

The presence of **18** was confirmed through authentic comparison; those of **12** and **15** are based upon spectral assignment.

Kinetic Study on Tosylate 9. Purified²² acetic acid containing acetic anhydride (1% (v/v)) was the solvent. The reactions were performed on a 0.03-M scale in the presence of sodium acetate (0.04 M). The well-known titrimetric procedure was followed, using crystal violet (0.03% solution in acetic acid) as indicator and standardized *p*-toluenesulfonic acid as the titrant. The kinetic data were processed by computer for the values in Table II.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American

Chemical Society, for support of this research.

Registry No. 1, 70179-05-4; 2, 10469-27-9; 3, 70179-04-3; 4, 70179-03-2; 5, 70179-02-1; 6, 70179-01-0; 7, 70179-00-9; 8, 70178-99-3; 8 acetate, 70178-98-2; 9, 70178-97-1; 12, 70178-96-0; 13 (X = OH), 70178-95-9; 13 (X = OAc), 70178-94-8; 14 (X = OH), 70178-93-7; 14 (X = OAc), 70178-85-7; 15, 53847-13-5; 16 (X = OH), 70178-86-8; 16 (X = OAc), 70178-87-9; 17 (X = OH), 70178-88-0; 17 (X = OAc), 70178-89-1; 18, 38553-10-5; 19, 13694-30-9; *tert*-butyl alcohol, 75-65-0; (*E*)- γ -phenylpiperylene, 70178-90-4; (*Z*)- γ -phenylpiperylene, 64035-02-5; 2-benzalicyclopentanone, 5679-13-0; 2-benzyl-2-cyclopentanone, 22354-39-8; 3-phenyl-1-hexyl acetate, 70178-91-5; 3-benzyl-1-pentyl acetate, 70178-92-6.

Host-Guest Complexation. 19. Cyclic, Bicyclic, and Tricyclic Polyether Systems^{1,2}

Roger C. Helgeson, Thomas L. Tarnowski, and Donald J. Cram*

Department of Chemistry, University of California at Los Angeles, Los Angeles, California 90024

Received January 18, 1979

Eighteen new macrocyclic polyethers are described, many of which are multistranded. The free energies of complexation in CDCl₃ at 25 °C of these hosts with Li⁺, Na⁺, K⁺, Rb⁺, Cs⁺, and NH₄⁺ picrates are reported. In the following line structures, the letters stand for the following units: E is CH₂CH₂; M is CH₂; D is 1,1'-dinaphthyl substituted in the 2,2'-positions by OCH₃, OH, or (OE)_nO bridges and in the 3,3'-positions by M(OE)_nOM or (OE)_nO bridges or CH₃ groups; T is 1,1'-ditetralyl substituted in the 2,2'-positions by (OE)_nO bridges and in the 3,3'-positions by H, M(OE)_nOM, or M(SE)_nSM bridges. The substituents (or bridges) attached to the 2,2'-positions of the units designated as D or T are written on the right, whereas those attached to the 3,3'-positions are written on the left, the exception being when two D or T units are involved. When bridges connect the 2- and 3-positions to one another, the bridges are written on both sides. The hosts containing a single bridge connecting the 3,3'-positions of D are as follows: E(OEOM)₂D(OCH₃)₂, **8**; O(EOEOM)₂D(OCH₃)₂, **9**; E(OEOEOM)₂D(OCH₃)₂, **10**; E(OEOM)₂D(OH)₂, **11**; O(EOEOM)₂D(OH)₂, **12**; E(OEOEOM)₂D(OH)₂, **13**. Hosts containing two bridges connecting the 2- to the 2'- and 3- to the 3'-positions are O(EOEOM)₂D(OEOEO)₂E, **16**, and E(OEOEOM)₂D(OEOEO)₂E, **17**. An example of a host with two bridges connecting two D units through their 2,2'-positions and a bridge connecting the 3,3'-positions of one D unit is O(EOEOM)₂D(OEOEO)₂D, (*S,S*)-**19**. For comparison, host (CH₃)₂D(OEOEO)₂E (**35**), whose bridge connects the 2,2'-positions, was included. The $-\Delta G^{\circ}_{av}$ values (kcal/mol) for each host binding the six ions decreased in the following order: O(EOEOM)₂D(OEOEO)₂E (**8.7**), Nap(OEOEO)₂E (**8.7**), (CH₃)₂D(OEOEO)₂E (**8.5**), E(OEOEO)₂D(OEOEO)₂E (**8.2**), O(EOEO)₂MDM(OEOEO)₂O (**8.2**), BrNap(OEOEO)₂E (**7.9**), E(OEOM)₂D(OCH₃)₂ (**7.8**), O(EOEOM)₂D(OCH₃)₂ (**7.4**), (*R,S*)-T(MOEOM)₂(OEOEO)₂T (**7.1**), E(OEOEOM)₂D(OCH₃)₂ (**6.8**), (*R,R*)(*S,S*)-T(MOEOM)₂(OEOEO)₂T (**6.7**), O(EOEOM)₂D(OH)₂ (**6.6**), E(OEOEOM)₂D(OH)₂ (**6.4**), Br₂Nap(OEOEO)₂E (**5.8**), E(OEOM)₂D(OH)₂ (**5.5**), (*R,R*)(*S,S*)-(CH₃)₂D-(MOM)₂D(OCH₃)₂ (**4.9**), (*R,R*)-T(MSESM)₂(OEOEO)₂T (≥ 4.6). A similar order was followed for maximum selectivity in binding the six ions, as measured by $-\Delta(\Delta G^{\circ})_{max}$ (kcal/mol). The values ranged from a high of 5.3 kcal/mol for O(EOEOM)₂D(OEOEO)₂E to a low of 0.5 kcal/mol for (*R,R*)(*S,S*)-(CH₃)₂D-(MOM)₂D(OCH₃)₂. The four-stranded host with the most enclosed cavity, (*R,R*)(*S,S*)-T(MOEOM)₂(OEOEO)₂T, gave the relatively high $-\Delta(\Delta G^{\circ})_{max}$ of 4.3 kcal/mol for its relatively low $-\Delta G^{\circ}_{av}$ of 6.7 kcal/mol. This host gave the very high $-\Delta G^{\circ}$ difference of 3.7 kcal/mol for K⁺ and Cs⁺. The highly rigid host with seven well-organized oxygen binding sites, O(EOEOM)₂D(OEOEO)₂E, gave the highest $-\Delta G^{\circ}$ value of 11.1 kcal/mol for K⁺. The two hosts with "jaws"-type organization of 10 to 12 oxygen binding sites, E(OEOEO)₂D(OEOEO)₂E and O(EOEO)₂MDM(OEOEO)₂O, gave the highest $-\Delta G^{\circ}$ values (kcal/mol) observed for Cs⁺ of 9.3 and 9.2, respectively. Their complexes with the larger ions probably possess a sandwich-type structure. Hosts containing two D units with bridges connecting the 3- to 3- and 3'- to 3'-positions are (CH₃)₂D-(MOM)₂D(OCH₃)₂, (*S,S*)-**20** and (*R,R*)(*S,S*)-**20**, and (HO)₂D-(MOM)₂D(OH)₂, (*R,R*)(*S,S*)-**22**. Stereoisomeric hosts containing two T units with bridges connecting their 2- to 2- and 2'- to 2'-positions are T(OEOEO)₂T, (*R,S*)-**23** and (*R,R*)(*S,S*)-**23**. Stereoisomeric hosts containing two T units with two (OE)₂O bridges connecting their 2- to 2- and 2'- to 2'-positions and two other kinds of bridges connecting their 3- to 3- and 3'- to 3'-positions are T(MOEOM)₂(OEOEO)₂T, (*R,R*)-**25**, (*R,R*)(*S,S*)-**25**, and (*R,S*)-**25**, and T(MSESM)₂(OEOEO)₂T, (*R,R*)-**26**. Two hosts with bridges connecting the 2- to the 3- and 2'- to 3'-positions of a D unit are E(OEOEO)₂D(OEOEO)₂E, **27**, and O(EOEO)₂MDM(OEOEO)₂O (M's at 3,3'-positions), **34**. Hosts based on 2,3-naphtho-18-crown-6 (**30**), Nap(OEOEO)₂E, with Br in their 1- or 1- and 4-positions are BrNap(OEOEO)₂E, **31**, and Br₂Nap(OEOEO)₂E, **32**.

The literature is rich in descriptions of macrocyclic ligand systems synthesized to complex alkaline metal ions.³

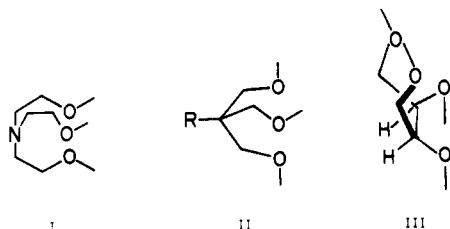
(1) The authors thank the Division of Basic Sciences of the Department of Energy for a contract (AT(04-3)34, P.A. 218), which supported this research.

(2) Two small parts of this paper appeared as parts of previous Communications: (a) K. E. Koenig, R. C. Helgeson, and D. J. Cram, *J. Am. Chem. Soc.*, **98**, 4018-20 (1976); (b) T. L. Tarnowski and D. J. Cram, *J. Chem. Soc., Chem. Commun.*, 661-3 (1976).

The cavities of most of these hosts are defined by a monocycle whose chain is conformationally flexible enough so that the binding sites can be nearly coplanar or their chains can coil in a variety of ways to adapt to the propensities of potential metal ion guests. A relatively small

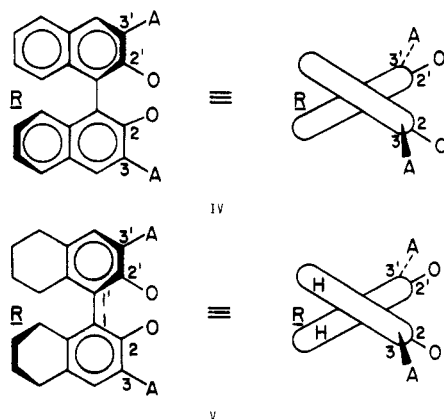
(3) J. S. Bradshaw in "Synthetic Multidentate Macrocyclic Compounds", R. M. Izatt and J. J. Christensen, Eds., Academic Press, New York, 1978, Chapter 2.

number of hosts have been prepared in which a three-dimensional cavity is defined by an integrated polycyclic system or by orientation of two monocyclic systems through their attachment to a rigid orienting unit. Integrated polycyclic systems usually involve bridgeheads to which three strands of the polycyclic system are attached. The cryptands of Lehn⁴ make extensive use of unit I, whose nitrogen serves both as a binding site and as a



bridgehead. The bicyclic polyethers of Stoddart⁵ involve unit II with tetrahedral carbon as a bridgehead. One "clam-shaped" bicyclic polyether system has been reported⁶ that makes use of III as a "hinging" unit.

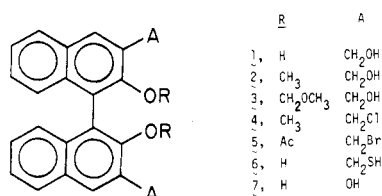
This paper reports the syntheses and binding properties of a number of macrocyclic polyether systems in which a three-dimensional orientation of binding sites is enforced through use of units IV and V. The four semiconvergent,



substitutable 2-, 2', 3-, and 3'-positions of these two rigid units, coupled with their chirality, provide a means of assembling three-dimensional ligand systems whose binding sites line cavities of a variety of shapes and sizes.

Results

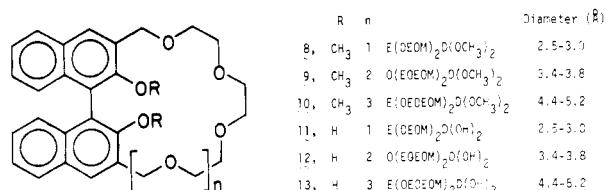
Syntheses. The tetrasubstituted 1,1'-dinaphthyl starting materials 1-7 either were available from earlier



studies^{7,2b} or were synthesized by ordinary procedures (see

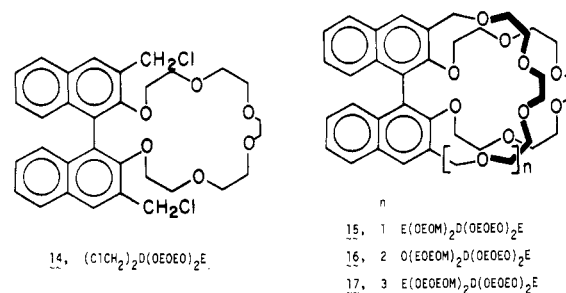
Experimental Section). The dinaphthyl unit imparts chirality to these compounds. The previous preparation⁷ of (*R*)- and (*S*)-1 of known configuration and maximum rotation allowed some of the following syntheses to be directed toward selected diastereomeric ligand systems.

Treatment of (*R*)(*S*)-diol 2 with triethylene, tetraethylene, and pentaethylene glycol ditosylates⁸-NaH-THF gave cycles 8, 9, and 10 in 40, 40, and 20% yields, re-



spectively. Similar ring closures with (*R*)(*S*)-diol 3 gave the corresponding acetals (not isolated) which were cleaved (H₃O⁺Cl⁻) to the diphenols to provide (overall yields) 11 (40%), 12 (30%), and 13 (15%), respectively.

An examination of the Corey-Pauling-Koltun (CPK) molecular model of polycycle 15 indicates it could be



assembled with least strain by threading the bridge reaching from the 3,3'-positions through the hole of the cycle formed by attachment of the 1,1'-dinaphthyl unit at the 2,2'-positions. In models, macrocycles 16 and 17 could be most easily constructed with the more central ring unthreaded. Dichloride (*R*)(*S*)-14⁷ when treated with triethylene glycol-NaH-THF failed to give monomeric material in detectable amounts. However, with tetraethylene glycol⁸-NaH-THF, and pentaethylene glycol⁸-NaH-THF, (*R*)(*S*)-14 gave 16 (40%) and 17 (44%), respectively. An X-ray structure of 16 revealed it did not possess the threaded structures,⁹ and it is reasonable to think that 17 does not either. The threaded structures in models are somewhat hindered and provide only divergent locations of oxygen electron pairs unfavorable for cooperatively binding ions.

Dichloride (*S,S*)-18 was prepared from its corresponding (*S,S*)-diol¹⁰ by treatment with SOCl₂. When (*S,S*)-18 was mixed with tetraethylene glycol⁸ and added to THF-NaH, polycycle (*S,S*)-19 was produced (30%). The compound's complexing properties toward alkylammonium ions clearly demonstrated (see Discussion) that the substance does not possess the threaded structure.

