Preparation and enantiomer recognition behaviour of azophenolic crown ethers containing *cis*-1-phenylcyclohexane-1,2-diol as the chiral subunit and 2,4-dinitrophenylazophenol as the chromophore[1]

Koichiro Naemura,*[a] Koji Ueno,[a] Sachiko Takeuchi,[a] Keiji Hirose,[a] Yoshito Tobe,[a] Takahiro Kaneda[b] and Yoshiteru Sakata[b]

[a] *Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan*

[b] *The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka, Ibaraki, Osaka 567, Japan*

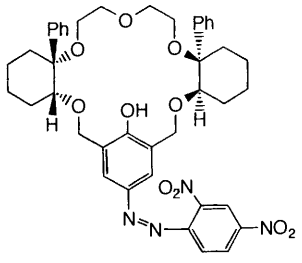
Optically active azophenolic crown ethers 1 and 2 incorporating two *cis*-1-phenylcyclohexane-1,2-diol chiral subunits and a *p*-(2,4-dinitrophenylazo)phenol moiety as a chromophore have been prepared and the enantiomer recognitive coloration in complexation with chiral ethylamine and 2-aminoethanol derivatives has been examined. The observed enantiomer selectivities of crown ethers 1 and 2 have been interpreted on the basis of CPK molecular model examination of the diastereoisomeric complexes.

Introduction

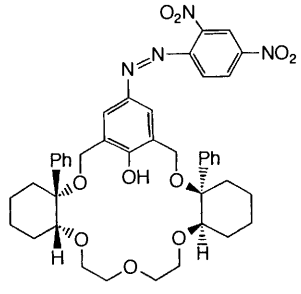
Various types of crown ethers have been prepared and their characteristic complexation has been widely examined. The design and preparation of crown ethers possessing a chromophore, and which selectively bind guest species, causing a synchronous colour change, have recently been considered an interesting subject in host–guest chemistry[2] and enantioselective coloration in complexation of chiral crown ethers with chiral guests is worthy of detailed study because it is capable of providing basic information for the development of colour indicators used to judge the absolute configuration of chiral guests. Chiral crown ethers incorporating a 2,4-dinitrophenylazophenol moiety are of special interest because not only is a 2,4-dinitrophenylazo group at the *para* position of the phenol moiety an effective chromophore but also it increases the acidity of the phenolic OH group, thereby increasing its binding ability towards neutral amines.

We have also reported the preparation of a variety of optically active crown ethers containing a synthetic chiral subunit[3] and our continuing interest in the enantiomer-recognition behaviour of crown ethers led us to prepare a chiral crown ether incorporating a chromophore and to examine enantioselective coloration in its complexation with chiral guests. Herein we report the preparation of isomeric azophenolic crown ethers **1** and **2** containing two *cis*-1-phenylcyclohexane-1,2-diol moieties as a chiral centre and the *p*-(2,4-dinitrophenylazo)phenol moiety, which serves as, in addition to a chromophore, a binding site for neutral amines. Their chiral-recognition behaviour towards chiral ethylamine and 2-aminoethanol derivatives is also described and the enantiomer selectivities observed have been interpreted on the basis of CPK molecular model examination of the diastereoisomeric complexes.

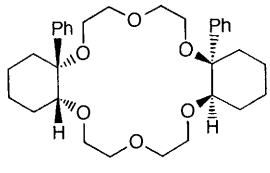
One of the CH_2OCH_2 moieties of crown ether (*R*,*R*)(*R*,*R*)-**3**[4] containing two *cis*-1-phenylcyclohexane-1,2-diol chiral subunits is replaced with the *p*-(2,4-dinitrophenylazo)phenol residue to give isomeric azophenolic crown ethers (*R*,*R*)(*R*,*R*)-**1** and (*R*,*R*)(*R*,*R*)-**2**, which possess a similarly shaped cavity but a different placement of the phenyl barriers with respect to the phenolate oxygen atom. As the phenolate oxygen atom participates in binding to amines, isomeric crown ethers **1** and **2** possess a chiral cavity with opposite configurational biases, as shown in the predicted conformations of their complexes with chiral amines.



(*R*,*R*)(*R*,*R*)-**1**



(*R*,*R*)(*R*,*R*)-**2**



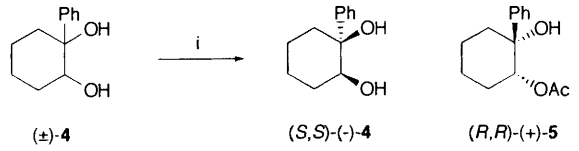
(*R*,*R*)(*R*,*R*)-**3**

Results and discussion

cis-1-Phenylcyclohexane-1,2-diol **4** has previously been resolved by pig liver esterase-mediated hydrolysis of racemate (±)-**5** in phosphate buffer solution.[4] Now we report the kinetic resolution of diol **4** by lipase QL (from *Alcaligenes sp.*)-mediated acylation, which is more practical for the preparation of a large quantity of our chiral subunit because this lipase is readily available at relatively low cost and because operations of enzymic reaction in organic solvents are easier than those in aqueous media.[5] Enantiomer-selective acylation of racemate (±)-**4** was carried out with isopropenyl acetate as an acylating agent in diisopropyl ether at 30 °C and terminated close to 50% of the esterification point by filtration of the enzyme. Chromatographic separation of the product gave diol (1*S*,2*S*)-(−)-**4** (91% ee)† and acetate (1*R*,2*R*)-(+)-**5** (Scheme 1) which

