Host–Guest Complexation. 29. Expanded Hemispherands[1]

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Abstract: Four new hemispherands and one new open-chain analogue were synthesized, one crystal structure was determined, and the five hosts were examined for their differential binding properties toward alkali metal, ammonium, and alkylammonium ions. Four of the hosts are composed of six anisyl units attached to one another, and at their ends through their 2,6-positions. This sequence is symbolized by $(A)_6$. The ligand systems are completed by attachment of CH_2OH, $(CH_2)_2S$, $(CH_2)_2SO_2$, or $(CH_2)_2$ groups to the ends of the $(A)_6$ unit. In the fifth system, four like-substituted anisyl groups $(A)_4$ were incorporated into a ring by attaching at its ends the unit $(BOCH_2)_2B$, in which B is 1,2-disubstituted benzene. The hosts examined possessed the structures $(A)_6(CH_2OH)_2$ (**5**), $(A)_6(CH_2)_2S$ (**6**), $A_6(CH_2)_2SO_2$ (**7**), $A_6(CH_2)_2$ (**8**), and $A_4(BOCH_2)_2B$ (**9**). The crystal structure of $(A)_6(CH_2)_2S$ (**6**) was determined. The molecule is chiral, contains an approximate C_2 axis, and has six oxygens which possess a roughly octahedral arrangement. Of the six attached methyl groups, the two at the ends of the sexiaryl chain turn inward to fill the cavity defined by the six oxygens and the other four are oriented away from the cavity in an alternating up–down–up–down arrangement. The unshared electron pairs of the sulfur and its two closest neighboring oxygens turn outward, whereas those of the other oxygens are oriented inward and are preorganized for binding. The binding free energies $(-\Delta G°)$ in $CDCl_3$ saturated with D_2O were determined by the extraction technique at 25 °C for **5–9** binding the picrate salts of Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $CH_3NH_3^+$, and $t\text{-}BuNH_3^+$. The patterns of $-\Delta G°$ values (kcal mol^{-1}) varied with ring size. For open-chain compound $A_6(CH_2OH)_2$ (**5**), peak binding was reached with Cs^+ at 9.1 kcal mol^{-1}. The CH_2OH ends of the sexiphenyl chain probably hydrogen bond one another to close a ring with seven binding oxygens. The 21-membered ring hosts $(A)_6(CH_2)_2S$ (**6**) and $(A)_6(CH_2)_2SO_2$ (**7**) bind very similarly, showing peak binding for K^+ at 10.1 and 10.2 kcal mol^{-1}, respectively. The binding of the 20-membered ring, $(A)(CH_2)_2$ (**8**), peaked with Na^+ and K^+ with values of 10.1 and 10.2 kcal mol^{-1}, respectively. The 24-membered ring, $(A)_4(BOCH_2)_2B$ (**9**), was such a poor complexing agent as to be off scale (<6 kcal mol^{-1}) for all ions but Rb^+ and Cs^+ (5.8 kcal mol^{-1}). These results are interpreted in terms of the principles of complementarity and preorganization.

Spherands based on the 2,6-disubstituted-4-methylanisyl (A′) unit (e.g., $(A′)_6$ (**1**)) are unique hosts in the sense that they not only have preorganized cavities lined with 24 unshared electrons but these electrons are located at an interface between the vacuum of the cavity and their hydrocarbon support structure composed of six methyl and six aryl groups. Thus the activity of these electrons should be between what they would be in a vacuum and in a hydrocarbon medium. As a consequence, $(A′)_6$ (**1**) binds exclusively lithium and sodium picrates in $CDCl_3$ saturated with D_2O at 25 °C with $-\Delta G° > 23$ and 19.3 kcal mol^{-1}, respectively. In contrast, the open-chain analogue $H(A′)_6H$ (**2**) binds the same ions with <6 kcal mol^{-1}. Thus $(A′)_6$ represents an extreme example of the application of the principle of preorganization to host design and the importance of this principle to selectivity and binding free energies.[2]

Hemispherands have been defined as hosts, at least half of whose cavities are preorganized during synthesis, but some parts of which must undergo conformational reorganization during the complexing act.[3] Anisole hemispherands $(A′)_3(CH_2OCH_3)_3$ (**3**)[4] and $(A)_4(CH_2OCH_3)_2$ (**4**)[5] are both 18-membered ring hosts which show peak binding with Na^+ at the $-\Delta G° = 12.2$ and 13.5 kcal mol^{-1} levels, respectively. In the search for compounds more than half self-organizing (during synthesis) but which show peak binding with the ions larger than Na^+, we designed with the help of CPK molecular models expanded hemispherands **6–8** whose cavities are complementary to the larger ions and whose four central anisyl units appear in CPK molecular models to be self-organizing. Open-chain relative **5** in models appears capable of completing its ring system by hydrogen bonding between the terminal hydroxymethylene group and was included in the study because it is a synthetic intermediate and one unlike any previously

examined by us. The larger cycle **9** was prepared to see how far self-organization could be pushed as the cavity expands. For convenience, the hosts will be denoted with line formulas in which A stands for the 2,6-disubstituted-anisyl unit, A′ for the 2,6-disubstituted-4-methylanisyl unit, and B for the 1,2-disubstituted-benzene unit.

Results

Syntheses. Diol $(A)_6(CH_2OH)_2$ (**5**) was prepared from 2,2′-dimethoxy-1,1′-biphenyl as the initial starting material. This compound was dimetalated with BuLi, and the organometallic produced was treated with iodine to give 3,3′-diiodo-2,2′-dimethoxy-1,1′-biphenyl (**10**, 46%). This compound was cross-coupled[6] with two moles of dibenzofuranylphenylmagnesium bromide (**11**) in the presence of $Ni(Ph_3P)_2Cl_2$ in ether to produce sexiaryl compound **12** (75%). Dimetalation of **12** and substitution of the organometallic with ethyl chloroformate gave diester **13** (54%). When fused in NaOH–KOH at 300 °C, **13** underwent ester hydrolysis and its two furan rings opened to give a sexiphenolic diacid. This compound without characterization was octamethylated with $(CH_3)_2SO_4$–K_2CO_3 to yield diester **14** (88% overall), reduction of which with $LiAlH_4$ produced diol **5** (88%). Chlorination of **5** with N-chlorosuccinimide–triphenylphosphine[7] gave dichloride **15**. This compound was ring closed with Na-H–$(CH_2)_4O$–CH_3CSNH_2 under high dilution conditions to produce macroring **6** (75%). Use of C_6H_6–EtOH–KOH–CH_3CSNH_2[8] or C_6H_6–$(CH_2)_4O$–t-BuOK–CH_3CSNH_2 in this ring closure gave 11 and 15% yields, respectively. Oxidation of sulfide **6** with m-chloroperbenzoic acid gave sulfone **7** (89%). Photoextrusion[9] of SO_2 from **7** in C_6H_6 produced host **8** (75%).

The synthesis of macrocycle **9** involved trisphenol **16** as the starting material,[4a] two of whose hydroxyl groups were protected by ketalization[10] to give the 7-membered cycle **17** (95%). Molecular models indicate that formation of the alternative ketal involving the two terminal hydroxyl groups would produce a highly

(1) We thank the Division of Basic Sciences of the Department of Energy, Contract AT(04-3), for support of all the research reported here except that dealing with the crystal structure **24**. That work was supported by NSF Grant GP80-22526.

