Kinetics with $K_2S_2O_8$. Reactions were conducted under dry oxygen free nitrogen in vessels equipped with a magnetic stirrer and immersed in a thermostat bath at 75 °C. Samples were withdrawn at intervals, and their peroxide contents were determined according to the procedure of Kolthoff and Carr.[6] Each peroxide estimation was carried out in duplicate, and each run was duplicated.

Good straight lines were obtained plotting the logarithm of the $K_2S_2O_8$ concentration against time for the initial 70% conversions. The apparent first-order rate constants obtained from the initial slopes of the graphs and the reaction conditions are reported in Table V.

Reaction Products with $K_2S_2O_8$. In a 100-mL flask, equipped with a magnetic stirrer, were introduced the reagents (in the amounts reported in Table V). The solution was flushed with N_2, and the flask was immersed in a bath at 75 °C for 4 h and then made basic with 10% NaOH and extracted with CH_2Cl_2 (4 × 10 mL). The combined extracts were quantitatively analyzed by GLC using quinoxaline as the internal standard.

The 2-isopropyl-4-methylquinoline (**9**) has been isolated by silica gel chromatography and identified by comparison (TLC, GLC, IR, NMR, and MS) with an authentic sample.[18] The results are reported in Table V.

Acknowledgment. This work was supported by "Progetto Finalizzato Chimica Fine e Secondaria" CNR, Roma.

Registry No. **3**, 33787-85-8; **4**, 33787-74-5; **5**, 30721-98-3; **6**, 30721-99-4; **7**, 56947-80-9; **8**, 91879-70-8; **9**, 91879-71-9; $(CH_3)_2CH\cdot$, 2025-55-0; $C_{11}H_{23}\cdot$, 55101-35-4; $K_2S_2O_8$, 7727-21-1; $(CH_3)_2CHCO_2H$, 79-31-2; $HOCH_2\cdot$, 2597-43-5; $(CH_3)_2NCO\cdot$, 23686-93-3; $OHCN(CH_3)CH_2\cdot$, 17526-06-6; $FeOH(OAc)_2$, 10450-55-2; dioxane, 123-91-1; dioxanyl radical, 4598-47-4; lepidine, 491-35-0; lepidine conjugate acid, 41229-57-6; lauroyl peroxide, 645-66-9; methanol, 67-56-1; dimethylformamide, 68-12-2; cyclohexyl iodide, 626-62-0; cyclohexane, 110-82-7; cyclohexyl radical, 3170-58-9; benzoyl peroxide, 94-36-0; potassium isobutyrate, 19455-20-0.

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Host–Guest Complexation. 32. Spherands Composed of Cyclic Urea and Anisyl Units[1,2]

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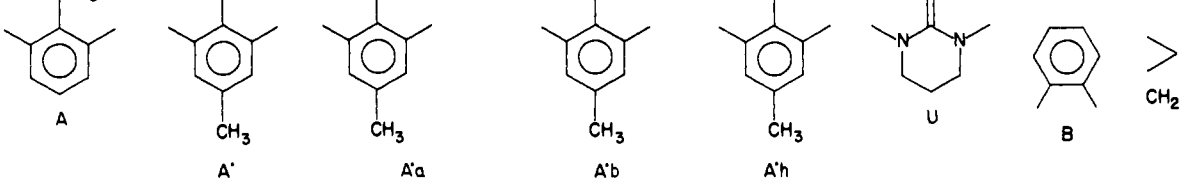
Abstract: Five new spherands and three new hemispherands containing cyclic urea units have been designed and synthesized, and their binding properties have been examined. Formally, these macrocycles are composed by attaching to one another the following units: 2,6-disubstituted anisyl, or A; 2,6-disubstituted 4-methylanisyl, or A′; N,N-disubstituted tetrahydro-2-pyrimidinone, or U; 2,6-disubstituted 1-(allyloxy)-4-methylbenzene, or A′a; 2,6-disubstituted 1-(benzyloxy)-4-methylbenzene, or A′b; 2,6-disubstituted 4-methylphenol, or A′h; 1,2-disubstituted benzene, or B; and CH_2 groups. Host structures and key



intermediates are visualized by line formulas in which adjacent letters indicate bonded units. The macroring acts as a semirigid support structure for the convergently arranged carbonyl and methoxy groups. Key ring-closing reactions involve urea NH group substitution of $ArCH_2Br$ in $(CH_2)_4O$–NaH under high dilution. Treatment of $U(A'UH)_2$ with $(BrCH_2)_2B$ gave $U(A'UCH_2)_2B$ (**1**, 7%), of $A(AUH)_2$ with $(BrCH_2)_2B$ gave $A(AUCH_2)_2B$ (**2**, 11%), of $A(AUH)_2$ with $(BrCH_2)_2A'$ gave $A(AUCH_2)_2A'$ (**3**, 32%), of $A'b(A'UH)_2$ with $(BrCH_2)_2A'a$ gave $A'b(A'UCH_2)_2A'a$ (**4**, 41%), deallylation of which with Pd–EtOH–TsOH gave $A'b(A'UCH_2)_2A'h$ (**5**, 25%), of $U(A'CH_2Br)_2$ with $(HU)_2A'$ gave $U(A'CH_2U)_2A'$ (**6**, 60%), and of $A'b(A'CH_2Br)_2$ with $(HU)_2A'b$ gave $A'b(A'CH_2U)_2A'b$ (**7**, 41%), which was hydrolytically debenzylated to give $A'h(A'CH_2U)_2A'h$ (43%), methylation of which produced $A'(A'CH_2U)_2A'$ (**8**, 71%). These compounds were generally purified as their NaBr complexes, which were decomplexed by crystallizing the free host from MeOH–H_2O mixtures by MeOH evaporation (a phase-transfer process). Crystal structures of complexes $A(AUCH_2)_2A'\cdot NaBr\cdot H_2O$ (**3**·NaBr·H_2O) and $A(AUCH_2)_2A'\cdot CsClO_4\cdot H_2O$ (**3**·$CsClO_4$·H_2O) are discussed. Association constants (K_a) between host and guest to give complexes were determined by extracting picrate salts (guests) from D_2O into $CDCl_3$ in the absence and presence of hosts at 25 °C. The rates of extraction were essentially instantaneous on the human time scale. The free energies for complexation for the seven hosts with picrate salts of Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $CH_3NH_3^+$, and t-$BuNH_3^+$ were determined. These $-\Delta G°$ values (kcal mol^{-1}) ranged from a high of ~18.3 ($U(A'UCH_2)_2B$ (**1**)) for Li^+ to a low of 7.2 ($U(A'CH_2U)_2A'$ (**6**)) for $(CH_3)_3CNH_3^+$. Interesting structural recognition factors ($K_a^G/K_a^{G'}$) for a host distinguishing between two similar guests (G and G′) are as follows: Li^+/Na^+, $U(A'UCH_2)_2B$ (**1**), 30; Na^+/Li^+, $A'b(A'CH_2U)_2A'b$ (**7**), 3400; Na^+/K^+, $A(AUCH_2)_2B$ (**2**), 2300; K^+/Na^+, $A(AUCH_2)_2A'$ (**3**), 3; K^+/Rb^+, $A'b(A'UCH_2)_2A'a$ (**4**), 110; Rb^+/Cs^+, $A'b(A'UCH_2)_2A'a$ (**4**), 25; Cs^+/Rb^+, $U(A'UCH_2)_2B$ (**1**), 2; $NH_4^+/CH_3NH_3^+$, $A(AUCH_2)_2A'$ (**3**), 9; $CH_3NH_3^+/NH_4^+$, $U(A'UCH_2)_2B$ (**1**), 1.7; $CH_3NH_3^+/t$-$BuNH_3^+$, $A'b(A'UCH_2)_2A'a$ (**4**), 4600; t-$BuNH_3^+/CH_3NH_3^+$, $U(A'UCH_2)_2B$ (**1**), 6. Correlations between the structures of hosts and guests and their free energies of binding are interpreted in terms of the principles of complementarity and of preorganization. In general, these hosts exist as a mixture of conformers equilibrating rapidly on the human time scale but slowly on the ^1H NMR time scale. When guest is added, they produce a single complex instantaneously on the human time scale.

Complexes as we use the term are composed of hosts (convergently arranged binding sites) and guests (divergently arranged binding sites) held together in solution in a definite structural relationship. Since each binding site provides at most a few

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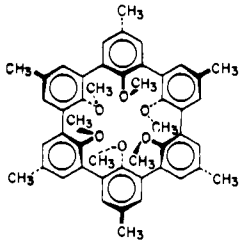
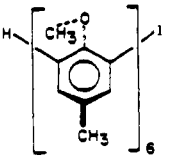
kilocalories per mole of binding free energy, a number of spatially and electronically compatible binding sites are required to structure a host–guest complex. The design of such complexes is aided by two self-evident guiding principles. The principle of complementarity points to the fact that *to complex, hosts must have binding sites that cooperatively contact and attract the binding sites of guests without generating strong nonbonded repulsions.* The principle of preorganization states that *the smaller the changes in organization of host and guest required for complexation, the stronger the binding.*[3]

Solvation is nonstructured complexation that competes with structured complexation between the two complexing partners. Thus changes in organization of host and guest that might occur during complexation includes both conformational and solvent reorganizations. Structural recognition in complexation depends on both complementarity and preorganization and is measured in terms of differences in free energy of complexation between possible complexing partners and of each complexing with their solvent shells.[3]

Spherand $A'(A'A')_2A'$ provides an extreme example of a host preorganized to be complementary to Li^+ and Na^+ ions whose picrate salts in $CDCl_3$ at 25 °C are bound with $-\Delta G°$ values of >23 and 19.2 kcal mol^{-1}, respectively. This host binds no other ions detectably. The free host possesses an enforced octahedral arrangement of six oxygens whose 24 unshared electrons provide the lining of a cavity that is shielded from solvation by six phenyls and six methyl groups. In contrast, the open-chain model compound $H(A')_6H$ binds Li^+ and Na^+ picrates with $-\Delta G° < 6$ kcal mol^{-1}. It exists in over 1000 conformations, only two of which are fully organized for cooperative binding. Most of these conformations expose the unshared electrons to solvation.[4]



$A'(A'A')_2A'$



HA'_6H

This paper reports an investigation of the syntheses and binding properties of eight new hosts (**1–8**) composed of various combinations of substituted anisyl (A) and cyclic urea (U) units, with CH_2 and ortho phenylene (B) units as spacers. The formulas and symbols for these units are listed at the end of the abstract. Host **9** has been previously reported[5] and will be compared with **1–8**. The use of the cyclic urea unit (U) was inspired by these facts and expectations. (1) When incorporated into a semirigid macrocycle by bonding through its two nitrogens, the U unit orients its carbonyl group toward the cavity in much the same way that a 2,6-disubstituted anisyl unit orients its oxygen (CPK model examination). (2) The urea carbonyl group is a much stronger hydrogen bonding unit than ether groups[6] and is likely to be a much better ligand for many of the metal ions as well. (3) The cyclic urea unit (U) provides less shielding to the cavity of its hosts than the anisyl unit. The cavity of $A'(A'A')_2A'$ is limited to binding only by encapsulation, whereas interspersing A with U units should provide space for formation of both nesting and perching complexes. (4) The rates of complexation–decomplexation and of extraction of guests were anticipated to be much faster for spherands containing U units than for those composed only of A units.[7,8] (5) Incorporation of U units in spherands introduces additional degrees of freedom into the design of structure and of solubility properties for these strongly binding hosts.

In the first section, the syntheses of **1–8** are outlined. Section two describes the crystal structures of two complexes of $A(AUCH_2)_2A'$ (**3**). In the third section the binding free energies of **1–8** with alkali-metal, ammonium, and alkylammonium cations are correlated with their structures and are compared with those of other hosts. Section four is concerned with the conformational equilibria that involve **1–8** (Chart I), and what happens to these conformations upon complexation.

Results and Discussion

Syntheses. Host $U(A'UCH_2)_2B$ (**1**) was prepared in 7% yield by adding *o*-xylene dibromide to a dilute solution of the disodium salt of $U(A'UH)_2$ (**10**) formed from **10** and NaH in $(CH_2)_4O$. The synthesis of the important intermediate **10** was reported in connection with the preparation of macrocycle **9**.[5] The assembly of the second key intermediate $A(AUH)_2$ (**11**) begins with the metalation (BuLi) of dibenzofuran and bromination of the organometallic to give **12**[9] (81%), which was coupled with *o*-$CH_3OC_6H_4MgBr$ to produce **13** (>80%). This substance was demethylated with BBr_3, and the resulting monophenol was fused with NaOH–KOH to generate terphenol (>80%), which was methylated to give $A(AH)_2$ (**14**, 88%). Thus $A(AH)_2$ (**14**) was produced from dibenzofuran in an overall yield of 49%. Demetalation and carbonation of $A(AH)_2$ (**14**) gave $A(ACO_2H)_2$ (**15**, 95%). This diacid through its diacid chloride was converted to its diacyl azide $A(ACON_3)_2$, which when heated rearranged to the bis(isocyanate) $A(ANCO)_2$. This material readily added two moles of $BrH_3N(CH_2)_3Br$ to produce $A[ANHCONH(CH_2)_3Br]_2$ (**16**, 59% overall), which unlike its three immediate precursors, was characterized. When treated with KOBu-*t*, **16** underwent a double-ring closure to give $A(AUH)_2$ (**17**, 96%). This bis(urea) compound under high dilution conditions ($(CH_2)_4O$–NaH) when treated with *o*-xylyl dibromide gave $A(AUCH_2)_2B$ (**2**, 3.5%), and with 2,6-bis(bromomethyl)-4-methylanisole[10] gave $A(AUCH_2)_2A'$ (**3**, 30%). Both macrocycles were purified through their NaBr complexes (Scheme I).

Hosts $A'b(A'UCH_2)_2A'a$ (**4**) and $A'b(A'UCH_2)_2A'h$ (**5**) involved terphenol **18** as the starting material.[10] Benzylation of **18** with 1 mol of $C_6H_5CH_2Br$–K_2CO_3 gave **19** (73%) in which only the centrally located phenolic hydroxyl group was alkylated. This regioselectivity may reflect a higher acidity of this central hydroxyl group due to the electron-withdrawing effect of the two attached aryl groups. The resulting diphenol was dibrominated to give **20** (60%) with 2,4,4,6-tetrabromocyclohexadienone[11] (TBC), which is nonacid-generating and therefore compatible with the benzyl ether groups of **19** and **20**. Dibromide **20** was methylated (CH_3I–K_2CO_3) to provide $A'b(A'Br)_2$ (**21**, 91%). This substance was metalated and carbonated to give $A'b(A'CO_2H)_2$ (**22**, 73%). The diacid with $SOCl_2$ gave $A'b(A'COCl)_2$ that was converted directly with NaN_3 to $A'b(A'CON_3)_2$ that without characterization was thermally rearranged to $A'b(A'NCO)_2$. When $Br(CH_2)_3NH_3Br$ was added to this uncharacterized bis(isocyanate), the bis(urea) compound $A'b[A'NHCONH(CH_2)_3Br]_2$ (**23**) was

(1) We warmly thank the National Science Foundation, Grant CHE 81-09532, for support of this research.

(2) Some of this work was communicated: (a) Cram, D. J.; Dicker, I. B.; Knobler, C. B.; Trueblood, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 6828–6830. (b) Cram, D. J.; Dicker, I. B. *J. Chem. Soc., Chem. Commun.* **1982**, 1219–1221.

(3) (a) Cram, D. J. In "Host-Guest Complexation Chemistry, IUPAC Chemistry for the Future"; Grünewald, H., Ed.; Pergamon Press: Oxford, 1984; pp 3–10. Cram, D. J.; Cram, J. M. *Workshop Conf. Hoechst* **1983**, *14*, 44–64.

(4) (a) Cram, D. J.; Kaneda, T.; Helgeson, R. C.; Lein, G. M. *J. Am. Chem. Soc.* **1979**, *101*, 6752–6754. (b) Cram, D. J.; Lein, G. M.; Kaneda, T.; Helgeson, R. C.; Knobler, C. B.; Maverick, E.; Trueblood, K. N. *Ibid.* **1981**, *103*, 6228–6232.

(5) Cram, D. J.; Katz, H. E.; Dicker, I. B. *J. Am. Chem. Soc.* **1984**, *106*, 4977–4987.

(6) (a) Mitsky, J.; Jaris, L.; Taft, R. W. *J. Am. Chem. Soc.* **1972**, *94*, 3442–3445. (b) Aitken, H. W.; Gilkerson, W. R. *Ibid.* **1973**, *95*, 8551–8559.

(7) Lein, G. M.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1982**, 301–304.

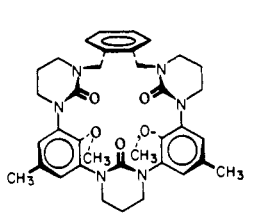
(8) Anthonsen, T.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1983**, 414–416.

(9) Gilman, H. *J. Am. Chem. Soc.* **1939**, *61*, 1365–1371.

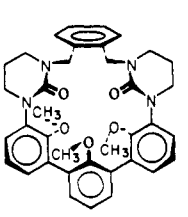
(10) Koenig, K. E.; Lein, G. M.; Stückler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3553–3566.

(11) Calo, V.; Ciminale, F.; Lopez, L.; Todesco, P. E. *J. Chem. Soc. C* **1971**, 3652–3653.

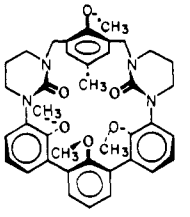
Chart I



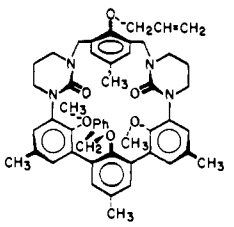
1, U(A·UCH$_2$)$_2$B



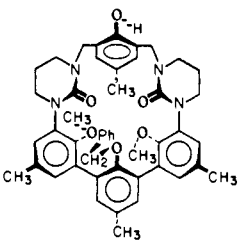
2, A(AUCH$_2$)$_2$B



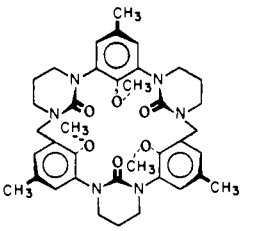
3, A(AUCH$_2$)$_2$A·



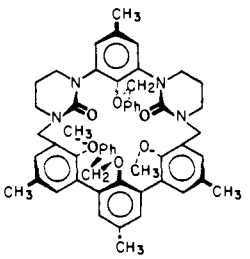
4, A·b(A·UCH$_2$)$_2$A·a



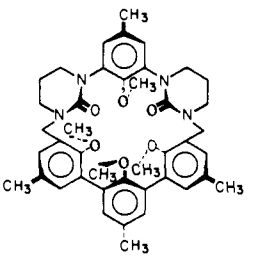
5, A·b(A·UCH$_2$)$_2$A·h



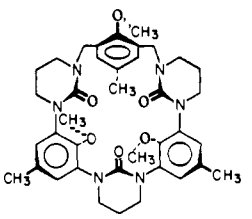
6, U(A·CH$_2$U)$_2$A·



7, A·b(A·CH$_2$U)$_2$A·b

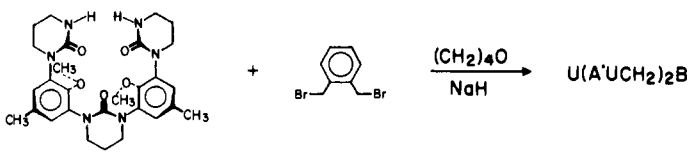


8, A·(A·CH$_2$U)$_2$A·

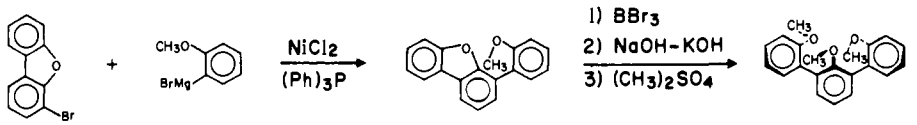


9, U(A·UCH$_2$)$_2$A·

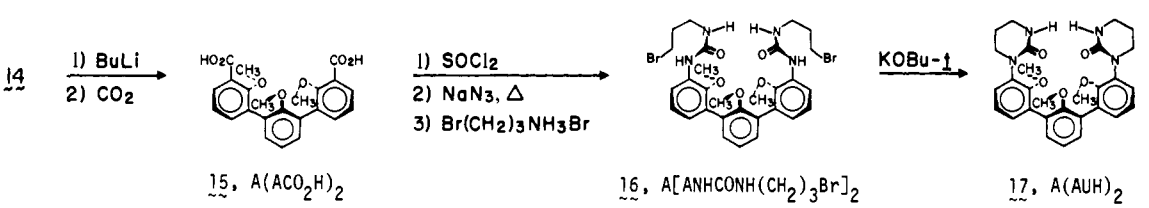
Scheme I



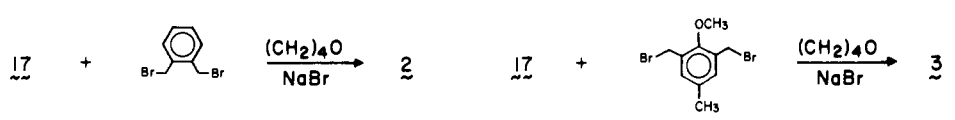
10, U(A·UH)$_2$ 1



12 13 14, A(AH)$_2$

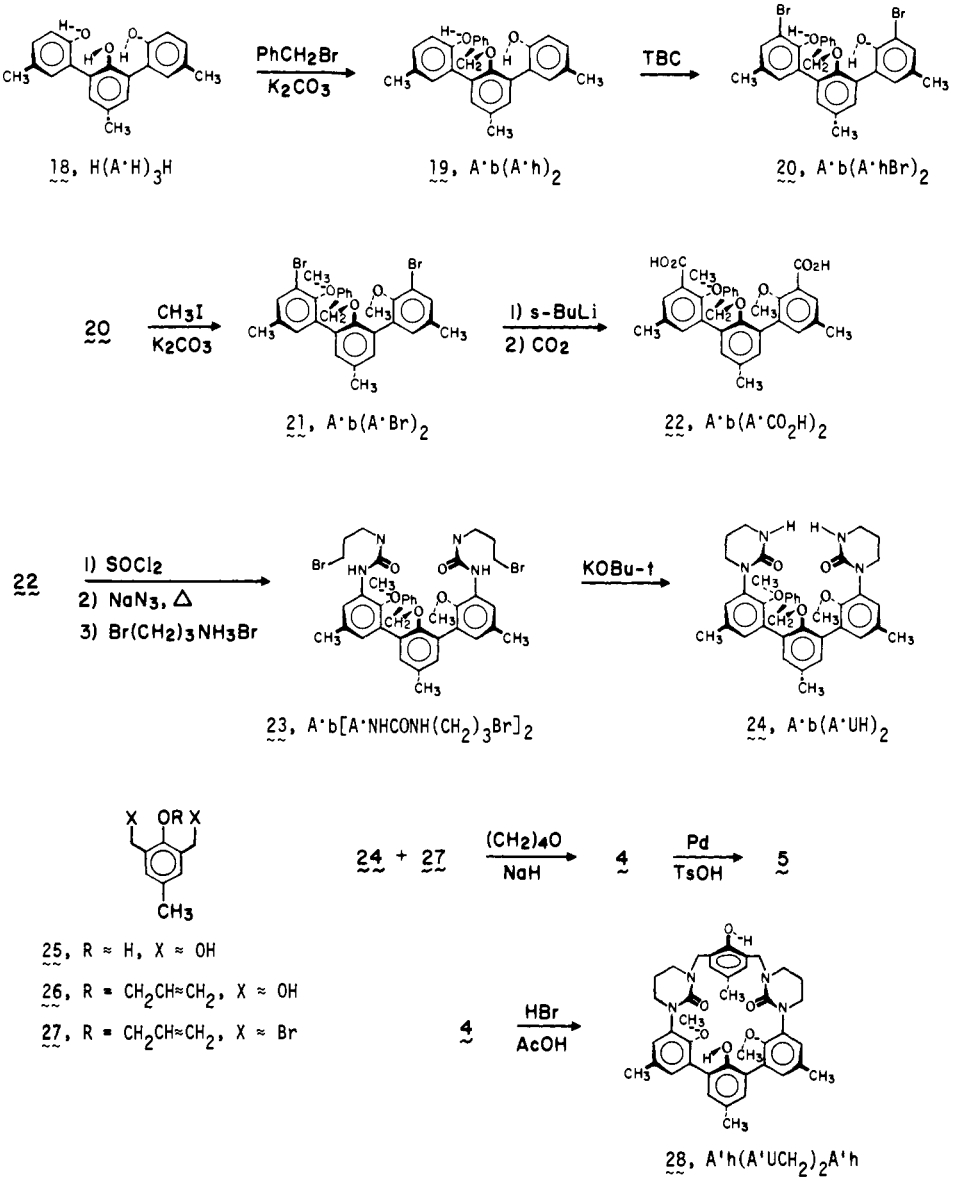


14 15, A(ACO$_2$H)$_2$ 16, A[ANHCONH(CH$_2$)$_3$Br]$_2$ 17, A(AUH)$_2$



17 + 2 17 + 3

Scheme II



produced in 79% overall yield from **22**. Treatment of **23** with KOBu-*t* gave A'b(A'UH)$_2$ (**24**, 89%).