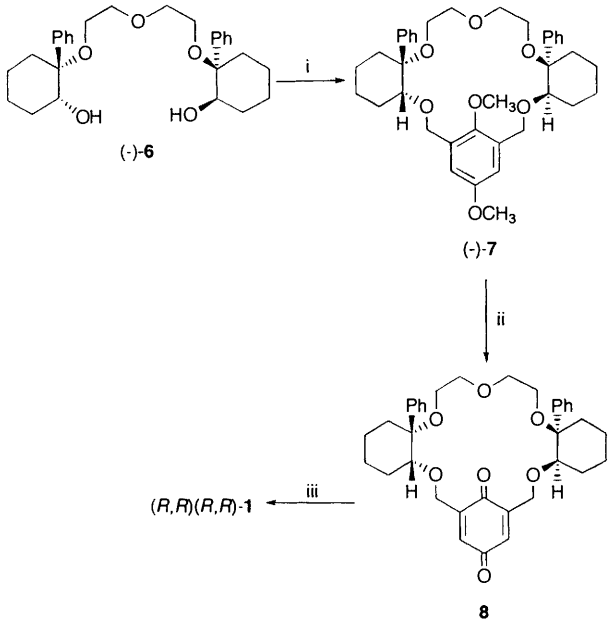
† ee = enantiomeric excess.

on hydrolysis with methanolic sodium hydroxide provided (1*R*,2*R*)-(+)-**4** (95% ee). The optical purity of diol **4** was easily improved by recrystallisation from hexane, enantiomerically pure (−)-**4** and (+)-**4** being obtained (>99% ee). The determination of enantiomeric purity of diol **4** was carried out by HPLC analysis using a chiral column.



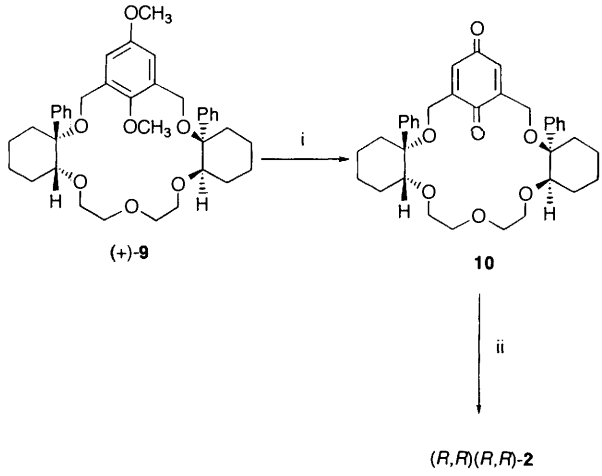
Scheme 1 *Reagent:* i, lipase QL, isopropenyl acetate

The preparation of crown ether **7** with the homotopic faces, whose chiral subunits were linked with a *m*-phenylene unit and a diethylene glycol unit, was carried out stepwise; that is, the condensation of 2 mol equiv. of the chiral subunits of the same chirality with diethylene glycol bis(methanesulfonate) followed by ring closure of the resulting C_2-diol **6** with 1,3-bis(bromomethyl)-2,5-dimethoxybenzene. The preparation of C_2-diol (*R*,*R*)(*R*,*R*)-(−)-**6** from diol (1*R*,2*R*)-(+)-4 has been reported in our previous paper.[4] High-dilution condensation of C_2-diol (*R*,*R*)(*R*,*R*)-(−)-**6**, $[\alpha]_D$ -7.52×10^{-1} deg cm^2 g^{-1} ($CHCl_3$), with 1,3-bis(bromomethyl)-2,5-dimethoxybenzene[6] in the presence of sodium hydride and potassium tetrafluoroboranuide in dry tetrahydrofuran (THF) gave crown ether (*R*,*R*)(*R*,*R*)-(−)-**7**, $[\alpha]_D$ -97.1×10^{-1} deg cm^2 g^{-1} ($CHCl_3$) in 80% yield. Oxidation of crown ether (*R*,*R*)(*R*,*R*)-(−)-**7** with cerium(IV) ammonium nitrate (CAN) in methylene dichloride–acetonitrile–water gave quinone **8**, which was immediately treated with 2,4-dinitrophenylhydrazine in a mixture of conc. H_2SO_4, ethanol and methylene dichloride followed by chromatography on silica gel and crystallisation from ethanol to give azophenolic crown ether (*R*,*R*)(*R*,*R*)-**1** as a red solid in 56% overall yield for the two steps (Scheme 2). Our previous



