Temperature dependent inversion of enantiomer selectivity in the complexation of optically active azophenolic crown ethers containing alkyl substituents as chiral barriers with chiral amines[1]

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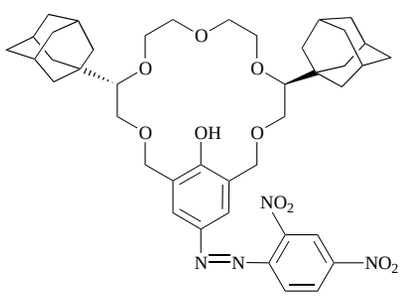
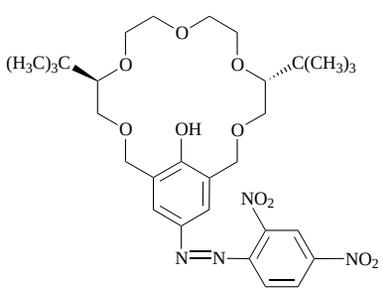
Azophenolic crown ethers (*S*,*S*)-1, (*R*,*R*)-2 and (*S*,*S*)-3 have been prepared in enantiomerically pure forms by using (*S*)-1-(1′-adamantyl)ethane-1,2-diol, (*R*)-3,3-dimethylbutane-1,2-diol and (*S*)-propane-1,2-diol, respectively, as chiral subunits, and the association constants for their complexes with chiral amines have been determined by ^{1}H NMR or UV–VIS spectroscopic methods at various temperatures. The enantiomer selectivities of crown ethers (*S*,*S*)-1 and (*R*,*R*)-2 in complexation with 2-aminopropan-1-ol are reversed at *ca.* 6 °C and increase with increasing temperature above the isoenantioselective temperature.

Enantiomer recognition has been widely studied in various types of chemical and biochemical transformations.[2] While it is the generally accepted view that lower temperatures enhance enantiomer discrimination in chiral processes, a few papers have reported that the enantiomer selectivity of a chiral process increased with increasing temperature; the enantiospecificity ratio of alcohol dehydrogenase-catalysed oxidation of secondary alcohols increased with increasing temperature above the 'racemic temperature',[3] the enantiomeric purities of compounds resolved by GLC using a chiral stationary phase was enhanced with increasing column temperature[4] and the optical yield of photochemically induced enantiomeric isomerization improved with increasing irradiation temperature.[5] Various types of optically active crown ethers have been prepared and their enantiomer recognition behaviour in complexation with chiral guests has been well documented.[6] But as far as we know there has been no report of the temperature dependent inversion of the enantiomer selectivity in complexation of a crown ether with a chiral amine in solution. It is important to seek information on how the temperature might influence the enantiomer selectivity in complexation of crown ethers with chiral amines because temperature dependent inversion of the enantiomer selectivity in complexation is a fundamental problem for the estimation of the configuration of guest species on the basis of the enantiomer selectivity in host–guest complexation. We here describe the preparation of optically active azophenolic crown ethers (*S*,*S*)-**1**, (*R*,*R*)-**2** and (*S*,*S*)-**3** containing alkyl substituents as chiral barriers by using (*S*)-1-(1′-adamantyl)ethane-1,2-diol **6**, (*R*)-3,3-dimethylbutane-1,2-diol **8** and (*S*)-propane-1,2-diol **10**, respectively. These crown ethers also possess a phenol moiety bearing an intraannular OH group as a binding site for neutral amines and the additional 2,4-dinitrophenylazo group at its *para*-position which acts not only as a chomophore but also to enhance the binding ability towards neutral amines.[7] The enantiomer selectivity in complexation of the crown ethers **1**, **2** and **3** with chiral 2-aminoethanol derivatives in chloroform was evaluated at various temperatures to observe the temperature dependent reversal of the enantiomer selectivity in complexation of crown ethers (*S*,*S*)-**1** and (*R*,*R*)-**2** with 2-aminopropan-1-ol at *ca.* 6 °C. The thermodynamic parameters for complexation were calculated on the basis of the association constants of the complexes determined at different temperatures.



(*S*,*S*)-**1**



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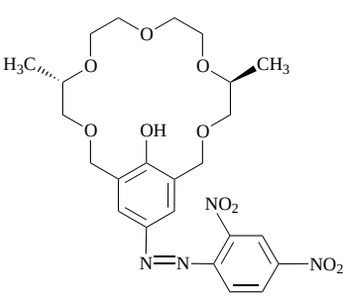
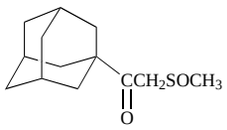


(*S*,*S*)-**3**

Results and discussion

We previously reported the preparation of the racemic diol (±)-**6** from 1-adamantylacetic acid but in rather low yield (37% overall)[8] and, therefore, it was our first task to modify the preparation of the diol (±)-**6**. Treatment of ethyl adamantane-1-carboxylate with sodium hydride and dimethyl sulfoxide (DMSO) gave compound **4**, which was reacted with acetic anhydride and sodium acetate[9] to give the compound **5**. Reduction of compound **5** with $LiAlH_4$ gave the diol (±)-**6** in 75% overall yield from ethyl adamantane-1-carboxylate. The chiral subunit (*S*)-**7**, $[\alpha]_D^{23}$ +20.8 (10^{-1} deg cm^2 g^{-1}) ($CHCl_3$), was pre-



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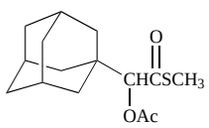

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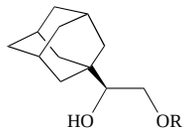
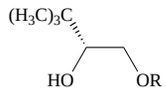
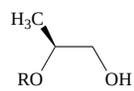


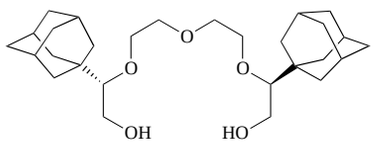
(*S*)-**6** R=H
(*S*)-**7** R=CPh$_3$



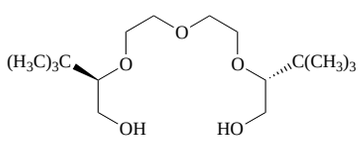
(*R*)-**8** R=H
(*R*)-**9** R=CPh$_3$



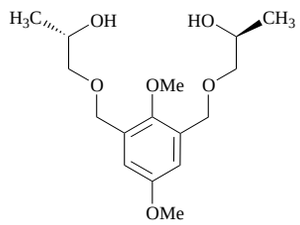
(*S*)-**10** R=H
(*S*)-**11** R=THP



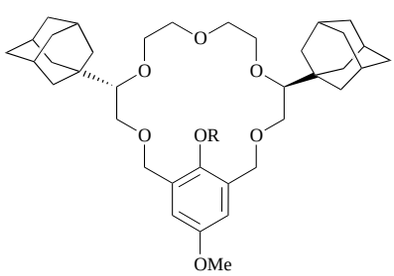
(*S*,*S*)-**12**



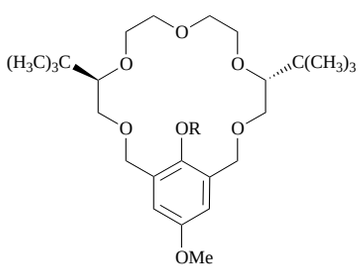
(*R*,*R*)-**13**



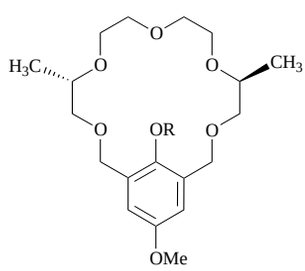
(*S*,*S*)-**14**



(*S*,*S*)-**15** R=CH$_3$
(*S*,*S*)-**16** R=H



(*R*,*R*)-**17** R=CH$_3$
(*R*,*R*)-**18** R=H



(*S*,*S*)-**19** R=CH$_3$
(*S*,*S*)-**20** R=H

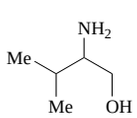
pared from the racemate (±)-**6** according to the reported procedures:[8] optical resolution of the racemate (±)-**6** using (−)-camphanic chloride as a resolving agent followed by the protection of the primary hydroxy group of the resulting diol (*S*)-**6**, $[\alpha]_D^{24}$ +18.0 (ethanol).

