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Tuning the Chiral Cavity of Macrocyclic Receptor for Chiral Recognition and Discrimination

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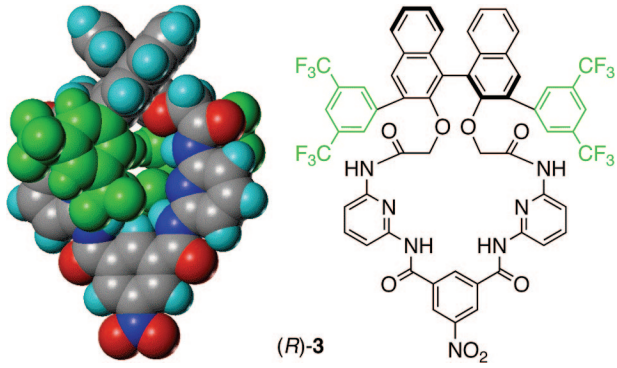
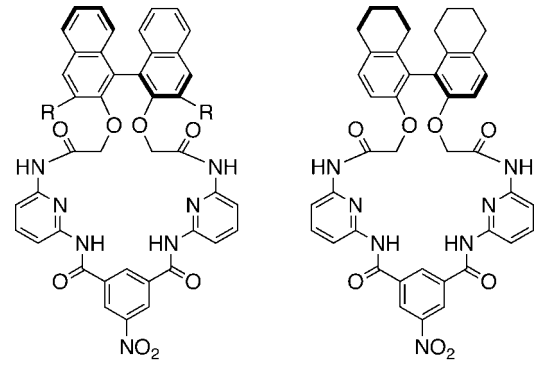


The size and shape of the chiral cavity of a macrocyclic receptor were tuned by the alteration of the binaphthyl moiety to improve the chiral recognition/discrimination ability. For example, host **3** with the 3,5-bis(trifluoromethyl)phenyl group at the 3,3′-positions showed improved enantioselectivity for small molecules such as 2-chloropropionic acid and methyl lactate as evaluated by the binding constants. This host **3** also had an excellent ability as an NMR chiral solvating agent.

Chiral recognition is important from various viewpoints, such as (i) biological and pharmaceutical activity,[1] (ii) resolution technology with GC or HPLC,[2] (iii) reagents for determining the enantiomeric purity and absolute configuration,[3] (iv) asymmetric synthesis,[4] (v) fundamental host−guest chemistry,[5]and (v) supramolecular material science.[6] Chirality and chiral recognition is inevitably significant because chiral biomolecules such as proteins, nucleic acids, and carbohydrates play a central role in life. Hydrogen bonding, capable of showing a high degree of complementarity and directionality, is frequently used for chiral recognition. We have recently reported that chiral macrocycle **1** with multiple hydrogen bonding sites in the cavity, named Chirabite-AR, can be used as an NMR chiral solvating agent for a variety of chiral compounds.[7] In that study, we noticed that the binaphthyl moiety is orthogonal to the plane of the lower segment in **1**, which is important for chiral discrimination in NMR.[7] We considered that, because of this specific structure, the facile and efficient alteration of the chiral pocket of **1** might be possible just by modifying the binaphthyl moiety. To substantiate this idea, we decided to investigate the potential for new derivatives **2**−**4**. Here we report that the chiral cavity could be tuned well by modifying the binaphthyl moiety, which led to elaborate chiral recognition and discrimination in terms of differential free energy ($\Delta\Delta G°$) and chemical shift nonequivalence ($\Delta\Delta\delta$), respectively.



