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Preparation of Homochiral Crown Ether containing (*S*)-1-(1-Adamantyl)ethane-1,2-diol as a Chiral Subunit and its Enantioselective Complexation with an Organic Ammonium Cation

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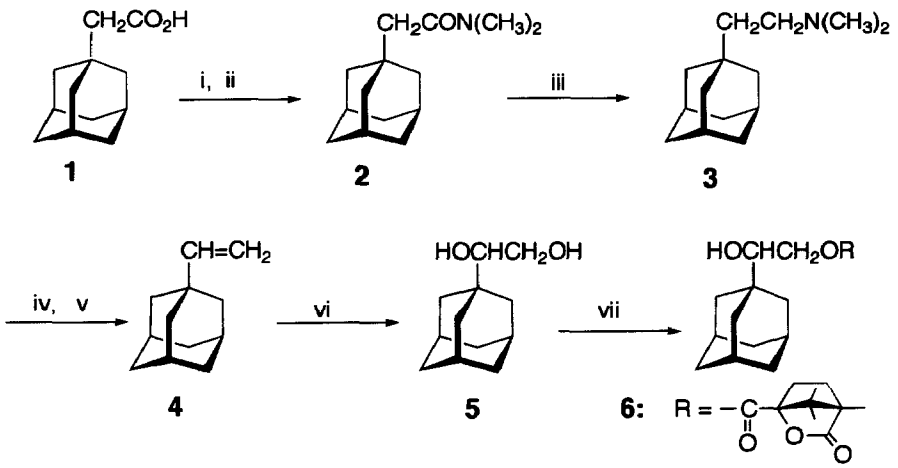
Abstract: Homochiral 1-(1-adamantyl)ethane-1,2-diol (**5**) was prepared and its absolute configuration was determined to be (*S*)-(+)-**5** by enzymatic and ^{1}H n.m.r. spectroscopic methods. Using (*S*)-(+)-**5** as a chiral subunit, the homochiral crown ether (+)-**18** was synthesized and its enantioselectivity in complexation of methionine methyl ester perchlorate was also examined by the ^{1}H n.m.r. spectroscopic method.

Various kinds of chiral crown ethers exhibiting enantiomer recognition behaviour for alkylammonium salts have been prepared.[1] For the purpose of the synthesis of these compounds, a variety of natural and synthetic optically active compounds have been employed as chiral subunits and among them chiral 1,2-ethanediol derivatives such as 3,3-dimethylbutane-1,2-diol and 1,2-diphenylethane-1,2-diol are of interest because of the bulky substituents at the stereogenic centers. Recently, the preparations of some crown ethers having tert-butyl substituents as chiral barriers and their high enantiomer recognition behaviour have been reported.[2] As the adamantyl group is bulkier than the tert-butyl group, 1-(1-adamantyl)ethane-1,2-diol (**5**) is expected to use to be an effective chiral building block of crown ethers, but no chiral host molecule having the adamantyl chiral barrier has never been prepared. The situation prompted us to prepare optically active **5** and to confirm its absolute configuration. In addition, we prepared the homochiral crown ether (+)-**18** using (*S*)-(+)-**5** as a chiral subunit and examined its enantiomer recognition behaviour.

RESULTS AND DISCUSSION

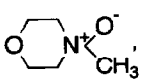
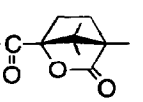
The first task is the preparation and resolution of 1-(1-adamantyl)ethane-1,2-diol (**5**). Treatment of 1-adamantylacetic acid (**1**)[3] with thionyl chloride was followed by a reaction with dimethylamine to give the amide **2**, $LiAlH_4$ reduction of which gave the amine **3** in 66% overall yield for the three-step process. Cope elimination of the N-oxide derived from **3** was carried out at 200 °C under reduced pressure to give 1-ethenyladamantane (**4**) in 78% yield. Oxidation of **4** with performic acid-NaOH and *m*-chloroperbenzoic acid-$HClO_4$ gave poor yields (16% and 42%, respectively) of (±)-**5**. In an alternative approach, treatment of **4** with osmium tetraoxide and N-methylmorpholine-N-oxide in tert-BuOH and pyridine at 70 °C provided (±)-**5** in 73% yield. Resolution of (±)-**5** was performed with (-)-camphanic acid as the resolving agent. Recrystallization of the diastereomeric esters **6** from MeOH gave (+)-**6**

(23% yield), $[\alpha]_D$ +37.1 (acetone), mp 193-195 °C, as a sparingly soluble solid, which was confirmed to be diastereomerically pure by its ^{1}H n.m.r. spectrum. The ^{1}H n.m.r. spectrum of the mixture of the diastereomers shows two double doublet signals (J = 2 and 9 Hz) due to the methine proton of the diol moiety at δ=4.95 and at δ=4.77 for (+)-**6** and (-)-**6**, respectivery, and in that of (+)-**6**, $[\alpha]_D$ +37.1, the latter signal completely disappeared. Hydrolysis of (+)-**6** provided homochiral (+)-**5**, $[\alpha]_D$ +19.2 (EtOH), mp 125-127 °C.



