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Host–Guest Complexation. 7. The Binaphthyl Structural Unit in Host Compounds[1,2]

Evan P. Kyba,[3a] George W. Gokel, Feike de Jong,[3b] Kenji Koga,[3c] Lynn R. Sousa,[3d] Merrell G. Siegel, Lester Kaplan, G. Dotsevi Y. Sogah,[3e] and Donald J. Cram*

Contribution No. 3833 from the Department of Chemistry, University of California at Los Angeles, Los Angeles, California 90024

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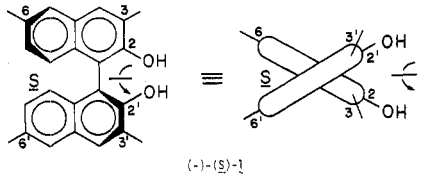
Reported here are the resolutions, optical stabilities, and maximum rotations of the enantiomers of 2,2′-dihydroxy-1,1′-binaphthyl (1), whose absolute configurations are known [(+)-1 is (*R*)-1]. Enantiomers, racemates, and meso forms of macrocycles have been prepared that are held together by ether linkages composed *formally* by the loss (of the elements) of water from the following units: 2,2′-dihydroxy-1,1′-binaphthyl (A); 2,2′-dihydroxy-1,1′-biphenyl (B); ethylene glycol (D); catechol (E); pentamethylenediol (F); *cis*-2,5-bis(hydroxymethyl)tetrahydrofuran (G); 1,3-bis(hydroxymethyl)benzene (J); 2,6-bis(hydroxymethyl)pyridine (K). The ring closures all involved base-catalyzed substitution by ArO^- on RCl, RBr or ROTs. In general, the larger the number of bonds made to produce a cycle in a single reaction mixture, the poorer the yield. When six bonds were made, yields were as low as 0.4%, with four, yields were usually 10–20%, with two, yields were about 45–60%. Pure enantiomers and/or diastereomers are reported that possess structures represented by the following abbreviated formulas: B–D_5; A–D; A–D_2; A–D_3; A–D_4; A–D_5; A–K; A–K–A–K; A–D_2–A–D_2; A–D_2–E–D_2; A–D–A–D_3; A–D_2–A–K; A–D_2–A–J; A–D_2–A–G; A–D_2–A–F; A–F–A–K; A–J–A–K; A–D–A–D–A–D; A–D–A–D. In several cases, the same cycles were assembled by different synthetic routes, particularly A–D_2–A–D_2 and A–D–A–D–A–D. Although optically stable at 100 °C for 24 h in dioxane–water, (−)-1 racemized 72% with HCl (~1.2 N) present. It also racemized 69% at 118 °C for 23 h in 1-butanol–0.67 M in KOH. In oxygen-free diethylene glycol, (−)-A–D_2–A–D_2 underwent 0% rotational loss in 6 h and 8.6% in 202 h. The maximum rotations and absolute configurations of all macrocycles are reported. The symmetry properties and shapes of certain of the cycles are discussed. The diastereoisomeric racemates of A–D–A–D–A–D each gave a 1:1 equilibrium mixture of the two racemates when heated at 340 °C for 7 min.

Structural recognition in molecular complexation between organic entities depends on the complementary placement of binding sites and steric barriers in hosts and guests. Paper 1[4a] of this series dealt with the general phenomenon of complexation, and parts 2–5[4b-e] dealt with the location of binding sites in disk-shaped hosts which did not extend far into a third dimension. Paper 6[4f] described the use of the [2.2]paracyclophanyl unit, which when incorporated into hosts extends rigidly into a third dimension. The [2.2]-paracyclophane unit also provides points for attachment of convergent steric barriers that might shape the environment of the binding site.

This paper describes the syntheses and properties of hosts that contain as part of their major ring systems the 1,1′-binaphthyl group. The macrorings include oxygens attached at the 2,2′ positions of the binaphthyl group, and thus, 2,2′-dihydroxy-1,1′-binaphthyl (1) is the key starting material in the syntheses. Cycles containing a 2,2′-bisoxy-1,1′-binaphthyl unit rigidly extend in three dimensions in such a way as to place one naphthalene ring above and in a plane tangent to the macrocycle, and the second naphthalene below and tangent to the macrocycle. The planes of the naphthalene rings are perpendicular to the best plane of the macroring. The dihedral angle between the two naphthalene rings of 1 in Corey–Pauling–Koltun (CPK) molecular models appears capable of varying between extremes of about 60 and 120°. With an angle of about 75°, the two oxygens are located with respect to one another about the same as they are in gauche ethylene glycol.



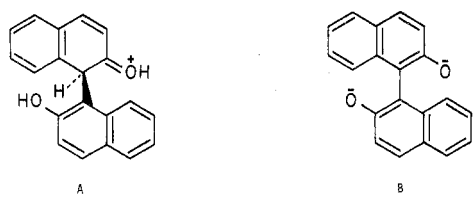
(−)-(S)-1

This binaphthyl unit possesses useful symmetry properties. It has a C_2 axis (indicated by the curved arrow with a horizontal line through it), and thus does not impart the unwanted property of "sidedness" to hosts. The unit is chiral, and the aryl rings are potential *chiral barriers* that should impart to hosts the property of *chiral recognition* toward appropriate guest compounds. The 3 and 3′ positions when substituted extend the chiral barriers, and the substituents are directed along the sides (above and below) of the macroring. The 6 and 6′ positions diverge from the binding sites of the macroring, and attached substituents can be used to manipulate solubility properties, or to bond hosts to solid supports. These structural

properties will be exploited in hosts described in this and subsequent papers.

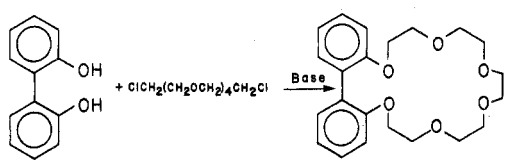
Resolution, Absolute Configuration, Optical Purity, and Configurational Stability of 2,2'-Dihydroxy-1,1'-binaphthyl (1). The resolution of **1** through its mono-*l*-menthoxyacetic ester was in progress when the resolution of **1** through the cinchonine salt of its phosphate ester was reported.[5] The former method provided a maximum rotation for (−)-**1** of $[\alpha]^{25}_D$ −33.6°,[6] whereas the latter and superior method gave $[\alpha]^{25}_D$ −33.9°[6] and $[\alpha]^{25}_D$ +33.8°[6] as maximum rotations for the two enantiomers. The absolute configurations of the enantiomers of **1** have been established by the x-ray method.[7] Although optically stable at 100 °C for 24 h in dioxane–water, (−)-(*S*)-**1** racemized 72% under those conditions when the solution was 1.2 N in HCl. In butanol 0.67 M in KOH at 118 °C for 23 h, (−)-(*S*)-**1** racemized 69%. These data set rough limits to the reaction conditions for converting (−)-(*S*)-**1** or (+)-(*R*)-**1** to other substances without loss of optical purity.

Molecular models (CPK) of **1** protonated or hydroxylated in either the 1 or 8 positions appear to offer less of a steric barrier to Ar–Ar rotation than that of **1** itself. Furthermore, the steric barrier is undoubtedly affected by the presence of charge that can be distributed in these positions. Possibly the acid-catalyzed racemization involves a transition state such as A, and the base-catalyzed a transition state such as B. Kinetic analyses and other mechanistic probes of the racemization should provide interesting results.



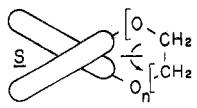
A B

Synthesis of Systems Containing One Biaryl Unit. As a prototype reaction, 2,2'-dihydroxy-1,1'-biphenyl was treated with pentaethylene glycol ditosylate[4e,8] and sodium hydroxide in dioxane–butanol[9] to give **2** (12%). Higher yields of cycles were obtained when (−)-(*S*)-**1**, (+)-(*R*)-**1**, or racemic **1** was treated with the various polyethylene glycol ditosylates [4e,8] in THF–*t*-BuOK under N_2 at reflux.



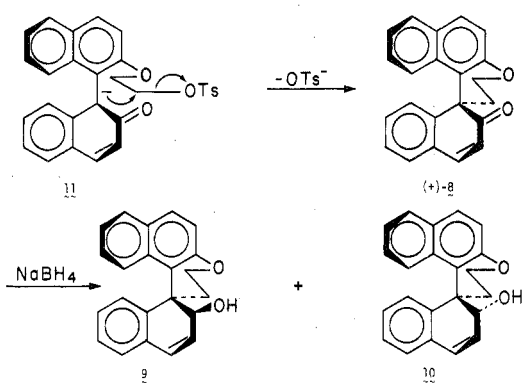
2

Cycles containing one binaphthyl and from one to five ethylene glycol units (**3**–**7**) were prepared from optically pure (−)-(*S*)-**1** or (+)-(*R*)-**1** for studies of the ORD and CD spectra.[10] When heated in oxygen-free diethylene glycol (sealed tube) at 205 °C, (−)-(*S*)-**6** underwent 0% rotational loss in 6 h, and 9% in 202 h. Thus both starting material and product were optically stable to the reaction conditions, and the same is undoubtedly true for the other cycles reported here.



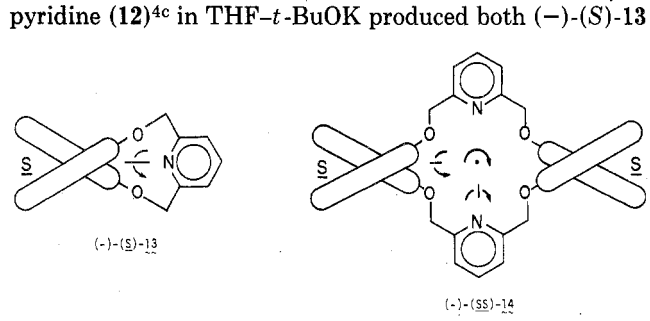
No.	n	%
(+)-(S)-3	1	23 (65)
(+)-(S)-4	2	2
(−)-(S)-5	3	65
(−)-(S)-6	4	52
(−)-(S)-7	5	64

The reaction of racemic **1** with ethylene glycol ditosylate gave ketone **8** as the main product (44%, mp 198–200 °C), as well as 23% of **3** and higher oligomers. The Rast and mass spectral molecular weights of **3** differentiated it from its higher oligomers. The structure of ketone **8** was derived from its UV, IR, and ^{1}H NMR spectra.[11] When reduced with $NaBH_4$, racemic **8** gave a 20:1 ratio of the diastereomeric diols **9** and **10**, in which **9** is more likely to be the dominant isomer. Ketone **8** is the product of alkylation by ethylene glycol ditosylate of the oxygen of one ring of **1**, and of C-1′ of the other ring of **1**. Substitution of dimethylformamide (DMF) for THF as solvent in the reaction of **1** with ethylene glycol ditosylate gave a 65% yield of **3** and no detectable **8**. With (−)-(*S*)-**1** as starting material, (+)-**8** was obtained (45%). The sharp melting point of (+)-**8** (187–188 °C) suggested that no racemization had occurred during formation and that the alkylation had occurred stereospecifically. Since (−)-(*S*)-**1** owes its asymmetry to restricted rotation and (+)-**8** to the presence of an asymmetric carbon, the reaction represents an interesting example of conversion of torsional into atomic asymmetry. The configuration assigned to (+)-**8** arises reasonably from the configuration of (−)-(*S*)-**1**, and involves as intermediate the asymmetric carbanion **11**. Others have reported that 1-substituted 2-naphthol anions under anhydrous conditions alkylate at C-1.[12] The reactions leading to (+)-**8**, **9**, and **10** are formulated.



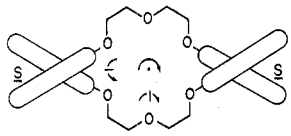
11 (+)-**8** **8** **9** **10**

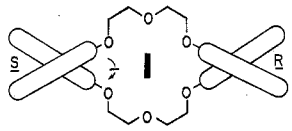
Syntheses of Systems Containing Two Binaphthyl Units. Treatment of (−)-(*S*)-**1** with 2,6-bis(chloromethyl)-pyridine (**12**)[4c] in THF–*t*-BuOK produced both (−)-(*S*)-**13** (not characterized) and (−)-(*S,S*)-**14** (26%). As CPK molecular models suggest should be the case, the two sets of β hydrogens on the pyridine rings of (−)-(*S,S*)-**14** are in different magnetic environments and have different ^{1}H NMR chemical shifts, one at δ 6.32 and the second at δ 6.40. Racemic **14** was also prepared.



(−)-(S)-13 (−)-(SS)-14

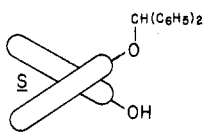
Treatment of (*R*),(*S*)-**1** with diethylene glycol ditosylate (THF–*t*-BuOK) gave a mixture of products from which were isolated (*R*),(*S*)-**4** (4%, mp 226–227 °C), (*R,R*),(*S,S*)-**15** (15%, phase change at 244–251 °C), and (*R,S*)-**15** (2%, mp 283–284 °C). When (−)-(*S*)-**1** was used as starting material, (+)-(*S*)-**4** (2%) and (−)-(*S,S*)-**15** (31%, mp 123–126 °C as C_6H_6–c-C_6H_{12} solvate) were obtained. The ^{1}H NMR spectrum of (−)-(*S,S*)-**15** was identical with that of (*R,R*),(*S,S*)-**15**, but different from that of (*R,S*)-**15**. Starting material (−)-(*S*)-**1** can

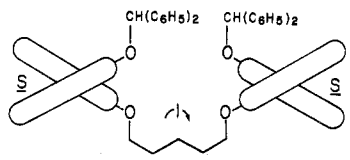

(-)-(SS)-15


(RS)-15

give (−)-(*S*,*S*)-**15**, but not (*R*,*S*)-**15**, whereas (*R*),(*S*)-**1** can give both (*R*,*S*)-**15** and (*R*,*R*),(*S*,*S*)-**15**. A spectral comparison identified the configurations of the latter two substances.

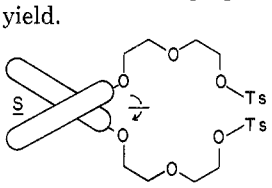
Compound (−)-(*S*,*S*)-**15** was also prepared by a second method which was multistep. Treatment of (−)-(*S*)-**1** with benzhydryl bromide for steric reasons gave mainly monosubstituted product (+)-(*S*)-**16** (73%). When treated with

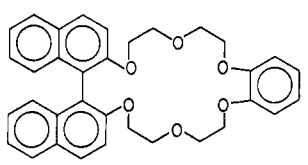

(+)-(S)-16

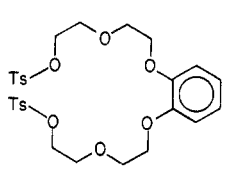

(-)-(SS)-17

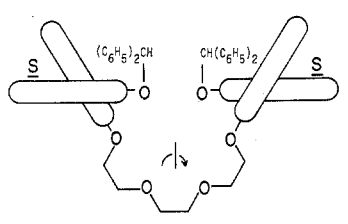
diethylene glycol ditosylate (THF, KOH), (+)-(*S*)-**16** gave (−)-(*S*,*S*)-**17** (73%). The benzhydryl protecting groups were removed with acid, and the resulting diol produced was converted directly to (−)-(*S*,*S*)-**15** with diethylene glycol ditosylate (THF–KOH) in a yield of 47% for the two steps.

