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Synthesis and Enantiomer Recognition of Dipodands and Crown Ethers Containing the 2,3:6,7-Dibenzobicyclo[3.3.1]nona-2,6-diene Residue as the Chiral Subunit

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Five new optically active crown ethers and six optically active dipodands are reported. The crown ethers were synthesized by using (+)-(1*S*,4*R*,5*S*,8*R*)-2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene-4,8-diol and (+)-(1*S*,4*R*,5*S*,8*R*)-4,8-bis(hydroxymethyl)-2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene as a chiral subunit and the dipodands contained the 2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene residue as a chiral anchor group. The enantiomer recognition behaviour of these compounds was evaluated by the enantiomer differential transport of methyl (±)-phenylglycinate and (±)-1,2-diphenylethylamine hydrochloride through bulk liquid membrane.

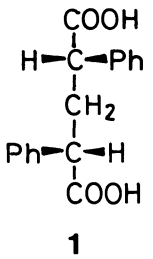
A large number of chiral crown ethers have been synthesized and numerous reports have described their chiral recognition properties.[1] Chiral discrimination of an open-chained equivalent of crown ether, to which Vögtle and Weber have suggested the term "podand",[2] is also interesting in the host-guest chemistry. Although a variety of optically active podands have been prepared,[1] as far as we know, little has been reported on their chiral recognition behavior.

In a recent publication,[3] we have reported on the preparation of optically active crown ethers and dipodands, and their chiral recognition properties. The crown ethers contained the *trans*-tetrahydrofuran-2,5-diylbis(hydroxymethylene) residue as a chiral subunit and dipodands contained the same residue as a chiral anchor group. All of the dipodands showed the enantiomer selectivity toward chiral primary ammonium salts examined and the dipodand having two 2,3-benzo-1,4,7-trioxa-2-octen-1-yl groups as a donor arm as well as the chiral tetrahydrofuran anchor group exhibited higher enantiomer selectivity than the crown ether having the same chiral subunit. It was also showed that the enantiomer selectivity of dipodands in transport was considerably changed by selection of the end group.

These recent results prompted us to examine the chiral recognition property of dipodands and crown ethers, and to acquire further information about the change of the enantiomer selectivity of dipodands produced by the variation in the structure of donor arm. In this paper, we report the preparation of optically active crown ethers and dipodands having a chiral anchor group. These compounds contained the 2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene residue as a chiral subunit. Their enantiomer recognition behavior was evaluated by the enantiomer differential transport of racemic primary ammonium salts through bulk liquid membrane.

Results and Discussion

(+)-(2*S*,4*S*)-2,4-Diphenylglutaric acid (**1**), $[\alpha]_D$ +81.3° (EtOH), was obtained by treatment of the sparingly soluble quinine salt with concentrated hydrochloric acid followed by recrystallization from ethanol.[4] The absolute configuration of the compound has been unambigously determined by a chemical correlation with (−)-(*R*)-3-phenylbutanoic acid.[4] Treatment of (+)-**1** with concentrated sulfuric acid at 80—90 °C for 1 h gave (−)-**2** in 77% yield, recrystallization of which from methanol provided the optically pure specimen **2**, mp 195—197 °C; $[\alpha]_D$ −340° (EtOH).[4] Reduction of (−)-**2** with $LiAlH_4$ in dry tetrahydrofuran (THF) yielded (+)-**4**, mp 192—194 °C; $[\alpha]_D$ +87.2° (EtOH), in 97% yield. Reaction of (+)-**4** with methyl *p*-toluenesulfonate and NaH in dry *N*,*N*-dimethylformamide (DMF) at 45 °C gave (−)-**11**, mp 169—170 °C; $[\alpha]_D$ +15.0° ($CHCl_3$), in 57% yield. The another chiral subunit (+)-**5** having two hydroxymethyl groups was prepared from (−)-**2** as follows. Wittig reaction of



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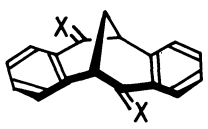
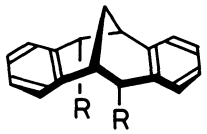


2 X = O

3 X = CH_2



4 R = OH

5 R = CH_2OH

(−)-**2** with methyltriphenylphosphonium bromide using potassium *t*-butoxide and THF[5] gave (−)-**3**, mp 126—127 °C; $[\alpha]_D$ −391° (EtOH), in 92% yield. Treatment of (−)-**3** with diborane in THF led to the corresponding organoborane which was converted into (+)-**5**, mp 170—172 °C; $[\alpha]_D$ +143° (EtOH), in 85% overall yield by oxidation with 30% H_2O_2 in THF followed by treatment with 3 M (1 M=1 mol dm^{-3}) aqueous sodium hydroxide.