Scheme 1

i; $SOCl_2$ ii; $(CH_3)_2NH$ iii; $LiAlH_4$ iv; H_2O_2, MeOH v; pyrolysis

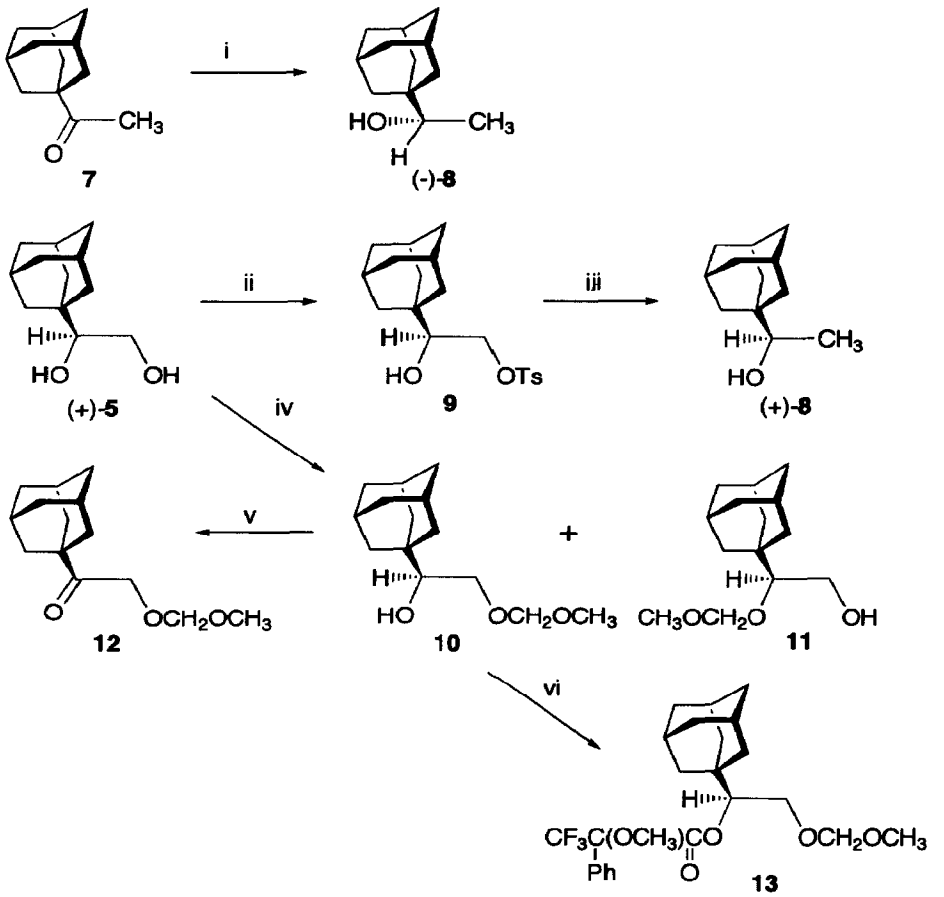
vi; OsO_4  , H_2O, t-BuOH, pyridine vii;  , pyridine

The absolute configuration of (+)-**5** was determined as follows. Enzymatic reduction of 1-acetyladamantane (**7**) with *Rhodotorula rubra*[4] gave (-)-1-(1-adamantyl)ethanol (**8**), $[\alpha]_D$ -1.21 ($CHCl_3$) (91% e.e. by HPLC analysis of its phenylcarbamate). Application of Prelog rule[5], which shows the stereochemistry of an alcohol formed preferentially by *R. rubra* mediated reduction of a corresponding ketone, to the present result allowed assignment of the *S* configuration to (-)-**8**, because it is obvious that the adamantyl substituent is larger than the methyl substituent. On the other hand, treatment of the tosylate **9**, which was prepared from (+)-**5**, with $LiAlH_4$ provided (*R*)-(+)-**8** and the chemical correlation determined the absolute configuration to be (*S*)-(+)-**5**.

Additional supportive evidence came from ^{1}H n.m.r. spectra of **13R** and **13S**. Treatment of (+)-**5** with chloromethyl methyl ether gave the mixture of methoxymethyl ethers **10** (55% yield) and **11** (13%). After separation, the structure of the major product was unambigously identified as the secondary alcohol **10** by oxidation with PCC to give the ketone **12** whose ^{1}H n.m.r. spectrum exhibited two singlet signals at δ=4.39 and 4.67 due to methylene groups. Treatment of (+)-**10** with (*R*)- and (*S*)-2-methoxy-2-phenyl-2-(trifluoromethyl)acetic acid, 4-dimethylaminopyridine, and 1,3-dicyclohexylcarbodiimide

(DCC) gave **13R** and **13S**, respectively.