A third method of preparing (−)-(*S*,*S*)-**15** proved to be the best. Treatment of (−)-(*S*)-**1** with 2-(2′-chloroethoxy)ethyl 2″-tetrahydropyranyl ether and NaH in DMF (or NaOH in butanol) produced the bispyranyl ether, which was cleaved to diol and converted to ditosylate (−)-(*S*)-**18**. Similarly, (+)-(*R*)-**18** and (*R*),(*S*)-**18** were prepared. Treatment of (−)-(*S*)-**18** with (−)-(*S*)-**1** (THF, KOH) gave (−)-(*S*,*S*)-**15** (37%), and treatment of (+)-(*R*)-**18** with (+)-(*R*)-**1** gave (+)-(*R*,*R*)-**15** (42%). Catechol and (*R*),(*S*)-**18** in *n*-BuOH–KOH gave (*R*),(*S*)-**19** (41%), which was also obtained from (*R*),(*S*)-**1** and **20** (prepared in 47% yield similarly to **18**) in 50% yield.


(-)-(S)-18

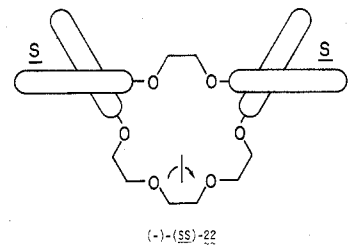

(R)(S)-19

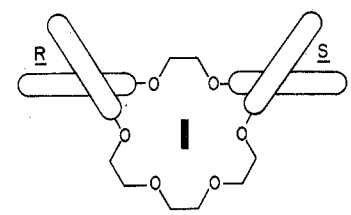

20


(-)-(SS)-21

The rotations of the three samples of (−)-(*S*,*S*)-**15** made by the three different methods were essentially identical and equal in magnitude with the sample of (+)-(*R*,*R*)-**15** prepared. Thus no racemization occurred during these syntheses, and the products were optically pure. The enantiomers of **15** formed a highly cyrstalline and stable solvate with CCl_4, as well as one containing 0.5 mol of benzene and 0.5 mol of cyclohexane.

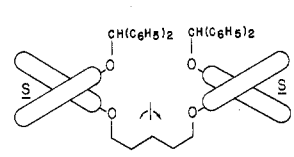
Cycles isomeric to **15** were also prepared. Treatment of racemic benzhydryl derivative **16** with triethylene glycol ditosylate (THF–KOH) gave **21** as a mixture of diastereoisomers (60%), whereas (+)-(*S*)-**16** gave (−)-(*S*,*S*)-**21**. The diastereomeric mixture (**21**) was cleaved with acid, and the resulting mixture of diols without separation was converted in 50% yield with ethylene glycol ditosylate (THF–KOH) to a mixture of

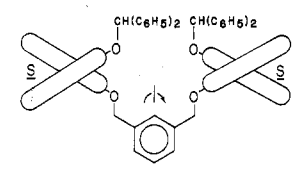

(-)-(SS)-22

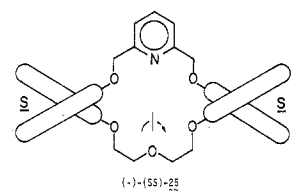

(RS)-22

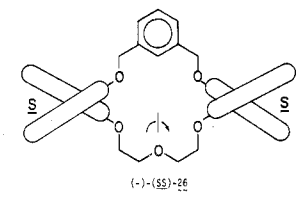
(*R*,*S*)-**22** and (*R*,*R*),(*S*,*S*)-**22** (50%). These diastereoisomers were separated and characterized. Similarly (−)-(*S*,*S*)-**21** was converted to (−)-(*S*,*S*)-**22** (60%).

Intermediates (−)-(*S*,*S*)-**17** (see above), (−)-(*S*,*S*)-**23**, and (−)-(*S*,*S*)-**24** were used to introduce other units into cycles

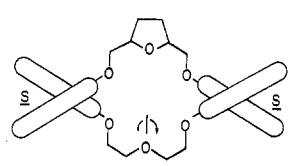

(-)-(SS)-23

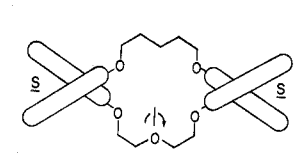

(-)-(SS)-24


(-)-(SS)-25


(-)-(SS)-26

related to **15**. Treatment of (+)-(*S*)-**16** with pentamethylene glycol ditosylate (THF–KOH) provided (−)-(*S*,*S*)-**23** (54%), and with 1,3-bis(bromomethyl)benzene[4d] (−)-(*S*,*S*)-**24** (67%). These benzhydryl protected intermediates were cleaved with acid to give their respective bisphenols, which without characterization were used in their ring-closing reactions. The bisphenol from (−)-(*S*,*S*)-**17** with 2,6 bis(chloromethyl)pyridine[4c] gave (−)-(*S*,*S*)-**25** (43%), with 1,3-bis(bromomethyl)benzene[4d] gave (−)-(*S*,*S*)-**26** (13%), and with *cis*-2,5-bis(tosyloxymethyl)tetrahydrofuran[4b] gave (−)-(*S*,*S*)-**27** (26%). The bisphenol from (−)-(*S*,*S*)-**23** with diethylene glycol ditosylate gave (−)-(*S*,*S*)-**28** (41%) and with 2,6-bis(chloromethyl)pyridine[4c] gave (−)-(*S*,*S*)-**29** (29%). The bisphenol from (−)-(*S*,*S*)-**24** with 2,6-bis(chloromethyl)pyridine[4c] gave (−)-(*S*,*S*)-**30** (43%). The ring-closing reactions involved THF–*t*-BuOK or THF–KOH.


(-)-(SS)-27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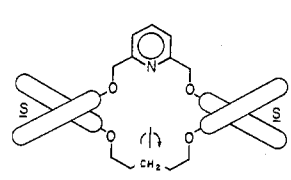
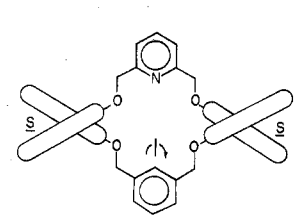
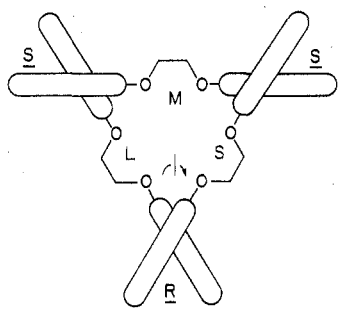
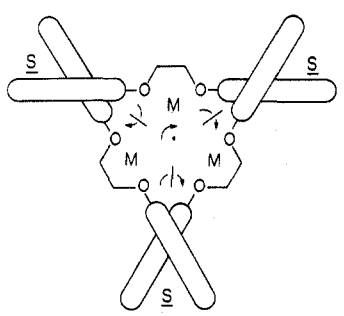

(-)-(SS)-29


(-)-(SS)-30

Synthesis of Systems Containing Three Binaphthyl Units. When (*R*),(*S*)-1 was treated with ethylene glycol ditosylate (THF–*t*-BuOK), besides (*R*),(*S*)-**3** and ketone (*R*),(*S*)-**8** (see above) there were produced three higher cyclic oligomers, X, Y, and Z (<1% yields). Their mass spectral molecular ions indicated their compositions, but not their configurations: X, $C_{44}H_{32}O_4$, mp 355 °C dec; Y, $C_{66}H_{48}O_6$, mp 188–190 °C; Z, $C_{66}H_{48}O_6$, mp 338–342 °C dec. The UV spectra of X and Y were very similar (five bands), but the λ_{max} in X and Y at 335–336 nm was moved to 355 nm in Z. This lowest energy band is probably associated with delocalization of the oxygen's electrons into the naphthalene rings, and is conformation dependent. The conformations in turn are dependent on the diastereomeric relationships between the binaphthyl units. The high-melting racemates (X and Z) were too insoluble for ^{1}H NMR spectral determinations. When (−)-(*S*)-**1** was used in the same reaction, in addition to (+)-(*S*)-**3** and ketone (+)-**8**, only *one* higher cyclic oligomer was produced (TLC), whose UV spectrum and TLC behavior identified it as one enantiomer of racemate Z. This evidence alone suggested X and Y must contain binaphthyl units of the *R* configuration, and that X was (*R*,*S*)-**32**, Y was (*R*,*S*,*S*),(*S*,*R*,*R*)-**31**, and Z was (*R*,*R*,*R*),(*S*,*S*,*S*)-**31**. The absence of (*R*,*R*),-



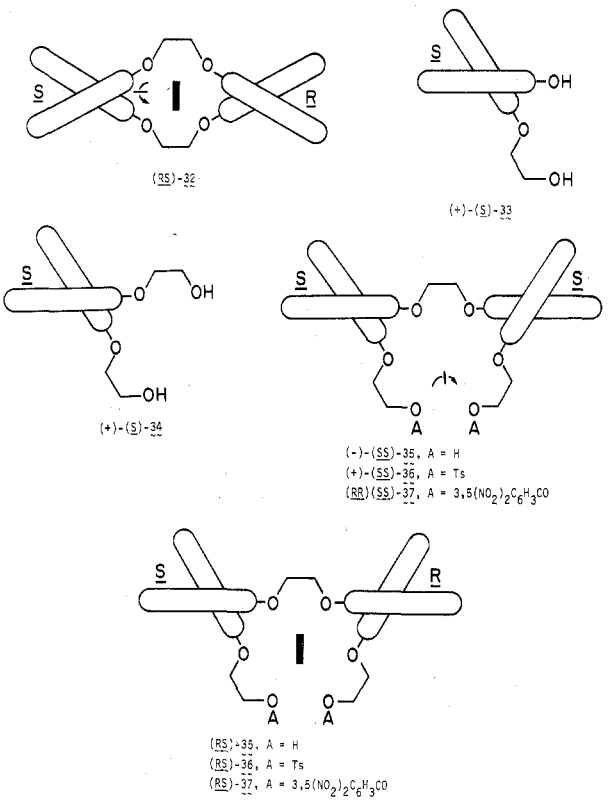
(−)-(RSS)-31



(−)-(SSS)-31

(*S*,*S*)-**32** or (*S*,*S*)-**32** in the reaction products indicates that the transition states leading to these isomers are of higher energy than those leading to (*R*,*S*)-**32** for steric–conformational reasons.

Rational, stepwise syntheses of (−)-(*R*,*S*,*S*)-**31** and (−)-(*S*,*S*,*S*)-**31** and their racemates proved more satisfactory. Treatment of (−)-(*S*)-**1** or (*R*),(*S*)-**1** with ethyl chloroacetate (THF–*t*-BuOK) gave mixtures of esters that were reduced ($LiAlH_4$) to mixtures of **33** and **34**, which were separated by distribution between ether and water–methanol–KOH mixtures. From (−)-(*S*)-**1** was produced (+)-(*S*)-**33** (43%) and (+)-(*S*)-**34** (19%), and from (*R*),(*S*)-**1**, (*R*),(*S*)-**33** (40%) and (*R*),(*S*)-**34** (15%) were produced. Treatment of (+)-(*S*)-**33** with ethylene glycol ditosylate (THF–*t*-BuOK) gave (−)-(*S*,*S*)-**35** (85%). Likewise (*R*),(*S*)-**33** gave a mixture of (*R*,*S*)-**35** and (*R*,*R*),(*S*,*S*)-**35**, which was separated through their 3,5-dinitrobenzoate esters (**37**) to give overall yields of 18% (*R*,*S*)-**35** and 25% (*R*,*R*),(*S*,*S*)-**35**. The ^{1}H NMR spectra and TLC behavior of these diastereomers were different. These properties were identical for (−)-(*S*,*S*)-**35** and for one



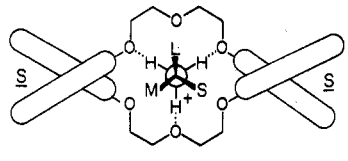
of the diastereomers, namely that of the (*R*,*R*),(*S*,*S*) configuration.

Tosylation of (−)-(*S*,*S*)-**35**, (*R*,*R*),(*S*,*S*)-**35**, and (*R*,*S*)-**35** gave (+)-(*S*,*S*)-**36**, (*R*,*R*),(*S*,*S*)-**36**, and (*R*,*S*)-**36** in 37, 50, and 52% yields, respectively. Treatment of (+)-(*S*,*S*)-**36** with (−)-(*S*)-**1** (DMF, K_2CO_3) gave (−)-(*S*,*S*,*S*)-**31** (46%), whereas (+)-(*S*,*S*)-**36** with (+)-(*R*)-**1** gave (−)-(*R*,*S*,*S*)-**31** (58%). Treatment of (*R*,*S*)-**36** with (*R*),(*S*)-**1** gave only (*R*,*S*,*S*),-(*S*,*R*,*R*,)-**31** (60%), whereas (*R*,*R*),(*S*,*S*)-**36** with (*R*),(*S*)-**1** gave (*R*,*S*,*S*),(*S*,*R*,*R*)-**31** (30%) and (*R*,*R*,*R*),(*S*,*S*,*S*)-**31** (16%). Enantiomer to racemate relationships among the stereoisomers of **31** were confirmed by the identity or nonidentity of their UV or ^{1}H NMR spectra and the TLC behavior. Diastereomers (−)-(*R*,*S*,*S*)-**31** and (−)-(*S*,*S*,*S*)-**31** possessed distinctly different ^{1}H NMR spectra, presumably due to different placements of the C-3 hydrogens of one naphthalene ring relative to the shielding or deshielding cones of a second transannular naphthalene ring in the two diastereoisomers. Two C-3 naphthalene protons were shielded and moved upfield to δ 6.58–6.78 per *S*,*S* or *R*,*R* relationship, whereas the *R*,*S* relationships provided no such shifts. Thus the doublet at δ 6.58–6.75 for (−)-(*S*,*S*,*R*)-**31** integrated to only two protons, whereas that at δ 6.62–6.78 for (−)-(*S*,*S*,*S*)-**31** integrated to six protons.

Symmetry Properties and Shapes of Host Compounds. The parent crown compounds exist in solution in all gauche conformations with the oxygens turned inward.[14] The cycles and their precursors containing the chiral binaphthyl unit possess interesting symmetry properties. Their formulas have been drawn with all oxygens turned inward. Rotation of (−)-(*S*)-**1** through 180° about the axis appended to its formula reproduces the formula, and hence the substance contains a C_2 axis. This symmetry element is carried into most of the cycles as is indicated by the curved arrow with a vertical line through it or a 180° curved arrow with a dot in it inserted into their formulas. Most of the cycles containing *both* (*R*)- and (*S*)-binaphthyl units contain mirror planes indicated in the formulas by the solid rectangular box [e.g., (*R*,*S*)-**15**, (*R*,*S*)-**22**, and (*R*,*S*)-**32**]. Interestingly, of these three meso isomers, (*R*,*S*)-**15** and (*R*,*S*)-**32** each contain a C_2 axis and are not

"sided," whereas (*R,S*)-**22** does not and is sided. Some of the cycles contain several C_2 axes. In particular, (−)-(*S,S*)-**14** and (−)-(*S,S*)-**15** contain three mutually perpendicular C_2 axes to give the molecule D_2 symmetry. Cycle (−)-(*S,S,S*)-**31** contains three C_2 axes all lying in the same plane and perpendicular to a C_3 axis (indicated in the formula by a 120° curved arrow with a dot in it), which gives the molecule overall D_3 symmetry. These symmetry properties seldomly are encountered in organic compounds and have important consequences with respect to possible host–guest complex structure.

Hosts that contain a C_2 axis in principle can complex alkylammonium ions from either face to produce the same structure (or family of structures of equilibrating conformers). Hosts that possess D_2 symmetry in principle form complexes, some of whose conformations duplicate one another. For example, if host (*S,S*)-**15** complexes LMSC*NH_3^+ (L is a large, M a medium, and S a small group), the two conformations **38** and **39** of the complex formed from one enantiomer of the



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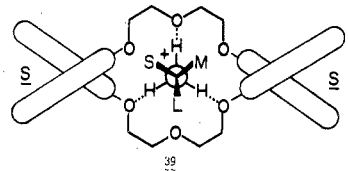

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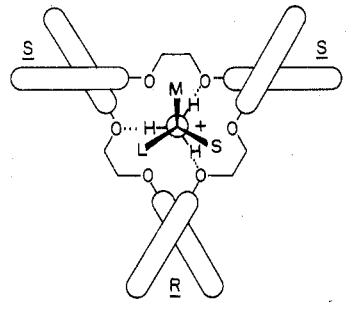
guest are superimposable on one another and on the two corresponding complexes formed with the guest protruding from the opposite face of the best plane of the macroring.

