Synthesis of Chiral Crown Ethers Derived from *trans, trans*- and *cis, trans*-2,2′-Spirobiindan-1,1′-diols. Their Chiral Recognition and Complexation Properties

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Synopsis. *trans,trans*-2,2′-Spirobiindan-1,1′-diol (**1**) was resolved as its (−)-ω-camphanic ester and the absolute rotation of the glycol **1** was determined. Two crown ethers and the acyclic analog were derived from (+)-**1**. Two crown ethers incorporating (+)-*cis,trans*-2,2′-spirobiindan-1,1′-diol were also prepared. Their chiral recognition properties in transport of methyl (±)-phenylglycinate hydrochloride and abilities to extract alkali metal picrates were investigated.

In the preceding paper,[1] we reported the preparation of optically active crown ethers incorporating *trans*-2,5-bis(hydroxymethyl)tetrahydrofuran as the chiral center. Our continuing interest in chiral macrocyclic polyether prompted us to incorporate 2,2′-spirobiindan-1,1′-diol with known absolute configuration into crown ether, and in this paper we report the preparation of some optically active crown ethers composed of the glycol as well as their chiral recognition properties and complexation properties.

Among three possible diastereomers of 2,2′-spirobiindan-1,1′-diol, *trans,trans*-glycol (C_2 symmetry) **1** and *cis,trans*-glycol (C_1 symmetry) **2** were isolated in optically active forms.[2-4] There is, however, no report of the determination of the absolute rotation of *trans,trans*-glycol **1**. Reduction of (±)-diketone **3** with LiAlH(OBu^t)$_3$ gave (±)-**1** in 95% yield. Treatment of (±)-**1** with 1 equiv of (−)-ω-camphanic acid chloride gave half ester **4** which was recrystallized from acetone to afford (−)-**4**, $[\alpha]_D$ −144°. Reduction of (−)-**4** with $LiAlH_4$ gave (−)-**1** whose ^1H NMR spectrum was in agreement with the reported ^1H NMR spectral data for *trans,trans*-2,2′-spirobiindan-1,1′-diol (**1**).[3] Jones oxidation of (−)-**1**, $[\alpha]_D$ −15.2°, to (2*R*)-(−)-diketone 3,[4] $[\alpha]_D$ −147°, permitted to assign the (1*S*,1*S*′,2*R*) configuration to (−)-**1**. The enantiomeric excess of (−)-**3**, $[\alpha]_D$ −147°, was determined to be >98% by means of HPLC with a chiral column.[5] The antipode; (+)-**1** was also prepared from (+)-**2** as follows. (+)-*cis,trans*-glycol **2**, $[\alpha]_D$ +13.5°, prepared *via* (−)-**5**,[3] was oxidized with Jones reagent to give (2*S*)-(+)-**3**, $[\alpha]_D$ +150°, from which (+)-**1**, $[\alpha]_D$ +15.0°, was prepared by LiAlH(OBu^t)$_3$ reduction.

Condensation of (+)-**1** with pentaethylene glycol ditosylate in THF–NaH gave crown ether **6** in 69% yield. Crown ether **7** was obtained in 35% yield by condensation of (+)-**1** with tetraethylene glycol ditosylate. Similarly crown ethers **8** and **9** were derived from (+)-**2**. Acyclic polyether **10** was obtained in 63% yield by condensation of (+)-**1** with diethylene glycol monomethyl ether tosylate. Table 1 lists the chiral recognition behaviour of crown ethers and acyclic polyether with methyl (±)-phenylglycinate hydrochloride. The cationbinding ability of polyethers was assessed by solvent extraction of aqueous solution of alkali metal picrates with $CHCl_3$ solution containing polyethers **6**—**10**. The results are given in Table 2.

TABLE 1. DIFFERENTIAL TRANSPORT OF METHYL (±)-PHENYLGLYCINATE HYDROCHLORIDE

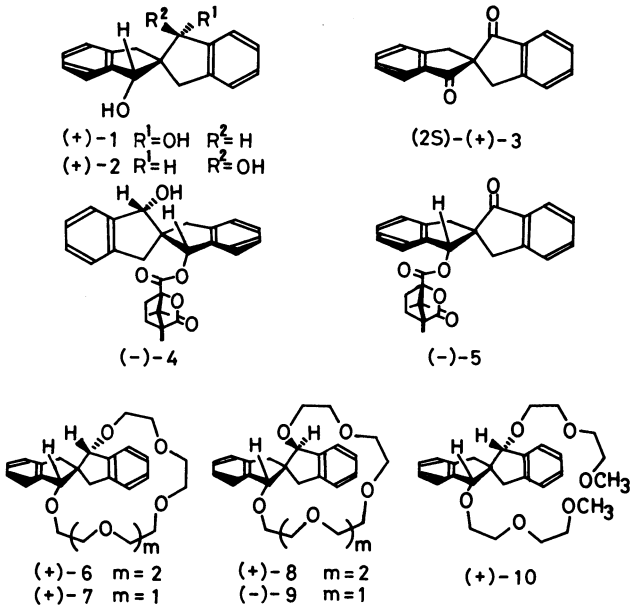
Host	Time/h	Transport/%	Configuration of dominant enantiomer	Optical purity/%
(+)−**6**	2	5.9	S	5.9
(+)−**7**	22	5.5	R	5.4
(+)−**8**	4	5.5	R	13.0
(−)−**9**	70	4.7	R	4.0
(+)−**10**	90	4.9	S	8.0

