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Synthesis and Optical Resolution of a Series of Inherently Chiral Calix[4]crowns with Cone and Partial Cone Conformations

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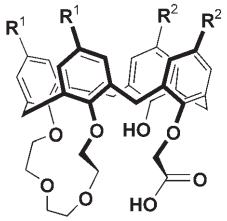
Abstract: A series of inherently chiral calix[4]arenes with cone and partial cone conformations and with crown ether moieties of variable size have been readily synthesized. By taking advantage of the carboxy appendage on the lower rim, these were condensed with the chiral auxiliary (*S*)-BINOL to form diastereomers which, in most cases, could be separated by preparative TLC, or more desirably, by column chromatography on silica gel (diastereomeric excess >99% based on HPLC analysis). Seven enantiopure antipodes of inherently chiral calix[4]crowns were obtained after hydrolysis. It has been found that both the size of the crown moiety and alkylation of the last phenolic hydroxy group (accompanied with or without a change in the conformation) affect the separation of the diastereomers.

Keywords: calixarenes · chirality · crown compounds · optical resolution · synthesis

Introduction

Inherently chiral calixarenes, whose chirality originates from the unsymmetrical array of achiral functionalities on the cavity-shaped calixarene skeletons (upper rim and/or lower rim, as well as other positions), have enriched the variety of chiral molecules and attracted increasing attention in recent years owing to their potential use in chiral discrimination and asymmetric catalysis.[1] Compared with chiral calix[4]arenes with chiral functionalities attached directly to the calixarene skeleton, the synthesis of calix[4]arenes with inherent chirality tends to be more challenging as there are always regio- and stereoselective problems involved in their synthesis. Moreover, optical resolution of the racemates usually requires the use of HPLC methods (chiral columns for racemates[2] and nonchiral columns for diastereomers of inherently chiral calix[4]arenes[2e,3]), which is inappropriate for scale-up. In only two cases has optical resolution been realized by conventional column chromatography on silica gel.[4] Clearly, the difficult access to optically pure, inherently chiral calix[4]arenes has impeded the research into their chiral discrimination and asymmetric catalytic abilities. For this reason, until now, only one report each on the chiral discrimination and asymmetric catalysis of inherently chiral calix[4]arenes has been published.[2h,4a]

In a preliminary paper[5] we reported a convenient approach to enantiopure antipodes of AABH-type inherently chiral calix[4]crown-4 molecules through the reaction of racemic calix[4]crown derivatives **1** with (*S*)-BINOL, followed by the separation of the diastereomers formed by preparative TLC and subsequent cleavage of the (*S*)-BINOL auxiliary. Their successful synthesis and resolution encouraged us to investigate the generality of these methods. In addition we may have gained some insight into the relationship between the structure of these calix[4]crown-4 molecules and their optical resolution. There are two ways to modify the structure of compound **1**: 1) by changing the size of the crown ether moiety and 2) by alkylating or esterifying the phenolic hydroxy group with or without changing the conformation. The carboxy group is retained for further condensation with the chiral auxiliary. Herein we report the synthesis of a series of inherently chiral calix[4]crowns with cone or partial cone conformations and their optical resolution by separation of the diastereomers derived from (*S*)-BINOL by preparative TLC or column chromatography on silica gel and the subsequent hydrolysis of the chiral auxiliary.



1a $R^1=R^2=H$
1b $R^1=t$Bu, $R^2=H$

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Results and Discussion

Changing the crown-4 moiety to crown-5, crown-6 or open chain analogues: 1,2-Calix[4]crown-5 (**2a**) and 1,2-calix[4]-crown-6 (**2b**) were synthesized according to literature procedures.[6] As indicated in Scheme 1, reaction of **2a** or **2b** with 1.1 equivalents of ethyl bromoacetate in the presence of one equivalent of Cs_2CO_3 in dry DMF at 60–70 °C furnished the tri-*O*-alkylated compound **3a** or **3b** as racemates in good yields. Their complicated NMR spectra suggested the absence of symmetry. Signals arising from the $ArCH_2Ar$ carbon atoms appeared at around $\delta = 31$ ppm, indicating that they all adopted the cone conformation.[7] Similar to the behavior observed by Pappalardo and co-workers,[2f] the outcome of this reaction is determined by the ability of the cone conformation of the phenolate intermediate to be stabilized by strong hydrogen bonding rather than by metal template effects. Thus, the tri-*O*-alkylated cone conformer can be obtained regardless of the size of the 1,2-crown ether moiety. Compounds **3a** and **3b** were efficiently resolved by HPLC using Chiralpak AD column (*n*-hexane/2-propanol 9:1, 0.5 mL min^{-1}, 25 °C). The retention times for the enantiomers of the crown-5 derivative **3a** are 7.8 and 31.9 min (enantiomeric ratio 49:51), yet for the crown-6 derivative **3b** the retention times are 9.7 and 12.9 min (enantiomeric ratio 50:50).

Although the enantiomers of **3a** and **3b** can be resolved by HPLC, it is more attractive to convert them to diastereomers and to separate these. Thus, compounds **3a** and **3b** were directly hydrolyzed to furnish the carboxylic acid derivatives **4a** and **4b** whose structures were confirmed by their spectroscopic data. Compounds **4a** and **4b**, which possess a carboxylic group, were then treated with (*S*)-BINOL in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) in CH_2Cl_2 at room temperature to furnish **5a** and **5b** as pairs of diastereomers. We successfully separated the diastereomeric mixture of crown-5 **5a** (ca. 1:1 ratio) to yield **5a-1** and **5a-2** (diastereomeric excess, $de > 99\,\%$ by HPLC analysis) by preparative TLC. In fact, among other chiral auxiliaries such as L-menthol, L-cinchonidine, and several L-amino acid esters, (*S*)-BINOL proved to be the most efficient. So it seems that the close proximity of the rigid structure of the axial chiral BINOL moiety to the inherently chiral calixarene backbone can favor the separation of the diastereomers. The separation of the diastereomeric mixture of crown-6 **5b**, on the other hand, failed. The diastereomers of compound **5b** appeared as two overlapping spots on TLC sheets even after several rounds of development.

The ^{1}H NMR spectra of **5a-1** and **5a-2** are shown in Figure 1 (*t*Bu groups are not included). In general, the signals arising from the calix[4]arene skeleton and the (*S*)-

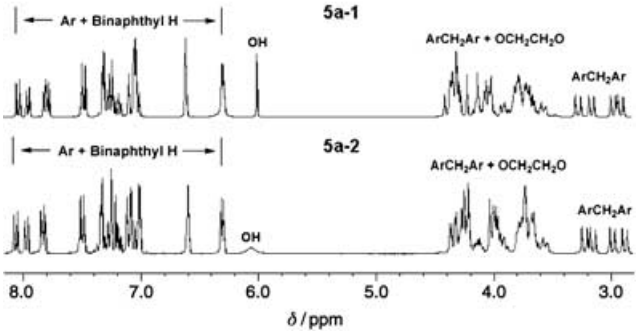
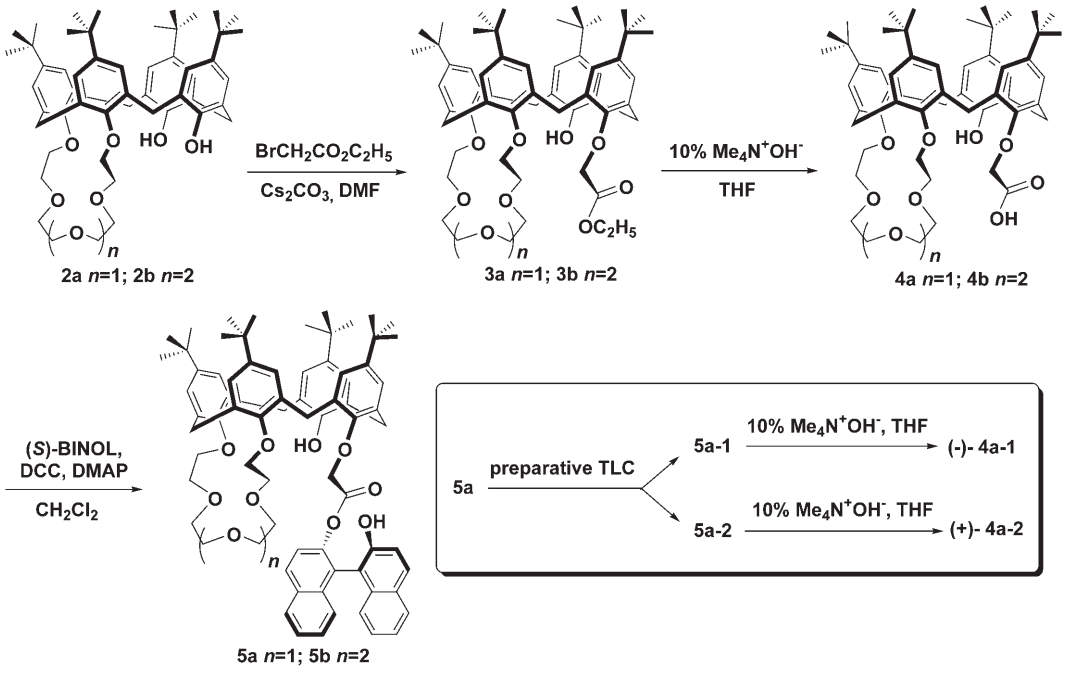
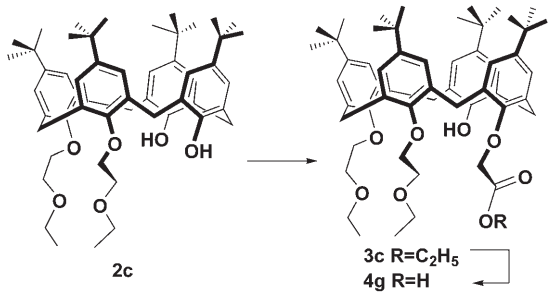


Figure 1. Partial ^{1}H NMR spectra of diastereomers **5a-1** and **5a-2**.



