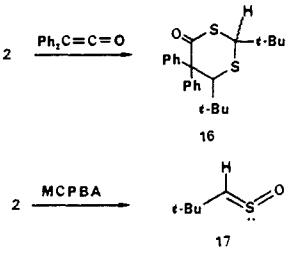
Then, 0.10 mL of a 1.72 M hexane solution of *n*-butyllithium was added via syringe, and the mixture was stirred for 1 h. It was warmed to room temperature overnight and quenched with $H_2O$. The aqueous layer was extracted with pentane, and the organic portions were combined, dried over $MgSO_4$, filtered, and evaporated. The resulting brown oil was eluted through a short silica gel plug with pentane to afford 11.0 mg (75%) of (*E*)-2,2-dimethyl-6-phenyl-3-hexene: oil, separated on silica gel 60 F254, 2% ether-hexane, $R_f$ = 0.58; *m/e*, exact mass for $C_{14}H_{20}$ 188.156, found 188.1565; error = 2.6 ppm; IR (neat, 1/cm) (*t*-Bu) 1380, (C=C) 1670; 270 MHz NMR ($CDCl_3$, ppm) 7.3-7.13 (5 H, m), 5.44 (1 H, dd, *J* = 15.6 Hz), 5.34 (1 H, dt, *J* = 15.6, 5.8 Hz), 2.65 (2 H, dd, *J* = 7.3, 9.6 Hz), 2.28-2.24 (2 H, m), 0.97 (9 H, s).

**Oxidation of 2 with mCPBA.** A solution of **2** in 1 mL of $CDCl_3$ (+repared as above from 5.6 mg of polymer **3**) was cooled to -78 °C under $N_2$, and 182 μL of a 100 mg/mL $CDCl_3$ solution of *m*-chloroperbenzoic acid (Aldrich, 80-85%, 55 μmol) was titrated via syringe to a colorless endpoint. Direct NMR analysis of the reaction medium showed signals corresponding to *m*-chlorobenzoic acid, a trace of trimers 4 and sulfine **17** (identified as the *E* isomer by comparison with literature spectra[22]) in the molar ratio 9.5:1:8.

**Reaction of 2 with Diphenylketene.** Two milliliters of a $CDCl_3$ solution of **2** (generated as above from 12 mg of **3**) were treated under $N_2$ with 0.15 mL of a 0.50 M solution of diphenylketene[26] in benzene. After the pink color had diminished (1 h), solvent was evaporatd and the resulting residue was eluted on a PTLC plate (20% ether-hexane). The $R_f$ 0.59 band was isolated as a 3:1 inseparable mixture of diasteriomers of **16** (11.2 mg, 0.0282 mmol).




**16**: oil, separated on silica gel 60 F254, 20% ether-hexane, $R_f$ 0.59; *m/e*, base = 105 amu; exact mass for $C_{24}H_{30}OS_2$ 398.1731, found 398.1739; error = 2 ppm; IR ($CDCl_3$, 1/cm) (C=O) 1670; 200 MHz NMR ($CDCl_3$, ppm) 7.75-7.28 (10 H, m), 4.8 (1 H, s), 4.43 (1 H, s) 1.19 (9 H, s), 0.76 (9 H, s). Isomer: 200 MHz NMR ($CDCl_3$, ppm) 7.75-7.28 (10 H, m), 4.51 (1 H, s), 4.32 (1 H, s) 1.15 (9 H, s), 0.73 (9 H, s).

**Acknowledgment.** This work was supported by NIH Grant CA17918.

(25) The method of Weinreb was used to synthesize **13**: Hatch, R. P.; Shringapure, J.; Weinreb, S. M. *J. Org. Chem.* **1978**, *43*, 4172.

(26) Zubovics, Z.; Ishikawa, N. *J. Fluorine Chem.* **1976**, *8*, 43.

# Host-Guest Complexation. 38. Cryptahemispherands and Their Complexes[1]

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**Abstract:** Syntheses and crystal structures are reported for a new class of hosts, their complexes, and their precursors. The cryptahemispherands **5-8** are composed of molecular modules that are half spherand **1** and half cryptand **3**. They were synthesized by the reactions of diacid chloride **20** with cyclic diamines **21-23** to produce diamides **13-16**, reduction of which gave the desired hosts **5-8**. These diamines were best purified, stored, and handled through their respective hydroborane complexes, **9-12**. Hosts **6** and **7** are diastereomeric, as are diamides **14** and **15** and hydroborane complexes **10** and **11**. Diamines **6** and **7** equilibrate rapidly at 25 °C probably by ring inversion of the methoxyl groups to give a 5:1 ratio of **6** over **7**. Diamides **14** and **15** equilibrate readily at 90 °C to give only **14** in detectable amounts. Hydroborane complexes **10** and **11** do not equilibrate at 90 °C. Cryptahemispherands **5**, **6**, and **8** formed a variety of complexes with the alkali metal cations, diamides **14** and **16** exhibited a low level of binding power, and hydroborane complexes **10** and **12** had no detectable affinity for the alkali metal cations. Hemispherand **17** was synthesized for comparison purposes. Crystal structures were determined for the isomeric diamides **14** and **15**, for hydroborane complex **9**, and for alkali cation complexes **5**·$NaB(Ph)_4$, **6**·KSCN, **8**·NaSCN, **8**·KSCN, and **8**·$CsClO_4$. The trisanisyl modules of all eight compounds possess the same preorganized conformation, with the unshared electron pairs of the three methoxyl groups turned inward and the methyl groups outward. The potential cavities of **9**, **14**, and **15** are filled with inward-turned hydrogens of the ethylene bridges. In the alkali metal ion complexes, the unshared electron pairs of the heteroatoms are all turned inward toward the guest metal ion. The use of CPK molecular models in predicting the structures of complexes is evaluated.

Structures **1-4** portray a prototypical spherand, a hemispherand, a cryptand, and a chorand, respectively. In prior studies, we compared the binding abilities of these types of hosts toward the alkali metal ions in $CDCl_3$ at 25 °C. We concluded that the spherands > cryptands > hemispherands > chorands > podands > solvents in their binding power toward complementary alkali metal ions. The same order applies to their states of organization for binding and being unsolvated prior to complexation. Extensive examinations of the relationships between structure and binding provided the corollary that the highest specificities in alkali metal ion binding were associated with the most highly preorganized systems.[2,3]

The anisyl groups of the hemispherands are self-organizing, whereas the bridging ethyleneoxy groups can turn their unshared electron pairs and methylene groups either inward or outward, depending on the demands of solvent or guests.[4] Because of this

(1) We gratefully acknowledge support from the Division of Basic Sciences of the Department of Energy for the research on the design, synthesis, and binding properties of the cryptahemispherands (Cram, D. J.; Ho, S. P.) and from the National Science Foundation for support on the crystal structure determinations (Knobler, C. B.; Maverick, E.; Trueblood, K. N.).

(2) Gram, D. J.; Kaneda, T.; Helgeson, R. C.; Brown, S. B.; Knobler, C. B.; Maverick, E.; Trueblood, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 3645-3657.
(3) Cram, D. J.; Lein, G. M. *J. Am. Chem. Soc.* **1985**, *107*, 3657-3668.

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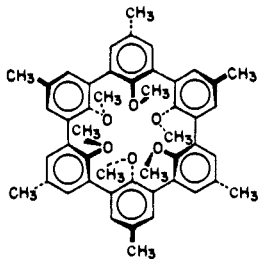
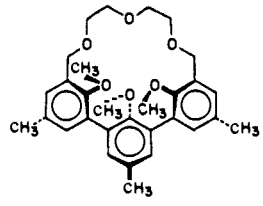


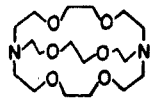
spherand

1



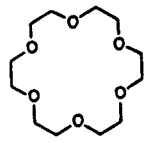
hemispherand

2



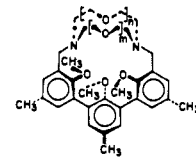
cryptand

3



chorand

4



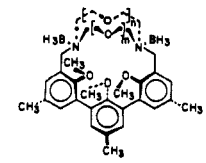
cryptahemispherands

5, m = n = 1

6, m = 2, n = 1

7, m = 1, n = 2

8, m = n = 2



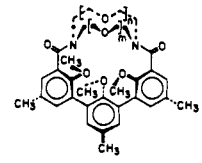
hydroborane complexes

9, m = n = 1

10, m = 2, n = 1

11, m = 1, n = 2

12, m = n = 2

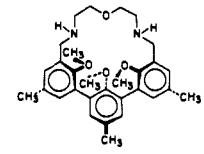


13, m = n = 1

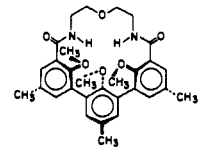
14, m = 2, n = 1

15, m = 1, n = 2

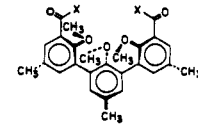
16, m = n = 2



17

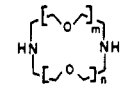


18



19, X = OH

20, X = Cl



21, m = n = 1

22, m = 2, n = 1

23, m = n = 2

blend of rigidity and flexibility, the hemispherands proved to be a particularly good vehicle for studies of structure-binding correlations. Additionally, the hemispherands provide high rates of complexation-decomplexation, chemical stability, and good correlations between predictions based on CPK molecular model examination and their solution and crystal structures.[5,6]

This paper reports the synthesis of the cryptahemispherands **5–8**, hydroborane complexes **9–12**, precursors **20** and **21**, several alkali metal-ion complexes of hosts **5–8**, and eight crystal structures of these macrobicyclic systems. In CPK molecular models, these compounds appear to be more highly preorganized than the cryptands but less than the spherands. We, therefore, anticipated that they should be very strong and specific binders of the alkali metal ions. The diazahemispherand **17** was also prepared for comparison purposes. A companion paper compares the free energies of binding by the cryptands and cryptahemispherands of the alkali metal picrate salts in $CDCl_3$.[7,8]

## Results and Discussion

**Synthesis.** The critical ring-closing reactions to form bicyclic diamides **13–16** involved condensation of diacid chloride **20** with diazachorands **21–23** by procedures similar to those used to prepare the cryptands.[9-11] Diacid **19** has been reported[12] and was converted to **20** with $SOCl_2$ (72%). The experimental part records an improved procedure for making diamine **21**.[13] Diamines **22** and **23** were purchased.[14] The acylations of **20** were conducted at 15–20 °C in benzene by double high dilution addition of each component to a benzene solution of $Et_3N$. The yields of the cyclic diamides decreased with decreasing ring size. Thus **16** was prepared in 90% yield, a mixture of **14** and **15** in 72%, and **13** in 47% yield. As expected, the retention volumes of these cyclic diamides upon purification by gel permeation chromatography increased with decreasing ring size.

Diamides **14** and **15** are geometrical isomers which in principle can interconvert provided all three methoxyl groups ring invert. Examination of CPK molecular models suggested that these isomers should be isolable at room temperature but might interconvert at higher temperatures. In practice, **14** and **15** were separated by HPLC, and **14** was found to dominate in the mixture by a factor of 2:1 when the ring closure was run below 25 °C and by a factor of 12:1 if the reaction temperature was allowed to reach 50 °C. Molecular model examination indicated that the isomer with the longer bridge syn to the *two* methoxyl groups should be less strained than that with the longer bridge syn to the single methoxyl group. Furthermore, in the models of **14** and **15**, the methyls of the methoxy groups on the flanking benzenes of **14** were forced less than those of **15** into the shielding cone of the central benzene, and the methyl on the oxygen of the central benzene was forced more into the shielding cone of the flanking benzene rings. Comparison of the $^1H$ NMR spectra of the two isomers showed that in the dominant isomer, the outer methoxy signal was downfield (less shielded) and the inner methoxy signal was upfield of the corresponding signals of the subordinate isomer. This allowed the dominant isomer to be assigned structure **14** and the subordinate isomer structure **15**. This assignment was confirmed by crystal-structure determination of both isomers (see below).