Allylation of triol A'h(CH$_2$OH)$_2$ (**25**)[10] with 1 mol of CH$_2$=CHCH$_2$Br–KOH produced a mixture from which A'a(CH$_2$OH)$_2$ (**26**, 10%) was isolated. Bromination of this compound with PBr$_3$ gave A'a(CH$_2$Br)$_2$ (**27**, 54%). Condensation of A'b(A'UH)$_2$ (**24**) with A'a(CH$_2$Br)$_2$ (**27**) under high dilution conditions ((CH$_2$)$_4$O–NaH) gave A'b(A'UCH$_2$)$_2$A'a (**4**, 54%) purified through its NaBr complex. The allyl group of **4**·NaBr was removed by stirring its solution in 95% EtOH with 10% Pd/C and TsOH[12] to give after decomplexation host A'b(A'UCH$_2$)$_2$A'h (**5**, 50%). It appeared that a Pd complex (uncharacterized) was also formed in this reaction. Treatment of A'b(A'UCH$_2$)$_2$A'a (**4**) with HBr–AcOH produced the bis(phenol) A'h(A'UCH$_2$)$_2$A'h (**28**, 68%). An attempt to bridge the two phenolic hydroxyls of **28** by treatment of the substance with 2,6-bis(bromomethyl)pyridine[13] ((CH$_2$)$_4$O–NaH) led only to polymer (Scheme II).

Host U(A'CH$_2$U)$_2$A' (**6**) was produced in a highly convergent synthesis by condensation of the two moieties U(A'CH$_2$Br)$_2$ (**29**) and (HU)$_2$A' (**30**), whose syntheses are described. Treatment of commercially available 2-amino-4-methylanisole with COCl$_2$ in (CH$_2$)$_4$O gave the disubstituted urea (**31**, 89%), which was cyclized with Br(CH$_2$)$_3$Br(NaH–(CH$_2$)$_4$O) to give U(A'H)$_2$ (**32**, 59%). Bromination of this compound led not to the desired U(A'Br)$_2$ (**37**) but to the isomeric dibromide **33** (49%), indicating that the combined ortho, para-directing abilities of the cyclic urea and methyl groups outweighed the ortho-directing propensity of the methoxy group. Metalation of **32** with *t*-BuLi and carbonation of the organometallic produced gave **34** (75%) rather than the hoped for U(A'CO$_2$H)$_2$ (**38**). Apparently the ability of the cyclic urea unit to direct metalation ortho in an attached benzene ring is stronger than that of a methoxyl group even though the former position is the more hindered. Accordingly, U(A'H)$_2$ (**32**) was demethylated with either BBr$_3$ or HBr–AcOH to give U(A'hH)$_2$ (**35**) in 94% and 77% yields, respectively. Bromination of U(A'hH)$_2$ (**35**) with 2,4,4,6-tetrabromocyclohexadienone[11] produced U(A'hBr)$_2$ (**36**, 95%), which was methylated with CH$_2$N$_2$ to give U(A'Br)$_2$ (**37**, 70%). Metalation of this dibromide with *t*-BuLi and carbonation gave U(A'CO$_2$H)$_2$ (**38**, 99%), methylation of which with CH$_2$N$_2$ led to U(A'CO$_2$CH$_3$)$_2$ (**39**, 100%). Reduction of **39** with LiAlH$_4$ produced U(A'CH$_2$OH)$_2$ (**40**, 83%), which with PBr$_3$ provided U(A'CH$_2$Br)$_2$ (**29**, 76%) (Scheme III).

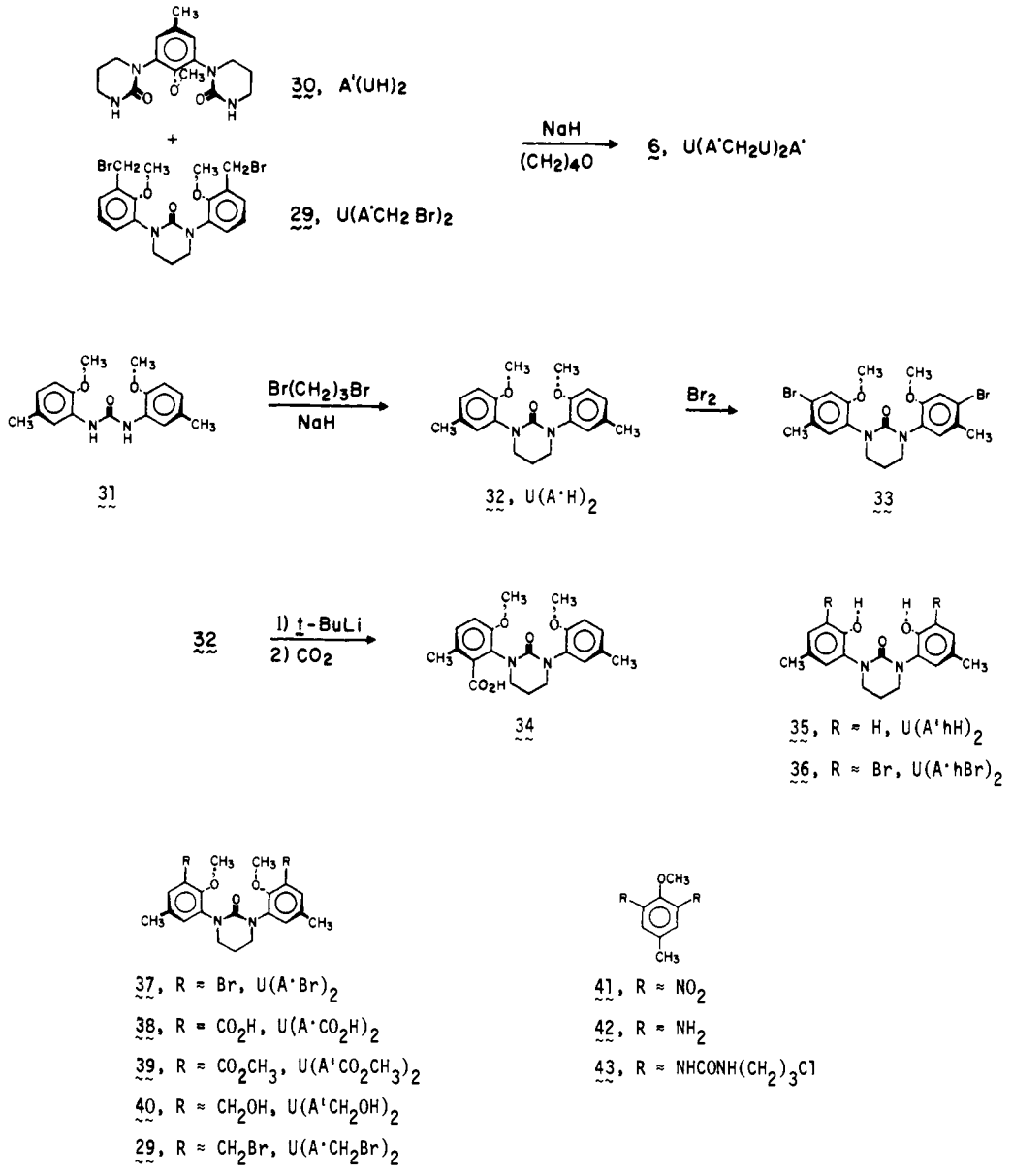
Reduction of 2,6-dinitro-4-methylanisole (**41**)[14] with H$_2$–Pt gave 2,6-diamino-4-methylanisole (**42**, 96%). Treatment of this diamine

(12) Boss, R.; Scheffold, R. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 558–559.

(13) Newcomb, M.; Timko, J.; Walba, D. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6392–6398.

(14) Baroni, E.; Kleinau, W. *Monatsh. Chem.* **1936**, *68*, 251–260.

Scheme III



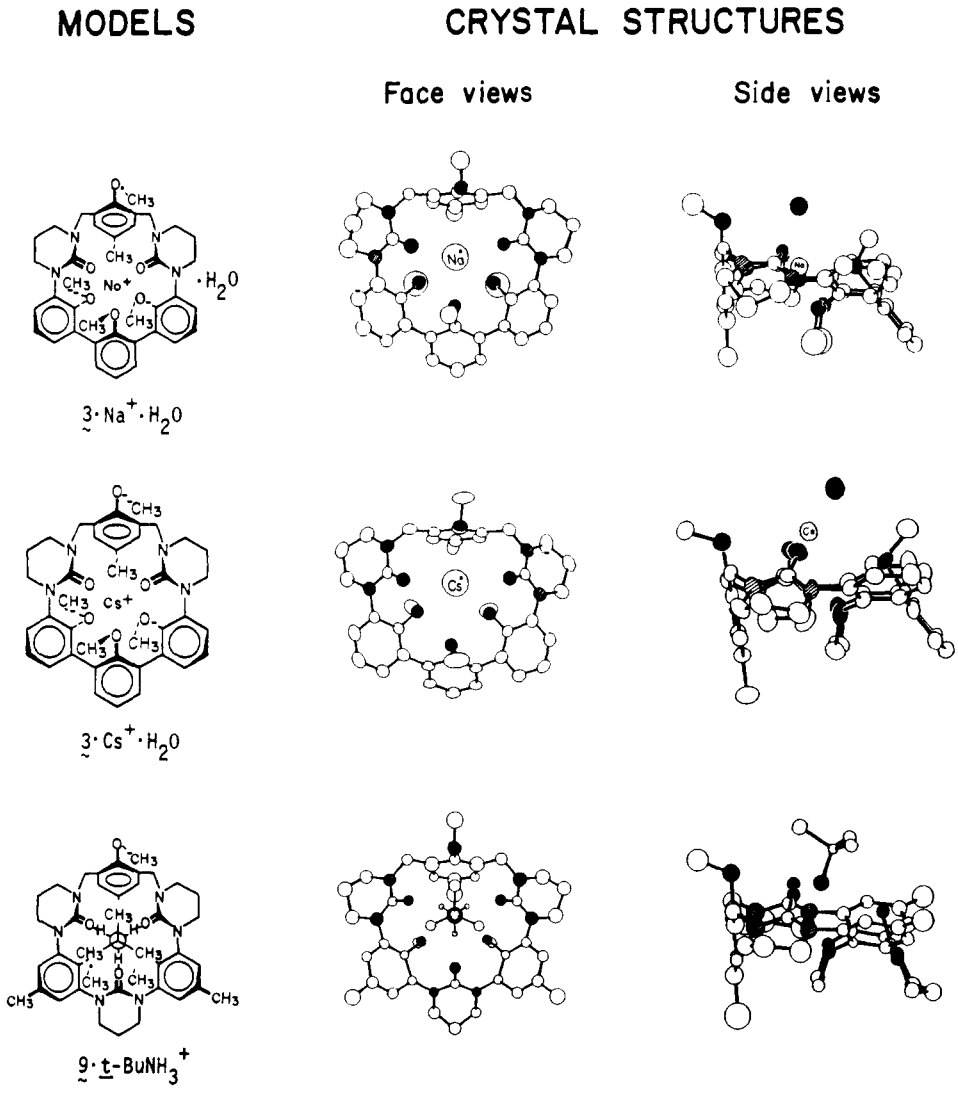
with isocyanate $Cl(CH_2)_3NCO$[15] produced the bis(urea) compound **43**, which was not fully characterized but was doubly annulated with NaH–$(CH_2)_4O$ to give A'$(UH)_2$ (**30**, 23% overall). Under high dilution conditions, A'$(UH)_2$ (**30**) and U(A'$CH_2Br)_2$ (**29**) were condensed (NaH–$(CH_2)_4O$) to provide U(A'$CH_2U)_2$A' (**6**, 48%), which was purified through its NaBr complex.

A convergent synthesis of host A'b(A'$CH_2U)_2$A'b (**7**) was realized by the condensation of A'b(A'$CH_2Br)_2$ (**44**) and $(HU)_2$A'b (**45**), whose syntheses are now described. Treatment of 2,6-dibromo-4-methylphenol[16] with benzyl bromide (K_2CO_3, NaI) gave the corresponding benzyl ether (**46**, 65%), which upon metalation with *sec*-BuLi and carbonation produced 2-(benzyloxy)-5-methylisophthalic acid (**47**, 72%). This material was converted with $SOCl_2$ to its diacid chloride (uncharacterized), which with NaN_3 gave its diacyl azide (uncharacterized). This material was thermally rearranged to the corresponding bis(isocyanate) (uncharacterized). Addition of $Br(CH_2)_3NH_3Br$ to this compound gave the open-chain bis(urea) compound **48** (43% overall) that was doubly annulated with KOBu-*t* to give A'b$(UH)_2$ (**45**, 83%). Diacid A'b(A'$CO_2H)_2$ (**22**) was esterified with CH_2N_2 to provide A'b(A'$CO_2CH_3)_2$ (**49**, 100%), which was reduced with $LiAlH_4$ to A'b(A'$CH_2OH)_2$ (**50**, 91%). This compound with PBr_3 gave A'b(A'$CH_2Br)_2$ (**44**, 65%). Under high dilution conditions, A'b(A'$CH_2Br)_2$ (**44**) and $(HU)_2$A'b (**45**) were condensed (NaH–$(CH_2)_4O$) to give A'b(A'$CH_2U)_2$A'b (**7**, 41%). This host was doubly debenzylated with HBr–AcOH to give diol A'h-(A'$CH_2U)_2$A'h (**51**, 43%) that was methylated with $(CH_3)_2SO_4$–NaOH to provide host A'(A'$CH_2U)_2$A' (**8**, 71%). In an attempt to bridge the pseudopara hydroxyl oxygens of A'h-(A'$CH_2U)_2$A'h (**51**) this bis(phenol) was mixed with O-$(CH_2CH_2OTs)_2$–K_2CO_3–$(CH_2)_4O$, but only polymer and starting material were recovered (Scheme IV).

Crystal Structures. Single-crystal X-ray structures of A-$(AUCH_2)_2$A'·NaBr·H_2O (**3**·NaBr·H_2O), A$(AUCH_2)_2$A'·$CsClO_4·H_2O$ (**3**·$CsClO_4·H_2O$), and U(A'$UCH_2)_2$A'·$(CH_3)_3CNH_3ClO_4$ have been reported.[2a] Face and side views of each are shown in Chart II. The gross structural features of these complexes, coupled with those of A'(A'A')$_2$A'·Li^+,[17] neatly illustrate three different ways guests can be bound to hosts. In A'(A'A')$_2$A'·Li^+, the Li^+ guest is surrounded on all sides by the six *p*-methylanisyl units so that no other molecules can approach the guest (capsular complex). In **3**·Na^+·H_2O, the Na^+ lies deep

(15) Mahood, S. A.; Schaffner, P. V. L. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, pp 160–163.
(16) Kohn, M.; Segel, A. *Monatsh. Chem.* **1925**, *46*, 661–669.
(17) Trueblood, K. N.; Knobler, C. B.; Maverick, E.; Helgeson, R. C.; Brown, S. B.; Cram, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 5594–5596.

Chart II



in a cavity defined by the five ligating oxygens of the host. Since the Na^+ guest is accessible on one side, **3**·Na^+ is a nesting complex. The bottom face is shielded by hydrocarbon groups. The top face is open, and the Na^+ is ligated by a water molecule. In **3**·Cs^+·H_2O and **9**·$(CH_3)_3CNH_3$, the guests are too large to nest in the cavity, and they are forced to perch on the ligating oxygens.

The general conformations of the $A(AUCH_2)_2A'$ and $U(A'UCH_2)_2A'$ hosts in these complexes are nearly guest independent. All oxygens converge on the cavity, and the attached methyl groups diverge from the cavity. Each oxygen of the UA'UA'U or UAAAU assembly is anti to its flanking oxygen. The oxygen of the additional $CH_2A'CH_2$ unit is syn to its flanking oxygens. The plane of this unit is tilted away from the open face of the host at an angle not far from 90° to the best plane defined by the atoms connecting the six units. This arrangement brings the aryl methyl of the $CH_2A'CH_2$ unit into contact with the methyls of the methoxyls of the two nearest A or A' groups to form a closed surface of carbon–hydrogen or carbon–carbon bonds on the bottom face of the complexes. The conformations of these complexes are compatible with expectations derived from CPK model examinations that led to the design and synthesis of the hosts.

Although a detailed account of these crystal structures will be published elsewhere, a few interesting features of **3**·Na^+·H_2O and **3**·Cs^+·H_2O will be pointed out here. The Na^+ in its complex has six ligating sites with an average distance of 2.56 Å. If one assumes the oxygens have a diameter of 2.80 Å, the effective diameter of Na^+ is 2.32 Å, considerably larger than the 1.75 Å for Na^+ in $A'(A'A')_2A'$·Na^+.[17] The distances of the urea oxygens to the Na^+ are 2.447 and 2.568 Å, the more distant oxygen being close enough to the water's oxygen (2.826 Å) to be hydrogen bonded to it. The central methoxyl oxygen is 2.447 Å, the two flanking oxygens are 2.723 and 2.665 Å, and the water oxygen is 2.56 Å from the Na^+. These distances place the Na^+ 0.554 Å below the plane defined by the two urea and central methoxyl oxygens, too distant from the oxygen of the $CH_2A'CH_2$ unit to be ligated. The angle of tilt of this A' group with respect to the best plane of the macroring is 107°. The average dihedral angle between the A units is 63° and between the A and U units is 60°.

The Cs^+ ion in **3**·Cs^+·H_2O has seven oxygen contacts with an average distance of 3.15 Å, providing Cs^+ with an effective diameter of 3.50 Å. The distances of the urea oxygens to the Cs^+ are 2.843 and 2.901 Å, and the water molecule ligating the Cs^+ at a distance of 3.378 Å is close enough to that urea oxygen with the longer cesium contact to infer the presence of a hydrogen bond between the carbonyl and the water molecule. The oxygen of the central A group is 2.996 Å, those of the flanking oxygens are 3.460 and 3.760 Å, and that of the A' group is 3.232 Å distant from the Cs^+. The 3.760-Å distance is too long for the oxygen involved to be ligating the Cs^+. The seventh binding site for the Cs^+ is an oxygen of a carbonyl group in a neighboring complex in the crystal. Thus two hosts appear to be held together by two Cs^+ guests and probably by the hydrogen bonds of two water molecules to form a crystallographic dimeric complex. The Cs^+ ion is located 0.786 Å above the plane defined by the two urea and the central A unit oxygens. The angle of tilt of the A' group with respect to the best plane of the macroring is 104.9°. The average dihedral angle between the A units is 65°, whereas that between the A

Scheme IV

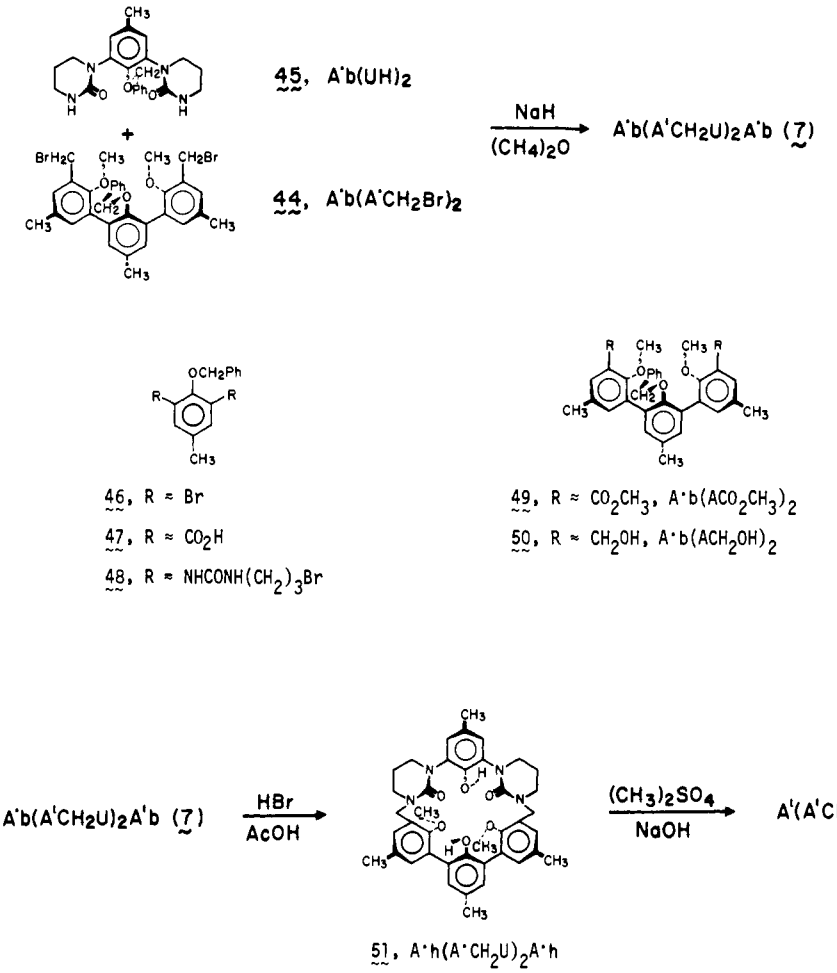


Table I. Association Constants (Ka) and Binding Free Energies ($-\Delta G°$) of Hosts for Picrate Salt Guests in $CDCl_3$ Saturated with D_2O at 25 °C

			guest cation							
host structure	no.	K_a[a] or $-\Delta G°$[b]	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+	$CH_3NH_3^+$	$(CH_3)_3CNH_3^+$
$U(A'UCH_2)_2B$	1	$-\Delta G°$	~18.3	16.3	12.4	11.4	11.8	11.8	12.1	13.2
$A(AUCH_2)_2B$	2	$-\Delta G°$	16.6	15.4	10.8	9.4	10.5	10.4	9.7	7.8
$A(AUCH_2)_2A'$	3	$-\Delta G°$	12.0	14.5	15.2	12.9	11.5	13.3	12.0	9.9
$A'b(A'UCH_2)_2A'a$	4	$-\Delta G°$	12.6	16.5	17.1	14.3	12.4	14.4	14.3	9.3
$A'b(A'UCH_2)_2A'h$	5	$-\Delta G°$	10.7	12.9	12.0	10.4	9.8	10.3	9.2	7.6
$U(A'CH_2U)_2A'$	6	$-\Delta G°$	7.6	12.1	10.4	8.2	7.4	8.6	8.2	7.2
$A'b(A'CH_2U)_2A'b$	7	$-\Delta G°$	11.1	15.9	13.1	10.8	10.9	11.0	10.1	8.6
$A'(A'CH_2U)_2A'$	8	$-\Delta G°$		11.4	10.5					
$U(A'UCH_2)_2A'$	9	$-\Delta G°$	12.1	15.4	15.6	14.2	13.1	14.4	14.4	13.2
$Nap(OEOEO)_2E$	52	$-\Delta G°$	5.9	8.3	10.8	9.6	8.3	9.5	7.5	6.9
$U(A'UCH_2)_2B$	1	K_a	2.5×10^{13}	8.7×10^{11}	1.2×10^9	2.2×10^8	4.4×10^8	4.4×10^8	7.3×10^8	4.6×10^9
$A(AUCH_2)_2B$	2	K_a	1.4×10^{12}	1.9×10^{11}	8.1×10^7	7.7×10^6	4.9×10^7	4.1×10^7	1.3×10^7	5.2×10^5
$A(AUCH_2)_2A'$	3	K_a	6.1×10^8	4.2×10^{10}	1.4×10^{11}	2.8×10^9	2.6×10^8	5.5×10^9	6.1×10^8	1.8×10^7
$A'b(A'UCH_2)_2A'a$	4	K_a	1.7×10^9	1.2×10^{12}	3.3×10^{10}	3.0×10^{10}	1.2×10^9	3.5×10^{10}	3.0×10^{10}	6.5×10^6
$A'b(A'UCH_2)_2A'h$	5	K_a	6.9×10^7	2.8×10^9	6.1×10^8	4.1×10^7	1.5×10^7	3.5×10^7	5.5×10^6	3.7×10^5
$U(A'CH_2U)_2A'$	6	K_a	3.7×10^5	7.3×10^8	4.1×10^7	1.0×10^6	2.6×10^5	2.0×10^6	1.0×10^6	1.9×10^5
$A'b(A'CH_2U)_2A'b$	7	K_a	1.3×10^8	4.4×10^{11}	3.9×10^9	8.1×10^7	9.6×10^7	1.1×10^8	2.5×10^7	2.0×10^6
$A'(A'CH_2U)_2A'$	8	K_a		2.2×10^8	4.9×10^7					
$U(A'UCH_2)_2A'$	9	K_a	7.2×10^8	1.6×10^{11}	2.2×10^{11}	1.4×10^{10}	3.9×10^9	3.5×10^{10}	3.5×10^{10}	4.5×10^9
$Nap(OEOEO)_2E$	52	K_a	2.3×10^4	1.2×10^6	8.6×10^7	1.1×10^7	1.3×10^6	9.9×10^6	3.3×10^5	1.1×10^5

[a] Units for K_a, mol^{-1}. [b] Units for $-\Delta G°$, kcal mol^{-1}.

