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Synthesis, Optical Resolution and Enantiomeric Recognition Ability of Novel, Inherently Chiral Calix[4]arenes: Trial Application to Asymmetric Reactions as Organocatalysts

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Newly designed, inherently chiral calix[4]arenes containing amino phenol structures have been synthesized and resolved to optically pure forms. The enantiomeric recognition ability of one chiral calix[4]arene was examined with mandelic acid by ^{1}H NMR spectroscopy, and we found that the inherently chiral calix[4]arene could be used as a chiral NMR solvating agent to determine the enantiopurity of mandelic acid at ambient temperature. In addition, the chiral calix[4]arenes were used as organocatalysts in asymmetric Michael-type addition reactions of thiophenols, and high catalytic efficiency with low enantioselectivity was observed.

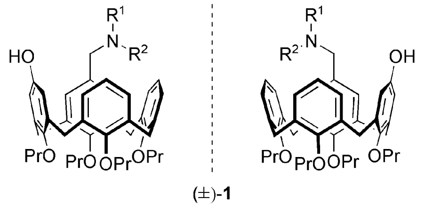
Introduction

The chemistry of chiral calixarenes has received increasing interest in recent years because it relates to the development of new chiral receptors for asymmetric recognition and provides potent tools for the stereochemical understanding of biochemical systems.[1] Hence, many chiral calixarenes containing chiral residues at either the wide or the narrow rim have been prepared as chiral receptors[2] and catalysts.[3] A more challenging and attractive approach to introduce chirality is to make the calixarene "inherently" chiral by creating an asymmetric structure.[4] Over the past two decades, many inherently chiral calixarenes have been prepared, and some of them have been resolved into individual enantiomers either by chiral preparative HPLC[5] or by the formation of diastereomers with a chiral auxiliary linked through covalent bonds.[6,7] In spite of these efforts, only a few examples of enantiomeric recognition with inherently chiral calixarenes have been reported.[5f,5j,6a,6c,6j] This paper describes the design, synthesis and optical resolution of functionalized inherently chiral calixarenes and their chiral recognition ability. The enantiomeric recognition ability of a novel, inherently chiral calix[4]arene was examined through ^{1}H NMR and UV/Vis titration experiments with mandelic acid. In addition, the chiral calix[4]arenes were used in asymmetric Michael-type addition reactions as organocatalysts.[8]

Results and Discussion

Synthesis and Optical Resolution

The novel, inherently chiral calix[4]arenes synthesised in this work are shown in Figure 1. The chiral calix[4]arenes **1** possess amino and hydroxy groups, which are involved in molecular recognition, at proximal positions on the wide rim. Such amino phenol (alcohol) structures are often present in useful chiral building blocks, such as cinchonidine, ephedrine and prolinol. Also, the conformations of the chiral calix[4]arenes **1** are fixed in the cone conformation, which provides a rigid chiral environment.



(±)-**1**

1a : $R^1 = R^2 = Bu$
1b : $R^1 = PhCH_2$, $R^2 = Et$,
1c : $R^1 = p\text{-MeO-}C_6H_4CH_2$, $R^2 = Et$
1d : $R^1 = p\text{-}F_3C\text{-}C_6H_4CH_2$, $R^2 = Et$

Figure 1. Functionalized inherently chiral calix[4]arenes **1**.

The requisite chiral calix[4]arenes **1a**–**d**, which contain different alkyl substituents on the nitrogen atom, can be prepared in a similar manner from the already reported proximally *p*-dibrominated calix[4]arene **2**[9] in a four-step sequence, as outlined in Scheme 1. Thus, *p*-dibromocalix[4]arene **2** was transformed into the monoformylated compound **3** by treatment with 1.0 equiv. of *n*BuLi and subse-

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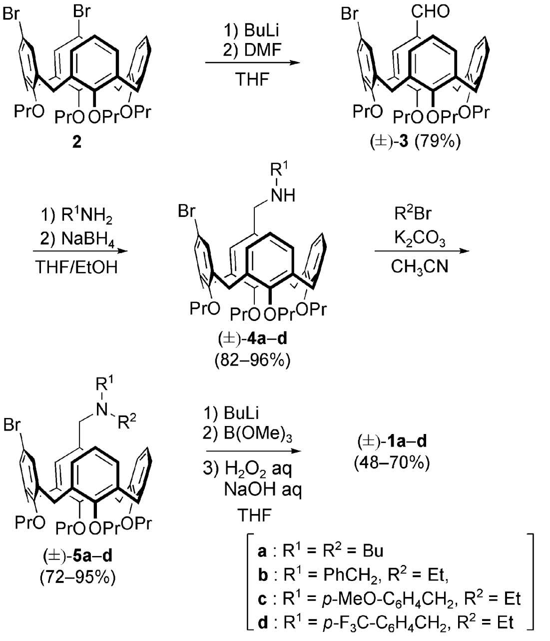
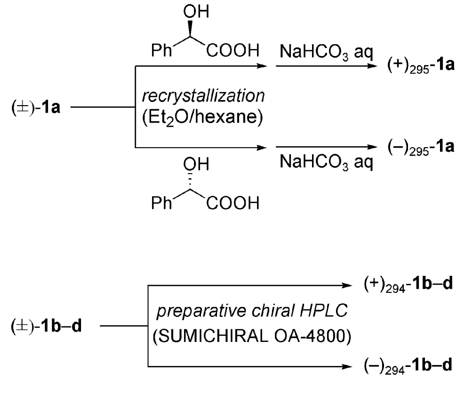
quent addition of *N*,*N*-dimethylformamide. The reductive amination of the formyl group of **3** with primary amines gave the corresponding secondary amines **4a**–**d** in 82–96% yields. Compounds **4a**–**d** were transformed with *n*-butyl or ethyl bromide to the tertiary amines **5a**–**d** in 72–95% yields.



Scheme 1. Synthesis of inherently chiral calix[4]arenes **1a**–**d**.

Lithiation of **5a**–**d** and trapping of the resulting anion with $B(OMe)_3$ gave the corresponding boronates. The boronates were oxidized by H_2O_2 using a one-pot method to give the target calix[4]arenes **1a**–**d** as racemates in 48–70% yields.

Efficient optical resolution of the racemic calix[4]arene **1a** was achieved by recrystallization after complexation with chiral mandelic acid (Scheme 2). The optical purity of the chiral calix[4]arene **1a** was confirmed by means of chiral HPLC analysis.[10] To the best of our knowledge, this is the first example of the optical resolution of an inherently chiral calix[4]arene by diastereomeric complexation without covalent bonding between chiral molecules.[11] The other ra-



Scheme 2. Optical resolution of the inherently chiral calix[4]arenes **1a**–**d**.