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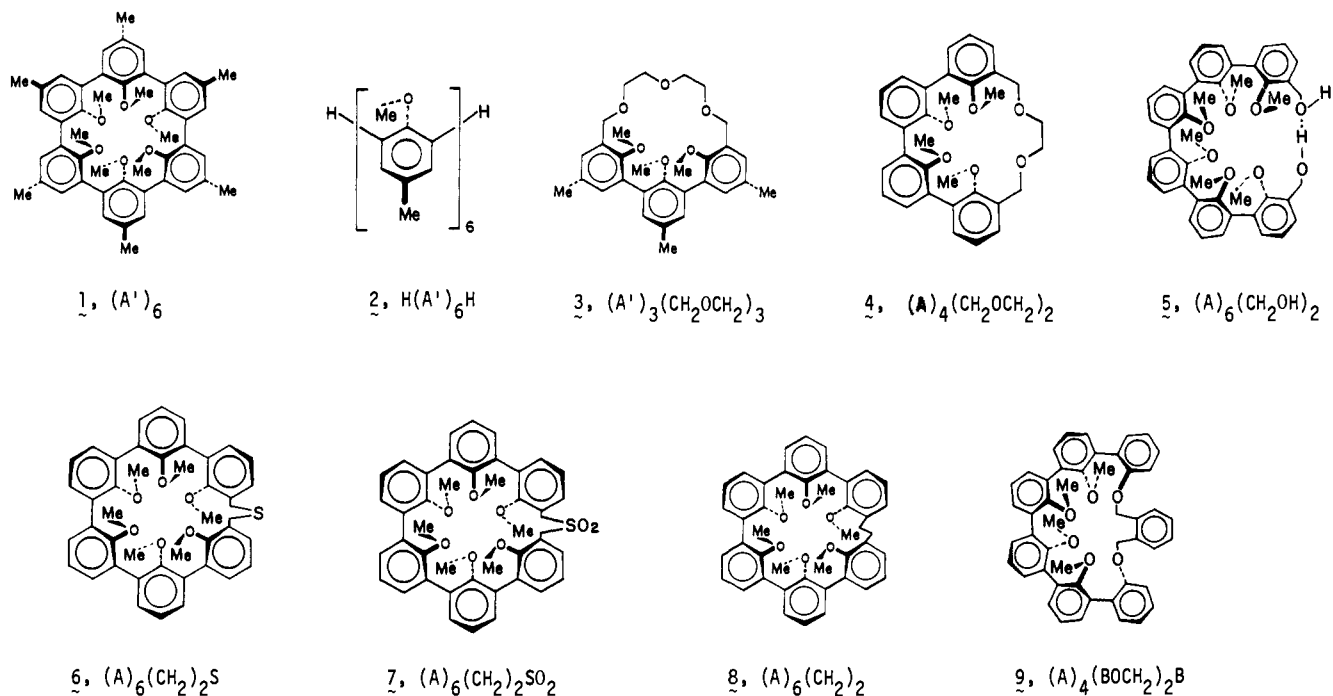
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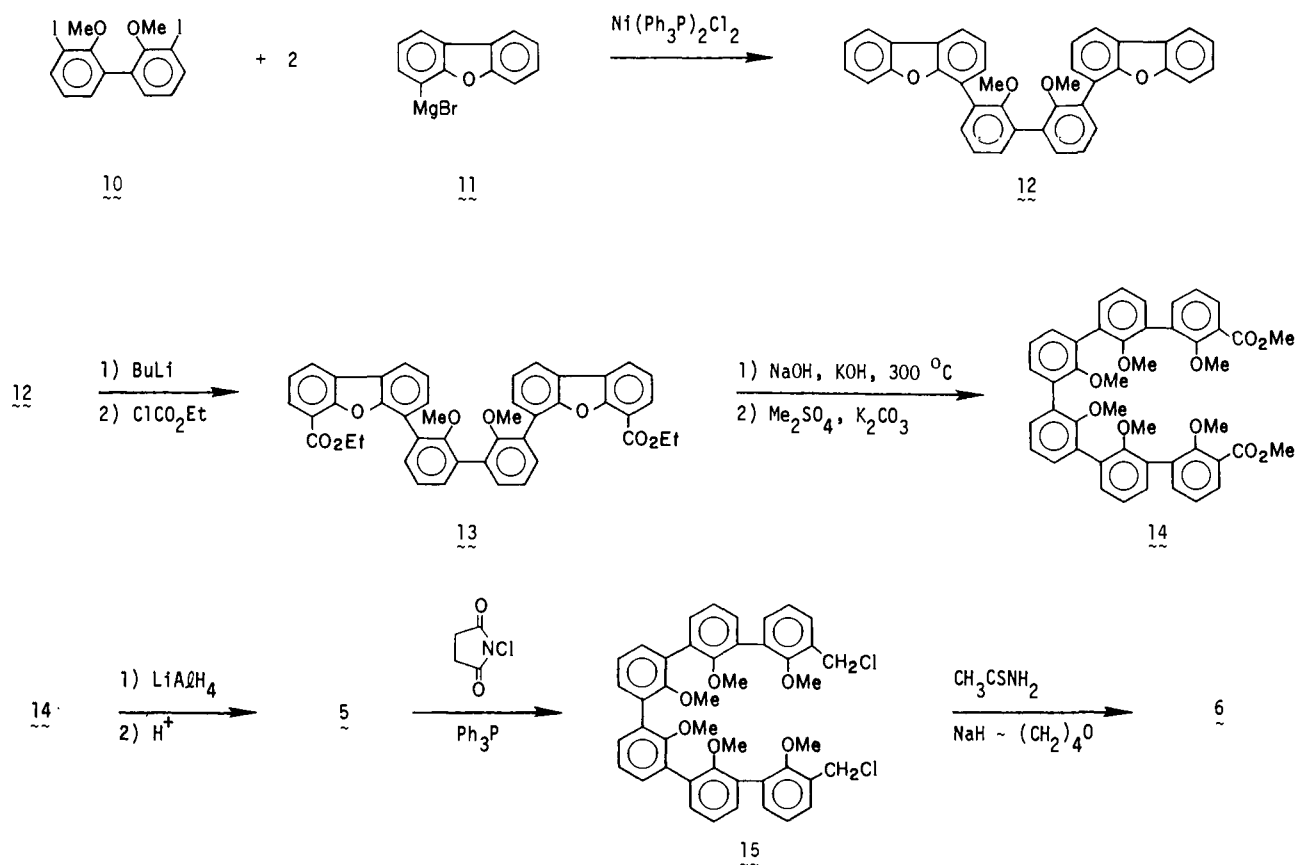(8) Hammerschmidt, E.; Bieber, W.; Vogtle, F. *Chem. Ber.* **1978**, *111*, 2445–2447.

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Expanded Hemispherands

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Chart I

1, (A')$_6$

2, H(A')$_6$H

3, (A')$_3$(CH$_2$OCH$_2$)$_3$

4, (A)$_4$(CH$_2$OCH$_2$)$_2$

5, (A)$_6$(CH$_2$OH)$_2$

6, (A)$_6$(CH$_2$)$_2$S

7, (A)$_6$(CH$_2$)$_2$SO$_2$

8, (A)$_6$(CH$_2$)$_2$

9, (A)$_4$(BOCH$_2$)$_2$B

Scheme I

10   11   12

12 $\xrightarrow[\text{2) ClCO}_2\text{Et}]{\text{1) BuLi}}$ 13 $\xrightarrow[\text{2) Me}_2\text{SO}_4, \text{K}_2\text{CO}_3]{\text{1) NaOH, KOH, 300 °C}}$ 14

14 $\xrightarrow[\text{2) H}^+]{\text{1) LiAlH}_4}$ 5 $\xrightarrow[\text{Ph}_3\text{P}]{}$ 15 $\xrightarrow[\text{NaH} \sim \text{(CH}_2)_4\text{O}]{\text{CH}_3\text{CSNH}_2}$ 6

strained, 10-membered ring. The remaining hydroxyl group of 17 was benzylated to give 18 (100%). The ketal function was hydrolyzed to free the two hydroxyl groups to give 19 (97%), which was brominated with 2,4,4,6-tetrabromocyclohexa-2,5-dienone[11] to yield 20 (93%). Other more acidic or basic brominating agents gave bad mixtures. The bisphenol was methylated with Me$_2$SO$_4$–NaOH to produce 21. This compound was dilithiated with BuLi, and the resulting organometallic was oxidatively coupled with Fe(acac)$_3$ in C$_6$H$_6$ to give 22 (51%).[12] The benzyl protecting groups of 21 were removed with H$_2$–Pd to yield sexiaryl

