Host–Guest Complexation. 8. Macrocyclic Polyethers Shaped by Two Rigid Substituted Dinaphthyl or Ditetralyl Units[1,2]

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Reported here are the syntheses and characterization of a large number of stereoisomeric macrocyclic polyethers (hosts) that contain rigid chiral units for studies of chiral recognition in molecular complexation with racemic alkylammonium salts (guests). These macrocyclic compounds contain six oxygens hexagonally arranged and held together by four ethylene (E) units and two differently substituted 1,1′-dinaphthyl units (D) bound to oxygen in their 2,2′ positions to give the general structure $D(OEOEO)_2D$. Also reported are similarly shaped compounds in which 1,1′-ditetralyl units (T) are bound to oxygen in their 2,2′ positions to give the general structures $T(OEOEO)_2D$ and $T(OEOEO)_2T$. The general shape of these compounds with all oxygens coplanar and turned inward places the naphthalene or tetralin rings in planes perpendicular to the plane of the macroring, with the two aryl rings protruding from each face of the macroring. Between the walls formed by these rigid units are chiral cavities, which are shaped further by substituents in the 3,3′ positions of the dinaphthyl or ditetralyl units. These 3,3′ substituents include CH_3, CH_2Cl, CH_2OH, $C(CH_3)_2OH$, $CH(CH_3)_2$, $CH_2OCH_2CO_2CH_3$, $CH_2OCH_2CO_2H$, $CH_2N(CH_2CH_2)_2O$, and Br. Substituents in the 6 position of the dinaphthyl unit diverge from the macroring and the cavities, and are used to manipulate solubility properties or to bond the hosts to solid supports. They are remote from the macroring binding sites and chiral barriers. These 6 substituents include Br, $Si(CH_3)_2OCH_3$, $COCH_3$, CO_2CH_3, CO_2H, $CH_2CO_2CH_3$, CH_2CH_2OH, $CH{=}CH_2$, $SO_3Ba_{1/2}$, and $C(CH_3)_3$. Optical resolutions of 3,3′-dimethyl-2,2′-dihydroxy-1,1′dinaphthyl and of 3,3′-dicarboxy-2,2′-dihydroxy-1,1′-dinaphthyl are reported. Catalytic reductions of the enantiomers of 2,2′-dihydroxy-1,1′-dinaphthyl, 3,3′-dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl, and dinaphthyl-containing macrocyclic polyethers converted the 1,1′-dinaphthyl units into the 5,5′,6,6′,7,7′,8,8′-octahydro-1,1-dinaphthyl (1,1′-ditetralyl) units with full preservation of configuration. The configurational stabilities to heat and catalysts and the maximum rotations of compounds containing chiral units were determined. The critical ring-closing steps were conducted without high dilution and went in yields that varied between about 17 and 64%. They were conducted under conditions that fully preserved the configurations of the chiral units. Generalizations useful in developing synthetic strategies emerged from this work: (1) Substituents in the 3 position of the dinaphthyl system had to be introduced before ring closure. (2) Alkyl, CH_2OH, $(CH_3)_2COH$, Br, and $CH_2N(CH_2CH_2)_2O$ substituents did not interfere with the ring-closing reactions. (3) Electrophilic substitution reactions of the macrocyclic ethers occurred in the 6 positions of the dinaphthyl and in the 3 positions of the ditetralyl units. (4) Only the Mannich reaction on 2,2′-dihydroxy-1,1′-dinaphthyl (dinaphthol) could be used to introduce substituents directly into the 3 positions of the dinaphthyl unit. (5) The chiral diphenolic starting materials and the macrocycles were configurationally stable to the conditions of the reactions to which they were submitted with the exception of the Mannich reaction. (6) The ring closures were the most satisfactory when $D(OEOEOTs)_2$ or $T(OEOEOTs)_2$ was treated with $D(OH)_2$ or $T(OH)_2$ in refluxing THF–KOH. The symmetry properties and shapes of the host compounds reported here are discussed.

Paper 7 of this series[4] reports the syntheses of a variety of macrocyclic host compounds containing one, two, or three chiral 1,1-dinaphthyl units incorporated into ring systems. Ether oxygen or pyridine nitrogen-containing units attached to the 2,2′ positions of the dinaphthyl group (or groups) were used to complete the cycles. The dinaphthyl units act as chiral barriers, and the heteroatoms provide binding sites for hydrogen bonding to the ammonium ions of amine salts, which are the guests in complexation.

Molecular models (Corey–Pauling–Koltun, or CPK) of hosts that contain two dinaphthyl units and six ether oxygens such as **1** indicate that the six oxygens in their more stable gauche conformations are about equally spaced from one another in a plane. The four naphthalene rings occupy four different planes each of which is perpendicular to that of the macrocycle. Two of the aromatic rings are above and tangent to the macroring and two are below and tangent to the macroring. Thus the space above and below the macroring is divided into two chiral cavities by the naphthalene rings which act as walls or steric barriers. Systems containing two cavities on each face are referred to as dilocular, since the substituents attached to an alkylammonium ion complexed on one face must be distributed in these two cavities. Dilocular hosts possess shapes remarkably dependent on the relative configurations of the two dinaphthyl units. When they possess the same configuration as in **1**, the naphthalene walls occupy parallel planes, the cavities are of about equal size, and the molecule is chiral. When the two dinaphthyl units possess opposite configurations, the naphthalene walls occupy planes that converge, as in **2**. On each face, one of the cavities is large and the other is small. If the dinaphthyl units are similarly substituted, these compounds are meso and achiral.

The shapes of the cavities are subject to the number and nature of substituents A and A′ attached at the 3 and 3′ positions of the naphthalene rings in **1** and **2**. Such substituents extend the chiral barriers and converge on the molecular parts of guests bound by the oxygens of the macroring. Substituents B and B′ attached to the 6 positions of the naphthalene rings in **1** and **2** diverge from the binding site and have little effect on the shapes of the cavities. Substituents in these positions can be used to manipulate the physical properties of such hosts or to attach them to solid supports.

The degree and direction of chiral recognition in complexation exhibited by dilocular hosts such as **1** have been reported to depend on substituents A.[2a,b,5] Dilocular hosts such as **1** have been attached through B substituents to solid supports for optical resolution of guests by chromatography.[2c,d] This paper reports the syntheses of compounds **1** and **2** in which substituents A and B have been extensively varied. Also reported are cycles in which the outer benzene rings of **1** and **2** have been reduced to their tetrahydro derivatives. The first Results section deals with the starting materials for ring clo-

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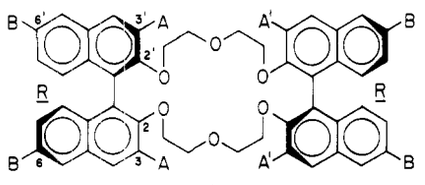
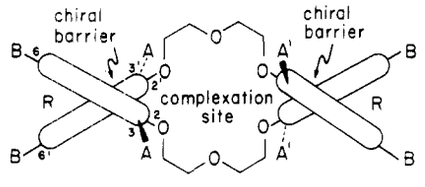


1



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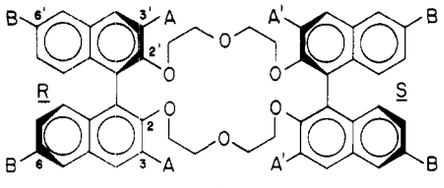

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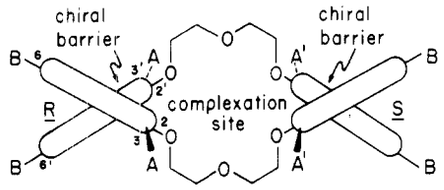
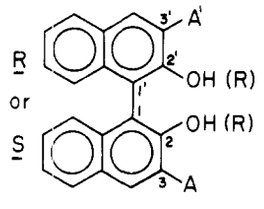


2 (projection formula)

sures. The second section describes the syntheses of the ring systems, and the manipulation of substituents once the rings are closed. The third section reports on how the dinaphthyl can be converted to ditetralyl units either before or after the rings are closed, and how both types of units can be incorporated into the same compounds. The first section under Discussion reports on the configurational stability of compounds that contain the dinaphthyl and ditetralyl units. The second section points to the symmetry properties and shapes of the host compounds of this paper. The results of complexation of many of these host compounds are described in future papers of this series.

Results

Dinaphthols, Ditetralols, and Derivatives. Use of 4-(butoxymethyl)morpholine[6] in a modified Mannich reaction



3, A=A'=H

4, A=A'=$CH_2N(CH_2CH_2)_2O$

5, A=H, A'=$CH_2N(CH_2CH_2)_2O$

6, A=A'=$CH_2N(CH_3)_2$

7, A=A'=CH_2OAc, R=Ac

8, A=CH_2OAc, R=H
A'=$CH_2N(CH_2CH_2)_2O$

9, A=A'=CH_2OH

10, A=H, A'=CH_2OH

11, A=CH_2OH, A'=$CH_2N(CH_2CH_2)_2O$

12, A=A'=CH_2Br

13, A=A'=CH_3

14, A=CH_3, A'=CH_2OH

15, A=CH_3, A'=$CH_2N(CH_2CH_2)_2O$

16, A=A'=CO_2H

17, A=A'=CO_2CH_3

18, A=A'=$C(CH_3)_2OH$

19, A=A'=CH_3, R=$(CH_2CH_2O)_2H$

20, A=A'=CH_3, R=$(CH_2CH_2O)_2Ts$

21, A=A'=H, R=$(CH_2CH_2O)_2Ts$

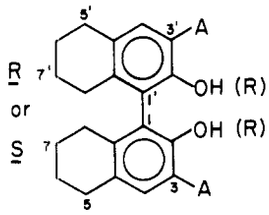
(160 °C) with 2,2'-dihydroxy-1,1'-dinaphthyl (3) gave mainly disubstituted product 4 (61%) but a small amount of monosubstituted compound 5 (15%) as well. Similarly, the bisamine 6 was prepared (33%).[7] When heated in acetic anhydride, 4 gave tetraacetate 7 (46%) and monoacetate 8 (39%), reduction of which with $LiAlH_4$ gave tetrol 9[8] (98%) and triol 11 (75%), respectively. Applications of similar procedures to aminodiol 5 gave triol 10 (80%). Substitution of propionic anhydride at reflux for acetic anhydride gave a better conversion to the tetraester, reduction of which gave tetrol 9 in 85% overall yield.

Key intermediate 3,3'-dimethyl-2,2'-dihydroxy-1,1'dinaphthyl (13) was prepared in several ways. Treatment of tetrol 9 with HBr in AcOH gave dibromide 12 (85%), reduction of which with $LiAlH_4$ gave 13 (98%). Direct but not exhaustive catalytic reduction of tetrol 9 with palladium and hydrogen gave diol 13 (33%) as well as incompletely reduced triol 14 (32%). Direct reduction of diaminodiol 4 with palladium and hydrogen produced 13 (44%) as well as aminodiol 15 (20%).

Racemic dimethyldiol 13 was resolved easily through the cinchonine and strychnine salts of its phosphoric acid diester, the former of which produced a 34% yield (racemate = 100%) of optically pure (+)-(*R*)-13, and the latter a 20% yield of optically pure (−)-(*S*)-13. The absolute configurations of these enantiomers were determined by their synthesis from optically pure diacids (+)-(*R*)-16 and (−)-(*S*)-16 (respectively) of established absolute configurations.[9] An improved preparation of 16[10] (41%) and its optical resolution to give its pure enantiomers[10] are also reported here, (+)-(*R*)-16 in 34% and (−)-(*S*)-16 in 30% yield. Reduction with $LiAlH_4$ of (+)-(*R*)-16 of maximum rotation gave (+)-(*R*)-9 (77%) and of (−)-(*S*)-16 gave (−)-(*S*)-9 (79%). Hydrogenolysis of each enantiomer with hydrogen and palladium gave (+)-(*R*)-13 (94%) and (−)-(*S*)-13 (98%), respectively. The four separately prepared samples of one or the other enantiomers of dimethyldiol 13 gave rotations of essentially the same values (disregarding signs), which points to their optical purities (see Experimental Section). Treatment of optically pure diacid (+)-(*R*)-16 gave diester (+)-(*R*)-17[9a] (76%), reduction of which with $LiAlH_4$ gave (+)-(*R*)-9 (63%), of essentially the same rotation observed for the compound prepared from diacid (+)-(*R*)-16 directly. Diester (+)-(*R*)-17 with CH_3Li gave tetrol (+)-(*R*)-18 (87%) as a benzene solvate.

As starting materials for directed ring closures (next section) involving two different kinds of biarylol units, $OCH_2CH_2OCH_2CH_2OH$ "arms" were attached at the 2,2' positions of the 3,3'-dimethyl-1,1'-dinaphthyl system. Treatment of optically pure (−)-(*S*)-3,3'-dimethyl-2,2'-dihydroxy-1,1'-dinaphthyl [(−)-(*S*)-13)] with NaH and $ClCH_2CH_2OCH_2CH_2OTHP$[4] (THP is the tetrahydropyranyl protecting group) gave the corresponding bis(THP) derivative, which was cleaved with acid to give dimethyldiol, (+)-(*S*)-19 (90%). Similarly, (+)-(*R*)-13 was converted to (−)-(*R*)-19 (68%). These two diols were converted to their respective ditosylates, (+)-(*S*)-20 (92%) and (−)-(*R*)-20 (93%), whose rotations were equal in magnitude and opposite in sign. Of all the dinaphthyl compounds prepared, only 19 and 20 coupled the (*R*) configuration with a (−) rotation and the (*S*) configuration with a (+) rotation. The ditosylates without the 3-methyl groups substituted in the naphthalene ring (21) were reported previously.[4]

Catalytic reduction of certain of the above 1,1'-dinaphthyl derivatives with platinum and hydrogen in glacial acetic acid gave the corresponding 1,1'-ditetralyl derivatives. As expected both on steric and electronic grounds, the outer aromatic rings were reduced selectively to leave the biphenyl moiety intact. Importantly for our purposes, when conducted at 25 °C, the reduction went with no loss in optical purity. Thus reduction of optically pure (+)-(*R*)-2,2'-dihydroxy-1,1'-dinaphthyl



22, A=H
23, A=CH_3
24, A=H, R=$(CH_2CH_2O)_2Ts$
25, A=CH_3, R=$(CH_2CH_2O)_2H$
26, A=CH_3, R=$(CH_2CH_2O)_2Ts$
27, A=Br

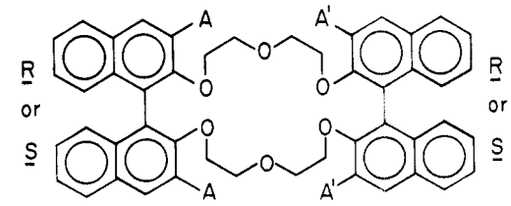
[(+)-(*R*)-**3**] at 25 °C over a 7-day period gave (+)-(*R*)-**22** (92%) as sharp-melting crystals. Similar reduction of optically pure (−)-(*S*)-**3** at 65 °C over a 3-day period gave (−)-(*S*)-**22** (92%) which melted over a 3 °C range, and whose rotations at four wavelengths were 8 ± 1% lower in magnitude than those for (+)-(*R*)-**22.** Apparently at 65 °C for three days, 4% of the material at some stage underwent inversion of configuration. The configurational stability to heat of compounds containing the 2,2′-disubstituted-1,1′-ditetralyl unit are discussed in a future section of this paper.

As a further test of the stereospecificity of the reduction reaction, optically pure dimethyldiol, (+)-(*R*)-**13,** was converted to its ditetralyl derivative (+)-(*R*)-**23** by two different routes. In the first, (+)-(*R*)-**13** was reduced directly to (+)-(*R*)-**23** (94%) to give a sharp-melting solid. In the second, the two phenolic hydroxyl groups of (+)-(*R*)-**13** were methoxymethylated to give the derivative with the more bulky and nonketolizable OCH_2OCH_3 groups. This derivative was then reduced with platinum and hydrogen in glacial acetic acid at 25 °C and the mixed acetal protective groups were removed to give (+)-(*R*)-**23** (81% overall) of the same melting point and rotation as that produced by direct reduction. These results make it highly unlikely that any racemization occurs during reductions conducted at 25 °C. Attempts to rearomatize **22** to give **3** under mild conditions failed.

Other 1,1′-dinaphthyl compounds with ether groups appended in the 2,2′ positions were similarly reduced to their 1,1′-ditetralyl derivatives. Thus the two hydroxyl groups of optically pure (−)-(*S*)-**3** were converted to OCH_2CH_2O-CH_2CH_2OH groups as before,[4] and this polyetherdiol was reduced and tosylated to give (−)-(*S*)-**24** (69% overall). Similarly, optically pure dimethyl two "armed" diol (+)-(*S*)-**19** was reduced to (+)-(*S*)-**25** (98%), and (−)-(*R*)-**19** gave (−)-(*R*)-**25.** These reduced diols were converted to their ditosylates, (+)-(*S*)-**26** and (−)-(*R*)-**26,** in 97 and 70% yields, respectively. The magnitudes of the optical rotations of these two sets of enantiomers were in satisfactory agreement with one another considering rotations were taken on incompletely chemically purified materials (all were glasses, and only a few milligrams were purified for analysis). Interestingly, the coupling of the (*R*) configuration with levorotatory character was carried over from **19** and **20** to their corresponding ditetralyl derivatives, **25** and **26.**

The substitution patterns in the bromination of 2,2′-dihydroxy-1,1′-ditetralyl [(+)-(*R*)-**22**] proved to be simpler than those observed with 2,2′-dihydroxy-1,1′-dinaphthyl (**3**). With the former compound (optically pure) bromination in CH_2Cl_2 at −30 °C gave (+)-(*R*)-**27** (98%) as a sharp melting solid. Bromination of **3** in CH_2Cl_2 at reflux led to 5,5′,6,6′-tetrabromo-2,2′-dihydroxy-1,1′-dinaphthyl (**28**), 81%, identified by its analysis and ^1H NMR and mass spectra. Bromination of 2,2′-dimethoxy-1,1′-dinaphthyl[12] gave 4,4′,6,6′-tetrabromo-2,2′-dimethoxy-1,1′-dinaphthyl, 91%, identified by its analysis and ^1H NMR and mass spectra.[13]

Macrocyclic Polyethers Containing Substituted Dinaphthyl Units. In the following ring-closing reactions, yields were not maximized nor were high dilution conditions employed. Dry THF and KOH (35%) as a reaction medium (at reflux) in general gave the highest yields.



(RR)(SS)-**29**, A=CH_3, A'=H
(RS)(SR)-**29**, A=CH_3, A'=H
(+)-(RR)-**29**, A=CH_3, A'=H
(−)-(SS)-**29**, A=CH_3, A'=H
(+)-(SR)-**29**, A=CH_3, A'=H
(RR)(SS)-**30**, A=CH_2OH, A'=H
(RS)(SR)-**30**, A=CH_2OH, A'=H
(+)-(RR)-**30**, A=CH_2OH, A'=H
(+)-(RR)-**31**, A=CH_2Cl, A'=H
(RR)(SS)-**32**, A=A'=CH_3
(RS)-**32**, A=A'=CH_3
(+)-(RR)-**32**, A=A'=CH_3
(−)-(SS)-**32**, A=A'=CH_3
(+)-(RR)-**33**, A=$C(CH_3)_2OH$, A'=H
(+)-(RR)-**34**, A=$CH(CH_3)_2$, A'=H
(RR)(SS)-**35**, A=$CH_2OCH_2CO_2CH_3$, A'=H
(RS)(SR)-**35**, A=$CH_2OCH_2CO_2CH_3$, A'=H
(+)-(RR)-**35**, A=$CH_2OCH_2CO_2CH_3$, A'=H
(RS)(SR)-**36**, A=$CH_2OCH_2CO_2H$, A'=H
(RR)(SS)-**36**, A=$CH_2OCH_2CO_2H$, A'=H
(+)-(RR)-**36**, A=$CH_2OCH_2CO_2H$, A'=H
(RR)(SS)-**37**, A=A'=CH_2OH
(RS)-**37**, A=A'=CH_2OH
38, A=A'=$CH_2N(CH_2CH_2)_2O$

Because of the high chiral recognition in complexation exhibited by the dimethyl substituted cycles **29,**[2b] all of its stereoisomers were prepared and characterized. Treatment of the racemic two-armed ditosylate[4] **20** with racemic diol **3** in DMF–NaH led to a mixture of diastereomers that was separated by chromatography to give (*R,S*),(*S,R*)-**29** (12%) and (*R,R*),(*S,S*)-**29** (8%), both of which were high melting solids. The ^1H NMR spectral chemical shift of the methyl groups of the (*R,R*),(*S,S*) isomer occurred at 0.1 ppm higher field than that for the (*R,S*),(*S,R*) isomer. Molecular models (CPK) of (*R,R*),(*S,S*)-**29** indicate that conformations are available which allow the methyl groups attached to one naphthalene ring to approach the face of a transannular naphthalene ring. In models of (*R,S*),(*S,R*)-**29,** these conformations are not available. The spectra of the two diastereomers differed even more in the OCH_2 region. Optically pure (*R,R*)-**29** was prepared in 32% yield from (*R*)-**3** and (*R*)-**20** in THF, KOH, and H_2O, whereas (*S,S*)-**29** was obtained (64%) from (*S*)-**3** and (*S*)-**20** (minimum of water). Optically pure (*S,R*)-**29** (16%) was prepared similarly from the reaction of optically pure dimethyldiol (*S*)-**13** and optically pure two-armed ditosylate, (*R*)-**21.** Comparisons of the ^1H NMR spectra of those isomers made by the stereodirected syntheses with those prepared from racemic materials identified the configurations of the two racemates. Although the two racemates were crystalline solids melting well over 200 °C, the (*S,R*), (*R,R*), and (*S,S*) enantiomers could not be induced to crystallize. They were purified carefully by both absorption and gel permeation chromatography, and the (*R,R*) and (*S,S*) isomers possessed rotations of the same magnitude but of opposite sign. The magnitude of rotation of (*S,R*)-**29** was much smaller than that of its diastereomers, a fact which correlates with its more "meso-like" structure.

Treatment of racemic tetrol **9** with racemic two-armed ditosylate **21** likewise produced (*R,R*),(*S,S*)-**30** (16%) and (*R,S*),(*S,R*)-**30** (8%) both as high melting solids with different ^1H NMR spectra. From (*R*)-**9** and (*R*)-**21,** (*R,R*)-**30** was prepared as a glass (28%) whose ^1H NMR spectrum served to differentiate between the two racemates. As expected, the greater acidity of the two phenolic hydroxyl groups of tetrol **9** led to their alkylation in the presence of 2 equiv of base in preference to the CH_2OH groups in the production of **30.** Treatment of (*R,R*)-**30** with thionyl chloride gave dichloride

(*R,R*)-**31** (76%), reduction of which with $LiAlH_4$ gave (*R,R*)-**29** (80%). The optical rotations of the two samples of (*R,R*)-**29** prepared by the two entirely different routes are in exact agreement with one another at λ 578 nm and have the exact magnitude as that of (*S,S*)-**29** at this wavelength. Furthermore, the magnitudes of the optical rotations of (*R,R*)-**29** prepared from dichloride (*R,R*)-**31** were the same at λ 546 and at λ 436 nm as the sample of (*S,S*)-**29** prepared by the other route.

