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**PAPER**

# Synthesis of chiral calix[4]arenes bearing aminonaphthol moieties and their use in the enantiomeric recognition of carboxylic acids†

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Two armed chiral calix[4]arenes **8–16** functionalized at the lower rim with chiral aminonaphthol units have been prepared and the structures of these receptors characterized by FTIR, $^{1}$H, and $^{13}$C, DEPT and COSY NMR spectroscopy and elemental analysis. The enantioselective recognition of these receptors with various carboxylic acids has been studied by $^{1}$H NMR and UV/Vis spectroscopy. The receptors exhibited different chiral recognition abilities towards the enantiomers of racemic materials and formed 2 : 1 or 1 : 1 complexes between host and guest. It was also demonstrated that chiral calix[4]arenes **9** and **16** could be used as chiral NMR solvating agents to determine the enantiomeric purity of mandelic acid.

## Introduction

Molecular recognition is a very important concept due to the role of chirality in many biological processes.[1] Because natural living systems are mostly composed of chiral biological molecules, which exist only in one of the possible enantiomeric forms, they interact differently with each stereoisomer of a racemic drug, as well as metabolize each enantiomer by way of a separate pathway to produce different pharmacological activities. Therefore, one stereoisomer may produce the desired therapeutic activities, while the other may be inactive or produce harmful effects. Detailed understanding of the interactions between biological molecules will be helpful for the development of novel enantioselective sensors, asymmetric catalysts and other molecular devices.[2]

Chiral carboxylic acids and their derivatives are organic molecules involved in a wide variety of biological processes and also play an important role in the area of design and preparation of pharmaceuticals, as they are part of the synthesis process in the production of drug intermediates and protein-based drugs.[3] The growing use of enantiomerically pure chiral carboxylic acids has given rise to the need for the development of fast and accurate methodologies for the determination of the enantiomeric composition of chiral carboxylic acids.[4]

The widespread research on molecular recognition of guests by artificial receptors has stimulated chemists to design chiral macrocyclic ligands for chiral recognition and chiral catalysis.[5,6] Calixarenes are versatile platforms in constructing supramolecular receptors for selective recognition of ions and neutral molecules.[7] The introduction of chirality into calixarene framework by attaching chiral units at one of the calix rims offers the possibility of studying chiral recognition phenomena in host–guest interactions.[8] Therefore our interest focused on new methods of synthesizing enantiomerically pure calixarenes.

In recent years, we have reported the synthesis of novel chiral calix[4]arenes containing various functionalities including amides,[9] Schiff bases,[10] and quaternary ammonium salts[11] as well as their catalytic activities and enantiomeric recognition properties toward chiral amines and amino acid derivatives. In the present study, we report the synthesis of novel calix[4]arene derivatives bearing chiral aminonaphthol moieties at the lower rim and their recognition abilities for carboxylic acids by $^{1}$H NMR and UV-Vis spectroscopy.

## Results and discussion

### Design and synthesis of calix[4]arene based receptors

This work is mainly focused on the synthesis and application of chiral calix[4]arene derivatives bearing aminonaphthol moieties. For the desired goal, first, a Mannich reaction was carried out, using a chiral or achiral amine, β-naphthol and benzaldehyde as starting materials, to yield the aminonaphthols **1–4** (Fig. 1). Compounds **1–3** were synthesized stereoselectively under solvent free conditions, starting from benzaldehyde, 2-naphthol and (*R*)-1-phenylethylamine or (*R*)-1-(2-naphthyl)-ethylamine respectively according to the literature procedures.[12] The pyrrolidinyl derivative of racemic aminonaphthol **4** was easily prepared using benzaldehyde, 2-naphthol and pyrrolidine in ethanol at 78 °C.[13] Racemic aminonaphthol derivative **4** was resolved using L-(+)-tartaric acid and enriched in the (*R*)-(−)enantiomer (97% ee). Then, coupling of the aminonaphthols with the corresponding

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† Electronic supplementary information (ESI) available: $^{1}$H, $^{13}$C, DEPT and COSY NMR spectra of compounds, $^{1}$H NMR and UV/Vis titration data. See DOI: 10.1039/c0ob00399a

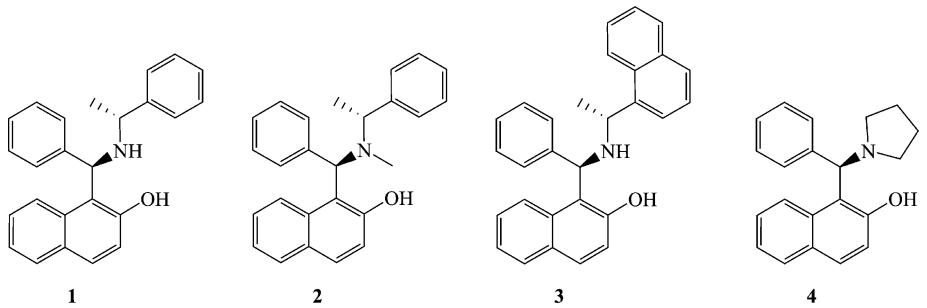



**Fig. 1** Chiral aminonaphthol derivatives appended to calix[4]arene.

calix[4]arene dibromide derivatives **5–7**[14] in DMF with anhydrous $K_2CO_3$ at room temperature led to the formation of the chiral calix[4]arene derivatives in moderate to good yields (Scheme 1). The products were characterized by a combination of $^1$H NMR, $^{13}$C NMR, FTIR and elemental analysis.

The stereogenic centers of receptors disturb the planar symmetry of the parent rings, resulting in more aromatic carbon signals in the $^{13}$C NMR spectra of the receptors. This pattern is similar to those observed in the $^{13}$C NMR spectra of other chiral calix[4]arenes.[15] The $^1$H NMR spectra of chiral calix[4]arenes exhibit two sets of doublets due to the bridging methylene protons and two sets of singlets due to the *tert*-butyl groups. This indicates that chiral *p-tert*-butylcalix[4]arene derivatives adopt a cone conformation in $CHCl_3$.

### Enantiomeric recognition study of chiral calix[4]arenes for racemic carboxylic acids by $^1$H NMR spectroscopy

Chiral macrocyclic compounds have been recognized as successful and promising chiral receptors for molecular recognition, mainly due to their inherent reduced flexibility and complexation ability.[16] With the optically pure calix[4]arene derivatives bearing aminonaphthol moieties in hand, we then studied the chiral recognition ability of these receptors toward racemic carboxylic acids, mandelic acid, *o*-chloro mandelic acid, dibenzoyl tartaric acid, hydroxyisovaleric acid and 2-chloropropionic acid (**a–e**) shown in Fig. 2. Because the signals of the methine or methyl hydrogens of all these guests do not overlap with the peaks of the other proton signals in their $^1$H NMR spectra after they interact with the host molecules, they are ideal probes for the present study. Preliminary $^1$H NMR studies of the chiral calix[4]arenes were performed with equimolar amounts of racemic mandelic acid.[17,18]

When the solution of racemic mandelic acid (10 mM in $CDCl_3$) was gradually added to the 10 mM solution of hosts **11–13** in $CDCl_3$, the CH proton signal of guest **a** moved to upfield without displaying any resolution (Fig. 3e–g). As a result of diastereomeric complexation, clear signal splitting ($\delta$ = 4.90 and 4.86 ppm for host **9**, $\delta$ = 5.01 and 4.99 ppm for host **14** and $\delta$ = 4.99 and 4.96 ppm for host **16**; Fig. 3b, Fig. 3d and Fig. 3c) with an upfield shift of the signal of the benzylic proton of racemic mandelic acid ($\delta$ = 5.25 ppm; Fig. 3a) was observed. The C═O stretch (1716 cm$^{-1}$ for mandelic acid) disappeared in the FTIR spectra of a 1 : 1 mixture of **9** and mandelic acid, and the observed intensities increased at 1624 cm$^{-1}$ (the $COO^-$ stretch) which demonstrated that the carboxyl group of the acid was ionized.