Using the diols (+)-**4** and (+)-**5** as a chiral subunit, we prepared optically active crown ethers. One of the ethylene glycol unit of 18-crown-6 and 15-crown-5 was replaced by the chiral diol (+)-**4** to give the chiral crown ethers **6** and **7** respectively. High-dilution condensation of (+)-**4** with pentaethylene glycol ditosylate in the presence of NaH in refluxing THF provided the crown ether (−)-**6**,[6] mp 115—117 °C; $[\alpha]_D$ −1.5° ($CHCl_3$), in 16% yield after alumina chromatography followed by recrystallization from hexane–benzene, and the formation of the dimeric crown ether formed by the condensation of two molecules of the diol **4** with two ditosylate molecules was not detected. By use of the same procedure, (+)-**4** was condensed with tetraethylene glycol ditosylate to give the mixture of crown ethers. Alumina chromatography of the mixture furnished (+)-**7**,[6] mp 72—74 °C; $[\alpha]_D$ +42.6° ($CHCl_3$) and the dimeric crown ether (+)-**8**,[6] mp 166—168 °C; $[\alpha]_D$ +5.4° ($CHCl_4$), in 11% and 12% yield, respectively. Their structures were confirmed on the basis of their mass and ^{1}H NMR spectra as well as elemental analyses. Analogously, condensation of (+)-**5** with pentaethylene glycol and tetraethylene glycol ditosylate in the presence of NaH in THF gave (+)-**9**,[6] $[\alpha]_D$ +51.2° ($CHCl_3$), (a glassy solid 12% yield) and (+)-**10**,[6] $[\alpha]_D$ +24.0° ($CHCl_3$), (a glassy solid 11% yield), respectively. In both cases, the formation of dimeric crown ethers was not detected and the dehydrated product (−)-**3** was isolated.

Cation-binding abilities for alkali metal ions (Li^+, Na^+, K^+, and Rb^+) of the crown ethers **6** and **7** were estimated by solvent extraction of aqueous solution of metal picrates with a chloroform solution containing crown ether, and the results are given in Table 1. As

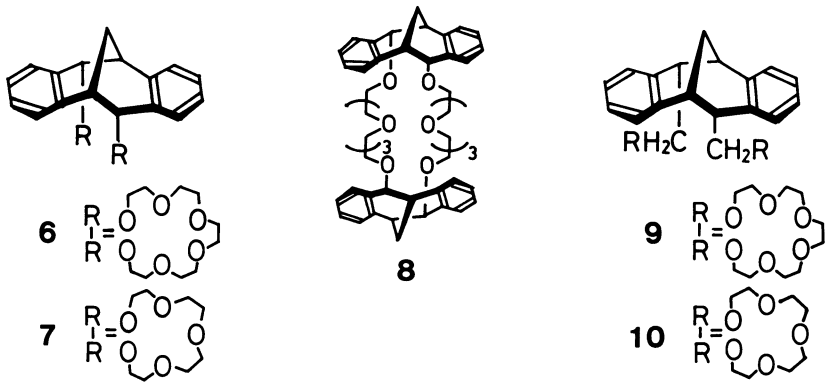
Table 1. Extraction of Alkali Metal Picrates with Crown Ethers **6** and **7**

Crown ether	Extractability/%			
	Li^+	Na^+	K^+	Rb^+
6	<0.1	6	2	1
7	<0.1	5	1	<0.1

can be seen from Table 1, both crown ethers show almost negligible extractabilities for any of the alkali metal ions examined in this study. The introduction of the chiral subunit (+)-**4** into 18-crown-6 and 15-crown-5 enlarges a cavity of the crown ether ring and this may be the major reason for the extremely low extractability of the crown ethers **6** and **7**.