Addition of an equimolar mixture of dichloride (*S*)-4⁷ and diol (*S*)-2⁷ to NaH-THF at high dilution gave (*S,S*)-20

(4) J. M. Lehn, *Struct. Bonding (Berlin)*, **16**, 1-69 (1973).

(5) A. C. Coxon and J. F. Stoddart, *J. Chem. Soc., Chem. Commun.*, 537 (1974).

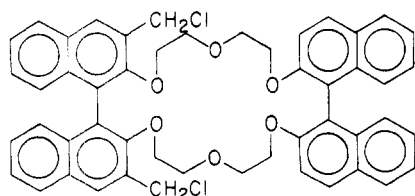
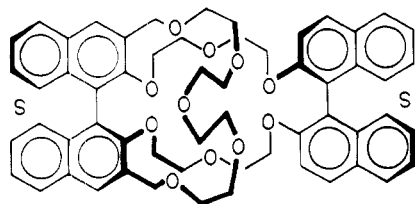
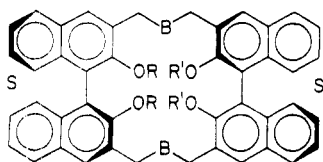
(6) R. C. Helgeson, G. R. Weisman, J. R. Toner, T. L. Tarnowski, Y. Chao, J. M. Mayer, and D. J. Cram, *J. Am. Chem. Soc.*, in press.

(7) (a) D. J. Cram, R. C. Helgeson, K. Koga, E. P. Kyba, K. Madan, L. R. Sousa, M. G. Siegel, P. Moreau, G. W. Gokel, J. M. Timko, and G. D. Y. Sogah, *J. Org. Chem.*, **43**, 2758-72 (1978); (b) R. Helgeson and G. D. Y. Sogah, unpublished results.

(8) M. Newcomb, S. S. Moore, and D. J. Cram, *J. Am. Chem. Soc.*, **99**, 6405-10 (1977).

(9) We warmly thank Dr. K. N. Trueblood and Dr. C. Knobler for information about these X-ray structure determinations in advance of publication.

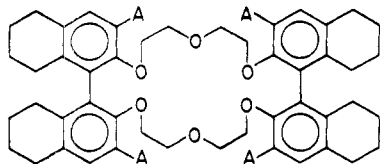
(10) D. J. Cram, R. C. Helgeson, S. C. Peacock, L. J. Kaplan, L. A. Domeier, P. Moreau, K. Koga, J. M. Mayer, Y. Chao, M. G. Siegel, D. H. Hoffman, and G. D. Y. Sogah, *J. Org. Chem.*, **43**, 1930-46 (1978).

(SS)-18, $(\text{ClCH}_2)_2\text{D}(\text{OEEOE})_2\text{D}$ (SS)-19, $\text{D}(\text{EOEOM})_2\text{D}(\text{OEEOE})_2\text{D}$ 

(SS)-20, $\text{R} = \text{O}$, $\text{P} = \text{O}$, $\text{Q} = \text{CH}_3$ or, $(\text{CH}_3\text{O})_2\text{D}(\text{MOM})_2\text{D}(\text{OCH}_3)_2$
 (RR)(SS)-21, $\text{B} = \text{S}$, $\text{P} = \text{Ac}$, $\text{R} = \text{H}$
 (RR)(SS)-22, $\text{B} = \text{S}$, $\text{R} = \text{H}$ or, $(\text{HO})_2\text{D}(\text{MOM})_2\text{D}(\text{OH})_2$

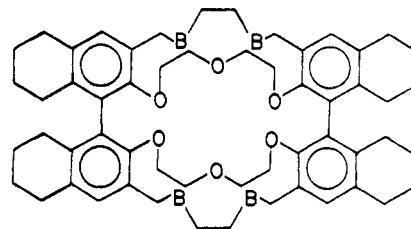
(20%). Similarly, (*R*)(*S*)-4 and (*R*)(*S*)-2 gave (*R,R*)(*S,S*)-20 (11%), whose configurational identity was established by ^1H NMR comparison with (*S,S*)-20. The meso isomer (*R,S*)-20 was not detected among the reaction products. Molecular model comparisons of (*S,S*)-20 and (*R,S*)-20 indicate the latter to be considerably more hindered than the former. In a somewhat analogous reaction, dibromide (*R*)(*S*)-5 and dithiol (*R*)(*S*)-6, when mixed in acetone in the presence of diisopropylethylamine, gave what is probably the (*R,R*)(*S,S*) diastereomer of 21 (42%), which on hydrolysis gave (*R,R*)(*S,S*)-22 (91%). The absence of isomeric product from the ring-closing reaction and the analogy of this to the synthesis of its oxygen analogue (*R,R*)(*S,S*)-21 are the bases of our tentative configurational assignments to 21 and 22.

Chloromethylation of macrocyclic polyethers containing the 2,2'-disubstituted 1,1'-dinaphthyl unit led to substitution in the 6-position of each naphthalene nucleus.⁷ To bridge two biaryl units with four polyether strands, substitution in only the 3,3'-positions was required. Catalytic reduction of 1,1'-dinaphthyl-containing hosts had been demonstrated previously to lead to 1,1'-ditetralyl-containing compounds in which only the outer rings were reduced. The chiral 2,2'-disubstituted 1,1'-ditetralyl unit had also been demonstrated to be thermally stable to configurational changes.¹⁰ Accordingly, (*R,R*)(*S,S*)-23 and (*R,S*)-23 were prepared (~98% yields) by catalytic re-



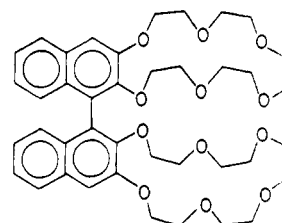
(RS) and (RR)(SS)-23, $\text{A} = \text{H}$ or, $\text{T}(\text{OEEOE})_2\text{T}$
 (RR)(RS) and (RR)(SS)-24, $\text{A} = \text{CH}_2\text{Cl}$ or, $(\text{ClCH}_2)_2\text{T}(\text{OEEOE})_2\text{T}(\text{CH}_2\text{Cl})_2$

duction of their corresponding dinaphthyl precursors¹¹ with hydrogen and platinum in glacial acetic acid. Optically pure (*R,R*)-23 had been prepared previously. These three compounds were chloromethylated in the 3-positions of all four benzene rings with paraformaldehyde-hydrochloric acid to give in 94–97% yields (crude) the corresponding three stereoisomeric tetrachloromethylated compounds (*R,R*)-24, (*R,S*)-24, and (*R,R*)(*S,S*)-24. These isomers without full characterization were mixed with ethylene glycol and added to NaH-THF to give the corresponding four-stranded hosts (*R,R*)-25 (38%), (*R,S*)-25 (79%), and (*R,R*)(*S,S*)-25 (43%). Similarly, (*R,R*)-24, 1,2-ethanedithiol, and NaH gave (*R,R*)-26 (20%).

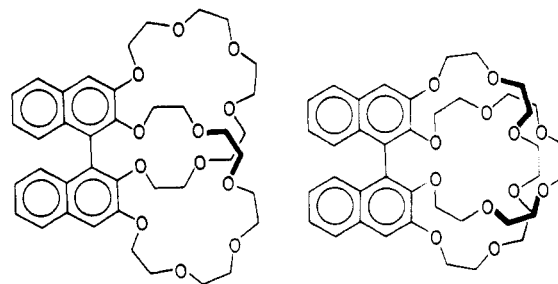


(RR)-, (RS)- and (RR)(SS)-25, $\text{B} = \text{O}$ or, $\text{T}(\text{MOEOM})_2(\text{OEEOE})_2\text{T}$
 (RR)-26, $\text{B} = \text{S}$ or, $\text{T}(\text{MESM})_2(\text{OEEOE})_2\text{T}$

The synthesis of 27 was accomplished in 30% yield by

27, $\text{E}(\text{OEEOE})_2\text{D}(\text{OEEOE})_2\text{E}$

mixing (*R*)(*S*)-7 with pentaethylene glycol ditosylate⁸-KOH-THF. The interesting isomeric structures 28 and 29 were also potential products from these starting ma-



28

29

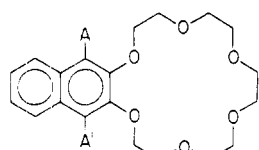
terials. In 28, each macroring involves both naphthalene rings, whereas in 29, one ring is threaded through the other.

Any question as to the structure of what was isolated from the above reaction of tetrol 7 was dismissed by a second and unambiguous synthesis of 27. Bromination of 30¹³ gave dibromo compound 31 (6%) and monobromo compound 32 (65%). The latter substance was trans-

(11) E. P. Kyba, W. G. Gokel, F. de Jong, K. Koga, L. R. Sousa, M. G. Siegel, L. Kaplan, G. D. Y. Sogah, and D. J. Cram, *J. Org. Chem.*, **42**, 4173–84 (1977).

(12) H. Wanzlick, M. Lehman-Horchler, and S. Mohrman, *Chem. Ber.*, **90**, 2521–6 (1957).

(13) E. P. Kyba, R. C. Helgeson, K. Madan, G. W. Gokel, T. L. Tarnowski, S. S. Moore, and D. J. Cram, *J. Am. Chem. Soc.*, **99**, 2564–71 (1977).



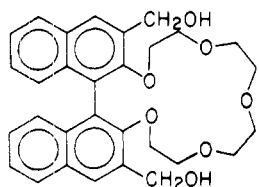
30. A = A' = H or, Nap(OEEOE)₂E

31. A = -, A' = Br or, BrNap(OEEOE)₂E

32. A = A' = Br or, S₂Nap(OEEOE)₂E

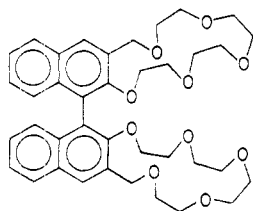
formed into its Grignard reagent, which underwent oxidative coupling when treated with CoCl₂¹⁴ to give **27** (3%) and **30** (18%). The samples of **27** prepared by the two methods exhibited identical properties.

The reaction of tetrol **1** with 1 mol of tetraethylene glycol ditosylate⁸ and 2 mol of NaOH in THF-H₂O was reported previously to give macrocyclic ether **33** in about 10% yield.⁷



33

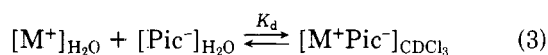
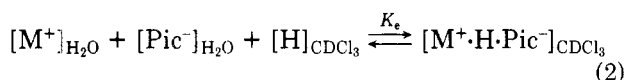
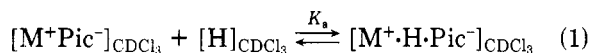
In the present study, we found that when tetrol **1** was treated with 2 mol of the same ditosylate and 4 mol of NaOH in the same solvent, the only product isolated was the bis-macrocyclic ether **34** (23%). The constitution of



34. (OEEOE)₂MDM(OEEOE)₂O

34 was established by X-ray crystal structure determination.⁹ Apparently compounds analogous to **28** and **29** if formed at all in this reaction were produced in only very low yields.

Free Energies of Association between Ligand Systems and Metal and Ammonium Picrates. Association constants, K_a , were determined as before^{6,15} for the binding of metal and ammonium picrates in CDCl₃ at 24–26 °C by the macrocyclic ethers. The extraction technique was used in which Li⁺, Na⁺, K⁺, Rb⁺, Cs⁺, and NH₄⁺ picrates in water were equilibrated with CDCl₃ in both the presence and absence of host (H). The extraction constants (K_e) and distribution constants (K_d) were determined from absorbances at 380 nm in the UV spectra of the CDCl₃ layers at equilibrium. Equations 1–3 define



(14) M. S. Kharasch and E. K. Fields, *J. Am. Chem. Soc.*, **63**, 2316–20 (1941).

(15) (a) K. E. Koenig, G. M. Lein, P. Stückler, T. Kaneda, and D. J. Cram, *J. Am. Chem. Soc.*, in press; (b) L. J. Kaplan, G. R. Weisman, and D. J. Cram, *J. Org. Chem.*, in press.

these constants. Values of K_a were calculated from those of K_e and K_d and eq 4. Free energy values ($-\Delta G^\circ$) were

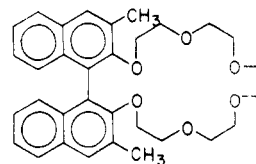
$$K_a = K_e/K_d \quad (4)$$

calculated from K_a values and eq 5. Table I records values

$$\Delta G^\circ = -RT \ln K_a \quad (5)$$

for K_a , for $-\Delta G^\circ$, and for R , which is the molar ratio of picrate ion to host in the organic layer at equilibrium. The values for the parameters are reported to more figures than are significant until $-\Delta G^\circ$'s are compared. The $-\Delta G^\circ$ values are significant to about ± 0.1 kcal/mol when R values are 0.6 or lower and to about ± 0.3 kcal/mol when R values are 0.6 or higher.

The general binding ability of each host for the six ions is measured by the parameter $-\Delta G^\circ_{av}$, whose values are also included in Table I. Also reported are the $-\Delta(\Delta G^\circ)_{max}$ values, which equal the difference between $-\Delta G^\circ$ for the most strongly bound minus $-\Delta G^\circ$ for the least strongly bound of these six salts. This parameter provides a general indication of the ability of each host to differentiate between the six ions. In a few cases, the Rb⁺ picrate complexes precipitated, and the $-\Delta G^\circ_{av}$ and $-\Delta(\Delta G^\circ)_{max}$ values were calculated based on the remaining five salts. The data given for macrocycle **35**⁶ are included for comparison purposes.¹⁶



35. (CH₃)₂O(OEEOE)₂E

Discussion

Many of the macrocycles reported here were synthesized and tested because of their unusual shapes and symmetry properties. Because the 1,1'-dinaphthyl and 1,1'-ditetralyl units are chiral and nearly rigid, attachment of oxygens at their 2,2'- and 3,3'-positions or CH₂O groups at the 3,3'-positions imposes interesting constraints on the positions of the binding sites relative to one another in the macrocycles. Hosts that are diastereomeric possess quite different arrangements of their oxygens.

Since systematic names of the compounds are useless in discussion and repetition of structural formulas is space consuming, the structures are symbolized by letters that stand for structural units strung together to form cycles. The symbols adopted are as follows: D, 1,1'-dinaphthyl, and T, 1,1'-ditetralyl substituted in the 2,2'-positions by O and sometimes in the 3,3'-positions by O or CH₂ (symbolized by M); E, CH₂CH₂; Nap, naphthalene substituted in the 2,3-positions by O and sometimes in the 1- or 1,4-positions by Br; S, sulfur.