We expected that the introduction of the CO_2Me group or the 3,5-bis(trifluoromethyl)phenyl group into the 3,3′-positions of the binaphthyl moiety would accentuate the chiral shape of the cavity, enhancing the chiral recognition power. The shape of the chiral cavity could also be altered by the replacement of the binaphthyl group by the 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl group. The three BINOL derivatives were employed because they are commercially available. The macrocycles **2**−**4** were synthesized basically in the same way as reported

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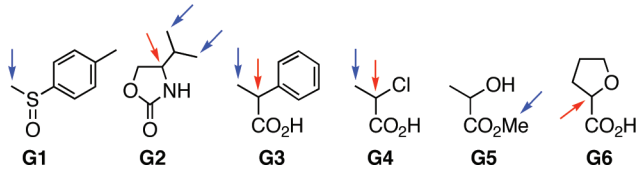

FIGURE 1. Chemical structures of guests **G1**−**G6**. The degree of chiral discrimination of the protons indicated by the arrows is shown in Figure 3.

TABLE 1. Binding Constants and Enantioselectivity of Hosts (*R*)-1−4 for Guests G1−G6

guest	K_a (M^{-1})[a] enantioselectivity[b]							
	(*R*)-**1**[c]		(*R*)-**2**		(*R*)-**3**		(*R*)-**4**	
(*R*)-**G1**	610	4.3	230	4.5	66	1.4	420	2.7
(*S*)-**G1**	2600		1030		93		1130	
(*R*)-**G2**	510	1.8	56	2.5	14	1.1	370	1.8
(*S*)-**G2**	280		22		13		210	
(*R*)-**G3**	1670	1.8	750	2.1	550	1.4	1300	1.2
(*S*)-**G3**	3050		1540		760		1510	
(*R*)-**G4**	3100	1.0	1610	1.6	1470	6.0	1570	1.1
(*S*)-**G4**	3080		2530		8760		1720	
(*R*)-**G5**	140	1.2	63	1.7	63	5.7	97	1.3
(*S*)-**G5**	120		37		11		77	
(*R*)-**G6**	770	3.0	320	1.9	340	4.4	600	2.3
(*S*)-**G6**	2340		620		1480		1360	

[a] In $CDCl_3$ at 22 °C. The K_a values were calculated by the nonlinear least-squares method. [b] Ratio of the K_a values. [c] The K_a values of (*R*)-**1** for **G1**−**G3** were taken from ref 7.

previously for **1**.[7] Although the yields of the macrocyclization giving **2** and **3** were lower than those giving **1** and **4**, all of them were successfully synthesized.[8]

The chiral recognition abilities of (*R*)-**1**−**4** for **G1**−**G6** (Figure 1) were evaluated by the binding constants (K_a) determined by NMR titrations as reported previously.[7,9] The data are summarized in Table 1. The K_a values for each guest tend to decrease in the following order: **1** > **4** > **2** > **3**. This order is quite reasonable when an increase in bulkiness, which can be seen from the structures of **1**−**4** optimized by the MM calculations (Figure 2), is taken into consideration. It is likely that steric repulsion takes place around the binaphthyl moiety of **1**−**4**, together with hydrogen bonding at the two amide NH groups of the lower segment.[7] The octahydro derivative **4** showed lower enantioselectivity for **G1**, **G3**, and **G6** than **1**. The dihedral angle between the biphenyl rings in **4** (92°) is slightly larger than that between the two naphthalene rings in **1** (88°), which makes the cavity of **4** slightly smaller than that of **1**. As a result, the binding of the (*S*)-enantiomers is suppressed by **4**, as compared to **1**, to a degree greater than that of the corresponding (*R*)-enantiomers (Table 1). This derivative **4** was found to be comparable or inferior to **1** in all cases. In the case of receptor **2**, to our delight, enantioselectivity was improved in most cases. Obviously, the 3,3′-positions of the binaphthyl moiety are the "hot spots" that are effective for the improvement of enantioselectivity. Replacement of the CO_2Me group by the 3,5-bis(trifluoromethyl)phenyl group increased enantioselectivity for **G4**−**G6**, and the chiral recognition energy of **3** for **G4** amounted to −1.0 kcal mol^{-1} as calculated from $-RT \ln\{K_a(S)/K_a(R)\}$. On the other hand, enantioselectivity for **G1**−**G3** was

