New Chiral Hosts Derived from Dimeric Tartaric Acid: Efficient Optical Resolution of Aliphatic Alcohols by Inclusion Complexation

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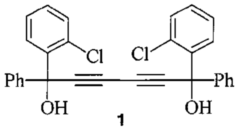
The novel, chiral, host compounds **8** and **9** were derived from tartaric acid. Inclusion complexation with these host compounds permitted highly efficient resolution of some aliphatic alcohols (**10**–**13**). The symmetrical dimer host compound **8** is effective for optical resolution of alcohols **10**, **12**, and **13** by a combination of enantioselective inclusion complexation and distillation techniques. The unsymmetrical dimer host compound **9** is effective for optical resolution of cyanohydrin **11**. The crystal structures of the inclusion complexes were analyzed by X-ray diffraction methods in order to elucidate the mechanism of the efficient chiral recognition in the inclusion crystals.

Introduction

The design of new lattice inclusion systems has been of interest in recent years because of their potential applications in analytical, synthetic, and material sciences.[1] Of the various kinds of chiral host compounds which we have designed to date {for example: *(S,S)*-(−)-1,6-bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**1**),[2] *(S,S)*-(−)-*trans*-1,4-bis[3-(*o*-chlorophenyl)-3-hydroxy-3-phenylprop-1-ynyl]-1,4-dihydroxycyclohexa-2,5-diene (**2**),[3] *(S,S,S,S,S,S)*-(−)-hexakis[3-(*o*-chlorophenyl)-3-hydroxy-3-phenylprop-1-ynyl]benzene (**3**),[4] *(S,S)*-2,2′-dihydroxy-1,1′-binaphthyl (**4**),[5] and *(R,R)*-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4,5]decane (**5**),[6] Scheme 1}, tartaric acid derivatives such as **5** are very useful hosts for the optical resolution of racemic guests[7] and for the enantioselective reaction of prochiral guests.[8] In some cases, however, **5** does not form an inclusion complex with relatively voluminous guest molecules. This is probably due to the molecular size of **5**: the void space created by the relatively small host molecule is too small to include relatively large guest molecules. In order to solve this problem, dimeric derivatives of tartaric acid were designed to act as hosts which should be able to accommodate guests of large molecular size.



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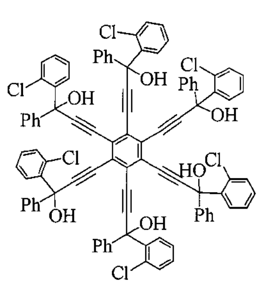

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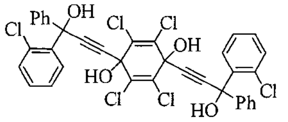

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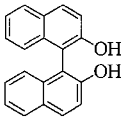

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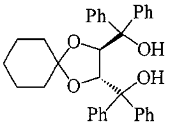

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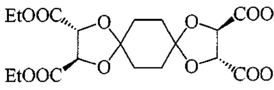

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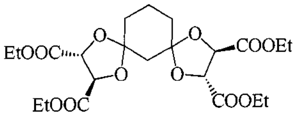

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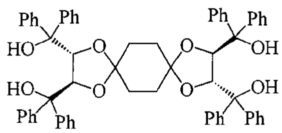

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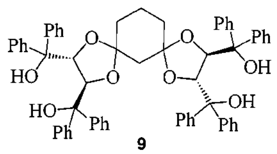

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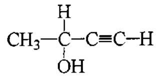
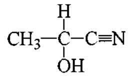


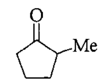
$CH_3-\underset{OH}{\overset{H}{C}}-C\equiv C-H$

10



$CH_3-\underset{OH}{\overset{H}{C}}-C\equiv N$

11



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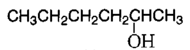
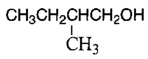


$CH_3CH_2CH_2CH_2\underset{OH}{C}HCH_3$

12



$CH_3CH_2\underset{CH_3}{C}HCH_2OH$

13

Results and Discussion

Heating a solution of (+)-diethyl tartrate and 0.5 molar equivalents of cyclohexane-1,4-dione in toluene at reflux containing a catalytic amount of TsOH gave tetraester **6** in 92% yield. Reaction of **6** with PhMgBr in THF gave crude crystals of (−)-*trans,trans*-2,3,10,11-tetrakis(hydroxydiphenylmethyl)-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradecane

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(**8**). Recrystallization of **8** from EtOH gave the 1:2 inclusion complex of **8** with EtOH as colorless prisms, which, upon heating, gave pure **8** as the free host compound. By the same method, the unsymmetrical dimer host compound (−)-*trans,trans*-2,3,9,10-tetrakis(hydroxydiphenylmethyl)-1,4,8,11-tetraoxadispiro[4.1.4.3]tetradecane **(9)** was prepared from **7**, which in turn was obtained by the condensation reaction of (+)-diethyl tartrate with cyclohexane-1,3-dione. The dimeric host compounds **8** and **9** showed a higher inclusion ability for some typical guest compounds than the monomeric host compound **5**. In particular, the symmetrical dimer host **8** took up all guest compounds tested (Table 1).