The four stereoisomeric tetramethyl compounds **32** were also prepared, but in lower yields for the ring closures. From the reaction of racemic dimethyldiol **13** with racemic two-armed ditosylate **20** was isolated a 10% yield of the (*R,R*)-(*S,S*)-**32** and a 7% yield of (*R,S*)-**32,** both of which are high melting solids. These two compounds were also prepared in 5 and 4% respective yields by the reaction of diethylene glycol ditosylate with **13.** A smaller cycle closed by the reaction of one molecule of each reactant with one another was also produced in 8% yield. From (*R*)-**13** and (*R*)-**20,** (*R,R*)-**32** was obtained (28%), and from (*S*)-**13** and (*S*)-**20,** (*S,S*)-**32** was produced (28%). These compounds are also glasses and possess rotations of almost identical magnitude. They possess ^1H NMR spectra identical to that of (*R,R*),(*S,S*)-**32** but distinctly different from that of (*R,S*)-**32.** These comparisons were used to assign the configurations to the racemate [(*R,R*),(*S,S*)-**32**] and to the *meso* compound [(*R,S*)-**32**].

Isopropyl groups were introduced as substituents into the 3,3′ positions of the dilocular system as follows. Treatment of the tertiary diol (+)-(*R,R*)-**18** with the two-armed ditosylate (+)-(*R*)-**21** gave diol (+)-(*R,R*)-**33** (28%). This compound was dehydrated by heating it at 175 °C with pyridine-treated alumina,[14] and the two 2-propenyl groups were reduced to two isopropyl groups with hydrogen and palladium to give (+)-(*R,R*)-**34** (75%).

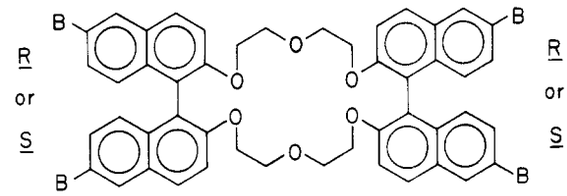
Carboxyl-terminated side chains were introduced into the hosts with the cyclic diols **30** as starting materials. For example, (*R,R*),(*S,S*)-**30** when mixed with NaH followed by methyl bromoacetate gave diester (*R,R*),(*S,S*)-**35** (71%). Similarly, (*R,S*),(*S,R*)-**30** gave (*R,S*),(*S,R*)-**35** (50%) and (*R,R*)-**30** gave (*R,R*)-**35** (77%). Hydrolysis of diesters (*R,S*),-(*S,R*)-**35,** (*R,R*),(*S,S*)-**35,** and (*R,R*)-**35** gave the corresponding diacids (*R,S*),(*S,R*)-**36** (94%), (*R,R*),(*S,S*)-**36** (83%), and (*R,R*)-**36** (76%).

Tetrols **37** are potential starting materials for preparation of polycyclic hosts in which four bridges link two dinaphthyl units. A mixture of the diastereomeric cyclic tetrols **37** was produced by treatment of racemic open-chain tetrol **9** with diethylene glycol ditosylate in THF–KOH. The two diastereoisomers produced were separated by chromatography and exhibited identical melting points. When mixed, the diastereomers gave a 20 °C melting point depression. They also exhibited different chromatographic behavior and ^1H NMR spectra. Their configurational identification made use of the fact that one was a racemate [(*R,R*),(*S,S*)-**37**] and the other a meso compound [(*R,S*)-**37**].

The structures were assigned to these diastereomers by a new partitioning method. Each was distributed between two layers composed of a mixture of $CDCl_3$, CD_3CO_2D, D_2O, (+)-α-phenylethylammonium bromide, and $NaPF_6$, whose composition was adjusted to allow nearly half of the host to be in each layer (^1H NMR spectra). The amine salt remained almost completely in the D_2O-rich layer. The layers were separated, the host was isolated from each layer, and optical rotations were taken on the four host samples produced. The rotation of product isolated from the $CDCl_3$-rich layer was positive and from the D_2O-rich layer was negative for the sample originally of the (*R,R*),(*S,S*) configuration. Zero rotation was observed for the product isolated from each layer when the (*R,S*) material was used. The yield of (*R,R*),(*S,S*)-**38** isolated from the original reaction mixture was 10%, and the yield of (*R,S*)-**38** was also 10%.

In a similar ring-closing reaction, racemic diaminodiol **4** was treated with diethylene glycol ditosylate in THF–*t*-BuOK. A 36% yield of 2,3,4,5-di-1,2-(3-*N*-morpholinomethylnaphtho)-1,6,9-trioxaundeca-2,4-diene was isolated and characterized (cyclic product of reaction of 1 mol of diethylene glycol ditosylate and of **4**). Also produced was a 51% yield of a sharp-melting compound which appeared to be either (*R,R*),(*S,S*)-**38** or (*R,S*)-**38.** The configuration was not determined, but the compound probably possesses the (*R,R*),-(*S,S*) configuration. Molecular models (CPK) of each diastereoisomer indicate the meso or (*R,S*) isomer to be somewhat more sterically congested than the (*R,R*) isomer.

Fortunately the dilocular systems were subject to direct electrophilic substitution, the 6 positions being the point of attack. The various stereoisomers of parent compound **39**



(RR)(SS)-**39**, B=H
(RS)-**39**, B=H
(+)-(RR)-**39**, B=H
(-)-(SS)-**39**, B=H
(RR)(SS)-**40**, B=Br
(RS)-**40**, B=Br
(+)-(RR)-**40**, B=Br
(RS)-**41**, B=$Si(CH_3)_2OCH_3$
(RR)(SS)-**42**, B=CH_3CO
(-)-(SS)-**42**, B=CH_3CO
(RR)(SS)-**43**, B=CO_2CH_3
(RR)(SS)-**44**, B=CO_2H
(-)-(SS)-**45**, B=$CH_2CO_2CH_3$
(SS)-**46**, B=CH_2CH_2OH
(-)-(SS)-**47**, B=$CH{=}CH_2$
(-)-(SS)-**48**, B=$SO_3(Ba)_{1/2}$
(-)-(SS)-**49**, B=$C(CH_3)_3$

listed were available from a previous study.[4] The chiral isomers used were optically pure and were freed from their crystalline solvates before use. Bromination of (*R,R*),(*S,S*)-**39** with excess bromine at 2 °C gave tetrabromide (*R,R*),(*S,S*)-**40** (88%). That the compound contained four bromine atoms was demonstrated by its analysis and mass spectrum. Similarly, (*R,S*)-**39** gave (*R,S*)-**40** (90%), and (*R,R*)-**39** gave (*R,R*)-**40.** The splitting patterns of the aryl protons in the ^1H NMR spectra of these compounds demonstrated the 6 positions were substituted. As a model reaction for attachment of dilocular systems to silica gel,[2c] (*R,S*)-**40** was tetralithiated with butyllithium, and this organometallic was added to a very large excess of dichlorodimethylsilane followed by methanol. Thus four dimethylmethoxysilyl groups were introduced into the 6 positions of the naphthalene rings to give (*R,S*)-**41** (84%).

Acetylation of (*R,R*),(*S,S*)-**39** with acetyl chloride in nitrobenzene at 25 °C gave the tetraacetyl derivative, (*R,R*),-(*S,S*)-**42** (93%). Similarly, (*S,S*)-**39** gave (*S,S*)-**42** (89%). The aryl proton splitting pattern in the ^1H NMR spectrum of this isomer was uniquely interpretable on the basis of substitution in the 6 positions of the naphthalene rings. Oxidation of (*R,R*),(*S,S*)-**42** with NaOBr and esterification of the tetraacid product gave tetraester (*R,R*),(*S,S*)-**43** (77%), whose ^1H NMR spectrum confirmed the substituents occupied the 6 positions. Hydrolysis of this tetraester gave tetracarboxylic acid (*R,R*),(*S,S*)-**44** (77%). This compound was almost totally insoluble in organic solvents but was readily soluble in aqueous alkali. The symmetrical distribution of the four CO_2^- groups prevented the salt from being a soap. Thus the highly lipophilic host **39** can be converted into a highly hydrophilic host by introduction of four carboxylate ions in the 6 positions.

Tetraacetyl compound (*S,S*)-**42** was used to prepare the

tetravinyl compound (*S,S*)-**47.** This compound was prepared for use as a highly chiral cross-linking agent for use in the polymerization of styrene and other vinyl monomers. Polymers cross-linked with (*S,S*)-**47** are visualized as containing chiral cavities potentially useful for resolving racemates by chromatography.[15]

Oxidative rearrangement[16] of (*S,S*)-**42** was accomplished with thallium trinitrate in methanol–perchloric acid–CH_2Cl_2. Tetraester (*S,S*)-**45** was produced in 98% yield, reduction of which gave tetrol (*S,S*)-**46** (90%). This compound was converted to its tetratosylate, which without characterization was treated with *t*-BuOK–Me_2SO to give the tetravinyl compound (*S,S*)-**47** (47%).

Sulfonation of (*S,S*)-**39** gave the tetrasulfonic acid characterized as its barium salt, (*S,S*)-**48** (50%). The aryl proton splitting pattern in the ^1H NMR spectrum of this compound established that sulfonation had occurred in the 6 position. This barium salt was converted to its lithium salt (a nonsoap), which was readily soluble in water and totally insoluble in organic media. This material was used in chiral recognition experiments conducted in aqueous media with chiral alkylammonium salts.[17]

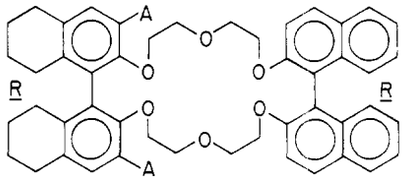
Attachment of long hydrocarbon chains (e.g., $C(CH_3)_2(CH_2)_{16}CH_3$) to the 6 position of these dilocular hosts would not only make them extremely lipophilic but also would produce high molecular weight waxes potentially useful as liquid phases for optical resolution in GLC chromatography. As a model experiment for attachment of such chains to these hosts, (*S,S*)-**39** was treated at −78 °C in dry CH_2Cl_2 with *t*-BuCl and $AlCl_3$ to give (*S,S*)-**49** (45%). The aromatic proton splitting pattern in the ^1H NMR spectrum of this compound was too complicated to be interpreted. However, it was similar enough to those of **45** and **47** that contain $CH_2CO_2CH_3$ and $CH{=}CH_2$ groups respectively in their 6 positions to make it clear that the four *tert*-butyl groups had entered the 6 positions as well.

Macrocyclic Polyethers Containing Ditetralyl Units. Molecular models of hosts containing the 2,2′-disubstituted 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-dinaphthyl (ditetralyl) unit are very similar in shape to those containing the dinaphthyl unit. However, their π base properties and aromatic substitution patterns were expected to be different from their parent dinaphthyl compounds. Therefore syntheses were undertaken of hosts containing two of these units and six oxygens incorporated into 22-membered macrocyclic rings.

Two general approaches proved viable. In the first, the cycles containing two dinaphthyl units were reduced directly to produce cycles containing two ditetralyl units. In the second and more flexible approach, the rings were assembled by combining ditetralyl with dinaphthyl units to give hosts containing one unit of each type.

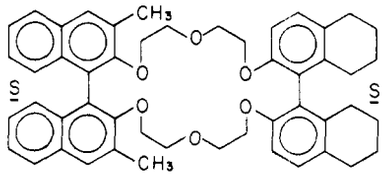
Reduction of unsubstituted bisdinaphthyl host (−)-(*S,S*)-**39**[4] with hydrogen in platinum–acetic acid at 25 °C for several days gave (−)-(*S,S*)-**50** in yields of 95–99%. Unlike the starting material, this product crystallized without forming a solvate. The same compound, (−)-(*S,S*)-**50,** of the same rotation was obtained in 54% yield by treatment of diol (−)-(*S,S*)-**22** with the reduced two-armed ditosylate (−)-(*S*)-**24** (THF–KOH). The enantiomer, (+)-(*R,R*)-**50,** was obtained by similar reduction of the cycle containing one dinaphthyl and one ditetralyl unit [(+)-(*R,R*)-**55**] whose synthesis is described later in this section. The rotations and melting points of the two enantiomers corresponded, a fact that indicates the reductions occurred without loss of optical purity. Similarly, dimethyl bisdinaphthyl host (+)-(*R,R*)-**29** was reduced to the dimethyl bisditetralyl host (+)-(*R,R*)-**51** (70%). The same compound was prepared by ring closing the ditetralyl two-armed ditosylate (+)-(*R*)-**24** with dimethyldiol (+)-(*R*)-**13** to make (+)-(*R,R*)-**57** which was reduced to (+)-(*R,R*)-**51.** The fact that the rotations of the two samples of (+)-(*R,R*)-**51** were within 2% of one another indicates that no loss of optical purity occurred during the reactions. Similarly, tetramethyl bisdinaphthyl system (+)-(*R,R*)-**32** was reduced to (+)-(*R,R*)-**52** (88%). The ^1H NMR and mass spectra of these reduced compounds and their elemental analyses indicated that only the outer rings underwent catalytic reduction. This result correlates with the facts that these outer rings are much less sterically hindered than the inner biphenyl systems, which appear to resist reduction. Reduction of the outer rings of **50** allows substituents to be introduced directly into the 3 position of the cycles. Thus bromination of (−)-(*S,S*)-**50** gave (+)-(*S,S*)-**53** (96%).

Ring closure of dibromodiol (+)-(*R*)-**27** and dinaphthyl two-armed ditosylate (+)-(*R*)-**21**[4] gave the dibromocycle (+)-(*R,R*)-**54** (68%) which contains one ditetralyl and one

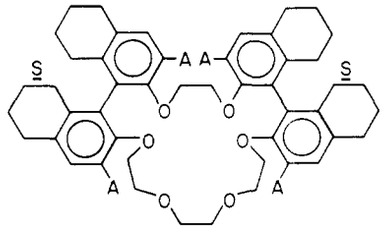


(+)-(RR)-54, A=Br (+)-(RR)-56, A=CH_3
(+)-(RR)-55, A=H

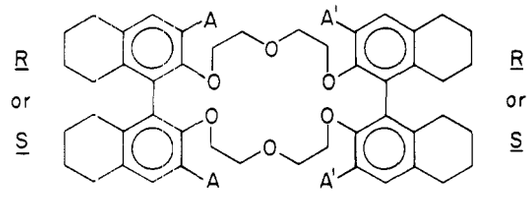
dinaphthyl unit. Lithiation of this substance and protonation of the organometallic produced gave (+)-(*R,R*)-**55** (96%), catalytic reduction of which gave (+)-(*R,R*)-**50** (92%). Dimethylditetralol, (+)-(*R*)-**23,** and dinaphthyl two-armed ditosylate (+)-(*R*)-**21** cyclized to produce (+)-(*R,R*)-**56** (70%), which contains a dimethylditetralyl unit on one side of the macrocycle and a dinaphthyl unit on the other. The isomer of this compound in which the methyl groups are on the dinaphthyl unit, (−)-(*S,S*)-**57,** was produced in 42% yield by treating dimethyldinaphthyl two-armed ditosylate (+)-(*S*)-**20** with ditetralol (−)-(*S*)-**22.**



(-)-(SS)-57



(-)-(SS)-58, A=H
(+)-(SS)-59, A=Br



(-)-(SS)-50, A=A'=H (+)-(RR)-52, A=A'=CH_3
(+)-(RR)-52, A=A'=H (+)-(SS)-53, A=A'=Br
(+)-(RR)-51, A=CH_3, A'=H

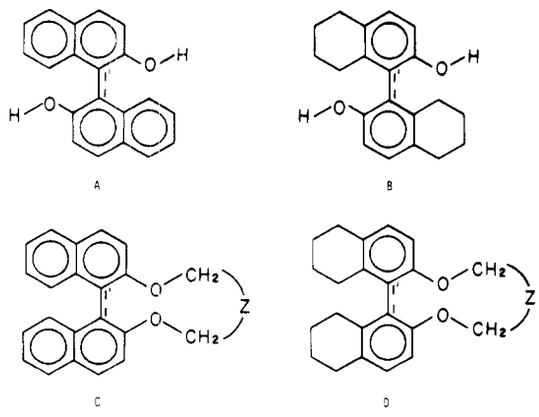
The isomer of **39** containing two dinaphthyl units of the (*S*) configuration connected by one $-OCH_2CH_2O-$ and one $-O(CH_2CH_2O)_3-$ bridge was catalytically reduced to give (−)-(*S,S*)-**58** (85%). Bromination of this compound gave (+)-(*S,S*)-**59** (94%) in which the bromine atom specifically entered the 3,3′ position of the ditetralyl units (^{1}H NMR spectra).

Discussion

Configurational Stabilities of Compounds Containing the Ditetralyl Units. Since many of the hosts described here were prepared for quantitative chiral recognition studies, their optical purities are important. Thus questions of what reaction conditions might induce reversal of the configurations of the dinaphthyl or ditetralyl units had to be answered. Studies already showed the cyclic hosts containing the dinaphthyl units were stable to temperatures of more than 200 °C.[4] Here we describe comparisons of the configurational stabilities of both the starting materials and cycles that contain the ditetralyl and dinaphthyl units. When heated in butanol at 118 °C for 24 h (+)-(*R*)-2,2′-dihydroxy-1,1′-dinaphthyl [(+)-(*R*)-**3**] lost ~1% of its rotation, whereas (+)-(*R*)-2,2′-dihydroxy-5,5′,6,6′,7,7′8,8′-octahydro-1,1′-dinaphthyl [(+)-(*R*)-**22**] lost ~2% of its rotation. When heated for 24 h at 100 °C in dioxane–water, 1.2 M in HCl, (+)-(*R*)-**3** lost 56% of its rotation whereas (+)-(*R*)-**22** lost <1% of its rotation. When heated at 118 °C for 24 h in butanol, 0.7 M in KOH, (+)-(*R*)-**3** lost 20% of its rotation, whereas (+)-(*R*)-**22** lost 7% of its rotation. Care was taken in the isolation of the compounds after treatment to avoid optical fractionation (rotations were taken on total samples). Small amounts of the rotational losses could reflect slight compound decomposition. Interestingly, the ditetralyl unit appears somewhat more configurationally stable to base and particularly to acid than the dinaphthyl unit. This latter fact correlates with the expectation that direct protonation of a 1,1-dinaphthyl system in the 1 or 1′ positions to give a configurationally unstable cation[4] occurs more readily than protonation in the 1 or 1′ positions of a 1,1′-ditetralyl system.[4]

The optical stabilities of bisdinaphthyl system (+)-(*R,R*)-**39** and bisditetralyl system (+)-(*R,R*)-**50** were compared by heating each in ampules at 226 °C in diphenyl ether for 1 week and reisolating the compounds. During the reisolation, traces of solvent and decomposition products were removed (silica gel chromatography). Since both compounds were glasses and total samples were used, no fractionation occurred. The rotations of the respective starting materials and recovered cycles were within 3% of one another, which indicates the compounds were essentially optically stable at this temperature for this time period.

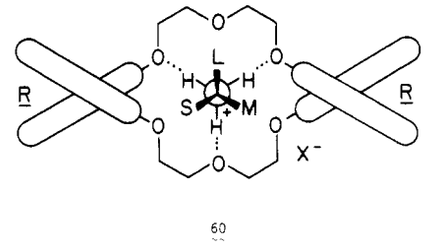
A comparison of CPK molecular models of dinaphthol **3** and ditetralol **22** suggests that the barriers to rotation in the two units should be somewhere nearly comparable. In both compounds, the transition states for racemization undoubtedly involve conformations A and B rather than C and D. The protons in A and B might well be in the 1 or 1′ positions, rather than on oxygen. Incorporation of the dinaphthyl and ditetralyl units in cycles containing 22-ring members or less forces racemization to occur via conformations C and D. Molecular model (CPK) examinations provide this conclusion and indicate that C and D are much higher energy than A and B.



The important question arises as to whether adsorption on platinum during catalytic reduction of the enantiomers of dinaphthyl **3** to those of ditetralol **22** also catalyzes the interconversion of enantiomers at some stage. Conceivably transition states for stereoisomer interconversion (e.g., A and B) that are much more planar than starting materials might be stabilized by adsorption on a platinum surface. Alternatively, platinum might transfer hydrogen atoms reversibly to the 1,1′ positions to produce short-lived intermediates with lower rotation barriers than those of A–D. Although such catalysis might exist, the barriers to interconversion must remain high enough to have allowed the reductions of dinaphthol **3** and dimethyldinaphthol **13** when carried out at 25 °C to have gone with negligible configurational loss. The evidence for this conclusion was discussed in an earlier section.

The question remains whether the *cycles* containing dinaphthyl units underwent configuration modification during reduction to ditetralyl units through stabilization of planar structures (e.g., C and D). Evidence that the cycles were stable to the conditions used in the reduction reactions is found in the fact that the same (or enantiomeric) compounds assembled in different reaction sequences gave rotations whose magnitudes were very close to one another. In the sequences compared, catalytic reduction in one of the two sequences was carried out before ring closure and the other after ring closure. In the first example, cycle (−)-(*S,S*)-**39** was reduced to (−)-(*S,S*)-**50,** which gave the same magnitude of rotation and mp as (+)-(*R,R*)-**50** obtained by a route that involved (+)-(*R,R,*)-**22** as one starting material. In the second example, cycle (+)-(*R,R*)-**29** was reduced to (+)-(*R,R*)-**51,** which gave a rotation only 2% higher than that obtained for a sample of (+)-(*R,R*)-**51** prepared from (+)-(*R*)-**24** (which contains a ditetralyl unit) as one starting material. In the latter synthetic route, the intermediates and the final product were not crystalline and the purification procedures depended on chromatographic procedures in which fractionation of enantiomers is highly improbable.

Symmetry Properties and Shapes of Host Compounds. These macrocyclic polyethers were prepared for study as host compounds for their chiral recognition properties in the complexation of enantiomeric primary amine salts as guests. Structure **60** is an idealized representation of the sterically

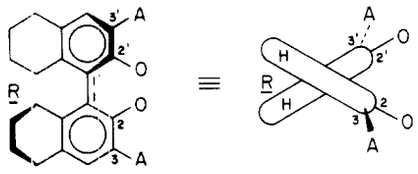


60

more stable diastereomeric complex between (*R,R*)-**39** and $LMSC^*NH_3{}^+X^-$, in which L is a large, M a medium, and S a small group. All of the hosts reported here possess three oxygens that can be spaced to hydrogen bond, in the tripod-like arrangement of structure **60,** with the $NH_3{}^+$ group of the guest (CPK models). Such an arrangement in a complex makes the C–N bond of the guest perpendicular to the best plane of the oxygens of the host. The L, M, and S groups are

distributed in the two chiral cavities between the naphthalene walls that protrude from that face of the complex from which the N–C bond protrudes.

