Molecular Architecture. 1. Sodium, Potassium, and Strontium Complexes of a Hexaazamacrocycle, an 18-Crown-6/Torand Analogue

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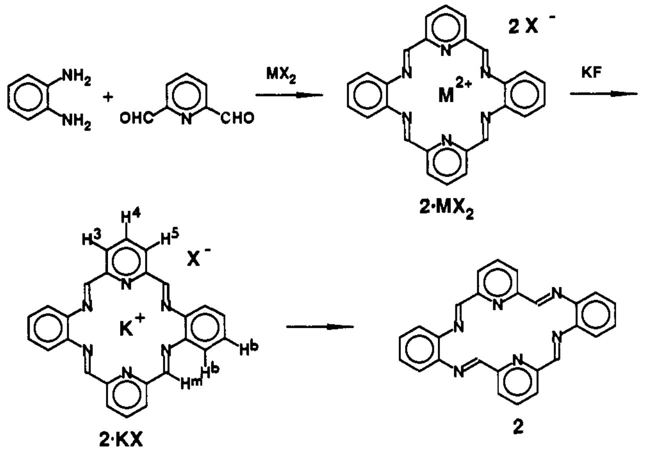
Abstract: Complexes of 4,5:15,16-dibenzo-3,6,14,17,23,24-hexaazatricyclo[17.3.1.$1^{8,12}$]tetracosa-1(23),4,8-(24),9,11,15,19,21-octaene (**2**) with $Sr(CF_3SO_3)_2$ and SrI_2 have been prepared by templated 2 + 2 cyclocondensation reactions of pyridine-2,6-dicarboxaldehyde and benzene-1,2-diamine. Complexes **2**·$KClO_4$, **2**·KI, and **2**·KCF_3SO_3 were prepared by reaction of the corresponding Sr complexes with KF. Free ligand **2** was prepared by reaction of **2**·KCF_3SO_3 with 18-crown-6 (**1**) and **2**·$NaCF_3SO_3$ was prepared from **2**. The X-ray crystal structure of **2**·$Sr(CF_3SO_3)_2$ was determined, showing two molecules per asymmetric unit. In both complexes Sr is nine-coordinate with Sr–N distances ranging from 2.65–2.82 Å. The stability constants of **2**·KCF_3SO_3 and **2**·$NaCF_3SO_3$ in DMSO were determined by NMR and potentiometric methods as log K_s = 3.7 and 3.1, respectively. Molecular mechanics calculations were performed on **2**·$SrCl_2$, **2**, and a tetramethyl analogue (**9**). Computational and structural studies of the complexes of **2** indicated an optimum hole size corresponding to metal ionic radii of 1.4–1.55 Å. Spectroscopic, structural, and computational results demonstrated that **2** is not preorganized for complexation, and the minimum energy conformer in solution is elliptical rather than circular. The K/Na selectivities and binding strengths of **1**, **2**, and torand **3** are compared, concluding that guest encapsulation is not required for strong binding and that preorganization does not ensure selectivity.

Despite the biological significance of alkali metals and extensive research on their complexes with macrocycles,[1] the structural factors controlling alkali metal–macrocycle interactions are still poorly understood. Lacking general quantitative models for predicting or explaining relative stabilities of host–guest complexes,[1c,2] chemists tend to discuss structure-stability relationships in broad qualitative terms. Examples are the chelate, macrocyclic, and macrobicyclic(cryptate) effects[1c,3] and the concept of ligand preorganization,[4] which encompasses these effects. In most alkali metal complexes that have been studied thermodynamically,[1] ligand preorganization is accompanied by guest encapsulation (shielding from solvent). This and related studies explore the preorganization (rigidifcation) of 18-crown-6 (**1**) in the absence of guest encapsulation. Thus, **1**, tetraimine macrocycle **2**,[5] and torand **3**[5b,6] are viewed as a host series of increasing rigidity and planarity.

In the heuristic transformation of **1** → **3**, six oxygen atoms are replaced by sp^2-hybridized nitrogens. Frensdorf showed that replacement of one or two oxygen atoms of 18-crown-6 by sp^3-hybridized nitrogen drastically decreases the stabilities of the potassium complexes in methanol.[7] This effect is consistent with the dominance of electrostatic attraction among the host/alkali metal interactions[2b] and with the smaller dipole moment of trimethylamine (0.61 D) compared with dimethyl ether (1.30 D).[8] Despite the larger dipole moment of pyridine (2.20 D),[8] replacement of $-CH_2OCH_2-$ moieties by 2,6-pyridinediyl in crown ethers,[1c,9] cryptands,[1c,9] and hemispherands[4b,10] does not generally increase the stabilities of alkali metal complexes.

Transition-metal complexes of polyazamacrocycles have been extensively studied,[1c,11] but quantitative studies of alkali metal complexes of such ligands remain rare.[5b–e,6,12] The 1:1 complexes of macrocyclic Schiff base **2** with Ca^{2+}, Sr^{2+}, and Pb^{2+} were previously prepared by condensation of benzene-1,2-diamine and pyridine-2,6-dicarboxaldehyde in the presence of perchlorate salts of these metals.[5f] These are among the first complexes of "hard" alkaline earth ions with hosts containing only "soft" nitrogen donors.[9b] Preliminary reports have also described the isolation of **2**·$KClO_4$,[5d,e] **2**·$K(CF_3SO_3)$,[5b,c] metal-free **2**,[5b,c] and **2**·$Na(CF_3SO_3)$,[5b] as shown in Scheme I. The X-ray crystal structures of **2**·$Cd(ClO_4)_2$,[5f] **2**·$Pd(ClO_4)_2$,[5f] metal-free **2**,[5c] and the Pr^{3+} complex of the tetramethyl analogue[13] are known, but the structure of an alkali metal or alkaline earth complex of **2** has not previously

Scheme I



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been reported. Described herein are potentiometric stability constant measurements for **2**·Na$^+$ and **2**·K$^+$, which were previously estimated by NMR methods.[5d,e] Molecular mechanics studies of **2** in the metal-free and complexed conformations and the crystal structure of **2**·Sr(ClO$_4$)$_2$ are also reported.

Experimental Section

General Methods. Reagent grade solvents were used as supplied, except methanol, which was stored over 3A sieves, and dimethyl sulfoxide (DMSO), which was distilled from CaH$_2$ in vacuo. Acetonitrile and chloroform were HPLC grade. ^{1}H NMR data were obtained at 300 MHz and are reported in ppm relative to the following values for residual protonated solvents: CDCl$_3$, 7.26; DMSO-*d*$_6$, 2.49; pyridine-*d*$_5$, 8.70. ^{13}C NMR spectra were recorded at 75.5 MHz. Melting points were determined on a Mel-Temp apparatus and are uncorrected. Mass spectra were obtained at 70 eV by electron impact ionization. Microanalyses were performed by Galbraith Laboratories, Inc., and results for **2**, **2**·KClO$_4$, **2**·KCF$_3$SO$_3$, **2**·NaCF$_3$SO$_3$, and **4** (or **5**) are given in the supplementary material.

Starting Materials. Pyridine-2,6-dicarboxaldehyde was prepared by the method of Papadopoulos et al.,[14] and benzene-1,2-diamine was practical grade (Kodak), recrystallized from 1% aqueous sodium thiosulfate with decolorization by Norit. The trifluoromethanesulfonate (triflate) salts of Na$^+$, K$^+$, and Sr^{2+} were prepared by a procedure reported for Mg^{2+} and Zn^{2+} triflates.[15] Thus a solution of 20 mmol of the carbonate salt in methanol was added dropwise with stirring of 56 mmol of trifluoromethanesulfonic acid (3M Corp.) over a period of 50 min (**Caution:** vigorous reaction and evolution of CO$_2$). The resulting solution was heated under reflux for 2 h, and then solvent was removed by rotary evaporation. KCF$_3$SO$_3$ was recrystallized from methanol, whereas NaCF$_3$SO$_3$ and Sr(CF$_3$SO$_3$)$_2$ were recrystallized from ethanol/diethyl ether. Yields ranged from 85 to 95%.