Application of Mosher's method[6] to the ^{1}H n.m.r. data of **13R** and **13S** summarized in Table 1 led to the assigment of the *S* configuration to (+)-**10** and (+)-**5**.



Scheme 2

i; *Rhodotorula rubra*, phosphate buffer (pH 7.0)

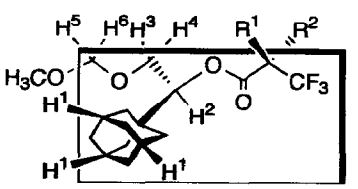
ii; TsCl, pyridine iii; $LiAlH_4$ iv; $ClCH_2OCH_3$, $NEt(i\text{-}Pr)_2$

v; PCC vi, $CF_3C(OCH_3)PhCO_2H$, 4-dimethylaminopyridine, DCC

Table 1. The selected ^{1}H n.m.r. data for **13R** and **13S** (in $CDCl_3$)

	Chemical shifts (δ)						
	H^1	H^2	H^3	H^4	H^5	H^6	CH_3
δ_S	1.93	5.02	3.85	3.62	4.66	4.54	3.34
δ_R	1.97	5.00	3.79	3.53	4.55	4.41	3.27
Δδ	-0.04	+0.02	+0.06	+0.09	+0.11	+0.13	+0.07

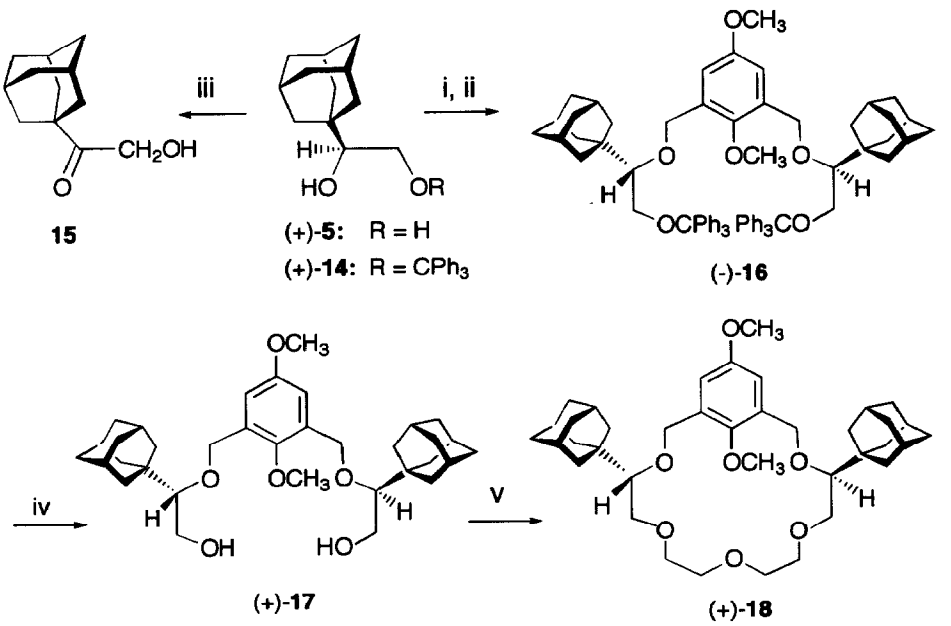
δ_S: for **13S** δ_R: for **13R** Δδ: δ_S-δ_R



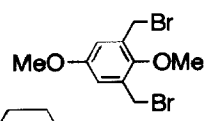
13S: R^1=Ph R^2=OCH_3

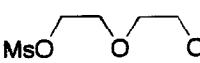
13R: R^1=OCH_3 R^2=Ph

Using (*S*)-(+)-**5** as a chiral subunit, we prepared the homochiral crown ether **18** having the adamantyl chiral barrier. After some unsuccessful attempts to regiospecifically block the primary hydroxyl group of (+)-**5**, treatment of (+)-**5** with triphenylmethyl bromide, triethylamine, and dimethylaminopyridine in CH_2Cl_2 gave exclusively the secondary alcohol (+)-**14**, $[\alpha]_D$ +20.4 ($CHCl_3$) in 80% yield, the structure of which was confirmed by oxidation with PCC to provide the ketone **15** whose IR spectrum showed ketonic carbonyl stretches. Condensation of (+)-**14** with 2,6-bis(bromomethyl)-1,4-dimethoxybenzene in the presence of NaH in dry THF gave (-)-**16**, $[\alpha]_D$ -12.5 ($CHCl_3$) in 83% yield. After treatment of (-)-**16** with *p*-toluenesulfonic acid and MeOH, the resulting diol (+)-**17**, $[\alpha]_D$ +1.48 ($CHCl_3$) was condensed with ethyleneglycol bis(methanesulfonate) in the presence of NaH and KBF_4 in dry THF to give (*S,S*)-(+)-**18**, $[\alpha]_D$ +28.6 ($CHCl_3$) in 41% yield.