Scheme 2 *Reagents:* i, 1,3-bis(bromomethyl)-2,5-dimethoxybenzene, NaH, KBF_4; ii, cerium(IV) ammonium nitrate; iii, 2,4-dinitrophenylhydrazine, conc. H_2SO_4

paper has described the preparation of crown ether (*S*,*S*)(*S*,*S*)-(−)-**9** from diol (1*S*,2*S*)-(−)-**4**.[7] On oxidation with CAN followed by treatment with 2,4-dinitrophenylhydrazine, crown ether (*R*,*R*)(*R*,*R*)-(+)-**9**, $[\alpha]_D$ $+45.6 \times 10^{-1}$ deg cm^2 g^{-1} ($CHCl_3$) prepared from diol (1*R*,2*R*)-(+)-**4** was converted into azophenolic crown ether (*R*,*R*)(*R*,*R*)-**2** *via* quinone **10** in 56% overall yield for two steps (Scheme 3). The enantiomers



Scheme 3 *Reagents:* i, cerium(IV) ammonium nitrate; ii, 2,4-dinitrophenylhydrazine, conc. H_2SO_4

(*S*,*S*)(*S*,*S*)-**1** and (*S*,*S*)(*S*,*S*)-**2** were also prepared from diol (1*S*,2*S*)-(−)-**4** by the same sequence of reactions. Both crown ethers **1** and **2** showed an absorption maximum at 418 nm in a UV–visible spectrum, and the absorption maximum of complexes of crown ethers **1** and **2** with chiral and achiral amines appeared in the region 574–600 nm.

The observed association constants for the complexes of azophenolic crown ethers **1** and **2** with chiral and achiral amines were determined by the Benesi–Hildebrand method[8] on the basis of the absorption maximum in the UV–visible spectrum at 25 °C in $CHCl_3$. The K_a-values together with the λ_{max}-values for complexes with chiral amines are summarised in Table 1.

The association constants for the diastereoisomeric complexes of crown ethers **1** and **2** with ethylamine derivatives (*S*)-**11** and (*S*)-**12** demonstrated that the change in placement of the phenolate binding site with respect to the chiral barriers resulted in the reversal of enantiomer selectivity in complexation. On the basis of CPK molecular model examination of the complexes using the assumption that the phenolate oxygen atom necessarily participates in binding to an amine[9] and the smallest group of an amine occupies the most hindered site near the bulky phenyl barrier in the complex, the predicted geometries **20** and **22** are illustrated for the complexes of (*S*,*S*)(*S*,*S*)-**1** and (*R*,*R*)(*R*,*R*)-**1**, respectively, with the (*S*)-ethylamine derivative (L, M and S are the large, the medium and the small-sized groups of the amine and the sequence of groups is L > M > S) and the geometries **21** and **23**, respectively, for the complexes of (*R*,*R*)(*R*,*R*)-**2** and (*S*,*S*)(*S*,*S*)-**2** with the (*S*)-ethylamine derivative.

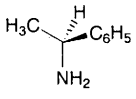
Assuming that a steric interaction between the phenyl barrier and the ligand L makes the complex with the geometry **22** less stable than the complex with the geometry **20**, we suggest that amines (*S*)-**11** and (*S*)-**12** showed better complementarity to crown ether (*S*,*S*)(*S*,*S*)-**1** than to crown ether (*R*,*R*)(*R*,*R*)-**1**. On the other hand, crown ether (*R*,*R*)(*R*,*R*)-**2** formed more stable complexes with amines (*S*)-**11** and (*S*)-**12** than crown ether (*S*,*S*)(*S*,*S*)-**2** did and the enantiomer selectivities observed are similarly interpreted in terms of a steric interaction between the phenyl barrier and the ligand L as shown in the geometries **21** and **23**.

The association constants for the complexes of crown ethers **1** and **2** with 2-aminoethanol derivatives **13**, **14** and **15** were larger than those for complexes with ethylamine derivatives **11** and **12**, suggesting that the hydroxy group of 2-aminoethanols occupies the site near the phenol residue of the crown ether to make the additional hydrogen bonding between the phenolate oxygen

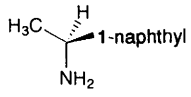
Table 1 Association constants K_a (dm^3 mol^{-1}), absorption maxima λ_{max} and the ratio of K_a-values for the complexes of chiral crown ethers with chiral amines[a]

