of host and guest in $CDCl_3$ (K_a, see eq 1), K_d, and K_e.

$$[t\text{-BuNH}_3^+]_{D_2O} + [X^-]_{D_2O} \overset{K_d}{\rightleftharpoons} [t\text{-BuNH}_3^+ \cdot X^-]_{CDCl_3} \quad (12)$$

$$[H]_{CDCl_3} + [t\text{-BuNH}_3^+]_{D_2O} + [X^-]_{D_2O} \overset{K_e}{\rightleftharpoons} [t\text{-BuNH}_3^+ \cdot H \cdot X^-]_{CDCl_3} \quad (13)$$

$$K_e = \frac{R}{(1 - R)\{[t\text{-BuNH}_3{}^+{}_i]_{D_2O} - R[H_i]_{CDCl_3}(V_{CDCl_3}/V_{D_2O})\}^2} \quad (14)$$

$$K_e = K_aK_d \quad (15)$$

The values of R and of K_a (normalized when scale C involving t-$BuNH_3SCN$ was employed[3]) are recorded in Table II. When 18-crown-6 (**17**) and pyridyl-18-crown-6 (**1**) were employed, the small amount of host that dissolved in the D_2O layer at equilibrium was corrected for by using the concentration of host in $CDCl_3$ at equilibrium in place of $[H_i]_{CDCl_3}$ in eq 17 (see footnotes *c*, *d*, *e*, and *f*, Table II).

Distribution of *tert*-Butylammonium Chloride between Deuterium Oxide and Deuteriochloroform in the Absence of Hosts. The K_d values for t-$BuNH_3{}^+Cl^-$ were determined by the fluorometric technique applied previously to t-$BuNH_3{}^+SCN^-$. The technique with respect to concentrations, volumes, and temperatures was identical except that the chloride was substituted for the thiocyanate salt.[3] The original D_2O solutions of t-$BuNH_3{}^+Cl^-$ were adjusted to pH 1 with HCl before being extracted with $CDCl_3$. Because the amounts of salt extracted at 24 °C were only slightly in excess of the blanks at 24 °C, the K_d value could only be grossly estimated to be $\approx 0.93 \times 10^{-6}$. At 0 °C, the aqueous layer was extracted successively with three $CDCl_3$ portions, which after subtraction of the blank (0.713×10^{-6}) gave K_d values of 1.07×10^{-6}, 1.75×10^{-6}, and 1.07×10^{-6} M^{-1}, respectively. The average value of $1.3 \pm 0.3 \times 10^{-6}$ M^{-1} was used in the calculation of K_a values of Table II.

References and Notes

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Host–Guest Complexation. 4. Remote Substituent Effects on Macrocyclic Polyether Binding to Metal and Ammonium Ions[1]

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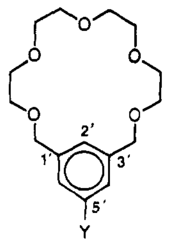
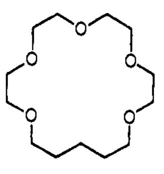
Abstract: Seven 5′-substituted 1′,3′-xylyl-18-crown-5 macrocyclic polyethers (hosts) are reported with substituents H (**1**), Br (**2**), $C(CH_3)_3$ (**3**), $CO_2C_2H_5$ (**4**), OCH_3 (**5**), SCH_3 (**6**), and CN (**7**). The association constants (K_a) of these hosts at 24 °C with *tert*-butylammonium thiocyanate, perchlorate, and picrate and the picrate salts of lithium, sodium, ammonium, potassium, rubidium, and cesium in $CDCl_3$ were measured by D_2O extraction-spectroscopic techniques. The K_a values obtained were submitted to Hammett linear free energy treatments. For *tert*-butylammonium, ammonium, potassium, rubidium, and cesium, the K_a values were only poorly correlated by existing σ constants. For lithium and sodium, no trends were visible in the data. For *tert*-butylammonium perchlorate as guest, the complex with **7** as host was about 2.4 kcal/mol less stable than with **3** as host. For ammonium, potassium, rubidium, and cesium ions, the differences between the complexes with **7** vs. **5** as host ranged from ~1.4 to ~1.7 kcal/mol. The OCH_3 substituent stabilized and the CN destabilized the complexes relative to H. Good linear free energy correlations were observed when ammonium picrate as a standard guest was compared with *tert*-butylammonium perchlorate and thiocyanate, potassium picrate, rubidium picrate, and cesium picrate as alternative guests. The effects of the substituents on the π basicity of the benzene ring appear to control the patterns of changes in K_a values with changes in substituent. The ^1H NMR spectra of the complexes of *tert*-butylammonium salts with **1–3** and **5** gave signals for the *tert*-butyl protons that were about 0.4 ppm upfield of the complex with 18-crown-6 and varied little with changes in substituent and counterion. This fact indicates that the complexes possess a conformation that places the *tert*-butyl group in the shielding cone of the aryl group.

The synthesis and properties of macrocyclic polyethers[2,3] and polythioethers[4] whose structures incorporate 1,3-xylyl units have been investigated recently. The complexing properties have been reported of host compounds containing 1,3-xylyl units substituted in the 2 position with functional groups whose *convergence* on bound guest ions is enforced by the rigidity of the aryl group.[5] We report here a study of the binding properties of cycles **1–7** in which substituents in the 5′ position of the 1′,3′-xylyl group are both remote and *divergent* from the site of complexation.[6] The association constants (K_a) defined by eq 1 have been determined at 24 °C in $CDCl_3$ in which H is the host, G^+X^- is the guest salt, and $G^+{\cdot}H{\cdot}X^-$ is the com-



1, Y = H
2, Y = Br
3, Y = C(CH$_3$)$_3$
4, Y = CO$_2$C$_2$H$_5$
5, Y = OCH$_3$
6, Y = SCH$_3$
7, Y = CN



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plex. The guests include t-BuNH$_3^+$SCN$^-$, t-BuNH$_3^+$ ClO$_4^-$, and the picrate salts of t-BuNH$_3^+$, NH$_4^+$, Li$^+$, Na$^+$, K$^+$, Rb$^+$, and Cs$^+$.

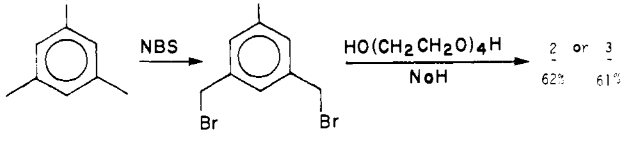
$$\mathrm{H + G^+X^-} \underset{\mathrm{CDCl_3}}{\overset{K_a}{\rightleftharpoons}} \mathrm{G^+{\cdot}H{\cdot}X^-} \qquad (1)$$

In an earlier study,[2b] the abilities of 18-crown-6, 18-crown-5 (**8**), and 1′,3′-xylyl-18-crown-5 (**1**) to complex t-BuNH$_3^+$SCN$^-$ in CDCl$_3$ were compared. Replacement of one oxygen atom of 18-crown-6 by a methylene unit as in **8** decreased K_a by a factor of greater than 10^3, whereas replacement of one CH$_2$CH$_2$OCH$_2$CH$_2$ unit of 18-crown-6 with a 1,3-xylyl unit as in **1** decreased K_a by a factor of 700. The difference between the K_a for **1** and that for **8** suggested that the π-electron system of **1** might be involved in the binding of the guest ions, and that a study of the remote substituent effects on K_a might provide clues as to the nature of that role. Corey-Pauling-Koltun (CPK) molecular models of complexes of **1** with various cations indicate that the ion contacts the π system of the benzene ring at the 2′ position of **1**. The models suggest that the complexes might resemble a point on the reaction coordinate for formation of the σ complexes of electrophilic aromatic substitution.

