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Synthesis of new chiral crown ethers containing a (*p*-methoxyphenoxy)methyl moiety and their chiral recognition ability towards amino acid esters

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Abstract—Novel crown ethers **9**–**13** containing a chiral subunit derived from 3-(*p*-methoxyphenoxy)propane-1,2-diol **7** were prepared in enantiomerically pure forms. Chiral recognition properties of these receptors towards L- and D-amino acid derivatives were examined by the UV–vis titration method. These receptors exhibit good chiral recognition towards the isomers (up to $K_L/K_D = 5.81$, $\Delta\Delta G_0 = 4.30$ kJ mol^{-1}) in $CHCl_3$ at 25 °C.

1. Introduction

The chemistry of crown ethers has developed rapidly in the years since Pedersen first described their synthesis.[1] Over the last two decades, a wide interest in the chemistry of chiral crown ethers has been shown. A major incentive for this research has been the discovery that chiral recognition and catalytic activity, two important properties of natural enzymes, can be displayed by these macrocycles.[2] Amino acids are the most important targets for molecular recognition by artificial host compounds. This is due to their rich chemistry. For this reason, chemists have been studying host–guest binding of amino acids as an instrument for manipulation of their reactivity.

Since Cram et al. reported the use of chiral macrocyclic ligands in enantiomeric recognition,[3] a great number of chiral artificial receptors have been developed, such as cyclophanes,[4] crown ethers[5] and cyclodextrins.[6] There is still a strong requirement for novel types of host molecules in order to improve the enantioselectivity. Evidence has accumulated over the past two decades that cation–π interactions play an important role in macromolecular organization and in molecular recognition.[7] Thus, alkali metal cation–π complexes of C-pivot and N-pivot crown ethers having methyl and ethylene side arms, attached to aromatic π-donors have been reported.[8,9] In addition to this, a number of protein structures, having a flexible side arm, have been described to demonstrate ammonium cation–π interactions.[10] It is known that the chiral nature of a crown ether, the rigidity of the microenvironment of its cavity and the quality of the side arm are all expected to play an important role in enantioselective induction.

In light of these observations and requirements for novel types of host molecules to improve enantioselectivity, we therefore undertook the design and synthesis of a group of crown ethers replete with donor groups appended to the macroring as a part of a flexible arm. We report herein, the synthesis of new chiral crown ethers **9**–**13** from 3-(*p*-methoxyphenoxy)propane-1,2-diol **7**, which is also used for precursor of β-blockers. The host–guest interaction involving these receptors **10**–**13** and chiral amino acid derivatives were characterized.

2. Results and discussion

2.1. Synthesis

The glycerol unit could be incorporated by the primary and secondary hydroxyls, which can be used as nucleophiles for the formation of the macrocycle rings and side arm attached via the secondary hydroxyl. Thus, a number