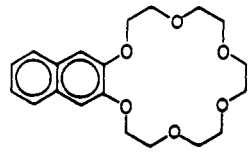
and U units is 56°. Thus although the general structures of the two complexes are rather similar, the units have adapted in a large number of small ways to accommodate the large difference in diameters of the two guests.

Correlation between Structure and Binding Free Energies. The association constants (K_a) and free energies of association ($-\Delta G°$) of macrocyclic hosts **1–8** in $CDCl_3$ saturated with D_2O at 25 °C were measured by the picrate salt extraction method.[18,19] Solutions of Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $CH_3NH_3^+$ and *t*-$BuNH_3^+$ picrates in D_2O were extracted with $CDCl_3$ in the absence and presence of host. The hosts and their complexes are

(18) 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.

(19) Artz, S. P.; Cram, D. J. *J. Am. Chem. Soc.* **1984**, *106*, 2160–2171.

soluble essentially only in the $CDCl_3$ layer. The K_a and $-\Delta G°$ values at 25 °C in $CDCl_3$ saturated with D_2O were calculated from the results and are recorded in Table I. The values are the average of two determinations. This method provides precisions in $-\Delta G°$ values that usually vary between ±1.4 and ±3.1%.[18] Those in the 15–18 kcal mol^{-1} range grow increasingly error prone (±6%) as they increase in value.[19] The K_a and $-\Delta G°$ values for the lipophilic chorand Nap(OEOEO)$_2$E (**52**)[18] and U(A′UCH$_2$)$_2$A′ (**9**)[5] were included in Table I for comparison purposes.



52, Nap(OEOEO)$_2$E

Hosts U(A′UCH$_2$)$_2$B (**1**) and A(AUCH$_2$)$_2$B (**2**) are composed of 19-membered macrorings containing only five oxygens, whereas **3–9** are 20-membered macrorings with six oxygens, and Nap(OEOEO)$_2$E is an 18-membered macroring containing six oxygens. Molecular models (CPK) of U(A′UCH$_2$)$_2$B (**1**) and A(AUCH$_2$)$_2$B (**2**) indicate these systems are more rigid and have smaller cavities than the other macrocycles. The constraints imposed by the enforced coplanarity of the CH$_2$–B–CH$_2$ unit appears to provide **1** and **2** with the highest $-\Delta G°$ values observed for binding Li$^+$ (~18.3 and 16.6 kcal mol^{-1}, respectively). Although these are below the values observed for A′(A′A′)$_2$A′ binding Li$^+$ (>23 kcal mol^{-1}, capsular complex), **1** and **2** possess the advantage over A′(A′A′)A′ of exhibiting faster complexing–decomplexing and extraction rates. Host U(A′UCH$_2$)$_2$B (**1**) in CPK models possesses a more adaptable and less shielded cavity than A(AUCH$_2$)$_2$B (**2**), which accounts for the greater discrimination shown by **2** in complexing the eight cations. In CPK models, **1** and **2** are complementary to Li$^+$ and Na$^+$ (nesting complexes), but the other ions are structurally limited to forming perching complexes. Host U(A′UCH$_2$)$_2$B (**1**) provides a $-\Delta G°_{av}$ for the eight cations of 13.4 kcal mol^{-1}, whereas A(AUCH$_2$)$_2$B (**2**) gives $-\Delta G°_{av}$ = 11.3 kcal mol^{-1}. Host U(A′UCH$_2$)$_2$B (**1**) shows the highest discrimination for Li$^+$ over Na$^+$ observed in this series with $K_a^{Li^+}/K_a^{Na^+}$ = 30. Macrocycle A(AUCH$_2$)$_2$B (**2**) provides $K_a^{Na^+}/K_a^{K^+}$ = 2300, the highest value observed for **1–9** or **52**. However, A′(A′A′)$_2$A′ (which forms only capsular complexes) shows the much higher ratios of >110 for $K_a^{Li^+}/K_a^{Na^+}$ and >5 × 10^{11} for $K_a^{Na^+}/K_a^{K^+}$.[4b] Cycle U(A′UCH$_2$)$_2$B (**1**) shows the highest discrimination of the series for $CH_3NH_3^+$ over NH_4^+ ($K_a^{CH_3NH_3^+}/K_a^{NH_4^+}$ = 1.7) and for *t*-BuNH_3^+ over $CH_3NH_3^+$ ($K_a^{t\text{-}BuNH_3^+}/K_a^{CH_3NH_3^+}$ = 6).

A comparison between the $-\Delta G°$ values for A(AUCH$_2$)$_2$A′ (**3**) and A′b(A′UCH$_2$)$_2$A′a (**4**) is instructive since the compounds differ only in the hydrocarbon groups attached to their oxygens and benzene rings. The $-\Delta G°_{av}$ for A′b(A′UCH$_2$)$_2$A′a (**4**) is 13.9 kcal mol^{-1}, whereas that for the A(AUCH$_2$)$_2$A′ (**3**) is 12.7 kcal mol^{-1}. This difference is attributed partially to the electron-releasing effects of the three methyl groups attached to the anisyls and partially to the steric inhibition of solvation by the benzyl group in A′b(A′UCH$_2$)$_2$A′a (**4**). These groups are absent in A(AUCH$_2$)$_2$A′ (**3**). Host A′b(A′UCH$_2$)$_2$A′a (**4**) exhibits interestingly high values of $K_a^{Na^+}/K_a^{Li^+}$ = 700, $K_a^{K^+}/K_a^{Rb^+}$ = 110, $K_a^{Rb^+}/K_a^{Cs^+}$ = 25, and $K_a^{CH_3NH_3^+}/K_a^{t\text{-}BuNH_3^+}$ = 4600. The much higher structural recognition shown by A′b(A′UCH$_2$)$_2$A′a (**4**) for these guests as compared to its analogue A(AUCH$_2$)$_2$A′ (**3**) is attributed to the increased space occupation by the CH$_2$CH=CH$_2$ side chains, which cannot turn inward to fill the cavity and which generally rigidify the cavity. Cycle A(AUCH$_2$)$_2$A′ (**3**) does show the highest discrimination of this series that favors potassium over sodium, but the value of $K_a^{K^+}/K_a^{Na^+}$ = 3 is modest indeed.

Toward the metal and NH_4^+ ions, A(AUCH$_2$)$_2$A′ (**3**) and U(A′UCH$_2$)$_2$A′ (**9**) are very close to one another in their $-\Delta G°$ values, differing only by $\Delta(\Delta G°_{av})$ = 0.8 kcal mol^{-1}. The substantially higher values observed for the tris(urea) system U(A′UCH$_2$)$_2$A′ (**9**) binding $CH_3NH_3^+$ and *t*-BuNH_3^+ than is found for A(AUCH$_2$)$_2$A′ (**3**) is probably associated mainly with steric inhibition of complexation associated with the methyl group of the central A unit in **3**.

Hosts A′b(A′UCH$_2$)$_2$A′a (**4**) and A′b(A′UCH$_2$)$_2$A′h (**5**) differ structurally only by the former compound containing an OCH$_2$CH=CH$_2$ group in place of an OH group of the latter. This small change reduces $-\Delta G°_{av}$ for **4** from 13.9 to 10.4 for **3** and destroys the high structural recognition of the former compound. Models of **3** indicate the presence in the free host of a spatially favorable intramolecular hydrogen bond of the type ArOH···O=C, which must be broken before a guest can enter the cavity.

Hosts U(A′UCH$_2$)$_2$A′ (**9**) and U(A′CH$_2$U)$_2$A′ (**6**) differ only in the placement of their two CH$_2$ groups. Molecular model examination indicates that when the two CH$_2$ groups are attached to the same benzene ring, as in **9**, the macrocycle is more rigid than when the CH$_2$ groups are attached to different benzene rings. The effect of the greater rigidification is to provide much stronger binding (principle of preorganization). Thus U(A′UCH$_2$)$_2$A′ (**9**) has a $-\Delta G°_{av}$ of 14.0 kcal mol^{-1}, whereas U(A′CH$_2$U)$_2$A′ (**6**) has a $-\Delta G°_{av}$ value of only 8.7 kcal mol^{-1}. Both systems are relatively indiscriminate in their binding except for U(A′CH$_2$U)$_2$A′ (**6**) complexing Na$^+$ vs. Li$^+$ ($K_a^{Na^+}/K_a^{Li^+}$ = 2000).

Ligand systems A′b(A′CH$_2$U)$_2$A′b (**7**) and A′(A′CH$_2$U)$_2$A′ (**8**) differ from one another only in the sense that the former contains two benzyl groups attached to oxygens whereas the latter contains methyls. Unfortunately, too little of **8** was prepared to allow measurement of more than two $-\Delta G°$ values (those for Na$^+$ and K$^+$). However, it is clear that the two benzyl groups play an important role in enhancing the binding free energies of **7**. Thus A′b(A′CH$_2$U)$_2$A′b (**7**) binds Na$^+$ 4.5 and K$^+$ 2.6 kcal mol^{-1} better than does A′(A′CH$_2$U)$_2$A′ (**8**). This striking effect is attributed to the cavity-organizing ability of two $C_6H_5CH_2$ vs. two CH_3 groups. In molecular models, the benzyl groups cannot orient inward to fill the cavity, whereas the methyl can (principle of preorganization). The benzyl groups also inhibit solvation of the binding sites more effectively than do the methyl groups. The macroring of A′b(A′CH$_2$U)$_2$A′b (**7**) is intrinsically rather flexible, but the benzyl groups provide enough organization to provide a $-\Delta G°_{av}$ value of 11.4 kcal mol^{-1}. Interestingly, **7** provides the highest $K_a^{Na^+}/K_a^{Li^+}$ value (3400) observed in this series of hosts.

These urea–anisole unit-containing hosts are both stronger binding and show higher structural recognition in their complexation than the model chorand Nap(OEOEO)$_2$E (**52**). This system provides $-\Delta G°_{av}$ of only 8.7 kcal mol^{-1}, and the maximum structural recognition it shows is K^{K^+}/K^{Na^+} = 70. We attribute the superior properties of the urea–anisyl macrocycles to the fact that they are more highly organized for complexation during synthesis and are less highly solvated than the chorands (principle of preorganization). Although the anisyl oxygen is probably intrinsically a poorer ligand than either a CH$_2$OCH$_2$ or a cyclic urea oxygen, its ability to self organize more than compensates for its innately nonbasic character. When bulkier groups are substituted for the methyl of the anisyl unit, this self-organizing feature appears to be enhanced, as is suggested by molecular models. The intrinsically powerful binding ability of the cyclic urea unit is undoubtedly attenuated by its being heavily solvated by water. This water must be at least partially displaced during complexation. When combined with anisyl or substituted anisyl units in a macrocycle, this solvation is probably somewhat inhibited by the hydrocarbon groups attached to the anisyl oxygens. Furthermore, these hydrocarbon groups generally reduce the number of conformations available to the urea units, an effect that can be used to preorganize the cavity.

Conformational Equilibria. Molecular model (CPK) examination of the 19-membered macroring hosts U(A′UCH$_2$)$_2$B (**1**) and A(AUCH$_2$)$_2$B (**2**) indicates that each can exist in two strain-free forms that should equilibrate rapidly on the human time scale but that are potentially observably on the ^{1}H NMR time scale. Both contain enforced cavities lined with unshared electron pairs of five oxygens, each of which is anti to its neigh-

boring oxygen. The methyl groups all diverge from the cavity. The two forms of each host differ in the location of the phenylene of the *o*-xylyl group, whose plane is roughly perpendicular to the best plane of the macroring, and which is oriented either syn or anti to the two flanking urea oxygens. In the drawings of **1** and **2**, the *o*-xylyl and flanking urea oxygens are anti to one another. Interconversion of the two conformations involves only the two methylenes passing through the cavity, which in models appears to be a facile process. The cavity is complementary to spheres the diameters of Li^+ and Na^+ in a nesting arrangement but is complementary to those of the larger ions only if the π electrons of the carbonyl groups serve as binding sites. Consequently, it is likely that the larger ions only form perching complexes. Both hosts are clearly spherands, since the cavities are enforced, and conformations with inward turned methyl or methylene groups introduce considerable strain into the system.

The ^1H NMR spectra of $U(A'UCH_2)_2B$ (**1**) and $A(AUCH_2)_2A$ (**2**) are consistent with the conformational analyses based on models. The CH_3O hydrogens of the methoxyls at 5 and 7 o'clock of **1** and **2** (outer methoxyls) exist as a broad singlet and the benzyl protons as very broad singlets. Each host when mixed with Na^+ or *t*-$BuNH_3^+$ forms single complexes. The aryl methoxyls exhibit sharp singlets (for **1**) or two sharp singlets present in an intensity ratio of 2:1 (for **2**), and the diastereotopic methylenes become normal AB quartets. As expected, complexation freezes out conformational equilibration. The resonances of the outer methoxyl protons are shifted upfield (0.152 ppm for **1** and 0.146 ppm for **2**) when their hosts are complexed with Na^+. This observation suggests that in these complexes the methyl groups are syn to and are shielded by the magnetic current of the *o*-xylyl group. When complexed with *t*-$BuNH_3^+$, the outer methoxyl protons of **1** were shifted downfield relative to free **1** by 0.091 ppm, suggesting the OCH_3 and *o*-xylyl groups are anti to one another, and that the perching *t*-Bu group and *o*-xylyl groups are syn to one another.

These hypotheses are compatible with conclusions based on molecular models of **1** and **2** and their respective complexes. In models of $U(A'UCH_2)_2B$·*t*-$BuNH_3^+$ in the conformation with the *t*-Bu and *o*-xylyl groups syn to one another, one methyl of the *t*-Bu group contacts the *o*-xylyl group, and the other two are more distant from but are over the two A′ groups. These locations should result in shielding of the CH_3 groups, which is observed. The chemical shifts of *t*-$BuNH_3SCN$ and *t*-$BuNH_3ClO_4$ and of the complex $E(OEOEO)_2E$·*t*-$BuNH_3SCN$ gave δ values in $CDCl_3$ of 1.49, 1.47 and 1.34 ppm, respectively. Furthermore, the δ values for the *t*-Bu protons for 1,3-$C_6H_4(CH_2OEOE)_2O$·*t*-$BuNH_3X$ were 0.94, 0.86, and 0.96 ppm as X was changed from thiocyanate to perchlorate to picrate, respectively.[20] Thus the chemical shift of the *t*-Bu protons of $E(OEOEO)_2E$·*t*-$BuNH_3Pic$ in $CDCl_3$ are likely to be at about δ 1.34. With this value as standard, the *t*-Bu protons of $U(A'UCH_2)_2B$·*t*-$BuNH_3Pic$ moved upfield relative to the standard by about 0.66 ppm.

A syn arrangement of the *t*-Bu and *o*-xylyl groups is also consistent with the fact that $U(A'UCH_2)_2B$ (**1**) complexes the three ammonium ions with $-\Delta G°$ values that decrease in the unusual order *t*-$BuNH_3^+ > CH_3NH_3^+ > NH_3^+$. Possibly small van der Waals attractions between the CH_3 and *o*-xylyl groups determine this order.

In CPK molecular models, the 20-membered macrocycles containing a *m*-xylyl moiety (**3–5** and **9**) also appear to be least strained in a conformation in which the five oxygens not attached to the *m*-xylyl group occupy positions anti to their most proximate neighboring oxygens. The *m*-xylyl groups appear capable of existing in either of two stable conformations with their attached oxygens either syn or anti to their most proximate neighboring (urea) oxygens. The methylenes and cyclic urea oxygens easily pass through the cavity, and the methoxyl groups as well, with somewhat more difficulty. The arylmethyl of the *m*-xylyl group also appears able to go through the cavity, but only by generating considerable strain. The allyloxy and benzyloxy groups seem completely unable to do so. The alkyl groups attached to oxygens do not appear to produce stable conformations with these alkyl groups turned inward and filling the cavity except possibly in $U(A'UCH_2)_2A'$ (**9**) that is more flexible than $A(AUCH_2)_2A'$ (**3**) or $A'b(A'UCH_2)_2A'a$ (**4**). Thus **3** and **4** appear to be spherands (enforced cavities lined with binding sites). The cavity of $A'b(A'UCH_2)_2A'h$ (**5**) is probably occupied by a O–H···O=C. Thus **5** and **9** are classified as hemispherands.[21]

In models of perching complexes of **3–5** and **9**, that conformation whose *m*-xylyl oxygen is syn to the flanking cyclic urea oxygens appears to be the more stable. This conformation is illustrated in the crystal structure of $U(A'UCH_2)_2A'$·*t*-$BuNH_3^+$. However, more strain appears to be involved in having all six oxygens simultaneously ligate a metal ion guest in this conformation than in one in which all six oxygens are anti to their flanking oxygens. Probably some of the complexes of these hosts involve the conformations in which all oxygens are anti to their flanking oxygens.

The ^1H NMR spectrum of the sample of $A(AUCH_2)_2A'$·NaBr (**3**·NaBr) isolated directly from the reaction mixture was a mixture of two complexes in a ratio of 86:14. When the free host was precipitated by heating the complex in methanol–water, its ^1H NMR spectrum indicated the presence of a single conformer. Recomplexation of the material with $NaClO_4$ or NaPic gave the spectrum of only the major isomer of the original mixture. Thus the ring closure appears to be templated, and the minor isomer is a kinetic product. The crystal structure of the major product reveals that the methoxyl of the *m*-xylyl unit is syn to the urea oxygens.

Host $A'b(A'UCH_2)_2A'a$ (**4**) was also isolated as a mixture of two NaBr complexes whose ratio was ~84:16 when the ring closure was performed either at 0 °C or in refluxing $(CH_2)_4O$. Decomplexation of this mixture by washing its $CHCl_3$ solution six times with water gave free cycle in two forms in a ratio of 70:30. When refluxed in ethyl acetate, this mixture produced only the major isomer in detectable amounts (^1H NMR). When recomplexed with NaBr, the free major isomer produced only the major complex. By analogy with the behavior of $A(AUCH_2)_2A'$ (**3**) and its complexes, the major isomers of $A'b(A'UCH_2)_2A'$ (**4**) and their complexes probably possess that conformation with the allyloxy group syn to the flanking urea oxygens. Since neither the benzyloxy nor the allyloxy groups can pass through the cavity of **4**, the isomerization of the minor to the major isomer of **4** at 60 °C (hot EtOAc) must have involved passing the arylmethyl of the *m*-xylyl unit through the cavity at a rate observable on the human time scale.

The ^1H NMR spectrum of $A'b(A'UCH_2)_2A'h$ (**5**) and of **5**·NaBr revealed the presence of one isomer or of several isomers rapidly equilibrating on the ^1H NMR time scale. In models of **5**, the hydroxyl and methylenes of **5** can easily pass through the cavity with only a small steric barrier. The same is true of $A'h(A'UCH_2)_2A'h$ (**28**). The ^1H NMR spectra of both **28** itself and **28**·NaBr represented the equivalent of single conformers. The complicated conformational behavior of $U(A'UCH_2)_2A'$ (**9**) has already been discussed.[5]

In CPK molecular models of the 20-membered macrocycle $U(A'CH_2U)_2A$ (**6**) there is no enforced cavity and strain-free conformations appear possible in which one or another of the methyl groups occupy the cavity. Although the ^1H NMR spectrum of **6** is the equivalent of a single conformation, it probably represents a mixture of conformers equilibrating rapidly on the ^1H NMR time scale. The ^1H NMR spectrum of **6**·NaBr is equally simple but probably represents a single conformation. Molecular models suggest that the all-anti conformation provides the best possible conformation for nesting complexes of this host.