TABLE 2. EXTRACTION OF ALKALI METAL PICRATES

Host	Extractability/%[a]				
	Li^+	Na^+	K^+	Rb^+	Cs^+
6	1	1	26	11	2
7	1	4	0	0	0
8	0	0	1	0	0
9	0	1	1	0	0
10	0	0	0	0	0
18-crown-6	3	6	66	59	33

a) Defined as % picrate extracted into the organic phase.

A number of features in these Tables deserve comment. (1) Crown ethers containing six oxygens carried the amino ester salt more rapidly than did crown ethers containing five oxygens. (2) Crown ethers incorporating *trans,trans*-glycol moiety transported the amino ester salt more rapidly than did crown ethers composed of *cis,trans*-glycol moiety. (3) The enantiomer selectivity of acyclic polyether **10** is comparable to that of crown ethers. (4) Crown ether containing six oxygens as well



as *trans,trans*-glycol moiety showed fairly high relative selectivity for K^+ and Rb^+.

2,2′-Spirobiindan-1,1′-diols are conformationally rigid, so that complexation properties of the crown ethers incorporating these units are extremely depend on the length of polyether bridge as well as the configuration at C 1 and C 1′ of the glycol moiety.

Experimental

(+)-cis,trans-2,2′-Spirobiindan-1,1′-diol (2). This compound was prepared by Dynessen's method;[3] $[\alpha]_D^{26}$ +13.5° (*c* 0.511, THF) (lit,[3] $[\alpha]_D$ +10.9° (THF)); mp 152—154°C; Anal. ($C_{17}H_{16}O_2$) C, H.

(±)-trans,trans-2,2′-Spirobiindan-1,1′-diol (1). A solution of (±)-**3**[3] (8.13 g, 32.8 mmol) in dry THF (180 mL) was added to a solution of $LiAlH(OBu^t)_3$ (25.7 g, 98.2 mmol) in dry THF (260 mL). The mixture was refluxed for 13 h and cooled in an ice-bath. To the chilled reaction mixture was added water (80 mL), and an inorganic solid was filtered off. After filtrate was concentrated, the residue was dissolved in $CHCl_3$, washed with water, and dried. The solvent was removed to give a solid which was recrystallized from ethanol to give (±)-**1** (7.85 g, 95% yield); mp 220—222°C; Found: C, 80.89; H, 6.36%. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39%.

Optical Resolution of (±)-1. (±)-*trans,trans*-Glycol **1** (10.1 g, 39.8 mmol) was treated with (−)-ω-camphanic acid chloride (17.1 g, 39.8 mmol) by the similar procedure reported for the preparation of the ester **5**.[3] The product was recrystallized from acetone to give (−)-**4** (2.12 g); $[\alpha]_D^{25}$ −144° (*c* 0.292, $CHCl_3$); mp 158—160°C; Found: C, 75.11; H, 6.55%. Calcd for $C_{27}H_{28}O_5$: C, 74.98; H, 6.53%.

The (−)-ester **4** (2.06 g, 4.76 mmol) was refluxed with $LiAlH_4$ (2.71 g, 71.4 mmol) in dry THF (120 mL) for 8 h. After a usual workup, the product was recrystallized from acetone to give (−)-**1** (636 mg, 53% yield); $[\alpha]_D^{25}$ −15.2° (*c* 0.309, THF); mp 234—236°C; Found: C, 80.96; H, 6.40%. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39%.

(+)-2,2′-Spirobiindan-1,1′-dione (3). Oxidation of (+)-**2**, $[\alpha]_D$ +13.5° (252 mg, 1.00 mmol) with 8N Jones reagent was carried out according to literature[3] to give (+)-**3** (220 mg, 89% yield); $[\alpha]_D^{28}$ +150° (*c* 0.290, $CHCl_3$). Recrystallization from ethanol furnished colorless needles; $[\alpha]_D^{28}$ +149° (*c* 0.363, $CHCl_3$) (lit,[3] $[\alpha]_D$ +151.86° ($CHCl_3$)); mp 218—219°C; Anal. ($C_{17}H_{12}O_2$) C, H.

(−)-2,2′-Spirobiindan-1,1′-dione (3). Oxidation of (−)-**1**, $[\alpha]_D$ −15.2°, (100 mg, 0.396 mmol) with 8N Jones reagent gave (−)-**3** (74 mg, 75% yield); $[\alpha]_D^{24}$ −147° (*c* 0.339, $CHCl_3$); mp 219—220°C; Found: C, 82.18; H, 4.85%. Calcd for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87%.

