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Determination of alkali metal cation selectivities of dibenzo-16-crown-5 lariat ethers with ether pendant groups by using electrospray ionization quadrupole ion trap mass spectrometry

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Abstract

The alkali metal cation selectivities of six lariat ethers with ether pendant groups were evaluated by electrospray ionization mass spectrometry in four methanolic solvent systems. The observed binding selectivities are affected by the number of oxygen atoms in the pendant ether group, the presence of a geminal propyl group, and to a lesser extent the polarity of the solvent environment. The presence of a dioxapentyl group in conjunction with a propyl sidearm yields the most Na^+-selective lariat ether. A longer trioxaoctyl pendant group exhibits a preference for complexation of K^+ over Na^+ due to the optimization of the interactions between the metal ion and the oxygen atoms of the trioxaoctyl group. Ab initio calculations suggest that the addition of a dioxapentyl or trioxaoctyl group pulls the Na^+ above the crown ether oxygens, increasing interaction with the former at the expense of interaction with the latter. (Int J Mass Spectrom 212 (2001) 389–401) © 2001 Elsevier Science B.V.

Keywords: Electrospray ionization; Binding selectivity; Metal complexation; Lariat ether; Quadrupole ion trap

1. Introduction

The use of electrospray ionization mass spectrometry (ESI-MS) [1–4] has proven to be successful for the analysis of a wide variety of noncovalently bound complexes. Moreover, numerous recent studies have shown that the equilibrium distribution of complexes in solution is reflected in the intensities of complexes observed in the mass spectra obtained upon ESI-MS of the solutions [5–35]. For determination of binding selectivities in host–guest chemistry, the intensities of complexes produced by ESI of solutions containing defined concentrations of one host and multiple guests are compared. ESI-MS analysis of binding selectivities has some advantages over the more conventional potentiometric, spectrophotometric, and NMR titrimetric methods [36], such as reduced sample consumption, tolerance of a wide variety of solvent conditions and reduced analysis times.

This ESI-MS method for measuring selectivities has been investigated in great detail in our laboratory [21–29] for hosts such as crown ethers and other

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Dedicated to R. Graham Cooks on the occasion of his sixtieth birthday.

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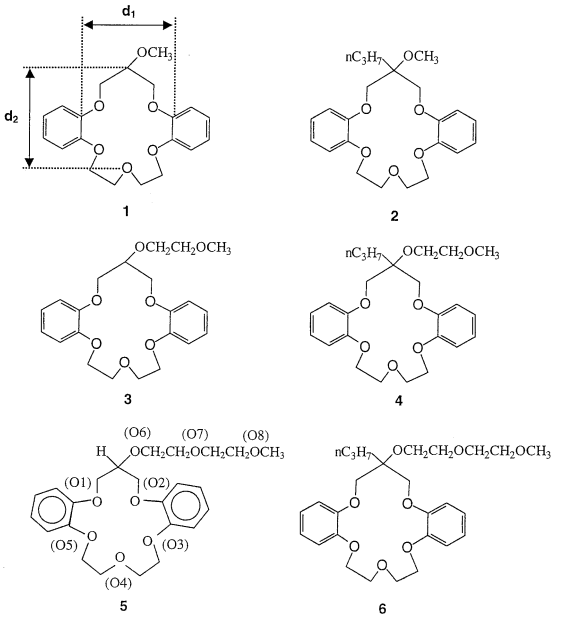


Fig. 1. Lariat ether structures (d_1 and d_2, as defined in **1**, represent the center to center distances between the indicated atoms for **1** and for the analogs **2**–**6**; these distances are tabulated in Table 2; the numbering system of the oxygens for lariat ethers **1**–**6**, as it is used in this article, is shown in **5**).

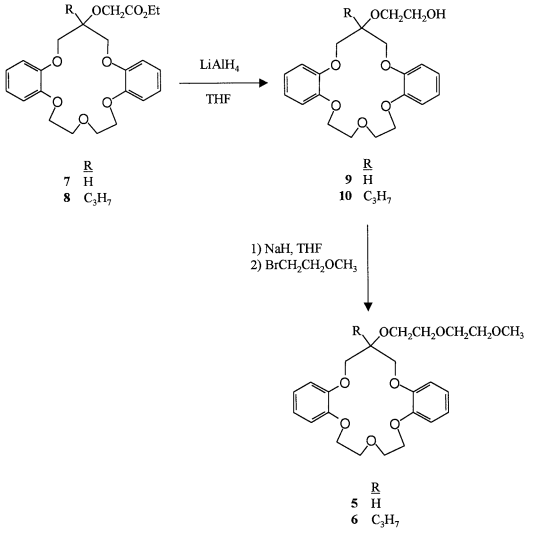
macrocycles with guests like alkali metal, transition metal, heavy metal, and ammonium ions. The ESI-MS method is most successful for analysis of host selectivities for a series of similar cations, resulting in the analysis of complexes with similar solvation energies. Thus, in these cases the resulting ESI mass spectral distributions of complexes generally agree well with the equilibrium distribution of complexes in solution, thus allowing the correlation of host structure/selectivity relationships. In the present work, ESI-MS is used to analyze the alkali metal binding selectivities of the six lariat ethers shown in Fig. 1 in several solvent systems. All six of the lariat ethers have the same dibenzo-16-crown-5 skeleton, but they differ in the substituents attached to the center carbon of the three-carbon bridge. The first substituent consists of an ether of varied length and number of oxygen binding sites, and the second sidearm is either a hydrogen or a geminal propyl group.