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

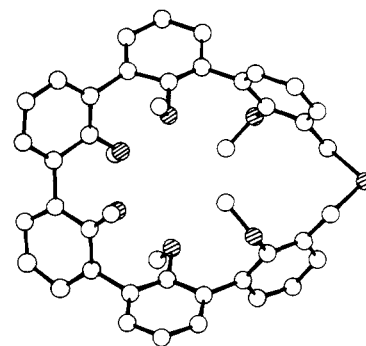| host structure	guest cation	K_a, M^{-1}	$-\Delta G^\circ$, kcal mol^{-1}
(A)$_6$(CH$_2$)$_2$ (8)	Li$^+$	1.3×10^4	5.6
	Na$^+$	2.5×10^7	10.1
	K$^+$	3.0×10^7	10.2
	Rb$^+$	4.4×10^5	7.7
	Cs$^+$	1.1×10^4	5.5
	NH$_4^+$	9.6×10^4	6.8
	CH$_3$NH$_3^+$	5.4×10^3	5.1
	t-BuNH$_3^+$	2.2×10^2	3.2
(A)$_6$(CH$_2$)$_2$S (6)	Li$^+$	$<2.5 \times 10^4$	<6
	Na$^+$	7.2×10^5	8.0
	K$^+$	2.5×10^7	10.1
	Rb$^+$	5.5×10^6	9.2
	Cs$^+$	2.2×10^5	7.3
	NH$_4^+$	1.2×10^6	8.3
	CH$_3$NH$_3^+$	3.5×10^4	6.2
	t-BuNH$_3^+$	9.5×10^1	2.7
(A)$_6$(CH$_2$)$_2$SO$_2$ (7)	Li$^+$	1.3×10^4	5.6
	Na$^+$	2.4×10^6	8.7
	K$^+$	3.0×10^7	10.2
	Rb$^+$	1.4×10^6	8.4
	Cs$^+$	3.5×10^4	6.2
	NH$_4^+$	3.1×10^5	7.5
	CH$_3$NH$_3^+$	1.1×10^4	5.5
	t-BuNH$_3^+$	9.5×10^1	2.7
(A)$_6$(CH$_2$OH)$_2$ (5)	Li$^+$	$<2.5 \times 10^4$	<6
	Na$^+$	3.5×10^4	6.2
	K$^+$	4.4×10^5	7.7
	Rb$^+$	2.0×10^6	8.6
	Cs$^+$	4.6×10^6	9.1
	NH$_4^+$	3.1×10^5	7.5
	CH$_3$NH$_3^+$	2.1×10^4	5.9
	t-BuNH$_3^+$	4.3×10^2	3.6
(A)$_4$(BOCH$_2$)$_2$B (9)	Li$^+$	$<2.5 \times 10^4$	<6
	Na$^+$	$<2.5 \times 10^4$	<6
	K$^+$	$<2.5 \times 10^4$	<6
	Rb$^+$	1.8×10^4	5.8
	Cs$^+$	1.8×10^4	5.8
	NH$_4^+$	1.7×10^3	4.4
	CH$_3$NH$_3^+$	$<2.5 \times 10^4$	<6
	t-BuNH$_3^+$	$<2.5 \times 10^4$	<6

24, (A)$_6$(CH$_2$)$_2$S

compound **23** (97%), whose internal aryls are anisyl and whose terminal aryls are phenolic. A mixture of this compound with *o*-xylyl dibromide when added under high dilution conditions to NaH–(CH$_2$)$_4$O gave the desired macrocycle **9** (20%).

Free Energies of Complexation. The association constants (K_a) and free energies of association ($-\Delta G^\circ$) of the open-chain system (A)$_6$(CH$_2$OH)$_2$ (5) and macrocycles (A)$_6$(CH$_2$)$_2$S (6), (A)$_6$(CH$_2$)$_2$SO$_2$ (7), (A)$_6$(CH$_2$)$_2$ (8), and A$_4$(BOCH$_2$)$_2$B (9) were determined by the picrate extraction method.[13] Solutions of Li$^+$, Na$^+$, K$^+$, Rb$^+$, Cs$^+$, NH$_4^+$, CH$_3$NH$_3^+$, and (CH$_3$)$_3$CNH$_3^+$ picrate in D$_2$O were extracted with CDCl$_3$ in the absence and presence of host. The hosts and their complexes are essentially insoluble in the D$_2$O layer. The K_a and $-\Delta G^\circ$ values at 25 °C in CDCl$_3$ saturated with D$_2$O were calculated from the results and the use of the equation $\Delta G^\circ = -RT \ln K_a$. Table I reports the values obtained, which are the average of two determinations. The $-\Delta G^\circ$ values have a precision ranging from ± 1.4 to $\pm 3.1\%$.[13]

Discussion

Crystal Structure of (A)$_6$(CH$_2$)$_2$S (6). The results of the crystal structure determination for host (A)$_6$(CH$_2$)$_2$S (6) are indicated by formula **24**.[14] The molecule is chiral and contains an ap-

proximate C_2 axis which passes through the S atom and the center of the (A)$_3$–(A)$_3$ bond. Each of the six oxygen atoms occupies a position on the side of the best plane of the macrocycle opposite to that of its two nearest oxygens. The methyl groups of the four anisyl units bonded only to other anisole units (inner anisoles) are oriented away from the cavity, and the unshared electron pairs of their attached oxygens are in orbitals that converge on the cavity. The methyl groups of the two anisole units bonded to CH$_2$ groups (outer anisoles) are oriented into the cavity, and the unshared electron pairs of their attached oxygens are in orbitals that diverge from the cavity. These two methyl groups essentially fill the cavity and thus **6** is not a spherand but a hemispherand since at least half of the cavity is enforced by the self-organizing up–down–up–down arrangement of the methoxyl groups of the four internal anisole units. For complexation to occur between **6** and any of the alkali metal ions, 180° rotations must occur around the Ar–OCH$_3$ bonds of the outer anisole units. Such a conformational reorganization generates a cavity in CPK molecular models of ~2.7 Å minimum diameter, which is complementary to the diameter of K$^+$ (2.7 Å). In CPK molecular models, other combinations of two methyl groups in **6** can turn inward; however, more strain is generated when either of them is part of an anisyl flanked by two other anisyls than when the anisyl is at the end of the sexianisyl chain. The same thing is true in models of (A)$_6$(CH$_2$)$_2$, (A)$_6$(CH$_2$)$_2$SO$_2$, and (A)$_6$(CH$_2$OH)$_2$ (the ends of the last compound probably are hydrogen bonded to form a cycle).

Correlation of Structure with Binding. Host (A)$_6$(CH$_2$)$_2$ (8) possesses a 20-membered ring whose methoxyl oxygens can assume a strain-free, nearly octahedral conformation. In this conformation, the six methyl groups are oriented outward. The orbitals of the 24 unshared electrons line a cavity which in molecular models has a diameter adjustable from a low of about 1.7 to a high of about 3.0 Å, depending on the dihedral angles between adjacent aryl groups. A sphere the diameter of Li$^+$ (1.5 Å) cannot contact more than four oxygens simultaneously. A sphere the diameter of Cs$^+$ (3.3 Å) can be inserted into the model, but the aryl–aryl bonds are deformed in the model complex, and the orbitals of the electron pairs cannot all focus on the Cs$^+$ simultaneously. The binding free energies (Table I) for (A)$_6$(CH$_2$)$_2$ (8) peak with Na$^+$ and K$^+$ as guests at 10.1 and 10.2 kcal mol^{-1}, respectively, and are very low for Li$^+$, Cs$^+$, CH$_3$NH$_3^+$, and t-BuNH$_3$ (5.6–3.2 kcal mol^{-1}). Intermediate values of 7.7 for Rb$^+$ and 6.8 kcal mol^{-1} for NH$_4^+$ are observed. Thus expanding the 18-membered rings of (A')$_6$ (1) or (A)$_4$(CH$_2$OCH$_2$)$_2$ (4) to the 20-membered ring of (A)$_6$(CH$_2$)$_2$ destroys the selectivity of Na$^+$ over K$^+$, and markedly decreases the peak binding free energy. Host (A')$_6$ (1) binds Na$^+$ with 19.3 kcal mol^{-1} [2] and (A)$_4$-(CH$_2$OCH$_2$)$_2$ (4) with 13.5 kcal mol^{-1}.[5]

The 21-membered ring cycles (A)$_6$(CH$_2$)$_2$S (6) and (A)$_6$(CH$_2$)$_2$SO$_2$ (7) in molecular models closely resemble one another. These two compounds show peak binding with K$^+$ as guest at the 10.1–10.2-kcal mol^{-1} level, exceeding that of Na$^+$ by 1.5–2.0 kcal mol^{-1} and Rb$^+$ by 0.9–1.8 kcal mol^{-1}. Host (A)$_6$(CH$_2$)$_2$S binds Cs$^+$ at the 7.3- and (A)$_6$CH$_2$)$_2$SO$_2$ at the 6.2-kcal mol^{-1} level. In models of (A)$_6$(CH$_2$)$_2$S, the unshared electron pairs of the sulfur

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(14) Space group *Cc*, *a* = 12.693 (4) Å, *b* = 18.382 (9) Å, *c* = 16.009 (7) Å, *β* = 99.50 (3)° at 295 K, *Z* = 4. Final *R* = 0.090 for 3034 unique reflections with *I* ≥ σ(*I*).