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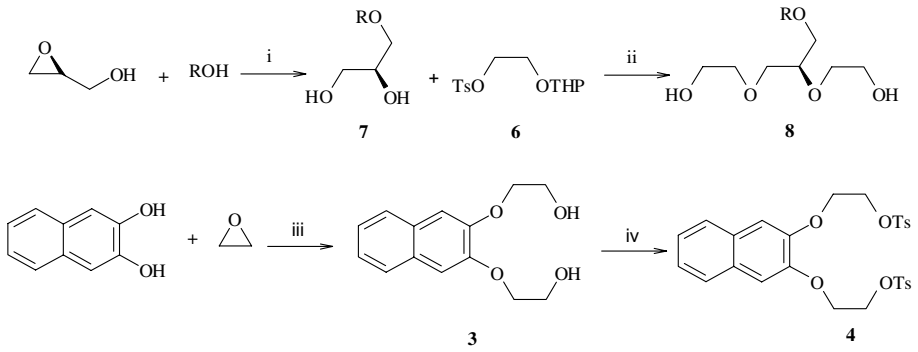
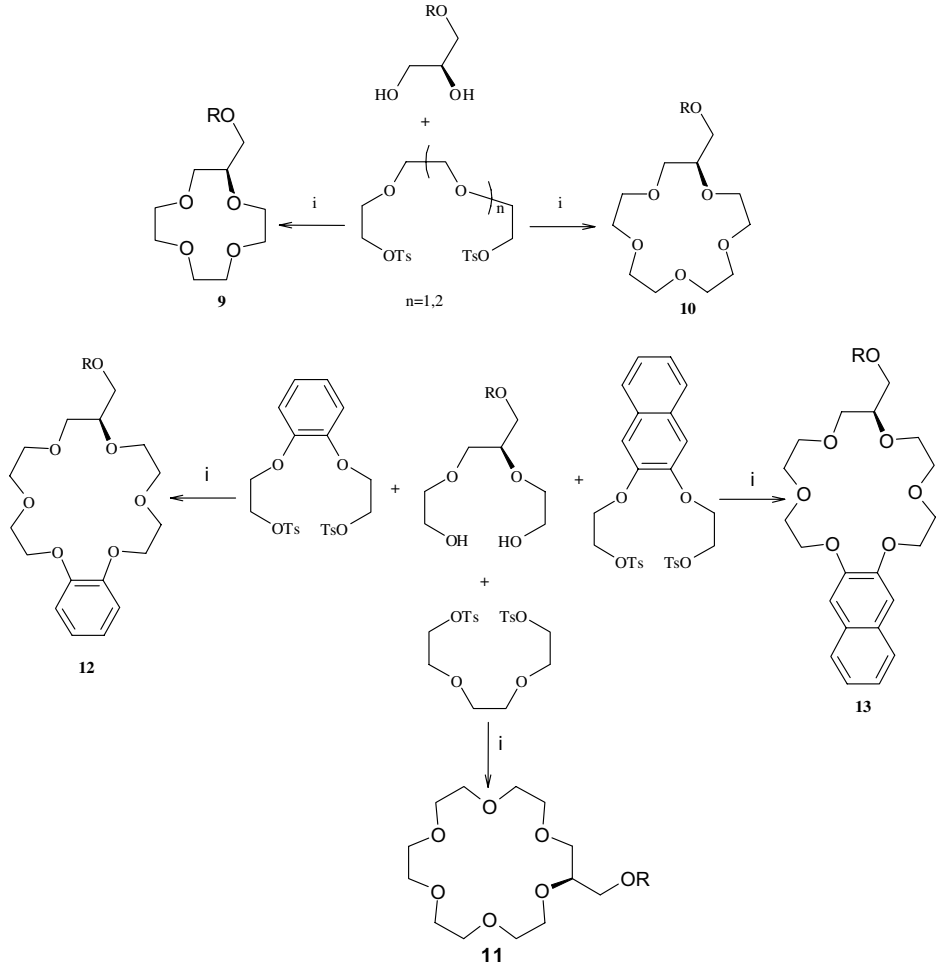
of side arms can be incorporated quite readily. In this study, a (*p*-methoxyphenoxy)methyl flexible side arm was chosen due to its donor groups, which are analogous to the structures already reported.[8,9] Chiral subunit diol **7**, was prepared from (*S*)-glycidol, *p*-methoxyphenol and catalytic amounts of piperidine hydrochloride in high yield and enantiopurity according to our previous report.[11] As shown in Scheme 1, building block diol **8** was prepared according to the procedure reported.[12] First, ethylene glycol was pseudoselectively monoprotected with 3,4-2*H*-dihydropyran to give 2-(tetrahydropyranyloxy)ethanol and then the remaining free hydroxyl group in 2-(tetrahydropyranyloxy)ethanol was tosylated to obtain **6** in a nearly quantitative yield. The condensation of 2 equiv of **6** with **7** in the presence of NaH followed by removal of the THP protection groups, provided **8** in 69% overall yield, which is the common precursor of 18-crown-6 ethers **11**–**13** as shown in Scheme 2.