The ability of lariat ethers to effectively complex metals has led to their development and optimization for use in ion selective electrode membranes [37–40]. Of these six lariat ethers, **1**–**4** have been investigated previously by conventional methods. Bartsch and co-workers incorporated each of these lariat ethers into PVC membranes and analyzed their alkali metal cation (Li^+, Na^+, and K^+) selectivities by using a fixed interference method in aqueous solutions [39]. Based on the diameters of the metal ions (Li^+:1.36 Å, Na^+: 1.96 Å, K^+: 2.66 Å, Rb^+: 2.98 Å, Cs^+: 3.30 Å [41]), the cavity of unsubstituted dibenzo-15-crown-5 is expected to be optimal for complexation of Na^+ [39]. The potentiometric measurements revealed that both **1** and **2** showed modest selectivity (i.e. less than half an order of magnitude difference in binding constants) for Na^+ over K^+ and pronounced selectivity for Na^+ over Li^+ (i.e. over three orders of magnitude difference in binding constants). Lariat ether **3** showed a comparable degree of selectivity for Na^+ over Li^+ and K^+ as **1** and **2**, but **4** exhibited substantially higher Na^+/K^+ selectivity than the other three, with a difference in Na^+ and K^+ binding constants of over an order of magnitude. The enhanced Na^+/K^+ selectivity on going from **2** to **4** was attributed to the ability of the second ether oxygen in the sidearm of **4** to coordinate the metal ion with optimization of the binding conformation provided by the presence of the propyl group. In general, the presence of a propyl group as the second pendant group assists in optimal pre-organization of the ether pendant group relative to the cavity, thus enhancing the overall Na^+/K^+ binding selectivity.

2. Experimental methods

2.1. Synthesis of lariat ethers **1**–**6**

Lariat ethers **1**–**4** were prepared by the reported methods [37,38]. Lariat ethers **5** and **6** were prepared by the method shown in Scheme 1. Thus, lariat ether esters **7** [42] and **8** [43] were transformed into the corresponding lariat ether alcohols **9** and **10** in 90% and 88% yields by a published method in which ethyl-sym-(methyl)dibenzo-16-crown-5-oxyacetate was the reactant [44]. In the second step, the protect-



Scheme 1.

ing mineral oil was removed from 1.0 g of KH (35% dispersion, 9.0 mmol) by washing with pentane under nitrogen and 3.0 mmol of **9** or **10** in 100 mL of dry THF was added. After the mixture was stirred for 30 min at room temperature, 0.56 mL (6.0 mmol) of 1-bromo-2-methoxyethane was added. After refluxing the mixture for 5 h, the excess of KH was destroyed by careful addition of water and the THF was evaporated in vacuo. To the residue was added 150 mL of dichloromethane and 100 mL of water. The dichloromethane layer was separated, washed with water (2×50 mL), dried over magnesium sulfate and evaporated in vacuo to give the crude product.

1-[sym-Dibenzo-16-crown-5-oxy]-3,6-dioxaheptane (**5**). Chromatography of the crude product on alumina with ethyl acetate as eluent gave a colorless oil in 30% yield. IR (neat): 1257 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.39 (s, 3H); 3.55–4.40 (m, 21H), 6.82–7.02 (m, 8H). Anal. Calcd. For $C_{24}H_{32}O_8$: C, 64.27; H, 7.19. Found: C, 64.41; H, 6.90.

1-[sym-(Propyl)dibenzo-16-crown-5-oxy]-3,6-dioxaheptane (**6**). Chromatography of the crude product on alumina with diethyl ether as eluent gave a colorless oil in 32% yield. IR (neat): 1257 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.94–1.01 (t, 3H); 1.40–1.55 (m, 2H); 1.87–1.96 (m, 2H); 3.38 (s, 3H); 3.51–4.32 (m, 20H); 6.80–6.97 (m, 8H). Anal. Calcd. For $C_{27}H_{38}O_8$: C, 66.10; H, 7.81. Found: C, 65.99; H, 7.84.

2.2. Mass spectrometry

All mass spectrometry experiments were performed with a Finnigan ion trap mass spectrometer (ThermoFinnigan, San Jose, CA) operating in the mass selective instability mode with modified electronics to allow axial modulation and equipped with an in-house built electrospray source. The electrospray interface is based on a design developed by Oak Ridge National Laboratories (Oak Ridge, TN) involving a differentially pumped region containing ion focusing lenses [45]. The Harvard syringe pump system (Harvard Apparatus Inc., Holliston, MA) operated at a flow rate of 3.0 μL/min for all solutions. Neither a heated desolvation capillary nor a sheath flow gas was used. The ESI needle voltage was 3.0 kV. Each spectrum taken was an average of 30 scans. Reported values are the average of 120–240 scans.

For screening of the alkali metal cation selectivities of lariat ethers **1–6**, solutions containing a single host with multiple metal ions were analyzed. Previous studies have shown that only minimal correction factors (i.e. corrections for different spray efficiencies), if any, are needed when using the ratio of the peak areas of two complexes (same host, different metal ions) to determine the alkali metal cation selectivities of each host [21–25], primarily because the host–metal complexes within a series have similar structures and solvation energies. Solutions containing one part of host and two parts of each metal ion were analyzed for each lariat ether in 99% methanol/1% chloroform, 75% methanol/25% chloroform, 50% methanol/50% chloroform, and 5% methanol/95% acetonitrile. The excess of metal ions relative to the lariat ether creates a more competitive binding environment for complexation with the host compound. Throughout the study, the minimum one part concentration of host was 5.0×10^{-5} M and concentrations of the metal ions were 1.0×10^{-4} M. The choices of 5.0×10^{-5} M in lariat ether and 1.0×10^{-4} M in each alkali metal salt were used to ensure solubility of all salts in the solvent medium whereas

Table 1
Alkali metal cation selectivity of dibenzo-18-crown-6 in methanol

	% $(DB18C6 + Na)^+$	% $(DB18C6 + K)^+$	% $(DB18C6 + Rb)^+$
1:1:1:1 in CH_3OH			
Theoretical equilibrium distribution[a,b]	20	52	28
Experimental ESI-MS distribution[b]	9	61	30
1:5:5:5 in CH_3OH			
Theoretical equilibrium distribution[c]	15	60	24
Experimental ESI-MS distribution[c]	7	68	25

[a]Theoretical values obtained using MINEQL + solution equilibria software, version 4.01 (Environmental Research Software, Hallowell, ME), and the following log *K* values reported in the literature: $Na^+ = 4.4$, $K^+ = 5.0$, $Rb^+ = 4.6$ [46].
[b]The initial concentrations of DB18C6 and the three metal chlorides are each 2.0×10^{-4} M.
[c]The initial concentration of DB18C6 is 2.0×10^{-4} M and the three metal chlorides are each 1.0×10^{-3} M.

maintaining conditions for increased selectivity over solutions containing one part host and one part of each guest metal ion. All metals salts used for these experiments were purchased from Aldrich Chemical Co. (Milwaukee, Wisconsin) and used without further purification. Theoretical values of solution equilibria conditions were obtained using MINEQL+ solution equilibria software, version 4.01 (Environmental Research Software, Hallowell, ME).