Although $LiAlH_4$ or $H_3B$·THF reduction of model compound *o*-methoxy-*N*,*N*-dimethylbenzamide went well under a variety of conditions, the cyclic diamides produced many side products. Furthermore, the diamines produced were unstable in chromatography on silica gel. Diamide **13** was successfully reduced only with diborane generated in situ ($NaBH_4 + F_3B{\cdot}O(Et)_2 + THF$)[15] at −78 °C, **14** and **15** as a mixture with the same reagent at 25

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(8) Throughout this paper, the free hosts are drawn in conformations that suggest the presence of cavities. Actually, these cavities are filled either with inward turned methylene groups or with parts of solvent.
(9) Dietrich, B.; Lehn, J.-M.; Sauvage, J. P.; Blanzet, J. *Tetrahedron* **1973**, *29*, 1629–1645.
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(15) Kelley, H. C.; Edwards, J. O. *J. Am. Chem. Soc.* **1960**, *82*, 4842–4846.

°C, and **16** with $H_3B{\cdot}S(CH_3)_2$.[16] The products were isolated as their hydroborane complexes **9–12** (69–78%). These complexes proved stable to chromatographic purification on silica gel. The ratio of **10**:**11** produced in various reductions varied between 5 to 1 and 2 to 1, with **10** as the dominant isomer. Complexes **9–12** were crystalline and could be stored (**9** only at −78 °C). Their $^1H$ NMR spectra suggested the compounds possessed a mirror plane, which indicates that both moles of $BH_3$ are complexed either on the outside or on the inside of the cavity. Since none of the cavities are larger enough to accommodate 2 mol of $BH_3$, the complexing electron pairs on the nitrogens must face outward to coordinate the $BH_3$ on the surfaces of the macrocycles. This conclusion was confirmed by the crystal structure determination of **9** (see below).

Although these complexes were decomposed as expected,[17] upon treatment with hydrochloric acid in THF at reflux, this temperature was high enough to partially cleave the benzyl–nitrogen bonds and to isomerize **7** to **6**. The use of tetramethylenediamine in the isolation was also unsatisfactory, since excess reagent and temperatures higher than 50 °C were required.[17] The hydroborane complexes **9** and **12** were, therefore, oxidatively cleaved with $I_2$[18] in the presence of $Mg(OAc)_2$ buffer (NaOAc provided unwanted host·$Na^+$ complexes). The products in $CH_2Cl_2$ solution were washed with aqueous $(CH_3)_4NOH$ to give unprotonated and noncrystalline cryptahemispherands, **5** and **8**, in 78% and 94% yields, respectively. These hosts slowly decomposed even in the absence of light and air at 0 °C and were, therefore, best freed from their borane complexes just before use. Oxidative decomplexation of **10** gave a product whose $^1H$ NMR spectrum indicated it might be **6**·$I^+I^-$. The spectrum resembled that produced when $I_2$ and **5** were mixed in $CDCl_3$ to give what is probably **5**·$I^+I^-$, identified by its FABMS ($M + I^+$) peak. The cryptands have been found to form stable complexes with $I_2$.[19] When **10** was held at reflux in hydrochloric acid–THF, the $^1H$ NMR spectrum of the product showed it to be a mixture of **6** and **7** and a minor amount of material produced by benzyl–nitrogen cleavage. The mixture was stirred with aqueous KSCN to give **6**·KSCN, identified by crystal-structure determination. Oxidative decomplexation of **11** with $I_2$ gave a product whose $^1H$ NMR spectrum resembled those observed from products similarly produced from **9** and **12** but more complicated. In addition to spectra due to **6** and **7**, less symmetrical isomers also seemed to be present. Treatment of the mixture with KSCN provided **6**·KSCN. We conclude that host compounds **6** and **7** interconvert at room temperature at rates rapid on the human time scale. Complexes **6**·$Li^+$ picrate, **6**·$Na^+$ picrate, and **6**·$K^+$ picrate were prepared and characterized through their $^1H$ NMR spectra. Although **6**·$Na^+$ picrate could be purified by chromatography, **6**·$Li^+$ picrate and **6**·$K^+$ picrate exchanged their metal ions for sodium ions on thick-layer plates of silica gel. Free hosts **8–11** could not be chromatographed without complexing the sodium salts absorbed on stationary phases.

The cryptahemispherands and their complexes were found by $^1H$ NMR experiments to behave somewhat similarly to the cryptands when their metal ion complexes were treated with acid.[20] For example, when $CF_3CO_2D$ was added to a $CDCl_3$ solution of **8**·$Na^+$ picrate, the material decomplexed and formed the diprotonated host ($^1H$ NMR spectral experiments). In a similar experiment with **6**·$Li^+$ picrate, decomplexation also occurred. However, attempts to wash the lithium salts away with water resulted in considerable loss of protonated host due to its dissolution in the aqueous phase. Addition of $CF_3CO_2D$ to **5** in $CDCl_3$ at 25 °C gave the cyclic diammonium salt, which proved to be somewhat soluble in $D_2O$. When a $CDCl_3$ solution of **5** was shaken with $D_2O$ (pH ~5 due to $D_2CO_3$), **5** became protonated, presumably on the outside of the cavity. When excess 3 N aqueous HCl was added to a $CDCl_3$ solution of **5**, the internally diprotonated compound was formed, which gave broad $^1H$ NMR signals. When the excess acid was washed away, the signals sharpened. Stirring the resulting solution at 25 °C for 12 h with 6 N aqueous tetramethylammonium hydroxide failed to deprotonate the amines. This result is similar to that observed for [1.1.1]cryptand and [2.1.1]cryptand.[21,22] Although the cavity of **5** is larger than that of either of those cryptands, it is small enough to hinder fast proton transfer to and from the nitrogens inside the cavity. These experiments indicated that the use of strong acid to convert the hydroborane complexes **9–12** to free hosts **5–8** is troublesome.

Diazahemispherand **18** was prepared for comparison purposes by condensing diacid chloride **20** with $O(CH_2CH_2NH_2)_2$ to give diamide **18** (75%), which was reduced to **17** with $LiAlH_4$ in THF at reflux. Various hydroborane reducing agents gave only bad mixtures of products.

**Isomerization of Diamides 14 and 15.** When bicyclic diamide **15** was held at reflux for 1 h in anhydrous THF (66 °C), $^1H$ NMR spectral measurements showed 80% had isomerized to **14**. A similar experiment run in $(CD_3)_2SO$ at 90 °C for 15 min provided 86% isomerization, whereas prolonged heating (5 h) gave >95% conversion of **15** to **14** (based on a 5% detection limit for **15**). When **14** was submitted to 5 h of heating at 90 °C in $(CD_3)_2SO$, no **15** could be detected in its $^1H$ NMR spectrum. From these experiments, the first-order rate constant for **15** → **14** is estimated to be $\sim 2.3 \times 10^{-3}$ s$^{-1}$ ($\Delta G^{\ddagger} \sim 26$ kcal mol$^{-1}$), and **14** → **15** is $< 5.6 \times 10^{-7}$ s$^{-1}$ ($\Delta G^{\ddagger} > 32$ kcal mol$^{-1}$). Since the same transition state is involved in these two reactions, these values suggest that $\Delta(\Delta G^{\circ})$ for the conversion of **15** → **14** is at least −6 kcal mol$^{-1}$ at 90 °C. When hydroborane complexes **10** and **11** were each heated at 90 °C in $(CD_3)_2SO$ for 5 h, no isomerization could be detected.

During the syntheses described in the last section, acid-catalyzed hydrolysis of hydroborane complex **10** at 66 °C and oxidative cleavage of hydroborane complex **11** at 25 °C both led to mixtures of diamines **6** and **7** in which isomer **6** dominated. Additionally, reduction of diamide **15** with diborane at 25 °C gave mixtures of hydroborane complexes **10** and **11** containing 20–50% of the former isomer. Since **10**, **11**, and **15** were stable to isomerization under the conditions of the above experiments, the results point to **6** and **7** occurring as rapidly interconverting intermediates in the conversions of diamide **14** and **15** to hydroborane complexes, **10** and **11**. The results suggest that at equilibrium at 25 °C, **6** dominates over **7** by a factor of about 5.

These experiments taken in sum indicate the probable order of stability with respect to ring inversion of the three methoxyl groups to be the following: hydroborane complexes > diamides > diamines. This order correlates with expectations based on CPK model examinations of the six compounds involved, coupled with the crystal structure results. Coordination of the outward-turned electron pairs of the two nitrogen atoms to $BH_3$ elongates the molecules along their N to N axis and shrinks them in the dimensions perpendicular to the N to N axis, especially near the mirror plane. Ring inversion requires swelling of the molecules in the region close to their mirror planes to allow the methyl groups to pass through the centers of the macrobicycles. Thus N·$BH_3$ complexation opposes ring inversion. In the diamides, **14** and **15**, both CPK models and the crystal structures indicate that the C=O oxygens are turned outward away from the cavity. The delocalization of electrons in the amide bond requires near coplanarity of the attached substituents. To ring invert **14** or **15**, the $\pi$-orbitals of the C=O groups and the nitrogen lone pair must uncouple. Thus the two diamides resist ring inversion at ambient temper-

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(22) Cox, B. G.; Murray-Rust, P.; van Truong, N.; Schneider, H. *J. Am. Chem. Soc.* **1984**, *106*, 1694–1698.

ature. In contrast, the two bridges of the diamines **6** and **7** are conformationally more flexible. Accordingly, **6** and **7** adapt more readily to the steric requirements of ring inversions of the three methoxyl groups at ambient temperature.

**Qualitative Complexation Experiments.** In contrast to the cryptahemispherands **5**, **6**, and **8**, which were difficult to handle because of their propensity for complexing $Na^+$, the diamides **14** and **15** and the hydroborane complexes **10** and **12** were very poor binders of the alkali metal ions. When solutions of **14** or **16** in $CH_2Cl_2$ were shaken with aqueous solutions of $Li^+$, $Na^+$, $K^+$, $Rb^+$, or $Cs^+$ picrates, **14** extracted only traces of potassium picrate, and **16**, only traces of cesium picrate. When submitted to the usual picrate salt extraction method for determining $-\Delta G°$ values at 25 °C in $CDCl_3$ saturated with $D_2O$, **14** and **16** gave $-\Delta G°$ values of <6 kcal $mol^{-1}$ binding free energies for all ions.[23] When sodium tetraphenyl borate was added as a solid to **16** in $CDCl_3$, it dissolved, and complexation changed the methoxy proton $^1H$ NMR spectral signals by as much as 0.11 ppm. When shaken with $D_2O$, the original spectrum of free **16** was regenerated, indicating the salt decomplexed and washed into the $D_2O$ layer. The low binding power of these diamides is attributed to the repulsions between the partial positive charges on the two nitrogens (which line the cavity) and the positively charged guests. Similar attempts to complex hydroborane derivatives **10** and **12** gave completely negative results. Molecular model examinations of **10** and **12** indicate that formation of cavities in these molecules involves considerable strain.