Scheme 1.

BINOL moiety of **5a-1** resemble the corresponding signals of **5a-2**. This indicates that the introduction of the outer chiral moiety distorts the skeletons of the calixarene enantiomers similarly. Combined with the results reported previously, the fact that the diastereomers of calix[4]crown-4 and -crown-5 could be separated by TLC while those of calix[4]-crown-6 could not implies that increasing the size or the flexibility of the crown ether moiety has a detrimental effect on the separation of the diastereomers. To confirm this, an open-chain calix[4]arene analog **4g** was also synthesized (Scheme 2). The diastereomers derived from this compound produced only one spot on TLC analysis.



Scheme 2.

The isolated diastereomers **5a-1** and **5a-2** were hydrolyzed under alkaline conditions to give optically pure **4a-1** and **4a-2**, respectively. Their CD spectra (Figure 2) are mirror images. The $[\alpha]_D^{25}$ values of the enantiomers **4a-1** and **4a-2** are -16 and $+16$ ($c=0.5$ in chloroform), respectively, which shows their enantiomeric nature and high *ee* values.

Alkylation of the remaining phenolic OH; retention of the cone conformation: Besides changing the size of the crown ether moiety, we also alkylated the last phenolic hydroxy group of compounds **3a** and **3b**. The reactions of **3a** and **3b** with alkylating agents *n*PrI and BnBr (2.0 equiv) in the presence of NaH (5.0 equiv) in dry DMF and subsequent hydrolysis with water provided the tetra-*O*-alkylated derivatives **4c–4f** in 66–88% yields (Scheme 3).

In general, the clear splitting pattern of four pairs of doublets due to the methylene protons of the $ArCH_2Ar$ moieties in the ^1H NMR spectra of compounds **4c–4f** and the corresponding carbon resonances at around $\delta=31$ ppm in their ^{13}C NMR spectra corroborate their molecular asymmetry and cone conformations. They were then treated with (*S*)-BINOL. We found that the reaction of **4c–4f** with (*S*)-BINOL is slower than those of **4a** and **4b**. This may be a result of steric hindrance at the lower rim caused by the introduction of the alkyl group. According to previous reports,[2f,g,8] the alkylation of the last hydroxy group of racemates of inherently chiral calix[4]crown ethers is detrimental to their resolution by HPLC. However, we found that the diastereomeric crown-5 derivatives **5c** and **5d**, and even the crown-6 derivatives **5e** and **5f** could, with sufficient care, be separated by column chromatography on silica gel ($de>99\%$ by HPLC analysis).

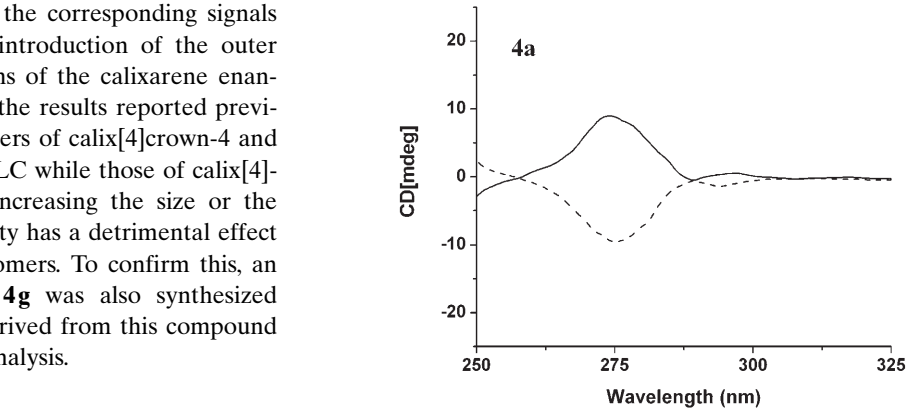
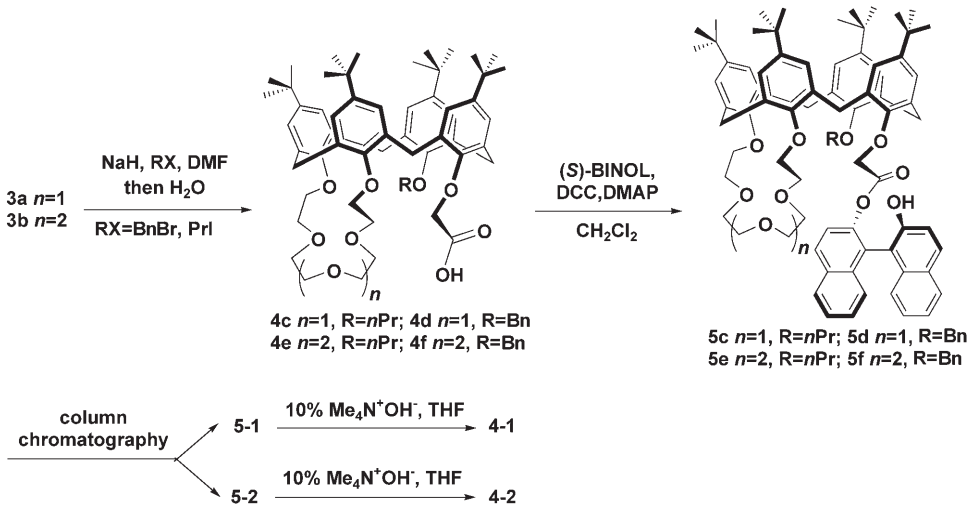


Figure 2. CD spectra (CH_2Cl_2, 25°C) of the enantiomers **4a-1** (solid line) and **4a-2** (dotted line).

By comparing the ^1H NMR spectra of **5c-1** and **5c-2** (Figure 3), we can see that there are more discernible differences than between **5a-1** and **5a-2**. The proton signals arising from the binaphthyl moiety appear in the region of $\delta=$ 8.00–7.00 ppm and have slightly different chemical shifts and splitting patterns. The signals below $\delta=7.00$ ppm are attributed to the calixarene moiety. The signals arising from the aromatic rings of **5c-1** exhibit a single peak at $\delta=6.91$ ppm, a pair of doublets at approximately $\delta=6.90$ ppm (partly buried in the former), and a singlet at $\delta=6.59$ ppm. Yet for **5c-2**, there is a single peak at $\delta=6.81$ ppm and three pairs



Scheme 3.

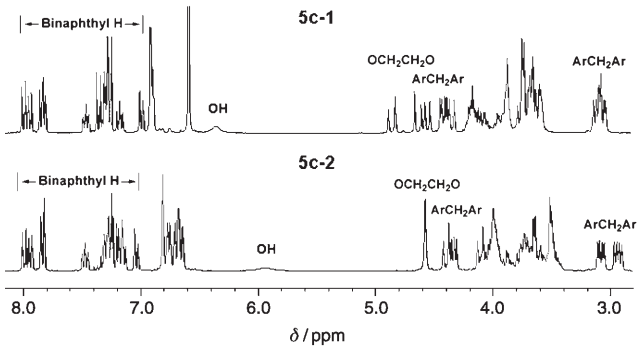


Figure 3. Partial ^{1}H NMR spectra of diastereomers **5c-1** and **5c-2**.

of doublets at approximately $\delta = 6.76$, 6.69, and 65 ppm (partly overlapping). The hydroxy signal of **5c-1** appears at $\delta = 6.36$ ppm, whilst that of **5c-2** is at $\delta = 5.95$ ppm. For the signals of the OCH_2CO_2 methylene protons, **5c-1** exhibits a pair of doublets at $\delta = 4.85$ and 4.63 ppm, whereas **5c-2** exhibits a pseudosinglet at $\delta = 4.58$ ppm, which indicates that the OCH_2CO_2 group of the latter can rotate more freely than the former. The protons of the $ArCH_2Ar$ moieties exhibit four pairs of doublets for both diastereomers, with those of **5c-1** at $\delta = 4.55$, 4.42, 4.40, 4.34, 3.11, 3.09, 3.06, and 3.05 ppm and those of **5c-2** at $\delta = 4.40$, 4.36, 4.33, 4.11, 3.09, 3.07, 2.95, and 2.93 ppm. It is interesting that the chemical shifts of the bridging methylene protons of **5c-2** are at lower fields than the corresponding shifts of **5c-1**. The ^{1}H NMR spectra of the diastereomers of **5d–5f** also show significant differences (refer to the corresponding spectroscopic data) in most regions. As a result of the significant differences in the ^{1}H NMR spectra of each pair of tetra-*O*-alkylated diastereomers and improvements in their separation compared with the tri-*O*-alkylated diastereomers, we speculate that alkylation of the last hydroxy group increases the steric hindrance at the lower rim, so that under the influence of the bulky outer chiral moiety (*S*)-BINOL, the calix skeletons of the tetra-*O*-alkylated diastereomers may suffer distortion to quite different degrees. It is reasonable to suggest that the differences in the structures of these diastereomers facilitate their separation.

