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HOST-GUEST COMPLEXATION. 43. SYNTHESIS AND BINDING PROPERTIES OF A MACROCYCLE COMPOSED OF TWO PHENANTHROLINES AND TWO SULFONAMIDE UNITS ǂ

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Abstract - Treatment of 2,9-bis(chloromethyl)-1,10-phenanthroline with toluenesulfonamide and K_2CO_3 in $HCON(CH_3)_2$ gave macrocycle 1 (21%) composed of two phenanthroline units bonded to each other through two $CH_2N(Ts)CH_2$ bridges. The 18-membered inner ring system contains six nitrogens, each of which is separated by two carbons. A crystal structure of $1.2H_2O$ indicated the two faces of the phenanthrolines approach each other to place their four nitrogens nearly in a plane bridged by a water dimer held in position by bifurcated hydrogen bonds. The two $ArSO_2N$ groups are turned outward, and the hydrogens of their attached CH_2 groups are oriented inward toward the water dimer, which serves as a guest. Complexation was indicated by addition of a variety of salts to a solution of 1 in $(CD_3)_2SO$, which caused changes in the ^1H NMR by as much as 1.5 ppm. Complexing ions include Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, Ag^+, Cu^+, Tl^+, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+}; noncomplexing ions are Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, UO_2^{2+}, and Ce^{3+}. A correlation between the chemical shifts of the CH_3 and tolyl aryl protons of the host and the ionic radii of the guests is interpreted in terms of three different host conformations in the various complexes. Equilibrations of the guest cations between 1 and cryptaplexes of Na^+, K^+, Rb^+, Cs^+, and NH_4^+ picrates in $(CD_3)_2SO$ provided the following estimates of the $-\Delta G°$ values of binding of these salts by 1: 8.4, 8.5, 6.8, <3.5, and 8.85 kcal mol^{-1}, respectively.

The 1,10-phenanthroline nucleus provides an attractive building block for incorporation into hosts. The unit is rigid, and provides two aromatic nitrogens whose unshared electron pairs are beautifully placed to act cooperatively in binding cations. These nitrogens strongly and usefully ligate the transition metals,[1] and crystalline alkali metal complexes of 1,10-phenanthroline have been characterized.[2] The 2,9-positions are well-spaced and chemically manipulable to provide sites for incorporation of the unit into interesting cyclic or polycyclic systems of dimensions amenable to cation binding.[3]

We report the synthesis, crystal structure, and cation binding properties of perazacorand 1. This compound contains an 18-membered inner ring system whose six regularly spaced nitrogens provide potential ligating sites of limited

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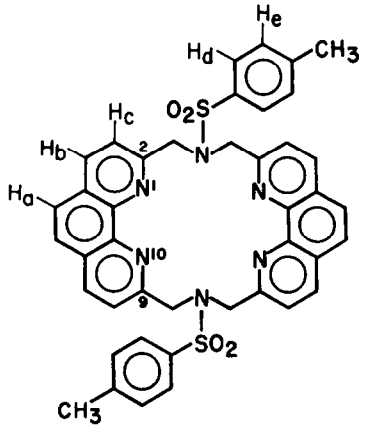
ǂ Dedicated to Prof. Dr. Hans Wynberg on the occasion of his 65th birthday.

conformational mobility. Thus **1** is somewhat preorganized. We are interested in correlations between preorganization, binding power, and ion selectivity in complexation.[4] Host **1** possesses the practical advantages of being only weakly basic, resistant to oxidation, and containing several benzylic proton-ring current combinations useful in ^{1}H NMR spectral analysis of conformations of complexes of **1**. Compound **1** was also a possible intermediate in a projected synthesis of the highly preorganized cryptand **2**, whose elegantly simple synthesis was reported by Lehn[5] after **1** was in hand.



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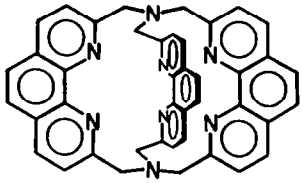

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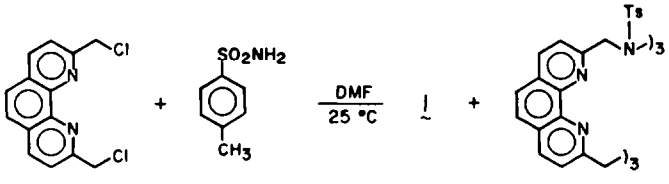
Synthesis

Azacorand **1** was prepared in 21% yield by slowly adding a mixture of dichloride **3**[3c,6] and sulfonamide **4** to a mixture of K_2CO_3 and $HCONMe_2$ under high dilution conditions. The relative insolubility of **1** made it easy to isolate by crystallization. The higher oligomer, **5**, present in trace amounts, proved more soluble. It was only spectrally characterized (MS and ^{1}H NMR).

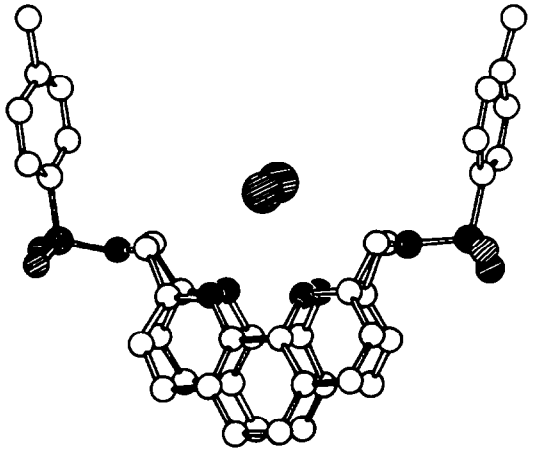


Crystal structure

The crystal structure of **1** complexed to a water dimer is shown in Chart 1 as drawings **6** and **7**. In **6**, the two phenanthrolines approach each other to produce a wedge shape, which minimizes the distances between the four phenantholine nitrogens. The planes of the phenanthrolines intersect at an angle of 12.6°. The phenanthrolines are offset with respect to each other, which destroys what would otherwise be a mirror plane (that of the page), but the molecule retains a pseudo-C_2 axis of symmetry. The orbitals of the unshared electron pairs of the four nitrogens converge on one another enough to nicely hydrogen bond the water dimer. The oxygen-oxygen distance in the water dimer is 2.89 Å, the nitrogen-to-near-water oxygen distances for one phenanthroline are 3.071 and 3.098 Å, and for the other phenanthroline are 3.207 Å and 3.083 Å.