In the following projection formulas of hosts whose syntheses have been described here, the presence of C_2 axes in the compounds they represent are indicated by the symbols ⊣ or ⌒, and planes of symmetry by the symbol ▮. The presence of the hosts of a citetralyl unit substituted in the 3 positions by A groups is indicated by partial structures **61.**

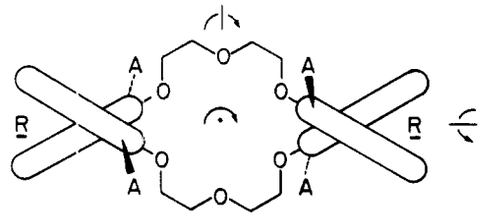


61

Hosts that contain at least one C_2 axis form the same complex when a guest is attached to either face. Such hosts are said to be nonsided, since each side is the stereochemical equivalent of the other. Hosts that contain three mutually perpendicular C_2 axes (D_2 symmetry) possess two cavities on each face between their naphthalene walls which although chiral are the stereochemical equivalent of one another. As a result, superimposable complexes are produced when L is distributed in any of the four cavities on the two faces of a host with D_2 symmetry. For example, if L were distributed in the lower and S and M in the upper cavity by conformational reorganization (180° rotation of the guest only about the C–N bond) in complex **60,** the new complex would be superimposable on the original by rotation of the whole new complex 180° around the C–N bond.

The shapes and symmetry properties of these macrocycles are affected both by the substituents in the 3 positions of the aryl units and by reduction of the outer rings of the dinaphthyl units. Structure **62** which possesses D_2 symmetry represents the shapes of several compounds reported here. In (*R,R*)-**32,** the A's are methyl groups, which are coplanar with their attached naphthalene rings and bonded oxygens. Thus the methyl groups extend the chiral barriers and decrease the cavity sizes.

In CPK molecular models of host **62** with A = H, we estimated that each naphthalene ring protruding from each face occupies ~65° of the 360° of that cylinder of space whose axis is perpendicular to the best plane of the oxygens and is centered equidistant from all six oxygen atoms turned inward. In the model used for this estimate, each oxygen was equidistant from its two nearest oxygen neighbors. Since two naphthalene rings protrude from each face, in **62** with A = H each cavity exposes ~115° of the cylinder.[4] Examination of models of **62** with A = CH_3 (*R,R*-**32**) suggests that each 3-methylnaphthyl group occupies about ~80°, which leaves only about 100° for each of the two cavities on each face. In **62** with A = CH_2OH (*R,R*-**37**), the two OH groups on each face are close enough to hydrogen bond one another with no conformation adjustments except those involving rotations about

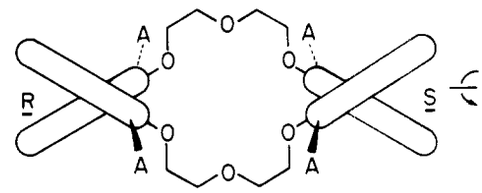


62

D_2-symmetry

the CH_2–O and O–H bonds. In such a conformation, no space is available for an alkylammonium ion guest. The close proximity of these pairs of $ArCH_2OH$ groups to one another suggests that the gas liberated when the racemate (*R,R*),-(*S,S*)-**37** melts at 170 °C is water and that the high temperature introduces two extra CH_2OCH_2 groups into the cycle. Interestingly, the mass spectrum of the cycle gives a strong M^+ minus $2H_2O$ peak. When the CH_2OH groups are turned outward, away from the axis of the cylinder, their space occupation of the cavities is only slightly greater than those of CH_3 groups. When the A groups of **62** are Br [(*R,R*)-**53**], again only about 100° of the cylinder is left for each cavity.

Structure **63** is the meso form of **62.** The naphthalene walls and their A substituents that protrude from each face converge on one another. When A = H as in (*R,S*)-**39,** ~60° of the cylinder is available in one cavity, ~170° remaining in the other. When A = CH_3 as in (*R,S*)-**32,** the methyl groups are close to touching one another. Only about 30° of the cylinder remains open to the small cavity, but the other cavity remains at ~170°. In **63** with A = CH_2OH [(*R,S*)-**37**], the OH groups

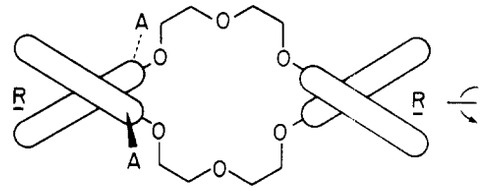


63

One mirror plane plus a C_2 axis

on the same face in the proper conformation can easily hydrogen bond one another. The gas liberated when (*R,S*)-**37** melts at 168–170 °C is probably water, a fact that correlates with the appearance in the mass spectrum of an ion with M^+ minus $2H_2O$. The (*R,S*) four-stranded cycle that possibly is formed looks in CPK models about comparably compressed to that of the (*R,R*) configuration.

Compound **64** with A = CH_3 [(*R,R*)-**29**] is chiral and possesses a C_2 axis, which means the two faces are stereochemically equivalent and the guest is nonsided. The larger of the

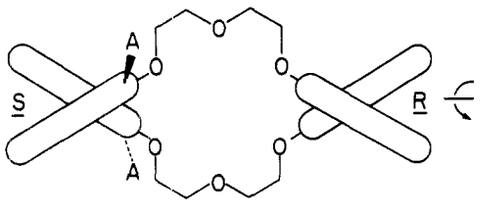


64

One C_2 axis

two cavities has available 115° and the smaller 100° of the imaginary cylinder of space. When A = CH_2OH [(*R,R*)-**30**] with the OH group turned outward, the cavity sizes are close to those of the compound with A = CH_3. With A = $C(CH_3)_2OH$ [(*R,R*)-**33**], either a CH_3 or OH is turned inward, and the smaller of the two cavities shrinks to ~90° or less, depending on whether an OH or CH_3 is turned toward the opposite naphthalene wall. When A = $CH(CH_3)_2$, the smaller of the cavity sizes can be as large as 100° with H turned inward, but as small as 60° with CH_3 inward.

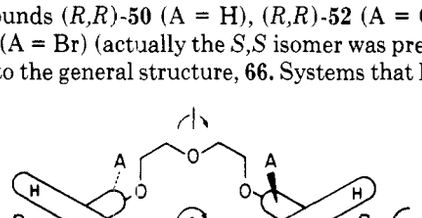
When A = H in **65,** the structure contains a mirror plane and a C_2 axis, as in (*R,S*)-**39.** However, when A = CH_3 as in (*S,R*)-**29,** the compound is chiral, possesses a C_2 axis, and is therefore nonsided. The two cavities on each face are different from those of any of the other compound. The smaller of the two has available only 45% of the cylinder and the larger 170° of the cylinder.



65
One C_2 axis

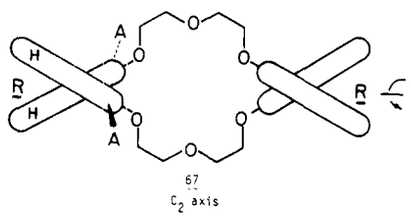
The compounds that contain two ditetralyl units with similar substituents (A groups) in their 3 positions are represented by projection structure **66**. Like structure **62**, **66** exhibits D_2 symmetry which means all four cavities are chiral and are stereochemically equivalent to one another. Most importantly, the molecules represented by **66** are nonsided. The substitution of these ditetralyl for the dinaphthyl units has in CPK molecular models only minor effects on their shapes and cavity sizes. *Provided the four methylene groups of the ditetralyl units are in the proper conformations,* the dihedral angles between the planes of the diphenyl part unit can be as small as the 60° estimated for the dinaphthyl units. This allows the two oxygens attached to each biaryl unit to be as close to one another as the oxygens of *gauche*-ethylene glycol. Again given the proper conformations, the dihedral angle appears able to be as large as ~120° without causing bond angle deformations of any consequence. When in the conformation with all oxygens turned inward and close together, the macroring places the oxygen's unshared electron pairs in positions that resemble those of 18-crown-6 (CPK molecular models). The main difference in shape between compounds **66** and **62** (provided the A groups are the same) occurs only in those parts of the cavities most distant from the axis of the imaginary cylinder. The saturated portions of the tetralin rings are thicker than the corresponding unsaturated portions of the naphthalene rings. Therefore the effects of the spacial differences between the ditetralyl and dinaphthyl systems on host–guest relationships are expected to be small except when guests possess large groups that extend far from the axis of the cylinder in the complexes. However, the basicities of the aryl oxygens and the π base strengths of the two types of units are expected to be somewhat different.

Compounds (*R,R*)-**50** (A = H), (*R,R*)-**52** (A = CH_3), and (*R,R*)-**53** (A = Br) (actually the *S,S* isomer was prepared) all conform to the general structure, **66**. Systems that lose two of

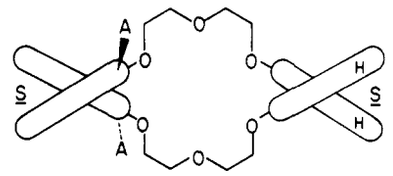


66
D_2-symmetry

their C_2 axes by combining a dinaphthyl with a ditetralyl unit are represented by general structures **67** and **68**. Compounds (*R,R*)-**54** (A = Br), (*R,R*)-**55** (A = H), and (*R,R*)-**56** (A = CH_3) all possess the general shape of **67**, whereas (*S,S*)-**57** conforms



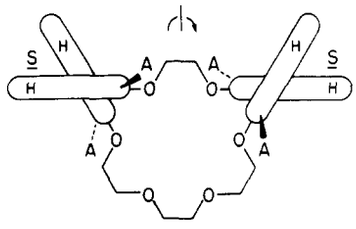
67
C_2 axis



68
C_2 axis

to the general shape of **68** in which A = CH_3. The cavity sizes in all of these compounds are estimated to be similar to those of the corresponding dinaphthyl parent compounds.

Compounds (*S,S*)-**58** (A = H) and (*S,S*)-**59** (A = Br) possess entirely different shapes than **62–66**. The two ditetralyl groups in these compounds are attached by one ethylene glycol unit and by a triethylene glycol unit. They possess the general shape suggested by **69**, which is chiral, but possess a C_2 axis



69
C_2 axis

and are therefore nonsided. The compound with A = H possesses cavities in CPK models similar to those of the parent bisdinaphthyl system.[4] The smaller of the two cavities on one face has ~55° of the imagined cylinder available whereas the larger has ~ 175°. When A = Br, the smaller cavity is narrowed to ~30°, and the larger to ~160°.

These results demonstrate feasibility for synthesizing a variety of potential host compounds whose symmetry properties, shapes, hydrophilicity, and lipophilicity are subject to manipulation. The syntheses reported here are highly modular. A few rigid units with different shapes and symmetry properties have been strung together with more flexible spacing and binding units to provide desired compounds. These syntheses make possible a semisystematic attack on the problem of host–guest complexation phenomena.

Experimental Section

General. Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. All ^1H NMR chemical shifts are given as δ in ppm from internal Me_4Si unless otherwise indicated and were recorded on a Varian HA-100 or T-60 spectrometer. Optical rotations were obtained with a Perkin-Elmer 141 polarimeter in a 1 dm thermostated cell. Gel permeation chromatograms were run on a $\frac{3}{8}$ in. by 20 ft column of styragel 100-Å beads in CH_2Cl_2 (30–70 μm particle size, exclusion limit of 1500 molecular weight) at a flow rate of 4 mL m^{-1} and a pressure of 200–400 lb/in.^{2}. Mass spectra were taken at 70 eV on an AEI Model MS-9 double-focusing spectrometer. All chemicals were reagent grade. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately prior to use. Dimethylformamide (DMF) was distilled from CaH_2 prior to use. All reactions that involved KOH, KO-*t*-Bu, $LiAlH_4$, or NaH were conducted in an inert atmosphere. All organic solutions were dried with magnesium sulfate. All noncrystalline macrocycles, once synthesized, were air sensitive and were therefore stored under argon at 0 °C.

3,3′-Bis(*N*-morpholinomethyl)-2,2′-dihydroxy-1,1′-dinaphthyl (4) and 3-*N*-Morpholinomethyl-2,2′-dihydroxy-1,1′-dinaphthyl (5). A solution of 100 g (0.35 mol) of 2,2′-dihydroxy-1,1′-dinaphthyl (3) in 850 g (4.9 mol) of 4-(butoxymethyl)morpholine[6] was heated at 160 °C under N_2 for 5 days (a precipitate of 4 started to form after 6 h). The reaction mixture was cooled, 300 mL of benzene was added with stirring, and after the mixture had stood 10 h at 25 °C the solid was collected, washed with 300 mL of ether, and dried at 25 °C (30 mm) to give 104 g (61%) of **4**. A sample of 5 g of this material was recrystallized from $CHCl_3$ and EtOAc to give 4.5 g of **4**, mp 300 °C. The 60 MHz ^1H NMR spectrum in $CDCl_3$ gave δ 7.60 (m, ArH, 4 H), 7.05

(m, ArH, 6 H), 3.98 (ABq, J_{AB} = 14 Hz, $ArCH_2N$, 4 H), 3.64 (m, OCH_2, 8 H), and 2.60 (m, NCH_2, 8 H). The mass spectrum gave M^+ 484. Anal. Calcd for $C_{30}H_{32}O_4N_2$: C, 74.36; H, 6.66; N, 5.78. Found: C, 74.23; H, 6.75; N, 5.66.

From the filtrate of the original reaction by chromatography was obtained **5** in 15% yield, mp 226–228 °C. Anal. Calcd for $C_{25}H_{23}O_3N$: C, 77.90; H, 6.01. Found: C, 77.84; H, 5.99.

3,3′-Bis(dimethylaminomethyl)-2,2′-dihydroxy-1,1′-dinaphthyl (6). Application of the same procedure to 42.9 g (0.15 mol) of 2,2′-dihydroxy-1,1′-dinaphthyl and 131 g (1 mol) of dimethylaminoisobutoxymethane[7] in 400 mL of isobutyl alcohol gave after 9 days at 160 °C 19.8 g (33%) of diamine **6**, mp 256–258 °C, M^+ 400. Anal. Calcd for $C_{26}H_{28}N_2O_2$: C, 77.97; H, 7.05. Found: C, 78.20; H, 6.88.

3,3′-Diacetoxymethyl-2,2′-diacetoxy-1,1′-dinaphthyl (7). A solution of 50 g (0.105 mol) of **4** in 1200 mL of acetic anhydride was refluxed for 8 days. The solution was cooled and evaporated at 30 mm, and the residue was dissolved in 150 mL of benzene. The residue was chromatographed on 1 kg of silica gel in hexane–benzene (2:1, v:v). Elution of the column with hexane–benzene mixtures eluted the desired product, **7**, which was recrystallized from ether to give 24.5 g (46%) of tetraacetate, mp 113–114 °C. Anal. Calcd for $C_{30}H_{26}O_8$: C, 70.03; H, 5.09. Found: C, 70.18; H, 5.18. Further elution of the column with ether–benzene produced 3-acetoxymethyl-3′-*N*-morpholinomethyl-2,2′-dihydroxy-1,1′-dinaphthyl (**8**), which was recrystallized from benzene–ether to give 16.5 g (39%), mp 115–117 °C. Anal. Calcd for $C_{28}H_{27}NO_5$: C, 73.51; H, 5.95. Found: C, 73.72; H, 6.04. Substitution of propionic anhydride at reflux for 4 days for acetic anhydride gave an 85% yield of the corresponding tetraester, which without characterization was converted to tetrol **9** (see next section).

3,3′-Bis(hydroxymethyl)-2,2′-dihydroxy-1,1′-dinaphthyl (9). To a refluxing suspension of 10.0 g (0.21 mol) of $LiAlH_4$ suspended in 1.5 L of dry ether was added dropwise 18.5 g (0.036 mol) of tetraacetate **7** dissolved in 100 mL of THF. The mixture was refluxed for 6 h and cooled, and ethanol was added dropwise at 0 °C to decompose excess reagent. To the mixture was added 400 mL of 15% hydrochloric acid and 300 mL of THF. The solution was stirred for 12 h and the organic layer was washed with 10% $NaHCO_3$ solution, and dried. The ether was evaporated at 30 mm, and the concentrated solution (250 mL) was refluxed with continuous replacement of THF by benzene. Tetrol **9** crystallized from hot benzene to give 12.5 g (98%), mp 222–224 °C (lit.[8] mp 231 °C), M^+ 346. Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.29; H, 5.24. Found: C, 76.44; H, 5.35.

3-Hydroxymethyl-2,2′-dihydroxy-1,1′-dinaphthyl (10). Application of the above procedures to 3-*N*-morpholinomethyl-2,2′-dihydroxy-1,1′-dinaphthyl **5** gave triol **10** (80%), mp 206–207 °C, M^+ 316. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.70; H, 5.29.

3-Hydroxymethyl-3′-*N*-morpholinomethyl-2,2′-dihydroxy-1,1′-dinaphthyl (11). Application of the above procedure to compound **8** gave triol **11** (75%), mp 190–192 °C, M^+ 415. Anal. Calcd for $C_{26}H_{25}O_4N$: C, 75.16; H, 6.06. Found: C, 75.07; H, 5.95.

3,3′-Bis(bromomethyl)-2,2′-dihydroxydinaphthyl (12). A slow stream of dry HBr was bubbled through a stirred suspension of 8.5 g of tetrol **9** in 120 mL of glacial acetic acid. After 10 min, the solid dissolved, the temperature increased, and a heavy precipitate formed. The mixture after standing 1 h was filtered and the filtrate was evaporated. The residue and filtrate were dissolved in 500 mL of ether and the solution was washed with water and then with a saturated solution of $NaHCO_3$. The solution was dried and evaporated to give 11 g of solid. One crystallization of this material from benzene gave 9.5 g (85%) of **12**: mp 215–216 °C; ^1H NMR (CD_3COCD_3) δ 8.05 (s, ArH^4, 2 H), 7.84 (q, ArH^5, 2 H), 7.22 (m, $Ar^{6,7}$, 4 H), 6.94 (m, ArH^8, 2 H), 4.84 (s, $ArCH_2Br$, 4 H); M^+ 472. Anal. Calcd for $C_{22}H_{16}O_2Br_2$: C, 55.96; H, 3.41. Found: C, 55.94; H, 3.53.

3,3′-Dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl (13). To a suspension of 3.0 g of $LiAlH_4$ in 350 mL of dry ether was added 7.08 g of the above dibromide **12** dissolved in 100 mL of THF. The mixture was refluxed for 4 h and stirred at 25 °C for 12 h more. At 0 °C, 25 mL of 95% ethanol was cautiously added, followed by 300 mL of 15% hydrochloric acid and 100 mL of THF. The layers were separated and the organic layer was washed twice with 10% $NaHCO_3$ solution and with water and was dried and evaporated. The residue was crystallized from benzene to give 4.7 g (98%) of dimethyldiol **13**, mp 205 °C. The ^1H NMR spectrum in $CDCl_3$ gave δ 7.76 (m, $ArH^{4,5}$, 4 H), 7.17 (m, ArH, 6 H), 5.05 (s, OH, 2 H), and 2.47 (s, CH_3, 6 H); mass spectrum M^+ 314. Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.98; H, 5.85.

Dimethydiol **13** was also prepared by catalytic reduction of tetrol **9**. A solution of 6.0 g of **9** in 60 mL of 95% ethanol was stirred with 3.0 g of 10% palladium on charcoal under 1 atm of hydrogen for 8 h. The mixture was filtered and the filtrate was evaporated under vacuum and chromatographed on 100 g of silica gel. Elution of the column with benzene gave dimethyldiol **13**, 1.83 g (33%), mp 205 °C, undepressed by admixture with an authentic sample. Elution with 1:1 (v:v) benzene–CH_2Cl_2 gave 1.9 g (32%) of 3′-hydroxymethyl-3-methyl-2,2′-dihydroxy-1,1′-dinaphthyl (**14**): mp 204 °C (from benzene); M^+ 330; ^1H NMR ($CDCl_3$) δ 7.82 (m, $ArH^{4,5}$, 4 H), 7.16 (m, ArH, 6 H), 4.93 (s, $ArCH_2$, 2 H), and 2.50 (s, CH_3, 3 H). Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.96; H, 5.68.

Elution of the column with 98:2 (v:v) CH_2Cl_2–isopropyl alcohol gave 1.0 g (17%) of starting tetrol, **9**.

Reduction of diaminediol **4** gave dimethyldiol **13** and 3-*N*-morpholinomethyl-3′-methyl-2,2′-dihydroxy-1,1′-dinaphthyl (**15**). A mixture of 2.0 g of diaminediol **4**, 80 mL of glacial acetic acid, 120 mL of 95% ethanol, and 1.0 g of 10% palladium on charcoal was stirred under 1 atm of H_2 for 15 h. The product was isolated by chromatography on 100 g of silica gel. Benzene eluted 0.56 g (44%) of dimethyldiol **13**, mp 206 °C, undepressed by admixture with an authentic sample. Elution of the column with 1:1 benzene–CH_2Cl_2 gave 0.280 g (20%) of aminodiol **15**, mp 185 °C, from CH_2Cl_2–ether: M^+ 399; ^1H NMR ($CDCl_3$) δ 7.72 (m, $ArH^{4,5}$, 4 H), 7.16 (m, ArH, 6 H), 3.96 (s, $ArCH_2N$, 2 H), 3.66 (t, CH_2O, 4 H), 2.60 (t, CH_2N, 4 H), and 2.49 (s, CH_3, 3 H). Anal. Calcd for $C_{26}H_{25}O_3N$: C, 78.17; H, 6.31. Found: C, 78.09; H, 6.37.

Optical Resolution of 3,3′-Dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl (13). A slurry of 146 g of racemic **13**, 750 mL of CH_2Cl_2, and 84.5 g of $POCl_3$ was stirred under N_2 and 111.3 g of triethylamine was added slowly at a rate that maintained gentle reflux. After addition was complete, the solution was stirred an additional hour and extracted twice with 300 mL of water. The solution was dried and evaporated and the crude chlorophosphate was stirred with 750 mL of THF and 200 mL of water at 50 °C for 1 h. To this solution, 700 mL of ethyl acetate was added, the layers were separated, and the organic layer was washed with 200 mL of water and with 200 mL of brine, dried, and evaporated under vacuum to produce white crystals of the phosphoric acid diester of weight 129 g (75%), mp >300 °C, M^+ 376.

A mixture of 60 g (0.160 mol) of the above acid ester, 47.0 (0.160 mol) of cinchonine, and 800 mL of methanol was warmed to reflux, and to the solution was added 149 mL of water. The solution was cooled to 25 °C, and the crystalline salt that separated was collected, washed, and dried to give 40.8 g of salt (38% based on racemate = 100%). This material was recrystallized three times from methanol–water to give 32.0 g (30%) of salt: $[\alpha]^{25}_{578}$ −291°, $[\alpha]^{25}_{546}$ −339°, $[\alpha]^{25}_{436}$ −632° (*c* 1.1, DMF).

The (−)-salt, 40.0 g (0.06 mol), was shaken with 1 L of ether and 500 mL of 5 M hydrochloric acid. The resulting slurry was extracted with ether in a continuous extractor until all solids dissolved (4 days). The ether layer was evaporated to give a white foam: weight 21.5 g (95%); $[\alpha]^{25}_{436}$ −1121°, $[\alpha]^{25}_{546}$ −650°, $[\alpha]^{25}_{578}$ −561° (*c* 1.0, MeOH); mp >300 °C. In 200 mL of dry THF was suspended 2.0 g (0.53 mol) of $LiAlH_4$, and dropwise a 50 mL of THF solution of this acid diester was added at a rate to maintain a gentle reflux. The reaction mixture was cooled to 25 °C and stirred for 8 h. Excess reducing agent was destroyed by adding cautiously 10 ml of ethyl acetate. The aluminum salts produced were treated in succession with 2 mL of water, 2 mL of 40% NaOH solution, and 3 mL of water. The salts were filtered and washed with fresh THF. The organic layers were combined and evaporated under vacuum. The resulting oil was dissolved in CH_2Cl_2, washed with water and brine, and dried. Evaporation of the solvent at reduced pressure gave 14.9 g (90%) of white crystals, recrystallization of which from benzene gave dimethyldiol, (+)-(*R*)-**13**, which after heating for 8 h at 110 °C (0.05 mm) to remove benzene gave mp 200–201 °C: ^1H NMR ($CDCl_3$) δ 7.76 (m, ArH, 4 H), 7.17 (m, ArH, 6 H), 5.05 (s, OH, 2 H), 2.47 (s, 6 H); M^+ 314; $[\alpha]^{25}_{436}$ +131.3°, $[\alpha]^{25}_{546}$ +45.7°, and $[\alpha]^{25}_{578}$ +37.3° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.92; H, 5.85.