In order to investigate the role of a spacer between the basic nitrogen atom and the calixarene backbone, we also synthesized chiral calixarenes (**8**, **10** and **15**) containing different methylene spacers. Although the methine proton signals of racemic mandelic acid split into two singlets with these hosts, the chemical shift non-equivalencies ($\Delta\Delta\delta$) were lower (Table 1, entry 1, 3 and 8). From the results shown in Table 1, it can be observed that the chiral receptors with a three-methylene spacer afforded relatively better results than the others. In addition, different proportions of both enantiomers of mandelic acid were treated with **9** and **16**, and different signal intensities for both (*S*)- and (*R*)-mandelic acid were observed depending on the proportions (Fig. 4). These results clearly indicate that these chiral calix[4]arenes could be used as chiral NMR solvating agents to determine the enantiomeric purity of mandelic acid at appropriate temperature.

Furthermore, $^1$H NMR titration studies of the chiral calix[4]arenes **9** and **16** with different molar ratios of (*R*)- or (*S*)-mandelic acid were examined (Fig. 5). Even in the presence of a less than stoichiometric amount of **16**, different chemical shifts of the benzylic proton of (*R*)- and (*S*)-mandelic acid were observed. Interestingly, the degree of signal separation of both guests did not depend on the molar ratio of chiral calix[4]arene/guest, although many chiral solvating agents depend greatly on the molar ratio of the chiral agent.

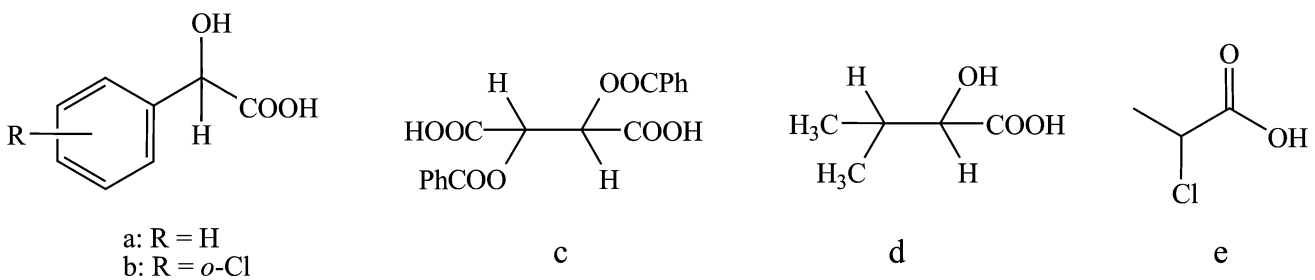
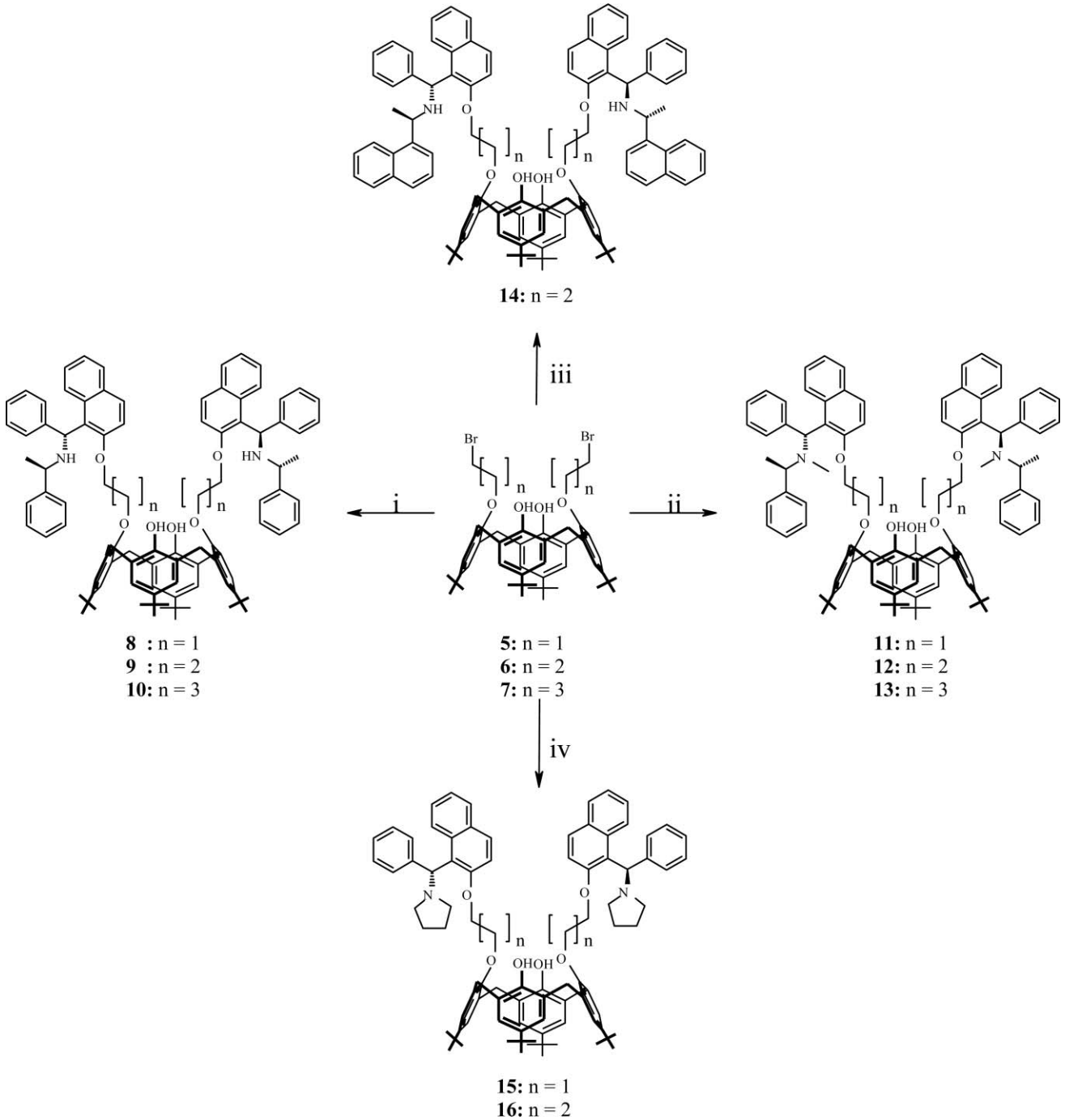



**Fig. 2** Chemical structures of the guests employed.




**Scheme 1** Reagents and conditions: (i)–(iv) Appropriate chiral aminonaphthol **1–4**, $K_2CO_3$, DMF, rt.

Also the magnitude of the upfield shifts of the signals of the benzylic proton gradually increased with an increase in the molar ratio of calixarenes. However, the addition of more than two equimolar amount of compounds **9** and **16** showed no further change in the chemical shifts of the mandelic acids. These results indicate that chiral calix[4]arenes **9** and **16** and mandelic acid form a 2 : 1 complex (see Supplementary Information for the Job plot analysis†).

Also the stoichiometry of the complexes between the receptors and the guest **c** (*rac*-dibenzoyltartaric acid) was determined by a continuous variation plot. The total concentration of the hosts and the guest was kept constant (10 mM) in $CDCl_3$, whilst the molar fraction of the guest {[G]/([H]+[G])} was continuously varied. The Job plots of **16** with (L)- and (D)-dibenzoyltartaric acid are illustrated in Fig. 6. A minimum of $\Delta\delta X$ at $X = 0.5$ was observed when the molar ratio of the compound **16** and (L)- or (D)-dibenzoyltartaric acid was 1 : 1, which indicated that host **16** and the guest formed 1 : 1 instantaneous complexes. It is apparent that the chemical shift changes of (L)-dibenzoyltartaric acid were greater than that of the corresponding (D)-dibenzoyltartaric acid in the presence of compound **16**.