Scheme II
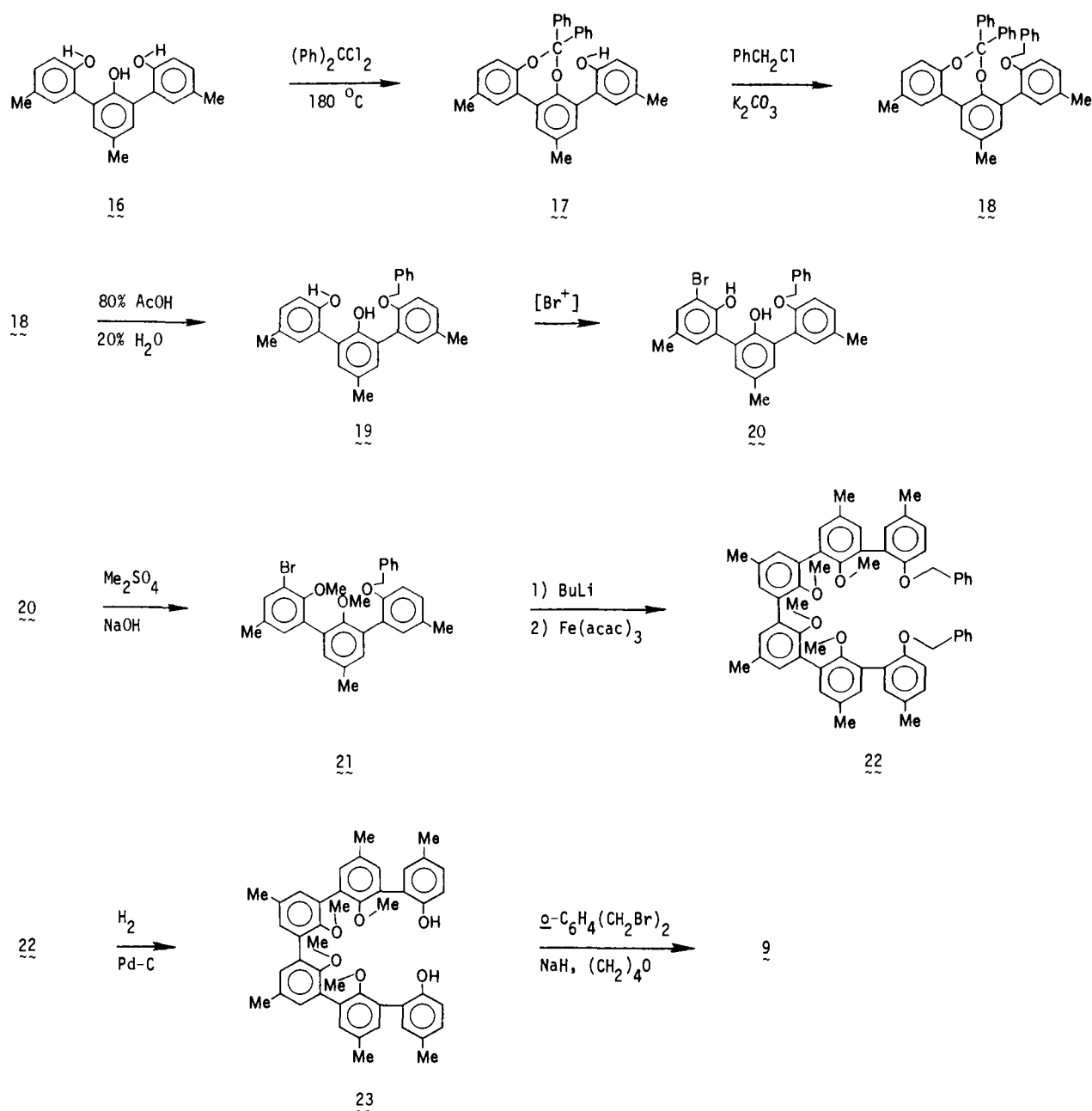
can turn inward to participate in the binding particularly well with the larger ions, Rb$^+$ and Cs$^+$, but much less well with K$^+$. In models of (A)$_6$(CH$_2$)$_2$SO$_2$, either one or both of the oxygens of the SO$_2$ group can orient inward to contact metal spheres of diameters ranging from 2.7 to 3.0 Å. The similarity in both the patterns and the values themselves for these two hosts suggests that neither S nor SO$_2$ is involved in the binding.

Open-chain host (A)$_6$(CH$_2$OH)$_2$ (5) gives peak binding with Cs$^+$ as guest at the 9.1-kcal mol^{-1} level, and the values decrease to 8.6 with Rb$^+$, to 7.7 with K$^+$, to 6.2 with Na$^+$, and to <6 kcal mol^{-1} with Li$^+$. Similarly, the values decrease to 7.5 with NH$_4^+$, to 5.9 with CH$_3$NH$_3^+$, and to 3.6 kcal mol^{-1} with t-BuNH$_3^+$. In contrast, analogue H(A′)$_6$H (2) binds these eight ions with $-\Delta G°$ values of <6 kcal mol^{-1}. Clearly the terminal CH$_2$OH groups of (A)$_6$(CH$_2$OH)$_2$ (5) play an important role in either organizing the system or providing additional binding sites or most probably both. In molecular models, seven of the eight oxygens of (A)$_6$-(CH$_2$OH)$_2$·Cs$^+$ can simultaneously and without strain contact the Cs$^+$ guest. The eighth CH$_2$OH oxygen may act as an acceptor of a hydrogen bond from the other terminal CH$_2$OH group, but it cannot participate in the binding of the guest. In models of

(A)$_6$(CH$_2$OH)$_2$·Rb$^+$, (A)$_6$(CH$_2$OH)$_2$·K$^+$, and (A)$_6$(CH$_2$OH)$_2$·Na$^+$, six oxygens (one from a CH$_2$OH group and five from CH$_3$O groups) in a roughly octahedral arrangement can contact the spheres in conformations of increasing strain as the sphere diameter decreases. In these structures, a terminal and binding CH$_2$OH donates a hydrogen bond to the *sequentially* most distant OCH$_3$ group, which, like the remaining CH$_2$OH group, does not participate in the binding. These observed values of binding for (A)$_6$(CH$_2$OH)$_2$ make it appear likely that the host exists in its uncomplexed state as a ring system of one of the above two varieties, or possibly both. It is interesting that (A)$_6$(CH$_2$OH)$_2$ distinguishes between K$^+$ and Na$^+$ by a power of ten in K_a value in spite of its rather flexible structure.

Host (A)$_4$(BOCH$_2$)$_2$B (9) contains a 22-membered ring and a total of six oxygens. In models of the uncomplexed compound, the two methylenes can turn inward to fill the cavity in an apparently strain-free conformation. Alternatively, in this larger ring system, the methyls of the two outer anisyl units can turn inward without any apparent strain. A cavity with a minimum diameter of about 2.4 Å can be formed in models in which the four anisyl methoxyls have the usual up–down–up–down ar-

rangement, the two benzyl oxygens lying roughly in the best plane of the macrocycle, with the plane of the xylyl group tilted to provide a dihedral angle of about 45° between the two planes. Although this cavity resembles that of $(A)_4(CH_2OCH_2)_2$ (4) in shape and the number of binding oxygens, $(A)_4(BOCH_2)_2B$ (9) is a much poorer binder, whose $-\Delta G°$ values for all eight ions are all <6 kcal mol^{-1}. This difference undoubtedly reflects the larger numbers of degrees of conformational freedom that must be frozen out for $(A)_4(BOCH_2)_2B$ to complex in comparison to the number in $(A)_4(CH_2OCH_2)_4$. In the latter 18-membered ring compound, all four anisyl groups are preorganized conformationally, and only the $CH_2OCH_2CH_2OCH_2$ bridge must reorganize.[5] In the 22-membered ring, the four anisyls as well as the bridge must probably be reorganized during complexation.

As model examination suggests should be the case, none of the hosts of this study show even moderately good binding of $CH_3NH_3^+$ and t-BuNH$_3^+$. These ions must perch on their NH···O hydrogen bonding systems in complexes, and the aryl oxygens of 5–9 are noncomplementary to the tripod arrangement required for binding the three hydrogens of RNH$_3^+$. In contrast, the NH$_4^+$ ion can nest in the cavities of these hosts, and a $-\Delta G°$ value as high as 8.3 kcal mol^{-1} is observed for $(A)_6(CH_2)_2S$ (6). For the four hosts whose values could be measured, Rb$^+$ is bound better than NH$_4^+$ by the relatively constant values of 1 ± 0.1 kcal mol^{-1}, which supports the suggestion that NH$_4^+$, like Rb$^+$, forms nesting complexes.