The mother liquors from the above cinchonine salt formation and purification were evaporated under vacuum to a gel, which when dried at 100 °C under vacuum gave 68.2 g of fine powder. This material was suspended in 1 L of 5 M HCl solution and continuously extracted with ether until a homogeneous aqueous solution was obtained. The ether was evaporated to yield a white foam, weight 34.8 g (58% of original acid), $[\alpha]^{25}_{436}$ +923° (73% optically pure).

In 52 mL of hot ethanol, 2.0 g (0.053 mol) of the above (+)-acid and 1.77 g (0.053 mol) of strychnine were mixed to give a solution. When cooled, fine white crystals separated, which were recrystallized from methanol–water to give 2.0 g (48%) of salt, $[\alpha]^{25}_{436}$ +672.0° (*c* 1.0, DMF), which did not change on further recrystallization. This salt (1.0 g) was converted to its acid by the same procedure as that used

for the cinchonine salt to give 0.47 g (89%) of (+)-acid diester, $[\alpha]^{25}_{436}$ +1218°, $[\alpha]^{25}_{546}$ +869°, $[\alpha]^{25}_{578}$ +566° (*c* 1.0, MeOH). Recrystallization of this material from methanol did not change these rotations. By the same procedure used for the (−)-acid diester, 0.300 g of this (+)-acid diester was converted to 0.224 g of dimethyldiol (−)-(*S*)-**13**, which after recrystallization from benzene and drying for 8 h at 110 °C (0.05 mm) to remove benzene gave 0.203 g (82%) of white crystals: $[\alpha]^{25}_{436}$ −129.8°, $[\alpha]^{25}_{546}$ −45.1°, and $[\alpha]^{25}_{578}$ −36.9° (*c* 1.0, $CHCl_3$); mp 200–202 °C; ^1H NMR ($CDCl_3$) δ 7.72 (m, ArH, 4 H), 7.17 (m, ArH, 6 H), 2.48 (s, CH_3, 6 H); M^+ 314. Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 84.01; H, 5.70.

2,2′-Dihydroxy-1,1′-dinaphthyl-3,3′-dicarboxylic Acid (16). A mixture of 3-hydroxy-2-naphthoic acid (72 g, 0.383 mol) and NaOH (14.4 g, 0.36 mol) in 1 L of water was heated to reflux in a 12-L flask. With vigorous stirring and refluxing, a hot solution of $FeCl_3 \cdot 6H_2O$ (108 g, 0.4 mol) in 200 mL of water was added dropwise (15 min). The mixture foamed as greenish-brown precipitates separated. After being stirred at reflux for 45 min, the mixture was cooled and a solution of 80 g (2 mol) of NaOH in 1 L of water was added, followed by 600 mL of concentrated hydrochloric acid. The mixture was stirred for 20 min, and the yellow precipitate that separated was filtered, washed with 350 mL of 10% HCl and 600 mL of H_2O, and dried. To a hot solution of the 73.5 g of dried solid in 370 mL of THF was added 59.8 g (0.59 mol) of triethylamine. The solution produced large brown plates when cooled to 25 °C for 1 day and to 0 °C for 1 day, which were collected and washed with cold THF to give 47 g of salt. This material was dissolved in 200 mL of 5% aqueous NaOH, and the resulting solution was washed once with ether. The aqueous layer was filtered, and the filtrate was acidified with concentrated hydrochloric acid to pH ~1. The deposited solid (**16**) was collected, water washed, and dried to give a yellow powder (29.5 g, 41%), mp >285 °C. This material was used directly in the following optical resolution.

Resolution of 2,2′-Dihydroxy-1,1′-dinaphthyl-3,3′-dicarboxylic Acid (16). To a suspension of 61.2 g (0.164 mol) of racemic **16** in 700 mL of methanol was added a solution in 20 mL of methanol of 50.0 g (0.345 mol) of optically pure L-leucine methyl ester, $[\alpha]^{25}_{589}$ +15.3° (neat). The reddish-brown solution was heated on a steam bath for 5 min and cooled to 25 °C for 1 day and to 0 °C for 1 day. The salt that separated was filtered, washed with a small amount of methanol, and dried to give 50.3 g (92%) of yellow crystals. The crystals were powdered in a mortar, and the powder was digested in three successive portions of 200 mL of hot methanol at reflux with stirring for 1 h. The rotations (*c* 0.3, MeOH) and weights of the solids obtained at each stage were as follows: before digestion, $[\alpha]^{25}_{578}$ +99.7°, weight 50.0 g; first digestion, $[\alpha]^{25}_{578}$ +117.8°, weight 43 g; second digestion, $[\alpha]^{25}_{578}$ +124.9°, weight 39.6 g; third digestion, $[\alpha]^{25}_{578}$ +123.0°, weight 37.5 g. The final powder was dissolved in 200 mL of water containing 6 g of NaOH. The resulting solution was washed with ether, filtered, and acidified to pH 1 to give a yellow precipitate, which was collected, washed, and dried at ca. 110 °C under vacuum to give (+)-(*R*)-**16**, 20.9 g (34%, racemate = 100%). An analytical sample was recrystallized from glacial acetic acid and had to be dried at 138 °C for 24 h at 0.05 mm to free it of solvent: needles; mp >285 °C; $[\alpha]^{25}_{578}$ +194°, $[\alpha]^{25}_{589}$ +185° (*c* 1.08, pyridine), reported[10a] $[\alpha]^{15}_{589}$ +179° (pyridine). Anal. Calcd for $C_{22}H_{14}O_6$: C, 70.58; H, 3.77. Found: C, 70.48; H, 3.94.

The mother liquor from the original salt was evaporated to a brown oil which was mixed with 60 mL of methanol and filtered from an insoluble yellow powder (which was methanol washed), and the oil was evaporated. The residual salt was converted back (see above) to diol diacid **16** enriched in the (−) isomer, 29.1 g. To a suspension of 29.0 g of this powder in 200 mL of methanol was added 23.5 g (0.233 mol) of triethylamine, and the resulting hot clear dark-red solution was allowed to stand at 25 °C for 2 days. The solid that separated was air dried (36.5 g) and recrystallized from 365 mL of methanol containing 3 mL of triethylamine to give 29.6 g of large plates of the salt. This material was converted to its acid (see above) to give after drying at 110 °C under vacuum for 24 h (−)-(*S*)-**16** as a yellow powder: 18.2 g (30%, racemate = 100%); mp >285 °C; $[\alpha]^{25}_{546}$ −246°, $[\alpha]^{25}_{578}$ −203°, $[\alpha]^{25}_{589}$ −190° (*c* 0.750, pyridine), reported[10b] $[\alpha]^{20}_{589}$ −171° (pyridine). The ^1H NMR spectra in dimethylacetamide of the two enantiomers were identical to one another.

(+)-(*R*)-3,3′-Bis(hydroxymethyl)-2,2′-dihydroxy-1,1′-dinaphthyl, (+)-(*R*)-9, and (−)-(*S*)-9. A solution of the above diacid diol (+)-(*R*)-**16** (7.49 g or 20 mmol) in 60 mL of THF was added to a suspension of $LiAlH_4$ (6.08 g or 160 mmol) in 200 mL of THF, which was refluxed for 9 h. The cooled reaction mixture was stirred with 90 mL of 50% hydrochloric acid and 100 mL of ether. The organic layer was separated, and the aqueous layer was extracted with a mixture of ether–THF. The combined organic layers were washed with brine, dried, and evaporated with added benzene to give a yellow solid. Recrystallization of this material from THF–benzene gave prisms (solvate) which when dried at 138 °C at 0.05 mm for 24 h gave (+)-(*R*)-**9**: 5.35 g (77%); mp 192–195 °C; $[\alpha]^{25}_{546}$ +78.7° (*c* 1.2, THF). Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.28; H, 5.24. Found: C, 76.39; H, 5.36.

A similarly conducted reduction of optically pure (−)-(*S*)-**16** gave (−)-(*S*)-**9** in 79% yield: mp 190–193 °C; $[\alpha]^{25}_{546}$ −77.8° (*c* 1.1, THF). This material gave M^+ 349 and the same ^1H NMR spectrum in CD_3COCD_3 as (*R*)(*S*)-**9** as follows: δ 7.98 (s, Ar^4H, 2 H), 7.80 (m, Ar^5H, 2 H), 7.18 (m, ArH, 6 H), and 4.92 (s, CH_2, 4 H).

(+)-(*R*)-3,3′-Dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl, (+)-(*R*)-13, from (+)-(*R*)-2,2′-Dihydroxy-1,1′-dinaphthyl-3,3′-dicarboxylic Acid, (+)-(*R*)-16, and (−)-(*S*)-13 from (−)-(*S*)-16. Diacid diol (+)-(*R*)-**16**, $[\alpha]^{25}_{589}$ +185° (*c* 1.08, pyridine), was reduced to tetrol (+)-(*R*)-**9** by the above procedure and the tetrol reduced to dimethyldiol (+)-(*R*)-**13** as follows. A mixture of 1 g (2.9 mmol) of (+)-(*R*)-**9**, 60 mL of ethyl acetate, and 1 g of 10% palladium on charcoal was reduced at 25 °C for 20 h under 3 atm of H_2 on a Parr apparatus. The mixture was filtered and evaporated and the product was chromatographed on 60 g of silica gel in CH_2Cl_2 to give product recrystallized from benzene and dried at 110 °C at 0.05 mm for 8 h to remove benzene to give 0.85 g (94%) of (+)-(*R*)-**13**: mp 197–199 °C; $[\alpha]^{25}_{436}$ +125.0°, $[\alpha]^{25}_{546}$ +44.2°, $[\alpha]^{25}_{578}$ +36.3° (*c* 1, $CHCl_3$). The ^1H NMR spectrum and TLC behavior of this material were identical to those of (+)-(*R*)-**13** prepared by direct resolution.

Similarly, diacid diol (−)-(*S*)-**16**, $[\alpha]^{25}_{589}$ −190° (*c* 1, pyridine), was reduced to tetrol (−)-(*S*)-**9**, 1.0 g (2.9 mmol) of which was hydrogenated to give 0.89 g (98%) of dried (8 h at 110 °C (0.05 mm)) (−)-(*S*)-**13**, which gave: mp 199–121 °C; $[\alpha]^{25}_{436}$ −128.8°, $[\alpha]^{25}_{546}$ −45.1°, and $[\alpha]^{25}_{578}$ −36.8° (*c* 1, $CHCl_3$).

(+)-(*R*)-3,3′-Dicarbomethoxy-2,2′-dihydroxy-1,1′-dinaphthyl, (+)-(*R*)-17. To a solution of 5.48 g (14.6 mmol) of diacid diol (+)-(*R*)-**16** (see above), $[\alpha]^{25}_{578}$ +190° (*c* 1.1, pyridine), in 70 mL of THF was added a solution of CH_2N_2 in 70 mL of ether (prepared from 7.0 g or 47 mmol of *N*-methyl-*N*-nitrosourea). Excess CH_2N_2 was decomposed immediately with 4 mL of AcOH, and the solution was evaporated to dryness. The residual solid was dissolved in CH_2Cl_2, and the solution was washed successively with water, saturated aqueous $NaHCO_3$, water, and brine. The solution was dried and evaporated, and 6.9 g of residual solid was chromatographed on silica gel in $CHCl_3$. The diester product [(+)-(*R*)-**17**] was recrystallized from benzene–pentane to give transparent plates, drying of which at 110 °C under vacuum converted them to nontransparent plates (4.5 g, 76%): mp 243–245 °C (lit.[9a] 239–240 °C); $[\alpha]^{25}_{436}$ +675°, $[\alpha]^{25}_{546}$ +227°, $[\alpha]^{25}_{578}$ +184°, $[\alpha]^{25}_{589}$ +172° (*c*, 0.815, THF), reported[9a] $[\alpha]^{25}_{589}$ +159° (*c* 1.0, THF). This material gave M^+ 402, and the ^1H NMR ($CDCl_3$) (60 MH_2) δ 6.00 (s, CH_3, 6 H), 2.85–2.55 (m, ArH, 6 H), 2.0–2.3 (m, ArH, 2 H), 1.33 (s, ArH, 2 H), −0.7 (s, OH, 2 H). Anal. Calcd for $C_{24}H_{18}O_6$: C, 71.63; H, 4.51. Found: C, 71.66; H, 4.65.

Reduction of this diester with $LiAlH_4$ gave (+)-(*R*)-**9** in 63% yield, mp 191–193.5 °C; $[\alpha]^{25}_{546}$ +77.1°, $[\alpha]^{25}_{578}$ +63.8° (*c*, 1.24, THF), whose ^1H NMR spectrum was identical to that of the sample prepared directly from (+)-(*R*)-**16** (see above).

(+)-(*R*)-3,3′-Di(2-hydroxy-2-propyl)-2,2′-dihydroxy-1,1′-dinaphthyl, (+)-(*R*)-18. To a solution of 5.0 g (12.4 mmol) of (+)-(*R*)-3,3′-dicarbomethoxy-2,2′-dihydroxy-1,1′-dinaphthyl [(+)-(*R*)-**17**], $[\alpha]^{25}_{578}$ +184° (*c* 1.0, THF), in 300 mL of dry THF at 0 °C under N_2 was added 70 mL of CH_3Li (1.6 M in hexane) in a single portion. The mixture was stirred for 1 h at 25 °C, CH_3OH was added dropwise to decompose the excess CH_3Li, the solution was diluted with 150 mL of water, and 12 M hydrochloric acid was added dropwise with stirring until a pH of 4 was attained. The mixture was shaken with 400 mL of CH_2Cl_2 and 600 mL of $NaHCO_3$ saturated aqueous solution; the organic layer was dried and evaporated under reduced pressure. The residue was crystallized from benzene to give 5.2 g (87%) of light-yellow needles that were dried at 25 °C and atmospheric pressure, mp ~175 °C (decompose), of a 1:1 benzene solvate of (+)-(*R*)-**18**: M^+ 402; ^1H NMR (CD_3COCD_3) δ 7.92 (m, ArH, 4 H), 7.20 (m, ArH, 6 H), 1.83 (s, CH_3, 12 H); $[\alpha]^{25}_{546}$ +132°, $[\alpha]^{25}_{578}$ +109°, and $[\alpha]^{25}_{589}$ +103°. When heated at 110 °C (0.05 mm) for 8 h, the solvate showed significant decomposition (TLC and ^1H NMR). A sample dried at 0.05 mm for 48 h at 25 °C gave an analysis consistent with 0.5 mol of benzene of solvation. Anal. Calcd for $C_{26}H_{26}O_4 \cdot 0.5C_6H_6$: C, 78.88; H, 6.62. Found: C, 78.82; H, 6.62.

(+)-(*S*)-3,3′-Dimethyl-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl [(+)-(*S*)-19] and (−)-(*R*)-19. In 150 mL of dry DMF (stored under 4A molecular sieves) at 50 °C was dissolved 20 g (63.7 mmol) of (−)-(*S*)-3,3′-dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl [(−)-(*S*)-**13**], $[\alpha]^{25}_{578}$ −36.9°, $[\alpha]^{25}_{436}$ −129.8° (*c* 1.0, $CHCl_3$). Under dry N_2, 6.4 g (128 mmol) of a 50% NaH dispersion in oil was carefully added. After H_2 evolution ceased, 26.5 g (127 mmol) of 2-

(2-chloroethoxy)ethyl 2-tetrahydropyranyl ether[4] in 50 mL of dry DMF was added. The resulting mixture was stirred at 70 °C for 40 h and then an additional 0.65 g (13 mmol) of NaH and 2.65 g (12.7 mmol) of the above chloro ether were added. The mixture was stirred for an additional 2 days, and mixed with 600 mL of water. After standing 24 h, the water was decanted from the precipitated oil, which was shaken with 200 mL of CH_2Cl_2 and 200 mL of water. The organic layer was washed with three 200-mL portions of water, dried, and filtered through a column of 50 g of activated alumina (MCB), which was subsequently washed free of product with CH_2Cl_2. The resulting solution was evaporated to 150 mL, and 150 mL of methanol and 10 mL of concentrated hydrochloric acid were added. After stirring for 2 h at 25 °C, the mixture was shaken with 100 mL of $NaHCO_3$ in water to neutralize the acid, the aqueous layer was saturated with NaCl and washed twice with CH_2Cl_2, the combined CH_2Cl_2 solutions were washed twice with water and dried, and the solvent was evaporated. The residue was magnetically stirred and heated at 120 °C for 2 h (0.1 mm) and cooled, and the mineral oil was rinsed from the oil with three successive 20 mL pentane portions. The product was dried to give 28.4 g (90%) of (+)-(*S*)-**19** as a soft white glass dried at 75 °C at 50 μm for 24 h: ^{1}H NMR ($CDCl_3$) δ 8, 2.53 (s, CH_3, 6 H), 3.17 (m, CH_2O-CH_2CH_2O, 12 H), 3.50 (m, $ArOCH_2$ and OH, 6 H), 7.09 (m, ArH, 6 H), 7.74 (m, ArH, 4 H); $[\alpha]^{25}_{578}$ +106.4°, $[\alpha]^{25}_{546}$ +124.4°, $[\alpha]^{25}_{436}$ +246.3° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found: C, 73.37; H, 7.00.

Similarly, from (+)-(*R*)-3,3′-dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl, (+)-(*R*)-**13**, $[\alpha]^{25}_{436}$ +125.0° (*c* 1, $CHCl_3$), (−)-(*R*)-**19** was prepared in 68% yield (15.4 g scale), M^+ 462, whose ^{1}H NMR spectrum was identical to its enantiomer.

(+)-(*S*)-3,3′-Dimethyl-2,2′-bis(5-tosyloxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl [(+)-(*S*)-20], (−)-(*R*)-20, and (*RS*)-20. To a solution of 20.0 g (40.8 mmol) of diol (+)-(*S*)-**19** in 75 mL of dry pyridine cooled to −20 °C was added 20 g (105 mmol) of tosyl chloride in 50 mL of dry pyridine at −20 °C. The mixture was swirled for 1 min and stored at −20 °C for 48 h. The mixture was poured onto 500 g of crushed ice, and the aqueous layer was decanted from the precipitated oil. The oil was dissolved in CH_2Cl_2 and washed with water, cold 5% hydrochloric acid, and 5% aqueous $NaHCO_3$. The solution was dried and evaporated under vacuum to give after drying at 40 °C (0.1 mm) for 30 h 30.2 g (92%) of (+)-(*S*)-**20** as a white glass: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, *p*-CH_3, 6 H), 2.46 (s, 3-CH_3, 6 H), 2.90–4.00 (m, OCH_2, 16 H), 6.90–7.40 (m, ArH, 10 H), 7.57–7.87 (m, ArH, 8 H); $[\alpha]^{25}_{578}$ +69.3°, $[\alpha]^{25}_{546}$ +80.8°, $[\alpha]^{25}_{436}$ +158° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{44}H_{46}O_{10}S_2$: C, 66.15; H, 5.80. Found: C, 66.16; H, 5.91.

Similarly, from (−)-(*R*)-**19** (see above) was prepared 22.9 g (93%) of (−)-(*R*)-**20**, $[\alpha]^{25}_{578}$ −69.7° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{44}H_{46}O_{10}S_2$: C, 66.14; H, 5.80. Found: C, 66.27; H, 6.05.

Similarly from (*R*),(*S*)-**13** was prepared (*R*),(*S*)-**19** (59%), which was converted to (*R*),(*S*)-**20** (90%), which was a glass, and possessed an ^{1}H NMR spectrum identical to that of (+)-(*S*)-**20**. Anal. Calcd for $C_{44}H_{46}O_{10}S_2$: C, 66.15; H, 5.80. Found: C, 66.40; H, 6.16.

(+)-(*R*)-2,2′-Dihydroxy-5,5′,6,6′,7,7′,8,8′,-octahydro-1,1′-dinaphthyl [(+)-(*R*)-22) and (−)-(*S*)-22. A mixture of 10.0 g (0.0275 mol) of (+)-(*R*)-2,2′-dihydroxy-1,1′-dinaphthyl [(+)-(*R*)-**3**], $[\alpha]^{25}_{589}$ +34.2° (*c* 1.0, $CHCl_3$), 1.2 g of PtO_2, and 250 mL of glacial acetic acid was shaken in a Parr apparatus under 3 atm of hydrogen at 25 °C for 7 days. The mixture was filtered through a Celite pad, and the filtrate was shaken with 400 mL of $CHCl_3$ and 1.5 L of water. The organic layer was washed with two 1-L portions of water and 1 L of 10% $NaHCO_3$ solution, dried, and evaporated. The residue was dissolved in 50 mL of CH_2Cl_2 and the solution was passed through a 150-g silica gel column. The product eluted with 2 L of CH_2Cl_2 and was crystallized from heptane to give 9.7 g (94%) of (+)-(*R*)-**22**: mp 165–166 °C; M^+ 294; ^{1}H NMR ($CDCl_3$) δ 6.90 (ABq, ArH, 4 H), 4.60 (s, OH, 2 H), 2.70 (m, $ArCH_2$, 4 H), 2.20 (m, $ArCH_2$, 4 H), and 1.66 (m, CCH_2CH_2C, 8 H); $[\alpha]^{25}_{436}$ +137.3°, $[\alpha]^{25}_{546}$ +65.2°, $[\alpha]^{25}_{578}$ +55.5°, $[\alpha]^{25}_{589}$ + 52.8° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.40; H, 7.38.

Similarly (−)-(*S*)-**3** of $[\alpha]^{25}_{589}$ −34.3° (*c* 1.0, $CHCl_3$) was reduced at 25 °C to (−)-(*S*)-**22** (95%): M^+ 294; ^{1}H NMR identical to its enantiomer; $[\alpha]^{25}_{578}$ −55.5°; mp 165–166 °C.

A similar conversion was applied to 5.0 g of (−)-(*S*)-**3** of $[\alpha]^{25}_{589}$ −34.3° (*c* 1.0, $CHCl_3$), except the reaction was conducted at 65 °C for 3 days. The product, 4.7 g (92%), gave: mp 164–167 °C; M^+ 294; ^{1}H NMR identical to its enantiomer; $[\alpha]^{25}_{436}$ −125°, $[\alpha]^{25}_{546}$ −60.1°, $[\alpha]^{25}_{578}$ −50.5°, and $[\alpha]^{25}_{589}$ −49.4° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.70; H, 7.54. These rotations are 8 ± 1% below those observed for (+)-(*R*)-**22**, a fact compatible with 4% of the material undergoing inversion at some stage during the reduction at this higher temperature.