Hammett-type linear free energy relationships[7] have been shown to correlate the physical properties of free-base tetraarylporphyrins[8] and their metal derivatives.[9] These studies revealed that substantial effects were obtained by placing substituents at places considerably removed from the binding site. One of the motives for our investigation was to determine whether linear free energy treatments of remote substituent effects on K_a values correlated the complexation data when the π system of an aryl group was one of the complexing sites.

Results

Preparation of Macrocycles. Macrocycles **1**,[2b] **2**, and **3** were prepared by adding dropwise an equimolar mixture of tetraethylene glycol and the appropriate 5-substituted 1,3-xylyl dibromide in dry tetrahydrofuran (THF) to a refluxing mixture of NaH and THF. The reaction was rapid enough to occur under moderately high dilution conditions to produce cycles in approximately 60–62% yields.



9, Y = Br
10, Y = C(CH$_3$)$_3$
11, Y = Br
12, Y = C(CH$_3$)$_3$

Treatment of **2** with butyllithium followed by ethyl chloroformate gave ester **4** (50%). The syntheses of cycles **5–7** involved cuprous iodide catalyzed nucleophilic aromatic substitutions on cyclic aromatic bromide **2**.[10] With sodium methoxide and catalyst, **2** gave **5** (86%), with lithium methiolate, **2** gave **6** (30%), and with cuprous cyanide, **2** gave **7** (62%). The reaction conditions were not varied to maximize yields.

Table I. Remote Substituent Effects for 5′-Y-1′,3′-Xylyl-18-crown-5 Hosts Complexing Picrate Salt Guests in CDCl$_3$ at 24 °C

Host No.	Host Y	Guest cation	R^a × 10^3	$K_a \times 10^{-3}$,^{b} M^{-1}	Log [(K_a)$_Y$/(K_a)$_H$]
1	H	Li$^+$	0.04	0.10	0.00
2	Br	Li$^+$	0.04	0.10	0.00
3	C(CH$_3$)$_3$	Li$^+$	0.08	0.25	+0.40
5	OCH$_3$	Li$^+$	0.13	0.40	+0.60
7	CN	Li$^+$	0.40	1.0	+1.0
1	H	Na$^+$	0.65	1.7	0.00
2	Br	Na$^+$	0.42	1.1	−0.19
3	C(CH$_3$)$_3$	Na$^+$	0.63	1.6	−0.03
5	OCH$_3$	Na$^+$	0.101	2.6	+0.18
7	CN	Na$^+$	0.063	1.6	−0.03
1	H	K$^+$	53.0	109	0.00
2	Br	K$^+$	19.7	36.4	−0.48
3	C(CH$_3$)$_3$	K$^+$	53.3	109	0.00
5	OCH$_3$	K$^+$	62.0	131	+0.08
7	CN	K$^+$	6.51	11.6	−0.96
1	H	NH$_4^+$	80.9	115	0.00
2	Br	NH$_4^+$	26.4	31.6	−0.56
3	C(CH$_3$)$_3$	NH$_4^+$	83.7	120	+0.018
5	OCH$_3$	NH$_4^+$	84.5	122	+0.03
7	CN	NH$_4^+$	9.39	10.7	−1.03
1	H	Rb$^+$	27.6	65.7	0.00
2	Br	Rb$^+$	8.40	18.9	−0.54
3	C(CH$_3$)$_3$	Rb$^+$	29.4	70.4	+0.03
5	OCH$_3$	Rb$^+$	32.2	77.7	+0.07
7	CN	Rb$^+$	2.49	5.49	−1.08
1	H	Cs$^+$	25.4	50.7	0.00
2	Br	Cs$^+$	7.34	13.8	−0.56
3	C(CH$_3$)$_3$	Cs$^+$	23.7	51.4	+0.006
5	OCH$_3$	Cs$^+$	27.7	55.7	+0.041
7	CN	Cs$^+$	1.79	3.33	−1.18

[a] [Guest]/[host] in CDCl$_3$ layer at equilibrium. [b] Association constant defined by eq 3.

Determination of Association Constants. By a technique described in the Experimental Section, solutions of cycles **1–3**, **5**, and **7** in CDCl$_3$ were used to extract H$_2$O solutions of lithium, sodium, potassium, cesium, rubidium, and ammonium picrates. From the measurement of the ultraviolet (UV) absorbance of the organic phase at 380 nm, the molar ratios of picrate to host (R) were determined at 24 °C. With eq 2,[2b] K_a values defined by eq 3 were calculated. In eq 2 K_d is the distribution constant (see eq 4) of the picrate salts between the two layers in the absence of host, $[\mathrm{G_i}]_{\mathrm{H_2O}}$ is the initial concentration of the guest (picrate salt) in H$_2$O, $[\mathrm{H_i}]_{\mathrm{CDCl_3}}$ is the initial host concentration in CDCl$_3$, $V_{\mathrm{CDCl_3}}$ is the volume of CDCl$_3$, and $V_{\mathrm{H_2O}}$ is the volume of H$_2$O. Table I reports the values of K_a obtained.

$$K_a = \frac{R}{(1-R)K_d\{[\mathrm{G_i}]_{\mathrm{H_2O}} - R[\mathrm{H_i}]_{\mathrm{CDCl_3}}(V_{\mathrm{CDCl_3}}/V_{\mathrm{H_2O}})\}^2} \qquad (2)$$

$$\mathrm{H + M^+\ Pic^-} \underset{\mathrm{CDCl_3}}{\overset{K_a}{\rightleftharpoons}} \mathrm{M^+{\cdot}H{\cdot}Pic^-} \qquad (3)$$

$$K_d = \frac{[\mathrm{G^+\ X^-}]_{\mathrm{CDCl_3}}}{[\mathrm{G^+}]_{\mathrm{H_2O}}\,[\mathrm{X^-}]_{\mathrm{H_2O}}} \qquad (4)$$

Smid et al.[11] found that the main UV absorption band of picrate salts undergoes pronounced bathochromic shifts when their cations are complexed by crown ethers. The magnitude of the shift of the absorption maximum ($\lambda_{\max}$) indicates whether the complexed salt exists as a crown-coordinated

Table II. Remote Substituent Effects for 5′-Y-1′,3′-Xylyl-18-crown-5 Hosts Complexing t-$BuNH_3^+$ X^- Salt Guests in $CDCl_3$ at 24 °C

Host No.	Host Y	Guest anion	R^a	K_a,[b] M^{-1}	[Log $(K_a)_Y/(K_a)_H$]	δ of t-Bu, ppm from Me_4Si
1	H	SCN^-	0.25	3 300	0.00	0.94
2	Br	SCN^-	0.04	330	−1.00	1.01
3	$C(CH_3)_3$	SCN^-	0.32	5 200	+0.20	0.94
4	$CO_2C_2H_5$	SCN^-	0.07	620	−0.72	1.01
5	OCH_3	SCN^-	0.25[c]	3 200	−0.008	0.98
1	H	ClO_4^-	0.60[d]	211 400	0.00	0.86
2	Br	ClO_4^-	0.17	23 300	−0.96	0.90
3	$C(CH_3)_3$	ClO_4^-	0.72	360 400	+0.23	0.83
5	OCH_3	ClO_4^-	0.61[e]	227 000	+0.031	0.88
6	SCH_3	ClO_4^-	0.34	64 600	−0.52	0.91
7	CN	ClO_4^-	0.06	6 670	−1.50	0.90
1	H	Pic^-	0.124[f]	3 460	0.00	0.96
2	Br	Pic^-	0.036[g]	760	−0.66	
3	$C(CH_3)_3$	Pic^-	0.15[h]	4 580	+0.12	0.96

[a] [Guest]/[host] in $CDCl_3$ layer at equilibrium determined by ^1H NMR. [b] Association constant defined by eq 1. [c] Average of 0.24 and 0.26 involving different preparations of host. [d] Two determinations gave 0.60 and 0.59. [e] Average of 0.62 and 0.60 involving different preparations of host. [f] Determined by UV method to be 0.13; average used. [g] Determined by UV method only. [h] Determined by UV method to be 0.16; average used.

contact ion pair or a crown-separated ion pair. The absorption maxima in $CDCl_3$ of the 1:1 complexes between sodium picrate and 4′-methylbenzo-15-crown-5, between potassium picrate and benzo-15-crown-5, and between ammonium picrate and 4′-carbomethoxybenzo-15-crown-5 were 356,[11a] 362,[11b] and 353 nm,[11c] respectively. The UV spectra of the picrate salt complexes of **1** in $CDCl_3$ obtained in the above extraction experiments gave λ_{max} values as follows: sodium picrate, 360 nm; potassium picrate, 366 nm; rubidium picrate, 363 nm; cesium picrate, 363 nm; and ammonium picrate, 358 nm. The magnitudes of these values indicate our complexes are crown-coordinated contact ion pairs, and are therefore 1:1. The formation of complexes composed of two crowns and one salt are excluded since λ_{max} for such species should be close to 380 nm. For instance, the 2:1 complexes between potassium and ammonium picrates and 4′-methylbenzo-15-crown-5 give λ_{max} 381[11b] and 378 nm,[11c] respectively.