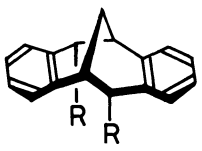
Our next task was the preparation of optically active dipodands having the 2,3:6,7-dibenzobicyclo[3.3.1]-nona-2,6-diene residue as a chiral anchor group. Condensation of (+)-**4** with 3-oxabutyl *p*-toluenesulfonate and NaH in dry DMF at 45—50 °C gave the dipodand (−)-**12** which possessed the methyl end group and two oxygen atoms in each donor arm. Both of the dipodands (−)-**13** and (−)-**14** contained two methyl end groups and they differed from each other in the number of donor atoms in a side chain. The dipodands (−)-**13** having three oxygen atoms in each side arm was prepared by condensation of (+)-**4** with 3,6-dioxaheptyl *p*-toluenesulfonate and the dipodand (−)-**14** having four oxygen atoms in each side arm was obtained from (+)-**4** and 3,6,9-trioxadecyl *p*-toluenesulfonate. The dipodands (−)-**15**, (−)-**16**, and (−)-**17**, all of which contained three oxygen atoms in a donor arm, differed from one another in the end group. Treatment of (+)-**4** with 3,6-dioxaoctyl, 3,6-dioxadecyl, and 7-phenyl-3,6-dioxaheptyl *p*-toluenesulfonate gave (−)-**15** having two ethyl end groups, (−)-**16** having two butyl end groups, and (−)-**17** having two benzyl end groups, respectively. All of the dipodands were obtained as a colorless oil and their structures were confirmed on the basis of their mass spectra as well as their ^{1}H NMR spectra.

Cation binding abilities of podands **13** and **14** were



examined, but both compounds extracted hardly any of the metal ions.

Next we turned attention to examine the enantiomer recognition behavior of these crown ethers and dipodands in transport[7] of (±)-1,2-diphenylethylamine and methyl (±)-phenylglycinate hydrochloride through bulk liquid membrane containing the optically active host molecules. The results are summarized in Table 2.



11 R = OCH_3

12 R = $O\frown O\frown OCH_3$

13 R = $O\frown O\frown O\frown OCH_3$

14 R = $O\frown O\frown O\frown O\frown OCH_3$

15 R = $O\frown O\frown OC_2H_5$

16 R = $O\frown O\frown OC_4H_9$

17 R = $O\frown O\frown OCH_2Ph$

As can be seen from Table 2, all crown ethers and dipodands transported dominantly 1,2-diphenylethylamine hydrochloride of the *S*-configuration and methyl phenylglycinate hydrochloride of the *R*-configuration. Entries 29 and 30 were carried out using the chloroform membrane which did not contain any host molecule. In these cases, methyl phenylglycinate hydrochloride scarcely transferred to the inner aqueous phase, but 4.0% of 1,2-diphenylethylamine hydrochloride moved to the receiving phase after 10 h. Entries 1, 2, 15, and 16 shows that the chiral compounds (+)-**4** and (−)-**11** containing no donor arm exhibited enantiomer selectivity, but their transportabilities were low. In Entries 3 and 4, the transport experiments were performed using the chloroform solution containing (+)-**4** and a small amount of achiral 18-crown-6. In these cases, the rate of transport of the guest molecules was obviously enhanced and the enantiomer selectivity was hardly changed by addition of 18-crown-6.

Table 2. Differential Transport of Enantiomeric Molecules through Bulk Liquid Membrane Containing Chiral Crown Ethers and Chiral Dipodands

Entry	Host	Guest[a]	Time	Transport	Configuration of dominant enantiomer	Optical purity
			h	%		%
1	(+)-**4**	a	10	7.0	*S*	37
2	(+)-**4**	b	180	5.0	*R*	4
3[b]	(+)-**4**	a	12	10	*S*	36
4[b]	(+)-**4**	b	44	11	*R*	6
5	(−)-**6**	a	2.5	10	*S*	69
6	(−)-**6**	b	36	10	—	0
7	(+)-**7**	a	2.4	10	*S*	67
8	(+)-**7**	b	8.5	10	*R*	25
9	(+)-**8**	a	1.5	12	*S*	53
10	(+)-**8**	b	42	11	*R*	5
11	(+)-**9**	a	2.2	10	*S*	32
12	(+)-**9**	b	36	12	—	0
13	(+)-**10**	a	1.7	10	*S*	80
14	(+)-**10**	b	24	11	*R*	11
15	(−)-**11**	a	5.0	11	*S*	29
16	(−)-**11**	b	180	2.0	—	—[d]
17	(−)-**12**	a	2.2	10	*S*	33
18	(−)-**12**	b	180	5.0	*R*	4
19	(−)-**13**	a	1.5	11	*S*	84
20	(−)-**13**	b	52	11	*R*	8
21	(−)-**14**	a	1.6	10	*S*	30
22	(−)-**14**	b	48	11	*R*	3
23	(−)-**15**	a	1.6	10	*S*	50
24	(−)-**15**	b	100	5.4	*R*	6
25	(−)-**16**	a	2.0	11	*S*	45
26	(−)-**16**	b	96	5.6	*R*	5
27	(−)-**17**	a	1.0	10	*S*	19
28	(−)-**17**	b	48	11	*R*	3
29[c]	No	a	10	4.0	—	—
30[c]	No	b	72	1	—	—

a) a: (±)-1,2-Diphenylethylamine hydrochloride, b: methyl (±)-phenylglycinate hydrochloride. b) The chloroform solution contained (+)-**4** (0.005 M) and 18-crown-6 (0.0005 M). c) The chloroform solution did not contain any host molecule. d) Circular dichroism was not measured.