Table 1. Host-guest ratios in the inclusion complexes of **5**, **8**, and **9** with typical guest compounds

Guest	5	8	9
MeOH	1:1	1:2	1:1
Acetone	2:1	1:2	1:1
Cyclopentanone	2:1	1:1	1:1
Ethyl acetate	–[a]	1:1	1:1
γ-Butyrolactone	1:1	1:2	1:1
THF	1:1	1:2	2:1
DMF	1:1	1:2	1:1
DMSO	2:1	1:1	1:1
Toluene	–[a]	1:1	1:1
Cyclohexane	–[a]	1:1	–[a]

[a] No complexation occurred.

The chiral discrimination ability of **8** and **9** was studied; both showed extremely high chiral recognition ability towards relatively small chiral alcohols which could not be resolved efficiently by the monomeric host compound **5**. For example, when a mixture of **8** and *rac*-but-3-yn-2-ol (**10**) was ground together with a mortar and pestle for a few minutes and kept at room temperature for one day, it gave a 1:1 inclusion complex of **8** and (+)-**10**. During the reaction, the opposite enantiomer, which was not incorporated into the host-guest complex, evaporated due to its low boiling point. Heating the inclusion complex in vacuo gave (+)-**10** (59% *ee*) in 77% yield. When the complexation was repeated, (+)-**10** (99% *ee*) was obtained in 28% yield. The optical purity of (+)-**10** was determined by GC, using a Chiral-DEX CB capillary column.[9] By similar complexation with **8**, *rac*-2-hexanol (**12**) and *rac*-2-methyl-1-butanol (**13**) were also resolved efficiently, and gave optically pure (+)-**12** and (−)-**13** in 34 and 5% yields, respectively. The resolution of **10**, **12**, and **13** by this simple distillation method[10] is a valuable tool for chiral resolution because the preparative methods reported to date for optically active aliphatic alcohols are not efficient. For example, optically active **10** (70% *ee*) has been prepared by enzymatic transesterification in 31% yield.[11]

The optical resolution of carbonyl compounds by complexation with **8** was less efficient. For example, when a neat solution of **8** in (±)-**14** was kept at room temperature for 24 h, a 1:1 inclusion complex of **8** and (−)-**14** was formed as colorless prisms, which upon heating in vacuo gave (−)-**14** (15% *ee*) as a distillate.

The unsymmetrical dimeric host **9** also displays interesting chiral recognition properties. Compound **9** incorporates *rac*-cyanohydrin **11** in a 1:2 ratio in the absence of toluene, but, in the presence of toluene, takes up (+)-**11** together with a toluene molecule. For example, when a solution of a 1:2 mixture of **9** and (±)-**11** in toluene (20 mL) was kept at room temperature for 8 h, 1:1:1 inclusion crystals of **9**, (+)-**11**, and toluene were formed as colorless prisms in 72% yield. One recrystallization of these crystals from toluene gave pure inclusion crystals, which upon heating in vacuo gave (+)-**11** (100% *ee*) in 24% yield as a distillate. On the other hand, when a neat solution of **9** in (±)-**11** was kept at room temperature for 3 h, a 1:2 inclusion complex of **9** and (±)-**11** was formed as colorless prisms, which upon heating in vacuo gave (±)-**11** as a distillate.

The role of multiple recognition sites and their topology in the performance in the chiral discrimination process of these newly designed host molecules was studied in the solid state by X-ray diffraction methods. The host molecules **8** and **9** both consist of two terminal hydrophilic 1,4-diol units and two voluminous hydrophobic areas, flanked by phenyl rings located above and below the cyclohexane ring.