Host	Amine	K_a (dm^3 mol^{-1})	(λ_{max}/nm)	Relative ratio of K_a-values
(*R*,*R*)(*R*,*R*)-**1**	none		(418)	
(*R*,*R*)(*R*,*R*)-**1**	(*S*)-**11**	5.3 ± 0.3	(588)	1
(*S*,*S*)(*S*,*S*)-**1**	(*S*)-**11**	11.1 ± 0.4	(585)	2.01
(*R*,*R*)(*R*,*R*)-**1**	(*S*)-**12**	4.3 ± 0.2	(586)	1
(*S*,*S*)(*S*,*S*)-**1**	(*S*)-**12**	8.3 ± 0.3	(584)	1.95
(*R*,*R*)(*R*,*R*)-**1**	(*S*)-**13**	78.4 ± 2.3	(577)	1
(*S*,*S*)(*S*,*S*)-**1**	(*S*)-**13**	88.3 ± 0.6	(578)	1.13
(*R*,*R*)(*R*,*R*)-**1**	(*S*)-**14**	18.6 ± 0.3	(574)	1
(*S*,*S*)(*S*,*S*)-**1**	(*S*)-**14**	19.3 ± 0.2	(574)	1.04
(*R*,*R*)(*R*,*R*)-**1**	(*S*)-**15**	197 ± 1	(583)	1
(*S*,*S*)(*S*,*S*)-**1**	(*S*)-**15**	270 ± 2	(577)	1.37
(*R*,*R*)(*R*,*R*)-**2**	none		(418)	
(*R*,*R*)(*R*,*R*)-**2**	(*S*)-**11**	18.8 ± 0.7	(599)	1.89
(*S*,*S*)(*S*,*S*)-**2**	(*S*)-**11**	9.97 ± 0.43	(597)	1
(*R*,*R*)(*R*,*R*)-**2**	(*S*)-**12**	7.81 ± 0.31	(595)	1.38
(*S*,*S*)(*S*,*S*)-**2**	(*S*)-**12**	5.66 ± 0.15	(598)	1
(*R*,*R*)(*R*,*R*)-**2**	(*S*)-**13**	126 ± 2	(583)	1.40
(*S*,*S*)(*S*,*S*)-**2**	(*S*)-**13**	90.0 ± 1.5	(585)	1
(*R*,*R*)(*R*,*R*)-**2**	(*S*)-**14**	9.79 ± 0.3	(579)	1
(*S*,*S*)(*S*,*S*)-**2**	(*S*)-**14**	11.3 ± 0.2	(580)	1.15
(*R*,*R*)(*R*,*R*)-**2**	(*S*)-**15**	583 ± 7	(589)	1.17
(*S*,*S*)(*S*,*S*)-**2**	(*S*)-**15**	499 ± 4	(588)	1

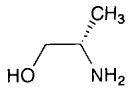
[a] Determined by the Benesi–Hildebrand method at 25 °C in $CHCl_3$.



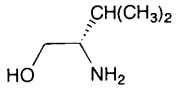
(*S*)-**11**



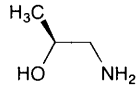
(*S*)-**12**



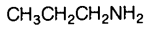
(*S*)-**13**



(*S*)-**14**



(*S*)-**15**



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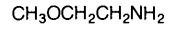

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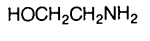

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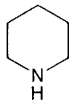

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atom and the hydroxy group of 2-aminoethanols stabilising the complexes.

On the assumption that the hydroxymethyl group of 2-aminoethanols occupies the less hindered site near the phenol residue, the geometries **24** and **25** are excluded because of a steric repulsion between the hydroxymethyl group of the amine and the phenyl barrier and the predicted geometries **26**–**29** are visualised for the complexes of crown ethers **1** and **2** with amines (*S*)-**13** and (*S*)-**14**.

On the basis of the geometries **26**–**29**, the observed enantiomer selectivity of crown ether **1** towards amine (*S*)-**13** and (*S*)-**14** and of crown ether **2** towards amine (*S*)-**13** are interpreted in terms of a steric repulsion between the phenyl barrier and the ligand R [R = CH_3 for (*S*)-**13** and R = $CH(CH_3)_2$ for (*S*)-**14**] making the complexes with the geometries **26** and **29** less stable than their corresponding diastereoisomeric complexes. However, the observed enantiomer selectivity of crown ether **2** towards amine (*S*)-**14** is not explicable on the basis of the predicted geometries **28** and **29**. The relatively small K_a-values for the complexes of crown ethers **1** and **2** with amine (*S*)-**14** are assumed to be due to a large steric repulsion between the bulky isopropyl group of amine (*S*)-**14** and the phenyl barrier.

Both diastereoisomeric complexes of the crown ether **1** with 1-substituted 2-aminoethanol (*S*)-**15** showed higher K_a-value than the complexes of crown ether **1** with 2-substituted 2-aminoethanols (*S*)-**13** and (*S*)-**14**. The relatively large K_a-values observed are interpreted from the geometries **30** and **31**, where the hindered sites near the phenyl barrier are occupied by the hydrogen atoms of the amine and the $CH(CH_3)OH$ group is allowed to occupy the less hindered site, and thus significant steric interactions between the chiral barrier and ligands of the amine are not appreciable in both complexes. In regard to the enantiomer selectivity, amine (*S*)-**15** showed better complementarity to crown ether (*S*,*S*)(*S*,*S*)-**1** than to crown ether (*R*,*R*)(*R*,*R*)-**1**. This chiral recognition would be due to steric interaction between the cyclohexane residue and the methyl group of the amine destabilising the (*R*,*R*)(*R*,*R*)-**1**–(*S*)-**15** complex with the geometry **30**. The enantiomer selectivity of crown ether **2** towards amine (*S*)-**15** is interpreted in terms of a similar steric interaction making the (*S*,*S*)(*S*,*S*)-**2**–(*S*)-**15** complex with the geometry **33** less stable than the (*R*,*R*)(*R*,*R*)-**2**–(*S*)-**15** complex with the geometry **32**.