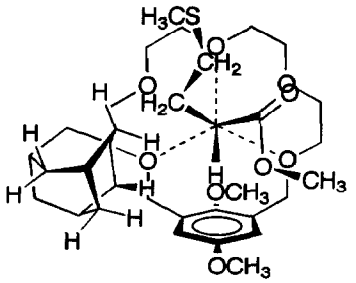
Scheme 3

i; Ph_3CBr, DMAP, Et_3N, CH_2Cl ii;  NaH, THF iii; PCC

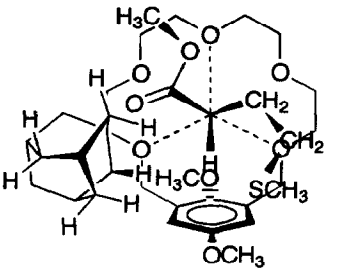
iv; TsOH, MeOH v;  NaH, KBF_3, THF

We examined enantioselectivity in complexation of (*S,S*)-(+)-**18** with methionine methyl ester perchlorate in $CDCl_3$ at 25 °C by the ^1H n.m.r. spectroscopic method. The method determined the association constant K_a (M^{-1}) value to be 1.7×10^2 for the (*S,S*)-**18** · (*R*)-guest complex and 1.2×10^2 for the (*S,S*)-**18** · (*S*)-guest complex. The ^1H n.m.r. spectra of the complexes also showed that triplet signal for the methine proton of the guest was shifted upfield by 0.95 ppm ((*S,S*)-**18** · (*R*)-guest) and by 0.77 ppm ((*S,S*)-**18** · (*S*)-guest) comparted with its respective chemical shift (δ=4.47 in $CDCl_3$) in the spectrum of methionine methyl ester perchlorate.

The CPK molecular model examination together with the spectral data suggests that the shielded methine proton of the guest occupied the narrow space over the aromatic ring of the host, which is nearly perpendicular rather than coplanar to the macrocyclic ring and functions as a rather bulky steric barrier in the complex. Thus the diastereomeric complexes are illustrated as shown in the structures **19** and **20**. We assume that a steric replusion between the phenyl barrier and the large $CH_2CH_2SCH_3$ group destabilized the (*S,S*)-**18** · (*S*)-guest complex **20**.



19



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EXPERIMENTAL SECTION

General ^{1}H-NMR spectra were obtained on a JASCO JNM-MH-100 spectrometer for solutions in $CDCl_3$ with $SiMe_4$ as internal standard and *J* Values are given in Hz. Mass spectroscopic analyses were carried out on a JEOL-DX-303-HF spectrometer. IR spectra were recorded on a Hitachi 260-10 spectrometer. Elemental analyses were carried out by Yanagimoto CHN-Corder, Type 2. Optical rotations were measured using a JASCO DIP-40 polarimeter and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. HPLC analyses were carried out on a Shimazu LC-6A chromatograph using chiral column Opti-Pak XC (waters). The culture of *R. rubra* was obtained from the Institute of Fermentation, Osaka, Japan.

N,N-Dimethyl-1-adamantylacetamide (**2**) A mixture of 1-adamantylacetic acid (**1**)[3] (7.90 g, 40.7 mmol) and thionyl chloride (12.0 g, 0.101 mol) was stirred at room temperature for 20 h and then excess of thionyl chloride was removed under reduced pressure. The residue was dissolved in dry benzene (70 cm^3) and the solution was added to a solution of dimethylamine (8.00 g, 0.177 mol) in dry benzene (70 cm^3). After stirring for 12 h, the reaction mixture was poured into ice-water, acidified with hydrochloric acid, and extracted with diethyl ether. Usual work-up gave **2** (8.51 g, 95%) as a white solid, which was used for the next reaction without further purification, IR (KBr) 2900, 2850, 1660, 1640 cm^{-1}.

N,N-Dimethyl-2-(1-adamantyl)ethylamine (**3**) A solution of **2** (8.51 g, 38.5 mmol) in dry diethyl ether (180 cm^3) was added to a suspension of $LiAlH_4$ (1.75 g, 46.2 mmol) in dry diethyl ether (70 cm^3) and then the mixture was refluxed for 17 h. After excess of aqueous NaOH solution was carefully added to the chilled reaction mixture, an inorganic solid was filtered off and the filtrate was concentrated under reduced pressure. The residue was distilled to give **3** (5.46 g, 69%), bp 122-124 °C at 5 mmHg, IR (neat film) 2900, 2850, 2820, 2750 cm^{-1}. Anal. Calc'd for $C_{14}H_{25}N$: C 81.09%, H 12.15%, N 6.76%.