**Crystal Structures.** Crystal structures of the following eight representative macrobicyclic systems were obtained: diamides **14** and **15**; hydroborane complex **9**; and alkali metal complexes **5**·$NaB(Ph)_4$, **6**·KSCN, **8**·NaSCN, **8**·KSCN, and **8**·$CsClO_4$. Common to all eight crystal structures is the conformational arrangement of the trisanisyl module. The unshared electron pairs of the three methoxy oxygens all face inward toward the potential cavity, which is filled with either methylene hydrogens of the bridges or the encapsulated metal ions. The methyl groups of the methoxyls all face outward away from the potential cavity, those attached to the flanking benzenes being syn to one another and anti to that of the central benzene. Throughout this paper, all structures are viewed from the face of the macroring that places the two $OCH_3$ groups nearer to the eye. The up-down-up arrangement of the $OCH_3$ groups appears to be a property of the molecular module to which the bridging $CH_2OCH_2$ and $CN(CH_2)_2$ units adapt, depending on whether and how the hosts are complexed. Thus the spherand-like module is *preorganized* for binding, whereas the cryptand-like module must conformationally reorganize to allow guests to enter the cavity.[8] These results further substantiate the generalizations that relate the class of host to the state of conformational organization of the cavity prior to the complexing act. Thus the spherands are totally preorganized, the hemispherands and cryptahemispherands are partially preorganized, and the cryptands and chorands are not conformationally preorganized for binding.[2] The spherands, hemispherands, and cryptahemispherands were all designed through examination of CPK molecular models. These eight crystal structures further illustrate the utility of these models for designing new hosts and for predicting their states of preorganization.

In Charts I and II ordinary drawings of the macrocycles are coupled with stereodrawings of the eight crystal structures in which the counterions are omitted unless they coordinate the guest.[8] Only an overview of the structural features are presented here. The details and many interesting comparisons will be published elsewhere.

A comparison of the crystal structures of diamides **14** and **15** indicates why the former is the more stable. The amide modules in the two molecules are essentially normal. In **14**, the average distance of the two N atoms from the plane of their three attached carbons is 0.06 Å; in **15** that distance is 0.08 Å. For both isomers, the distance of the N from the C—C=O plane is 0.00 Å, and the bond lengths and angles are not far from being normal. However, the N···N distance in **14** at 6.48 Å is greater than in **15** at 5.45 Å, which reflects the different effective lengths of the bridges syn to the two methoxyl groups in the two isomers. In the more stable isomer **14** the $OCH_2CH_2O$ conformations are more staggered than they are in **15**. The longer bridge in **15** is more folded and compressed than in **14**. In effect, **14** is more stable than **15** because the longer bridge in **14** is located on the same side of the macroring as the two methoxyl groups, where the route required to span the two nitrogens is longer than on the opposite side.

**Table I.** Molecular Parameters of the Cryptahemispherand Complexes of Alkali Metal Ions

| | **5**·$Na^+$ | **6**·$K^+$ [a] | **8**·$Na^+$ | **8**·$K^+$ [b] | **8**·$Cs^+$ [c] |
|---|---|---|---|---|---|
| | | Distances (Å) | | | |
| N···N | 4.64 | 5.48 | 6.68 | 6.36 | 6.67 |
| N···$M^+$ | 2.64 | 3.09[d] | 3.18 | 3.22 | 3.40 |
| | 2.61 | 3.09[d] | 3.64 | 3.25 | 3.36 |
| O···$M^+$ (av) | 2.40 | 2.84 | 2.68 | 2.88 | 3.03 |
| O···$M^+$ (limits) | 2.34 | 2.73 | 2.53 | 2.83 | 2.91 |
| | 2.46 | 3.21 | 2.78 | 2.94 | 3.15 |
| $M^+$ (diam)[e] | 2.08 | 2.96 | 2.46 | 3.08 | 3.36 |
| | | Angles (deg) | | | |
| Ar–Ar dihedral | 54.1 | 62.6[d] | 50.1 | 55.4 | 55.7 |
| | 54.7 | 62.6[d] | 63.8 | 53.4 | 56.5 |
| N···$M^+$···N | 125 | 125 | 156 | 159 | 161 |
| Ar–O bond to 1,2,6-C Ar plane | 4.15 | 2.72[d] | 0.5 | 1.5 | 0.4 |
| | 0.03 | 2.56 | 1.7 | 0.3 | 3.4 |
| | 1.35 | 2.72[d] | 0.2 | 1.8 | 1.9 |
| | | No. of Ligands | | | |
| | 7 | 8 | 5 | 9 | 9 |

[a] $K^+$ is contact ion-paired to N of $NCS^-$, N···$M^+$ distance, 3.12 Å. [b] $H_2O$ (1 mol) ligates the $K^+$, $K^+$···$OH_2$ distance, 3.44 Å. [c] $H_2O$ (1 mol) ligates the $Cs^+$, $Cs^+$···$OH_2$ distance, 3.56 Å. [d] The identity of these pairs of values is associated with the crystallographic mirror symmetry in the molecule. [e] Calculated assuming the O-atom radius equals 1.40, and the N-atom radius is 1.50 Å.

The crystal structure of hydroborane adduct **9** provides a N···N distance of 5.96 Å and aryl–aryl dihedral angles of 67°. The N–B bond lengths are 1.58 Å, close to the average C–N bond lengths of 1.57 Å. These bond lengths differ from the N–B distance of 1.66 Å and the N–C distances of 1.52 Å observed in the crystal structure of the bishydroborane complex of [2.2.2] cryptand.[24] The fact that the $BH_3$ groups lie outside the cavity forces the N–C bonds to be directed inward, which in turn leads to congestion of the two bridges, a pushing apart of the two nitrogens, and an expansion of the Ar–Ar dihedral angles as compared to complexes where the guests occupy the cavity.

Table I lists some structural parameters of the five cryptahemispherand complexes of the alkali metal ions. Of these, **5**·$Na^+$, **6**·$K^+$, and **8**·$Cs^+$ are very stable complexes based on picrate salt binding studies in $CDCl_3$.[7] The sodium ion in **5**·$Na^+$ exhibits strong interactions with all of its ligands. The $Na^+$···N and $Na^+$···O distances are all close to the standard values of 2.66 Å and 2.35 Å, respectively.[25] There are no interactions with external ligands; molecular models indicate there is little room for any. The Ar–Ar dihedral angles are ~55°. The diameter of $Na^+$ bound to the seven heteroatoms is 2.14 Å, which is greater than the diameter of 1.75 Å for $Na^+$ bound to six ligands in **1**·$Na^+$.[2] As expected from the short bridges, the N···N distance of 4.64 Å is shorter than is observed in any of the other eight crystal structures.

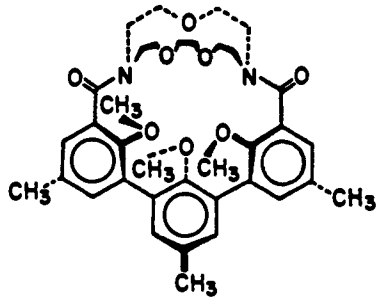
The potassium ion in **6**·$K^+$ interacts strongly with seven of its eight ligands. The $K^+$···N distance of 3.09 Å is not far from the standard value of 2.83 Å.[25] For reasons not understood, the central

(23) Helgeson, R. C.; Weisman, G. R.; Toner, J. L.; Tarnowski, T. L.; Chao, Y.; Mayer, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 4928–4941.

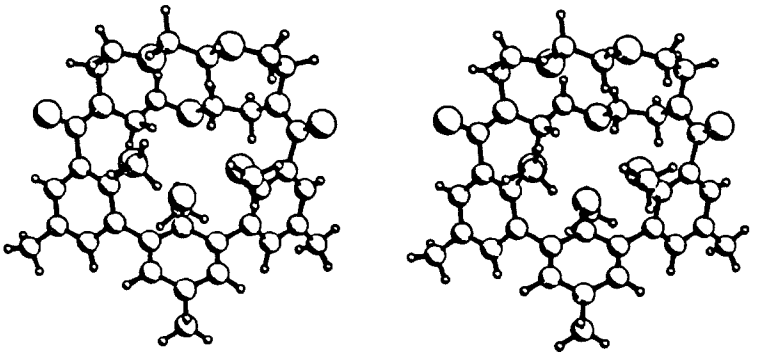
(24) Metz, B.; Moras, D.; Weiss, R. *J. Chem. Soc. Perkin Trans. 2* **1976**, 423–429.

(25) These values were obtained by adding the ionic radii of the metal ions to the van der Waals radii of the ligating atoms. Values were taken from Pauling, L. C. *Nature of the Chemical Bond*, 2nd ed.; Cornell: Ithaca, New York, 1940; pp 189, 350.

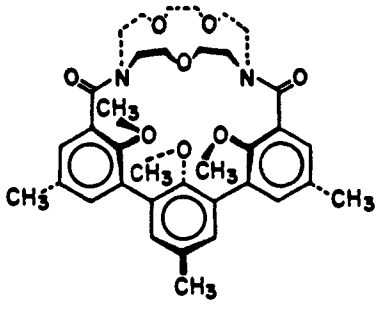
Chart I



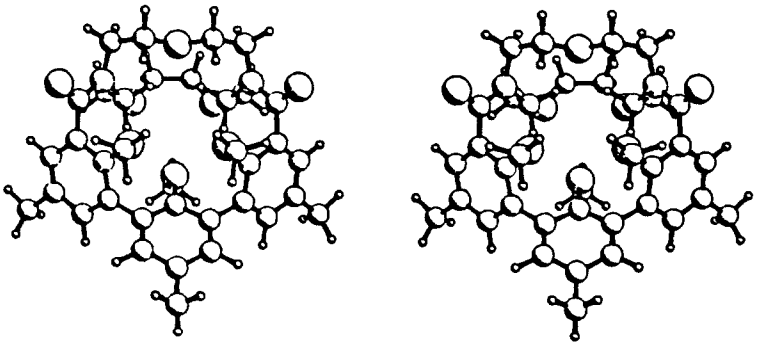
14



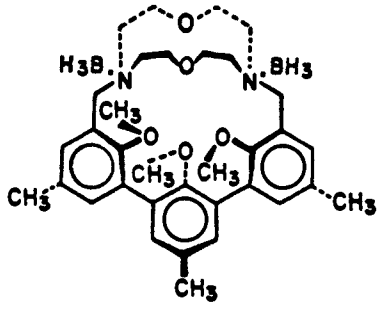
14



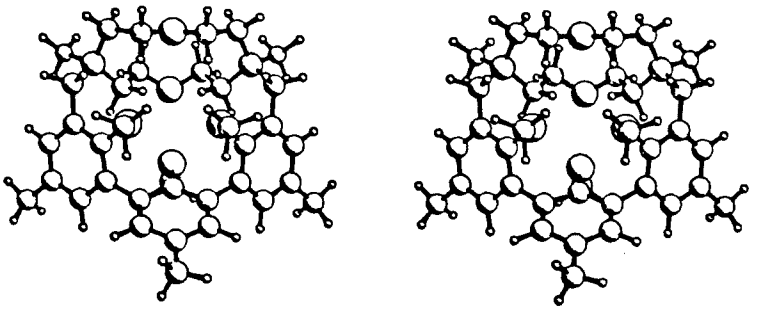
15



15



9



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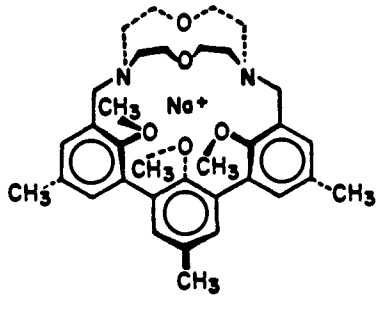
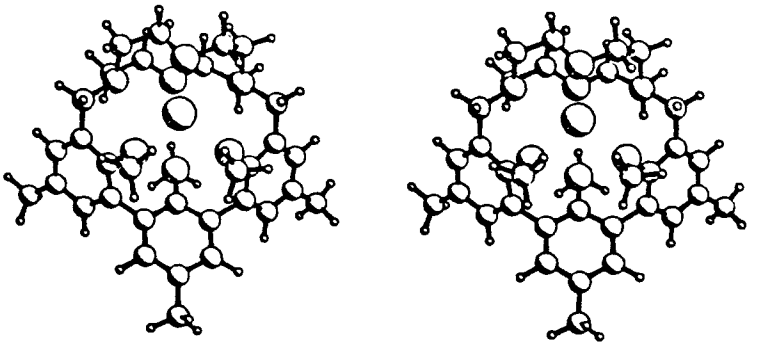
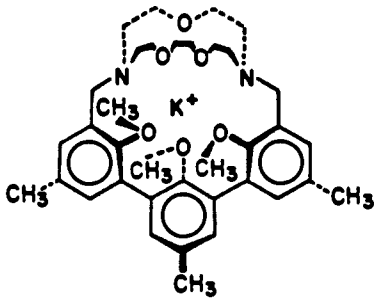