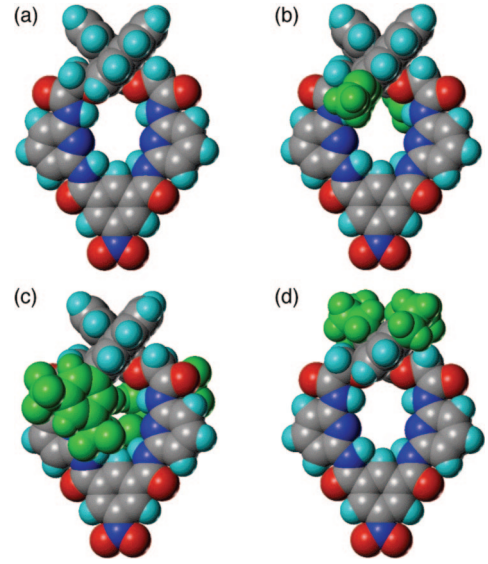

FIGURE 2. Optimized structures for (a) (*R*)-**1**, (b) (*R*)-**2**, (c) (*R*)-**3**, and (d) (*R*)-**4**. The altered moiety is shown in green. The geometries were optimized by using the MM3 force field on CAChe 5.02 (Fujitsu) and were drawn with Sybyl 6.4 (Tripos Inc.).

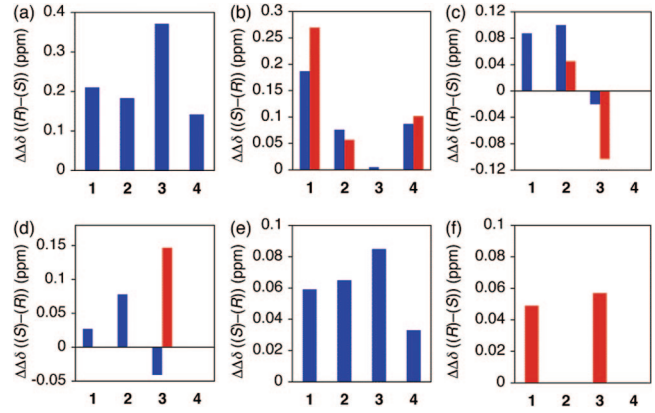

FIGURE 3. Comparison of the chiral discrimination abilities of **1**−**4**. The chemical shift nonequivalences ($\Delta\Delta\delta$) observed for (a) **G1**, (b) **G2**, (c) **G3**, (d) **G4**, (e) **G5**, and (f) **G6** are indicated by the height of the vertical bars. Those for the methyl group and the proton attached to the asymmetric carbon, which are indicated by the blue and red arrows in Figure 1, are shown in blue and red, respectively. NMR spectra are given in the Supporting Information.

deteriorated by the attachment of the 3,5-bis(trifluoromethyl)phenyl group. These results clearly indicate that host **3**, bearing the most compact cavity (Figure 2), is endowed with the ability to recognize the chirality of small molecules. In contrast, hosts **1** and **4** with less crowded binding sites exhibited higher enantioselectivity for a larger guest (**G1**), while **1** and **4** showed lower enantioselectivity for smaller guests (**G4** and **G5**). Thus, the trend in Table 1 suggests that the size complementarity is important for enantioselectivity.

The chiral recognition of 2-chloropropionic acid (**G4**) by **3** is noteworthy because the slight difference in size between the methyl group and the chlorine atom (effective van der Waals radii of 1.80 and 1.73 Å, respectively)[10] was discriminated successfully. Because of the steric repulsion caused by the 3,5-bis(trifluoromethyl)phenyl group, (*R*)-**3** showed lower affinity