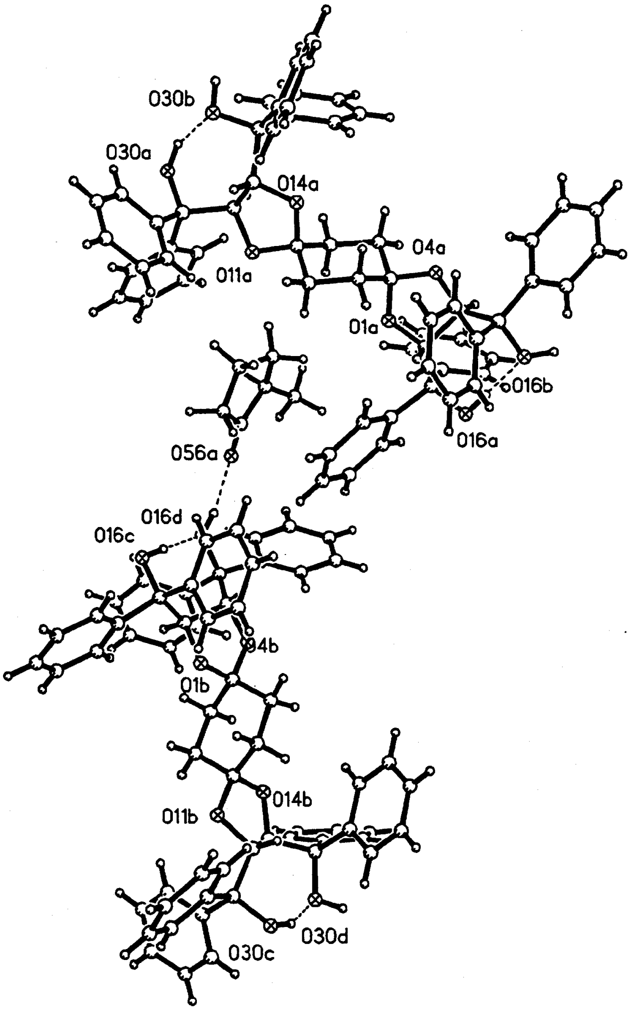

Figure 1. ORTEP drawing of the 1:1 complex of (*R,R,R,R*)-(−)**8** and (*R*)-(−)-**14**, showing both hydrogen bonding and incorporation of the guest molecule as a clathrate

Recently, solid state studies of (*R,R*)-(−)-*trans*-2,3-bis[hydroxy(diphenyl)methyl]-1,4-dioxaspiro[5,4]decane (**5**), containing one such unit, and its molecular complexes, explained its universal complexation properties. It appears that one hydroxy group of the diol moiety forms an intramolecular $O-H\cdots O$ hydrogen bond, whereas the other, sterically hindered, one is either unbound in the free compound or acts as a hydrogen bond donor or acceptor during the molecular recognition process.[12] Inspection of the packing diagrams of several complexes formed in the solid state by **8** and **9** allows some interesting rationalization for their differing recognition properties. The molecular structure of the 1:1 complex between (*R,R,R,R*)-(−)-**8** and (*R*)-(−)-**14** is shown in Figure 1. The diol moieties form a pair of strong intramolecular hydrogen bonds ($O\cdots O$ separations of 2.66−2.67 Å), leaving two OH groups available for interactions. One of these (O16d in Figure 1) forms a hydrogen bond with carbonyl O65a of the host. The second generates chains made up of host molecules. Two nonparallel sets of chains found in the crystal permit location of the cyclopentanone ring in the hydrophobic cavity of the neighboring host molecule. Most interesting is the molecular structure of the 1:2 complex of (−)-**8** and (−)-**13**, shown in Figure 2. One alcohol hydroxy group (O70′) donates an H atom to the O30 oxygen of the host, forming an intermolecular hydrogen bond. A second guest molecule of the same chirality acts both as hydrogen bond donor and acceptor, forming an extended hydrogen-bonded network of host molecules: $HOST-OH\cdots O(70)-H\cdots O-HOST$. These chains are held together by noncovalent forces other than hydrogen bonding. The hydrogen atom from the sterically hindered O15 hydroxy moiety remains unbound.

The molecular structure of the 1:1:1 complex of (*R,R,R,R*)-(−)-**9** with (+)-(**11**) and toluene is shown in Figure 3, and the molecular structure of the 1:2 complex of (*R,R,R,R*)-(−)-**9** and (±)-(**11**) is shown in Figure 4. As can be clearly seen, the O16 hydroxy groups provide an enantioselective binding site; i.e. the same enantiomer of cyanohydrin is hydrogen bonded, regardless of whether the complex is formed from the single enantiomer or from (±)-**11**. The two remaining hydroxy groups form host-to-host hydrogen-bonded chains. The recognition process is solvent-dependent; the hydrophobic cavities formed by the isomeric host **9** are of different size and shape than those formed by host **8**. Their shape is that of an open jaw and could be easily adjustable by conformational rearrangement of the five-membered rings. The torsion angles in the central ring are almost the same in the three crystal structures, and describe conformations of slightly flattened chairs (a regular chair in the case of **8**), whereas those in the outer five-membered rings vary. Small differences in conformation in the latter can cause large differences in the location of the terminal phenyl rings. The cavities can discriminate between the to-