5·Na$^+$

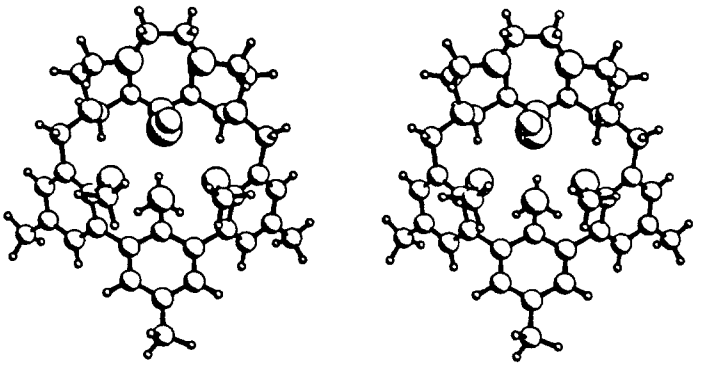


5·Na$^+$

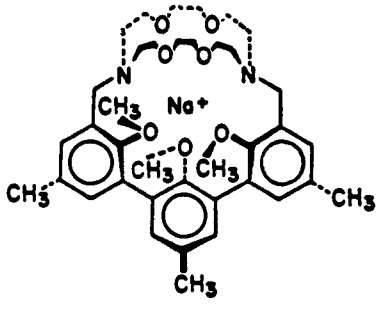
Chart II



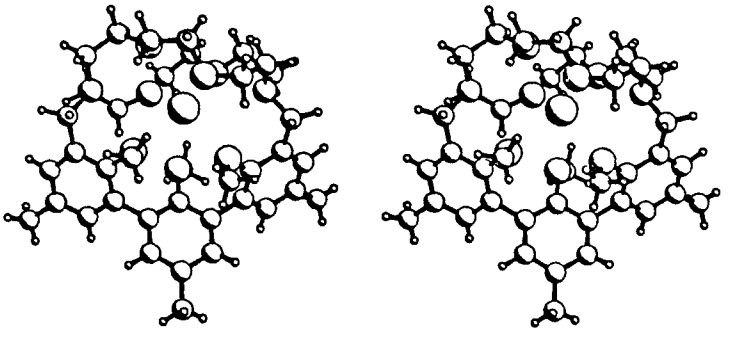

6·K+



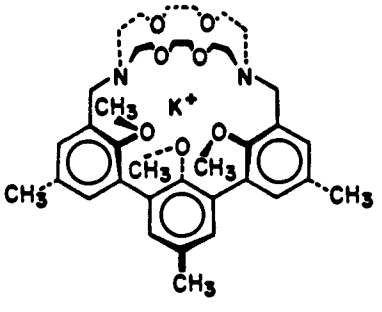
6·K+



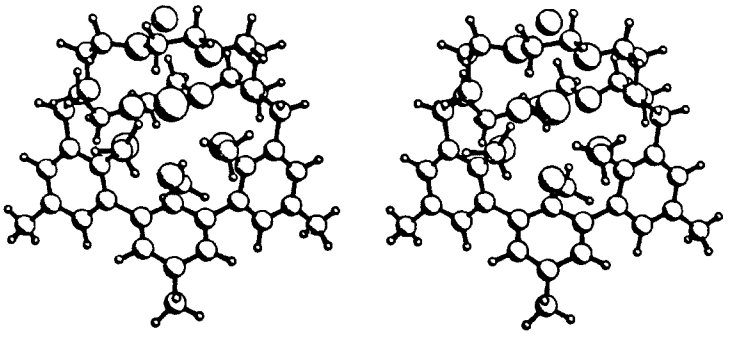

8·Na+



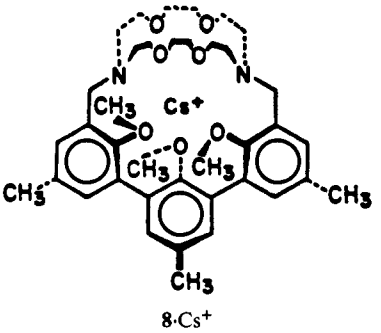
8·Na+



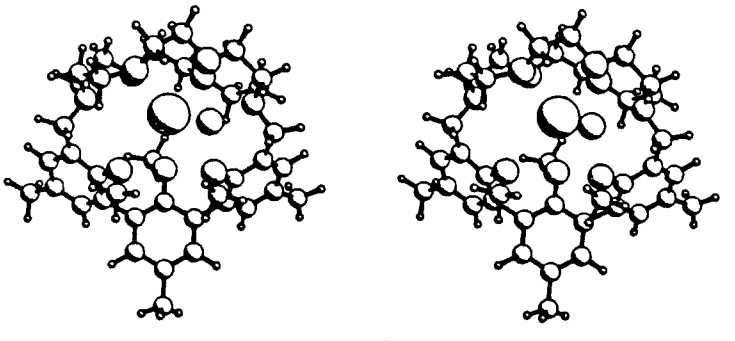

8·K+



8·K+




8·Cs+



8·Cs+

methoxy oxygen is 3.21 Å from the $K^+$, which is also reflected in the high aryl–aryl dihedral angle of 63°. The N of the thiocyanate coordinates the $K^+$ in complex in the middle of the area defined by the two syn methoxyl groups and the two oxygens of the longer bridge. The distance from $K^+$ to the N of the counterion is 3.12 Å, close to the $K^+$···N distance for the two neutral nitrogen ligands (3.09 Å).

Molecular model examination of **8**·$Na^+$, **8**·$K^+$, and **8**·$Cs^+$ suggests good complementarity for **8**·$Cs^+$, moderate complementarity for **8**·$K^+$, and poor complementarity for **8**·$Na^+$. The crystal structures of the three complexes confirmed the expectation and show how the hosts in **8**·$Na^+$ and **8**·$K^+$ adapt to their smaller-than-ideal guests. The two $Na^+$···N distances are 3.18 and 3.64 Å, well-above the standard value of 2.45 Å.[25] Five of the $Na^+$···O distances are between 2.53 and 2.69 Å, while the other two are 2.78 and 2.85 Å, compared to the standard distance of 2.35 Å.[25] Because of spacial constraints, the cavity of **8** is unable to contract enough to allow all eight of its heteroatoms to ligate the $Na^+$ at the same time. As a consequence, the cavity diameter is not notably dissimilar from that of **8**·$Cs^+$. This is shown by the facts that the N···N distances are almost identical (6.68 Å for **8**·$Na^+$ and 6.67 Å for **8**·$Cs^+$) and the average Ar–Ar dihedral angles are very similar (57° for **8**·$Na^+$ and 56° for **8**·$Cs^+$). In effect, the $Na^+$ ligates the five oxygens close to one of the nitrogens, and the cavity is unfilled except in this region. The apparent $Na^+$ diameter is 2.56 Å, much greater than normal. In solution, the $Na^+$ in **8**·$Na^+$ is undoubtedly "rattling around" in the cavity.

The host is **8**·$K^+$ adapts somewhat differently. The normal diameter of $K^+$ *is* large enough for all nine ligating sites to be within reach of the metal ion with a small contraction of the cavity. Thus the N···N distance in **8**·$K^+$ shrinks to 6.36 Å, and the Ar–Ar dihedral angle shrinks to an average value of 54°. The N···$K^+$ distances are 3.22 and 3.25 Å compared to the standard values of 2.83.[25] The average O···$M^+$ distance is 2.88 Å (seven values ranging only from 2.83–2.94) compared to the standard value of 2.73 Å.[25] These comparisons suggest that the $K^+$ ion is ligated by all nine heteroatoms to give a $K^+$ diameter of 2.96 Å. Water (1 mol) also coordinates the $K^+$ at a $H_2O$···$K^+$ distance of 3.44 Å. Its oxygen is surrounded by the four oxygens and the two nitrogens of the bridge. A simple way to visualize the complex is to notice that the four oxygens and two nitrogens in the bridges compose a diaza-18-crown-6 whose heteroatoms are within ±0.4 Å of being coplanar. On one face of the best plane are found the three methoxy oxygens, and centered on the other face is the oxygen of the ligating water molecule.

Comparisons of the N···$Cs^+$ and O···$Cs^+$ distances in **8**·$Cs^+$ with the standard values of 3.19 and 3.09 Å, respectively,[25] show that $Cs^+$ has strong interactions with all nine ligands of the host. The two N···$Cs^+$ distances are 3.40 and 3.36 Å, whereas the O···$Cs^+$ average distance is 3.03 Å, the values ranging from 2.91 to 3.15 Å. Thus **8** appears to be a nearly ideal host for $Cs^+$. It provides a $Cs^+$ diameter of 3.26 Å. Interestingly, **8**·$Cs^+$ is also bound to a mol of water located in a position different from that in **8**·$K^+$. The oxygen of the water lies between the two oxygens of the syn-methoxy groups and the two oxygens of the proximate bridge, similar to where the $SCN^-$ counterion contacts $K^+$ in **6**·$K^+$.

The N···$M^+$···N angles provide a general measure of how much the diazacrown moiety is folded about the axis of the two nitrogens in the five metal-ion complexes. This angle would be 180° in the absence of folding. In **5**·$Na^+$ and **6**·$K^+$, the N···$M^+$···N angles are both 125°, which provides 180° − 125° = 55° of folding of the bridging ring. In **8**·$Na^+$, **8**·$K^+$, and **8**·$Cs^+$, the folds of the bridging ring are 24, 21, and 19°, respectively.

A comparison of the structural parameters of the parent spherand complex **1**·$Na^+$[2] with those of **5**·$Na^+$ is instructive. The respective values are as follows: $Na^+$ diameter, 1.75 Å (six ligands), 2.14 Å (seven ligands); average aryl–aryl dihedral angles, 61 and 56°; average angle between aryl–oxygen bond and the 1,2,6-aryl carbon plane, 1.8 and 1.8°; average angle of fold of aryl around the O–Ar–$CH_3$ axis, 4.8 and 5.4°; average angle between $CH_3OC$ plane and the best aryl plane, 84 and 77°; and the average $ArOCH_3$ bond angle, 114 and 113° (normal angle is 118°). Taken in sum, these parameters are remarkably alike considering that half of one complex differs radically from half of the other complex.