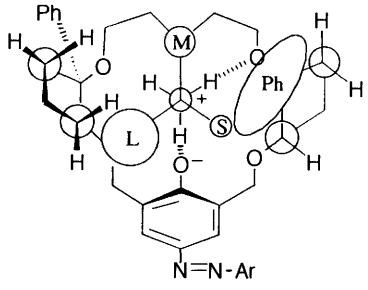
Table 2 provides the K_a-values and the λ_{max}-values of complexes of crown ethers **1** and **2** with achiral amines **16**–**19**. Crown ether **1** bound primary amines **16**, **17** and **18** more weakly than did crown ether **2** presumably due to the following steric requirement. CPK molecular models of the complexes of crown ether **1** with primary amines suggest that the axial hydrogen atoms of the cyclohexane residue cover the donor oxygen atom at the 2 and 10 o'clock position in crown ether (*R*,*R*)(*R*,*R*)-**1** and (*S*,*S*)(*S*,*S*)-**1**, respectively, to weaken Cram's three-point binding mode.[10] On the other hand, the donor oxygen atom at the 10 and 2 o'clock position in crown ether (*R*,*R*)(*R*,*R*)-**2** and (*S*,*S*)(*S*,*S*)-**2**, respectively, is not covered by the hydrogen atom of the cyclohexane residue to form favourably the three-point binding mode in the complexes of crown ether **2**. This may be one reason for the relative weakness in the binding ability of crown ether **1** towards amines examined here.

As mentioned here, the results demonstrated that *cis*-1-phenylcyclohexane-1,2-diol served as an effective chiral barrier of crown ethers and the change in placement of the binding sites with respect to the chiral barriers caused the reversal in enantiomer selectivity.

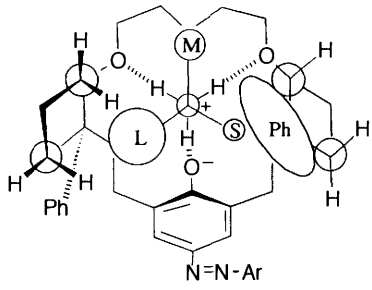
Experimental

General procedure

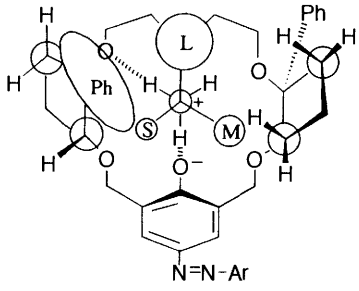
^1H NMR spectra were recorded at 270 MHz on a JASCO JNM-MH-270 spectrometer for solutions in $CDCl_3$ with $SiMe_4$ as internal standard and *J*-values are given in Hz. Mass spectra were recorded on a JEOL-DX-303-HF spectrometer. Elemental analyses were carried out by a Yanagimoto CHN-Corder, Type 2. Mps were measured on a Yanagimoto micro melting point apparatus and are uncorrected. UV and visible spectra were recorded on a Hitachi 330 spectrometer. IR spectra were measured on a Hitachi 260-10 spectrometer. Optical rotations were measured using a JASCO DIP-40 polarimeter at ambient temperature and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. GLC analyses were performed on a Shimadzu GS 8A chromatography using an SE-52-on-Uniport HP 2 m × 2.6 mm column. HPLC analyses were carried out on a Shimadzu LC-6A using a chiral column Opti-Pak AD (Waters), 250 mm × 4.6 mm [hexane–ethanol (9:1); 1.0 cm^3 min^{-1}]. Lipase QL (from *Alcaligenes sp.*) was supplied from the Meito Sangyo Co. (Japan) and used without further purification.