The preparation of the crown ethers (*S*,*S*)-**1** and (*R*,*R*)-**2** having the substituents located near the diethylene glycol bridge and the homotopic faces was carried out stepwise; chiral subunits of the same chirality were linked successively with the diethylene glycol unit and with the *m*-phenylene unit. Condensation of 2 mol equiv. of the chiral subunit (*S*)-**7** with diethylene glycol bis(toluene-*p*-sulfonate) in the presence of sodium hydride in tetrahydrofuran (THF) gave the 1,11-*O*-blocked tetraethylene glycol derivative in 74% yield, which was deprotected with methanol containing toluene-*p*-sulfonic acid to give the C_2-diol (*S*,*S*)-**12**, $[\alpha]_D^{22}$ +4.66 ($CHCl_3$), in 98% yield. High dilution condensation of the diol (*S*,*S*)-**12** with 1,3-bis(bromomethyl)-2,5-dimethoxybenzene in THF containing sodium hydride and potassium tetrafluoroboranuide gave the crown ether (*S*,*S*)-**15**, $[\alpha]_D^{19}$ +44.3 ($CHCl_3$), in 66% yield. The intraannular methyl group of the crown ether (*S*,*S*)-**15** was selectively cleaved with sodium ethanethiolate in DMF at 100 °C[10] to give the phenolic crown ether (*S*,*S*)-**16**, $[\alpha]_D^{25}$ +23.2 ($CHCl_3$), in 64% yield. Oxidation of the phenolic crown ether (*S*,*S*)-**16** with cerium(IV) ammonium nitrate (CAN) in acetonitrile gave the corresponding quinone which was immediately treated with 2,4-dinitrophenylhydrazine in a mixture of conc. H_2SO_4, ethanol and methylene dichloride to give the azophenolic crown ether (*S*,*S*)-**1** in 82% yield.

The diol (*R*)-**8**, $[\alpha]_D^{28}$ −25.3 ($CHCl_3$), which was prepared according to the procedures described in the literature[11] was reacted with triphenylmethyl chloride in the presence of triethylamine and 4-dimethylaminopyridine to give the chiral subunit (*R*)-**9**, $[\alpha]_D^{28}$ −16.5 ($CHCl_3$), in 70% yield. The C_2-diol (*R*,*R*)-**13**, $[\alpha]_D^{25}$ −2.73 ($CHCl_3$), was derived from the chiral subunit (*R*)-**9** in 28% yield by condensation with diethylene glycol bis(toluene-*p*-sulfonate) followed by deprotection. High dilution condensation of the C_2-diol (*R*,*R*)-**13** with 1,3-bis(bromomethyl)-2,5-dimethoxybenzene gave the crown ether (*R*,*R*)-**17**, $[\alpha]_D^{24}$ −27.0 ($CHCl_3$), in 48% yield. Demethylation of the crown ether (*R*,*R*)-**17** gave the phenolic crown ether (*R*,*R*)-**18** in 95% yield, which was transformed to the azophenolic crown ether (*R*,*R*)-**2** in 50% yield.

According to the published route,[12] protection of the hydroxy group followed by $LiAlH_4$ reduction, the chiral subunit (*S*)-**11** was prepared from ethyl (*S*)-lactate as a mixture of two diastereoisomers. Condensation of the chiral subunit (*S*)-**11** with 1,3-bis(bromomethyl)-2,5-dimethoxybenzene followed by deprotection with ethanol and pyridinium toluene-*p*-sulfonate gave the C_2-diol (*S*,*S*)-**14**, $[\alpha]_D^{20}$ +19.2 ($CHCl_3$), in 55% yield. Ring closure of the diol (*S*,*S*)-**14** with diethylene glycol bis(toluene-*p*-sulfonate) under high dilution conditions gave the crown ether (*S*,*S*)-**19**, $[\alpha]_D^{24}$ +22.1 ($CHCl_3$), in 50% yield, which was transformed to the azophenolic crown ether (*S*,*S*)-**3** in 72% yield *via* the phenolic crown ether (*S*,*S*)-**20**.

Enantiomer recognition of the crown ethers (*S*,*S*)-**1**, (*R*,*R*)-**2** and (*S*,*S*)-**3** towards chiral amines: 2-amino-3-methylbutan-1-ol **21**, 2-aminopropan-1-ol **22** and 1-aminopropan-2-ol **23** was



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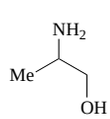

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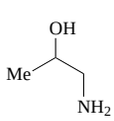

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evaluated at various temperatures. Association constants for complexes of (*S*,*S*)-**1** with **21**, **22** and **23**, (*R*,*R*)-**2** with **21**, **22** and **23** and (*S*,*S*)-**3** with **21** were calculated by the non-linear least-squares method on the basis of the ^{1}H NMR spectral data in $CDCl_3$. As association constants for complexes of (*S*,*S*)-**3** with **22** and **23** were so large that it was difficult to get accurate data at lower temperature by ^{1}H NMR titration, they

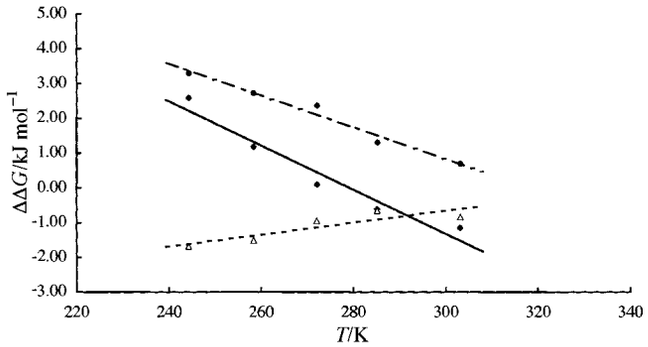


Fig. 1 Temperature dependence of $\Delta\Delta G$ ($\Delta G_S - \Delta G_R$) for the complexation of crown ether (*S*,*S*)-**1** with amines in chloroform: 2-amino-3-methylbutan-1-ol (△), 2-aminopropan-1-ol (◆) and 1-aminopropan-2-ol (●)

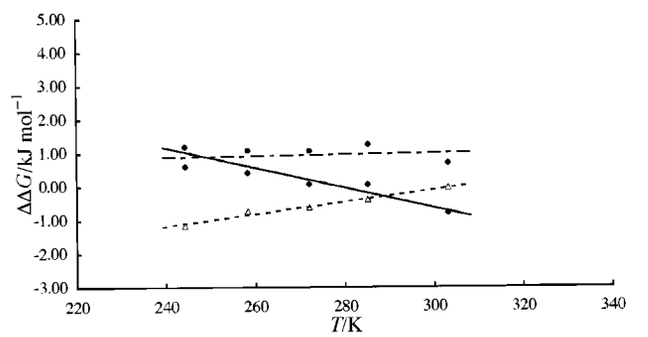


Fig. 2 Temperature dependence of $\Delta\Delta G$ ($\Delta G_S - \Delta G_R$) for the complexation of crown ether (*S*,*S*)-**2** with amines in chloroform: 2-amino-3-methylbutan-1-ol (△), 2-aminopropan-1-ol (◆) and 1-aminopropan-2-ol (●)

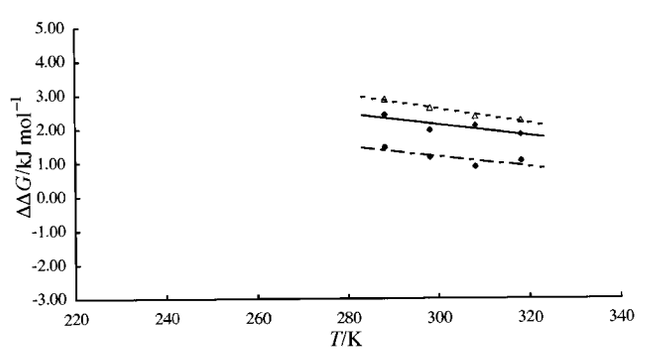


Fig. 3 Temperature dependence of $\Delta\Delta G$ ($\Delta G_S - \Delta G_R$) for the complexation of crown ether (*S*,*S*)-**3** with amines in chloroform: 2-amino-3-methylbutan-1-ol (△), 2-aminopropan-1-ol (◆) and 1-aminopropan-2-ol (●)

were determined by the Rose–Drago method[13] on the basis of the absorption in the UV–VIS spectrum in $CHCl_3$. The observed K_a-values of the complexes and the thermodynamic parameters for complexation calculated on the basis of K_a-values determined at different temperatures are summarized in Tables 1 and 2. The results show that the association constants of all complexes increased with decreasing temperature but that K_a^R/K_a^S values were influenced by changes in temperature.