Found: C 80.77%, H 12.05%, N 6.66%.

1-Ethenyladamantane (**4**) To a chilled solution of **3** (5.46 g, 26.4 mmol) in MeOH (10 cm^3) was added 30% H_2O_2 solution (13 cm^3) by portions with care and then the mixture was stirred for 30 h at room temperature. The mixture was treated with 5% Pd on carbon (100 mg) to destroy the remaining H_2O_2 and the catalyst was filtered off. After concentration under reduced pressure, the residual glass was pyrolyzed at 200 °C under reduced pressure until effusion of a liquid was ceased. The product was washed with 5% hydrochloric acid, saturated $NaHCO_3$, and water, and dried ($MgSO_4$). Distillation of the product gave **4** (3.35 g, 78%), bp 102-103 °C at 30 mmHg, IR (neat film) 3080, 2900, 2850, 1640, 1000, 910 cm^{-1}; δ_H(270 MHz; $CDCl_3$) 1.54~1.76 (12H, adamantyl CH_2), 1.99 (3H, br s, adamantyl CH), 4.84 (1H, d, *J* 11, CH=), 4.86 (1H, d, *J* 17.5, CH=), 5.71 (1H, dd, *J* 11 and 17.5, CH=). Anal. Calc'd for $C_{12}H_{18}$: C 88.82%, H 11.18%. Found: C 88.65%, H 11.01%.

1-Adamantylethane-1,2-diol (**5**) A solution of osmium tetraacetate (90 mg, 0.354 mmol) in t-BuOH (30 cm^3) was added to a mixture of **4** (19.1 g, 0.118 mol), N-methylmorpholine-N-oxide (22.3 g, 0.165 mol), pyridine (8 cm^3), t-BuOH (100 cm^3), and H_2O (60 cm^3) and the mixture was heated at 70 °C for 27 h under nitrogen atomosphere. To the mixture was then added $Na_2S_2O_4$ (1.0 g) and H_2O (25 cm^3) and the reaction mixture was extracted with ethyl acetate. After usual work-up, evaporation of the solvent gave a solid, which was recrystallized from hexane to give **5** (17.0 g, 73%), mp 128-130 °C, IR (KBr) 3300, 2900, 2850, 1090, 1065, 1055, 1030 cm^{-1}; δ_H(270 MHz; $CDCl_3$) Anal. Calc'd for $C_{12}H_{20}O_2$: C 73.43%, H 10.27%. Found: C 73.35%, H 10.20%.

Resolution of (±)-1-Adamantylethane-1,2-diol (**5**) (-)-(1*S*)-Camphanic chloride (17.0 g, 78.4 mmol) was added to a solution of (±)-**5** (7.00 g, 35.7 mmol) in pyridine (30 cm^3) with ice-cooling by portions. After stirring for 12 h at room temperature, the reaction mixture was poured into ice-water and extracted with CH_2Cl_2. The extract was washed with 5% hydrochloric acid, aqueous $NaHCO_3$, and water, and dried ($MgSO_4$). Evaporation of the solvent gave a solid (15.6 g, 79%), $[\alpha]_D^{23}$ -2.69 (c 1.04, acetone), which was recrystallized from MeOH three times to give (+)-**6** (4.61 g, 23%), $[\alpha]_D^{24}$ +37.1 (c 0.85, acetone, >99% d.e.), m.p. 193~195 °C, IR (KBr) 2960, 2910, 2850, 1780, 1750, 1740 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 0.90~1.15 (18H, m), 1.50~1.80 (15H, m), 1.82~2.20 (7H, m), 2.30~2.50 (2H, m), 4.12 (1H, dd, *J* 9 and12, CH_2), 4.77 (1H, dd, *J* 2 and12, CH_2), 4.95 (1H, dd, *J* 2 and 9, CH). Anal. Calc'd for $C_{32}H_{44}O_8$: C, 69.04%; H, 7.94%. Found: C, 68.65%; H, 7.93%.

A solution of (+)-**6** (4.59 g, 8.25 mmol) in 5% KOH solution (80 cm^3, H_2O:MeOH, 1:1) was stirred for 3.5 h at 65 °C and then concentrated. The residue was extracted with diethyl ether and worked-up in the usual way. Evaporation of the solvent followed by recrystallization from hexane gave (+)-**5** (1.56 g, 95%), $[\alpha]_D^{22}$ +19.2 (c 1.00, EtOH), m.p. 125~127 °C, IR (KBr) 3350, 2900, 2850, 1090, 1065, 1055, 1030 cm^{-1}; δ_H(270 MHz; $CDCl_3$) 1.52~1.88 (12H, m, CH_2), 1.99 (3H, s, CH), 3.23 (1H, dd, *J* 3 and 9, CH_2), 3.56 (1H, dd, *J* 9 and 11, CH), 3.75 (1H, dd, *J* 3 and 11, CH_2). Anal. Calc'd for $C_{12}H_{20}O_2$: C, 73.43%; H, 10.27%. Found: C, 73.40%; H, 10.22%.