**Table 1** Chemical shift changes ($\Delta\delta$) and non-equivalencies ($\Delta\Delta\delta$) of the methine proton of guest **a** in the presence of chiral hosts by $^1$H NMR spectroscopy (400 MHz) in $CDCl_3$ at 25 °C

| Entry | Host | Guest | Ratio | $\Delta\delta$ (ppm) | $\Delta\Delta\delta$ (ppm) | Enantiomer[a] |
|---|---|---|---|---|---|---|
| 1 | **8** | **a** | 1 : 1 | — | 0.012 | (*S*) |
| 2 | **9** | **a** | 1 : 1 | — | 0.042 | (*S*) |
| 3 | **10** | **a** | 1 : 1 | — | 0.003 | (*S*) |
| 4 | **11** | **a** | 1 : 1 | 0.308 | — | — |
| 5 | **12** | **a** | 1 : 1 | 0.212 | — | — |
| 6 | **13** | **a** | 1 : 1 | 0.177 | — | — |
| 7 | **14** | **a** | 1 : 1 | — | 0.020 | (*S*) |
| 8 | **15** | **a** | 1 : 1 | — | 0.025 | (*S*) |
| 9 | **16** | **a** | 1 : 1 | — | 0.030 | (*S*) |

[a] Enantiomer showing higher upfield shift.

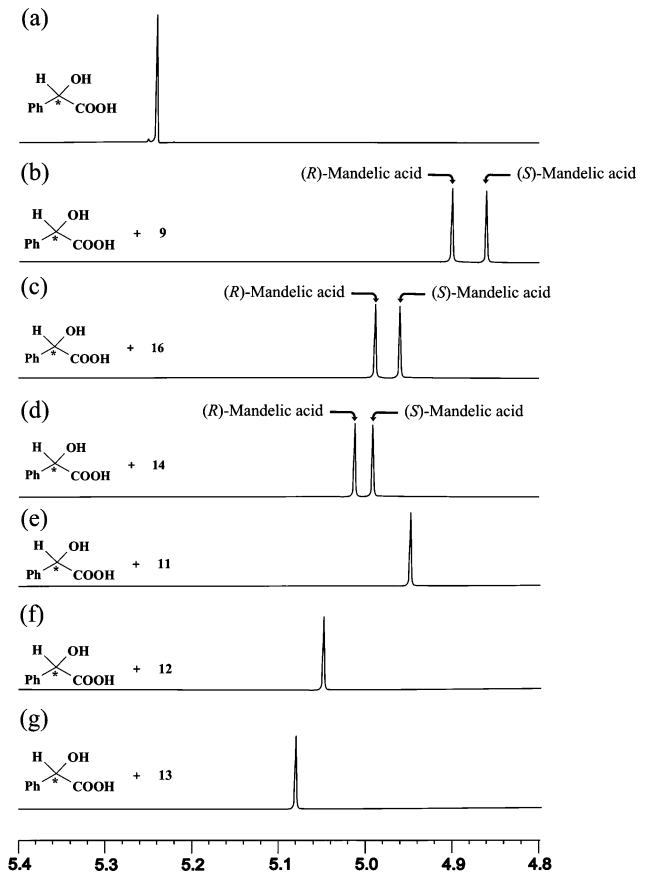



**Fig. 3** $^1$H NMR spectra of racemic mandelic acid in the absence and presence of chiral hosts in $CDCl_3$ at 25 °C [mandelic acid/host = 1 : 1].

Next, we examined the relationship between the absolute configuration and the upfield shift of the proton signals of the carboxylic acids in the presence of hosts. For all the tested compounds, the signals of the (*S*)-enantiomer appeared at a higher magnetic field than that of the (*R*)-enantiomer in the presence of hosts (Table 1).

A variety of racemic carboxylic acids (Fig. 1, (b–e)) were chosen as guests to screen the potential of **9**, **14** and **16** as chiral shift reagents by using $^1$H NMR spectroscopy. Table 2 shows chemical shift non-equivalencies ($\Delta\Delta\delta$) of the guests in the presence of chiral hosts. Generally for the carboxylic acids tested **b–d**, the signals for the protons attached to the stereogenic center were split. While the

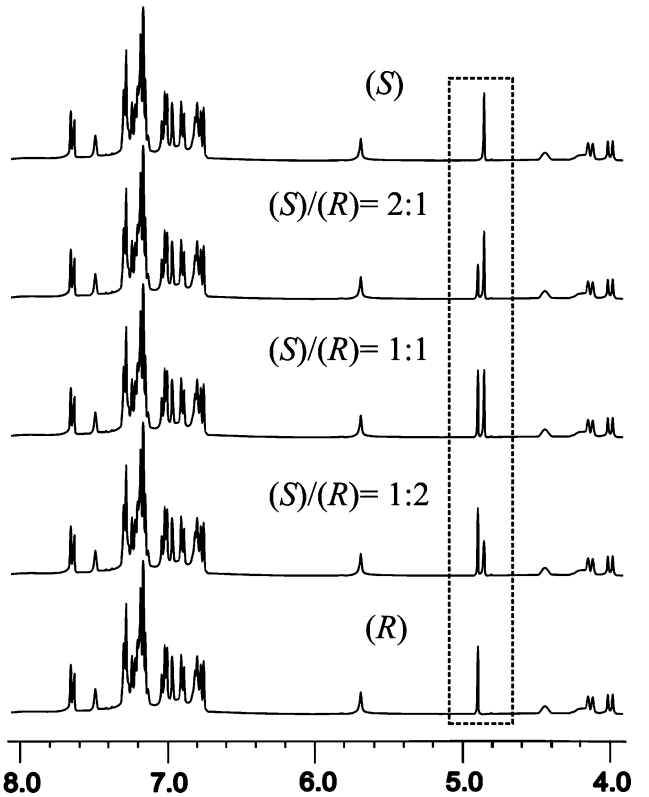



**Fig. 4** $^1$H NMR spectra of different enantiomeric ratios of mandelic acid in the presence of **9** in $CDCl_3$ at 25 °C [mandelic acid/**9** = 1 : 1].