Molecular models of $A'b(A'CH_2U)_2A'b$ (**7**) indicate that neither of the benzyloxy groups have any possibility of passing through the cavity, although the methylene, the urea oxygens and

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the methoxyl groups can do so easily. Thus two isomers are possible, although only one was isolated. Only one isomer of **7**·NaBr was isolated, although a second isomeric complex was detected by ^{1}H NMR as present in <5% amounts in the mother liquors from crystallization of the major component from the reaction mixture. In molecular models, that isomer looks the more stable in which each oxygen is flanked by only anti oxygens. The resulting octahedral arrangement of oxygens appears well arranged to strongly ligate in a nesting arrangement all of the alkali-metal ions. Although adaptable, the cavity diameter appears to be most complementary to the diameters of Na^+ and K^+, which it binds the most strongly. Although either of the methyl groups attached to oxygens can turn inward in this isomer to occupy the cavity, the resulting conformations appear more strained than when all of the alkyl groups diverge from the cavity. It seems probable that the isomer obtained is a spherand. The benzyl groups in models appear to play a determining role in inhibiting collapse of the cavity by conformational reorganization.

Molecular models of A′(A′CH$_2$U)$_2$A′ (**8**) provide a much more flexible system than those of A′b(A′CH$_2$U)$_2$A′b. The ^{1}H NMR spectrum of the compound is that of either a single conformation or a rapidly equilibrating group of conformers. The latter is the more probable. In that conformer of **8** in which the methoxyl groups at 12 and 6 o'clock are syn to one another, one methyl group can easily occupy the cavity without introducing strain into the system. Thus **8** is not a spherand.

These results taken in sum illustrate the importance of preorganization to both high binding free energies and to high structural recognition. One relatively rigid form of preorganized host is found in A(AUCH$_2$)$_2$B (**2**), which owes the conformational arrangement of its parts to the tightness of its macroring. A second form is illustrated by A′b(A′UCH$_2$)$_2$A′a (**4**) and A′b-(A′CH$_2$U)$_2$A′b (**7**), which are more flexible. Their organization is preserved by the presence of bulky appendages that inhibit collapse of the cavity. Still another form of preorganized host is illustrated by U(A′UCH$_2$)$_2$A′ (**9**), which is conformationally very mobile, but most of its conformations are strongly binding. As a result, this host binds all ions tested rather indiscriminately.

Experimental Section

General Data. All chemicals were reagent grade. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl. Methanol, tetramethylethylenediamine (TMEDA), and toluene were dried over 3 Å sieves. Diisopropylethylamine was distilled from *p*-toluenesulfonyl chloride (100 mL/g). Gaseous phosgene (99%) (Matheson Corp.) was used directly. Solutions of *sec*-butyllithium and *tert*-butyllithium (Alfa-Ventron Corp.) were titrated to a 1,10-phenanthroline endpoint before use. Potassium *tert*-butoxide and solutions of borane in THF were obtained from Aldrich Chemical Co. Medium-pressure chromatography was performed on either a 250 mm × 25 mm or a 1000 mm × 25 mm Altex column packed with silica gel 60 (E. M. Merck, particle size 0.040–0.063 mm, 230–400 mesh, ASTM) with flow rates between 6 and 12 mL/min. Gravity chromatography was done on either silica gel 60 (E. M. Merck, particle size 0.063–0.200 mm) or neutral alumina (MCB, activated alumina, 80–325 mesh). Flash chromatography involved silica gel 60 (E. M. Merck, particle size 0.040–0.063 mm, 230–400 mesh, ASTM). Preparative thin-layer chromatography was done on silica gel 60 (E. M. Merck, layer thickness either 0.5 mm or 2.0 mm). Reported R_f's were obtained on thin-layer plates of silica gel 60 (E. M. Merck, layer thickness 0.25 mm). Gel permeation chromatography was performed on a 20 ft × 0.375 in. o.d. column packed with 200 g of 100 Å styragel (Waters Associates) with CH_2Cl_2 as the mobile phase at flow rates of 3.5–4.0 mL/min. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. NMR spectra were obtained on a Bruker WP-200 (200 MHz) spectrometer. Chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Coupling constants are reported in hertz (Hz) and splitting patterns are designated as s (singlet), d (doublet), t (triplet), m (multiplet), AB (AB quartet), b (broad), and d of d (doublet of doublets). Mass spectra were recorded on an AE-1 Model MS-9 double-focusing spectrometer interfaced by Kratos Co. to a Data General Nova 3; IR spectra were recorded on a Perkin-Elmer Model 297 spectrophotometer.

34,36,37-Trioxo-35,38-dimethoxy-4,27-dimethyl-1,7,11,20,24,30-hexaazaheptacyclo[28.3.1.1^{2,6}.1^{7,11}.1^{20,24}.1^{25,29}.1^{1,30}.0^{13,18}]octaconta-35-(2),3,5,13(14),15,17,38(25),26,28-nonaene (1). A mixture of 1.328 g (2.47 mmol) of tris(urea) compound U(A′UH)$_2$ (**10**,[5] 0.50 g of 50% NaH (washed with hexane), and 850 mL of THF was refluxed under argon until a solution was obtained. The reaction mixture was cooled to −78 °C, and, all at once, 0.680 g of 96% pure (2.574 mmol) 1,2-bis(bromomethyl)benzene in 5 mL of THF was added. The mixture was allowed to come to 25 °C over 15 h, and stirring was continued for a total of 36 h. Water was then added to destroy excess NaH, and the THF was removed under reduced pressure. To the residue was added 100 mL of CH_2Cl_2, 100 mL of distilled water, and 10 g of NaBr. The mixture was stirred vigorously for 10 min, and the phases were separated. The aqueous layer was extracted with 50 mL of CH_2Cl_2, and the combined organic extracts were dried (Na_2SO_4), filtered, and evaporated to dryness. Benzene (25 mL) was added, the mixture was swirled and allowed to stand for 10 min, and 25 mL of benzene was added. The solid that separated was filtered and washed with benzene. Recrystallization of this material from CH_2Cl_2/THF gave 0.2340 g of a white solid. The mother liquors were added to the benzene filtrate, the solvents were removed, and the residue was gel chromatographed. The fraction of retention volume 153–180 mL was collected, evaporated to dryness, and dissolved in 20 mL of CH_2Cl_2. Benzene was added to the cloudpoint, and a small amount of flocculent material was filtered and discarded. The filtrate, when diluted with benzene and heated to reflux, gave a white precipitate (0.3161 g), which after being washed with benzene, was identified as a mixture of the open-chain alcohol (HUA′UA′UCH$_2$BCH$_2$OH) and the sodium bromide complex of **1**. This mixture of materials was combined with the first solid originally collected prior to the gel chromatography (total 0.5501 g) and subjected to a decomplexation procedure designed to enable separation of the free host **1** from the open-chain alcohol. This material was dissolved in 40 mL of methanol and heated to reflux. Distilled water (130 mL) was added dropwise. After 15 h a precipitate that had formed (0.1 g) was cooled, filtered, and washed well with distilled water. The filtrate was evaporated to dryness and again dissolved in methanol (20 mL). Distilled water heated to 100 °C was added at a rate so as to maintain a reflux. After 24 h the condenser was removed and solvent allowed to evaporate until a white precipitate again formed (approximately 50 mL of solvent was left at this point). The mixture was cooled to 25 °C, and the solid (0.2 g) was filtered and combined with the former precipitate. The mother liquors were discarded. The ^{1}H NMR spectrum of these materials indicated them to be a mixture of **1** (uncomplexed) and open-chain alcohol. The mixture was heated to reflux with 30 mL of toluene. Some of the material dissolved, and the toluene was decanted. This procedure was repeated five more times with 30 mL of toluene each time. The insoluble solid was collected, leaving behind a yellow oil which adhered to the walls of the flask. The toluene-soluble fraction was evaporated, and the product that separated was recrystallized from ethanol and dried at 100 °C under vacuum to yield 0.1052 g (6.7%) of **1**, mp 250 °C dec. The insoluble mobile solid was filtered, washed with benzene, and recrystallized from $CHCl_3$/CH_3CN to yield 0.13 g of HUA′UA′UCH$_2$BCH$_2$OH (8.0%), mp 240 °C dec. The oil adhering to the flask was mainly oligomeric impurities and was discarded.

Free host **1**: ^{1}H NMR ($CDCl_3$) δ 2.10–2.20 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$N), 2.273 (s, 6 H, ArCH$_3$), 3.297 (b s, 2 H, ArCH$_2$N), 3.69–3.850 (b m, 8 H, NC*H*$_2$CH$_2$C*H*$_2$N), 3.613 (b s, 6 H, ArOCH$_3$), 4.750 (b s, 2 H, ArCH$_2$N), 6.927 (s, 2 H, ArH), 6.957 (s, 2 H, ArH), 7.22–7.4 (m, 4 H, *o*-xylyl); MS (70 eV, 235 °C), *m/e* 638 (M$^+$, 1), 607 (M$^+$ − 31, 100). Anal. Calcd for $C_{36}H_{42}N_6O_5$: C, 67.69; H, 6.63; N, 13.16. Found: C, 67.29; H, 6.51; N, 12.84.

1·(CH$_3$)$_3$CNH$_3$ picrate: ^{1}H NMR ($CDCl_3$) δ 0.688 (s, 9 H, (CH$_3$)$_3$C), 2.252–2.399 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$N), 2.252 (s, 6 H, ArCH$_3$), 3.545–3.943 (m, 12 H, NC*H*$_2$CH$_2$C*H*$_2$N), 3.704 (s, 6 H, ArOCH$_3$), 4.544 (AB, *J* = 15.1 Hz, 2 H, ArCH$_2$N), 4.748 (AB, *J* = 15.1 Hz, 2 H, ArCH$_2$N), 6.942 (s, 4 H, ArH), 7.220–7.349 (m, 4 H, *o*-oxlyl), 8.774 (s, 2 H, picrate).

1·NaBr complex: ^{1}H NMR ($CDCl_3$) δ 2.250–2.481 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$N), 2.275 (s, 6 H, ArCH$_3$), 3.461 (s, 6 H, ArOCH$_3$), 3.772 (AB, *J* = 15.9 Hz, 2 H, ArCH$_2$N), 3.805–4.144 (m, 12 H, NC*H*$_2$CH$_2$C*H*$_2$N), 5.368 (AB, *J* = 15.9 Hz, 2 H, ArCH$_2$N), 6.894 (s, 2 H, ArH), 6.945 (s, 2 H, ArH), 7.439–7.551 (m, 4 H, *o*-xylyl).

HUA′UA′UCH$_2$BCH$_2$OH: ^{1}H NMR ($CDCl_3$) δ 2.015–2.281 (b m, 12 H, ArCH$_3$, NCH$_2$C*H*$_2$CH$_2$N), 3.15–3.90 (b m, 18 H, OCH$_3$, NC*H*$_2$CH$_2$C*H*$_2$N), 6.997 (s, 2 H, ArH), 7.068 (s, 2 H, ArH), 7.300 (s, 4 H, ArH); MS (70 eV, 250 °C), *m/e* 650 (M$^+$, 1), 625 (M$^+$ − 31, 2); osmometric mol wt 730 ± 10%. Anal. calcd for $C_{36}H_{44}N_6O_6$: C, 65.83; H, 6.75; N, 12.80. Found: C, 65.78; H, 6.49; H, 12.74.

4-Bromodibenzofuran (12).[9] To a solution of 67.3 g (0.40 mol) of dibenzofuran in 700 mL of THF was added under argon at −40 °C 180 mL of a 2.4 M solution of BuLi in hexane (0.43 mol). The mixture was allowed to warm to 25 °C and was maintained at this temperature for 5 h. The mixture was cooled to −78 °C, and a solution of 109 g (0.85 mol) of 1,2-dibromoethane in 50 mL of THF was slowly added with stirring. The mixture was allowed to warm to 25 °C, at which temper-

ature it was stirred for 2 h. The solvent was evaporated, the residue was dissolved in CH_2Cl_2, and the solution was washed with 1 N HCl in H_2O. The organic layer was dried and evaporated, and the crystals that separated were recrystallized to give **12**: 80 g (81%); mp 67–69 °C; MS (70 eV, 250 °C), *m/e* 246 (M^+). Anal. Calcd for $C_{12}H_7BrO$: C, 58.32; H, 2.86; Br, 32.34. Found: C, 58.37; H, 2.85; Br, 32.22.

4-(2-Methoxyphenyl)dibenzofuran (13). To a suspension of 7.0 g (0.3 mol) of Mg in 30 mL of Et_2O was very slowly added at gentle reflux 75.0 g (0.3 mol) of **12** dissolved in 400 mL of Et_2O. The mixture was refluxed for 12 h, decanted from unreacted Mg, and slowly added to a solution of 55 g (0.3 mol) of 2-bromoanisole and 2.0 g of $Ni[P(C_6H_5)_3]_2Cl_2$ in 100 mL of Et_2O. The mixture was refluxed for 24 h and poured over crushed ice. The mixture was acidified with dilute HCl in H_2O, and the organic layer was washed with water, dried, and evaporated, and the mixture dissolved in CH_2Cl_2 was passed through a filter column of silica gel to remove catalyst. The column filtrate was evaporated to give 82 g (>80%) of **13** contaminated with dibenzofuran, but of direct use for the next step. A small sample was purified by chromatography and recrystallization from CH_2Cl_2/pentane to give pure **13**: mp 90–91 °C; ^1H NMR ($CDCl_3$) δ 3.8 (s, CH_3O, 3 H); MS (70 eV, 250 °C), *m/e* 274 (M^+). Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 82.96; H, 5.15.

4-(2-Hydroxyphenyl)dibenzofuran. Crude **12** (81 g) was dissolved in 700 mL of CH_2Cl_2, and the solution was cooled to −78 °C. To the stirred mixture was added 30 mL of BBr_3, and the mixture was allowed to warm to 25 °C over a 12-h period, and it was poured over crushed ice. The CH_2Cl_2 layer was separated, and the remaining mixture of water and solid was shaken with Et_2O to dissolve the solid. The organic layers were combined, dried, and evaporated to give a mixture of products used directly in the next step, yield >80%. A small sample of the title compound was obtained pure by chromatography on silica gel (CH_2Cl_2) and recrystallization (CH_2Cl_2/pentane): mp 112–113 °C; ^1H NMR ($CDCl_3$) δ (b s, OH, 1 H); MS (70 eV, 250 °C), *m/e* 260 (M^+). Anal. Calcd for $C_{18}H_{12}O_2$: C, 83.06; H, 4.65. Found: C, 83.17; H, 4.71.

2,2′,2″-Trihydroxy-1,1:3′,1″-terphenyl. The crude, dry mixture (no solvents) from the above demethylation was placed in a 1-L stainless-steel container with 800 g of KOH pellets, and the mixture was slowly heated with a Bunsen burner. When the first pellets melted, a stainless-steel stirrer was started. A temperature (~220 °C) was maintained that provided a smooth evaporation from the melt of H_2O. After 30 min at this temperature, water evolution slowed down, and the temperature was raised to 300–320 °C for 18 min. The paste was poured out on a steel pan, pulverized, and dissolved in 700 mL of H_2O, and the solution was cooled to 0 °C and acidified cautiously with 10 N HCl/H_2O. The resulting mixture was cooled and shaken with four successive 500-mL portions of ether, and the combined ether layers were dried with $MgSO_4$. The solution was evaporated, and the residue was mixed with CH_2Cl_2 (400 mL). The mixture was cooled to 0 °C for 24 h, and the insoluble tris(phenol) was collected as white crystals. The mother liquors were filter chromatographed on silica gel (EtOAc), and additional product was isolated by crystallization from CH_2Cl_2 to give a total of 57.6 g (69% from **12**) of nearly pure tris(phenol): mp 168–170 °C; MS (70 eV, 240 °C), *m/e* 278 (M^+). Anal. Calcd for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.79; H, 5.14.

2,2′,2″-Trimethoxy-1,1′:3′,1″-terphenyl (14). To a refluxing mixture of 57.6 g of the above tris(phenol), 100 g of K_2CO_3, and 3 L of acetone was added with vigorous stirring over a 48-h period 60 mL of $(CH_3)_2SO_4$. The K_2SO_4 that separated was filtered and washed with acetone. The filtrate was concentrated, and the product was crystallized from a $(CH_3)_2CO$/EtOH solution of the residue to give a first crop of **14**. The filtrate was evaporated, and the residual oil was again methylated (30 g of K_2CO_3 and 20 mL of $(CH_3)_2SO_4$) to give a second crop of **14**. The filtrates were subjected to filter chromatography to give a third crop of **14**: total weight, 58.1 g (88%, or 49% overall based on dibenzofuran); mp 117–118 °C; ^1H NMR ($CDCl_3$) δ 3.17 (s, CH_3, 3 H), 3.79 (s, CH_3, 6 H), 6.9–7.4 (m, ArH, 11 H); MS (70 eV, 240 °C), *m/e* 320 (M^+). Anal. Calcd for $C_{21}H_{20}O_3$: C, 79.73; H, 6.29. Found: C, 78.61; H, 6.37.

2,2′,2″-Trimethoxy-3,3″-dibromo-1,1′:3′,1″-terphenyl (BrAAABr). To a solution of 9.6 g (30 mmol) of **14** and 7.5 mL (90 mmol) of TMEDA in 400 mL of Et_2O was added 36 mL of a 2.3 M solution of BuLi (83 mmol) in hexane. The mixture was stirred 12 h and cooled to −78 °C, and 5 mL of Br_2 (98 mmol) was added. The mixture was allowed to warm to 25 °C, and H_2O was added cautiously. The mixture was evaporated, and the residue was shaken with CH_2Cl_2/H_2O. The organic layer was dried and evaporated, and the residue was subjected to silica gel chromatography (pentane/toluene, 1/10, v/v, then with increasing toluene concentration). The product was recrystallized from CH_2Cl_2/pentane to give 4.3 g (30%) of BrAAABr: mp 122–123 °C; ^1H NMR ($CDCl_3$) δ 3.2 (s, OCH_3, 3 H), 3.6 (s, OCH_3, 6 H), 7.0–7.6 (m, ArH, 9 H); MS (70 eV, 240 °C), *m/e* 478 (M^+). Anal. Calcd for $C_{21}H_{18}O_3Br_2$: C, 52.75; H, 3.79; Br, 33.42. Found: C, 52.74; H, 3.70; Br, 33.40.

2,2′,2″-Trimethoxy-3,3″-dicarboxy-1,1′:3′,1″-terphenyl (15). To a dry stirred mixture (under argon) of HAAAH (**14**) (4.95 g or 0.0155 mol), 160 mL of Et_2O, and 5.14 mL of TMEDA was added 15.1 mL of a 2.3 M solution of BuLi in hexane. After 6 h, an additional 5 mL of 2.3 M BuLi solution was added and stirring was continued (18.5 h). The dianion was quenched with gaseous CO_2, and the resulting mixture was shaken with EtOAc and H_2O. The mixture was acidified with 50% HCl/H_2O, and the layers were separated. The aqueous layer was extracted with an additional two 50-mL portions of EtOAc. The combined extracts were dried ($MgSO_4$), filtered, and evaporated to dryness to give a white solid. The product was triturated with pentane and dried to give 5.9 g (93%) of the diacid (TLC, silica gel, 6% MeOH/EtOAc + 3 drops of AcOH, R_f 0.20, minor impurities at R_f 0.25, 0.3, 0.35). An analytical sample was prepared by recrystallization of the crude material from CH_2Cl_2/Et_2O; mp 230–232 °C; ^1H NMR ($CDCl_3$) δ 3.194 (s, 3 H, OCH_3), 3.655 (s, 6 H, OCH_3), 7.329–7.488 (m, 5 H, ArH), 7.610–8.239 (dd, 4 H, ArH); MS (70 eV, 190 °C), *m/e* 408 (M^+). Anal. Calcd for $C_{23}H_{20}O_7$: C, 67.64; H, 4.94. Found: C, 67.54; H, 4.85.

2,2′,2″-Trimethoxy-3,3″-bis[3-(3-bromopropyl)ureido]-1,1′:3′,1″-terphenyl (16). A mixture of 5.9 g (0.0145 mol) of **15** and 10 mL of thionyl chloride was refluxed for 70 min (a $CaCl_2$ tube protected against moisture). The excess thionyl chloride was evaporated under reduced pressure. Toluene (20 mL) was added to the residual oil, and the solution was evaporated to dryness under reduced pressure. An additional 20 mL of toluene was added and evaporated. The residue was placed under high vacuum to give a viscous oil. Acetone (45 mL) was added, the solution was cooled to 0 °C, and a solution of 2.45 g of sodium azide in 7.5 mL of water was added. After 15 min of stirring, the mixture became viscous. The flask was swirled manually an additional 5 min, and the contents were poured into 500 mL of ice water. The precipitate was collected on a medium-sintered glass-fritted funnel, washed well with water, and allowed to air dry under vacuum for 30 min. A minimal amount of toluene was then added to the filter, and the dissolved acyl azide was filtered. The filtrate was cooled to 0 °C, dried (a large amount of $MgSO_4$), and refiltered. The $MgSO_4$ was washed with 100 mL of dried (3-Å sieves) toluene. The filtrate (250 mL) was heated under argon by immersing its container in an oil bath heated to 150 °C. Within 5 min, the Curtius rearrangement was complete as evidenced by the cessation of nitrogen evolution. Heating was continued until the toluene began to reflux. The hot solution was then immediately cooled to 0 °C, and 5.1 mL (0.029 mol) of freshly distilled diisopropylethylamine and 6.5 g (0.0297 mol, 98% pure) of 3-bromopropylamine–hydrobromide were added. The mixture was stirred vigorously for 30 min at 0 °C, the ice bath was removed, and stirring was continued for 30 h. TLC (5–10% MeOH/CH_2Cl_2) indicated the presence of mainly one component. Water (150 mL) was added, and the mixture was filtered. The solid was washed with 100 mL of water, 200 mL of CH_2Cl_2, methanol, and, finally, pentane. The layers of the combined filtrates were separated, and the organic layer was dried (Na_2SO_4), filtered, condensed to a small volume under reduced pressure, and diluted with EtOAc until product precipitated. The precipitate was collected, washed with a small amount of CH_2Cl_2, and combined with the previously filtered product. The combined sample was dried (100 °C/30 mm) to give 5.85 g (59.4%) of **16**. In some runs, an additional 10–30% of **16** was recovered from the filtrates by chromatography. The success of this reaction is dependent upon the dryness of the acyl azide solution prior to the rearrangement. The isocyanate formed is readily decomposed by any moisture present. An analytical sample of **16** was prepared by its recrystallization from methanol/water: mp 185.5–187.5 °C; ^1H NMR ($CDCl_3$) δ 2.110–2.174 (m, 4 H, $NCH_2CH_2CH_2N$), 3.066 (s, 3 H, OCH_3), 3.400–3.532 (m, 14 H, NCH_2, CH_2Br, OCH_3), 5.150 (b s, 2 H, $HNCH_2$), 6.989–7.380 (m, 7 H, ArH), 8.025 (dd, 2 H, $HC{=}CN(CO)N$); MS (70 eV, 200 °C) *m/e* 518 [M^+ − 158 (^{79}Br), 1], 516 [M^+ − 162 (^{81}Br), 1]. Anal. Calcd for $C_{29}H_{34}Br_2N_4O_5$: C, 51.34; H, 5.05; N, 8.26. Found: C, 51.23; H, 4.81; N, 7.97.