The enantiomer selectivity of (+)-**7** and (+)-**10**, the cavity of which is smaller than that of (+)-**6** and (+)-**9**, is higher than the selectivity of (+)-**6** and (+)-**9**. The enantiomer selectivity of (+)-**10** toward 1,2-diphenylethylamine hydrochloride is the highest in crown ethers examined here and comparable to that of biphenanthryl crown ether,[8] which has been known to be a crown ether having a high chiral recognition property. The crown ether (+)-**7** is nearly equal to biphenanthryl crown ether with regard to its enantiomer recognition behavior toward methyl phenylglycinate hydrochloride.

Entries 17—22 shows that, among dipodands (−)-**12**, (−)-**13**, and (−)-**14**, all of which have two methyl end groups, the enantiomer selectivity of (−)-**13** having three oxygen atoms in each side chain is the highest of all and comparable to that of (+)-**10**. Transportability of (−)-**12** having only two donor atoms in each side chain is low, and a significant difference was not found in transportabilities of (−)-**13** and (−)-**14**. In Entries 19, 20, and 23—28, among dipodands (−)-**13**, (−)-**15**, (−)-**16**, and (−)-**17**, all of which contain three oxygen atoms in each side chain, (−)-**13** having two methyl end groups has the highest enantiomer selectivity. The bulky end groups reduce the enantiomer selectivity of dipodand, but there is no significant difference in transportabilities of these dipodands.

As noted above, the degree of enantiomer selectivity of dipodands in transport varied widely with variation in the structure of the donor arms, and in the case of dipodands reported here, the 1,4,7-trioxaoctyl group is the best subunit as the donor arm of the chiral dipodands.

Experimental

Melting points are uncorrected. Infrared spectra were recorded on a Hitachi 260-10 spectrometer. Ultraviolet spectra were taken on a Hitachi 220A spectrophotometer and circular dichroism data were corrected with a JASCO J-40 spectropolarimeter. Optical rotations were measured with a JASCO DIP-40 automatic polarimeter. ^{1}H NMR spectra were obtained from a JNM-MH-100 and a JNM-C-60 and chemical shift are reported in parts per million (δ) down field from tetramethylsilane. Mass spectra were taken with a Hitachi RMS-4 spectrometer.

(−)-2,3:6,7-Dibenzobicyclo[3.3.1]nona-2,6-diene-4,8-dione (2). (+)-2,4-Diphenylglutaric acid (**1**) (6.00 g, 0.0211 mol) $[\alpha]_D^{22}$ +79.1° (EtOH), which was obtained from the sparingly soluble quinine salt, was stirred in concentrated sulfuric acid (40 mL) for 1 h at 80—90 °C. The mixture was cooled to room temperature, poured into an ice-water, and extracted with benzene. The extract was washed with aqueous solution of sodium hydrogencarbonate and water, dried over $MgSO_4$, and concentrated in vacuo to give **2** (4.00 g, 77% yield), which was recrystallized from methanol to furnish (−)-**2**, mp 195—197 °C; $[\alpha]_D^{22}$ −340° (*c* 0.0220, EtOH). Found: C, 82.01; H, 4.81%. Calcd for $C_{17}H_{12}O_2$: C, 82.24; H, 4.67%.