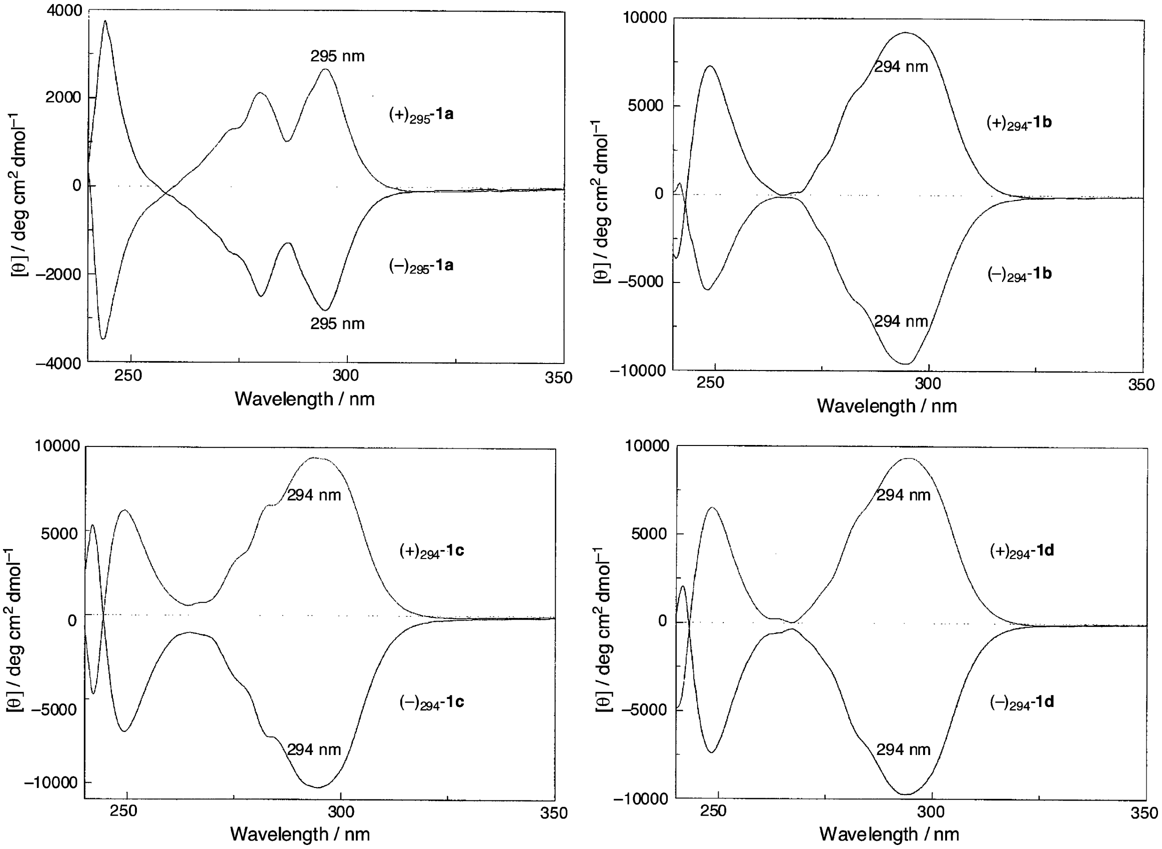


Figure 2. CD spectra of enantiomers of calix[4]arenes **1a**–**d** in hexane.

cemic calix[4]arenes **1b–d** were resolved in optically pure forms by preparative chiral HPLC using a SUMICHIRAL OA-4800 column (2.0 × 25 cm). The circular dichroism (CD) spectra of the separated enantiomers of **1a–d** showed perfect mirror images (Figure 2).[12]

Enantiomeric Recognition Ability of 1a for Mandelic Acid

With an efficient synthetic scheme for the synthesis of inherently chiral calix[4]arenes in hand, the ability of the chiral calix[4]arene **1a** to recognize enantiomers was investigated. ^{1}H NMR studies of the chiral calix[4]arene $(+)_{295}$-**1a** were performed with equimolar amounts of racemic mandelic acid.[13] As a result of diastereomeric complexation, clear signal splitting (δ = 4.93 and 4.96 ppm; Figure 3b) with an upfield shift of the signal of the benzylic proton of racemic mandelic acid (δ =5.26 ppm; Figure 3a) was observed. In addition, different proportions of both enantiomers of mandelic acid were treated with $(+)_{295}$-**1a**, and different signal intensities for both (*R*)- and (*S*)-mandelic acid were observed depending on the proportions (Figure 4). These results clearly indicate that inherently chiral calix[4]arene **1a** could be used as a chiral NMR solvating agent to determine the enantiopurity of mandelic acid at ambient temperature. Furthermore, ^{1}H NMR studies of the chiral calix[4]arene $(+)_{295}$-**1a** with different molar ratios of (*R*)- or (*S*)-mandelic acid were examined (Figure 5). Even in the presence of a less than stoichiometric amount of $(+)_{295}$-**1a**, different chemical shifts of the benzylic proton of (*R*)- and (*S*)-mandelic acid were observed. Interestingly, the degree of signal separation of (*R*)- and (*S*)-mandelic acid ($\Delta\Delta\delta \approx$ 0.03 ppm) did not depend on the molar ratio of **1a**/mandelic acid, although many chiral solvating agents depend greatly on the molar ratio of the chiral agent.[13] Also the magnitude of the upfield shifts of the signals of the benzylic proton gradually increased with an increase in the molar ratio of $(+)_{295}$-**1a**. However, the addition of more than an equimolar amount of $(+)_{295}$-**1a** showed no further change in the chemical shifts of the mandelic acids. These results indicate that inherently chiral calix[4]arene **1a** and mandelic acid form a 1:1 complex.

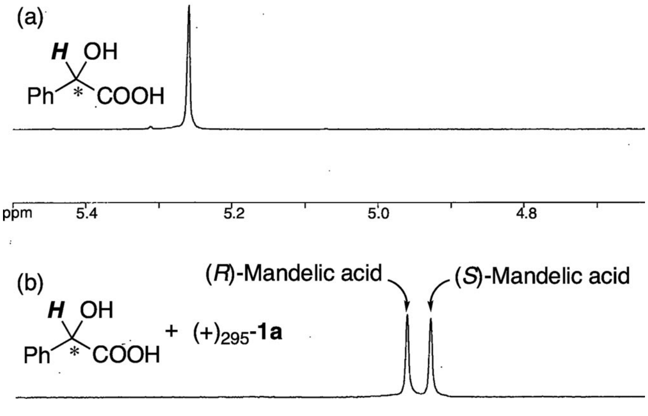


Figure 3. ^{1}H NMR spectra of racemic mandelic acid in the absence and presence of $(+)_{295}$-**1a** in CDCl$_3$ at 27 °C [mandelic acid/$(+)_{295}$-**1a** = 1:1].

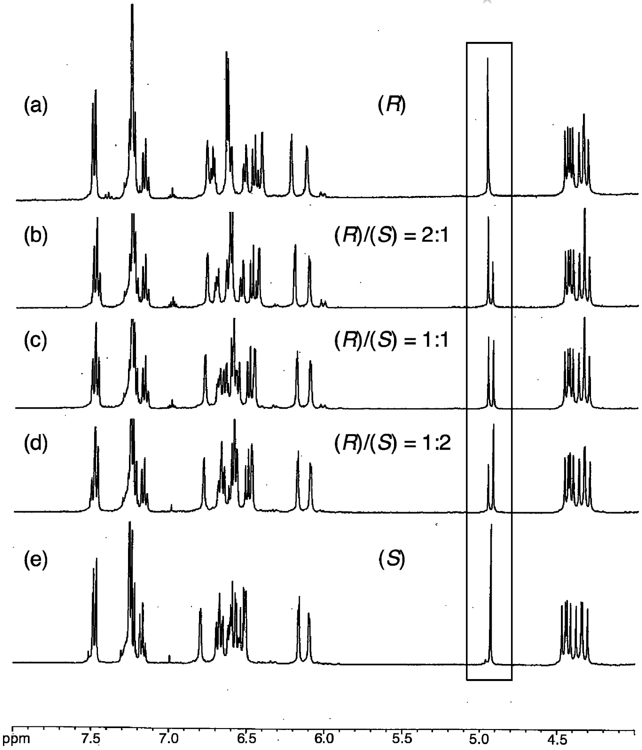


Figure 4. ^{1}H NMR spectra of various enantiomeric ratios mandelic acid in the presence of $(+)_{295}$-**1a** in CDCl$_3$ at 27 °C [mandelic acid/$(+)_{295}$-**1a** = 1:1].