In Figs. 1, 2 and 3 are plotted $\Delta\Delta G$ values ($\Delta G_S - \Delta G_R$) of complexation of the crown ethers (*S*,*S*)-**1**, (*S*,*S*)-**2** and (*S*,*S*)-**3**, respectively, with the amines **21**, **22** and **23** as a function of temperature. The most important features shown in Figs. 1 and 2 are that the sign of $\Delta\Delta G$ values for the complexation of the crown ethers (*S*,*S*)-**1** and (*S*,*S*)-**2** with **22** reverses at *ca.* 6 °C; the isoenantioselective temperature (T_{iso}) and the *S*-selectivity towards **22** increased with increasing temperature above T_{iso}. The enantiomer selectivities in complexation of the other combinations of crown ethers and amines, except for that of the crown ether (*S*,*S*)-**2** and **23**, showed also an unambiguous temperature dependent enantiomer selectivity; reversal of the selectivity was not observed within the experimental temperature range because of high T_{iso} values which were estimated by calculation from ΔH and ΔS values and are listed in Tables 1 and 2.

Next, on the basis of CPK molecular models, we give an explanation for the enantiomer selectivities observed below T_{iso} which are governed by $-\Delta_{R,S}\Delta H$ in terms of steric interactions between ligands of the amine and the steric barriers of the crown ether in the complex. For predicting the geometry of the complex of a phenolic crown ether with a 2-aminoethanol derivative, we use as a working hypothesis[14] that the phenolate oxygen atom necessarily serves as a binding site for amines and the hydroxymethyl group of 2-aminoethanol derivatives occupies the area near the phenolate oxygen atom to form the fourth hydrogen bond between the phenolate oxygen atom and the hydroxy group of the guest. Judging from CPK molecular models and the observed enantiomer selectivities, we infer that the pseudo-equatorial substituent at C-5 (open circle in the geometries) makes the methylene group at C-4 and the methine group at C-5 an effective steric barrier on the β-face of the complex: 'the ethylenoxy barrier' (shaded ellipse in the geometries **24**–**29**).

Figs. 1, 2 and 3 show that the crown ethers (*S*,*S*)-**1** and (*S*,*S*)-**2** having bulky substituents showed better complementarity to (*S*)-**21** than to (*R*)-**21** but the crown ether (*S*,*S*)-**3** having the small methyl substituents showed the reverse complementarity below T_{iso}. The predicted geometries **24** and **25** are illustrated for the complexes of the (*S*,*S*)-crown ethers **1**, **2** and **3** with (*R*)-**21** and with (*S*)-**21**, respectively, on the basis of CPK molecular models of the complexes. The *S*-selectivity of the crown ethers (*S*,*S*)-**1** and (*S*,*S*)-**2** towards **21** is rationalized in terms of steric repulsion between the bulky substituent and the bulky isopropyl group destabilizing the (*S*,*S*)-crown ether–(*R*)-**21** complex with the geometry **24** (shaded circle indicates the 1-adamantyl group or the *tert*-butyl group). As both the chiral substituent barrier and the ligand of the amine are bulky, the crown ethers **1** and **2** recognize **21** by the chiral substituent barrier. On the other hand, the steric interaction between the small substituent and the ligand of the amine is not dominant and the crown ether **3** recognizes **21** by 'the ethylenoxy barrier'; steric repulsion between 'the ethylenoxy barrier' and the isopropyl group made the (*S*,*S*)-crown ether–(*S*)-**21** complex with the geometry **25** (shaded circle indicates the methyl group) less stable than the diastereoisomeric complex.

Analogously, it is assumed that the crown ethers **1**, **2** and **3** recognize **22** by 'the ethylenoxy barrier' because the steric interaction between the small ligand of the amine and the substituent of the crown ether is not dominant. The *R*-selectivity of all (*S*,*S*)-crown ethers towards **22** observed below T_{iso} is rationalized from the geometries **26** and **27** which are illustrated for the stable (*S*,*S*)-crown ether–(*R*)-**22** complex and the less stable (*S*,*S*)-crown ether–(*S*)-**22** complex, respectively. The *S*-selectivity of the (*S*,*S*)-crown ethers **1** and **2** towards **22** observed above T_{iso} is not explicable.

The geometries **28** and **29** are illustrated for the complexes of the (*S*,*S*)-crown ethers with (*R*)-**23** and with (*S*)-**23**, respectively. The *R*-selectivity of all (*S*,*S*)-crown ethers towards **23** is assumed to be due to a steric repulsion between the methyl group of the chiral centre of **23** and the substituent of the crown ether making the (*S*,*S*)-crown ether–(*S*)-**23** complex with the geometry **29** less stable than the diastereoisomeric complex with the geometry **28**.

An inversion of the sign of enantiomer selectivity dependent upon temperature is predictable since the enthalpy change and the entropy change compensate each other, as can be seen in Tables 1 and 2, and the entropy change contributes to the stability of the complex.[15] The previous failure to observe such a

Table 1 Association constants for the complexes and thermodynamic parameters for complexation of crown ethers (*S*,*S*)-**1** and (*R*,*R*)-**2**

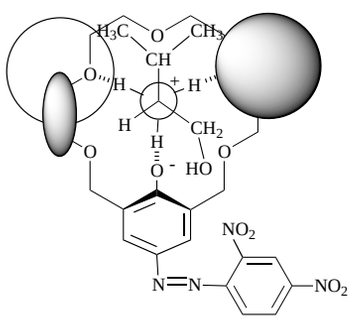
Crown ether	Amine	K_a/M^{-1}							
		−30 °C	−15 °C	0 °C	15 °C	30 °C	ΔH/kJ mol^{-1}	ΔS/J K^{-1} mol^{-1}	T_{iso}[a]/°C
(*S*,*S*)-**1**	(*R*)-**21**	(7.90 ± 1.69) × 10^3	(1.74 ± 0.10) × 10^3	(4.68 ± 0.20) × 10^2	(1.64 ± 0.04) × 10^2	(4.77 ± 0.16) × 10^1	(−5.35 ± 0.26) × 10^1	(−1.45 ± 0.11) × 10^2	
(*S*,*S*)-**1**	(*S*)-**21**	(1.82 ± 0.98) × 10^4	(3.51 ± 0.48) × 10^3	(7.11 ± 0.20) × 10^2	(2.17 ± 0.06) × 10^2	(6.66 ± 0.19) × 10^1	(−5.96 ± 0.62) × 10^1	(−1.63 ± 0.26) × 10^2	62.1
(*R*,*R*)-**2**	(*R*)-**21**	(1.53 ± 0.48) × 10^4	(2.82 ± 0.21) × 10^3	(5.93 ± 0.32) × 10^2	(1.60 ± 0.07) × 10^2	(4.38 ± 0.08) × 10^1	(−6.20 ± 0.45) × 10^1	(−1.74 ± 0.18) × 10^2	
(*R*,*R*)-**2**	(*S*)-**21**	(8.64 ± 1.58) × 10^3	(2.01 ± 0.09) × 10^3	(4.49 ± 0.24) × 10^2	(1.35 ± 0.04) × 10^2	(4.31 ± 0.32) × 10^1	(−5.66 ± 0.49) × 10^1	(−1.56 ± 0.20) × 10^2	32.5
(*S*,*S*)-**1**	(*R*)-**22**	(2.40 ± 1.05) × 10^4	(4.32 ± 0.50) × 10^3	(9.56 ± 0.98) × 10^2	(2.19 ± 0.12) × 10^2	(4.38 ± 0.81) × 10^1	(−6.63 ± 0.23) × 10^1	(−1.87 ± 0.09) × 10^2	
(*S*,*S*)-**1**	(*S*)-**22**	(6.74 ± 1.43) × 10^3	(2.49 ± 0.24) × 10^3	(9.17 ± 0.54) × 10^2	(2.84 ± 0.06) × 10^2	(6.94 ± 0.41) × 10^1	(−4.80 ± 0.79) × 10^1	(−1.22 ± 0.33) × 10^2	5.0
(*R*,*R*)-**2**	(*R*)-**22**	(7.49 ± 1.27) × 10^3	(2.24 ± 0.12) × 10^3	(7.63 ± 0.35) × 10^2	(2.35 ± 0.06) × 10^2	(8.00 ± 0.43) × 10^1	(−4.81 ± 0.34) × 10^1	(−1.22 ± 0.14) × 10^2	
(*R*,*R*)-**2**	(*S*)-**22**	(1.34 ± 0.74) × 10^4	(2.70 ± 0.26) × 10^3	(7.80 ± 0.53) × 10^2	(2.41 ± 0.15) × 10^2	(5.83 ± 0.08) × 10^1	(−5.66 ± 0.15) × 10^1	(−1.53 ± 0.06) × 10^2	5.3
(*S*,*S*)-**1**	(*R*)-**23**	(1.35 ± 0.32) × 10^4	(3.72 ± 0.68) × 10^3	(9.97 ± 0.87) × 10^2	(2.24 ± 0.22) × 10^2	(6.57 ± 1.21) × 10^1	(−5.71 ± 0.64) × 10^1	(−1.54 ± 0.27) × 10^2	
(*S*,*S*)-**1**	(*S*)-**23**	(2.65 ± 0.21) × 10^3	(1.05 ± 0.11) × 10^3	(3.50 ± 0.28) × 10^2	(1.29 ± 0.04) × 10^2	(4.98 ± 0.34) × 10^1	(−4.26 ± 0.41) × 10^1	(−1.08 ± 0.17) × 10^2	45.3
(*R*,*R*)-**2**	(*R*)-**23**	(3.37 ± 0.63) × 10^3	(9.85 ± 0.74) × 10^2	(3.60 ± 0.20) × 10^2	(1.07 ± 0.03) × 10^2	(2.51 ± 0.13) × 10^1	(−5.10 ± 0.62) × 10^1	(−1.40 ± 0.26) × 10^2	
(*R*,*R*)-**2**	(*S*)-**23**	(4.54 ± 0.52) × 10^3	(1.63 ± 0.22) × 10^3	(5.77 ± 0.10) × 10^2	(1.82 ± 0.05) × 10^2	(3.29 ± 0.09) × 10^1	(−5.11 ± 1.06) × 10^1	(−1.37 ± 0.44) × 10^2	—