Cycles **1–5** were used to determine K_a values for t-$BuNH_3^+SCN^-$, **1–3** and **5–7** K_a values for t-$BuNH_3^+$ ClO_4^-, and **1–3** values for t-$BuNH_3^+$ Pic^- in $CDCl_3$ at 24 °C. The previously developed D_2O-$CDCl_3$ extraction methods were employed for the thiocyanate salt,[2b,12] the perchlorate salt,[13] and the picrate salt of *tert*-butylamine. The R values of eq 2 were determined with ^1H NMR techniques for the thiocyanate and perchlorate salts, while both the ^1H NMR and UV techniques were applied for the picrate salt. The K_d value for the perchlorate salt at 24 °C was found to be 9.6×10^{-6} M^{-1} (see Experimental Section), and that for the thiocyanate was 5.2×10^{-5} M^{-1}.[12] The K_a values obtained are recorded in Table II.

Discussion

These experiments involve host compounds whose Y substituents in CPK molecular models are rigidly held in positions too remote from the binding sites to sterically influence binding constants. The shapes of the binding sites in the seven hosts are the same, and only the electronic effects of the substituents should influence binding abilities of the hosts. The nine guest salts differ from one another in two respects; seven different cations and three different anions are represented. The solvent and temperature were kept constant. In the first of the following sections is discussed the variation of K_a values with changes in the cations of the picrate salts. The second section deals with the linear free energy relationships between K_a values when cations and Y substituents are varied independently. In the third section is discussed the effect of anion on the response to changes in Y of K_a values of t-$BuNH_3^+$ cation. The structures of the complexes are discussed in the fourth section.

Effects of Changes in Guest Cations on Association Constants. The values of K_a for the seven picrate salts and the parent host with Y = H vary from a low of about 10^2 for Li^+ to a high of over 10^5 for K^+ and NH_4^+. When Y changes from H to Br or $C(CH_3)_3$, the overall spread in K_a values decreases to factors of 10^3, $10^{2.5}$, and $10^{1.5}$, respectively. For all the picrates and for all hosts with Y = H, Br, or $C(CH_3)_3$, the K_a values for the different guest cations decrease in the following order: $NH_4^+ \sim K^+ > Rb^+ \sim Cs^+ > t\text{-}BuNH_3^+ \sim Na^+ > Li$. For dicyclohexyl-18-crown-6 (isomer A) in water at 25 °C, the K_a values varied by a maximum of about 40, and decreased in the following order: $K^+ > Na^+ \gtrsim Rb^+ \gtrsim NH_4^+ \gtrsim Cs^+ > Li^+$.[14] The larger spread in values associated with changes in ions in our work is probably due more to the solvent difference ($CDCl_3$ vs. H_2O) than to the difference in host structure. For dicyclohexyl-18-crown-6, larger differences in K_a values have been observed for some of these ions in methanol than in water.[14b] Even the relative positions of Na^+ and Cs^+ in the hierarchy are inverted in passing from water to methanol.[14b]

The most striking deviation in the order of K_a values for **1** in $CDCl_3$ from what has been observed with 18-crown-6 hosts[14b] in water involves NH_4^+. Host **1** in $CDCl_3$ binds this ion as well as it binds K^+, whereas dicyclohexyl-18-crown-6 in water binds K^+ considerably better than NH_4^+ which lies between Cs^+ and Rb^+. A better comparison involves K_a values for 2,3-naphtho-18-crown-6 complexing picrate salts in $CDCl_3$ (the same technique as reported here). With this host, the order of binding was $K^+ \sim Rb^+ > NH_4^+ > Cs^+ > Na^+ > Li^+$.[5b] An attractive explanation attributes the deviation for NH_4^+ in the 1′,3′-xylyl-18-crown-5 series to the following structural feature. The cavity sizes of 18-crown-6 and of 1′,3′-xylyl-18-crown-5 with its phenyl tilted out of the best plane of the oxygens are about the same. More of the binding of the NH_4^+ ion by 18-crown-6 cycles probably occurs through the three $NH^+\cdots O$ site interactions arranged in the tripod than through the three $N^+\cdots O$ site interactions. For K^+, Rb^+, and Cs^+, the binding site interactions are equally distributed among six $M^+\cdots O$ interactions. Substitution of one $N^+\cdots\pi$-Ar for one $N^+\cdots O$ interaction is probably less costly in binding energy than substitution of an $M^+\cdots\pi$-Ar for one $M^+\cdots O$ interaction.

Relationships between Association Constants, Remote Substituents in Hosts, and Cation Structure in Guests. In Tables I and II are listed values for log $[(K_a)_Y/(K_a)_H]$ for the various host-guest combinations. For lithium and sodium picrates, no patterns of their response to changes in Y substituents are visible. However, the values of log $[(K_a)_Y/(K_a)_H]$ for ammonium, potassium, rubidium, and cesium picrates for hosts with any given substituent are remarkably similar. This similarity in their response to remote substituents suggests that these four ions are complexed in much the same manner. Molecular model (CPK) examination of complexes of **1** with NH_4^+ and with spheres whose diameters correspond to those of the metal ions in question demonstrate that Li^+ and Na^+ do not fill the cavity of **1** (benzene ring tilted), K^+ just fills the cavity, and NH_4^+, Rb^+, and Cs^+ more than fill the cavity. Thus unlike NH_4^+, K^+, Rb^+, and Cs^+, Li^+ and Na^+ do not contact all six binding sites simultaneously but probably select between them. The structures of the complexes of Li^+ and Na^+ can vary somewhat with changes in the electronic character of the remote substituents, whereas the structures of the other complexes cannot. The "too small" ions minimize their free energies by selecting the most basic sites, whereas the "just right" or "too large" ions minimize their free energies by contacting all sites.