2.3. Ab initio calculations

Molecular mechanics conformational searches were performed using MMFF (Merck) force fields followed by ab initio calculations using a Restricted Hartree-Fock model at the 3-21G* level of theory with Spartan© software (Wavefunction Inc., Irvine, CA) undertaken on a Silicon Graphics O2 computer workstation with an IRIX 6.5 operating system and 300 MHz MIPS R5000 processor (Silicon Graphics Inc., Mountain View, CA).

3. Results and discussion

3.1. ESI-MS strategy

Prior to mass spectrometric evaluation of the binding selectivities of lariat ethers **1**–**6**, studies of solutions containing dibenzo-18-crown-6, a model host, and alkali metal cations were undertaken to verify the correlation between ESI mass spectral intensities and the equilibrium distribution of complexes in solution. The known log *K* values for the dibenzo-18-crown-6/metal ion complexes in methanol are: 4.4 for Na^+, 4.8–5.0 for K^+, and 4.4–4.6 for Rb^+ [46]. For our calculations of the equilibrium distributions, the log *K* values of 4.4 for Na^+, 5.0 for K^+, and 4.6 for Rb^+ were utilized. From these log *K* values, the expected distribution of complexes in solution can be calculated for any initial concentrations of dibenzo-18-crown-6 and alkali metal cations, and then compared to the distribution of complexes detected in the mass spectra. Two sets of results are summarized in Table 1 for this type of experiment, involving either 1:1:1:1 or 1:5:5:5 methanolic solutions of dibenzo-18-crown-6 and three alkali metal cations, Na^+, K^+, and Rb^+. For both solutions, dibenzo-18-crown-6 preferentially binds K^+ over Rb^+ and Na^+, in good agreement with the calculated equilibrium preferences. Moving from a 1:1:1:1 host/metal ions mixture to a 1:5:5:5:5 host/metal ions mixture enhances the observed selectivity to a modest degree because the greater excess of metal ions increases the competition between the various metal ions for the available host molecules. This trend in enhanced selectivity is reflected in both the calculated equilibrium distribution and the experimentally observed distribution of complexes.

Modest differences in the distribution of complexes and the degree of selectivity obtained for the ESI-MS results relative to the calculated equilibrium values are attributed to two factors. First, the range in the reported log *K* values for dibenzo-18-crown-6 [46] indicates a degree of variability that could alter the expected distribution of complexes by up to 10%. Second, formation of droplets in the electrospray process occurs in a partially humid laboratory atmosphere, thus meaning that the 100% methanolic environment is difficult to maintain. A small amount of water in the spray process may alter the observed alkali metal cation selectivity of dibenzo-18-crown-6 due to the modification of the polarity of the solvent.

3.2. Alkali metal cation selectivities of lariat ethers

For evaluation of the alkali metal cation selectivities of lariat ethers **1**–**6**, each lariat ether was mixed with alkali metal salts in a 1:2:2:2:2 ratio (host: Li^+ : Na^+ : K^+ : Rb^+). Four different solvent environments were investigated for effects on binding selectivity: 99% methanol/1% chloroform (1% chloroform is required for solubilization of the lariat others), 75% methanol/25% chloroform, 50% methanol/50% chloroform, and 5% methanol/95% acetonitrile. Negligible differences in spray efficiencies are observed within each set of host/alkali metal cation complexes, based on examination of the intensities of lariat ether/alkali metal cation complexes for solutions containing a single lariat ether in excess and only one metal ion (data not shown). Figs. 2 and 3 illustrate examples of the mass spectra obtained in the four methanolic solvent systems for lariat ethers **1** and **4**. The spectra illustrate the 1:1 lariat ether/metal complexes are the dominant species and solvated adducts are not observed, so that only the intensities of the former need to be quantified. Moreover, it is evident that the solvent environment influences the selectivity of alkali metal cation complexation more significantly for lariat ether **1** than for **4**, as explained later. Fig. 4 summarizes the complete set of ESI-MS results obtained for the distributions of alkali metal cation complexes of the six lariat ethers, as measured by mass spectral peak intensities. Note that these experiments give a way of evaluating the selectivities, but not the absolute avidities, of the lariat ethers for the metal ions. Fig. 4 illustrates that complexation of either Li^+ or Rb^+ is generally less favorable than complexation of Na^+ or K^+ for each of the lariat ethers, which is due to Na^+ and K^+ having ionic diameters closer to the diameter of the 16-crown-5 ring of the lariat ethers so that Li^+ is too small and Cs^+ is too large to complex as effectively as Na^+ and K^+. Thus, the Na^+/ K^+ selectivities provide the most relevant comparisons, as highlighted in Fig. 5.