2·Sr(CF$_3$SO$_3$)$_2$. A mixture of 0.81 g (6 mmol) of pyridine-2,6-dicarboxaldehyde, 0.65 g (6 mmol) of benzene-1,2-diamine, 1.16 g (3 mmol) of Sr(CF$_3$SO$_3$)$_2$, and 450 mL of acetonitrile was stirred under N$_2$ at reflux temperature for 12 h. Rotary evaporation left a yellow residue, which was heated with 300 mL of boiling acetonitrile. The hot solution was filtered through a fine mesh glass Buchner funnel, and then the filtrate was reheated with 100 mL of benzene. The product was allowed to crystallize at room temperature for 2 days and then collected by vacuum filtration. Concentration of the filtrate to 100 mL gave a second crop, total yield, 1.36 g (57%, dec 410 °C): ^{1}H NMR (DMSO-*d*$_6$) δ 9.19 (s, H^m, 4 H), 8.43 (t, J = 7.7 Hz, H^4, 2 H), 8.19 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.60–7.86 (m, H^b, 8 H); (pyridine-*d*$_5$) δ 9.23 (s, H^m, 4 H), 8.45 (t, J = 7.6 Hz, H^4, 2 H), 8.16 (d, J = 7.6 Hz, H^{3,5}, 4 H), 7.62–7.77 (m, H^b, 8 H); IR (KBr, cm^{-1}) 3100 w, 1655 m, 1580 s, 1500 m, 1460 m, 1390 m, 1310 (br) s, 1255 (br) s, 1235 s, 1170 s, 1045 s, 1018 m, 980 m, 825 s, 765 s, 750 s, 650 s; UV (CH$_3$CN, nm ($\epsilon \times 10^{-3}$)) λ_{max} 338 (40.5), 270 (34.8), 225 (34.3); MS (*m/z*), 44 (100), 81 (82), 100 (60), 207 (20), 414 (M – Sr(CF$_3$SO$_3$)$_2$, 7%).

2·Sr(ClO$_4$)$_2$. A mixture of 0.68 g (5 mmol) of pyridine-2,6-dicarboxaldehyde, 0.54 g (5 mmol) of benzene-1,2-diamine, 0.80 g (2.5 mmol) of Sr(ClO$_4$)$_2$·6H$_2$O, and 200 mL of methanol was stirred under N$_2$ at reflux temperature for 3.5 h. After the reaction mixture cooled to room temperature, the yellow precipitate was collected by vacuum filtration, washed with a few milliliters of methanol, and dried in vacuo, yielding 0.92 g (53%): ^{1}H NMR (DMSO-*d*$_6$) δ 9.20 (s, H^m, 4 H), 8.44 (t, J = 7.7 Hz, H^4, 2 H), 8.20 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.60–7.86 (m, H^b, 8 H).

2·SrI$_2$. A mixture of 0.41 g (3 mmol) of pyridine-2,6-dicarboxaldehyde, 0.33 g (3 mmol) of benzene-1,2-diamine, 0.51 g (1.5 mmol) of SrI$_2$, and 140 mL of methanol was stirred under N$_2$ at reflux temperature for 8 h. The solution was concentrated to 30 mL and then cooled to 0 °C. The yellow precipitate was collected by vacuum filtration, washed with cold methanol, and dried to yield 0.52 g (48%): ^{1}H NMR (DMSO-*d*$_6$) δ 9.21 (s, H^m, 4 H), 8.41 (t, J = 7.7 Hz, H^4, 2 H), 8.21 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.60–7.87 (m, H^b, 8 H).

2·KCF$_3$SO$_3$. A mixture of 1.0 g (1.25 mmol) of **2**·Sr(CF$_3$SO$_3$)$_2$, 0.47 g (5 mmol) of KF·2H$_2$O, and 300 mL of acetonitrile was stirred under N$_2$ at reflux temperature for 1 h. The hot solution was filtered through a fine mesh glass Buchner funnel, and the filtrate was concentrated to dryness by rotary evaporation. The resulting yellow solid was dissolved in 150 mL of boiling acetonitrile, 50 mL of benzene was added, and the solution stood at room temperature overnight in an open beaker. The resulting fine yellow needles were collected by vacuum filtration and dried in vacuo, yielding 0.60 g (74%), mp 379–382 °C dec: ^{1}H NMR (DMSO-*d*$_6$) δ 8.84 (s, H^m, 4 H), 8.16 (t, J = 7.7 Hz, H^4, 2 H), 7.91 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.37–7.52 (m, H^b, 8 H), 7.36 (s, 0.5 (C$_6$H$_6$), 3 H); (pyridine-*d*$_5$) δ 8.86 (s, H^m, 4 H), 8.04 (t, J = 7.7 Hz, H^4, 2 H), 7.85 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.43–7.51 (m, H^b, 8 H), 7.33 (s, 0.5 (C$_6$H$_6$), 3 H); ^{13}C NMR (DMSO-*d*$_6$, ppm relative to solvent at 39.5) δ 159.2 (C^2), 153.3 (C^m), 144.2 (4°-C^b), 139.3 (α-C^b), 129.2 (C^4), 128.6 (C$_6$H$_6$), 128.2 (β-C^b), 118.3 (C^{3,5}); IR (KBr, cm^{-1}) 3090 w, 1635 m, 1590 s, 1485 m, 1455 w, 1300 (br) s, 1270 (br) s, 1235 m, 1165 (br) s, 1050 s, 1005 m, 820 m, 745 m, 710 m, 650 s; UV (CH$_3$CN, nm ($\epsilon \times 10^{-3}$)) λ_{max} 325 (28.6), 275 (39.3), 240 (37.2); MS (*m/z*), 44 (100), 60 (42), 207 (28), 413 (42), 414 (M – KCF$_3$SO$_3$, 39%). Anal. (C, H, N, K) **2**·KCF$_3$SO$_3$·(C$_6$H$_6$)$_{0.5}$·(H$_2$O)$_{0.5}$.

2·KClO$_4$. A mixture of 0.20 g (0.28 mmol) of **2**·Sr(ClO$_4$)$_2$, 94 mg (1 mmol) of KF·2H$_2$O, and 60 mL of methanol was stirred under N$_2$ at reflux temperature for 1 h and then allowed to cool to room temperature. The orange precipitate was collected by vacuum filtration and recrystallized from acetonitrile to afford 87 mg (56%) of yellow needles, mp 386–388 °C dec: ^{1}H NMR (DMSO-*d*$_6$) δ 8.91 (s, H^m, 2 H), 8.23 (t, J = 7.7 Hz, H^4, 2 H), 7.98 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.45–7.59 (m, H^b, 4 H); IR (KBr, cm^{-1}) 3050 w, 3000 w, 1620 m, 1580 s, 1480 m, 1440 m, 1365 w, 1255 m, 1080 (br) s, 800 m, 725 m. Anal. (C, H, N, K).

2·KI. A mixture of 100 mg (0.13 mmol) of **2**·SrI$_2$, 40 mg (0.43 mmol) of KF·2H$_2$O, and 60 mL of acetonitrile was stirred under N$_2$ at reflux temperature for 1.7 h. The hot solution was filtered through a fine mesh glass Buchner funnel, and the filtrate was concentrated to 50 mL by boiling. Cooling to 0 °C produced orange crystals, which were collected by vacuum filtration under N$_2$. Recrystallization from acetonitrile and drying in vacuo gave 46 mg (61%), dec 360 °C: ^{1}H NMR (DMSO-*d*$_6$) 8.88 (s, H^m, 4 H), 8.18 (t, J = 7.7 Hz, H^4, 2 H), 7.95 (d, J = 7.7 Hz, H^{3,5}, 4 H), 7.41–7.96 (m, H^b, 8 H).

4,5:15,16-Dibenzo-3,6,14,17,23,24-hexaazatricyclo[17.3.1.1^{8,12}]tetracosa-1(23),4,8(24),9,11,15,19,21-octaene (2). To a solution of 0.51 g (0.78 mmol) of **2**·KCF$_3$SO$_3$ in 300 mL of acetonitrile was added 2.1 g (7.8 mmol) of 18-crown-6. The solution was stirred under N$_2$ at room temperature for 1.25 h. The resulting yellow precipitate was collected by vacuum filtration and then dissolved in 100 mL of boiling pyridine. Benzene (50 mL) was added, and the solution was left in an open beaker at room temperature for 2 days. The yellow crystals were collected by vacuum filtration and dried in vacuo, yielding 0.19 g (50%), mp 307–309 °C dec: ^{1}H NMR (pyridine-*d*$_6$) δ 9.52 (s, H^m, 4 H), 8.02 (d, J = 7.6 Hz, H^{3,5}, 4 H), 7.79 (t, J = 7.6 Hz, H^4, 2 H), 7.34–7.66 (m, H^b, 8 H); IR (KBr, cm^{-1}) 3070 w, 1620 m, 1580 m, 1475 m, 1455 m, 1375 w, 1335 w, 1205 w, 1165 m, 1120 m, 1095 m, 955 s, 900 m, 815 s, 765 s, 745 s; UV (CH$_3$CN, nm ($\epsilon \times 10^{-3}$)) λ_{max} 272 (25.5), 240 (29.1); MS (*m/z*), 207 (45), 208 (61), 413 (M – 1, 100) 414 (M$^+$, 82%). Anal. (C, H, N).