In Figure 1, values of log $[(K_a)_Y/(K_a)_H]_{NH_4^+}$ for the five substituents are plotted against values for log $[(K_a)_Y/(K_a)_H]_{M^+}$ where $M^+ = K^+$, Rb^+, or Cs^+. The deviation of the points from the line whose slope, ρ, is set equal to unity provides a measure of how differently each of the three metal ions responds to changes in Y as compared to the response of NH_4^+. The least-squares line generated from all of the points gives a slope (ρ) of 1.03 ± 0.29.[16] The proximity of this ρ to unity indicates how uniformly the four ions respond in their complexation to changes in Y. The slope of the least-squares line for K^+ is 0.942 ± 0.12;[16] for Rb^+ is 1.05 ± 0.09;[16] and for Cs^+ is 1.12 ± 0.13.[16] Equation 5 expresses the relationship exhibited in Figure 1.

$$\rho \log [(K_a)_Y/(K_a)_H]_{NH_4^+} = \log [(K_a)_Y/(K_a)_H]_{M^+} \quad (5)$$

Values of log $[(K_a)_Y/(K_a)_H]$ for NH_4^+ and M^+ when plotted against $\sigma_I{}^q$ values of Grob[15] provided linear correlations[7] which, although better than with other existing σ substituent constants, were still not good. The point for Y = OCH_3 fell well on one side of the least-squares line (substituent more stabilizing) and the point for Y = CN well on the other side (substituent less stabilizing than expected based on a σ-bonded electrostatic quinuclidine model).[15] The OCH_3 and CN groups provide the maximum differences in free energy for hosts **1**, **2**, **3**, **5**, and **7** complexing ammonium, potassium, rubidium, and cesium picrates. The ratios of $(K_a)_{OCH_3}/(K_a)_{CN}$ for NH_4^+, K^+, Rb^+, and Cs^+ were 11, 11, 14, and 17, respectively (Table I). These ratios correspond to $\Delta\Delta G$ values (eq 6) of −1.43 for NH_4^+, −1.44 for K^+, −1.57 for Rb^+, and −1.66 kcal/mol for Cs^+. Thus the methoxyl group is the most electron-releasing and stabilizing substituent and the cyano group the most electron-withdrawing and destabilizing substituent of the five examined for these guests. The results suggest that the methoxyl group distributes some negative charge and the cyano group some positive charge into the π-binding site at the 2′ position of the benzene ring closest to the positively charged guest ion. Smaller electronic effects also probably are transmitted through the σ bond system to the benzyl oxygens which hydrogen bond the guest. The fact that σ^+ fails to correlate the data indicates that the complexes provide poor models for the transition states of electrophilic aromatic substitution reactions.[7] Partial σ bonding to aromatic carbon in the transition states for those reactions makes much greater electronic demands on substituents than simple π-complexation.

$$\Delta\Delta G = -RT \ln [(K_a)_{OCH_3}/(K_a)_{CN}] \quad (6)$$

The response of K_a values to remote substituents in our 1′,3′-xylyl-18-crown-6 system in $CDCl_3$ shows interesting similarities to those observed by Smid et al.,[6] who studied the complexation by 4′-substituted benzo-18-crown-6 of sodium and potassium tetraphenylborates in acetone at 25 °C. Changes in the remote substituents from a methyl to a nitro group resulted in a reduction in K_a values by a factor of about 8 for K^+, but only about 3 for Na^+. No Hammett correlation was observed for either ion, although a good correlation was observed for Na^+ and 4′-substituted benzo-15-crown-5 hosts. With this type of host, a 4′-amino substituent produced a K_a value which was a factor of 22 higher than a 4′-nitro substituent when N^+ was guest. In the hosts of this system, the remote substituents exerted their effects by changing the basicity of the aryl oxygen binding sites.

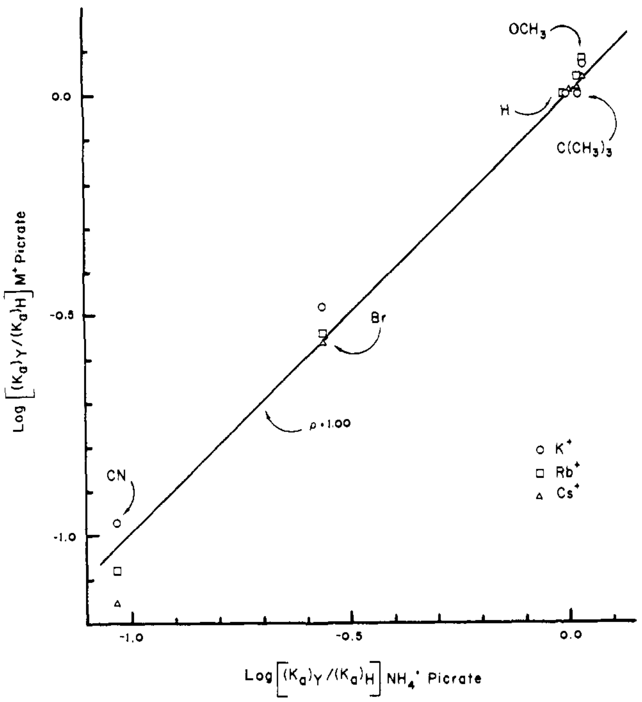


Figure 1. Plot of linear free energy relationship (eq 5) which indicates that the association constants between NH_4^+, K^+, Rb^+, Cs^+, and 5′-Y-1′,3′-xylyl-18-crown-5 hosts respond similarly to changes in remote substituent Y.

The t-$BuNH_3^+$ salts of Table II as guests provide association constants that are more sensitive to remote substituents in the host than those of any of the other cations. The most completely studied series involved the perchlorate salt and six substituents. The K_a value for host **3** (Y = $C(CH_3)_3$) was the highest and exceeded the K_a value for host **7** (Y = CN, which gave the lowest K_a) by a factor of 54. The K_a value for the host bearing OCH_3 (**5**) exceeded that with CN by a factor of 34, well above that observed for the same substituent changes applied to the complexes for the other cations. The factor of 54 provides $\Delta\Delta G = -2.4$ kcal/mol difference in stability of the complex with Y = $C(CH_3)_3$ vs. CN, and the factor of 34 gives $\Delta\Delta G = -2.1$ kcal/mol difference for complexes with OCH_3 vs. CN. The greater sensitivity of the t-$BuNH_3^+$ ion to remote substituent effects compared to the other cations is attributed to the nonpolar character and umbrella shape of the t-Bu group. In the complex, this hydrocarbon group shields the five oxygens of the host and the NH_3^+ group of the guest from contact with solvent on one side of the complex. The effect is a local lowering of the dielectric constant in the environment of the N^+. As a result, the N^+ makes greater demands on the π system of the aryl binding site which in turn is sensitive to the remote substituent.

Figure 2 records a least-squares plot of log $[(K_a)_Y/(K_a)_H]_{t\text{-}BuNH_3ClO_4}$, log $[(K_a)_Y/(K_a)_H]_{t\text{-}BuNH_3SCN}$, and log $[(K_a)_Y/(K_a)_H]_{t\text{-}BuNH_3\,picrate}$ against log $[(K_a)_Y/$

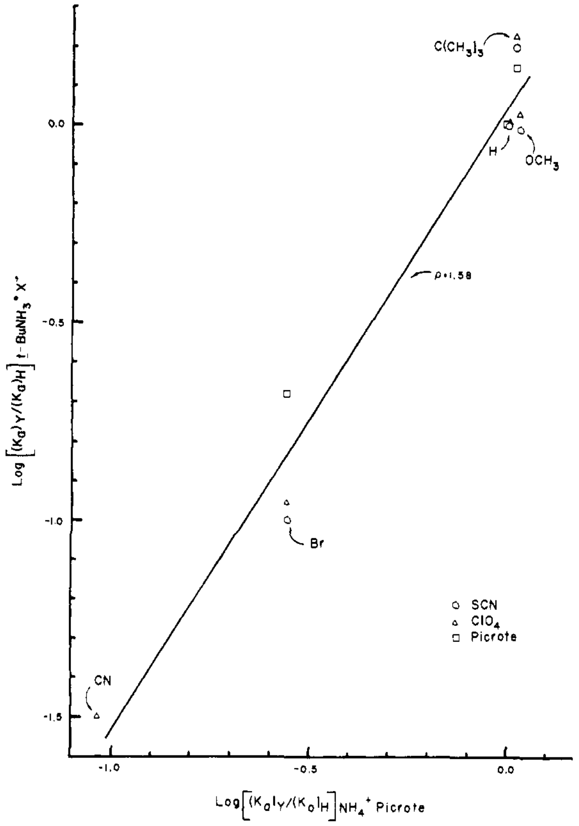


Figure 2. Linear free-energy correlation which indicates how similarly t-BuNH$_3^+$ and NH$_4^+$ salts respond in their complexation with 5′-Y-1′,3′-xylyl-18-crown-5 to changes in Y substituents in the 5′ position.