The close internuclear nitrogen-to-nitrogen distances are 3.308 and 3.300 Å. These distances suggest that the two oxygens hydrogen bond each other, and that the oxygen dimer guest is bound to the two phenanthrolines by hydrogen bonds that are possibly bifurcated. The crystal structure did not refine well enough to locate these hydrogens due to the presence of disordered acetone in the lattice. Drawing **7** of Chart 1 shows the relative positions of the two oxygens and the four nitrogens involved in host-guest binding.

Notice that in **6**, the eight hydrogens of the four CH_2 groups line the cradle-like cavity occupied by the water dimer. The carbon-to-near oxygen distances range from 3.60 to 4.04 Å, not close enough to suggest hydrogen bonding of the type $CH_2\cdots O$, although these hydrogens are slightly acidified by the inductive effects of the phenanthroline and sulfonamide substituents. As a consequence of these hydrogens turning inward, the sulfonamide nitrogens turn outward. The attached tolyl groups further define the cavity.



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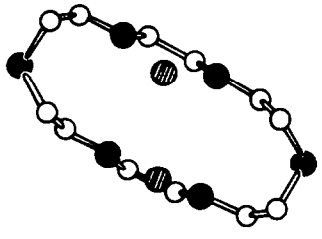

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Chart 1

Qualitative complexation experiments

A FAB mass spectrum (Xenon with a copper alloy probe) of **1** gave M + 63 and M + 65 peaks, indicating that **1** complexed the two isotopes of Cu^+ well enough to remove them from the probe. When the probes were free of Cu^+, the normal $M + H^+$ molecular ion was observed.

Only very polar solvents such as $(CD_3)_2SO$ and $(CD_3)_2NCDO$ dissolved enough **1** to serve as media suitable for ^1H NMR spectral experiments. The ^1H NMR spectrum of **1** in $(CD_3)_2SO$ provided the expected four doublets (coupling constants of 8 Hz) and one singlet in the aromatic region, which were assigned with the aid of decoupling experiments. The methylene protons appeared as broad singlets which

sharpened at higher temperature, suggesting the presence of temperature-dependent interconversions of conformers. The methyl signal of the p-toluenesulfonamide moiety of **1** is obscured by protio impurities in $(CD_3)_2SO$, but is visible in $(CD_3)_2NCDO$.

When less than one equivalent of guest salt was added to a solution of **1** in $(CD_3)_2SO$, the ^1H NMR spectrum showed the presence of both free and complexed material. The spectrum was composed of peaks superimposable on the spectrum of free **1** and completely complexed **1**. When a mixture of two ions was added to a solution of **1**, the spectrum obtained was a combination of the spectra of the two complexes taken independently. Thus the exchange rates for transfer of ions between host molecules are slow on the ^1H NMR time scale.

The ^1H NMR spectra were determined for complexes formed in $(CD_3)_2SO$ by addition of stoichiometric excesses of the following salts to **1**: LiPicrate; $NaBF_4$; KPicrate; RbPicrate; NH_4Picrate; CuCl; $Pb(NO_3)_2$; $AgNO_3$; $Cd(NO_3)_2$; and $HgCl_2$. Changes in peak positions as high as 1.5 ppm were observed upon complexation of **1** with the above salts. No changes were observed with $Mg(OAc)_2$, $Ca(Picrate)_2$, $Sr(Picrate)_2$, $Ba(Picrate)_2$, $UO_2(NO_3)_2$, or $Ce(NO_3)_3$.

Figure 1 is a plot of the chemical shifts (δ) of the $ArC\underline{H}_3$ protons of **1** in the various complexes against the ionic radii (Å) of the ionic guests. Figure 2 contains similar plots of the chemical shifts of the two sets of $Ar\underline{H}$ protons, H_d or ortho and H_e or meta to the sulfonyl (see formula **1**) of the tolyl groups in the complexes against the ionic radii of the guests.[7] All three curves exhibit a shape which suggests that the complexes fall into three general conformational classes, depending on the ionic radii of the guests. Class A includes ions of between 1.3 and 1.5 Å, such as K^+, Rb^+, and NH_4^+. In the complexes of these three ions, all three kinds of protons of the tolyl group are moved maximally upfield. Examination of Corey-Pauling-Koltun (CPK) molecular models of **1** suggests that Class A complexes possess conformation **8**, which contains a circular cavity, with a radius of about 1.4 Å lined with the orbitals of the unshared electron pairs of six nitrogens arranged in roughly hexagonal fashion.