Shapes of the Macrocyclic Hosts. The binding abilities of the hosts are dictated by the shapes and sizes of their cavities. Compounds **8–13**, which contain one dinaphthyl unit, possess six to eight oxygens. The two hydroxy or methoxy oxygens have enforced conformations which push one or both of them out of the best plane of the other macroring oxygens. By inserting graded spheres of known diameter (ball bearings) into their cavities, we estimated the approximate range of their cavity diameters with the oxygens turned inward and without folding the macroring. These estimates are listed beneath their

(16) We warmly thank Dr. J. R. Toner for determining the binding parameters for host (R,R)(S,S)-**20**.

Table I. Equilibrium and Free Energy Parameters for Association between Hosts and Metal or Ammonium Picrates in CDCl₃ at 24-26 °C

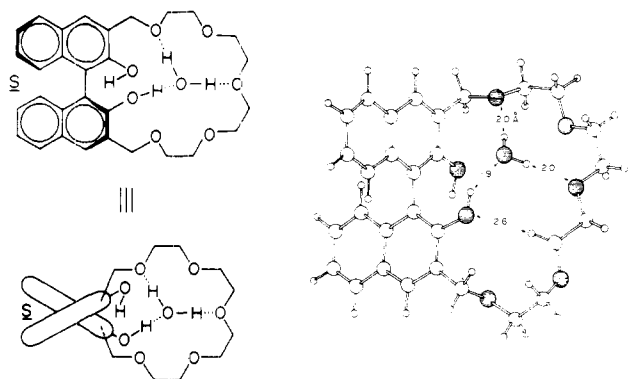
ligand system		M ⁺ of picrate	R _{CDCl₃} ^b	K _a × 10 ⁻³ M ⁻¹ ^c	-ΔG ^o , kcal/ mol	-ΔG ^o _{av} , ^d kcal/mol	-Δ(ΔG ^o) _{max} , ^e kcal/mol
structure ^a	no.						
E(OEOM) ₂ D(OCH ₃) ₂	8	Li	0.0051	16	5.74	7.8	2.6
		Na	0.23	1 200	8.30		
		K	0.42	3 700	8.97		
		Cs	0.172	560	7.85		
		NH ₄	0.276	800	8.06		
O(OEOEM) ₂ D(OCH ₃) ₂	9	Li	0.0059	19	5.84	7.4	2.6
		Na	0.016	43	6.33		
		K	0.24	950	8.16		
		Rb	0.26	1 400	8.39		
		Cs	0.23	950	8.16		
		NH ₄	0.21	480	7.76		
E(OEOEOM) ₂ D(OCH ₃) ₂	10	Li	0.0041	13	5.62	6.8	2.0
		Na	0.013	33	6.17		
		K	0.096	230	7.32		
		Rb	0.093	270	7.42		
		Cs	0.13	360	7.59		
		NH ₄	0.080	110	6.88		
E(OEOM) ₂ D(OH) ₂	11	Li	0.00071	2.2	4.56	5.5	1.7
		Na	0.0031	7.9	5.32		
		K	0.022	40	6.28		
		Cs	0.013	25	6.01		
		NH ₄	0.0052	5.85	5.14		
O(OEOEM) ₂ D(OH) ₂	12	Li	0.00225	7.1	5.26	6.6	2.2
		Na	0.0059	15	5.70		
		K	0.099	240	7.35		
		Rb	0.095	310	7.50		
		Cs	0.083	200	7.24		
		NH ₄	0.054	71	6.62		
E(OEOEOM) ₂ D(OH) ₂	13	Li	0.0016	4.9	5.04	6.4	2.3
		Na	0.012	31	6.13		
		K	0.052	105	6.86		
		Rb	0.046	120	6.94		
		Cs	0.091	220	7.29		
		NH ₄	0.041	51	6.43		
O(OEOEM) ₂ D(OEOEO) ₂ E	16	Li	0.0056	18	5.81	8.7	5.3
		Na	0.33	2 900	8.82		
		K	0.78	130 000	11.1		
		Rb	0.51	9 200	9.51		
		Cs	0.17	530	7.82		
		NH ₄	0.57	7 900	9.42		
(CH ₃) ₂ D(OEOEO) ₂ E	35	Li	0.0078	22.8	5.95	8.5	4.5
		Na	0.273	1 730	8.52		
		K	0.718	42 800	10.4		
		Rb	0.437	4 700	9.10		
		Cs	0.181	576	7.87		
		NH ₄	0.464	3 260	8.89		
(R,R)(S,S)-(CH ₃ O) ₂ D(MOM) ₂ - D(OCH ₃) ₂	(R,R)(S,S)-20	Li	0.00168	5.28	5.08	4.9	0.5
		Na	0.00158	4.05	4.93		
		K	0.00286	5.03	5.05		
		Rb	0.00256	5.64	5.12		
		Cs	0.00168	3.12	4.77		
		NH ₄	0.00235	2.62	4.66		
(R,R)-T(OEOEO) ₂ T	(R,R)-23	K	0.010	18	5.81		
		NH ₄	0.011	12	5.57		
(R,R)(S,S)-T(MOEOM) ₂ (OEOEO) ₂ T	(R,R)(S,S)-25	Li	0.0010	3.1	4.77	6.7	4.3
		Na	0.0019	51	6.43		
		K	0.56	4 200	9.04		
		Rb	0.135	390	7.63		
		Cs	0.0046	8.5	5.37		
		NH ₄	0.0765	99	6.82		
(R,S)-T(MOEOM) ₂ (OEOEO) ₂ T	(R,S)-25	Li	0.0064	20	5.87	7.1	2.5
		Na	0.0046	130	6.98		
		K	0.34	1 300	8.35		
		Rb	0.135	390	7.63		
		Cs	0.042	84	6.72		
		NH ₄	0.077	100	6.83		
(R,R)-T(MSESM) ₂ (OEOEO) ₂ T	(R,R)-26	Li	0.0018	5.7	5.13	>4.6	>2.8
		Na	0.0063	16.5	5.76		

Table I (Continued)

ligand system		M ⁺ of			-ΔG ^o ,		
structure ^a	no.	picrate	R _{CDCl₃} ^b	K _a × 10 ⁻³ M ^{-1 c}	kcal/ mol	-ΔG ^o _{av, d} kcal/mol	-Δ(ΔG ^o) _{max, e} kcal/mol
E(OEOEO) ₂ D(OEOEO) ₂ E	27	K	0.0099	18	5.81		
		Rb	0.00066	1.4	4.30		
		Cs	0.0000		< 3.00		
		NH ₄	0.00064	0.71	3.89		
		Li	0.0045	14	5.66	8.2	4.4
		Na	0.152	540	7.83		
		K	0.83	24 000	10.1		
O(OEOEO) ₂ MOM(OEOEO) ₂ O	34	Cs	0.66	6 400	9.29		
		NH ₄	0.42	1 300	8.35		
		Li	0.0067	21	5.90	8.2	4.1
		Na	0.081	240	7.35		
		K	0.82	22 000	10.0		
		Cs	0.59	5 200	9.17		
Nap(OEOEO) ₂ E	30	NH ₄	0.555	2 600	8.76		
		Li	0.00704	22.5	5.94	8.7	4.8
		Na	0.226	1 220	8.31		
		K	0.740	85 900	10.8		
		Rb	0.524	11 300	9.63		
		Cs	0.262	1 250	8.33		
		NH ₄	0.575	9 850	9.55		
BrNap(OEOEO) ₂ E	31	Li	0.0094	30	6.11	7.9	2.9
		Na	0.18	865	8.11		
		K	0.435	4 200	9.04		
		Rb	0.23	1 100	8.25		
		Cs	0.235	970	8.17		
		NH ₄	0.153	280	7.44		
Br ₂ Nap(OEOEO) ₂ E	32	Li	0.00076	2.4	4.62	5.8	2.0
		Na	0.0072	19	5.84		
		K	0.037	72	6.63		
		Rb	0.013	29	6.09		
		Cs	0.0072	14	5.66		
		NH ₄	0.0077	14	5.66		

^a In these structures, the letters stand for the following units: E is CH₂CH₂; M is CH₂; D is 1,1'-dinaphthyl substituted in the 2,2'-positions by OCH₃, OH, or (OE)_nO bridges and in the 3,3'-positions by M(OE)_nOM or (OE)_nO bridges or CH₃ groups; T is 1,1'-ditetralyl substituted in the 2,2'-positions by (OE)_nO bridges and in the 3,3'-positions by H, M(OE)_nOM, or M(SE)_nSM bridges. ^b Ratio of picrate to host in CDCl₃ phase at equilibrium obtained by direct measurement, except for hosts 30 and 35 with ions other than Li⁺, where *R* was calculated by difference from measurements made on the aqueous phase. ^c The method for determining *K*_a values has been described in ref 6 and 15. ^d Average -Δ*G*^o values for each host binding the five or six ions. ^e The -Δ(Δ*G*^o)_{max} value for each host equals the highest -Δ*G*^o value minus the lowest -Δ*G*^o value.

formulas. The general shape of E(OEOM)₂D(OH)₂ (11) with 1 mol of water as guest is indicated by its X-ray structure, 36.¹⁷ Although the structure formulated



36

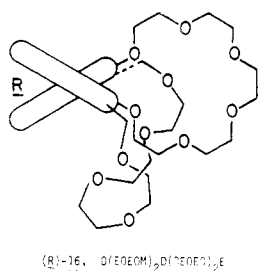
possesses the (*S*) configuration, the X-ray structure involved racemic material. This structure explains why it was so difficult to expel the water from the cavity (see Experimental Section) and shows how neatly the cavity

is filled by the triply hydrogen bonded water and by one inward-turning methylene group.

Although CPK models of E(OEOM)₂D(OEOEO)₂E (15) can be constructed, no accessible conformation produces a cavity. The shortness of the extra bridge extending from the 3,3'-positions of the dinaphthyl unit forces the 20-membered ring that involves the 2,2'-positions to collapse into its own cavity. The inability of the ether oxygens to act cooperatively in closing the final ring explains our inability to obtain the compound. The next higher analogue, O(OEOEO)₂D(OEOEO)₂E (16), in models can form a compact cavity embraced by the 20-membered ring system of the bridge attached to the dinaphthyl unit at the 2,2'-positions. In that conformation with the most oxygen lone pairs convergent on the cavity, the naphthyl-naphthyl dihedral angle is minimal. With the six oxygens of the 20-membered ring nearly coplanar, the cavity has a "floor" composed of one benzyl oxygen of the other bridge. The cavity diameter is relatively invariant at about 2.6 Å, since the naphthyl-naphthyl hinge is frozen in place by the shortness of the second bridge.

In the X-ray structure of uncomplexed 16, the electron pairs of the potentially convergent benzyl oxygen are divergent, as are those of two oxygens of the 20-membered ring that provides the potential cavity. The cavities of uncomplexed crown compounds are similarly filled with CH₂ groups when uncomplexed.¹⁸ The naphthyl-naphthyl

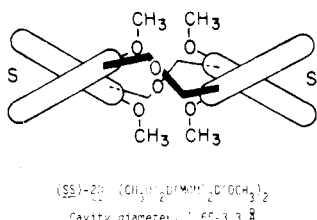
(17) We warmly thank Dr. Israel Goldberg for information regarding these structures in advance of publication.



dihedral bond angle is 80° , and this bond does not quite lie in the plane of each naphthalene ring. Thus the system is somewhat strained by the two bridges. In molecular models the next higher analogue, 17, is much more flexible and less crowded and was formed in a comparable yield during ring closure.

The addition of the extra bridge extending from the 3,3'-positions of the dinaphthyl unit formed a new 21-membered ring when dichlorides 14 and 18 were converted to 16 and 19, respectively. In these conversions, the C_2 axes of 14 and 18 were destroyed, and "nonsided" starting materials became "sided" products. In 16 and 19, guest ions can enter and leave the cavity of the central ring from only one side, since the opposite side is blocked by the strand of the second bridge passing across its face. The C_2 axis of dichlorides 14 and 18 was a useful structural feature in the syntheses of 16 and 19, since the same stereoisomers were produced irrespective of which end of the new bridge converged and which end diverged from the central cavity. Thus stereoisomeric mixtures were avoided in turning nonsided into sided hosts.¹⁹

In molecular models, the shape of $(\text{CH}_3\text{O})_2\text{D}(\text{MOM})_2\text{D}(\text{OCH}_3)_2$ ((S,S)-20) depends on the naphtha-



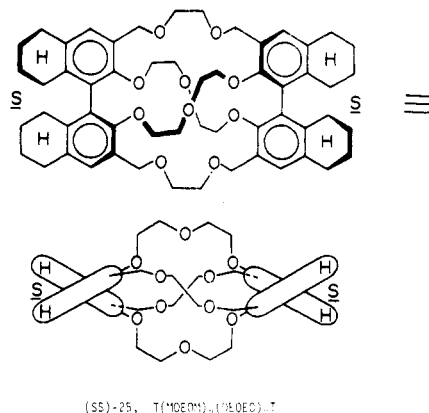
lene-naphthalene dihedral angles. With the dihedral angle as high as 90° , one of the four methyl groups can orient inward and occupy the cavity. With all four methyl groups oriented away from the center of the cavity, the four oxygens of the CH_3O groups are nearly tetrahedrally arranged, thus forming a cavity of about 1.65-Å diameter when the aryl-aryl dihedral angles are minimal. When the aryl-aryl dihedral angles are maximal, the six oxygens are nearly octahedrally arranged around a cavity of about 3.3 Å.

The sulfur-containing macrocycle $(\text{HO})_2\text{D}(\text{MSM})_2\text{D}(\text{OH})_2$ ((R,R)(S,S)-22) in molecular models resembles $(\text{CH}_3\text{O})_2\text{D}(\text{MOM})_2\text{D}(\text{OCH}_3)_2$ in general shape. However, the four convergent hydroxyl groups of $(\text{HO})_2\text{D}(\text{MSM})_2\text{D}(\text{OH})_2$ undoubtedly hydrogen bond one another, and these hydrogen bonds would have to be broken before a cavity could form. This effect is probably responsible for our inability to measure the free energy of binding of metal ions by this potential host.

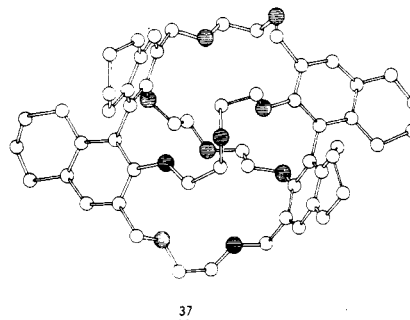
(18) (a) J. D. Dunitz, M. Dobler, P. Seiler, and R. P. Phizackerly, *Acta Crystallogr., Sect. B*, 30, 2733–8 (1974), and immediately preceding papers; (b) M. R. Truter, *Struct. Bonding (Berlin)*, 16, 71–111 (1973).