$(K_a)_H]_{NH_4 picrate}$. The slope of $m = +1.58 \pm 0.45^{16}$ provides a collective measure of the greater demands made on the substituents by t-BuNH$_3^+$ as compared to NH$_4^+$. The fact that the data for the four series correlate with reasonable linearity suggests that the complexes of the four series possess similar structures. Plots of log $[(K_a)_Y/(K_a)_H]_{t\text{-BuNH}_3ClO_4}$ against $\sigma_1{}^{q\,15}$ provided a linear correlation for Y = H, C(CH$_3$)$_3$, SCH$_3$, and Br, but again the OCH$_3$ substituent was substantially above and the CN substituent was substantially below the line, and no overall correlation was visible.

Effects of Changes in Guest Anions on Association Constants. The anions were varied only in the t-BuNH$_3^+$ salts, and the K_a values for the thiocyanate, perchlorate, and picrate salts are listed in Table II. Only hosts with Y = H, Br, and C(CH$_3$)$_3$ were studied with all three salts. Values of K_a decrease in the order perchlorate > thiocyanate ~ picrate. The perchlorate values are an average of about 60 times higher than the picrate or thiocyanate values.

A plot of values of log $[(K_a)_Y/(K_a)_H]_{t\text{-BuNH}_3ClO_4}$ against those of log $[(K_a)_Y/(K_a)_H]_{t\text{-BuNH}_3SCN}$ generates a least-squares line of slope $m = 0.99 \pm 0.14^{16}$ for the four substituents common to the two series (H, Br, C(CH$_3$)$_3$, and OCH$_3$). This correlation suggests that the eight complexes represented possess similar structures and that the demands the t-BuNH$_3^+$ makes on the substituent in the complexes are independent of whether the counterions are SCN$^-$ or ClO$_4^-$. The scanty data available for the picrate anions suggest that the same conclusion applies. All three of these anions are soft, and this type of conclusion probably applies only to such anions, particularly in solvents as nonpolar as chloroform and to hosts as poor at complexing as **1–7.** If all three hydrogens of RNH$_3^+$ are engaged in complexing in a tripod arrangement, then a hydrogen bond such as RNH$_3^+\cdots$X$^-$ must be broken during the complexation process. This is not true for the NH$_4^+$ ion, whose fourth hydrogen can remain hydrogen bonded to the counterion in the complex, particularly in nonpolar media.

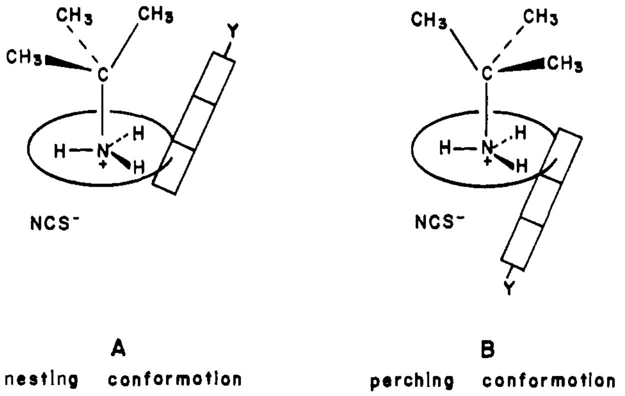
Structures of Complexes in Solutions. A central question in host–guest complexation is that of the structure in solution of complexes held together by noncovalent bonds. In complexation of **1** with potassium picrate, molecular models (CPK plus graded spheres) suggest that K$^+$ can lie in the best plane of the oxygens when that plane and the plane of the phenyl group form an angle of about 135° with one another. The complex is "sided" since the 2′-C-H of the aryl is on one side and the 4′,5′,6′-C-H's of the aryl are on the other side of the best plane of the macroring. In CDCl$_3$, the complex is probably ion paired, so with potassium picrate, the only structural ambiguity concerns the location of the picrate on one or the other face of the ion pair.

In the complexes of **1** with Rb$^+$, Cs$^+$, NH$_4^+$, and t-BuNH$_3^+$ salts, the cationic part of the complex can exist in two conformations. Since these guest cations are too large to pass in their entirety into the best plane of the macrocycle, what remains must extend outward from one face or the other. The side of the host from which protrudes the 2′-C-H provides a "perch" for the guest, and the side from which protrudes the 4′,5′,6′-C-H's provides a "nest" for the guest. The bound part of the guest can contact the 2′ position of the π system of the aryl in either the *nesting* or *perching* conformations.

The nesting conformation places at least two hydrogens of the t-Bu group in the shielding region of the aryl ring in the complex between t-BuNH$_3^+$ClO$_4^-$ and **1,** whereas in the perching conformation, the hydrogens of the t-Bu group are far removed from the magnetic field of the aryl group. Comparisons of the ^{1}H NMR chemical shifts of the t-Bu hydrogens for complexes in CDCl$_3$ of t-BuNH$_3^+$ salts with **1–7** and with 18-crown-6 provided information regarding which conformation applies to the former complexes.

Solutions of cycle in CDCl$_3$ were shaken with solutions of salt in D$_2$O, the layers were carefully separated, and the ^{1}H NMR spectra of the CDCl$_3$ layers were taken. Table II records the molar ratio of guest to host (R, determined by peak integrations), which ranged from 0.04 to 0.72. Table II also records the chemical shifts of the t-Bu protons for the complexes of **1–7** relative to Me$_4$Si. A solution of t-BuNH$_3^+$SCN$^-$ prepared directly in CDCl$_3$–Me$_4$Si gave δ 1.49, whereas t-BuNH$_3^+$ClO$_4^-$ gave δ 1.47. Extraction experiments with 18-crown-6, 18-crown-5, and dicyclohexyl-18-crown-6 of t-BuNH$_3^+$SCN$^-$ gave t-Bu proton chemical shifts in CDCl$_3$ relative to Me$_4$Si of δ 1.34, 1.38, and 1.40, respectively. These upfield shifts relative to uncomplexed salt of 0.15–0.09 ppm probably reflect the reduction of positive charge on NH$_3^+$ when complexed as compared to uncomplexed.

Much larger upfield chemical shifts of t-Bu protons were observed for the complexes of **1–7** (Table II). The values of δ ranged from 0.83 to 1.01 ppm as the remote substituents and counterions were varied. When the counterions were the same, the maximum change with changes in Y were only 0.07 ppm. Thus the chemical shifts of the t-Bu protons remained remarkably constant although the binding constants between host and guest varied by $\sim 10^{1.5}$. This fact indicates that the conformations of the complexes change very little with respect to the relative locations of the t-Bu protons and the aryl group. The fact that the t-Bu protons are moved upfield by 0.33–0.51 ppm relative to those of the complex with 18-crown-6 indicates that nesting conformation A makes a substantial contribution to the equilibrium between the two possible conformations (A and B) and is probably the dominant structure. In the nesting conformation, the anion can better contact the complexed N$^+$ and less charge separation results than in the perching conformation. In the nesting conformation, the angle between the aryl and oxygen plane is about 135°, whereas in the perching conformation, the angle is 90° or less. When the bulky aryl and



A nesting conformation

B perching conformation

t-Bu groups protrude from opposite sides of the cycle as in the perching conformation, they sterically inhibit close contact between the charges of the ion pair. This effect may well make the perching conformation the less stable in RNH_3^+ complexes with **1** in nonpolar media. With NH_4^+, Rb^+, and Cs^+, no such effect would exist and no reasonable guess can be made as to which conformation dominates.