Scheme 1. Reagents and conditions: (i) Piperidine hydrochloride, 70–80 °C, 4 h; (ii) NaH, THF then HCl, MeOH; (iii) piperidine hydrochloride; (iv) TsCl, pyridine, R = –C_6H_4–*p*-OMe.



Scheme 2. Reagents and conditions: (i) NaH, THF, reflux, 56 h.

The synthesis of crown ether **9** was initiated from the ring closure of **7** with triethylene glycol di(*p*-toluenesulfonate) in the presence of NaH in THF under high dilution conditions to give **9** in 15% yield, which was not used for host–guest interaction due to its small cavity size. Receptor **10** was prepared by essentially the same procedure as that used for the preparation of **9** by using tetraethylene glycol di(*p*-toluenesulfonate) to give **10** in 39% yield. The racemic form of this receptor has been synthesized by similar ways and studied thoroughly for different purposes such as its biological activity,[13] muscle contractility influence[14] and binding properties.[13,15] The enantiomerically pure chiral building block **8** was employed simply for the synthesis of 18-membered ethers **11**–**13**. Thus, treatment of **8** with triethylene glycol di(*p*-toluenesulfonate) as described for **9** gave **11** in 18% yield. In order to investigate the effect of the benzo unit on the macrocycle ring for the molecular recognition, which is known to increase the enantioselectivity of aza-15-crown-5 ether derivatives towards chiral ammonium cations,[16] crown ether **12** was prepared by the ring closure of **8** with ditosylate **2** in 12% yield. Ditosylate **4** is an example of ditosylate containing a naphtho unit for the extended rigidity of macrocycle **13** as seen in Scheme 1. Thus, the ring opening reaction of ethylene oxide with 2,3-dihydroxynaphthalene and piperidine hydrochloride as catalyst gave diol **3** according to the reported procedure,[17] then tosylated **3** gave **4** in overall 50% yield. The ring closure of **8** with **4** gave **13** in 12% yield, which can be easily crystallized from ethanol. The structures purposed for these macrocycles are consistent with the data obtained from ^{1}H NMR, ^{13}C NMR, IR spectra and elemental analysis.

2.2. Molecular recognition and UV–vis

The main purpose of synthesizing these receptors is to study their molecular recognition for guest molecules. UV–vis spectroscopy is a convenient and widely used method for the study of this binding phenomena. When the receptor absorbs light at different wavelengths in the free and complexed states, the difference in the UV–vis spectra is sufficient for the estimation of molecular recognition thermodynamics. In UV spectroscopic titration experiments, the addition of a varying concentration of guest molecules results in a gradual increase or decrease of characteristic absorption of 1:1 stoichiometry. The complexation of ammonium cations (G) with chiral crown ether type molecular (H) is expressed by Eq. 1:

$$\mathrm{H}+\mathrm{G} \rightleftharpoons \mathrm{H}\cdot\mathrm{G} \tag{1}$$

Under the conditions employed herein, chiral amino acid esters were selected as the guest molecules. The association constants of the supramolecular system formed, were calculated according to the modified Benesi–Hilderbrand equation,[18] Eq. 2, where $[H]_0$ and $[G]_0$ refer to the total concentration of crown ether and amino acid ester, respectively, $\Delta\varepsilon$ is the change in molar extinction co-efficient between the free and complexed crown ether and ΔA denotes the absorption change of crown ether on the addition of amino acid esters.

$$[\mathrm{H}]_0[\mathrm{G}]_0/\Delta A = 1/K_\mathrm{a}\Delta\varepsilon + [\mathrm{G}]_0/\Delta\varepsilon \tag{2}$$

For all the guest molecules examined, plots of calculated $[H]_0[G]_0/\Delta A$ values as a function of $[G]_0$ values gave excellent linear relationships, supporting the 1:1 complex formation. The binding constant (K_a) and free energy changes ($-\Delta G_0$) of these host with guest molecules obtained from usual curve fitting analyses (R >0.98) of observed absorbance changes are summarized in Table 1. The binding constant K_a of the complexes of crown ethers **10**–**13** with amino acid ester salts was determined by the Benesi–Hilderbrand equation on the basis of the UV–vis spectrum of the