(19) Compound (S,S)-19 unfortunately was not examined as a host for metal ions but was examined for its ability to complex differentially the enantiomers of phenylglycine and of methionine. Differential complexation was observed (S. C. Peacock and D. J. Cram) and will be reported in another paper.

The geometries of the diastereomers of $T(\text{MOEOM})_2(\text{OEEOE})_2\text{T}$, (S,S)-25 and (R,S)-25, are particularly in-

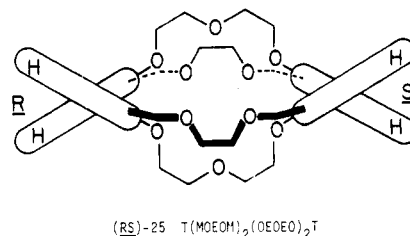


teresting, since four bridges connect two rigid 1,1'-ditetralyl units²⁰ to form a cage potentially lined with electron pairs of ten oxygens. The molecular shapes in models of the two diastereomers differ markedly from one another. Isomer (S,S)-25 possesses D_2 symmetry, and with all unshared electron pairs in convergent positions, two "eight-oxygen" cavities are produced, six of whose oxygens are common to each cavity. Insertion of graded spheres into the two cavities indicates that two spheres of about 2.6-Å diameter can be accommodated at the same time with seven oxygen contacts each, or one sphere of 3.4 Å can be surrounded by three strands and eight oxygen contacts. The X-ray structure of uncomplexed (S,S)-25 was determined,¹⁷ and structure 37 shows one view of the compound. As in other



uncomplexed crystalline hosts,¹⁸ the cavities are filled with inward-turning methylene groups. Attempts to form crystalline complex salts of this compound have thus far failed.

Isomer (R,S)-25 possesses a plane of symmetry. Mo-

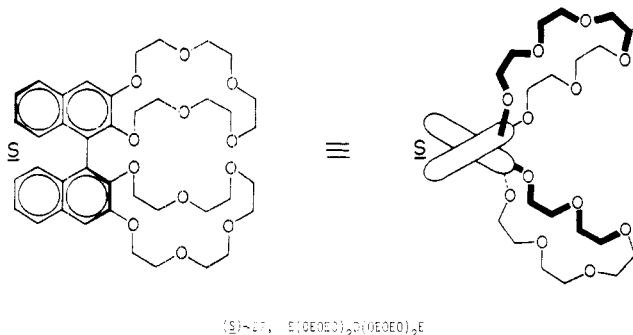


lecular models of the substance indicate that a maximum of only six oxygens can act cooperatively in binding a single ion that is fully inserted into the hole of the central ring ($\text{D}(\text{OEEOE})_2\text{D}$). The diameter of the cavity formed by this ring was from about 2.5 to 3.3 Å, depending on the

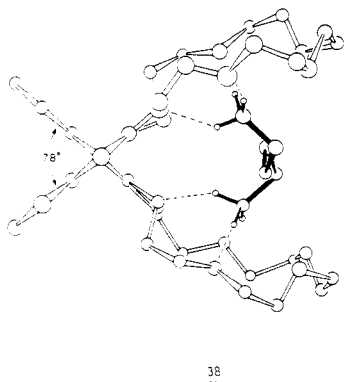
(20) The geometry of $T(\text{OEEOE})_2\text{T}$ (23) was discussed in ref 10. Although the X-ray structure was actually determined on (R,R)-25, the formulas of the models drawn are those of (S,S)-25, since the machine drawing 36 was made of (S,S)-25.

aryl-aryl dihedral angles which act as hinges. With the spheres of the greatest diameter (e.g., that of Cs^+) and the central hole contracting to 2.5 Å, the ion "perches" on the six central oxygens and contacts the two oxygens of one MOEOM bridge in models of potential complexes.

The shape in a molecular model of the sulfur-containing macrocycle $\text{T}(\text{MSESM})_2(\text{OEOEO})_2\text{T}$ (*R,R*-26) resembles that of (*R,R*)-25. Molecular models of the bis-macrocycle $\text{E}(\text{OEOEO})_2\text{D}(\text{OEOEO})_2\text{E}$ (27) reveal that the substance

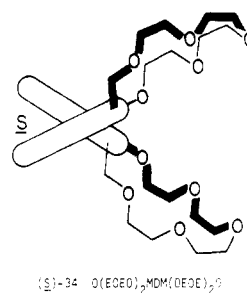


possesses a "jaws"-like shape, in which the dinaphthyl unit serves as the hinge. With the oxygens turned inward, the two cavities each possess the same diameter as that of $\text{Nap}(\text{OEOEO})_2\text{E}$ (30), namely, about 2.5–2.7 Å. The two "jaws" of the host in models can close on one another enough so the two macrocycles can "sandwich" a metal ion only with sphere diameters of about 3.0–3.3 Å. In models of such complexes, only 10 or 11 out of the total of 12 possible oxygens can concurrently contact the guest ion. Although X-ray structures of neither 27 nor any metal salt complex have been determined, the X-ray structure of the complex of 27 with $\text{F}_6\text{P}^+\text{H}_3\text{N}(\text{CH}_2)_4\text{NH}_3^+\text{PF}_6^-$ turned out to be as expected (see 38).²⁰



Host $\text{O}(\text{EOEO})_2\text{MDM}(\text{OEOE})_2\text{O}$ (34) also possesses a "jaws"-like structure with 10 potentially binding oxygens. The two macrorings are 16-membered and in molecular models possess cavity diameters of about 1.9 Å. Spheres of diameters of 2.7–3.5 Å can contact all 10 oxygens of 34 when sandwiched between the two macrorings. The two methylene groups attached to the 3,3'-positions of the 1,1'-dinaphthyl unit of 34 act as spacers that bring the 10 oxygens closer together than is possible for all 12 oxygens of 27. The X-ray structure of uncomplexed 34 indicates the substance possesses the general "jaws" configuration, the aryl-aryl dihedral angle being 75°. The structure of (*S*)-34 illustrated here is a cross-section of the molecular model viewed along the axis of the Ar-Ar bond. The X-ray structure of the KCNO complex of 34 possesses the expected sandwich structure with ten oxygen to K^+ contacts.⁹

Relationships between Binding Properties and Structure. The $-\Delta G_{\text{av}}^\circ$ parameter of Table I measures the general abilities of the hosts to bind Li^+ , Na^+ , K^+ , Rb^+ ,



Cs^+ , and NH_4^+ ions in CDCl_3 at 25 °C. The $-\Delta(\Delta G^\circ)_{\text{max}}$ values roughly measure the hosts' capacity to differentiate between the ions in complexation. In many of the following comparisons, $\text{Nap}(\text{OEOEO})_2\text{E}$ (30) will serve a standard crown compound and $(\text{CH}_3)_2\text{D}(\text{OEOEO})_2\text{E}$ (35) as a standard macrocyclic ether containing a 3,3'-dinaphthyl-2,2'-disubstituted-1,1'-dinaphthyl unit. A context for the following discussion is provided by their decreasing order: $\text{O}(\text{EOEOM})_2\text{D}(\text{OEOEO})_2\text{E}$ (8.7), $\text{Nap}(\text{OEOEO})_2\text{E}$ (8.7), $(\text{CH}_3)_2\text{D}(\text{OEOEO})_2\text{E}$ (8.5), $\text{E}(\text{OEOEO})_2\text{D}(\text{OEOEO})_2\text{E}$ (8.2), $\text{O}(\text{EOEO})_2\text{MDM}(\text{OEOE})_2\text{O}$ (8.2), $\text{BrNap}(\text{OEOEO})_2\text{E}$ (7.9), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ (7.8), $\text{O}(\text{EOEOM})_2\text{D}(\text{OCH}_3)_2$ (7.4), (*R,S*)- $\text{T}(\text{MOEOM})_2(\text{OEOEO})_2\text{T}$ (7.1), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ (6.8), (*R,R*)(*S,S*)- $\text{T}(\text{MOEOM})_2(\text{OEOEO})_2\text{T}$ (6.7), $\text{O}(\text{EOEOM})_2\text{D}(\text{OH})_2$ (6.6), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$ (6.4), $\text{Br}_2\text{Nap}(\text{OEOEO})_2\text{E}$ (5.8), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$ (5.5), (*R,R*)(*S,S*)- $(\text{CH}_3\text{O})_2\text{D}(\text{MOM})_2\text{D}(\text{OCH}_3)_2$ (4.9), (*R,R*)- $\text{T}(\text{MSESM})_2(\text{OEOEO})_2\text{T}$ (≥ 4.6). The $-\Delta(\Delta G^\circ)_{\text{max}}$ values (kcal/mol) for each host decreased in a slightly different order: $\text{O}(\text{EOEOM})_2\text{D}(\text{OEOEO})_2\text{E}$ (5.3), $\text{Nap}(\text{OEOEO})_2\text{E}$ (4.8), $(\text{CH}_3)_2\text{D}(\text{OEOEO})_2\text{E}$ (4.5), $\text{E}(\text{OEOEO})_2\text{D}(\text{OEOEO})_2\text{E}$ (4.4), (*R,R*)(*S,S*)- $\text{T}(\text{MOEOM})_2(\text{OEOEO})_2\text{T}$ (4.3), $\text{O}(\text{EOEO})_2\text{MDM}(\text{OEOE})_2\text{O}$ (4.1), $\text{BrNap}(\text{OEOEO})_2\text{E}$ (2.9), (*R,R*)- $\text{T}(\text{MSESM})_2(\text{OEOEO})_2\text{T}$ (≥ 2.8), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ (2.6), $\text{O}(\text{EOEOM})_2\text{D}(\text{OCH}_3)_2$ (2.6), (*R,S*)- $\text{T}(\text{MOEOM})_2(\text{OEOEO})_2\text{T}$ (2.5), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$ (2.3), $\text{O}(\text{EOEOM})_2\text{D}(\text{OH})_2$ (2.2), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ (2.0), $\text{Br}_2\text{Nap}(\text{OEOEO})_2\text{E}$ (2.0), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$ (1.7), (*R,R*)(*S,S*)- $(\text{CH}_3\text{O})_2\text{D}(\text{MOM})_2\text{D}(\text{OCH}_3)_2$ (0.5).

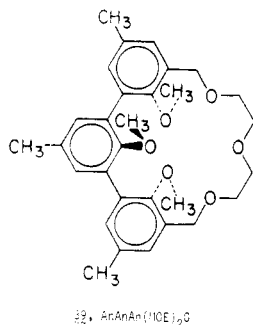
Hosts 8–13 all contain the 1,1'-dinaphthyl unit substituted in the 2,2'-positions with OCH_3 or OH in the 3,3'-positions with bridges composed of $\text{M}(\text{OE})_n\text{OM}$ units. These six hosts and the two standards provide the following decreasing order of $-\Delta G_{\text{av}}^\circ$ values (kcal/mol): $\text{Nap}(\text{OEOEO})_2\text{E}$ (8.7), $(\text{CH}_3)_2\text{D}(\text{OEOEO})_2\text{E}$ (8.5), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ (7.8), $\text{O}(\text{EOEOM})_2\text{D}(\text{OCH}_3)_2$ (7.4), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ (6.8), $\text{O}(\text{EOEOM})_2\text{D}(\text{OH})_2$ (6.6), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$ (6.4), $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$ (5.5). The $-\Delta(\Delta G^\circ)_{\text{max}}$ values decrease in essentially the same order from a high of 4.8 kcal/mol for $\text{Nap}(\text{OEOEO})_2\text{E}$ to a low of 1.7 kcal/mol for $\text{E}(\text{OEOEOM})_2\text{D}(\text{OH})_2$. It is concluded that the six-oxygen arrangement of $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ is inferior to the six-oxygen arrangements of the two standards, both for overall binding and for selectivity. As expected based on analogies with the crowns, the six-oxygen system > seven-oxygen system > eight-oxygen system in complexing and complexing selectively.²² Even the host containing the structurally similar disubstituted 1,1'-dianisyl unit $\text{AnAn}(\text{MOEO})_2\text{E}^6$ proved to bind better ($-\Delta G_{\text{av}}^\circ = 8.2$ kcal/mol) and more selectively ($-\Delta(\Delta G^\circ)_{\text{max}} = 3.3$ kcal/mol) than $\text{E}(\text{OEOEOM})_2\text{D}(\text{OCH}_3)_2$ ($-\Delta G_{\text{av}}^\circ = 7.8$ and $-\Delta(\Delta G^\circ)_{\text{max}} = 2.6$ kcal/mol). Intramolecular hydrogen bonding and the presence of complexed water which has

(21) I. Goldberg, *Acta Crystallogr., Sect. B*, 33, 472–9 (1977).

(22) C. J. Pedersen in Chapter 1 of the monograph of ref 3.

to be displaced or reorganized when the cations enter the cycles explain why the hydroxyl-containing hosts are poorer binders than their methoxyl-containing counterparts.

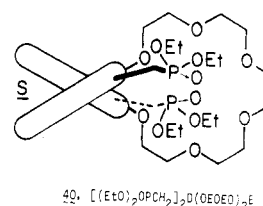
The best host of this study proved to be O-(EOEOM)₂D(OEOEO)₂E (**16**) with $\Delta G^\circ_{av} = 8.7$ kcal/mol and $-\Delta(\Delta G^\circ)_{max} = 5.3$ kcal/mol. The extra O-(EOEOM)₂ bridge of **16** provides a seventh potentially binding oxygen which can act as a "floor" for the cavity and should also rigidify the whole system conformationally, as compared to the model system (CH₃)₂D(OEOEO)₂E without the extra bridge. As expected from the match between the hole diameter of O-(EOEOM)₂D(OEOEO)₂E (2.6 Å) and the ionic radius of K⁺ (2.66 Å), this ion is the best bound ($-\Delta G^\circ = 11.1$ kcal/mol) of the six examined. This value compares with 10.4 and 10.8 kcal/mol for (CH₃)₂D(OEOEO)₂E and Nap(OEOEO)₂E, respectively. The $-\Delta(\Delta G^\circ)_{max}$ value of 5.3 kcal/mol is the highest for any system thus far examined except AnAnAn(MOE)₂O (**39**),



which gave the same value but was a much better general binder ($-\Delta G^\circ_{av} = 10.2$ kcal/mol).^{15a} Both systems are relatively rigid, which probably accounts for their high selectivity.