2·NaCF$_3$SO$_3$. A mixture of 45 mg (0.11 mmol) of crude **2**, 19 mg (0.11 mmol) of NaCF$_3$SO$_3$, and 30 mL of acetonitrile was stirred under N$_2$ at reflux temperature for 2 h. The resulting clear yellow solution was concentrated to 10 mL and cooled to 0 °C. The precipitated yellow-orange plates were collected by vacuum filtration and dried in vacuo to afford 38 mg (59%), mp 260–264 °C dec: ^{1}H NMR (pyridine-*d*$_5$) δ 8.99 (s, H^m, 4 H), 8.01 (t, J = 8 Hz, H^4, 2 H), 7.87 (d, J = 8 Hz, H^{3,5}, 4 H), 7.45–7.61 (m, H^b, 8 H); ^{13}C NMR (pyridine-*d*$_5$, ppm relative to solvent at 149.9) δ 158.4 (C^2), 153.4 (C^m), 144.9 (4°-C^b), 139.8 (α-C^b), 129.6 (C^4), 129.2 (β-C^b), 118.8 (C^{3,5}); IR (KBr, cm^{-1}) 3070 w, 3020 w, 1625 m, 1585 m, 1485 m, 1450 m, 1270 (br) s, 1160 (br) s, 1035 (br) s, 815 m, 760 m, 695 m, 645 m; UV (CH$_3$CN, nm ($\epsilon \times 10^{-3}$)) 327 (23.1), 270 (34.2), 240 (32.4); MS (*m/z*), 44 (42), 311 (100), 414 (M – NaCF$_3$SO$_3$, 70%). Anal. (C, H, N, Na).

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Attempted recrystallization of **2**·$NaCF_3SO_3$ from methanol gave a product, mp 240–242 °C dec: ^1H NMR (DMSO-d_6) δ 8.84 (s, 2 H), 8.22 (t, J = 7.7 Hz, 2 H), 7.95 (d, J = 7.7 Hz, 2 H), 7.72 (d, J = 7.7 Hz, 2 H), 7.31 (d, J = 7.6 Hz, 2 H), 7.14–7.24 (m, 6 H), 6.81 (t, J = 7.6 Hz, 2 H), 6.09 (d, J = 6 Hz, 2 H), 3.00 (s, 6 H); IR (KBr, cm^{-1}) 3400 m, 3100 w, 3040 w, 2980 w, 2850 w, 1605 s, 1595 s, 1510 s, 1435 m, 1330 m, 1260 m, 1185 m, 1150 m, 1070 s, 905 m, 820 s, 760 s; UV (DMSO, nm ($\epsilon \times 10^{-3}$)) λ_{max} 390 (13.4), 275 (37.3); MS (m/z), 207 (30), 208 (41), 413 (100), 414 (M − $2CH_3OH$, 73), 446 (M − CH_3OH, 3%). Anal. (C, H, N) **4**·$(H_2O)_{0.1}$ or **5**·$(H_2O)_{0.1}$.

2_2·Ba(ClO_4)$_2$.[5f] A mixture of 0.54 g (5 mmol) of benzene-1,2-diamine, 0.68 g (5 mmol) of pyridine-2,6-dicarboxaldehyde, 0.42 g (1.25 mmol) of $Ba(ClO_4)_2$, and 200 mL of methanol was stirred under N_2 at reflux temperature for 6 h and then allowed to cool to room temperature. The resulting orange precipitate was collected by vacuum filtration and recrystallized from acetonitrile/methanol, yielding 0.38 g (26%), dec 400 °C: ^1H NMR (DMSO-d_6) δ 8.53 (s, H^m, 4 H), 8.06 (t, J = 7.7 Hz, H^4, 2 H), 7.56 (d, J = 7.7 Hz, $H^{3,5}$, 4 H), 7.10–7.20 (m, H^b, 8 H).

2·Pb(ClO_4)$_2$.[5f] A mixture of 54 mg (0.5 mmol) of benzene-1,2-diamine, 68 mg (0.5 mmol) of pyridine-2,6-dicarboxaldehyde, 89 mg (0.25 mmol) of $Pb(ClO_4)_2·3H_2O$, and 80 mL of methanol was stirred under N_2 at reflux temperature for 14 h. The reaction mixture was concentrated to 40 mL by boiling and cooled to 0 °C. The yellow precipitate was collected by vacuum filtration and dried in vacuo, affording 150 mg (73%), dec 310 °C: ^1H NMR (DMSO-d_6) 9.71 (s, H^m, 4 H), 8.58 (t, J = 7.7 Hz, H^4, 2 H), 8.32 (d, J = 7.7 Hz, $H^{3,5}$, 4 H), 7.65–7.93 (m, H^b, 8 H); IR (KBr, cm^{-1}) 3090 w, 1625 w, 1585 m, 1285 m, 1185 m, 1125 (br) s, 1050 (br) s, 825 m, 775 m, 750 m, 640 m.

2,6-Bis((phenylimino)methyl)pyridine (6). A mixture of 0.20 g (1.5 mmol) of pyridine-2,6-dicarboxaldehyde, 0.28 g (3 mmol) of aniline, 1 drop of concentrated H_2SO_4, and 150 mL of methanol was stirred under N_2 at room temperature for 16 h. The solvent was removed by rotary evaporation, and the residue was recrystallized from acetonitrile, yielding 0.29 g (68%), dec 300 °C: ^1H NMR (DMSO-d_6) δ 8.68 (s, H^m, 2 H), 8.25 (d, J = 7.7 Hz, $H^{3,5}$, 2 H), 8.11 (t, J = 7.7 Hz, H^4, 1 H), 7.39 (m, H^b, 10 H); IR (KBr, cm^{-1}) 3080 w, 2900 w, 1635 w, 1590 s, 1350 m, 1210 m, 1150 (br) m, 830 m, 775 m, 750 m.

Crystallography. Crystals of **2**·$Sr(CF_3SO_3)_2$ were obtained by slow evaporation of an acetonitrile/benzene solution. Crystal data are as follows: $[SrL(CF_3SO_3)_2]$, $[SrL(OH_2)(CF_3SO_3)_2]$, $Sr_2N_{12}C_{58}H_{36}F_{12}S_4O_{13}$, M = 1615.8, $F(000)$ = 1616, triclinic, a = 17.255 (13) Å, b = 18.992 (21) Å, c = 11.077 (10) Å, α = 89.6 (1)°, β = 109.9 (1)°, γ = 109.8 (1)°, U = 3187.7 Å^3, d_c = 1.68 g cm^{-3}, d_m = 1.70 g cm^{-3}, Z = 4, λ = 0.7107 Å, μ = 19.9 cm^{-1}, space group $P\bar{1}$.

A crystal of approximate size 0.4 × 0.3 × 0.25 mm was set up to rotate about the a axis on a Stoe Stadi2 diffractometer, and data were collected via variable width ω scan. Background counts were for 20 s, and a scan rate of 0.0333°/s was applied to width of (1.5 + sin μ/tan θ). A total of 9201 independent reflections were measured of which 3943 with $I > 3\sigma(I)$ were used in subsequent refinement. An empirical absorption correction was applied.[16] The structure was determined by the heavy atom method. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in calculated positions. The structure was given a weighting scheme in the form $w = 1/[\sigma^2(F) + 0.003F^2]$. The final R value was 0.073 (R_w = 0.073). Calculations were carried out by using SHELX76[17] and some original programs on an Amdahl 5870 computer at the University of Reading, although final cycles of least-squares refinement were carried out on a Cray X-MP at the University of London Computer Centre. In the final cycle of refinement, the maximum shift/error ratio was 0.13. The maximum and minimum peaks in the final difference Fourier map were 0.72 and −0.57 eÅ^{-3}, respectively. Distances in the two coordination spheres are given in Table I. Positional parameters, thermal parameters, remaining dimensions in the molecules, hydrogen atom positions, and observed and calculated structure factor tables are included in the supplementary material.

Table I. Distances (Å) in the Two Coordination Spheres of **2**·$Sr(ClO_4)_2$[a]

molecule A		molecule B	
O(42)–Sr(1)	2.594 (0.020)	O(22)–Sr(2)	2.536 (0.021)
O(44)–Sr(1)	2.952 (0.014)	O(31)–Sr(2)	2.558 (0.017)
O(52)–Sr(1)	2.524 (0.019)	W(1)–Sr(2)	2.640 (0.020)
N(11)–Sr(1)	2.816 (0.014)	N(21)–Sr(2)	2.752 (0.018)
N(14)–Sr(1)	2.651 (0.016)	N(24)–Sr(2)	2.760 (0.018)
N(17)–Sr(1)	2.727 (0.015)	N(27)–Sr(2)	2.758 (0.016)
N(110)–Sr(1)	2.761 (0.014)	N(210)–Sr(2)	2.744 (0.015)
N(113)–Sr(1)	2.658 (0.017)	N(213)–Sr(2)	2.733 (0.012)
N(116)–Sr(1)	2.776 (0.015)	N(216)–Sr(2)	2.746 (0.018)

[a] Estimated standard deviations in parentheses.