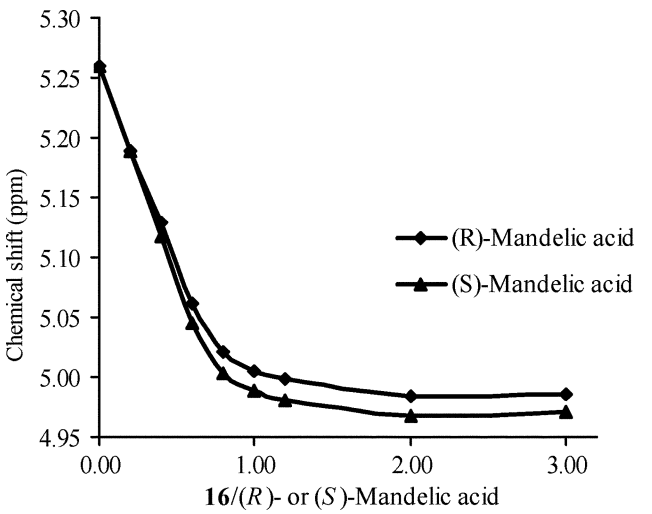


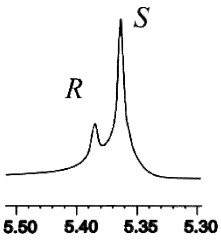
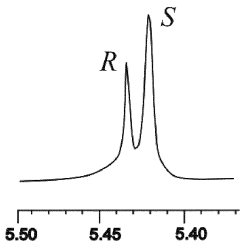
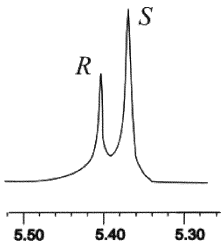
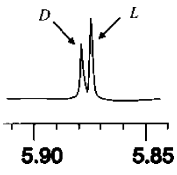
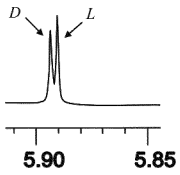
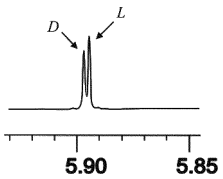
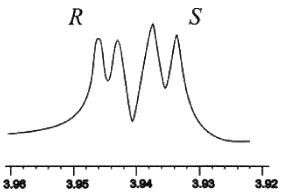
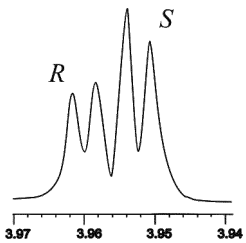
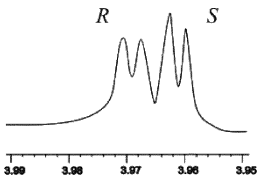
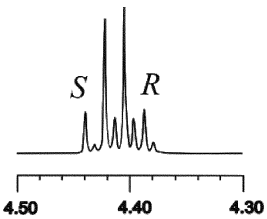
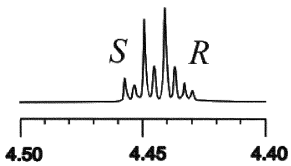
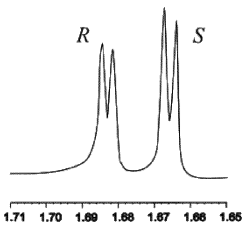

**Fig. 5** $^1$H NMR titration curves of compound **16** with (*R*)- and (*S*)-mandelic acids.

methyl proton signal of **e** was efficiently split into two doublets with chiral host **16**, the CH proton signal was split into two quartets with chiral hosts **9** and **14**.

The formation of diastereomeric host–guest complexes possibly occurs through interaction of the basic nitrogen atom in chiral receptors and the carboxyl group in the chiral carboxylic acid. The protonated amine groups would lead to the formation of the corresponding diastereomeric salt with chiral carboxylic acids. Though the number of recognition sites that are necessary for producing chiral recognition is due to the shape of the receptor,

**Table 2** Chemical shift non-equivalencies ($\Delta\Delta\delta$) of the methine and α-methyl protons of guests in the presence of chiral hosts by $^1$H NMR spectroscopy (400 MHz) in $CDCl_3$ at 25 °C

| Acid | Proton spectra | Compound **9** spectra | Compound **14** spectra | Compound **16** spectra |
|---|---|---|---|---|
| **b** | α-H |  |  |  |
| **c** | α-H |  |  |  |
| **d** | α-H |  |  |  |
| **e** | α-H or $CH_3$ |  |  |  |

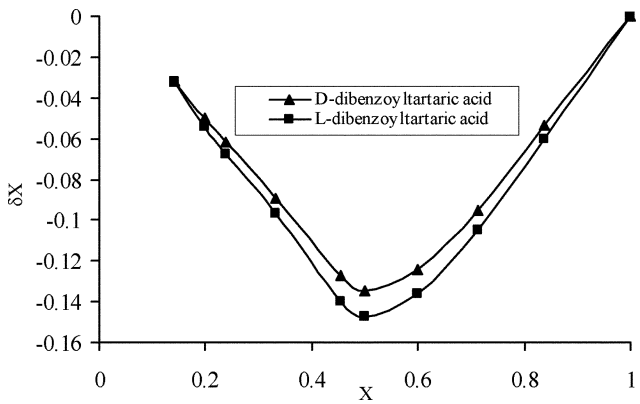



**Fig. 6** Job plots of **16** with (L)- and (D)-dibenzoyltartaric acid [$X$ = molar fraction of dibenzoyltartaric acid, $\Delta\delta$ = chemical shift change of the methine proton of (L)- and (D)-dibenzoyltartaric acid]. (■) With pure (L)- dibenzoyltartaric acid, (▲) with pure (D)-dibenzoyltartaric acid.

three ordinary recognition sites are required in the receptor molecules.[19] In this study, chiral calix[4]arenes interact with a minimum of three of the possible recognition groups (phenoxy oxygen, amine nitrogen, phenyl groups and hydroxy groups) in order to exhibit enantioselective binding to the chiral carboxylic acids. Among the guest molecules, mandelic acid derivatives contain a hydroxy group at the α-position of the carbonyl group. This oxygen function may act as an additional binding site and play a crucial role for chiral recognition. Since the methine protons are adjacent to the hydroxy group, these protons must be significantly influenced by the possible recognition groups of the chiral hosts.

## UV spectral titrations

UV-Vis spectroscopic method is a convenient and widely used method for the study of binding phenomena.[20] When the receptors absorb light at different wavelengths in the free and complexed states, the differences in the UV-Vis spectra may suffice for the estimation of molecular and enantiomeric recognition thermodynamics. In order to obtain the association constants ($K$) and the thermodynamic quantities ($\Delta H$ and $\Delta S$) for the stoichiometric 1 : 1 inclusion complexation of **9** and **16** with (D)- or (L)-dibenzoyltartaric acid, spectrophotometric titrations

have been performed in $CHCl_3$ at 25–35 °C. Upon addition of (L)-dibenzoyltartaric acid to the $CHCl_3$ solution containing chiral receptor **9** ($1.0 \times 10^{-5}$ M, 25 °C), the absorbance of **9** at 241 nm decreased and the one at 285 nm increased, with an isosbestic point at 248 nm (Fig. 7). A similar spectral change was observed when the other receptor was used as host and was believed to be due to hydrogen bonding and π–π stacking.

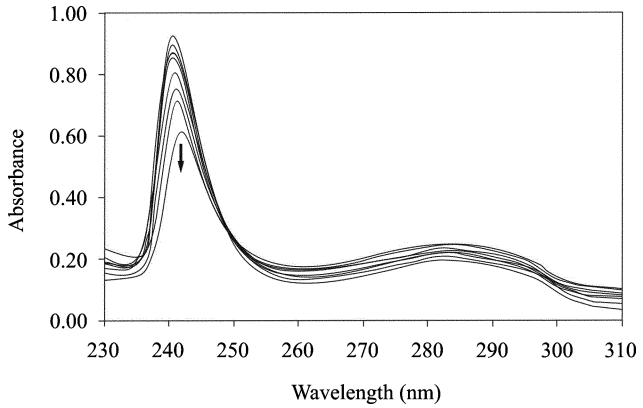



**Fig. 7** UV/Vis spectra of chiral calix[4]arene **9** ($1.00 \times 10^{-5}$ M) in the presence of (L)-dibenzoyltartaric acid ($0.10–3.00 \times 10^{-4}$ M) in $CHCl_3$.

The complexation of carboxylic acid derivative (G) with chiral calix[4]arene (H) is expressed by eqn (1):

$$H + G \underset{}{\overset{K}{\rightleftharpoons}} H \cdot G \tag{1}$$

Under the conditions employed, the concentration of calix[4]arene derivatives ($1.00 \times 10^{-5}$ M) is much smaller than that of guest, *i.e.* $[H]_0 \ll [G]_0$. Therefore, the stability constant of the supramolecular system formed can be calculated according to the modified Hildebrand–Benesi equation,[21] eqn (2), where $[G]_0$ denotes the total concentration of carboxylic acid, $[H]_0$ refers to the total concentration of calix[4]arene derivative, $\Delta\varepsilon$ is the difference between the molar extinction coefficient for the free and complexed calix[4]arene derivative, $\Delta A$ denotes the changes in the absorption of the modified calix[4]arene on adding carboxylic acid derivative.