The poorest all-oxygen ligand system proved to be (CH₃O)₂D(MOM)₂D(OCH₃)₂ (**20**), which gave $-\Delta G^\circ_{av} = 4.9$ and $-\Delta(\Delta G^\circ)_{max} = 0.5$ kcal/mol. Although molecular models of this system suggest it should provide a somewhat spherical cavity for complexing the larger ions Cs⁺ and Rb⁺, the $-\Delta G^\circ$ values for these ions are lower than those observed for the other hosts. It appears likely that the actual conformations required for complexation are of higher energy than are suggested by molecular model examination.

The four-stranded host (*R,R*)(*S,S*)-T(MOEOEM)₂(OEOEO)₂T ((*R,R*)(*S,S*)-**25**) proved to be a disappointing ligand system from the point of view of showing high binding ability. Although molecular models suggested that eight well-arranged oxygens might bind ions such as K⁺, $-\Delta G^\circ$ for this ion was 9.0 kcal/mol, only 2.2 kcal/mol higher than that of the model compound T(OEOEO)₂T. The four-stranded cycle gave $-\Delta G^\circ_{av} = 6.7$ kcal/mol and a relatively high $-\Delta(\Delta G^\circ)_{max}$ of 4.3 kcal/mol. The difference between $-\Delta G^\circ$ for K⁺ and Na⁺ was 2.6 kcal/mol, higher than was observed for any of the other systems of this paper except O-(EOEO)₂MDM(OEOE)₂O, which gave 2.7 kcal/mol. The greatest difference observed for any system examined thus far was for the host *trans*-(*o*-ClC₆H₄)₂E(OEOEO)₂E, whose difference for the two ions was 3.1 kcal/mol (the $-\Delta G^\circ_{av}$ value was 9.1 kcal/mol).⁶ More striking is the $-\Delta(\Delta G^\circ)$ difference of 3.7 kcal/mol for (*R,R*)(*S,S*)-T(MOEOEM)₂(OEOEO)₂T binding K⁺ vs. Cs⁺. The only system known for which an equal difference exists is [(EtO)₂OPCH₂]₂D(OEOEO)₂E (**40**),⁶ and this latter system has the second highest $-\Delta G^\circ_{av}$ (10 kcal/mol) yet observed. The two systems with the next highest difference (kcal/mol) between these two ions are O-(EOEOM)₂D(OEOEO)₂E (**3.3**) and AnAnAn(MOE)₂O



(**3.3**). All but **40** of these four systems possesses universally rigid cavities of a diameter that is difficult to expand.

Interestingly, the meso isomer of the four-stranded system, (*R,S*)-T(MOEOEM)₂(OEOEO)₂T ((*R,S*)-**25**), possesses a higher $-\Delta G^\circ_{av}$ value (7.1 kcal/mol) and lower $-\Delta(\Delta G^\circ)_{max}$ value (2.5 kcal/mol) than its (*R,R*)(*S,S*) isomer. The meso isomer possesses a much more open and adaptable structure than the chiral isomer. The relatively low $-\Delta G^\circ_{av}$ values for both isomers are attributed to the fact that four of the eight oxygens that can be employed at any one time to bind an ion are of the less basic ArO variety. The low $-\Delta G^\circ$ value of 5.8 kcal/mol for (*R,R*)-T(OEOEO)₂T binding K⁺ reflects this effect.

The sulfur analogue of the four-stranded oxygen system, (*R,R*)-T(MSESM)₂(OEOEO)₂T ((*R,R*)-**26**), turned out to be the poorest overall ligand system of this series, with a ΔG°_{av} of ≥ 4.6 kcal/mol. In this compound, the two extra sulfur-containing strands do not affect the binding for K⁺ ($-\Delta G^\circ = 5.8$ kcal/mol), since (*R,R*)-T(OEOEO)₂T which does not contain these extra bridges gives the same value.

The two "jaws"-type hosts E(OEOEO)₂D(OEOEO)₂E (**27**) and O-(EOEO)₂MDM(OEOE)₂O (**34**) both give $-\Delta G^\circ_{av}$ values of 8.2 kcal/mol and similar $-\Delta(\Delta G^\circ)_{max}$ values of 4.4 and 4.1 kcal/mol, respectively. Molecular models of the two systems indicate that in sandwich-type complexes with the larger ions, a maximum of 10 oxygen-to-metal ion contacts can be made to each host at any one time. The two oxygens attached to the 3,3'-positions of **27** are too far from one another to allow them to act cooperatively in finding these spherical ions. Not surprisingly, these two systems provide almost the best ligands for binding Cs⁺ that have yet been examined. Thus E(OEOEO)₂D(OEOEO)₂E gives $-\Delta G^\circ$ for Cs⁺ of 9.3, and O-(EOEO)₂MDM(OEOE)₂O gives 9.2 kcal/mol. Only the system [(EtO)₂OPCH₂]₂D(OEOEO)₂O^{15c} (the analogue of **40** with one more EO unit in the cycle), which possesses up to 11 well-located oxygen binding sites, surpasses these systems to give $-\Delta G^\circ = 10.1$ kcal/mol for Cs⁺.

Successive substitutions of bromine in the 1- and 4-positions of Nap(OEOEO)₂E (**30**) to give BrNap(OEOEO)₂E (**31**) and Br₂Nap(OEOEO)₂E (**32**) reduces $-\Delta G^\circ_{av}$ and $-\Delta(\Delta G^\circ)_{max}$ values (kcal/mol) from 8.7 to 7.9 to 5.8 and 4.8 to 2.9 to 2.0, respectively. This effect probably is mainly steric in origin, since the CH₂ group of the ArOCH₂ is dislocated from its normal position by an ortho bromine. As a result, the lone pairs on the oxygen are diverted somewhat from their more normal convergent positions.

Apparently, Nap(OEOEO)₂E provides the best tripod arrangement for binding NH₄⁺, since $-\Delta G^\circ = 9.6$ kcal/mol. The next best system for binding this ion is the relatively rigid compound O-(EOEOM)₂D(OEOEO)₂E, with $-\Delta G^\circ = 9.4$ kcal/mol. None of the noncrown compounds examined thus far exceed the $-\Delta G^\circ$ value for NH₄⁺ of 10.7 kcal/mol observed for dicyclohexano-18-crown-6.⁶

None of the new systems reported here showed particularly high binding energies toward Na⁺ or Li⁺, nor did they show a greater affinity for Na⁺ than for K⁺. One of the two poorest ligand systems examined, (*R,R*)(*S,S*)-(CH₃O)₂D(MOM)₂D(OCH₃)₂, showed very little discrimination between all six ions. The $-\Delta G^\circ$ value (kcal/mol)

for Li^+ was 5.1 and that for Na^+ was 4.9. The general bias these systems have shown for binding K^+ and Rb^+ over the other smaller and larger ions reflects the bias in their design. No doubt systems can also be designed to selectively and powerfully bind the ions of the lower diameter as well.

Experimental Section

General Procedure. Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. All ^1H NMR spectra were recorded on a Varian HA-100 or T-60 spectrophotometer. Optical rotations were taken on a Perkin-Elmer 141 polarimeter in a 1-dm thermostated cell. Mass spectra were taken at 70 eV on an AEI Model MS-9 double-focusing spectrometer. Tetrahydrofuran (THF) was distilled from benzophenone ketyl immediately prior to use. Dichloromethane was fractionally distilled before use, and all solvents were reagent grade. All organic solutions were dried with MgSO_4 before concentrating or being submitted to chromatography. Gel permeation chromatograms were run in CH_2Cl_2 on a $3/8$ in. \times 30 ft column of Styragel 100-Å beads (30–70 μm particle size, exclusion limit of 1500 mol wt) at a flow rate of 4 mL/min and a pressure of 200–400 lb/in.²

Starting Materials. The preparations of pure samples of (R)(S)-, (R)-, and (S)-3,3'-bis(hydroxymethyl)-2,2'-dihydroxy-1,1'-dinaphthyl (1) have been reported,¹¹ as well as (R)(S)-2,2'-bis(hydroxymethyl)-2,2'-dimethoxy-1,1'-dinaphthyl, (R)(S)-2.⁶ By the same procedure used for preparation of (R)(S)-2,⁶ 15 g (106 mmol) of optically pure (R)-1 was converted to (R)-2: 14.65 g (86% after film drying at 110 °C (0.01 mm) for 12 h), obtained as a glass, pure to TLC and ^1H NMR;⁶ $[\alpha]_{589}^{25} -147^\circ$, $[\alpha]_{578}^{25} -155^\circ$, $[\alpha]_{546}^{25} -180^\circ$, and $[\alpha]_{436}^{25} -357^\circ$ (c 0.99, CHCl_3). Anal. Calcd for $\text{C}_{24}\text{H}_{20}\text{O}_4$: C, 76.99; H, 5.92. Found: C, 76.92; H, 5.84. Similarly, 10 g (29 mmol) of optically pure (S)-1 was converted to (S)-2 as a glass: 9.5 g (88%), pure to TLC (silica gel, 4:1 (v/v), C_6H_6 - Et_2O); $[\alpha]_{589}^{25} +147^\circ$, $[\alpha]_{578}^{25} +155^\circ$, $[\alpha]_{546}^{25} +181^\circ$, $[\alpha]_{436}^{25} +359^\circ$ (c 1, CHCl_3) and $[\alpha]_{589}^{25} +52^\circ$, $[\alpha]_{578}^{25} +55^\circ$, $[\alpha]_{546}^{25} +65^\circ$, $[\alpha]_{436}^{25} +128^\circ$ (c 1.02, THF). Anal. Calcd for $\text{C}_{24}\text{H}_{20}\text{O}_4$: C, 76.99; H, 5.92. Found: C, 76.75; H, 5.77. Compound (R)(S)-3,3'-bis(hydroxymethyl)-2,2'-dimethoxy-1,1'-dinaphthyl (4) has been reported.⁶ By the same procedure, 3 g (8.0 mmol) of optically pure (+)-(S)-2 was converted to 2.8 g (85% after chromatography on 100 g of silica gel-benzene and film drying) of (S)-4, whose ^1H NMR spectrum was identical with that of racemic material:⁶ $[\alpha]_{589}^{25} +128^\circ$, $[\alpha]_{578}^{25} +134^\circ$, $[\alpha]_{546}^{25} +155^\circ$, $[\alpha]_{436}^{25} +287^\circ$ (c 0.99, CHCl_3). Anal. Calcd for $\text{C}_{24}\text{H}_{20}\text{Cl}_2\text{O}_2$: C, 70.08; H, 4.90. Found: C, 70.18; H, 4.84.

3,3'-Bis(hydroxymethyl)-2,2'-bis(methoxymethoxy)-methoxy-1,1'-dinaphthyl (3). To a solution of 20 g (58 mmol) of racemic tetrol 1 in 600 mL of THF under N_2 was added 13.5 g (120 mmol) of *t*-BuOK, and the suspension of salt was stirred 15 min at 25 °C. After 10 g (125 mmol) of $\text{ClCH}_2\text{OCH}_3$ was added, stirring was continued for 30 min, and the mixture was shaken with 600 mL each of CH_2Cl_2 and H_2O . The organic layer was extracted with two 100-mL portions of CH_2Cl_2 and the combined extracts were dried, evaporated (50 °C (30 mm)), dissolved in 50 mL of CHCl_3 , and chromatographed on 800 g of silica gel- C_6H_6 . The column was washed with C_6H_6 (2 L) and 19:1 (v/v) C_6H_6 - Et_2O (3 L), and product was eluted with 4 L of 9:1 (v/v) C_6H_6 - Et_2O and 3 L (v/v) of 4:1 C_6H_6 - Et_2O as a colorless oil. After film drying at 50 °C (0.01 mm) for 12 h the yield was 13.8 g (55%): M^+ , m/e 434; ^1H NMR, 60 MHz, CDCl_3 , δ 3.04 (s, OCH_3 , 6 H), 3.53 (s, broad, OH, 2 H), 4.44 (s, OCH_2 , 4 H), 4.91 (s, broad, ArCH_2 , 4 H), 7.22 (m, ArH, 6 H), 7.83 (m, ArH, 2 H), 8.01 (s, ArH, 2 H). Anal. Calcd for $\text{C}_{26}\text{H}_{26}\text{O}_6$: C, 71.87; H, 6.03. Found: C, 71.95; H, 6.31.

3,3'-Bis(bromomethyl)-2,2'-diacetoxy-1,1'-dinaphthyl (5). A mixture of 115 g (0.24 mol) of 3,3'-bis(bromomethyl)-2,2'-dihydroxy-1,1'-dinaphthyl¹⁰ and 100 g (0.81 mol) of AcBr in 400 mL of CHCl_3 was heated at 50 °C for 12 h. The solution was evaporated under reduced pressure to a tan solid, 133 g (98%), which gave one spot on TLC (silica gel, 9:1 (v/v), C_6H_6 - Et_2O), and was used in subsequent reactions without purification. An analytical sample was recrystallized from CH_2Cl_2 - C_6H_{12} to give material: mp 168–169 °C (after drying at 100 °C (0.01 mm) for 12 h); M^+ , m/e 554 (^{79}Br); ^1H NMR, 60 MHz, CDCl_3 , δ 1.88 (s,

CH_3 , 6 H), 4.60 (s, ArCH_2 , 4 H), 7.28 (m, ArH, 6 H), 7.88 (m, ArH, 2 H), 8.02 (s, ArH, 2 H). Anal. Calcd for $\text{C}_{26}\text{H}_{20}\text{Br}_2\text{O}_4$: C, 56.14; H, 3.62. Found: C, 56.38; H, 3.72.

3,3'-Bis(mercaptopomethyl)-2,2'-dihydroxy-1,1'-dinaphthyl (6). A solution of dibromide 5, 72 g (0.13 mol), and 23 g (0.30 mol) of thiourea in 300 mL of DMF under N_2 was heated at 70 °C for 4 h. The solution was evaporated (80 °C (30 mm)), and the residue was dissolved in 300 mL of morpholine. After being heated at 100 °C for 3 h under N_2 , the solution was evaporated (80 °C (30 mm)), and the residue was diluted with CHCl_3 (500 mL) and 3 N HCl (1 L). The organic layer was dried and concentrated to 100 mL. The solution was chromatographed on 500 g of silica gel- C_6H_6 . Elution of the column with 10 L of C_6H_6 gave 23.7 g (48%) of 6, mp 176–177 °C, which was recrystallized from C_6H_6 - C_6H_{12} and dried at 100 °C (0.01 mm) for 3 h: M^+ , m/e 378; ^1H NMR, 60 MHz, CDCl_3 , δ 2.10 (t, SH, 2 H), 3.90 (d, ArCH_2 , 4 H), 5.27 (s, OH, 2 H), 7.18 (m, ArH, 6 H), 7.80 (m, ArH, 2 H), 7.90 (s, ArH, 2 H). Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{O}_2\text{S}_2$: C, 69.84; H, 4.79. Found: C, 69.64; H, 4.83.