(+)-trans,trans-2,2′-Spirobiindan-1,1′-diol (1). (+)-Diketone **3**, $[\alpha]_D$ +150°, (808 mg, 3.26 mmol) was reduced with $LiAlH(OBu^t)_3$ (3.31 g, 13.0 mmol) in dry THF (75 mL) by the same manner as described for (±)-**1** to give (+)-**1** (756 mg, 92% yield); $[\alpha]_D^{26}$ +15.0° (*c* 0.353, THF); mp 233—234°C; Found: C, 80.88; H, 6.37%. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39%.

(+)-(1S,5R,22R)-3,4:23,24-Dibenzo-6,9,12,15,18,21-hexaoxatricyclo[20.3.0.0^{1,5}]pentacosa-3,23-diene (6). To a boiling suspension of NaH (150 mg, 6.25 mmol) in dry THF (40 mL) was added a solution of (+)-**1** (528 mg, 2.00 mmol) and pentaethylene glycol ditosylate (1.15 g, 2.22 mmol) in dry THF (70 mL) dropwise over an 8 h period under N_2. The reaction mixture was refluxed for further 16 h under N_2, cooled in an ice-bath, and quenched with water (2 mL). After a usual workup, the crude product was chromatographed on alumina (benzene eluent) to give a solid which was recrystallized from hexane to furnish (+)-**6** (625 mg, 69% yield); $[\alpha]_D^{27}$ +45.3° (*c* 0.371, $CHCl_3$); mp 101—102°C; Found: C, 71.20; H, 7.51%. Calcd for $C_{27}H_{34}O_6$: C, 71.34 H, 7.54%.

(+)-(1S,5R,19R)-3,4:20,21-Dibenzo-6,9,12,15,18-pentaoxatricycylo[17.3.0.0^{1,5}]docosa-3,20-diene (7). A procedure similar to that for **6** using (+)-**1** (510 mg, 2.02 mmol) and tetraethylene glycol ditosylate (1.02 g, 2.03 mmol) gave (+)-**7** (274 mg, 35% yield) as colorless crystals from hexane; $[\alpha]_D^{25}$ +81.3° (*c* 0.200, $CHCl_3$); mp 106°C; Found: C, 73.15; H, 7.44%. Calcd for $C_{25}H_{30}O_5$: C, 73.14; H, 7.37%.

(+)-(1S,5S,22R)-3,4:23,24-Dibenzo-6,9,12,15,18,21-hexaoxatricyclo[20.3.0.0^{1,5}]pentacosa-3,23-diene (8). Condensation of (+)-**2** (816 mg, 3.11 mmol) with pentaethylene glycol ditosylate (1.78 g, 3.44 mmol) was carried out by the same procedure as described for **6**. The product was chromatographed on alumina (benzene eluent) to give (+)-**8** (465 mg, 33% yield) as a colorless oil; $[\alpha]_D^{27}$ +2.77° (*c* 0.433, $CHCl_3$); Found: C, 71.19; H, 7.48%. Calcd for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54%.

(−)-(1S,5S,19R)-3,4:20,21-Dibenzo-6,9,12,15,18-pentaoxatricyclo[17.3.0.0^{1,5}]docosa-3,20-diene (9). A procedure similar to that for **6** using (+)-**2** (680 mg, 2.69 mmol) and tetraethylene glycol ditosylate (1.36 g, 2.70 mmol) gave (−)-**9** (270 mg, 24% yield); $[\alpha]_D^{27}$ −23.0° (0.390, $CHCl_3$); mp 86—87°C; Found: C, 73.09; H, 7.41%. Calcd for $C_{25}H_{30}O_5$: C, 73.14; H, 7.37%.

(+)-(1R,1′R,2S)-1,1′-Bis(5-methoxy-3-oxapentyloxy)-2,2′-spirobiindan (10). After a mixture of (+)-**1** (400 mg, 1.58 mmol), NaH (150 mg, 6.25 mmol), and DMF (30 mL) was stirred at 30°C for 2 h, to the mixture was added a solution of Methyl Carbitol tosylate (960 mg, 3.49 mmol) in DMF (20 mL). The mixture was stirred at 45°C for 24 h under N_2 and quenched with water (1 mL). Workup followed by chromatography on alumina (hexane–benzene 1:1 eluent) gave (+)-**10** (440 mg, 61% yield) as a colorless oil; $[\alpha]_D^{25}$ +46.8° (*c* 0.948, $CHCl_3$); Found: C, 71.30; H, 7.89%. Calcd for $C_{27}H_{36}O_6$: C, 71.02; H, 7.95%.

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 0.005 M $CHCl_3$ solution of the host separated the inner aqueous phase (0.1 M HCl (1 M=1 mol dm^{-3})) and the outer aqueous phase (0.08 M HCl) which contained $LiPF_6$ (0.4 M) and methyl (±)-phenylglycinate hydrochloride (0.04 M). The $CHCl_3$ layer was stirred at 20°C, and transport was followed by monitoring the absorbance at 261 nm and $[\theta]_{261}$ of the inner aqueous phase.

Extraction Procedure. Aqeous solution (5 mL) of metal picrate (2.4×10^{-4} M) and a $CHCl_3$ solution (5 mL) containing the host (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 picrate was followed by monitoring the absorbance at 357 nm of the aqueous phase.

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