Direct Correlation of Cation Binding Strengths to Hammett Parameters in Substituted *N*-Benzylaza-15-crown-5 Lariat Ether and *N,N'*-Dibenzyl-4,13-diaza-18-crown-6 BiBLE Derivatives

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Silver (Ag^+), sodium (Na^+), and lithium (Li^+) cation binding affinities (log K_S, acetonitrile, 25 °C) have been determined by using potentiometric methods for 18 lariat ethers and bibracchial lariat ethers (BiBLEs) including nine previously unreported compounds. The *N*-benzylaza-15-crown-5 derivatives **1–9** bear the following substituents on the aromatic ring: H, 2-nitro, 4-nitro, 2-cyano, 4-cyano, 2-chloro, 4-chloro, 2-methoxy, and 4-methoxy. Nine derivatives of *N,N'*-dibenzyl-4,13-diaza-18-crown-6 **10–18** were also prepared having the same range of substituents. The ratio of binding constants, K/K_H, for all three cations correlates well with the Taft inductive constants (σ^0) with the best correlation observed for Ag^+. ρ values for the binding reactions between monoaza and diaza crowns, respectively, with the indicated cations are Ag^+, −1.08 and −1.28; Li^+, −1.00 and −0.78; and Na^+, −1.91 and −1.00.

Introduction

After more than 2 decades of study, the ability of macrocyclic polyether compounds to complex various ionic species remains their most studied property. We[1-4] and others[5-7] have been especially interested in the complexation and selectivity profiles of single-armed lariat ethers[1,2,5,6] and two-armed bibracchial lariat ethers (BiBLEs)[3,4,7] with alkali and alkaline-earth cations. These macrocycles form alkali metal complexes that are similar to those formed by certain naturally occurring ionophores.[8,9]

To date, most cation binding studies of either lariat ethers or BiBLEs have been conducted in anhydrous methanol solution. Data from our own work are exclusively in this solvent and primarily for sodium, potassium, calcium, and ammonium cations. The important application of lariat ethers as electrochemically switched cation carriers[10-13] has been conducted in acetonitrile solution. Lithium cation binding by these species in acetonitrile solution is also of considerable interest but few data were available. Acetonitrile, the solvent used in the electrochemical studies, required a technique different from our standard one[14] since the usual ion-selective electrode technique is unreliable in anhydrous acetonitrile solution.

We report here the preparation of several novel lariat ether and BiBLE compounds and stability constants for their complexes with Li^+, Na^+, and Ag^+. In addition, we report correlations of the Hammett type for these structures. There is an excellent correlation between silver binding in acetonitrile and Taft inductive constants (σ^0).

Results and Discussion

Syntheses. The compounds used in this study (except for **7**, **8**, **16**, and **17**, see below) were prepared by simple alkylation of aza-15-crown-5 or diaza-18-crown-6 (CH_3CN, Na_2CO_3, reflux) using the appropriately substituted benzyl halides. After alkylation, compounds **1–6** and **9** were purified by column chromatography and/or Kugelrohr distillation to obtain pure products in yields ranging from 72% to 96%. Compounds **10–15** and **18** were similarly prepared. The products (70–90%) crystallized upon workup and were recrystallized to purity. Compounds **7** and **8** were prepared by treating the appropriate N-substituted diethanolamine (NaH, THF, reflux) with triethylene glycol dimesylate.[2] The yields for these cyclizations were 40% and 46%, respectively. Compound **16** was prepared by our recently developed, two-step cyclization method.[4] Reaction of *N,N'*-dibenzyl-1,8-diamino-3,6-dioxaoctane with 1,2-bis(2-iodoethoxy)ethane (CH_3CN, Na_2CO_3, NaI, reflux) gave **16** in 66% yield.[4] Compound **17** was prepared by our one-step cyclization reaction.[3] Heating 2-methoxybenzylamine with 1,2-bis(2-iodoethoxy)ethane (CH_3CN, Na_2CO_3) for 24 h gave **17** in 30% yield.[3]

Selection of Substituent Constants. Using the Hammett equation, Smid and co-workers[15] showed that cation binding of Na^+ in acetone at 25 °C by 4'-substituted benzo-15-crown-5 derivatives correlate well with $\sigma_p^- + \sigma_m$. ρ for this reaction was −0.47. Such a relationship is expected for benzocrown derivatives since the macroring donor atoms are directly conjugated to the 4'-substituents through the aromatic ring and the substituent is meta to one macroring oxygen and para to the other.

The binding results presented in this paper are for 15-membered ring nitrogen-pivot lariat ethers (compounds **1–9**) and 18-membered ring bibracchial lariat ethers (compounds **10–18**) as shown below.