The general shape of most of the hosts described here depends on the number of binaphthyl units they contain. The central hole is designed to bind the NH_3^+ group of alkylammonium hosts, and the alkyl group in complexes protrudes approximately perpendicularly from the best plane of the oxygens. If (LMS)C is a generalized alkyl group, the substituents L, M, and S occupy the space in a complex above and around one face of the host. Since the naphthalene rings of a binaphthyl unit also extend perpendicularly above and below the face of the host, they divide the space available for L, M, and S into compartments. Hosts containing one binaphthyl unit, such as **6,** have one compartment on each face. Hosts with two binaphthyl units, such as (*S,S*)-**15** or (*S,S*)-**22,** have two compartments into which L, M, and S must fit in a complex. Hosts with three units, such as (*S,S,S*)-**31,** have three compartments. It is convenient to classify the hosts as having one, two, or three compartments on each face as monolocular, dilocular, or trilocular,[13] respectively. Hosts **2–7, 13,** and **19** are monolocular, **14, 15, 22, 25–30,** and **32** are dilocular, and the isomers of **31** are trilocular.

In CPK molecular models of these hosts, the naphthalene rings protruding from each face occupy ~65° of the 360° of the cylinder of space whose axis is perpendicular to the plane of the oxygens and is centered equidistant from all six oxygens. For the monolocular systems, this leaves ~295° of the cylinder for distribution of substituents L, M, and S in a single asymmetric cavity in host–guest complexes. For the dilocular and trilocular systems, the sizes of the compartments on each face depend both on the relative configurations and arrangements of the binaphthyl units. Dilocular hosts (*S,S*)-**15** and (*R,S*)-**15** are diastereomeric. In (*S,S*)-**15,** the two naphthalenes that extend from one face occupy roughly parallel planes that provide two spatially equivalent asymmetric cavities, each exposing ~115° of the cylinder. In (*R,S*)-**15** the planes of the two naphthalene rings converge to provide two cavities, one of ~60° and one of ~170°, each of which contains a mirror plane. Although (*S,S*)-**15** and (*S,S*)-**22** are isomeric and contain binaphthyl units of the same configuration, (*S,S*)-**15** has two equivalent cavities of ~115°, but (*S,S*)-**22** has one cavity of ~55° and one of ~175°. In (*S,S*)-**22,** an extension of the plane of one naphthalene ring would intersect the second naphthalene ring that protrudes from the same face. Isomer (*R,S*)-**22** is sided, since it contains no C_2 axis. On one side the aryls occupy planes that converge, and one cavity is ~70° and the other ~160°. On the opposite side, the aryls occupy the same plane, and one cavity is ~25° and the other ~205°.

The divisions of the cylinder of space in the trilocular systems **31** are particularly interesting. In the more symmetrical *S,S,S* isomer, the three cavities are similarly shaped, and they each expose ~55° of the cylinder. In the less symmetrical *R,S,S* isomer, the space is unevenly divided into a relatively large cavity (L) of 85°, a medium cavity (M) of ~55°, and a small cavity (S) of ~25°. In (*S,S,S*)-**31,** the cavities themselves are all *asymmetric,* whereas in (*R,S,S*)-**31,** cavity M is asymmetric, and L and S both have a mirror plane. Host (*R,S,S*)-**31** was designed to have a complementary relationship for one enantiomer of guest ions such as LMSC*NH_3^+, whereas (*S,S,S*)-**31** was designed for one enantiomer of $LMSCCH_2NH_3^+$. Complexes **40** and **41** indicate the complementary character of host and guest envisioned.



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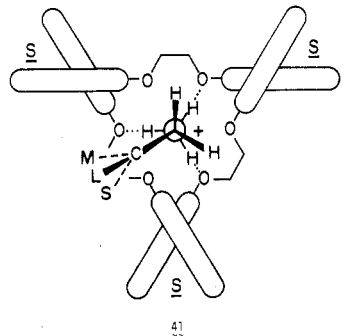

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The introductions of the 2,6-pyridine, pentamethylene, benzo, 1,3-benzene, or 2,5-tetrahydrofuran units into the dilocular systems (**14, 19, 25–30**) do not change the cavity shapes much, since these units roughly lie in the planes of the oxygens and provide about the same space between the naphthalene walls. Of these compounds, only (*S,S*)-**14** possesses the three C_2 axes found in the parent system, (*S,S*)-**15.** The unsymmetrical distributions of some of the units of the others destroy all but one of the C_2 axes found in the parent system, (*S,S*)-**15.** These hosts are not sided, however.

Equilibration of Diastereomeric Trilocular Systems. When melted and held at 340 °C for 7 min, (*R,R,S*),(*S,S,R*)-**31** and (*R,R,R*),(*S,S,S*)-**31** each gave an approximately equal mixture of the two diastereoisomers. Thus, $\Delta\Delta G \sim 0$ for the two racemates. The symmetry number for the isomer with D_3 symmetry [(*R,R,R*)-**31** or (*S,S,S*)-**31**] is 6, and that for the isomer with C_2 symmetry is 2 [(*R,R,S*)-**31** or (*S,S,R*)-**31**]. If

the intra- and intermolecular interactions of all the units in each diastereoisomer in the melt are additive, then $\Delta\Delta G = -RT \ln (6/2) = -1340$ cal/mol for the difference in free energy for the two diastereomers, and the equilibrium mixture would be 75% (*R,R,R*),(*S,S,S*)-**31** and 25% (*R,R,S*),(*S,S,R*)-**31**. The results indicate that the interactions of the units in each diastereoisomer of **31** are not additive, and suggest that either intra- or intermolecular interactions tend to slightly destabilize the (*R,R,R*),(*S,S,S*) isomer relative to the (*R,R,S*),(*S,S,R*) isomer. The two diastereoisomers possess different overall shapes and undoubtedly pack differently in the melt. Possibly the less symmetrical (*R,R,S*),(*S,S,R*) isomer produces a more dense melt with fewer holes and more contact points than the more symmetrical (*S,S,S*),(*R,R,R*) isomer.

The binding properties of the hosts described here will be reported in later papers of this series.

Experimental Section

General. All temperatures are in degrees Celsius. Alumina used in chromatography was MCB AX 611. Tetrahydrofuran (THF) and dioxane were distilled from sodium benzophenone ketyl immediately before use. Dimethylformamide (DMF) was distilled from CaH_2 prior to use. Magnesium sulfate was used as drying agent for organic extracts. All reactions involving NaH, *t*-BuOK, KOH, or $LiAlH_4$ were conducted under N_2. All melting points were taken on a Thomas-Hoover apparatus and are uncorrected. All ^1H NMR chemical shifts are given in δ parts per million from added Me_4Si in $CDCl_3$ and were recorded on a Varian HA-100 spectrometer. Mass spectra were taken on an AEI Model MS-9 double focusing mass spectrometer at 70 eV. Optical rotations were recorded with a Perkin-Elmer 141 polarimeter in a 1-dm thermostated cell. Gel permeation chromatographs were run on $\frac{3}{8}$ in. × 20 ft columns at flow rates of 3–4 mL/min with either THF or CH_2Cl_2 as solvent. Column A was packed with Bio-Rad CS-8 beads (1000 molecular weight exclusion limit), and column B with Styragel 100-Å beads (37–70 μm particle size, exclusion limit 1500 molecular weight). Since very similar procedures were applied to different starting materials, they will be illustrated, labeled, and then referred to by label. Systematic names will be illustrated, but are so cumbersome that semisystematic "crown" nomenclature will be more commonly used, along with compound numbers already assigned. Optically pure 2,2′-dihydroxy-1,1′-binaphthyl was used in all syntheses unless otherwise specified.

Resolution of 2,2′-Dihydroxy-1,1′-binaphthyl (1). From 2.71 g of *l*-menthoxyacetyl chloride and 2.20 g of **1** in THF–pyridine at 25 °C for 1 h was prepared the monoester, which was purified by chromatography on silica gel and crystallization from cyclohexane to give 0.40 g (9%) of product: mp 139–140.5 °C; $[\alpha]^{25}_D$ −14.4° (*c* 1.0, $(CH_3)_2CO$); M^+, 482. Anal. Calcd for $C_{32}H_{34}O_4$: C, 79.64; H, 7.10. Found: C, 79.56; H, 6.83. This material was hydrolyzed with KOH in CH_3OH to give (−)-(*S*)-**1** (70%) [mp 207–209 °C; $[\alpha]^{25}_D$ −33.4° (*c* 0.76, THF)] undepressed by admixture with diol prepared through phosphate salt (see below).

The better method is a modification of that of others,[5] and is outlined here. Racemic **1** (600 g, 2.09 mol) was slurried with 2 L of CH_2Cl_2, and under N_2 was added 450 g (2.93 mol) of $POCl_3$, followed by the slow addition with stirring of triethylamine (517 g, 5.1 mol) so as to maintain gentle reflux. After 1 h of additional stirring, the reaction mixture was washed with water, dried, and evaporated. This crude acid chloride was stirred for 1 h in 3.5 L of THF and 1 L of water at 50 °C for 1 h. Ethyl acetate (3 L) was shaken with the mixture, and the aqueous layer was washed with CH_2Cl_2. The organic layers were combined, washed with 0.5 L of water (twice) and 1 L of brine, dried, and evaporated to give 684 g (94%) of the acid phosphate of **1**. This material was mixed with 578 g (1.96 mol) of cinchonine in 8.3 L of hot CH_3OH, 3.6 L of water was added, and the mixture was filtered free of a flocculent impurity. The salt crystallized (532 g, or 84% of theory for one pure diastereomer), and its rotation did not change on recrystallization. This salt (total sample) in 1915 mL of absolute ethanol was heated to boiling, and 1915 mL of very hot 6 N HCl solution was added with vigorous stirring. After 3 days at 0 °C the white platelets were collected and digested (twice) with stirring with 1 L of hot 6 N HCl solution for 12 h, and once with 600 mL of cold water (2 h) to give after drying 222 g of the phosphate acid ester: $[\alpha]^{25}_{546}$ +722°, $[\alpha]^{25}_{436}$ +1329° (*c* 0.9, MeOH); yield based on enantiomer present in racemic **1** used, 59%.

The filtrate from the initial crystallization of the cinchonine salt was evaporated, the residue was dissolved in 3.1 L of refluxing absolute ethanol, and 3.1 L of hot 6 N HCl was added with stirring at a rate to aid crystallization and inhibit oiling. The product was digested, as with its enantiomer, and dried to give 115.3 g of (−)-(*R*)-acid ester: $[\alpha]^{25}_{546}$ −734°, $[\alpha]^{25}_{436}$ −1355° (*c* 0.9, MeOH). The filtrates were reworked to give 52.4 g of additional (redigested) material ($[\alpha]^{25}_{546}$ −714°, $[\alpha]^{25}_{436}$ −1315° (*c* 0.57, MeOH)) to give a total of 168 g of (−)-(*R*)-acid, or 46% of theory. Partially optically pure (−)-(*R*)-acid ester was brought to optical purity by one crystallization of its cinchonidine salt. The acid ester recovered (65% of theoretical maximum) gave $[\alpha]^{25}_{546}$ −728°, $[\alpha]^{25}_{436}$ −1346° (*c* 1.1, MeOH).

The acid phosphate ester of (+)-(*R*)-**1** was reduced to (*R*)-(+)-**1** as follows. Acid ester (115.4 g, 0.331 mol, $[\alpha]^{25}_{546}$ −734°) was mixed with 1 L of THF at 0 °C under N_2, and $LiAlH_4$ (31.4, 0.83 mol) was added in small portions during 1 h with stirring. An additional 400 mL of THF was added, and the mixture was stirred at 25 °C for 17 h, cooled to 0 °C, and cold 6 N HCl (250 mL) added slowly and cautiously. The upper phase was decanted, and the lower phase was mixed with 300 mL of 6 N HCl and 150 mL of THF. The phases were again separated and the lower phase extracted with ether. The combined organic phases were washed with brine, decolorized with Norite, and evaporated. The oil was dissolved in 1 L of benzene, which was evaporated to induce crystallization. The solid that separated (90.6 g, 96%, mp 202–207 °C) was recrystallized from benzene to give 84.5 g, 89% (mp 207.5–208.5 °C), of (+)-(*R*)-**1**: $[\alpha]^{25}_{589}$ +34.3°, $[\alpha]^{25}_{546}$ +50.9° (*c* 1.0, THF). The overall yield in the resolution was ~41% of theory.

Similar reduction of 198 g of (+)-(*S*)-acid phosphate ($[\alpha]^{25}_{546}$ +722°, *c* 0.9, MeOH) gave 88% of (−)-(*S*)-**1** [mp 207–208 °C; $[\alpha]^{25}_{589}$ −33.3°, $[\alpha]^{25}_{578}$ −37.8°, $[\alpha]^{25}_{546}$ −51.3°, $[\alpha]^{25}_{436}$ −228° (*c* 1.1, THF)], or 52% yield in the resolution. Several preparations were made by different experimentalists using a variety of procedures, but each preparation gave the same rotations and melting points for (+)- and (−)-**1**.

Racemization Experiments with 2,2′-Dihydroxy-1-binaphthyl (1). A solution of (−)-**1** (0.1 g in 12 mL of dioxane and 10 mL of H_2O) gave $[\alpha]^{25}_D$ −0.106°. After 7 and 26 h respectively at 100 °C under N_2, the solutions gave $[\alpha]^{25}_D$ −0.110° and −0.106°. A solution of 95 mg (0.331 mmol) in 10 mL of butanol containing 47 mg (0.71 mmol) of KOH gave $[\alpha]^{25}_D$ +0.734°. After 13 and 23 h respectively under N_2 at 118 °C, the solutions gave $[\alpha]^{25}_D$ +0.408 and +0.230°. A solution of 100 mg of (−)-**1** in 12 mL of dioxane and 10 mL of 20% aqueous HCl gave $[\alpha]^{25}_D$ −0.158°. After 7 and 26 h respectively at 100 °C under nitrogen, the solutions gave $[\alpha]^{25}_D$ −0.099 and −0.044°.

2,3:4,5-Dibenzo-1,6,9,12,15,18-hexaoxacycloeicosa-2,4-diene [2,2′-Biphenyl-20-crown-6 (2)]. Procedure I. A mixture of 10.0 g (53.8 mmol) of 2,2′-dihydroxy-1,1′-biphenyl and 110 mL of butanol was purged with N_2 and 4.5 g (112 mmol) of NaOH was added. After the solution had refluxed for 1 h under N_2, 14.8 g (53.8 mmol) of pentaethylene glycol dichloride in 30 mL of butanol was added (0.5 h). After 17 h at reflux under N_2, the solution was shaken with 100 mL of $CHCl_3$ and 100 mL of water. The layers were separated, and the $CHCl_3$ layer was washed with water, dried, and concentrated to give 22 g of oil, which was chromatographed on 700 g of neutral alumina (activity I). Elution with 4 L of (3:2, v/v) benzene–ether gave 8.7 g of oil, which was molecularly distilled to give 2.66 g of bp 135–140 °C (20 μm) and 3.26 g of bp 177–183 °C (20 μm). The latter material crystallized and was recrystallized from heptane to give 2.5 g (12%) of **2**: mp 64–65 °C; ^1H NMR δ 3.6 (m, CH_2CH_2O, 16 H), 4.5 (m, $ArOCH_2$, 4 H), 6.9 (m, ArH, 10 H), 7.2 (m, ArH, 10 H); M^+ 388 (base peak). Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27. Found: C, 68.01; H, 7.32.