2,2′,2″-Trimethoxy-3,3″-bis(hexahydro-2-oxopyrimidinyl)-1,1′:3′,1″-terphenyl (17). A mixture of 4.61 g (6.8 mmol) of **16**, 300 mL of $(CH_3)_3COH$, and 3.0 g (0.027 mol) of $(CH_3)_3COK$ was stirred for 48 h. The mixture was diluted with 250 mL of water, stirred 12 h, filtered through a fine frit, and washed well with water. The filtrates were refiltered and washed with water, and the combined solids were washed with ether and dried to give 3.36 g (96%) of **17**: mp 240–245 °C; pure to TLC (10% MeOH/CH_2Cl_2, R_f 0.2) and ^1H NMR analysis. A sample was recrystallized from acetonitrile: mp 276.5–279 °C; ^1H NMR ($CDCl_3$) δ 2.027–2.142 (m, 4 H, $NCH_2CH_2CH_2N$), 3.249 (s, 3 H, $ArOCH_3$), 3.419–3.544 (m, 4 H, $HNCH_2$), 3.595 (s, 6 H, $ArOCH_3$), 3.55–3.70 (m, 4 H, $ArNCH_2$), 5.117 (b s, 2 H, NH); MS (70 eV, 230 °C), *m/e* 516 (M^+). Anal. Calcd for $C_{29}H_{32}N_4O_5$: C, 67.42; H, 6.24; N, 10.85.

Found: C, 67.27; H, 6.21; N, 10.94.

34,38-Dioxo-33,35,36,37-tetramethoxy-31-methyl-3,7,23,27-tetraazaheptacyclo[27.3.1.1^{3,7}.1^{8,12}.1^{13,17}.1^{18,22}.1^{23,27}]octaconta-1(33),8(35),9,11,13(36),14,16,18(37),19,21,29,31-dodecaene (3). Sodium hydride (0.6 g of a 50% mull washed with pentane) was added under argon to 1.50 g (2.90 mmol) of **17** mixed with 900 mL of THF. The mixture was heated to reflux for 1.75 h and cooled to −78 °C, and 0.89 g (2.89 mmol) of 2,6-bis(bromomethyl)-4-methylanisole[10] in 5 mL of THF was added with stirring. The mixture was allowed to warm to 25 °C over a 12-h period, and stirring was continued for a total of 14 h. The reaction mixture was heated to reflux for 1 h, cooled to 25 °C, quenched with water (5 mL), and evaporated to dryness under reduced pressure. The residue was partitioned between 80 mL of CH_2Cl_2 and 100 mL of water, the layers were separated, and the aqueous layer was extracted again with two 20-mL portions of CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. The residual oil was subjected to gel chromatography, the fraction of retention volume 168–193 mL separating cleanly from oligomer and polymer. THF (50 mL) was added to the residue. After 45 min a white microcrystalline solid (0.9063 g, 40.8%) of **3**·NaBr had formed. This material was filtered and washed with THF. The mother liquors were concentrated to a small volume and gave an additional 0.064 g (2.9%) of **3**·NaBr, mp 250 °C dec. A flame test on the sample was strongly positive for Na^+. A sample of the NaBr complex was recrystallized from CH_2Cl_2/THF to give material used for the crystal structure determination. The ^1H NMR spectrum (200 MHz, $CDCl_3$) of the material revealed that the complex existed in two forms. Integration of the benzyl protons or the protons of the para methyl group showed the presence of 11–17% of the minor isomer. A sample of the material was decomplexed as follows. A mixture of 0.104 g (0.1360 mol) of **3**·NaBr, 10 mL of methanol, and 2 mL of water was heated at reflux for 12 h. The condenser was then removed, and the solvent was allowed to evaporate until a white precipitate had formed. The mixture was cooled to 25 °C and filtered through a fine glass frit, and the solid was washed well with conductivity water and dried at 100 °C at 0.1 mm to give 0.0663 g (74%) of **3**, mp 252–284 °C dec. The overall yield of free cycle for both the cyclization and decomplexation was 32.3%. For analysis, a sample was recrystallized from ethanol/water to give small dots (dried 200 °C/0.1 mm), mp 285–287 °C. In contrast, to the complex, the free host exists as one conformation (^1H NMR). Recomplexation of the free host with $Na^+ClO_4^-$ (acetonitrile) gave a single conformation (^1H NMR). It was recrystallized from CH_2Cl_2/THF to give crystals for X-ray analysis.

Free host **3**: ^1H NMR ($CDCl_3$) δ 2.171–2.259 (m, 4 H, $NCH_2CH_2CH_2N$), 2.290 (s, 3 H, $ArCH_3$), 2.874 (s, 3 H, $ArOCH_3$), 3.279 (s, 6 H, $ArOCH_3$), 3.438 (AB, J = 14.6 Hz, 2 H, $ArCH_2N$), 3.556–3.802 (m, 8 H, $NCH_2CH_2CH_2N$), 3.934 (s, 3 H, $ArOCH_3$), 5.611 (AB, J = 14.6 Hz, 2 H, $ArCH_2N$), 7.039–7.321 (m, 11 H, ArH); MS (70 eV, 190 °C), m/e 662 (M^+, 3), 631 (M^+ − 31, 98). Anal. Calcd for $C_{39}H_{42}N_4O_6$: C, 70.68; H, 6.39; N, 8.45. Found: C, 70.59; H, 6.48; N, 8.48.

3·NaPic complex, major conformer: ^1H NMR ($CDCl_3$ saturated with D_2O) δ 2.271 (s, 3 H, $ArCH_3$), 2.295–2.395 (m, 4 H, $NCH_2CH_2CH_2N$), 2.739 (s, 3 H, $ArOCH_3$), 3.179 (s, 6 H, $ArOCH_3$), 3.693 (s, 3 H, $ArOCH_3$), 3.612–4.126 (m, 8 H, $NCH_2CH_2CH_2N$), 3.749 (AB, J = 15.1 Hz, 2 H, $ArCH_2N$), 5.127 (AB, J = 15.1 Hz, 2 H, $ArCH_2N$), 7.049–7.393 (m, 11 H, ArH), 8.744 (s, 2 H, picrate); MS (70 eV, 200 °C) of **3**·NaBr, m/e 670 (M^+ − 15). Anal. Calcd for $C_{39}H_{42}N_4O_6NaBr$: C, 61.18; H, 5.53; N, 7.32; Na, 3.00; Br, 10.44. Found: C, 61.32; H, 5.72; N, 7.37; Na, 2.92; Br, 10.38.

34,38-Dioxo-35,36,37-trimethoxy-3,7,23,27-tetraazaheptacyclo[27.3.0.1^{3,7}.1^{8,12}.1^{13,17}.1^{18,22}.1^{23,27}]octaconta-1(33),8(35),9,11,13(36),14,16,18(37),19,21,29,31-dodecaene (2). A mixture of NaH (0.6 g of 50% washed with pentane), 1.5 g (2.9 mmol) of **17**, and 900 mL of THF was refluxed under argon for 1.75 h. The reaction mixture was cooled to −78 °C. Under an argon stream with stirring, 0.79 g (2.9 mmol) of 1,2-bis(bromomethyl)benzene (96% pure) in 5 mL of THF was added. The mixture was allowed to warm to 25 °C over a 12-h period, and stirring continued for a total of 12.5 h. The reaction mixture was heated to reflux for 1 h, cooled to 25 °C, quenched with water (5 mL), and evaporated to dryness under reduced pressure. The residue was partitioned between 100 mL of water and 80 mL of CH_2Cl_2 (drops of concentrated HCl in H_2O were added to break up an emulsion). The layers were separated, and the aqueous layer was extracted with two 20-mL portions of CH_2Cl_2. The combined extracts were dried ($MgSO_4$), filtered, evaporated to dryness, and subjected to gel chromatography to give (after removing the CH_2Cl_2) an oil, retention volume 162–178 mL. This oil was triturated with 25 mL of THF. The grayish tan solid that precipitated was filtered, washed with THF, and dried. It gave a strong positive sodium flame test. Recrystallization of this material from CH_2Cl_2/THF gave 0.085 g (4.1% assuming bromide as the counterion) of a white powder whose ^1H NMR spectrum indicated it to be **2**·Na^+. The mother liquor (from both precipitation and recrystallization steps) were combined, solvent was removed, and 10 mL of CH_2Cl_2 was added. This solution was stirred 12 h with 20 mL of 1 M NaBr in H_2O. The CH_2Cl_2 layer was separated and evaporated to dryness, and THF was added. No additional sodium complex of **2** precipitated. After slow evaporation of the THF over 1 week, a white powder slowly precipitated. The mother liquor was carefully removed, and the solid was washed with a small amount of THF. This material gave a negative sodium flame test. Recrystallization of this material from $CH_3CN/CHCl_3$ gave 0.2639 g (14%) of the open-chain alcohol $HUAUAUCH_2BCH_2OH$, mp 260 °C dec.

The sodium complex of **2** was decomplexed as follows: 85 mg of **2**·NaBr was dissolved in 15 mL of MeOH. The mixture was stirred magnetically, the solvent was heated to reflux, and 5 mL of conductivity water was added. After the mixture had refluxed for 15 h, the condenser was removed and approximately 5 mL of solvent was evaporated. Water (5 mL) was added, and reflux was continued 12 h, after which time a white powdery precipitate had formed. The mixture was cooled to 25 °C, filtered, washed well with conductivity water, and dried at 100 °C at 0.1-mm pressure to give 56.1 mg (3.1% overall) of uncomplexed **2**, mp 252–254 °C dec. Recrystallization of this material from ethanol/water gave beautiful crystals (solvate) of **1**·H_2O: mp 252–283 °C dec; ^1H NMR ($CDCl_3$) δ 2.091–2.142 (m, 4 H, $NCH_2CH_2CH_2N$), 2.767 (s, 3 H, $ArOCH_3$), 3.10–3.80 (b m, 8 H, $NCH_2CH_2CH_2N$), 3.343 (b s, 6 H, OCH_3), 4.511 (b s, 2 H, $ArCH_2N$), 5.045 (b s, 2 H, $ArCH_2N$), 7.051–7.480 (m, 13 H, ArH); MS (70 eV, 200 °C), m/e 618 (M^+, 1), 587 (M^+ − 31, 100). Anal. Calcd for $C_{37}H_{38}N_4O_5$: C, 71.83; H, 6.19; N, 9.06. Found: C, 71.71; H, 6.21; N, 8.98.

Open-chain alcohol $HUAUAUCH_2BCH_2OH$: ^1H NMR ($CDCl_3$) δ 2.040 (m, 4 H, $NCH_2CH_2CH_2N$), 3.240–3.780 (b m, 14 H, $NCH_2CH_2CH_2N$, $ArOCH_3$), 4.778 (b s, 4 H, $ArCH_2N$), 7.081–7.376 (m, 13 H, ArH); MS (70 eV, 240 °C), m/e 636 (M^+); osmometric mol wt 630 ± 10%. Anal. Calcd for $C_{37}H_{40}N_4O_6$: C, 69.79; H, 6.33; N, 8.80. Found: C, 70.64; H, 6.10; N, 8.89.

2,2″-Dihydroxy-5,5′,5″-trimethyl-2″-(phenylmethoxy)-1,1′:3,1″-terphenyl (19). To 42.0 g (0.1311 mol) of tris(cresol), **18**,[10] in 300 mL of acetone was added 18.85 g (0.136 mol, 4% excess) of K_2CO_3 and 23.5 mL (0.198 mol) of benzyl bromide. This mixture was stirred at 25 °C in the dark for 71 h and then concentrated to dryness. The residue was partitioned between 500 mL of EtOAc and 250 mL of H_2O. The organic layer was washed with 250 mL of H_2O and dried over Na_2SO_4. The solvent was evaporated, leaving an oil which was chromatographed (flash column, silica gel, 15% ether/benzene) to give 39.56 g (74%) of **19** as a white foam, which was stored at −20 °C: ^1H NMR ($CDCl_3$) δ 2.39 (s, 3 H, $ArCH_3$), 2.33 (s, 6 H, $ArCH_3$), 4.32 (s, 2 H, $PhCH_2O$) 6.64–7.34 (m, 13 H, ArH); MS (70 eV, 250 °C), m/e 618 (M^+). Anal. Calcd for $C_{28}H_{26}O_3$: C, 81.92; H, 6.38. Found: C, 81.75; H, 6.36.

2,2″-Dihydroxy-2′-(phenylmethoxy)-3,3″-dibromo-5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (20). To a stirred solution of 32.2 g (0.0784 mol) of **19** in 1.5 L of $CHCl_3$ at 0 °C was added 65.5 g (0.160 mol) of 2,4,4,6-tetrabromocyclohexadienone. The stirred solution became green within a few minutes. After 80 min a solution of 1.35 g of Na_2SO_3 in 50 mL of water was added, and the solution was stirred 12 h. The $CHCl_3$ layer was separated, dried ($MgSO_4$), and filtered, and the solvent was evaporated under reduced pressure. The residue was mixed with 300 mL of pentane, and a portion of the side product 2,4,6-tribromophenol crystallized. This material was washed with pentane and discarded. The filtrates were evaporated and chromatographed at medium pressure on 284 g of silica gel packed in 2/1 CH_2Cl_2/pentane (elution with 2.5 L of 2/1 CH_2Cl_2/pentane and 1 L of CH_2Cl_2 at a flow rate of 50 mL/min). The fractions containing product were combined and rechromatographed at medium pressure on 800 g of silica gel packed in 4/1 pentane/CH_2Cl_2. Elution of the column with 6.5 L of 4/1 pentane/CH_2Cl_2 and 3.5 L of 1/2 pentane/CH_2Cl_2 (at 50 mL/min) gave, after crystallization from CH_2Cl_2/pentane, 27.0 g (60%) of **20**, pure by TLC (silica, 2/1 CH_2Cl_2/pentane, R_f 0.3) and ^1H NMR analysis. The mother liquors were evaporated to give 6.5 g of an oil, mainly the desired product by TLC. This material was not purified. For analysis, a sample of **20** was recrystallized from CH_2Cl_2/pentane: mp 144–147 °C; ^1H NMR ($CDCl_3$) δ 2.292 (s, 6 H, $ArCH_3$), 2.391 (s, 3 H, $ArCH_3$), 4.317 (s, 2 H, OCH_2Ar), 6.462 (s, 2 H, ArOH), 6.639–6.685 (m, 2 H, ortho ArH of benzyl), 7.008 (d, J_{meta} = 1.9 Hz, 2 H, ArH), 7.070–7.188 (m, 5 H, ArH), 7.355 (d, J_{meta} = 1.9 Hz, 2 H, ArH); MS (70 eV, 205 °C), m/e 566 (M^+). Anal. Calcd for $C_{28}H_{24}Br_2O_3$: C, 59.17; H, 4.26; Br, 28.12. Found: C, 59.19; H, 4.21; Br, 28.21.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-dibromo-5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (21). A mixture of 12.6 g (0.0222 mol) of **20**, 6.73 g (0.0486 mol) of K_2CO_3, 350 mL of acetone, and 5.5 mL of MeI (0.088

mol) was stirred for 40 h at 25 °C. An additional 1.0 g of K_2CO_3 was then added, and after being stirred 70 h, the mixture was filtered and washed with acetone and the filtrate was evaporated under reduced pressure. The residue was partitioned between 150 mL of water and 75 mL of CH_2Cl_2. The CH_2Cl_2 layer was separated, and the aqueous layer was extracted with 50 mL of CH_2Cl_2. The combined extracts were dried ($MgSO_4$), filtered, and evaporated. The residual oil was dissolved in 200 mL of CH_2Cl_2, and silica gel was added until all the solvent had been absorbed. The silica was then washed well with CH_2Cl_2 until the washings were no longer UV active. The combined washings were evaporated under reduced pressure and placed under high vacuum to give a foam. The product, 12.0 g (90.7%), was pure to TLC (silica gel, 40/60 pentane/CH_2Cl_2, R_f 0.6) and ^1H NMR analyses. Crystals of **21** slowly formed over a 2-month period. A sample was recrystallized from pentane at −20 °C to give bundles of sharp needles: mp 122–123 °C; ^1H NMR ($CDCl_3$) δ 2.269 (s, 6 H, $ArCH_3$), 2.367 (s, 3 H, $ArCH_3$), 3.579 (s, 6 H, OCH_3), 4.335 (s, 2 H, OCH_2Ar), 6.680–6.726 (m, 2 H, ortho ArH of benzyl), 7.097–7.378 (m, 9 H, ArH); MS (70 eV, 210 °C), *m/e* 594 (^{79}Br) (M^+, 6), 562 (M^+ − 32, 8). Anal. Calcd for $C_{30}H_{28}Br_2O_3$: C, 60.42; H, 4.73. Found: C, 60.44; H, 4.77.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-dicarboxy-5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (22). To 14.1 g (0.0236 mol) of **21** in 800 mL of THF at −78 °C stirred under argon was added 51 mL of a 1.45 M solution of *sec*-butyllithium (0.0725 mol) in hydrocarbon. The pale orange solution was stirred for 10 min and then quenched with a vigorous stream of CO_2. The mixture was allowed to warm to 25 °C, the THF was evaporated under reduced pressure, and the residue was partitioned between 100 mL of CH_2Cl_2 and 60 mL of water. The CH_2Cl_2 layer was separated, and the aqueous layer was extracted with 100 mL of CH_2Cl_2. The combined organic extracts were washed with 100 mL of water, and the combined aqueous washings were acidified with 2 N hydrochloric acid to pH 0. The diacid was extracted with 100 mL of CH_2Cl_2 and two additional 50-mL portions of CH_2Cl_2. The CH_2Cl_2 extracts were combined, washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a white solid. The solid was dissolved in 300 mL of hot acetone, evaporated to 80-mL total volume, and layered over with 100 mL of pentane. After 1 day, crystals had formed. The flask was cooled to −20 °C for an additional 3 days. The mother liquor was then decanted, and the product was washed with pentane and dried to give 8.4 g (67.5%) of **22**. An additional 0.68 g (5.5%) of **22** was recovered from the filtrate. A sample of **22** was recrystallized from acetone/pentane to give beautiful crystals: mp 195–196.5 °C; ^1H NMR ($CDCl_3$) δ 2.371 (s, 6 H, $ArCH_3$), 2.429 (s, 3 H, $ArCH_3$), 3.627 (s, 6 H, OCH_3), 4.256 (s, 2 H, OCH_2Ar), 6.559–6.598 (m, 2 H, ortho ArH of benzyl), 7.067–7.971 (m, 9 H, ArH); MS (70 eV, 210 °C), *m/e* 526 (M^+, 2), 494 (M^+ − 32, 40). Anal. Calcd for $C_{32}H_{30}O_7$: C, 72.99; H, 5.74. Found: C, 73.21; H, 5.74.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-bis[3-(3-bromopropyl)ureldo]5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (23). A mixture of 6.4 g (0.0122 mol) of **22** and 8 mL of thionyl chloride was stirred and heated to reflux for 20 min, and the excess reagent was evaporated under reduced pressure. Toluene (20 mL) was added to the residue, the mixture was evaporated to dryness under reduced pressure (temperature less than 70 °C), and the flask was evacuated at 0.01 mm for 20 min. Toluene (20 mL) was again added and removed as before, and the residue was again placed under vacuum to remove the last traces of thionyl chloride. This diacid chloride of **22** was used directly in the next step. (A small sample was converted to its dimethyl ester, whose TLC showed it to be one component and whose ^1H NMR (200 MHz) showed the benzyl group to be intact.) Acetone (38 mL) was added, and the mixture was placed in a sonicator for 3 min until it was homogeneous. The solution was quickly cooled to 0 °C, and a solution of 2.12 g (0.0326 mol) of sodium azide in 6.3 mL of water was added with stirring. The mixture was stirred for 15 min, 1 g more of sodium azide (0.015 mol) was added, and the mixture was stirred for 5 min and then poured onto 550 mL of ice water. No solid separated so the acyl azide was extracted carefully with 50 mL of toluene. The milky toluene layer was quickly separated and cooled to 0 °C. A large excess of $MgSO_4$ was then added, and the mixture was stirred. The original aqueous layer was again extracted with toluene (30 mL), and the toluene layer was added to the previous extract. The mixture was stirred for 5 more min at 0 °C and then filtered into a very dry flask. The filter cake was washed with 25 mL of dried (3-Å sieves) toluene. The solution was stirred under argon, and the flask (fitted with a condenser) containing the solution was immediately lowered into an oil bath held at 150 °C. Nitrogen evolution began at an internal temperature below reflux (20 min). The oil bath was then removed and quickly replaced with an ice water bath. After the solution had cooled to 0 °C, 5.5 g (0.025 mol) of 1-amino-3-bromopropane–hydrobromide and 4.3 mL (0.025 mol) of freshly distilled ethyldiisopropylamine were added. The ice bath was removed, and the mixture was vigorously stirred for 17.5 h, after which time the product had separated as a solid. TLC (silica, 10% MeOH/CH_2Cl_2, R_f 0.5) showed only one spot. Water (250 mL) was added, and the mixture was filtered onto a 150-mL coarse sintered glass funnel. The filter cake was washed well with 100 mL of toluene and 100 mL of water and dried (100 °C, 30 mm, 24 h) to give 7.7 g (79.5%) of **23**, which was used directly in the next step. A sample was recrystallized from $CHCl_3/CH_3CN$ and dried (120 °C/0.01 mm, 8 h) to give **23**: mp 228 °C dec; ^1H NMR ($CDCl_3$) δ 2.009–2.140 (m, 4 H, $NCH_2CH_2CH_2N$), 2.331 (s, 6 H, $ArCH_3$), 2.398 (s, 3 H, $ArCH_3$), 3.307–3.489 (m, 14 H, $BrCH_2$, $HNCH_2$, OCH_3), 4.124 (s, 2 H, OCH_2Ar), 5.155 (b s, 2 H, $HNCH_2$), 6.459–6.498 (m, 2 H, ortho ArH of benzyl), 6.763 (d, J_{meta} = 1.6 Hz, 2 H, ArH), 6.986–7.163 (m, 5 H, ArH), 7.831 (d, J_{meta} = 1.6 Hz, 2 H, ArH); MS (70 eV, 220 °C), *m/e* 641 (M^+ − 153). Anal. Calcd for $C_{38}H_{44}Br_2N_4O_5$: C, 57.29; H, 5.57; N, 7.03. Found: C, 57.43; H, 5.51; N, 7.09.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-bis(hexahydro-2-oxopyrimidinyl)-1,1′:3′,1″-terphenyl (24). A mixture of 7.3 g (9.16 mol) of **23** suspended in 450 mL of $(CH_3)_3COH$ (distilled from CaH_2) was stirred with 4.05 g (0.036 mol) of $(CH_3)_3COK$. The dense insoluble starting material dissolved after 15 min to give a mixture with the appearance of a "thin" suspension. After 20 h, TLC (silica, 10% MeOH/CH_2Cl_2, R_f 0.2) of the product showed primarily one spot. The mixture was diluted with water to a volume of 4 L and stirred for 2 h, and the precipitated product was poured onto a medium-sintered glass-fritted funnel, washed well with water, filtered, and dried (100 °C, 30 mm, 15 h) to give 5.18 g (89%) of **24**, pure by ^1H NMR and TLC. A sample was recrystallized from CH_3CN to give crystals: mp 269–271 °C; ^1H NMR ($CDCl_3$) δ 1.979–2.037 (m, 4 H, $NCH_2CH_2CH_2N$), 2.296 (s, 6 H, $ArCH_3$), 2.369 (s, 3 H, $ArCH_3$), 3.371–3.467 (m, 4 H, $HNCH_2$), 3.583 (s, 6 H, OMe), 4.334 (s, 2 H, OCH_2Ar), 4.920 (b s, 2 H, HN), 6.646–6.694 (m, 2 H, ortho ArH of benzyl), 7.034–7.130 (m, 9 H, ArH); MS (70 eV, 240 °C), *m/e* 634 (M^+, 1), 603 (M^+ − 31, 100). Anal. Calcd for $C_{38}H_{42}N_4O_5$: C, 71.90; H, 6.67; N, 8.83. Found: C, 71.85; H, 6.67; N, 8.71.