Stability Constant Measurements. The K_s value fo **2**·$KClO_4$ in DMSO-d_6 was estimated in ^1H NMR competition experiments with 18-crown-6.[5e] A weighed sample of **2**·$KClO_4$ (4–5 mg) was dissolved in 0.45–0.50 mL of DMSO-d_6 (Aldrich, 99.9 atom % D). The solution (approximately 2 × 10^{-2} M) was transferred to an NMR tube, and a spectrum was obtained. Small amounts of purified 18-crown-6[18] were added with mixing, and spectra were recorded after each addition. The total concentration of 18-crown-6 was measured by integration relative to the signals of **2**·K^+ and free **2**. All species were in rapid exchange, as observed by ^1H NMR at 300 MHz. The fraction of complexed 18-crown-6 (s) was determined from its chemical shift according to eq 1, where $C·K^+$ represents 18-crown-6·K^+, $[C]_t = [C] + [C·K^+]$, δ is the observed chemical shift of 18-crown-6, δ_c is the chemical shift of 18-crown-6 (3.494 ppm) in the absence of **2**·K^+, and δ_o is the chemical shift of $C·K^+$ (3.543 ppm), which was calculated by an iterative method[19] from separate dilution experiments. For each data point the free potassium

$$s = \frac{[C·K^+]}{[C]_t} = \frac{\delta - \delta_c}{\delta_o - \delta_c} \tag{1}$$

concentration was calculated by eq 2 employing the stability constant (K_c) for $C·K^+$. This value (log K_c = 3.2) was also determined by iterative treatment of dilution data.[19] The concentrations of **2**·K^+ and free **2** were

$$[K^+] = \frac{s}{K_c(1 - s)} \tag{2}$$

calculated by means of conservation eqs 3 and 4. Stability constant values for each NMR measurement were averaged to afford the estimated K_s value for **2**·K^+ in DMSO-d_6.

$$[\mathbf{2}·K^+] = [\mathbf{2}·K^+]_o - [K^+] - [C·K^+] \tag{3}$$

$$[\mathbf{2}] = [\mathbf{2}·K^+]_o - [\mathbf{2}·K^+] \tag{4}$$

Ion-selective electrode (ISE) measurements in anhydrous DMSO employed a Corning Model 150 pH/ion meter, a Corning Model 477364 temperature probe, and a Corning Model 46067 Ag/AgCl reference electrode. For potassium determinations, a Corning Model 476220 monovalent cation electrode was conditioned in 0.01 M KCF_3SO_3 in DMSO for 2 days, and the outer reference electrode compartment was filled with 1 M aqueous $NaNO_3$. For sodium determinations, a Corning Model 476210 sodium electrode was conditioned in 0.1 M $NaCF_3SO_3$ in DMSO for 2 days, and the outer reference electrode compartment was filled with 1 M aqueous KNO_3. Stability constants of $NaCF_3SO_3$ and KCF_3SO_3 complexes of 18-crown-6 were determined by titration of solid 18-crown-6 into solutions of the triflate salts. In a typical experiment, the electrode pair was calibrated with 1 × 10^{-4} M and 1 × 10^{-5} M solutions of KCF_3SO_3, giving a slope of log [K^+] vs potential (mv) equal to 59.31. Eight 1–2-mg additions of 18-crown-6 were made to a 1 × 10^{-4} M solution of KCF_3SO_3 in DMSO. Analogous experiments were performed with 18-crown-6 and $NaCF_3SO_3$.

Ion-selective electrode determinations of K_s for **2**·$NaCF_3SO_3$ and **2**·KCF_3SO_3 were performed by competition with 18-crown-6. Solutions of the complexes in DMSO were prepared ranging from 10^{-2} to 10^{-4} M. For each series of measurements the electrode pair was calibrated by using appropriate concentrations of the metal salt in DMSO. For each measurement [$C·K^+$] was calculated by means of eq 5, and then K_s values were calculated as described above for ^1H NMR experiments. Data and calculations for representative ISE titrations are included in the supplementary material.

$$[C·K^+] = \frac{K_c[K^+][C]_t}{1 + K_c[K^+]} \tag{5}$$

Computational Chemistry. Molecular mechanics calculations were carried out on an Amdahl 5870 computer at the University of Reading. Calculations on the metal complexes employed a version of Allinger's MM2 (1980) program[20] which was modified to allow for coordination

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(17) SHELX76 Package for Crystal Structure Determination; Sheldrick, G. M., University of Cambridge, 1976.

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(19) Hartley, F. R.; Burgess, C.; Alcock, R. M. *Solution Equilibria*; Ellis Horwood: Chichester, U.K., 1980; pp 149–152.

(20) Allinger, N. L.; Yuh, Y. H. QCPE Program No. 423, Quantum Chemistry Program Exchange, Department of Chemistry, Indiana University, Bloomington, In 47405, modified version of 1980.

Table II. Molecular Mechanics Parameters Used for Modeling **2**·$SrCl_2$[a]

Bond Stretching

bond	force constant k_s (mdyn Å^{-1})	ideal bond length r_0 (Å)
M–N(py)	99.0	2.4–3.3
M–N(im)	99.0	2.4–3.3
M–Cl	99.0	2.4–3.3
C(ar)–C(ar)	8.067	1.3923
C(ar)–N(im)	4.75	1.475
C(ar)–C(im)	5.20	1.475
C(im)–N(im)	9.60	1.250
C(ar)–N(py)	8.07	1.345

Angle Bending

angle	k_b (mdyn Å^{-1} rad^{-2})	θ_0 (deg)
Cl–M–Cl	0.30	180.0
Cl–M–N	0.30	90.0
N(py)–M–N(py)	0.30	180.0
N(py)–M–N(im)	0.30	60.0, 120.0
N(im)–M–N(im)	0.30	60.0, 120.0, 180.0
M–N(py)–C(ar)	0.30	120.0
N(py)–C(ar)–C(ar)	0.45	120.0
M–N(im)–C(ar)	0.45	120.0
M–N(im)–C(im)	0.45	120.0
N(py)–C(ar)–C(im)	0.63	119.9
C(ar)–N(py)–C(ar)	0.45	120.0
N(py)–C(ar)–C(ar)	0.45	120.0
C(im)–C(ar)–N(py)	0.45	120.0
C(im)–N(im)–C(ar)	0.55	121.4
N(im)–C(im)–C(ar)	0.45	117.2
N(im)–C(im)–H	0.45	120.0

Torsional Strain

angle	V_1 (kcal mol^{-1})	V_2 (kcal mol^{-1})	V_3 (kcal mol^{-1})
M–N(py)–C(ar)–C(ar)	0.00	2.00	0.00
M–N(py)–C(ar)–C(im)	0.00	2.00	0.00
M–N(im)–C(im)–C(ar)	0.00	2.00	0.00
M–N(im)–C(im)–H	0.00	2.00	0.00
M–N(im)–C(ar)–C(ar)	0.00	2.00	0.00
N(im)–C(im)–C(ar)–N(py)	0.00	3.00	0.00
N(im)–C(im)–C(ar)–C(ar)	0.00	3.00	0.00
N(im)–C(ar)–C(ar)–N(im)	0.00	6.00	−1.06
C(im)–N(im)–C(ar)–C(ar)	0.00	3.00	0.00
C(im)–C(ar)–N(py)–C(ar)	−0.27	6.60	0.00
C(ar)–N(py)–C(ar)–C(ar)	0.00	6.00	−1.06
C(ar)–N(py)–C(ar)–C(im)	−0.93	5.33	0.00
N(py)–C(ar)–C(im)–H	0.00	3.00	0.00
N(py)–C(ar)–C(ar)–C(ar)	−0.27	6.00	0.00
H–C(ar)–C(ar)–H	0.00	10.00	0.00
N(py)–C(ar)–C(ar)–H	0.00	6.00	−1.06
C(ar)–C(im)–N(im)–C(ar)	−0.93	8.00	0.00
C(ar)–C(im)–N(im)–H	0.00	12.25	0.00
N(im)–C(ar)–C(ar)–C(ar)	−0.27	6.66	0.00
N(im)–C(ar)–C(ar)–H	0.00	6.00	−1.06

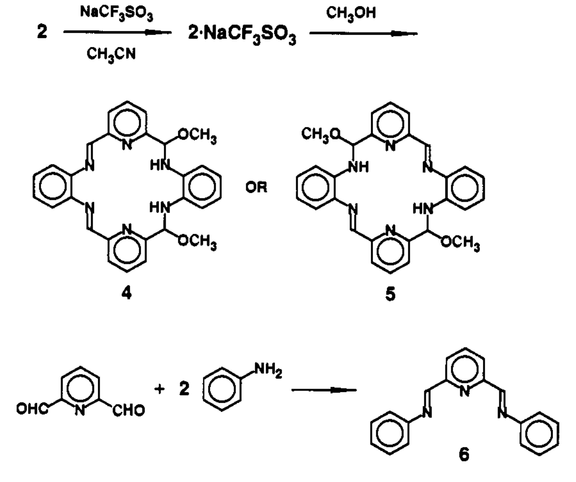
[a] Parameters for other atoms are available in the MM2(80) program (ref 20).

numbers greater than 4[21] and to include periodicity at metal angles. Torsional barriers about coordinate bonds were neglected, and other parameters are listed in Table II. Calculations on the metal-free macrocycles employed the MM2 (1987) program, including special treatment of hydrogen atoms[22] and improved parameters for imines and pyridines.[23] Allinger's method for the treatment of torsion angles within aromatic rings[24] was used with both programs.