(−)-4,8-Bis(methylene)-2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene (3). To a suspension of methyltriphenylphosphonium bromide[9] (36.0 g, 0.101 mol) in dry THF (450 mL) was added a suspension of potassium *t*-butoxide (11.3 g, 0.101 mol) in dry THF (190 mL), and then the mixture was stirred for 1 h at room temperature. A solution of (−)-**2** (5.00 g, 0.0202 mol); $[\alpha]_D$ −340°, in dry THF (30 mL) was added to the mixture and it was stirred for an additional 4 h at room temperature under nitrogen atmosphere. After water (15 mL) was added to the reaction mixture, it was stirred at room temperature for 1 h and an inorganic solid was filtered off. The filtrate was concentrated in vacuo and the residue was extracted with ether. The extract was washed with water, dried over $MgSO_4$, and concentrated in vacuo. After addition of hexane (200 mL) to the residue, the precipitated phosphine oxide was filtered off and the solvent was removed. The residue was chromatographed on alumina (eluted with hexane–benzene 1:1 v:v) to provide a solid, which was recrystallized from methanol to give (−)-**3** (4.52 g, 92% yield), mp 126—128 °C, $[\alpha]_D^{27}$ −391° (*c* 0.022, EtOH) (lit,[4] mp 124.2—124.6 °C; $[\alpha]_D$ +392° (EtOH)). Found: C, 93.25; H, 6.61%. Calcd for $C_{19}H_{16}$: C, 93.40; H, 6.60%.

(+)-2,3:6,7-Dibenzobicyclo[3.3.1]nona-2,6-diene-4,8-diol (4). To a suspension of $LiAlH_4$ (1.60 g, 0.0421 mol) in dry THF (50 mL) was added a solution of (−)-**2** (2.65 g, 0.0107 mol) in dry THF (50 mL) at 0 °C and then the mixture was stirred for 1 h at room temperature. After addition of 10% sulfuric acid to the reaction mixture with ice-cooling, an inorganic solid was filtered off and the filtrate was concentrated in vacuo. The residue was extracted with chloroform. The extract was washed with diluted HCl, aqueous solution of sodium hydrogencarbonate, and water, and dried over $MgSO_4$. The solvent was removed in vacuo to give a solid, which was recrystallized from hexane–benzene to provide (+)-**4** (2.48 g, 92% yield), mp 192—194 °C; $[\alpha]_D^{22}$ +87.0° (*c* 0.159, EtOH). Found: C, 80.75; H, 6.36%. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39%.

(+)-4,8-Bis(hydroxymethyl)-2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene (5). A freshly prepared solution of diborane (44.1 mL, 16.5 mmol) in THF was slowly added to a solution of (−)-**3** (4.04 g, 16.5 mmol) in dry THF (100 mL), and then the mixture was stirred for 1 h at room temperature under nitrogen atmosphere. After addition of a small amount of water, the reaction mixture was concentrated in vacuo to give a solid (7.78 g). The solid was dissolved in THF (100 mL), 3 M aqueous solution of sodium hydroxide (35 mL) was added, and the mixture was heated at 40 °C. 30% hydrogen peroxide (5.7 g) was added to the mixture and it was heated for an additional 2 h at this temperature. After water (50 mL) was added to the mixture, the organic phase was withdrawn and the aqueous solution was extracted with ether. The combined organic solutions were washed with water, dried over $MgSO_4$, and concentrated to give a solid, which was recrystallized from benzene to afford (+)-**5** (3.88 g, 85% yield), mp 170—172 °C; $[\alpha]_D^{27}$ +143° (*c* 0.524, EtOH); ^{1}H NMR (DMSO-d_6) δ=2.18 (2H, t J=3 Hz), 3.21 (2H, br s), 3.50 (2H, br s), 4.0—4.1 (4H, m), 4.70 (2H, br s), 6.9—7.5 (8H, m). Found: C, 81.20; H, 7.15%. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19%.

(−)-20,21:23,24-Dibenzo-2,5,8,11,14,17-hexaoxatricyclo[16.3.3.1^{19,22}]pentacosa-20,23-diene (6). To a suspension of NaH (140 mg, 5.83 mmol) in dry THF (30 mL) was slowly

added a mixture of (+)-**4** (500 mg, 1.98 mmol) and pentaethylene glycol ditosylate[10] (1.20 g, 2.20 mmol) in dry THF (60 mL) over a period of 6 h under reflux in nitrogen atmosphere. After the mixture was refluxed for an additional 24 h, a small amount of water was added to the reaction mixture and the mixture was concentrated in vacuo. The residue was extracted with dichloromethane and the extract was washed with diluted HCl and aqueous solution of sodium hydrogencarbonate, and dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was chromatographed on alumina (eluted with chloroform) to give a solid, which was recrystallized from hexane–benzene to furnish (−)-**6** (140 mg, 16% yield), mp 115—117 °C; $[\alpha]_D^{26}$ −1.5°, $[\alpha]_{435}^{27}$+30.7° (*c* 0.384, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.20 (2H, d *J*=3 Hz), 3.3—4.1 (22H, m), 4.67 (2H, d *J*=4.5 Hz), 6.9—7.5 (8H, m); MS *m/z* 454 (M^+). Found: C, 71.03; H, 7.44%. Calcd for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54%.