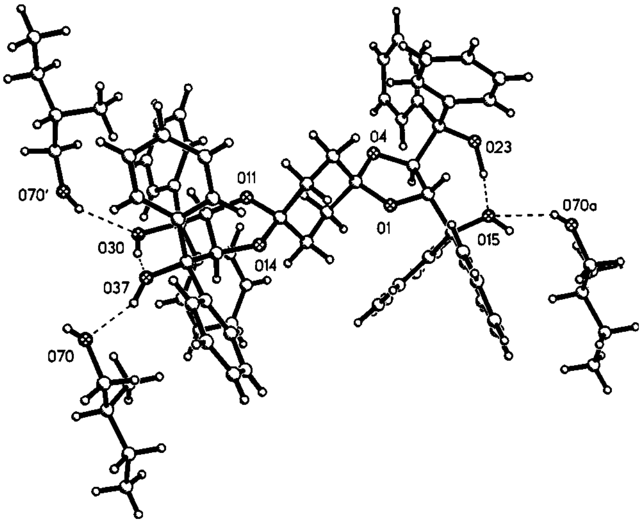

Figure 2. ORTEP drawing of the 1:2 complex of (*R,R,R,R*)-(−)-**8** and (−)-**13**

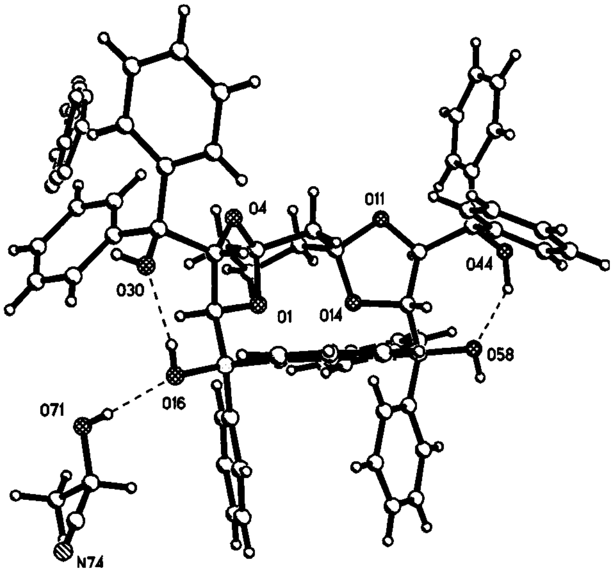

Figure 3. ORTEP drawing of the 1:1:1 complex of (*R,R,R,R*)-(−)-**9**, (+)-**11**, and toluene

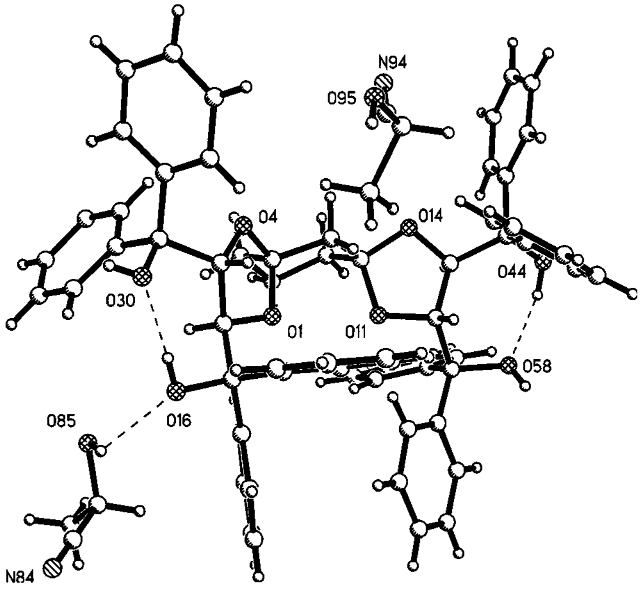

Figure 4. ORTEP drawing of the 1:2 complex of (*R,R,R,R*)-(−)-**9** and (±)-**11**