Results

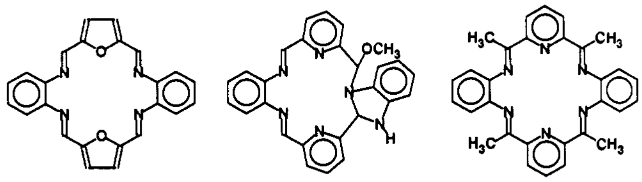
Synthesis. Condensation of benzene-1,2-diamine with pyridine-2,6-dicarboxaldehyde was performed under various conditions. In the absence of a metal salt, the ^1H NMR signals of macrocycle **2** could not be observed in the mixture of crude, apparently polymeric products. Similar product mixtures were obtained when condensations were performed in the presence of sodium or potassium salts (e.g., F^-, I^-, BF_4^-, ClO_4^-, and $CF_3SO_3^-$). Only in the case of KI was an appreciable yield of macrocycle obtained (approximately 12%). Of the six strontium salts attempted (acetate, Br^-, I^-, NO_3^-, ClO_4^-, and $CF_3SO_3^-$) only SrI_2, $Sr(ClO_4)_2$, and $Sr(CF_3SO_3)_2$ gave solid **2**·SrX_2 complexes.

Scheme II



4 5 6

Scheme III



7 8 9

The strontium complexes were all treated with KI, and corresponding potassium complexes (**2**·KX) were isolated by slightly different procedures. Flames tests demonstrated the absence of Sr and the presence of K in the product from **2**·SrI_2, but microanalytical data were not consistent with rational compositions incorporating **2**·KI. This complex was very air-sensitive and decomposed on storage, even under N_2. Correct analytical data were obtained initially for **2**·$KClO_4$, which was used for stability constant estimation by ^1H NMR;[5e] however, the synthesis of analytically pure **2**·$KClO_4$ from **2**·$Sr(ClO_4)_2$ was not reproducible. The triflate complex (**2**·KCF_3SO_3) was reliably obtained from **2**·$Sr(CF_3SO_3)_2$ in high yield and purity, so later complexation and synthetic experiments focused on this material.

Free ligand **2** was obtained by treatment of **2**·KCF_3SO_3 with a large excess of 18-crown-6 in acetonitrile. Macrocycle **2** has low solubility in most solvents and precipitates from the reaction mixture after several minutes. Analytically pure material was obtained after a single recrystallization. This compound may be obtained less economically by reaction of **2**·CF_3SO_3 with 1 equiv of [2.2.2]cryptand. The sodium complex (**2**·$NaCF_3SO_3$) was readily produced by combination of the components in acetonitrile, as shown in Scheme II. The complex could also be formed by reaction of **2**·$Sr(CF_3SO_3)_2$ with excess NaF; however, separation from strontium and sodium salts proved difficult. Attempted recrystallization of **2**·$NaCF_3SO_3$ from methanol led to a metal-free bis-adduct of **2** with methanol, according to spectral and microanalytical data, which are consistent with either structure **4** or **5** (Scheme II). For purposes of spectral comparison, the complexes **2**·$Pb(ClO_4)_2$[5f] and $\mathbf{2}_2$·$Ba(ClO_4)_2$[5f] and compound **6** were synthesized (Scheme II).

Stability Constants. As described previously,[5e] the ^1H NMR chemical shifts of **2**·$KClO_4$ in DMSO-d_6 varied with concentration and in the presence of competing complexing agents. All ligand resonances shifted to lower field with dilution, whereas the effect of adding 18-crown-6 depended on the initial concentration of **2**·$KClO_4$. This behavior suggested that free **2** associated with **2**·$KClO_4$ to form a weaker, but strongly shielded, 2:1 complex.[5e]

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[21] Drew, M. G. B.; Hollis, S.; Yates, P. C. *J. Chem. Soc., Dalton Trans.* **1985**, 1829–1834.

[22] (a) Reference 20, version of 1987. (b) Allinger, N. L.; Kok, R. A.; Iman, M. R. *J. Comput. Chem.* **1988**, *9*, 591–595.

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Table III. Stability Constant Values (K_s) Determined by Titration of **2**·MX with 18-Crown-6

MX	method	[**2**·M$^+$]$_0$^{a} (M)	log K_s (SD)
$KClO_4$^{b}	^1H NMR	1.8×10^{-2}	4.1 (0.3)
$KClO_4$^{b}	^1H NMR	1.7×10^{-2}	4.1 (0.2)
KCF_3SO_3^{c}	ISE	1.0×10^{-2}	4.7 (0.3)
KCF_3SO_3^{c}	ISE	6.0×10^{-3}	3.68 (0.06)
KCF_3SO_3^{c}	ISE	2.3×10^{-3}	3.66 (0.08)
KCF_3SO_3^{c}	ISE	2.5×10^{-4}	3.66 (0.04)
$NaCF_3SO_3$^{c}	ISE	2.1×10^{-4}	3.06 (0.02)
$NaCF_3SO_3$^{c}	ISE	1.2×10^{-4}	3.05 (0.03)

[a] Initial concentration of **2**·MX. [b] Experiment performed in DMSO-d_6. [c] Experiment performed in DMSO.

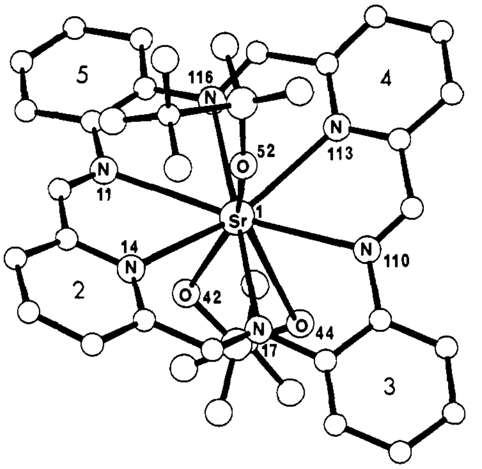

Figure 1. Non-hydrogen atom positions, numbering, and ring labeling for molecule A of **2**·$Sr(CF_3SO_3)_2$.

This phenomenon, the limited solubility range of the complexes, and the poorer solubility of free **2** dictated the determination of K_s values by addition of a competing ligand to solutions of **2**·$KClO_4$, **2**·KCF_3SO_3, or **2**·$NaCF_3SO_3$. As a test of the chemical shift of 18-crown-6 as an indicator of the rapid complexation equilibrium with potassium ion, the stability constant (K_c) of 18-crown-6·$KClO_4$ was determined from a dilution series in DMSO-d_6 by an iterative method.[19] The resulting value of log K_c = 3.4 was previously reported,[5c] but later experiments refined this value to log K_c = 3.2 ∓ 0.2. This is in agreement with the potentiometrically determined value of log K_c = 3.1 for 18-crown-6·$KClO_4$ in DMSO.[25]

By incremental addition of 18-crown-6 to NMR tubes containing $1.7-1.8 \times 10^{-2}$ M solutions of **2**·$KClO_4$ in DMSO-d_6, the stability constant of **2**·K^+ was calculated as log K_s = 4.1. Since this method depends on very small changes in the chemical shift of 18-crown-6 (<0.05 ppm), potentiometric titration was used for more accurate measurement of K_s values for **2**·KCF_3SO_3 and **2**·$NaCF_3SO_3$. In these experiments, glass ion-selective electrodes were used to determine K^+ activity after each incremental addition of 18-crown-6. Resulting log K_s values are compared in Table III with values determined by NMR for **2**·$KClO_4$. The initial concentrations of the complexes are given as [**2**·M^+]$_0$, and errors are expressed as the standard deviations of the 8–16 data points obtained in each titration. Solubility limitations precluded direct determination of K_s by adding the ligand to DMSO solutions of the metal salts.[25]

Structure and Conformation. In the crystal structure of **2**·$Sr(ClO_4)_2$ there are two molecules (A and B) per asymmetric unit with slightly different coordination spheres. These are shown in Figures 1 and 2 together with the numbering scheme. There are no intermolecular contacts shorter than the sum of van der Waals radii. In both molecules the metal atom is bonded to all six nitrogen atoms of the macrocycle (Sr–N = 2.65–2.82 Å in molecule A and 2.73–2.76 Å in molecule B). In molecule A the Sr atom is also bonded to two triflate anions, one via two oxygen atoms (Sr–O = 2.59, 2.95 Å) and the other through just one oxygen (2.52 Å). In molecule B on the other hand, the Sr atom is bonded to two triflate ions, both via only one oxygen atom (Sr–O = 2.54, 2.56 Å) and to a water molecule (2.64 Å). Thus, the Sr atoms in both molecules are formally nine-coordinate. In both molecules, the macrocycles are severely buckled (saddle-shaped), as shown by the least-squares planes calculations given in Table IV. In each structure the four imino groups are approximately planar with the Sr atom on one side of the plane and the two pyridine nitrogen atoms on the other.