## Experimental Section

**General Methods.** THF and diethyl ether were freshly distilled from sodium benzophenone ketyl just prior to use, $CH_2Cl_2$ from $CaH_2$, and benzene from $LiAlH_4$. All other solvents were dried over 3-Å molecular sieves. All chemicals were reagent grade. All reactions were conducted under an argon atmosphere. Flash chromotography was carried out on silica gel 60 (E. M. Merck, particle size 0.040–0.063 mm, 230–400 mesh ASTM). Gravity columns were packed with silica gel 60 (E. M. Merck, particle size 0.063–0.200 mm, 70–230 mesh ASTM). Gel permeation chromatography was performed on a 20 ft by 0.375 in. (o.d.) column packed with 200 g of styragel (Waters Associates) with $CH_2Cl_2$ as mobile phase at flow rates of approximately 4.0 mL per min. Preparative thin-layer chromotography was effected on 0.5 mm, 1 mm, or 2 mm silica gel plates (E. M. Merck, 60 $F_{254}$) or 1 mm reverse phase silica gel plates (PLKC 18F, Whatman). Thin-layer chromatography was conducted on plastic-backed precoated silica gel plates (E. M. Merck, $F_{254}$, 0.2 mm thickness) and reverse phase plates (Whatman, KC 18F, 0.2-mm thickness). High-pressure liquid chromatography was performed on a Waters Prep LC/System 500A liquid chromatograph. The compounds were purified on either one or two PrepPAK silica cartridges containing approximately 500 g of silica gel each. Melting points below 240 °C were measured on a Thomas-Hoover melting point apparatus. Those above 240 °C were measured on a Mel-Temp apparatus. All melting points are uncorrected. Infrared spectra were obtained on a Perkin-Elmer 297 grating spectrophotometer. Ultraviolet spectra were recorded on a Varian Cary 219 spectrophotometer. Mass spectroscopy was performed on an AE1 model MS-9 double-focusing spectrometer interfaced by Kratos Company to a Data General Nova 3. Regular mass spectra were recorded at 16 or 70 eV at the temperatures indicated. FABMS were conducted by using xenon ionization techniques at 25 °C (6 kV, 1 mA) in a thioglycerol matrix. Proton NMR spectra were obtained at 200.1 MHz on a Bruker WP-200 spectrometer. Chemical shifts refer to tetramethylsilane as standard and $CHCl_3$ at $\delta$ 7.24 as reference. All elemental analyses were within 0.30% of theory unless otherwise listed.

**2,2′,2″-Trimethoxy-5,5′,5″-trimethyl[1,1′:3′,1″-terphenyl]-3,3″-dicarbonyl Dichloride (20).** Diacid **19** (1.0 g, 2.2 mmol) was placed in a flask capped with a septum and flushed with argon. Thionyl chloride (1.6 mL, 22.2 mmol) which had been purified by distilling from triphenyl phosphite was added. The resulting mixture was stirred at 25 °C. The diacid was gradually dissolved. After 45 min, 30 mL of dry benzene was added to the paste, and the solution was evaporated to remove the excess thionyl chloride. This procedure was repeated twice. The product (97%, 1.1 g) was dried on the vacuum pump and used directly in the next reaction: $^1H$ NMR ($CDCl_3$) $\delta$ 2.37 (s, 3 H, Ar$CH_3$), 2.42 (s, 6 H, Ar$CH_3$), 3.20 (s, 3 H, O$CH_3$), 3.57 (s, 6 H, O$CH_3$), 7.18 (s, 2 H, Ar*H*), 7.46 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.83 (d, 2 H, $J$ = 1.9 Hz, Ar*H*); IR 1770 $cm^{-1}$.

**1,7-Dioxa-4,10-diazacyclododecane (21).** Phosphorus pentachloride (58 g, 0.28 mol) was added to diglycolic acid (16 g, 0.12 mol), and the mixture was dissolved in 200 mL of $CHCl_3$. After stirring for 15 min at 25 °C, the solution was refluxed for 2 h, and the $POCl_3$ and HCl were evaporated. The residue was fractionally distilled at 0.1–0.4 mmHg, and the 2,2-oxybis(acetyl chloride) was collected between 39–42 °C, the bath temperature being maintained below 80 °C. The product [13.1 g (64%); $^1H$ NMR $\delta$ 4.57 (s, 2 H, C$H_2$)] was used to react directly with 1,5-diamino-3-oxapentane, which was prepared as follows. Ammonia gas was bubbled for 30 min through a vigorously stirred suspension of 2,2-oxybis(ethylamine) dihydrochloride (3.0 g, 17 mmol) in 50 mL of $CHCl_3$–10% $CH_3OH$ (v). The suspension dissolved and was replaced by a white precipitate, which was collected. The solvent of the filtrate was evaporated under reduced pressure to give the diamine, which was distilled at 8 mmHg [bp 42–44 °C; 1.7 g (94%); $^1H$ NMR ($CDCl_3$) $\delta$ 1.40 (s, 4 H, N$H_2$), 2.87 (t, 4 H, $J$ = 5.1 Hz, $CH_2$N), 3.49 (t, 4 H, $J$ = 5.1 Hz, $CH_2$O)]. This diamine (3 g, 26.3 mmol) in 50 mL of anhydrous benzene and 2,2-oxybis(acetyl chloride) (2.45 g, 13.2 mmol) in 50 mL of anhydrous benzene were placed in separate gas-tight syringes and added via a syringe pump to a 2-L Morton flask containing 1 L of violently stirred anhydrous benzene (25 °C, 20 min). The precipitate was collected and washed with hot $CHCl_3$, and the filtrates were evaporated to give a residue which was recrystallized from $CHCl_3$–heptane to produce 1.6 g (60%) of 5,9-dioxo-1,7-dioxa-4,10-diazacyclododecane [mp 169–173 °C (lit.[13] mp 182–183 °C), $^1H$ NMR $\delta$ 3.47 (t, 4 H, $J$ = 4.9 Hz, $CH_2$NH), 3.65 (t, 4 H, $J$ = 4.9 Hz, $CH_2$O), 4.12 (s, 4 H, CO$CH_2$O), 7.16 (brs, 2 H, N*H*)]. The diamine salt produced as the other product was recovered and recycled. The above lactam (2.0 g, 10 mmol) was

placed in a paper thimble of a Soxlet. A solution of $LiAlH_4$ (2.0 g) in 300 mL of freshly distilled THF (purity is important) was refluxed for 3 days to slowly dissolve the lactam and reduce it. The flask was cooled and stirred successively with 1.2 mL of $H_2O$, 4 mL of pure THF (purity is important), 2.2 mL of 15% aqueous NaOH, 3.6 mL of $H_2O$, and 6 mL of pure THF. The white gelatinous precipitate was rinsed with 250 mL of pure THF. The combined organic layers were evaporated to give white crystals of **21** [1.60 g (93%), mp 80–83 °C (lit.[13] 83–84 °C), $^1H$ NMR ($OCl_3$) $\delta$ 2.16 (brs, 2 H, N*H*), 2.78–2.87 (m, 8 H, $CH_2$N), 3.60–3.68 (m, 8 H, $CH_2$O)].

**36,37,38-Trimethoxy-5,10,15-trimethyl-22,25,30,33-tetraoxa-1,19-diazapentacyclo[17.8.8.1$^{3,7}$.1$^{13,17}$]octatriaconta-3,5,7(38),8,10,12-(37),13,15,17(36)-nonaene-2,18-dione (16). Procedure A.** Diacyl chloride **20** (2.44 g, 5.01 mmol) was dissolved in 250 mL of anhydrous benzene and transferred in 50-mL portions to a 50-mL gas-tight syringe. Similarly, diamine **23** (1.31 g, 5.01 mmol) together with triethylamine (1.52 mL, 10.9 mmol, distilled from tosyl chloride) in 150 mL of anhydrous benzene was transferred to a 50-mL gas-tight syringe. These solutions were added (3 h) via a syringe pump to an oven-dried 2-L Morton flask containing 1200 mL of vigorously stirred anhydrous benzene. The precipitated $Et_3NHCl$ was collected, the filtrate was evaporated, and the residue was purified by gel chromatography with $CH_2Cl_2$ as the mobile phase. Fractions of the main peak of retention volume of 132 mL were combined and evaporated to give 3.05 g (90%) of **16** which was pure by $^1H$ NMR. A small sample was recrystallized from $CHCl_3$–$CH_3OH$ for elemental analysis: mp 309–320 °C dec; $^1H$ NMR ($CDCl_3$) $\delta$ 2.34 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.71 (s, 3 H, O$CH_3$), 3.37 (s, 6 H, O$CH_3$), 3.07–3.50, 3.60–3.95 (m, 22 H, N$CH_2$, O$CH_2$), 4.29 (d, 2 H, $J$ = 14.0 Hz, $CH_2$N), 7.08 (d, 2 H, $J_m$ = 0.5 Hz, Ar*H*), 7.15 (d, 2 H, $J_m$ = 0.5 Hz, Ar*H*), 7.24 (s, 2 H, Ar*H*); IR 1625 cm$^{-1}$; MS (180 °C 16 eV), 676 ($M^+$, 85), 645 ($M^+ - OCH_3$, 100). Anal. Calcd for $C_{38}H_{48}N_2O_9$: C and H.

**33,34,35-Trimethoxy-5,10,15-trimethyl-22,25,30-trioxa-1,19-diazapentacyclo[17.8.5.1$^{3,7}$.1$^{13,17}$]pentatriaconta-3,5,7(35),8,10,12-(34),13,15,17(33)-nonaene-2,18-dione (14 and 15).** Diamine **22**, a highly deliquescent compound, was quickly weighed (0.45 g, 2.06 mmol) and dried on the vacuum pump for 2 days. It was submitted to procedure A along with $Et_3N$ (0.63 mL, 4.49 mmol) and **20** (1.0 g, 2.06 mmol) with an addition time of 1 h. The fractions with a retention volume of 146 mL (gel permeation chromatography) produced 0.93 g (72%) of a mixture of isomers **14** and **15** pure to $^1H$ NMR [MS (180 °C, 16 eV), 632 ($M^+$, 68), 601 ($M^+ - OCH_3$, 100)]. The mixture of isomers pure to $^1H$ NMR, was separated by HPLC, 500 mg at a time, with two 500-g columns connected in series with $CH_2Cl_2$–1% $CH_3OH$ (v) as the mobile phase with essentially base line separation in a 5:2 ratio. The major isomer **14** was crystallized from $CH_2Cl_2$–$(CH_3)_2CO$, mp 337–345 °C dec; $^1H$ NMR ($CDCl_3$) $\delta$ 2.34 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.62 (s, 3 H, O$CH_3$), 3.38 (s, 6 H, O$CH_3$), 2.95–3.30, 3.65–4.23 (m, 18 H, N$CH_2$), 4.42 (d, 2 H, $J$ = 15.2 Hz, N$CH_2$), 7.11 (s, 2 H, Ar*H*), 7.13 (s, 2 H, Ar*H*), 7.25 (s, 2 H, Ar*H*); IR 3000, 1615 cm$^{-1}$; UV ($CHCl_3$) $\lambda_{max}$ 284 nm, $\epsilon$ 7355. Anal. Calcd for $C_{36}H_{44}N_2O_8$: C and H.

The minor isomer **15** was crystallized from $CH_2Cl_2$–$CH_3OH$ and decomposes without melting above 350 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 2.36 (s, 6 H, Ar$CH_3$), 2.44 (s, 3 H, Ar$CH_3$), 2.72 (s, 3 H, O$CH_3$), 3.28 (s, 6 H, O$CH_3$), 2.94–3.10, 3.15–3.83 (m, 18 H, N$CH_2$, O$CH_2$), 4.70 (d, 2 H, $J$ = 17.0 Hz, N$CH_2$), 7.04 (s, 2 H, Ar*H*), 7.23 (s, 2 H, Ar*H*), 7.25 (s, 2 H, Ar*H*); IR 3000, 1625 cm$^{-1}$; UV ($CHCl_3$) $\lambda_{max}$, 285 nm, $\epsilon$ 5268. Anal. Calcd for $C_{36}H_{44}N_2O_8$: C and H.