1-(2-Propenyl-1-oxy)-2,6-(dihydroxymethyl)-4-methylbenzene (26). To a 0.5-L Parr shaker bottle was added 19.3 g (0.115 mol) of triol **25**,[10] a solution of 5.12 g (0.128 mol) of NaOH in 50 mL of water, and 15 mL (0.173 mol) of allyl bromide. The tightly stoppered mixture was shaken for 48 h and filtered. The solid that had formed was washed well with water, air dried, dissolved in EtOAc, dried ($MgSO_4$), filtered, and evaporated to dryness. The resulting material was predominately the desired product but was contaminated with bis- and tris-allylated materials. Recrystallization of the material from ether/pentane gave 2.45 (10.2%) of **26**, mp 87.5–92 °C, which was used directly in the next step. A sample was purified for analysis by recrystallization again from ether/pentane: mp 95–97 °C; ^1H NMR ($CDCl_3$) δ 2.314 (s, 3 H, $ArCH_3$), 4.401–4.443 (m, 2 H, OCH_2CHCH_2), 4.678 (s, 4 H, $ArCH_2OH$), 5.248–5.471 (m, 2 H, OCH_2CHCH_2), 6.002–6.196 (m, 1 H, OCH_2CHCH_2), 7.130 (s, 2 H, ArH); MS (70 eV, 145 °C), *m/e* 208 (M^+, 34). 150 (M^+ − 58, 100). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.20; H, 7.74. Found: C, 69.27; H, 7.78.

1-(2-Propenyl-1-oxy)-2,6-bis(bromomethyl)-4-methylbenzene (27). To a stirred mixture of 1.48 g (7.11 mmol) of **26** and 70 mL of benzene was added phosphorus tribromide (0.74 mL, 7.87 mmol). The insoluble starting material dissolved within 2 min and was replaced by a gummy precipitate. After the mixture was stirred for an additional 40 min, the precipitate dissolved and 120 mL of water saturated with $NaHCO_3$ was added. The layers were separated. The benzene layer was washed with two 50-mL portions of brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a solid. This material was dissolved in 2 mL of CH_2Cl_2 and chromatographed on 20 g of silica gel packed in CH_2Cl_2 and eluted with 50 mL of CH_2Cl_2. The solvent was removed under reduced pressure to give 1.42 g (60%) of **27** as an off-white solid. Recrystallization of this material from pentane gave 1.27 g (53.7%) of **27**: mp 77–79 °C; ^1H NMR ($CDCl_3$) δ 2.301 (s, 3 H, $ArCH_3$), 4.523 (s, 4 H, CH_2Br), 4.604–4.645 (m, 2 H, OCH_2CHCH_2), 5.307–5.580 (m, 2 H, OCH_2CHCH_2), 6.08–6.15 (m, 1 H, OCH_2CHCH_2), 7.180 (s, 2 H, ArH); MS (70 eV, 145 °C), *m/e* 332 (^{79}Br) (M^+, 3), 253 (M^+ − 79, 17). Anal. Calcd for $C_{12}H_{14}Br_2O$: C, 43.15; H, 4.22. Found: C, 43.06; H, 4.09.

34,38-Dioxo-33-(2-propenyl-1-oxy)-35,37-dimethoxy-36-(phenylmethoxy)-10,15,20,31-tetramethyl-3,7,23,27-tetraazaheptacyclo-[27.3.1.1^{3,7}.1^{8,12}.1^{13,17}.1^{18,22}.1^{23,27}]octaconta-1(33),8(35),9,11,13-(36),14,16,18(37),19,21,29,31-dodecaene (4). A stirred mixture of 1.69 g (2.66 mmol) of **24**, 850 mL of THF, and 1.0 g of 50% sodium hydride (washed with pentane) was heated to reflux under argon for 5.5 h, cooled to −78 °C, and 0.8776 g (2.63 mmol) of **27** in 50 mL of THF was added. The stirred mixture was allowed to rise to 25 °C, and stirring was continued for a total of 12 h, after which time the mixture was heated to reflux for 2 h. The THF was evaporated until ~100 mL remained, and

the mixture was evaporated to dryness under reduced pressure. The residue was partitioned between 150 mL of CH_2Cl_2 and 50 mL of H_2O, a few drops of 6 N HCl being added to break up an emulsion. The CH_2Cl_2 layer was separated, the aqueous layer was extracted with 20 mL of CH_2Cl_2, and the combined organic extracts were washed with two 75-mL portions of an 0.8 M aqueous solution of NaBr. The organic layer was dried ($MgSO_4$), filtered, and evaporated to dryness. Gel chromatography of the residue gave virtually one peak of retention volume 144–171 mL centered at 157 mL. This fraction was evaporated to an oil and dissolved in 30 mL of THF. The THF was removed under reduced pressure to give a white foam. Another 50 mL of THF was added to this foam, and a white solid precipitated. After 6 h, this solid was filtered through a fine-sintered glass funnel, washed with 10 mL of THF, then 10 mL of ether, and dried to give 1.209 g (50.7%) of **4**·NaBr. Solvent was removed from the mother liquor under reduced pressure. The residue was dissolved in 5 mL of THF, and a second crop of **4**·NaBr was filtered and washed with THF and then ether. After being dried an additional 0.072 g (3.1%) **4**·NaBr was obtained. The ^1H NMR spectrum of this complex indicated the presence of only one geometrical isomer. This material gave a brilliant sodium flame test and a positive test for bromine with silver nitrate in ethanol. Decomplexation of **4**·NaBr was accomplished as follows. To a 50-mL centrifuge tube was added 0.2021 g (0.222 mmol) of **4**·NaBr, 10 mL of $CHCl_3$, and 10 mL of conductivity water. The mixture was vortexed for 2 min and centrifuged for 3 min, and the upper, aqueous layer removed with a pipette. The $CHCl_3$ was treated, as above, five times more with 10-mL portions of conductivity water. The $CHCl_3$ solution was then evaporated under reduced pressure. Residual water was removed under high vacuum, and the residue was crystallized from EtOAc and dried (120 °C, 0.01 mm) 24 h: 0.1381 g (77%, from complex); mp 249–255 °C. The overall yield of the free host **4** for both the cyclization and decomplexation steps is 41.4%. The ^1H NMR spectrum of **4**·NaBr isolated directly from the cyclization (one isomer) carried out at −78 °C is as follows: ($CDCl_3$) δ 2.25–2.45 (m, 4 H, $NCH_2CH_2CH_2N$), 2.332 (s, 9 H, $ArCH_3$), 2.423 (s, 3 H, $ArCH_3$), 3.194 (s, 6 H, OCH_3), 3.765 (s, 2 H, OCH_2Ar), 3.687 (AB, J = 15.6 Hz, 2 H, $ArCH_2N$), 4.179 (d, J = 5.4 Hz, 2 H, OCH_2CHCH_2), 4.974 (AB, J = 15.6 Hz, 2 H, $ArCH_2N$), 5.238–5.438 (m, 2 H, OCH_2CHCH_2), 5.921–6.058 (m, 1 H, OCH_2CHCH_2), 6.277 (d, J = 6.8 Hz, 2 H, O-ortho ArH of benzyl) 6.795–7.144 (m, 11 H, ArH). The ^1H NMR partial spectrum of the minor isomer of **4**·NaBr produced in the cyclization carried out at 25 °C is as follows: ($CDCl_3$) δ 3.220 (s, OCH_3), 5.02, 5.1 (AB, J = 15 Hz). The ^1H NMR of the crystallized free host **4** (single conformer) obtained from the −78 °C ring closure is as follows: ($CDCl_3$) δ 2.1–2.3 (m, 4 H, $NCH_2CH_2CH_2N$), 2.242 (s, 9 H, $ArCH_3$), 2.328 (s, 3 H, $ArCH_3$), 3.099 (s, 6 H, OCH_3), 3.470 (AB, J = 15.6 Hz, 2 H, $ArCH_2N$), 3.601–4.011 (m, 8 H, $NCH_2CH_2CH_2N$), 4.048 (s, 2 H, OCH_2Ar), 4.95–5.75 (m, 3 H, OCH_2CHCH_2), 4.828 (m, 2 H, OCH_2CHCH_2) 6.524–6.570 (m, 2 H, ortho ArH of benzyl), 6.787–7.036 (m, 11 H, ArH); MS (16 eV, 240 °C), m/e 806 (M^+, 1), 775 ($M^+ - 31$, 100). Anal. Calcd for $C_{50}H_{54}N_4O_6$: C, 74.42; H, 6.76; N, 6.94. Found: C, 74.20; H, 6.70; N, 6.78. The ^1H NMR partial spectrum of the minor isomer of **4** is as follows: ($CDCl_3$) δ 2.454 (s, $ArCH_3$), 3.035 (s, OCH_3), 4.199 (s, OCH_2Ar), 6.646–6.683 (m, ortho ArH of benzyl).

By integration of the signals in the ^1H NMR spectra for the two geometric isomers that were adequately separated from one another, the amounts of the minor isomers were made as follows: **4**·NaBr from ring closure at refluxing THF, 10–15% minor, 90–85% major isomer; **4** from the same reaction, 28–33% minor, 72–67% major isomer; **4**·NaBr from ring closure initiated at −78 °C, ≤5% minor, 95–100% major isomer; **4** from same reaction, 83% major, 17% minor isomer.

34,38-Dioxo-35,37-dimethoxy-36-(phenylmethoxy)-10,15,20,31-tetramethyl-3,7,23,27-tetraazaheptacyclo[27.3.1.1^{3,7}.1^{8,12}.1^{13,17}.1^{18,22}.1^{23,27}]octaconta-1(33),8(35),9,11,13(36),14,16,18(37),19,21,29,31-dodecaen-33-ol (5). A mixture of 0.330 g (0.3627 mmol) of **4**, 0.409 g (0.384 mmol) of 10% palladium/carbon, 0.1063 g (0.559 mmol) of p-$CH_3C_6H_4SO_3H$, and 42.5 mL of 95% ethanol was stirred under argon for 48 h. Sodium carbonate (0.1 g) was added, and the mixture was filtered over a celite pad. The ethanolic filtrates were colorless. When the pad was washed with CH_2Cl_2, a very dark amber color appeared in the filtrate. The filtrate was evaporated to dryness under reduced pressure, and the dark residue was transferred, with 10 mL of $CHCl_3$, to a 50-mL centrifuge tube. Water (10 mL, conductivity) was added, the mixture was vortexed for 2 min and centrifuged for 3 min, and the upper aqueous layer was removed. This operation was repeated four more times. Magnesium sulfate was added to the $CHCl_3$ layer, and the mixture was filtered, washed with CH_2Cl_2, and evaporated to dryness under reduced pressure to give a dark viscous oil. To the oil was added 8 mL of 95% ethanol. The deallylated product crystallized and was washed with 95% ethanol to give 0.1084 g (39%) of **5** containing some grayish black material imbedded in the crystals. It appeared to be colloidal palladium that had been in the solution and was apparently the cause of at least part of the color in the crude product. These crystals were dissolved in CH_2Cl_2 and filtered through a medium-sintered glass funnel to give a colorless filtrate. The filtrate was condensed and refiltered over a celite pad on top of a fine-sintered glass funnel. The colorless filtrate was evaporated to dryness, and the residue was recrystallized from a small amount of 95% ethanol to give 0.0688 g (24.7%) of **5**, mp >265 °C dec. The mother liquor from the first recrystallization was evaporated and gave 0.1514 g of an oil that by ^1H NMR (200 MHz) was a 2/7 mixture of two materials, the minor component being identical with the material which had crystallized. The major component was clearly deallylated, and in *all respects was consistent with the expected product* **5**, except for an unexplained singlet at δ 5.392. When this mixture of materials was dissolved in 20 mL of toluene (clear, homogeneous) and heated to reflux for 24 h, a dark gray film appeared on the walls of the flask. The ^1H NMR spectrum (200 MHz) of the material recovered from this treatment and revealed that the ratio of the two components was then 55/38 and that the previously crystallized material had increased from 22 to 55%. From this mixture, an additional 0.0681 g (24.5%) of **5** was crystallized by an addition of a small amount of 95% ethanol. The mother liquor was still a mixture of both components, neither of which could be separated by another recrystallization. Host **5**: ^1H NMR ($CDCl_3$) δ 2.00–2.30 (m, 4 H, $NCH_2CH_2CH_2N$), 2.249 (s, 6 H, $ArCH_3$) 2.267 (s, 3 H, $ArCH_3$), 2.337 (s, 3 H, $ArCH_3$), 3.365–3.55 (m, 8 H, $NCH_2CH_2CH_2N$), 3.396 (AB, J = 14.6 Hz, 2 H, $ArCH_2N$), 3.557 (s, 6 H, OCH_3), 4.050 (s, 2 H, $OCH_2C_6H_5$), 5.641 (AB, J = 14.6 Hz, 2 H, $ArCH_2N$), 6.673–7.046 (m, 8 H, ArH); MS (70 eV, 230 °C), m/e 766 (M^+, 1), 735 ($M^+ - 31$, 100). Anal. Calcd for $C_{47}H_{50}N_4O_6$: C, 73.61; H, 6.57; N, 7.31. Found: C, 73.74; H, 6.53; N, 7.22.

34,38-Dioxo-35,37-dimethoxy-10,15,20,31-tetramethyl-3,7,23,27-tetraazaheptacyclo[27.3.1.1^{3,7}.1^{8,12}.1^{13,17}.1^{18,22}.1^{23,27}]octaconta-1(33),8(35),9,11,13(36),14,16,18(37),19,21,29,31-dodecaene-33,36-diol (28). Through a stirred solution of 1.0003 g (1.0090 mmol) of **4** in 30 mL of acetic acid was vigorously bubbled HBr gas for 5 min. The solution became cloudy and then homogeneous as the temperature increased to 55 °C. The flask was stoppered and left for 1 h. Water (170 mL) was added, and a solid quickly separated and floated on top of the liquid. The mixture was stirred 0.5 h and filtered, and the solid was air dried for 2 h, dissolved in CH_2Cl_2, dried ($MgSO_4$), filtered, and evaporated to dryness to give a white foam. This foam was dissolved in 10 mL of 95% ethanol. Crystals of **28** formed, and after 1 day at 25 °C, the mixture was cooled to −20 °C for 1 h. The crystals were collected, washed with 95% ethanol, and dried (0.01 mm, 120 °C) to give 0.4553 g (61.2%) of **28**, mp >265 °C dec. The filtrate was evaporated to give an additional 0.0494 g (6.6%) of **28**: ^1H NMR ($CDCl_3$) δ 2.076–2.406 (m, 4 H, $NCH_2CH_2CH_2N$), 2.267 (s, 3 H, $ArCH_3$), 2.308 (s, 6 H, $ArCH_3$), 2.325 (s, 3 H, $ArCH_3$), 3.284 (s, 6 H, OCH_3), 3.422 (AB, J = 15.1 Hz, 2 H, $ArCH_2N$), 3.499–3.845 (m, 8 H, $NCH_2CH_2CH_2N$), 3.558 (AB, J = 15.1 Hz, 2 H, $ArCH_2N$), 6.924 (s, 2 H, ArH), 6.970 (s, 4 H, ArH), 7.044 (s, 2 H, ArH); MS (70 eV, 150 °C), no M^+. Anal. Calcd for $C_{40}H_{44}N_4O_6$: C, 70.99; H, 6.55. Found: C, 70.67; H, 6.59.

1,3-Bis(2-methoxy-5-methylphenyl)urea (31). To a stirred mixture of 94.85 g (0.691 mol) of 4-methyl-2-aminoanisole, 61 mL of dry pyridine, and 500 mL of THF held at reflux was added over a 2-h period a solution of 35.8 g (0.360 mol) of $COCl_2$ dissolved in 450 mL of THF. The solution was refluxed an additional 3 h, the THF was distilled, and the precipitated mass was filtered onto a large Büchner funnel and washed well with 1 L of water and 4 L of CH_2Cl_2. Some solid remained undissolved. The filtrate was poured into a separatory funnel, the CH_2Cl_2 layer was separated, the aqueous layer was extracted with three 50-mL portions of water, and the combined extracts were evaporated under reduced pressure. The residue was recrystallized from 2 L of hot *sec*-butyl alcohol to give 61.84 g (59.6%) of **31**. The mother liquors were evaporated, and an additional 10.24 g (9.9%) of **31** was obtained. The cake of material that was not dissolved by the original CH_2Cl_2/H_2O wash was boiled in *sec*-butyl alcohol, an insoluble solid was filtered, and the solution, upon cooling, gave another 15.48 g (14.9%) of **31**. Upon evaporation of the mother liquor, 4.86 g (4.7%) more of **31** crystallized to give a total of 92.36 g (89%) of **31**. A sample from a previous reaction that had been recrystallized from a large amount of methanol (1.9 g in 100 mL) was used for characterization: mp 185 °C IR ($CHCl_3$) 3424 (s), 1680 (vs), 1600 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 2.310 (s, 6 H, $ArCH_3$), 3.851 (s, 6 H, OCH_3), 6.75–6.85 (m, 4 H, ArH), 7.058 (b s, 2 H, NH), 7.973 (b s, 2 H, ArH); MS (70 eV, 180 °C), m/e 300 (M^+). Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33. Found: C, 67.97; H, 6.76; N, 9.40.

1,3-Bis(2-methoxy-5-methylphenyl)tetrahydro-2-pyrimidinone (32). A mixture of 2 L of THF, 235.7 g (0.78 mol) of **31**, and 75 g of 50% NaH was stirred under N_2 for 70 min. THF (500 mL) was added, the mixture

was heated to reflux for 45 min, and 632 g (3.13 mol) of 1,3-dibromopropane was added dropwise (exotherm) over 20 min. The reaction mixture was held at reflux for 24 h. Since an aliquot showed the presence of starting material, an additional 50 g of 50% NaH was added, the mixture was refluxed for 24 h more, and 270 mL of THF was distilled. The residue was partitioned between 500 mL of water and 500 mL of ether (7 mL of concentrated hydrochloric acid was added to break an emulsion), and the layers were separated. The aqueous layer was extracted with 300 mL of ether. The combined ethereal extracts were washed with three 100-mL portions of brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to approximately 800 mL. Pentane (2 L) was added. After being left sitting 1 day, the product that separated was filtered and washed with pentane to give after being dried 130 g of crude **32**. The mother liquor was evaporated under reduced pressure and placed under high vacuum at 40 °C to remove the excess 1,3-dibromopropane. The residue was dissolved in ether, and additional product that crystallized was filtered, washed with ether, and dried to give 26 g of crude **32**. Recrystallization of all of the recovered crude **32** from CH_2Cl_2/Et_2O gave 124 g (46.4%) of pure product. The mother liquors were twice recrystallized to provide an additional 18.5 g (6.9%) of **32**. The final mother liquor from the last recrystallization was chromatographed over 300 g of silica gel packed in CH_2Cl_2. Products were eluted with 200 mL of CH_2Cl_2, followed by 1 L of EtOAc. From the latter fractions an additional 10.6 g (4.0%) of **32** was obtained, total yield 153.1 g (57.3%). A sample recrystallized from CH_2Cl_2/Et_2O gave the following: mp 140–141.5 °C; IR (neat) 1644 (s), 1510 (s), 1028 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 2.15–2.3 (m, 2 H, $NCH_2CH_2CH_2N$), 2.249 (s, 6 H, $ArCH_3$), 3.657 (t, J = 5.86 Hz, 4 H, NCH_2), 3.818 (s, 6 H, OCH_3), 6.783–7.110 (m, 6 H, ArH); MS (70 eV, 180 °C), m/e 340 (M^+, 23), 309 ($M^+ - 31$, 100). Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.57; H, 7.11; N, 8.23. Found: C, 70.38; H, 7.04; N, 8.15.

As a byproduct, 1,3-bis(2-methoxy-5-methylphenyl)-1,3-bis(2-propenyl)urea was isolated as the faster moving chromatographic component. It was crystallized and recrystallized from pentane in 20% yield: mp 93–94 °C; IR (neat) 1640 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 2.049 (s, 6 H, $ArCH_3$), 3.954 (s, 6 H, OCH_3), 4.056 (d, J = 6.35 Hz, 4 H, NCH_2CHCH_2), 4.960–5.053 (m, 4 H, NCH_2CHCH_2), 5.846–6.046 (m, 2 H, NCH_2CHCH_2), 6.353–6.724 (m, 6 H, ArH); MS (70 eV, 180 °C), m/e 380 (M^+). Anal. Calcd for $C_{22}H_{28}N_2O_5$: C, 71.71; H, 7.66; N, 7.60. Found: C, 71.66; H, 7.42; N, 7.48.

1,3-Bis(2-methoxy-4-bromo-5-methylphenyl)tetrahydro-2-pyrimidinone (33). To a solution of 90.0 mg (0.18 mmol) of **32** in 2 mL of CH_2Cl_2 was added 58 μL of Br_2 (1.1 mmol). The solution was stirred at 25 °C for 30 min, and 1 mL of saturated $Na_2S_2O_5$ aqueous solution was added, followed by 10 mL of water and 10 mL of CH_2Cl_2. The layers were separated, and the aqueous phase was extracted twice with 5-mL portions of CH_2Cl_2. The combined CH_2Cl_2 fractions were dried ($MgSO_4$) and evaporated to dryness to yield 125 mg of a viscous oil. Crystallization from acetone/pentane gave 64.4 mg (48.8%) of **33** as crystals: mp 164–165 °C (the yield in this reaction is nearly quantitative since the mother liquor contained nearly pure **33**); ^1H NMR ($CDCl_3$) δ 2.140–2.25 (m, 2 H, $NCH_2CH_2CH_2N$), 2.281 (s, 6 H, OCH_3), 3.623 (t, J = 5.86 Hz, 4 H, NCH_2), 3.816 (s, 6 H, OCH_3), 7.080 (s, 2 H, ArH), 7.146 (s, 2 H, Ar); MS (70 eV, 180 °C); m/e 496 (^{79}Br, M^+). Anal. Calcd for $C_{20}H_{22}Br_2N_2O_3$: C, 48.22; H, 4.45; N, 5.62. Found: C, 48.37; H, 4.50; N, 5.70.

1-(2-Carboxy-3-methyl-6-methoxyphenyl)-3-(2-methoxy-5-methylphenyl)tetrahydro-2-pyrimidinone (34). To a solution of 0.59 g (1.73 mmol) of **32** in 100 mL of THF was added 0.57 mL (3.8 mmol) of tetramethylenediamine. The solution was stirred and cooled to −78 °C under argon, and 3.1 mL of a 1.2 M *tert*-butyllithium (3.72 mmol) solution was added. The solution became deep yellow. After 19 min the mixture was quenched with carbon dioxide, evaporated to dryness, and shaken with CH_2Cl_2 and water (50 mL of each). The layers were separated, and the aqueous layer was acidified with concentrated hydrochloric acid extracted with two 25-mL portions of CH_2Cl_2. The extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a white solid (0.5 g, 75%) pure by ^1H NMR and TLC. For analysis, a sample was recrystallized from CH_2Cl_2/Et_2O to give **34**: mp 206–207 °C; ^1H NMR ($CDCl_3$) δ 2.237–2.4 (m, 2 H, $NCH_2CH_2CH_2N$), 2.267 (s, 3 H, $ArCH_3$), 2.328 (s, 3 H, $ArCH_3$), 3.569–3.691 (m, 4 H, $NCH_2CH_2CH_2N$), 3.838 (s, 3 H, OCH_3), 3.872 (s, 3 H, OCH_3), 6.807–7.171 (m, 5 H, ArH); MS (70 eV, 210 °C), m/e 384 (M). Anal. Calcd for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.56; H, 6.27; N, 7.14.