Experimental Section

General. All reactions with alkoxides and organometallics were run under nitrogen. Tetrahydrofuran (THF) was distilled from benzophenone ketyl under nitrogen. All other solvents were reagent grade. All reported temperatures are uncorrected. Characterizing ^1H NMR spectra were recorded in $CDCl_3$ on a Varian T-60 NMR spectrometer, whereas analytical spectra involved a Varian HA-100 spectrometer with Me_4Si as internal standard. Gel permeation chromatography was performed on a 10 ft by $^3/_8$ in. column of 60 Å styragel. Gas-liquid partition chromatography (GLC) was run on a 3.5 ft by $^1/_4$ in. column of 15% SE-30 on 60/80 firebrick. All analytical samples and samples of hosts used for association constant determination were subjected to GLC purification just before use. Mass spectra were taken on an AEI Model MS-9 double-focusing mass spectrometer at 70 eV. Melting points were taken on a Thomas-Hoover apparatus and are uncorrected.

5-*tert*-Butyl-1,3-bis(bromomethyl)benzene (12), 5-Bromo-1,3-bis(bromomethyl)benzene (11), and 1,3-Bis(bromomethyl)benzene. A mixture of 16.2 g (0.10 mol) of 5-*tert*-butyl-1,3-xylene (**10**)[17] and 37.4 g (0.21 mol) of *N*-bromosuccinimide in 350 mL of anhydrous CCl_4 was brought to reflux and 0.3 g of dibenzoyl peroxide was added. After refluxing for 10 h, the mixture was cooled, filtered, washed with water, dried, and evaporated in vacuo. The solid residue was recrystallized from cyclohexane to give 11.0 g of **12** (34%) as white needles, mp 110–112 °C. An analytical sample was obtained by sublimation at 90 °C and 180 μ: ^1H NMR spectrum δ 1.3 (s, 9, $(CH_3)_3$), 4.4 (s, 4, $ArCH_2$), and 7.3 (m, 3, ArH); mass spectrum *m/e* 318 (M ^{79}Br). Anal. Calcd for $C_{12}H_{16}Br_2$: C, 45.03; H, 5.03. Found: C, 45.11; H, 4.95.

By a similar procedure, 5-bromo-1,3-dimethylbenzene[18] (**9**) was converted in 20% yield to 5-bromo-1,3-bis(bromomethyl)benzene (**11**): mp 97–98.5 °C; ^1H NMR δ 4.4 (s, 4, $ArCH_2$), 7.2–7.6 (m, 3, ArH). Anal. Calcd for $C_8H_7Br_3$: C, 28.02; H, 2.06. Found: C, 27.89; H, 2.22.

Diethyl isophthalate was reduced with $LiAlH_4$ in the usual way, and the diol product was converted with 48% aqueous hydrobromic acid (reflux for 37 h) to crude 1,3-bis(bromomethyl)benzene, mp 71–75 °C (lit.[19] 76–77 °C), which was used directly in ring-closing reactions (see next section).

5′-*tert*-Butyl-1′,3′-xylyl-18-crown-5 (3), 5′-Bromo-1′,3′-xylyl-18-crown-5 (2), and 1′,3′-Xylyl-18-crown-5 (1). The prototype ring-closing reaction is exemplified by the preparation of **3**. To a refluxing mixture of 2.70 g (57 mmol) of NaH (50% mineral oil) in 300 mL of THF was added dropwise over 18 h a solution of 5.3 g (16.5 mmol) of dibromide **12** and 3.20 g (16.5 mmol) of tetraethylene glycol in 200 mL of THF. The reaction mixture was then cooled to 25 °C and stirred for 8 h. Excess NaH was decomposed carefully by the addition of water. The reaction mixture was filtered and the THF evaporated in vacuo. The residue was shaken with dilute hydrochloric acid and CH_2Cl_2. The aqueous phase was washed with CH_2Cl_2, and the combined organic phases were dried and evaporated in vacuo. The residue was chromatographed on 225 g of silica gel with 2% methanol in ether (v) as eluting agent to give **3**, 3.2 g (61%), as a low-melting solid: ^1H NMR δ 1.4 (s, 9, $(CH_3)_3$), 3.7 (s, 16, CH_2CH_2), 4.6 (s, 4, $ArCH_2$), 7.2 (s, 2, ArH), 7.5 (s, 1, ArH); mass spectrum *m/e* 326 (M^+). Anal. Calcd for $C_{20}H_{32}O_5$: C, 68.16; H, 9.17. Found: C, 68.22; H, 9.10.

Application of this procedure to tribromide **11** gave bromocycle **2** in 62% yield after gel permeation chromatography: mp 45–60 °C; ^1H NMR ($CDCl_3$) δ 3.6 (s, 12, CH_2CH_2), 4.5 (s, 4, $ArCH_2$), 7.2 (s, 2, ArH), 7.6 (s, 1, ArH). Anal. Calcd for $C_{16}H_{23}BrO_5$: C, 51.21; H, 6.18. Found: C, 51.32; H, 6.26.

By the same procedure, **1**[2] was prepared from *m*-xylyl dibromide in 60% yield.

5′-Carboethoxy-1′, 3′-xylyl-18-crown-5 (4). Under nitrogen, a solution of 2.6 g (7 mmol) of bromocycle **2** in 100 mL of dry THF was cooled to −78 °C. A solution of about 10 mmol of butyllithium in hexane was added, the mixture was stirred for 30 min, and 1.6 mL (2.2 g, 20 mmol) of ethyl chloroformate was added. After an additional 30 min of stirring at −78 °C, the stirred solution was allowed to warm to 25 °C and stirring was continued for an additional 12 h. Excess water was added, and the solvent was evaporated in vacuo. The residue was shaken with water and CH_2Cl_2, and the organic layer was dried and evaporated in vacuo. The residue was chromatographed on 50 g of silica gel. Ethyl pentanoate eluted with CH_2Cl_2, and a mixture of **1** and **4** eluted with 5% acetone (by volume) in CH_2Cl_2 to give 1.8 g of material. Analytical GLC indicated that 70% of the mixture was **4** and the rest **1**. Preparative GLC at 260 °C gave 1.3 g (50%) of **4** as a glass: ^1H NMR ($CDCl_3$) δ 1.3 (t, 3, J = 12 Hz, CH_2CH_3), 4.4 (q, 2, J = 12 Hz, CO_2CH_2), 3.7 (s, 16, CH_2CH_2), 4.6 (s, 4, $ArCH_2$), 7.7 (s, 2, ArH), 7.8 (s, 1, ArH); mass spectrum *m/e* 368 (M^+). Anal. Calcd for $C_{19}H_{28}O_7$: C, 61.94; H, 7.66. Found: C, 61.76; H, 7.62.

5′-Methoxy-1′,3′-xylyl-18-crown-5 (5). To 1.37 g (3.7 mmol) of bromocycle **2** in 15 mL of 2.6-lutidine and 6.95 g (36.5 mmol) of CuI was added a solution of 9.6 g (219 mmol) of sodium methoxide in 20 mL of absolute methanol. The solution was refluxed under nitrogen for 30 h. The mixture was cooled and shaken with 75 mL of 6 N hydrochloric acid and 100 mL of CH_2Cl_2. The aqueous layer was washed with two 100-mL portions of CH_2Cl_2. The organic layers were combined, washed twice with water, dried, and evaporated in vacuo. The residue was chromatographed on 25 g of silica gel with 5% acetone in CH_2Cl_2 (v) as eluting agent to give 1.04 g (86%) of **5** as a low-melting wax: ^1H NMR δ 3.7 (s, 16, CH_2CH_2), 3.8 (s, 3, CH_3), 4.6 (s, 4 $ArCH_2$), 6.7 (s, 2, ArH), and 7.3 (s, 1, ArH); mass spectrum *m/e* 326 (M^+). Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.65; H, 8.03.