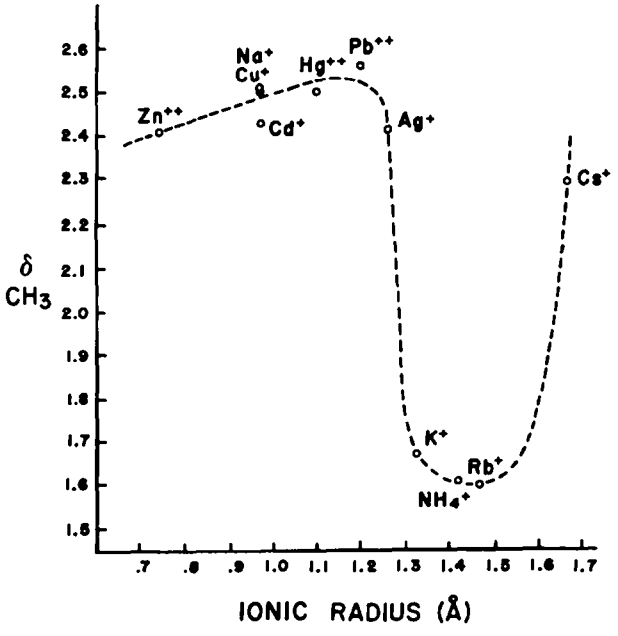


Figure 1

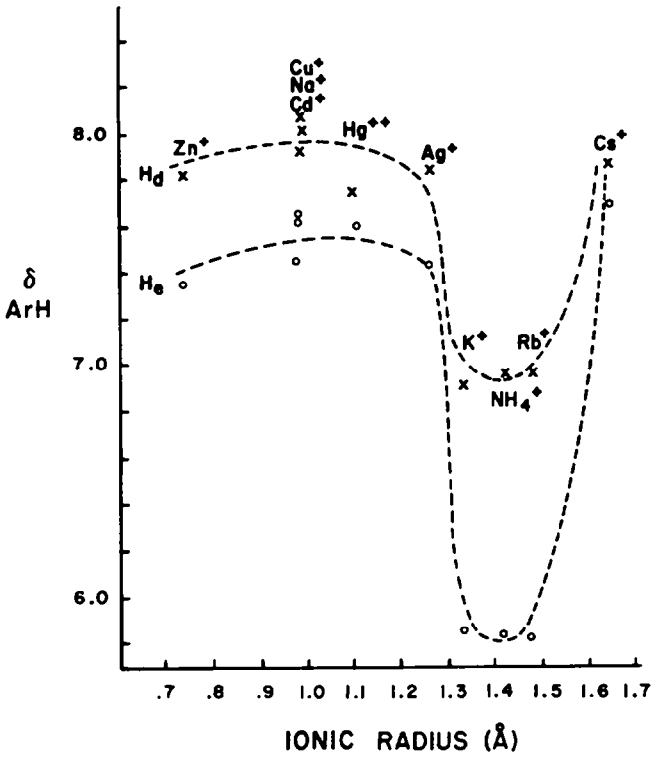
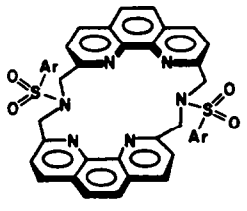


Figure 2

In conformation **8**, the two phenanthrolines are coplanar, and the p-$CH_3C_6H_4SO_2$ groups appear to be free to rotate around the N-S bond. Models indicate, however, that random distribution places the CH_3 and C_6H_4 protons in the large shielding region of the two phenanthroline nuclei much of the time, which explains the observed upfield shifts of these protons. In conformation **8**, the two CH_2 protons are in very different magnetic environments. Only one of the two protons in each CH_2 group is near a SO_2N pi system, whose field should affect its chemical shift. The interconversion of these two protons requires



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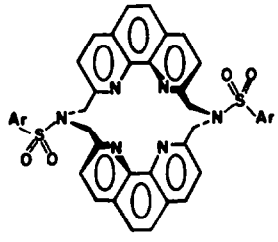

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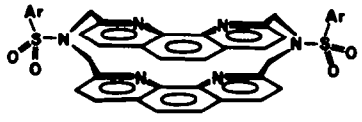

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that the methylene groups rotate through the 18-membered macroring, which is unlikely to occur rapidly on the NMR time scale while the host complexes a large cation. As a consequence, the methylene protons of Class A complexes exhibit AB quartet patterns.

Class B complexes include metals of between 0.7 and 1.25 Å ionic radii, such as Zn^{2+}, Na^{+}, Cu^{+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, and Ag^{+}. The ^1H NMR spectra of these complexes are characterized by the lack of large chemical shift changes in the $CH_3C_6H_4SO_2$ proton signals, a variety of types of methylene proton absorptions, and often a modest downfield shift in the ArH protons of the phenanthroline units. Molecular model examination indicates that in conformation **9**, the four nitrogens of the phenanthroline units are arranged in a flattened tetrahedral arrangement, and that the two p-$CH_3C_6H_4SO_2N$ nitrogens are distant from the cavity. The resulting cavity radius can be as small as 0.7 Å or as large as 1.2 Å. Complexes possessing this structure should exist as a pair of enantiomerically related helical conformers, each with a C_2 axis. Interconversions of these enantiomers can occur without CH_2 ring inversions simply by rotations of the p-$CH_3C_6H_4SO_2N$ groups, a process which interconverts the two protons of each of the four methylenes. Formally, conformation **8** is a possible transition state for interconversions of enantiomerically related complexes of the **9** conformation. Thus during an enantiomeric interconversion process, **1** undergoes a large increase in cavity size. Small ions with high complexation energies should form complexes with slow interconversion rates, and larger ions with low binding energies should interconvert faster.