1,3-Bis(2-hydroxy-5-methylphenyl)tetrahydro-2-pyrimidinone (35). To 2.32 g (0.682 mmol) of **32** in 30 mL of CH_2Cl_2 was added 1.55 mL of BBr_3. After 24 h, water (50 mL) was added, and a suspension of the product formed. The suspension was filtered and the solid dissolved in 500 mL of hot acetone, dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was crystallized from ethanol to give 2.0096 g (94.4%) of **35**. An analytical sample was prepared by recrystallizing it from acetic acid to give crystals, mp 245–247 °C dec. On a 25-g scale, it was found to be more convenient to demethylate with HBr/AcOH as follows: To a solution of 30.3 g (.089 mol) of **32** in 50 mL of AcOH stirred at reflux was added 250 mL of 48% HBr in H_2O. After 63 h, the solution was cooled to 25 °C. Water (1 L) was added, and the mixture was stirred 14 h and filtered, and the **35** obtained was dried under vacuum to give 21.2 g (77%): ^1H NMR ($CDCl_3$) δ 2.262–2.315 (m, 8 H, $NCH_2CH_2CH_2N$, $ArCH_3$), 3.848 (t, J = 5.9 Hz, 4 H, NCH_2), 6.894–6.988 (m, 6 H, ArH); MS (70 eV, 180 °C), m/e 312 (M^+). Anal. Calcd for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.20; H, 6.36; N, 8.98.

1,3-Bis(2-hydroxy-3-bromo-5-methylphenyl)tetrahydro-2-pyrimidinone (36). A stirred solution was formed from 19.08 g (.047 mol) of 2,4,4,6-tetrabromocyclohexadienone, 100 mL of $CHCl_3$, and 6.36 g (0.0204 mol) of **35** under argon. Dissolution took 12 min, and after 17 min, the product began to precipitate. After 14 h the $CHCl_3$ was evaporated under reduced pressure and the remaining solid was thoroughly washed with ether to completely remove the 2,4,6-tribromophenol formed. The material remaining after being dried was 9.08 g (94.9%) of **36**, suitable for use in subsequent steps. A sample was recrystallized for analysis from AcOH: mp 237–239 °C dec; ^1H NMR ($CDCl_3$) δ 2.15–2.3 (m, 2 H, $NCH_2CH_2CH_2N$), 2.237 (s, 6 H, $ArCH_3$), 3.740 (t, J = 5.9 Hz, 4 H, NCH_2), 6.943 (b s, 2 H, ArH), 7.224 (b s, 2 H, ArH); MS (70 eV, 180 °C), m/e 468 (M^+). Anal. Calcd for $C_{18}H_{18}Br_2N_2O_3$: C, 45.98; H, 3.86; Br, 33.99. Found: C, 45.87; H, 3.77; Br, 34.08.

1,3-Bis(2-methoxy-3-bromo-5-methylphenyl)tetrahydro-2-pyrimidinone (37). To a stirred suspension of 1.10 g (2.13 mol) of **36** in 20 mL of CH_2Cl_2 at 0 °C was added excess diazomethane in ether. After 25 min, the mixture was homogeneous. Formic acid was added to destroy any excess diazomethane. The solution was dried ($MgSO_4$), filtered, evaporated to dryness under reduced pressure, and chromatographed over 30 g of silica gel packed in 5% Et_2O/CH_2Cl_2. Product was eluted with 400 mL of the same solvent to give 0.821 g (70.4%) of **37**. A sample was recrystallized from CH_2Cl_2/Et_2O: mp 181–183 °C; ^1H NMR ($CDCl_3$) δ 2.184–2.3 (m, 2 H, $NCH_2CH_2CH_2N$), 2.274 (s, 6 H, $ArCH_3$), 3.701 (b s, 4 H, NCH_2), 3.874 (s, 6 H, OCH_3), 7.073 (b s, 2 H, ArH), 7.279 (b s, 2 H, ArH); MS (70 eV, 230 °C), m/e 496 (M^+). Anal. Calcd for $C_{20}H_{22}Br_2N_2O_3$: C, 48.22; H, 4.45; Br, 32.08. Found: C, 48.23; H, 4.43; Br, 31.89.

1,3-Bis(2-methoxy-3-carboxy-5-methylphenyl)tetrahydro-2-pyrimidinone (38). To a solution of $(C_6H_5)_3CBr$ in 500 mL of dry THF stirred under argon at −78 °C was added 0.2 mL of a 1.36 M solution of *tert*-butyllithium, followed by 5.3298 g (0.0107 mol) of **37** as a finely crushed powder. The red color persisted. *tert*-Butyllithium (32 mL of 1.36 M solution) was then added, and the solution was stirred until all of the starting material had dissolved (1.2 h). Carbon dioxide was then vigorously admitted, the mixture was allowed to warm to 25 °C, and the THF was evaporated under reduced pressure. The residue was dissolved in 230 mL of water. The resulting solution was extracted with two 50-mL portions of CH_2Cl_2. The aqueous layer was acidified with 6 N hydrochloric acid and extracted with 100 mL and two additional 25-mL portions of CH_2Cl_2. The combined extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give 4.56 g (99%) of **38** as a white powder. This material was pure by ^1H NMR analysis and was used directly in subsequent reactions. An analytical sample was obtained by recrystallization from ethanol/water: mp 225–232 °C; ^1H NMR ($CDCl_3$) δ 2.301–2.45 (m, 2 H, $NCH_2CH_2CH_2N$), 2.354 (s, 6 H, $ArCH_3$), 3.75 (b s, 4 H, NCH_2), 4.016 (s, 6 H, OCH_3), 7.354 (b s, 2 H, ArH), 7.841 (b s, 2 H, ArH); MS (16 eV, 200 °C), m/e 428 (M^+). Anal. Calcd for $C_{22}H_{24}N_2O_7$: C, 61.68; H, 5.65; N, 6.54. Found: C, 61.51; H, 5.56; N, 6.50.

1,3-Bis(2-methoxy-3-carbomethoxy-5-methylphenyl)tetrahydro-2-pyrimidinone (39). To 4.4 g (0.010 mol) of **38** dissolved in ether was added excess diazomethane in ether. The excess diazomethane was then destroyed with formic acid. The solution was dried ($MgSO_4$), filtered, and evaporated to dryness to give 4.6 g (100%) of a slightly yellow oil, pure by ^1H NMR and TLC (silica gel, 25% Et_2O/CH_2Cl_2, R_f = 0.4). An analytical sample was prepared by crystallization from ether/pentane: mp 143–144 °C; ^1H NMR ($CDCl_3$) δ 2.20–2.35 (m, 2 H, $NCH_2CH_2CH_2N$), 2.318 (s, 6 H, $ArCH_3$), 3.723 (b s, 4 H, NCH_2), 3.887 (s, 6 H, $ArOCH_3$ or $ArCO_2CH_3$), 3.913 (s, 6 H, $ArOCH_3$ or $ArCO_2CH_3$), 7.307 (s, 2 H, ArH), 7.546 (s, 2 H, ArH); MS (70 eV, 220 °C), m/e 456 (M^+). Anal. Calcd for $C_{24}H_{28}N_2O_7$: C, 63.15; H, 6.18; N, 6.14. Found: C, 63.12; H, 6.08; N, 6.23.

1,3-Bis(2-methoxy-3-hydroxymethyl-5-methylphenyl)tetrahydro-2-pyrimidinone (40). To a solution of 0.212 g (0.465 mmol) of **39** in 12 mL of THF at 0 °C under argon was added 0.19 g of $LiAlH_4$. After being stirred for 25 min, the reaction was quenched with EtOAc and 10%

aqueous NaOH. The mixture was dried ($MgSO_4$), filtered, and washed with EtOAc, and the filtrates were evaporated under reduced pressure to give, after recrystallization from $CHCl_3/Et_2O$, 0.153 g (83%) of **40**, mp 201–203 °C. A sample was recrystallized from ethanol/water for analysis: mp 201–202 °C; ^1H NMR ($CDCl_3$) δ 2.2–2.4 (m, 2 H, $NCH_2CH_2CH_2N$), 2.289 (s, 6 H, $ArCH_3$), 3.723 (b s, 4 H, NCH_2), 3.865 (s, 6 H, OCH_3), 4.670 (s, 4 H, $ArCH_2OH$), 7.061 (s, 4 H, ArH); MS (70 eV, 180 °C), *m/e* 400 (M^+). Anal. Calcd for $C_{22}H_{28}N_2O_5$: C, 65.98; H, 7.05; N, 7.00. Found: C, 66.07; H, 7.10; N, 6.89.

1,3-Bis(2-methoxy-3-bromomethyl-5-methylphenyl)tetrahydro-2-pyrimidinone (29). To 1.0512 g (2.628 mol) of **40** suspended in 100 mL of benzene under argon was added 300 mL of PBr_3. The mixture was stirred for 18 h. A saturated aqueous $NaHCO_3$ solution (125 mL) was added, and the mixture was shaken with 125 mL of EtOAc. The organic layer was washed with two 120-mL portions of saturated aqueous $NaHCO_3$ and evaporated to dryness under reduced pressure. The residual oil was chromatographed on 30 g of silica gel packed in CH_2Cl_2. Product was eluted with 300 mL of 15% Et_2O/CH_2Cl_2 to give 1.02 g (76%) of **29**: mp 191.2–194.5 °C; ^1H NMR ($CDCl_3$) δ 2.1–2.3 (m, 2 H, $NCH_2CH_2CH_2N$), 2.276 (s, 6 H, $ArCH_3$), 3.735 (b s, 4 H, NCH_2), 3.940 (s, 6 H, OCH_3), 4.528 (s, 4 H, $ArCH_2Br$), 7.088 (s, 4 H, ArH); MS (70 eV, 180 °C), *m/e* 524 (^{79}Br) (M^+). Anal. Calcd for $C_{22}H_{26}Br_2N_2O_3$: C, 50.19; H, 4.98; N, 5.33. Found: C, 50.29; H, 5.16; N, 5.30.

2,6-Bis(hexahydro-2-oxopyrimidinyl)-4-methylbenzene (30). A mixture of 2.82 g (0.0133 mol) of 2,6-dinitro-4-methylanisole (**41**),[14] 30 mL of a 3/1 EtOAc/EtOH solution, and a catalytic amount of PtO_2 were hydrogenated at 50 psi for 1 h. The solution was filtered through Celite, washed well with CH_2Cl_2, and evaporated to dryness to give 1.94 g (0.0127 mol, 96%) of 2,6-diamino-4-methylanisole (**42**), one spot by TLC (silica gel, 10% CH_2Cl_2, R_f 0.3). To this material were added 50 mL of CH_2Cl_2 and 3.5 g (0.0293 mol) of 3-chloropropane isocyanate.[15] The homogeneous mixture quickly became an orange and then a red color. After 5.5 h, a suspension that had formed was filtered and washed with CH_2Cl_2. The mother liquors were boiled in acetone, and some additional product that precipitated was filtered and added to the first precipitate, giving 4.54 g of **43** (approximate yield 91% from diamine **42**), one main spot by TLC (silica gel, 10% Et_2O/CH_2Cl_2 eluted three times, R_f 0.2). Of the above material, 3.72 g was added to 300 mL of THF and 0.75 g of 50% NaH (washed first with pentane). The mixture was heated to reflux for 75 h, cooled to 25 °C, quenched with water, and evaporated to a 100-mL volume. Dichloromethane and water were added. The CH_2Cl_2 layer was separated, dried ($MgSO_4$), filtered, and evaporated to dryness, and 10 mL of CH_2Cl_2 was added. Crystals quickly formed and were filtered and washed with CH_2Cl_2 to give 0.8 g of **30** (26.4% from **43**); mp > 270 °C. The overall yield of **30** from diamine **42** is 23%: ^1H NMR ($CDCl_3$) δ 2.037–2.127 (m, 2 H, $NCH_2CH_2CH_2N$), 2.275 (s, 3 H, $ArCH_3$), 3.393–3.462 (d of t, J^4 = 5.9 Hz, J'^4 = 2.2 Hz, 4 H, $HNCH_2$), 3.578 (*t*, J^4 = 5.7 Hz, 4 H, $ArNCH_2$), 3.830 (s, 3 H, OCH_3), 4.980 (b s, 2 H, HN), 6.992 (s, 2 H, ArH); MS (70 eV, 170 °C), *m/e* 318 (M^+). Anal. Calcd for $C_{16}H_{22}N_4O_3$: C, 60.36; H, 6.97; N, 17.60. Found: C, 60.18; H, 6.79; N, 17.48.

33,35,37-Trioxo-34,36,38-trimethoxy-4,15,26-trimethyl-1,8,12,18,22,29-hexaazaheptacyclo[27.3.1.1^{2,6}.1^{8,12}.1^{13,17}.1^{18,22}.1^{24,28}]octaconta-2(34),3,5,13(36),14,16,24(38),25,27-nonaene (6). To 950 mL of THF was added 0.7444 g (2.34 mmol) of **30** and 1.0 g of 50% NaH (washed with pentane). The mixture was stirred, heated to reflux under argon for 2 h, and cooled to −78 °C, and then 1.23 g (2.34 mmol) of **29** in 50 mL of THF was added. The stirred mixture was maintained at −78 °C for 4.3 h and allowed to warm to 25 °C over a 12-h period. Stirring was continued for a total of 14 h, and then the mixture was heated to reflux for 1 h. Most of the THF was then distilled off over a 2-h period, and the mixture was cooled, quenched with 10 mL of water, and evaporated to dryness under reduced pressure. The residue was partitioned between 350 mL of water and 100 mL of CH_2Cl_2 (6 N hydrochloric acid was added to break an emulsion). The CH_2Cl_2 layer was separated, and the aqueous layer was extracted with two 25-mL portions of CH_2Cl_2. The combined organic extracts were washed with 100 mL of 1 M aqueous NaBr, dried ($MgSO_4$), and filtered, and most of the solvent was removed under reduced pressure to give a faintly colored solution in 15 mL of CH_2Cl_2. Tetrahydrofuran (80 mL) was then carefully layered over this solution, and after a few hours, **6**·NaBr crystallized. This material was washed with THF and dried under vacuum to give 1.1014 g (60.2%) of **6**·NaBr: ^1H NMR ($CDCl_3$) δ 2.054–2.442 (m, 8 H, $NCH_2CH_2CH_2N$), 2.276 (s, 3 H, $ArCH_3$), 2.362 (s, 6 H, $ArCH_3$), 3.216 (s, 3 H, OCH_3), 3.485 (AB, J^3 = 13.7 Hz, 2 H, $ArCH_2N$), 3.430–3.872 (m, 10 H, $NCH_2CH_2CH_2N$), 3.809 (s, 6 H, OCH_3), 5.501 (AB, J^3 = 13.7 Hz, 2 H, $ArCH_2N$), 6.853 (s, 2 H, ArH), 7.088 (s, 4 H, ArH).

Decomplexation of **6**·NaBr was accomplished as follows. To a stirred refluxing mixture of 0.800 g (1.018 mmol) of **6**·NaBr in 20 mL of methanol was added dropwise 10 mL of conductivity water. After 1.5 h at reflux, the condenser was removed, and one-third of the solvent evaporated. By that time, the clear solution had become cloudy. Three more milliliters of conductivity water was added over a 5-min period, the condenser was replaced, and reflux was continued until the product precipitated as a white powder. The mixture was cooled to 25 °C, diluted with 25 mL of conductivity water, filtered through a fine-sintered glass filter, washed with 150 mL of water, and dried under vacuum to give 0.6329 g (91% from complex) of **6**. This material gave a negative flame test. Recrystallization of the material from $EtOH/D_2O$ gave 0.4529 g (65.1%) of **6**, mp 237–241 °C. After being dried (200 °C, 0.01 mm), this material had a melting point of 255 °C dec. The mother liquor was condensed, and an additional 0.0968 g (13.9%) of **6** was obtained. The overall yield of **6** for the cyclization, decomplexation, and recrystallization steps was 47.5%: ^1H NMR ($CDCl_3$) δ 1.900–2.179 (m, 6 H, $NCH_2CH_2CH_2N$), 2.276 (b s, 9 H, $ArCH_3$), 3.128 (s, 3 H, OCH_3), 3.289–3.826 (m, 12 H, NCH_2), 3.349 (AB, J^3 = 14.2 Hz, 2 H, $ArCH_2N$), 3.862 (s, 6 H, OCH_3), 5.833 (AB, J^3 = 14.2 Hz, 2 H, $ArCH_2N$), 6.973 (b s, 6 H, ArH); MS (70 eV, 230 °C), 682 (M^+). Anal. Calcd for $C_{38}H_{46}N_6O_6$: C, 66.84; H, 6.79; N, 12.31. Found: C, 66.81; H, 6.81; N, 12.32.

1-(Phenylmethoxy)-2,6-dibromo-4-methylbenzene (46). A mixture of 35.9 g (0.135 mol) of 2,6-dibromo-4-methylphenol,[16] 25 g (0.146 mol) of benzyl bromide, 21 g (0.15 mol) of K_2CO_3, and 500 mL of acetone was stirred for 24 h. The mixture was filtered, and the filtrate was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed once with water, dried ($MgSO_4$), filtered, and evaporated. The syrupy residue was diluted with pentane, and crystals of **46** formed: 31.62 g (65%); mp 75–76 °C; ^1H NMR ($CDCl_3$) δ 2.252 (s, 3 H, $ArCH_3$), 4.980 (s, 2 H, $ArOCH_2$), 7.311–7.607 (m, 7 H, ArH); MS (70 eV, 170 °C), *m/e* 358 (M^+, ^{81}Br). Anal. Calcd for $C_{14}H_{12}Br_2O$: C, 47.23; H, 3.40. Found: C, 47.20; H, 3.35.

1-(Phenylmethoxy)-2,6-dicarboxy-4-methylbenzene (47). To a very dry solution of 5.00 g (0.014 mol) of **46** in 250 mL of THF stirred under argon at −78 °C was added 50 mL of a 1.5 M *sec*-butyllithium solution. After 12 min, the red solution was quenched with CO_2. After being warmed to 25 °C, the mixture was evaporated under reduced pressure and partitioned between 400 mL of water and 100 mL of ether. The layers were separated, the aqueous layer was again extracted with ether, and the combined ethereal extracts were washed with 50 mL of water. The combined aqueous washings were then acidified (6 N hydrochloric acid), and the product precipitated. After 2 h, the white solid was filtered, washed well with water, and air dried to give 3.68 g (92%) of crude **47**. The material was swirled with 50 mL of CH_2Cl_2 and allowed to sit for 2 h. After the mixture was filtered, washed with CH_2Cl_2, and dried, 2.9 g (72%) of pure **47** was obtained. A sample recrystallized from acetone/pentane gave the following: mp 133.5–134.5 °C; ^1H NMR ($CDCl_3$) δ 2.446 (s, 3 H, $ArCH_3$), 5.178 (s, 2 H, OCH_2Ph), 7.383–7.511 (m, 5 H, ArH), 8.137 (s, 2 H, ArH); MS (70 eV, 150 °C), *m/e* 286 (M^+). Anal. Calcd for $C_{16}H_{14}O$: C, 67.13; H, 4.93. Found: C, 67.01; H, 4.89.

2,6-Bis[3-(3-bromopropyl)ureido]-4-methylbenzene (48). A mixture of 7.3 g (0.025 mol) of **47**, 6 mL of thionyl chloride, and 2 drops of dimethyl formamide was heated to reflux for 20 min, diluted with 100 mL of toluene, and evaporated under reduced pressure. Toluene (50 mL) was added to the residue, the solution was evaporated under reduced pressure, and toluene (50 mL) was again added and evaporated under reduced pressure. The residue was dried under vacuum. Acetone (75 mL) was added, the solution was cooled to 0 °C, and 4.2 g (0.065 mol) of sodium azide in 13 mL of water was added with stirring. After being stirred 40 min, the mixture was shaken with ice water and 100 mL of toluene. The phases were separated, and the aqueous layer was extracted with two 25-mL portions of toluene. The combined toluene extracts were maintained at 0 °C, stirred for 5 min with a large excess of magnesium sulfate, and filtered into a 500-mL flame-dried flask with 50 mL more of dried toluene (3-Å sieves). A stirring bar was added, and a reflux condenser under argon was affixed to the flask. The flask was heated over a 10-min period until the onset of a vigorous reflux and quickly cooled to 0 °C, and 11.2 g (0.0512 mol) of 1-amino-3-bromopropane–hydrobromide and 8.8 mL (0.051 mol) of ethyldiisopropylamine (freshly distilled) were added. The mixture was stirred for 30 min at 0 °C, allowed to warm to 25 °C, and stirred for an additional 24 h. After this time, the reaction had a gelatin-like appearance. Water (100 mL) was added, and the mixture was filtered (with difficulty) through a coarse-sintered glass funnel. The mass was washed well with water, then with benzene, and finally with ether. The crumbly solid that remained was dissolved in 1.5 L of hot acetone, dried (Na_2SO_4), filtered, and evaporated to a 100-mL volume. A granular solid separated and was filtered and washed with acetone. After being dried, 3.48 g (24.6%) of **48**, mp 174 °C, was obtained, pure by elemental analysis. The mother liquor

was condensed to a 50-mL volume, and an additional 1.9 g (13.4%) of **48** was recovered. TLC indicated that more product was in the mother liquor. The compound gave the following: ^{1}H NMR ($CDCl_3$) δ 2.008–2.176 (m, 4 H, $NCH_2CH_2CH_2Br$), 2.286 (s, 3 H, $ArCH_3$), 3.301–3.462 (m, 8 H, $NCH_2CH_2CH_2Br$), 4.704 (b s, 2 H, $CONHCH_2$), 4.860 (s, 2 H, OCH_2Ph), 6.365 (s, 2 H, $ArNHCO$), 7.264–7.427 (m, 7 H, ArH); MS (70 eV, 200 °C), *m/e* 394 (M^+ – 180). Anal. Calcd for $C_{22}H_{28}Br_2N_4O_3$: C, 47.50; H, 5.07; N, 10.07. Found: C, 47.44; H, 4.97; N, 10.08.