After hydrolysis of **5c–5f**, four pairs of enantiomers were obtained. Their CD spectra all show symmetrical images (Figure 4) and their specific rotations have the same magnitudes with opposite signs.

Alkylation of the free phenolic OH; changing to partial cone conformations: The successful separation of the tetra-*O*-alkylated diastereomeric cone conformers **5c–5f** prompted us to investigate the possibility of synthesizing and optically resolving partial cone conformers. So far tetra-*O*-alkylated inherently chiral calix[4]arenes with partial cone conformations have been synthesized by reacting 1,2-di-*O*-substituted calix[4]arenes with suitable alkylating agents using Cs_2CO_3 as the base.[2d,f,4b,9] It has been proven that the first alkylation reaction occurs on the same side as the di-*O*-sub-

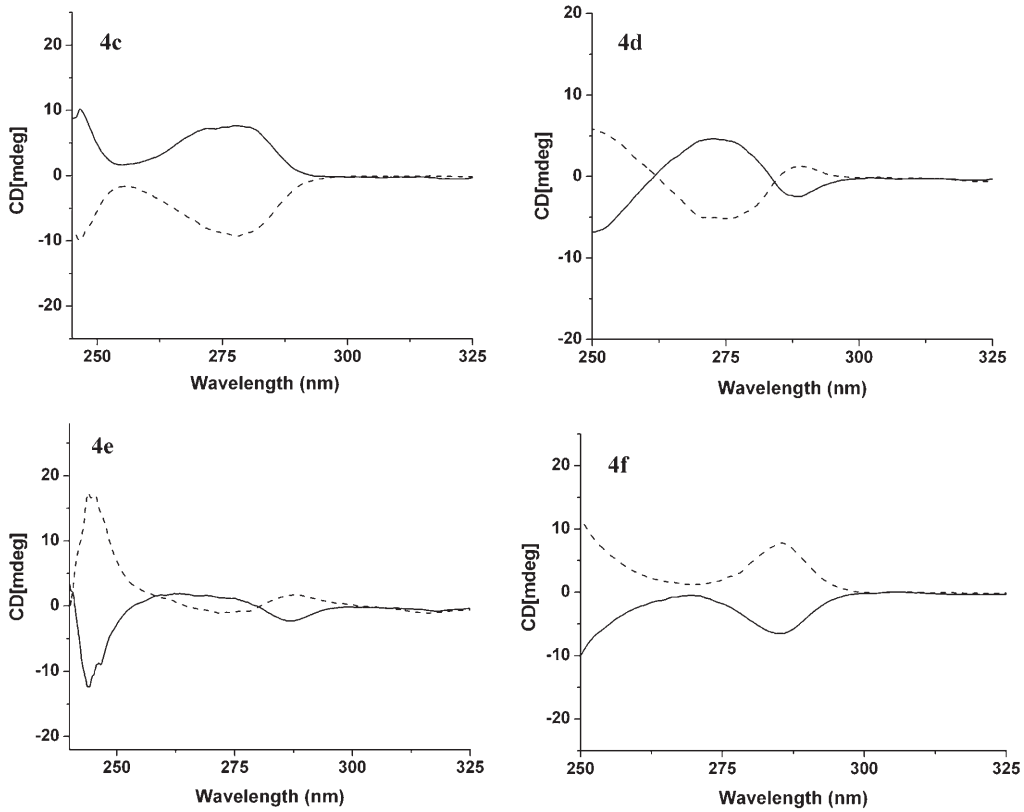
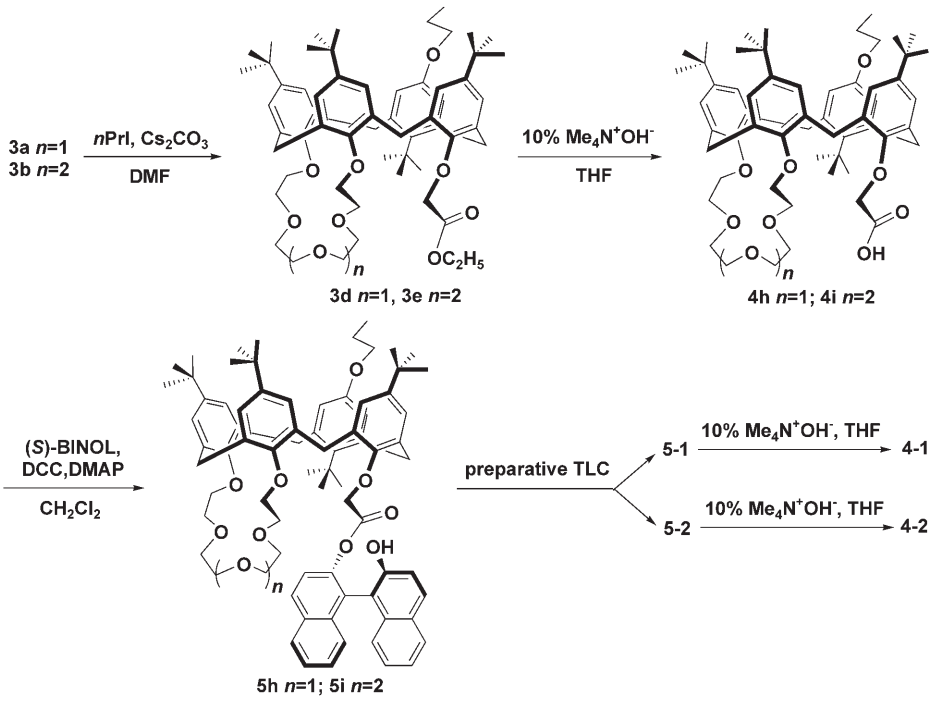


Figure 4. CD spectra (CH_2Cl_2, 25 °C) of the enantiomers of **4c–4f** (the solid lines and the dotted lines denote **4–1** and **4–2**, respectively).

stituted moieties to yield a tri-*O*-alkylated cone conformer intermediate. However, under the template effect of the Cs^+ cation, the second alkylation reaction has to occur on the opposite side to avoid steric hindrance, giving tetra-*O*-alkylated products with partial cone conformations. We treated compounds **3a** and **3b** with *n*PrI (10 equiv) in DMF in the presence of Cs_2CO_3 (10 equiv) at 70 °C for two days. As expected, compounds **3d** and **3e** with partial cone conformations were obtained in moderate yields (Scheme 4). The NMR spectra of **3d** and **3e** resemble each other. The resonances arising from the bridging methylene carbon atoms are observed at $\delta = 37.92$, 37.62, 31.63, and 31.05 ppm for **3d** and at $\delta = 38.11$, 37.81, 31.32, and 30.74 ppm for **3e**, respectively. Because only the unsubstituted aromatic ring of **3a** and **3b** can rotate as the other three are immobilized by the substituents, we can deduce that **3d** and **3e** adopt partial cone conformations. Indeed, because of the diamagnetic shielding effect, the methyl and methylene protons of the inverted *O*-propyl groups in **3d** and **3e** appear at a higher field than those of **4c** and **4e** cone conformers bearing a propyl group. Hydrolysis of **3d** and **3e** afforded the carboxylic acid derivatives **4h** and **4i**, respectively. Compared with those of **3d** and **3e**, all the signals arising from the methyl and methylene protons in the inverted *O*-propyl group of **4h** and **4i** are positioned at remarkably high fields. This phenomenon indicates that the inverted propyl group is deeply buried in the hydrophobic cavity generated by the three remaining phenol units in a sort of "self-inclusion" complex. It is still not clear why this simple hydrolysis reaction can cause such significant conformational adjustment.



Scheme 4.

Compounds **4h** and **4i** were then treated with (*S*)-BINOL to furnish **5h** and **5i**, respectively, each as a pair of diastereomers. Similarly, both the tetra-*O*-alkylated diastereomeric crown-5 and crown-6 partial cone conformers **5h** and **5I**, respectively, can readily be separated by preparative TLC ($CHCl_3$:AcOEt = 4:1, $de > 99\%$). After hydrolysis, two pairs of enantiomers were obtained. Their CD spectra show symmetrical images (Figure 5) and their specific rotations have the same magnitudes with opposite signs.