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

For all guest molecules examined, plots of calculated $1/\Delta A$ values as a function of $1/[G]_0$ values give good straight lines, supporting the 1 : 1 complex formation. Typical plots are shown for the complexation of compound **9** with (L)-DBTA in Fig. 8.

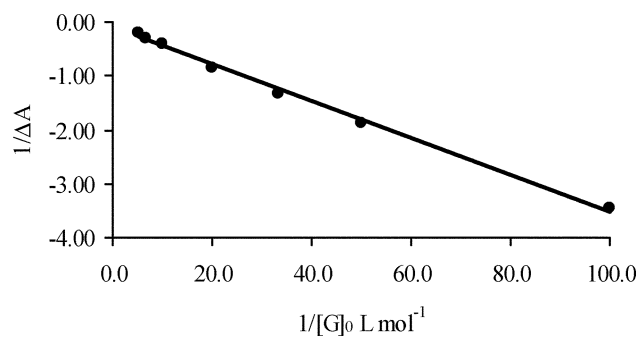



**Fig. 8** Typical Benesi–Hildebrand plot of $1/\Delta A$ *versus* $1/[G]_0$.

The free-energy change ($\Delta G$) for inclusion complexes formed by chiral calix[4]arene derivatives and guest carboxylic acid is calculated from the equilibrium constant $K$ by eqn (3):

$$\Delta G = -RT \ln K \tag{3}$$

and is related to the enthalpic and entropic changes ($\Delta H$ and $\Delta S$) through the Gibbs–Helmholtz equation [eqn (4)]. Combining eqn (3) and (4), we obtain eqn (5) which describes the temperature dependence of $K$. Thus, plots of the ln $K$ values as a function of the inverse of temperature gave good linear relationships for the working temperature range (Fig. 9).

$$\Delta G = \Delta H - T\Delta S \tag{4}$$

$$\ln K = -\Delta H/RT + \Delta S/R \tag{5}$$

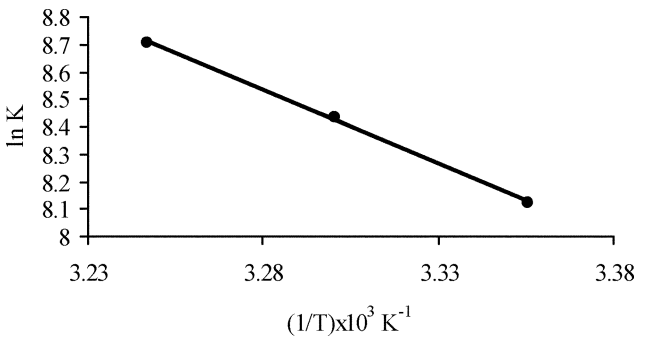



**Fig. 9** The plot of ln K *versus* $1/T$ for the host–guest complexation of **9** and (L)-DBTA in $CHCl_3$ at 25 °C.

The association constants ($K$), the free-energy change ($-\Delta G_0$) calculated from the slope and the intercept, and the thermodynamic parameters are summarized in Table 3, along with the enantioselectivity $K_L/K_D$ for the complexation of D/L-dibenzoyltartaric acid by these hosts.

UV-Vis spectroscopic studies indicate that chiral receptors **9** and **16** show strong binding and good recognition ability for the enantiomers of dibenzoyltartaric acid. This is presumably due to multiple hydrogen bonding and π–π stacking interactions between the receptor and the aromatic side chain of the guest. From the data shown in Table 3, all hosts have greater $K$ values toward the (L)-enantiomer of dibenzoyltartaric acid than the (D)-enantiomer, which is probably due to the more complementary structure of the (L)-enantiomer with receptors. Table 3 also shows the enantiomeric discrimination of the guest **c**, characterized by the value of $K_L/K_D$, which are 2.27 and 1.40 for chiral calix[4]arene receptors **9** and **16**. It was found that chiral calix[4]arene **9** containing a secondary amine moiety and an extra aromatic ring gave stronger binding and better recognition ability for the guest when compared with receptor **16**. As can be recognized readily from Table 3, all the values of the enthalpy changes ($\Delta H°$) and the entropy changes ($\Delta S°$) of the resulting complexes are positive. These results indicate that the complexation of chiral calix[4]arenes (**9** and **16**) with D/L-dibenzoyltartaric acid is driven predominantly by the favorable entropic change, typically showing large positive entropy changes ($\Delta S°$ = 341.68–377.81 J mol$^{-1}$) and somewhat smaller positive enthalpy changes ($\Delta H°$ = 83.80–94.87 kJ mol$^{-1}$). One possible explanation for the complexation of the large entropy driving force

**Table 3** Binding constants ($K$), enantioselectivities ($K_L/K_D$) and thermodynamic parameters for the complexation of (L)- and (D)-dibenzoyltartaric acid with the chiral hosts **9** and **16** in $CHCl_3$ at 25 °C

| Entry | Host | Guest | $K\times10^3/M^{-1}$ | $K_L/K_D$ | $-\Delta G$/kJ mol$^{-1}$ | $-\Delta\Delta G^a$ | $\Delta H$/kJ mol$^{-1}$ | $\Delta\Delta H^b$ | $\Delta S$/J mol$^{-1}$ | $\Delta\Delta S^c$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **9** | (D)-DBTA | 1.41 ± 0.03 | 2.27 | 18.03 ± 0.18 | 1.87 | 83.80 ± 0.92 | 2.09 | 341.68 ± 6.07 | 13.32 |
| 2 | **9** | (L)- DBTA | 3.20 ± 0.06 | | 19.90 ± 0.22 | | 85.89 ± 1.35 | | 355.00 ± 7.68 | |
| 3 | **16** | (D)-DBTA | 0.91 ± 0.02 | 1.40 | 17.00 ± 0.26 | 0.72 | 89.10 ± 0.75 | 5.77 | 356.03 ± 5.42 | 21.78 |
| 4 | **16** | (L)- DBTA | 1.27 ± 0.05 | | 17.72 ± 0.34 | | 94.87 ± 1.43 | | 377.81 ± 8.17 | |

[a] $\Delta\Delta G = \Delta G_L - \Delta G_D$. [b] $\Delta\Delta H = \Delta H_L - \Delta H_D$. [c] $\Delta\Delta S = \Delta S_L - \Delta S_D$.

is that both dissociated guest and free calix[4]arene derivatives are heavily solvated by hydrogen-bonding interactions.

## Conclusions

In this study, novel chiral calix[4]arenes bearing aminonaphthol moieties were developed for the recognition of various chiral carboxylic acids. The chiral calix[4]arenes **9** and **16** could be used as chiral NMR solvating agents to determine the enantiomeric purity of mandelic acid at ambient temperature. Further studies of the chiral calix[4]arenes to allow asymmetric catalysis are now in progress in our laboratory.

## Experimental

### General

Melting points were determined on an Electrothermal 9100 apparatus in a sealed capillary and are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded at room temperature on a Varian 400 MHz spectrometer in $CDCl_3$. IR spectra were obtained on a Perkin Elmer Spectrum 100 FTIR spectrometer using KBr pellets. UV/Vis spectra were measured with a Perkin Elmer Lambda 25 spectrometer. Optical rotations were measured on an Atago AP-100 digital polarimeter. The HPLC measurements were carried out on Agilent 1100 equipment connected with a Zorbax RX-C18 column. Elemental analyses were performed using a Leco CHNS-932 analyzer. Analytical TLC was performed using Merck prepared plates (silica gel 60 F254 on aluminium). Flash chromatography separations were performed on a Merck Silica Gel 60 (230–400 Mesh). All reactions, unless otherwise noted, were conducted under a nitrogen atmosphere. All starting materials and reagents used were of standard analytical grade from Fluka, Merck and Aldrich and used without further purification. Toluene was distilled from $CaH_2$ and stored over sodium wire. Other commercial grade solvents were distilled, and then stored over molecular sieves. The drying agent employed was anhydrous $MgSO_4$.