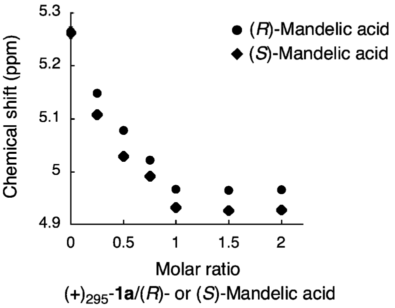


Figure 5. ^{1}H NMR chemical shift of the signal of the benzylic proton of mandelic acid with various molar ratios of $(+)_{295}$-**1a**/(*R*)- or (*S*)-mandelic acid in CDCl$_3$ at 27 °C.

Next, the association constants of $(+)_{295}$-**1a** with (*R*)- or (*S*)-mandelic acid were measured by titration experiments using UV/Vis spectral measurements (Figure 6). From the changes in absorption intensity at 279 nm along with the concentration of mandelic acid, the association constants, K_a, were calculated by the non-linear least-squares method. The association constant, K_a, for $(+)_{295}$-**1a** with (*S*)-mandelic acid (3.5×10^5 dm^{-3}mol^{-1}) was 2.2 times larger than that with (*R*)-mandelic acid (1.6×10^5 dm^{-3}mol^{-1}). Although the mechanism of enantiomeric recognition by chiral calix[4]arene **1a** is not yet clear at this stage, one can speculate that not only the amino and hydroxy groups of **1a**, but also the cavity of the calixarene, cooperate in chiral molecular recognition.

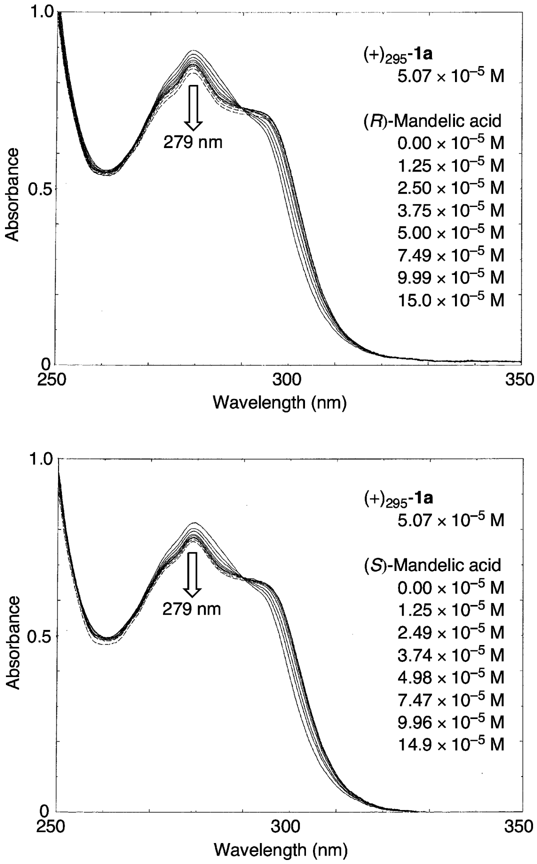
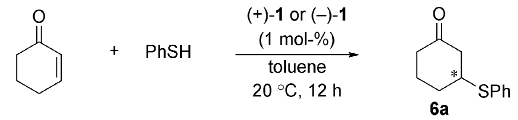


Figure 6. Absorption spectra of the chiral calix[4]arene $(+)_{295}$-**1a** in the presence of (*R*)- or (*S*)-mandelic acid in $CHCl_3$ at 25 °C.

Asymmetric Michael-Type Addition Reactions Catalysed by Inherently Chiral Calix[4]arenes 1

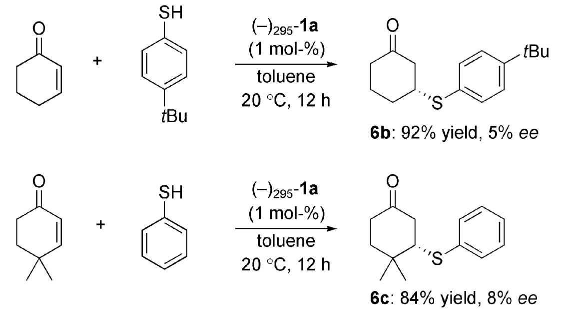
The application of an inherently chiral calix[4]arene **1** as a chiral organocatalyst[14] is a challenge in organic synthesis. In a preliminary trial, an asymmetric Michael-type addition reaction of thiophenol, which is known to be catalysed by chiral amino alcohols, was selected as a model reaction (Table 1).[15] Both enantiomers, $(+)_{295}$-**1a** and $(-)_{295}$-**1a**, promoted the reaction efficiently and gave a Michael addition product **6a** in excellent yields. The chiral induction of the product was observed to be 15% *ee*, and the configuration of the major enantiomer was (*S*) with $(+)_{295}$-**1a**, (*R*) with $(-)_{295}$-**1a** (Entries 1 and 2). Although the observed enantioselectivity of the product was poor, a certain amount of chiral induction was observed. Note that this is the first example of an inherently chiral calixarene with no chiral residue being applied to asymmetric catalysis.[16] Reaction at a lower temperature led to a slight increase in the enantioselectivity with no loss of reactivity (Entry 3). Compounds **1b–d** were also examined as catalysts in the reaction, but gave poor selectivity regardless of the electronic properties of the benzyl substituent in the tertiary amine on the catalyst (Entries 4–7). Other substrates were also subjected to the Michael-type addition reactions, and selected examples are shown in Scheme 3.

Table 1. Asymmetric Michael-type addition reactions of thiophenol catalysed by (+)- or (–)-**1**.



Entry	Catalyst	Yield[a]	*ee* (config.)[b]
1	$(+)_{295}$-**1a**	91%	15% (*S*)
2	$(-)_{295}$-**1a**	93%	15% (*R*)
3[c]	$(-)_{295}$-**1a**	95%	16% (*R*)
4	$(+)_{294}$-**1b**	65%	3% (*S*)
5	$(-)_{294}$-**1b**	62%	3% (*R*)
6	$(-)_{294}$-**1c**	67%	3% (*R*)
7	$(-)_{294}$-**1d**	45%	3% (*R*)

[a] Isolated yield. [b] Determined by a previously reported procedure, see ref.[15a] [c] Reaction temp. –40 °C.



Scheme 3. Asymmetric Michael-type addition reactions catalysed by $(-)_{295}$-**1a**.