In these benzyl-substituted nitrogen-pivot systems, a methylene group insulates the para substituent from the macroring nitrogen atom. Resonance effects are thus assumed to be negligible. Since σ_p^- constants were developed for substituents that show through-resonance interactions, these values cannot be used to correlate binding properties in **1–18**. There are, however, σ constants for compounds in which through-resonance interactions are presumed to

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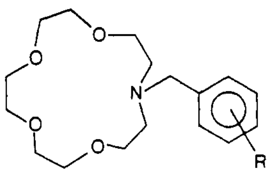
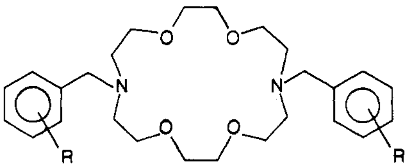


1, R = 2-NO$_2$
2, R = 4-NO$_2$
3, R = 2-CN
4, R = 4-CN
5, R = 2-Cl
6, R = 4-Cl
7, R = H
8, R = 2-CH$_3$O
9, R = 4-CH$_3$O



10, R = 2-NO$_2$
11, R = 4-NO$_2$
12, R = 2-CN
13, R = 4-CN
14, R = 2-Cl
15, R = 4-Cl
16, R = H
17, R = 2-CH$_3$O
18, R = 4-CH$_3$O

be negligible.[16] Van Bekkum, Verkade, and Wepster[17] have developed a series of σ^n values based on the acidity constants of benzoic acid derivatives having substituents in which there is little or no resonance interaction. Taft developed the so-called σ^0 values are based on the ionization of substituted phenylacetic and 3-phenylpropanoic acid derivatives and from the rates of hydrolysis of phenyl-substituted ethyl phenylacetate and ethyl 3-phenylpropanoate derivatives.[18] The placement of one or two methylene groups between the aromatic ring and the carboxyl group prohibits resonance interactions.

We report here the binding of Li$^+$, Na$^+$, and Ag$^+$ cations to substituted $C_6H_5CH_2NR_2$ groups, in which R_2 corresponds to the macroring. In these reactions, the aromatic ring is insulated from the macroring nitrogen by a methylene group. We have chosen Taft's σ^0 constants for the present study because his systems and ours involve equilibrium between a group I cation and an oxygen or nitrogen atom.

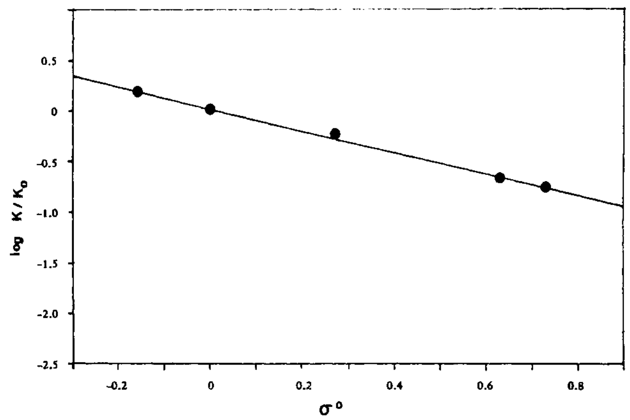


Figure 1. Plot of Ag$^+$ binding (log K/K_H) as a function of σ^0 for the para-substituted-aza-15-crown-5 derivatives.

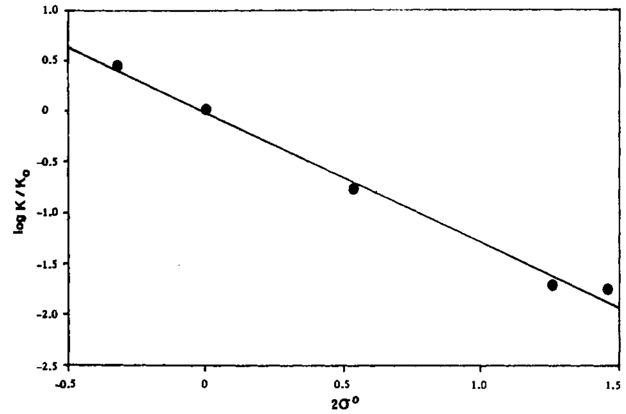


Figure 2. Plot of Ag$^+$ binding (log K/K_H) as a function of σ^0 for the para-substituted diaza-18-crown-6 derivatives.

Binding Data. Binding constant data for 15-membered ring aza lariat ethers (compounds **1**–**9**) and 18-membered ring diaza bibracchial lariat ethers (BiBLEs, compounds **10**–**18**) are shown in Table I. Cation binding constants were measured in anhydrous acetonitrile solution at 25 °C by using modifications of the procedures reported by Gutknecht[19] and Cox[20-22] (see Experimental Section). Data were obtained first for Ag$^+$ and then for Li$^+$ and Na$^+$ by competition with Ag$^+$. The Taft inductive constants (σ^0) for all para-substituted benzyl substituents are also shown in Table I. Note that the σ constants are those reported by Taft for nonhydroxylic solvents.[18]

The ortho- and para-substituted systems in both the aza-15-crown-5 and the diaza-18-crown-6 systems show an increase in binding with a decrease in the Taft inductive constants. In the para-substituted compounds, inductive effects are responsible for the observed results while steric effects probably influence binding in the ortho-substituted compounds.