2,2',3,3'-Tetrahydroxy-1,1'-dinaphthyl (7). The literature procedure¹² was employed except that the initial solution of 2,3-naphthalenediol was filtered hot to remove insoluble material. The crude tetrol was recrystallized from THF, and the resulting solvate was heated at 130 °C (0.01 mm) for 12 h to give 7 as a white, solvent-free powder: 60%; mp >300 °C (decomposition); M^+ , m/e 318; ^1H NMR, 60 MHz, $(\text{CD}_3)_2\text{SO}$, δ 6.6–7.3 (m, ArH, 8 H), 7.4–7.7 (m, ArH, 2 H), 8.2 (s, OH, 2 H), 9.9 (s, OH, 2 H). Anal. Calcd for $\text{C}_{20}\text{H}_{14}\text{O}_4$: C, 75.45; H, 4.44. Found: C, 75.29; H, 4.64.

2,3,4,5,6,7-Bis[1,3-(2-methoxynaphtho)]-9,12,15,18-tetraoxacyclooctadeca-3,5-diene (8). Procedure A. To 400 mL of THF under N_2 was added NaH (2.5 g, 52 mmol) as a 50% mineral oil dispersion. To this refluxing suspension was added (2 h) a mixture of 3.7 g (9.9 mmol) of (R)(S)-diol 2 and 4.7 g (10 mmol) of triethylene glycol ditosylate in 200 mL of THF. The mixture was refluxed for 48 h and then cooled, excess NaH was decomposed with CH_3OH , and the solution was shaken with 600 mL each of CH_2Cl_2 and H_2O . The aqueous layer was extracted with three 100-mL portions of CH_2Cl_2 . The organic extracts were dried and evaporated under reduced pressure. The residue was chromatographed on 200 g of alumina- Et_2O , the mineral oil was washed from the column with 0.5 L of Et_2O , and the product was eluted with 2 L of Et_2O . The product was subjected to gel permeation chromatography on column A (retention volume 198 mL of CH_2Cl_2) to give 1.9 g (40%) of 8 as a white foam: M^+ , m/e 488; ^1H NMR, 60 MHz, CDCl_3 , δ 3.18 (s, OCH_3 , 6 H), 3.64 (m, OCH_2 , 12 H), 4.71 (ABq, ArCH_2 , 4 H), 7.28 (m, ArH, 6 H), 7.80 (m, ArH, 2 H), 7.87 (s, ArH, 2 H). Anal. Calcd for $\text{C}_{30}\text{H}_{32}\text{O}_6$: C, 73.55; H, 6.60. Found: C, 73.77; H, 6.66.

2,3,4,5,6,7-Bis[1,3-(2-methoxynaphtho)]-9,12,15,18,21-pentaoxacycloheneicos-3,5-diene (9). Application of procedure A to 3.7 g (9.9 mmol) of (R)(S)-diol 3, 5.2 g (10.4 mmol) of tetraethylene glycol ditosylate,⁸ and 2.5 g (52 mmol) of NaH in 600 mL of THF gave 2.1 g (40%) of 9 as a white foam: gel permeation retention volume, 188 mL of CH_2Cl_2 ; M^+ , m/e 532; ^1H NMR, 60 MHz, CDCl_3 , δ 3.42 (s, OCH_3 , 6 H), 3.60 (m, OCH_2 , 16 H), 4.77 (ABq, ArCH_2 , 4 H), 7.25 (m, ArH, 6 H), 7.83 (m, ArH, 2 H), 7.90 (s, ArH, 2 H). Anal. Calcd for $\text{C}_{32}\text{H}_{36}\text{O}_7$: C, 72.16; H, 6.81. Found: C, 72.18; H, 6.78.

2,3,4,5,6,7-Bis[1,3-(2-methoxynaphtho)]-9,12,15,18,21,24-hexaoxacyclotetracos-3,5-diene (10). Application of procedure A to 3.7 g (9.9 mmol) of (R)(S)-diol 2, 5.6 g (10.3 mmol) of pentaethylene glycol ditosylate,⁸ and 2.5 g (52 mmol) of NaH in 600 mL of THF gave 1.15 g (20%) of 10 as a white foam: gel permeation chromatogram retention volume, 184 mL of CH_2Cl_2 ; M^+ , m/e 576; ^1H NMR, 60 MHz, CDCl_3 , δ 3.37 (s, OCH_3 , 6 H), 3.60 (m, OCH_2 , 20 H), 4.83 (ABq, ArCH_2 , 4 H), 7.20 (m, ArH, 6 H), 7.86 (m, ArH, 2 H), 7.97 (s, ArH, 2 H). Anal. Calcd for $\text{C}_{34}\text{H}_{40}\text{O}_8$: C, 70.81; H, 6.99. Found: C, 70.97; H, 7.13.

2,3,4,5,6,7-Bis[1,3-(2-hydroxynaphtho)]-9,12,15,18-tetraoxacyclooctadeca-3,5-diene (11). Procedure B. To a solution of 2.3 g (5.3 mmol) of racemic diol 3 and 2.7 g (5.9 mmol) of triethylene glycol ditosylate in 600 mL of THF under N_2 was added 3.0 g (63 mmol) of NaH as a 50% mineral oil dispersion. The mixture was refluxed for 48 h and then cooled, and the excess NaH was decomposed with CH_3OH . The solution was shaken

with 300-mL portions of water and CH_2Cl_2 , and the aqueous layer was washed with two 100-mL portions of CH_2Cl_2 . The combined organic layers were dried, evaporated at 50 °C (30 mm), and dissolved in 200 mL of CHCl_3 . To this solution was added 400 mL of CH_3OH and 5 mL of concentrated HCl aqueous solution, and the mixture was stirred for 2 h at 25 °C. The mixture was shaken with 400 mL of H_2O , and the aqueous layer was extracted with two 100-mL portions of CHCl_3 . The combined organic layers were dried, evaporated under reduced pressure, and chromatographed on 150 g of silica gel- CH_2Cl_2 . The column was washed with 3 L of CH_2Cl_2 . The product was eluted with 3 L of 5% THF in CH_2CH_2 (v/v) to give 1.0 g (40%) of 11 as a monohydrate; mp 214–215 °C after recrystallization from CH_2Cl_2 -EtOAc. The melting point of this monohydrate occurs without any visual indication of loss of H_2O below 214 °C. The material can be dehydrated by heating at 200 °C (0.01 mm) for 12 h. The dried substance gave the following: M^+ , m/e 460; $^1\text{H NMR}$, 60 MHz, CDCl_3 , δ 3.58 (m, OCH_2 , 12 H), 4.97 (ABq, ArCH_2 , 4 H), 7.24 (m, ArH, 6 H), 7.74 (s, ArH, 4 H), 7.80 (m, ArH, 2 H). Anal. Calcd for $\text{C}_{28}\text{H}_{28}\text{O}_6 \cdot \text{H}_2\text{O}$: C, 70.28; H, 6.32. Found: C, 70.52; H, 6.27. Anal. Calcd for $\text{C}_{28}\text{H}_{28}\text{O}_6$: C, 73.03; H, 6.13. Found: C, 72.84; H, 6.32.

2,3,4,5,6,7-Bis[1,3-(2-hydroxynaphtho)]-9,12,15,18,21-pentaoxacycloheneicoso-3,5-diene (12). Application of procedure B to 2.3 g (5.3 mmol) of (*R*)(*S*)-diol 3, 2.9 g (5.8 mmol) of tetraethylene glycol ditosylate,⁸ and 3 g (63 mmol) of NaH gave crude product as an oil which after chromatography on 150 g of silica gel- CH_2Cl_2 (column washed with 1 L of CH_2Cl_2 and 2 L of 5% THF in CH_2Cl_2 (v/v); product eluted with 3 L of 10% THF in CH_2Cl_2 (v/v)) gave 0.8 g (30%) of 12 as a white solid, mp 188–189 °C, after recrystallization from CH_2Cl_2 -EtOAc: M^+ , m/e 504; $^1\text{H NMR}$, 60 MHz, CDCl_3 , δ 3.63 (m, OCH_2 , 16 H), 4.94 (ABq, ArCH_2 , 4 H), 7.21 (m, ArH, 6 H), 7.80 (m, ArH, 2 H), 7.83 (s, ArH, 4 H). Anal. Calcd for $\text{C}_{30}\text{H}_{32}\text{O}_7$: C, 71.41; H, 6.39. Found: C, 71.22; H, 6.42.

2,3,4,5,6,7-Bis[1,3-(2-hydroxynaphtho)]-9,12,15,18,21,24-hexaoxacyclotetraeicoso-3,5-diene (13). Application of procedure B to 2.3 g (5.3 mmol) of racemic diol 3, 3.1 g (5.7 mmol) of pentaethylene glycol ditosylate,⁸ and 3 g (63 mmol) of NaH gave, after removal of the protecting group, product as a crude oil. This material was chromatographed on 150 g of silica gel- CH_2Cl_2 . The column was washed with 1 L of CH_2Cl_2 , 2 L of 5% THF in CH_2Cl_2 (v/v), and 3 L of THF in CH_2Cl_2 (v/v), and product was eluted with 2 L of 20% THF in CH_2Cl_2 (v/v) to give 0.435 g (15%) of 13; mp 162–163 °C after recrystallization from CH_2Cl_2 -EtOAc and drying at 110 °C (0.01 mm) for 12 h. The substance gave the following: M^+ , m/e 546; $^1\text{H NMR}$, 60 MHz, CDCl_3 , δ 3.64 (m, OCH_2 , 20 H), 4.93 (ABq, ArCH_2 , 4 H), 7.01 (s, OH, 2 H), 7.20 (m, ArH, 6 H), 7.78 (m, ArH, 2 H), 7.81 (s, ArH, 4 H). Anal. Calcd for $\text{C}_{32}\text{H}_{36}\text{O}_8$: C, 70.06; H, 6.61. Found: C, 69.88; H, 6.48.

2,3,23,24-Dibenzo-7,10,13,16,19,27,30,33,36,39,42-undecaoxatetracyclo[23.18.0.0^{5,43}.0^{21,26}]tritetraconta-1(43),2,4,21,23,25-hexaene (16). To a refluxing solution of 3.0 g (62.5 mmol) of NaH (50% suspension in mineral oil) in 300 mL of THF stirred under N_2 was added over a 2-h period a solution of 3.6 g (6.2 mmol) of racemic 2,3,4,5-bis[1,2-(3-chloromethylnaphtho)]-1,6,9,12,15,18-hexaoxacycloeicoso-2,4-diene⁷ (14) and 1.3 g (6.7 mmol) of tetraethylene glycol⁸ in 150 mL of THF. The mixture was refluxed for 24 h and then cooled, excess NaH was decomposed with CH_3OH , and the mixture was shaken with 0.5 L of CHCl_3 and 1 L of H_2O . The organic layer was dried and evaporated under reduced pressure, and the residue was dissolved in 30 mL of CH_2Cl_2 and chromatographed on 100 g of alumina-Et₂O. Elution of the column with 6 L of Et₂O gave 1.75 g (40%) of 16; mp 103–104 °C after recrystallization from CH_2Cl_2 -EtOAc and drying at 90 °C (0.01 mm) for 12 h. This compound exhibited a single peak at 167 mL of CH_2Cl_2 on gel permeation chromatography. M^+ , m/e 712; $^1\text{H NMR}$ spectrum, 60 MHz, CDCl_3 , δ 3.40 (m, OCH_2 , 34 H), 4.30 (m, OCH_2 , 2 H), 4.63 (m, ArCH_2 , 2 H), 5.18 (m, ArCH_2 , 2 H), 6.65 (m, ArH, 1 H), 7.20 (m, ArH, 5 H), 7.80 (m, ArH, 2 H), 7.87 (s, ArH, 4 H), 8.12 (s, ArH, 4 H). Anal. Calcd for $\text{C}_{40}\text{H}_{50}\text{O}_{11}$: C, 67.97; H, 7.13. Found: C, 68.12; H, 7.23.

2,3,26,27-Dibenzo-7,10,13,16,19,22,30,33,36,39,42,45-dodecaoxatetracyclo[26.18.0.0^{5,46}.0^{24,29}]hexatetraconta-1(46),2,4,24,26,28-hexaene (17). To a refluxing suspension of 2.0 g (42

mmol) of NaH in 500 mL of THF under N_2 was added over an 8-h period a solution of 1.6 g (2.7 mmol) of racemic dichloride 14⁷ and 0.7 g (2.9 mmol) of pentaethylene glycol⁸ in 300 mL of THF. The reaction mixture was refluxed an additional 24 h and the crude product isolated as usual (see preparation of 16), which was subjected to alumina-ether and finally gel permeation chromatography. The final product (17) gave a retention volume of 163 mL of CH_2Cl_2 , 0.9 g (44%); mp 116–117 °C after recrystallization from CH_2Cl_2 -Et₂O and drying at 100 °C (0.01 mm) for 12 h; M^+ , m/e 750; $^1\text{H NMR}$, 60 MHz, CDCl_3 , δ 3.43 (m, OCH_2 , 40 H) 4.92 (ABq, ArCH_2 , 4 H), 7.13 (m, ArH, 6 H), 7.86 (m, ArH, 2 H), 7.99 (s, ArH, 4 H). Anal. Calcd for $\text{C}_{42}\text{H}_{54}\text{O}_{12}$: C, 67.18; H, 7.25. Found: C, 66.82; H, 7.13.