As seen in Fig. 4, in a 99% methanol/1% chloroform solution, lariat ethers **1, 3, 4**, and **6** show the same selectivity trend: $Na^+ > K^+ > Rb^+ > Li^+$, whereas for **2** and **5** the order of Na^+ and K^+ is reversed. Addition of a geminal propyl group has been used in synthetic design strategies to assist in pre-organization of the lariat ether binding cavity and ether pendant group for enhanced Na^+ selectivity. However, this expected enhancement in selectivity was marginal in the potentiometric studies of the methoxy-substituted lariat ethers as well as in the present ESI-MS study [39], likely because the methoxy oxygen is not on a sufficiently long tether to allow it to optimally align its dipole with the alkali metal cation bound in the cavity. Addition of the geminal propyl group (i.e. in **2**) forces the methoxy group closer to the crown ether ring cavity through steric effects. Consequently, while the methoxy group in **1** was too short to interact well with either Na^+ or K^+ bound in the cavity, pushing the methoxy group closer to the cavity (i.e. in **2**) allows more optimal alignment of the dipole associated with the methoxy oxygen with the K^+ ion which is perched above the cavity of **2**, but does not enhance the interaction with the Na^+ ion which is nested within the cavity. A net decrease in Na^+/K^+ selectivity is thus observed for **2**. Lariat ether **3** exhibits a modest increase in Na^+/K^+ selectivity compared to **1** and **2**, presumably because the longer dioxapentyl ether pendant group can interact favorably to further stabilize the binding of Na^+ as it nests within the dibenzo-16-crown-5 cavity. Lariat ether **4** shows a further increase in Na^+/K^+ selectivity and has the greatest Na^+ selectivity of all of the six lariat ethers in this study. The Na^+ selectivity is

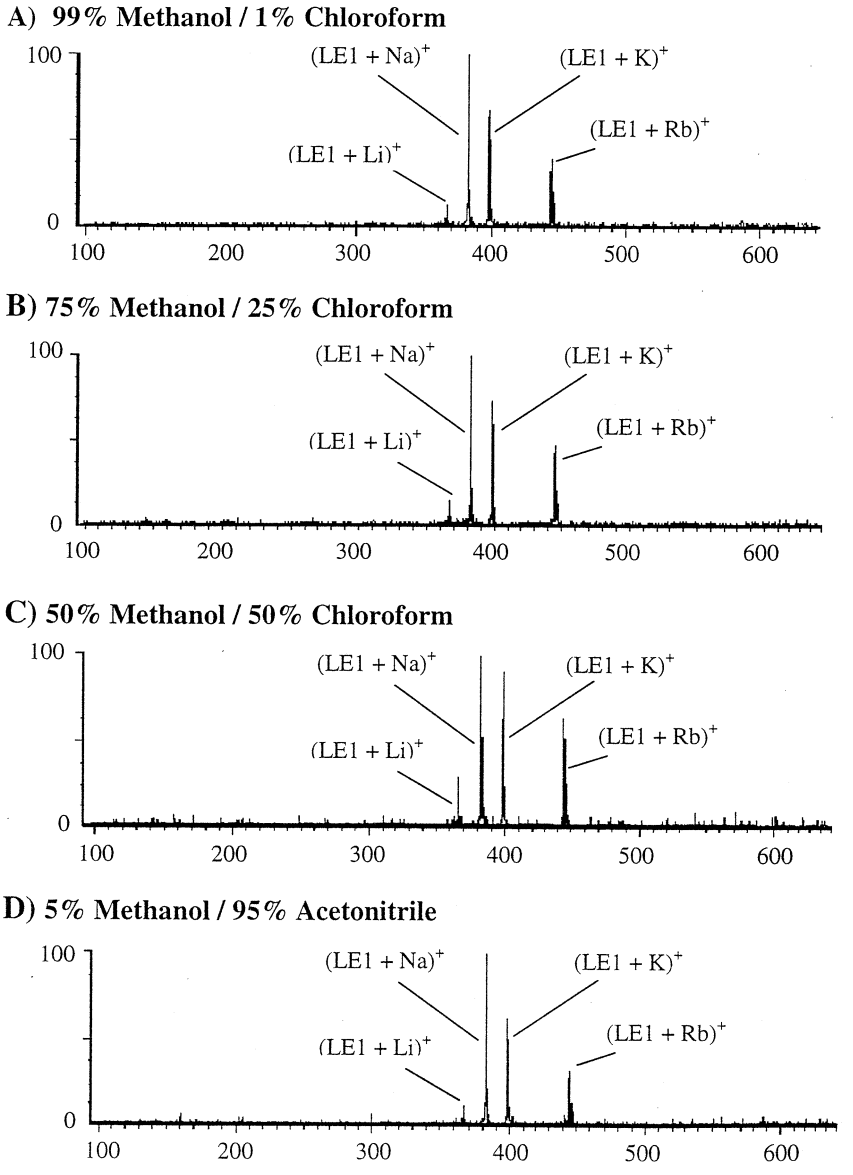


Fig. 2. ESI mass spectra of lariat **1** with LiCl, NaCl, KCl, and RbCl (1:2:2:2:2) (A) 99% methanol / 1% chloroform, (B) 75% methanol/ 25% chloroform, (C) 50% methanol/50% chloroform, and (D) 5% methanol/ 95% acetonitrile.

enhanced for **4** because the propyl group enforces the conformation of the dioxapentyl group relative to the cavity, thus enhancing the exclusion of K^+. The alkali metal cation selectivities observed for **5** and **6** are particularly interesting because it was not intuitively obvious whether a longer ether pendant group (i.e. trioxaoctyl) would further anchor Na^+ in the cavity or enhance the stabilization of K^+ perching above the cavity. The ESI-mass spectrometric results confirm the latter for **5**, with a preference for complexation of K^+ over Na^+. Addition of a geminal propyl group reverses this selectivity, and thus lariat ether **6** shows a selectivity that is more similar to that of **1**. Apparently the propyl group in **6** does not assist the