Table 1. Binding constants (K_a), the Gibbs free energy changes ($-\Delta G_0$), enantioselectivities K_L/K_D and $-\Delta\Delta G_0$ calculated from $-\Delta G_0$ for the complexation of L/D guest with the chiral host **10**, **11**, **12** and **13** at 241 and 291 nm in $CHCl_3$ at 25 °C

Host[a]	Guest[b]	K (dm^3 mol^{-1})	K_L/K_D	$-\Delta G_0$ (kJ mol^{-1})	[c]$\Delta\Delta G_0$ (kJ mol^{-1})
10	L-Ala-OMe·HCl	6.16×10^4		27.3	
	D-Ala-OMe·HCl	1.06×10^4	5.81	23.00	4.30
	L-Phe-OMe·HCl	6.00×10^3		21.60	
	D-Phe-OMe·HCl	5.43×10^3	1.08	21.30	0.30
11	L-Ala-OMe·HCl	3.33×10^3		20.10	
	D-Ala-OMe·HCl	3.80×10^3	0.87	20.40	−0.30
	L-Phe-OMe·HCl	3.25×10^3		20.10	
	D-Phe-OMe·HCl	3.60×10^3	0.84	20.30	−0.20
12	L-Ala-OMe·HCl	2.75×10^3		19.60	
	D-Ala-OMe·HCl	3.00×10^3	0.91	19.80	−0.20
	L-Phe-OMe·HCl	4.25×10^3		20.00	
	D-Phe-OMe·HCl	3.86×10^3	1.10	20.50	−0.30
13[d]	L-Ala-OMe·HCl	3.00×10^3		19.80	
	D-Ala-OMe·HCl	4.14×10^3	0.72	20.60	−1.20
	L-Phe-OMe·HCl	3.33×10^3		20.10	
	D-Phe-OMe·HCl	7.78×10^3	0.42	20.20	−2.10

[a] The concentration of the hosts = 2.00×10^{-4} mol dm^{-3}.
[b] Ala-OMe·HCl: alanine methyl ester hydrochloride; Phe-OMe·HCl: phenylalanine methyl ester hydrochloride.
[c] $\Delta\Delta G_0 = \Delta G_0(\mathrm{L}) - \Delta G_0(\mathrm{D})$.
[d] 2.00×10^{-5} mol dm^{-3}.

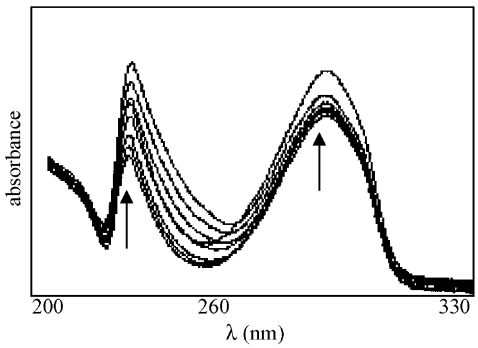


Figure 1. UV–vis spectra of 10 (2×10^{-4} mol dm^{-3}) in presence of L-ala-OMe·HCl in $CHCl_3$ at 25 °C.

complexes in $CHCl_3$ at 25 °C. The typical UV spectral changes upon addition of L-ala-OMe hydrochloride to **10** are shown in Figure 1 while typical plots are shown for the complexation of **10** with L-ala-OMe hydrochloride in Figure 2.

We have shown that crown ethers **10**–**13** formed complexes of appreciable stability constants towards isomers of ala-OMe hydrochloride and phe-OMe hydrochloride ($K_a = 2.75 \times 10^3$–6.16×10^4 dm^3 mol^{-1}). It is thought that the macroring would envelop the cation in a fashion normally associated with crown ether binding while the donor groups attached to the flexible side arm would further solvate the bound cation. The data presented herein are superior than those obtained with a chiral cyclophane receptor, which was applied also towards amino acid derivatives.[4d] As shown in Table 1, the crown receptor shows chiral recognition ability for the amino acid derivatives, while **11** and **12** cannot recognize the chirality of the L- and D-isomer ($K_L/K_D \cong 1$).