(*R*),(*S*)-2,3:4,5-Di(1,2-naphtho)-1,6,9,12,15,18-hexaoxacycloeicosa-2,4-diene [2,2′-Binaphthyl-20-crown-6 ((*R*),(*S*)-7)]. Procedure I (without distillation of the product) applied to 4.86 g of (*R*),(*S*)-**1** gave 2.75 g (33%) of (*R*),(*S*)-**7** after recrystallization from benzene–heptane: mp 130–130.5 °C; ^1H NMR spectrum δ 3.5 (complex m, CH_2OCH_2, 16 H), 4.04 (m, $ArOCH_2$, 4 H), 7.26 (m, ArH, 8 H), 7.83 (m, ArH, 4 H); M^+ 488 (base peak). Anal. Calcd for $C_{30}H_{32}O_6$: C, 73.75; H, 6.60. Found: C, 73.88; H, 6.76.

Racemic and (−)-(*S*)-2,2′-Binaphthyl-20-crown-6 ((−)-(*S*)-7) by Procedure II. Potassium *tert*-butoxide (2.36 g, 21 mmol) was added to a stirred solution under N_2 of 3.00 g (10.5 mmol) of (−)-(*S*)-**1** dissolved in 140 mL of pure THF. To the resulting suspension was added 5.72 g (10.5 mmol) of pentaethylene glycol ditosylate. The mixture produced was heated at reflux for 5 h and evaporated under reduced pressure. The residue was shaken with water and CH_2Cl_2, and the organic layer was washed with brine and dried. Evaporation of the solvent gave 6.1 g of oil, which was absorbed on 23 g of alumina and placed on the top of a chromatograph column prepared from a slurry of alumina and ether. The (−)-(*S*)-**7** was eluted with ether, and evaporation of the eluate gave a colorless oil, which was dried as a foam for 24 h at 35 °C and 0.07 mm, yield 3.1 g, (64%). The ^1H NMR and

mass spectra were identical with racemic 7 and gave $[\alpha]^{25}_{D}$ −70.5°, $[\alpha]^{25}_{546}$ −89.8° (c 1.0, THF). Anal. Calcd for $C_{30}H_{32}O_6$: C, 73.76; H, 6.60. Found: C, 73.62; H, 6.45. When carried out at 25 °C for 16 h, procedure II gave a 52% yield of (−)-(S)-7 of identical properties. When applied to racemic 1, racemic 7 resulted: 60%; mp 130–130.5 °C.

Optical Stability of (−)-(S)-2,2′-Binaphthyl-20-crown-6 ((−)-(S)-7). When a solution (1 M) of optically pure (−)-(S)-7 in oxygen-free diethylene glycol in a tube sealed under vacuum was heated at 205 °C for 6 h, the compound underwent no rotational loss. In 202 h at 205 °C, 9% rotational loss was observed. In a second experiment, two samples (0.50 g each) of (−)-(S)-7 of $[\alpha]^{25}_{578}$ −74.5° (c 1.0, THF) were sealed in ampules under vacuum as solutions in 10 mL of diphenyl ether. One tube was heated at 226 °C for 6 days and the other was held at 25 °C. The cycles were recovered by chromatography. The heated sample gave $[\alpha]^{25}_{578}$ −41.9° and the unheated gave $[\alpha]^{25}_{578}$ −74.2° (c 1, THF).

Applications of Procedure II to the Preparation of (−)-(S)-2,2′-Binaphthyl-14-crown-4 ((−)-(S)-5) and (−)-(S)-2,2′-Binaphthyl-17-crown-5 ((−)-(S)-6). From (−)-(S)-1 and triethylene glycol ditosylate was obtained (−)-(S)-5 (65%) as a gum: M^+ 400; $[\alpha]^{25}_{589}$ −127° (c 0.91, $CHCl_3$). Anal. Calcd for $C_{26}H_{24}O_4$: C, 78.00; H, 6.00. Found: C, 78.04; H, 5.96. From (−)-(S)-1 and tetraethylene glycol ditosylate was obtained (−)-(S)-6 (52%) as a gum: $[\alpha]^{25}_{589}$ −63°, $[\alpha]^{25}_{578}$ −67° (c 1.89, $CHCl_3$). Anal. Calcd for $C_{28}H_{28}O_5$: C, 75.68; H, 6.31. Found: C, 75.75; H, 6.31.

(R),(S)-2,3:4,5-Di(1,2-naphtho)-1,6,9-trioxacycloundeca-2,4-diene ((R),(S)-4) and (R,S)- and (R,R),(S,S)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene ((R,R),(S,S)-15 and (R,S)-15). By procedure I, 10.9 g of (±)-1, 5.5 g of diethylene glycol dichloride, and 1.6 g of NaOH were converted to a mixture of the three title products, which were separated on 500 g of neutral alumina with benzene and 4:1 (v/v) benzene–ether as eluting agents. Benzene eluted 2,2′-binaphthyl-11-crown-3 ((R),(S)-4), which was sublimed [195 °C (50 μm)] to give 0.50 g (4%) of material: mp 226–227 °C; ^{1}H NMR spectrum, δ 3.5 (m, 4 H, CH_2), 4.01 (8 lines, 2 H, CH_2), 4.32 (8 lines, 2 H, CH_2) as a whole ABX_2 pattern, 7.2 (complex m, ArH, 8 H), 7.8 (m, ArH, 4 H); M^+ 356 (base peak). Anal. Calcd for $C_{24}H_{20}O_3$: C, 80.88; H, 5.66. Found: C, 81.01; H, 5.77.

Benzene–ether eluted a mixture of (R,S)- and (R,R),(S,S)-15, which was crystallized and recrystallized from 1:1 (v/v) benzene–cyclohexane to give 0.22 g (2%) of (R,S)-15; mp 283–284 °C. It proved necessary to heat the sample to 165 °C (50 μm) to completely rid the sample of solvent. The material gave: ^{1}H NMR δ 3.29 (m, CH_2OCH_2, 8 H), 3.90 (m, $ArOCH_2$, 8 H), 7.20 (complex m, ArH, 16 H), 7.76 (m, ArH, 8 H); M^+ 712 (base peak). Anal. Calcd for $C_{48}H_{40}O_6$: C, 80.88; H, 5.66. Found: C, 80.88; H, 5.84.

From the filtrates was crystallized by fractional crystallization from benzene–cyclohexane (R,R),(S,S)-15, 2.0 g (15%), phase change at mp 244–251 °C. This isomer was much more soluble in $CDCl_3$ than (R,S)-15, and gave a different ^{1}H NMR fine structure: ^{1}H NMR δ 3.18 (m, CH_2OCH_2, 8 H), 3.81 (m, $ArOCH_2$, 8 H), 7.2 (complex m, ArH, 16 H), 7.83 (m, ArH, 8 H); M^+ 712 (base peak). Anal. Calcd for $C_{48}H_{40}O_6$: C, 80.88; H, 5.66. Found: C, 81.05; H, 5.92.

(+)-(S)-2,2′-Dinaphthyl-11-crown-3 ((+)-(S)-4), (−)-(S,S)-Bis(binaphtho)-22-crown-6 ((−)-(S,S)-15), and (+)-(R,R)-15. By procedure II, 14 g of diethylene glycol ditosylate, 10.0 g of (−)-(S)-1, and 8 g of t-BuOK produced a mixture of (+)-(S)-4 and (−)-(S,S)-15. Separation of these oligomers by chromatography on 1 kg of neutral alumina gave 4.3 g of (−)-(S,S)-15 as white needles containing 0.5 mol each of benzene and cyclohexane (^{1}H NMR integration): mp 123–126 °C. Anal. Calcd for $C_{48}H_{40}O_6 \cdot \frac{1}{2}C_6H_{12} \cdot \frac{1}{2}C_6H_6$: C, 81.69; H, 6.22. Found: C, 81.71; H, 6.06. The material also formed a solvate with CCl_4 (needles). The initial solvate when heated 17 h at 170 °C (50 μm) gave 3.9 g (31%) of (−)-(S,S)-15 as a foam: ^{1}H NMR identical with (+)-15; M^+ 712 (base peak); $[\alpha]^{25}_{578}$ −220°, $[\alpha]^{25}_{546}$ −262°, $[\alpha]^{25}_{436}$ −599°, $[\alpha]^{25}_{365}$ −1620° (c 1.1, CH_2Cl_2).

From the mother liquors from the crystallization of (−)-(S,S)-15 was obtained by sublimation and resublimation 0.24 g (2%) of (+)-(S)-4, mp 231–232 °C, whose ^{1}H NMR spectrum was identical with (±)-4: M^+ 356 (base peak); $[\alpha]^{25}_{578}$ +72.0°, $[\alpha]^{25}_{546}$ +78.0°, $[\alpha]^{25}_{436}$ +40.0°, $[\alpha]^{25}_{365}$ −672° (c 0.88, CH_2Cl_2). Anal. Calcd for $C_{24}H_{20}O_3$: C, 80.88; H, 5.66. Found: C, 80.81; H, 5.55.

Similarly, (+)-(R,R)-15 was prepared in 22% yield: $[\alpha]^{25}_{578}$ +221°, $[\alpha]^{25}_{546}$ +262°, $[\alpha]^{25}_{436}$ +600°, $[\alpha]^{25}_{365}$ +1630° (c 0.87, CH_2Cl_2).

(+)-2,2′-Bis(5-tosyloxy-3-oxa-1-pentyloxy)-1,1′-binaphthyl ((R),(S)-18), (−)-(S)-18, and (+)-(R)-18. The required intermediate 2-(2′-chloroethoxy)ethyl 2″-tetrahydropyranyl ether was reported previously.[4a]

A solution of 120 g (575 mmol) of 2-(2′-chloroethoxy)ethyl 2″-tetrahydropyranyl ether in 700 mL of butanol was added (15 min) to a stirred, boiling mixture of 60 g (0.217 mol) of (±)-1 and 20 g (0.500 mol) of NaOH in 700 mL of butanol. The resulting mixture was stirred and refluxed for 10 h (pH 7–8), and then 6.0 g (0.15 mol) more of NaOH and 60 g (0.278 mol) of the chloro ether in 100 mL of butanol was added. The mixture was stirred at reflux for an additional 10 h. The procedure was repeated with 6.0 g (0.15 mol) of NaOH and 20 g (0.096 mol) of the chloro ether in 50 mL of butanol and a 15-h reflux period. The reaction mixture was cooled and filtered, and the filtrate was concentrated under vacuum, ultimately at 150 °C (50 μm) to remove the excess chloro ether. The residue (140 g) was heated at 100 °C and 5 g (0.044 mol) of pyridine hydrochloride was added. The resulting mixture was heated at 190 °C (50 μm) *with stirring* for 2 h to give, upon cooling, 98.3 g of a light brown glass (diol precursor to (±)-18). A solution of 104 g (0.545 mol) of tosyl chloride in 300 mL of dry pyridine at 0 °C was added to 98.3 g (0.210 mol) of this diol dissolved in 400 mL of dry pyridine at 0 °C. The reaction mixture was allowed to stand at 0 °C for 24 h, poured onto 2 kg of ice water, and stirred for 2 h. The mixture was extracted with 2-L portions of CH_2Cl_2. The extracts were combined, washed with two 1-L portions of cold 6 N hydrochloric acid and 100 mL of brine, and dried. The solvent was evaporated to give 138 g of a brown glass which was chromatographed on 2 kg of silica gel with chloroform as eluent. Elution with 4 L of solvent brought 6 g of material off the column which was discarded. Elution with an additional 16 L of solvent gave upon evaporation ditosylate (R),(S)-18, which was pure by TLC. The material was film dried at 105 °C (50 μm) for 24 h to give 101 g (63%): ^{1}H NMR δ 2.35 (s, CH_3, 6 H), 2.95 (m, CH_2, 4 H), 3.30 (m, CH_2, 4 H), 3.61 (m, CH_2, 4 H), 3.95 (m, CH_2, 4 H), 7.2 (m, ArH, 12 H), 7.7 (m, ArH, 8 H). The material crystallized from CH_3CN–CH_3OH gave mp 69–71 °C. Anal. Calcd for $C_{42}H_{42}O_{10}S_2$: C, 65.44; H, 5.49. Found: C, 65.64; H, 5.36.

A different procedure was applied to (−)-(S)-18. To a solution of 50.0 g of (−)-(S)-1 in 1 L of dry DMF was added 19.5 g of NaH (50% oil dispersion). The mixture was heated to 70 °C with stirring under N_2. After 1 h, 2-(2′-chloroethoxy)ethyl 2″-tetrahydropyranyl ether (83.2 g) was added. The reaction mixture was stirred at 70 °C for 48 h under N_2, cooled, and shaken with 2 L of water. The mixture was extracted with CH_2Cl_2, and the combined organic layers were washed with water, dried, and evaporated. The residue in 1:1 pentane–CH_2Cl_2 was filtered through 250 g of basic alumina, which was washed with additional solvent. The eluent was concentrated, and the oil was dissolved in 300 ml of CH_2Cl_2 to which was added 150 mL of methanol and 10 mL of concentrated hydrochloric acid. The solution was stirred for 1 h at 25 °C and neutralized with aqueous $NaHCO_3$, and the organic layer was separated and combined with CH_2Cl_2 washes of the aqueous layer. The organic layer was dried and evaporated, and the oil was washed with pentane to remove the mineral oil. The oil was dried at 90 °C (0.1 mm) to give 57.4 g (70%) of diol as a gum. This material, 31.7 g, in 300 mL of dry pyridine was cooled to −20 °C, and 30.0 g of tosyl chloride was added in small portions during 15 min, during which time and for an additional 1.5 h the mixture was cooled and stirred. After standing at −20 °C for 24 h, the mixture was stirred into 1000 g of ice. The water was decanted, and the residual oil was shaken with CH_2Cl_2 and 10% aqueous hydrochloric acid. The organic layer was washed with the same acid, then with 10% aqueous $NaHCO_3$ and water. The solution was dried, evaporated at 25 °C under vacuum, and dried at 0.01 mm (25 °C) to give 41.5 g (80%) of (−)-(S)-18 as a gum. This material possessed a ^{1}H NMR spectrum identical with racemic 18: $[\alpha]^{25}_{578}$ −30.7° (c 1.0, THF). Anal. Calcd for $C_{42}H_{42}O_{10}S_2$: C, 65.44; H, 5.49. Found: C, 65.40; H, 5.30.

Similarly, (+)-(R)-18 was prepared (68%): $[\alpha]^{25}_{578}$ +31.0° (c 1.0, THF).

(−)-(S,S)-Bis(binaphtho)-22-crown-6 ((−)-(S,S)-15) from (−)-(S)-2,2′-Bis-(5-tosyloxy-3-oxa-1-pentyloxy)-1,1′-binaphthyl ((−)-(S)-18), and (+)-(R,R)-15 from (+)-(R)-18. Procedure III. To a solution of 15.4 g (0.54 mol) of (−)-(S)-1 in 1 L of THF was added under N_2 7.15 g (0.108 mol) of KOH (85%) in 50 mL of water. The solution was refluxed under N_2 for 1 h and 41.5 g (0.54 mol) of (−)-(S)-18 was added. The solution was refluxed for 50 h, evaporated at 25 mm to 150 mL, and shaken with 150 mL of CH_2Cl_2 and 150 mL of water. The phases were separated, the aqueous phase was extracted with two 150-mL portions of CH_2Cl_2, and the combined organic phases were washed successively with 10% aqueous KOH and water. The solution was dried and evaporated under vacuum to give 40.0 g of oil, which was chromatographed on 850 g of silica gel with CH_2Cl_2 as eluting agent to give (−)-(S,S)-15, which was crystallized from benzene–cyclohexane to give 16.2 g of the solvate: mp 123–124 °C. When heated to 170 °C (0.06 mm) for 10 h, this material gave 14.0 g (37%) of (−)-(S,S)-15 as a glass: $[\alpha]^{25}_{578}$ −220° (c 1.0, CH_2Cl_2).