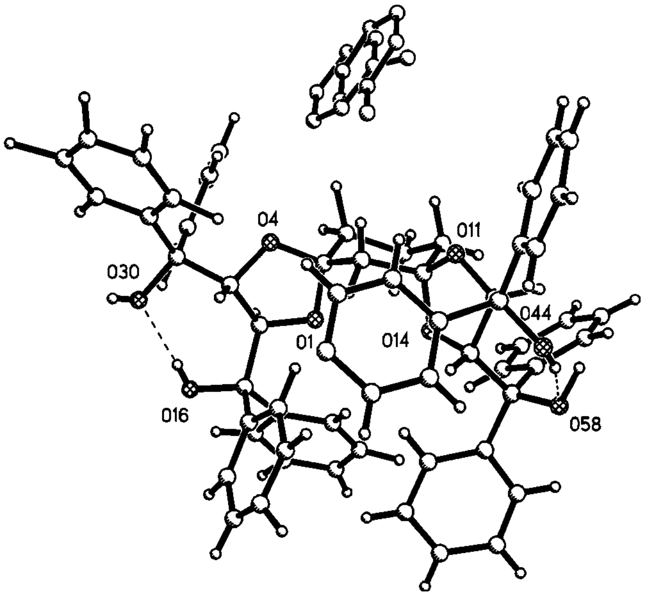

Figure 5. ORTEP drawing of the 1:1 complex of (*R,R,R,R*)-(−)-**9** and toluene

pologies of cyanohydrin and toluene molecules. In the absence of toluene, one molecule of (−)-**11** is incorporated into the crystal as a clathrate (see Figure 4). When cyanohydrin complexation is performed in toluene, a disordered solvent molecule is included in the cavity (0.7:0.3 occupancy), expelling a molecule of (−)-**11**. When no cyanohydrin is present, the cavity is occupied by a disordered toluene molecule (0.5:0.5 occupancy) and the 1:1 complex of (−)-**9** and toluene shown in Figure 5 is formed. The packing patterns of the 1:1:1 complex of (−)-**9** with (+)-**11** and toluene, and of the 1:2 complex with (±)-**11**, are shown in Figure 6 and Figure 7, respectively. The cavities located between hydrogen-bonded chains of the host matrix take up toluene or cyanohydrin in approximately the same space. Interestingly, the latter does not participate in any hydrogen bonding.

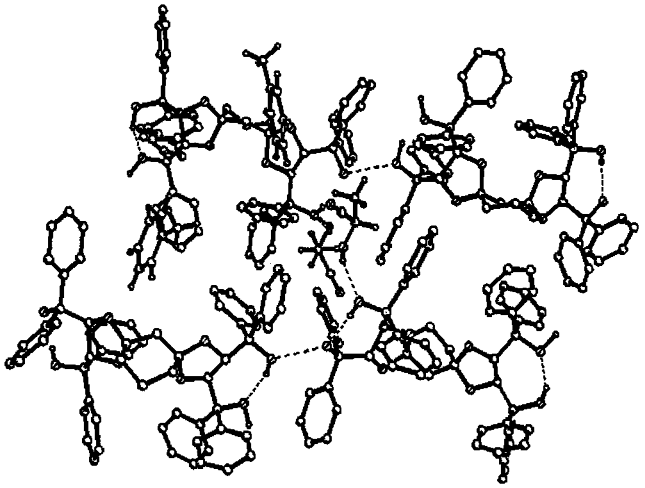

Figure 6. Packing pattern of the 1:1:1 complex of (*R,R,R,R*)-(−)-**9**, (+)-**11**, and toluene; host molecules (solid lines) form hydrogen-bonded networks; between them, hydrogen-bonded (+)-**11** and disordered toluene molecules (70% population) are shown (open lines)

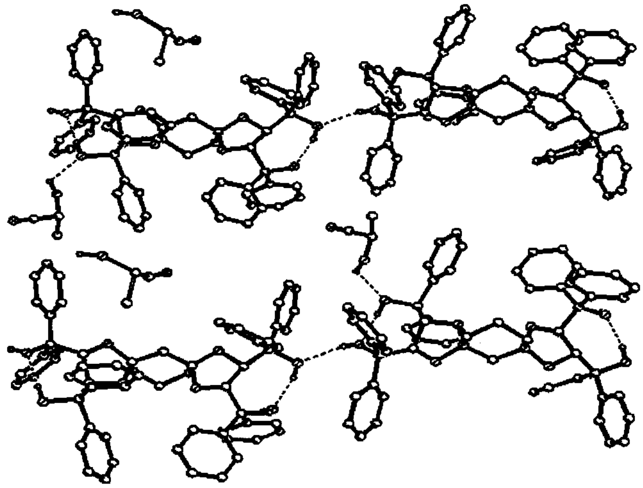

Figure 7. Packing pattern of the 1:2 complex of (*R,R,R,R*)-(−)-**9** and (±)-**11**; host molecules (solid lines) form hydrogen-bonded networks; between them, hydrogen-bonded (−)-**11** and (−)-**11** taken up as a clathrate are shown (open lines)

Conclusion

In summary, the basic factors playing an important role in the chiral recognition process in the new hosts (−)-**8** and (−)-**9** are: the number of 1,4-diol units, their chiral environment, and the topology of the hydrophobic cavities available for take-up of the guests as clathrates. Although the new hosts contain two 1,4-diol units, one of these is mostly involved in the formation of the host-to-host networks. The only exception, the 1:2 complex of (−)-**8** and (−)-**13**, is a case in which the second guest molecule is included in the polar network. The dimeric 1,4-diol units in the host **8** have the best topology for selective binding of two guest molecules of the same chirality. The large void space created between the recognition centers of (−)-**9** can be occupied by neutral solvent molecules, by hydrophobic parts of the guest molecules, or by nonspecifically attached molecules of the second enantiomer.

Experimental Section

General Remarks: NMR spectra were recorded on a Jeol Lambda 300 instrument. − IR spectra were recorded with a Jasco FT-IR 200 spectrometer. Optical rotations were determined with a Jasco DIP 1000 polarimeter.