[a] The predicted isoenantioselective temperatures are calculated from ΔH and ΔS values.

Table 2 Association constants for the complexes and thermodynamic parameters for complexation of crown ethers (*S*,*S*)-**3**

	K_a/M^{-1}						
Amine	15 °C	25 °C	35 °C	45 °C	ΔH/kJ mol^{-1}	ΔS/J K^{-1} mol^{-1}	T_{iso} [a]/ °C
(*R*)-**21**	(7.05 ± 0.44) × 10^3	(2.62 ± 0.07) × 10^3	(1.17 ± 0.12) × 10^3	(5.20 ± 0.06) × 10^2	(−6.58 ± 0.41) × 10^1	(−1.55 ± 0.16) × 10^2	
(*S*)-**21**	(2.13 ± 0.25) × 10^3	(9.12 ± 0.42) × 10^2	(4.66 ± 0.09) × 10^2	(2.22 ± 0.05) × 10^2	(−5.68 ± 0.42) × 10^1	(−1.33 ± 0.16) × 10^2	148
(*R*)-**22**	(1.99 ± 0.01) × 10^4	(7.04 ± 0.33) × 10^3	(2.64 ± 0.02) × 10^3	(1.12 ± 0.02) × 10^3	(−7.33 ± 0.27) × 10^1	(−1.72 ± 0.10) × 10^2	
(*S*)-**22**	(7.27 ± 0.12) × 10^3	(3.20 ± 0.07) × 10^3	(1.17 ± 0.01) × 10^3	(5.63 ± 0.11) × 10^2	(−6.62 ± 0.82) × 10^1	(−1.56 ± 0.31) × 10^2	156
(*R*)-**23**	(1.42 ± 0.01) × 10^4	(5.10 ± 0.09) × 10^3	(1.92 ± 0.07) × 10^3	(9.05 ± 0.10) × 10^2	(−7.06 ± 0.66) × 10^1	(−1.66 ± 0.25) × 10^2	
(*S*)-**23**	(7.75 ± 0.03) × 10^3	(3.18 ± 0.01) × 10^3	(1.36 ± 0.42) × 10^2	(6.06 ± 0.19) × 10^1	(−6.47 ± 0.13) × 10^1	(−1.50 ± 0.05) × 10^2	103

[a] The predicted isoenantioselective temperatures are calculated from ΔH and ΔS values.



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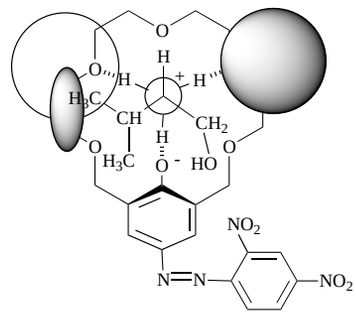

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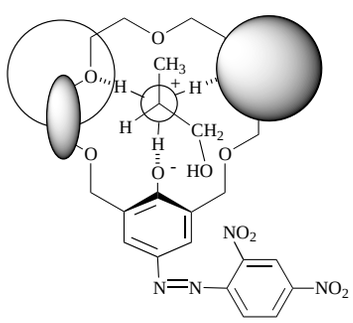

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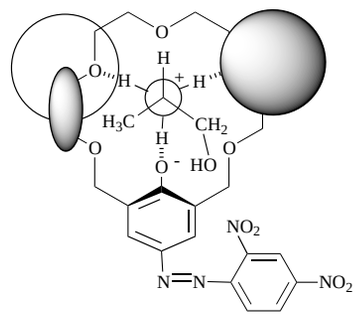

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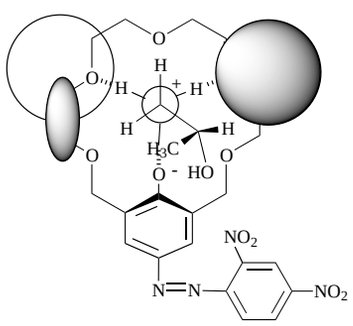

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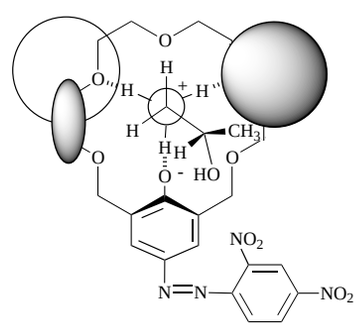

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temperature dependent inversion of the enantiomer selectivity in host–guest complexation in solution would appear to be due largely to the T_{iso} value generally being high and the association constant of the complex decreasing markedly with increasing temperature. The present results are the first observed examples of the temperature dependent reversal of the enantiomer selectivity in complexation of crown ethers with amines in solution.

Experimental

General

^{1}H NMR spectra were obtained on JEOL GSX-270 and JEOL GSX-400 spectrometers for solutions in $CDCl_3$ with $SiMe_4$ as an internal standard, and *J* values are given in Hz. ^{13}C NMR spectra were recorded on a JASCO JNM-MH-270 spectrometer and chloroform (δ_C 77.0) was used as a chemical-shift reference.

UV and visible spectra were recorded on a Hitachi 330 spectrometer. Mass spectroscopic analyses were carried out on a JEOL JMS-DX303HF mass spectrometer using *m*-nitrobenzyl alcohol as a matrix. IR spectra were recorded on a Hitachi 260-10 spectrometer. Elemental analyses were carried out on a Yanagimoto CHN-Corder, Type 2. HPLC analyses were carried out on a Shimazu GS 8A chromatograph equipped with a UV spectrophotometric detector (wavelength 254 nm) using an Inertsil ODS (GL Sciences) 250 mm × 4.6 mm column. Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were measured using a JASCO DIP-40 polarimeter and $[M]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. The guest amines (*R*)- and (*S*)-2-amino-3-methylbutan-1-ol, (*R*)- and (*S*)-2-aminopropan-1-ol and (*R*)- and (*S*)-1-aminopropan-2-ol were purchased from Aldrich Chemical Company Inc. and used without further purification.

1-(1′-Adamantyl)-2-methylsulfinylethanone 4

A mixture of DMSO (275 g, 3.52 mol) and sodium hydride (16.1 g, 670 mmol) was stirred for 30 min at 65–72 °C under a nitrogen atmosphere. After the evolution of hydrogen had ceased, the reaction mixture was cooled to room temperature. A solution of ethyl adamantane-1-carboxylate (46.0 g, 221 mmol) in dry THF (150 cm^3) was added dropwise to the reaction mixture. The reaction mixture was stirred for 40 min at room temperature and then saturated aq. ammonium chloride (10 cm^3) was added. The mixture was poured into ice–water, acidified (pH 3–4) with dilute hydrochloric acid and extracted with ethyl acetate. The combined extracts were washed with aq. sodium hydrogen carbonate and water and dried (K_2CO_3). Removal of the solvent gave a solid, which was recrystallized from hexane to give the title compound **4** (48.4 g, 93%); mp 104–105 °C; ν_{max}(KBr)/cm^{-1} 2900, 2850, 1780, 1450, 1340, 1280, 1160, 1040, 1010, 960, 930, 810, 760 and 690; δ_H(270 MHz; $CDCl_3$) 1.66–1.83 (12H, m, adamantyl CH_2), 2.09 (3H, s, adamantyl CH), 2.72 (3H, s, SCH_3), 3.78 (1H, d, *J* 15.0, $COCH_2SO$) and 4.16 (1H, d, *J* 15.0, $COCH_2SO$), MS (FAB) *m/z* 240 (M^+) and 241 (MH^+) (Found: C, 64.81; H, 8.3. $C_{13}H_{20}O_2S$ requires C, 64.96; H, 8.39%).