Reduction of 1-Acetyladamantane (**7**) *with Rhodotorura rubra* The grown mycelium was collected,

washed with sterilized water, and suspended again in phosphate buffer solution (pH 7.0) (100 cm^3). To the solution was added **7** (100 mg, 0.56 mmol) and 95% EtOH (2 cm^3) and the whole was stirred for 15 days at 30 °C. After the solid was filtered off, the filtrate was extracted with ethyl acetate. The extract was washed with water and concentrated. The products were separated on a preparative TLC (Silica gel, hexane:diethyl ether, 1:1) to give **8** (35 mg, 35%), $[\alpha]_D^{22}$ -1.21 (c 0.98, $CHCl_3$) (91% e.e. by HPLC of its phenylcarbamate); IR (KBr) 3340, 2900, 2850, 1070 cm^{-1}.

Conversion of (+)-**5** *into 1-(1-Adamantyl)ethanol* (**8**) To a solution of **5**, $[\alpha]_D^{22}$ +7.96 (46% e.e.) (200 mg, 1.02 mmol) in pyridine (1 cm^3) was added *p*-toluenesulfonyl chloride (233 mg, 1.22 mmol) and the mixture was stirred for 12 h with ice-cooling. After pouring into ice-water, the reaction mixture was extracted with diethyl ether and usual work-up gave **9** (345 mg), which was dissolved in dry diethyl ether (10 cm^3). The whole was added to a suspension of $LiAlH_4$ (77 mg, 2.03 mmol) in dry diethyl ether (15 cm^3) and then the mixture was refluxed for 6 h. After saturated NH_4Cl was carefully added to the chilled reaction mixture, an inorganic solid was filtered off and the filtrate was concentrated. Silica gel chromatography of the product gave **8** (hexane:diethyl ether, 4:1) (119 mg, 65%), $[\alpha]_D^{22}$ +0.60 (c 0.99, $CHCl_3$)

1-(1-Adamantyl)-2-methoxymethoxyethanol (**10**) To a mixture of **5**, $[\alpha]_D$ +37.1, (3.00 g, 15.3 mmol), diisopropylethylamine (2.20 g, 16.8 mmol), and $CHCl_3$ (100 cm^3) was added chloromethyl methyl ether (1.40 g, 16.8 mmol) and then the mixture was stirred at 50 °C for 30 h. After dilution with diethyl ether, the mixture was washed with water and dried ($MgSO_4$). Removal of the solvent followed by silica gel chromatography of the residue gave 1-(1-adamantyl)-2-methoxymethoxyethanol (**10**) (hexane:diethyl ether, 7:3) (2.03 g, 55%) as a colourless oil and 2-(1-adamantyl)-2-methoxymethoxyethanol (**11**) (hexane:diethyl ether 7:3) (460 mg, 13%) as a colourless oil.

For **10**: $[\alpha]_D^{22}$ +15.7 (c 1.25, $CHCl_3$), IR (neat film) 3440, 2880, 2840, 1140, 1110, 1030 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 1.55~1.75 (12H, m, CH_2), 1.98 (3H, br s, CH), 2.28 (1H, br s, OH), 3.29 (1H, dd, *J* 9 and 3 CH), 3.38 (3H, s, OCH_3), 3.45 (1H, dd, *J* 9 and 10, CH_2O), 3.75 (1H, dd, *J* 3 and 10, CH_2O), 4.65 (1H, d, *J* 7, OCH_2O), 4.68 (1H, d, *J* 7, OCH_2O). Anal. Calc'd for $C_{14}H_{24}O_3$ C, 69.96%; H, 10.07%. Found C, 69.65%; H, 9.98%.

For **11**: IR (neat film) 3460, 2880, 2840, 1150, 1110, 1020 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 1.55~1.75 (12H, m, CH_2), 1.98 (3H, br s, CH), 2.96 (1H, dd, *J* 2 and 9, OH), 3.36 (1H, dd, *J* 2 and 10 CH), 3.43 (3H, s, OCH_3), 3.54 (1H, ddd, *J* 2, 9 and 13, CH_2O), 3.74 (1H, ddd, *J* 2, 10, and 13, CH_2O), 4.58 (1H, d, *J* 7, OCH_2O), 4.78 (1H, d, *J* 7, OCH_2O).