### Syntheses

**General procedure for the synthesis of compounds 8–16.** Compounds **8–16** were synthesized using a modified procedure originally reported by Zhang *et al.*[22] To a suspension of appropriate aminonaphthol (1 mmol) and $K_2CO_3$ 1.38 g (10 mmol) in dry DMF (15 mL) was added a solution of *p-t*-butylcalix[4]arene dibromide derivatives (0.5 mmol) in dry DMF (15 mL) dropwise. The mixture was stirred at room temperature for 48 h. Then it was poured into 50 mL water and extracted with toluene (10 mL × 3), washed with water (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$, filtered, evaporated and purified by flash chromatography.

**25,27-Bis[(1-((*R*)-phenyl{[(1′*R*)-1′-phenylethyl]amino}-methyl)-naphthalen-2-yloxy)ethoxy]-26,28-dihydroxy-5,11,17,23-tetra-(*tert*-butyl)calix[4]arene (8).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 25) to afford **8** as a white solid. Yield 45%; Mp 142–144 °C; $[\alpha]_D^{25}$ = +28.0 (*c* 1, $CHCl_3$). IR (KBr): 3353, 2957, 1622, 1235, 1028, 749, 700 cm$^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.73 (d, 2H, *J* = 7.4 Hz, Ar*H*), 7.66 (d, 4H, *J* = 9.0 Hz, Ar*H*), 7.43 (d, 4H, *J* = 7.5 Hz, Ar*H*), 7.37–7.29 (m, 10H, Ar*H* + ArO*H*), 7.26–7.16 (m, 6H, Ar*H*), 7.14–7.03 (m, 12H, Ar*H*), 6.81–6.77 (m, 4H, Ar*H*), 5.62 (bs, 2H, NHC*H*), 4.67–4.57 (m, 2H, C*H*CH$_3$), 4.31 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 4.23 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 3.88–3.58 (m, 8H, OC$H_2$C$H_2$O) 3.25 (d, 4H, *J* = 12.9 Hz, ArC$H_2$Ar), 2.85–2.60 (br, 2H, N*H*), 1.31 (s, 18H, C(C$H_3$)$_3$), 1.13 (d, 6H, *J* = 6.1 Hz, CHC$H_3$), 0.91 (s, 18H, C(C$H_3$)$_3$); $^{13}$C-NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 155.1, 150.7, 150.1, 147.1, 146.7, 141.7, 132.8, 132.5, 129.8, 129.5, 128.9, 128.5, 128.3, 128.0, 127.9, 127.3, 126.8, 126.7, 125.9, 125.6, 125.4, 125.3, 124.1, 89.5, 74.2, 69.1, 58.7, 55.8, 54.9, 34.2, 34.1, 32.1, 32.0, 31.8, 31.3, 26.2, 22.9, 14.4. Anal. Calcd for $C_{98}H_{106}N_2O_6$ (1407.90): C, 83.60, H, 7.59, N, 1.99%. Found: C, 83.84; H, 7.36; N, 1.72%.

**25,27-Bis[(1-((*R*)-phenyl{[(1′*R*)-1′-phenylethyl]amino}-methyl)-naphthalen-2-yloxy)propoxy]-26,28-dihydroxy-5,11,17,23-tetra-(*tert*-butyl)calix[4]arene (9).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 20) to afford compound **9** as a white solid. Yield 70%; Mp 132–135 °C; $[\alpha]_D^{25}$ = +25.0 (*c* 2, $CHCl_3$). IR (KBr): 3340, 2956, 1623, 1238, 1068, 749, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.67–7.65 (m, 2H, Ar*H*), 7.60 (s, 2H, ArO*H*), 7.56 (d, 4H, *J* = 9.0 Hz, Ar*H*), 7.30 (d, 4H, *J* = 7.5 Hz, Ar*H*), 7.24–7.19 (m, 8H, ArH), 7.17–7.13 (m, 6H, Ar*H*), 7.10 (d, 2H, *J* = 7.0 Hz, Ar*H*), 7.07–6.96 (m, 8H, Ar*H*), 6.93–6.87 (m, 2H, Ar*H*), 6.79–6.77 (m, 4H, Ar*H*), 5.52 (bs, 2H, NHC*H*), 4.31 (q, 2H, *J* = 6.6 Hz, C*H*CH$_3$), 4.17 (d, 2H, *J* = 12.7 Hz, ArC$H_2$Ar), 4.06 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 3.82 (b, 2H, OC$H_2$), 3.75–3.69 (m, 2H, OC$H_2$), 3.60–3.58 (m, 2H, OC$H_2$), 3.49 (q, 2H, *J* = 6.5 Hz, OC$H_2$), 3.20 (d, 4H, *J* = 12.9 Hz, ArC$H_2$Ar), 1.99–1.92 (m, 2H, OCH$_2$C$H_2$CH$_2$O), 1.83–1.77 (m, 2H, OCH$_2$C$H_2$CH$_2$O), 1.21 (s, 18H, C(C$H_3$)$_3$), 1.10 (d, 6H, *J* = 6.5 Hz, CHC$H_3$), 0.95 (s, 18H, C(C$H_3$)$_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 153.8, 149.6, 148.5, 146.0, 145.2, 144.3, 140.5, 131.8, 131.6, 128.2, 127.6, 127.2, 126.8, 126.7, 126.6, 126.1, 125.7, 125.5, 125.3, 124.7, 124.6, 122.4, 71.6, 64.8, 54.6, 33.0, 32.8, 30.9, 30.8, 30.7, 30.1, 29.0, 25.0. Anal. Calcd for $C_{100}H_{110}N_2O_6$ (1435.95): C, 83.64, H, 7.72, N, 1.95%. Found: C, 83.80; H, 7.50; N, 1.82%.

**25,27-Bis[(1-((*R*)-phenyl{[(1′*R*)-1′-phenylethyl]amino}-methyl)-naphthalen-2-yloxy)butoxy]-26,28-dihydroxy-5,11,17,23-tetra-(*tert*-butyl)calix[4]arene (10).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 15) to afford compound **10** as a white solid. Yield 54%; Mp 128–131 °C; $[\alpha]_D^{25}$ = +22.0 (*c* 1.4, $CHCl_3$). IR (KBr): 3360, 2953, 1623, 1239, 1028, 753, 700 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.78 (d, 2H, *J* = 9.1 Hz, Ar*H*), 7.63 (d, 4H, *J* = 9.1 Hz, Ar*H*), 7.45–7.43 (m, 6H, Ar*H*), 7.36–7.06 (m, 26H, Ar*H* + ArO*H*), 6.84 (s, 4H, Ar*H*), 5.64 (s, 2H, NC*H*), 4.28 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 4.26 (d, 2H, *J* = 13.0 Hz, ArC$H_2$Ar), 4.17–4.12 (m, 2H, OC$H_2$), 3.87–3.80 (m, 6H, OC$H_2$($CH_2$)$_2$C$H_2$O), 3.62 (q, 2H, *J* = 6.5 Hz, C*H*$CH_3$), 3.36 (d, 2H, *J* = 13.0 Hz, ArC$H_2$Ar), 3.35 (d, 2H, *J* = 13.0 Hz, ArC$H_2$Ar), 1.89–1.84 (m, 4H, OC$H_2$($CH_2$)$_2$C$H_2$O), 1.83–1.73 (m, 4H, OC$H_2$($CH_2$)$_2$C$H_2$O), 1.34 (s, 18H, C(C$H_3$)$_3$), 1.23 (d, 6H, *J* = 6.6 Hz, CHC$H_3$), 1.00 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 155.1, 151.0, 150.1, 147.1, 146.6, 145.6, 141.7, 132.8, 129.4, 128.9, 128.5, 128.0, 127.4, 127.0, 126.9, 126.6, 126.0, 125.7, 125.6, 125.3, 123.6, 114.9, 55.9, 34.2, 34.1, 32.0, 31.3, 26.7, 26.4, 26.3. Anal. Calcd for $C_{102}H_{114}N_2O_6$ (1464.00): C, 83.68, H, 7.85, N, 1.91%. Found: C, 83.86; H, 7.62; N, 1.80%.