(*S,S*)-2,3,23,24-Dibenzo[naphtho[2',1':34,35]naphtho[1',2':36,37]-7,10,13,16,19,27,30,33,38,41,44-undecaoxatetracyclo[23.20.0.0^{5,45}.0^{21,26}]pentatetraconta-1(45),2,4,21,23,25,34,36-octaene ((*S,S*)-19). The starting dichloro compound (*S,S*)-18 was prepared from the corresponding optically pure (*S,S*)-diol¹⁰ by the same method used to prepare (*R,R*)-18.¹⁰ The spectral and chromatographic properties of the two enantiomers were identical. To a refluxing suspension of 2 g (42 mmol) of NaH in 500 mL of THF stirred under N_2 was added over a 12-h period a solution of optically pure (*S,S*)-18 (2.8 g, 3.5 mmol) and tetraethylene glycol⁸ (0.8 g, 4 mmol). The mixture was refluxed for an additional 24 h, and the product was isolated in the usual manner (see above) and chromatographed on 250 g of alumina-Et₂O. The desired product was eluted with 5 L of Et₂O and then submitted to gel permeation chromatography to give a retention volume of 152 mL of CH_2Cl_2 . The product, (*S,S*)-19, was isolated as a white foam which was dried at 50 °C (0.01 mm) for 24 h: 0.96 g (30%); M^+ , m/e 930; $^1\text{H NMR}$, 60 MHz, CDCl_3 , δ 3.45 (m, OCH_2 , 32 H), 4.70 (m, ArCH_2 , 4 H), 6.67 (m, ArH, 1 H), 7.21 (m, ArH, 13 H), 7.90 (m, ArH, 8 H); $[\alpha]_{589}^{25}$ -138°, $[\alpha]_{578}^{25}$ -146°, $[\alpha]_{546}^{25}$ -171°, $[\alpha]_{436}^{25}$ -371° (c 1.03, CHCl_3). Anal. Calcd for $\text{C}_{58}\text{H}_{58}\text{O}_{11}$: C, 74.82; H, 6.29. Found: C, 74.82; H, 6.33.

(*R,R*)(*S,S*)- and (*S,S*)-2,3,4,5,6,7:11,12,13:14,15,16-Tetrakis[1,3-(2-methoxynaphtho)]-9,18-dioxacyclooctadeca-2,5,11,14-tetraene ((*R,R*)(*S,S*)-20 and (*S,S*)-20). To a refluxing suspension of 3.0 g (62.5 mmol) of NaH in 500 mL of THF stirred under N_2 was added over a 24-h period 6.1 g (14.8 mmol) of (*R*)(*S*)-dichloride 4⁷ and 5.6 g (14.9 mmol) of (*R*)(*S*)-diol 2⁷ in 500 mL of THF. The mixture was refluxed an additional 24 h and then cooled, and the excess NaH was decomposed with CH_3OH . The mixture was shaken with 500 mL of CHCl_3 and 1 L of H_2O . The aqueous layer was extracted with two 100-mL portions of CHCl_3 . The combined organic extracts were dried and evaporated under reduced pressure. The residue in 50 mL of CHCl_3 was chromatographed on 300 g of silica gel- C_6H_6 . The column was washed with 1 L of C_6H_6 , 2 L of 1% Et₂O in C_6H_6 (v/v), 2 L of 2% Et₂O in C_6H_6 (v/v), and 3 L of 5% Et₂O in C_6H_6 (v/v). Product eluted with 3 L of 10% Et₂O in C_6H_6 (v/v), to give 1.2 g (11%) of (*R,R*)(*S,S*)-20: mp 320 °C (decomposition) after recrystallization from CH_2Cl_2 -Et₂O; M^+ , m/e 712; $^1\text{H NMR}$, 60 MHz, CDCl_3 , δ 2.77 (s, OCH_3 , 12 H), 4.77 (ABq, ArCH_2 , 8 H), 7.25 (m, ArH, 12 H), 7.88 (m, ArH, 4 H), 8.00 (s, ArH, 4 H). Anal. Calcd for $\text{C}_{48}\text{H}_{40}\text{O}_6$: C, 80.88; H, 5.66. Found: C, 80.79; H, 5.80.

(*S,S*)-20 was similarly prepared from optically pure (*S*)-4⁷ (3.1 g) and (*S*)-2⁷ (2.9 g) to give 1.1 g (20%) of product (*S,S*)-20 as a white foam, with gel permeation retention volume (189 mL of CH_2Cl_2), TLC behavior, and $^1\text{H NMR}$ spectrum identical with those of (*R,R*)(*S,S*)-20. The substance gave $[\alpha]_{589}^{25}$ +136°, $[\alpha]_{578}^{25}$ +143°, $[\alpha]_{546}^{25}$ +170°, and $[\alpha]_{436}^{25}$ +363° (c 1.01, CHCl_3). Anal. Calcd for $\text{C}_{48}\text{H}_{40}\text{O}_6$: C, 80.88; H, 5.66. Found: C, 80.92; H, 5.51.

An attempt to prepare (*R*)(*S*)-20 from (*S*)-4 and (*R*)-2 by the above method gave only higher molecular weight oligomers (retention volume on gel permeation chromatography of 160 mL CH_2Cl_2) which were not characterized.

2,3,4,5,6,7:11,12,13:14,15,16-Tetrakis[1,3-(2-hydroxynaphtho)]-9,18-dithiacyclooctadeca-2,5,11,14-tetraene (22). To a solution of 15.9 g (28.7 mmol) of racemic dibromide 5 and 11.3 g (29.9 mmol) of dithiol 6 in 2.4 L of acetone stirred under N_2 was added 7.8 g (60 mmol) of diisopropylethylamine in 100 mL of acetone. The mixture was stirred for 48 h at 25 °C, refluxed for 24 h, and concentrated under reduced pressure to about 1-L volume. The mixture was shaken with 1 L of CH_2Cl_2 and 1.5 L of H_2O , and the organic layer was dried and concentrated under

reduced pressure to 100-mL volume. This solution was chromatographed on 500 g of silica gel-C₆H₆. Elution of the column with 10 L of C₆H₆ gave 9.4 g (42%) of the diacetate **21** as a white foam dried at 50 °C (0.01 mm) for 24 h. This material gave one spot on a silica gel TLC plate (C₆H₆) and a singlet absorption in its ¹H NMR spectrum for the CH₃ group, which suggests only one isomer was formed: M⁺, *m/e* 772; ¹H NMR, 60 MHz, CDCl₃, δ 0.88 (s, CH₃, 6 H), 3.93 (m, ArCH₂, 8 H), 5.26 (s, OH, 2 H), 7.08 (m, ArH, 12 H), 7.80 (m, ArH, 4 H), 8.13 (s, ArH, 4 H), 8.24 (s, ArH, 4 H). This material was not further characterized.

A solution of 7.6 g (9.8 mmol) of this diacetate (**21**) in 150 mL of morpholine was heated under N₂ for 1 h. The white solid that precipitated during the course of the reaction (and afterward when the mixture was cooled to 25 °C) was filtered to give 4.15 g of material. The filtrate was evaporated at 80 °C (30 mm) and the residue was shaken with 300 mL of CHCl₃ and 500 mL of 1 N HCl in water. The organic layer was dried, evaporated under reduced pressure to 15 mL, and diluted with 50 mL of Et₂O to give 2.0 g of product, identical with the filtered material (TLC and ¹H NMR). The total product (**22**) was 6.15 g (91%): mp 202–203 °C after drying at 200 °C (0.01 mm) for 12 hr; M⁺, *m/e* 688; ¹H NMR, 60 MHz, CDCl₃, δ 3.93 (ABq, ArCH₂, 8 H), 5.52 (s, OH, 4 H), 7.10 (m, ArH, 12 H), 7.78 (m, ArH, 4 H), 8.01 (s, ArH, 4 H). Anal. Calcd for C₄₄H₃₂O₄S₂: C, 76.73; H, 4.68. Found: C, 76.62; H, 4.73.

(R,R)(S,S)- and (R,S)-2,3:4,5:13,14:15,16-Tetrakis[1,2-(5,6,7,8-tetrahydronaphtho)]-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene ((R,R)(S,S)-23, (R,S)-23). To a hot solution of 7.0 g (9.8 mmol) of **(R,R)(S,S)-23**, 2,3:4,5:13,14:15,16-tetra(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene¹¹ in 1 L of glacial acetic acid was added 1.0 g of PtO₂ and the resulting mixture was shaken under 3 atm of H₂ for 7 days. The resulting mixture was filtered, and the filtrate was shaken with 1 L of CH₂Cl₂ and 2 L of H₂O. The organic layer was washed with three 1-L portions of water and two 1-L portions of 10% aqueous NaHCO₃, dried, and evaporated under reduced pressure. The residue was chromatographed on a 30-g column of alumina-CH₂Cl₂. Elution of the column with 1 L of CH₂Cl₂ gave 7.0 g (98%) of **(R,R)(S,S)-23**; mp 215–216 °C, after recrystallization from CH₂Cl₂-cyclohexane. The ¹H NMR spectrum of the material was identical with that of **(R,R)-23**.¹⁰ Anal. Calcd for C₄₈H₅₆O₆: C, 79.09; H, 7.74. Found: C, 79.07; H, 7.68.

By a similar procedure, from 5.0 g of **(R,S)-2,3:4,5:13,14:15,16-tetra(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene**¹¹ was prepared 5.0 g (98%) of **(R,S)-23**: mp 200–201 °C (from CH₂Cl₂-cyclohexane); M⁺, *m/e* 728; ¹H NMR, 60 MHz, CDCl₃, δ 1.67 (m, CCH₂CH₂C, 16 H), 2.17 (m, ArCH₂, 8 H), 2.72 (m, ArCH₂, 8 H), 3.57 (m, OCH₂, 16 H), 6.79 (ABq, ArH, 8 H). Anal. Calcd for C₄₈H₅₆O₆: C, 79.09; H, 7.74. Found: C, 79.07; H, 7.68.

(R,R)(S,S)-, (R,R)-, and (R,S)-12,15,18,39,42,53,56,59,62,65-Decaoxanonacyclo[27.22.9.6^{10,20}.0^{3,8}.0^{22,27}.0^{30,35}.0^{37,60}.0^{44,52}.0^{46,51}]hexahexaconta-1-(52),2,8,10,19,21,27,29,35,37(60),44,46(51)-dodecaene ((R,R)-(S,S)-25, (R,R)-25, (R,S)-25). A solution of 2.7 g (3.7 mmol) of **(R,R)(S,S)-23** in 50 mL of CHCl₃ was diluted with 200 mL of acetic acid and heated to 65 °C. To this solution was added 9.0 g (300 mmol) of paraformaldehyde and 39 mL of concentrated HCl aqueous solution, and the resulting mixture was stirred at 65 °C for 4 h. The solution was cooled and then shaken with 300 mL of CHCl₃ and 1 L of H₂O, and the organic layer was washed with two 500-mL portions of water and 700 mL of a 10% NaHCO₃ aqueous solution. The organic layer was dried and then concentrated to 25 mL under reduced pressure, and the residue was chromatographed on 100 g of silica gel-CH₂Cl₂. Elution of the column with 2 L of CH₂Cl₂ gave 3.3 g (97%) of the tetrachloro compound **(R,R)(S,S)-24** as an oil: M⁺, *m/e* 920 (³⁵Cl); ¹H NMR, 60 MHz, CDCl₃, δ 1.67 (m, CCH₂CH₂C, 16 H), 2.14 (m, ArCH₂, 8 H), 2.77 (m, ArCH₂, 8 H), 3.58 (m, OCH₂, 16 H), 4.52 (ABq, CH₂Cl, 8 H), 7.08 (s, ArH, 4 H). This compound was used directly in the next reaction without further purification.

To a refluxing suspension of 3.0 g (62.5 mmol) of NaH (50% suspension in mineral oil) in 250 mL of THF stirred under N₂ was added over a period of 2 h a solution of 3.3 g (3.6 mmol) of the above **(R,R)(S,S)-24** and 0.5 g (8.1 mmol) of dry ethylene glycol in 250 mL of THF. The mixture was refluxed for 48 h and then cooled, the excess NaH was decomposed with CH₃OH, and the

mixture was shaken with 0.5 L of CHCl₃ and 1 L of H₂O. The organic layer was dried and then evaporated under reduced pressure, and the residue was dissolved in 30 mL of CH₂Cl₂ and chromatographed on 100 g of alumina-Et₂O. Elution of the column with 5 L of Et₂O gave 1.4 g (43%) of **(R,R)(S,S)-25** as a white solid: mp 300 °C (decomposition) after recrystallization from CH₂Cl₂-Et₂O and drying at 165 °C (0.01 mm) for 12 h; M⁺, *m/e* 900; ¹H NMR, 60 MHz, CDCl₃, δ 1.68 (m, CCH₂CH₂C, 16 H), 2.17 (m, ArCH₂, 8 H), 2.73 (m, ArCH₂, 8 H), 3.13 (m, OCH₂, 8 H), 3.68 (m, OCH₂, 16 H), 4.70 (ABq, ArCH₂O, 8 H), 7.02 (s, ArH, 4 H). Anal. Calcd for C₅₆H₆₈O₁₀: C, 74.64; H, 7.61. Found: C, 74.43; H, 7.57.

Application of the above chloromethylation procedure to 2.7 g of optically pure **(R,R)-23**¹⁰ gave 3.3 g (97%) of crude tetrachloro compound **(R,R)-24**, which was converted by the above procedure to 1.24 g (38%) of **(R,R)-25**; mp 310 °C (decomposition) after recrystallization from CH₂Cl₂-Et₂O and drying at 200 °C (0.01 mm) for 12 h. The ¹H NMR spectrum and the behavior of the compound were identical with those of its racemate, **(R,R)(S,S)-25**. The **(R,R)-25** sample gave [α]_D²⁵₅₇₈ +70°, [α]_D²⁵₅₄₆ +78°, and [α]_D²⁵₄₃₆ +132° (c 1, CHCl₃). Anal. Calcd for C₅₆H₆₈O₁₀: C, 74.64; H, 7.61. Found: C, 74.37; H, 7.50.

Application of the above chloromethylation procedure to 2.7 g of **(R,S)-23** gave 3.2 g (94%) of **(R,S)-24**: mp 280 °C (decomposition) after alumina-Et₂O chromatography and recrystallization from CH₂Cl₂-Et₂O; M⁺, *m/e* 920 (³⁵Cl); ¹H NMR, 60 MHz, CDCl₃, δ 1.66 (m, CCH₂CH₂C, 16 H), 2.12 (m, ArCH₂, 8 H), 2.72 (m, ArCH₂, 8 H), 3.48 (m, OCH₂, 16 H), 4.71 (ABq, ArCH₂Cl, 8 H), 7.10 (s, ArH, 4 H). Anal. Calcd for C₅₂H₆₀Cl₄O₆: C, 67.68; H, 6.55. Found: C, 68.02; H, 6.82.