Oxidation of 1-(1-Adamantyl)-2-methoxymethoxyethanol (**10**) To a solution of pyridinium chlorochromate (PCC) (192 mg, 0.891 mmol) in CH_2Cl_2 (10 cm^3) was added a solution of **10** (107 mg, 0.445 mmol) in CH_2Cl_2 (5 cm^3) and then the mixture was stirred for 12 h at room temperature. Silica gel chromatography of the reaction mixture gave **12** (hexane:diethyl ether, 4 : 1) (57 mg, 54%) as a colourless oil, IR (neat film) 1710 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 1.60~1.90 (12H, m, CH_2), 2.06 (3H, s, CH), 3.38 (3H, s, CH_3), 4.39 (2H, s, CH_2), 4.67 (2H, s CH_2); HRMS Calc'd for $C_{14}H_{23}O_3$ 239.1647, Found 239.1631.

(S)-MTPA ester **13S** To a solution of (*S*)-2-methoxy-2-phenyl-2-trifluoromethylacetyl chloride (23 mg, 97 μmol), 4-dimethylaminopyridine (12 mg, 97μmol), DCC (29 mg, 140 μmol), and CH_2Cl_2 (1 cm^3) was added a solution of (+)-(**10**) (10 mg, 42 μmol) in CH_2Cl_2 (1 cm^3) and then the mixture was stirred at room temperature for 12 h. A preparative TLC (silica gel, hexane:benzene, 1:1) of the reaction mixture gave **13S** (8 mg, 42%), δ_H(270 MHz; $CDCl_3$) 1.370-1.800 (12H, m, CH_2), 1.933 (3H, br s, adamantyl CH), 3.337 (3H, s, OCH_3), 3.600 (3H, s, OCH_3 (MTPA)), 3.621 (1H, dd, *J* 9 and 11, OCH_2), 3.846 (1H, dd, *J* 3 and 11, OCH_2), 4.539 (1H, d, *J* 7, OCH_2O), 4.657 (1H, d, *J* 7, OCH_2O), 5.023 (1H, dd, *J* 3 and 9, OCH), 7.32-7.68 (5H, m, aromatic CH).
For (*R*)-MTPA ester **13R**; δ_H(270 MHz; $CDCl_3$) 1.400-1.900 (12H, m, CH_2), 1.973 (3H, br s, adamantyl CH), 3.266 (3H, s, OCH_3), 3.528 (1H, dd, *J* 9 and 11, OCH_2), 3.550 (3H, s, OCH_3 (MTPA)), 3.792 (1H, dd, *J* 3 and 11, OCH_2), 4.414 (1H, d, *J* 7, OCH_2O), 4.552 (1H, d, *J* 7, OCH_2O), 5.007 (1H, dd, *J* 3 and 9, OCH), 7.38-7.60 (5H, m, aromatic CH).

(S)-(+)-1-(1-Adamantyl)-2-triphenylmethyloxyethanol **(14)** To a solution of (+)-**5** (1.00 g, 5.09 mmol) in CH_2Cl_2 (10 cm^3) was added a mixture of triphenyl bromide (3.30 g, 10.2 mmol), triethylamine (620 mg, 6.11 mmol), and 4-dimethylaminopyridine (31 mg, 0.255 mmol) and then the mixture was stirred for 12 h at room temperature. After diluting with diethyl ether, the reaction mixture was washed with water and dried ($MgSO_4$). The solvent was removed and the residue was chromatographed on silica gel to give **14** (hexane:diethyl ether, 95:5) (1.76 g, 79%), mp 138-139 °C, $[\alpha]_D^{23}$ +20.4 (c 0.93, $CHCl_3$); IR (KBr) 3550, 3050, 2900, 2850, 1600, 760 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 1.40~1.80 (12H, m, CH_2), 1.90 (3H, br s, CH), 2.34 (1H, d, *J* 3, OH), 3.10~3.40 (3H, m, CH_2 and CH), 7.06~7.54 (15H, m, aromatic CH). Anal. Calc'd for $C_{31}H_{34}O_2$ C, 84.89%; H, 7.81%. Found: C, 84.82%; H, 7.85%.

1-Adamantyl triphenylmethoxymethyl ketone **(15)** To a mixture of PCC (192 mg, 0.891 mmol) in CH_2Cl_2 (10 cm^3) was added a solution of the (±)-**14** (200 mg, 0.445 mmol), prepared from (±)-**5** by the same manner described above, in CH_2Cl_2 (5 cm^3) and the mixture was stirred for 12 h at room temperature. Silica gel chromatography of the reaction mixture gave **15** (hexane) (104 mg, 54%) as a colourless oil, IR (neat film) 1710, 1600, 760 cm^{-1}. Anal. Calc'd for $C_{31}H_{32}O_2$ requires C, 85.28%; H, 7.22%. Found: C, 85.20%; H, 7.22%.