(+)-17,18:20,21-Dibenzo-2,5,8,11,14-pentaoxatricyclo[13.3.3.1^{16,19}]docosa-17,20-diene (7) and (+)-35,36:38,39:40,41:42,43-Tetrabenzo-2,5,8,11,14,20,23,26,29,32-decaoxapentacyclo[31.3.3.2^{15,18}.2^{16,19}.1^{34,37}]tetratetracosa-35,38,40,42-tetraene (8). Condensation of (+)-**4** (500 mg, 1.98 mmol) with tetraethylene glycol ditosylate[10] (1.10 g, 2.19 mmol) and NaH (140 mg, 5.83 mmol) was carried out according to a similar procedure described for the preparation of **6**. After the same work-up, chromatography on alumina provided **7** (90 mg, 11% yield, eluted with benzene) and **8** (100 mg, 12% yield, eluted with benzene–chloroform 4:1 v:v).

7: Mp 72—74 °C (recrystallized from hexane–benzene); $[\alpha]_D^{25}$ +42.6° (*c* 0.402, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.18 (2H, t *J*=3 Hz), 2.7—3.7 (18H, m), 5.20 (2H,d *J*=7.5 Hz), 7.0—7.6 (8H, m); MS *m/z* 410 (M^+). Found: C, 72.80; H, 7.29%. Calcd for $C_{25}H_{30}O_5$: C, 73.14; H, 7.37%.

8: Mp 166—168 °C (recrystallized from benzene); $[\alpha]_D^{25}$ +5.4° (*c* 0.459, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.12 (4H, t *J*=3 Hz), 3.1—3.4 (4H, m), 3.6—4.1 (32H, m), 4.63 (4H, d *J*=4.5 Hz), 6.8—7.4 (16H, m); MS *m/z* 820 (M^+). Found: C, 72.85; H, 7.33%. Calcd for $C_{50}H_{60}O_{10}$: C, 73.14; H, 7.37%.

(+)-21,23:25,26-Dibenzo-3,6,9,12,15,18-hexaoxatricyclo[18.3.3.1^{21,24}]heptacosa-22,25-diene (9). To a suspension of NaH (130 mg, 5.42 mmol) in dry THF (30 mL) was added a mixture of (+)-**5** (500 mg, 1.81 mmol) and pentaethylene glycol ditosylate (1.10 g, 2.01 mmol) in dry THF (60 mL) over a period of 15 h under reflux and then the mixture was refluxed for an additional 29 h in nitrogen atmosphere. After the same work-up described for the preparation of **6**, the crude product was chromatographed on alumina. Fractions eluted with benzene gave (−)-**3** (53 mg, 12% yield) and fractions eluted with benzene–chloroform (9:1 v:v) gave (+)-**9** (100 mg, 12% yield) as a glassy solid, $[\alpha]_D^{23}$ +51.2° (*c* 0.775, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.20 (2H, br s), 3.2—4.0 (28H, m), 7.0—7.6 (8H, m); MS *m/z* 482 (M^+). Found: C, 71.80; H, 7.88%. Calcd for $C_{29}H_{38}O_6$: C, 72.17; H, 7.94%.

(+)-19,20:22,23-Dibenzo-3,6,9,12,15-pentaoxatricyclo[15.3.3.1^{18,21}]tetracosa-19,22-diene (10). The reaction of (+)-**5** (500 mg, 1.81 mmol) with tetraethylene glycol ditosylate (1.00 g, 1.99 mmol) and NaH (130 mg, 5.42 mmol) was performed by the same procedure described for the preparation of **6**. Alumina chromatography gave (−)-**3** (95 mg, 39% yield, eluted with benzene) and (+)-**10** (87 mg, 11% yield, eluted with benzene–chloroform 9:1 v:v) as a glassy solid, $[\alpha]_D^{24}$ +24.0° (*c* 0.566, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.20 (2H, m), 3.3—4.0 (24H, m), 7.0—7.6 (8H, m); MS *m/z* 402 (M^+). Found: C, 71.45; H, 8.35%. Calcd for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51%.