**25,27-Bis[(1-((*R*)-phenyl{methyl[(1′*R*)-1′-phenylethyl]amino}-methyl)naphthalen-2-yloxy)ethoxy]-26,28-dihydroxy-5,11,17,23-tetra(*tert*-butyl)calix[4]arene (11).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 25) to afford compound **11** as a white solid. Yield 40%; Mp 123–126 °C; $[\alpha]_D^{25}$ = –19.0 (*c* 0.5, $CHCl_3$). IR (KBr): 3385, 2954, 1623, 1263, 746, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 9.55 (d, 2H, *J* = 8.8 Hz, Ar*H*), 7.69 (d, 4H, *J* = 7.2 Hz, Ar*H*), 7.56–7.54 (m, 2H, Ar*H*), 7.51–7.43 (m, 4H, Ar*H*), 7.36–7.24 (m, 10H, Ar*H*), 7.23–7.16 (m, 6H, Ar*H*+ ArO*H*), 7.13–7.06 (m, 8H, Ar*H*), 7.00–6.96 (m, 2H, Ar*H*), 6.87–6.85 (m, 4H, Ar*H*), 5.90 (s, 2H, NC*H*), 4.67–4.62 (m, 2H, OC$H_2$), 4.50 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 4.47 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 4.45–4.38 (m, 6H, OC$H_2$C$H_2$O), 4.21 (q, 2H, *J* = 6.8 Hz, C*H*$CH_3$), 3.41 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 3.38 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 2.03 (s, 6H, NC$H_3$), 1.35 (d, 6H, *J* = 6.9 Hz, CHC$H_3$), 1.33 (s, 18H, C(C$H_3$)$_3$), 1.00 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 154.1, 150.8, 150.1, 147.4, 143.6, 142.9, 141.8, 133.4, 132.8, 132.7, 130.1, 129.6, 128.6, 128.4, 128.2, 128.0, 127.9, 126.9, 126.7, 126.4, 126.1, 126.0, 125.9, 125.5, 124.7, 123.8, 115.0, 74.7, 68.3, 64.3, 57.0, 34.2, 34.1, 33.8, 32.1, 31.9, 31.3, 13.8. Anal. Calcd for $C_{100}H_{110}N_2O_6$ (1435.95): C, 83.64, H, 7.72, N, 1.95%. Found: C, 83.86; H, 7.38; N, 1.81%.

**25,27-Bis[(1-((*R*)-phenyl{methyl[(1′*R*)-1′-phenylethyl]amino}-methyl)naphthalen-2-yloxy)propoxy]-26,28-dihydroxy-5,11,17,23-tetra(*tert*-butyl)calix[4]arene (12).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 20) to afford compound **12** as a white solid. Yield 58%; Mp 182–184 °C; $[\alpha]_D^{25}$ = –21.0 (*c* 1, $CHCl_3$). IR (KBr): 3320, 2959, 1623, 1266, 1238, 740, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 9.60 (d, 2H, *J* = 8.8 Hz, Ar*H*), 7.96 (s, 2H, Ar*H*), 7.64 (d, 4H, *J* = 7.8 Hz, Ar*H*), 7.55–7.43 (m, 6H, Ar*H*), 7.33–7.22 (m, 10H, Ar*H* + ArO*H*), 7.16–6.93 (m, 18H, Ar*H*), 5.77 (s, 2H, NC*H*), 4.40 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 4.32 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 4.20–4.10 (m, 8H, OC$H_2$C$H_2$C$H_2$O), 4.00 (q, 2H, *J* = 6.6 Hz, C*H*$CH_3$), 3.39 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 3.32 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 2.37–2.29 (m, 4H, OC$H_2$C$H_2$C$H_2$O), 2.00 (s, 6H, NC$H_3$), 1.36 (d, 6H, *J* = 6.6 Hz, CHC$H_3$), 1.31 (s, 18H, C(C$H_3$)$_3$), 1.07 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 154.1, 151.0, 150.0, 147.4, 143.7, 142.2, 141.9, 133.4, 133.1, 133.0, 129.6, 129.4, 128.6, 128.5, 128.2, 128.1, 127.9, 126.7, 126.4, 125.9, 125.5, 123.4, 123.3, 114.1, 97.0, 73.6, 65.8, 64.4, 57.0, 34.3, 34.1, 33.8, 32.3, 32.2, 31.9, 31.3, 30.7, 14.3. Anal. Calcd for $C_{102}H_{114}N_2O_6$ (1464.00): C, 83.68, H, 7.85, N, 1.91%. Found: C, 83.92; H, 7.46; N, 1.83%.

**25,27-Bis[(1-((*R*)-phenyl{methyl[(1′*R*)-1′-phenylethyl]amino}-methyl)naphthalen-2-yloxy)butoxy]-26,28-dihydroxy-5,11,17,23-tetra(*tert*-butyl)calix[4]arene (13).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 15) to afford compound **13** as a white solid. Yield 48%; Mp 130–134 °C; $[\alpha]_D^{25}$ = –14.0 (*c* 2, $CHCl_3$). IR (KBr): 3335, 2954, 1624, 1238, 746, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 9.45 (d, 2H, *J* = 9.6 Hz, Ar*H*), 7.58–6.74 (m, 40H, Ar*H* + ArO*H*), 5.80 (s, 2H, NC*H*), 4.29 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 4.27 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 4.19–4.06 (m, 6H, OC$H_2$ + C*H*$CH_3$), 4.00 (br s, 4H, OC$H_2$($CH_2$)$_2$C$H_2$O), 3.29 (d, 2H, *J* = 12.9 Hz, ArC$H_2$Ar), 3.28 (d, 2H, *J* = 13.1 Hz, ArC$H_2$Ar), 2.17 (br s, 8H, OC$H_2$($CH_2$)$_2$C$H_2$O), 1.91 (s, 6H, NC$H_3$), 1.28 (d, 6H, *J* = 6.8 Hz, CHC$H_3$), 1.23 (s, 18H, C(C$H_3$)$_3$), 0.91 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 154.3, 151.0, 150.1, 147.2, 143.7, 142.7, 141.8, 133.4, 132.9, 129.7, 129.5, 128.6, 128.5, 128.4, 128.2, 128.0, 126.8, 126.6, 126.4, 126.0, 125.8, 125.4, 123.9, 114.4, 69.0, 64.1, 56.9, 34.2, 34.1, 33.7, 32.1, 32.0, 31.3, 27.3, 27.0, 13.5. Anal. Calcd for $C_{104}H_{118}N_2O_6$ (1492.06): C, 83.72, H, 7.97, N, 1.88%. Found: C, 83.91; H, 7.84; N, 1.76%.