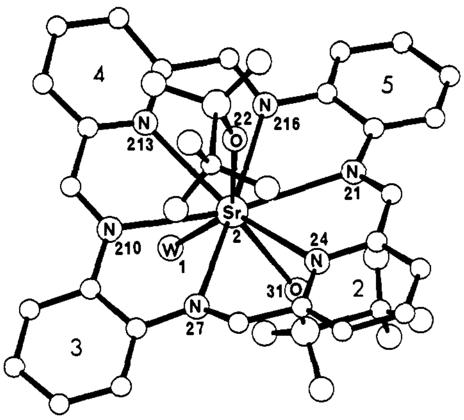

Figure 2. Non-hydrogen atom positions, numbering, and ring labeling for molecule B of **2**·$Sr(CF_3SO_3)_2$, containing one water molecule (W).

Table IV. Least-Squares Planes Calculations for **2**·$Sr(CF_3SO_3)_2$^{a}

molecule A	molecule B
plane 1	plane 1
Sr(1) −0.27, N(11) −0.06, N(14) 0.38, N(17) −0.19, N(110) −0.06, N(113) 0.38, N(116) −0.19	Sr(2) −0.40, N(21) −0.01, N(24) 0.37, N(27) −0.16, N(210) −0.01, N(213) 0.37, N(216) −0.16
plane 2^b (pyridine)	plane 2^b (pyridine)
C(13), N(14), C(15), C(119), C(120), C(121)	C(23), N(24), C(25), C(219), C(220), C(221)
plane 3^b (benzene)	plane 3^b (benzene)
C(18), C(19), C(122), C(123), C(124), C(125)	C(28), C(29), C(222), C(223), C(224), C(225)
plane 4^b (pyridine)	plane 4^b (pyridine)
C(112), N(113), C(114), C(126), C(127), C(128)	C(212), N(213), C(214), C(226), C(227), C(228)
plane 5^b (benzene)	plane 5^b (benzene)
C(117), C(118), C(129), C(130), C(131), C(132)	C(217), C(218), C(229), C(230), C(231), C(232)
plane 6 (imine nitrogens)	plane 6 (imine nitrogens)
N(11) −0.06, N(17) 0.06, N(110) −0.06, N(117) 0.06, Sr(1)^c 0.14, N(14)^c −0.51, N(113)^c −0.49	N(21) −0.06, N(27) 0.07, N(210) −0.07, N(217) 0.07, Sr(2)^c 0.32, N(24)^c −0.45, N(213)^c −0.46
angles between planes (deg)	angles between planes (deg)
2∠3 26.9, 2∠4 39.1, 3∠4 21.1, 2∠5 26.1, 3∠5 31.0, 4∠5 26.1	2∠3 19.4, 2∠4 39.1, 3∠4 21.6, 2∠5 18.0, 3∠5 24.6, 4∠5 25.1
angles between planes in **2**·$Cd(ClO_4)_2$^{d}	
2∠3 32.4, 2∠4 47.9, 3∠4 34.7, 2∠5 36.5, 3∠5 51.5, 4∠5 34.9	

[a] Deviations of atoms from planes given in Å. [b] Planar within experimental error. [c] Atom not contributing to plane. [d] Reference 5f.

Conformations of the macrocycle and cavity size were modeled by molecular mechanics calculations by a method used previously[21,26] for a range of hosts, including 18-crown-6.[26b] In this method the M–N bond lengths are fixed at a specific value by assigning a bond stretching force constant of 99.0 mdyn Å^{-1}. All other parameters in the force field are set at reasonable estimated

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[25] Kohltoff, I. M.; Chantooni, M. K. *Anal. Chem.* **1980**, *52*, 1039–1044.

[26] (a) Drew, M. G. B.; Yates, P. C. *Pure Appl. Chem.* **1989**, *61*, 835–840. (b) Drew, M. G. B.; Nicholson, D. G. *J. Chem. Soc., Dalton Trans.* **1986**, 1543–1549.

Table V. Steric Energies and Geometries of **2**·$SrCl_2$ as a Function of Sr–N Bond Length According to Molecular Mechanics Calculations[a]

M–N bond lengths (Å)	energy (kcal/mol)	angles between planes (deg)		deviations from plane 6 (Å)	
		2∠4	3∠5	M	N(14), N(113)
2.40[b]	35.21	55.6	67.3	−0.25	−0.71
2.50[b]	22.12	49.2	59.4	−0.21	−0.62
2.60[b]	11.98	41.8	50.2	−0.16	−0.52
2.70[b]	4.87	33.2	39.4	−0.12	−0.40
2.80[b]	1.03	23.3	29.2	−0.07	−0.27
2.90[b]	1.24	16.6	19.8	−0.02	−0.11
3.00[b]	6.72	6.6	8.0	−0.01	−0.06
3.10[b]	19.20	3.8	4.4	0.00	−0.03
3.20[b]	38.89	3.3	3.7	0.00	−0.03
3.30[b]	65.74	2.9	3.1	0.00	−0.02
3.00[c]	4.83	29.8	17.6	0.54	−0.31

[a] Planes defined as in Table IV. [b] Hexagonal-bipyramidal geometry fixed with bond stretching force constant of 99.0 mdyn $Å^{-1}$ and L–Sr–L angle force constant of 0.3 mdyn $Å^{-1}$ rad^{-2}. [c] Bond stretching force constant = 99.0 mdyn $Å^{-1}$; L–Sr–L angle force constant reduced to 0.03 mdyn $Å^{-1}$ rad^{-2}.

values. As the structure is minimized, it adjusts to conform to these M–N bond lengths, and the calculated strain energy indicates how well the macrocycle can conform to the stereochemical requirements of the metal atom. The energy is calculated for a series of M–N distances, resulting in a plot of steric energy as a function of M–N bond length. Most of the calculations assumed a hexagonal-bipyramidal coordination geometry produced by six nitrogen atoms in a hexagonal-planar arrangement together with two axial chlorine atoms. The L–M–L angles were essentially fixed at the ideal values of 60, 90, 120, and 180°, by using an angle bending force constant of 0.3 mdyn $Å^{-1}$ rad^{-2}.

The results of molecular mechanics calculations for **2**·$SrCl_2$ are shown in Table V, which lists Sr–N bond lengths, total energies, and least-squares planes calculations. The steric energy of the macrocycle is a minimum at Sr–N bond lengths of 2.845 Å, producing a slightly folded structure (22.9° between pyridine rings and 28.9° between benzene rings). When the Sr–N bond lengths are decreased below 2.9 Å, the macrocyclic ring becomes more severely puckered in the observed saddle conformation. As can be seen from Table V, the angles between the two pyridine rings increase considerably as the M–N bond length is decreased. When the Sr–N bond length is increased above 2.9 Å the six nitrogen atoms, and the four aromatic rings become almost coplanar. Even for very large Sr–N distances (3.2–3.3 Å) the metal atom stayed in the plane, causing severe bond angle strain in the macrocycle. With the hexagonal-bipyramidal coordination constraints at an Sr–N distance of 3.2 Å, the metal was drawn into the plane even when minimization was started from a nonplanar geometry. On the other hand, when the L–Sr–L bending force constant was reduced to 0.03 mdyn $Å^{-1}$ rad^{-2}, a lower energy, distorted hexagonal-bipyramidal structure resulted in which the metal atom resided 0.54 Å above the tetraimine plane (cf. Table V, last entry).

The relative energies of the circular and elliptical conformations of ligand **2** were examined computationally. The crystal structure coordinates of **2**·Sr^{2+} and free **2** were input for minimization by the MM2(87) molecular mechanics program.[22] The MM2(80) calculations on **2**·$SrCl_2$ did not employ explicit nitrogen lone pairs, and C–N dipoles were set to zero because of the difficulty of assigning realistic charges to metal atoms. Calculations on the free ligand were performed first by using the bond moments in the 1987 program: 0.58 D for C–N and 0.60 D for N–LP (lone pair). These results were inconclusive, since the observed elliptical conformation for free **2** had a calculated energy of 7.71 kcal/mol, and the energy of the circular conformation was 8.33 kcal/mol. When the four imine hydrogen atoms were designated type 28 (potentially hydrogen bonding), these energies decreased to −19.76 and −18.5 kcal/mol, respectively. This change also caused the elliptical form to flatten and produced a transannular H–N contact of 2.02 Å, which is shorter than that observed in the crystal structure of **2** (2.1 Å).[5c] The imine hydrogens were then assumed non-hydrogen bonding, but the C–N and N–LP dipoles were increased to 1.07 and 1.11 D, respectively, to simulate the dipole moment of pyridine (2.2 D).[23] This change increased the energies of the elliptical and circular forms to 13.74 and 30.04 kcal/mol, respectively.