With a method for the synthesis of calix[4]arenes with partial cone conformations in hand, we synthesized a conformational isomer of **4h** that also adopts a partial cone conformation, the only difference being that it has a different inverted aromatic ring (Scheme 5). 1,2-Calix[4]crown-5 **2a** was

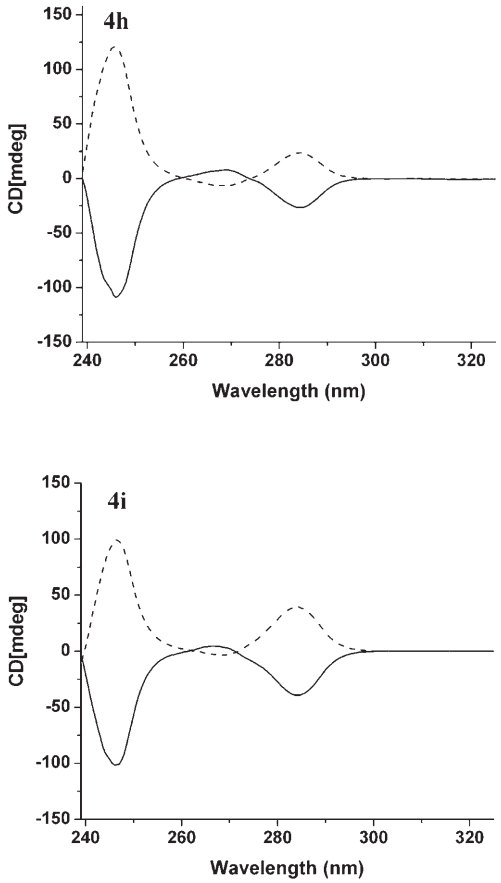
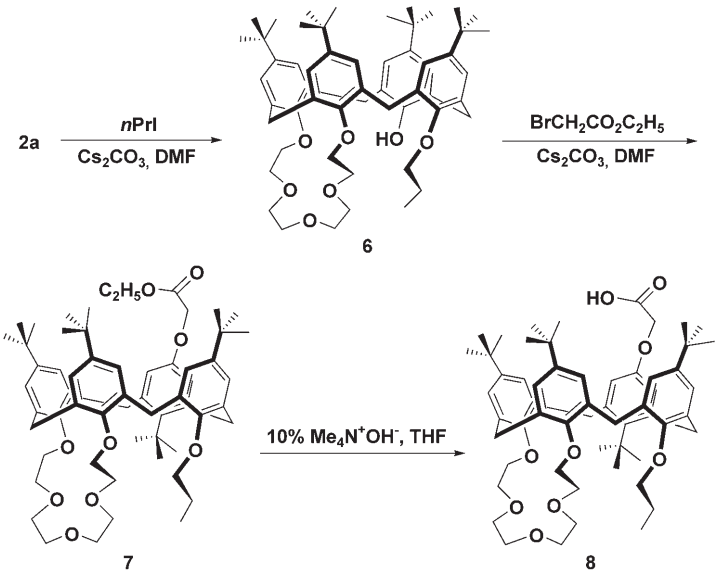


Figure 5. CD spectra (CH_2Cl_2, 25 °C) of the enantiomers of **4h** and **4i** (the solid lines and the dotted lines denote **4–1** and **4–2**, respectively).



Scheme 5.

treated with *n*PrI under the same reaction conditions as used for the alkylation of compounds **3a** and **3b** to yield inherently chiral racemate **6** with a cone conformation. Compound **6** was then subjected to the same reaction conditions as used to esterify **2a** to yield **7** with a partial cone conformation, which was confirmed by its spectroscopic data. Compound **7**, with the inverted aromatic ring bearing the ethoxycarbonylmethyl group, was then hydrolyzed to give carboxylic acid derivative **8**. Compound **8** was then treated with (*S*)-BINOL to yield a diastereomeric mixture. However, TLC analysis of compound **8** showed only one spot with various developing solvents and attempts to separate it failed. So it seems that in our system, it is essential that the carboxylic group is *syn* to the crown moiety if the diastereomeric mixture is to be separated by conventional chromatography methods.

Conclusions

In conclusion, we have demonstrated a facile way to synthesize a series of tri- and tetra-*O*-alkylated inherently chiral calix[4]crowns with cone and partial cone conformations. By taking advantage of the carboxylic group appended on the lower rim of **4**, diastereomers **5a–5i** were formed by condensation with chiral auxiliary (*S*)-BINOL. Chemical resolution was effected by preparative TLC for compounds **5a**, **5h**, and **5i**, and by conventional column chromatography on silica gel for **5c–5f**. After hydrolysis, the (*S*)-BINOL unit was removed and seven pairs of optically pure enantiomers of **4** were obtained. Structural modification has a profound effect upon the separation of the diastereomers. It seems that 1) increasing the size or the flexibility of the crown ether moiety has a detrimental effect upon the separation of diastereomers; 2) in contrast, alkylation of the last phenolic hydroxy group with or without changing the conformation has a beneficial effect upon the separation of the diastereomers; 3) for our resolution method, it is necessary for the carboxylic group to be on the same side of the calixarene as the crown moiety at the lower rim. Enantiomers **4** possess crown moieties and carboxylic groups that may serve as recognition sites. We believe the reactions described in this work provide a convenient access to optically pure inherently chiral calix[4]crowns on a large scale and will facilitate the research into their chiral discrimination and asymmetric catalytic abilities which is now under investigation in our laboratory.

Experimental Section

General remarks: Melting points were determined on an electrothermal melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained at 300.13 and 75 MHz on a Bruker DMX300 NMR spectrometer ($CDCl_3$ and TMS as internal standard), respectively. MALDI-TOF MS were recorded with a Bruker BIFLEXIII spectrometer with CCA (2-cyano-4′-hydroxycinnamic acid) as the matrix. CD spectra were recorded with a JASCO *J*-810 spectrometer. NaH (80% in oil, Merck) was washed twice with petroleum ether (30–60 °C) and stored in a desiccator. All other chemicals were reagent grade and were used without further purification. Self-made preparative TLC plates were prepared using silica gel HF_{254} (10–40 μm) and carboxymethylcellulose (CMC) as adhesive. Column chromatography was performed on silica gel (200–300 mesh). Petroleum ether used for column chromatography refers to of the 60–90 °C fraction.

5,11,17,23-Tetra-*tert*-butyl-25,26-bis[(ethoxyethyl)oxy]-27,28-dihydroxycalix[4]arene (2c): NaH (0.924 g, 5.0 equiv) was added to a suspension of *p-tert*-butylcalix[4]arene (5 g, 7.7 mmol) in DMF (500 mL) and the reaction mixture was stirred at room temperature for 1 h. Then bromoethyl ethyl ether (2.83 g, 2.2 equiv) was added and the mixture was stirred at 60 °C for 24 h. Methanol (40 mL) was added dropwise to remove excess NaH. After removal of the solvent under reduced pressure, the residue was partitioned between 10% HCl (300 mL) and CH_2Cl_2 (2×300 mL). The organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography (SiO_2, petroleum ether/AcOEt 9:1) to give **2c** as a white solid. Yield 56%; m.p. 205–207 °C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ = 8.53 (s, 2H; OH), 6.97–6.87 (m, 8H), 4.57 (d, J = 12.6 Hz, 1H; ArCH_2Ar), 4.39 (d, J = 13.2 Hz, 2H; ArCH_2Ar), 4.28 (d, J = 14.3 Hz, 1H; ArCH_2Ar), 4.11–3.61 (m, 12H; CH_2CH_2OCH_2CH_3), 3.28 (d, J = 12.7 Hz, 4H; ArCH_2Ar), 1.29 (t, J = 6.9 Hz, 6H; OCH_2CH_3), 1.18 (s, 18H), 1.06 ppm (s, 18H); ^{13}C NMR: δ = 151.81, 148.91, 146.01, 141.91, 133.79, 133.65, 128.48, 127.69, 125.78, 125.73, 125.08, 125.05, 74.36, 69.68, 66.70, 33.96, 33.82, 32.44, 31.73, 31.13, 31.55, 31.29, 15.23 ppm; IR (KBr): $\tilde{\nu}$ = 3366, 1484, 1200, 1122 cm^{-1}; MALDI-TOF MS: *m*/*z*: 792.2 $[M]^+$, 815.2 $[M+Na]^+$, 831.2 $[M+K]^+$; elemental analysis calcd (%) for $C_{52}H_{72}O_6$: C, 78.75; H, 9.15; found: C, 78.67; H, 9.20.

Reaction of 2a–2c with ethyl bromoacetate: General procedure for the preparation of cone conformers 3a–3c: A stirred mixture of **2a–2c** (3.7 mmol), ethyl bromoacetate (0.68 g, 1.1 equiv), and Cs_2CO_3 (1.21 g, 1.0 equiv) in DMF (250 mL) was heated at 60 °C for 6 h. Then 10% HCl (4 mL) was added to quench the reaction. After removal of the solvent under reduced pressure, the residue was partitioned between water and CH_2Cl_2. The organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography to give **3a–3c** as white solids.