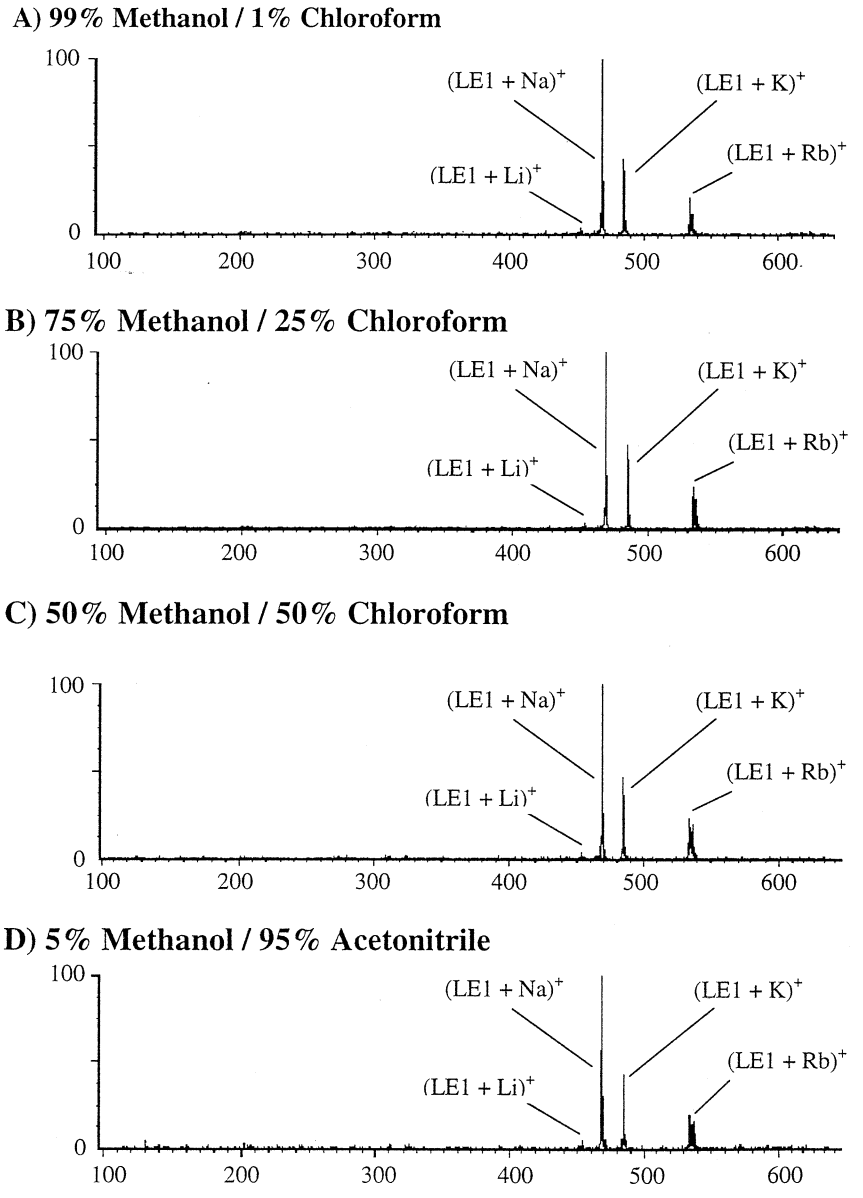


Fig. 3. ESI mass spectra of lariat **4** with LiCl, NaCl, KCl, and RbCl (1:2:2:2:2) (A) 99% methanol/1% chloroform, (B) 75% methanol/25% chloroform, (C) 50% methanol/ 50% chloroform, and (D) 5% methanol/ 95% Acetonitrile.

trioxaoctyl group in stabilizing the larger K^+ ion because pushing of the trioxaoctyl group further toward the 16-crown-5 cavity reduces the encapsulation volume to a size more amenable to Na^+ complexation.

Solvent-dependent changes in selectivity are also evident upon examination of the ESI-MS results obtained for the less polar 75% methanol/25% chloroform, 50% methanol/50% chloroform, and more polar 5% methanol/95% acetonitrile solvent systems (electric dipole moments of solvents: $\mu_{CHCD} = 1.01$ D, $\mu_{MeOH} = 1.70$ D, $\mu_{ACN} = 3.92$ D [47]). As

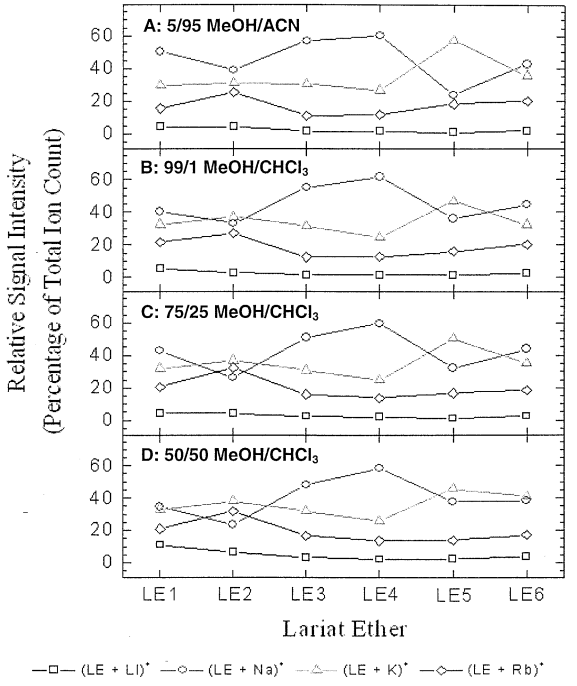


Fig. 4. Variations in metal selectivities of lariat ethers in various solvent systems.