The plot of Ag$^+$ binding constant (log K/K_H) vs. σ^0 for the para-substituted aza-15-crown-5 derivatives is shown in Figure 1. ρ for this reaction is −1.08. The plot of Ag$^+$ binding vs. $2\sigma^0$ for diaza-18-crown-6 derivatives is shown in Figure 2. ρ for this reaction is −1.28. The correlation between silver binding and σ^0 for both reactions is excellent.

The correlation of Li$^+$ and Na$^+$ binding constants with σ^0 is not as good as that observed for Ag$^+$. This is probably due to the fact that Li$^+$ and Na$^+$ do not interact with nitrogen as strongly as does Ag$^+$. The principal effect of aromatic ring substituents will be felt on the macroring nitrogens. The binding of cations that interact strongly with nitrogen should correlate well with σ^0.

As expected, Li$^+$ and Na$^+$ binding is higher than Ag$^+$ binding with aza-15-crown-5 derivatives but lower in the diaza-18-crown-6 series. The only exceptions to this trend are compounds **10** and **12**. These compounds have very strongly electron withdrawing residues (nitro and cyano) in the ortho positions. Since the nitrogen atoms contribute strongly to Ag$^+$ binding in diaza crowns,[23] the effect of these substituents is magnified. Sodium cation binding,

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Table I. Cation Binding Constants and Hammett Parameters for Aza-15-crown-5 and Diaza-18-crown-6 Derivatives[a]

			log K_S (MeCN)			lot K/K_H		
no.	substit.	σ^0	Ag^+	Li^+	Na^+	Ag^+	Li^+	Na^+
Aza-15-crown-5 Derivatives								
1	2-NO_2		2.47	3.39	4.39	−1.22	−1.24	−1.29
2	4-NO_2	+0.73	2.92	3.70	3.97	−0.77	−0.93	−1.71
3	2-CN		3.06	3.75	5.04	−0.63	−0.88	−0.64
4	4-CN	+0.63	3.01	4.31	4.52	−0.68	−0.32	−1.16
5	2-Cl[b]							
6	4-Cl	+0.27	3.45	4.46	4.70	−0.24	−0.17	−0.98
7	H	0.00	3.69	4.63	5.68	0.00	0.00	0.00
8	2-OCH_3		4.22	5.22	5.80	0.53	0.59	0.12
9	4-OCH_3	−0.16	3.88	4.82	5.74	0.19	0.19	0.06
4,13-Diaza-18-crown-6 Derivatives								
10	2-NO_2		3.17	<2	3.18	−2.69	−2.24	−1.72
11	4-NO_2	+0.73	4.10	3.19	3.34	−1.76	−1.05	−1.56
12	2-CN		3.57	3.02	4.58	−2.29	−1.22	−0.32
13	4-CN	+0.63	4.15	3.23	3.44	−1.71	−1.01	−1.46
14	2-Cl[b]							
15	4-Cl	+0.27	5.08	3.92	4.65	−0.78	−0.32	−0.25
16	H	0.00	5.86	4.24	4.90	0.00	0.00	0.00
17	2-OCH_3		6.20	5.11	5.93	0.34	0.87	1.03
18	4-OCH_3	−0.16	6.30	4.55	4.97	0.44	0.31	0.07

[a] Determined in acetonitrile at 25.0 ±1.0 °C; see Experimental Section. [b] Compound insoluble in acetonitrile.

Table II. Reaction Constants (ρ) for the Binding of Cations by Macrocycles

cation	monoaza crowns	diaza crowns
Ag^+	−1.08	−1.28
Li^+	−1.00	−0.78
Na^+	−1.91	−1.00

on the other hand, is dominated by oxygen interactions.[23,24] As a result, these substituents do not present a problem in the single-armed lariat ethers **1** and **3**.

The nitrogen affinity of Ag^+ in the diaza crowns compared to the Li^+ and Na^+ preference of oxygen in the lariat ethers is apprent from the binding properties. Silver cation binding by diaza crowns is invariably greater than Li^+ or Na^+ binding. Binding of Ag^+ by **16** is 2 powers of ten greater than that for compound **7**. In contrast, binding by Na^+ and Li^+ decreases from **16** to **7** by factors of 0.78 and 0.39, respectively. This trend holds for all of the para-substituted compounds. When the ratio nitrogen: oxygen macroring donors is high (diaza-18-crown-6, 0.5) Ag^+ binding is high and alkali metal cation binding is low. As the ratio decreases (aza-15-crown-5, 0.25), Ag^+ binding decreases and alkali metal cation binding increases.

Reaction Constants. The reaction constants for the binding of Ag^+, Li^+, and Na^+ to the aza crowns and diaza crowns are shown in Table II. All ρ values are negative and opposite to that observed for the ionization of substituted phenylacetic acid and 3-phenylpropanoic acid derivatives.[18] Of course, cation binding is the reverse of proton ionization from a carboxylic acid. The signs of the ρ values are opposite because the equilibria are assessed in opposite directions.