Conclusions

In this study, novel, inherently chiral calix[4]arenes were developed for the recognition of chiral molecules. The inherently chiral calix[4]arene **1a** could be used as a chiral NMR solvating agent to determine the enantiopurity of mandelic acid at ambient temperature. In addition, the chiral calix[4]arenes were used as organocatalysts in asymmetric Michael-type addition reactions of thiophenols. Further improvements in the structures of the chiral calix[4]arenes to allow more efficient asymmetric catalysis are now in progress in our laboratory.

Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 spectrometer in $CDCl_3$. Tetramethylsilane (TMS) served as the internal standard (δ = 0 ppm) for ^1H and ^{13}C NMR spectroscopy. IR spectra were measured with a Bio-Rad FTS-60A spectrometer. Circular dichroism (CD) spectra were measured by using a Jasco J-820 spectrometer. UV/Vis spectra were measured with a Shimadzu UV-2400PC spectrophotometer. High-performance liquid chromatography (HPLC) was carried out with a Hitachi 655 liquid chromatograph instrument and a SUMICHIRAL OA-4800 column (0.46 × 25 cm). Optical rotations were measured with a Jasco DIP-1000 digital polarimeter. MS data were measured with a JEOL JMS-AX500 mass spectrometer (EI, 70 eV) coupled to a GC. Preparative gel-permeation chromatography (GPC) and preparative HPLC were performed by using a Jai model 908 liquid chromatograph with JAIGEL 1-H and 2-H columns and with a SUMICHIRAL OA-4800 column (2.0 × 25 cm), respectively. Analytical thin-layer chromatography (TLC) and column chromatography were carried out on precoated silica gel 60 F_{254} plastic sheets (E. Merck) and with silica gel 60 (spherical 0.040–0.100 mm, Kanto), respectively. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone.

5-Bromo-11-formyl-25,26,27,28-tetrapropoxycalix[4]arene [(±)-3]: *n*BuLi (8.0 mmol, 1.5 M in hexane) was added to a solution of 5,11-dibromo-25,26,27,28-tetrapropoxycalix[4]arene (**2**)[9] (8.0 mmol) in THF (120 mL) at –78 °C under argon, and the mixture was stirred at this temperature for 30 min. Dry *N*,*N*-dimethylformamide (12 mmol) was then added, and the mixture was stirred at –78 °C for 15 min. The reaction was quenched with aq. 0.2 N HCl (60 mL), and organic materials were extracted with $CHCl_3$ (50 mL × 2). The organic extracts were washed with water and dried with $MgSO_4$. Evaporation of the solvents and purification of the residue by column chromatography on silica gel ($CHCl_3$/hexane = 3:2 as eluent) afforded **3a** in 79% yield (4.42 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.72 (s, 1 H), 7.21–7.25 (m, 2 H), 6.48–6.73 (m, 8 H), 4.49 (d, J = 13.7 Hz, 1 H), 4.43 (d, J = 13.7 Hz, 1 H + 1 H), 4.39 (d, J = 13.6 Hz, 1 H), 3.73–4.01 (m, 8 H), 3.26 (d, J = 13.8 Hz, 1 H), 3.19 (d, J = 13.8 Hz, 1 H), 3.17 (d, J = 13.5 Hz, 1 H), 3.10 (d, J = 13.6 Hz, 1 H), 1.83–1.94 (m, 8 H), 0.94–1.03 (m, 12 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.70, 162.68, 156.77, 156.20, 155.49, 137.38, 136.81, 136.14, 135.84, 135.64, 134.95, 134.62, 133.72, 131.08, 130.89, 130.63, 130.47, 130.01, 128.69, 128.46, 128.16, 127.91, 122.45, 122.13, 114.88, 76.93, 76.86, 76.77, 76.71, 31.00, 30.97, 30.86, 30.83, 23.30, 23.19, 23.18, 23.12, 10.41, 10.35, 10.21, 10.17 ppm. IR: ṽ = 2963, 2932, 2875, 1692, 1456, 1297, 1206, 1004, 766 cm^{-1}. $C_{41}H_{47}BrO_5$ (699.71): calcd. C 70.38, H 6.77; found C 69.93, H 6.72.

5-Bromo-11-[(butylamino)methyl]-25,26,27,28-tetrapropoxycalix[4]arene [(±)-4a]: *n*-Butylamine (20 mmol) was added to a solution of **3** (4.0 mmol) in THF (40 mL)/ethanol (40 mL) at room temperature, and the mixture was stirred for 24 h. $NaBH_4$ (4.0 mmol) was then added, and the mixture was stirred for 30 min. The reaction was quenched with aq. satd. NH_4Cl, and organic materials were extracted with $CHCl_3$ (50 mL × 2). The organic extracts were washed with water and dried with $MgSO_4$. Evaporation of the solvents and purification of the residue by column chromatography on silica gel ($CHCl_3$/AcOEt = 1:3 as eluent) afforded **4a** in 82% yield (2.48 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68–6.82 (m, 5 H), 6.59 (t, J = 7.6 Hz, 1 H), 6.39–6.49 (m, 4 H), 4.44 (d, J = 13.5 Hz, 1 H), 4.42 (d, J = 13.4 Hz, 1 H), 4.39 (d, J = 13.4 Hz, 1 H), 4.37 (d, J = 13.5 Hz, 1 H), 4.13 (br. s, 1 H), 3.73–3.91 (m, 8 H), 3.59 (s, 2 H), 3.16 (d, J = 13.5 Hz, 1 H), 3.14 (d, J = 13.5 Hz, 1 H), 3.08 (d, J = 13.5 Hz, 1 H), 3.07 (d, J = 13.5 Hz, 1 H), 2.58 (t, J = 7.3 Hz, 2 H), 1.84–1.92 (m, 8 H), 1.47–1.52 (m, 2 H), 1.34–1.38 (m, 2 H), 0.90–1.04 (m, 15 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.10, 156.59, 155.95, 155.23, 136.79, 136.62, 136.11, 136.04, 135.10, 135.01, 134.31, 134.13, 131.07, 130.47, 130.43, 129.16, 128.80, 128.54, 128.24, 127.81, 122.20, 121.86, 114.72, 76.80, 76.69, 76.62, 52.69, 48.02, 31.11, 30.97, 30.95, 30.83, 23.34, 23.24, 23.11, 20.46, 13.98, 10.53, 10.47, 10.11 ppm. IR: ṽ = 2961, 2930, 2874, 1586, 1463, 1214, 1007, 758 cm^{-1}. $C_{45}H_{58}BrNO_4$·0.2$CHCl_3$ (756.85·0.2$CHCl_3$): calcd. C 69.55, H 7.49, N 1.79; found C 69.63, H 7.50, N 1.72.