We found that receptor **13** exhibits a stronger binding and better enantioselectivity towards phe-OMe hydrochloride ($K_D/K_L = 2.38$), whereas receptor **13** has a poor recognition ability for the ala-OMe hydrochloride ($K_D/K_L = 1.39$). Thus, receptor **13** exhibits stronger binding and better enantioselectivity for amino acid esters containing an aromatic group than those possessing a small aliphatic side chain, inferring that the π–π stacking interaction between the receptor and the aromatic side chain of amino acid is the principle attractive interaction involved and that this result is consistent with those demonstrated previously.[4d] In addition to this, the rigidity of **13** may also play an important role in enantioselective recognition.

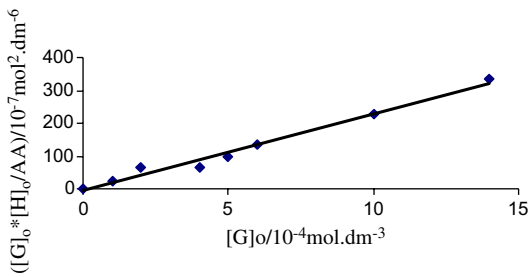


Figure 2. Typical plot of $[H]_0[G]_0/\Delta A$ versus $[G]_0$ for the host–guest complexation of **11** and L-Ala-OMe·HCl in $CHCl_3$ at 25 °C.

Significant results were obtained with receptor **10**, which was found to be the strongest binding constant and the best enantioselectivity towards ala-OMe hydrochloride. The binding constants of **10** towards L- and D-ala-OMe hydrochloride were found to be 6.16×10^4 dm^3 mol^{-1} and 1.06×10^4 dm^3 mol^{-1}, respectively. The L-form was 5.81 times more stable than the D-form of ala-OMe hydrochloride, while receptor **10** had no enantioselectivity towards phe-OMe hydrochloride ($K_D/K_L = 1.08$). It is known that for enantiomeric recognition, the steric repulsion between the substituent on the stereogenic centre and the substituent of ammonium cation,[19] cation–π interaction,[4d,8,9] is expected to be an important factor. The enhanced chiral recognition ability has been suggested to arise from cation–π interaction and the cavity size of **10** when compared with those of 18-membered rings and small aliphatic side chain of alanine to make favourable recognition ability for receptor **10**. These results show that the cavity size, structural rigidity of hosts, π–π stacking and cation–π interactions between host and guest, and steric repulsion between the substituent on the stereogenic centre and on the ammonium cation may be the most important factors for the enantioselective recognition of amino acid derivatives.

3. Conclusion

In conclusion, general classes of crown compounds **10**–**13** have been prepared in order to investigate hosts capable of recognizing the chirality of the amino acid derivatives. Moderate enantiomeric recognition of amino acid esters was achieved with chiral (***S***)-**10** and (***S***)-**13**.

4. Experimental

4.1. General information

Melting points were determined with a Gallenkamp Model apparatus with open capillaries. Infrared spectra were recorded on a Midac-FTIR Model 1700 spectrophotometer. The UV–vis spectra were measured by Shimadzu 160 UV spectrophotometer. The Elemental analyses were obtained with Carlo Erba Model 1108 apparatus. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Bruker DPX-400 high performance digital FT-NMR spectrometer with tetramethysilane as the internal standard solu- tions in deuteriochloroform. *J* Values are given in hertz. Optical rotations were recorded using Perkin–Elmer Model 341 polarimeter. All chemicals were of reagent grade unless otherwise specified. THF was dried (on sodium benzophenone ketyl) and distilled prior to use.

4.2. 1,2-Bis-(2-hydroxyethoxy)benzene 1

This compound was prepared according to the procedure recorded in the literature[17] from catechol (11.0 g, 0.1 mol) diethylamine hydrochloride (as a catalyst) and

ethylene oxide (9.8 mL, 0.2 mol) to give 18.8 g, 95%; mp 81–83 °C.