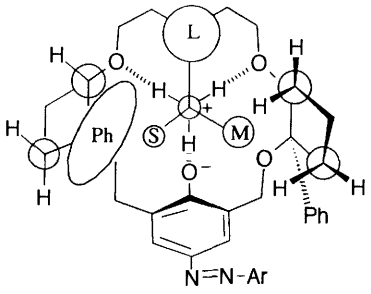
20 [(*S*,*S*)(*S*,*S*)-**1**:(*S*)-amine]



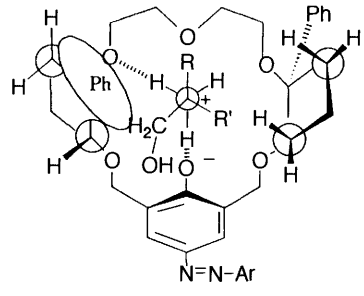
21 [(*R*,*R*)(*R*,*R*)-**2**:(*S*)-amine]



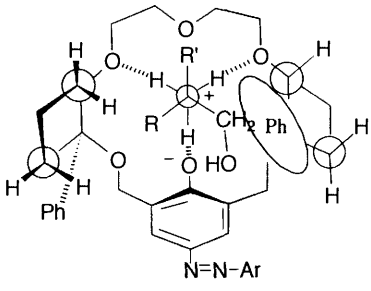
22 [(*R*,*R*)(*R*,*R*)-**1**:(*S*)-amine]



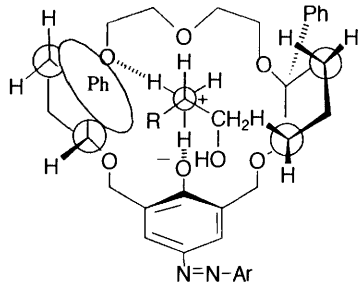
23 [(*S*,*S*)(*S*,*S*)-**2**:(*S*)-amine]



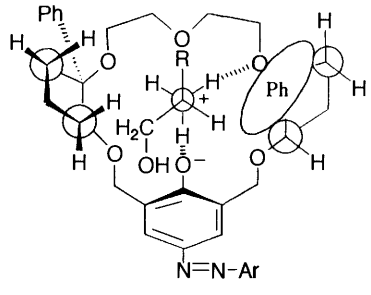
24 [(*R*,*R*)(*R*,*R*)-**1**:2-aminoethanol]



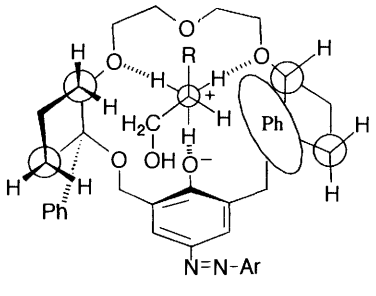
25 [(*R*,*R*)(*R*,*R*)-**2**:2-aminoethanol]



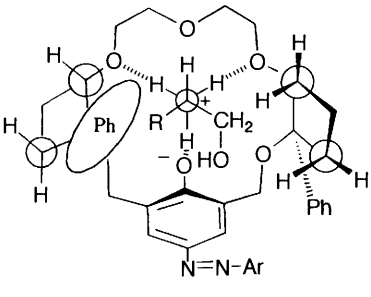
26 [(*R*,*R*)(*R*,*R*)-**1**:(*S*)-amine]



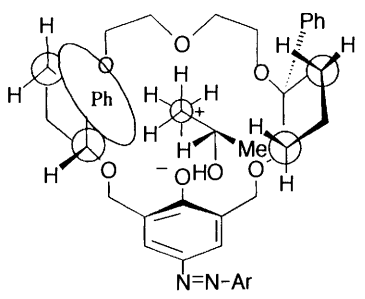
27 [(*S*,*S*)(*S*,*S*)-**1**:(*S*)-amine]



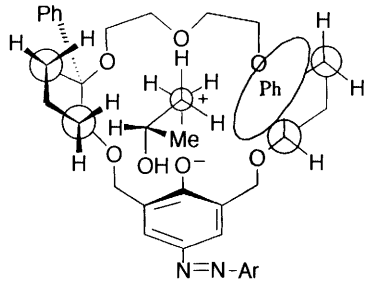
28 [(*R*,*R*)(*R*,*R*)-**2**:(*S*)-amine]



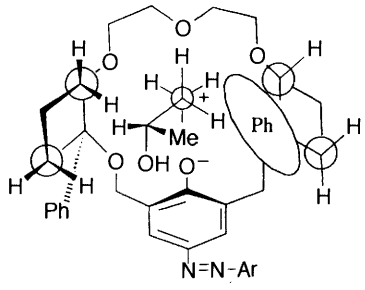
29 [(*S*,*S*)(*S*,*S*)-**2**:(*S*)-amine]



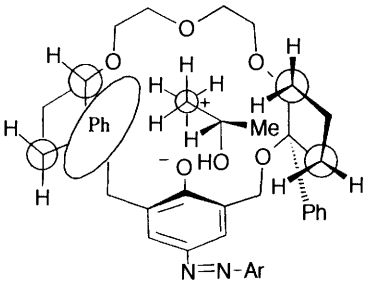
30 [(*R,R*)(*R,R*)-**1**:(*S*)-**15**]



31 [(*S,S*)(*S,S*)-**1**:(*S*)-**15**]



32 [(*R,R*)(*R,R*)-**2**:(*S*)-**15**]



33 [(*S,S*)(*S,S*)-**2**:(*S*)-**15**]

Table 2 Association constants K_a (dm^3 mol^{-1}), absorption maxima λ_{max} for the complexes with achiral amines[a]