***(R,R,R,R)*-(−)-*trans*,*trans*-2,3,10,11-Tetrakis(hydroxydiphenylmethyl)-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradecane (8):** A solution of (+)-diethyl tartrate (275 g, 1.33 mol) and cyclohexane-1,4-dione (74 g, 0.66 mol) in toluene (500 mL) containing a catalytic amount of TsOH was heated under reflux for 120 h. The tetraester **6** was obtained in 92% yield after recrystallization from toluene (297 g, colorless prisms), m.p. 73−75 °C. − $[\alpha]_D = -21.6$ ($c = 1.0$, $CHCl_3$). A solution of **6** (21.4 g, 0.044 mol) in dry THF (50 mL)

was added with stirring to a solution of PhMgBr in THF (500 mL), prepared from Mg (15.8 g, 0.65 mol) and bromobenzene (100 g, 0.64 mol), and the mixture was stirred for 6 h. Conventional workup gave crude crystals of (*R*,*R*,*R*,*R*)-(−)-*trans*,*trans*-2,3,10,11-tetrakis(hydroxydiphenylmethyl)-1,4,9,12-tetraoxadispiro[4.2.4.2]-tetradecane (**8**). Recrystallization of the crude crystals from EtOH gave the 1:2 inclusion complex of **8** with EtOH as colorless prisms, which, upon heating, gave pure **8** as a white powder in 35% yield, m.p. 267−270 °C. − $[\alpha]_D = -28.0$ (c = 1.0, $CHCl_3$).
8: IR (nujol): $\tilde{\nu}$ = 3448 cm^{-1}, 3237 (OH). − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.06−1.25 (m, 8 H, CH_2), 3.91 (s, 4 H, OH), 4.53 (s, 4 H, CH),7.23−7.46 (m, 40 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 33.4, 78.2, 80.4, 109.1, 127.2, 127.6, 128.2, 128.5, 142.4,145.9. − $C_{62}H_{56}O_8$ (929.1164): calcd. C 80.15, H 6.08; found C 80.03, H 6.25.

***(R,R,R,R)*-(−)-*trans*,*trans*-2,3,9,10-Tetrakis(hydroxydiphenylmethyl)-1,4,8,11-tetraoxadispiro[4.1.4.3]tetradecane (9):** A solution of (+)-diethyl tartrate (110 g, 0.53 mol) and cyclohexane-1,3-dione (25 g, 0.22 mol) in toluene (300 mL) containing a catalytic amount of TsOH was heated under reflux for 120 h. The tetraester **7** was obtained in 43% yield after recrystallization from toluene (46 g, colorless prisms), m.p. 63−65 °C. − $[\alpha]_D = -38.3$ (c = 1.0, $CHCl_3$). A solution of **7** (11.6 g, 0.024 mol) in dry THF (30 mL) was added with stirring to a solution of PhMgBr in THF (300 mL), prepared from Mg (7.0 g, 0.29 mol) and bromobenzene (46 g, 0.29 mol), and the mixture was stirred for 6 h. Conventional workup gave crude crystals of (−)-*trans*,*trans*-2,3,9,10-tetrakis(hydroxydiphenylmethyl)-1,4,8,11-tetraoxadispiro[4.1.4.3]tetradecane (**9**). Recrystallization of **9** from MeOH gave the 1:2 inclusion complex of **9** with MeOH as colorless prisms, which, upon heating, gave pure **9** as a white powder in 24% yield,m.p. 259−261 °C. − $[\alpha]_D = -140$ (c = 1.0, $CHCl_3$).
9: IR (nujol): $\tilde{\nu}$ = 3369, 3313 (OH) cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.70, 0.89,1.47 (each m, 2 H, CH_2), 1.50 (s, 2 H, CH_2), 3.51, 4.48 (each s, 2 H, OH), 4.52, 4.58 (each d, J = 7.7 Hz, 2 H, CH), 6.9 −7.6 (m, 40 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.7, 35.2, 46.3, 77.6, 78.4, 80.8, 81.0, 110.1, 127.0, 127.1, 127.2, 127.3, 127.4, 127.5, 128.0, 128.2, 128.7, 129.0, 142.2, 143.1, 146.0,146.1. − $C_{62}H_{56}O_8$ (929.1164): calcd. C 80.15, H 6.08; found C 80.10, H 6.02.

Optical Resolution of But-3-yn-2-ol (10): A mixture of **8** (5.5 g, 5.9 mmol) and (±)-but-3-yn-2-ol (**10**, 0.9 g, 13 mmol) was ground in a mortar and pestle for a few minutes and kept at room temperature for 1 day. A 1:1 inclusion complex of **8** and (+)-**10** was obtained. Heating of the inclusion complex at 200 °C/30 Torr gave (+)-**10** (59% *ee*, 0.32 g, 77% yield) as a distillate. When this complexation was repeated, (+)-**10** (0.12 g, 28% yield) of 99% *ee* was obtained, with $[\alpha]_D = +50.6$ (c = 0.33, dioxane). The optical purity of (+)-**10** was determined by GC, using a Chiral-DEX CB capillary column.[9]