According to the Hammett correlation, the larger the ρ value, the greater the influence substituents have on binding. It is apparent from the data in Table II that Na^+ cation binding is most affected by substituents in the aza crown series and that Ag^+ binding is most affected in the BiBLE series. Indeed, Na^+ binding is highest in the aza crown series while Ag^+ binding is highest in the BiBLE series.

Cation binding by these systems should be affected by all of the donors sterically accessible to the cation when complexed and by those aromatic ring substituents whose influence should be felt through the ring-nitrogen atom. It is well-known that the affinity of Ag^+ for nitrogen atoms is greater than that of either Li^+ or Na^+ and that this influence is especially strong when the nitrogen atoms are in an anti-linear arrangement (i.e., 180° apart and on opposite sides of the cation). In contrast, the affinity of alkali metal cations for oxygen is known to exceed that for nitrogen. Of course, overall binding of alkali metal cations would be stronger in a five-oxygen donor (15-crown-5) system compared to a six-oxygen donor (18-crown-6) system. The differences in binding reflect the difference in donor number and the presence of nitrogen. Likewise, the ρ values reflect these differences so that Li^+ and Na^+ show the expected order in both macroring systems. The larger ρ value for Ag^+ cation in the 18-membered ring system reflects the cation's nitrogen affinity.

Conclusion

The binding constant data presented for two groups of macrocycles, benzyl-substituted 15-membered ring aza lariat ethers **1**–**9** and dibenzyl-substituted 18-membered ring diaza bibracchial lariat ethers (BiBLEs) **10**–**18**, indicate an excellent correlation between Ag^+ binding in acetonitrile and Taft substituent inductive constants. The correlation is only slightly poorer for Li^+ and Na^+ binding probably because of the weak interaction between alkali metal cations and nitrogen donor atoms. In general, Ag^+ binding is high when the ratio of nitrogen to oxygen heteratoms is high. When the ratio is low, alkali metal binding is higher than that of Ag^+. These results are important because they allow one to make predictions about the binding properties of alkali metal and silver cations to lariat ethers and BiBLEs.

Experimental Section

General. ^1H NMR spectra were recorded on a Varian EM 360A spectrometer or on a Hitachi Perkin-Elmer R-600 high resolution NMR spectrometer and are reported in ppm (δ) downfield from internal Me_4Si. IR spectra were recorded on a Perkin-Elmer 298 or a Perkin-Elmer 599 infrared spectrophotometer and were calibrated against the 1601-cm^{-1} band of polystyrene. Melting points were determined on a Thomas Hoover apparatus in open capillaries and are uncorrected. All combustion analyses were performed by Atlantic Microlab, Inc., Atlanta, GA,

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and are reported as percents. Preparative chromatography columns were packed with activated aluminum oxide (MCB 80-325 mesh, chromatographic grade, AX 611) or with Kieselgel 60 (70–230 mesh).

All reactions were conducted under an atmosphere of dry nitrogen. Sodium carbonate was purchased from J. T. Baker Chemical Co. and was anhydrous. Acetonitrile was purchased from Alfa Products and was used without further purification. All alkylating agents were purchased from Aldrich Chemical Company unless otherwise noted. All chromatography solvents (CH_2Cl_2, 2-propanol, hexanes) were of commercial grade and were distilled prior to use.

Preparation of Nitrogen-Pivot Lariat Ethers. Aza-15-crown-5 was prepared in 55% yield by using the general procedure of Okahara et al.[25]

***N*-(2-Nitrobenzyl)aza-15-crown-5 (1)** was prepared by treating aza-15-crown-5 with 2-nitrobenzyl chloride in the presence of a refluxing acetonitrile solution containing anhydrous sodium carbonate.[26] The purified yellow oil (96%) possessed physical properties identical with those previously reported.[12]

***N*-(4-Nitrobenzyl)aza-15-crown-5 (2)** was prepared using 4-nitrobenzyl bromide as described for **1**.[26] The purified yellow oil (85%) possessed physical properties identical with those previously reported.[12]

***N*-(2-Cyanobenzyl)aza-15-crown-5 (3) was** prepared from 2-cyanobenzyl bromide as described for **1** and **2**.[26] Column chromatography (alumina, 2% 2-propanol/hexanes) followed by bulb-to-bulb distillation on a Kugelrohr apparatus (175 °C, 0.1 Torr) gave **3** as a transparent oil (2.7 g, 82%): ^1H NMR ($CDCl_3$) 2.82 (t, 4 H, NCH_2), 3.65 and 3.90 (s, and m, 18 H, benzyl and OCH_2), 7.26–7.65 ppm (m, 4 H, aromtic); IR (neat) 2900 (s), 2230, 1470, 1370, 1140 (s), 780 cm^{-1}. Anal. Calcd for $C_{18}H_{26}N_2O_4$: C, 64.64; H, 7.85; N, 8.38. Found: C, 64.46; H, 7.89; N, 8.33.