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for (*R*)-**G4** than (*R*)-**1**, as expected. On the other hand, surprisingly, (*R*)-**3** showed higher affinity for (*S*)-**G4** than (*R*)-**1**; the additional energy operating between (*R*)-**3** and (*S*)-**G4** can be calculated from $-RT \ln\{K_a(\mathbf{3})/K_a(\mathbf{1})\}$ to be −0.61 kcal mol^{-1}. Although this increased affinity of (*R*)-**3** for (*S*)-**G4** was unexpected from the cavity half-closed by the 3,5-bis(trifluoromethyl)phenyl group (Figure 2c), the fact that the complexation-induced shift value for the lower amide NH groups of (*R*)-**3** ($\Delta\delta_\infty$ = 1.64 ppm) is as large as that of (*R*)-**1** ($\Delta\delta_\infty$ = 1.33 ppm) indicates that (*S*)-**G4** is bound in the crowded cavity of (*R*)-**3** with hydrogen bonding. An attractive interaction, such as van der Waals force and the CH/π interaction,[11,12] may take place between the 3,5-bis(trifluoromethyl)phenyl group of (*R*)-**3** and (*S*)-**G4**. The conformational change of (*R*)-**3** is likely to take place upon binding of (*S*)-**G4**.

In view of the results shown above, we decided to compare the abilities of hosts **1**−**4** to discriminate between the enantiomers of **G1**−**G6** in NMR. The fundamental data obtained with variants **1**−**4** must become useful in developing the next generation of chiral solvating agents.[13] The extents of signal splitting induced upon addition of 1 equiv of host ($\Delta\Delta\delta$) were measured, and the results are summarized in Figure 3. Surprisingly, despite the lower affinity of **3** (Table 1), **3** brought about larger splitting than **1** in many cases. In particular, the signals for the proton attached to the asymmetric carbon in **G3**, **G4**, and **G6** were resolved completely by host **3** (Supporting Information, Tables S5, S7, and S9). We attribute this enhanced performance of **3** to the ring-current effect resulting from the 3,5-bis(trifluoromethyl)phenyl group.

In summary, the size and shape of the chiral cavity of the macrocyclic receptor were tuned successfully by the alteration of the binaphthyl moiety to improve the chiral recognition/discrimination ability. For example, host **3** with the 3,5-bis(trifluoromethyl)phenyl group showed enantioselective binding for small molecules such as 2-chloropropionic acid and methyl lactate. Host **3** also showed excellent chiral discrimination in NMR. By synthesizing other derivatives according to the scenario demonstrated here, the scope of chiral recognition/discrimination will be expanded further in the future.[14]

Experimental Section

Macrocycles **2**, **3**, and **4** were prepared via **5**, **7**, and **8**, respectively, as described below.

(*R*)-Dimethyl 2,2′-Bis[(*tert*-butoxycarbonyl)methoxy]-1,1′-binaphthalene-3,3′-dicarboxylate ((*R*)-5). A mixture of (*R*)-dimethyl 2,2′-dihydroxy-1,1′-binaphthalene-3,3′-dicarboxylate (2.03 g, 5.04 mmol), *tert*-butyl bromoacetate (1.64 mL, 11.2 mmol), and K_2CO_3 (1.56 g, 11.3 mmol) in acetone (50 mL) was heated at reflux for 18 h under N_2. The mixture was filtered and concentrated. The product was purified by basic alumina column chromatography (hexane/EtOAc (7:1)) to give (*R*)-**5** as white crystals (3.13 g, 98%): mp 119 °C; $[\alpha]^{25}_D$ +5.60 (*c* 0.822, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.23 (s, 18H), 3.96 (s, 6H), 4.15 (d, J = 15.3 Hz, 2H), 4.57 (d, J = 15.3 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 7.34 (t, J = 8.2 Hz, 2H), 7.45 (t, J = 8.2 Hz, 2H), 7.96 (d, J = 8.2 Hz, 2H), 8.58 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 27.8, 52.4, 71.4, 81.0, 124.7, 125.6, 125.9, 126.6, 128.8, 129.2, 129.8, 133.8, 135.6, 152.8, 166.4, 167.6; IR (KBr) 3009, 2986, 2955, 1747, 1724, 1447, 1277, 1234, 1157, 1084, 1069, 752 cm^{-1}; HRMS (FAB, nitrobenzyl alcohol) calcd for $C_{36}H_{39}O_{10}$ 631.2543, found 631.2500 (M + H).