4.3. 1,2-Bis-(2-*p*-tolylsulfonyl ethoxy)benzene 2

This compound was prepared according to the procedure recorded in the literature[17] from 1, 2-bis-(2-hydroxyethoxy)benzene (26.73 g, 0.135 mol), pyridine (110 mL) at −10 °C and *p*-toluenesulfonylchloride (51.43 g, 0.27 mol) to give 66 g, 96%; mp 95–95.5 °C.

4.4. 2,3-Bis-(2-hydroxyethoxy)naphthalene 3

It was synthesized as described by the above method by using 2,3-dihydroxynaphthalene (16.0 g, 0.1 mol), piperidine hydrochloride (as catalyst) and ethylene oxide (10 mL, 0.2 mol) to give 17.36 g (70%), mp 146–147 °C.

4.5. 2,3-Bis-[2-(*p*-tolylsulfonyl)ethoxy]naphthalene 4

This compound was synthesized in the usual manner using 2,3-bis-(2-hydroxyethoxy)naphthalene (20.0 g, 0.08 mol), pyridine (100 mL) at −10 °C and *p*-toluenesulfonylchloride (30.64 g, 0.16 mol) to give 30 g (68.2%); mp 111–112 °C. ^{1}H NMR δ: 2.42 (s, 6H), 4.28–4.31 (q, 4.5 Hz, 2H), 4.43–4.45 (q, 4 Hz, 2H), 7.28–7.38 (m, 8H), 7.62–7.66 (dd, 2H), 7.82–7.85 (m, 4H). IR *v*: 3063, 2950, 1636, 1602, 1509, 1490, 1463, 1363, 1265, 1189, 1113, 1027, 935, 816, 789, 670, 552 cm^{-1}.

4.6. Tetra(ethylene glycol)di(*p*-toluenesulfonate) 5

p-Toluenesulfonylchloride (10.47 g, 55.00 mmol) in small portions was added to tetra(ethylene glycol) (4.45 g, 25.0 mmol) in 30 mL of distilled pyridine at −10 °C. The mixture was kept overnight at 4 °C. Then, the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The organic layer was extracted with 6 M HCl at 0 °C. The combined organic layers were washed with water (2 × 25 mL) and saturated $NaHCO_3$ solution and dried with $CaCl_2$ and the solvent evaporated. Purification by flash column chromatography (eluent: ethanol–CH_2Cl_2, 98/2) yielded 10.59 g (84%) of tetraethylene glycol di(*p*-toluenesulfonate).

4.7. Synthesis of 1-(tetrahydropyranyloxy)-2-[(*p*-tolylsulfonyl)oxy]ethane 6

This compound was prepared from ethylene glycol according to the method reported[12] and the crude product was purified by silica gel column chromatography using methanol–dichloromethane (2/98) as eluent to give pure product.

4.8. (*S*)-3-(*p*-Methoxyphenoxy)propane-1,2-diol 7

This compound was prepared by the method described[11] from (*S*)-glycidol (3.7 g, 0.05 mol), *p*-methoxyphenol (6.2 g, 0.05 mol) and piperidine hydrochloride (0.3 g, 2.5 mmol) as a catalyst to give 8.51 g (86%); mp 80–82 °C, $[\alpha]_D^{20} = +10.5$ (*c* 0.5, MeOH). ^{1}H NMR δ: 3.65–3.77 (m, 7H), 3.93–3.94 (m, 2H), 4.01 (m, 1H), 6.76–6.83 (m, 4H). ^{13}C NMR δ: 63.15, 64.16, 69.49, 71.50, 114.98, 121.62, 129.62, 158.54. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.45; H, 7.10.