General Procedure for the Preparation of Monotosylates. To a solution of 2-(2-methoxyethoxy)ethanol (5.00 g, 0.0416 mol) in pyridine (30 mL) was slowly added *p*-toluenesulfonyl chloride (11.9 g, 0.0624 mol) with ice-cooling, and the mixture was kept overnight in a refrigerator. The reaction mixture was poured into ice-water, acidified with hydrochloric acid, and extracted with benzene. The extract was washed with aqueous solution of sodium hydrogencarbonate and water, and dried over $MgSO_4$. The solvent was throughly removed in vacuo to give 10.2 g (90% yield) of 3,6-dioxaheptyl *p*-toluenesulfonate which was used in the next reaction without further purification. The other monotosylates were prepared by the same procedure described here.

(−)-4,8-Dimethoxy-2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-diene (11). A mixture of (+)-**4** (302 mg, 1.20 mmol), NaH (115 mg, 4.79 mmol), and dry DMF (30 mL) was heated at 45 °C for 1 h. A solution of methyl *p*-toluenesulfonate (894 mg, 4.80 mmol) in dry DMF (20 mL) was added to the reaction mixture at 45 °C and then it was heated for an additional 48 h at 45—50 °C. After a small amount of water was added to the reaction mixture at room temperature, a solid was filtered off and the filtrate was concentrated in vacuo. To the residue was added diluted HCl and a precipitated solid was collected, washed with water, and recrystallized from ether–hexane to give (+)-**11** (190 mg, 57% yield), mp 169—170 °C; $[\alpha]_D^{25}$ +15.0° (*c* 0.360, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.29 (2H, t *J*=3 Hz), 3.3—3.5 (2H, m), 3.70 (6H, s), 4.54 (2H, d *J*=5.2 Hz), 7.0—7.5 (8H, m). Found: C, 81.20; H, 7.16%. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19%.

(−)-4,8-(1,3-dioxapentyl)-2,3:6,7-dibenzobicyclo[3.3.1]-nona-2,6-diene (12). To a suspension of NaH (144 mg, 6.00 mmol) in dry DMF (30 mL) was added (+)-**4** (378 mg, 1.50 mmol) and the mixture was stirred for 1 h at room temperature. A solution of 3-oxabutyl *p*-toluenesulfonate (863 mg, 3.75 mmol) in dry DMF (20 mL) was added to the reaction mixture and then it was stirred for 24 h at 45—50 °C in nitrogen atmosphere. After a small amount of water was added to the reaction mixture, the solvent was removed in vacuo. The residue was extracted with chloroform and the extract was washed with water, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on alumina and fractions eluted with hexane–benzene (1:1 v:v) gave a solid, which was recrystallized from hexane to provide (−)-**12** (435 mg, 79% yield), mp 66—67 °C; $[\alpha]_D^{20}$ −10.3° (*c* 0.283, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.30 (2H, t *J*=3 Hz), 3.40 (6H, s), 3.3—4.3 (10H, m), 4.74 (2H, d *J*=5.2 Hz), 7.0—7.5 (8H, m). Found: C, 75.11; H, 7.70%. Calcd for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66%.

(−)-4,8-Bis(1,4,7-trioxaoctyl)-2,3:6,7-dibenzobicyclo[3.3.1]-nona-2,6-diene (13). By using the same procedure described for the preparation of (−)-**12**, the compound **13** (650 mg, 86% yield) was obtained from (+)-**4** (470 mg, 1.66 mmol), 3,6-dioxaheptyl *p*-toluenesulfonate (1.14 mg, 4.15 mmol), and NaH (159 mg, 6.64 mmol) as a colorless oil after chromatography on alumina (eluted with hexane–benzene 1:1 v:v); $[\alpha]_D^{20}$ −34.0° (*c* 0.351, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.32 (2H, t *J*=3 Hz), 3.36 (6H, s), 3.3—4.2 (18H, m), 4.74 (2H, d *J*=5.2 Hz), 7.0—7.5 (8H, m); MS *m/z* 456 (M^+). Found:

C, 69.98; H, 7.90%. Calcd for $C_{27}H_{36}O_6$: C, 71.02; H, 7.95%.

(−)-4,8-Bis(1,4,7,10-tetraoxaundecyl)-2,3:6,7-dibenzobicyclo-[3.3.1]nona-2,6-diene (14). The compound **14** (205 mg, 25% yield) was obtained from (+)-**4** (378 mg, 1.50 mmol), 3,6,9-trioxadecyl *p*-toluenesulfonate (1.19 g, 3.75 mmol), and NaH (144 mg, 6.00 mmol) as a colorless oil after chromatography on alumina (eluted with hexane–benzene 1:1 v:v); $[\alpha]_D^{20}$ −10.5° (*c* 0.721, $CHCl_3$); ^1H NMR ($CDCl_3$); δ=2.19 (2H, t *J*=3 Hz), 3.30 (6H, s), 3.3—4.2 (26H, m), 3.73 (2H, d *J*=4.5 Hz), 6.9—7.5 (8H, m); MS *m/z* 544 (M^+). Found: C, 68.28; H, 8.08%. Calcd for $C_{31}H_{44}O_8$: C, 68.36; H, 8.14%.