***S*-Methyl 2-acetoxy-2-(1′-adamantyl)thioacetate 5**

A mixture of compound **4** (60.0 g, 250 mmol), acetic anhydride (540 g, 5.29 mol) and sodium acetate (45.1 g, 550 mmol) was stirred for 4 h at 100–110 °C. Then the reaction mixture was poured into ice–water and extracted with benzene. The combined extracts were washed with water and dried (Na_2SO_4). Evaporation of the solvent gave a solid, which was recrystallized from ethanol to give the title compound **5** (58.4 g, 83%); mp 86–87 °C; ν_{max}(KBr)/cm^{-1} 2930, 2860, 1740, 1700, 1420, 1370, 1240, 1200, 1045 and 970; δ_H(270 MHz; $CDCl_3$) 1.68–1.73 (12H, m, adamantyl CH_2), 1.98 (3H, br s, adamantyl CH), 2.05 (3H, s, $COCH_3$), 2.13 (3H, s, SCH_3) and 6.21 (1H, s, CH); MS (FAB) *m/z* 282 (M^+), 283 (MH^+) (Found: C, 63.88; H, 7.8. $C_{15}H_{22}O_3S$ requires C, 63.80; H, 7.85%).

(±)-1-(1′-Adamantyl)ethane-1,2-diol 6

A solution of compound **5** (31.4 g, 111 mmol) in dry THF (200 cm^3) was added slowly to a suspension of lithium aluminium hydride (6.19 g, 163 mmol) in dry THF (300 cm^3) and then the mixture was refluxed for 3 h under a nitrogen atmosphere. The reaction mixture was cooled to 0–5 °C and then ethyl acetate (40 cm^3) and saturated aq. ammonium chloride (20 cm^3) were successively added. After the deposited solid had been removed by filtration, the solvent was evaporated under reduced pressure to give a solid, which was recrystallized from hexane to give the diol **6** (21.3 g, 97%); mp 128–130 °C; ν_{max}(KBr)/cm^{-1} 3300, 2900, 2850, 1090, 1065, 1055 and 1030; δ_H(270 MHz; $CDCl_3$) 1.52–1.88 (14H, m, adamantyl CH_2 and OH), 1.99 (3H, s, adamantyl CH), 3.23 (1H, dd, *J* 2.8 and 9.0, CH_2), 3.56 (1H, dd, *J* 9.0 and 11.0, CH_2) and 3.75 (1H, dd, *J* 2.8 and 11.0, CH) (Found: C, 73.35; H, 10.2. $C_{12}H_{20}O_2$ requires C, 73.43; H, 10.27%).

Optical resolution of (±)-6. According to the procedure reported in our previous paper,[8] reaction of the racemate (±)-**6** (10.0 g, 50.9 mmol) with (−)-camphanic chloride (24.0 g, 111 mmol) in pyridine (40 cm^3) gave a mixture of diastereoisomeric esters as a solid (18.4 g, 65%), $[a]_D^{21}$ +7.79 (*c* 1.14, acetone), which showed two double doublet signals due to the methine proton of the diol moiety at δ 4.95 and 4.77 in its ^{1}H NMR spectrum. The mixture was recrystallized three times from methanol until the signal at δ 4.77 disappeared completely to give the diastereomerically pure ester as colorless needles (7.40 g, 26%); mp 193–195 °C; $[M]_D^{24}$ +201.3 (*c* 1.01, acetone); ν_{max}(KBr)/cm^{-1} 2960, 2910, 2850, 1780, 1750 and 1740 (Found: C, 68.99; H, 8.0. $C_{32}H_{44}O_8$ requires C, 69.04; H, 7.97%).

Hydrolysis of the (+)-ester (11.3 g, 20.3 mmol) in a mixture of aq. potassium hydroxide (5%; 100 cm^3) and methanol (100 cm^3) gave a solid, which was recrystallized from hexane to give the diol (*S*)-(+)-**6** (3.50 g, 89%); mp 125–127 °C, $[M]_D^{24}$ +35.3 (*c* 0.973, ethanol). The spectral data completely agreed with those of the racemate (±)-**6** (Found: C, 73.31; H, 10.2%).

(*S*)-1-(1′-Adamantyl)-2-triphenylmethoxyethanol 7

According to the procedure reported in our previous paper,[8] the diol (*S*)-**6** (4.28 g, 21.4 mmol) was reacted with triphenylmethyl chloride (13.8 g, 42.8 mmol), triethylamine (4.3 cm^3) and 4-dimethylaminopyridine (131 mg, 1.07 mmol) in methylene dichloride (40 cm^3) at room temperature for 12 h and silica gel column chromatography of the products gave compound (*S*)-**7** (hexane–diethyl ether, 95:5, as eluent) (7.00 g, 75%); mp 138–140 °C (after recrystallization from ethanol); $[M]_D^{23}$ +91.9 (*c* 0.937, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3550, 3050, 2900, 2850, 1600, 1480, 1440, 1090, 1070, 770, 760 and 700; δ_H(270 MHz; $CDCl_3$) 1.40–1.80 (12H, m, adamantyl CH_2), 1.90 (3H, br s, adamantyl CH), 2.36 (1H, d, *J* 2.5, OH), 3.12 (1H, dd, *J* 8.7 and 8.6, CH_2), 3.27 (1H, ddd, *J* 8.6, 2.7 and 2.5, CH), 3.33 (1H, dd, *J* 8.7 and 2.7, CH_2) and 7.06–7.54 (15H, m, ArH) (Found: C, 84.82; H, 7.8. $C_{31}H_{34}O_2$ requires C, 84.89; H, 7.85%).

(*R*)-3,3-Dimethyl-1-triphenylmethoxybutan-2-ol 9

Treatment of the diol (*R*)-**8**, $[a]_D^{28}$ −25.3 (*c* 0.860, $CHCl_3$) (5.88 g, 49.8 mmol), which was prepared by the procedure reported in the literature,[11] with triphenylmethyl chloride (15.5 g, 54.7 mmol), triethylamine (5.5 cm^3) and 4-dimethylaminopyridine (168 mg, 1.37 mmol) followed by column chromatography of the products on alumina gave compound (*R*)-**9** (12.5 g, 70%); mp 81–82 °C; $[M]_D^{28}$ −60.1 (*c* 1.07, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3550, 3050, 2950, 2875, 1600, 1480, 1450, 1230, 1080, 770, 760 and 700; δ_H(270 MHz; $CDCl_3$) 0.78 [9H, s, $C(CH_3)_3$], 2.46 (1H, d, *J* 2.5, OH), 3.07 (1H, dd, *J* 9.4 and 8.9, CH_2), 3.32 (1H, dd, *J* 9.4 and 3.0, CH_2), 3.24 (1H, ddd, *J* 8.9, 3.0 and 2.5, CH) and 7.20–7.45 (15H, m, ArH) (Found: C, 83.57; H, 7.8. $C_{25}H_{28}O_2$ requires C, 83.29; H, 7.83%).

(*S*)-2-Tetrahydropyranyloxypropan-1-ol 11

A mixture of ethyl (*S*)-lactate (91.3 g, 773 mmol), 3,4-dihydro-2*H*-pyran (98.7 ml, 1.08 mol) and three drops of hydrochloric acid was stirred for 12 h at room temperature and then aq. sodium hydrogen carbonate was added to the reaction mixture. The organic phase was separated, washed with water and dried ($MgSO_4$). Removal of the volatile materials under reduced pressure gave ethyl 2-tetrahydropyranyloxypropionate (141 g, 90%) as a colorless oil, which was dissolved in dry THF (400 cm^3). The solution was added slowly to a suspension of lithium aluminium hydride (25.0 g, 660 mmol) in dry THF (450 cm^3) at 0–5 °C and then the mixture was refluxed for 4 h under a nitrogen atmosphere. The reaction mixture was cooled to 0–5 °C and then saturated aq. ammonium chloride was carefully added to the chilled mixture. After the deposited solid had been removed by filtration, the filtrate was evaporated under reduced pressure.