Similarly prepared (+)-(*R,R*)-**15** (from (+)-(*R*)-**18**, 42%) gave $[\alpha]^{25}_{578}$ +221° (*c* 1.0, CH_2Cl_2).

(*R*),(*S*)-2-Benzhydryloxy-2′-hydroxy-1,1′-binaphthyl ((*R*),(*S*)-16) and (+)-(*S*)-16. A mixture of 28.6 g (0.10 mol) of **1**, 300 mL of THF, and 12.0 g (0.11 mol) of *t*-BuOK was stirred under N_2 (5 min), and benzyhydryl bromide (27.1 g or 0.11 mol) in 200 mL of THF was added. The mixture was heated at reflux for 24 h, cooled, and evaporated under vacuum. The residue was partitioned between CH_2Cl_2 and 10% NaOH solution. The aqueous layer on acidification gave 4 g of recovered **1**. The organic layer was washed with brine, dried, and evaporated (vacuum) to give an oil that crystallized as a solvate of diethyl ether from that solvent: weight 31.6 g (60%); mp 103–105 °C (bubbles). Anal. Calcd for $C_{33}H_{24}O_2 \cdot C_4H_{10}O$: C, 84.38; H, 6.51. Found: C, 84.27; H, 6.35. This material crystallized from pentane gave: melting behavior, translucent at 62 °C, cloudy at 84 °C, liquid at 138–140 °C; M^+ 452. Anal. Calcd for $C_{33}H_{24}O_2$: C, 87.58; H, 5.35. Found C, 87.73; H, 5.37.

From (−)-(*S*)-**1** (28.6 g) by the same procedure was obtained 33 g (73%) of (+)-(*S*)-**16**, except the material was purified by chromatography on 700 g of alumina (CH_2Cl_2–pentane eluting agent). The material was a foam: $[\alpha]^{25}_{589}$ +18.7°, $[\alpha]^{25}_{578}$ +19.6°, $[\alpha]^{25}_{546}$ +21.3° (*c* 0.55, THF). Anal. Calcd. for $C_{33}H_{24}O_2$: C, 87.58; H, 5.35. Found: C, 87.49; H. 5.57.

(−)-(*S,S*)-1,17-Bisbenzyhydryl-2,3:4,5:13,14:15,16-tetra-(1,2-naphtho)-1,6,9,12,17-pentaoxaheptadecyl-2,4,13,15-tetraene ((−)-(*S,S*)-17). From 9.05 g of (+)-(*S*)-**16**, 6.14 g of diethylene glycol ditosylate, and 2.45 g of KOH by procedure III (THF–H_2O, reflux, 48 h) was obtained an oil that was chromatographed on 500 g of alumina developed with CH_2Cl_2 in pentane. The product came off with 40% CH_2Cl_2–60% pentane (by volume) to give 7.15 g (73%) of (−)-(*S,S*)-**17** as a white foam: $[\alpha]^{25}_{578}$ −3.04°, $[\alpha]^{25}_{546}$ −5.18°, $[\alpha]^{25}_{436}$ −30.25° (*c* 1.0, $CHCl_3$); M^+ 974. Anal. Calcd for $C_{70}H_{54}O_5$: C, 86.21; H, 5.58. Found: C, 86.08; H, 5.69.

(−)-(*S,S*)-Bis(binaphtho)-22-crown-6 ((−)-(*S,S*)-15) from (−)-(*S,S*)-17, Procedure IV. A solution of 4.35 g of bisbenzhydryl ether (−)-(*S,S*)-**17** in 50 mL of CH_2Cl_2, 50 mL of methanol, and 5 mL of concentrated hydrochloric acid was stirred for 20 h at 25 °C. The mixture was shaken with 200 mL of ice water and 200 mL of CH_2Cl_2, and the organic phase was water washed, dried, and evaporated under vacuum. The resulting mixture of diphenylmethoxymethane and the bisphenol was mixed with 200 mL of THF, 1.85 g of diethylene glycol ditosylate, and 0.65 g of KOH in 1 mL of water. The solution was heated at reflux under N_2 for 24 h, and the impure product isolated as usual and chromatographed on 200 g of alumina. Elution of the column with 1:9 CH_2Cl_2–pentane (v/v) gave 1.51 g (85%) of diphenylmethoxymethane. Elution with 1:1 CH_2Cl_2–pentane (v/v) gave (−)-(*S,S*)-**15**, which was purified through crystallization of its benzene–cyclohexane solvate and dried: weight 1.48 g (47%); $[\alpha]^{25}_{578}$ −215°, $[\alpha]^{25}_{546}$ −255° (*c* 0.31, CH_2Cl_2). Its ^1H NMR was superimposable on authentic material.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-8,9,10:19,20,21-bis(1,3-benzo)-9,20-diaza-1,6,12,17-tetraoxacyclodocosa-2,4,8,13,15,19-hexaene ((−)-(*S,S*)-14). To a solution of 14.3 g (0.050 mol) of (−)-(*S*)-**1** in 500 mL of THF was added under N_2 12.3 g (0.11 mol) of *t*-BuOK along with 350 mL of additional THF. The initial solution became a slurry during 15 min of stirring at 25 °C. In one portion, 8.8 g (0.050 mol) of 2,6-bis(chloromethyl)pyridine was added with 1 L of THF. The reaction mixture was stirred and heated at reflux under N_2 for 96 h and cooled, and the THF was evaporated under vacuum. The residue was shaken with CH_2Cl_2 and water, and the organic layer was washed with water, dried, and evaporated. The residue was dissolved in hot THF and cooled, and the THF disolvate that crystallized was collected to give, after drying in vacuo at 25 °C for 48 h, 7.2 g (31%) of (−)-(*S,S*)-**14**·2$(CH_2)_4O$: mp 295–298 °C dec; ^1H NMR δ 1.76 (m, 8 H, $(CH_2)_4$), 3.66 (m, 8 H, $(CH_2)_4$), 4.82 (s, 8 H, pyrCH_2), 6.32, 6.40 (portion of A_2B, 4 H, pyr-H-3), 6.8–7.9 (m, 26 H, naphthyl-H); M^+ 778 (solvate lost); $[\alpha]^{25}_{589}$ −250°, $[\alpha]^{25}_{578}$ −264°, $[\alpha]^{25}_{546}$ −319°, $[\alpha]^{25}_{436}$ −772° (*c* 1.1, $CHCl_3$, rotation adjusted for solvate). Material obtained by evaporation of a solution of (−)-(*S,S*)-**14** in CH_2Cl_2 was free of solvate. Anal. Calcd for $C_{54}H_{38}N_2O_4$: C, 83.27; H, 4.92. Found: C, 83.20; H, 5.03.

The filtrates from the crystallizations were evaporated and chromatographed on silica gel (350 g). Elution of the products with CH_2Cl_2 gave first (−)-(*S,S*)-**14**, then mixtures, and finally the oligomer composed of one binaphthyl and one pyrido unit ((−)-(*S*)-**13**), whose ^1H NMR py-CH_2O protons came at δ 5.07. This material was not characterized.

1,2-Bis(5-tosyloxy-3-oxa-1-pentyloxy)benzene (20). A solution of 68.0 g (0.326 mol) of 2-(2-chloroethoxy)ethyl 2-tetrahydrofuranyl ether in 150 mL of butanol was added dropwise under N_2 to a mixture of 11.0 g (0.100 mol) of catechol and 8.2 g (0.200 mol) of NaOH in 300 mL of boiling butanol. The mixture was stirred under N_2 for 15 h, and an additional 2.9 g (0.07 mol) of NaOH was added. The mixture was refluxed for an additional 16 h. The mixture was cooled and filtered from 14.9 g (94%) of NaCl, the filtrate was evaporated to an oil at 20 mm, and the oil was heated to 120 °C (50 μm) to give 47 g of residue. This material was stirred with 1 g of pyridine hydrochloride for 1 h at 155–160 °C (50 μm). The product was distilled, and the 1,1-bis(5-hydroxy-3-oxa-1-pentyloxy)benzene was collected as a colorless oil (19.5 g or 68%) at 185–187 °C (50 μm). Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75. Found: C, 59.03; H, 7.87.

To 5.7 g (20 mmol) of this diol in 130 mL of dry pyridine at 0 °C was added 15.2 g (60 mmol) of tosyl chloride. The mixture was stirred at 0 °C until homogeneous, and stored at 0 °C for 24 h. The usual extraction procedure gave 9.8 g of a brown oil, which was dissolved in 400 mL of 49:1 (v/v) $CHCl_3$–ether and run through a column of 20 g of silica gel. The column eluate was concentrated and the residue dried at 50 °C (20 μm) for 15 h to give 8.2 g (69%) of **20** as a viscous oil: ^1H NMR δ 2.40 (s, CH_3, 6 H), 3.75 (m, $CH_2CH_2OCH_2$, 8 H), 4.10 (m, $ArOCH_2$ and CH_2OTs, 8 H), 6.89 (m, benzo Ar-H, 4 H), 7.29–7.79 (m, ArH, 4 H). Anal. Calcd for $C_{28}H_{34}O_{10}S_2$: C, 56.55; H, 5.75. Found: C, 56.24; H, 5.90.

2,3-Benzo-11,12:13,14-di(1,2-naphtho)-1,4,7,10,15,18-hexaoxacycloeicosa-2,11,13-triene or Benzo-2,2′-binaphtho-20-crown-6 (19). A mixture of 20.8 g (35.0 mmol) of ditosylate **20** in 40 mL of butanol was added to a mixture of 10.0 g (35.0 mmol) of (±)-**1** and 2.88 g (70 mmol) of NaOH in 70 mL of boiling butanol stirred under N_2. The mixture was refluxed for 20 h. The crude product was isolated in the usual way and chromatographed on 800 g of neutral alumina with benzene–ether as eluting agent to give crystalline (±)-**19**, which was recrystallized from cyclohexane–benzene to give 9.3 g (50%) of needles: mp 147–148 °C; ^1H NMR δ 3.6 (m, $CH_2CH_2OCH_2$, 8 H), 4.0 (complex m, $ArOCH_2$, 8 H), 6.84 (narrow m, benzo ArH, 4 H), 7.20 (complex m, naphthyl ArH, 8 H), 7.80 (m, naphthyl ArH, 4 H); M^+ 536 (base peak). Anal. Calcd for $C_{34}H_{32}O_6$: C, 76.10; H, 6.01. Found: C, 75.78; H, 5.99.

Cycle **20** was also prepared by procedure I from ditosylate (±)-**18** and catechol in 41% yield, mp 147–148 °C, undepressed by admixture with authentic material.

Mixture of (*R,S*)- and (*R,R*),(*S,S*)-1,20-Bis(benzhydryl)-2,3:4,5:16,17:18,19-tetra(1,2-naphtho)-1,6,9,12,15,20-hexaoxaeicosa-2,4,16,18-tetraene ((*R,S*)-21 and (*R,R*),(*S,S*)-21) and (−)-(*S,S*)-21. From 10.5 g (0.020 mol) of (*R*),(*S*)-**16** as its etherate (monobenzhydryl ether of **1**), potassium hydroxide, and triethylene glycol ditosylate (4.6 g, 0.010 mol) was prepared crude **21** (12.3 g) by procedure III which was chromatographed on 400 g of alumina with CH_2Cl_2–pentane (1:5, v/v) as eluting agent to remove impurities, and 1:1 to bring off 6 g (60%) of the diastereomeric mixture **21**: white foam; M^+ 1018. Anal. Calcd for $C_{72}H_{58}O_6$: C, 84.84; H, 5.73. Found: C, 84.88; H, 5.84.

Similarly from (+)-(*S*)-**16** (29.3 g or 0.0647 mol), KOH (4.70 g or 0.0712 mol), and triethylene glycol ditosylate (14.82 g or 0.0324 mol) was obtained 24.0 g (73%) of (−)-(*S,S*)-**21**: M^+ 1018; ^1H NMR δ 2.67 (s, central CH_2OCH_2, 4 H), 3.15 (pseudo t, $ArOCH_2CH_2$, 4 H), 3.84 (m, $ArOCH_2$, 4 H), 6.04 (s, Ar_2CH, 2 H), 6.8–7.9 (complex m, ArH, 44 H); $[\alpha]^{25}_{589}$ −3.04°, $[\alpha]^{25}_{578}$ −3.40°, $[\alpha]^{25}_{546}$ −5.25°, $[\alpha]^{25}_{436}$ −28.7° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{72}H_{58}O_6$: C, 84.84; H, 5.73. Found: C, 85.01; H, 5.67.

(*R,R*),(*S,S*)-, (*R,S*)-, and (−)-(*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 ((*R,R*),(*S,S*)-22, (*R,S*)-22, and (−)-(*S,S*)-22). A solution of 4.9 g of the above mixture of racemic and *meso*-**21** in 300 mL of THF and 100 mL of concentrated hydrochloric acid was allowed to stand at 25 °C for 16 h. The solution was evaporated under vacuum until it became turbid, at which point it was shaken with 200 mL of water and 200 mL of CH_2Cl_2. The aqueous phase was extracted with additional CH_2Cl_2, and the combined organic layers were washed with water and evaporated. Toluene (150 mL) and enough concentrated ammonium hydroxide to neutralize the residue were added, and the solution was evaporated under vacuum. The toluene–ammonium hydroxide–evaporative treatment was repeated, and the phenolic oil produced was used directly in the next step. This material was dissolved in 100 mL of THF, and 3 g of potassium hydroxide dissolved in 15 mL of water was added. To the resulting mixture was added 3.7 g of ethylene glycol ditosylate in 75 mL of tetrahydrofuran. The solution was refluxed for 36 h, and an additional 1.5 g of potassium hydroxide and 1.5 g of ethylene glycol ditosylate were added. The resulting mixture was refluxed for an additional 12 h, filtered, and shaken with 200 mL of CH_2Cl_2 and 200 mL of water. The organic phase was washed with 10% sodium hydroxide solution, water, and

brine. The solution was dried and evaporated, and the resulting oil was chromatographed on neutral alumina (500 g) made up in 1:1 CH_2Cl_2–pentane. The column was washed with the same solvent mixture, and 75-mL fractions were cut. Cycle **22** was eluted in fractions 5–14, 1.7 g (50%), as a 3:7 mixture of (*R,S*) and (*R,R*),(*S,S*) isomers. A sample of this material was molecularly distilled at 250 °C (10 μm) to give material for analysis: M^+ 712. Anal. Calcd for $C_{48}H_{40}O_6$: C, 80.87; H, 5.66. Found: C, 80.59; H, 5.94.

A solution of 100 mg of (*R,S*)- and (*R,R*),(*S,S*)-**21** mixture was submitted to thick-layer chromatography on silica gel (1-mm thick plate) with $CHCl_3$–cyclohexane as developer (six times). The bands were scraped from the plate, and the products were recovered by repeated washing of the silica gel with 1:3 methanol–chloroform. The *R,S* isomer (R_f 0.13, SiO_2–$CHCl_3$) was crystallized from ethanol: mp 118–121 °C (bubbles at 180 °C). The (*R,R*),(*S,S*) isomer (R_f 0.28, SiO_2–$CHCl_3$) was crystallized and recrystallized from ethanol: mp 132–135 °C after recrystallization (bubbles at 180 °C).

The ^1H NMR spectrum of dried (*R,R*),(*S,S*)-**22** gave δ 2.9–4.0 (m, OCH_2CH_2O, 16 H), 6.75 and 6.86 (d, Ar^3-H, 2 H), 7.03–8.0 (complex m, ArH, 22 H). The ^1H NMR spectrum of the dried (*R,S*)-**22** gave δ 3.0–4.0 (m, OCH_2CH_2O, 16 H), 6.9–7.9 (complex m, ArH, 24 H). The spectra of other cycles containing two binaphthyl units *of the same configuration* separated by a single ethylenedioxy unit exhibit signals at ca. δ 6.76 and 6.86, and are assigned to those protons at the 3 positions of the naphthalene rings that thrust into the face of a naphthalene ring of the attached binaphthyl unit, and are thus moved upfield by the shielding cone of the aromatic system.