The observed spectra of the Class B complexes are interpreted in terms of their existing in conformations such as **9**. Ions such as Ag^{+} and Hg^{2+} have relatively large radii of 1.26 and 1.10 Å, respectively. The complexes, **1**·Ag^{+} and **1**·Hg^{2+} exhibit broad singlets for their CH_2 protons, suggesting enantiomer interconversions that are moderately fast on the ^1H NMR time scale. The complexes of Na^{+} and Cd^{2+} also provide singlets for their CH_2 protons, suggesting that enantiomer interconversions are fast because of relatively low binding free energies. However, complexes **1**·Cu^{+} and **1**·Zn^{2+} both give AB quartet patterns for their CH_2 protons. These metal ions have both small ionic radii and probably high binding energies. The broad AB patterns collapsed to broad singlets when the solutions were heated.

Class C complexes are composed of **1** binding metals with greater than 1.5 Å ionic radii, Cs^{+} with a 1.65 Å radius being our only example. Molecular model examination suggests that Class C complexes involved conformation **10**, which resembles that observed in the crystal structure of **1**·$2H_2O$ (**6**). In this conformation, the four phenanthroline nitrogens occupy the base of a square pyramid, the p-$CH_3C_6H_4SO_2N$ nitrogens being remote from the cavity. One host in this conformation contacts only one side of a large ion, which suggests that either solvent or a second host molecule might ligate the other side. In the ^1H NMR spectrum of **1**·Cs^{+}, the p-$CH_3C_6H_4$ proton signals are so broad at 25 °C as to be almost unobservable. When the temperature was increased to 87 °C, the signals tended to sharpen.

Estimates of the free energies for complexation

Estimates of the relative free energies of complexation of **1** with sodium, potassium, rubidium, cesium, and ammonium picrates were made through competition experiments utilizing ^1H NMR spectral analysis. The ^1H NMR spectrum of **1**·LiPic was too ill-defined to be included in this study. That the ions studied formed only 1:1 complexes was established by the fact that the ^1H NMR spectra of the complexes did not change as both the absolute and relative concentrations of **1** and each guest were varied over the concentration ranges used in the competition

experiment. When the salts were added incrementally to solutions of 1, the spectrum of free 1 and that of each complex were additive, the signals of free 1 decreasing in intensity proportionately as the signals of complexed 1 increased in intensity. When host and guest were present in equal stoichiometric amounts, the signals of free host were absent, and only those of complexes of 1 were present. In all cases, the total concentrations of picrate salt present were determined by integration of the picrate proton singlet at δ 8.6 to 8.8. A relaxation delay of 5 seconds was required to obtain a valid integral for these protons. The concentrations of free and complexed 1 were each determined by integrations of appropriate proton signals of host and complex. The spectra of free and complexed host, and of different complexes, were sufficiently different to provide at least one set of peaks that could be integrated to provide ratios of either host to complex, or of two complexes relative to each other.

In the first type of experiment, host was added to a solution containing a known ratio of picrate salt of two different ions, each present in excess of host. The relative amounts of the two complexes at equilibrium were determined by ^{1}H NMR integrations. Equilibrium was reached by the time the solutions were put into the spectrometers. Equation (1) expresses the relevant equilibrium, and K the equilibrium constant. Equations (2), (3), (4), and (5) follow. Equation (5) expresses K in terms of the following measurable parameters: X_a and X_b are the initial mole fractions of the two guest cations, G_a^+ and G_b^+; $[G_a^+]$ and $[G_b^+]$ are the relative concentrations of uncomplexed cations at equilibrium; $[1 \cdot G_a^+]$ and $[1 \cdot G_b^+]$ are the relative concentrations of complexed guest cations at equilibrium; $[Pic^-]$ is the relative total concentration of picrate ion measured at equilibrium. Table 1 reports the results. Although cesium picrate was included in these competition experiments, no cesium complex could be detected, even when the mole fraction of cesium picrate exceeded that of rubidium picrate by a factor of 44. We assumed that had as much as 10% $1 \cdot Cs^+$ been formed, our instrument could have detected it. We set limits on the K value for Cs^+, accordingly. Attempts to get any of the transition metal guests on this scale failed, due to 1 binding them much more strongly than the alkali metal ions.

Table 1. Values of equilibrium constants (K) between complexes composed of 1 and two different guest (G) picrate salts

				Rel. concns. at equil.				$\Delta(\Delta G°)$[a]
G_a^+	G_b^+	X_a	X_b	$[1 \cdot G_a^+]$	$[1 \cdot G_b^+]$	$[Pic^-]$	K	(kcal mol^{-1})
Rb^+	K^+	0.913	0.087	1	1	63	12.7	
								+ 1.6
Rb^+	K^+	0.913	0.087	1.15	1	26.5	15.4	
Na^+	K^+	0.928	0.072	12	1	600	1.1	
								+ 0.1
Na^+	K^+	0.504	0.496	7	1.2	38.6	1.22	
NH_4^+	K^+	0.493	0.507	1.5	1	9.4	0.56	- 0.35
Cs^+	Rb^+	0.912	0.088	no $1 \cdot Cs^+$ detected			>90[b]	
Cs^+	Rb^+	0.978	0.022	no $1 \cdot Cs^+$ detected			>400[b]	>+ 5

[a]Free energy of formation of $1 \cdot G^+$ for various cations relative to that for $1 \cdot K^+$.