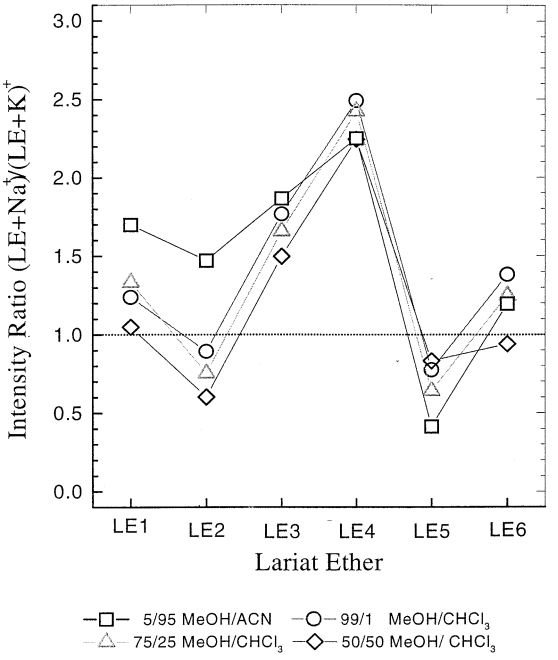


Fig. 5. Variation in Na^+/K^+ selectivity in various solvent systems.

shown in Fig. 5, a recurring loss in the Na^+/K^+ selectivity with decreasing solvent polarity is generally observed for **1**–**2**. Both **1** and **2** show more dramatic changes in Na^+/K^+ selectivity with solvent environment than are observed for **3**–**6**, confirming that the ether pendant group plays an important role in shielding the bound metal ion from external solvent changes, making the complexes with the longer ether pendant group less susceptible to changes in stability with variation of the solvent polarity. Diminution of the Na^+/K^+ selectivity with reduced solvent polarity for **1**–**2** is due mainly to increases in complexation of both K^+ and Li^+ relative to Na^+ complexation (see Fig. 4). The size of Na^+ is most similar to the cavity size of the 16-crown-5 ring, whereas the other ions have poorer fits which allow greater accessibility and potential for interaction with solvent molecules. Thus, there are greater enhancements in the interactions of the oxygen atoms of the 16-crown-5 cavity with Li^+ and K^+ in the less polar solvents, with the methoxy group having a minor influence on complexation. A large shift toward higher Na^+ selectivity is seen for **1** and **2** in the 5% methanol/95% acetonitrile solution as solvent molecules more polar than methanol interact with the more poorly fitting Li^+ and K^+. In addition, Na^+ has a larger decrease in solvation energy in acetonitrile versus methanol compared to the change in solvation energy for K^+ [48], a factor which also may contribute to the enhancement in the formation of the lariat ether/Na^+ complexes for **1** and **2**. For **5** reverse trend in selectivity is observed; in this case, K^+ possesses the best fit to the cavity formed by the 16-crown-5 ring and the trioxaoctyl pendant group. For lariat ether **4**, the small variation in selectivity with changes in solvent polarity is related to the presence of a pendant ether substituent which is long enough to anchor the nested Na^+ ion and whose conformation relative to the 16-crown-5 ring is stabilized by the geminal propyl substituent, yet has sufficiently few oxygens to prohibit pulling the nested Na^+ ion out of the 16-crown-5 ring, as is apparently the case for **5** and **6**.

Table 2
RHF 3-21G* ab inito calculations for lariat ethers **1–6** with Na^+ and K^+

Complex	*E* (kJ/mol)	Distances (Å) O1, M	O2, M	O3, M	O4, M	O5, M	O6, M	O7, M	O8, M	O, M ave.	d_1 (Å)[a]	d_2 (Å)[a]
1 + Na	361	2.31	2.27	2.33	2.25	2.22	2.28			2.28	5.75	5.00
1 + K	474	2.71	2.63	2.66	2.62	2.61	2.66			2.65	5.88	5.85
3 + Na	401	2.37	2.40	2.43	2.34	2.40	2.36	2.40		2.39	5.61	5.46
3 + K	515	2.73	2.65	2.69	2.69	2.66	2.64	2.70		2.68	5.83	5.88
4 + Na	431	2.36	2.41	2.43	2.34	2.38	2.41	2.36		2.38	5.63	5.52
4 + K	546	2.68	2.65	2.72	2.65	2.66	2.68	2.67		2.67	5.76	5.93
5 + Na	441	2.42	2.44	2.35	2.35	2.59	2.36	2.35	2.47	2.43	4.33	5.41
5 + K	555	2.72	2.70	2.81	2.73	2.70	2.67	2.75	2.73	2.73	5.80	5.91

[a]Refer to the depiction of **1** in Fig. 1 for definitions of d_1 and d_2.

3.3. Molecular models and computational results

The results of molecular modeling and ab initio calculations for lariat ethers **1, 3, 4**, and **5** with Na^+ and K^+ are presented in Table 2 together with plots of their cross-ring distances in Fig. 6. As examples of the calculated structures, the Na^+ complexes of **1, 3**, and **5** (the three lariat ethers without the propyl groups) are illustrated in Fig. 7. In these models the pendant ether group hovers above the metal ion, and the cavity adopts a rather concave shape. The methoxy pendant group is not positioned to strongly interact with the metal ion, unlike the longer dioxapentyl and trioxaoctyl groups. As shown in Fig. 6, the distance between the inner carbons of the two opposing aryl rings (d_1 in Fig. 1) as well as the cross-ring distance between the carbon to which the pendant groups are attached and the crown ether ring oxygen opposite it (d_2 in Fig. 1) give an indication of the cavity sizes of the lariat ethers, as influenced by the associated pendant group(s). For instance, the distance between the aromatic rings (d_1) decreases slightly from 5.75 Å for $(\mathbf{1} + Na)^+$ to 5.63 Å for $(\mathbf{4} + Na)^+$, then drops dramatically from 5.63 to 4.33 Å from $(\mathbf{4} + Na)^+$ to $(\mathbf{5} + Na)^+$, respectively, indicating a compaction of the 16-crown-5 ring. For **4** and **5** in 99% methanol, the corresponding Na^+/K^+ selectivity likewise drops significantly from about 2.5 to about 0.8. Simultaneously, the other cross-ring distance (d_2) increases for the Na^+ complexes from 5.00 to 5.52 Å from **1** to **4**, respectively, as the Na^+/K^+ selectivity correspondingly increases from about 1.3 to 2.5, then decreases to 5.41 Å for $(\mathbf{5} + Na)^+$ as the Na^+/K^+ selectivity