By a similar procedure, (−)-(*S,S*)-**21** was converted (60%) to (−)-(*S,S*)-**22**: foam; M^+ 712; ^1H NMR spectrum identical with (*S,S*),(*R,R*)-**22**; $[\alpha]^{25}_{589}$ −212°, $[\alpha]^{25}_{578}$ −223°, $[\alpha]^{25}_{546}$ −265° (*c* 4.5, $CHCl_3$). Anal. Calcd for $C_{48}H_{40}O_6$: C, 80.88; H, 5.66. Found: C, 80.96; H, 5.95.

(−)-(*S,S*)-1,1,19,19-Tetraphenyl-3,4:5,6:14,15:16,17-tetra(1,2-naphtho)-2,7,13,18-tetraoxanonadeca-3,5,14,16-tetraene ((−)-(*S,S*)-23). A solution of (+)-(*S*)-2′-benzhydryloxy-2-hydroxy-1,1′-binaphthyl ((+)-(*S*)-**16**) (17.7 g or 0.0391 mol), 1,5-pentanediol ditosylate (8.06 g or 0.0196 mol), and KOH (2.84 g, 85% pellets, 0.043 mol in 10 mL of H_2O) in 400 mL of THF was refluxed for 24 h. The precipitated KOTs was filtered, the filtrate was evaporated in vacuo, and the residual oil was chromatographed on 500 g of alumina. The desired product was eluted with CH_2Cl_2–pentane (3:7, v/v): weight 10.35 g (54%); white foam; ^1H NMR δ 0.92 (m, $OCH_2(CH_2)_3$, 6 H), 3.44 (t, $ArOCH_2$, 4 H), 6.00 (s, Ar_2CH, 2 H), 7.0, 7.7 (m, m, ArH, 48 H); M^+ 972; $[\alpha]^{25}_{578}$ −20.8°, $[\alpha]^{25}_{546}$ −25.5°, $[\alpha]^{25}_{436}$ −69.3° (*c* 0.8, $CHCl_3$). Anal. Calcd for $C_{71}H_{56}O_4$: C, 87.62; H, 5.80. Found: C, 87.32; H, 5.58.

(−)-(*S,S*)-1,1,19,19-Tetraphenyl-3,4:5,6:14,15:16,17-tetra(1,2-naphtho)-9,10,11-(1,3-benzo)-2,7,13,18-tetraoxanonadeca-3,5,9,14,16-pentaene ((−)-(*S,S*)-24). To a solution of 19.9 g (0.044 mol) of (+)-(*S*)-**16** in 400 mL of THF was added 4.93 g (0.044 mol) of *t*-BuOK. The solution was stirred under nitrogen for 10 min, and a solution of 5.80 g (0.022 mol) of 2,6-bis(bromomethyl)benzene in 100 mL of THF was added. The mixture was heated at reflux for 36 h, the solvent was evaporated *in vacuo*, and the residue was chromatographed on 700 g of alumina. The desired product eluted with CH_2Cl_2–pentane (1:3, v/v) to give 14.9 g (67%) of white foam: M^+ 1006; $[\alpha]^{25}_{578}$ −8.9°, $[\alpha]^{25}_{546}$ −11.7°, $[\alpha]^{25}_{436}$ −34.7° (*c* 0.6, $CHCl_3$). Anal. Calcd for $C_{74}H_{54}O_4$: C, 88.24; H, 5.40. Found: C, 88.02; H, 5.40.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-8,9,10-(1,3-benzo)-9-aza-1,6,12,17,20-pentaoxacyclodocosa-2,4,8,13,15-pentaene ((−)-(*S,S*)-25). Procedure IV was used except as follows. The benzhydryl groups were removed from 7.65 g (0.784 mmol) of (−)-(*S,S*)-**17**, and the derived bisphenol was mixed with *t*-BuOK (1.93 g, 1.725 mmol) and 2,6-bis(chloromethyl)pyridine (1.40 g, 7.84 mmol) in 200 mL of THF. The product was chromatographed on 250 g of alumina, and the desired product was eluted with from 2:3 to 1:1 CH_2Cl_2–pentane (v/v) to give 2.54 g (43%) of (−)-(*S,S*)-**25** as a foam dried at 110 °C for 20 h at 50 μm: ^1H NMR δ 2.9 (m, CH_2OCH_2, 4 H), 3.62 (pseudo-t, $ArOCH_2$, 4 H), 4.89 (s, pyCH_2, 4 H), 6.68, 6.76 (s, s, py-H-3, 2 H), 7.0–7.4, 7.7–7.9 (m, m, ArH, 27 H); $[\alpha]^{25}_{578}$ −241.9°, $[\alpha]^{25}_{546}$ −288.2°, $[\alpha]^{25}_{436}$ −664.9° (*c* 0.7, $CHCl_3$). Anal. Calcd for $C_{51}H_{39}NO_5$: C, 82.12; H, 5.27. Found: C, 82.33; H, 5.43.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-8,9,10-(1,3-benzo)-1,6,12,17,20-pentaoxacyclodocosa-2,4,8,13,15-pentaene ((−)-(*S,S*)-26). Proceudre IV was used except as follows. The benzhydryl groups were removed from 9.15 g (9.34 mmol) of (−)-(*S,S*)-**17**, and the bisphenol was mixed with 2.30 g (0.020 mol) of *t*-BuOK and 2.47g (9.34 mmol) of 1,3-bis(bromomethyl)benzene in 200 mL of THF. After 69 h of reflux under N_2, the products were isolated and chromatographed on 400 g of alumina, the desired product being eluted with 2:3 (v/v) CH_2Cl_2–pentane, which dried to a white foam: weight 0.9 g (13%); M^+ 744; ^1H NMR δ 2.78 (m, CH_2OCH_2, 4 H), 3.52 (t, $ArOCH_2$, 4 H), 4.80 (s, $ArOCH_2$, 4 H), 6.7–7.9 (complex m, ArH, 28 H); $[\alpha]^{25}_{589}$ −214.9°, $[\alpha]^{25}_{578}$ −230.5°, $[\alpha]^{25}_{546}$ −274.9°, $[\alpha]^{25}_{436}$ −629.9° (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{52}H_{40}O_5$: C, 83.85; H, 5.41. Found: C, 83.92; H, 5.57.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-8,9,10-(1,3-cyclopentano)-1,6,9,12,17,20-hexaoxacyclodocosa-2,4,13,15-tetraene ((−)-(*S,S*)-27). Proceudre IV was used except as follows. The benzhydryl groups were removed from 3.31 g (3.4 mmol) of (−)-(*S,S*)-**17**, and the derived bisphenol in 100 mL of THF was mixed with 0.60 g (9.00 mmol) of KOH in 5 mL of water and 3.96 g (9.00 mmol) of *cis*-2,5-bis(tosyloxymethyl)tetrahydrofuran[4b] in 20 mL of THF. After the mixture had refluxed under N_2 for 100 h, another 2.0 g (4.5 mmol) of the ditosylate and 0.30 g (4.5 mmol) of KOH was added, and the refluxing was continued for 100 h. The isolated mixed products were chromatographed on 200 g of alumina, and the desired product was eluted with CH_2Cl_2–pentane (1:1, v/v) to give after drying 0.65 g (26%) of (−)-(*S,S*)-**27** as a white glass: ^1H NMR δ 1.1–1.4 (m, $C(CH_2)_2C$, 4 H), 2.9–4.2 (m, 14 H, all other aliphatic H), 6.8–7.4 (m, ArH-3,6,7,8, 16 H), 7.6–8.1 (m, ArH-4,5, 8 H); M^+ 738; $[\alpha]^{25}_{589}$ −218°, $[\alpha]^{25}_{578}$ −229°, $[\alpha]^{25}_{546}$ 270°, $[\alpha]^{25}_{436}$ −599° (*c* 0.56, $CHCl_3$). Anal. Calcd for $C_{50}H_{42}O_6$: C, 81.28; H, 5.73. Found: C, 81.09; H, 5.67.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-1,6,9,12,17-pentaoxacyclodocosa-2,3,13,15-tetraene ((−)-(*S,S*)-28). Procedure IV was used except as follows. The benzhydryl groups were removed from 4.51 g (4.64 mmol) of (−)-(*S,S*)-**23**, and the bisphenol was mixed in 200 mL of THF with 1.14 g (10 mmol) of *t*-BuOK and diethylene glycol ditosylate (2.02 g, 4.9 mmol). The solution was refluxed for 48 h, and the product mixture was chromatographed on 200 g of alumina. The desired product was eluted with 3:7 (v/v) CH_2Cl_2–pentane to give after drying 1.36 g (41%) of (−)-(*S,S*)-**28** as a white foam: ^1H NMR δ 1.18 (m, $C(CH_2)_3C$, 6 H), 3.06 (m, CH_2OCH_2, 4 H), 3.70 (m, $ArOCH_2$, 8 H), 7.14, 7.80 (m, m, ArH, 24 H); M^+ 710 (base peak); $[\alpha]^{25}_{589}$ −193°, $[\alpha]^{25}_{578}$ −203°, $[\alpha]^{25}_{546}$ −241°, $[\alpha]^{25}_{436}$ −553° (*c* 0.15, $CHCl_3$). Anal. Calcd for $C_{49}H_{42}O_5$: C, 82.79; H, 5.96. Found: C, 82.80; H, 5.88.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-8,9,10-(1,3-benzo)-9-aza-1,6,12,17-tetraoxacyclodocosa-2,4,8,13,15-pentaene ((−)-(*S,S*)-29). Procedure IV was used except as follows. The benzhydryl groups were removed from 4.51 g (4.64 mmol) of (−)-(*S,S*)-**23** to give the bisphenol, which in 200 mL of THF was mixed with 1.14 g (10.21 mmol) of *t*-BuOK and 0.86 g (4.87 mmol) of 2,6-bis(chloromethyl)pyridine[4c] and refluxed for 48 h. The crude reaction product was chromatographed on 300 g of alumina, and the desired product was eluted with 2:3 (v/v) CH_2Cl_2–pentane to give after drying a white foam: weight 1.5 g (29%); ^1H NMR δ 0.80 (br s, $C(CH_2)_3C$, 6 H), 3.52 (br s, $ArOCH_2$, 4 H), 4.88 (s, py-CH_2, 4 H), 6.62, 6.73 (s, s, py-H-3,5, 2 H), 7.0–7.9 (complex m, ArH and py-H-4, 25 H); M^+ 743; $[\alpha]^{25}_{589}$ −240°, $[\alpha]^{25}_{578}$ −250°, $[\alpha]^{25}_{546}$ −301°, $[\alpha]^{25}_{436}$ −702° (*c* 0.50, $CHCl_3$). Anal. Calcd for $C_{52}H_{41}NO_4$: C, 83.96; H, 5.56. Found: C, 83.98; H, 5.69.

(−)-(*S,S*)-2,3:4,5:13,14:15,16-Tetra(1,2-naphtho)-8,9,10:19,20,21-di(1,3-benzo)-9-aza-1,6,12,17-tetraoxacyclodocosa-2,4,8,13,15,20-hexaene ((−)-(*S,S*)-30). Procedure IV was used except as follows. The benzhydryl groups were removed from 15.8 g (0.016 mol) of (−)-(*S,S*)-**24** to give the bisphenol, which in 300 mL of THF was mixed with 3.86 g (0.0345 mol) of *t*-BuOK and 2.76 g (0.016 mol) of 2,6-bis(chloromethyl)pyridine[4c] in 100 mL of THF. The mixture was refluxed for 42 h, an additional 1.0 g of 2,6-bis(chloro)-pyridine and 1.5 g of *t*-BuOK were added, and refluxing was continued for an additional 24 h. The product mixture was chromatographed on 500 g of alumina, and the desired product was eluted with from 1:1 CH_2Cl_2–pentane (v/v) to pure CH_2Cl_2 to give after drying (−)-(*S,S*)-**30** as a white foam: weight 5.3 g (43%); ^1H NMR δ 4.57 (s, $ArOCH_2$, 4 H), 4.82 (AB, J = 4 Hz, $ArOCH_2$, 4 H), 6.40–7.90 (complex m, ArH, 31 H); M^+ 777; $[\alpha]^{25}_{589}$ −269°, $[\alpha]^{25}_{578}$ −283°, $[\alpha]^{25}_{546}$ −339°, $[\alpha]^{25}_{436}$ −798° (*c* 0.54, $CHCl_3$). Anal. Calcd for $C_{55}H_{39}O_4N$: C, 84.92; H, 5.05. Found: C, 84.83; H, 5.18.

Syntheses of (*R*),(*S*)- or (+)-(*S*)-2,3:4,5-Di(1,2-naphtho)-1,6-dioxacycloocta-2,4-diene ((*R*),(*S*)-3 and (+)-(*S*)-3), (*R,S*)-2,3:4,5:10,11:12,13-Tetra(1,2-naphtho)-1,6,9,14-tetraoxacyclohexadeca-2,4,10,12-tetraene ((*R,S*)-32), (*R,R,R*),(*S,S,S*)-, (*R,S,S*),(*S,R,R*)-, and (−)-(*S,S,S*)-2,3:4,5:10,11:12,13:18,19:20,21-hexaene ((*R,R,R*),(*S,S,S*)-31, (*R,S,S*),(*S,R,R*)-31, and (−)-(*S,S,S*)-31), and of Anomalous Ketone 8 and (+)-8 from Diethylene Glycol Ditosylate and (*R*),(*S*)- or (−)-(*S*)-2,2′-Dihydroxy-1,1′-binaphthyl ((±)-1 and (−)-(*S*)-1). A mixture of (±)-1 (10.0 g, 34.9 mmol), *t*-BuOK (7.83 g, 69.8 mmol), and ethylene glycol ditosylate (12.93 g, 34.9 mmol) in 600 ml of THF was prepared. The