***N*-(4-Cyanobenzyl)aza-15-crown-5 (4)** was prepared from 4-cyanobenzyl bromide as described for **1** and **2**.[26] Column chromatography (alumina, 2% 2-propanol/hexanes) followed by recrystallization (hexanes) gave **4** as a white crystalline solid (2.7 g, 82%, mp 45–46 °C): ^1H NMR ($CDCl_3$) 2.77 (t, 4 H, NCH_2), 3.66 and 3.76 (s and m, 18 H, benzyl and OCH_2), 7.55 ppm (s, 4 H, aromatic); IR (neat) 2900 (s), 2230, 1365, 1140 (s), 950 cm^{-1}. Anal. Calcd for $C_{18}H_{26}N_2O_4$: C, 64.64; H, 7.85; N, 8.38. Found: C, 64.50; H, 7.88; N, 8.30.

***N*-(2-Chlorobenzyl)aza-15-crown-5 (5)** was prepared from 2-chlorobenzyl chloride as described for **1** and **2**.[26] Bulb-to-bulb distillation on a Kugelrohr apparatus (148 °C, 0.08 mm) followed by filtration of the resulting sample through a pad of silica gel 60 (1% $MeOH/CH_2Cl_2$ as solvent) gave **5** as a transparent oil (0.62 g, 72%): ^1H NMR ($CDCl_3$) 2.90 (t, 4 H, NCH_2), 3.65 and 3.88 (s and m, 18 H, benzyl and OCH_2), 7.16–7.75 ppm (m, 4 H, aromatic); IR (neat) 2900 (s), 1140 (s), 760 cm^{-1}. Anal. Calcd for $C_{17}H_{26}NO_4Cl$: C, 59.37; H, 7.64; N, 4.07. Found: C, 59.28; H, 7.66; N, 3.91.

***N*-(4-Chlorobenzyl)aza-15-crown-5 (6)** was prepared from 4-chlorobenzyl chloride as described for **1** and **2**.[26] Column chromatography (alumina, 2% 2-propanol/hexanes) gave **6** as a transparent oil (0.86 g, 80%): ^1H NMR ($CDCl_3$) 2.76 (t, 4 H, NCH_2), 3.65 (m, 18 H, benzyl and OCH_2), 7.25 ppm (s, 4 H, aromatic); IR (neat) 2900 (s), 1145 (s), 1030 cm^{-1}. Anal. Calcd for $C_{17}H_{26}NO_4Cl$: C, 59.37; H, 7.64; N, 4.07. Found: C, 59.32; H, 7.64; N, 4.04.

***N*-Benzylaza-15-crown-5 (7)** was prepared from *N*-benzyldiethanolamine and triethylene glycol dimesylate as previously described in the literature.[2] The purified transparent oil (46%) possessed physical properties identical with those previously reported.[2]

***N*-(2-Methoxybenzyl)aza-15-crown-5 (8)** was prepared from *N*-(2-methoxybenzyl)diethanolamine and triethylene glycol dimesylate as previously described.[2] The purified transparent oil (40%) possessed physical properties identical with those previously reported.[2]

***N*-(4-Methoxybenzyl)aza-15-crown-5 (9)** was prepared from 4-methoxybenzyl chloride as described for **1** and **2**.[26] Column chromatography (alumina, 2% 2-propanol/hexanes) followed by filtration of the resulting sample through a pad of silica gel 60 (1% $MeOH/CH_2Cl_2$ as solvent) gave **9** as a transparent oil (0.70 g, 83%): ^1H NMR ($CDCl_3$) 2.76 (t, 4 H, NCH_2), 3.65 and 3.77 (s and m, 21 H, benzyl, OCH_2 and OCH_3), 6.82 (d, 2 H, aromatic), 7.25 ppm (d, 2 H, aromatic); IR (neat) 2900 (s), 1530 (s), 1320, 1260 (s), 1140 (s), 1050 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NO_5$: C, 63.68; H, 8.63; N, 4.13. Found: C, 63.57; H, 8.70; N, 4.07.