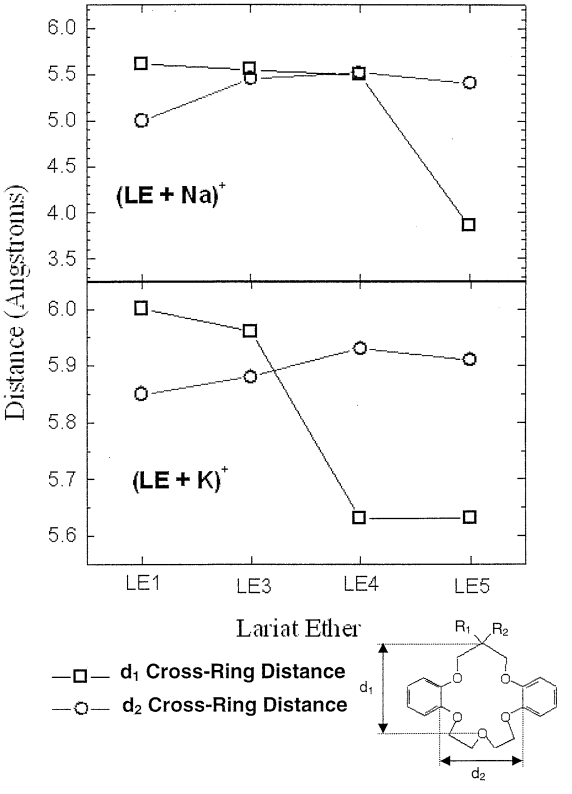


Fig. 6. Variation in size of the lariat ether's 16-crown-5 cavity.

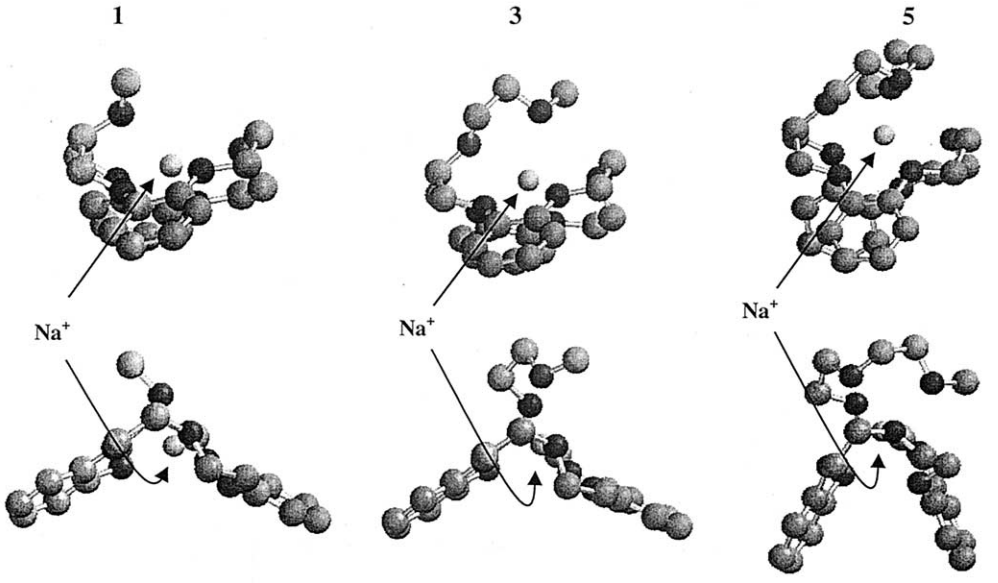


Fig. 7. Complexation of Na^+ of lariat ethers **1, 3**, and **5** (models in the lower half of the figure are rotated 90° about the vertical axis with respect to the upper models; oxygens are the darker atoms, carbons are the lighter atoms, and hydrogens are excluded for greater clarity).

drops. There is comparatively little change in the ring sizes of the K^+ complexes with variation in pendant groups (Fig. 6). The compaction of the 16-crown-5 ring for the $(\mathbf{5} + Na)^+$ complexes that mirrors the drop in selectivity may occur because the pendant arm retains the ion above the ring and the oxygens crowd beneath it to maximize interactions.

From Table 2, the increase in average oxygen-

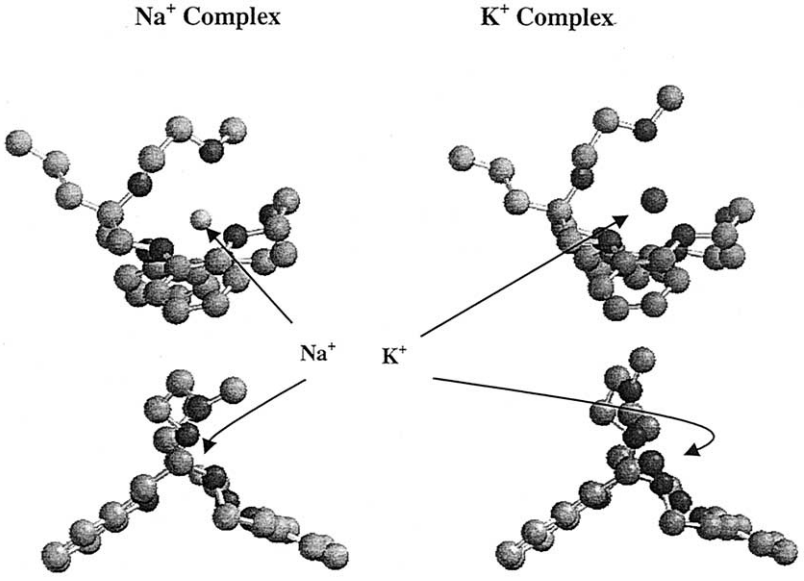


Fig. 8. Complexation of Na^+ and K^+ by lariat ether **4** (models in the lower half of the figure are rotated 90° about the vertical axis with respect to the upper models; oxygens are the darker atoms, carbons are the lighter atoms, and hydrogens are excluded for greater clarity).