(+)-(*R*)-3,3′-Dimethyl-5,5′,6,6′,7,7′,8,8′-octahydro-2,2′-dihydroxy-1,1′-dinaphthyl [(+)-(*R*)-23]. A mixture of 3 g (9.5 mmol) of optically pure (+)-(*R*)-3,3′-dimethyl-2,2′-dihydroxy-1,1′-dinaphthyl [(+)-(*R*)-**13**], $[\alpha]^{25}_{578}$ +37.3° (*c* 1, $CHCl_3$), 0.25 g of PtO_2, 100 mL of glacial acetic acid, and 20 mL of ethyl acetate was shaken in a Parr apparatus under 3 atm of H_2 for 6 days. The product was isolated as in the reduction of (+)-(*R*)-**3** but was crystallized from hexane to give 2.9 g (94%) of (+)-(*R*)-**23** as white needles: mp 164–166 °C; M^+ 322; $[\alpha]^{25}_{436}$ +190°, $[\alpha]^{25}_{546}$ +94°, and $[\alpha]^{25}_{578}$ +84° (*c* 1.04, THF); ^{1}H NMR ($CDCl_3$) δ 6.88 (s, ArH, 2 H), 4.57 (s, OH, 2 H), 2.72 (m, $ArCH_2$, 4 H), 2.21 (m, $ArCH_2$, 4 H), 2.20 (s, $ArCH_3$, 6 H), and 1.68 (m, CCH_2CH_2C, 8 H). Anal. Calcd for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.83; H, 7.92.

The same compound, (+)-(*R*)-**23**, was prepared from the same (+)-(*R*)-**13** by first protecting the two OH groups with OCH_2OCH_3 groups to inhibit possible racemization, reducing the tetraether, and deprotecting the reduced product. To a solution of 3 g (9.5 mmol) of (+)-(*R*)-**13** in 150 mL of THF under N_2 at 25 °C was added 2 g of NaH as a 50% oil dispersion. The mixture was stirred 15 min, 3 g (37.5 mmol) of chloromethyl methyl ether was added, and the mixture was stirred for 12 h. The excess NaH was decomposed by dropwise addition of CH_3OH; the resulting solution was shaken with CH_2Cl_2 and H_2O (400 mL of each). The organic layer was dried and evaporated under vacuum to an oil. An ^{1}H NMR spectrum of this product (a small mineral oil contaminant) in $CDCl_3$ gave δ 7.78 (m, ArH, 4 H), 7.22 (m, ArH, 6 H), 4.52 (AB quartet, OCH_2, 4 H), 2.80 (s, OCH_3, 6 H), and 2.53 (s, $ArCH_3$, 6 H). This protected (tetraether) phenol was reduced similarly to its parent (+)-(*R*)-**13**, and the reduced product was chromatographed in benzene on 100 g of silica gel made up in cyclohexane. Elution of the column with 2 L of benzene gave mineral oil, whereas elution with 2 L of 19:1 (v:v) benzene to ether gave the tetraether as a colorless oil. Its ^{1}H NMR spectrum in $CDCl_3$ gave δ 6.82 (s, ArH, 2 H), 4.80 (s, OCH_2, 4 H), 2.90 (s, OCH_3, 6 H), 2.72 (m, $ArCH_2$, 4 H), 2.22 (m, $ArCH_2$, 4 H), 2.21 (s, $ArCH_3$, 6 H), and 1.68 (m, CCH_2CH_2C, 8 H). This oil was mixed with 200 mL of $CHCl_3$, 300 mL of CH_3OH, and 5 mL of concentrated hydrochloric acid, and the mixture was stirred for 18 h at 25 °C. A saturated aqueous solution of $NaHCO_3$ (800 mL) was cautiously added, the mixture was shaken, and the organic layer was dried and evaporated under vacuum. The residue was crystallized from hexane to give 2.5 g (81% overall) of white needles of (+)-(*R*)-**23**, mp 164–166 °C, whose ^{1}H NMR spectrum was identical to that of directly prepared material, and which gave $[\alpha]^{25}_{436}$ +190°, $[\alpha]^{25}_{546}$ +94°, and $[\alpha]^{25}_{578}$ +80° (*c* 1.08, THF).

(−)-(*S*)-2,2′-Bis(5-tosyloxy-3-oxa-1-pentyloxy)-5,5′,6,6′,-7,7′,8,8′-octahydro-1,1′-dinaphthyl [(−)-(*S*)-24]. The diol, (*S*)-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl (20.9 g or 45.2 mmol), prepared as before[4] from optically pure (−)-(*S*)-2,2′-dihydroxy-1,1′-dinaphthyl [(−)-(*S*)-**3**] was dissolved in 250 mL of glacial acetic acid. Platinum oxide (250 mg) was added and the mixture was stirred under 1 atm of H_2 for 4 days at 25 °C. The solution was filtered, and the filtrate was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, and the solution was washed with aqueous $NaHCO_3$, dried, and evaporated to give 21.0 g (99%) of the corresponding octahydrodiol as a viscous oil. This material was dissolved in 50 mL of dry pyridine, the solution was cooled to 0 °C, and 20 g (105 mmol) of tosyl chloride in 30 mL of dry pyridine cooled to 0 °C was added. The solutions were mixed and allowed to stand at −20 °C for 5 days and then poured onto 500 g of crushed ice. The mixture was brought to 25 °C, the water was decanted, and the precipitated oil was dissolved in CH_2Cl_2. The solution was washed with cold 5% hydrochloric acid and water, dried, and evaporated under vacuum to give 34.0 g (98%) of a viscous white gum. A small sample was purified by silica gel TLC to give (−)-(*S*)-**24**: ^{1}H NMR ($CDCl_3$) δ 1.67 (m, CCH_2CH_2C, 8 H), 2.17 (m, $ArCH_2$, 4 H), 2.42 (s, $ArCH_3$, 6 H), 2.70 (m, $ArCH_2$, 4 H), 3.40 (m, CH_2OCH_2, 8 H), 3.90 (m, $ArOCH_2$ and CH_2OTs, 8 H), 6.67 and 7.00 (d, d, diphenyl ArH, 4 H), 7.32 and 7.75 (d, d, tosyl ArH, 8 H); $[\alpha]^{25}_{578}$ −26.2° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{42}H_{50}O_{10}S_2$: C, 64.76; H, 6.47. Found: C, 64.71; H, 6.63.

(+)-(*S*)-3,3′-Dimethyl-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1-dinaphthyl [(+)-(*S*)-25] and (−)-(*R*)-25. A mixture of 100 mL of glacial acetic, 10 g of diol (+)-(*S*)-**19** (see above), and 0.10 g of PtO_2 was stirred under 1 atm of H_2 at 25 °C for 3 days. The mixture was filtered, the acetic acid was evaporated under reduced pressure, and the residue was distributed between CH_2Cl_2 and aqueous $NaCHO_3$. The organic layer was washed with water, dried, and evaporated under vacuum to give after drying under vacuum 10 g (98%) of (+)-(*S*)-**25** as a white glass: ^{1}H NMR ($CDCl_3$) δ 1.67 (m, CCH_2CH_2C), 2.20 (m, $ArCH_2$, 4 H), 2.27 (s, $ArCH_3$, 6 H), 2.70 (m, $ArCH_2$, 4 H), 3.93 (m, OCH_2, 16 H), 6.85 (s, ArH, 2 H); $[\alpha]^{25}_{589}$ +25.0°, $[\alpha]^{25}_{578}$ +26.3° (*c* 1.0, $CHCl_3$). An analytical sample

was prepared by TLC on silica gel. Anal. Calcd for $C_{30}H_{42}O_6$: C, 72.26; H, 8.49. Found: C, 72.40; H, 8.51.

Similarly 17.0 g of (−)-(*R*)-**19** (see above) was reduced to give 20.0 g (98%) of (−)-(*R*)-**25**: $[\alpha]^{25}_{589}$ −24.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.67 (m, CCH_2CH_2C, 8 H), 2.18 (m, $ArCH_2$, 4 H), 2.25 (s, CH_3, 6 H), 2.68 (m, $ArCH_2$ and OH, 6 H), 3.25–3.84 (m, OCH_2, 16 H), 6.86 (s, ArH, 2 H). A small sample was purified by preparative TLC on silica gel for analysis. Anal. Calcd for $C_{30}H_{42}O_6$: C, 72.26; H, 8.49. Found: C, 72.27; H, 8.23.

(−)-(*R*)-3,3′-Dimethyl-2,2′-bis(5-tosyloxy-3-oxa-1-pentyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-dinaphthyl [(−)-(*R*)-26] and (+)-(*S*)-26. From 17.4 g (34.5 mmol) of diol (−)-(*R*)-**25** and 15.0 g (78.7 mmol) of tosyl chloride in 50 mL of pyridine for 3 days at −20 °C was obtained product which was filtered through 100 g of alumina in CH_2Cl_2. The product, (−)-(*R*)-**26**, 27 g (97%), was a white glass: ^1H NMR ($CDCl_3$) δ 1.65 (m, CCH_2CH_2C, 8 H), 2.15 (m, $ArCH_2$, 4 H), 2.18 (s, CH_3 of naphthyl, 6 H), 2.40 (s, CH_3 of tosyl, 6 H), 2.72 (m, $ArCH_2$, 4 H), 3.17–4.08 (m, OCH_2, 16 H), 6.83 (s, diphenyl ArH, 2 H), 7.27 (d, tosyl ArH, 4 H), 7.58 (d, tosyl ArH, 4 H); $[\alpha]^{25}_{589}$ −14.4° $[\alpha]^{25}_{578}$ −14.0° (*c* 0.5, $CHCl_3$). An analytical sample was prepared by TLC on silica gel. Anal. Calcd for $C_{44}H_{54}O_{10}S_2$: C, 65.48; H, 6.74. Found: C, 65.24; H, 6.77.

Similarly, from 10 g of diol (+)-(*S*)-**25** was prepared 11.2 g (70%) of (+)-(*S*)-**26** as a white glass, $[\alpha]^{25}_{578}$ +13.4° (*c* 0.5, $CHCl_3$), whose ^1H NMR spectrum was essentially identical to that of its enantiomer. An analytical sample was prepared by TLC on silica gel. Anal. Calcd for $C_{44}H_{54}O_{10}S_2$: C, 65.48; H, 6.74. Found: C, 65.62; H, 6.70.

(+)-(*R*)-3,3′-Dibromo-2,2′-dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-dinaphthyl, (+)-(*R*)-27. To a solution of 4.6 g (16 mmol) of (+)-(*R*)-**22**, $[\alpha]^{25}_{546}$ +65.2° (*c* 1.1, $CHCl_3$), in 150 mL of CH_2Cl_2 at −30 °C was added 5.8 g (36 mmol) of Br_2 in a single portion. The mixture was stirred for 15 min, 200 mL of $NaHSO_3$ saturated aqueous solution was added, and the mixture was allowed to warm to 25 °C and was stirred for 1 h. The CH_2Cl_2 layer was separated, washed with 10% $NaHCO_3$ (300 mL), dried, and evaporated and the residue was crystallized from heptane to give 6.9 g (98%) of (+)-(*R*)-**27**: mp 142–143 °C; M^+ 450 (^{79}Br); ^1H NMR ($CDCl_3$) δ 7.18 (s, ArH, 2 H), 5.17 (s, OH, 2 H), 2.70 (m, $ArCH_2$, 4 H), 2.20 (m, $ArCH_2$, 4 H), and 1.66 (m, CCH_2CH_2C, 8 H); $[\alpha]^{25}_{436}$ +65.0°, $[\alpha]^{25}_{546}$ +35.3°, $[\alpha]^{25}_{578}$ +30.5°, and $[\alpha]^{25}_{589}$ +29.2° (*c* 1.05, $CHCl_3$). Anal. Calcd for $C_{20}H_{20}Br_2O_2$: C, 53.12; H, 4.46. Found: C, 53.24; H, 4.46.

5,5′,6,6′-Tetrabromo-2,2′-dihydroxy-1,1′-dinaphthyl (28).[13] To a solution of 2,2′-dihydroxy-1,1′-dinaphthyl (5.72 g or 0.020 mol) in 200 mL of CH_2Cl_2 was added Br_2 (10 mL, 31.96 g or 0.20 mol) in one portion, and the resulting solution was held at reflux for 19 h. The solution was cooled, washed with two 100-mL portions of 20% aqueous $NaHSO_3$, with 5% aqueous $NaHCO_3$, and with water. The solution was dried and evaporated to give a white solid purified by trituration with CH_2Cl_2: 9.75 g (81%); M^+ 598 (^{79}Br); ^1H NMR (CD_3COCD_3) δ 6.88, 6.97 (d of d, half of A_2B_2q, $J_{7,8}$ = 9 Hz, $J_{4,8}$ of the epi H^1s = 0.9 Hz, H_8, 2 H), 7.34, 7.43 (d, half of A_2B_2q, $J_{7,8}$ = 9 Hz, H_7, 2 H); 7.37, 7.46 (d, half of A_2B_2q, $J_{3,4}$ = 9.5 Hz, H_3, 2 H), 8.22, 8.32 (d of d, half of A_2B_2q, $J_{3,4}$ = 9.5, H_4, J_{epi} = 0.9 Hz, H_4, 2 H). Anal. Calcd for $C_{20}H_{10}Br_4O_2$: C, 39.91; H, 1.68. Found: C, 39.52; H, 2.12.

4,4′,6,6′-Tetrabromo-2,2-dimethoxy-1,1-dinaphthyl.[13] To 1.57 g (0.005 mol) of 2,2′-dimethoxy-1,1-dinaphthyl,[12] mp 195 °C, in 80 mL of $CHCl_3$ was added at 25 °C dropwise a solution of 2 mL or 6.2 g of Br_2 (0.0388 mol) in 20 mL of $CHCl_3$. After the resulting solution has stood 18 h it was treated with 25 mL of 20% aqueous $NaHSO_3$ with cooling. The resulting mixture was shaken with water and CH_2Cl_2, the organic phase was washed with aqueous K_2CO_3 solution, dried, and evaporated under vacuum. The product was chromatographed on 200 g of neutral alumina, and the product was eluted with 25% (v) CH_2Cl_2 in pentane to give 2.86 g (91%) of product, which was recrystallized from CCl_4–ethanol and dried at 135 °C (1 mm): mp 225–227 °C; M^+ 626 (^{79}Br); ^1H NMR ($CDCl_3$) δ 3.68 (s, CH_3O, 6 H), 6.81, 6.90 (half of ABq, *J* = 9 Hz, H_8, 1 H), 7.20, 7.29 (d, d, *J* = 2 Hz, H_7 coupled to H_5, half of ABq coupled to H_8, *J* = 9 Hz, H_7, 1 H), 7.68 (s, H_3, 2 H), 8.35 (d, *J* = 2 Hz, H_5 coupled to H_7, 2 H). Anal. Calcd for $C_{22}H_{14}Br_4O_2$: C, 41.94; H, 2.24. Found: C, 41.69; H, 2.47.

(*R,R*),(*S,S*)-2,3,4,5-Di-1,2-(3-methylnaphtho-13,14,15,16-di(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-29], (*R,S*),(*S,R*)-29, (−)-(*R,S*)-29, (+)-(*R,R*)-29, and (−)-(*S,S*)-29. To a solution of 0.570 g of **3** in 15 mL of dry DMF stirred at 25 °C under N_2 was added 0.22 g of NaH (57% dispersion in mineral oil), followed by 1.6 g of two-armed dimethyl ditosylate, **20**, in 25 mL of dry DMF. The mixture was stirred at 45 °C until it became homogeneous and then at 60 °C for 48 h. The mixture was cooled, the solvent was evaporated under reduced pressure, and the residue was shaken with CH_2Cl_2 and water. The organic layer was washed with water and brine, dried, and evaporated, and the residue was dried as a foam at 80 °C and 50 μm for 3 h, weight 1.3 g. This material was chromatographed on 200 g of silica gel. Hexane eluted unreacted **3** (0.13 g or 23%), whereas 2:3 hexane–CH_2Cl_2–methane eluted first (*R,S*),(*S,R*)-**29** (mp 249 °C, 0.176 g, 12%, from CH_2Cl_2), then a mixture of diastereomers (0.12 g, 8%), and finally (*R,R*),(*S,S*)-**29** (mp 222–223 °C, 0.147 g, 10%, from CH_2Cl_2). Both diastereomers gave M^+ 740. The ^1H NMR spectrum in $CDCl_3$ of the (*R,S*),(*S,R*) isomer gave δ 7.72 (m, ArH, 8 H), 7.36 (s, ArH, 2 H), 7.12 (m, ArH, 12 H), 3.96 (m, CH_2O, 4 H), 3.69 (m, CH_2O, 4 H), 3.33 (m, CH_2O, 4 H), 2.88 (m, CH_2O, 4 H), and 2.50 (s, CH_3, 6 H); that of the (*R,R*),(*S,S*) isomer gave δ 7.80 (m, ArH, 8 H), 7.38 (s, ArH, 2 H), 7.09 (m, ArH, 12 H), 4.00 (m, OCH_2, 4 H), 3.50 (m, CH_2O, 8 H), 3.04 (m, CH_2O, 4 H), and 2.40 (s, CH_3, 6 H). Anal. Calcd for each isomer $C_{50}H_{44}O_6$: C, 81.06; H, 5.99. Found for (*R,S*),(*S,R*)-**29**: C, 80.84; H, 6.23. Found: C, 80.63; H, 6.12.

Procedure II (see below) was applied to 1.80 g of optically pure (−)-(*S*)-**13** and 4.40 g of optically pure (−)-(*R*)-**19** (two-armed ditosylate) to give 0.68 g (16%) of (+)-(*S,R*)-**29** as a foam, $[\alpha]^{25}_{589}$ +41.4°, $[\alpha]^{25}_{578}$ +44.2°, $[\alpha]^{25}_{546}$ +53.4°, and $[\alpha]^{25}_{436}$ +142.3° (*c* 1, $CHCl_3$). The ^1H NMR spectrum of this compound was identical to that of (*R,S*),(*S,R*)-**29** but different from that of (*R,R*),(*S,S*)-**29**. Anal. Calcd for $C_{50}H_{44}O_6$: C, 81.06; H, 5.99. Found: C, 81.12; H, 6.20.

Procedure I. Isomer (+)-(*R,R*)-**29** was synthesized from optically pure binaphthol (+)-(*R*)-**3** and dimethyl two-armed ditosylate (−)-(*R*)-**20** as follows. To 1 L of THF, 6.04 g (0.021 mol) of (+)-(*R*)-**3**, $[\alpha]^{25}_{589}$ +34.1° (*c* 1.0, $CHCl_3$), and 2.8 g (0.0042 mol) of KOH (85%) dissolved in 30 mL of water were added and the solution was held at reflux 30 min. Optically pure (−)-(*R*)-**20** [$[\alpha]^{25}_{578}$ −69.7°, *c* 1.0, $CHCl_3$] was added and the mixture was refluxed for 180 h. The reaction mixture was evaporated under reduced pressure and shaken with water–CH_2Cl_2; the CH_2Cl_2 layer was water washed, dried, and evaporated to give 5.6 g of oil. This oil was chromatographed on 250 g of neutral alumina and eluted with 1:10 (v:v) acetone–CCl_4, the last 900 mL of 1600 mL of which gave 4.97 g (32%) of product as a white foam: M^+ 740, M^{2+} 370, gel permeation column retention volume 152 mL of CH_2Cl_2; $[\alpha]^{25}_{578}$ +152° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.8–6.9 (m, ArH, 22 H), 4.20–2.85 (m, CH_2O, 16 H), 2.35 (s, CH_3, 6 H). Anal. Calcd for $C_{50}H_{44}O_6$: C, 81.06; H, 5.99. Found: C, 81.10; H, 6.13.

Procedure II. A mixture of 100 mL of THF, 1.0 g of optically pure binaphthol, (−)-(*S*)-**3** (0.0032 mol, $[\alpha]^{25}_{589}$ −34.3°, *c* 1.0, $CHCl_3$), and 0.40 g (0.0064 mol) of KOH (85%) was stirred for 1 h and then 2.54 g (0.0032 mol) of optically pure (+)-(*S*)-**20** (dimethyl two-armed ditosylate, $[\alpha]^{25}_{578}$ +70.0°, *c* 1.0, $CHCl_3$) in 100 mL of THF was added; the mixture was refluxed under N_2 for 175 h. The crude product (2.62 g) was isolated as before and purified by gel permeation chromatography to give 1.50 g (64%) of (−)-(*S,S*)-**29** as a white foam; M^+ 740, M^{2+} 370, gel permeation retention volume 152 mL of CH_2Cl_2; $[\alpha]^{25}_{436}$ −380°, $[\alpha]^{25}_{546}$ −171°, $[\alpha]^{25}_{578}$ −152° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.80–6.90 (m, ArH, 22 H), 4.2–2.85 (m, CH_2O, 16 H), 2.35 (s, CH_3, 6 H). Anal. Calcd for $C_{50}H_{44}O_6$: C, 81.06; H, 5.99. Found: C, 81.38; H, 6.03.

(*R,R*),(*S,S*)-2,3,4,5-Di-1,2-(3-hydroxymethylnaphtho)-13,-14:15,16-di(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-30], (*R,S*),(*S,R*)-30, and (+)-(*R,R*)-30. A solution of 23 g of tetrol **9** in 2 L of THF, 5.4 g of NaOH in 60 mL of H_2O, and 56 g of 2,2′-di(5-tosyloxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl (**21**)[4] was stirred under N_2 at reflux for 100 h. The crude product was isolated as in procedure I and chromatographed on 1.5 kg of alumina. The column was washed with 3 L of ether, and the products were eluted with ether–isopropyl alcohol mixtures to give 17.0 g (33%) of crude **30**. The faster moving diastereomer was fractionally crystallized from CH_2Cl_2–ethyl acetate to give (*R,S*)-,(*S,R*)-**30**: 4.25 g (8%); mp 197–198 °C; M^+ 772; ^1H NMR ($CDCl_3$) δ 8.00–6.98 (m, ArH, 22 H), 4.94 (m, $ArCH_2$, 4 H), and 4.40–2.76 (m, OCH_2, 16 H). Anal. Calcd for $C_{50}H_{44}O_8$: C, 77.70; H, 5.74. Found: C, 77.50; H, 5.96.

Fractional crystallization of the slower moving racemate from CH_2Cl_2 and ethyl acetate gave 8.5 g (16%) of (*R,R*),(*S,S*)-**30**: mp 230–231 °C; M^+ 772; ^1H NMR ($CDCl_3$) δ 7.80 (m, ArH, 8 H), 7.18 (m, ArH, 14 H), 4.70 (m, $ArCH_2$, 4 H), and 4.22–3.78 (m, OCH_2, 16 H). Anal. Calcd for $C_{50}H_{44}O_8$: C, 77.70; H, 5.74. Found: C, 77.48; H, 6.01.

By the same procedure from optically pure (+)-(*R*)-**21**[4] and (+)-(*R*)-**9** (see above) was produced in 28% yield (+)-(*R,R*)-**30** as a glass, pure to TLC, $[\alpha]^{25}_{578}$ +120°, $[\alpha]^{25}_{546}$ +115°, $[\alpha]^{25}_{436}$ +318° (*c* 1.0, $CHCl_3$). The ^1H NMR spectra of (+)-(*R,R*)-**30** and that of (*R,R*),-(*S,S*)-**30** (see above) were identical but decidedly different from that of (*R,S*),(*S,R*)-**30** (see above).