4.9. (*S*)-4-(*p*-Methoxyphenoxy)methyl-3,6-dioxa-1,8-octanediol 8

This compound was synthesized as described above[12] by using (*S*)-3-(4-methoxyphenoxy)propane-1,2-diol (4.95 g, 0.025 mol) and 1-(tetrahydropyranyloxy)-2-[(*p*-tolylsulfonyl)oxy]ethane (15 g, 0.05 mol) to give 4.93 g (69%) of pure product as a colourless viscous oil, which was purified by silica gel column chromatography [eluent: EtOAc–hexane–EtOH–triethylamine (14/7/2/2)]. $[\alpha]_D^{24} = +9.5$ (*c* 0.25, MeOH). ^{1}H NMR δ: 3.12 (br s, 2H, OH), 3.62–3.65 (m, 2H), 3.68–3.78 (m, 10H), 3.8–3.84 (m, 2H), 3.99–4.0 (d, 5.28 Hz, 2H), 6.81–6.86 (m, 4H). IR *v*: 3413, 3049, 2942, 2873, 1898, 1516, 1460, 1246, 1127, 1058, 894, 831, 756 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_6$: C, 59.00; H, 8.00. Found: C, 59.20; H, 7.96.

4.10. 2-[(*p*-Methoxyphenoxy)methyl]-12-crown-4 9

To a suspension of 0.886 g (29 mmol 80% in mineral oil) of NaH in 150 mL of dry THF at 0 °C was added a solution of 1.30 g (6.56 mmol) of (*S*)-3-(*p*-methoxyphenoxy)propane-1,2-diol in 250 mL of THF. The reaction mixture was refluxed for 2 h. After cooling to 0 °C, a solution of triethylene glycol di-(*p*-toluenesulfonate) 3 g (6.56 mmol) in 250 mL of THF was slowly added. The suspension was refluxed for 56 h. The solvent was evaporated after which 100 mL of water was added to the residue. The mixture was extracted with CH_2Cl_2 (4 × 20 mL) and the combined organic layers washed with 50 mL of water, dried over $MgSO_4$ and the solvent evaporated. To the solution of crude product in toluene was added a solution of $NaClO_4{\cdot}H_2O$ in EtOAc then the crystallized complex was filtered to give the pure product. Free ligand was obtained by the silica gel column chromatography of complex (eluent: EtOAc–hexane–triethylamine, 5/5/1) to yield 0.2 g (15%) as a viscous oil. $[\alpha]_D^{30} = -9.5$ (*c* 5, $CHCl_3$). The spectral data of this complex is as follows: ^{1}H NMR δ: 6.68–6.73 (m, 4H), 3.54–4.01 (m, 20H). ^{13}C NMR δ: 154.01, 152.62, 115.22, 114.67, 73.21, 67.14, 66.37, 66.24, 65.89, 65.39, 65.19, 55.71. IR *v*: 3042, 2924, 2878, 1595, 1509, 1470, 1238, 1100, 1020, 921, 842, 750, 624 cm^{-1}.

4.11. (*S*)-2-[(*p*-Methoxyphenoxy)methyl]-15-crown-5 10

This compound was prepared in a manner similar to that described for the preparation of **9** by using diol **7** (1.30 g, 6.56 mmol) and tetraethylene glycol di(*p*-toluenesulfonate) (3.29 g, 6.56 mmol). The crude product was purified by column chromatography (eluent: EtOAc–hexane–triethylamine, 5/5/1) to yield as a viscous oil 0.91 g (39%) of pure product. $[\alpha]_D^{30} = -14.5$ (*c* 7, $CHCl_3$). ^{1}H NMR δ: 3.64–4.03 (m, 24H); 6.81–6.88 (m, 4H). ^{13}C NMR δ: 153.75, 152.82, 115.34, 114.61, 77.66, 77.58, 77.43, 77.12, 75.86, 70.82, 70.62, 70.58, 70.15, 68.56, 65.42, 55.69. IR *v*: 3043, 2940, 2874, 1602, 1509, 1463, 1233, 1133, 1041, 941, 829,

743 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.92. Found: C, 60.45; H, 8.05.