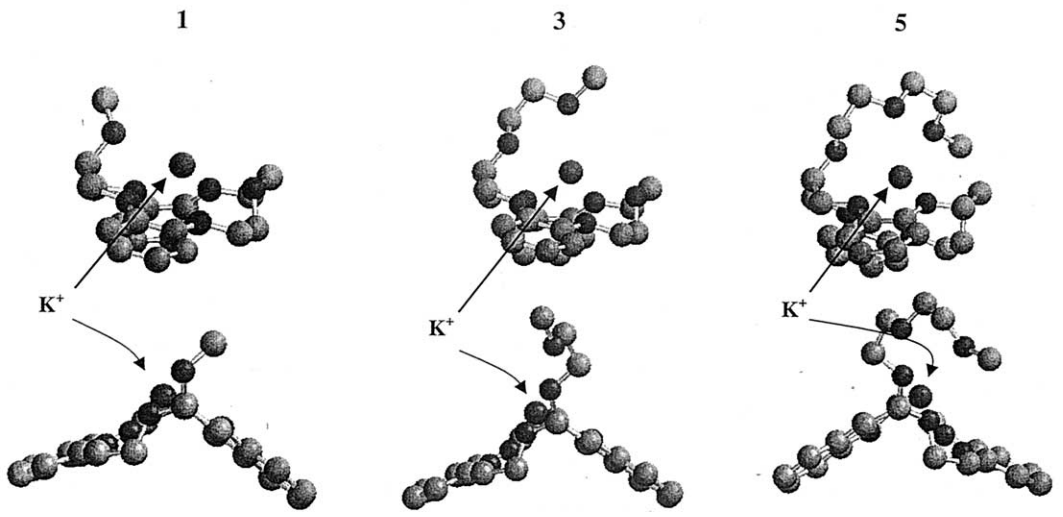


Fig. 9. Complexation of K^+ by lariat ethers **1, 3**, and **5** (Models in the lower half of the figure are rotated 90° about the vertical axis with respect to the upper models; oxygens are the darker atoms, carbons are the lighter atoms, and hydrogens are excluded for greater clarity).

metal ion distance on going from lariat ether **1** to **3** to **5** is due to the interactions of the longer ether group of **3** or **5** with Na^+ above the crown ether ring, thus effectively pulling Na^+ out of the cavity. The strengths of binding interactions involving the metal ion with the 16-crown-5 oxygens are reduced as the interactions with the longer ether pendant group are optimized.

The most important effect of the metal being pulled out of the crown ether cavity is to decrease the overall energy of binding to the crown ether ring while increasing the overall number of oxygen–metal ion bonds. This factor may contribute to the reduction in solvent effects on selectivities for **3**–**6** compared to **1** and **2**, along with the solvent shielding properties of the pendant ether substituent discussed above. The loss of fit of the 16-crown-5 cavity may result in increased interactions of Na^+ with solvent molecules, such that ionic-polar interactions between Na^+ and the 16-crown-5 oxygens may consequently be more affected by solvent polarity. Such an effect occurs to a far lesser extent for K^+ which has a volume more similar to that of the enclosure formed between the pendant ether arm and crown ether ring, resulting in diminished solvent-dependent selectivity trends for **3** and **5**, and the absence of any clear solvent-dependent trends for **4** and **6**.

Models for both the Na^+ and K^+ complexes of **4**, the most selective lariat ether, are shown in Fig. 8. These models demonstrate that although Na^+ can nest within the crown ether cavity, K^+ must perch above because its larger size prevents it from fitting into the ring. This ability of Na^+ to interact more effectively with the crown ether oxygens contributes to the selectivity for Na^+ over K^+ in the dibenzo-16-crown-5 lariat ethers. As shown in Table 2 and Fig. 8, the propyl group of lariat ether **4** significantly enhances interaction of the terminal oxygen atom with the Na^+ ion.

From the ab initio models shown in Figs. 7 and 8, in the Na^+ complexes of **1**–**4**, Na^+ is nested within the 16-crown-5 ring. However, for the Na^+ complex of **5**, Na^+ is suspended between the pendant arm and the 16-crown-5 ring, allowing it easier movement from the host to the solvent. As previously stated, for **6**, the added propyl geminal group pushes the trioxaoctyl group forward, thus forcing Na^+ further into the 16-crown-5 ring, resulting in its better encapsulation. From Figs. 8 and 9, it can be seen that for K^+ complexes of **1**–**5**, K^+ remains virtually unchanged in

its position perched above the 16-crown-5 ring. However, for the complex with **5**, the trioxaoctyl group is able to fully encapsulate K^+, thus restricting its access to the solvent compared to **1**–**4**. For **6**, the trioxaoctyl group is forced closer to the 16-crown-5 ring, thus creating an encapsulated area small enough to hinder entrance of K^+ into the crevice formed between the cyclic polyether cavity and pendant ether group.

4. Conclusions

The use of ESI mass spectrometry allows rapid, efficient screening of binding selectivities in a variety of solvents. The preferences for binding different alkali metal cations can be monitored simultaneously, thus reducing the sample consumption and time for analysis. For the six lariat ethers studied in the present report, the presence of a dioxapentyl group in conjunction with a propyl sidearm (i.e. in **4**) creates the most Na^+ selective lariat ether. Addition of a longer trioxaoctyl pendant group results in a preference for complexation of K^+ over Na^+ because of optimization of interactions between the metal ion and the oxygen atoms of the trioxaoctyl group. Addition of a second sidearm, a propyl group, regenerates Na^+ selectivity because of a greater degree of pre-organization of the cavity in conjunction with optimization of the anchoring interaction with the metal ion provided by the ether pendant group. Decreases in polarity/dielectric constant of the solvent media generally lowers the Na^+/K^+ selectivity, possibly due to favorably increasing the electrostatic interaction between K^+ and the 16-crown-5 ring while the Na^+ interactions with the ring are comparatively little affected. Ab initio calculations show that the addition of the dioxapentyl or trioxaoctyl group pulls Na^+ above the crown ether ring oxygens, increasing interaction with the former at the expense of interaction with the latter. The calculations also suggest that changes in pendant groups cause significant alterations in crown ether ring shape, which reveal a role of the pendant arm as the primary site of metal-oxygen interaction for ions with a poor fit to the encapsulated area of the lariat ether.

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