Host	Amine	K_a (dm^3 mol^{-1})	(λ_{max}/nm)
(*R,R*)(*R,R*)-**1**	**16**	2.56 × 10^2	(598)
(*R,R*)(*R,R*)-**1**	**17**	5.94 × 10	(600)
(*R,R*)(*R,R*)-**1**	**18**	4.13 × 10^2	(579)
(*R,R*)(*R,R*)-**1**	**19**	1.31 × 10	(592)
(*R,R*)(*R,R*)-**2**	**16**	1.79 × 10^3	(598)
(*R,R*)(*R,R*)-**2**	**17**	3.47 × 10^2	(599)
(*R,R*)(*R,R*)-**2**	**18**	9.53 × 10^2	(588)
(*R,R*)(*R,R*)-**2**	**19**	7.11	(598)

[a] Determined by the Benesi–Hildebrand method at 25 °C in $CHCl_3$.

Optical resolution of *cis*-1-phenylcyclohexane-1,2-diol 4

A mixture of (±)-*cis*-1-phenylcyclohexane-1,2-diol **4**[5] (10.0 g, 0.0521 mol), isopropenyl acetate (11.8 g, 0.118 mol), lipase QL (2.00 g) and diisopropyl ether (200 cm^3) was stirred at 30 °C. The progress of the reaction was monitored by GLC. After the mixture had been stirred for 11 h, the reaction was terminated close to 50% of the esterification point by filtering off the enzyme. The volatile materials were evaporated off under reduced pressure. The residue was chromatographed on silica gel to give (+)-acetate **5** [hexane–diethyl ether (4:1) eluent] (5.64 g, 48%) and (−)-diol **4** (91% ee by HPLC) [hexane–diethyl ether (2:1) eluent] (5.00 g, 50%). Recrystallisation of (−)-diol **4** from hexane gave enantiomerically pure *species* (−)-**4** (4.40 g), $[\alpha]_D^{22}$ −19.4 (*c* 1.00, benzene) (>99% ee; t_R = 12 min by HPLC); mp 121–121.5 °C (Found: C, 74.9; H, 8.3. $C_{12}H_{16}O_2$ requires C, 74.97; H, 8.39%).

A solution of (+)-acetate **5** (5.20 g, 0.0222 mol) in 5% methanolic NaOH (300 cm^3) was stirred at room temperature for 12 h. The reaction mixture was then neutralised with dil. HCl and concentrated under reduced pressure. After extraction with diethyl ether, the extract was washed successively with aq. sodium hydrogen carbonate and water, and then was dried ($MgSO_4$). The solvent was removed to give (+)-diol **4**, (95% ee by HPLC), which was recrystallised from hexane to give enantiomerically pure species (+)-**4** (3.83 g, 90%), $[\alpha]_D^{22}$ +19.3 (*c* 1.00, benzene) (>99% ee; t_R = 72 min by HPLC); mp 120.5–121 °C (Found: C, 74.8; H, 8.3%).

(4*R*,9*R*,17*R*,22*R*)-(−)-27,29-Dimethoxy-9,17-diphenyl-3,10,13,16,23-pentaoxatetracyclo[23.3.1.0^{4,9}.0^{17,22}]nonacosa-1(29)-25,27-triene 7

A solution of diol (*R,R*)(*R,R*)-(−)-**6**,[4] $[\alpha]_D^{22}$ −7.52 (*c* 0.550, $CHCl_3$) (1.60 g, 3.50 mmol) and 1,3-bis(bromomethyl)-2,5-dimethoxybenzene (1.15 g, 3.50 mmol) in dry THF (370 cm^3) was added dropwise to a boiling mixture of sodium hydride (340 mg, 14.1 mmol), potassium tetrafluoroboranuide (443 mg, 3.51 mmol) in dry THF (150 cm^3) over a 10 h period and then the mixture was refluxed for a further 20 h under dry nitrogen. After the reaction mixture had been cooled in an ice-bath, a small amount of water was slowly added and the solvent was removed under reduced pressure. The residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (Mg_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on silica gel to give *crown ether* **7** as a glass (1.74 g, 80%) [from hexane–diethyl ether (1:1)]; $[\alpha]_D^{22}$ −97.1 (*c* 1.01, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2930, 2855, 1610, 1480, 1390, 1330, 1250, 1090, 860, 760 and 700; δ_H 1.10–2.06 (16 H, m, CH_2), 2.90–3.36 (8 H, m, OCH_2), 3.73 (3 H, s, OCH_3), 3.97 (3 H, s, OCH_3), 3.99–4.10 (2 H, m, CH), 4.53 (4 H, dd, *J* 10.0 and 25.4, $ArCH_2$), 6.71 (2 H, s, CH_3OAr) and 7.14–7.57 (10 H, m, ArH); *m/z* 616 (M^+) (Found: C, 73.8; H, 7.7. $C_{38}H_{44}O_7$ requires C, 74.00; H, 7.84%).