3-{[(Ethoxycarbonyl)methyl]oxy}-*p-tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (3a): Column chromatography (SiO_2, petroleum ether/AcOEt 4:1). Yield 77%; m.p. 154–155 °C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ = 7.11 (s, 2H), 7.06 and 7.02 (2d, J = 2.1 Hz, 1H each), 6.66 (s, 2H), 6.45 (s, 1H), 6.44 (s, 1H), 4.56 (d, J = 15.7 Hz, 1H; CH_2CO$_2$), 4.52–3.66

(m, 21H), 3.26 (d, J=14.1 Hz, 1H; ArCH_2Ar), 3.23 (d, J=11.3 Hz, 1H; ArCH_2Ar), 3.21(d, J=13.5 Hz, 1H; ArCH_2Ar), 3.19 (d, J=11.8 Hz, 1H; ArCH_2Ar), 1.33 (t, J=7.2 Hz, 3H; CH_2CH_3), 1.32 (s, 18H), 0.93 (s, 9H), 0.77 ppm (s, 9H); ^{13}C NMR: δ=169.8, 153.6, 152.5, 150.7, 146.1, 145.8, 145.2, 141.0, 135.9, 135.4, 132.9, 132.0, 132.01, 131.7, 129.3, 128.1, 125.8, 125.6, 125.4, 125.2, 125.1, 125.0, 124.8, 124.74, 76.22, 72.42, 72.28, 72.06, 70.99, 70.37, 69.88, 69.61, 68.41, 60.88, 34.15, 33.84, 33.61, 31.79, 31.68, 31.07, 31.34, 30.98, 30.80, 14.3 ppm; IR (KBr): $\tilde{\nu}$=3480, 1755, 1482, 1202, 1123 cm^{-1}; MALDI-TOF MS: m/z: 915.8 $[M+Na]^+$, 931.8 $[M+K]^+$; elemental analysis calcd (%) for $C_{56}H_{76}O_9$: C, 75.30; H, 8.58; found: C, 75.32; H, 8.58.

3-{[(Ethoxycarbonyl)methyl]oxy}-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, cone conformer (3b): Column chromatography (SiO_2, petroleum ether/acetone 8:1). Yield 82%; m.p. 152–154°C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ=7.11 (s, 2H), 7.05 and 7.02 (2d, J=2.1 Hz, 1H each), 6.62 (s, 2H), 6.48 (s, 2H), 5.82 (s, 1H; OH), 4.53 (s, 2H; CH_2CO_2), 4.48 (d, J=11.7 Hz, 1H; ArCH_2Ar), 4.42 (d, J=13.2 Hz, 1H; ArCH_2Ar), 4.29–3.61 (m, 24H), 3.28 (d, J=12.5 Hz, 1H; ArCH_2Ar), 3.24 (d, J=11.6 Hz, 1H; ArCH_2Ar), 3.20 (d, J=12.1 Hz, 1H; ArCH_2Ar), 3.17 (d, J=12.7 Hz, 1H; ArCH_2Ar), 1.32 (t, J=7.3 Hz, 3H; CH_2CH_3), 1.31 (s, 18H), 0.88 (s, 9H), 0.78 ppm (s, 9H); ^{13}C NMR: δ=169.64, 153.61, 152.18, 150.81, 150.53, 145.86, 145.74, 145.38, 141.32, 135.86, 135.56, 132.88, 131.88, 131.81, 131.76, 129.33, 128.34, 125.67, 125.61, 125.23, 125.17, 125.08, 124.94, 124.84, 124.79, 74.92, 72.31, 71.85, 71.14, 70.76, 70.62, 69.69, 69.58, 60.92, 34.12, 33.82, 33.75, 33.62, 31.74, 31.65, 31.04, 31.00, 31.52, 31.33, 30.87, 14.24 ppm; IR (KBr): $\tilde{\nu}$=3467, 1737, 1482, 1202, 1124 cm^{-1}; MALDI-TOF MS: m/z: 958.8 $[M+Na]^+$, 975.8 $[M+K]^+$; elemental analysis calcd (%) for $C_{58}H_{80}O_{10}$: C, 74.33; H, 8.60; found: C, 74.31; H, 8.63.

5,11,17,23-Tetra-*tert*-butyl-25,26-bis[(ethoxyethyl)oxy]-27-{[(ethoxycarbonyl)methyl]oxy}-28-hydroxycalix[4]arene, cone conformer (3c): Column chromatography (SiO_2, petroleum ether/AcOEt 9:1). Yield 62%; m.p. 117–120°C; ^{1}H NMR: δ=7.07 (s, 2H), 7.02 (d, J=2.3 Hz, 1H), 7.00 (d, J=2.3 Hz, 1H), 6.64 (s, 1H), 6.63 (s, 1H), 6.52 (s, 2H), 5.98 (s, 1H; OH), 4.63 and 4.53 (2d, J=15.8 Hz, 1H each, CH_2CO_2), 4.56 (d, J=12.8 Hz, 1H; ArCH_2Ar), 4.44 (d, J=12.9 Hz, 2H; ArCH_2Ar), 4.34 (d, J=13.3 Hz, 1H; ArCH_2Ar), 4.30–3.79 (m, 10H), 3.62 (q, J=7.2 Hz, 2H; CH_2CH_3), 3.59 (q, J=7.2 Hz, 2H; CH_2CH_3), 3.24 (d, J=13.5 Hz, 1H; ArCH_2Ar), 3.23 (d, J=11.4 Hz, 1H; ArCH_2Ar), 3.20 (d, J=12.8 Hz, 1H; ArCH_2Ar), 3.17 (d, J=12.6 Hz, 1H; ArCH_2Ar), 1.33 (t, J=7.1 Hz, 3H; $CO_2CH_2CH_3$), 1.24 (t, J=7.2 Hz, 3H; OCH_2CH_3), 1.23 (t, J=7.2 Hz, 3H; OCH_2CH_3), 1.29, 1.28, 0.90 and 0.82 ppm (4s, 9H each); ^{13}C NMR: δ=169.89, 153.51, 152.38, 151.02, 150.49, 145.73, 145.60, 145.38, 141.16, 135.63, 135.38, 132.87, 132.12, 132.06, 132.01, 129.10, 128.43, 125.64, 125.58, 125.18, 125.12, 125.03, 124.95, 124.93, 124.81, 74.72, 72.31, 71.95, 69.34, 69.26, 66.60, 66.33, 60.94, 34.10, 33.82, 33.78, 33.67, 31.74, 31.65, 31.10, 31.07, 31.39, 30.99, 15.50, 15.30, 14.24 ppm; IR (KBr): $\tilde{\nu}$=3538, 1759, 1481, 1203 cm^{-1}; MALDI-TOF MS: m/z: 901.1 $[M+Na]^+$; elemental analysis calcd (%) for $C_{56}H_{78}O_8$: C, 76.50; H, 8.94; found: C, 76.28; H, 8.94.

Hydrolysis of compounds 3a–3c: General procedure for the preparation of 4a, 4b, and 4g: Compounds **3a–3c** (1.8 mmol) in THF (100 mL) were refluxed with aqueous 10% tetramethylammonium hydroxide solution (8.18 mL, 5 equiv) for 12 h. After removal of the solvent, 10% HCl (40 mL) was added. The aqueous solution was extracted with CH_2Cl_2 (2×40 mL). The organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was crystallized from CH_2Cl_2/CH_3OH to give the products **4a, 4b**, and **4g** as white solids.

3-[(Carboxymethyl)oxy]-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (4a): Yield 80%; m.p. 128–130°C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ=7.03 and 6.97 (2d, J=2.4 Hz, 1H each, ArH), 6.95 (s, 3H; ArH), 6.85 (d, J=2.3 Hz, 1H; ArH), 6.82 and 6.77 (2d, J=2.4 Hz, 1H each, ArH), 4.84 and 4.37 (2d, J=16.0 Hz, 1H each, CH_2CO_2), 4.44 (d, J=12.5 Hz, 1H; ArCH_2Ar), 4.30 (d, J=12.4 Hz, 1H; ArCH_2Ar), 4.26 (d, J=13.5 Hz, 1H; ArCH_2Ar), 4.21 (d, J=12.9 Hz, 1H; ArCH_2Ar), 4.33–3.66 (m, 16H), 3.36 (d, J=13.6 Hz, 1H; ArCH_2Ar), 3.28 (d, J=12.6 Hz, 1H; ArCH_2Ar), 3.27 (d, J=13.3 Hz, 1H; ArCH_2Ar), 3.26 (d, J=12.5 Hz, 1H; ArCH_2Ar), 1.23, 1.13, 1.08, and 1.01 ppm (4s, 9H each, C(CH_3)$_3$); ^{13}C NMR: δ=171.13, 152.38, 151.35, 150.33, 149.26, 147.07, 146.53, 146.03, 142.51, 134.24, 134.01, 133.95, 133.40, 132.21, 132.14, 129.04, 128.20, 126.08, 125.80, 125.78, 125.68, 125.65, 125.45, 125.41, 125.07, 75.82, 74.37, 72.15, 71.28, 70.91, 70.69, 70.22, 70.15, 69.74, 34.02, 34.01, 33.89, 33.86, 31.54, 31.35, 31.20, 31.16, 32.24, 32.08, 31.27, 30.48 ppm; IR (KBr): $\tilde{\nu}$=3446, 1760, 1482, 1248, 1201, 1123 cm^{-1}; MALDI-TOF MS: m/z: 887.2 $[M+Na]^+$, 903.2 $[M+K]^+$; elemental analysis calcd (%) for $C_{54}H_{72}O_9$: C 74.97, H 8.39; found: C 74.99, H 8.32.