(+)-(*R,R*)-2,3,4,5-Di-1,2-(3-chloromethylnaphtho)-13,14:15,16-di(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene, (+)-(*R,R*)-31. To a solution of 0.90 g (1.2 mmol) of (+)-(*R,R*)-**30** in 40 mL of benzene was added 4.0 g (34 mmol) of thionyl chloride in a single portion. The solution was stirred at 25 °C for 10 h and evaporated at 30 mm of pressure and 60 °C. The residue was dissolved in 50 mL of CH_2Cl_2 and the solution was extracted with 30 mL of 10% $NaHCO_3$. The organic layer was dried and concentrated to 15 mL, and the residue was chromatographed on 50.0 g of silica gel. Elution of the column with 2 L of CH_2Cl_2 gave 0.72 g (76%) of (+)-(*R,R*)-**31** as a glass, which was dried at 50 μm and 50 °C for 10 h. The compound gave the ^1H NMR spectrum in $CDCl_3$ of δ 8.05–6.90 (m, ArH, 22 H), 4.70 (ABq, $ArCH_2$, 4 H), and 4.16–2.78 (m, OCH_2, 16 H); $[\alpha]^{25}_{589}$ +116°, $[\alpha]^{25}_{578}$ +122°, $[\alpha]^{25}_{546}$ +145°, and $[\alpha]^{25}_{436}$ +335°. Anal. Calcd for $C_{50}H_{42}Cl_2O_6$: C, 74.15; H, 5.24. Found: C, 74.50; H, 5.26.

(+)-(*R,R*)-Dimethyldinaphtho-22-crown-6 [(+)-(*R,R*)-29] from (+)-(*R,R*)-31. To a solution of 1.5 g (39 mmol) of $LiAlH_4$ in 150 mL of THF under N_2 was added 0.7 g (0.87 mmol) of (+)-(*R,R*)-**31** in 20 mL of THF. The mixture was refluxed for 3 h and cooled to 5 °C and the excess $LiAlH_4$ was decomposed by dropwise addition of water. Ether (150 mL) and 100 mL of 6 N hydrochloric acid were added and the resulting mixture was stirred at 25 °C for 6 h. The organic layer was separated, and the aqueous phase was extracted with 100 mL of ether. The combined organic extracts were washed with 100 mL of 10% $NaHCO_3$ solution, dried, and concentrated to 30 mL. The residue was chromatographed on 50 g of neutral alumina. Elution of the column with 2.5 L of ether gave 0.51 g (80%) of (+)-(*R,R*)-**29** as a colorless glass, dried at 50 μm and 100 °C for 5 h. The ^1H NMR spectrum in $CDCl_3$ gave δ 8.00–6.90 (m, ArH, 22 H), 4.24–2.90 (m, OCH_2, 16 H), and 2.40 (s, CH_3, 16 H); $[\alpha]^{25}_{589}$ +145°, $[\alpha]^{25}_{578}$ +152°, $[\alpha]^{25}_{546}$ +170°, and $[\alpha]^{25}_{436}$ +381° (*c* 1.0, $CHCl_3$).

(*R,R*),(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2,(3-methylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-32], (*R,S*)-32, (+)-(*R,R*)-32, and (−)-(*S,S*)-32. From 0.942 g of racemic **13**, 2.4 g of racemic **20**, and 0.377 g of KOH in 60 mL of THF and 1 mL of water refluxed for 40 h was obtained an isomeric mixture that was chromatographed on 400 g of silica gel. Benzene elution of the chromatogram and recrystallization of the product gave 0.155 g (7%) of (*R,S*)-**32**: mp 314–315 °C; M^+ 768; ^1H NMR ($CDCl_3$) δ 7.73 (d, $ArH^{4,5}$, 8 H), 7.10 (m, ArH, 12 H), 3.68 (m, CH_2O, 8 H), 3.26 (m, CH_2O, 4 H), 2.86 (m, CH_2O, 4 H), and 2.52 (s, CH_3, 12 H). Anal. Calcd for $C_{52}H_{48}O_6$: C, 81.22; H, 6.29. Found: C, 81.01; H, 6.28. Elution of the chromatographic column with 20:1 (v:v) benzene–ether gave (*R,R*),(*S,S*)-**32**, which after recrystallization from CH_2Cl_2–ether gave: 0.22 g (10%); mp 158–160 °C; M^+ 768; ^1H NMR ($CDCl_3$) δ 7.70 (m, $ArH^{4,5}$, 8 H), 7.12 (m, ArH, 12 H), 3.50 (m, CH_2O, 8 H), 2.92 (m, CH_2O, 8 H), 2.45 (d, CH_3, 12 H). Anal. Calcd for $C_{52}H_{48}O_6$: C, 81.22; H, 6.29. Found: C, 80.93; H, 6.28.

When racemic **13** was treated similarly with diethylene glycol ditosylate, (*R,S*)-**32** (4%), mp 314–315 °C, (*R,R*),(*S,S*)-**32** (5%), mp 158–160 °C, and (*R*),(*S*)-2,3,4,5-di-1,2-(3-methylnaphtho)-1,6,9-trioxaundeca-2,4-diene (8%), mp 285 °C (from benzene), were produced. This monolocular material gave: M^+ 384; ^1H NMR ($CDCl_3$) δ 7.72 (m, $Ar^{4,5}$, 4 H), 7.20 (m ArH, 6 H), 4.06 (m, CH_2O, 4 H), 3.28 (t, CH_2O, 4 H), and 2.58 (s, CH_3, 6 H). Anal. Calcd for $C_{26}H_{24}O_3$: C, 81.22; H, 6.29. Found: C, 81.45; H, 6.44.

From a mixture of 8.60 g (0.0274 mol) of (+)-(*R*)-**13**, $[\alpha]^{25}_{578}$ +37.3° (*c* 1.0, $CHCl_3$), 21.9 g (0.027 mol) of (−)-(*R*)-**20**, $[\alpha]^{25}_{578}$ − 67.9 °C (*c* 1.0, $CHCl_3$), 4.2 g (0.0636 mol) of KOH (85%) in 75 mL of water, and 1.5 L of THF at reflux for 231 h was obtained by procedure I (and a CH_2Cl_2 solution filtration through 50 g of alumina to remove polymer) 6.4 g of crude product. This material was chromatographed on 300 g of alumina and eluted with the last 900 mL of 1.8 L of acetone–CCl_4 (1:10, v:v) to produce 5.8 g (28%) of (+)-(*R,R*)-**32** as a glass: M^+ 768; ^1H NMR ($CDCl_3$) δ 7.8–6.9 (m, ArH, 20 H), 4.2–2.8 (m, CH_2O, 16 H), 2.35 (s, CH_3, 6 H); $[\alpha]^{25}_{436}$ +321°, $[\alpha]^{25}_{546}$ +156.5°, $[\alpha]^{25}_{578}$ +135° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{52}H_{48}O_6$: C, 81.23; H, 6.28. Found: C, 80.92; H, 6.14.

Similarly, (−)-(*SS*)-**32** was prepared as a glass (28%), $[\alpha]^{25}_{578}$ −134° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{52}H_{48}O_6$: C, 81.23; H, 6.28. Found: C, 81.38; H, 6.02.

(+)-(*R,R*)-2,3,4,5-Di-1,2-[3-(2-hydroxy-2-propyl)naphtho]-13,14:15,16-di(1,2-naphtho)-1,6,9,12,16,20-hexaoxacyclodocosa-2,4,13,15-tetraene, (+)-(*R,R*)-33. From 3.6 g (9 mmol) of (+)-(*R*)-3,3′-(2-hydroxy-2-propyl)-2,2′-dihydroxy-1,1′-dinaphthyl (see above), 7.0 g (9 mmol) of optically pure (+)-(*R*)-2,2′-di(5-tosyloxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl,[4] 750 mL of THF, and 20 mL of water (procedure I) after 7 days of reflux was obtained crude material that was chromatographed on 100 g of activity 1 neutral alumina (in ether). The column was washed with 300 mL of ether, and the product was eluted with 49:1 (v:v) ether–isopropyl alcohol to give 2.1 g (28%) of (+)-(*R,R*)-**33** as a white foam; M^+ 828 (weak), $M^+ - H_2O$ 810 (strong), $M^+ - 2H_2O$ 792 (strong); ^1H NMR ($CDCl_3$) δ 7.78 (m, ArH, 8 H), 7.12 (m, ArH, 14 H), 3.55 (m, OCH_2, 16 H), 1.60 (s, CH_3, 6 H), and 1.70 (s, CH_3, 6 H); $[\alpha]^{25}_{436}$ +222°, $[\alpha]^{25}_{546}$ +88°, $[\alpha]^{25}_{578}$ +73°, $[\alpha]^{25}_{589}$ +589° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{54}H_{52}O_8$: C, 78.24; H, 6.32. Found: C, 78.20; H, 6.43.

(+)-(*R,R*)-2,3,4,5-Di-1,2-(3-isopropylnaphtho)-13,14,15,16-di-(1,2-naphtho)-1,6,9,12-hexaoxacyclodocosa-2,4,13,15-tetraene, (+)-(*R,R*)-34. To a solution of 0.450 (0.54 mmol) of (+)-(*R,R*)-**33** (see above) in 25 mL of CH_2Cl_2 was added 7 g of neutral alumina, activity 1, pretreated with 2% pyridine.[14] The suspension was evaporated at 25 °C (30 mm), and the residue was heated at 175 °C for 5 h under 30 mm of pressure. The solid was extracted five times with 50-mL portions of CH_2Cl_2 at 25 °C, and the combined extracts were evaporated. The residue was dissolved in 50 mL of ethyl acetate and hydrogenated under 2 atm of H_2 with 1 g of 10% Pd on C in a Parr apparatus for 30 min. The suspension was filtered, the filtrate was evaporated, and the residue was dissolved in CH_2Cl_2 and chromatographed on 50 g of neutral activity 1 alumina in ether. Elution of the column with 1.5 L of ether gave 325 mg (75%) of (+)-(*R,R*)-**34** as a white foam: M^+ 796; ^1H NMR ($CDCl_3$) δ 7.80 (m, ArH, 8 H), 7.14 (m, ArH, 14 H), 3.38 [m, OCH_2, $CH(CH_3)_2$, 18 H] and 1.39 (d, CH_3, 12 H); $[\alpha]^{25}_{436}$ +207°, $[\alpha]^{25}_{546}$ +86°, $[\alpha]^{25}_{578}$ +71°, and $[\alpha]^{25}_{589}$ +67° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{54}H_{52}O_6$: C, 81.38; H, 6.58. Found: C, 81.46; H, 6.57.

(*R,R*),(*S,S*)-2,3,4,5-Di-1,2-[3-(2,5-dioxa-4-oxohexa)]-13,14,-15,16-di(1,2-naphthol)-1,6,9,12,16,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-35], (*R,S*),(*S,R*)-35, and (+)-(*R,R*)-35. To a solution of (*R,R*),(*S,S*)-**30**, 2.4 g or 3.1 mmol, in 200 mL of THF under N_2 was added NaH (2.0 g, 42 mmol) as a 50% mineral oil dispersion. The mixture was stirred for 15 min, methyl bromoacetate (3.0 g, 20 mmol) in 10 mL of THF was added, and the mixture was refluxed for 18 h. The reaction mixture was cooled, filtered, and evaporated under reduced pressure. The residue was shaken with 200 mL each of water and CH_2Cl_2, the water layer was extracted with CH_2Cl_2, and the combined organic layers were dried and evaporated under reduced pressure. The residue in 10 mL of benzene was chromatographed on 100 g of silica gel (cyclohexane). The column was washed with 500 mL of cyclohexane, 1 L of benzene, and 2 L of 49:1 (v:v) benzene–ether to give impurities, and the product was eluted with 2 L of 9:1 (v:v) benzene–ether as 2.0 g (71%) of a colorless oil: M^+ 916; ^1H NMR ($CDCl_3$) δ 7.90 (m, ArH, 8 H), 7.20 (m, ArH, 14 H), 4.72 (broad s, $ArCH_2$, 4 H), 4.03 (s, OCH_2O, 4 H), 3.63 (s, CH_3O, 6 H), and 4.22–2.90 (m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{56}H_{52}O_{12}$: C, 73.35; H, 5.72. Found: C, 73.29; H, 5.75.

By the same procedure, (*R,S*),(*S,R*)-**30** was converted to (*R,S*),-(*S,R*)-**35** (50%) which was a glass: M^+ 916; ^1H NMR ($CDCl_3$) δ 8.07–6.85 (m, ArH, 22 H), 4.97 (s, $ArCH_2$, 4 H), 4.20 (s, CH_2CO_2, 4 H), 3.66 (s, OCH_3, 6 H), and 4.40–2.50 (m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{56}H_{52}O_{12}$: C, 73.35; H, 5.72. Found: C, 73.30; H, 5.60.

Similarly, (+)-(*R,R*)-**30** (see above) was converted to (+)-(*R,R*)-**35** (77%) which was a glass: $[\alpha]^{25}_{589}$ +110°, $[\alpha]^{25}_{578}$ +116°, $[\alpha]^{25}_{546}$ +137°, $[\alpha]^{25}_{436}$ +311° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) identical to (*R,R*),(*S,S*)-**35**. Anal. Calcd for $C_{56}H_{52}O_{12}$: C, 73.35; H, 5.72. Found: C, 73.19; H, 5.59.

(*R,S*),(*S,R*)-2,3:4,5-Di-1,2-[3-(2,5-dioxa-4-oxopenta)]-13,14:15,16-di(1,2-naphtho)-1,6,9,12,16,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,S*),(*S,R*)-36), (*R,R*),(*S,S*)-36, and (+)-(*R,R*)-36. To a solution of diester (*R,S*),(*S,R*)-**35** (see above) (0.6 g, 0.65 mmol) in 60 mL of ethanol was added NaOH (2.0 g, 50 mmol) in 10 mL of water. The solution was refluxed for 12 h, concentrated at 60 °C (30 mm) to about 5 mL, and diluted with water to 100 mL. The suspension was extracted with two 50-mL portions of CH_2Cl_2; the aqueous layer was acidified with HCl to pH 1. The mixture was stirred with 200 mL of CH_2Cl_2 until the two phases were transparent (2 h). The layers were separated, and the aqueous layer was extracted with 50 mL of CH_2Cl_2. The combined CH_2Cl_2 layers were washed with water, dried, and evaporated to give 550 mg (94%) of product as a white powder: M^+ 888; ^1H NMR δ 8.10–6.90 (m, ArH, 22 H), 5.00 (broad s, $ArCH_2$, 4 H), 4.22 (broad s, CH_2CO_2, 4 H), 4.30–2.80 (m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{54}H_{48}O_{12}$: C, 72.96; H, 5.44. Found: C, 72.90; H, 5.32.

Similarly, (*R,R*),(*S,S*)-**35** (see above) was hydrolyzed to (*R,R*),-(*S,S*)-**36** (83%), which was a colorless glass: M^+ 888; ^1H NMR (CD_3CO_2D) δ 8.15–6.80 (m, ArH, 22 H), 4.80 (s, $ArCH_2$, 4 H), 4.18 (s, OCH_2CO_2, 4 H), and 4.20–2.75 (m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{54}H_{48}O_{12}$: C, 72.96; H, 5.44. Found: C, 73.12; H, 5.51.

Similarly, (+)-(*R,R*)-**35** (see above) was converted to (+)-(*R,R*)-**36** (76%): glass; $[\alpha]^{25}_{589}$ +104°, $[\alpha]^{25}_{578}$ +110°, $[\alpha]^{25}_{546}$ +131°, and $[\alpha]^{25}_{436}$

+304° (*c* 1.0, THF); ^{1}H NMR δ 8.15–6.35 (m, ArH, 22 H), 4.68 (broad s, $ArCH_2$, 4 H), 3.98 (broad s, OCH_2CO_2, 4 H), and 430–2.80 (m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{54}H_{48}O_{12}$: C, 72.96; H, 5.44. Found: C, 73.10; H, 5.56.

(*R,R*),(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(3-hydroxymethylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-37] and (*R,S*)-37. From 3.5 g (10.1 mmol) of tetrol **9**, 4.1 g (10 mmol) of diethylene glycol ditosylate, 1.15 g (20.3 mmol) of KOH in 210 mL of THF, and 16 mL of water refluxed under N_2 for 5 days was obtained 5.5 g of crude product (procedure I). Chromatography of this material on silica gel with 20:1 (v:v) ether–methanol gave after further chromatography on alumina 0.50 g (10%) of (*R,R*),(*S,S*)-**37**: mp 168–170 °C (bubbles); M^+ 832 (weak) $M^+ - 2H_2O$ 796; ^{1}H NMR ($CDCl_3$) δ 7.76 (m, ArH, 8 H), 7.10 (m, ArH, 12 H), 4.76 (s, $ArCH_2$, 8 H), 3.36–2.96 (m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{52}H_{48}O_{10}$: C, 74.98; H, 5.81. Found: C, 74.86; H, 6.00.

Further elution of the silica gel column with 92% ether–8% methanol (v:v) gave 0.52 g (10%) of (*R,S*)-**37**: mp 168–170 °C (bubbles); $M^+ - 2H_2O$ 796; ^{1}H NMR ($CDCl_2$) δ 7.80 (m, ArH, 8 H), 7.10 (m, ArH, 12 H), 4.80 (broad s, $ArCH_2$, 8 H), 3.83–2.48 (complex m, OCH_2CH_2O, 16 H). Anal. Calcd for $C_{52}H_{48}O_{10}$: C, 74.98; H, 5.81. Found: C, 75.14; H, 6.00.

These two diastereomers give a mmp 148–160 °C (bubbles). Thorough mixing of (*R,R*),(*S,S*)-**37** (83 mg), 0.20 mL of $CDCl_3$, 0.40 mL of CD_3CO_2D, 0.11 mL of D_2O, 20.2 mg of optically pure (+)-α-phenylethylammonium bromide, and 10 mg of $NaPF_6$ gave two layers, whose ^{1}H NMR spectra indicated the macrocycle was 40% in the aqueous-rich and 60% in the chloroform-rich phase. The amine salt was almost completely in the aqueous layer. The macrocycle in each layer was isolated. Material from the $CDCl_3$ layer gave $[\alpha]^{25}_{578}$ +0.1 ± 0.05° (*c* 2, $CHCl_3$), and that from the water layer gave $[\alpha]^{25}_{578}$ −0.2 ± 0.1° (*c* 2, $CHCl_3$). A similar distribution experiment performed with (*R,S*)-**37** gave optical rotations of 0.0°.

2,3,4,5,13,14,15,16-Tetra-1,2-(3-*N*-morpholinomethylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene (38). From 19.36 g (40 mmol) of diaminodiol **4**, 29 g (80 mmol) of *t*-BuOK, and 16.56 g (40 mmol) of diethylene glycol ditosylate in 800 mL of THF held at 25 °C for 12 h and at reflux for 90 min was isolated (procedure I) 34.8 g of material which was chromatographed on 900 g of neutral alumina with ether as eluting agent. Fractions 3–7 (500-mL fractions) contained 2,3:4,5-di-1,2-(3-*N*-morpholinomethylnaphtho)-1,6,9-trioxaundeca-2,4-diene, which after further purification by alumina chromatography gave 7.9 g (36%) of pure material as an oil, dried at 60 °C (20 mm) for 24 h, M^+ 554. Anal. Calcd for $C_{34}H_{38}O_5N_2$: C, 73.64; H, 6.86. Found: C, 73.92; H, 7.08. Fractions 9–14 of the original chromatograph column contained **38**, which precipitated as a microcrystalline material on evaporation of the ether solution: weight 11.2 g (51%); mp 130–132 °C; M^+ 1108; one component on TLC. Anal. Calcd for $C_{68}H_{76}O_{10}N_4$: C, 73.64; H, 6.86. Found: C, 73.32; H, 7.16. The configuration of this material was not determined.

(*R,R*),(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-bromonaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-40], (*R,S*)-40, and (+)-(*R,R*)-40. Cycle (*R,R*),(*S,S*)-bisdinaphthyl-22-crown-6 [(*R,R*),(*S,S*)-**39**)],[4] 6.82 g (9.57 mmol) in 400 mL of CH_2Cl_2, was stirred under argon at 2 °C. Bromine (4.0 mL or 78.4 mmol) dissolved in 100 mL of CH_2Cl_2 was added dropwise (30 min) with stirring. After an additional 30 min, 50 mL of a 10% $NaHSO_3$ solution was added, the organic phase was separated, anhydrous K_2CO_3 was added, and the mixture was refluxed for 10 min and filtered. The filtrate was filtered through a 100-g column of activity IV alumina, and the column filtrate was evaporated to leave a light yellow oil. This material crystallized from CH_2Cl_2–ether (1:1, v:v), and the solid that separated was collected and slurried with hot ethyl acetate, cooled, and filtered to give 8.65 g (88%) of white crystals of (*R,R*),(*S,S*)-**40**: mp 299–300 °C; ^{1}H NMR ($CDCl_3$) δ 7.25 (d, ArH^3, $J_{3,4}$ = 9 Hz, 4 H), 7.80 (d, ArH^4, 4 H), 7.97 (d, ArH^5, $J_{5,7}$ = 2 Hz, 4 H), 7.20 (d of d, ArH^7, $J_{7,8}$ = 9 Hz, 4 H), 6.85 (d, ArH^8, 4 H), 3.81 (m, $ArOCH_2$, 8 H), and 3.17 (m, CH_2OCH_2, 8 H). Anal. Calcd for $C_{48}H_{36}Br_4O_6$: C, 56.06; H, 3.58. Found: C, 56.25; H, 3.50.

Similarly, (*R,S*)-**39** gave (*R,S*)-**40** in 90% yield, mp 334–335 °C (from $CHCl_3$–heptane), M^+ 1024. Anal. Calcd for $C_{48}H_{36}Br_4O_6$: C, 56.06; H, 3.53. Found: C, 56.30; H, 3.57.

Similarly, optically pure (+)-(*R,R*)-**39**[4] gave (+)-(*R,R*)-**40** (91%): mp 179–180 °C (from $CHCl_3$–heptane); $[\alpha]^{25}_{589}$ +108°, $[\alpha]^{25}_{578}$ +124°, $[\alpha]^{25}_{546}$ +148° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{48}H_{36}Br_4O_6$: C, 56.06; H, 3.53. Found: C, 56.27; H, 3.12.

(*R,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-dimethylmethoxysilylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,S*)-41]. In a dry system under pure dry argon was placed 250 mL of pure dry 1,2-dimethoxymethane (distilled from CaH_2) containing a trace amount of triphenylmethane indicator. A few drops of butyllithium solution in hexane were added until a pink color persisted. Then 6 mL of a 2.2 M solution of butyllithium in hexane (13.2 mmol) was added dropwise under argon to the solution stirred at −75 °C. Tetrabromide (*R,S*)-**40** (2.05 g) was added and the resulting mixture was stirred for 3 h at −75 °C and then added rapidly under argon to 12 g of dichlorodimethylsilane stirred at −75 °C. The stirred mixture was allowed to warm to 25 °C, and after 4 h at 25 °C the mixture was heated to reflux for 10 h. The mixture was cooled and filtered, the filter cake was washed with dry 1,2-dimethoxyethane, and the solvent was evaporated under reduced pressure to give a glass, which was stirred with 25 mL of dry methanol. The resulting solution was evaporated and the residue was chromatographed on silica gel in CH_2Cl_2 to give 1.8 g (84%) of (*R,S*)-**41**: mp 95–96 °C; M^+ 1064. Anal. Calcd for $C_{60}H_{72}Si_4O_{10}$: C, 67.67; H, 6.77. Found: C, 67.45; H, 6.89.