4.12. (*S*)-2-[(*p*-Methoxyphenoxy)methyl]-18-crown-6 11

This compound was prepared in a manner similar to that described for the preparation of **9** by using diol **8** (1.45 g, 5 mmol) and triethylene glycol di(*p*-toluenesulfonate) (2.8 g, 5 mmol) to give 0.35 g (18%) of **11** as a viscous oil. Crude product was purified by chromatography as described for **10**. $[\alpha]_D^{30} = -8.8$ (*c* 4.66, $CHCl_3$). ^{1}H NMR δ: 6.71–6.78 (m, 4H), 3.54–3.97 (m, 28H). ^{13}C NMR δ: 153.84, 152.99, 115.53, 114.55, 77.82, 77.74, 77.34, 71.31, 70.96, 70.85, 70.83, 70.72, 70.69, 70.65, 70.10, 68.67, 67.90, 55.68. IR *v*: 3049, 2937, 2871, 1602, 1516, 1470, 1358, 1290, 1238, 1120, 1041, 988, 948, 829, 750 cm^{-1}. Anal. Calcd for $C_{20}H_{32}O_8$: C, 60.0; H, 8.0. Found: C, 59.87; H, 8.20.

4.13. (*S*)-12-[(4-Methoxyphenoxy)methyl]-2,3-benzo-18-crown-6 12

This compound was prepared in a manner similar to that described for the preparation of **9** by using diol **8** (1 g, 3.5 mmol) and 2,3-bis-[2-(*p*-tolylsulfonyl)ethoxy]benzene (1.77 g, 3.5 mmol) to give 0.20 g (12%) of pure **12** as a viscous oil, whose crude product was purified by silica gel column chromatography (eluent: petroleum ether (60–80)–EtOAc–triethylamine, 80/17/3). $[\alpha]_D^{30} = -2.7$ (*c* 2, $CHCl_3$). ^{1}H NMR: δ 3.71–3.84 (m, 12H), 3.89–4.01 (m, 8H), 4.15–4.20 (m, 4H), 6.78–6.85 (m, 4H), 6.90–6.94 (m, 4H). ^{13}C NMR δ: 152.96, 151.94, 149.43, 121.63, 114.31, 113.85, 113.38, 73.80, 71.93, 70.95, 70.42, 70.02, 69.97, 69.88, 69.32, 67.52, 67.34, 66.82, 54.20; IR *v*: 3069, 2924, 2871, 1615, 1509, 1451, 1233, 1133, 1041, 935, 829, 750 cm^{-1}. Anal. Calcd for $C_{24}H_{32}O_8$: C, 64.0; H, 7.0. Found: C, 64.38; H, 7.24.

4.14. (*S*)-12-[(4-Methoxyphenoxy)methyl]-2,3-naphtho-18-crown-6 13

This compound was prepared in a manner similar to that described for the preparation of **9** by using diol **8** (1.45 g, 5 mmol) and 2,3-bis-[2-(*p*-tolylsulfonyl)ethoxy]naphthalene **4** (2.72 g, 5 mmol) to give 0.30 g (12%) of pure **13** as a white solid, whose crude product was purified by crystallization from ethanol, mp 88–89 °C. $[\alpha]_D^{30} = -8.6$ (*c* 3.76, $CHCl_3$). ^{1}H NMR δ: 7.58–7.56 (dd, 2H), 7.16–7.25 (dd, 2H), 7.01–7.02 (d, 2.8 Hz, 2H); 6.60–6.69 (m, 4H), 4.12–4.20 (m, 4H), 3.80–3.94 (m, 8H), 3.59–3.75 (m, 12H). ^{13}C NMR δ: 152.74, 151.89, 148.05, 128.25, 125.27, 123.13, 114.39, 113.45, 106.87, 76.92, 70.49, 70.24, 70.05, 69.94, 69.15, 68.45, 67.70, 67.59, 67.34, 54.58. IR *v*: 3056, 2931, 2884, 1610, 1516, 1457, 1240, 1120, 1060, 941, 823, 743 cm^{-1}. Anal. Calcd for $C_{28}H_{34}O_8$: C, 67.0; H, 6.0. Found: C, 66.85; H, 6.22.

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