Experimental Section

General. All reactions were conducted under an atmosphere of dry argon or nitrogen. Tetrahydrofuran (THF) or diethyl ether were freshly distilled from sodium benzophenone ketyl just prior to use. Benzene, dimethylformamide (DMF), and thionyl chloride were purified as usual.[15] All other solvents were fractionally distilled before use. Flash chromatography was carried out on silica gel 60 (E. M. Merck, particle size 0.040–0.063 mm, 230–240 mesh ASTM). Medium-pressure chromatography (120 psi at ca. 10 mL/min) was conducted on either of three Altex columns: 250 mm × 15 mm (column A), 1000 mm × 25 mm (column B), or 600 mm × 25 mm (column C). Medium-pressure columns were packed with the same silica gel as described for flash chromatography. Gravity columns were packed with silica gel 60 (E. M. Merck, particle size 0.063–0.200 mm) or aluminum oxide (E. M. Merck, neutral grade, particle size 0.063–0.200 mm, 70–230 mesh ASTM). Gel permeation chromatography was performed on a 20 ft × 0.375 in. (outer diameter) column packed with 200 g of 100-Å styragel (Waters Associates) with CH$_2$Cl$_2$ as the mobile phase at flow rates of 3.5–4.0 mL/min. Thin-layer chromatography was conducted on precoated silica gel plates (E. M. Merck, F$_{254}$, thickness 0.2 mm). Melting points below 240 °C were measured on a Thomas-Hoover and those above 240 °C on a Mel-Temp apparatus. Infrared spectra were taken on a Perkin-Elmer 297 grating spectrophotometer. Mass spectra were recorded on an AE-1 Model MS-9 double-focusing spectrometer interfaced by Kratos Co. to a Data General Nova 3. Mass spectra were reported at 70 eV. Proton NMR spectra were obtained on a 200-MHz WP-200 spectrometer and ^{13}C NMR at 50.29 MHz on the same instrument or at 22.49 MHz on a Jeol-90 spectrometer. All chemical shifts are reported in parts per million downfield from internal $(CH_3)_4$Si in CDCl$_3$ unless otherwise indicated. Elemental analyses were within 0.30% of theory. Association constants were determined at 0.015 M concentrations of host and guest by the published procedure.[13]

3,3'-Diiodo-2,2'-dimethoxy-1,1'-biphenyl (10). To a suspension of 52.12 g (243.2 mmol) of 2,2'-dimethoxy-1,1'-biphenyl and 75.0 mL (469.9 mmol) of tetramethylethylenediamine in 600 mL of dry ether at −78 °C was added 582 mmol of butyllithium in hexane. The reaction mixture was allowed to warm to room temperature. The reaction mixture was stirred for 5 h, and the dilithiate suspension was cooled to 0 °C. To the mixture was added by cannulation a solution of 165 g (650.1 mmol) of iodine in 1 L of dry ether (the solubility of iodine in ether at room temperature is 0.18 g/mL). The reaction mixture was stirred at 0 °C for 10 min and then at room temperature for 1.5 h. The mixture was quenched with 500 mL of water saturated with Na$_2$SO$_3$. The organic phase was dried over MgSO$_4$ and concentrated under reduced pressure. The residue was crystallized from CH$_2$Cl$_2$/hexane at −20 °C. The crude product dissolved in a minimum of dichloromethane was flash chromatographed through a short Florisil column packed and eluted with 1/1

CH$_2$Cl$_2$/hexane to afford the product as a white solid. Recrystallization of this material from CH$_2$Cl$_2$/heptane at −20 °C provided analytically pure diiodide as thick, white rods: 51.81 g (46%); mp 101–102.5 °C; ^{1}H NMR δ 3.48 (s, 3 H, OCH$_3$), 6.89 (t, 1 H, ArH$_4$, J = 7.7 Hz), 7.34 (d of d, 1 H, ArH$_5$, J_o = 7.7 Hz, J_m = 1.3 Hz), 7.81 (d of d, 1 H, ArH$_6$, J_o = 7.7 Hz, J_m = 1.3 Hz); MS, m/e, M$^+$ 466. Anal. Calcd for C$_{14}$H$_{12}$I$_2$O$_2$: C, H, and I.

4,4'-(2,2'-Dimethoxy[1,1'-biphenyl]-3,3'-diyl)bis(dibenzofuran) (12). A mixture of 48.38 g (195.80 mmol) of 4-bromodibenzofuran,[16] 6.70 g (275.6 mmol) of Mg, 250 mL of the dry ether, and a trace of iodine was refluxed for 2 h. This Grignard mixture was cooled and transferred via cannula into a mixture of 30.09 g (64.56 mmol) of diiodide 10 and 4.24 g (6.5 mmol) of Ni(Cl)$_2$(Ph$_3$P)$_2$[6] in 250 mL of dry ether at 0 °C. The black mixture was stirred at 0 °C for 30 min and at reflux for 6 h and then at room temperature for 61 h. The reaction mixture was poured into ice/hydrochloric acid and the organic phase was removed. The aqueous phase was extracted with 2 × 500 mL of CH$_2$Cl$_2$. The combined organic phases were evaporated in vacuo. The residue was flash chromatographed (SiO$_2$, 6 × 42 cm, hexane → 1/1 CH$_2$Cl$_2$/hexane) to afford the crude product. Recrystallization of the crude product from CH$_2$Cl$_2$/hexane gave pure 12 as a white crystalline solid: 26.58 g (75%); mp 192–194 °C. Anal. Calcd for C$_{38}$H$_{26}$O$_4$: C and H.[17]

4-Bromodibenzofuran. To a solution of 67.3 g (0.40 mol) of dibenzofuran in 700 mL of dry THF was added at −40 °C 180 mL of a 2.4 M BuLi solution in hexane (0.43 M). The mixture was allowed to warm to 25 °C and stirred at this temperature for 5 h. The solution was cooled to −78 °C and 109 g (0.85 mol) of 1,2-dibromomethane dissolved in 50 mL of THF (dry) was added dropwise with stirring. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The solvent was evaporated and the residue was dissolved in CH$_2$Cl$_2$, washed with water and aqueous K$_2$CO$_3$ solution, and dried (MgSO$_4$). The solvent was evaporated, and the residue was recrystallized from CH$_2$Cl$_2$/pentane to give product as white crystals: 80.0 g (81%); mp 67–69 °C. Anal. Calcd for C$_{12}$H$_7$BrO: C, H, and Br.

Diethyl 6,6'-(2,2'-Dimethoxy[1,1'-biphenyl]-3,3'-diyl)bis(4-dibenzofuran)carboxylate (13). To a solution of 3.58 g (6.55 mmol) of 12 in 70 mL of dry THF at −78 °C was added 18.9 mmol of butyllithium in hexane. The reaction mixture was allowed to warm to 25 °C. After being stirred for 4 h, the dilithiate suspension was cooled to −78 °C. To this was added 25.2 mL (264 mmol) of ethyl chloroformate in one portion. The yellow solution was warmed to 25 °C. After being stirred at 25 °C for 18 h, the reaction mixture was concentrated under reduced pressure. The residue was partitioned between 200 mL of CH$_2$Cl$_2$ and 100 mL of water. The organic layer was dried (MgSO$_4$) and evaporated in vacuo. The residue was flash chromatographed (SiO$_2$, 6 × 26 cm, CH$_2$Cl$_2$) to give the crude product which was recrystallized from CH$_2$Cl$_2$/hexane to afford pure 13 as a slightly yellow crystalline solid: 2.43 g (54%); mp 175–177 °C. An analytical sample was prepared by recrystallization from CH$_2$Cl$_2$/hexane to give colorless crystals; mp 177.5–179 °C; ^{1}H NMR δ 1.35 (t, 3 H, OCH$_2$CH$_3$, J = 7.1 Hz), 3.36 (s, 3 H, OCH$_3$), 4.40 (q, 2 H, OCH$_2$CH$_3$, J = 7.1 Hz), 7.28–8.18 (m, 9 H, ArH); MS, m/e, M$^+$ 690. Anal. Calcd for C$_{44}$H$_{38}$O$_8$: C and H.

Dimethyl 2,2',2'',2''',2'''',2'''''-Hexamethoxy-[1,1':3',1'':3'',1''':3''', 1'''':3'''',1''''':3'''''-sexiphenyl]-3,3'''''-dicarboxylate (14). Approximately half of a mixture of 75.6 g (1.89 mol) of NaOH and 125.4 g (1.90 mol) of KOH was heated in a steel crucible to 200 °C whereupon fusion occurred. To the molten base was added 17.45 g (25.26 mmol) of diester 13 followed by the remaining NaOH/KOH mixture in such a way that the organic material was covered by the solid base. The mixture was then mechanically stirred as the temperature was raised to 300 °C and not allowed to go higher. The frothing, creamy mixture was stirred for 1 h (timed from the addition of the diester) and then poured into a shallow pan. After being cooled, the solid was dissolved in water and filtered through a coarse fritted glass funnel to remove insoluble impurities. The collected material (if any) was washed with water, and the combined filtrates were cooled in an ice bath. This aqueous solution was carefully acidified with concentrated hydrochloric acid and filtered. The collected solid was washed with water and dried over P$_2$O$_5$ in vacuo. The slightly purplish solid was added to 123.91 g (896.5 mmol) of K$_2$CO$_3$, 53 mL (560.1 mmol) of dimethyl sulfate, and 1000 mL of acetone. This mixture was mechanically stirred at reflux for 29 h. The reaction mixture was filtered, and the collected solid was washed liberally with acetone. The mother liquor was concentrated under reduced pressure, and the residue was partitioned between 500 mL of ether and 100 mL of 1/1 concentrated NH$_4$OH/water. The aqueous phase was extracted with 100 mL of ether, and the combined organic phases were dried (MgSO$_4$) and concentrated in vacuo. The residue was flash chromatographed (SiO$_2$,

(15) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. "Purification of Laboratory Chemicals"; Pergamon Press: Oxford, U.K., 1980.