[b]These values calculated assuming that 10% $1 \cdot Cs^+$ could have been detected.

$$1\cdot G_a^+Pic^- + G_b^+Pic^- \overset{K}{\rightleftharpoons} 1\cdot G_b^+Pic^- + G_a^+Pic^- \quad (1)$$

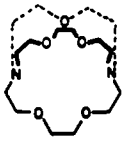
$$[G_a^+] = X_a[Pic^-] - [1\cdot G_a^+] \quad (2)$$

$$[G_b^+] = X_b[Pic^-] - [1\cdot G_b^+] \quad (3)$$

$$K = \frac{[1\cdot G_b^+][G_a^+]}{[1\cdot G_a^+][G_b^+]} \quad (4)$$

$$K = \frac{[1\cdot G_b^+](X_a[Pic^-] - [1\cdot G_a^+])}{[1\cdot G_a^+](X_b[Pic^-] - [1\cdot G_b^+])} \quad (5)$$

In a second type of experiment carried out in $(CD_3)_2SO$ at 25 °C, [2.2.1]cryptaplexes or [2.2.2]cryptaplexes[8] of potassium or rubidium picrate[9] were equilibrated with **1**. In equation (6) describing this equilibrium, Crd stands for cryptand **11** or **12**, $Crd\cdot G^+$ for cryptaplexes derived from **11** or **12**, and K' is the equilibrium constant. Enough **1** was added to solutions of $Crd\cdot G^+Pic^-$ so that both free and complexed **1** were visible in the ^1H NMR spectra. Their relative concentrations were readily measured by integration, and equilibrium was reached by the time measurements could be made. In two of the five runs, the cryptands and cryptaplexes provided similar enough spectra to make separate integrations untenable. Since the initial cryptaplex picrates used in the equilibrations were one-to-one, the sum of the concentrations of cryptand and cryptaplex at equilibrium were always equal to the concentrations of the picrate ion, whose protons were easily integrated in the ^1H NMR spectra. Thus equation (7) applies. Every molecule of $1\cdot G$ formed must produce a molecule of free Crd, as is expressed in equation (8). Equations (9), (10), and (11) follow, applying in each case to the relative concentrations of species present at equilibrium.



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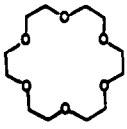

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$$Crd\cdot G^+Pic^- + 1 \overset{K'}{\rightleftharpoons} Crd + 1\cdot G^+Pic^- \quad (6)$$

$$[Crd] + [Crd\cdot G^+] = [Pic^-] \quad (7)$$

$$[Crd] = [1\cdot G^+] \quad (8)$$

$$[Crd\cdot G^+] = [Pic^-] - [1\cdot G^+] \quad (9)$$

$$K' = \frac{[1\cdot G^+][Crd]}{[Crd\cdot G^+][1]} \quad (10)$$

$$K' = \frac{[1\cdot G^+]^2}{[1]([Pic^-] - [1\cdot G^+])} \quad (11)$$

Four different competition experiments were carried out involving **11**·KPic, **11**·RbPic, **12**·KPic, and **12**·RbPic. In a fifth experiment, **11**·$KClO_4$ was substituted for the corresponding picrate. The relative concentrations at equilibrium of **1**, **1**·G^+, and Pic^- were measured in runs 1 and 3-5, and of (Crd + Crd·G^+) in runs 2, 4, and 5 by integrations of appropriate protons in the ^1H NMR spectra. When values for [Pic^-] and ([Crd] + [Crd·G^+]) could both be measured (e.g., runs 3 and 4), they were within 10% of one another. When different integrations were used to measure the same entity, the values were averaged. Table 2 records the results. When a small amount of D_2O was added to the

Table 2. Relative values in arbitrary units of [**1**], [**1**·G^+], [Pic^-], and ([Crd] + [Crd·G^+]) measured by ^1H NMR proton integrations at equilibrium in $(CD_3)_2SO$ at 25 °C, and derived K' values.[a]

Run 1 with **11**·K^+Pic^-, K' = 1.3, $\Delta(\Delta G°)'$ = - 0.16 kcal mol^{-1}
[**1**]: ArH_b, 5.25; 0.5(ArH_a + ArH_c) = 3.4; ArH_c = 5.25; average, 4.6
[**1**·K^+]: ArH_b, 9.25; ArH_c, 7.5; ArH_d = 7.5; $ArCH_2N$ at δ 5.39, 8.25; CH_3, 6.2; average, 7.7
[Pic^-]: ArH, 17.5

Run 2 with **11**·$K^+ClO_4^-$, K' = 1.3, $\Delta(\Delta G°)'$ = - 0.16 kcal mol^{-1}
[**1**]: ArH_b, 3.0; 0.5(ArH_a + ArH_c), 2.25; ArH_c, 3.25; average, 2.8
[**1**·K^+]: ArH_b, 3.75; ArH_c, 2.75; $ArCH_2N$ at δ 5.39, 3.0; average, 2.2
([**11**] + [**11**·K^+]): 6

Run 3 with **12**·K^+Pic^-, K' = 0.21, $\Delta(\Delta G°)'$ = + 0.93 kcal mol^{-1}
[**1**]: ArH_b, 4.25; ArH_d, 4.25; $ArCH_2N$, 4.25; CH_3, 2.7; average, 3.9
[**1**·K^+]: ArH_b = 7.0; 0.5(ArH_a + ArH_c) = 5.25; ArH_d = 6.75; average, 6.3
[Pic^-]: ArH, 15.5

Run 4 with **11**·Rb^+Pic^-, K' = 2.5, $\Delta(\Delta G°)'$ = - 0.54 kcal mol^{-1}
[**1**]: 0.5(ArH_a + ArH_c), 1.1
[**1**·Rb^+]: ArH_b, 4.75; ArH_d, 4.0; ArH_e, 3.75; $ArCH_2N$ at δ 5.46, 4.5; CH_3, 2.9; average, 4.25
[Pic_]: ArH, 11
([**11**] + [**11**·Rb^+]), 10.2; average, 10.6

Run 5 with **12**·Rb^+Pic^-, K' = 0.15, $\Delta(\Delta G°)'$ = + 1.1 kcal mol^{-1}
[**1**]: ArH_b, 5.0; 0.5(ArH_a + ArH_c), 3.4; ArH_d 5.0; average, 4.5
[**1**·K^+]: ArH_b, 4.0; ArH_d, 3.8; CH_3, 3.2; average 3.7
[Pic^-]: ArH, 23
([**12**] + [**12**·Rb^+]): 25
Average: 24

[a] A Bruker WP200 spectrometer (200 MHz) was employed.