**30,31,32-Trimethoxy-5,10,15-trimethyl-22,27-dioxa-1,19-diazapentacyclo[17.5.5.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]dotriaconta-3,5,7(32),8,10,12(31),13,15,17-(30)-nonaene-2,18-dione (13).** Diamine **21** (0.14 g, 0.8 mmol), 0.24 mL of $Et_3N$, and diacid chloride **20** (0.39 g, 0.8 mmol) were submitted to procedure A with an addition time of 40 min. The fractions with a retention volume of 153 mL (gel permeation chromatography) produced **13** mixed with $Et_3N$. The sample was dissolved in $CH_2Cl_2$, the solution was washed with water, 3 N aqueous NaOH, and brine, dried ($MgSO_4$), and evaporated to give 0.22 g (47%) of white crystals of **16**, a small sample of which was recrystallized from $CH_2Cl_2$–$(CH_3)_2CO$, mp 305–317 °C dec; $^1H$ NMR ($CDCl_3$) $\delta$ 2.37 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.70 (s, 3 H, O$CH_3$), 3.27 (s, 6 H, O$CH_3$), 3.10–3.35, 3.58–3.97 (m, 14 H, N$CH_2$, O$CH_2$), 4.68 (d, 2 H, $J$ = 14 Hz, N$CH_2$), 7.05 (d, 2 H, $J_m$ = 1.6 Hz, Ar*H*), 7.23 (d, 2 H, $J_m$ = 1.6 Hz, Ar*H*), 7.25 (s, 2 H, Ar*H*); IR 1630 cm$^{-1}$; MS (180 °C, 16 eV), 588 ($M^+$, 100), 557 ($M^+ - OCH_3$, 29). Anal. Calcd for $C_{34}H_{40}N_2O_7$: C and H.

**Hexahydro{(36,37,38-trimethoxy-5,10,15-trimethyl-22,25,30,33-tetraoxa-1,19-diazapentacyclo[17.8.8.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]octatriaconta-3,5,7-(38),8,10,12(37),13,15,17(36)-nonaene-$N^1$:$N^{19}$)}diboron (12). Procedure B.** Lactam **16** (0.24 g, 0.35 mmol) was dissolved in 40 mL of anhydrous THF and heated. When the solvent started to boil, borane methyl sulfide (9.9 mmol) was added, and the methyl sulfide was slowly distilled away. The reaction was followed by TLC. After about 50 min all the starting material had reacted, and TLC showed a main spot near the solvent front (10% $CH_3OH$ in $CH_2Cl_2$ (v)) and a very faint spot at the origin. The flask was cooled to 25 °C, and the solvent was evaporated. The residue was dissolved in $CH_2Cl_2$, and cold water was added cautiously to destroy the remaining borane reagent. The solution was stirred for 15 min, and the layers were separated. The organic phase was washed with water and filtered through anhydrous calcium sulfate. The solvent was evaporated, and the residue was purified by filtration through 15 g of regular silica gel in a coarse fritted funnel. Product **12** was eluted with 10% $CH_3OH$ in $CH_2Cl_2$ (v) and recrystallized from $CH_2Cl_2$ to give 0.107 g (87%), mp with dec above 189 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 2.36 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.78 (s, 3 H, O$CH_3$), 3.37 (s, 6 H, O$CH_3$), 2.50–4.16 (m, 24 H, N$CH_2$, O$CH_2$), 3.66 (d, 2 H, $J$ = 12.5 Hz, Ar$CH_2$N), 4.61 (d, 2 H, $J$ = 12.5 Hz, Ar$CH_2$N), 7.16 (d, 2 H, $J_m$ = 1.7 Hz, Ar*H*), 7.24 (s, 2 H, Ar*H*), 7.31 (d, 2 H, $J_m$ = 1.7 Hz, Ar*H*); MS (280 °C, 70 eV), 648 ($M^+ - (BH_3)_2$, 2), 617 ($M^+ - (BH_3)_2OCH_3$, 100). Anal. Calcd for $C_{38}H_{52}N_2O_7B_2H_6$: C, 67.46; H, 8.64; N, 4.14; B, 3.20. Found: C, 67.23; H, 8.73; N, 4.09; B, 3.32.

**Hexahydro{(33,34,35-trimethoxy-5,10,15-trimethyl-22,25,30-trioxa-1,19-diazapentacyclo[17.8.5.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]pentatriaconta-3,5,7-(35),8,10,12(34),13,15,17(33)-nonaene-$N^1$:$N^{19}$)}diboron (10).** Procedure B was applied to 0.101 g (0.16 mmol) of lactam **14** and 4.47 mmol of borane–methyl sulfide. After 30 min, TLC showed that all of **14** had reacted. The product **10** was recrystallized from $CH_2Cl_2$ to give 0.074 g (73%) of material, mp dec above 187 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 2.35 (s, 6 H, Ar$CH_3$), 2.46 (s, 3 H, Ar$CH_3$), 2.58 (s, 3 H, O$CH_3$), 3.35 (s, 6 H, O$CH_3$), 2.96–4.16 (m, 22 H, N$CH_2$, O$CH_2$, Ar$CH_2$N), 4.46 (d, 2 H, $J$ = 11.0 Hz, Ar$CH_2$N), 7.15 (d, 2 H, $J_m$ = 1.7 Hz, Ar*H*), 7.26 (s, 2 H, Ar*H*), 7.48 (d, 2 H, $J_m$ = 1.7 Hz, Ar*H*); MS (280 °C, 70 eV), 618 ($M - BH_3$, 0.7), 604 ($M^+ - (BH_3)_2$, 14), 573 ($M - (BH_3)_2OCH_3$, 100). Anal. Calcd for $C_{36}H_{42}N_2O_6B_2H_6 + 0.33H_2O$: C, 67.72; H, 8.63; N, 4.39; B, 3.39. Found: C, 67.94; H, 8.70; N, 4.25; B, 3.35.

**Hexahydro{(33,34,35-trimethoxy-5,10,15-trimethyl-22,25,30-trioxa-1,19-diazapentacyclo[17.8.5.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]pentatriaconta-3,5,7-(35),8,10,12(34),13,15,17(33)-nonaene-$N^1$:$N^{19}$)}diboron (11). Procedure C.** Lactam **15** (28.5 mg, 4.5 × $10^{-2}$ mmol) was dissolved in 12 mL of anhydrous THF. A THF solution of $LiBH_4$ (2 M, 2.7 mL) was added to the flask, and the mixture was stirred for 5 min. The flask was cooled to −78 °C, and 700 $\mu$L of boron trifluoride etherate (distilled from $CaH_2$ under reduced pressure) was added slowly. After the addition was completed, the solution was stirred for another 5 min before the cold bath was removed. The flask was allowed to warm to 25 °C. The reaction was followed by TLC and usually took 4–6 h. After 4.5 h, the flask was reimmersed in the cold bath, and water was added very cautiously to quench the remaining borane reagent. Methylene chloride and cold water were added, and the mixture was stirred for 10 min. The organic phase was washed once with water, dried ($Na_2SO_4$), and evaporated under vacuum. The residue was chromatographed on a 0.5-mm preparative TLC plate, and product was eluted with 2.5% $CH_3OH$ in $CH_2Cl_2$ (v). The less polar band ($R_f$ 0.62) corresponded to the diborane complex of the major isomer **10**. The more polar band ($R_f$ 0.53) corresponded to the diborane complex of **11**. About 20 mg of the mixture was obtained (69%). The ratio of the major to the minor isomers was 1:5; $^1H$ NMR ($CDCl_3$) $\delta$ 2.34 (s, 6 H, Ar$CH_3$), 2.47 (s, 3 H, Ar$CH_3$), 2.60 (s, 3 H, O$CH_3$), 3.33 (s, 6 H, O$CH_3$), 2.50–4.39 (m, 20 H, N$CH_2$), 3.60 (d, 2 H, $J$ = 13.9 Hz, Ar$CH_2$N), 4.50 (d, 2 H, $J$ = 13.9 Hz, Ar$CH_2$N), 6.99 (d, 2 H, $J_m$ = 1.7 Hz, Ar*H*), 7.17 (d, 2 H, $J_m$ = 1.7 Hz, Ar*H*), 7.29 (s, 2 H, Ar*H*). Anal. Calcd for $C_{36}H_{48}N_2O_6B_2H_6 + 2H_2O$: C, 64.68; H, 8.75; N, 4.19. Found: C, 64.71; H, 8.46; N, 4.36.

**Hexahydro{(30,31,32-trimethoxy-5,10,15-trimethyl-22,27-dioxa-1,19-diazapentacyclo[17.5.5.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]dotriaconta-3,5,7(32),8,10,12-(31),13,15,17(30)-nonaene-$N^1$:$N^{19}$)}diboron (9).** Lactam **13** (0.120 g, 0.20 mmol), 5.0 mL of 2 M $LiBH_4$ in THF, and 1.3 mL of boron trifluoride etherate were subjected to procedure C (−78 °C for 16 h). The excess borane was quenched at −78 °C with THF and water, the solution was evaporated under reduced pressure, and the residue was partitioned between $CH_2Cl_2$ and water. The organic phase was twice washed with water, dried ($Na_2SO_4$), and concentrated (vacuum) to 4 mL. A small amount of $CH_3OH$ was added, the crystals that separated were collected (50.3 mg) and the filtrate was chromatographed on 3 g of silica gel in a coarse fritted funnel with 10% ether in $CH_2Cl_2$ (v) as mobile phase to give 36 mg of additional **9**, total wt, 86.9 mg (72%), mp dec above 205 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 2.38 (s, 6 H, Ar$CH_3$), 2.46 (s, 3 H, Ar$CH_3$), 2.59 (s, 3 H, O$CH_3$), 3.27 (s, 6 H, O$CH_3$), 2.07–4.38 (m, 16 H, N$CH_2$, O$CH_2$), 4.06 (d, 2 H, $J$ = 11.0 Hz, Ar$CH_2$N), 4.40 (d, 2 H, J = 11.0 Hz, Ar$CH_2$N), 7.24 (d, 2 H, $J$ = 2.0 Hz, Ar*H*), 7.28 (s, 2 H, Ar*H*), 7.45 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*); MS (220 °C, 16 eV), 574 ($M^+ - BH_3$, 12), 573 ($M^+ - CH_3$, 25), 560 ($M^+ - (BH_3)_2$, 24), 529 ($M^+ - (BH_3)_2OCH_3$ 100). Anal. Calcd for $C_{34}H_{44}N_2O_5B_2H_6$: C, 69.41; H, 8.57; N, 4.76;

B, 3.67. Found: C, 69.49; H, 8.44; N, 4.78; B, 3.59.

**25,26,27-Trimethoxy-4,9,23-trimethyl-16-oxa-13,19-diazatetracyclo-[19.3.1.1$^{2,6}$.1$^{7,11}$]heptacosa-1(25),2,4,6(27),7,9,11(26),21,23-nonaene-12,20-dione (18).** Procedure A was applied to 2.39 g (4.9 mmol) of diacid chloride **20**, 0.51 g (4.9 mmol) of 3-oxa-1,5-pentanediamine, and 1.5 mL of $Et_3N$ with an addition time of 2 h at 15 °C. Product was collected from the gel permeation chromatograph column at 153-mL retention volume to give 1.91 g (75%) of **18**. A small sample was recrystallized from $CH_2Cl_2$–$CH_3OH$, mp 243 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 2.39 (s, 6 H, Ar$CH_3$), 2.46 (s, 3 H, Ar$CH_3$), 2.57 (s, 3 H, O$CH_3$), 3.33 (s, 6 H, O$CH_3$), 3.48–4.02 (m, 8 H, N$CH_2$, O$CH_2$), 7.28 (s, 4 H, Ar*H*), 7.78 (s, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 8.48 (brs, 2 H, N*H*); IR 1660 cm$^{-1}$; MS (200 °C, 70 eV), 518 ($M^+$, 100), 487 ($M^+ - OCH_3$, 7). Anal. Calcd for $C_{30}H_{34}N_2O_6$: C and H.