mixture was stirred under N_2 for 20 h at 25 °C, refluxed for 44 h, and cooled, and the product mixture was isolated as 11.2 g of tan solid. This material in CH_2Cl_2 was filtered through 100 g of neutral alumina to give 10.1 g of light yellow solid. This material was rechromatographed on 150 g of silica gel. Pentane–ether (94:6, v/v) eluted cycle **3**, then a mixture of **3** and ketone **8**, and finally **8** itself. Pentane–benzene (1:1, v/v) and then benzene eluted, in this order, **8**, cycle (*R,S*)-**32**, (*R,S,S*),(*S,R,R*)-**31**, and (*R,R,R*),(*S,S,S*)-**31**. The combined latter fractions were rechromatographed on 300 g of silica gel with benzene as eluting agent. Preparative thick-layer chromatography on silica gel plates with CH_2Cl_2–pentane (4:6 v/v) as developer applied to the appropriate fractions provided samples of the last three compounds. Cycle (±)-**3**, after recrystallization from pentane–ether, weighed 2.46 g (23%): mp 222–223 °C; UV spectrum in $CHCl_3$ gave λ_{max} at 325 (log ε 3.76) and 298 (log ε 4.07) with shoulders at 317 and 291 nm; M^+ 312; Rast molecular weight in camphor, 391; ^1H NMR δ 4.00–4.36 (m, $ArOCH_2$, 4 H), 7.40 (m, ArH, 8 H), 7.76–7.92 (m, ArH, 4 H). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.52; H, 5.33. Recrystallization of ketone **8** from pentane–ether gave 4.80 g (44%) of light yellow crystals: mp 196.5–198 °C, sublimation of which at 200 °C (10 μm) gave mp 198–200 °C; M^+ 312; Rast molecular weight in camphor, 338; UV spectrum ($CHCl_3$) gave λ_{max} at 289 (log ε 4.10) and 278 (log ε 4.00) and shoulders at 331 and 268 nm; IR spectrum (KBr), strong band at 1660 cm^{-1} (C=O); ^1H NMR δ 2.22 (symmetric m, CCH_2, 2 H), 4.18 (symmetric m, OCH_2, 2 H), 6.22–6.50 (m, CH=CH, 2 H) 6.68–7.70 (m, ArH, 10 H). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.61; H, 5.30. The smaller cycle (*R,S*)-**32** was separated from the larger (*R,S,S*),(*S,R,R*)-**31** by fractional sublimation at 250 °C (10 μm) to give 0.085 g (1%) of (*R,S*)-**32** as white crystals: mp 355 °C dec; M^+ 624; UV spectrum λ_{max} 336 (log ε 4.06), 323 (log ε 4.02), 292 (log ε 4.26), 282 (log ε 4.06), with a shoulder at 273 nm. Anal. Calcd for $C_{44}H_{32}O_4$: C, 84.59; H, 5.16. Found: C, 84.54; H, 5.03. Preparative thick-layer chromatography of the mixture of (*R,S*)-**32** and (*R,S,S*),(*S,R,R*)-**31** gave the latter, which was recrystallized from ether to give 52 mg (0.5%) of fine crystals: mp 188–190 °C; UV spectrum ($CHCl_3$) λ_{max} 355 (log ε 4.15), 324 (log ε 4.14), 292 (log ε 4.38) and 282 (log ε 4.44) with a shoulder at 273 nm; M^+ 937; ^1H NMR spectrum δ 3.62–4.02 (m, $ArOCH_2$, 12 H), 6.52–7.96 (br m, ArH, 36 H). Anal. Calcd for $C_{66}H_{48}O_6$: C, 84.59; H, 5.16. Found: C, 84.49; H, 5.08. Preparative thick-layer chromatography of the mixture of (*R,S,S*),(*S,R,R*)-**31** and (*S,S,S*),(*R,R,R*)-**31** led to pure (*S,S,S*),-(*R,R,R*)-**31**, which was recrystallized from a large volume of ether to give 30 mg of white crystals: mp 338–342 °C dec; UV spectrum λ_{max} 335 (log ε 4.12), 325 (log ε 4.17), 293 (log ε 4.41), and 282 (log ε 4.46) with a shoulder at 273 nm; M^+ 937. This material was too insoluble for a ^1H NMR spectrum. Anal. Calcd for $C_{66}H_{48}O_6$: C, 84.59; H, 5.16. Found: C, 84.47; H, 5.45.

When 8.6 g of (*R*),(*S*)-**1**, 6.75 g of *t*-BuOK, and 11.1 g of ethylene glycol ditosylate in 100 mL of DMF were stirred under nitrogen at 70 °C for 70 h, product was obtained which was chromatographed on alumina to give, after crystallization from ether–CH_2Cl_2, 6.1 g (65%) of (*R*),(*S*)-**3**: mp 221–223 °C, undepressed by admixture with authentic material.

Treatment of 0.50 g of (−)-(*S*)-**1** by the first procedure (THF–*t*-BuOK) gave (+)-(*S*)-**3**: weight 0.113 g (21%); mp 216.5–217 °C; UV and ^1H NMR spectra and TLC behavior identical with (±)-**3**; $[\alpha]^{25}_{578}$ +546°, $[\alpha]^{25}_{546}$ +628°, $[\alpha]^{25}_{436}$ +1116°, $[\alpha]^{25}_{365}$ +1427° (*c* 0.93, CH_2Cl_2). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.49; H, 5.10. Also produced was 0.221 g (40%) of ketone (+)-**8**: mp 187–188 °C; UV and ^1H NMR spectra and TLC behavior identical with (±)-**8**; $[\alpha]^{25}_{578}$ +247°, $[\alpha]^{25}_{546}$ +314°, $[\alpha]^{25}_{436}$ +1324° (*c* 0.97, CH_2Cl_2). Also obtained was 9 mg (1.7%) of (−)-(*S,S,S*)-**31**: glass; phase transition, 185–200 °C; M^+ 937; UV spectrum and TLC behavior identical with (*R,R,R*),(*S,S,S*)-**31**; analysis and ^1H NMR spectrum are recorded for the sample whose preparation is described in the next section.

Ketone (±)-**8**, 200 mg, was reduced in 15 mL of methanol containing 1 drop of 6 N NaOH solution with 200 mg of $NaBH_4$. The mixture was stirred at 25 °C for 0.5 h, then refluxed for an additional 0.5 h. The solvent was evaporated, and the residue was distributed between water and CH_2Cl_2. The organic phase was washed with water and dried, the solvent was evaporated, and the residual oil was submitted to thick layer chromatographic separation on a silica gel plate with CH_2Cl_2–pentane (4:6, v/v) as developer. The faster moving spot, probably **9**, gave 174 mg (87%) of crystalline material: mp 136–138 °C; IR spectrum, no C=O absorption, but O–H bonds at 3590 and 3400 cm^{-1}. Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.82; H, 6.05. The slower moving isomer, probably **10**, was obtained as 9 mg of crystalline material, mp 156–157 °C, and was not further characterized.

(*R*),(*S*)- and (−)-(*S*)-1,7-Dihydroxy-4,5:6,7-di(1,2-naphtho)-3-oxahepta-4,6-diene ((*R*),(*S*)-33 and (−)-(*S*)-33) and (*R*),(*S*)- and (−)-(*S*)-1,10-Dihydroxy-4,5:6,7-di(1,2-naphtho)-3,8-dioxadeca-4,6-diene ((*R*),(*S*)-34 and (−)-(*S*)-34). To a stirred solution of (*R*),(*S*)-**1** (50.0 g, 0.175 mol) in 1.8 L of THF was added 23.5 g (0.21 mol) of *t*-BuOK, and the mixture was heated to reflux under N_2. A solution of ethyl chloroacetate (25.8 g, 0.21 mol) in 30 mL of THF was added (30 min), and the reflux was continued for 14 h. The solvent was evaporated and the residue was distributed between 600 mL of ether and 400 mL of water. The ether layer was washed with water, dried, evaporated to 300 mL volume, and added dropwise to a slurry of 7.0 g (0.184 mol) of $LiAlH_4$ in 1.5 L of anhydrous ether. The mixture was stirred at 25 °C for 12 h, and 3 mL of ethyl acetate was added, followed by 400 mL of 6 N HCl solution. The mixture was stirred for 4 h, the **33** that separated was filtered, and the ether layer of the filtrate was extracted with three 80-mL portions of 2 N KOH in water–methanol (2:1, v/v). The ether layer was washed with water, dried, and evaporated, and the residue was crystallized from benzene–hexane to give 9.8 g (15%) of (*R*),(*S*)-**34**: mp 112–113 °C. Anal. Calcd for $C_{24}H_{22}O_4$: C, 76.99; H, 5.92. Found: C, 76.81; H, 5.76. The basic combined aqueous extracts were acidified with concentrated aqueous HCl, and the precipitate was filtered. This material was dissolved in a minimum amount of hot THF, and the solution was added to a threefold volume of ether. The precipitate (**33**) was collected, the filtrates were evaporated, and the process was repeated to give more **33**. From the final filtrates was recovered 10.0 g (20%) of **1**. The combined samples of **33** were recrystallized from ethanol–THF to give 23.2 g (40%) of fine crystals of (*R*),(*S*)-**33**: mp 209–211 °C; ^1H NMR (CD_3SOCD_3) δ 3.32 (m, OCH_2, 2 H), 3.92 (m, OCH_2, 2 H), 3.9 (s, OH, 2 H), 6.7–7.9 (m, ArH, 12 H). Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.77; H, 5.49.

A similar procedure applied to (−)-(*S*)-**1** gave (+)-(*S*)-**33** (43%) as an oil, $[\alpha]^{25}_{546}$ +12.9° (*c* 1.2, THF), whose spectral and TLC properties were the same as (*R*),(*S*)-**33**. Also obtained was (+)-(*S*)-**34** [19%, mp 133–134 °C, $[\alpha]^{25}_{546}$ +23.2° (*c* 1.05, THF)], whose spectral and TLC properties were the same as (*R*),(*S*)-**34**. The two compounds were easily separated by silica gel chromatography. The crude recovered (−)-(*S*)-**1** exhibited 98% of its original optical rotation.

(−)-(*S,S*)-, (*R,R*),(*S,S*)-, and (*R,S*)-1,18-Dihydroxy-4,5:6,7:12,13:14,15-tetra(1,2-naphtho)-3,8,11,16-tetraoxadeca-4,6,12,14-tetraene ((−)-(*S,S*)-35, (*R,R*),(*S,S*)-35, and (*R,S*)-35). A mixture of 6.5 g (0.058 mol) of *t*-BuOK was added to a stirred solution under N_2 of 18.9 g (0.057 mol) of (*R*),(*S*)-**33** in 600 mL of THF, followed by 10.7 g (0.029 mol) of ethylene glycol ditosylate in 100 mL of THF. The mixture was refluxed for 28 h, the solvent was evaporated (vacuum), and the oily residue was dissolved in a 4:1 (v/v) mixture of ether–CH_2Cl_2. This solution was washed three times with a 2 N KOH solution in 2:1 (v/v) water–methanol, then water, and was then dried. Evaporation of the solvent in small portions yielded, after drying under vacuum, 18.3 g (93%) of crude **35** (diastereomeric mixture) as a solid foam.

A solution of 8.5 g (0.012 mol) of this mixture in 30 mL of benzene was added to a solution of freshly prepared 3,5-dinitrobenzoyl chloride (8.5 g, 0.037 mol) in 100 mL of benzene. The mixture was refluxed for 12 h, the solvent was evaporated (vacuum), and the residual oil was chromatographed on 800 g of silica gel in CH_2Cl_2 to give first (*R,S*)-**37** and then (*R,R*),(*S,S*)-**37**. Each isomer was recrystallized from acetone–ether to produce 2.8 g (21%) of (*R,S*)-**37**, mp 124–126 °C, and 4.0 g (30%) of (*R,R*),(*S,S*)-**37**, mp 174–176 °C. The *R,S* isomer gave a ^1H NMR spectrum δ 4.05 (m, CH_2CH_2, 12 H), 6.80–8.0 (m, ArH, 24 H), 8.6 (d, ArH, 4 H), 9.10 (t, ArH, 2 H). Anal. Calcd for $C_{60}H_{42}O_{16}N_4$: C, 67.03; H, 3.94. Found: C, 66.78; H, 4.01. The (*R,R*),(*S,S*) isomer gave an ^1H NMR spectrum δ 3.95 (s, OCH_2, 4 H), 4.28 (m, OCH_2, 8 H), 6.82–8.0 (m, ArH, 24 H), 9.10 (t, ArH, 2 H). Anal. Calcd for $C_{60}H_{42}O_{16}N_4$: C, 67.03; H, 3.94. Found: C, 67.01; H, 3.80.

To a solution of (*R,R*),(*S,S*)-**37** (2.4 g, 2.23 mmol) in 60 mL of THF and 30 mL of water was added 0.350 g (6.2 mmol) of KOH. The mixture was stirred at 25 °C for 12 h, the solvent was evaporated, and the residue was dissolved in CH_2Cl_2. This solution was washed with water, dried, and evaporated under vacuum to give 1.4 g (91%) of (*R,R*),-(*S,S*)-**35** as a foam: transition point 95–105 °C; ^1H NMR δ 2.08 (s, OH, 2 H), 3.45 (m, OCH_2, 4 H), 3.82 (s, OCH_2, 4 H), 3.94 (m, OCH_2, 4 H), 6.78–8.00 (m, ArH, 24 H). Anal. Calcd for $C_{46}H_{38}O_6$: C, 80.44; H, 5.58. Found: C, 79.78; H, 5.50. By a similar procedure, (R,S)-**37** was converted to (*R,S*)-**35** (92%), which was a foam: transition point 95–105 °C; ^1H NMR δ 1.80 (s, OH, 2 H), 3.32 (m, OCH_2, 4 H), 3.81 (m, OCH_2, 8 H), 6.80–8.00 (m, ArH, 24 H). Anal. Calcd for $C_{46}H_{38}O_6$: C, 80.44; H, 5.58. Found: C, 80.30; H, 5.60.

By a procedure similar to that applied to the conversion of (*R*),-(*S*)-**33** to the mixture of (*R,R*)(*S,S*)-**35** and (*R,S*)-**35**, (−)-(*S*)-**33** was converted to (−)-(*S,S*)-**35** (85%, $[\alpha]^{25}_{546}$ −55.8° (*c* 1.0, THF)), which

was purified by chromatography on silica gel. The material gave the same NMR spectrum and TLC behavior as (*R,R*),(*S,S*)-**35**.

(−)-(*S,S*)-, (*R,R*),(*S,S*)-, and (*R,S*)-1,18-Ditosyloxy-4,5:6,7:12,13:14,15-tetra(1,2-naphtho)-3,8,11,16-tetraoxaoctadeca-4,6,12,14-tetraene ((−)-(*S,S*)-36, (*R,R*),(*S,S*)-36, and (*R,S*)-36). The procedure is illustrated as follows. The mixture of (*R,R*),(*S,S*)-**35** and (*R,S*)-**35** (see above), 10.0 g (14.6 mmol) in 80 mL of dry pure pyridine, was cooled to −3 °C, and 8.3 g (43 mmol) of tosyl chloride was added in one portion. The mixture was stirred for 30 min at 0 °C, and held at 0 °C for 7 days. The mixture was stirred in 500 mL of ice water for 45 min, and the precipitate was filtered, washed with water, and dried in vacuum over solid KOH. The crude material (12.5 g) was dissolved in 450 mL of CH_2Cl_2 and rapidly chromatographed on 70 g of silica gel to give 7.6 g (52%) of a mixture of (*R,R*),(*S,S*)-**36** and (*R,S*)-**36** as a white powder: mp 175–190 °C; ^1H NMR δ 2.30 (s, $ArCH_3$, 6 H), 3.9 (m, OCH_2, 12 H), 6.8–8.0 (m, ArH, 32 H).

Similarly (*R,R*),(*S,S*)-**35** was converted to (*R,R*),(*S,S*)-**36** (50%): mp 204–205.5 °C; ^1H NMR δ 2.30 (s, $ArCH_3$, 6 H), 3.90 (m, OCH_2, 12 H), 6.8–8.0 (m, ArH, 32 H). Anal. Calcd for $C_{60}H_{50}O_{10}S_2$: C, 72.42; H, 5.06. Found: C, 72.38; H, 4.97. Similarly (*R,S*)-**35** was converted to (*R,S*)-**36** (52%): mp 217–219 °C (too insoluble for an ^1H NMR spectrum). Anal. Calcd for $C_{60}H_{50}O_{10}S_2$: C, 72.42; H, 5.06. Found: C, 72.25; H, 5.03. Similarly (−)-(*S,S*)-**35** was converted to (+)-(*S,S*)-**36** (37%, mp 172–174 °C), whose ^1H NMR and TLC properties were identical with those of (*R,R*),(*S,S*)-**36**: $[\alpha]^{25}_{546}$ +68.2° (*c* 1.00, THF).