Chiral Macrocycle (*R*)-2. A solution of (*R*)-**5** (1.00 g, 1.59 mmol) in CF_3CO_2H (4.4 mL) was stirred at room temperature for 8 h. The solution was concentrated and dried in vacuo. The white precipitate was formed. To a suspension of diacid (502 mg, 0.968 mmol) in dry CH_2Cl_2 (60 mL) were added $(COCl)_2$ (0.64 mL, 7.5 mmol) and DMF (2 drops). The mixture was stirred at room temperature for 4 h. The volatiles were removed by rotary evaporation, and the residue was dried in vacuo for 3 h. The obtained acid chloride was used without further purification. A solution of acid chloride (538 mg, 0.968 mmol) in dry THF (100 mL) and a solution of *N*,*N*′-bis(6-amino-2-pyridinyl)-5-nitro-1,3-benzenedicarboxamide (**6**)[7] (300 mg, 0.763 mmol) and Et_3N (0.22 mL, 1.6 mmol) in dry THF (100 mL) were added dropwise simultaneously to dry THF (60 mL) at room temperature with vigorous stirring over 4 h. The mixture was stirred for an additional 12 h, and the volatiles were removed by rotary evaporation. The solid residue was dissolved in CH_2Cl_2, and the solution was washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (CH_2Cl_2/THF (50:1) to (15:1)) afforded (*R*)-**2** in 38%. Recrystallization from CH_2Cl_2/hexane afforded (*R*)-**2** as white crystals (132 mg, 20%): mp 267 °C dec; $[\alpha]^{22}_D$ +162 (*c* 0.797, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.66 (d, J = 14.6 Hz, 2H), 3.91 (s, 6H), 4.16 (d, J = 14.6 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 7.49 (t, J = 8.1 Hz, 2H), 7.57 (t, J = 8.1 Hz, 2H), 7.79 (t, J = 8.1 Hz, 2H), 7.94 (d, J = 8.1 Hz, 2H), 8.01 (d, J = 8.1 Hz, 2H), 8.08 (d, J = 8.1 Hz, 2H), 8.71 (s, 2H), 8.92 (br s, 1H), 9.07 (br s, 2H), 9.10 (d, J = 1.1 Hz, 2H), 9.30 (br s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 52.8, 73.2, 109.6, 110.3, 122.7, 125.1, 126.5, 126.9, 127.1, 128.7, 129.9, 129.99, 130.0, 135.4, 135.5, 135.8, 141.6, 148.7, 149.1, 149.8, 151.9, 161.3, 165.8, 166.7; IR (KBr) 3371, 1693, 1585, 1535, 1454, 1304, 1281, 1219, 1076, 802 cm^{-1}; HRMS (FAB, nitrobenzyl alcohol) calcd for $C_{46}H_{34}N_7O_{12}$ 876.2265, found 876.2272 (M + H).