$(CD_3)_2SO$ solutions, no significant changes in the integrations were observed, suggesting that the small amount of water present in the original solvent had little effect on the equilibrium. From the averaged concentrations and equation (11), K', and $\Delta(\Delta G°)'$ values were calculated, and are listed in Table 3. Changes in values of K' were insignificant when the absolute values of the initial concentrations of **1** and cryptaplex picrate salts were decreased by a factor of over 2. This fact, coupled with our inability to detect by direct ^1H NMR measurements any species other than one-to-one complexes of the type **1**·G^+, indicate that such complexes were involved in these equilibria.

The $-\Delta G°$ values (kcal mol^{-1}) for **1** binding the picrate salts of Na^+, K^+, Rb^+, and NH_4^+ in $(CD_3)_2SO$ at 25 °C were estimated from the K values of Table 1, the K' values of Table 2, and the stability constants (K_s) defined by equation (12) previously collected by Cox[10] for **11**·K^+, **11**·Rb^+, **12**·K^+, and **12**·Rb^+ in $(CH_3)_2SO$ at 25 °C. When more than one literature K_s value was given[10], the average value was used.[12]

$$\text{Crd} + \text{G}^+ \overset{K_s}{\rightleftharpoons} \text{Crd}\cdot\text{G}^+ \qquad (12)$$

These calculations were performed as follows. The $\Delta G°$ values for formation of **11**·K^+, **12**·K^+, **11**·Rb^+, and **12**·Rb^+ were calculated from the literature values[10] of K_s, and are listed in Table 3. The $\Delta(\Delta G°)'$ values for the cryptands vs. **1** binding K^+ and Rb^+ listed in Table 2 were added to the appropriate $\Delta G°$ values for the cryptands binding these ions. The resulting $\Delta G°$ values for **1** binding these ions are listed in Table 3. Addition of the $\Delta G°$ value for formation of **1**·K^+ to the $\Delta(\Delta G°)$ values of Table 1 gave the $\Delta G°$ values for formation of **1**·Na^+, **1**·Rb^+, **1**·Cs^+, and **1**·NH_4^+ listed in Table 3. The $\Delta G°$ value for 18-crown-6 (**13**) binding K^+ in $(CH_3)_2SO$ is also included for purposes of comparison.[11]

Table 3. Free energies of formation of complexes in dimethyl sulfoxide at 25 °C

Entry no	Complex	$\Delta G°$ (kcal mol^{-1})	Source of value[a]
1	**1**·Na^+	- 8.4	$\Delta(\Delta G°)$ and $\Delta G°_{av}$ for **1**·KPic
2	**1**·K^+	- 8.4	$\Delta(\Delta G°)'$ of run 1, $\Delta G°$ for **11**·KPic
3	**1**·K^+	- 8.4	$\Delta(\Delta G°)'$ of run 2, $\Delta G°$ for **11**·$KClO_4$
4	**1**·K^+	- 8.6	$\Delta(\Delta G°)'$ of run 3, $\Delta G°$ for **12**·KPic
5	**1**·K^+	- 8.5	average of values, or $\Delta G°_{av}$
6	**1**·Rb^+	- 6.8	$\Delta(\Delta G°)'$ of run 4, $\Delta G°$ for **11**·RbPic
7	**1**·Rb^+	- 6.8	$\Delta(\Delta G°)'$ of run 5, $\Delta G°$ for **12**·RbPic
8	**1**·Rb^+	- 6.9	$\Delta(\Delta G°)$ and $\Delta G°_{av}$ for **1**·K^+
9	**1**·Cs^+	>- 3.5	$\Delta(\Delta G°)$ and $\Delta G°_{av}$ for **1**·K^+
10	**1**·NH_4^+	- 8.85	$\Delta(\Delta G°)$ and $\Delta G°_{av}$ for **1**·K^+
11	**11**·K^+	- 8.2	reference 10
12	**11**·Rb^+	- 6.3	reference 10
13	**12**·K^+	- 9.55	reference 10
14	**12**·Rb^+	- 7.9	reference 10
15	**13**·K^+	- 4.4	reference 11

[a]Source of $\Delta(\Delta G°)$ values is Table 1, of $\Delta(\Delta G°)'$ values is Table 2.

Confidence in the validity of the $\Delta G°$ estimates of Table 3 is increased by the fact that when different kinds of equilibrations or different starting materials were involved in the determinations, the resulting values were either identical or within 0.2 kcal mol^{-1} of one another. For example, entries 2-4 of Table 3 provide $\Delta G°$ values for formation of **1**·K^+ which depend on equilibrations of **1** with **11**·KPic, **11**·$KClO_4$, or **12**·KPic. The resulting values are -8.5 ± 0.1 kcal mol^{-1}. Entries 7-9 give $\Delta G°$ values for formation of **1**·Rb^+ resulting from equilibrations of **1** with **11**·RbPic or **12**·RbPic, and equilibrations of **1**·KPic with **1**·RbPic coupled with those involving **1**·KPic with **11**·KPic and **12**·KPic. The resulting values are -6.85 ± 0.05 kcal mol^{-1}.