3-[(Carboxymethyl)oxy]-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, cone conformer (4b): Yield 83%; m.p. 125–127°C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ=7.75 (s, 1H; OH), 7.02–6.85 (m, 8H), 4.91 and 4.45 (2d, J=16.0 Hz, 1H each; CH_2CO_2), 4.50 (d, J=14.1 Hz, 1H; ArCH_2Ar), 4.34 (d, J=12.6 Hz, 1H; ArCH_2Ar), 4.26 (d, J=13.5 Hz, 1H; ArCH_2Ar), 4.24 (d, J=12.9 Hz, 1H; ArCH_2Ar), 4.53–3.67 (m, 20H), 3.34 (d, J=13.9 Hz, 1H; ArCH_2Ar), 3.29 (d, J=12.6 Hz, 1H; ArCH_2Ar), 3.27 (d, J=12.9 Hz, 2H; ArCH_2Ar), 1.17, 1.15, 1.10, and 1.05 ppm (4s, 9H each); ^{13}C NMR: δ=171.32, 152.05, 151.71, 151.09, 148.75, 146.81, 146.63, 145.84, 142.41, 134.16, 133.82, 133.54, 132.99, 132.70, 128.74, 128.00, 126.26, 125.85, 125.66, 125.64, 125.60, 125.55, 125.41, 125.32, 125.00, 75.40, 74.26, 72.06, 71.22, 70.70, 70.57, 70.40, 70.32, 70.26, 69.77, 34.04, 33.97, 33.90, 33.78, 32.30, 32.25, 30.97, 31.43, 31.29, 31.24 ppm; IR (KBr): $\tilde{\nu}$=3422, 1748, 1482, 1201, 1124 cm^{-1}; MALDI-TOF MS: m/z: 931.2 $[M+Na]^+$, 947.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{56}H_{76}O_{10}$: C 73.98, H 8.43; found: C 73.53, H 8.30.

5,11,17,23-Tetra-*tert*-butyl-25,26-bis[(ethoxyethyl)oxy]-27-[(carboxymethyl)oxy]-28-hydroxycalix[4]arene, cone conformer (4g): Yield 62%; m.p. 162–164°C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ=11.9 (s, 1H; COOH), 7.75 (s, 1H; OH), 7.09 and 7.02 (2d, J=2.0 Hz, 1H each), 7.03 and 7.00 (2d, J=2.2 Hz, 1H each), 6.86 and 6.80 (2d, J=2.0 Hz, 1H each), 6.75 and 6.74 (2s, 1H each), 4.76 and 4.61 (2d, J=15.7 Hz, 1H each, CH_2CO_2), 4.49 (d, J=12.7 Hz, 1H; ArCH_2Ar), 4.41 (d, J=12.5 Hz, 1H; ArCH_2Ar), 4.38 (d, J=13.4 Hz, 1H; ArCH_2Ar), 4.31 (d, J=12.9 Hz, 1H; ArCH_2Ar), 4.68–3.54 (m, 12H; C$H_2CH_2OCH_2CH_3$), 3.29 (d, J=13.5 Hz, 1H; ArCH_2Ar), 3.27 (d, J=12.3 Hz, 2H; ArCH_2Ar), 3.23 (d, J=12.6 Hz, 1H; ArCH_2Ar), 1.29 (t, J=6.9 Hz, 6H; CH_2CH_3), 1.23, 1.21, 1.11, and 0.96 ppm (4s, 9H each); ^{13}C NMR: δ=170.88, 151.76, 151.49, 151.09, 148.60, 146.96, 146.82, 145.93, 141.95, 134.48, 134.32, 134.24, 133.83, 133.28, 133.11, 128.39, 127.81, 126.31, 126.06, 125.64, 125.62, 125.41, 125.39, 125.16, 124.84, 75.16, 74.79, 71.47, 69.26, 68.88, 66.73, 66.58, 34.10, 33.86, 33.70, 32.14, 31.92, 31.28, 30.67, 31.44, 31.40, 31.37, 31.13, 15.19, 15.07 ppm; IR (KBr): $\tilde{\nu}$=3309, 1766, 1482, 1246, 1200, 1123 cm^{-1}; MALDI-TOF MS: m/z: 873.5 $[M+Na]^+$, 889.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{54}H_{74}O_8$: C 76.20, H 8.76; found: C 76.10, H 8.75.

Alkylation of the last phenolic OH group: general procedure for the preparation of cone conformers 4c–4f: Compound **3a** or **3b** (1.5 mmol) and NaH (0.18 g, 5.0 equiv) in DMF (100 mL) were stirred at room temperature for 1 h. Then alkylating agent was added and the temperature was kept at 70°C overnight. Water (15 mL) was added and the mixture was stirred for another 3 h. After removal of the solvent under reduced pressure, 10% HCl (50 mL) was added. The aqueous solution was extracted with CH_2Cl_2 (2×50 mL). The organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography (SiO_2, petroleum ether/AcOEt 1:1) to give **4c–4f** as white solids.

3-[(Carboxymethyl)oxy]-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (4c): Yield 88%; m.p. 186–188°C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ=11.28 (s, 1H; COOH), 7.18 (s, 2H), 7.15 (s, 2H), 6.62 (s, 2H), 6.53 (s, 2H), 4.89 and 4.55 (2d, J=15.7 Hz, 1H each, CH_2CO_2), 4.61 (d, J=12.5 Hz, 1H; ArCH_2Ar), 4.39 (d, J=12.6 Hz, 1H; ArCH_2Ar), 4.26 (d, J=13.0 Hz, 1H; ArCH_2Ar), 4.20 (d, J=13.8 Hz, 1H; ArCH_2Ar), 4.47–3.73 (m, 18H), 3.27 (d, J=12.9 Hz, 1H; ArCH_2Ar), 3.26 (d, J=13.5 Hz, 1H; ArCH_2Ar), 3.21 (d, J=12.5 Hz, 1H; ArCH_2Ar), 3.17 (d, J=12.0 Hz, 1H; ArCH_2Ar), 1.63–1.59 (m, 2H; $CH_2CH_2CH_3$), 1.37 and 0.85 (2s, 18H each), 1.00 ppm (t, J=7.4 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=170.83, 154.07, 152.01, 150.84, 150.82, 147.11, 145.33, 145.15, 145.00, 135.69, 135.00, 134.91, 134.87, 132.98, 132.55, 131.59, 131.35, 126.06, 125.87, 125.48, 125.34, 125.23, 125.19, 124.76, 124.57, 78.44, 75.41, 73.55, 71.49, 71.04, 70.67, 70.53, 70.45, 69.11, 34.21, 34.08, 33.66, 31.73, 31.60, 31.03, 31.19, 31.12, 30.89, 30.47, 23.02, 10.25 ppm; IR (KBr): $\tilde{\nu}$=3235,

1762, 1481, 1200 cm^{-1}; MALDI-TOF MS: *m/z*: 929.9 $[M+Na]^+$; elemental analysis calcd (%) for $C_{57}H_{78}O_9$: C 75.46, H 8.67; found: C 75.56, H 8.65.

3-[(Carboxymethyl)oxy]-4-benzyloxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (4d): Yield 66%; m.p. 128–130°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 7.38–7.34 (m, 5H; OCH_2Ph), 7.13–7.08 (m, 4H), 6.62 and 6.57 (2d, *J* = 1.7 Hz, 1H each), 6.48 (s, 2H), 4.97 and 4.83 (2d, *J* = 11.1 Hz, 1H each, OCH_2Ph), 4.85 and 4.42 (2d, *J* = 15.8 Hz, 1H each, CH_2CO_2), 4.58 (d, *J* = 12.5 Hz, 1H; $ArCH_2Ar$), 4.26 (d, *J* = 12.4 Hz, 1H; $ArCH_2Ar$), 4.17 (d, *J* = 12.3 Hz, 1H; $ArCH_2Ar$), 4.31–3.69 (m, 17H), 3.23 (d, *J* = 12.8 Hz, 1H; $ArCH_2Ar$), 3.14 (d, *J* = 12.6 Hz, 1H; $ArCH_2Ar$), 3.05 (d, *J* = 12.6 Hz, 1H; $ArCH_2Ar$), 2.88 (d, *J* = 13.0 Hz, 1H; $ArCH_2Ar$), 1.34, 1.33, 0.86, and 0.82 ppm (4s, 9H each); ^{13}C NMR: δ = 170.77, 154.13, 152.10, 150.87, 149.96, 147.00, 145.36, 145.27, 145.10, 136.41, 135.65, 134.87, 134.81, 134.77, 132.94, 132.74, 132.11, 131.30, 130.06, 128.42, 128.40, 126.02, 125.73, 125.40, 125.33, 125.24, 125.21, 124.75, 124.45, 78.50, 75.38, 73.50, 71.28, 71.07, 70.56, 70.49, 70.45, 69.06, 34.17, 34.06, 33.70, 33.64, 31.72, 31.57, 31.02, 31.16, 31.08, 30.53 ppm; IR (KBr): $\tilde{\nu}$ = 3246, 1761, 1480, 1199 cm^{-1}; MALDI-TOF MS: *m/z*: 977.1 $[M+Na]^+$; elemental analysis calcd (%) for $C_{61}H_{78}O_9$: C 76.70, H 8.23; found: C 76.43, H 8.26.