5-[(Benzylamino)methyl]-11-bromo-25,26,27,28-tetrapropoxycalix[4]arene [(±)-4b]: Calix[4]arene **4b** was prepared in a manner similar to that described for **4a** by using benzylamine instead of *n*-butylamine (96% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.36 (m, 5 H), 6.47–6.73 (m, 10 H), 4.43 (d, J = 13.4 Hz, 1 H + 1 H), 4.39 (d, J = 13.6 Hz, 1 H + 1 H), 3.76–3.89 (m, 8 H), 3.68 (s, 2 H), 3.57 (s, 2 H), 3.15 (d, J = 13.4 Hz, 1 H + 1 H), 3.07 (d, J = 13.5 Hz, 1 H + 1 H), 1.85–1.93 (m, 8 H), 0.92–1.03 (m, 12 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.86, 156.15, 155.91, 155.43, 140.39, 137.05, 137.02, 135.70, 135.55, 134.66, 134.59, 134.56, 134.53, 133.54, 130.54, 130.49, 128.67, 128.46, 128.34, 128.27, 128.13, 127.93, 127.89, 126.83, 122.16, 121.89, 114.65, 76.75, 76.69, 76.65, 52.94, 52.64, 30.97, 30.85, 23.29, 23.18, 23.14, 10.45, 10.39, 10.19, 10.17 ppm. IR: ṽ = 2963, 2923, 2876, 1456, 1213, 1196, 1006, 966, 766 cm^{-1}. $C_{48}H_{56}BrNO_4$·0.1$CHCl_3$ (790.87·0.1$CHCl_3$): calcd. C 71.97, H 7.03, N 1.74; found C 72.08, H 7.08, N 1.66.

5-Bromo-11-{[(4-methoxybenzyl)amino]methyl}-25,26,27,28-tetrapropoxycalix[4]arene [(±)-4c]: Calix[4]arene **4c** was prepared in a manner similar to that described for **4a** by using (4-methoxybenzyl)amine instead of *n*-butylamine (93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (d, J = 8.6 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 6.48–6.74 (m, 10 H), 4.44 (d, J = 13.3 Hz, 1 H), 4.43 (d, J = 13.4 Hz, 1 H), 4.39 (d, J = 13.5 Hz, 1 H), 4.38 (d, J = 13.4 Hz, 1 H), 3.77–3.87 (m, 8 H), 3.80 (s, 3 H), 3.61 (s, 2 H), 3.56 (s, 2 H), 3.152 (d, J = 13.4 Hz, 1 H), 3.148 (d, J = 13.4 Hz, 1 H), 3.08 (d, J = 13.4 Hz, 1 H + 1 H), 1.86–1.95 (m, 8 H), 0.93–1.03 (m, 12 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.54, 156.88, 156.16, 155.92, 155.45, 137.07, 137.04, 135.72, 135.57, 134.69, 134.60, 134.57, 134.54, 133.56, 132.51, 130.54, 130.49, 129.47, 128.69, 128.47, 128.15, 127.91, 122.15, 121.93, 114.64, 113.72, 76.77, 76.71, 76.67, 55.26, 52.50, 52.28, 30.98, 30.86, 23.30, 23.19, 23.15, 10.45, 10.39, 10.19, 10.17 ppm. IR: ṽ = 2963, 2934, 2876, 1513, 1457, 1247, 1212, 1196, 1038, 1006, 966, 766 cm^{-1}. $C_{49}H_{58}BrNO_5$ (820.89): calcd. C 71.69, H 7.12, N 1.71; found C 71.74, H 7.10, N 1.76.

5-Bromo-11-({[4-(trifluoromethyl)benzyl]amino}methyl)-25,26,27,28-tetrapropoxycalix[4]arene [(±)-4d]: Calix[4]arene **4d** was prepared in a manner similar to that described for **4a** by using [4-(trifluoromethyl)benzyl]amine instead of *n*-butylamine (93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 6.60–6.69 (m, 7 H), 6.54–6.56 (m, 2 H), 6.48 (t, J = 7.5 Hz, 1 H), 4.45 (d, J = 13.4 Hz, 1 H + 1 H), 4.40 (d, J = 13.5 Hz, 1 H + 1 H), 3.77–3.88 (m, 8 H), 3.67 (s, 2 H), 3.53 (s, 2 H), 3.15 (d, J = 13.4 Hz, 1 H + 1 H), 3.08 (d, J = 13.2 Hz, 1 H + 1 H), 1.86–1.95 (m, 8 H), 0.94–1.03 (m, 12 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.78, 156.33, 155.92, 155.61, 144.61, 137.31, 137.20, 135.55, 135.50, 134.86, 134.75, 134.51, 134.46, 133.24, 130.61, 129.24, 128.92, 128.60, 128.46, 128.39, 128.06, 128.04, 128.00, 127.84, 125.70, 125.30, 125.27, 125.23, 125.19, 122.99, 122.15, 121.85, 120.29, 114.62, 76.81, 76.75, 76.69, 52.56, 52.23, 31.00, 30.99, 30.88, 30.86, 23.29, 23.21, 23.19, 10.40, 10.34, 10.25, 10.23 ppm. IR: ṽ = 2966, 2935, 2877, 1457, 1326, 1213, 1197, 1164, 1126, 1067, 1006, 966, 766 cm^{-1}. $C_{49}H_{55}BrF_3NO_4$ (858.86): calcd. C 68.52, H 6.45, N 1.63; found C 68.40, H 6.45, N 1.55.

5-Bromo-11-[(dibutylamino)methyl]-25,26,27,28-tetrapropoxycalix[4]arene [(±)-5a]: *n*-Butyl bromide (3.6 mmol) was added to a mixture of **4a** (3.0 mmol), K_2CO_3 (7.5 mmol) and CH_3CN (100 mL), and the mixture was heated at reflux for 15 h. The mixture was cooled to room temperature, and the reaction was quenched with water. After the removal of CH_3CN by evaporation, organic materials were extracted with $CHCl_3$ (50 mL × 2), and the organic extracts were dried with $MgSO_4$. Evaporation of the solvents and purification of the residue by column chromatography on silica gel ($CHCl_3$/AcOEt = 3:1 as eluent) afforded **5a** in 72% yield (1.76 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.77–6.93 (m, 5 H), 6.53 (t, J = 7.5 Hz, 1

H), 6.28–6.39 (m, 4 H), 4.45 (d, J = 13.4 Hz, 1 H), 4.43 (d, J = 13.3 Hz, 1 H), 4.39 (d, J = 13.4 Hz, 1 H), 4.37 (d, J = 13.3 Hz, 1 H), 3.86–3.95 (m, 4 H), 3.70–3.77 (m, 4 H), 3.43 (s, 2 H), 3.16 (d, J = 13.4 Hz, 1 H), 3.14 (d, J = 13.4 Hz, 1 H), 3.08 (d, J = 13.5 Hz, 1 H), 3.07 (d, J = 13.4 Hz, 1 H), 2.37 (t, J = 7.4 Hz, 4 H), 1.84–1.93 (m, 8 H), 1.43–1.50 (m, 4 H), 1.28–1.36 (m, 4 H), 1.02–1.07 (m, 6 H), 0.90–0.93 (m, 12 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.38, 156.23, 155.66, 154.94, 136.53, 136.46, 136.43, 135.85, 135.42, 134.85, 134.02, 133.92, 132.73, 130.38, 130.20, 129.73, 129.11, 128.98, 128.41, 127.59, 127.54, 122.21, 121.93, 114.78, 76.82, 76.70, 76.62, 76.58, 57.95, 53.46, 31.00, 30.95, 30.88, 30.84, 29.19, 23.41, 23.30, 23.07, 20.77, 14.22, 10.64, 10.57, 10.05, 10.00 ppm. IR: $\tilde{\nu}$ = 2959, 2931, 2873, 1456, 1212, 1195, 1009, 763 cm^{-1}. C$_{49}$H$_{66}$BrNO$_4$ (812.96): calcd. C 72.39, H 8.18, N 1.72; found C 72.29, H 8.01, N 1.56.