**25,26,27-Trimethoxy-4,9,23-trimethyl-16-oxa-13,19-diazatetracyclo-[19.3.1.1$^{2,6}$.1$^{7,11}$]heptacosa-1(25),2,4,6(27),7,9,11(26),21,23-nonaene (17).** Lactam **18** (0.14 g, 0.27 mmol) was dissolved in 30 mL of anhydrous THF. A fourfold excess of 1 M $LiAlH_4$ solution in THF (Aldrich 1.1 mL) was added to the solution which was then heated to reflux. After 12 h, TLC indicated that all the starting material had reacted. The mixture was cooled to 25 °C, and the excess reagent was destroyed by adding 170 $\mu$L of 1 N aqueous NaOH. A precipitate formed which was filtered. The precipitate was rinsed with 2 portions of $CH_2Cl_2$ and 2 portions of $CH_3OH$. The combined organic fractions were evaporated, and the residue was partitioned between $CH_2Cl_2$ and aqueous $(CH_3)_4N$-OH. The organic layer was washed 3 times with the aqueous basic solution, and the organic solution was filtered through a piece of phase-separator filter paper. The solvent was evaporated to give a white foam, 110 mg (85%): $^1H$ NMR ($CDCl_3$) $\delta$ 2.30 (s, 6 H, Ar$CH_3$), 2.46 (s, 6 H, Ar$CH_3$, O$CH_3$), 3.38 (s, 6 H, O$CH_3$), 2.36–3.66 (m, 8 H, N$CH_2$, O$CH_2$), 3.31 (d, 2 H, $J$ = 13.7 Hz, Ar$CH_2$N), 4.24 (d, 2 H, $J$ = 13.7 Hz, Ar$CH_2$N), 6.95 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.01 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.26 (s, 2 H, Ar*H*).

The sodium picrate complex **17**·NaPic, was prepared by adding the salt as a solid to a solution of **17** in $CH_2Cl_2$. After having been stirred for several hours, the solution was filtered from the excess salt, and the filtrate was evaporated to give **17**·NaPic: $^1H$ NMR ($CDCl_3$) $\delta$ 2.34 (s, 6 H, Ar$CH_3$), 2.50 (s, 6 H, Ar$CH_3$, O$CH_3$), 3.44 (s, 6 H, O$CH_3$), 2.32–3.67 (m, 8 H, N$CH_2$, O$CH_2$), 3.29 (d, 2 H, $J$ = 12.2 Hz, Ar$CH_2$N), 4.30 (d, 2 H, $J$ = 12.2 Hz, Ar$CH_2$N), 6.96 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.10 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.32 (s, 2 H, Ar*H*), 8.85 (s, 2 H, Ar*H*, picrate; FABMS (xenon ionization, 25 °C), 513 (M + $Na^+$, 100).

**36,37,38-Trimethoxy-5,10,15-trimethyl-22,25,30,33-tetraoxa-1,19-diazapentacyclo[17.8.8.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]octatriaconta-3,5,7(36)-nonaene (8). Procedure D.** Hydroborane complex **12** (40 mg, 0.059 mmol) was dissolved in 3 mL of $CH_2Cl_2$, and 1.5 mL of an aqueous 0.7 M $Mg(OAc)_2$/AcOH buffer was added. Equivalents (6) of iodine (90 mg, 0.35 mmol) dissolved in 1 mL of THF was added dropwise (fiarly rapidly) to the solution. After having been stirred for 5 min at 25 °C, the layers were separated. The aqueous phase was washed with 1 portion of $CH_2Cl_2$, and the organic portions were combined. The organic phase was washed with 2 portions of dionized water and shaken for a few min at a time with 2 portions of aqueous (deionized water) $(CH_3)_4NOH$ or until the organic phase was colorless. The solution was filtered through a piece of phase-separator filter paper. The solvent was evaporated, and the white foam (30 mg, 78%) was dried on the vacuum pump: $^1H$ NMR ($CDCl_3$) $\delta$ 2.31 (s, 6 H, Ar$CH_3$), 2.41 (s, 3 H, Ar$CH_3$), 2.83 (s, 3 H, O$CH_3$), 3.55 (s, 6 H, O$CH_3$), 2.63–3.80 (m, 24 H, N$CH_2$, O$CH_2$), 3.04 (d, 2 H, $J$ = 11.8 Hz, Ar$CH_2$N), 4.12 (d, 2 H, $J$ = 11.8 Hz, Ar$CH_2$N), 6.95 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.03 (d, 2 H, $J_m$ = 1.9 Hz Ar*H*), 7.16 (s, 2 H, Ar*H*); MS (320 °C, 70 eV), 648 ($M^+$, 2) 617 ($M^+ - OCH_3$, 100). Anal. Calcd for $C_{38}H_{52}N_2O_7$: C, 70.34; H, 8.08; N, 4.32. Found: C, 70.15; H, 7.95; N, 4.15.

Complexes of compound **8** were prepared by stirring a $CH_2Cl_2$ solution of **8** with an aqueous solution of the salt in the presence of a small amount of $(CH_3)_4NOH$. The complex **8**·$CsClO_4$ was characterized as follows: mp dec above 185 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 2.35 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.73 (s, 3 H, O$CH_3$), 3.41 (s, 6 H, O$CH_3$), 2.20–4.18 (m, 26 H, N$CH_2$, O$CH_2$, Ar$CH_2$N), 4.12 (d, 2 H, $J$ = 7.2 Hz, Ar$CH_2$N), 7.00 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.12 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.23 (s, 2 H, Ar*H*). Anal. Calcd for $C_{38}H_{52}N_2O_7CsClO_4$: C, 51.79; H, 5.95. Found: C, 51.88; H, 5.91. The complex **8**·KSCN gave the following: $^1H$ NMR ($CDCl_3$) $\delta$ 2.29 (s, 6 H, Ar$CH_3$), 2.37 (s, 3 H, Ar$CH_3$), 2.75 (s, 3 H, O$CH_3$), 3.31 (s, 6 H, O$CH_3$), 2.07–4.06 (m, 24 H, N$CH_2$, O$CH_2$), 2.57 (d, 2 H, $J$ = 11.8 Hz, Ar$CH_2$N), 4.11 (d, 2 H, $J$ = 11.8 Hz, Ar$CH_2$N), 6.94 (d, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 7.06 (d, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 7.14 (s, 2 H, Ar*H*). The complex **8**·NaBr gave the following: $^1H$ NMR ($CDCl_3$) $\delta$ 2.37 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.88 (s, 3 H, O$CH_3$), 3.41 (s, 6 H, O$CH_3$), 2.55–3.97 (m, 24 H, N$CH_2$, O$CH_2$), 2.98 (d, 2 H, $J$ = 11.8 Hz, Ar$CH_2$N), 4.11 (d, 2 H, $J$ = 11.8 Hz, Ar$CH_2$N), 7.04 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.15 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.22 (s, 2 H, Ar*H*). The complex **8**·$NH_4$Pic gave mp 244–248 °C dec; $^1H$ NMR ($CDCl_3$) $\delta$ 2.36 (s, 6 H, Ar$CH_3$), 2.45 (s, 3 H, Ar$CH_3$), 2.74 (s, 3 H, O$CH_3$), 3.35 (s, 6 H, O$CH_3$), 2.10–4.09 (m, 24 H, N$CH_2$, O$CH_2$), 2.56 (d, 2 H, $J$ = 11.7 Hz, Ar$CH_2$N), 4.18 (d, 2 H, $J$ = 11.7 Hz, Ar$CH_2$N), 6.39 (t, 4 H, $J$ = 52.98 Hz, $NH_4^+$), 6.98 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.13 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.24 (s, 2 H, Ar*H*), 8.79 (s, 2 H, ArH picrate). Anal. Calcd for $C_{38}H_{52}N_2O_7NH_4C_8H_2N_3O_7$: C, 59.05; H, 6.53. Found: C, 58.87; H, 6.57.

**33,34,35-Trimethoxy-5,10,15-trimethyl-22,25,30-trioxa-1,19-diaza-pentacyclo[17.8.5.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]pentatriaconta-3,5,7(35),8,10,12-(34),13,15,17(33)-nonaene (6).** Hydroborane complex **10** (29 mg, 0.046 mmol) was dissolved in 5 mL of THF. Hydrochloric acid (1 M, 92 $\mu$L) was added to this solution which was heated to reflux. The reaction was follwed by TLC. After 30 min, all the starting material had reacted. The mixture was cooled to 25 °C, and the solvent was evaporated. The residue was dissolved in $CH_2Cl_2$, and the solution was washed twice with 3 N $(CH_3)_4NOH$. It was then stirred with aqueous sodium picrate containing a small amount of $(CH_3)_4NOH$. The layers were separated, and the organic phase was filtered through a piece of phase-separator filter paper. The solvent was evaporated, and the residue was chromatographed on a 1-mm preparative TLC plate with a 20% EtOH/$CH_2Cl_2$ (v) eluting solvent. The sodium picrate complex of **6** was obtained (22 mg, 56%). The lithium picrate complex of **6** was obtained by stirring a methanol solution of the sodium complex with a huge excess of ultra-pure LiCl (Alfa-Ventron) for 24 h. The methanol was evaporated, and the residue was partitioned between $CH_2Cl_2$ and water. The organic phase was washed with 2 more portions of water and then filtered through a piece of phase-separator filter paper. The solvent was evaporated to give the lithium picrate complex of **6**. The potassium picrate complex was obtained in a similar manner by stirring with potassium picrate in methanol.

Compound **6** was also obtained from the hydroborane complex **11**, the minor isomer. Complex **11** (20 mg, 0.032 mmol) was submitted to procedure D (48 mg of $I_2$ was used). The final $CH_2Cl_2$ solution of **6** and **7** was stirred with an aqueous solution of NaPic containing a trace of $(CH_3)_4NOH$ for 0.5 h. The organic phase was filtered through phase-separator filter paper. The solvent was evaporated, and the residue was chromatographed on a 1-mm preparative TLC plate with 20% EtOH in $CH_2Cl_2$ as the mobile phase. The complex **6**·NaPic was obtained (17 mg, 62%). These complexes of **6** were characterized as follows. Complex **6**·LiPic: $^1H$ NMR ($CDCl_3$) $\delta$ 2.36 (s, 6 H, Ar$CH_3$), 2.49 (s, 3 H, Ar$CH_3$) 2.57 (s, 3 H, O$CH_3$), 3.43 (s, 6 H, O$CH_3$), 2.33–4.00 (m, 20 H, N$CH_2$, O$CH_2$), 2.93 (d, 2 H, $J$ = 12.2 Hz, Ar$CH_2$N), 4.41 (d, 2 H, $J$ = 12.2 Hz, Ar$CH_2$N), 7.01 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.16 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.32 (s, 2 H, Ar*H*), 8.89 (s, 2 H, Ar*H*, picrate). Complex **6**·NaPic: $^1H$ NMR ($CDCl_3$) $\delta$ 2.34 (s, 6 H, Ar$CH_3$), 2.42 (s, 3 H, Ar$CH_3$), 2.49 (s, 3 H, O$CH_3$), 3.36 (s, 6 H, O$CH_3$), 1.88–4.24 (m, 20 H, N$CH_2$, O$CH_2$), 2.64 (d, 2 H, $J$ = 11.7 Hz, Ar$CH_2$N), 4.44 (d, 2 H, $J$ = 11.7 Hz, Ar$CH_2$N), 6.97 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.12 (d, 2 H, $J_m$ = 2.0 Hz, Ar*H*), 7.32 (s, 2 H, Ar*H*), 8.81 (s, 2 H, Ar*H*, picrate); FABMS (xenon ionization, 25 °C), 627.39 (M + $Na^+$, 18), 605.40 (M + $H^+$, 23). Complex **6**·KPic: $^1H$ NMR ($CDCl_3$) $\delta$ 2.23 (s, 3 H, Ar$CH_3$), 2.30 (s, 6 H, Ar$CH_3$), 2.49 (s, 3 H, O$CH_3$), 3.48 (s, 6 H, O$CH_3$), 1.88–4.14 (m, 22 H, N$CH_2$, O$CH_2$, Ar$CH_2$N), 4.33 (d, 2 H, $J$ = 14.0 Hz, Ar$CH_2$N), 6.95 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.02 (d, 2 H, $J_m$ = 1.9 Hz, Ar*H*), 7.32 (s, 2 H, Ar*H*), 8.82 (s, 2 H, Ar*H*, picrate).