(*R,R*)(*R,R*)-Azophenolic crown ether 1

A solution of CAN (2.70 g, 4.92 mmol) in acetonitrile (7 cm^3)–water (5 cm^3) was added to a solution of crown ether (−)-**7** (600 mg, 0.978 mmol) in a mixture of methylene dichloride (2 cm^3) and acetonitrile (15 cm^3). The mixture was stirred for 15 min at room temperature and then for another 1.5 h at 40 °C. After addition of water, the reaction mixture was extracted with chloroform and the extract was washed with water and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on silica gel to give quinone

8 as a yellow oil ($CHCl_3$ as eluent), which was immediately dissolved in a mixture of methylene dichloride (2 cm^3) and ethanol (20 cm^3). To the solution was added a solution of 2,4-dinitrophenylhydrazine (400 mg, 2.02 mmol) in a mixture of ethanol (20 cm^3) and conc. H_2SO_4 (2 cm^3) and then the mixture was stirred for 1.5 h at room temperature and diluted with water. After extraction with chloroform, the extract was washed successively with aq. sodium hydrogen carbonate and water, and was then dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel [hexane–ethyl acetate (1 : 1) as eluent] followed by further purification by TLC on silica gel [hexane–ethyl acetate (1 : 1) as eluent] to give compound **1** as a red oil, which was triturated with ethanol to give pure species **1** as a *red solid* (415 mg, 56%); mp 109–110 °C; ν_{max}(KBr)/cm^{-1} 3250, 2930, 1600, 1530, 1470, 1350, 1090, 840 and 705; λ_{max}($CHCl_3$)/nm 414 (ε 2.42 × 10^4 dm^3 mol^{-1} cm^{-1}); δ_H($CDCl_3$), 1.27–2.13 (16 H, m, CH_2), 3.26–3.37 (2 H, m, OCH_2), 3.38–3.47 (2 H, m, OCH_2), 3.57–3.82 (4 H, m, OCH_2), 3.90 (2 H, dd, *J* 4.98 and 2.49, CH), 4.66 (4 H, dd, *J* 8.2 and 11.9, $ArCH_2$), 7.25–7.54 (10 H, m, ArH), 7.71 (2 H, s, HOAr*H*), 7.80 (1 H, d, *J* 8.33, O_2NArH), 8.48 (1 H, dd, *J* 6.86 and 24.5, O_2NArH), 8.72 (1 H, d, *J* 2.45, O_2NArH) and 9.72 (1 H, s, OH); *m/z* 766 (M^+) (Found: C, 65.3; H, 6.1; N, 7.25. $C_{42}H_{46}N_4O_{10}$ requires C, 65.78; H, 6.05; N, 7.31%).

(*R*,*R*)(*R*,*R*)-Azophenolic crown ether 2

By the same procedure as described above, oxidation of crown ether (*R*,*R*)(*R*,*R*)-(+)-**9**, $[\alpha]_D$ +45.6 ($CHCl_3$) prepared from (1*R*,2*R*)-**4** (> 99% ee) [7] (570 mg, 0.973 mmol) with CAN (2.70 g, 4.92 mmol) followed by silica gel chromatography gave quinone **10** as a yellow oil ($CHCl_3$ as eluent). Treatment of quinone **10** with 2,4-dinitrophenylhydrazine (400 mg, 2.02 mmol) followed by column chromatography on silica gel [hexane–ethyl acetate (1 : 1) as eluent] gave a red oil, which was further purified on TLC on silica gel [hexane–ethyl acetate (1 : 1) as eluent] to give compound **2** as an oil, which was triturated with ethanol to give pure species **2** as a *red solid* (414 mg, 56%); mp 108–109.5 °C; ν_{max}(KBr)/cm^{-1} 3200, 2940, 1600, 1535, 1450, 1350, 1300, 840, 760 and 700; λ_{max}($CHCl_3$)/nm 418 (ε 2.35 × 10^4); δ_H($CDCl_3$) 1.27–2.13 (14 H, m, CH_2), 2.13–2.30 (2 H, m, CH_2), 3.24–3.35 (2 H, m, OCH_2), 3.57–3.68 (2 H, m, OCH_2), 3.70–3.84 (6 H, m, CH and OCH_2), 4.46 (4 H, dd, *J* 8.2 and 11.9, $ArCH_2$), 7.27–7.61 (10 H, m, ArH), 7.66 (2 H, s, HOAr*H*), 7.79 (1 H, d, *J* 8.96, O_2NArH), 8.44 (1 H, dd, *J* 6.72 and 2.24, O_2NArH), 8.72 (1 H, d, *J* 2.24, O_2NArH) and 9.98 (1 H, s, OH); *m/z* 766 (M^+) (Found: C, 65.6; H, 6.1; N, 7.3. $C_{42}H_{46}N_4O_{10}$ requires C, 65.78; H, 6.05; N, 7.31%).

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Paper 5/04479K
Received 10*th July* 1995
Accepted 9*th August* 1995