Preparation of BiBLEs. 4,13-Diaza-18-crown-6 was prepared in 92% yield from *N,N'*-dibenzyl-4,13-diaza-18-crown-6 according to the literature procedure.[4]

***N,N'*-Bis(2-nitrobenzyl)-4,13-diaza-18-crown-6 (10)** was prepared by treating 4,13-diaza-18-crown-6 with 2-nitrobenzyl chloride in the presence of refluxing acetonitrile solution containing anhydrous sodium carbonate.[4] The purified yellow solid (mp 77–78.5 °C) was obtained in 90% yield and possessed physical properties identical with those previously reported.[12]

***N,N'*-Bis(4-nitrobenzyl)-4,13-diaza-18-crown-6 (11)** was prepared in 90% yield from 4-nitrobenzyl bromide as described for **10**.[4] The purified yellow solid (mp 116–118 °C) possessed physical properties identical with those previously reported.[4]

***N,N'*-Bis(2-cyanobenzyl)-4,13-diaza-18-crown-6 (12)** was prepared from 2-cyanobenzyl bromide in 90% yield as described for **10**.[4] The purified white solid (mp 96–98 °C) possessed physical properties identical with those previously reported.[4]

***N,N'*-Bis(4-cyanobenzyl)-4,13-diaza-18-crown-6 (13)** was prepared from 4-cyanobenzyl bromide as described for **10**.[4] Column chromatography (alumina, 0–5% $MeOH/CHCl_3$) followed by recrystallization (EtOH) gave **13** as a white crystalline solid (1.7 g, 91%, mp 103–104 °C): ^1H NMR ($CDCl_3$) 2.80 (t, 8 H, NCH_2), 3.56–3.84 (m, 20 H, benzyl and OCH_2), 7.54 ppm (br s, 8 H, aromatic); IR (KBr) 2980 (s), 2840, 2220, 1610, 1520, 1460 (s), 1380 (s), 1120 (s), 1020, 960, 890, 740 cm^{-1}. Anal. Calcd for $C_{28}H_{36}N_4O_4$: C, 68.26; H, 7.38. Found: C, 68.22; H, 7.45.

***N,N'*-Bis(2-chlorophenyl)-4,13-diaza-18-crown-6 (14)** was prepared from 2-chlorobenzyl chloride as described for **10**.[4] Recrystallization (EtOH) gave **14** as a white crystalline solid (1.5 g, 82%, mp 94–95 °C): ^1H NMR ($CDCl_3$) 2.85 (t, 8 H, NCH_2), 3.45–3.80 (m, 20 H, benzyl and OCH_2), 7.10–7.70 ppm (m, 8 H, aromatic); IR (KBr) 2950 (s), 2890 (s), 1610, 1580, 1480, 1410, 1270, 1130 (s), 920, 840, 730 cm^{-1}. Anal. Calcd for $C_{26}H_{36}N_2O_4Cl_2$: C, 61.04; H: 7.10. Found: C, 61.11; H, 7.13.

***N,N'*-Bis(4-chlorobenzyl)-4,13-diaza-18-crown-6 (15)** was prepared from 4-chlorobenzyl chloride as described for **10**.[4] Recrystallization (EtOH) gave **15** as a white crystalline solid (1.4 g, 75%, mp 79–80 °C): ^1H NMR ($CDCl_3$) 2.82 (t, 8 H, NCH_2), 3.48–3.86 (m, 20 H, benzyl and OCH_2), 7.22 ppm (br s, 8 H, aromatic); IR (KBr) 2980 (s), 2820 (s), 1620, 1580, 1470, 1430, 1360, 1250, 1150 (s), 1030, 920, 730 cm^{-1}. Anal. Calcd for $C_{26}H_{36}N_2O_4Cl_2$: C, 61.04; H, 7.10. Found: C, 61.10; H, 7.14.

***N,N'*-Dibenzyl-4,13-diaza-18-crown-6 (16)** was prepared from *N,N'*-dibenzyl-1,8-diamino-3,6-dioxaoctane and 1,2-bis(2-iodoethoxy)ethane as previously described.[4] The purified solid (mp 80–81 °C) was obtained in 66% yield and possessed physical properties identical with those previously reported.[27]

***N,N'*-Bis(2-methoxybenzyl)-4,13-diaza-18-crown-6 (17)** was prepared (30%) from 2-methoxybenzylamine and 1,2-bis(2-iodoethoxy)ethane as previously described.[3] The purified solid (mp 86–87 °C) possessed physical properties identical with those previously reported.[3]

***N,N'*-Bis(4-methoxybenzyl)-4,13-diaza-18-crown-6 (18)** was prepared from 4-methoxybenzyl chloride as described for **10**.[4] Column chromatography (alumina, 0–5% $MeOH/CHCl_3$) followed by recrystallization (EtOH–hexanes, 2:1) gave **18** as a white crystalline solid (1.7 g, 91%, mp 65–66 °C): ^1H NMR ($CDCl_3$) 2.81 (t, 8 H, NCH_2), 3.58–3.82 (m, 26 H, benzyl, OCH_2 and OCH_3), 6.85 (d, 4 H, aromatic), 7.22 ppm (d, 4 H, aromatic); IR (KBr) 2960 (s), 2880 (s), 1620, 1510 (s), 1470, 1240, 1130, 1020, 730 cm^{-1}. Anal. Calcd for $C_{28}H_{42}N_2O_6$: C, 66.89; H, 8.44. Found: C, 67.00; H, 8.51.