5-{[(Benzyl)(ethyl)amino]methyl}-11-bromo-25,26,27,28-tetrapropoxycalix[4]arene [(±)-5b]: Calix[4]arene **5b** was prepared from **4b** in a manner similar to that described for **5a** by using ethyl bromide (3 equiv.) instead of *n*-butyl bromide (91% yield). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.16–7.32 (m, 5 H), 6.45–6.76 (m, 10 H), 4.42 (d, J = 13.4 Hz, 1 H + 1 H), 4.38 (d, J = 13.4 Hz, 1 H + 1 H), 3.76–3.88 (m, 8 H), 3.42 (s, 2 H), 3.33 (s, 2 H), 3.14 (d, J = 13.3 Hz, 1 H), 3.13 (d, J = 13.4 Hz, 1 H), 3.07 (d, J = 13.3 Hz, 1 H), 3.06 (d, J = 13.3 Hz, 1 H), 2.36 (q, J = 6.9 Hz, 2 H), 1.85–1.94 (m, 8 H), 0.92–1.05 (m, 15 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.78, 156.06, 155.71, 155.35, 140.05, 137.06, 136.99, 135.64, 135.15, 134.58, 134.52, 134.15, 132.75, 130.60, 130.37, 129.11, 128.80, 128.64, 128.56, 128.11, 128.08, 127.88, 127.81, 126.55, 122.17, 121.98, 114.65, 76.75, 76.72, 76.66, 76.62, 57.43, 57.00, 46.91, 30.95, 30.82, 23.28, 23.18, 23.12, 11.98, 10.45, 10.40, 10.21, 10.17 ppm. IR: $\tilde{\nu}$ = 2966, 2876, 1458, 1213, 1009, 964, 763, 738 cm^{-1}. C$_{50}$H$_{60}$BrNO$_4$·0.1CHCl$_3$ (818.92·0.1CHCl$_3$): calcd. C 72.43, H 7.28, N 1.69; found C 72.18, H 7.28, N 1.63.

5-Bromo-11-{[(ethyl)(4-methoxybenzyl)amino]methyl}-25,26,27,28-tetrapropoxycalix[4]arene [(±)-5c]: Calix[4]arene **5c** was prepared from **4c** in a manner similar to that described for **5a** by using ethyl bromide (3 equiv.) instead of *n*-butyl bromide (95% yield). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.19 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.45–6.75 (m, 10 H), 4.43 (d, J = 13.4 Hz, 1 H), 4.42 (d, J = 13.3 Hz, 1 H), 4.385 (d, J = 13.5 Hz, 1 H), 4.380 (d, J = 13.3 Hz, 1 H), 3.77–3.87 (m, 8 H), 3.80 (s, 3 H), 3.36 (s, 2 H), 3.33 (s, 2 H), 3.14 (d, J = 13.5 Hz, 1 H + 1 H), 3.08 (d, J = 13.4 Hz, 1 H), 3.07 (d, J = 13.5 Hz, 1 H), 2.35 (q, J = 7.0 Hz, 2 H), 1.85–1.96 (m, 8 H), 0.99–1.07 (m, 9 H), 0.90–0.97 (m, 6 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 158.36, 156.81, 156.09, 155.73, 155.37, 137.10, 137.02, 135.67, 135.17, 134.63, 134.61, 134.55, 134.17, 132.80, 131.92, 130.60, 130.38, 129.95, 129.16, 128.66, 128.58, 128.13, 127.89, 127.82, 122.17, 122.01, 114.64, 113.48, 76.77, 76.74, 76.69, 76.65, 56.81, 56.66, 55.23, 46.73, 30.96, 30.85, 23.29, 23.18, 23.13, 11.94, 10.46, 10.40, 10.21, 10.17 ppm. IR: $\tilde{\nu}$ = 2965, 2934, 2876, 1512, 1457, 1248, 1212, 1196, 1039, 1007, 966, 765 cm^{-1}. C$_{51}$H$_{62}$BrNO$_5$·0.1CHCl$_3$ (848.95·0.1CHCl$_3$): calcd. C 71.30, H 7.26, N 1.63; found C 71.22, H 7.27, N 1.62.

5-Bromo-11-({(ethyl)[4-(trifluoromethyl)benzyl]amino}methyl)-25,26,27,28-tetrapropoxycalix[4]arene [(±)-5d]: Calix[4]arene **5d** was prepared from **4d** in a manner similar to that described for **5a** by using ethyl bromide (3 equiv.) instead of *n*-butyl bromide (80% yield). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.58 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 7.9 Hz, 2 H), 6.51–6.70 (m, 9 H), 6.42 (t, J = 7.4 Hz, 1 H), 4.43 (d, J = 14.0 Hz, 1 H + 1 H), 4.39 (d, J = 13.6 Hz, 1 H), 4.38 (d, J = 13.6 Hz, 1 H), 3.76–3.87 (m, 8 H), 3.41 (s, 2 H), 3.30 (s, 2 H), 3.15 (d, J = 13.3 Hz, 1 H), 3.14 (d, J = 13.4 Hz, 1 H), 3.08 (d, J = 13.3 Hz, 1 H), 3.07 (d, J = 13.4 Hz, 1 H), 2.33 (q, J = 6.9 Hz, 2 H), 1.87–1.97 (m, 8 H), 0.92–1.08 (m, 15 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.67, 156.25, 155.73, 155.54, 144.64, 137.27, 137.24, 135.47, 135.12, 134.82, 134.77, 134.42, 134.10, 132.32, 130.63, 130.50, 128.97, 128.84, 128.66, 128.53, 128.43, 128.34, 128.02, 127.97, 127.93, 125.76, 125.06, 125.02, 123.06, 122.14, 121.93, 120.35, 114.59, 76.87, 76.76, 76.65, 57.03, 56.97, 47.17, 30.97, 30.84, 23.26, 23.24, 23.17, 12.05, 10.39, 10.34, 10.26, 10.22 ppm. IR: $\tilde{\nu}$ = 2966, 2935, 2877, 1458, 1326, 1213, 1163, 1125, 1067, 1006, 765 cm^{-1}. C$_{51}$H$_{59}$BrF$_3$NO$_4$ (886.92): calcd. C 69.06, H 6.71, N 1.58; found C 68.61, H 6.69, N 1.45.