Distillation of the products gave compound (*S*)-**11** (83.3 g, 75%) as a diastereoisomeric mixture; bp 130–135 °C at 40 mmHg. The diastereoisomeric mixture was used for the next reaction without further separation.

(2*S*,10*S*)-(+)-2,10-Di(1′-adamantyl)-3,6,9-trioxaundecane-1,11-diol 12

A solution of compound (*S*)-**7** (6.10 g, 13.9 mmol) in dry THF (80 cm^3) was added dropwise to a suspension of sodium hydride (1.70 g, 70.8 mmol) in dry THF (150 cm^3) and then the mixture was refluxed for 4 h. A solution of diethylene glycol bis(toluene-*p*-sulfonate) (2.60 g, 6.26 mmol) in dry THF (160 cm^3) was added slowly to the mixture under reflux and the reaction mixture was refluxed for an additional 10 h. The reaction mixture was cooled to 0–5 °C and then a small amount of cold water was added to the chilled mixture. After the solvent had been evaporated under reduced pressure, the residue was extracted with methylene dichloride. The combined extracts were washed with water and dried ($MgSO_4$). After removal of the solvent, the products were chromatographed on silica gel to give 2,10-di(1′-adamantyl)-1,11-bis(triphenylmethoxy)-3,6,9-trioxaundecane (4.40 g, 74%) (hexane–diethyl ether, 1:1, as eluent), which was dissolved in methanol (200 cm^3) containing toluene-*p*-sulfonic acid monohydrate (3.40 g, 17.7 mmol). The solution was stirred at room temperature for 7 h, neutralized with aq. sodium hydrogen carbonate and extracted with chloroform. The combined extracts were washed with aq. sodium hydrogen carbonate and water, dried (K_2CO_3) and evaporated under reduced pressure. Column chromatography of the residue on silica gel gave the diol (*S*,*S*)-**12** (2.00 g, 98%) (benzene–ethyl acetate, 1:1, as eluent) as a solid; $[M]_D^{22}$ +21.5 (*c* 0.964, $CHCl_3$); mp 83–85 °C; ν_{max}(KBr)/cm^{-1} 3350, 2900, 2850, 1460, 1440, 1420, 1340, 1230, 1100, 990, 940, 930, 810, 740 and 650; δ_H(270 MHz; $CDCl_3$) 1.67–1.53 (24H, m, adamantyl CH_2), 1.95 (6H, br s, adamantyl CH), 3.24–2.83 (2H, m, CH), 3.87–3.53 (12H, m, CH_2) and 4.38 (2H, br s, OH), MS (FAB) *m/z* 463 (MH^+) (Found: C, 72.58; H, 9.9. $C_{28}H_{46}O_5$ requires C, 72.69; H, 10.0%).

(2*R*,10*R*)-(−)-2,10-Di-*tert*-butyl-3,6,9-trioxaundecane-1,11-diol 13

By a similar procedure to that described for the preparation of the diol (*S*,*S*)-**12**, condensation of compound (*R*)-**9** (11.5 g, 31.3 mmol) with diethylene glycol bis(toluene-*p*-sulfonate) (5.84 g, 14.1 mmol) followed by hydrolysis gave an oily product, which was chromatographed on silica gel to give the diol (*R*,*R*)-**13** (1.49 g, 28%) (benzene–ethyl acetate, 1:1, as eluent) as a colorless oil; $[M]_D^{25}$ −8.38 (*c* 2.35, $CHCl_3$); ν_{max}(neat film)/cm^{-1} 3350, 3050, 2950, 2875, 1600, 1480, 1450, 1230, 1080, 770, 760 and 700; δ_H(270 MHz; $CDCl_3$) 0.90 [18H, s, $C(CH_3)_3$], 3.07 (2H, dd, *J* 3.0 and 8.4, CH), 3.50–3.80 (12H, m, CH_2) and 4.34 (2H, d, *J* 6.4, OH); δ_C(67.9 MHz; $CDCl_3$) 26.1 (q), 34.6 (s), 62.8 (t), 72.8 (t) and 90.7 (d); HRMS *m/z* 307.2507 (MH^+), $C_{16}H_{35}O_5$ requires 307.2485.

(*S*,*S*)-1,3-Bis(4′-hydroxy-2-oxapentyl)-2,5-dimethoxybenzene 14

A solution of compound (*S*)-**11** (10.0 g, 61.2 mmol) in dry THF (150 cm^3) was added dropwise to a suspension of sodium hydride (2.94 g, 123 mmol) in dry THF (150 cm^3) at room temperature and then the the mixture was stirred for 1 h under reflux. A solution of 1,3-bis(bromomethyl)-2,5-dimethoxybenzene (9.90 g, 30.6 mmol) in dry THF (250 cm^3) was added to the reaction mixture under reflux and refluxing was continued for an additional 10 h. The reaction mixture was cooled to 0–5 °C and then a small amount of cold water was added carefully. After the mixture had been concentrated under reduced pressure, the residue was extracted with a mixture of hexane and ethyl acetate. The combined extracts were washed with water, dried ($MgSO_4$) and evaporated under reduced pressure to give 1,3-bis(4′-tetrahydropyranyloxy-2-oxapentyl)-2,5-dimethoxybenzene as a yellow oil, which was dissolved in ethanol (350 cm^3) containing pyridinium toluene-*p*-sulfonate (1.54 g, 6.12 mmol). The solution was heated for 12 h at 60 °C and then concentrated under reduced pressure. The residue was directly chromatographed on silica gel to give the diol (*S*,*S*)-**14** (5.30 g, 55%) (hexane–ethyl acetate, 1:2, as eluent) as a colorless oil; $[M]_D^{24}$ +60.3 (*c* 1.07, $CHCl_3$); ν_{max}(neat film)/cm^{-1} 3400, 2950, 2900, 1480, 1100 and 1070; δ_H(400 MHz; $CDCl_3$) 1.15 (6H, d, *J* 6.4, CH_3), 2.43 (2H, br s, OH), 3.33 (1H, dd, *J* 9.5 and 8.2, CH_2), 3.51 (1H, dd, *J* 9.5 and 3.1, CH_2), 3.73 (3H, s, CH_3O), 3.78 (3H, s, CH_3O), 3.95–4.05 (1H, m, CH), 4.58 (4H, s, benzyl CH_2), 6.89 (2H, s, ArH); δ_C(67.9 MHz; $CDCl_3$) 18.6 (q), 55.0 (q), 61.9 (q), 65.8 (d), 67.5 (t), 75.7 (t), 113.9 (d), 131.7 (d), 149.5 (s) and 155.4 (s); HRMS *m/z* 314.1685 (M^+), $C_{16}H_{26}O_6$ requires M, 314.1729.

(5*S*,13*S*)-5,13-Di(1′-adamantyl)-19,21-dimethoxy-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-triene 15

A solution of the diol (*S*,*S*)-**12** (3.80 g, 8.21 mmol) and 1,3-bis(bromomethyl)-2,5-dimethoxybenzene (2.70 g, 8.33 mmol) in dry THF (1000 cm^3) was added dropwise to a mixture of sodium hydride (840 mg, 35.0 mmol) and potassium tetrafluoroboranuide (1.20 g, 8.58 mmol) in dry THF (450 cm^3) during 50 h under reflux and the reaction mixture was refluxed for an additional 8 h under a nitrogen atmosphere. After the reaction mixture had been cooled to 0–5 °C, a small amount of cold water was added carefully. The reaction mixture was acidified (pH 1) with dilute hydrochloric acid, evaporated under reduced pressure and extracted with diethyl ether. The combined extracts were washed with aq. sodium hydrogen carbonate and water, dried ($MgSO_4$) and evaporated under reduced pressure. Column chromatography of the residue on silica gel gave the crown ether (*S*,*S*)-**15** (4.40 g, 66%) (hexane–diethyl ether, 1:1, as eluent) as a solid; mp 127–129 °C; $[M]_D^{19}$ +276.4 (*c* 0.986, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3020, 2980, 2860, 1500, 1460, 1445, 1260, 1130, 1100 and 1060; δ_H(270 MHz; $CDCl_3$) 1.53–1.67 (24H, m, adamantyl CH_2), 1.95 (6H, s, adamantyl CH), 2.84 (2H, dd, *J* 2.5 and 7.0, OCH), 3.33–3.76 (12H, m, OCH_2), 3.80 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.34 (2H, d, *J* 10.8, benzyl CH_2), 4.65 (2H, d, *J* 10.8, benzyl CH_2) and 6.85 (2H, s, ArH); MS (FAB) *m/z* 625 (MH^+) (Found: C, 72.70; H, 8.9. $C_{38}H_{56}O_7$ requires C, 73.04; H, 9.03%).