**30,31,32-Trimethoxy-5,10,15-trimethyl-22,27-dioxa-1,19-diazapenta-cyclo[17.5.5.1$^{3,7}$.1$^{8,12}$.1$^{13,17}$]dotriaconta-3,5,7(32),8,10,12(31),13,15,17-(33)-nonaene (5).** Hydroborane complex **9** (20 mg, 0.034 mmol) and 52.8 mg (0.2 mmol) of iodine were submitted to procedure D to give **5** as a thin film, which was dried under high vacuum to give 18 mg (94%) of **5**: $^1H$ NMR ($CDCl_3$) $\delta$ 2.30 (s, 6 H, Ar$CH_3$), 2.44 (s, 3 H, Ar$CH_3$), 2.58 (s, 3 H, O$CH_3$), 3.30 (s, 6 H, O$CH_3$), 2.28–4.08 (m, 18 H, N$CH_2$, O$CH_2$, Ar$CH_2$N), 3.93 (d, 2 H, $J$ = 12.7 Hz, Ar$CH_2$N), 6.86 (d, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 7.06 (d, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 7.23 (s, 2 H, Ar*H*); FABMS (xenon ionization, 25 °C), 560 ($M^+$, 100), 546 ($M^+ - CH_3 + H$, 7), 530 ($M^+ - OCH_3 + H$).

Compound **5** was characterized as its $NaB(Ph)_4$ complex made by stirring **5** in $CH_2Cl_2$ with aqueous $NaB(Ph)_4$ containing a trace of $(CH_3)_4NOH$. The layers were separated, the organic phase was concentrated, and the **5**·$NaB(Ph)_4$ was crystallized by adding $CH_3OH$: $^1H$ NMR ($CDCl_3$) $\delta$ 2.38 (s, 6 H, Ar$CH_3$), 2.43 (s, 3 H, Ar$CH_3$), 2.51 (s, 3 H, O$CH_3$), 3.33 (s, 6 H, O$CH_3$), 1.94–3.60 (m, 16 H, N$CH_2$, O$CH_2$), 2.99 (d, 2 H, $J$ = 12.0 Hz, Ar$CH_2$N), 3.97 (d, 2 H, $J$ = 12.0 Hz, Ar$CH_2$N), 6.84–7.48 (m, 26 H, Ar*H*). Anal. Calcd for $C_{34}H_{44}N_2O_5$·$NaB(C_6H_5)_4$·0.8 $CH_2Cl_2$: C, 72.74; H, 6.81. Found: C, 72.58; H, 7.14. The crystal structure of **5**·$NaB(C_6H_5)_4$ contains $CH_2Cl_2$.

The diprotonated form of **5** gave the following $^1H$ NMR ($CDCl_3$) $\delta$ 2.36 (s, 6 H, Ar$CH_3$), 2.48 (s, 3 H, Ar$CH_3$), 2.49 (s, 3 H, O$CH_3$), 3.41

(s, 6 H, $OCH_3$), 2.23-4.40 (m, 16 H, $NCH_2$, $OCH_2$), 3.11 (d, 2 H, $J$ = 13.2 Hz, $ArCH_2N$), 4.09 (d, 2 H, $J$ = 13.2 Hz, $ArCH_2N$), 7.00 (d, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 7.15 (d, 2 H, $J_m$ = 1.5 Hz, Ar*H*), 7.34 (s, 2 H, Ar*H*).

What is probably **5**·$I^+I^-$ gave the following: $^1H$ NMR ($CDCl_3$) $\delta$ 2.35 (s, 6 H, $ArCH_3$), 2.46 (s, 3 H, $ArCH_3$), 2.62 (s, 3 H, $OCH_3$), 3.31 (s, 6 H, $OCH_3$), 2.96-3.87 (m, 16 H, $NCH_2$, $OCH_2$), 4.22 (d, 2 H, $J$ = 13.2 Hz, $ArCH_2N$), 4.34 (d, 2 H, $J$ = 13.2 Hz, $ArCH_2N$), 7.15 (d, 2 H, Ar*H*), 7.19 (d, 2 H, Ar*H*), 7.26 (s, 2 H, Ar*H*); FABMS (xenon ionization, 0 °C), 687 (M + $I^+$, 0.6), 561 (M + $H^+$, 100), 583 (M + $Na^+$, 21).

**Crystal Structures.** Compounds **5**·$Na^+$, **8**·$Na^+$, **8**·$K^+$, **8**·$Cs^+$, and **9** are crystallized in the monoclinic system in space groups $P2_1/n$, $Cc$, $P2_1/c$, $P2_1/c$ and $P2_1/m$, respectively. Unit cell dimensions are as follows: **5**·$Na^+$ $a$ = 19.919 (2) Å, $b$ = 14.725 (2) Å, $c$ = 21.387 (2) Å, $\beta$ = 111.85 (3)°, $Z$ (the number of molecules in the unit cell) = 4; **8**·$Na^+$ $a$ = 16.907 (6) Å, $b$ = 12.543 (4) Å, $c$ = 20.860 (7) Å, $\beta$ = 117.89 (3)°, $Z$ = 4; **8**·$K^+$ $a$ = 14.078 (4) Å, $b$ = 11.367 (3) Å, $c$ = 25.909 (7) Å, $\beta$ = 101.48 (2)°, $Z$ = 4; **8**·$Cs^+$ $a$ = 11.329 (3) Å, $b$ = 14.364 (5) Å, $c$ = 26.219 (10) Å, $\beta$ = 105.03 (3)°, $Z$ = 4; **9** $a$ = 15.605 (11) Å, $b$ = 15.799 (7) Å, $c$ = 15.023 (7) Å, $\beta$ = 94.43 (5)°, $Z$ = 4 (two crystallographically unrelated molecules each having a mirror plane through the molecule are found in this unit cell). Compounds **6**·$K^+$, **14**, and **15** crystallize in the orthorhombic system in space groups *Pnma*, $P2_1na$ and *Pnma*, respectively. Unit cell dimensions are as follows: **6**·$K^+$ $a$ = 21.210 (9) Å, $b$ = 14.745 (6) Å, $c$ = 11.808 (5) Å, $Z$ = 4 (the molecule contains a crystallographic mirror plane); **14** $a$ = 11.318 (3) Å, $b$ = 7.835 (1) Å, $c$ = 37.230 (8) Å, $Z$ = 4; **15** $a$ = 16.056 (4) Å, $b$ = 15.370 (4) Å, $c$ = 14.640 (3) Å, $Z$ = 4 (the molecule contains a crystallographic mirror plane). With the exception of **6**·$K^+$ and **5**·$Na^+$, which were examined on a modified Picker FACS1 diffractometer, all measurements were taken on a Syntex $P\bar{1}$ diffractometer. All measurements except for those of **15**, which involved Cu K$\alpha$ radiation, made use of Mo K$\alpha$ radiation. Measurements were made at ambient temperature except for **9** and **14**, which were made at 115 K. Refinement of the eight structures gave R values currently at **5**·$Na^+$ 0.16, **6**·$K^+$ 0.08, **8**·$Na^+$ 0.06, **8**·$K^+$ 0.14, **8**·$Cs^+$ 0.08, **9** 0.08, **14** 0.08, and **15** 0.08. All but **8**·$Cs^+$, which was solved by using heavy atom methods, were solved by using direct methods. Full details will be published elsewhere.

# Host-Guest Complexation. 39. Cryptahemispherands Are Highly Selective and Strongly Binding Hosts for Alkali Metal Ions[1]

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**Abstract:** The association constants ($K_a$, $M^{-1}$) and free energies of binding ($-\Delta G°$, kcal $mol^{-1}$) have been measured at 25 °C in $CDCl_3$ saturated with $D_2O$ for cryptahemispherands **1-3**, cryptands **9-11**, and diazahemispherand **4** binding the alkali metal picrate salts. Methods were used in which complexes whose $K_a$ values had been determined were equilibrated with hosts of unknown values. The equilibrium points were determined by $^1H$ NMR spectral methods. The cryptahemispherands as a class were found to be more powerful complexing agents than the cryptands. The two classes exhibited comparable ion selectivities. Plots of the $-\Delta G°$ values of the cryptands in $CDCl_3$-$D_2O$ vs. those in 95% $CH_3OH$-5% $H_2O$ were linear. The $-\Delta G°$ values for eight different sets of binding partners in $CDCl_3$-$D_2O$ were found to be 5.2 ± 0.4 kcal $mol^{-1}$ higher than the corresponding eight values in $CH_3OH$-$H_2O$. The results are discussed in terms of the relative states of preorganization for binding and desolvation of the various host classes.

The previous paper in this series reports the syntheses and crystal structures of complexes whose hosts belong to a new subclass called the cryptahemispherands, whose bicyclic structures are illustrated by **1-3**. The monocyclic diazahemispherand **4** was also prepared for purposes of comparison.[2] Hosts **1-3** combine certain structural features of the spherands (**5-7**),[3,4] the hemispherands (e.g., **8**),[5] and the cryptands (**9-11**),[6-8] which in turn are relatives of the chorands (e.g., **12**).[9] The trisanisyl molecular modules of **1-8** and the tetraanisyl module of reference compound **13**[10] are organized for binding during their syntheses rather than during the act of complexation. In these modules, the unshared electron pairs of the oxygens face inward toward the cavity, and their attached methyl groups are oriented outward, shielding the oxygens from solvation. In contrast, the $(CH_2OCH_2)_m$ and $(CH_2)_3N$ modules of **1-4** and **8-12** are conformationally mobile. The unshared electron pairs of their heteroatoms can face outward to be solvated or inward toward solvent parts occupying the cavity. The methylene groups can turn inward to fill the cavity or outward when the cavity is filled. Upon complexation with cations, the guest must conformationally reorganize these chains and displace solvent bound to their heteroatoms in the process.[3] The chorands, and particularly the cryptands, are *preorganized* for binding with respect to the sequences of their atoms but not with regard to their conformations or competitive complexation with solvent. The spherands are *preorganized* with respect to their atomic sequences, their conformations, and the unsolvated states of their heteroatoms.

This paper reports the association constants and free energies of complexation of alkali metal and ammonium picrates by cryptahemispherands **1-3**, diazahemispherand **4**, and cryptands **9-11** at 25 °C in $CDCl_3$ saturated with $D_2O$. The values obtained are compared with those reported for the spherands in the same

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