5-[(Dibutylamino)methyl]-11-hydroxy-25,26,27,28-tetrapropoxycalix[4]arene [(±)-1a]: *n*BuLi (8.0 mmol, 1.5 M in hexane) was added to a solution of **5a** (4.0 mmol) in THF (100 mL) at –78 °C under argon, and the mixture was stirred at this temperature for 30 min. B(OMe)$_3$ (16 mmol) was added, and the mixture was stirred at –78 °C for 1 h. Then 30% aq. H$_2$O$_2$ (15 mL) and 3 N aq. NaOH (15 mL) were added to the resulting reaction mixture, which was warmed to room temperature. After stirring at room temperature for 1 h, the reaction was quenched with Na$_2$S$_2$O$_3$·5H$_2$O (32 mmol), and the mixture was stirred for 30 min. After removal of THF by evaporation, organic materials were extracted with CHCl$_3$ (50 mL × 2). The organic extracts were washed with water and dried with MgSO$_4$. Evaporation of solvents and purification of the residue by column chromatography on silica gel (CHCl$_3$/AcOEt = 1:1 as eluent) afforded **1a** in 51% yield (1.53 g). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.76–6.86 (m, 4 H), 6.72 (t, J = 7.4 Hz, 1 H), 6.45 (t, J = 7.4 Hz, 1 H), 6.36–6.38 (m, 2 H), 5.81 (s, 2 H), 4.45 (d, J = 13.3 Hz, 1 H), 4.43 (d, J = 13.7 Hz, 1 H), 4.40 (d, J = 13.7 Hz, 1 H), 4.37 (d, J = 13.2 Hz, 1 H), 3.86–3.92 (m, 4 H), 3.77 (t, J = 7.1 Hz, 2 H), 3.69 (t, J = 7.1 Hz, 2 H), 3.39 (s, 2 H), 3.15 (d, J = 13.3 Hz, 1 H), 3.13 (d, J = 13.3 Hz, 1 H), 3.06 (d, J = 12.8 Hz, 1 H), 3.03 (d, J = 12.8 Hz, 1 H), 2.32 (t, J = 7.5 Hz, 4 H), 1.87–1.93 (m, 8 H), 1.41–1.47 (m, 4 H), 1.25–1.32 (m, 4 H), 1.01–1.06 (m, 6 H), 0.88–0.94 (m, 12 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.87, 156.30, 156.01, 150.79, 149.74, 135.43, 135.38, 135.33, 134.93, 134.87, 134.82, 130.40, 129.56, 129.50, 128.23, 128.22, 128.00, 127.92, 121.86, 121.74, 114.80, 76.74, 76.70, 76.66, 57.30, 52.81, 31.10, 31.07, 31.00, 28.39, 23.27, 23.20, 20.73, 14.15, 10.45, 10.41, 10.28, 10.24 ppm. IR: $\tilde{\nu}$ = 3386, 2961, 2932, 2874, 1592, 1466, 1212, 1006, 763 cm^{-1}. C$_{49}$H$_{67}$NO$_5$ (750.06): calcd. C 78.46, H 9.00, N 1.87; found C 78.14, H 8.85, N 1.72.

5-{[(Benzyl)(ethyl)amino]methyl}-11-hydroxy-25,26,27,28-tetrapropoxycalix[4]arene [(±)-1b]: Calix[4]arene **1b** was prepared from **5b** in a manner similar to that described for **1a** (48% yield). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.20–7.33 (m, 5 H), 6.74 (s, 1 H), 6.71 (s, 1 H), 6.62–6.64 (m, 2 H), 6.51–6.53 (m, 3 H), 6.44 (t, J = 7.4 Hz, 1 H), 5.91–5.94 (m, 2 H), 4.43 (d, J = 13.2 Hz, 1 H + 1 H), 4.37 (d, J = 13.2 Hz, 1 H + 1 H), 3.80–3.84 (m, 6 H), 3.74 (t, J = 7.3 Hz, 2 H), 3.28–3.42 (m, 4 H), 3.13 (d, J = 13.2 Hz, 1 H), 3.12 (d, J = 13.3 Hz, 1 H), 3.03 (d, J = 13.2 Hz, 1 H), 3.02 (d, J = 13.3 Hz, 1 H), 2.32–2.38 (m, 2 H), 1.87–1.95 (m, 8 H), 0.93–1.04 (m, 15 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.78, 156.26, 155.80, 150.17, 149.95, 139.89, 135.66, 135.59, 135.38, 135.11, 134.93, 134.78, 134.74, 132.12, 129.00, 128.82, 128.67, 128.23, 128.14, 127.94, 126.66, 121.79, 114.52, 114.47, 76.76, 76.68, 76.65, 57.07, 56.99, 47.08, 31.02, 30.95, 23.25, 23.21, 23.18, 23.16, 11.81, 10.44, 10.41, 10.25, 10.21 ppm. IR: $\tilde{\nu}$ = 3537, 2964, 2934, 2876, 1457, 1214, 1008, 967, 766 cm^{-1}. C$_{50}$H$_{61}$NO$_5$ (756.02): calcd. C 79.43, H 8.13, N 1.85; found C 78.99, H 8.11, N 1.77.

5-{[(Ethyl)(4-methoxybenzyl)amino]methyl}-11-hydroxy-25,26,27,28-tetrapropoxycalix[4]arene [(±)-1c]: Calix[4]arene **1c** was prepared from **5c** in a manner similar to that described for **1a** (70% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (d, J = 8.5 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 6.68 (d, J = 7.0 Hz, 2 H), 6.53–6.92 (m, 5 H), 6.42 (t, J = 7.4 Hz, 1 H), 5.98 (s, 2 H), 4.43 (d, J = 13.2 Hz, 1 H + 1 H), 4.37 (d, J = 13.1 Hz, 1 H + 1 H), 3.73–3.85 (m, 8 H), 3.78 (s, 3 H), 3.25–3.35 (m, 4 H), 3.13 (d, J = 13.2 Hz, 1 H), 3.12 (d, J = 13.3 Hz, 1 H), 3.024 (d, J = 13.2 Hz, 1 H), 3.016 (d, J = 13.2 Hz, 1 H), 2.30–2.35 (m, 2 H), 1.86–1.97 (m, 8 H), 0.93–1.02 (m, 15 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.33, 156.70, 156.34, 155.70, 150.19, 150.06, 135.72, 135.25, 135.01, 134.93, 134.88, 134.77, 134.61, 132.11, 131.70, 130.06, 128.90, 128.63, 128.20, 128.09, 128.01, 127.98, 121.82, 121.78, 114.59, 113.50, 76.77, 76.75, 76.71, 76.64, 56.75, 56.39, 55.24, 46.86, 31.03, 30.97, 23.24, 23.22, 23.17, 11.77, 10.41, 10.38, 10.28, 10.25 ppm. IR: $\tilde{\nu}$ = 3384, 2964, 2935, 2877, 1512, 1459, 1248, 1214, 1040, 1008, 967, 765 cm^{-1}. $C_{51}H_{63}NO_6\cdot 0.3CHCl_3$ ($786.05\cdot 0.3CHCl_3$): calcd. C 75.00, H 7.73, N 1.70; found C 74.90, H 7.79, N 1.74.