**25,27-Bis[(1-((*R*)-phenyl{[(1′*R*)-1′-naphthylethyl]amino}-methyl)-naphthalen-2-yloxy)propoxy]-26,28-dihydroxy-5,11,17,23-tetra-(*tert*-butyl)calix[4]arene (14).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 15) to afford compound **14** as a white solid. Yield 73%; Mp 144–146 °C; $[\alpha]_D^{25}$ = –12.6 (*c* 2, $CHCl_3$). IR (KBr): 3346, 2955, 1621, 1237, 777, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 8.01–7.65 (m, 16H, Ar*H*), 7.54–7.45 (m, 6H, ArH), 7.37 (t, 2H, *J* = 7.2 Hz, Ar*H*), 7.30–7.09 (m, 18H, Ar*H* + ArO*H*), 6.92 (s, 4H, Ar*H*), 5.83 (br s, 2H, NHC*H*), 4.49 (q, 2H, *J* = 6.2 Hz, C*H*$CH_3$), 4.40 (br, 2H, ArC$H_2$Ar), 4.24 (br, 4H, OC$H_2$), 4.12 (d, 2H, *J* = 12.7 Hz, ArC$H_2$Ar), 3.67 (br, 2H, OC$H_2$), 3.47 (br, 2H, OC$H_2$), 3.34 (d, 4H, *J* = 12.9 Hz, ArC$H_2$Ar), 1.90–1.64 (m, 2H, OC$H_2$C$H_2$C$H_2$O), 1.62–1.44 (m, 2H, OC$H_2$C$H_2$C$H_2$O), 1.38 (br s, 24H, CHC$H_3$ + C(C$H_3$)$_3$), 1.14 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 155.2, 150.8, 150.0, 149.7, 147.4, 145.6, 141.9, 134.2, 133.1, 133.0, 131.8, 129.6, 128.9, 128.2, 128.1, 127.9, 127.2, 126.8, 126.5, 126.2, 126.0, 125.8, 125.7, 125.5, 125.4, 125.3, 123.5, 72.7, 65.7, 54.6, 34.3, 34.1, 32.1, 32.0, 31.4, 29.9, 25.3. Anal. Calcd for $C_{108}H_{114}N_2O_6$ (1536.07): C, 84.45, H, 7.48, N, 1.82%. Found: C, 84.90; H, 7.28; N, 1.95%.

**25,27-Bis[(1-((*R*)-(α-pyrrolidinylbenzyl))naphthalen-2-yloxy)-ethoxy]-26,28-dihydroxy-5,11,17,23-tetra(*tert*-butyl)-calix[4]arene (15).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 15) to afford compound **15** as a white solid. Yield 42%; Mp 157–159 °C; $[\alpha]_D^{25}$ = –64.0 (*c* 0.5,

$CHCl_3$). IR (KBr): 3374, 2956, 1624, 1233, 1084, 748, 700 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 9.46 (d, 2H, $J$ = 8.8 Hz, Ar*H*), 7.66 (d, 6H, $J$ = 7.8 Hz, Ar*H*), 7.58 (d, 2H, $J$ = 9.0 Hz, Ar*H*), 7.44–7.41 (m, 4H, Ar*H* + *ArOH*), 7.31–7.27 (m, 2H, Ar*H*), 7.20–7.01 (m, 12H, Ar*H*), 6.87 (s, 4H, Ar*H*), 5.69 (s, 2H, NC*H*), 4.62–4.61 (m, 4H, ArC$H_2$Ar), 4.57–4.42 (m, 8H, OC$H_2$C$H_2$O), 3.43 (d, 2H, $J$ = 13.1 Hz, ArC$H_2$Ar), 3.32 (d, 2H, $J$ = 12.5 Hz, ArC$H_2$Ar), 2.58–2.56 (m, 4H, NC$H_2$), 2.30–2.26 (m, 4H, NC$H_2$), 1.54 (br, 8H, C$H_2$), 1.30 (s, 18H, C(C$H_3$)$_3$), 1.00 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 153.4, 150.9, 150.0, 147.3, 144.4, 141.6, 133.3, 133.1, 132.7, 129.9, 129.3, 128.3, 128.2, 128.0, 127.6, 127.0, 126.2, 126.0, 125.7, 125.6, 125.4, 125.3, 123.7, 114.2, 74.9, 68.3, 66.6, 53.6, 34.2, 34.0, 32.5, 32.0, 31.8, 31.3, 23.8, 23.6. Anal. Calcd for $C_{90}H_{102}N_2O_6$ (1307.78): C, 82.66, H, 7.86, N, 2.14%. Found: C, 82.94; H, 7.68; N, 2.01%.

**25,27-Bis[(1-((*R*)-(α-pyrrolidinylbenzyl))naphthalen-2-yloxy)-propoxy]-26,28-dihydroxy-5,11,17,23-tetra(*tert*-butyl)-calix[4]-arene (16).** The crude product was purified by flash chromatography on silica gel (EtOAc/Hexane 1 : 15) to afford compound **16** as white crystals. Yield 60%; Mp 140–142 °C; $[\alpha]_D^{25}$ = −30.0 (*c* 1, $CHCl_3$). IR (KBr): 3353, 2955, 2867, 1622, 1596, 1484, 1235, 748, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 9.40 (d, 2H, $J$ = 8.8 Hz, Ar*H*), 8.00 (s, 2H, ArO*H*), 7.68–7.43 (m, 12H, Ar*H*), 7.28–6.89 (m, 16H, Ar*H*), 5.60 (s, 2H, NC*H*), 4.45–4.40 (m, 6H, ArC$H_2$Ar + OC$H_2$), 4.33–4.22 (m, 6H, OC$H_2$), 3.42 (dd, 4H, $J_1$ and $J_2$ = 12.9 Hz, ArC$H_2$Ar), 2.63–2.61 (m, 4H, NC$H_2$), 2.47 (p, 4H, $J$ = 6.0 Hz, OCH$_2$C$H_2$CH$_2$O), 2.40–2.37 (m, 4H, NC$H_2$), 1.72 (br, 8H, C$H_2$), 1.34 (s, 18H, C(C$H_3$)$_3$), 1.09 (s, 18H, C(C$H_3$)$_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ (ppm): 23.9, 30.8, 31.4, 32.0, 32.4, 34.2, 34.4, 54.1, 66.0, 66.7, 73.5, 114.5, 123.5, 124.8, 125.5, 126.0, 126.3, 126.7, 127.9, 128.1, 128.2, 128.4, 129.4, 129.7, 133.2, 141.9, 144.4, 147.5, 149.9, 151.1, 153.7. Anal. Calcd for $C_{92}H_{106}N_2O_6$ (1335.84): C, 82.72, H, 8.00, N, 2.10%. Found: C, 82.90; H, 7.91; N, 2.04%.

### NMR host–guest titrations

Samples for analysis were obtained by mixing equimolar amounts of chiral hosts with the guests in $CDCl_3$, making the concentrations of the hosts (or guests) normally 10 mM. For NMR titrations the guest compound was dissolved in an appropriate amount of solvent and the resulting solution evenly distributed among 10 NMR tubes. The first NMR tube was sealed without any host. The host compound was also dissolved in the appropriate amount of solvent and added in increasing amounts to the NMR tubes, so that solutions with the following relative amounts (equiv) of host *versus* guest compound (concentration was $6.0 \times 10^{-2}$ M) were obtained: 0, 0.20, 0.40, 0.60, 0.80, 1.00, 1.20, 2.00, 3.00, 4.00, 6.00, 10.00.

### UV-Vis spectral measurement

Binding constants ($K$) were determined on the basis of the differential UV spectrometry in chloroform. The same concentrations of guest solution were added to the sample cell and reference cell (light path = 1 cm). The association constants were determined at 241 nm. The concentration of the hosts is $1.00 \times 10^{-5}$ mol $dm^{-3}$ with the increasing concentration between 0.10–3.00 $\times 10^{-4}$ mol $dm^{-3}$ of the added guest.

### Evaluation of the stoichiometric ratio of the host–guest complex (Job plots)

The stoichiometry of the complex between chiral hosts and enantiomers of carboxylic acids was determined by a continuous-variation plot (Job plot).[23] Equimolar amounts of host and guest compounds were dissolved in $CDCl_3$. These solutions were distributed among nine NMR tubes, with the molar fractions $X$ of host and guest in the resulting solutions increasing (or decreased) from 0.1 to 0.9 (and *vice versa*). The complexation induced shifts ($\Delta\delta$) were multiplied by $X$ and plotted against $X$ itself.

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