(16) We thank Dr. Manfred Lauer for preparation of these compounds.
(17) Gilman, H.; Van Ess, P. R. *J. Am. Chem. Soc.* **1939**, *61*, 1365–1371.

6 × 48 cm, 1/2 ethyl acetate/hexane) to afford the pure diester as a white foam after drying in vacuo: 16.76 g (88%); ^{1}H NMR δ 3.27 (s, 3 H, OCH$_3$), 3.33 (s, 3 H, OCH$_3$), 3.59 (s, 3 H, OCH$_3$), 3.92 (s, 3 H, CO$_2$CH$_3$), 7.15–7.81 (m, 9 H, ArH); MS, m/e, M$^+$ 754. Calcd for C$_{46}$H$_{42}$O$_{10}$: C and H.

2,2′,2″,2‴,2⁗,2⁗′-Hexamethoxy-[1,1′:3′1″:3″,1‴:3‴,1⁗:3⁗,1⁗′-sexiphenyl]-3,3⁗′-dimethanol (5). To a suspension of 16.00 g (21.19 mmol) of diester **14** in 500 mL of ether and 100 mL of THF cooled to −78 °C was added 1.78 g (44.56 mmol) of LiAlH$_4$. The reaction mixture was allowed to warm slowly to room temperature. The mixture was stirred at 25 °C for 20 h, cooled to 0 °C, and quenched with a 15% NaOH solution in water. The reaction mixture was filtered, and the filter cake was washed with ether. The organic phase was washed with 300 mL of water. The aqueous layer was neutralized to pH 7 with aqueous HCl followed by aqueous NaHCO$_3$ solution (saturated) and was then extracted with 500 mL of ether. The combined organic phases were dried (MgSO$_4$) and concentrated in vacuo. The residue was flash chromatographed (SiO$_2$, 6 × 42 cm, 1/1 ethyl acetate/hexane → 1/1 ethyl acetate/CH$_2$Cl$_2$) to provide the diol as a white solid: 13.02 g (88%); mp 176–178 °C. An analytical sample was prepared by recrystallization from CH$_2$Cl$_2$/hexane to give fragile, white clusters: mp 178–179.5 °C; ^{1}H NMR δ 3.28 (s, 3 H, OCH$_3$), 3.33 (s, 3 H, OCH$_3$), 3.50 (s, 3 H, OCH$_3$), 4.77 (s, 2 H, CH_2OH), 7.11–7.43 (m, 9 H, ArH); MS, m/e, M$^+$ 698. Anal. Calcd for C$_{44}$H$_{42}$O$_8$: C and H.

3,3⁗′-Bis(chloromethyl)-2,2′,2″,2‴,2⁗,2⁗′-hexamethoxy-1,1′:3′,1″:3″,1‴:3‴,1⁗:3⁗,1⁗′-sexiphenyl (15). A mixture of 2.278 g (8.69 mmol) of triphenylphosphine, 1.134 g (9.99 mmol) of *N*-chlorosuccinimide, and 250 mL of THF was stirred at 25 °C for 15 min. To this white suspension was added 2.493 g (3.57 mmol) of diol **5**. The reaction mixture was stirred at 25 °C for 8 h during which time it became an amber solution. The reaction mixture was partitioned between 250 mL of ether and 150 mL of water. The aqueous layer was extracted with 100 mL of ether, and the combined organic layers were washed with 50 mL of brine and dried (MgSO$_4$). Removal of the solvent in vacuo left a residue which was flash chromatographed (SiO$_2$, 3.5 × 40 cm, 10/1 hexane/ethyl acetate) to afford pure dichloride as a white foam after drying under vacuum: 2.598 g (99%); ^{1}H NMR δ 3.28 (s, 3 H, OCH$_3$), 3.34 (s, 3 H, OCH$_3$), 3.53 (s, 3 H, OCH$_3$), 4.73 (s, 2 H, CH$_2$Cl), 7.11–7.45 (m, 9 H, ArH); MS, m/e, M$^+$ (^{35}Cl) 734. Anal. Calcd for C$_{44}$H$_{40}$Cl$_2$O$_6$: C, H, and Cl.

34,35,36,37,38,39-Hexamethoxy-28-thiaheptacyclo-[28.3.1.1^{2,6}.1^{7,11}.1^{12,16}.1^{17,21}.1^{22,26}]nonatriaconta-1(34),2,4,6(39),7,9,11-(38),12,14,16(37),17,19,21(36),22,24,26(35),30,32-octadecaene (6). To a refluxing suspension of 514 mg (w/oil) (10.71 mmol) of NaH in 900 mL/dry THF was added by syringe pump a solution of 2.598 g (3.53 mmol) of dichloride **15** in 51 mL of THF and dropwise a solution of 267 mg (3.55 mmol) of thioacetamide in 51 mL of THF over a 24-h period. The reaction mixture was refluxed an additional 16 h, cooled, and quenched with water. The products were partitioned between 200 mL of ether and 200 mL of water. The aqueous phase was extracted with 100 mL of ether, and the combined organic phases were washed with 100 mL of brine, dried (MgSO$_4$), and evaporated in vacuo. The residue was flash chromatographed (SiO$_2$, 3.5 × 40 cm, 4/1 CH$_2$Cl$_2$/ethyl acetate → 2/1 CH$_2$Cl$_2$/ethyl acetate) to provide the pure cycle as a white solid, 1.85 g (75%). An analytical sample was prepared by recrystallization from CH$_2$Cl$_2$/hexane to give thick, colorless crystals: mp 249–252 °C; ^{1}H NMR δ 2.87 (s, 3 H, OCH$_3$), 3.05 (s, 3 H, OCH$_3$), 3.35 (s, 3 H, OCH$_3$), 3.62 (d, 1 H, –CH$_A$HS–, J = 12.8 Hz), 3.93 (d, 1 H, –CHH$_B$S–, J = 12.8 Hz), 7.03–7.42 (m, 9 H, ArH); ^{13}C NMR δ 30.7 (CH$_2$S), 60.0 (OCH$_3$), 60.3 (OCH$_3$), 61.2 (OCH$_3$), 122.3, 122.8, 123.2, 129.6, 130.0, 130.3, 130.6, 132.4, 132.8, 156.7, 156.9, 157.8; MS, m/e 698 (16), 697 (49), M$^+$ 696 (100), 681 (25), 666 (14), 665 (26), 664 (11), 663 (21), 649 (18), 617 (16), 325 (12), 317 (10). Anal. Calcd for C$_{44}$H$_{40}$O$_6$S: C, H, and S.

34,35,36,37,38,39-Hexamethoxy-28-thiaheptacyclo-[28.3.1.1^{2,6}.1^{7,11}.1^{12,16}.1^{17,21}.1^{22,26}]nonatriaconta-1(34),2,4,6(39),7,9,11-(38),12,14,16(37),17,19,21(36),22,24,26(35),30,32-octadecaene 28,28-Dioxide (7). To a solution of 1.40 g (2.01 mmol) of cycle **6** in 100 mL of CH$_2$Cl$_2$ at 0 °C was added a solution of 2.50 g (11.6 mmol) of *m*-chloroperbenzoic acid in 75 mL of CH$_2$Cl$_2$ dropwise over 15 min. The reaction mixture was stirred at 0 °C for 15 min and then at 25 °C for an additional 1.5 h. After being cooled again to 0 °C, the reaction mixture was quenched with 50 mL of water saturated with NaHSO$_3$. The products were partitioned between 250 mL of CH$_2$Cl$_2$ and 100 mL of water. The organic layer was washed with 2 × 100 mL of 1/1 saturated aqueous NaHCO$_3$ solution/water. The combined aqueous layers were extracted with 100 mL of CH$_2$Cl$_2$, and the combined organic layers were washed with 100 mL of brine, dried (MgSO$_4$), and concentrated under reduced pressure. The solid residue was flash chromatographed (SiO$_2$, 3.5 × 41 cm, CH$_2$Cl$_2$ → 2/1 → 1/1 → ^{1}/$_2$CH$_2$Cl$_2$/ethyl acetate

→ ethyl acetate) to provide the cyclic sulfone as a white solid, 1.307 g (89%). An analytical sample was prepared by recrystallization from CH$_2$Cl$_2$/hexane to give colorless crystals: mp 315–322 °C with gas evolution and dec; ^{1}H NMR δ 2.92 (s, 3 H, OCH$_3$), 3.06 (s, 3 H, OCH$_3$), 3.39 (s, 3 H, OCH$_3$), 4.29 (d, 1 H, –CH$_A$HSO$_2$–, J = 13.6 Hz), 4.64 (d, 1 H, –CHH$_B$SO$_2$–, J = 13.6 Hz), 7.10–7.52 (m, 9 H, ArH); ^{13}C NMR δ 53.7 (CH$_2$SO$_2$), 60.0 (OCH$_3$), 60.9 (OCH$_3$), 61.5 (OCH$_3$), 120.8, 122.6, 122.9, 123.2, 129.7, 131.8, 132.1, 132.8, 132.9, 157.2, 157.7, 157.8; MS, m/e, 729 (10), M$^+$ 728 (22), 666 (12), 665 (43), 664 (95), 634 (31), 633 (61), 619 (20), 618 (56), 617 (100), 602 (18), 601 (29), 587 (12), 586 (10), 585 (11). Anal. Calcd for C$_{44}$H$_{40}$SO$_8$: C, H, and S.