Correlation of structure and binding

The binding free energies listed in Table 3 indicate that the azacoraplex with **1** as host and Na^+, K^+, Rb^+, and NH_4^+ as guests are an average of ~4 kcal mol^{-1} more stable than **13**·K^+, the most stable of the all-oxygen coraplexes. Indeed, these coraplexes of **1** are of comparable stability to the cryptaplexes with the same guests. This is surprising, since cryptands **11** and **12** contain seven and eight binding sites, respectively, whereas **1** contains only six. Furthermore, the two nitrogens of the p-$CH_3C_6H_4SO_2N$: groups of **1** are not expected to be as strongly binding ligands as are the two $(CH_2)_3N$: groups in each of the cryptands. We conclude that the enforced preorganization of the two nitrogens in each of the phenanthrolines more than compensates for the poor ligating power of the tosylamide nitrogens. The sp^2 orbitals of the unshared electron pairs of each phenanthroline nitrogen converge on one another, and the resulting electron repulsion is somewhat compensated by ligating cations. The additional preorganization resulting from incorporating the two rigid phenanthrolines into the same 18-membered ring system appears to compensate for the lack of additional strong ligating sites. The two $(CH_2)_2NSO_2C_6H_4CH_3$-p bridges of **1** severely limit the distances the four phenanthroline nitrogens can be from one another. As importantly, in all of the conformations available to the macroring of **1** (**8**, **9**, and **10**), the orbitals of these four unshared electron pairs converge on one another.

The space occupied by the bridging units and the phenanthrolines severely limits the ability of the rather bulky $(CH_3)_2SO$ molecules to assume solvating geometries which might compensate for the C-N dipoles, an effect which likely further raises the free energy of **1**. Thus **1** is preorganized both with regard to the location of four of its binding sites and to sterically inhibiting solvation of these sites. Each of these two kinds of contributions to preorganization, one involving relative locations and the other, solvation of binding sites of the host, is expected to make both enthalpic and entropic contributions to the free energy of **1** binding cations. We believe the identification of the principle of preorganization[12] with only entropic effects to be in error. For example, the somewhat additive alignment of the C-N dipoles in each phenanthroline and the lack of compensating solvation effects should make substantial enthalpic contributions to the binding power of **1**.

The sp^2 hybridization of the phenanthroline binding site-electron pairs provides about 8% less p-character than is available to the orbitals occupied by the binding sites of ether oxygens. Since p-orbitals are more extended than s-orbitals, the higher the s-character of binding sites, the more important should be host preorganization to binding. Thus preorganizational effects in **1** account for the high $-\Delta G°$ values in general.

With hosts containing mainly oxygen binding sites, the $-\Delta G°$ values of Rb^+ and NH_4^+ are usually close to one another.[13] However, with **1**, NH_4^+ is 2 kcal mol^{-1} more strongly bound than Rb^+. This effect may reflect the hardness of the sp^2 binding sites of **1**, which induce a hardness in NH_4^+ by concentrating positive charge on the hydrogens of this ion.

The highest selectivity for **1** binding the alkali metal ions is most strikingly exhibited in the difference in $\Delta G°$ values for **1**·Rb^+ and **1**·Cs^+ of >-3.3 kcal mol^{-1}. This difference is larger than that for any corand of which we are aware, and is comparable or less than the difference of ~6 kcal mol^{-1} exhibited by cryptand **12** in the same medium.[10]

The diamine derived by desulfonation of **1** should provide a ligating system interesting both in its own right and as a starting point for synthesis of a variety of polycyclic systems with high preorganization, of which **2** is the simplest example.

EXPERIMENTAL

7,8,9,18,19,20-Hexahydro-18,19-bis((4-methylphenyl)-sulfonyl)-1,21:4,6:10,12:15,17-tetraethenodibenzo[b,k][1,4,7,10,13,16]hexaazacyclooctadecine (1). A solution of 552 mg (2 mmols) of 2,9-bis-(chloromethyl)-1,10-phenanthroline[3c] and 312 mg (2 mmols) of 4-methylbenzenesulfonamide in 50 mL of dry $(CH_3)_2NCHO$ was placed in a gas-tight syringe. A syringe pump was used to add this solution to a rapidly stirred mixture of 4 g of anhydrous K_2CO_3 powder in 500 mL of dry $(CH_3)_2NCHO$ over a 20 h period. The reaction mixture was then allowed to stir at 25 °C for an additional 2 days. The resulting solution was mixed with 3 L water and neutralized with dilute aqueous HCl to provide a white precipitate. This was removed by filtration through a fine-fritted glass funnel. The solids were added to 150 mL of absolute ethanol, and the mixture was heated to reflux and sonnicated in an ultrasonic cleaning bath. The undissolved solids (polymers) were removed by filtration through a fine-fritted glass funnel, and the filtrate was evaporated under vacuum. The resulting solids were mixed with 75 mL of absolute ethanol and sonnicated until all of the solids were suspended. The remaining undissolved material, which was almost pure 1, was filtered, washed, and dried at 10^{-5} torr for 24 h to give 150 mg (21%) of product. This material was recrystallized from acetone to give pure product, mp, >240 °C (decomposition); ^{1}H NMR (200 MHz, $(CD_3)_2SO$): δ 7.99 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 7.89 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 7.58 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 7.39 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.36 (s, 4H, Ar-H_a); 4.85 (broad s, 8H, $ArCH_2N$); 2.5 (under $(CH_3)_2SO$) (s, 6H, $ArCH_3$); ^{1}H NMR (200 MHz, $(CD_3)_2NCDO$: δ 8.03 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 7.92 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 7.64 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 7.44 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.40 (s, 4H, Ar-H_a); 4.88 (broad s, 8H, $ArCH_2N$); 2.54 (s, 6H,$ArCH_3$); I.R. (KBr pellet): 1160, 1325, 1340 cm^{-1} (sulfonamide). M.S. (Xe FAB, sulfolane + thioglycerol): m/e = 751 ($M + H^+$). Analysis calcd for $C_{42}H_{34}N_6O_4S_2$: C, 67.18; H, 4.56. Found: C, 66.77; H, 4.45.