(-)-1,3-Bis[1'-(1-adamantyl)-2'-(triphenylmethyloxyethoxymethyl]-2,5-dimethoxybenzene **(16)** A solution of (+)-**14** (2.30 g, 5.24 mmol) in dry THF (30 cm^3) was added to a suspension of NaH (435 mg, 9.06 mmol) in dry THF (30 cm^3) and then the mixture was refluxed for 10h. To the reaction mixture was added a solution of 1,4-dimethoxy-2,6-bis(bromomethyl)benzene (772 mg, 2.38 mmol) in dry THF (50 cm^3) at room temperature and then the mixture was refluxed for 20 h. After decomposition of excess NaH and removal of the solvent, the residue was dissolved in CH_2Cl_2, washed with water, and dried ($MgSO_4$). Silica gel chromatography of the product gave **16** (hexane:diethyl ether, 95:5) (2.05 g, 83%) as a colourless glass, $[\alpha]_D^{24}$ -12.5 (c 0.50, $CHCl_3$); δ_H (270 MHz; $CDCl_3$) 1.40~1.70 (24H, m, adamantyl CH_2), 1.86 (6H, br s, adamantyl CH), 3.10~3.50 (6H, m, CH_2 and CH), 3.63 (3H, s, CH_3O), 3.70 (3H, s, CH_3O), 4.60 (2H, d, *J* 15, benzylic CH_2), 5.05 (2H, d, *J* 15, benzylic CH_2), 7.04 (2H, s, aromatic CH), 7.15~7.60 (30H, m, aromatic CH).

(+)-1,3-Bis[1'-(1-adamantyl)-2'-hydroxyethoxymethyl]-2,5-dimethoxybenzene (**17**) A mixture of (-)-**16** (2.00 g, 1.92 mmol), *p*-toluenesulfonic acid monohydrate (1.46 g, 7.70 mmol), and MeOH (100 cm^3) was stirred for 12 h at room temperature. After addition of $NaHCO_3$, the reaction mixture was concentrated under reduced pressure and extracted with $CHCl_3$. The extract was worked up in the usual way and the product was chromatographed on silica gel to give **17** (diethyl ether) (788 mg, 74%) as a colourless glass, $[\alpha]_D^{24}$ +1.48 (c 0.52, $CHCl_3$); IR (KBr) 3400, 2900, 2850, 1100, 1060, 1020 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 1.50~1.80 (24H, m, adamantyl CH_2), 1.97 (6H, br s, adamantyl CH), 3.04 (2H, dd, *J* 4 and 7, CH), 3.68 (2H, dd, *J* 7 and 11, CH_2), 3.77 (3H, s, CH_3O), 3.78 (2H, dd, *J* 4 and 11, CH_2), 3.81 (3H, s, CH_3O), 4.61 (2H, d, *J* 15, benzylic CH_2), 4.74 (2H, d, *J* 11, benzylic CH_2), 6.96 (2H, s, aromatic CH), 7.15~7.60 (30H, m, aromatic CH); HRMS Calc'd for $C_{34}H_{50}O_6$. 554.3608, Found 554.3595.

(S,S)-(+)-Crown Ether **18** A solution of (+)-**17**, (750 mg, 1.35 mmol) and diethyleneglycol bis(methanesulfonate) (390 mg, 1.49 mmol) in dry THF (100 cm^3) was slowly added to a boiling mixture of NaH (195 mg, 4.06 mmol), KBF_4 (170 mg, 1.35 mmol) and dry THF (30 cm^3) over a 10 h period and the reaction mixture was then refluxed for further 32 h. After decomposition of excess of NaH with water followed by concentration under reduced pressure, the residue was dissolved in CH_2Cl_2. The solution was worked-up in the usual way. Chromatography of the product on silica gel gave (+)-**18** (hexane:diethyl ether, 2:1) (350 mg, 41%) as a colourless glass, $[\alpha]_D^{22}$ +28.6 (c 0.99, $CHCl_3$); IR (KBr) 2900, 2850, 1110 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 1.50~1.80 (24H, m, adamantyl CH_2), 1.97 (6H, br s, adamantyl CH), 3.07 (2H, dd, *J* 2 and 7, CH), 3.30~3.50 (10H, m, CH_2), 3.61 (2H, dd, *J* 2 and 11, CH_2); 3.70 (3H, s, OCH_3); 3.81 (3H, s, OCH_3); 4.65 (2H, d, *J* 13, benzylic CH_2); 4.88 (2H, d, *J* 13, benzylic CH_2); 6.97 (2H, s, aromatic CH); MS *m/z* 624 (M^+). Anal. Calc'd for $C_{38}H_{56}O_7$: C, 73.04%; H, 9.03%. Found: C, 72.80%; H, 8.90%.

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