(*R,R*),(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-acetylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-42]. Anhydrous $AlCl_3$ (10.68 g or 80 mmol) and acetyl chloride (3.14 g or 40 mmol) were added to 50 mL of nitrobenzene (distilled from P_2O_5 and stored over 4 Å molecular sieves) at 25 °C. The solution was stirred at 25 °C for 15 min, 1.0 g (1.4 mmol) of (*R,R*),(*S,S*)-**39**[4] was added, and the mixture was stirred at 25 °C for 2 h. The reaction mixture was poured onto a mixture of ice and hydrochloric acid, and the mixture was shaken with CH_2Cl_2. the water layer was extracted with CH_2Cl_2, and the combined organic phases were dried and evaporated (in vacuum), and the residue was chromatographed on 75 g of low activity silica gel with CH_2Cl_2–ethanol (98:2, v:v) as eluting agent to give 1.15 g (93%) of product, which was rechromatographed on 75 g of silica gel to give with 200:1 (v:v) CH_2Cl_2–ethanol, (*R,R*),(*S,S*)-**42**, which was dissolved in 40 mL of hot $CHCl_3$ and crystallized by the addition of 5 mL of ether to give 630 mg (51%) of pure product: mp 340–341 °C (decomposition); IR spectrum (KBr), carbonyl absorption at 1680 cm^{-1}. Anal. Calcd for $C_{48}H_{40}O_6$: C, 76.35; H, 5.49. Found: C, 76.10; H, 5.64.

Similarly, 2.0 g of optically pure (−)-(*S,S*)-**39**[4] was converted to 2.2 g (89%) of (−)-(*S,S*)-**42** (without chromatography, but precipitated with ether from nitrobenzene–CH_2Cl_2), 258–262 °C. An analytical sample recrystallized from ether–$CHCl_3$ gave: mp 264–265 °C dec; $[\alpha]^{25}_{578}$ −87°, $[\alpha]^{25}_{546}$ −105° (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.67 (s, CH_3, 12 H), 3.19 (m, $ArOCH_2$, 8 H), 3.83 (m, CH_2OCH_2, 8 H), 7.03 (d, $J_{7,8}$ = 9 Hz, 4 H), 7.34 (d, $J_{3,4}$ = 9 Hz, 4 H), 7.70 (d of d, $J_{7,8}$ = 9 Hz, $J_{5,7}$ = 2 Hz, 4 H), 8.08 (d, $J_{3,4}$ = 9 Hz, 4 H), 8.48 (d, $J_{5,7}$ = 2 Hz, 4 H); M^+ 880; IR spectrum (KBr), carbonyl absorption at 1670 cm^{-1}. Anal. Calcd for $C_{48}H_{40}O_6$: C, 76.35; H, 5.49. Found: C, 76.35; H, 5.69.

(*R,R*),(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-carbomethoxynaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-43]. A solution of 16 g of KOH (85%) and 11.2 g of NaOH in 72 mL of water was cooled to 0 °C and 8.0 mL (24.8 g or 155 mmol) of Br_2 was added. Tetraacetylcycle (*R,R*),(*S,S*)-**42** (1.2 g or 1.36 mmol) was added to the stirred solution followed by 120 mL of purified dioxane (refluxed 24 h with Na followed by distillation). The vigorously stirred solution was heated slowly to reflux (30 min), held there for 2 h, cooled, and mixed with 100 mL of 10% aqueous $NaHSO_3$. The solvent was evaporated at reduced pressure and the residue was dissolved in 80 mL of water. The solution was acidified with 15 mL of 20% aqueous H_2SO_4 to a pH of 1. The heavy precipitate of tetraacid was collected and washed with acetone and water to give 1.234 g of crude material, which was mixed with 350 mL of dry methanol and 56 drops of concentrated H_2SO_4. The mixture was stirred at reflux for 5 days, the methanol was about 75% evaporated, and the resulting solution was shaken with water and CH_2Cl_2. The organic layer was washed with water, dried, and evaporated under reduced pressure, and the residue was chromatographed on 300 g of silica gel deactivated with 15% water with CH_2Cl_2 as the developer to give 1.1 g of crude diester, which was recrystallized from CH_2Cl_2–acetone to give 1.0 g (77%) of (*R,R*),(*S,S*)-**43**: mp 300–301 °C; M^+ 994; ^{1}H NMR ($CDCl_3$) δ 7.30 (d, ArH^3, $J_{3,4}$ = 9 Hz, 4 H), 8.04 (d, ArH^4, 4 H), 8.60 (d, ArH^5, $J_{5,7}$ = 2 Hz, 4 H), 7.72 (d of d, ArH^7, $J_{7,8}$ = 9 Hz, 4 H), 7.02 (d, ArH^8, 4 H), 3.87 (m, $ArOCH_2$, 8 H), 3.17 (m, CH_2OCH_2, 8 H), and 3.88 (s, CH_3, 12 H). Anal. Calcd for $C_{56}H_{48}O_{14}$: C, 71.18; H, 5.12. Found: C, 71.08; H, 5.10.

(*R,R*),(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-carboxynaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*R,R*),(*S,S*)-44]. A mixture of 0.769 g (0.813 mmol) of (*R,R*),(*S,S*)-**43** and 150 mL of a 0.5 M LiOH solution of 50% purified dioxane–water (v) was heated at reflux for 12 h and the solvent was evaporated under reduced pressure to 30 mL. This solution was acidified with 120 mL of 1 N HCl, and the mixture was boiled to coagulate the product which was collected and water washed. The product was dissolved in 10 mL

of 0.25 M aqueous NaOH, the solution was washed twice with CH_2Cl_2, and the product was again precipitated and coagulated with 1 N HCl solution to pH 1.5. The product was collected and washed with 1 N HCl solution and dried at 0.1 mm at 165 °C for 24 h to give 0.557 g (77%) of (*R,R*),(*S,S*)-**44**; ^{1}H NMR (2.5 M NaOD in D_2O) δ 2.89 (m, OCH_2O, 8 H), 3.70 (m $ArOCH_2$, 8 H), 6.98 (d, ArH^3, $J_{3,4}$ = 9 Hz, 4 H), 7.40 (d, ArH^8, $J_{7,8}$ = 9 Hz, 4 H), 7.63 (d of d, ArH^7, $J_{7,8}$ = 9 Hz, $J_{5,7}$ = 1.3 Hz, 4 H), 8.28 (d, ArH^4, $J_{3,4}$ = 9 Hz, 4 H), and 8.54 (d, ArH^5, $J_{5,7}$ = 1.3 Hz, 4 H). Anal. Calcd for $C_{52}H_{40}O_{14}$: C, 70.26; H, 4.54. Found: C, 70.28; H, 4.71.

(−)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-[6-(3-oxa-2-oxobuta)-naphtho]-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-45]. Thallium trinitrate (4.2 g or 9.5 mmol)[16] was dissolved in a mixture of 83 mL of methanol and 70% aqueous perchloric acid (16 mL) cooled in an ice bath. A solution of optically pure tetraacetylcycle (−)-(*S,S*)-**42** (2.04 g or 2.32 mol) in 25 mL of CH_2Cl_2 was added. The initially homogeneous mixture was stirred for 1 h at 4 °C and 3 h at 25 °C and filtered from the precipitated thallous nitrate. The filtrate was diluted with 200 mL of water and extracted with 200 mL of CH_2Cl_2 twice, and the combined organic layers were dried. Evaporation of the solvent and drying of the residue under vacuum at 75 °C gave (−)-(*S,S*)-**45** as a foam; 2.27 g (98%); M^+ 1000; ^{1}H NMR ($CDCl_3$) δ 3.0–3.4 (m, och_2O, 8 H), 3.6–4.0 (m, $ArOCH_2$, 8 H), 3.67 (s, OCH_3, 6 H), 3.72 (s, $ArCH_2$, 4 H), 7.0–7.4 (m, ArH, 12 H), 7.7–8.0 (m, ArH, 8 H). Recrystallization of a small sample of the material from ether–chloroform gave mp 174–175 °C. Anal. Calcd for $C_{60}H_{56}O_{14}$: C, 71.99; H, 5.64. Found: C, 71.75; H, 5.85.

(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-[6-(3-oxapropana)naphtho]-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(*S,S*)-46]. Ester (−)-(*S,S*)-**45**, 1.65 g, was reduced with $LiAlH_4$ in THF in the usual way to give 1.3 g (90%) of (*S,S*)-**46** as a white foam: M^+ 888; ^{1}H NMR ($CDCl_3$) δ 1.67 (s, OH, 4 H), 2.92 (t, $ArCH_2CH_2$, J = 6 Hz, 8 H), 3.85 (t, $ArCH_2CH_2$, J = 6 Hz, 8 H), 3.0–3.4 (m, $ArOCH_2$, 8 H), 3.6–4.0 (m, OCH_2O, 8 H), 7.0–7.4 (m, ArH, 12 H), 7.7–8.0 (m, ArH, 8 H). An analytical sample was chromatographed on silica gel with gradient elution from CH_2Cl_2 to 6% methanol–CH_2Cl_2 (v), followed by drying at 160 °C (0.1 mm). Anal. Calcd for $C_{56}H_{56}O_{10}$: C, 75.65; H, 6.35. Found: C, 75.67; H, 6.34.

(−)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-vinylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-47]. To a solution of crude tetrol (*S,S*)-**46** (200 mg, 0.23 mmol) in 3 mL of puridine at 0 °C was added 300 mg or 1.6 mmol of tosyl chloride, and the solution was allowed to stand at 0 °C for 48 h. The tetratosylate was isolated in the usual way to give 0.310 mg or 0.21 mmol (88%) of crude product used directly in the next step. This material was dissolved in 4 mL of Me_2SO (4 mL, distilled from BaO and stored over 4 Å molecular sieves) and 112 mg (1 mmol) of *t*-BuOK was added to give a dark brown mixture that was stirred for 2 h at 25 °C. The mixture was shaken with 25 mL of 10% hydrochloric acid and 40 mL of CH_2Cl_2. The organic layer was washed with water, dried, and evaporated under reduced pressure to give a brown oil that was chromatographed on 7 g of silica gel in CH_2Cl_2 to give 80 mg (47%) of (−)-(*S,S*)-**47** as a colorless glass, dried at 25 °C (0.1 mm): M^+ 816; $[\alpha]^{25}_{578}$ −52°, $[\alpha]^{25}_{546}$ −62°, $[\alpha]^{25}_{435}$ −175° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 3.1–3.4 (m, $ArOCH_2$, 8 H), 3.7–4.0 (m, CH_2OCH_2, 8 H), 5.23, 5.71, and 6.84 (d of d, $CH{=}CH_2$ J = 1 and 11 Hz; J = 1 and 17 Hz; J = 11 and 17 Hz, respectively, 4 H each), 7.0–7.5 (m, ArH, 12 H), 7.7–8.0 (m, ArH, 8 H). For analysis the sample was dried at 140 °C (0.1 mm) for 72 h. Anal. Calcd for $C_{56}H_{48}O_6$: C, 82.35; H, 5.92. Found: C, 82.25; H, 6.02.

(−)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-barium sulfonatonaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-48]. Optically pure bisdinaphtho-22-crown-6 [(−)-(*S,S*)-**39**][4], 5.0 g or 7.02 mmol, was added at 25 °C with stirring to 25 mL of concentrated H_2SO_4. After 2 h of stirring at 25 °C the mixture was homogeneous and light brown. After 22 h of additional stirring at 25 °C, the solution was poured slowly into 125 mL of distilled water at 0 °C with stirring at 0 °C (ice bath). The solution was neutralized to pH 7.4 with $Ba(OH)_2{\cdot}8H_2O$. Because of the massive precipitate of $BaSO_4$ it was necessary to filter at an intermediate stage and then the neutralization was continued. The final mixture was heated to coagulate the $BaSO_4$ and the mixture was filtered through a fritted glass filter. The filter cake was thoroughly washed with boiling distilled water, and the clear filtrate was evaporated under reduced pressure to give 4.5 g (50% of (−)-(*S,S*)-**48**. An analytical sample of this salt dissolved in H_2O was purified by gel permeation chromatography (Bio-Gel P_2, 100–200 mesh, exclusion limit, 2600). The neutral UV-active fractions were combined and evaporated to dryness to give white crystals: mp >360 °C; $[\alpha]^{25}_{589}$ −165.5°, $[\alpha]^{25}_{578}$ −180.0°, $[\alpha]^{25}_{546}$ −216.4° (*c* 1.2, H_2O); ^{1}H NMR (D_2O) δ relative to $(CH_3)_2CO$ as internal standard 0.46 (broad s, OCH_2O, 8 H), 1.32 (broad s, $ArOCH_2$, 8 H), 4.66 (d, $J_{7,8}$ = 9 Hz, ArH^8, 4 H), 5.08 (m, ArH^3 + ArH^7, 8 H), 5.97 (d, $J_{3,4}$ = 10 Hz, ArH^4, 4 H), and 6.24 (s, ArH^5, 4 H). Anal. Calcd for $C_{48}H_{36}S_4O_{18}Ba_2$: C, 43.22; H, 2.78; Ba, 21.20. Found: C, 43.50; H, 3.02; Ba, 21.20.

An aqueous solution containing 1.5 g (1.1 mmol) of (−)-(*S,S*)-**48** in distilled water was passed through 10 g of Dowex 50 cationic exchange resin. The UV-active effluent was evaporated, and the remaining tetrasulfonic acid liquid was dried at 40 °C for 4 h. This material gave a neutralization equivalent with LiOH in distilled water to a phenolphthalein end point of 255 (Calcd 258) and was neutralized likewise to give after evaporation and drying 1.2 g (98%) of the tetralithium salt of the tetrasulfonic acid, whose ^{1}H NMR spectrum in D_2O was superimposable on that of the Ba salt.

(−)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(6-*tert*-butylnaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-49]. A solution of 391 mg (0.54 mmol) of optically pure (−)-(*S,S*)-**39**[4] in 5 mL of dry CH_2Cl_2 was cooled to −78 °C, and 0.51 g (5.4 mmol) of *tert*-butyl chloride was added followed by 0.72 g (5.4 mmol) of $AlCl_3$. The reaction mixture was stirred for 6 h at −78 °C and quenched with water. The mixture was shaken with CH_2Cl_2 and water, the organic phase was dried, and the solvent was evaporated under reduced pressure to give 0.40 g of crude product as a foam. This material was chromatographed on silica gel with CH_2Cl_2 as the mobile phase to give 230 mg (45%) of product, which after crystallization from ethanol–$CHCl_3$ gave (−)-(*S,S*)-**49**: mp 289–291 °C; M^+ 936; ^{1}H NMR ($CDCl_3$) δ 1.25 (s, CH_3, 36 H), 3.20 (m, CH_2OCH_2, 8 H), 3.8 (m, $ArOCH_2$, 8 H), 6.92 to 7.26 (m, ArH, 12 H), and 7.70 to 7.88 (m, ArH, 8 H). The aryl splitting pattern resembles that of tetraester **45** and that of tetravinyl compound **47**. The compound gave $[\alpha]^{25}_{589}$ −116.9°, $[\alpha]^{25}_{578}$ −122.4°, $[\alpha]^{25}_{546}$ −146.2°, $[\alpha]^{25}_{436}$ −342.3° (*c* 1.05, $CHCl_3$). Anal. Calcd for $C_{64}H_{72}O_6$: C, 82.01; H, 7.74. Found: C, 81.75; H, 7.91.

(−)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-50]. A 2.0-g sample (28 mmol) of (−)-(*S,S*)-**39**, $[\alpha]^{25}_{578}$ −221° (*c* 1.0, $CHCl_4$),[4] was dissolved with heating in 350 mL of glacial acetic acid–ethyl acetate (6:1, v:v) and 0.50 g of PtO_2 was added. The solution was hydrogenated in a Parr apparatus at 25 °C under 3 atm of hydrogen for 5 days. The solution was filtered, the solvent was evaporated under reduced pressure, and the residue in $CHCl_3$ was extracted with 10% $NaHCO_3$ to remove the acetic acid. Evaporation of the filtrate gave 2.0 g (98%) of product as white needles, which were recrystallized from cyclohexane to give (−)-(*S,S*)-**50**: mp 235–236 °C; M^+ 728; ^{1}H NMR ($CDCl_3$) δ 1.7 (m, CCH_2CH_2C, 16 H), 2.2 (m, CH_2 at C-8 of tetralin, 8 H), 2.8 (m, CH_2 at C-5 of tetralin, 8 H), 3.4 and 3.7 (m, m, OCH_2CH_2O, 16 H), 6.5 (d, ArH^3, 4 H), 6.9 (d, ArH^4, 4 H); $[\alpha]^{25}_{578}$ −55°, $[\alpha]^{25}_{546}$ −62°, $[\alpha]^{25}_{436}$ −106° (*c* 1.0 $CHCl_3$). Anal. Calcd for $C_{48}H_{56}O_6$: C, 79.09; H, 7.74. Found: C, 79.15; H, 7.96.

This same compound, (−)-(*S,S*)-**50**, was prepared in 54% yield by the ring-closing reaction of 1.1 g (3.7 mmol) of reduced diol (−)-(*S*)-**22**, $[\alpha]^{25}_{578}$ −55.5° (*c* 1.0 $CHCl_3$), with the reduced two-armed ditosylate (−)-(*S*)-**24**, $[\alpha]^{25}_{578}$ −26.2° (*c* 1.0, $CHCl_3$), in 300 mL of refluxing THF–H_2O (99:1, v:v) containing 0.42 g (7.5 mmol) of KOH (4 day reaction time). The cyclic product, after alumina chromatography and recrystallization from cyclohexane, gave mp 235–236 °C, an ^{1}H NMR spectrum identical with that of (−)-(*S,S*)-**50** prepared from (−)-(*S,S*)-**39**, and $[\alpha]^{25}_{578}$ −55°, $[\alpha]^{25}_{546}$ −62 °. and $[\alpha]^{25}_{436}$ −105° (*c* 1.0, $CHCl_3$).

(+)-(*R,R*)-2,3,4,5-Di-1,2-(3-methyl-5,6,7,8-tetrahydronaphtho)-13,14,15,16-di-1,2-(5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*R,R*)-51]. Procedure III. A sample of 1.23 g (1.66 mmol) of (+)-(*R,R*)-**29**, $[\alpha]^{25}_{578}$ +144.5° (*c* 1, $CHCl_3$), was dissolved with heating in 50 mL of glacial acetic acid, and 297 mg of PtO_2 was added. The mixture was stirred at 85 °C under 1 atm of H_2 for 5 days and filtered. The filtrate was evaporated under reduced pressure, and the residue in ether was passed through a short alumina column to remove the acetic acid. The material was then chromatographed in CH_2Cl_2 on silica gel to give 1.17 g (70%) of (+)-(*R,R*)-**51** as a white foam (dried at 50 °C (0.1 mm) for 20 h): M^+ 756; $[\alpha]^{25}_{578}$ +35.4°, $[\alpha]^{25}_{546}$ +39.2°, $[\alpha]^{25}_{436}$ +63.7° (*c* 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.7 (m, CCH_2CH_2C, 16 H), 2.2 (s and m superimposed, CH_3 and CH_2 at C-8 of tetralin ring, 14 H), 2.8 (m, CH_2 at C-5 at tetralin ring, 8 H), 3.4 and 3.7 (m, OCH_2CH_2O, 16 H), 6.5–7.0 (s at 6.8 superimposed on q, ArH, 6H). Anal. Calcd for $C_{50}H_{60}O_6$: C, 79.33; H, 7.99. Found: C, 79.31; H, 7.92.

In an alternative synthesis of (+)-(*R,R*)-**51** in which none of the intermediates were characterized, optically pure (+)-(*R*)-**3** was converted to (+)-(*R*)-bis-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl,[4] $[\alpha]^{25}_{578}$ +22.1° (*c* 1, $CHCl_3$), which was catalytically

reduced in acetic acid with PtO_2 and H_2 at 50 °C for 2 days to give (*R*)-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-5,5′-6,6′,7,7′,8,8′-octahydro-1,1′-dinaphthyl (68%) which was tosylated to give the ditosylate (*R*)-**24**, 45% (^{1}H NMR identical to (*S*)-**24**, see above). This material was ring closed by procedure II with (+)-(*R*)-**13** (optically pure) to give (+)-(*R,R*)-**57** (72%) (^{1}H NMR identical to (−)-(*S,S*)-**57**, see below) which was reduced in acetic acid, H_2, and PtO_2 at 80–90 °C for 5 days to give (+)-(*R,R*)-**51** (43%), $[\alpha]^{25}_{578}$ +34.8°, $[\alpha]^{25}_{546}$ +38.5°, $[\alpha]^{25}_{436}$ +62.0° (*c* 1.92, $CHCl_3$). These rotations are 98, 98, and 97% respectively of the sample of (+)-(*R,R*)-**51** prepared from (+)-(*R,R*)-**29**.

(+)-(*R,R*)-2,3,4,5,13,14,15,16-Tetra-1,2-(3-methyl-5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*R,R*)-52]. A 2.0-g sample (12.6 mmol) of (+)-(*R,R*)-**32**, $[\alpha]^{25}_{578}$ +134.8° (*c* 1.0, $CHCl_3$), 250 mL of glacial acetic acid, and 660 mg of PtO_2 was stirred at 60 °C. The product was isolated as in procedure III to give 1.84 g (88%) of (+)-(*R,R*)-**52** as a white foam: M^+ 784; $[\alpha]^{25}_{578}$ +22.2°, $[\alpha]^{25}_{546}$ +23.3°, $[\alpha]^{25}_{436}$ +33.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.6 (m, CCH_2CH_2C, 16 H), 2.2 (m and s, $ArCH_2$ at C-8 of decalin and $ArCH_3$, 20 H), 2.7 (m, $ArCH_2$ at C-5 of decalin, 8 H), 3.3 and 3.7 (m, m, OCH_2CH_2O, 16 H), 6.8 (s, ArH, 4 H). Anal. Calcd for $C_{52}H_{64}O_6$: C, 79.55; H, 8.21. Found: C, 79.33; H, 8.01.

(+)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(3-bromo-5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*S,S*)-53]. To a solution of 141 mg (0.194 mmol) of (−)-(*S,S*)-**50** (see above) dissolved in 10 mL of CH_2Cl_2 was added 0.05 mL of Br_2. The solution was immediately covered with foil and cooled to −45 °C for 1 h, by which time starting material had disappeared (TLC). After an additional 45 min, the reaction mixture was added to 10 mL of 10 aqueous $NaHSO_3$. The mixture was shaken, the aqueous layer was washed with CH_2Cl_2, and the combined organic layers were washed with water, dried, and evaporated to give (+)-(*S,S*)-**53** as a white foam which was dried at 50 °C (0.1 mm) for 24 h, 0.193 mg (96%). The material gave: M^+ 1040 (part of an isotopic cluster); $[\alpha]^{25}_{578}$ +98.1°, $[\alpha]^{25}_{546}$ +114°, $[\alpha]^{25}_{436}$ +223° (*c* 0.81, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.7, 2.2, and 2.7 [m, $(CH_2)_4$, 32 H], 3.4 and 3.7 (m, OCH_2CH_2O, 16 H), 7.3 (s, ArH, 4 H). Anal. Calcd for $C_{48}H_{52}O_6Br_4$: C, 55.19; H, 5.02. Found: C, 55.34; H, 5.05.