33,34,35,36,37,38-Hexamethoxyheptacyclo[27.3.1.1^{2,6}.1^{7,11}.1^{12,16}.1^{17,21}.1^{22,26}]octatriaconta-1(33),2,4,6(38),7,9,11(37),12,14,16-(36),17,19,21(35),22,24,26(34),29,31-octadecaene (8). A mixture of 750 mg (1.03 mmol) of cycle **7** and 200 mL of benzene (Spectro-grade) was degassed with argon under sonication (Sonicor, 60 Hz) for 30 min. The colorless solution was irradiated for 24 h with a 450-W Hanovia high-pressure lamp with use of a Vycor filter. Argon was bubbled into the reaction mixture throughout the irradiation time to remove SO$_2$. The solvent was removed in vacuo leaving a residue which was chromatographed (Al$_2$O$_3$, 2% water deactivated, 3 × 28 cm, CH$_2$Cl$_2$ → 10/1 → 5/1 → CH$_2$Cl$_2$/ethyl acetate) to provide 594 mg (87%) of the desired cycle. Recrystallization of this material from CH$_2$Cl$_2$/ethanol gave analytically pure **8** as white clusters: 511 mg (75%); mp 268–277 °C with slight dec; ^{1}H NMR δ 2.88 (s, 3 H, OCH$_3$), 2.95 (s, 3 H, OCH$_3$), 3.01–3.20 (m, 2 H, –CH$_2$CH$_2$–), 3.23 (s, 3 H, OCH$_3$), 7.07–7.42 (m, 9 H, ArH); ^{13}C NMR δ 30.46 (CH$_2$), 60.17 (OCH$_3$), 60.28 (OCH$_3$), 61.55 (OCH$_3$), 122.68, 122.93, 128.31, 129.25, 129.36, 129.51, 129.67, 129.71, 132.43, 132.55, 132.69, 132.79, 133.62, 137.04, 156.25, 157.54, 158.46; IR (KBr) 2940, 1455, 1400, 1230, 1175, 1010, 760; MS, m/e, 666 (11), 665 (48), M$^+$ 664 (100), 634 (11), 633 (21), 618 (19), 617 (34), 332 (19). Anal. Calcd for C$_{44}$H$_{40}$O$_6$: C and H.

2-(2,10-Dimethyl-6,6-diphenyldibenzo[*d,f*][1,3]dioxepin-4-yl)-4-methylphenol (17). A mixture of 8.21 g (25.62 mmol) of triol **16** and 6.11 g (25.77 mmol) of dichlorodiphenylmethane was heated to 180–190 °C whereupon fusion began. The frothing mixture was maintained at 180–190 °C for 35 min or until hydrogen chloride evolution had ceased. After cooling, the glass was dissolved in 200 mL of ether and the solution was washed with 2 × 50 mL of water saturated with NaHCO$_3$, 2 × 50 mL of water, and 50 mL of brine. The solution was dried (Na$_2$SO$_4$), and the solvent was evaporated under reduced pressure. The residue was chromatographed on 265 g of SiO$_2$ packed and eluted with 6/4 hexane/CH$_2$Cl$_2$ to provide ketal **17** as a white foam, 12.08 g (97%). An analytical sample was prepared by recrystallization from hexane to give white crystals: mp 170–171 °C; ^{1}H NMR δ 2.12 (s, 3 H, ArCH$_3$), 2.37 (s, 3 H, ArCH$_3$), 2.41 (s, 3 H, ArCH$_3$), 5.86–7.37 (m, 18 H, ArH); MS, m/e, M$^+$ 484 (100). Anal. Calcd for C$_{34}$H$_{28}$O$_3$: C and H.

2,10-Dimethyl-4-[5-methyl-2-(phenylmethoxy)phenyl]-6,6-diphenyldibenzo[*d,f*][1,3]dioxepin (18). To 22.96 g 47.38 mmol) of ketal **17** in 300 mL of acetone was added 14.31 g (103.54 mmol) of K$_2$CO$_3$ and 9.93 g (58.06 mmol) of benzyl bromide. This mixture was refluxed in the dark for 78 h, cooled, and concentrated in vacuo. The residue was partitioned between 250 mL of CH$_2$Cl$_2$ and 250 mL of water. The organic phase was dried (MgSO$_4$) and concentrated under pressure to afford **18** as a white solid homogeneous to TLC, 27.25 g (>99%). An analytical sample was prepared by recrystallization from CH$_2$Cl$_2$/ethanol to give large, white crystals: mp 177.5–179 °C; ^{1}H NMR δ 2.17 (s, 3 H, ArCH$_3$), 2.36 (s, 6 H, ArCH$_3$), 4.82 (s, 2 H, –OCH$_2$Ph), 6.45–7.35 (m, 23 H, ArH); MS, m/e, M$^+$ 574. Anal. Calcd for C$_{41}$H$_{34}$O$_3$: C and H.

5,5′,5″-Trimethyl-2″-(phenylmethoxy)-[1,1′:3′,1″-terphenyl]-2,2′-diol (19). To 27.25 g (47.4 mmol) of benzyl ketal **18** was added 40 mL of water and 160 mL of glacial acetic acid. The resulting emulsion was refluxed for 30 h during which time it became homogeneous. After cooling, the reaction mixture was concentrated in vacuo, and the residue was dissolved in 500 mL of CH$_2$Cl$_2$. The organic phase was washed with 100 mL of saturated aqueous NaHCO$_3$ solution. The aqueous phase was extracted with 50 mL of CH$_2$Cl$_2$, and the combined organic phases were dried (MgSO$_4$) and concentrated under reduced pressure. The residue was flash chromatographed (SiO$_2$, 28 × 8.5 cm, 10% ether/hexane → 20% ether/hexane) to provide diol **19** as a white foam after drying under vacuum: 18.94 g (97%); ^{1}H NMR δ 2.34 (s, 3 H, ArCH$_3$), 2.36 (s, 3 H, ArCH$_3$), 2.38 (s, 3 H, ArCH$_3$), 5.06 (s, 2 H, –OCH$_2$Ph), 6.15 (s, 1 H, OH), 6.84 (s, 1 H, OH), 6.90–7.28 (m, 13 H, ArH); MS, m/e, M$^+$ 410. Anal. Calcd for C$_{28}$H$_{26}$O$_3$: C and H.

3-Bromo-5,5′,5″-trimethyl-2″-(phenylmethoxy)-[1,1′:3′,1″-terphenyl]-2,2′-diol (20). To 18.94 g (46.13 mmol) of benzyl diol **19** in 1400 mL of CHCl$_3$ cooled to 0 °C was added 19.49 g (47.57 mmol) of 2,4,4,6-tetrabromocyclohexa-2,5-dienone. The reaction mixture was stirred at 0 °C for 4 h, and 100 mL of water and 100 mL of saturated aqueous Na$_2$SO$_3$ solution were added. The organic solution was removed,

dried (MgSO₄), and concentrated under reduced pressure. The residue was flash chromatographed (SiO₂, 32 × 8.5 cm, 10% ether/hexane → 20% ether/hexane) to afford the brominated diol 20 as a white foam after drying under vacuum: 21.08 g (93%); ¹H NMR δ 2.30 (s, 3 H, ArCH₃), 2.36 (s, 6 H, ArCH₃), 5.06 (s, 2 H, –OCH₂Ph), 6.20 (s, 1 H, OH), 6.73 (s, 1 H, OH), 6.96–7.33 (m, 12 H, ArH); MS, *m/e*, M⁺ (⁷⁹Br) 488. Anal. Calcd for C₂₈H₂₅BrO₃: C, H, and Br.