(5*S*,13*S*)-5,13-Di(1′-adamantyl)-19-methoxy-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-trien-21-ol 16

Ethanethiol (5.73 g, 92.2 mmol) was added slowly to a suspension of sodium hydride (3.07 g, 128 mmol) in dry DMF (50 cm^3) at 0 °C under a nitrogen atmosphere. To the resulting clear solution of sodium ethanethiolate in dry DMF was added slowly a solution of the crown ether (*S*,*S*)-**15** (2.20 g, 3.52 mmol) in dry DMF (80 cm^3) at room temperature and then the reaction mixture was heated for 4 h at 100 °C. The reaction was cooled to 0–5 °C and a small amount of cold water was carefully added. The mixture was acidified (pH 5) with hydrochloric acid and extracted with diethyl ether. The combined extracts were washed with aq. sodium hydrogen carbonate and water and dried ($MgSO_4$). After removal of the solvent, column chromatography of the residue on silica gel gave the phenolic crown ether (*S*,*S*)-**18** (1.37 g, 64%) (hexane–ethyl acetate, 1:1, as eluent); $[M]_D^{25}$ +141.5 (*c* 0.865, $CHCl_3$); mp 88–89 °C (from ethyl acetate–hexane); ν_{max}(KBr)/cm^{-1} 3340, 2980, 2925, 2850, 1490, 1360, 1255, 1100, 1050, 850, 750 and 660; δ_H(270 MHz; $CDCl_3$) 1.72–1.55 (24H, m, adamantyl CH_2), 1.95 (6H, s, adamantyl CH), 2.95 (2H, dd, *J* 2.5 and 7.5, OCH), 3.85–3.54 (12H, m, OCH_2), 3.75 (3H, s, OCH_3), 4.52 (2H, d, *J* 11.0, benzyl CH_2), 4.62 (2H, d, *J* 11.0, benzyl CH_2), 6.69 (2H, s, ArH) and 7.48 (1H, s, OH); MS *m/z* 610 (M^+) (Found: C, 72.58; H, 9.0. $C_{37}H_{54}O_7$ requires C, 72.76; H, 8.91%).

(5*R*,13*R*)-5,13-Di-*tert*-butyl-19,21-dimethoxy-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-triene 17

By a procedure similar to that described for the preparation of the crown ether (*S*,*S*)-**15**, condensation of the diol (*R*,*R*)-**13** (500 mg, 1.55 mmol) with 1,3-bis(bromomethyl)-2,5-dimethoxybenzene (500 mg, 1.55 mmol) followed by silica gel chromatography of the products gave the crown ether (*R*,*R*)-**17** (355 mg, 48%) (chloroform as eluent) as a colorless oil. HPLC analysis showed a single peak: t_R 5.86 min (acetonitrile, 1.0 cm^3 min^{-1}, as eluent); $[M]_D^{24}$ −126.4 (*c* 1.86, $CHCl_3$); ν_{max}(neat film)/cm^{-1} 2950, 2850, 1480, 1360, 1100 and 1050; δ_H(270 MHz; $CDCl_3$) 0.91 [18H, s, $C(CH_3)_3$], 3.00 (2H, dd, *J* 2.8 and 7.1, CH), 3.31–3.37 (12H, m, CH_2), 3.79 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.34 (2H, d, *J* 11.0, benzyl CH_2), 4.66 (2H, d, *J* 11.0, benzyl CH_2) and 6.85 (2H, s, ArH); δ_C(69.6 MHz; $CDCl_3$) 26.4 (q), 34.7 (s), 55.6 (q), 63.8 (q), 68.6 (t), 70.5 (t), 71.4 (t), 71.9 (t), 87.7 (d), 116.3 (d), 132.4 (s), 152.0 (s) and 155.0 (s); HRMS *m/z* 468.3096 (MH^+). $C_{26}H_{45}O_7$ requires 468.3087.

(5*R*,13*R*)-5,13-Di-*tert*-butyl-19-methoxy-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-trien-21-ol 18

By a procedure similar to that described for the preparation of the phenolic crown ether (*S*,*S*)-**16**, demethylation of the crown ether (*R*,*R*)-**17** (100 mg, 0.210 mmol) followed by purification by silica gel column chromatography gave the phenolic crown ether (*R*,*R*)-**18** (90 mg, 95%) (hexane–ethyl acetate, 1:1, as eluent) as a colorless oil, which was immediately used for the next reaction.

(5*S*,13*S*)-9,21-Dimethoxy-5,13-dimethyl-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-triene 19

A solution of the diol (*S*,*S*)-**14** (3.00 g, 9.54 mmol) and diethylene glycol bis(toluene-*p*-sulfonate) (4.00 g, 9.54 mmol) in dry THF (500 cm^3) was added dropwise to a mixture of sodium hydride (912 mg, 38.0 mmol) and potassium tetrafluoroboranuide (1.20 g, 9.54 mmol) in dry THF (200 cm^3) over a 9 h period under reflux and the reaction mixture was refluxed for an additional 20 h under a nitrogen atmosphere. After work-up as described above, silica gel column chromatography of the products gave the crown ether (*S*,*S*)-**19** (1.80 g, 50%) (hexane–ethyl acetate, 1:2 as eluent) as a colorless oil. HPLC analysis showed a single peak: t_R 5.07 min (acetonitrile, 1.0 cm^3 min^{-1}, as eluent); $[M]_D^{24}$ +84.9 (*c* 1.52, $CHCl_3$); ν_{max}(neat film)/cm^{-1} 3300, 2900, 1640, 1600, 1320, 1220 and 1060; δ_H(270 MHz; $CDCl_3$) 1.12 (6H, d, *J* 6.5, CH_3), 3.39–3.62 (14H, m, CH_2 and CH), 3.79 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 4.46 (2H, d, *J* 11.1, benzyl CH_2), 4.61 (2H, d, *J* 11.1, benzyl CH_2) and 6.84 (2H, s, ArH); δ_C(67.9 MHz; $CDCl_3$) 16.8 (q), 55.5 (q), 64.1 (t), 68.4 (t), 68.5 (t), 70.7 (t), 73.3 (t), 74.8 (d), 116.3 (d), 132.3 (s), 152.3 (s) and 154.9 (s); HRMS *m/z* 384.2185 (M^+). $C_{26}H_{44}O_7$ requires 384.2148.

(5*S*,13*S*)-19-Methoxy-5,13-dimethyl-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-trien-21-ol 20

By a procedure similar to that described for the preparation of the phenolic crown ether (*S*,*S*)-**16**, demethylation of the crown ether (*S*,*S*)-**19** (500 mg, 1.30 mmol) followed by purification by silica gel column chromatography gave the phenolic crown ether (*S*,*S*)-**20** (440 mg, 92%) (hexane–ethyl acetate, 1:1, as eluent) as a colorless oil; ν_{max}(neat film)/cm^{-1} 3400, 2900, 1660, 1610, 1500, 1480, 1380, 1260, 1100, 1060, 860 and 780; δ_H(270 MHz; $CDCl_3$) 1.12 (6H, d, *J* 6.4, CH_3), 3.46–3.81 (14H, m, CH_2 and CH), 3.79 (3H, s, OCH_3), 4.62 (4H, s, benzyl CH_2), 6.70 (2H, s, ArH) and 7.59 (1H, br s, OH); MS *m/z* 370 (M^+). This was used for the next reaction without further purification.