3-[(Carboxymethyl)oxy]-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, cone conformer (4e): Yield 67%; m.p. 152–154°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 7.15 (s, 2H), 7.14 and 7.12 (2d, *J* = 1.7 Hz, 1H each), 6.58 (s, 2H), 6.51 and 6.49 (2d, *J* = 2.5 Hz, 1H each), 4.78 and 4.53 (2d, *J* = 15.7 Hz, 1H each, CH_2CO_2), 4.58 (d, *J* = 13.0 Hz, 1H; $ArCH_2Ar$), 4.39 (d, *J* = 12.4 Hz, 1H; $ArCH_2Ar$), 4.22 (d, *J* = 12.7 Hz, 1H; $ArCH_2Ar$), 4.19 (d, *J* = 12.7 Hz, 1H; $ArCH_2Ar$), 4.05–3.60 (m, 22H), 3.23 (d, *J* = 12.8 Hz, 2H; $ArCH_2Ar$), 3.16 (d, *J* = 12.5 Hz, 1H; $ArCH_2Ar$), 3.14 (d, *J* = 12.5 Hz, 1H; $ArCH_2Ar$), 2.00–1.83 (m, 2H; $CH_2CH_2CH_3$), 1.34 (s, 18H each, $C(CH_3)_3$), 0.98 (t, *J* = 7.5 Hz, 3H; $CH_2CH_2CH_3$), 0.83 and 0.82 ppm (2s, 9H each); ^{13}C NMR: δ = 170.61, 154.27, 151.88, 150.83, 150.79, 147.14, 145.27, 145.16, 145.00, 135.50, 135.03, 135.01, 134.88, 132.96, 132.55, 131.59, 131.44, 126.07, 125.85, 125.50, 125.25, 125.18, 125.16, 124.76, 124.57, 78.38, 75.20, 73.17, 71.25, 70.92, 70.85, 70.73, 70.57, 70.27, 69.04, 34.21, 34.08, 33.66, 31.73, 31.60, 31.03, 31.19, 30.82, 30.73, 23.00, 10.29 ppm; IR (KBr): $\tilde{\nu}$ = 3230, 1762, 1481, 1200, 1123 cm^{-1}; MALDI-TOF MS: *m/z*: 973.8 $[M+Na]^+$, 989.8 $[M+K]^+$; elemental analysis calcd (%) for $C_{59}H_{82}O_{10}$: C 74.49, H 8.69; found: C 74.48, H 8.64.

3-[(Carboxymethyl)oxy]-4-benzyloxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, cone conformer (4f): Yield 66%; m.p. 103–105°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 7.36–7.32 (m, 5H; OCH_2Ph), 7.12 and 7.08 (2d, *J* = 2.1 Hz, 1H each), 7.11 and 7.07 (2d, *J* = 2.1 Hz, 1H each), 6.60 and 6.48 (2d, *J* = 1.4 Hz, 1H each), 6.55 and 6.46 (2d, *J* = 1.4 Hz, 1H each), 4.94 and 4.80 (2d, *J* = 11.1 Hz, 1H each, OCH_2Ph), 4.73 and 4.45 (2d, *J* = 15.8 Hz, 1H each, CH_2CO_2), 4.55 (d, *J* = 12.5 Hz, 1H; $ArCH_2Ar$), 4.27 (d, *J* = 12.4 Hz, 1H; $ArCH_2Ar$), 4.18 (d, *J* = 12.6 Hz, 1H; $ArCH_2Ar$), 4.39–3.57 (m, 21H), 3.22 (d, *J* = 12.8 Hz, 1H; $ArCH_2Ar$), 3.13 (d, *J* = 12.6 Hz, 1H; $ArCH_2Ar$), 3.02 (d, *J* = 12.5 Hz, 1H; $ArCH_2Ar$), 2.87 (d, *J* = 12.9 Hz, 1H; $ArCH_2Ar$), 1.32, 1.31, 0.84, and 0.81 ppm (4s, 9H each); ^{13}C NMR: δ = 170.53, 154.35, 152.00, 150.83, 150.02, 147.01, 145.34, 145.24, 145.14, 136.48, 135.44, 134.98, 134.87, 134.75, 132.90, 132.73, 132.07, 131.40, 130.00, 128.46, 128.44, 128.40, 126.00, 125.76, 125.54, 125.24, 125.07, 124.78, 124.46, 78.45, 75.19, 73.13, 71.23, 70.99, 70.83, 70.72, 70.57, 70.53, 70.23, 68.95, 34.17, 34.06, 33.70, 33.64, 31.72, 31.57, 31.02, 31.23, 30.95, 30.83 ppm; IR (KBr): $\tilde{\nu}$ = 3230, 1761, 1480, 1199, 1123 cm^{-1}; MALDI-TOF MS: *m/z*: 1021.0 $[M+Na]^+$, 1037.0 $[M+K]^+$; elemental analysis calcd (%) for $C_{63}H_{82}O_{10}$: C 75.72, H 8.27; found: C 75.73, H 8.34.

Alkylation of the last phenolic OH group: general procedure for the preparation of partial cone conformers 3d and 3e: Compound **3a** or **3b** (1.8 mmol), *n*PrI (3.06 g, 10 equiv), and Cs_2CO_3 (5.84 g, 10 equiv) in DMF (100 mL) were stirred at 70°C for 2 d. Then 10% HCl (15 mL) was added to quench the reaction. After removal of the solvent under reduced pressure, the residue was partitioned between water (50 mL) and CH_2Cl_2 (2×50 mL). The organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography and then recrystallized from CH_2Cl_2/CH_3OH to give **3d** or **3e** as a white solid.

3-{[(Ethoxycarbonyl)methyl]oxy}-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, partial cone conformer (3d): Column chromatography (SiO_2, petroleum ether/AcOEt 6:1). Yield 42%; m.p. 251–253°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 7.36 and 7.23 (2d, *J* = 2.4 Hz, 1H each), 7.05 (s, 2H), 6.87 and 6.86 (2d, *J* = 2.7 Hz, 1H each), 6.64 and 6.62 (2d, *J* = 2.4 Hz, 1H each), 4.50 and 4.36 (2d, *J* = 15.2 Hz, 1H each, CH_2CO_2), 4.33 (d, *J* = 12.3 Hz, 1H; $ArCH_2Ar$), 4.29 (d, *J* = 12.3 Hz, 1H; $ArCH_2Ar$), 4.25–3.51 (m, 22H), 3.19 (t, *J* = 7.8 Hz, 2H; $CH_2CH_2CH_3$), 3.11 (d, *J* = 13.0 Hz, 1H; $ArCH_2Ar$), 3.05 (d, *J* = 12.8 Hz, 1H; $ArCH_2Ar$), 1.63–1.50 (m, 2H), 1.43 and 1.31 (2s, 9H each), 1.29 (t, *J* = 7.2 Hz, 3H; $CO_2CH_2CH_3$), 1.05 (s, 18H), 0.70 ppm (t, *J* = 7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ = 169.74, 155.06, 153.81, 153.58, 153.49, 144.88, 144.33, 143.91, 143.21, 135.74, 134.91, 132.94, 132.69, 132.64, 132.04, 132.02, 132.00, 127.91, 127.63, 126.14, 126.04, 125.75, 125.56, 125.51, 125.44, 74.02, 73.00, 71.59, 71.36, 71.27, 70.83, 70.78, 70.58, 70.24, 69.34, 60.78, 37.92, 37.62, 31.63, 31.05, 34.04, 34.03, 33.75, 31.78, 31.68, 31.43, 31.37, 23.82, 14.20, 10.31 ppm; IR (KBr): $\tilde{\nu}$ = 1760, 1479, 1201, 1122 cm^{-1}; MALDI-TOF MS: *m/z*: 957.6 $[M+Na]^+$, 973.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{59}H_{82}O_9$: C 75.77, H 8.84; found: C 75.96, H 8.84.