^{1}H NMR Spectra of Complexes of 1 in Presence of Excess Guest Salt.

To solutions of 10 mg of **1** dissolved in 0.5 mL of $(CD_3)_2SO$ were added excess stoichiometric amounts of salt, and the 200 MHz spectra were taken to give the following data.

1·NaPic: δ 8.16 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 8.02 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 7.58 (d+d, 8H, Ar-H_c + Ar-H_e, J = 8 Hz); 7.56 (s, 4H, Ar-H_a); 4.95 (broad s, 8H, $ArCH_2N$); 2.5 (s, 6H, $ArCH_3$).

1·KPic: δ 8.10 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 7.55 (s, 4H, Ar-H_a); 7.46 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 6.91 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 5.86 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 5.38 (d, 4H, $ArCH_2N$, J = 14 Hz); 4.82 (d, 4H, $ArCH_2N$, J = 14 Hz); 1.67 (s, 6H, $ArCH_3$).

1·RbPic: δ 8.10 (d, 4H, Ar-H_b, J_{bc} = 8.5 Hz); 7.56 (s, 4H, Ar-H_a); 7.48 (d, 4H, Ar-H_c, J_{bc} = 8.5 Hz); 6.98 (d, 4H, Ar-H_d, J_{de} = 7.8 Hz); 5.83 (d, 4H, Ar-H_e, J_{de} = 7.8 Hz); 5.46 (d, 4H, $ArCH_2N$, J = 14 Hz); 4.68 (d, 4H, $ArCH_2N$, J = 14 Hz); 1.60 (s, 6H, $ArCH_3$).

1·CsPic: δ 7.95 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 7.88 (d broadened at 25 °C, 4H, Ar-H_e, J_{de} = 8 Hz); 7.52 (d broadened at 25 °C, Ar-H_e, J_{de} = 8 Hz); 7.40 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.39 (s, 4H, Ar-H_a); 4.9 (broad s, 8H, $ArCH_2N$); 2.25 (broad s, 6H, $ArCH_3$).

1·NH_4Pic: δ 8.11 (d, 4H, Ar-H_b, J_{bc} = 8.2 Hz); 7.56 (s, 4H, Ar-H_a); 7.49 (d, 4H, Ar-H_c, J_{bc} = 8.2 Hz); 7.19 (t, NH_4^+, J_N = 49 Hz); 6.97 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 5.84 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 5.40 (d, 4H, $ArCH_2N$, J = 13.7 Hz); 4.80 (d, 4H, $ArCH_2N$, J = 13.7 Hz); 1.61 (s, 6H, $ArCH_3$).

1·CuCl: δ 8.30 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 8.05 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 7.80 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.64 (s, 4H, Ar-H_a); 7.61 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 5.66 (d, 4H, $ArCH_2N$, J = 14.4 Hz); 4.84 (d, 4H, $ArCH_2N$, J = 14.4 Hz); 2.5 (s, 6H, $ArCH_3$).

1·$AgNO_3$: δ 8.69 (d broadened at 25 °C, 4H, Ar-H_b, J_{bc} = 8 Hz); 8.15 (s broadened at 25 °C, 4H, Ar-H_a); 7.85 (d+d, 8H, Ar-H_c + Ar-H_e, J = 8 Hz); 7.40 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 5.04 (broad s, 8H, $ArCH_2N$); 2.39 (s, 6H, $ArCH_3$).

1·$ZnCl_2$: δ 9.01 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 8.42 (s, 4H, Ar-H_a); 7.99 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.82 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 7.37 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 5.3 (broad d, 4H, $ArCH_2N$); 4.5 (broad d, 4H, $ArCH_2N$); 2.41 (s, 6H, $ArCH_3$).

1·$Cd(NO_3)_2$: δ 8.97 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 8.35 (s, 4H, Ar-H_a); 8.02 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.94 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 7.46 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 5.07 (s, 8H, $ArCH_2N$); 2.43 (s, 6H, $ArCH_3$).

1·$HgCl_2$: δ 8.42 (d, 4H, Ar-H_b, J_{bc} = 8 Hz); 8.03 (d, 4H, Ar-H_e, J_{de} = 8 Hz); 7.82 (d, 4H, Ar-H_c, J_{bc} = 8 Hz); 7.74 (s, 4H, Ar-H_a); 7.61 (d, 4H, Ar-H_d, J_{de} = 8 Hz); 5.1 (broad s, 8H, $ArCH_2N$; 2.5 (s, 6H, $ArCH_3$).

Equilibrations Between Different Complexes of 1 and Between the Cryptand Complexes.

The procedure used for these equilibrations was modeled after those reported previously for determining equilibria between different cryptaspheraplexes and between cryptaplexes and cryptaspheraplexes. The cryptaplexes used are those reported in this paper.[9]

Crystal Structure

Compound **1**·$2H_2O$·$0.5(CH_3)_2C{=}O$ crystallizes in the monoclinic system C2/c. Unit cell dimensions are a = 19.197(1), b = 16.4096(8), c = 25.942 Å, β = 104.292(2)°, V = 7912 $Å^3$, Z = 8. The crystal was examined on a modified PICKER FACS-1 diffractometer, MoKα radiation, at 295 K. The structure was determined by direct methods. Refinement of 290 parameters (5819 reflections with I>0) has an agreement value, R, currently = 0.109. Acetone is disordered about a two-fold axis at x=0, z=1/4. Full details will be published elsewhere.

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