To a warm (~40 °C) solution of 600 mg (0.65 mmol) of **(R,S)-24** and 120 mg (1.9 mmol) of ethylene glycol in 350 mL of THF under N₂ was added 1.0 g (21 mmol) of NaH, and the mixture was refluxed for 36 h. The crude product was isolated by the usual procedure, but without chromatography and, after crystallization from CH₂Cl₂-EtOAc, gave 465 mg (79%) of **(R,S)-25**: mp 325 °C (decomposition) after drying at 200 °C (0.01 mm) for 12 h; M⁺, *m/e* 900; ¹H NMR, 60 MHz, CDCl₃, δ 1.68 (m, CCH₂CH₂C, 16 H), 2.21 (m, ArCH₂, 8 H), 2.77 (m, ArCH₂, 8 H), 3.10 (m, OCH₂, 8 H), 3.64 (m, OCH₂, 16 H), 4.65 (ABq, ArCH₂O, 8 H), 7.01 (s, ArH, 4 H). Anal. Calcd for C₅₆H₆₈O₁₀: C, 74.64; H, 7.61. Found: C, 74.49; H, 7.60.

(R,R)-12,15,18,53,56,59-Hexaoxa-38,42,62,65-tetrathianocyclododecaene[27.22.9.6^{10,20}.0^{3,8}.0^{22,27}.0^{30,35}.0^{37,60}.0^{44,52}.0^{46,51}]hexahexaconta-1(52),2,8,10,19,21,27,29,35,37(60),44,46(51)-dodecaene ((R,R)-26). To a refluxing suspension of 3.0 g (62.5 mmol) of NaH (50%) in 250 mL of THF stirred under N₂ was added over a 2-h period a solution of 2.6 g (2.8 mmol) of tetrachloro compound **(R,R)-24** and 0.55 g (5.9 mmol) of 1,2-ethanedithiol in 250 mL of THF. The crude product was isolated in the usual manner and chromatographed on alumina-Et₂O to give 550 mg (20%) of **(R,R)-26**: mp 320 °C (decomposition), after recrystallization from CH₂Cl₂-Et₂O and drying at 165 °C (0.01 mm) for 12 h; M⁺, *m/e* 964; ¹H NMR, 60 MHz, CDCl₃, δ 1.61 (m, ArCH₂, 16 H), 2.08 (m, ArCH₂, 8 H), 2.73 (m, ArCH₂, SCH₂CH₂S, 16 H), 3.53 (m, OCH₂, 16 H), 3.64 (m, ArCH₂S, 8 H), 7.08 (s, ArH, 4 H); [α]_D²⁵₅₇₈ -271°, [α]_D²⁵₅₄₆ -316°, [α]_D²⁵₄₃₆ -616° (c 1, CHCl₃). Anal. Calcd for C₅₆H₆₈O₆S₄: C, 69.69; H, 7.10. Found: C, 69.94; H, 7.39.

2,2',3,3',5,5',6,6',8,8',9,9',11,11',12,12',14,14',15,15'-Eicosahydro-1,1',4,4',7,7',10,10',13,13',16,16'-dodecaoxabi(17,17'-cyclooctadeca[2',3'-b]naphthalene) ((R)(S)-27). To a refluxing solution stirred under N₂ of 0.318 g (1.00 mmol) of **(R)(S)-2,2',3,3'-tetrahydro-1,1'-dinaphthyl ((R)(S)-7)**¹² in 75 mL of dry THF was added dropwise a solution of 0.264 g (4.00 mmol) of 85% KOH in 8 mL of H₂O. The oily precipitate that separated was dispersed by addition of 8 mL of additional H₂O to produce a turbid suspension. To this stirred refluxing mixture was added in one portion 1.09 g (2.00 mmol) of pentaethylene glycol ditosylate⁸ dissolved in 2 mL of THF. The mixture was refluxed for 4 days, the solvent was evaporated under reduced pressure, and the residue was shaken with 25-mL portions of CH₂Cl₂ and H₂O. The aqueous layer was extracted with three 10-mL portions of CH₂Cl₂, and the combined organic extracts were dried and evaporated under reduced pressure to an oil. This material was chromatographed on a 6 × 1 in. diameter alumina dry column, which was eluted with mixtures of THF in CH₂Cl₂ to give an oil,

which after crystallization from $\text{Et}_2\text{O}-\text{CH}_2\text{Cl}_2$ gave the product as a solvate, which was dried at 142 °C (0.01 mm) for 2 days to give (*R,S*)-**27**, 0.23 g (30%): mp 160–161 °C; M^+ , m/e 722; ^1H NMR, 100 MHz, CDCl_3 , δ 3.1–3.9 (m, CH_2OCH_2 , 32 H), 3.9–4.2 (m, ArOCH_2 , 4 H), 4.2–4.4 (m, ArOCH_2 , 4 H), 7.05 (d, ArH, 4 H), 7.22 (s, ArH, 4 H), 7.1–7.4 (m, ArH, 2 H), 7.7 (d, ArH, 2 H). Anal. Calcd for $\text{C}_{40}\text{H}_{50}\text{O}_{12}$: C, 66.46; H, 6.97. Found: C, 66.28; H, 7.06.

2,3-(4-Bromo-2,3-naphtho)-1,4,7,10,13,16-hexaoxacyclooctadeca-2-ene (31) and 2,3-(1,4-Dibromo-2,3-naphtho)-1,4,7,10,13,16-hexaoxacyclooctadeca-2-ene (32). A solution of 0.42 mL of Br_2 (7.8 mmol) in 10 mL of CH_2Cl_2 was added dropwise to a solution stirred at 0 °C of 2.174 g (6.0 mmol) of 2,3-(2,3-naphtho)-1,4,7,10,13,16-hexaoxacyclooctadeca-2-ene (**30**)¹³ in 45 mL of CH_2Cl_2 . The material was stirred for 1 h, and washed with two 50-mL portions of 10% aqueous NaHSO_3 to destroy excess Br_2 . The combined aqueous layers were dried with MgSO_4 containing a little Li_2CO_3 . The solvent was evaporated under reduced pressure, and the residue was chromatographed on a 15 × 1 in. diameter silica gel dry column with Et_2O as mobile phase. Unlike the corresponding TLC behavior, the five bands on the column were ill-defined. The solid column was cut into five sections, and each was diluted with 10% EtOH in CH_2Cl_2 . The band with the highest R_f value produced on solvent evaporation crude dibromide **32**, which after recrystallization from EtOH gave 0.176 g (6%) of product as white needles: mp 109–110 °C; M^+ , m/e 518 (^{79}Br); ^1H NMR, 60 MHz, CDCl_3 , δ 3.75 (d, $\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2$, 12 H), 3.9–4.2 (m, $\text{ArOCH}_2\text{CH}_2$, 4 H), 4.2–4.5 (m, ArOCH_2 , 4 H), 7.4–7.7 (m, ArH,^{6,7} 2 H), 8.1–8.4 (m, ArH,^{5,8} 2 H). Anal. Calcd for $\text{C}_{20}\text{H}_{24}\text{Br}_2\text{O}_6$: C, 46.18; H, 4.65. Found: C, 46.23; H, 4.72.

The two bands with the next highest R_f values from the above column when eluted gave, upon evaporation of solvent and film drying at 50 °C (0.01 mm) for 24 h, monobromide **31** as a viscous oil: 1.70 g (65%); M^+ , m/e 440 (^{79}Br); ^1H NMR, 60 MHz, CDCl_3 , δ 3.7 (d, $\text{CH}_2\text{OCH}_2\text{CH}_2$, 12 H), 3.8–4.1 (m, $\text{ArOCH}_2\text{CH}_2$, 4 H), 4.1–4.5 (m, ArOCH_2 , 4 H), 7.05 (s, ArH,⁴ 1 H), 7.1–7.8 (m, ArH, 3 H), 7.8–8.2 (m, ArH,⁸ 1 H). Anal. Calcd for $\text{C}_{20}\text{H}_{23}\text{BrO}_6$: C, 54.44; H, 5.69. Found: C, 54.36; H, 5.54.

Conversion of 2,3-(4-Bromo-2,3-naphtho)-1,4,7,10,13,16-hexaoxacyclooctadeca-2-ene (31) to (*R*)(*S*)-27**.** To 0.0972 g (4.00 mmol) of dry Mg stirred under dry conditions (N_2) was added dropwise through a septum a solution of 1.50 g (3.41 mmol) of monobromide **31** in 4 mL of dry THF. A small amount of 1,2-dibromoethane was added to initiate the reaction. The mixture was stirred an additional 45 min after the addition was complete and was filtered under N_2 through a glass plug into a stirred mixture (N_2) of 39 mg (0.30 mmol) of anhydrous CaCl_2 ,¹⁴ 2 mL of THF, and 0.26 mL (3.4 mmol) of bromoethane. The resulting mixture was stirred for 1 h, warmed to reflux for 5 min, and shaken with 150 mL of H_2O and 0.7 mL of AcOH. The resulting mixture was extracted with four 20-mL portions of CH_2Cl_2 . The combined extracts were dried ($\text{MgSO}_4-\text{Li}_2\text{CO}_3$) and evaporated under reduced pressure to an oil. Addition of Et_2O to this oil precipitated 228 mg (18%) of debrominated material, **30**. Evaporation of the mother liquors gave an oil that was chromatographed on a 15 ×

0.5 in. diameter silica gel dry column with Et_2O as the mobile phase. The three UV-active bands were cut from the column, and product was eluted from each with 10% EtOH in CH_2Cl_2 (v/v). The fastest moving band gave 380 mg (25%) of starting bromide (**31**), the second band gave 73 mg (6%) of debrominated material **30**, and the slowest moving band gave 110 mg (9%) of crude product **27**. This material was recrystallized twice from $(\text{CH}_3)_2\text{CO}-\text{Et}_2\text{O}$ to give 29 mg (2.4%) of pure **27**, mp 160–161 °C, undepressed by admixture with **27** prepared by the alternative method (see above). The samples of **27** prepared by the two different routes give identical ^1H NMR and mass spectra (see above).

2,2',3,3',5,5',6,6',8,8',9,9',11,11',12,12'-Hexadecahydro-1,1',4,4',7,7',10,10',13,13'-decabi(20,20'-(14*H*)-cyclohexadeca[2',3'-*b*]naphthalene) (34). To a solution (stirred under N_2) of 14 g (40 mmol) of 3,3'-bis(hydroxymethyl)-2,2'-dihydroxy-1,1'-dinaphthyl (**1**)⁷ and 40.2 g (80 mmol) of tetraethylene glycol ditosylate⁸ in 1.5 L of THF was added 6.4 g (160 mmol) of NaOH in 30 mL of water. The mixture was refluxed for 72 h, concentrated to 600 mL under reduced pressure, and shaken with 1 L each of CH_2Cl_2 and H_2O . The aqueous layer was washed with two 100-mL portions of CH_2Cl_2 , and the organic extracts were dried (MgSO_4). The solvent was evaporated under reduced pressure. The residue was dissolved in 40 mL of CHCl_3 and chromatographed on 500 g of alumina (neutral, activity 1)- Et_2O . Elution of the column with 5 L of Et_2O and 4 L of 1% EtOH in Et_2O (v/v) gave 6.1 g (23%) of **34**: mp 103–104 °C, after recrystallization from $\text{Et}_2\text{O}-\text{CH}_2\text{Cl}_2$; M^+ , m/e 662; ^1H NMR, 60 MHz, CDCl_3 , δ 3.57 (m, OCH_2 , 32 H), 5.05 (ABq, ArCH_2 , 4 H), 7.18 (m, ArH, 6 H), 7.77 (m, ArH,⁵ 2 H), 8.03 (s, ArH,⁴ 2 H). Anal. Calcd for $\text{C}_{38}\text{H}_{46}\text{O}_{10}$: C, 68.86; H, 7.00. Found: C, 68.81; H, 7.11.

Registry No. (*R*)(*S*)-**1**, 55515-95-2; (*R*)-**2**, 70101-46-1; (*S*)-**2**, 70101-47-2; (*R*)(*S*)-**2**, 70144-24-0; (*R*)(*S*)-**3**, 70101-48-3; (*S*)-**4**, 70101-49-4; (*R*)(*S*)-**4**, 70144-25-1; (*R*)(*S*)-**5**, 70101-50-7; (*R*)(*S*)-**6**, 70101-51-8; (*R*)(*S*)-**7**, 61601-94-3; (*R*)(*S*)-**8**, 70101-52-9; (*R*)(*S*)-**9**, 70101-53-0; (*R*)(*S*)-**10**, 70101-54-1; (*R*)(*S*)-**11**, 70101-55-2; (*R*)(*S*)-**12**, 70101-56-3; (*R*)(*S*)-**13**, 70101-57-4; (*R*)(*S*)-**14**, 55442-54-1; (*R*)(*S*)-**16**, 70101-58-5; (*R*)(*S*)-**17**, 70101-59-6; (*S,S*)-**18**, 70144-26-2; (*S,S*)-**19**, 70101-60-9; (*R,R*)(*S,S*)-**20**, 70101-61-0; (*S,S*)-**20**, 70144-27-3; (*R,R*)(*S,S*)-**21**, 70101-62-1; (*R,R*)(*S,S*)-**22**, 70101-63-2; (*R,R*)(*S,S*)-**23**, 70144-28-4; (*R,S*)-**23**, 70144-29-5; (*R,R*)-**23**, 65390-92-3; (*R,R*)(*S,S*)-**24**, 70101-64-3; (*R,R*)-**24**, 70144-30-8; (*R,S*)-**24**, 70144-31-9; (*R,R*)(*S,S*)-**25**, 70101-65-4; (*R,R*)-**25**, 70144-32-0; (*R,S*)-**25**, 70144-33-1; (*R,R*)-**26**, 70101-66-5; (*R*)(*S*)-**27**, 61601-93-2; (*R*)(*S*)-**29**, 70101-67-6; **30**, 17454-52-3; **31**, 61602-03-7; **32**, 61601-95-4; (*R*)(*S*)-**34**, 70101-68-7; ClCH_2OMe , 107-30-2; (*R*)(*S*)-3,3'-bis(bromomethyl)-2,2'-dihydroxy-1,1'-dinaphthyl, 55442-33-6; thiourea, 62-56-6; triethylene glycol ditosylate, 19249-03-7; tetraethylene glycol ditosylate, 37860-51-8; pentaethylene glycol ditosylate, 41024-91-3; tetraethylene glycol, 112-60-7; pentaethylene glycol, 4792-15-8; (*R,R*)(*S,S*)-2,3:4,5:13,14:15,16-tetra(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene, 41024-97-9; (*R,S*)-2,3:4,5:13,14:15,16-tetra(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene, 41024-94-6; ethylene glycol, 107-21-1; 1,2-ethanedithiol, 540-63-6; Li^+ , 17341-24-1; Na^+ , 17341-25-2; K^+ , 24203-36-9; Cs^+ , 18459-37-5; NH_4^+ , 14798-03-9; Rb^+ , 22537-38-8.