(*R,R,R*),(*S,S,S*)-, (*R,S,S*),(*S,R,R*)-, (−)-(*S,S,S*)-, and (−)-(*R,S,S*)-2,3:4,5:10,11:12,13:18,19:20,21-hexa(1,2-naphtho)-1,6,9,14,17,22-hexaoxacyclotetracosa-2,4,10,12,18,20-hexaene ((*R,R,R*),(*S,S,S*)-, (*R,S,S*),(*S,R,R*)-, (−)-(*S,S,S*)-, and (−)-(*R,S,S*)-31). A mixture of (*R*),(*S*)-**1** (1.5 g, 5.25 mmol) and K_2CO_3 (0.75 g, 5.5 mmol) was heated for 2 h at 80 °C in 50 mL of DMF under N_2 with stirring. This mixture was added in one portion to a warm solution of 5 g (5.0 mmol) of the diastereomeric mixture of ditosylates (*R,R*),(*S,S*)- and (*R,S*)-**36** in 350 mL of DMF. The resulting mixture was stirred under N_2 for 30 h at 80 °C, the solvent was evaporated under vacuum, and the residue in 400 mL of CH_2Cl_2 was filtered through 150 g of silica gel to give 3.4 g (68%) of a mixture of diastereomeric cycles as a white solid. Extraction of this material with three 20-mL portions of CH_2Cl_2 left 0.6 g of (*R,R,R*),(*S,S,S*)-**31** undissolved. The extract was concentrated and chromatographed on 300 g of silica gel. The first fractions of CH_2Cl_2 eluate contained 2.0 g of pure (*R,S,S*),(*S,R,R*)-**31**, and the middle fractions contained 0.2 g of additional (*R,R,R*),(*S,S,S*)-**31**, which was combined with the first sample. The 0.8 g of (*R,R,R*),(*S,S,S*)-**31** was dissolved in 140 mL of hot dioxane, the solution was cooled, and 120 mL of ether was added. The pure (*R,R,R*),(*S,S,S*)-**31** crystallized: weight 0.72 g (14%); mp 335–340 °C (decomposition by isomerization); M^+ 936; ^1H NMR δ 3.49–3.94 (m, CH_2CH_2, 12 H), 6.62, 6.78 (d, ArH-3, 6 H), 6.85, 8.12 (m, ArH, 36 H). Anal. Calcd for $C_{66}H_{48}O_6$: C, 84.59; H, 5.16. Found: C, 84.47; H, 5.45. The (*R,S,S*),(*S,R,R*)-**31** was recrystallized from benzene–cyclohexane to give 1.8 g (36%) of pure isomer: mp 185–187 °C; M^+ 936; ^1H NMR δ 3.41–3.94 (m, $ArOCH_2$, 12 H), 6.58, 6.75 (d, ArH-3, 2 H), 6.85–8.13 (m, ArH, 36 H). Anal. Calcd for $C_{66}H_{48}O_6$: C, 84.59; H, 5.16. Found: C, 84.43; H, 5.25. Values for R_f were 0.65 and 0.75 on silica gel in CH_2Cl_2 for (*R,R,R*),(*S,S,S*)-**31** and (*R,S,S*),(*S,R,R*)-**31**, respectively.

In similar experiments, pure ditosylate (*R,S*)-**36** was treated with (*R*),(*S*)-**1** to give *only* (*R,S,S*),(*S,R,R*)-**31** (mp 185–187 °C; 60%) whereas pure ditosylate (*R,R*),(*S,S*)-**36** treated with (*R*),(*S*)-1 gave 30% (*R,S,S*),(*S,R,R*)-**31**, mp 185–187 °C, and 16% (*R,R,R*),(*S,S,S*)-**31**, mp 345–350 °C dec. Similarly, from ditosylate (+)-(*S,S*)-**36** and (−)-(*S*)-1 was obtained (−)-(*S,S,S*)-**31** (46%): white solid with a phase transition at 185–200 °C (solid → foam) and ~250 °C (foam to liquid); M^+ 936; $[\alpha]^{25}_{546}$ −175° (*c* 1.0, THF). Anal. Calcd for $C_{66}H_{48}O_6$: C, 84.59; H, 5.16. Found: C, 84.43; H, 5.31. Similarly, from ditosylate (+)-(*S,S*)-**36** and (+)-(*R*)-**1** was obtained (−)-(*S,S,R*)-**31** (58%): M^+ 936; mp 247–249 °C; $[\alpha]^{25}_{546}$ −141° (*c* 1.0, THF). Anal. Calcd for $C_{66}H_{48}O_6$: C, 84.59; H, 5.16. Found: C, 84.49; H, 5.20.

Comparisons of the ^1H NMR spectra of (−)-(*S,S,S*)-**31** and (−)-(*S,R,R*)-**31** showed differences in the ArH chemical shift region. Both compounds gave a high-field doublet (part of an AX system) at about δ 6.6–6.8 due to the H-3 protons of the binaphthyl system. Integration of the spectrum of (−)-(*S,S,S*)-**31** indicated the presence of six protons, whereas that of (−)-(*R,S,S*)-**31** gave only two such protons. Examination of CPK molecular models of the diastereomers indicates that when two binaphthyl units are connected by an ethylene glycol bridge, each *S,S* configurational relationship between binaphthyls places two naphthalene H-3 protons in the shielding cone of a transannular naphthyl group, whereas each *R,S* configurational relationship places two naphthalene H-3 protons in the deshielding cone of a transannular naphthyl group. Thus (−)-(*S,S,S*)-**31** has three *S,S*-binaphthyl relationships and should have six upfield shifted C-3 protons, and (−)-(*R,S,S*)-**31** has one *S,S* relationship and should have two upfield shifted C-3 protons, as was observed.

Thermal Equilibration of (*R,S,S*),(*S,R,R*)-31 and (*R,R,R*),-(*S,S,S*)-31. Vials of about 10 mg of each of the above diastereoisomers were sealed under vacuum and placed in a Woods metal bath at a temperature of 340 °C for 7 min. The vials were opened, and the material was dissolved in CH_2Cl_2 and the isomers separated by TLC on silica gel. The separate spots were eluted, and the relative amounts of each isomer were estimated to be about equal (±5%) from the intensities of their UV spectra compared to standards.

Registry No.—(±)-**1**, 41024-90-2; (+)-(*R*)-**1**, 18531-94-7; (−)-(*S*)-**1**, 18531-99-2; (−)-(*S*)-1 *l*-menthoxyacetyl chloride monoester, 63731-41-9; **2**, 41051-91-6; (±)-**3**, 55442-18-7; (+)-(*S*)-**3**, 55515-85-0; (±)-**4**, 41024-96-8; (+)-(*S*)-**4**, 41051-92-7; (−)-(*S*)-**5**, 55442-00-7; (−)-(*S*)-**6**, 55442-01-8; (±)-**7**, 53783-48-2; (−)-(*S*)-**7**, 41024-92-4; **8**, 55442-19-8; (+)-**8**, 55515-86-1; **9**, 63731-42-0; (−)-(*S,S*)-**14**, 54108-54-2; (*R,S*)-**15**, 41024-94-6; (*R,R*),(*S,S*)-**15**, 41024-97-9; (−)-(*S,S*)-**15**, 41024-93-5; (+)-(*R,R*)-**15**, 41024-95-7; (±)-**16**, 55515-79-2; (+)-(*S*)-**16**, 55442-12-1; (−)-(*S,S*)-**17**, 55442-13-2; (−)-(*S,S*)-**17** free alcohol, 57244-65-2; (±)-**18** free alcohol, 55441-93-5; (±)-**18**, 55441-94-6; (−)-(*S*)-**18**, 55515-77-0; (+)-(*R*)-**18**, 55821-78-8; (±)-**19**, 55442-86-9; **20**, 41024-87-7; **20** free alcohol, 41757-99-7; (*R,S*)-**21**, 55442-14-3; (*R,R*),(*S,S*)-**21**, 55515-80-5; (−)-(*S,S*)-**21**, 55515-83-8; (*R,S*)-**22**, 55442-15-4; (*R,R*),(*S,S*)-**22**, 55515-81-6; (−)-(*S,S*)-**22**, 55515-84-9; (−)-(*S,S*)-**23**, 57244-63-0; (−)-(*S,S*)-**23** free alcohol, 57244-66-3; (−)-(*S,S*)-**24**, 57244-64-1; (−)-(*S,S*)-**24** free alcohol, 57244-67-4; (−)-(*S,S*)-**25**, 59346-20-2; (−)-(*S,S*)-**26**, 59346-25-7; (−)-(*S,S*)-**27**, 63731-43-1; (−)-(*S,S*)-**28**, 57244-68-5; (−)-(*S,S*)-**29**, 59346-21-3; (−)-(*S,S*)-**30**, 59346-26-8; (*R,S,S*),(*S,R,R*)-**31**, 55528-99-9; (*S,S,S*),(*R,R,R*)-**31**, 55442-21-2; (−)-(*S,S,S*)-**31**, 55515-87-2; (−)-(*S,S,R*)-**31**, 55515-94-1; (±)-**32**, 55442-20-1; (±)-**33**, 55442-22-3; (+)-(*S*)-**33**, 55515-89-4; (±)-**34**, 55441-95-7; (+)-(*S*)-**34**, 55515-88-3; (*R,R*),(*S,S*)-**35**, 55442-24-5; (*R,S*)-**35**, 63731-44-2; (−)-(*S,S*)-**35**, 55515-93-0; (*R,S*)-**36**, 55515-92-9; (*R,R*),(*S,S*)-**36**, 55442-25-6; (+)-(*S,S*)-**36**, 55529-00-5; (*R,S*)-**37**, 63731-45-3; (*R,R*),(*S,S*)-**37**, 55442-23-4; *l*-menthoxyacetyl chloride, 15356-62-4; pentaethylene glycol dichloride, 5197-65-9; pentaethylene glycol ditosylate, 41024-91-3; triethylene glycol ditosylate, 19249-03-7; diethylene glycol dichloride, 111-44-4; 2-(2′-chloroethoxy)ethyl 2″-tetrahydropyranyl ether, 54533-84-5; tosyl chloride, 98-59-9; benzhydryl bromide, 776-74-9; diethylene glycol ditosylate, 7460-82-4; 2,6-bis(chloromethyl)pyridine, 3099-28-3; 2-(2-chloroethoxy)ethyl 2-tetrahydrofuranyl ether, 63731-46-4; catechol, 120-80-9; ethylene glycol ditosylate, 6315-52-2; 1,3-bis(bromomethyl)benzene, 626-15-3; *cis*-2,5-bis(tosyloxymethyl)tetrahydrofuran, 1472-00-0; ethyl chloroacetate, 105-39-5; 3,5-dinitrobenzoyl chloride, 99-33-2; 1,5-pentanediol ditosylate, 24293-28-5; tetraethylene glycol ditosylate, 37860-51-8.

References and Notes

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Application of the Salicylidenimino Chirality Rule to Chiral 1-Alkyl-2-propynylamines and 1-Alkyl-2-propenylamines[1]

Björn Ringdahl,[2a] Howard E. Smith,*[2b] and Fu-Ming Chen[2c]

Department of Organic Pharmaceutical Chemistry, Biomedical Center, University of Uppsala, S-751 23 Uppsala, Sweden, and Departments of Chemistry, Vanderbilt University, Nashville, Tennessee 37235, and Tennessee State University, Nashville, Tennessee 37203

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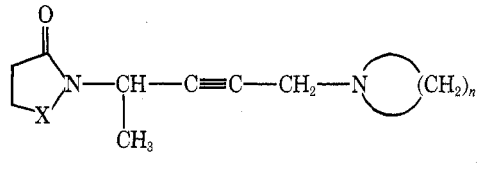
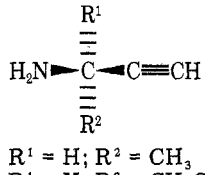
The sign of the Cotton effects near 255 and 315 nm in the circular dichroism (CD) spectra of the *N*-salicylidene derivatives of chiral 1-alkyl-2-propynylamines and 1-alkyl-2-propenylamines correlates with their absolute configurations. The Cotton effects are generated by the coupled oscillator mechanism and their sign is the same as the chirality (right-handed screw for positive chirality) of the triple and the double bond with the phenyl group–methine bond of the salicylidenimino chromophore. The chirality is determined by both the absolute configuration and the preferred conformation of the respective *N*-salicylidene derivatives. Thus those derivatives with the *R* configuration display negative Cotton effects near 255 and 315 nm, and those with the *S* configuration, positive.

In connection with the study of the stereospecific blockade of the motor effects of the muscarinic agent oxotremorine, *N*-(4-pyrrolidino-2-butynyl)-2-pyrrolidone, by *N*-(4-*tert*-amino-1-methyl-2-butynyl)-substituted succinimides (1) and 2-pyrrolidones (**2**),[3] the respective enantiomers of 1 and **2** were

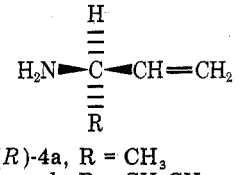


1a, X = CO; *n* = 4
b, X = CO; *n* = 6
2, X = CH_2; *n* = 4

prepared from the enantiomers of 1-methyl-2-propynylamine (**3a**),[3] the absolute configurations of the latter being rigorously

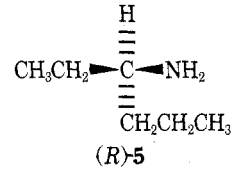


(*R*)-**3a**, R^1 = H; R^2 = CH_3
b, R^1 = H; R^2 = CH_3CH_2
c, R^1 = H; R^2 = $CH_3CH_2CH_2$
d, R^1 = CH_3; R^2 = CH_3CH_2



(*R*)-**4a**, R = CH_3
b, R = CH_3CH_2
c, R = $CH_3CH_2CH_2$

established in two ways.[3,4] For the possible synthesis of chiral analogues of **1** and **2**, the enantiomers of 1-ethyl-2-propynylamine (**3b**), 1-propyl-2-propynylamine (**3c**) and 1-ethyl-1-methyl-2-propynylamine (**3d**) were also prepared and their absolute configurations were also established by chemical transformations.[5,6] Partial reduction of (*R*)-**3a** and of the enantiomers of **3b** and **3c** with hydrogen over Lindlar's catalyst afforded (*R*)-1-methyl-2-propenylamine [(*R*)-**4a**] and the enantiomers of 1-ethyl-2-propenylamine (**4b**) and 1-propyl-2-propenylamine (**4c**).[7] Reduction of (*S*)-**3c** with hydrogen over Raney nickel gave (*R*)-1-ethylbutylamine [(*R*)-**5**].[7] Thus a group of chiral 1-alkyl-2-propynylamines (**3**) and 1-alkyl-2-propenylamines (**4**) of established configuration became available for a rigorous test of the salicylidenimino chirality rule[8] for the deduction of the absolute configurations of amines of this type.

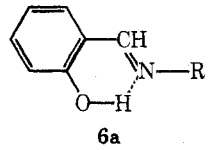


(*R*)-**5**

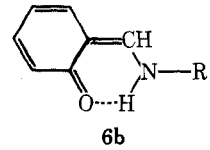
We now report the preparation of the *N*-salicylidene derivatives (**6**) of an enantiomer of each of these amines and the interpretation of the circular dichroism (CD) spectra of these derivatives.

Results and Discussion

Electronic Absorption Spectra. The electronic (isotropic) absorption (EA) spectra of the *N*-salicylidene derivatives of the 1-alkyl-2-propynylamines (**3**), of the 1-alkyl-2-propenylamines (**4**), and of 1-ethylbutylamine (**5**) in hexane exhibit three absorption bands with maxima at 318–320 (log ε 3.69–3.71), 254–255 (log ε 4.11–4.15), and 216 nm (log ε 4.40–4.42), designated as bands I, II, and III, respectively. These bands are assigned to transitions of the intramolecularly hydrogen-bonded salicylidenimino chromophore (**6a**).[8]



6a



6b

As is frequently the case,[9] band II also shows a shoulder at 260–261 nm (log ε 4.07–4.09) and at a slightly longer wavelength than the absorption maximum. In methanol, a broad band with maximum at 400–403 nm (log ε 2.03–2.19 for the derivatives of **3a–3d**, 2.97–2.99 for those of **4a–4c**, and 3.23 for that of **5**) becomes evident, and bands I, II, and III show a slight decrease in intensity. A shoulder near 260 nm is no