5′-Thiomethyl-1′,3′-xylyl-18-crown-5 (6). To 60 mL (0.150 mol) of butyllithium (2.5 M in hexane) was added dropwise at −78 °C 9.0 mL (0.165 mol, 1.1 equiv) of methanethiol. To this mixture was added 25 mL of anhydrous THF. The reaction mixture was stirred at −78 °C for 30 min and allowed to warm to 25 °C. The excess methanethiol and solvent were evaporated in vacuo, and the solid residue was dried under high vacuum for 10 h. To this material was added 1.25 g (3.4 mmol) of bromocycle **2** dissolved in 25 mL of 2,6-lutidine. Cuprous iodide (6.34 g, 33.3 mmol) was added and the reaction mixture was heated to 125 °C. After 28 h, 25 mL of anhydrous dimethylformamide was added, and the reaction was allowed to proceed for 96 h at 125 °C. The mixture was then cooled, the solvent was removed in vacuo, the residue was distributed between 250-mL portions of CH_2Cl_2, and the combined organic phases were washed with 50 mL of water, dried, and evaporated in vacuo. The residue was chromatographed on 25 g of silica gel with 5% ethanol in CH_2Cl_2 (v) as eluting agent to give 0.38 g (30%) of **6** as an oil: ^1H NMR spectrum δ 2.5 (s, 3, CH_3), 3.7 (s, 16, CH_2CH_2), 4.6 (s, 4, $ArCH_2$), 7.0 (s, 2, ArH), 7.5 (s, 1, ArH). Anal. Calcd for $C_{17}H_{26}O_5S$: C, 59.64; H, 7.65. Found: C, 59.65; H, 7.73.

5′-Cyano-1′,3′-xylyl-18-crown-5 (7). To a solution of 1.16 g (3.1 mmol) of bromocycle **2** dissolved in 20 mL of dry dimethyl sulfoxide was added 3.0 g (33.5 mmol) of CuCN. The resulting solution was stirred at 125 °C for 40 h. The reaction mixture was cooled and shaken with a mixture of 100 mL of CH_2Cl_2 and a solution of 8.3 g of $FeCl_3$ in 100 mL of 6 N hydrochloric acid. The aqueous layer was twice extracted with 100-mL portions of CH_2Cl_2, and the combined organic extracts were washed twice with water, dried, and evaporated in vacuo. The crude residue was chromatographed on 20 g of silica gel with 5% acetone in CH_2Cl_2 (v) as eluting agent to give 0.62 g (62%) of **7** as an oil: ^1H NMR spectrum δ 3.7 (s, 16, CH_2CH_2), 4.7 (s, 4, $ArCH_2$), 7.4 (s, 1, ArH), 8.0 (s, 1, ArH); mass spectrum *m/e* 321 (M^+). Anal.

Table III

Picrate salt	ϵ at 380 nm in CH_3CN	$[G^+]_{H_2O}$, M	$[G^+X^-]_{CHCl_3}$, M × 10^7	K_d, M^{-1} × 10^3
Li^+	16 900	0.0200	5.69	1.42
Na^+	16 900	0.0200	6.975	1.74
K^+	16 900	0.0200	10.2	2.55
Rb^+	16 900	0.0100	4.57	4.57
Cs^+	16 900	0.0100	5.41	5.41
NH_4^+	16 900	0.0200	16.1	4.02
t-$BuNH_3^+$	17 800	0.0150	530	237

Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.22. Found: C, 63.41; H, 7.37.

Determination of Spectra and of Association Constants (K_a) by the Ultraviolet Method. All ultraviolet (UV) measurements were made on a Beckman DU spectrometer at 380 nm at 24-26 °C. All volume transfers were done by syringe. The volume indicated by the position of the meniscus in the syringe before and after the addition provided the most reproducible results. Typically, five to seven complexation experiments were run simultaneously with a given host. Picrate salts[20] in distilled water in volumetric flasks (100 mL) were prepared that involved the following cations (concentrations); Li^+ (0.015 M); Na^+ (0.015 M); K^+ (0.015 M); Rb^+ (0.010 M); Cs^+ (0.010 M); NH_4^+ (0.015 M); and t-$BuNH_3^+$ (0.015 M). Solutions of the hosts, 0.075 M in $CDCl_3$, were also prepared in either 1.00- or 2.00-mL volumetric flasks.

Into a 12-mL centrifuge tube was introduced a measured volume of picrate solution. The volume for rubidium and cesium picrates was 1.0 mL; for all others it was 0.5 mL. A small magnetic stir bar was then added to the tube. To one tube was added 1.0 mL of H_2O to be used as a blank. To each of the tubes, including the one containing H_2O, was added 0.2 mL of the host solution. The tubes were stoppered to prevent evaporation and briefly centrifuged to cause the $CDCl_3$ layer to sink. The contents of each tube were then stirred vigorously for ca. 3 min by means of a magnetic stirrer placed on its side, and separated into two clear layers by centrifugation.

An aliquot of the $CDCl_3$ layer was measured and transferred by microsyringe into a 5-mL volumetric flask and diluted to the mark with CH_3CN. With more intensely colored layers (e.g., with **5** as host) only 0.01 mL was used. With less intensely colored layers (e.g., with **1-3** and **7**) 0.05 mL aliquots were used. For each size of aliquot, a blank was also made by measuring the desired volume from the $CDCl_3$ layer of the H_2O blank and diluting to the mark with CH_3CN in a 5-mL volumetric flask. The UV absorption of each 5-mL solution was measured against the appropriate blank solution at 380 nm. The same cell was always used for the blank, a second cell was always used for the unknown, and their orientation in the spectrophotometer was always kept the same. The absorbance of the sample cell at 380 nm relative to the absorbance of the blank cell when both were filled with CH_3CN was measured prior to each series of extractions. The value varies from −0.001 to +0.003 and was subtracted from all recorded absorbances in the calculations.

Calculations were based on the Beer's law relationship, $a = \epsilon bc$, where a is the absorbance, ϵ the extinction coefficient, b the path length of the cell, and c the concentration of the measured species. The total millimoles of picrate salt in the measured aliquot was equal to the product of c and the volume of the measured solution, which was 5 mL. The millimoles of host was the product of the host concentration and the aliquot volume. The guest to host molar ratio, R, which was the same in the measured aliquot as in the original $CDCl_3$ layer, was given by the millimoles of picrate salt divided by the millimoles of host.

Extinction coefficients (ϵ) for each salt in CH_3CN were determined in the concentration range of 10^{-6} to 10^{-4} M of standard solutions prepared by serial dilutions of 5.00×10^{-4} M solutions directly prepared from the pure salts. The average ϵ over this range (±5%) was used in the calculations. The extinction coefficients determined by this method are recorded in Table III. Values of K_a were calculated from eq 2, which has been derived elsewhere.[2b,12]

$$[G^+]_{H_2O} + [X^-]_{H_2O} \overset{K_d}{\rightleftharpoons} [G^+\,X^-]_{CDCl_3} \qquad (7)$$

The distribution constants (K_d) of the alkali and two ammonium picrates between water and chloroform were determined as follows. Picrate solutions of known concentrations (Table III) in 200 mL of distilled H_2O were shaken in a sealed separatory funnel with 300 mL of ethanol-free $CDCl_3$. The layers were allowed to separate and clarify (14 h), and the lower layer was very carefully transferred through the stopcock to a flask where the solvent was evaporated on a rotary evaporator under vacuum. The residue was quantitatively transferred with CH_3CN to a 5.00-mL volumetric flask and diluted with CH_3CN to the mark. By the above UV techniques, the amount of picrate salt extracted was calculated. Since so little salt was extracted from the aqueous layer, the final salt concentration was within error of the initial concentration. The values for K_d were calculated using eq 4, and are recorded in Table III.