The increased-dipole MM2(87) calculations on **2** produced a C_2-symmetric conformation very similar to that observed in the crystal.[5c] The C–N–C–C torsional angles were −28° and −172° for the benzene rings, and the N–C–C–N torsional angles were 12° and −164° for the pyridine rings. The transannular imine H–N contacts were more poorly simulated (2.39 Å). Comparable calculations on the circular form resulted in a shallow saddle conformation with torsional angles ranging from 157° to 160° for the benzene rings (C–N–C–C) and 7° to 8° for the pyridine rings (N–C–C–N).

Discussion

The Schiff base condensation of benzene-1,2-diamine with pyridine-2,6-dicarboxaldehyde (Scheme I) is one of several known 2 + 2 macrocyclization reactions successfully templated by alkaline earth salts.[9b,27] Despite the stabilities of **2**·Na^+ and **2**·K^+, alkali metal salts were far less effective in the template synthesis of **2**. This is consistent with the greater stability expected for alkaline earth complexes of **2** and its cyclization precursor because of the stronger electrostatic attraction between ligand dipoles and a doubly charged guest. The synthesis of **2**·KX from **2**·SrX_2 and KF would appear thermodynamically unfavorable from this point of view. On the other hand, this reaction may be driven either by precipitation of a product (SrX_2 from acetonitrile or **2** from methanol) or by the binding energy of F^- to Sr^{2+}. In contrast to bis(pyridine) macrocycle **2**, bis(furan) analogue **7** (Scheme III) may be obtained in good yield by a 2 + 2 Schiff base condensation templated by KI.[27c]

The availability of **2** makes possible the complexation of metals under very mild conditions. Previous attempts to form complexes of **2** with Mn^{2+}, Fe^{2+}, Co^{2+}, or Zn^{2+} were performed by heating $\mathbf{2}_2$·Ba^{2+} with the corresponding perchlorate salts in methanol.[28] In the resulting complexes the 18-membered ring contracted to the 15-membered ligand **8** (Scheme III). Macrocycle **2** is a stable, isolable all-sp^2 hexaaza[18]annulene, unlike tetramethyl analogue **9**. The latter ligand rearranges to a macrotricyclic derivative in the absence of a metal,[29] and **9**·$Pr(NO_3)_3$ is the only well-characterized complex of this ligand.[13] Limitations of **2** are its generally poor solubility (slightly soluble in CH_3CN, pyridine, and DMSO) and its susceptibility to imine addition reactions. An example of the latter is the conversion of **2**·$NaCF_3SO_3$ to **4** or **5**. The ^1H NMR pattern of this product suggests equivalent but unsymmetrically substituted benzene rings, favoring structure **5**. A methanol addition product was also observed for bis(furan) analogue **7**, although structures corresponding to **4**, **5**, or ring-contracted product **8** could not be distinguished.[27c]

The X-ray crystal structure of complex **2**·$Sr(CF_3SO_3)_2$, together with those of metal-free **2**[5c] [**2**·$Pb(OH_2)$][ClO_4]$_2$(H_2O),[5f] [**2**·$CdClO_4(OH_2)$]ClO_4·CH_3OH,[5f] **9**·$Pr(NO_3)_3$,[13] and the rearrangement product of **9**,[29] provide a good structural basis for comparison. The three complexes of **2** (Sr^{2+}, Pb^{2+}, and Cd^{2+}) all show saddle deformation of the ligand. Whereas Sr is nine-coordinate with the Sr–N contacts ranging from 2.65–2.82 Å, the eight-coordinate Pb and Cd complexes have M–N contacts ranging from 2.65 to 2.85 Å (Pb–N) and 2.50 to 2.79 Å (Cd–N). For Sr the oxygen contacts range from 2.52 to 2.59 Å with a longer

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Table VI. 300-MHz Proton NMR Chemical Shifts for Ligand **2** and Complexes (δ)

	H^m (solvent)		H^4 (solvent)	
compound	DMSO-d_6	C_5D_5N	DMSO-d_6	C_5D_5N
2·$NaCF_3SO_3$		8.99		8.01
2·KCF_3SO_3	8.92[a]	8.86	8.16[a]	8.04
2·$Sr(CF_3SO_3)_2$	9.19	9.23	8.43	8.45
2$_2$·$Ba(ClO_4)_2$	8.53		8.06	
2·$Cd(ClO_4)_2$[b]	9.27		8.50	
2·$Pb(ClO_4)_2$	9.71		8.58	
2		9.52		7.79
6	8.67		8.11	

[a] ^1H NMR chemical shifts were concentration dependent in DMSO-d_6; value calculated from dilution experiments. [b] Reference 5a.

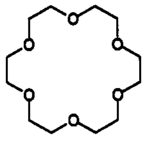
(2.95 Å) Sr–O interaction with a bridging triflate in molecule A and a ligating water (2.64 Å) in molecule B. Corresponding axial interactions for Pb are 2.45 Å for Pb–OH_2 and 2.83 Å with a disordered perchlorate, whereas Cd is bonded to a water molecule (2.24 Å) and to a perchlorate oxygen at 2.33 Å. In both structures the four imine nitrogens form an approximate plane with deviations of −0.30, 0.49, and 0.60 Å for Pb and the two pyridyl nitrogens and −0.11, 0.74, and 0.75 Å for Cd and the pyridyl nitrogens, respectively. As is seen from Table IV, Sr deviates from the imine plane by about the same degree as Pb, whereas the pyridyl rings are more coplanar in **2**·Sr^{2+} than in **2**·Pb^{2+}.

The recent structural study of **9**·$Pr(NO_3)_3$[13] shows an 11-coordinate metal atom bonded to the six nitrogens of the macrocycle (2.65–2.68 Å) and to five oxygen atoms of two bidentate nitrate anions and a solvent methanol molecule. The saddle distortion of this ligand is more severe than in **2**·Sr^{2+}. The crystal structures indicate that the 18-membered macrocycles provide cavities that, if planar, would be too large for Sr^{2+}, Pb^{2+}, Cd^{2+}, and Pr^{3+} and distort by tilting the pyridine and benzene rings to opposite sides of the tetraimine plane. The unusual ^{113}Cd NMR chemical shift of **2**·Cd^{2+} may be a consequence of this mismatch between ion size and cavity size.[5a]

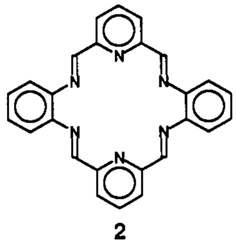
Some information about the solution structure of **2** and its complexes can be derived from a comparison of ^1H NMR data collected in Table VI, which shows the chemical shifts of the imine methine (H^m) and pyridine 4-position (H^4) protons. In part because of solubility limitations, some of the NMR data were obtained in DMSO-d_6 and some in pyridine-d_5; however, Table VI shows that the solvent shift is minor compared with the complexation shifts. All complexes of **2** have H^m and H^4 resonances at lower field than model compound **6**, except for **2**$_2$·Ba^{2+}. In this "sandwich" complex the two macrocyclic ligands apparently shield one another as has been reported for **7**$_2$·$Ba(ClO_4)_2$.[27c] For 1:1 complexes of **2** the H^m chemical shift values are in the order Pd > Cd > Sr > Na > K, in agreement with the corresponding series for **7** (Pb > Sr > Na > K).[27c] The smaller, more highly charged metal ions tend to shift the H^m and H^4 protons to lower field, apparently as a consequence of electrostatic polarization.