(+)-(*R,R*)-2,3,4,5-Di-1,2-(3-bromo-5,6,7,8-tetrahydronaphtho)-13,14,15,16-di(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*R,R*)-54]. To a stirred solution of 7.3 g (16 mmol) of dibromodiol (+)-(*R*)-**27** (see above) and 14.2 g (18 mmol) of the optically pure two-armed ditosylate (+)-(*R*)-**21**[4] in 1 L of THF under N_2 was added 1.8 g (36 mmol) of KOH in 30 mL of water. The mixture was refluxed for 7 days and the crude product was isolated in the usual way and chromatographed on 300 g of neutral activity I alumina in ether. The column was eluted with 5 L of ether to give 9.6 g (68%) of (+)-(*R,R*)-**54** as a white foam: M^+ 876 (^{79}Br); $[\alpha]^{25}_{436}$ +66°, $[\alpha]^{25}_{546}$ +20°, and $[\alpha]^{25}_{578}$ +16° (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.80 (m, ArH, 4 H), 7.24 (m, ArH, 10 H), 3.50 (m, OCH_2CH_2O, 16 H), 2.70 (m, $ArCH_2$, 4 H), 2.10 (m, $ArCH_2$, 4 H), and 1.62 (m, CCH_2CH_2C, 8 H). Anal. Calcd for $C_{48}H_{46}Br_2O_6$: C, 65.16; H, 5.28. Found: C, 65.78; H, 5.48.

(+)-(*R,R*)-2,3,4,5-Di-1,2-(5,6,7,8-tetrahydronaphtho)-13,14,15,16-di(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*R,R*)-55]. To a stirred solution of 1.5 g (1.7 mmol) of dibromocycle (+)-(*R,R*)-**54** (see above) in 200 mL of dry THF stirred under N_2 at −78 °C was added 20 mL of butyllithium (1.6 M in hexane). The mixture was stirred for 45 min, CH_3OH was added dropwise (20 mL), and the solution was allowed to warm to 25 °C. The crude product was isolated by the usual extraction–evaporation method to give a white solid which when crystallized from CH_2Cl_2–hexane gave 1.18 g (96%) of (+)-(*R,R*)-**55**: mp 211–212 °C, M^+ 720; $[\alpha]^{25}_{436}$ +251°, $[\alpha]^{25}_{546}$ +116°, and $[\alpha]^{25}_{578}$ +99° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.82 (m, ArH, 4 H), 6.96 (m, ArH, 12 H), 3.50 (m, OCH_2CH_2O, 16 H), 2.74 (m, $ArCH_2$, 4 H), 2.18 (m, $ArCH_2$, 4 H), and 1.68 (m, CCH_2CH_2C, 8 H). Anal. Calcd for $C_{48}H_{48}O_6$: C, 79.97; H, 6.71. Found: C, 80.22; H, 6.96.

(+)-(*R,R*)-2,3,4,5,13,14,15,16-Tetra-1,2-(5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*R,R*)-50]. A mixture of 300 mg (0.42 mmol) of (+)-(*R,R*)-**55** and 100 mg of PtO_2 and 50 mL of glacial acetic acid was hydrogenated at 25 °C for 5 days. The product was isolated as in procedure III to give 280 mg (92%) of white crystalline (+)-(*R,R*)-**50** (from CH_2Cl_2–hexane), mp 234–235 °C, whose ^{1}H NMR spectrum and TLC behavior were identical to that of (−)-(*S,S*)-**50** (see above), $[\alpha]^{25}_{436}$ +102°, $[\alpha]^{25}_{546}$ +60°, $[\alpha]^{25}_{578}$ +53° (*c* 1.0, $CHCl_3$).

(+)-(*R,R*)-2,3,4,5-Di-1,2-(3-methyl-5,6,7,8-tetrahydronaphtho)-13,14,15,16-di(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(+)-(*R,R*)-56]. To a stirred solution of 3.8 g (11.8 mmol) of reduced optically pure dimethyldiol, (+)-(*R*)-**23**, in 600 mL of THF under N_2 was added 1.35 g (24 mmol) of KOH in 10 mL of water. The mixture was stirred for 15 min at 25 °C, 9.5 g (12.3 mmol) of optically pure dinaphthyl two-armed ditosylate [(+)-(*R*)-**21**][4] in 400 mL of THF was added, and the mixture was refluxed for 7 days. The crude product was isolated as in procedure I and was chromatographed on 200 g of alumina in ether with ether as developer to give 6.2 g (70%) of product as a white foam after drying at 60 °C (0.1 mm) for 24 h. This (+)-(*R,R*)-**56** gave: M^+ 748; $[\alpha]^{25}_{436}$ +244°, $[\alpha]^{25}_{546}$ +110°, $[\alpha]^{25}_{578}$ +93°, and $[\alpha]^{25}_{589}$ +83° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.80 (m, ArH, 10 H), 7.08 (m, ArH, 10 H), 3.50 (m, OCH_2CH_2O, 16 H), 2.72 (m, $ArCH_2$, 4 H), 2.18 (s, $ArCH_3$, 6 H), 2.14 (m, $ArCH_2$, 4 H), and 1.64 (m, CCH_2CH_2C, 8 H). Anal. Calcd for $C_{50}H_{52}O_6$: C, 80.18; H, 7.00. Found: C, 80.09; H, 7.03.

(−)-(*S,S*)-2,3,4,5-Di-1,2-(3-methylnaphtho)-13,14,15,16-di-1,2-(5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-57]. To a solution of reduced ditetralyldiol (−)-(*S*)-**22**, $[\alpha]^{25}_{578}$ −49.4° (*c* 1.0, $CHCl_3$), in 150 mL of dry THF under N_2 was added 0.50 g (7.6 mmol) of KOH (85%), the mixture was refluxed for 30 min, and 2.62 g (3.4 mmol) of optically pure dimethyldinaphthyl two-armed ditosylate (+)-(*S*)-**20** ($[\alpha]^{25}_{578}$ +70.0°, *c* 1.0, $CHCl_3$) in 50 mL of dry THF was added. The mixture was refluxed for 160 h, and the crude product was isolated as in procedure I to give 1.45 g of material that was submitted to gel permeation chromatography to give after drying at 60 °C (0.1 mm) for 24 h 1.06 g (42%) of (−)-(*S,S*)-**57** as a white foam: M^+ 748; $[\alpha]^{25}_{436}$ −88.6°, $[\alpha]^{25}_{546}$ −47.6°, $[\alpha]^{25}_{578}$ −41.0°, and $[\alpha]^{25}_{589}$ −39.4°; ^{1}H NMR ($CDCl_3$) δ 7.9, 6.8 (m, m, ArH, 14 H), 3.1–4.0 (m, OCH_2CH_2O), 2.95 (m, $ArCH_2$, 4 H), 2.50 (s, CH_3, 6 H), 2.23 (m, $ArCH_2$, 4 H), 1.93 (m, CCH_2CH_2C, 8 H). Anal. Calcd for $C_{50}H_{52}O_6$: C, 80.18; H, 6.99. Found: C, 80.07; H, 7.03.

(−)-(*S,S*)-2,3,4,5,10,11,12,13-Tetra-1,2-(5,6,7,8-tetrahydronaphtho)-1,6,9,14,17,20-hexaoxacyclodocosa-2,4,10,12-tetraene [(−)-(*S,S*)-58]. A mixture of 1.013 g (1.41 mmol) of (−)-(*S,S*)-2,3,4,5,10,11,12,13-tetra-1,2-naphtho-1,6,9,14,17,20-hexaoxacyclodocosa-2,4,10,12-tetraene [$[\alpha]^{25}_{578}$ −223°, *c* 4.5, $CHCl_3$],[4] 48 mg of PtO_2, and 70 mL of glacial acetic acid was heated at 75–85 °C under 1 atm of H_2 with stirring for 7 days. The product was isolated as in procedure III and purified by chromatography on silica gel–CH_2Cl_2 to give 820 mg (85%) of (−)-(*S,S*)-**58**: M^+ 728; $[\alpha]^{25}_{578}$ −106°, $[\alpha]^{25}_{546}$ −121°, $[\alpha]^{25}_{436}$ −223° (*c* 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.7 (m, CCH_2CH_2C, 16 H), 2.2, 2.8 (m, m, $ArCH_2$, 16 H), 3.2, 3.5, 3.9 (m, OCH_2CH_2O, 16 H), 6.2–7.0 (m, ArH, 8 H). Anal. Calcd for $C_{48}H_{56}O_6$: C, 79.09; H, 7.74. Found: C, 79.10; H, 7.80.

(+)-(*S,S*)-2,3,4,5,10,11,12,13-tetra-1,2-(3-bromo-5,6,7,8-tetrahydronaphtho)-1,6,9,14,17,20-hexaoxacyclodocosa-2,4,10,12-tetraene [(+)-(*S,S*)-59]. To a solution of 581 mg (0.798 mmol) of (−)-(*S,S*)-**58** (see above) in 25 mL of CH_2Cl_2 in a foil-wrapped flask and cooled to −50 °C was added with stirring 0.25 mL of bromine. After 2 h, 15 mL of a 10% aqueous solution of $NaHSO_3$ was added, the layers were shaken, and the aqueous layer was washed with 10 mL of CH_2Cl_2. The combined organic layers were washed with water, dried, and evaporated under reduced pressure to give a white foam of (+)-(*S,S*)-**59**: 588 mg (94%); M^+ 1040 (isotopic cluster); $[\alpha]^{25}_{578}$ +47.6°, $[\alpha]^{25}_{546}$ +55.4°, $[\alpha]^{25}_{436}$ +109.6° (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.7, 2.1 and 2.7 [m, $(CH_2)_4$, 32 H], 3.4 and 3.8 (m, OCH_2CH_2O, 16 H), 7.3 (d, ArH, 4 H). Anal. Calcd for $C_{48}H_{52}Br_4O_6$: C, 55.19; H, 5.02. Found: C, 55.52; H, 5.03.

Optical Stability to Heat of (−)-(*S,S*)-2,3,4,5,13,14,15,16-Tetra-1,2-(5,6,7,8-tetrahydronaphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene [(−)-(*S,S*)-(50)]. A 77.8-mg sample of (−)-(*S,S*)-**50** was dissolved in 15 mL of diphenyl ether which had been passed through an alumina column. The rotations of the solution were measured at 25 °C in a 1-mL, 1-dm cell, α^{25}_{578} −0.110°, α^{25}_{546} −0.124°, α^{25}_{436} −0.168° (observed). An 8-mL aliquot of this solution was transferred to a thick-walled glass ampule which was evacuated, passed through two freeze–thaw cycles, frozen a third time, and sealed, all under high vacuum. The ampule was heated to 175 °C for 1 week and cooled and the rotations were measured, $[\alpha]^{25}_{578}$ −0.106°, $[\alpha]^{25}_{546}$ −0.122°, $[\alpha]^{25}_{436}$ −0.162°. The already heated material was transferred to a fresh ampule, similarly sealed and heated at 200 °C for 1 week and 223 °C for 1 week and the rotations were measured, $[\alpha]^{25}_{578}$ −0.106°, $[\alpha]^{25}_{546}$ −118°, $[\alpha]^{25}_{436}$ −156°. The already heated material was similarly recycled and held at 253 °C for 5 days to give $[\alpha]^{25}_{578}$ −0.106°, $[\alpha]^{25}_{546}$ −0.119°, and $[\alpha]^{25}_{436}$ −0.156°. These experiments demonstrate these ditetralyl systems are configurationally stable to temperatures as high as 250 °C for as long as 5 days.

In a similar experiment, (+)-(*R,R*)-**50** of rotation $[\alpha]^{25}_{578}$ +57.8° (*c* 0.83 $CHCl_3$) was heated in a sealed tube in diphenyl ether at 226

°C for 1 week. The material was reisolated and subjected to silica gel chromatography (a small amount of open-chain material was removed), and the (+)-(*R*,*R*)-**50** recovered gave $[\alpha]^{25}_{578}$ +60.2° (*c* 1.04, $CHCl_3$).

In an identical and parallel experiment, the bisdinaphthyl system (+)-(*R*,*R*)-**39** of rotation $[\alpha]^{25}_{578}$ +209° (*c* 1.0, CH_2Cl_2) was found to decrease in rotation to $[\alpha]^{25}_{578}$ +202° (*c* 1.1, CH_2Cl_2). During silica gel purification, again a small amount of open-chain material was removed.

Configurational Stability to Heat of (+)-(*R*)-2,2′-Dihydroxy-1,1′-dinaphthyl [(+)-(*R*)-3] and of (+)-(*R*)-2,2′-Dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-dinaphthyl [(+)-(*R*)-22]. The general procedures involved dissolving 100-mg samples of each diol in the appropriate solutions in parallel experiments and heating each solution with stirring under N_2 in the same oil bath. The optical purity of the isolated product was then determined. Neutral, acidic, and basic conditions were all examined.

A. Neutral Conditions. The diols were heated in 10 mL of butanol at 118 °C for 24 h, and the solutions were cooled and evaporated under reduced pressure to give white solids that were dried at 110 °C (0.05 mm) for 8 h. The total samples were dissolved and their rotations were taken.

B. Acidic Conditions. The diols were heated at 100 °C for 24 h in a solution of purified dioxane (12 mL) and 10 mL of 1.2 M aqueous hydrochloric acid. The solutions were cooled and shaken with 50 mL of $CHCl_3$ and 300 mL of water and the organic layer was dried and evaporated under reduced pressure to give a pale yellow foam dried at 110 °C (0.05 mm) for 8 h. Total samples were dissolved and their rotations were taken.

C. Basic Conditions. The diols were heated at 118 °C for 26 h in 10 mL of butanol that was 0.7 M in KOH. The solutions were cooled and shaken with 50 mL of $CHCl_3$ and 300 mL of dilute hydrochloric acid and the organic layer was washed with water, dried, and evaporated under reduced pressure. Each residue was dissolved in 10 mL of CH_2Cl_2 and chromatographed on 20 g of silica gel in CH_2Cl_2. The 500 mL of column eluate (CH_2Cl_2) was evaporated under reduced pressure to give white solids that were dried 8 h at 110 °C (0.05 mm).

Comparisons of the optical rotations before and after the heat treatments are as follows: Diol (+)-(*R*)-**3**, $[\alpha]^{24}_{589}$ +34.2° (*c* 1.0, THF), initial rotation gave after the above treatments: neutral conditions, $[\alpha]^{25}_{589}$ +33.7° (*c* 1.0, THF) or 1% loss in rotation; acidic conditions, $[\alpha]^{25}_{589}$ +14.9° (*c* 1.0, THF) or 56% loss in rotation; basic conditions, $[\alpha]^{25}_{589}$ +27.2° (*c* 1.0, THF) or 20% loss in rotation. Reduced diol, (+)-(*R*)-**22**, initial rotation $[\alpha]^{25}_{589}$ +52.8 (*c* 1.0, $CHCl_3$), gave after the above treatments: neutral conditions, $[\alpha]^{25}_{589}$ +51.6° (*c* 1.0, $CHCl_3$), 2% loss in rotation; acidic conditions, $[\alpha]^{25}_{589}$ +52.5° (*c* 1.0, $CHCl_3$), <1% loss in rotation; basic conditions, $[\alpha]^{25}_{589}$ +49.1° (*c* 1.0, $CHCl_3$), 7% loss in rotation.

Registry No.—(±)-**3**, 41024-90-2; (+)(*R*)-**3**, 18531-94-7; (−)(*S*)-**3**, 18531-99-2; (±)-**4**, 55442-26-7; (±)-**5**, 55442-27-8; (±)-**6**, 55442-28-9; (±)-**7**, 55442-29-0; (±)-**8**, 65355-15-9; (±)-**9**, 55515-95-2; (+)(*R*)-**9**, 42167-07-7; (−)(*S*)-**9**, 42167-06-6; (±)-**10**, 55442-32-5; (±)-**11**, 55442-31-4; (±)-**12**, 55442-33-6; (±)-**13**, 55442-34-7; (±)(*R*)-**13**, 55515-98-5; (−)(S)-**13**, 55515-99-6; (±)-**13** phosphoric acid diester, 65355-16-0; (+)(*R*)-**13** phosphoric acid diester cinchonine, 65391-02-8; (+)(*R*)-**13** phosphoric acid diester, 65391-01-7; (−)(*S*)-**13** phosphoric acid diester, 39648-68-5; (+)(*R*)-**13** strychnine, 65355-10-4; (+)(*R*)-**13** CH_2OCH_3 diether, 65355-11-5; (±)-**14**, 55442-35-8; (±)-**15**, 55442-36-9; (±)-**16**, 65390-98-9; (+)(*R*)-**16** L-leucine methyl ester, 65355-12-6; (+)(*R*)-**16**, 18531-92-5; (−)(*S*)-**16**, 42167-04-4; (+)-(*R*)-**17**, 18531-91-4; (+)(*R*)-**18**, 65355-13-7; (+)(*S*)-**19**, 65390-99-0; (−)(*R*)-**19**, 65391-00-6; (±)-**19**, 55442-38-1; (±)-**20**, 55442-39-2; (+)-(*S*)-**20**, 65337-83-9; (−)(*R*)-**20**, 65337-84-0; (±)-**21**, 55441-94-6; (+)(*R*)-**21**, 55821-78-8; (+)(*R*)-**22**, 65355-14-8; (−)(*S*)-**22**, 65355-00-2; (+)(*R*)-**23**, 65355-01-3; (+)(*R*)-**24**, 65355-02-4; (−)(*S*)-**24**, 65355-03-5; (+)(*S*)-**25**, 65355-04-6; (−)(*R*)-**25**, 65355-05-7; (−)(*R*)-**26**, 65355-06-8; (+)(*S*)-**26**, 65355-07-9; (+)(*R*)-**27**, 65355-08-0; (±)-**28**, 65355-09-1; (*R*,*S*),(*S*,*R*)-**29**, 55516-17-1; (*R*,*R*),(*S*,*S*)-**29**, 55516-16-0; (+)(*S*,*R*)-**29**, 65390-97-8; (+)(*R*,*R*)-**29**, 55516-22-8; (−)(*S*,*S*)-**29**, 55821-98-2; (*R*,*S*),(*S*,*R*)-**30**, 55442-69-8; (*R*,*R*),(*S*,*S*)-**30**, 55516-19-3; (+)(*R*,*R*)-**30**, 55516-20-6; (+)(*R*,*R*)-**31**, 55516-21-7; (*R*,*S*)-**32**, 55516-15-9; (*R*,*R*),(*S*,*S*)-**32**, 55442-67-6; (+)(*R*,*R*)-**32**, 65337-85-1; (−)(*S*,*S*)-**32**, 65390-94-5; (+)(*R*,*R*)-**33**, 65354-98-5; (+)(*R*,*R*)-**34**, 65354-99-6; (*R*,*R*),(*S*,*S*)-**35**, 55442-70-1; (*R*,*S*),(*S*,*R*)-**35**, 55516-23-9; (+)(*R*,*R*)-**35**, 55516-24-0; (*R*,*S*),(*S*,*R*)-**36**, 55442-71-2; (*R*,*R*),(*S*,*S*)-**36**, 65390-95-6; (+)-(*R*,*R*)-**36**, 55516-25-1; (*R*,*R*),(*S*,*S*)-**37**, 55442-64-3; (*R*,*S*)-**37**, 55527-98-5; (*R*,*R*),(*S*,*S*)-**38**, 65390-96-7; (*R*,*R*),(*S*,*S*)-**39**, 41024-97-9; (*R*,*S*)-**39**, 41024-94-6; (+)(*R*,*R*)-**39**, 41024-95-7; (−)(*S*,*S*)-**39**, 41024-93-5; (*R*,*R*)(*S*,*S*)-**40**, 55516-26-2; (*R*,*S*)-**40**, 55516-27-3; (+)-(*R*,*R*)-**40**, 55130-93-3; (*R*,*S*)-**41**, 55516-28-4; (*R*,*R*),(*S*,*S*)-**42**, 55442-74-5; (−)(*S*,*S*)-**42**, 65390-91-2; (*R*,*R*),(*S*,*S*)-**43**, 65354-86-1; (*R*,*R*)(*S*,*S*)-**44**, 55442-79-0; (−)(*S*,*S*)-**45**, 65354-87-2; (*S*,*S*)-**46**, 65354-88-3; (−)(*S*,*S*)-**47**, 65354-89-4; (−)(*S*,*S*)-**48**, 65354-90-7; (−)-(*S*,*S*)-**49**, 65354-91-8; (−)(*S*,*S*)-**50**, 65354-92-9; (+)(*R*,*R*)-**50**, 65390-92-3; (+)(*R*,*R*)-**51**, 65354-93-0; (+)(*R*,*R*)-**52**, 65354-94-1; (+)(*S*,*S*)-**53**, 65354-95-2; (+)(*R*,*R*)-**54**, 65354-96-3; (+)(*R*,*R*)-**55**, 65354-97-4; (+)(*R*,*R*)-**56**, 65378-55-4; (+)(*R*,*R*)-**57**, 65390-93-4; (−)(*S*,*S*)-**57**, 65354-80-5; (−)(*S*,*S*)-**58**, 65354-81-6; (+)(*S*,*S*)-**59**, 65354-82-7; 4-(butoxymethyl)morpholine, 5625-84-3; dimethylaminoisobutoxymethane, 50339-64-5; cinchonine, 118-10-5; 3-hydroxy-2-naphthoic acid, 92-70-6; L-leucine methyl ester, 2666-93-5; 2-(2-chloroethoxy)-ethyl-2-tetrahydropyranyl ether, 54533-84-5; tosyl chloride, 98-59-9; chloromethyl methyl ether, 107-30-2; (*S*)-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl, 65390-89-8; 4,4′,6,6′-tetrabromo-2,2-dimethoxy-1,1-dinaphthyl, 65354-83-8; 2,2′-dimethoxy-1,1-dinaphthyl, 2960-93-2; (*R*),(*S*)-2,3:4,5-di-1,2-(3-methylnaphtho)-1,6,9-trioxaundeca-2,4-diene, 55442-68-7; 2,3:4,5-di-1,2-(3-*N*-morpholinomethylnaphtho)-1,6,9-trioxaundeca-2,4-diene, 55442-62-1; dichlorodimethylsilane, 75-78-5; *tert*-butyl chloride, 507-20-0; (+)-(*R*)-bis-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-1,1′-dinaphthyl, 65390-90-1; (*R*)-2,2′-bis(5-hydroxy-3-oxa-1-pentyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1-dinaphthyl, 65354-85-0; (−)-(*S*,*S*)-2,3,4,5,10,11,12,13-tetra-1,2-naphtho-1,6,9,14,17,20-hexaoxacyclodocosa-2,4,10,12-tetraene, 55515-84-9.

References and Notes

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