1-(Phenylmethoxy)-2,6-bis(hexahydro-2-oxopyrimidinyl)-4-methylbenzene (45). To a solution of 3.4 g (6.11 mmol) of **48** in 300 mL of $(CH_3)_3COH$ was added 2.7 g of $(CH_3)_3COK$. The mixture was stirred vigorously for 17 h, the solvent was evaporated under reduced pressure, and the residue was extracted with 100 mL of CH_2Cl_2 from 100 mL of water (2 N hydrochloric acid was added to break an emulsion). The aqueous layer was extracted with two 50-mL portions of CH_2Cl_2. The organic extracts were combined, washed with 100 mL of brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to a volume at which the product began to crystallize (about 20 mL). Ether (30 mL) was layered carefully on top of the CH_2Cl_2, the flask was stoppered, and the product was filtered after 2 h and washed with ether to give 2.0 g (83%) of **45**, pure to ^{1}H NMR and TLC. For analysis a sample was recrystallized from CH_2Cl_2/Et_2O: mp 276–278 °C; ^{1}H NMR ($CDCl_3$) δ 1.854–1.912 (m, 4 H, $NCH_2CH_2CH_2N$), 2.298 (s, 3 H, $ArCH_3$), 3.297 (b s, 4 H, $HNCH_2$), 3.458 (b s, 4 H, $ArNCH_2$), 4.982 (s, 2 H, OCH_2Ph), 5.702 (b s, 2 H, *H*N), 7.018 (s, 2 H, ArH), 7.268–7.469 (m, 5 H, ArH); MS (70 eV, 180 °C), *m/e* 394 (M^+). Anal. Calcd for $C_{22}H_{26}N_4O_3$: C, 66.99; H, 6.64; N, 14.20. Found: C, 66.80; H, 6.59; N, 4.12.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-dicarbomethoxy-5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (49). To a solution of 2.08 g (3.95 mmol) of diacid **22** in 200 mL of ether was added excess diazomethane. Formic acid was added dropwise to destroy the excess diazomethane, and the mixture was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give 2.2 g (100%) of **49** as an oil. This material was pure by ^{1}H NMR and TLC (silica gel, 10% Et_2O/CH_2Cl_2, R_f 0.4), and was used without further purification. A sample was chromatographed over a 2-mm silica gel plate, eluted with 10% Et_2O/CH_2Cl_2 to give a colorless oil, and dried at 100 °C: ^{1}H NMR ($CDCl_3$) δ 2.308 (s, 6 H, $ArCH_3$), 2.367 (s, 3 H, $ArCH_3$), 3.579 (s, 6 H, $ArOCH_3$), 3.923 (s, 6 H, CO_2CH_3), 4.301 (s, 2 H, OCH_2Ph), 6.633 (d, J^4 = 6.3 Hz, 2 H, ortho ArH of benzyl), 7.056–7.590 (m, 9 H, ArH); MS (16 eV, 210 °C), *m/e* 554 (M^+). Anal. Calcd for $C_{34}H_{34}O_7$: C, 73.63; H, 6.18. Found: C, 73.58; H, 6.18.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-bis(hydroxymethyl)-5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (50). To a solution of 2.2 g (3.97 mmol) of **49** in 100 mL of ether stirred at 0 °C under argon was added 0.5 g of $LiAlH_4$. The mixture was stirred for 30 min. The reaction was quenched with EtOAc, and 4 mL of 2 N aqueous NaOH was added. The mixture was filtered, and the inorganic salts were washed with EtOAc. The filtrate was dried ($MgSO_4$), filtered, evaporated to dryness, and placed under vacuum to give 1.80 g (91%) of **50** as a white foam, which was used directly in the next step. A sample was crystallized from ether/pentane at −20 °C to give crystals: mp 124–125 °C; ^{1}H NMR ($CDCl_3$) δ 2.315 (s, 6 H, $ArCH_3$), 2.384 (s, 3 H, $ArCH_3$), 3.506 (s, 6 H, OCH_3), 4.306 (s, 2 H, $ArOCH_2$), 4.716 (b s, 4 H, CH_2OH), 6.612–6.658 (m, 2 H, ortho ArH of benzyl), 7.056–7.188 (m, 9 H, ArH); MS (70 eV, 180 °C), *m/e* 498 (M^+). Anal. Calcd for $C_{32}H_{34}O_5$: C, 77.08; H, 6.87. Found: C, 76.99; H, 6.89.

2,2″-Dimethoxy-2′-(phenylmethoxy)-3,3″-bis(bromomethyl)-5,5′,5″-trimethyl-1,1′:3′,1″-terphenyl (44). A mixture composed of 1.8 g (3.61 mmol) of **50**, 200 mL of benzene, and 0.33 mL (3.51 mmol) of phosphorus tribromide was stirred at 25 °C for 53 min, and 100 mL of saturated aqueous $NaHCO_3$ was added. The layers were separated. The benzene layer was washed with two 100-mL portions of water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to a small volume. This material was flash chromatographed at medium pressure over 60 g of silica gel packed in 1/1 pentane/CH_2Cl_2. Product was eluted with 250 mL of the same solvent to give 1.047 g (65%) of **44** as a white foam, which was used directly in the next step. A sample was chromatographed on a 2-mm silica gel plate. Product was eluted with 60/40 CH_2Cl_2/pentane to give **44** as a clear oil which dried to a glass: ^{1}H NMR ($CDCl_3$) δ 2.286 (s, 6 H, $ArCH_3$), 2.381 (s, 3 H, $ArCH_3$), 3.569 (s, 6 H, OCH_3), 4.296 (s, 2 H, OCH_2Ph), 4.611 (s, 4 H, $ArCH_2Br$), 6.611 (d, J^4 = 8.3 Hz, 2 H, ortho ArH of benzyl), 7.039–7.192 (m, 9 H, ArH); MS (70 eV, 210 °C), *m/e* 624 (^{81}Br) (M^+). Anal. Calcd for $C_{32}H_{32}Br_2O_3$: C, 61.55; H, 5.17; Br, 25.59. Found: C, 61.64; H, 5.05; Br, 25.50.

35,37-Dioxo-34,38-dimethoxy-33,36-bis(phenylmethoxy)-4,15,26,31-tetramethyl-8,12,18,22-tetraazaheptacyclo[27.3.1.1^{2,6}.1^{8,12}.1^{13,17}.1^{18,22}.1^{24,28}]octaconta-1(33),2(34),3,5,13(36),14,16,24(38),25,27,29,31-dodecaene (7). A mixture of 850 mL of THF, 0.88 g (2.23 mmol) of **45**, and 1.0 g of 50% NaH washed with pentane was heated to reflux for 2 h under argon and cooled to −78 °C, and 1.4 g (2.24 mmol) of **44** in 30 mL of THF was added. The mixture was stirred for 3 h at −78 °C and allowed to warm to 25 °C. The mixture was stirred for a total of 17 h, and then 700 mL of THF was evaporated over a 2-h period. The cooled mixture was quenched with water (10 mL), and the mixture was evaporated to dryness under reduced pressure. The residue was vigorously mixed with 180 mL of EtOAc and 50 mL of H_2O, the phases were separated, and the aqueous layer was extracted with 50 mL of EtOAc. The combined organic extracts were washed with three 20-mL portions of water, dried ($MgSO_4$), filtered, and evaporated to dryness. Gel chromatography of the mixture gave excellent separation of the desired component (retention volume 165–190 mL, center 177 mL), which was evaporated under reduced pressure. The residue was dissolved in 5 mL of 95% ethanol from which was obtained 0.5284 g (27.7%) of **7**. From the mother liquor an additional 0.1891 g (9.92%) was recovered. These materials were pure to TLC and ^{1}H NMR analysis. Recrystallization of a sample gave material of melting point 272–275 °C after being dried at 200 °C and 0.01 mm. The mother liquor was condensed to dryness, dissolved in 50 mL of CH_2Cl_2, and stirred for 0.5 h with 50 mL of aqueous 2 N NaBr. The organic layer was separated, dried ($MgSO_4$), and evaporated to dryness, and **7**·NaBr was isolated by crystallization from THF/ether. Spectral analysis (^{1}H NMR) indicated a very small amount of a minor isomer (≤5%) to be present. This material was stirred 2 h (the complex slowly dissolved) with 50 mL of water and 40 mL of EtOAc, the organic layer was separated, and the aqueous layer was extracted with 50 mL of EtOAc. The combined organic extracts were washed with two 25-mL portions of water, dried ($MgSO_4$), filtered, and condensed to dryness. This material was recrystallized from 95% ethanol to give 0.0698 g (3.7%) of pure **7** after being dried. Of all the hosts studied, this was the only one which was soluble when uncomplexed in EtOAc. The complex, first isolated after gel permeation chromatography, is insoluble in EtOAc. Stirring the complex with EtOAc/H_2O is, then, a method for the decomplexation of hosts that are insoluble in EtOAc in the complexed state. Crystalline **7** dissolved in $CDCl_3$ appears to be only one conformer: ^{1}H NMR ($CDCl_3$) δ 1.937–2.381 (m, 4 H, NCH_2, CH_2CH_2N), 2.2–2.45 (m, 6 H, NCH_2), 2.257 (s, 3 H, $ArCH_3$), 2.306 (s, 3 H, $ArCH_3$), 2.332 (s, 6 H, $ArCH_3$), 3.250 (s, 3 H, OCH_3), 3.348 (AB, J = 13.7 Hz, 2 H, $ArCH_2N$), 3.396 (s, 2 H, OCH_2Ph), 3.60–3.75 (m, 2 H, $ArCH_2NCH_2$), 4.916 (s, 2 H, OCH_2Ph), 5.906 (AB, J = 13.7 Hz, 2 H, $ArCH_2$), 6.245 (d, J^4 = 6.8 Hz, 2 H, ortho ArH of one benzyl), 6.585–7.041 (m, 16 H, ArH); MS (16 eV, 180 °C), *m/e* 856 (M^+). Anal. Calcd for $C_{54}H_{56}N_4O_6$: C, 75.68; H, 6.59; N, 6.54. Found: C, 75.52; H, 6.51; N, 6.50. The major isomer of **7**·NaBr: ^{1}H NMR ($CDCl_3$) δ 1.85–2.25 (m, 4 H, $NCH_2CH_2CH_2N$), 2.328 (s, 3 H, $ArCH_3$), 2.342 (s, 6 H, $ArCH_3$), 2.415 (s, 3 H, $ArCH_3$), 2.80–2.92 (m, 2 H, $ArCH_2NCH_2$), 3.328 (s, 6 H, OCH_3), 3.574 (AB, J = 13.67 Hz, 2 H, $ArCH_2N$), 3.799–3.848 (m, 6 H, $CH_2NCH_2CH_2CH_2N$), 4.026 (s, 2 H, OCH_2Ph), 4.406 (s, 2 H, OCH_2Ph), 5.421 (AB, J = 13.67 Hz, 2 H, $ArCH_2N$), 6.347 (d, J^4 = 7.32 Hz, 2 H, ortho ArH of one benzyl), 6.522 (d, J^4 = 6.84 Hz, 2 H, ortho ArH of other benzyl), 6.719–7.271 (m, 14 H, ArH). The minor isomer of **7**·NaBr (<5%): ^{1}H NMR ($CDCl_3$) δ 4.50 (s, OCH_2Ph), 5.6 (AB, J = 14 Hz).

35,37-Dioxo-34,38-dimethoxy-4,15,26,31-tetramethyl-8,12,18,22-tetraazaheptacyclo[27.3.1.1^{2,6}.1^{8,12}.1^{13,17}.1^{18,22}.1^{24,28}]octaconta-1(33),2(34),3,5,13(36),14,16,24(38),25,27,29,31-dodecaene-33,36-diol (51). Hydrogen bromide was vigorously admitted for 5 min through a gas dispersion tube to a stirred solution of 0.5053 g (0.5896 mol) of **7** in 30 mL of AcOH. The temperature increased to 50 °C. The flask was stoppered, stirred for 45 min, and diluted with 220 mL of distilled water. The product that separated floated on the liquid. It was filtered through a fine sintered glass funnel, washed well with 100 mL of water, and air dried. This material was dissolved in CH_2Cl_2, and the solution was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a white foam that smelled strongly of benzyl bromide. This material was crystallized from 10 mL of 95% ethanol, and product was collected, washed with 95% ethanol, and dried (200 °C/0.01 mm) to give 0.1703 (42.7%) of **51**: mp >255 °C dec; ^{1}H NMR ($CDCl_3$) δ 2.062–2.391 (m, 16 H, $ArCH_3$, $NCH_2CH_2CH_2N$), 3.108–3.90 (m, 8 H, NCH_2), 3.647 (s, 6 H, OCH_3), 5.186 (b AB, J = 14 Hz, 2 H, $ArCH_2N$), 5.983 (b AB, $J \simeq$ 14 Hz, 2 H, $ArCH_2N$), 6.836–7.390 (m, 8 H, ArH); MS (70 eV, 210 °C), *m/e* 676 (M^+). Anal. Calcd for $C_{41}H_{44}N_4O_6$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.80; H, 6.37; N, 8.30.

35,37-Dioxo-33,34,36,38-tetramethoxy-4,15,26,31-tetramethyl-8,12,18,22-tetraazaheptacyclo[27.3.1.1^{2,6}.1^{8,12}.1^{13,17}.1^{18,22}.1^{24,28}]octaconta-1(33),2(34),3,5,13(36),14,16,24(38),25,27,29,31-dodecaene (8). A clear stirred solution of 0.0600 g (0.0886 mmol) of **51** in 10 mL of THF and 4 mL of water was flushed for 5 min with a stream of argon, and 0.1 g of NaOH and 100 mL of $(CH_3)_2SO_4$ were added. After 23.5 h, 20 drops

of concentrated ammonium hydroxide was added. The solution was stirred for 5 h, condensed to dryness, and partitioned between 50 mL of CH_2Cl_2 and 50 mL of H_2O. A bad emulsion formed. After sitting 14 h, the CH_2Cl_2 layer was separated and the aqueous layer was extracted with 20 mL of CH_2Cl_2. The combined organic extracts were washed with 100 mL of water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a colorless oil. This material was crystallized from ethanol/water to give, after washing with three 1-mL portions of 7:3 ethanol/water and drying (160 °C/0.01 mm), 0.0442 g (70.7%) of **8**: mp >269 °C dec; ^1H NMR ($CDCl_3$) δ 1.945-2.262 (m, 4 H, $NCH_2CH_2CH_2N$), 2.303 (s, 3 H, $ArCH_3$), 2.337 (s, 3 H, $ArCH_3$), 2.359 (s, 6 H, $ArCH_3$), 3.033 (s, 3 H, $ArOCH_3$), 3.233 (s, 6 H, $ArOCH_3$), 3.303-3.367 (m, 6 H, $NCH_2CH_2CH_2N$), 3.355 (AB, J = 13.7 Hz, 2 H, $ArCH_2N$), 3.555 (s, 3 H, $ArOCH_3$), 3.608-3.716 (m, 2 H, $NCH_2CH_2CH_2N$), 5.853 (AB, J = 13.7 Hz, 2 H, $ArCH_2N$), 7.031-7.092 (m, 8 H, ArH); MS (70 eV, 220 °C), m/e 704 (M^+, 11), 674 (M^+ - 30, 100). Anal. Calcd for $C_{42}H_{48}N_4O_6$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.39; H, 6.82; N, 7.93.

Registry No. **1**, 83604-21-1; **1**·NaBr complex, 92184-73-1; **1**-Li·picrate, 92184-75-3; **1**-Na·picrate, 92184-77-5; **1**-K·picrate, 92184-79-7; **1**-Rb·picrate, 92184-81-1; **1**-Cs·picrate, 92184-83-3; **1**·NH_4^+·picrate, 92185-55-2; **1**·$CH_3NH_3^+$·picrate, 92185-56-3; **1**·$(CH_3)_3CNH_3^+$·picrate, 83604-22-2; **2**, 83604-24-4; **2**-Li·picrate, 92184-85-5; **2**-Na·picrate, 92184-87-7; **2**-K·picrate, 92269-44-8; **2**-Rb·picrate, 92184-89-9; **2**-Cs·picrate, 92184-91-3; **2**·NH_4^+·picrate, 92185-57-4; **2**·$CH_3NH_3^+$·picrate, 92185-58-5; **2**·$(CH_3)_3CNH_3^+$·picrate, 92185-59-6; **3**, 83604-25-5; **3**·NaBr complex, 83604-26-6; **3**-Li·picrate, 92184-93-5; **3**-Na·picrate, 92184-95-7; **3**-K·picrate, 92184-97-9; **3**-Rb·picrate, 92184-99-1; **3**-Cs·picrate, 92185-00-7; **3**·NH_4^+·picrate, 92185-60-9; **3**·$CH_3NH_3^+$·picrate, 92185-61-0; **3**·$(CH_3)_3CNH_3^+$·picrate, 92185-62-1; **4**, 84379-21-5; **4**·NaBr complex, 92185-01-8; **4**-Li·picrate, 92185-03-0; **4**-Na·picrate, 92185-05-2; **4**-K·picrate, 92185-64-3; **4**-Rb·picrate, 92185-07-4; **4**-Cs·picrate, 92185-09-6; **4**·NH_4^+·picrate, 92185-65-4; **4**·$CH_3NH_3^+$·picrate, 92185-66-5; **4**·$(CH_3)_6CNH_3^+$·picrate, 92185-67-6; **5**, 84379-22-6; **5**-Li·picrate, 92185-11-0; **5**-Na·picrate, 92185-13-2; **5**-K·picrate, 92185-15-4; **5**-Rb·picrate, 92185-17-6; **5**-Cs·picrate, 92185-19-8; **5**·NH_4^+·picrate, 92185-68-7; **5**·$CH_3NH_4^+$·picrate, 92185-69-8; **5**·$(CH_3)_3CNH_3^+$·picrate, 92185-70-1; **6**, 84379-24-8; **6**·NaBr complex, 92185-20-1; **6**-Li·picrate, 92185-22-3; **6**-Na·picrate, 92185-24-5; **6**-K·picrate, 92185-27-8; **6**-Rb·picrate, 92185-29-0; **6**-Cs·picrate, 92185-31-4; **6**·NH_4^+·picrate, 92185-71-2; **6**·$CH_3NH_3^+$·picrate, 92185-72-3; **6**·$(CH_3)_3CNH_3^+$·picrate, 92185-73-4; **7**, 84379-23-7; **7**·NaBr complex, 92185-32-5; 7-Li·picrate, 92185-34-7; 7-Na·picrate, 92185-36-9; 7-K·picrate, 92185-38-1; 7-Rb·picrate, 92185-40-5; 7-Cs·picrate, 92185-42-7; 7·NH_4^+·picrate, 92185-74-5; 7·$CH_3NH_3^+$·picrate, 92185-75-6; 7·$(CH_3)_3CNH_3^+$·picrate, 92185-76-7; 8, 92185-77-8; 8-Na·picrate, 92185-44-9; 8-K·picrate, 92185-46-1; 9, 83604-23-3; 9-Li·picrate, 92219-68-6; 9-Na·picrate, 92185-48-3; 9-K·picrate, 92185-50-7; 9-Rb·picrate, 92185-52-9; 9-Cs·picrate, 92219-70-0; 9·NH_4^+·picrate, 92219-71-1; 9·$CH_3NH_3^+$·picrate, 92185-78-9; 9·$(CH_3)_3CCNH_3^+$·picrate, 89482-94-0; **10**, 83604-32-4; **12i**, 89827-45-2; **13**, 92185-79-0; **14**, 83604-34-6; **15**, 83604-35-7; **16**, 83604-38-0; **17**, 83604-39-1; **18**, 71128-89-7; **19**, 84379-25-9; **20**, 84379-26-0; **21**, 84379-27-1; **22**, 84379-28-2; **23**, 84379-29-3; **24**, 84379-30-6; **25**, 91-04-3; **26**, 7259-92-9; **27**, 84379-31-7; **28**, 92185-80-3; **29**, 92185-81-4; **30**, 84379-43-1; **3u**, 84379-37-3; **32**, 84379-38-4; **33**, 92185-82-5; **34**, 92185-83-6; **35**, 84379-39-5; **36**, 83587-11-5; **37**, 84379-40-8; **38**, 84395-43-7; **39**, 92185-84-7; **40**, 83587-10-4; **41**, 29455-11-6; **42**, 37780-40-8; **43**, 92185-85-8; **44**, 84379-33-9; **45**, 84379-42-0; **46**, 84379-34-0; **47**, 84379-35-1; **48**, 84379-36-2; **49**, 92185-86-9; **50**, 84379-32-8; **51**, 92185-87-0; **52**, 17454-52-3; **52**-Li-picrate, 64799-51-5; **52**-Na·picrate, 64799-49-1; **53**-K·picrate, 64851-30-5; **52**-Rb·picrate, 64822-96-4; **52**-Cs·picrate, 64799-34-4; **52**·NH_4^+·picrate, 92185-88-1; **52**·$CH_3NH_3^+$·picrate, 92185-89-2; **52**·$(CH_3)_3CNH_3^+$·picrate, 92185-90-5; HUA′UA′UCH$_2$BCH$_2$OH, 92185-91-6; BrAAABr, 92185-92-7; HUAUAUCH$_2$BCH$_2$OH, 92185-93-8; $COCl_2$, 75-44-5; 1,2-bis(bromomethyl)benzene, 91-13-4; dibenzofuran, 132-64-9; 2-bromoanisole, 578-57-4; 4-(2-hydroxphenyl)dibenzofuran, 92185-94-9; 2,2′,2″-trihydroxy-[1,1:3′,1″]terphenyl, 92185-95-0; 2,4,4,6-tetrabromocyanohexadienone, 20244-61-5; 1-amino-3-bromopropane hydrobromide, 5003-71-4; 4-methyl-2-aminoanisole, 120-71-8; 1,3-dibromopropane, 109-64-8; 1,3-bis(2-methoxy-5-methylphenyl)-1,3-bis(2-propenyl)urea, 92185-96-1; 3-chloropropane isocyanate, 13010-19-0; 2,6-dibromo-4-methylphenol, 2432-14-6.

Chemical Consequences of Single-Electron Oxidation of Phenylmesityldiazoethane

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Abstract: Both thermolysis and photolysis of 1-phenyl-2-mesityldiazoethane (PMDE) lead exclusively to products derived from facile hydrogen or mesityl migration subsequent to, or concurrent with, loss of N_2. No detectable amounts of ketazine or any dimeric hydrocarbons are formed in these reactions—a result that is attributable to the steric hindrance about the diazo carbon in PMDE. Quite in contrast, the one-electron oxidation of this diazoalkane yields *no* monomeric products by simple hydrogen or mesityl migration; instead, ketazine and dimeric products are formed by two distinct paths. Dimerization of diazo radical cations followed by competing secondary reactions of the resulting dication is the favored path accounting for the major products. In a very much slower reaction, $PMDE^{+\cdot}$ attacks neutral PMDE to yield ketazine.

The ease with which diazoalkanes lose nitrogen to form transient carbenes has made this class of compounds the object of intensive mechanistic investigations.[1] Unfortunately, carbenes are such high-energy transients that their subsequent reactions are often indiscriminate and hence of little synthetic value.[2] The synthetic utility of diazoalkanes is realized more often in metal-salt-catalyzed reactions in which the nature of reactive intermediates derived from the diazoalkane is seldom understood.[3] However, a number of reports have appeared in the last decade which indicate that a general electron-transfer mechanism may explain much of the chemistry observed in catalyzed diazoalkane decompositions.[4] In many cases, diazo radical cations were proposed as discrete intermediates.

In 1971, Yamamoto and co-workers[5] reported that reactions of diphenyldiazomethane (DDM) can be induced by metal ions

(1) Patai, S., Ed. "The Chemistry of Diazonium and Diazo Groups"; Wiley: New York, 1978.

(2) Moss, R. A.; Jones, M., Jr. In "Reactive Intermediates"; Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1981; Vol. 2, Chapter 3. In contrast, diazonium ions have great synthetic utility. See Chapter 8 in ref 1 above.

(3) Wulfman, D. S.; Poling, B. In "Reactive Intermediates"; Abramovitch, R. A., Ed.; Plenum Press: New York, 1980; Vol. 1, Chapter 5.

(4) Despite the similarities between electrochemical and metal-catalyzed decompositions of diazo alkanes, the electrochemistry of diazo alkanes remains little studied by comparison. See Chapter 10 in ref 1 above.

(5) Shirafuji, T.; Yamamoto, Y.; Nozaki, H. *Tetrahedron* **1971**, *27*, 5353.

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