As previously reported,[5c] the ^1H NMR spectrum of **2**·K^+ complexes are concentration dependent in DMSO-d_6, the H^m and H^4 resonances shifting slightly to lower field upon dilution. Addition of competing ligands to solutions of **2**·K^+ in DMSO-d_6 produced opposite effects depending on initial concentration. Addition of [2.2.2]cryptand or 18-crown-6 to solutions of **2**·K^+ at higher concentration (approximately 10^{-2} M) gave upfield shifts of H^m and H^4, whereas initial **2**·K^+ concentrations of about 10^{-3} M led to a downfield shift of H^m and an upfield shift of H^4. At higher concentrations free **2** apparently associates with **2**·K^+, forming spectroscopically significant amounts of **2**$_2$·K^+, analogous to **2**$_2$·Ba^{2+}. The octacoordinate ionic radii of K^+ (1.51 Å)[30] and Ba^{2+} (1.42 Å)[30] are similar, but efforts to prepare **2**$_2$·K^+ were fruitless. Decomplexation of **2**·K^+ at lower concentrations gives free **2** as a consequence of the weakness of the sandwich complex (**2**$_2$·K^+ $\rightarrow$ **2**·K^+ + **2**). As seen from Table VI, free ligand **2** has an H^m resonance at even lower field than the Na, K, and Sr complexes, whereas the H^4 resonance occurs at higher field, as expected electrostatically. This result suggests that free ligand **2** exists as a rapidly interconverting mixture of elliptical conformers similar to the solid-state structure.[5c]

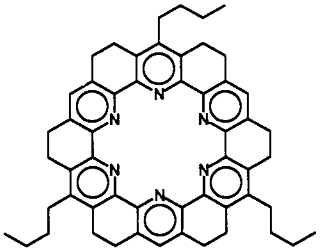
The preceding NMR data indicate that in solution all the complexes of **2** that have been investigated have conformations similar to those of **2**·Cd^{2+}, **2**·Pb^{2+}, and **2**·Sr^{2+}. Even for the alkali metals the slightly puckered ligand forms a distorted hexagonal-planar ligand array, leaving axial sites for two or three additional ligands (counterion and solvent). Host **2** is not completely preorganized, and some of the complexation energy must be used to orient all six nitrogen dipoles toward the cavity. The relative stabilities of **2**·Na^+ and **2**·K^+ are of particular interest in comparison with those of torand alkali metal complexes (**3**·Na^+ and **3**·K^+).[6a]



1



2



3

As observed in Table III, larger stability constants (K_s) were obtained for **2**·K^+ complexes when measured at higher initial concentrations. This suggests that one or more competing equilibria, perhaps involving **2**$_2$·K^+, occur at these concentrations and are not taken into account by the equations used to calculate K_s. At concentrations less than 6×10^{-3} M these equilibria are apparently unimportant, as consistent values of $\log K_s = 3.7$ were obtained by the 18-crown-6/ISE method. By the same method a lower value of $\log K_s = 3.1$ was determined for **2**·$NaCF_3SO_3$ in DMSO. The corresponding values for 18-crown-6 (**1**) are $\log K_s = 3.2$[25] for the potassium complex and $\log K_s = 1.46$[25] for the sodium complex. Hence **2** is a stronger potassium complexing agent than **1** by a factor of 3 but binds sodium by a factor of 140 better than **1**. The resulting K^+/Na^+ selectivity for **2** is only 5, whereas the K^+/Na^+ selectivity of **1** in DMSO-d_6 is 63. Unfortunately, the stability constants for **3**·Na^+ and **3**·K^+ in DMSO are not available; however, torand **3** binds both sodium and potassium very tightly with no observable selectivity in D_2O-saturated $CDCl_3$.[6a] Solvents of lower polarity tend to enhance K^+/Na^+ selectivities,[31] so the graduated change in host structure from **1** through **2** to **3** apparently causes tighter binding but poorer selectivity.

According to the simple notion of best fit between cavity size and ion size,[1c,31b] rigidification of a macrocyclic host would be expected to improve selectivity. In order to probe the effective hole size of **2**, molecular mechanics calculations were carried out by a method used previously for various macrocycles, including 18-crown-6.[21,26] The structure of $SrCl_2$ was constructed as eight-coordinate in order to investigate the relationships between the M–N bond length, macrocycle conformation, and steric energy. Treatment of angles in a nine-coordinate complex would unnecessarily complicate the comparison of folded structures having

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[30] Shannon, R. D. *Acta Crystallogr. A* **1976**, *32*, 751–767.

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short M–N lengths with more planar structures of larger metal atoms. The structural data indicated that two different M–N bond lengths for pyridine and imine nitrogens were not warranted. As indicated in Table II, torsional parameters for the C(im)–C(ar) and N(im)–C(ar) bonds were set to $V_1 = V_3 = 0.0$ and $V_2 = 3.0$ kcal mol^{-1} after some experimentation to model single bond sites of conjugation. In addition, nonbonded interaction parameters for the metal atom were estimated as r^*/Å = 2.50 and ϵ/kcal mol^{-1} = 0.260.

The steric energy of hexagonal-bipyramidal **2**·SrCl$_2$ is minimum for M–N distances between 2.8 and 2.9 Å, as indicated in Table V. This result is consistent with the earlier estimate of 2.8 Å by Honeybourne.[32] The mean M–N distances for known structures are 2.71 Å for Sr, 2.75 for Pb,[5f] and 2.65 for Cd.[5f] According to the appropriate ionic radii (1.31 Å for nine-coordinate Sr, 1.29 Å for eight-coordinate Pb, and 1.10 Å for eight-coordinate Cd),[30] the effective radii of the sp^2-hybridized N atoms of **2** would be 1.4–1.55 Å. Hence metal ions having radii ranging from 1.4 to 1.5 Å would best fit the hole size of host **2**, which is slightly puckered. This puckering or saddle deformation becomes more extreme as the nitrogen atoms move inward to bind smaller metal atoms.

Most of the results of Table V were calculated with a force constant of 0.30 kcal Å^{-1} rad^{-2} for the N–Sr–N angles. This constraint causes unreasonably high steric energies for large Sr–N distances, mostly as a consequence of C–C–N and C–N–C angle deformation in the nearly planar structures. The calculations were therefore repeated with a force constant of 0.03 kcal A^{-1} rad^{-2} for the N–Sr–N angles. The last entry of Table VI shows that for Sr–N = 3.0 Å a nonplanar (distorted hexagonal-bipyramidal) structure results. In this case the energy of the complex increases much less rapidly with the increasing Sr–N bond length, and an energy of only 24.86 kcal/mol is reached at Sr–N = 3.30 Å.

The molecular mechanics calculations on metal-free **2** are consistent with the solution NMR and crystal studies indicating that the elliptical conformation is of lowest energy. Whereas maximum conjugation would be expected in a planar, circular conformation, this appears to be destabilized by dipole–dipole and other interactions. Also in accord with the MM2(80) calculations on **2**·SrCl$_2$, the relaxed circular conformation is saddle-shaped with Ar–C and Ar–N torsions ranging from 7–23°. The corresponding angles in the two molecules of **2**·Sr(CF$_3$SO$_3$)$_2$ range from 0.3–34°. The imine units are more coplanar with the pyridine rings than with the benzene rings in all three cases. Torsion angles of 12–31°, as observed in the crystal structure of **2**, permit partial stabilization by conjugation. It is also suggested by the molecular mechanics calculations that the previously mentioned H–N contacts of 2.1 Å may be weakly hydrogen bonding. Replacement of these hydrogens by methyl groups in macrocycle **9** apparently destabilizes both the elliptical and circular conformations by steric interactions, providing a driving force for rearrangement to the macrotricyclic product isolated.[29] MM2(87) calculations were also performed on 9 and the rearrangement product, resulting in energies of 53.1 and 72.5 kcal/mol for the elliptical and circular conformations of **9**, respectively. On the other hand, the computed energy of the rearrangement product is only 28.6 kcal/mol.

Conclusion

Computational results and structural analysis of the known complexes of **2** both indicate a cavity radius of 1.4–1.55 Å. Potassium, with a nine-coordinate radius of 1.55 Å[30] is expected to fit better than sodium, for which an eight-coordinate radius (1.18 Å)[30] should be used because of its comparable size to Cd and Pb. This comparison makes it difficult to explain the relatively poor K/Na selectivity observed in DMSO. This property is probably not due to poor host preorganization because highly preorganized torand **3** shows even lower selectivity between these ions. A possibility common to **2** and **3** is their openness to axial ligand interactions. Ionic radii increase with coordination number, thus there is an interplay between host/guest fit and axial coordination to counterion and solvent. This is suggested by the formation of the 2:1 sandwich complex of Ba^{2+}, which has a 9-coordinate radius of 1.47 Å (a good 1:1 fit) and a 12-coordinate radius of 1.61 Å.[30] The titration results presented here suggested the equilibrium formation of a similar 2:1 complex of K$^+$, which has a 12-coordinate radius of 1.64 Å.[30] Both **2** and **3** demonstrate that guest encapsulation is not required for formation of strong alkali metal complexes, but more detailed thermodynamic data are required for full interpretation of binding strengths.

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Supplementary Material Available: Tables I–IV of atomic coordinates, remaining dimensions (bond lengths and angles), thermal parameters, and hydrogen atom positions for **2**·Sr(CF$_3$SO$_3$)$_2$, Tables VI–X of titration data and calculations for ISE determination of log K_s values for **2**·KCF$_3$SO$_3$ and **2**·NaCF$_3$SO$_3$, and Table XI of microanalytical data (23 pages); Table V of observed and calculated structure factors for **2**·Sr(CF$_3$SO$_3$)$_2$ (44 pages). Ordering information is given on any current masthead page.

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