Cation Stability Constants. Acetonitrile (Alfa Products) was purified by stirring for 2 days over calcium hydride (10 g/L),

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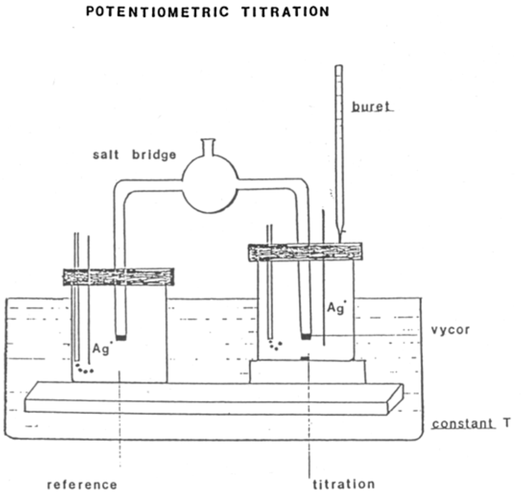

Figure 3. Salt bridge apparatus used for cation binding measurements.

followed by decantation and distillation from phosphorus pentoxide (5 g/L). Further purification involved heating at reflux for 12 h over calcium hydride and fractional distillation under a dry nitrogen atmosphere. The collected acetonitrile was then syringed out of the flask under a dry nitrogen atmosphere and used to prepare the solutions as needed.

Tetrabutylammonium perchlorate (TBAP, Fluka Chemical Corp.) was twice recrystallized from ethyl acetate and dried in vacuo for 24 h (110 °C, <0.3 Torr). Lithium and sodium perchlorate (Aldrich Chemical Co.) were recrystallized from distilled water, dried in vacuo for 24 h (110 °C, <0.3 Torr), and stored in a desiccator over calcium chloride. Silver nitrate (Aldrich Chemical Co.) was used without further purification.

The binding constant determination was based on the methods of Gutknecht[19] and Cox.[20-22] The experimental cell was constructed in our laboratory and is shown in Figure 3. The cell was thermostated at 25 ± 1 °C by a Cole-Palmer (Model 1252-00) circulator. Two silver wires served as the indicator electrodes and the potentials were measured on an Orion 701A ionalyzer. Both the reference and titration cells were kept under an atmosphere of dry nitrogen.

The salt bridge, shown in Figure 3, was glass blown in our laboratory. It was constructed of two glass tubes joined to a 5-mL round-bottomed flask. The ends of the tubes were fitted with Vycor frits (EG + G) and sealed to the tapered tubes by a Teflon sheath. The salt bridge was filled and stored in a solution of 0.05 M TBAP in acetonitrile. The bridge was purged with nitrogen prior to each experiment.

The salt bridge was calibrated as follows. A minimum of ten samples were prepared containing varying concentrations of $AgNO_3$ in 0.05 M $TBAP/CH_3CN$. The reference cell solution was kept constant at 0.01 M $AgNO_3$. Each solution was introduced into the cell, and the salt bridge was put in place and kept under a dry nitrogen atmosphere. Once thermal equilibrium was attained, the potential was recorded. The theoretical potential was calculated according to eq 1. The calibration experiment was

$$E = \frac{2.303RT}{F}\ \frac{\log\,[\mathrm{Ag}^+]}{[0.01\ \mathrm{M\ Ag}^+]_{\mathrm{ref}}} \tag{1}$$

repeated whenever there were changes made in the salt bridge composition (solvent, supporting electrolyte, etc.).

The stability constants were determined by a method based on a competition for the ligand by the alkali metal (Li^+ or Na^+) and silver, the latter being detected by a silver wire dipped in a $AgNO_3$ solution. The silver binding constant is determined first and is then used to calculate the alkali metal (or any metal) binding constant. The equilbria involved are indicated below.

$$\begin{aligned} \mathrm{Ag}^+ + \mathrm{L} &\overset{K_{\mathrm{Ag}}}{\rightleftharpoons} \mathrm{LAg}^+ \\ \mathrm{LAg}^+ + \mathrm{M}^+ &\rightleftharpoons \mathrm{LM}^+ + \mathrm{Ag}^+ \\ \mathrm{L} + \mathrm{M}^+ &\rightleftharpoons \mathrm{LM}^+ \end{aligned}$$

K_{Ag} was determined by simple potentiometric titration of a $AgNO_3$ solution (0.001 M $AgNO_3$/0.05 M TBAP/solvent) with a solution of the ligand (0.01 M L/0.05 M TBAP/solvent). The resulting emf is a measure of the free Ag^+ ion concentration. The following equations were used to calculate K_{Ag}. Using a similar experimental procedure, a solution of the alkali metal cation is titrated into the silver–ligand solution. For a solution containing M^+, Ag^+ and ligand (L), the total concentrations can be written as

$$[\mathrm{Ag}^+]_{\mathrm{T}} = [\mathrm{Ag}^+]_{\mathrm{F}} + [\mathrm{LAg}^+]$$