The values of λ_{max} for the picrate salts in the UV spectra were obtained as follows. A 3.0-mL solution of **1** in $CDCl_3$ (0.075 M) was prepared, and 0.40-mL aliquots (syringe) were transferred to 12.0-mL centrifuge tubes. To these tubes were added measured volumes of the standard picrate salt solutions prepared for K_a determinations. The volumes were as follows: for sodium, potassium, and ammonium picrates, it was 2.0 mL; for rubidium and cesium, it was 3.0 mL. The mixture in each tube was stirred magnetically at 24 °C for 3 min, then centrifuged to clearly separate the layers. The organic layer was carefully removed with the syringe and transferred to a 1-mm cell. The $CDCl_3$ solution containing the complex between **1** and sodium picrate was analyzed directly. The solutions of potassium and ammonium picrate were diluted to 0.2 of their original concentration, while those containing cesium and rubidium required dilution to 0.5 of their original concentrations. The UV spectra were recorded on a Cary 14 vis-UV spectrophotometer. The positions of λ_{max} observed are reported in the Results section.

Determination of Association Constants (K_a) and Chemical Shifts of *tert*-Butyl Protons for Complexes Using Proton Nuclear Magnetic Resonance Methods. The association constants that involved t-$BuNH_3^+SCN^-$ and t-$BuNH_3^+ClO_4^-$ were determined by procedures reported previously.[2b,12,13] Experimentally, the concentrations used in the extractions that involved t-$BuNH_3^+SCN^-$ were those of scale C, but the K_as calculated and reported in Table III are corrected to scale A by dividing by 2.[2b] The ^1H NMR procedure used for t-$BuNH_3^+$ picrate was essentially identical with those described for the other two salts except that the K_d values used in the calculation of K_a values of Table II had been determined by the UV method. In a typical K_a determination carried out at 24-26 °C, 0.50 mL of a 0.15 M solution of host in $CDCl_3$ and 5.0 mL of a 0.015 M of a guest picrate solution in D_2O were added to a 12-mL centrifuge tube containing a magnetic stirring bar. The tube was stoppered, briefly centrifuged, and then vigorously stirred for 3 min. The layers were separated by centrifugation of the stoppered tube, a 0.30-mL aliquot of the $CDCl_3$ layer was withdrawn carefully by syringe and placed in an NMR tube, and a drop of Me_4Si was added. The ^1H NMR spectrum was taken and integrated. The R values of Table II that involved the picrate salts other than the t-$BuNH_3^+$ were calculated from the integrations of the picrate protons (s, 2, ArH) at ca. δ 8.8 ppm relative to the CH_2CH_2 protons (s) of the host.

The chemical shifts of the t-Bu protons relative to Me_4Si that are reported in Table II were observed on the same solutions used to determine the R values of Table II. Saturated solutions of t-$BuNH_3^+ClO_4^-$ and t-$BuNH_3^+SCN^-$ in $CDCl_3$ in the absence of host at 24 °C gave chemical shifts (singlets) for the t-Bu protons at δ 1.4 and 1.47 ppm, respectively. The chemical shift of t-$BuNH_2$ in $CDCl_3$ was δ 1.15 ppm.

The K_a values for t-$BuNH_3^+SCN^-$ were calculated from R values determined by the ^1H NMR method previously described,[2] and the K_d value (eq 4) which was reported previously.[2] The R values for t-$BuNH_3^+ClO_4^-$ was determined by the ^1H NMR method developed for SCN^- salt. The K_d for t-$BuNH_3^+ClO_4^-$ was determined by the fluorometric method applied to the SCN^- and Cl^- salts.[2,12] The experimental technique with respect to concentrations, volumes, and temperature was identical with that used for the SCN^- and Cl^- salts.[2,12] The original D_2O solution of t-$BuNH_3^+ClO_4^-$ was adjusted to pH 4.5 with $HClO_4$, and extracted three times with $CDCl_3$. Values of K_d obtained from the three extractions were 0.96×10^{-5}, 0.92×10^{-5}, and 0.96×10^{-5} M^{-1} (after correction for a blank of 0.011×10^{-5}) to give an average value of 0.95×10^{-5} M^{-1}. A second series of extractions from a D_2O solution of t-$BuNH_3^+ClO_4^-$ at pH 0.5 ($HClO_4$) gave K_d values of 1.07×10^{-5}, 0.90×10^{-5}, and 0.93×10^{-5} M^{-1} (after correction for blank). The K_d value used in the calculations of K_a in this paper was the overall average of the six determinations, which was $0.96 \pm (0.04) \times 10^{-5}$ M^{-1}.

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Host-Guest Complexation. 5. Convergent Functional Groups in Macrocyclic Polyethers[1,2]

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Abstract: Thirteen 2′-R-1′,3′-xylyl-*m*-crown-*n*-macrocyclic polyethers are reported where R = CO_2CH_3 ($m = 15, n = 4$; $m = 18, n = 5$; $m = 21, n = 6$; $m = 30, n = 9$); where R = CO_2H ($m = 15, n = 4$; $m = 18, n = 5$; $m = 21, n = 6$; $m = 30, n = 9$); where R = CH_2OH, CH_2OCH_3, Br, Cl, or CN ($m = 18, n = 5$). The pK_as in water at 22 °C of the cycles with R = CO_2H were found to be $m = 15, n = 4$, 4.8; $m = 18, n = 5$, 4.8; $m = 21, n = 6$, 3.8; $m = 30, n = 9$, 3.4; acyclic model compound 2,6-bis(methoxymethyl)benzoic acid, 3.3. In the smaller cycles, the carboxylic acid group is the most thoroughly hydrogen bonded. Association constants (K_a) were determined for complexation of *tert*-butylammonium thiocyanate with nine of the cycles in $CDCl_3$ at 22 °C. For the R groups in the 18-membered ring hosts, $CO_2CH_3 \gg H > CH_2OCH_3 \sim CH_2OH > CO_2H > CN$ in their ability to stabilize the complexes. When R = CO_2CH_3, the hosts changed in complexing power as follows: 18-membered ≫ 21-membered > 30-membered > 15-membered macrocycle. These results correlated with expectations based on examination of scale molecular models of the complexes. The anionic form of the four cyclic acids and their model compound were tested for their abilities to lipophilize Li^+, Na^+, K^+, and Ca^{2+} by distributing their host salts at 22 °C between CH_2Cl_2 and water. Maximum lipophilization occurred when hosts and guests were coupled as follows: Li^+, 18-membered ring; Na^+, 21-membered ring; K^+, 30-membered ring; Ca^{2+}, 18-membered ring. For all ions, the 15-membered ring host was poorer than the open-chain model. The t-$BuNH_4^+$ salts of the same host acids were distributed between D_2O and $CDCl_3$ at 22 °C. The distribution constants for the 2′-carboxylate-1′,3′-xylyl host salts ($K_d = [\text{salt}]_{CDCl_3}/[\text{salt}]_{D_2O}$) ranged from 0.7 to 0.02 in the order 18-crown-5 > 21-crown-6 > 30-crown-9 > open-chain model > 15-crown-5. The ^1H NMR spectra of the t-$BuNH_3^+$ complexes of the 1′,3′-xylyl-18-crown-5 hosts indicated a structure that placed the t-Bu protons in the shielding cone of the xylyl group.

One of the problems central to the design of host compounds is that of the placement of substituents in positions that converge on the functional or binding sites of guest compounds. Molecular model (Corey-Pauling-Koltun, or CPK) examination of macrocyclic polyethers containing a 1,3-xylyl unit as part of the large ring indicates that substituents attached to the 2 position of the aryl group are directed inward toward the hole of the cycle. Earlier work demonstrated that substituent variation in the 5′ position of 1′,3′-xylyl-18-crown-5 produced changes in $CDCl_3$ at 24 °C of association constants between cycles and the cations of inorganic and organic salts by factors as large as 54.[3] Effects of this magnitude, exerted by substituents both remote and divergent from the point of complexation, have been interpreted as evidence that the π system of 1,3-xylyl unit acts as a binding site.[3] The present study is concerned with the effects of convergent substituents on the binding properties of hosts containing the 2-substituted 1,3-xylyl unit.

Syntheses. New cycles **1-4** were prepared from dibromide **16** and the appropriate polyethylene glycols as starting materials. Moderately high dilution conditions were realized by slow, dropwise addition of an equimolar mixture of dibromide