(*R*)-3,3′-Bis[3,5-bis(trifluoromethyl)phenyl]-2,2′-bis[(ethoxycarbonyl)methoxy]-1,1′-binaphthyl ((*R*)-7). A mixture of (*R*)-3,3′-bis[3,5-bis(trifluoromethyl)phenyl]-1,1′-bi-2-naphthol (384 mg, 0.540 mmol), ethyl bromoacetate (0.14 mL, 1.3 mmol), and K_2CO_3 (207 mg, 1.50 mmol) in acetone (3.2 mL) was heated at reflux for 6 h under N_2. The mixture was filtered and concentrated. The product was purified by silica gel column chromatography (hexane/EtOAc (10:1)) to give (*R*)-**7** as white crystals (464 mg, 97%): mp 65 °C; $[\alpha]^{20}_D$ −94.7 (*c* 0.714, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.95 (t, J = 6.8 Hz, 6H), 3.79 (dq, J = 1.8, 6.8 Hz, 4H), 3.83 (d, J = 15.6 Hz, 2H), 4.16 (d, J = 15.6 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.35 (dt, J = 1.4, 8.1 Hz, 2H), 7.50 (dt, J = 1.4, 8.1 Hz, 2H), 7.91 (s, 2H), 7.97 (d, J = 8.1 Hz, 2H), 8.03 (s, 2H), 8.23 (s, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.6, 60.8, 69.6, 121.4 (sept, J_{CF} = 4.0 Hz), 123.3 (q, J_{CF} = 271.5 Hz), 125.2, 125.6, 126.1, 127.8, 128.4, 129.7 (d, J_{CF} = 2.9 Hz), 130.9, 131.4, 131.8 (q, J_{CF} = 33.3 Hz), 132.0, 133.9, 140.2, 151.9, 167.6; ^{19}F NMR ($CDCl_3$, 565 MHz) δ −63.7; IR (KBr) 3069, 2986, 2908, 1761, 1379, 1281, 1182, 1136, 893, 683 cm^{-1}; HRMS (FAB, nitrobenzyl alcohol) calcd for $C_{44}H_{31}F_{12}O_6$ 883.1929, found 883.1943 (M + H).

Chiral Macrocycle (*R*)-3. To a solution of (*R*)-**7** (337 mg, 0.382 mmol) in EtOH (2 mL) was added 10% NaOH (2 mL), and the solution was heated at reflux for 10.5 h. After removal of EtOH, the mixture was acidified with 10% HCl. The white precipitate formed was filtered and dried in vacuo. To a suspension of diacid

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(14) Macrocycle **1** can also be used as a chiral selector in chiral HPLC by immobilization to silica gel: Ema, T.; Tanida, D.; Sugita, K.; Sakai, T.; Miyazawa, K.; Ohnishi, A. *Org. Lett.* **2008**, *10*, 2365–2368.

(220 mg, 0.266 mmol) in dry CH_2Cl_2 (18 mL) were added $(COCl)_2$ (0.20 mL, 2.3 mmol) and DMF (1 drop). The mixture was stirred at room temperature for 4 h. The volatiles were removed by rotary evaporation, and the residue was dried in vacuo for 3 h. The obtained acid chloride was used without further purification. A solution of acid chloride (230 mg, 0.266 mmol) in dry THF (27 mL) and a solution of diamine **6** (83.8 mg, 0.213 mmol) and Et_3N (62 μL, 0.45 mmol) in dry THF (27 mL) were added dropwise simultaneously to dry THF (18 mL) at room temperature with vigorous stirring over 3 h. The mixture was stirred for an additional 15 h, and the volatiles were removed by rotary evaporation. The solid residue was dissolved in CH_2Cl_2, and the solution was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated. The product was purified by silica gel column chromatography (CH_2Cl_2) to give (*R*)-**3** as a pale yellow solid (81 mg, 32%): mp 232 °C dec; $[\alpha]^{17}_D$ +64.9 (*c* 0.826, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.77 (d, J = 15.5 Hz, 2H), 3.80 (d, J = 15.5 Hz, 2H), 7.25 (d, J = 7.8 Hz, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.60 (t, J = 7.8 Hz, 2H), 7.69−7.75 (m, 6H), 8.01 (d, J = 8.0 Hz, 2H), 8.03 (d, J = 8.0 Hz, 2H), 8.08 (s, 2H), 8.13 (s, 4H), 8.21 (br s, 2H), 8.81 (s, 1H), 9.05 (br s, 2H), 9.16 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 71.9, 110.03, 110.05, 122.0 (m), 123.0 (q, J_{CF} = 271.8 Hz), 125.3, 125.8, 127.1, 127.2, 128.3, 128.7, 128.9, 129.3 (d, J_{CF} = 3.2 Hz), 131.1, 131.6, 132.1 (q, J_{CF} = 33.2 Hz), 132.3, 133.6, 136.0, 139.7, 141.6, 148.0, 149.1, 150.1, 150.7, 161.1, 165.2; ^{19}F NMR ($CDCl_3$, 565 MHz) δ −63.6; IR (KBr) 3379, 3074, 2916, 1701, 1585, 1522, 1456, 1279, 1136, 804 cm^{-1}; HRMS (FAB, nitrobenzyl alcohol) calcd for $C_{58}H_{34}F_{12}N_7O_8$ 1184.2277, found 1184.2252 (M + H).