Optical Resolution of 2-Hexanol (12): A mixture of **8** (3.0 g, 3.3 mmol) and (±)-2-hexanol (**12**, 0.66 g, 6.5 mmol) was ground in a mortar and pestle for a few minutes and kept at room temperature for 1 day. A 1:1 inclusion complex of **8** and (+)-**12** was obtained. Heating of the inclusion complex at 180 °C/30 Torr gave (+)-**12** (65% *ee*, 0.32 g, 97% yield) as a distillate. When the complexation was repeated, (+)-**12** (0.11 g, 34% yield) of 100% *ee* was obtained, with $[\alpha]_D = +12.0$ (c = 0.2, $CHCl_3$),. The optical purity of (+)-**10** was determined by GC, using a Chiral-DEX CB capillary column.[9]

Optical Resolution of 2-Methyl-1-butanol (13): A mixture of **8** (29 g, 31 mmol) and (±)-2-methyl-1-butanol (**13**, 11 g, 123 mmol) was ground in a mortar and pestle for a few minutes and kept at room temperature for 1 day. A 1:2 inclusion complex of **8** and (−)-**13** was obtained. Heating of the inclusion complex at 180 °C/30 Torr gave (−)-**13** (27% *ee*, 4.9 g, 91% yield) as a distillate. When the complexation was repeated three times, (−)-**13** (0.27 g, 5% yield) of 100% *ee* was obtained, with $[\alpha]_D = -6.9$ (c = 0.41, heptane). The optical purity of (+)-**10** was determined by GC, using a Chiral-DEX CB capillary column.[9]

Optical Resolution of 2-Methylcyclopentanone (14): A solution of **8** (2.1 g, 2.3 mmol) in (±)-**14** (10 g, 100 mmol) was kept at room temperature for 24 h. A 1:1 inclusion complex of **8** and (−)-**14** was formed as colorless prisms (2.2 g, 97% yield, no sharp m.p.), which upon heating in vacuo gave (−)-**14** (0.15 g, 68% yield) of 15% *ee*, with $[\alpha]_D = -16.2$ (c = 1.0, MeOH), as a distillate. The optical purity of (−)-**14** was determined by comparison of the measured $[\alpha]_D$ with the literature value.[12] Crystals suitable for X-ray analysis of the pure 1:1 complex of **8** and (−)-**14** were prepared by complexation of **8** with (−)-**14** of 100% *ee*, which was obtained by complexation with the host compound **2**.[3]

Optical Resolution of 2-Hydroxypropionitrile (11) in the Presence of Toluene: A solution of **9** (2.1 g, 2.3 mmol) and (±)-**11** (0.33 g, 4.6 mmol) in toluene (20 mL) was kept at room temperature for 8 h, forming 1:1:1 inclusion crystals of **9**, (+)-**11**, and toluene as colorless prisms (1.8 g, 72% yield). One recrystallization of the crystals from toluene gave pure inclusion crystals (0.83 g, 28% yield), m.p. 134−136 °C), which upon heating in vacuo gave (+)-**11** (0.04 g, 24% yield) of 100% *ee*, with $[\alpha]_D = +28.4$ (c = 0.51, MeOH), as a distillate.

Optical Resolution of 2-Hydroxypropionitrile (11) in the Absence of Toluene: A solution of **9** (1 g, 1.1 mmol) in (±)-**11** (2 g, 28 mmol) was kept at room temperature for 3 h, forming a 1:2 inclusion complex of **9** and (±)-**11** as colorless prisms (1.2 g, 100% yield), m.p. 133−135 °C.

X-ray Crystallographic Study: Crystal data for the 1:1 complex of (*R,R,R,R*)-(−)-**8** and (−)-**14**, $C_{68}H_{67}O_9$, M = 1028.22, monoclinic space group $P2_1$, (No. 4), a = 10.6546(6), b = 20.393(1), c = 13.859(1) Å, β = 111.388(5)°, V = 2803.9(3) Å^3, Z = 2, $D_{calcd.}$ = 1.218 Mg m^{-3}, μ(Cu-K_α) = 0.634 mm^{-1}, F(000) = 1094. An air-stable crystal of size 0.11 × 0.17 × 0.27 mm was used for data collection on the Nonius MACH3 diffractometer. A total of 4511 reflections were collected, 3561 unique reflections (R_{int} = 0.0193) were used for structure solution and refinement against F^2 using the SHELXS86[14] and SHELXL97[15] programs. Final R indices are: for $I > 2\sigma$ (I): $R_1 = 0.0458$, $wR_2 = 0.1254$. All non-hydroxy H-atoms were placed geometrically and refined with a riding model with the U_{iso} constrained to be 1.2 times that of U_{eq} of the carrier atom. Positions for hydroxy group H-atoms were found from difference mapping and refined with isotropic temperature factors. The configuration of the guest molecule was set relative to the known configuration of the host molecule.