(+)-4,8-Bis(1,4,7-trioxanonyl)-2,3:6,7-dibenzobicyclo[3.3.1]-nona-2,6-diene (15). The compound **15** (250 mg, 34% yield) was obtained from (+)-**4** (378 mg, 1.50 mmol), 3,6-dioxaoctyl *p*-toluenesulfonate (1.08 g, 3.75 mmol), and NaH (144 mg, 6.00 mmol) as a colorless oil after chromatography on alumina (eluted with benzene); $[\alpha]_D^{22}$ +40.0° (*c* 0.520, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=1.18 (6H, t *J*=6.8 Hz), 2.30 (2H, t *J*=3.2 Hz), 3.48 (4H, q *J*=6.8 Hz), 3.2—4.2 (18H, m), 4.74 (2H, d *J*=5.3 Hz), 7.0—7.6 (8H, m); MS *m/z* 484 (M^+). Found: C, 71.77; H, 8.28%. Calcd for $C_{29}H_{40}O_6$: C, 71.87; H, 8.32%.

(−)-4,8-Bis(1,4,7-trioxaundecyl)-2,3:6,7-dibenzobicyclo[3.3.1]-nona-2,6-diene (16). The compound **16** (380 mg, 54% yield) was obtained from (+)-**4** (327 mg, 1.30 mmol), 3,6-dioxadecyl *p*-toluenesulfonate (1.03 g, 3.25 mmol), and NaH (125 mg, 5.21 mmol) as a colorless oil after chromatography on alumina (eluted with benzene); $[\alpha]_D^{23}$ −9.80° (*c* 0.806, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=0.88 (6H, t *J*=7 Hz), 1.0—1.7 (8H, m), 2.29 (2H, t *J*=3 Hz), 3.3—4.2 (22H, m), 4.74 (2H, d *J*=5.2 Hz), 7.0—7.5 (8H, m); MS *m/z* 540 (M^+). Found: C, 73.19; H, 8.89%. Calcd for $C_{33}H_{48}O_6$: C,73.30; H, 8.95%.

(−)-4,8-Bis(8-phenyl-1,4,7-trioxaoctyl)-2,3:6,7-dibenzo-bicyclo[3.3.1]nona-2,6-diene (17). The compound **17** (339 mg, 25% yield) was prepared from (+)-**4** (378 mg, 1.50 mmol), 7-phenyl-3,6-dioxaheptyl *p*-toluenesulfonate (1.31 g, 3.75 mmol), and NaH (144 mg, 6.00 mmol) as a colorless oil after chromatography on alumina (eluted with benzene); $[\alpha]_D^{22}$ −5.91° (*c* 0.551, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.25 (2H, t *J*=3.2 Hz), 3.3—4.2 (20H, m), 4.72 (4H, d *J*=5.2 Hz), 7.0—7.5 (18H, m); MS *m/z* 608 (M^+). Found: C, 76.78; H, 7.15%. Calcd for $C_{39}H_{44}O_6$: C, 76.94; H, 7.29%.

Extraction Procedure. The aqueous solution (5 mL) of the metal picrate (2.4×10^{-4} M) and the chloroform solution (5 mL) containing the crown ether (2.4×10^{-4} M) were placed in a screw cap glass tube (30 mL) and the tube was shaken for 30 min at room temperature. Extraction of the picrate was followed by monitoring the absorbance at 357 nm of the aqueous phase.

Enantiomer Differential Transport. Enantiomer differential transport was carried out in a conventional apparatus which consisted of an outer cylindrical glass vessel (24.5 mm inner diameter) and a central glass tube (15.5 mm inner diameter). The 0.01 M chloroform solution of the optically active host molecule separated the inner aqueous phase (0.1 M hydrochloric acid) and the outer aqueous phase (0.08 M hydrochloric acid) which contained $LiPF_6$ (0.4 M) and the racemic guest molecule (0.08 M). The chloroform layer was gently stirred at a constant speed (60 rpm) at 20—25 °C, and transport was monitored by ultraviolet spectra and enantiomeric excess of the guest molecule transported was monitored by circular dichroism.

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