5-({(Ethyl)[4-(trifluoromethyl)benzyl]amino}methyl)-11-hydroxy-25,26,27,28-tetrapropoxycalix[4]arene [(±)-1d]: Calix[4]arene **1d** was prepared from **5d** in a manner similar to that described for **1a** (70% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.1 Hz, 2 H), 7.33 (d, J = 8.0 Hz, 2 H), 6.58–6.68 (m, 5 H), 6.46 (d, J = 7.5 Hz, 2 H), 6.28 (t, J = 7.5 Hz, 1 H), 6.10–6.14 (m, 2 H), 4.44 (d, J = 13.1 Hz, 1 H), 4.43 (d, J = 13.2 Hz, 1 H), 4.38 (d, J = 13.1 Hz, 1 H), 4.37 (d, J = 13.1 Hz, 1 H), 3.88 (t, J = 7.6 Hz, 2 H), 3.75–3.81 (m, 6 H), 3.30 (s, 2 H), 3.25 (s, 2 H), 3.13 (d, J = 13.2 Hz, 1 H), 3.12 (d, J = 13.3 Hz, 1 H), 3.02 (d, J = 13.2 Hz, 1 H), 3.01 (d, J = 13.2 Hz, 1 H), 2.26 (q, J = 7.0 Hz, 2 H), 1.85–1.97 (m, 8 H), 0.93–1.05 (m, 15 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.65, 156.43, 155.52, 150.45, 150.12, 144.33, 136.15, 136.12, 135.33, 134.86, 134.60, 134.51, 134.29, 131.55, 129.04, 128.99, 128.67, 128.55, 128.37, 128.16, 127.98, 127.85, 125.76, 125.05, 125.01, 124.97, 123.06, 121.80, 121.72, 120.64, 114.74, 76.88, 76.84, 76.72, 76.62, 56.82, 56.75, 47.14, 31.06, 31.01, 30.95, 23.29, 23.25, 23.18, 23.09, 11.86, 10.38, 10.36, 10.29, 10.26 ppm. IR: $\tilde{\nu}$ = 2966, 2936, 2877, 1460, 1326, 1215, 1164, 1125, 1067, 1006, 966, 765 cm^{-1}. $C_{51}H_{60}F_3NO_5\cdot 0.2CHCl_3$ ($824.02\cdot 0.2CHCl_3$): calcd. C 72.54, H 7.13, N 1.65; found C 72.81, H 7.30, N 1.68.

Optical Resolution of Chiral Calix[4]arene 1a: A racemic mixture of calix[4]arene **1a** (4.0 mmol) and (*R*)-mandelic acid (8.0 mmol) was dissolved in Et_2O (100 mL), and hexane (15 mL) was then gradually added to the solution. The solution was placed in a flask at room temperature for 2–3 d, which led to a white crystalline calix[4]arene **1a**–(*R*)-mandelic acid complex. The resulting white crystals were filtered and dried to yield chirally enriched calix[4]arene $(+)_{295}$-**1a**–(*R*)-mandelic acid complex. {The chirally enriched calix[4]arene $(-)_{295}$-**1a**–(*R*)-mandelic acid complex was obtained from the filtrate.} The white solid was dissolved in $CHCl_3$ (50 mL), and satd. aq. $NaHCO_3$ (50 mL) was added to the solution. After stirring at room temperature for 30 min, the organic layer was separated and washed with water (50 mL × 5). The organic solution was dried with $MgSO_4$, and the solvent was evaporated to give chirally enriched calix[4]arene $(+)_{295}$-**1a** (65–93% *ee*, 40–25% yield). Chirally enriched calix[4]arene $(+)_{295}$-**1a** was treated again with (*R*)-mandelic acid in the same manner as described above. After repeating this procedure 2–3 times, enantiomerically pure calix[4]arene $(+)_{295}$-**1a** was obtained. The optical purity of the chiral calix[4]arene **1a** was determined by chiral HPLC analysis [SUMICHIRAL OA-4800 column (0.46 × 25 cm) with hexane/*i*PrOH/MeOH/TFA = 90:5:5:0.3 as eluent].

Optical Resolution of Chiral Calix[4]arenes 1b–d: Optical resolution of (±)-**1b**–**d** was carried out by preparative HPLC using a SUMICHIRAL OA-4800 column (2.0 × 25 cm) with $CHCl_3$ as the eluent. The calix[4]arenes **1b**–**d** (100 mg) were loaded onto the preparative column, and enantiomerically pure calix[4]arene $(+)_{294}$-**1** (10.0–12.5 mg) and $(-)_{294}$-**1** (10.0–12.5 mg) were obtained.

Measurement of the Association Constants of Chiral Calix[4]arene $(+)_{295}$-1a with Mandelic Acid: Association constants (K_a) were determined in $CHCl_3$ solution with a UV/Vis spectrophotometer at 25 °C. A solution of $(+)_{295}$-**1a** (3 mL, 5.07×10^{-5} M in $CHCl_3$) was placed in the sample cell, and pure $CHCl_3$ (3 mL) was placed in the reference cell. A calculated amount of (*R*)- or (*S*)-mandelic acid (1.25×10^{-2} M stock solution in $CHCl_3$) was then added to the sample and reference cells, and absorption spectra were recorded. Additional amounts of mandelic acid solution were added to the two cells, and spectra were recorded after each addition. The wavelength selected for maximal intensity changes was 279 nm. From the absorption intensities at this wavelength and the mandelic acid concentration, the association constants (K_a) were calculated by using the non-linear least-squares method of Marquardt.

Catalytic Asymmetric Michael-Type Addition Reactions Catalysed by (+)- or (–)-1: 2-Cyclohexen-1-one (1.50 mmol) was added to a solution of (+)- or (–)-**1** (0.0150 mmol) and thiophenol (1.75 mmol) in toluene (3 mL) under argon at 20 °C, and the mixture was stirred at this temperature for 12 h. The reaction was quenched with 1 N aq. HCl (3 mL), and organic materials were extracted with $CHCl_3$ (3 mL × 2). The organic extracts were washed with water (5 mL) and dried with $MgSO_4$. Evaporation of the solvent and purification of the residue by preparative GPC afforded a Michael addition product. The absolute configuration of the product was determined by comparison of the observed optical rotation with the reported value, and the *ee* was determined by a previously reported procedure.[15a]

3-(Phenylthio)cyclohexanone (6a):[15a] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.43 (m, 2 H), 7.25–7.33 (m, 3 H), 3.39–3.45 (m, 1 H), 2.65–2.70 (m, 1 H), 2.28–2.40 (m, 3 H), 2.10–2.16 (m, 2 H), 1.66–1.78 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.71, 133.15, 132.96, 129.03, 127.74, 47.69, 46.04, 40.83, 31.15, 23.97 ppm. IR: $\tilde{\nu}$ = 2946, 1715, 1222, 745, 694 cm^{-1}. MS (EI): m/z = 206 [M]$^+$, 110, 97.

3-(4-*tert*-Butylphenylthio)cyclohexanone (6b):[15a] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.37 (m, 4 H), 3.33–3.39 (m, 1 H), 2.64–2.69 (m, 1 H), 2.25–2.39 (m, 3 H), 2.09–2.19 (m, 2 H), 1.66–1.77 (m, 2 H), 1.30 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.85, 151.13, 133.42, 129.26, 126.07, 47.83, 46.29, 40.84, 34.55, 31.22, 24.05 ppm. IR: $\tilde{\nu}$ = 2963, 1716, 734 cm^{-1}. MS (EI): m/z = 262 [M]$^+$, 166, 97.

4,4-Dimethyl-3-(phenylthio)cyclohexanone (6c):[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.41 (m, 2 H), 7.21–7.30 (m, 3 H), 3.15–3.19 (m, 1 H), 2.41–2.64 (m, 3 H), 2.27–2.32 (m, 1 H), 1.86–1.92 (m, 1 H), 1.60–1.67 (m, 1 H), 1.27 (s, 3 H), 1.21 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.93, 134.60, 132.66, 129.08, 127.39, 57.59, 45.38, 38.59, 37.84, 34.62, 29.02, 21.03 ppm. IR: $\tilde{\nu}$ = 2959, 1707, 737, 688 cm^{-1}. MS (EI): m/z = 234 [M]$^+$, 125, 110.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all new compounds as well as the HPLC charts of **1a**–**d**.

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