3-Bromo-2,2′-dimethoxy-5,5′,5″-trimethyl-2″-(phentylmethoxy)-1,1′:3′,1″-terphenyl (21). To 13.31 g (27.20 mmol) of diol 20 in 400 mL of THF was added 50 mL of water and 7.0 g (175 mmol) of NaOH. This mixture was stirred for 15 min, and then 10.3 mL (109 mmol) of (CH₃)₂SO₄ was added. The reaction mixture was refluxed for 1.5 h, cooled, quenched with concentrated NH₄OH, and partitioned between 200 mL of ether and 100 mL of water. The organic phase was washed with 100 mL of water and 100 mL of brine. The combined aqueous phases were extracted with 50 mL of ether, and the combined organic phases were dried (MgSO₄). The solvent was removed in vacuo, and the residue was dried at 100 °C under vacuum to give the ether 21 as a slightly yellow viscous oil, pure enough for use in subsequent reactions (14.09 g, >99%). An analytical sample prepared via preparatory TLC (SiO₂, 10% ether/hexane) gave 21 as a viscous oil: ¹H NMR δ 2.29 (s, 3 H, ArCH₃), 2.32 (s, 3 H, ArCH₃), 2.34 (s, 3 H, ArCH₃), 3.19 (s, 3 H, OCH₃), 3.48 (s, 3 H, OCH₃), 5.03 (s, 2 H, –OCH₂Ph), 6.90–7.35 (m, 12 H, ArH); MS, *m/e*, M⁺ (⁷⁹Br) 516. Anal. Calcd for C₃₀H₂₉BrO₃: C, H, and Br.

2,2′′′′′-Bis(phenylmethoxy)-2′,2″,2′′′,2′′′′-tetramethoxy-5,5′,5″,5′′′,5′′′′,5′′′′′-hexamethyl-1,1′:3′,1″:3″,1′′′:3′′′,1′′′′:3′′′′,1′′′′′-sexiphenyl (22). To a solution of 2.88 g (5.57 mmol) of triphenyl 21 in 75 mL of dry THF at –78 °C was added 5.88 mmol of butyllithium in hexane. The light yellow solution was stirred 10 min at –78 °C and then transferred via cannula into a refluxing solution of 3.95 g (11.18 mmol) of Fe(acac)₃ in 100 mL of benzene. The reaction mixture was refluxed for 2.5 h, cooled, and partitioned between 250 mL of ether and 200 mL of 1/1 concentrated hydrochloric acid/water. The organic phase was washed with 4 × 125 mL of water. The combined aqueous washings were extracted with 150 mL of ether, and the combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. The residue was chromatographed (medium pressure, SiO₂, columns A + B, 10% ether/hexane) to provide sexiphenyl 22 as a white foam after drying

under vacuum: 1.25 g (51%); ¹H NMR δ 2.31 (s, 3 H, ArCH₃), 2.34 (s, 6 H, ArCH₃), 3.24 (s, 3 H, OCH₃), 3.28 (s, 3 H, OCH₃), 5.02 (s, 2 H, –OCH₂Ph), 6.88–7.27 (m, 12 H, ArH); MS, *m/e*, M⁺ 874. Anal. Calcd for C₆₀H₅₈O₆: C and H.

2′,2″,2′′′,2′′′′-Tetramethoxy-5,5′,5″,5′′′,5′′′′,5′′′′′-hexamethyl-[1,1′:3′,1″:3″,1′′′:3′′′,1′′′′:3′′′′,1′′′′′-sexiphenyl]-2,2′′′′′-diol (23). A mixture of 1.25 g (1.43 mmol) of sexiphenyl 22, 750 mg of 10% palladium/carbon, 25 mL of ethyl acetate, and 25 mL of ethanol was hydrogenated under 2.5 atm of hydrogen in a Parr apparatus for 1 h at 25 °C. The reaction mixture was filtered through Whatman No. 50 hardened filter paper and concentrated under reduced pressure to afford the diol 23 as a white foam after drying under vacuum: 0.96 g (97%); ¹H NMR δ 2.35 (s, 3 H, ArCH₃), 2.38 (s, 3 H, ArCH₃), 2.40 (s, 3 H, ArCH₃), 3.31 (s, 3 H, OCH₃), 3.35 (s, 3 H, OCH₃), 6.91–7.25 (m, 14 H, ArH); MS, *m/e*, M⁺ 694. Anal. Calcd for C₄₆H₄₆O₆: C and H.

30,35-Dihydro-37,38,39,40-tetramethoxy-3,7,12,17,22,26-hexamethyl-5,9:10,14,15,19:20,24-tetramethenotribenzo[c,g,c][1,6]dioxacyclotriacontin (9). To a refluxing suspension of 351 mg (w/oil) of NaH (7.31 mmol) in 250 mL of THF was added dropwise with stirring a solution of 960 mg of diol 23 (1.382 mmol) and 188 mg (0.71 mmol) of 1,2-bis(bromomethyl)benzene in 200 mL of THF under high dilution over an 88-h period. The reaction mixture was refluxed an additional 103 h, cooled, and quenched with water. The solvent was removed in vacuo, and the residue was partitioned between 300 mL of CH₂Cl₂ and 100 mL of water. The organic layer was dried (MgSO₄) and concentrated under reduced pressure. The residue was chromatographed (medium pressure, SiO₂, column B, 15% ether/hexane) to yield the cycle as a white solid, 220 mg (20%). An analytical sample was prepared by recrystallization from CH₂Cl₂/methanol to give white crystals: mp 263–271 °C; ¹H NMR δ 2.33 (s, 6 H, ArCH₃), 2.35 (s, 3 H, ArCH₃), 2.78 (s, 3 H, OCH₃), 3.16 (s, 3 H, OCH₃), 4.90 (s, 2 H, J = 13.3 Hz, OCH₂), 5.15 (d, 2 H, J = 13.3 Hz, OCH₂), 6.71–7.33 (m, 18 H, ArH); ¹³C NMR δ 20.52 (ArCH₃), 20.72 (ArCH₃), 20.79 (ArCH₃), 59.80 (OCH₃), 60.26 (OCH₃), 66.91 (OCH₂), 112.29, 127.04, 128.31, 128.72, 129.15, 129.62, 130.00, 130.34, 130.85, 131.10, 131.36, 131.73, 132.02, 132.26, 132.65, 134.47, 154.34, 154.46, 154.58; IR (KBr) 2930, 1600, 1500, 1465, 1415, 1235, 1020, 865, 805, 750; M⁺, *m/e*, 798 (13), 797 (50), M⁺ 796 (100), 779 (22), 778 (41), 765 (20), 764 (18), 749 (15), 692 (17), 105 (15). Anal. Calcd for C₅₄H₅₂O₆: C and H.

Methyl Transfers. 8. The Marcus Equation and Transfers between Arsenesulfonates
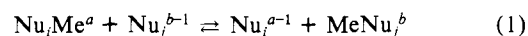
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Abstract: Using a ³⁵S label, rates of identity methyl-transfer reactions XC₆H₄*SO₃⁻ + CH₃O₃SC₆H₄X → XC₆H₄*SO₃CH₃ + XC₆H₄SO₃⁻ in sulfolane have been measured. For all five cases, these identity rates fit the Hammett equation with the rather large ρ of +0.6. Rates and equilibria for XC₆H₅SO₃Me + 3,4-Cl₂C₆H₃SO₃⁻ have been measured. The fit to the Marcus equation using averages of the experimental identity rates for the intrinsic rate is perfect, within experimental error. The absolute values of ρ for the forward and reverse reactions differ by an amount quantitatively consistent with the nonzero identity reaction ρ. The significance of the identity reaction ρ > 0 is discussed.

Introduction

Rates of chemical reactions have been of interest for years, and it has long been recognized that, although thermodynamically unfavorable reactions are often very slow, there is no general correlation of rates with free-energy change. There are numerous examples of thermodynamically highly favorable reactions which are quite slow, such as the decomposition of TNT. After separating from these slow reactions those which mechanistically pass through highly unstable intermediates, many one-step slow reactions remain. A useful concept for such apparently anomalously slow reactions has been the Marcus equation,[1] which expresses

the kinetic barrier as the sum of an intrinsic barrier and the thermodynamic barrier (together with higher order terms). The Marcus equation was initially designed for electron-transfer reactions in solution but later found application to hydrogen-atom transfers,[2] proton transfers,[3] and group transfers, especially methyl-transfer reactions.[4,5] eq 1. A form of the Marcus equation

$$Nu_iMe^a + Nu_j^{b-1} \rightleftharpoons Nu_i^{a-1} + MeNu_j^b \qquad (1)$$

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