(*R*)-2,2′-Bis[(ethoxycarbonyl)methoxy]-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl ((*R*)-8). A solution of (*R*)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthol (3.04 g, 10.3 mmol) in dry THF (15 mL) was added dropwise to a suspension of NaH (60% oil suspension, 1.22 g, 30.5 mmol) in dry THF (75 mL) under N_2 in an ice bath, and the mixture was stirred in an ice bath for 1 h. To the solution was added ethyl bromoacetate (2.6 mL, 23 mmol), and the mixture was stirred in an ice bath for an additional 3 h. The mixture was filtered through Celite and concentrated. The product was purified by basic alumina column chromatography (hexane/EtOAc (5:1)) to give (*R*)-**8** as a colorless viscous oil (3.11 g, 65%): $[\alpha]^{26}_D$ +34.0 (*c* 0.774, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.22 (t, J = 7.1 Hz, 6H), 1.61−1.75 (m, 8H), 2.06−2.10 (m, 2H), 2.44−2.49 (m, 2H), 2.75−2.76 (m, 4H), 4.14−4.19 (m, 4H), 4.45 (d, J = 16.8 Hz, 2H), 4.48 (d, J = 16.8 Hz, 2H), 6.65 (d, J = 8.1 Hz, 2H), 7.01 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.1, 23.0, 23.1, 26.9, 29.4, 60.9, 66.3, 110.2, 126.2, 128.8, 130.9, 137.4, 153.1, 169.7; IR (neat) 2982, 2928, 2855, 1759, 1732, 1474, 1292, 1196, 1103, 1034, 795 cm^{-1}; HRMS (FAB, nitrobenzyl alcohol) calcd for $C_{28}H_{35}O_6$ 467.2434, found 467.2399 (M + H).

Chiral Macrocycle (*R*)-4. Host (*R*)-**4** was prepared by using **6** and (*R*)-**8** in the same way as described for (*R*)-**3**. Purification by silica gel column chromatography (CH_2Cl_2/THF (15:1)) afforded (*R*)-**4** in 62% yield. Recrystallization from CH_2Cl_2 afforded (*R*)-**4** as pale yellow crystals (670 mg, 44%): mp 216 °C dec; $[\alpha]^{23}_D$ +29.6 (*c* 0.720, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.66−1.75 (m, 8H), 2.15−2.28 (m, 4H), 2.72−2.78 (m, 4H), 4.46 (br s, 4H), 6.89 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 8.3 Hz, 2H), 7.77−7.79 (m, 4H), 8.13 (d, J = 7.3 Hz, 2H), 8.61 (br s, 2H), 8.92 (br s, 1H), 9.08 (s, 2H), 9.37 (br s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 22.79, 22.84, 27.8, 29.2, 72.2, 110.3, 111.6, 114.8, 126.9, 127.4, 129.1, 130.1, 133.5, 135.5, 136.8, 141.1, 148.3, 149.5, 149.6, 153.8, 161.5, 168.3; IR (KBr) 3371, 2928, 2851, 1686, 1585, 1535, 1450, 1312, 1223, 1150, 1080, 802, 752 cm^{-1}; HRMS (FAB, nitrobenzyl alcohol) calcd for $C_{42}H_{38}N_7O_8$ 768.2782, found 768.2792 (M + H).

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Supporting Information Available: Synthetic schemes and CD spectra of (*R*)-**1**−**4**, copies of ^{1}H and ^{13}C NMR spectra of **2**−**5** and **7**−**8**, and a list of ^{1}H NMR spectra of **G1**−**G6** in the presence of **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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