(5*S*,13*S*)-5,13-Di(1′-adamantyl)-19-(2′,4′-dinitrophenylazo)-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-trien-21-ol 1

A solution of the phenolic crown ether (*S*,*S*)-**16** (950 mg, 1.57 mmol) in acetonitrile (150 cm^3) was added to a solution of CAN (2.20 g, 4.01 mmol) in acetonitrile (50 cm^3) and then the mixture was stirred for 2 h at room temperature. After water had been added to the reaction mixture, the solvent was evaporated under reduced pressure. The residue was extracted with chloroform and the combined extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent gave the corresponding quinone (1.00 g) as a yellow oil, which was immediately taken up in a mixture of ethanol (40 cm^3) and methylene dichloride (40 cm^3). To this solution was added a solution of 2,4-dinitrophenylhydrazine (3.30 g, 8.40 mmol) in a mixture of sulfuric acid (7 cm^3) and ethanol (90 cm^3) and then the mixture was stirred for 1.5 h at room temperature. After water had been added, the reaction mixture was extracted with chloroform. The combined extracts were washed with aq. sodium hydrogen carbonate and water, dried ($MgSO_4$) and evaporated under reduced pressure. Silica gel column chromatography of the residue gave the azophenolic crown ether (*S*,*S*)-**1** (982 mg, 82%) (chloroform as eluent) as an orange solid; mp 89–90 °C; λ_{max}($CHCl_3$)/nm; 403 (ε/dm^3 mol^{-1} cm^{-1} 2.46×10^4); ν_{max}(KBr)/cm^{-1} 3340, 2980, 2925, 2850, 1490, 1360, 1255, 1100, 1050, 850, 750 and 660; δ_H(270 MHz; $CDCl_3$) 1.56–1.69 (24H, m, adamantyl CH_2), 1.96 (6H, s, adamantyl CH), 2.98 (2H, dd, *J* 2.3 and 7.6, CH), 3.60–3.94 (12H, m, OCH_2), 4.67 (2H, d, *J* 11.4, benzyl CH_2), 4.76 (2H, d, *J* 11.4, benzyl CH_2), 7.80 (2H, s, HOArH), 7.82 [1H, d, *J* 8.9, $(O_2N)_2ArH$], 8.49 [1H, dd, *J* 8.9 and 2.6, $(O_2N)_2ArH$], 8.76 [1H, d, *J* 2.6, $(O_2N)_2ArH$] and 8.99 (1H, br s, OH); δ_C(69.6 MHz; $CDCl_3$) 28.3 (t), 36.9 (t), 37.1 (t), 38.7 (t), 70.2 (t), 70.8 (t), 71.4 (t), 72.1 (t), 87.5 (d), 120.0 (d), 125.2 (s), 126.4 (d), 127.5 (d), 145.7 (s), 146.5 (s), 147.0 (s), 148.9 (s) and 161.5 (s); MS (FAB) *m/z* 775 (MH^+) (Found: C, 64.78; H, 7.0; N, 7.28. $C_{42}H_{54}O_{10}N_4$ requires C, 65.10; H, 7.02; N, 7.23%).

(5*S*,13*S*)-5,13-Di-*tert*-butyl-19-(2′,4′-dinitrophenylazo)-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-trien-21-ol 2

As described for the preparation of the azophenolic crown ether (*S*,*S*)-**1**, oxidation of the phenolic crown ether (*R*,*R*)-**18** (90 mg, 0.200 mmol) with CAN followed by treatment with 2,4-dinitrophenylhydrazine gave solid products. Silica gel column chromatography gave the azophenolic crown ether (*R*,*R*)-**2** (60 mg, 50%) (chloroform as eluent) as a red solid; mp 65.0–66.5 °C; λ_{max}($CHCl_3$)/nm; 402 (ε/dm^3 mol^{-1} cm^{-1} 2.92×10^4); ν_{max}(KBr)/cm^{-1} 3300, 3000, 2900, 1620, 1560, 1490, 1380, 1320, 1140, 940, 870 and 790; δ_H(270 MHz; $CDCl_3$) 0.94 [18H, s, $C(CH_3)_3$], 3.16 (2H, dd, *J* 2.3 and 7.6, CH), 3.59–3.95 (12H, m, OCH_2), 4.68 (2H, d, *J* 11.2, benzyl CH_2), 4.76 (2H, d, *J* 11.2, benzyl CH_2), 7.80 (2H, s, HOArH), 7.82 [1H, d, *J* 8.9, $(O_2N)_2ArH$], 8.49 [1H, dd, *J* 8.9 and 2.3, $(O_2N)_2ArH$], 8.76 [1H, d, *J* 2.3, $(O_2N)_2ArH$] and 8.99 (1H, br s, OH); δ_C(69.6 MHz; $CDCl_3$) 26.5 (q), 34.9 (s), 70.3 (t), 70.8 (t), 72.1 (t), 72.5 (t), 87.2 (d), 120.0 (d), 120.2 (d), 125.2 (s), 126.4 (d), 127.6 (d), 145.8 (s), 147.0 (s), 147.1 (s), 149.0 (s) and 161.5 (s); MS (FAB) *m/z* 619 (MH^+). (Found: C, 57.90; H, 6.7; N, 8.65. $C_{30}H_{42}O_{10}N_4$ requires C, 58.24; H, 6.84; N, 8.65%).

(5*S*,13*S*)-5,13-Dimethyl-19-(2′,4′-dinitrophenylazo)-3,6,9,12,15-pentaoxabicyclo[15.3.1]henicosane-1(21),17,19-trien-21-ol 3

As described for the preparation of the azophenolic crown ether (*S*,*S*)-**1**, oxidation of the phenolic crown ether (*S*,*S*)-**20** (150 mg, 0.405 mmol) with CAN followed by treatment with 2,4-dinitrophenylhydrazine gave solid products, column chromatography of which on silica gel gave the azophenolic crown ether (*S*,*S*)-**3** (170 mg, 78%) (chloroform as eluent) as an orange solid. HPLC analysis showed a single peak: t_R 5.09 min, (acetonitrile, 1.0 cm^3 min^{-1}, as eluent); mp 42.0–42.5 °C; λ_{max}($CHCl_3$)/nm; 403 (ε/dm^3 mol^{-1} cm^{-1} 2.98×10^4); ν_{max}(KBr)/cm^{-1} 3300, 2950, 2900, 1640, 1600, 1500, 1480, 1400, 1320, 1100, 1060, 820 and 740; δ_H(270 MHz; $CDCl_3$) 1.16 (6H, d,

J 6.3, CH_3), 3.16–3.82 (14H, m, CH_2 and CH), 4.74 (4H, s, benzyl CH_2), 7.80 (2H, s, HOArH), 7.81 [1H, d, *J* 8.6, $(O_2N)_2ArH$], 8.48 [1H, dd, *J* 8.6 and 2.3, $(O_2N)_2ArH$], 8.75 [1H, d, *J* 2.3, $(O_2N)_2ArH$] and 9.04 (1H, br s, OH); δ_C(67.9 MHz; $CDCl_3$) 16.2 (q), 70.3 (t), 70.5 (t), 74.6 (t), 74.8 (t), 120.0 (d), 120.0 (d), 125.4 (s), 126.4 (d), 127.5 (d), 145.7 (s), 146.6 (s), 147.0 (s), 149.0 (s) and 161.7 (s); HRMS *m/z* 534.2003 (M^+). $C_{24}H_{30}O_{10}N_4$ requires 534.1962.

General procedures for evaluation of association constants of complexes

Association constants for complexes of (*S*,*S*)-**1** with **21**, **22** and **23**, (*R*,*R*)-**2** with **21**, **22** and **23** and (*S*,*S*)-**3** with **21** were calculated by the non-linear least-squares method on the basis of the ^{1}H NMR spectral data in $CDCl_3$ and those for complexes of (*S*,*S*)-**3** with **22** and **23** were determined by the Rose–Drago method[13] on the basis of the UV–VIS absorptions in $CHCl_3$. In order to evaluate K_a values precisely, the concentrations of the host and the guest were changed in each experiment and measurements were made on solutions ranging in concentration as follows; for ^{1}H NMR titration: 5.29×10^{-4}–4.88×10^{-2} M for the complexes with $K_a = 5.20 \times 10^3$–1.82×10^4; 1.05×10^{-3}–9.76×10^{-2} M for the complexes with $K_a = 1.60 \times 10^2$–2.40×10^4; 3.18×10^{-3}–2.64×10^{-1} M for the complexes with $K_a = 2.51 \times 10$–1.35×10^2; 1.31×10^{-3}–7.06×10^{-3} M for the complexes with $K_a = 4.54 \times 10^3$–1.53×10^4; 6.93×10^{-4}–9.53×10^{-3} M for the complexes with $K_a = 2.62 \times 10^2$–7.49×10^3; for the UV–VIS spectroscopic method: 3.18×10^{-5}–5.65×10^{-4} M for the complexes with $K_a = 3.20 \times 10^3$–1.99×10^4; 2.76×10^5–9.21×10^{-5} M for the complexes with $K_a = 2.64 \times 10^3$–7.04×10^3; 3.33×10^{-4}–6.24×10^{-3} M for the complexes with $K_a = 6.06 \times 10$–1.74×10^3; 1.11×10^4–8.35×10^{-4} M for the complexes with $K_a = 1.36 \times 10^2$–5.10×10^3.

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