Crystal Data for the 1:2 Complex of (*R,R,R,R*)-(−)-8 and (−)-13: $C_{72}H_{80}O_{10}$, M = 1105.36, space group $P1$, a = 9.3706(5), b = 13.7210(7), c = 14.1083(9) Å, α = 64.525(5), β = 72.913(5) γ = 84.741(5) deg., V = 1564.04(15) Å^3, Z = 1, $D_{calcd.}$ = 1.174 Mg·m^{-3}, μ(Cu-K_α) = 0.612 mm^{-1}, F(000) = 592. A colorless crystal of size 0.34 × 0.14 × 0.14 mm, sealed by epoxy glue, was used for data collection (ca. 5.4% decomposition during time of experiment). A total of 6844 reflections were collected on the Nonius MACH3 diffractometer; 3823 unique with [$I > 2\sigma$ (I)] were used for structure solution and refinement using the SHELXS86[13] and SHELXL97[14] programs. Final R indices are: for [$I > 2\sigma$ (I)]: R_1 =

0.0412, wR_2 = 0.1051. All but non-hydroxy H-atoms were placed geometrically and refined with a riding model, with the U_{iso} constrained to be 1.2 times that of U_{eq} of the carrier atom. Positions for hydroxy group H-atoms were found from difference mapping and refined with isotropic temperature factors. The configuration of the guest molecule was set relative to the known configuration of the host molecule.

Crystal Data for the 1:1:1 Complex of (*R,R,R,R*)-(−)-9, (+)-11 and Toluene: $C_{71}H_{67}NO_{10}$, M_w = 1094.26, orthorhombic space group $P2_12_12_1$ (No. 19), a = 14.3400(2), b = 15.1880(3), c = 27.6300(6) Å, V = 6017.7(2) Å^3, Z = 4, $D_{\text{calcd.}}$ = 1.208 Mg·m^{-3}, μ(Mo-K_α) = 0.080 cm^{-1}, F(000) = 2320. A total of 10584 unique reflections were collected on an Nonius Kappa CCD system, with 6309 reflections used in the structure analysis and refinement using the SHELXS86[14] and SHELXL97[15] programs. Final R_1 and wR_2 factors are 0.0528 and 0.1283, respectively. The disordered toluene molecule was fitted to the regular hexagon geometry and refined isotropically. All non-hydroxy H-atoms were placed geometrically and refined with a riding model with the U_{iso} constrained to be 1.2 times that of U_{eq} of the carrier atom. Positions for hydroxy group H-atoms were found from difference mapping and refined with isotropic temperature factors.

Crystal Data for the 1:2 Complex of (*R,R,R,R*)-(−)-9 and (±)-11: $C_{68}H_{66}N_2O_{10}$, M_w = 1071.23. Colorless crystals (sealed by epoxy glue, ca. 6% decomposition), crystallized in orthorhombic space group $P2_12_12_1$ (No. 19), a = 14.1920(6), b = 14.9610(6), c = 27.725(3) Å, V = 5886.8(7) Å ^{3}, Z = 4, $D_{\text{calcd.}}$ = 1.209, F(000) = 2272, μ(Cu-K_α) = 0.648 cm $^{-1}$. A total of 6723 reflections were collected on Nonius MACH3 diffractometer, and 3119 unique reflections were used in structure analysis and refinement using the SHELXS86[14] and SHELXL97[15] program systems. Final R_1 and wR_2 factors are 0.0584 and 0.1507, respectively. All non-hydroxy H-atoms were placed geometrically and refined with a riding model with the U_{iso} constrained to be 1.2 times that of U_{eq} of the carrier atom. The configurations of the two enantiomeric molecules of **9** were set relative to the known configuration of the host molecule.

Crystal Data for the 1:1 Complex of (*R,R,R,R*)-(−)-9 and Toluene: $C_{69}H_{64}O_8$, M_w = 1021.2. Colorless crystals, crystallized in monoclinic $P2_1$ space group (No. 4), a = 10.649(1), b = 22.180(2), c = 12.0333(8) Å, β = 101.42(1)°, V = 2785.9(4) Å^3, F(000) = 1084, μ(Cu-K_α) = 0.623 cm^{-1}, Z = 2, $D_{\text{calcd.}}$ = 1.217 Mg cm^{-1}. A total of 3119 reflections were collected on Nonius MACH3 diffractometer using a crystal protected by epoxy glue (4.3% decomposition during experiment). 2619 unique reflections were used in structure analysis and refinement using the SHELXS86[14] and SHELXL97[15] program systems. Final R_1 and wR_2 factors calculated for 2223 $F > 4\delta_F$ are 0.0574 and 0.1532, respectively. All non-hydroxy H-atoms were placed geometrically and refined with a riding model with the U_{iso} constrained to be 1.2 times that of U_{eq} of the carrier atom. The disordered toluene molecule was fitted to the regular hexagon geometry and refined isotropically.

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