$$[\mathrm{L}]_{\mathrm{T}} = [\mathrm{L}]_{\mathrm{F}} + [\mathrm{LAg}^+]$$

$$K_{\mathrm{Ag}} = [\mathrm{LAg}^+]/[\mathrm{Ag}^+]_{\mathrm{F}}[\mathrm{L}]_{\mathrm{F}}$$

$$[\mathrm{M}^+]_{\mathrm{T}} = [\mathrm{M}^+]_{\mathrm{F}} + [\mathrm{LM}^+]$$

$$[\mathrm{Ag}^+]_{\mathrm{T}} = [\mathrm{Ag}^+]_{\mathrm{F}} + [\mathrm{LAg}^+]$$

$$[\mathrm{L}]_{\mathrm{T}} = [\mathrm{L}]_{\mathrm{F}} + [\mathrm{LAg}^+] + [\mathrm{LM}^+]$$

$[Ag^+]_F$ was calculated as before, from the measured emf for the solution. The value of K_{Ag}, along with the mass balance equations, can be used to calculate $[L]_F$, $[M^+]_F$, and $[LM^+]$. The binding constant for the M^+–ligand interaction can be calculated as follows

$$K_S = [\mathrm{LM}^+]/[\mathrm{L}]_{\mathrm{F}}[\mathrm{M}^+]_{\mathrm{F}}$$

All binding constant determinations were perfomed in duplicate. Values of log *K* were reproducible to ±0.05 log unit.

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Registry No. **1**, 88548-59-8; **1**·Ag^+, 110116-90-0; **1**·Na^+, 108043-48-7; **1**·Li^+, 110117-18-5; **2**, 88548-60-1; **2**·Ag^+, 110116-91-1; **2**·Na^+, 108043-49-8; **2**·Li^+, 110117-19-6; **3**, 110116-81-9; **3**·Ag^+, 110116-92-2; **3**·Na^+, 110117-05-0; **3**·Li^+, 110117-20-9; **4**, 110116-82-0; **4**·Ag^+, 110116-93-3; **4**·Na^+, 110117-06-1; **4**·Li^+, 110117-21-0; **5**, 110116-83-1; **6**, 110116-84-2; **6**·Ag^+, 110116-94-4; **6**·Na^+, 110117-07-2; **6**·Li^+, 110117-22-1; **7**, 71089-11-7; **7**·Ag^+, 110116-95-5; **7**·Na^+, 79407-80-0; **7**·Li^+, 110117-23-2; **8**, 98269-24-0; **8**·Ag^+, 110116-96-6; **8**·Na^+, 110117-08-3; **8**·Li^+, 110117-24-3; **9**, 110116-85-3; **9**·Ag^+, 110116-97-7; **9**·Na^+, 110117-09-4; **9**·Li^+, 110117-25-4; **10**, 94978-65-1; **10**-Ag^+, 110116-98-8; **10**·Na^+, 110117-10-7; **10**·Li^+, 110117-27-6; **11**, 105400-16-6; **11**·Ag^+, 110116-99-9; **11**·Na^+, 110117-11-8; **11**·Li^+, 110117-26-5; **12**, 105400-14-4; **12**·Ag^+, 110117-00-5; **12**·Na^+, 110117-12-9; **12**·Li^+, 110117-28-7; **13**, 110116-86-4; **13**·Ag^+, 110117-01-6; **13**·Na^+, 110117-13-0; **13**·Li^+, 110117-29-8; **14**, 110116-87-5; **15**, 110116-88-6; **15**·Ag^+, 110117-02-7; **15**·Na^+, 110117-14-1; **15**·Li^+, 110117-30-1; **16**, 69703-25-9; **16**·Ag^+, 110117-03-8; **16**·Na^+, 110117-15-2; **16**·Li^+, 110117-31-2; **17**, 93000-66-9; **17**·Ag^+, 110117-04-9; **17**·Na^+, 110117-16-3; **17**·Li^+, 110117-32-3; **18**, 69703-26-0; **18**·Ag^+, 110142-30-8; **18**·Na^+, 110117-17-4; **18**·Li^+, 110117-33-4; *N*-(2-methoxybenzyl)diethanolamine, 98269-32-0; 4-methoxybenzyl chloride, 824-94-2; 4,13-diaza-1,8-crown-6, 23978-55-4; *N*,*N*′-dibenzyl-1,8-diamino-3,6-dioxaoctane, 110116-89-7; 1,2-bis(2-iodoethoxy)ethane, 36839-55-1; aza-15-crown-5, 66943-05-3; 2-nitrobenzyl chloride, 612-23-7; 4-nitrobenzyl bromide, 100-11-8; 2-cyanobenzyl bromide, 22115-41-9; *p*-cyanobenzyl bromide, 17201-43-3; 2-chlorobenzyl chloride, 611-19-8; 4-chlorobenzyl chloride, 104-83-6; *N*-benzyldiethanolamine, 101-32-6; triethyleneglycol dimesylate, 80322-82-3; 2-methoxybenzylamine, 6850-57-3.