3-{[(Ethoxycarbonyl)methyl]oxy}-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, partial cone conformer (3e): Column chromatography (SiO_2, petroleum ether/AcOEt 5:1). Yield 55%; m.p. 193–195°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 7.35 and 7.22 (2d, *J* = 2.4 Hz, 1H each), 7.07 (s, 2H), 6.89 and 6.87 (2d, *J* = 2.4 Hz, 1H each), 6.68 and 6.67 (2d, *J* = 2.5 Hz, 1H each), 4.50 and 4.37 (2d, *J* = 15.3 Hz, 1H each, CH_2CO_2), 4.35 (d, *J* = 11.9 Hz, 1H; $ArCH_2Ar$), 4.31 (d, *J* = 12.2 Hz, 1H; $ArCH_2Ar$), 4.28–4.18 (m, 2H; $CO_2CH_2CH_3$), 4.17–3.46 (m, 24H), 3.10 (d, *J* = 13.5 Hz, 1H; $ArCH_2Ar$), 3.05 (d, *J* = 13.7 Hz, 1H; $ArCH_2Ar$), 2.93 and 2.90 (2d, *J* = 7.2 Hz, 1H each, $CH_2CH_2CH_3$), 1.55–1.39 (m, 2H; $CH_2CH_2CH_3$), 1.42, 1.32, 1.07, and 1.05 (4s, 9H each), 1.30 (t, *J* = 6.9 Hz, 3H; $CO_2CH_2CH_3$), 0.53 ppm (t, *J* = 7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ = 169.75, 155.03, 155.80, 153.50, 152.98, 145.14, 144.29, 144.01, 143.33, 135.49, 135.42, 133.11, 132.92, 132.90, 132.36, 132.07, 132.05, 127.74, 127.45, 126.21, 126.19, 125.80, 125.56, 125.29, 125.25, 73.80, 72.11, 71.07, 70.83, 70.72, 70.45, 70.42, 70.30, 70.25, 69.82, 69.19, 60.77, 38.11, 37.81, 31.32, 30.74, 34.06, 34.00, 33.75, 33.74, 31.75, 31.66, 31.36, 31.30, 23.59 ppm; IR (KBr): $\tilde{\nu}$ = 1762, 1479, 1201 cm^{-1}; MALDI-TOF MS: *m/z*: 1001.5 $[M+Na]^+$, 1017.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{61}H_{86}O_{10}\cdot 0.5\,H_2O$: C 74.13, H 8.87; found: C 74.08, H 8.71.

3-[(Carboxymethyl)oxy]-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, partial cone conformer (4h): This compound was synthesized by hydrolysis of **3d** following the same procedure as used for the hydrolysis of **4a**, **4b**, and **4g**. Yield 99%; m.p. 209–211°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 9.49 (s, 1H; CO_2H), 7.22 (s, 2H), 7.20 (d, *J* = 2.2 Hz, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 2.1 Hz, 2H), 6.90 (d, *J* = 2.3 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H; $ArCH_2Ar$), 4.24 and 4.17 (2d, *J* = 15.5 Hz, 1H each, OCH_2CO_2), 4.06 (d, *J* = 12.0 Hz, 1H; $ArCH_2Ar$), 3.98 (d, *J* = 17.7 Hz, 1H; $ArCH_2Ar$), 4.13–3.52 (m, 19H), 3.28 (d, *J* = 12.2 Hz, 1H; $ArCH_2Ar$), 3.26 (d, *J* = 12.1 Hz, 1H; $ArCH_2Ar$), 2.24–2.19 (m, 1H), 1.93–1.86 (m, 1H), 1.37, 1.27, 1.26, and 1.11 (4s, 9H each), 0.27–0.07 (m, 2H), −0.31 ppm (t, *J* = 7.5 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ = 169.41, 154.12, 153.55, 150.96, 150.31, 147.38, 145.68, 145.46, 145.28, 136.01, 135.60, 134.48, 133.49, 132.80, 132.69, 132.09, 132.07, 127.86, 126.38, 126.01, 125.30, 125.27, 125.19, 125.15, 124.82, 75.58, 72.16, 71.25, 70.71, 70.62, 70.01, 69.23, 68.91, 39.62, 38.29, 30.94, 30.14, 34.19, 34.00, 31.56, 31.44, 31.35, 31.30, 22.29, 9.77 ppm; IR (KBr): $\tilde{\nu}$ = 3396, 1761, 1480, 1201, 1124 cm^{-1}; MALDI-TOF MS: *m/z*: 929.4 $[M+Na]^+$, 945.4 $[M+K]^+$; elemental analysis calcd (%) for $C_{57}H_{78}O_9$: C 75.46, H 8.67; found: C 75.31, H 8.71.

3-[(Carboxymethyl)oxy]-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, partial cone conformer (4i): This compound was synthesized by hydrolysis of **3e** following the same procedure as used for the hydrolysis of **4a**, **4b**, and **4g**. Yield 87%; m.p. 142–144°C (CH_2Cl_2/CH_3OH); ^1H NMR: δ = 9.55 (s, 1H; CO_2H), 7.21 (d, *J* = 2.3 Hz, 2H), 7.19 (d, *J* = 2.3 Hz, 1H), 7.08 (d, *J* = 2.3 Hz, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.95 (s, 2H), 6.91 (d, *J* = 2.4 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H; $ArCH_2Ar$), 4.22 and 4.16 (2d, *J* = 15.5 Hz, 1H each, CH_2CO_2), 4.13 (d, *J* = 12.3 Hz, 1H; $ArCH_2Ar$), 4.13–3.54 (m, 24H), 3.25 (d, *J* = 12.2 Hz, 2H; $ArCH_2Ar$), 2.29–2.22 (m, 1H),

1.96–1.89 (m, 1H), 1.37, 1.26, 1.25, and 1.12 (4s, 9H each), 0.22–0.16 (m, 2H), −0.34 ppm (t, J=7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=169.27, 154.07, 153.74, 150.79, 150.31, 147.27, 145.70, 145.38, 145.27, 135.65, 135.55, 134.42, 133.57, 132.89, 132.62, 132.40, 132.11, 127.80, 126.21, 125.93, 125.39, 125.26, 125.20, 125.06, 124.81, 74.91, 72.07, 71.09, 70.93, 70.68, 70.62, 70.57, 70.55, 69.31, 69.25, 69.00, 39.67, 38.25, 30.84, 30.39, 34.17, 33.98, 31.54, 31.42, 31.35, 31.29, 22.21, 9.67 ppm; IR (KBr): $\tilde{\nu}$= 3394, 1760, 1480, 1202, 1121 cm^{-1}; MALDI-TOF MS: m/z: 973.5 $[M+Na]^+$, 989.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{59}H_{82}O_{10}$: C 74.49, H 8.69; found: C 74.23, H 8.71.

Condensation of 4 with (*S*)-BINOL: general procedure for the preparation of diastereomers 5a–5i: Compound **4** (0.55 mmol), (*S*)-BINOL (0.173 g, 1.1 equiv), DCC (1.1 equiv for **4a** and **4b**, 3.0 equiv for **4c–4i**), and DMAP (0.014 g, 0.2 equiv) in CH_2Cl_2 (50 mL) were stirred at room temperature for a period of time (1 d for **4a** and **4b**, 5 d for **4c–4i**). After filtering off the insoluble DCC, CH_2Cl_2 was evaporated and a small amount of AcOEt was added. The insoluble DCC was again removed by filtration and the solvent was evaporated. The residue was purified by column chromatography and then subjected to preparative TLC (only for **4a**, **4b**, **4h**, and **4i**).

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (5a): First the crude product was purified by column chromatography (SiO_2, petroleum ether/AcOEt 4:1) and then the isolated diastereomeric mixture was subjected to preparative TLC ($CHCl_3$/AcOEt 5:1) to give **5a-1** and **5a-2** as white solids.

Compound **5a-1**: Yield 25%; m.p. 139–141°C; ^{1}H NMR: δ=8.09 (d, J= 8.9 Hz, 1H), 8.01 (d, J=8.2 Hz, 1H), 7.86 (d, J=7.7 Hz, 1H), 7.83 (d, J= 8.7 Hz, 1H), 7.54 (t, J=8.0 Hz, 1H), 7.53 (d, J=8.9 Hz, 1H), 7.37–7.06 (m, 10H), 6.66 (s, 2H), 6.35 and 6.34 (2s, 1H each), 6.02 (s, 1H; O*H*), 4.43 (d, J=13.8 Hz, 1H; ArC*H*$_2$Ar), 4.29 and 4.13 (2d, J=16.3 Hz, 1H each, C*H*$_2$CO$_2$), 4.39–3.59 (m, 19H), 3.31 (d, J=13.6 Hz, 1H; ArC*H*$_2$Ar), 3.19 (d, J=12.6 Hz, 1H; ArC*H*$_2$Ar), 3.01 (d, J=13.7 Hz, 1H; ArC*H*$_2$Ar), 2.94 (d, J=13.2 Hz, 1H; ArC*H*$_2$Ar), 1.39, 1.37, 0.93, and 0.74 ppm (4s, 9H each); ^{13}C NMR: δ=168.45, 153.56, 152.23, 151.94, 150.51, 150.38, 147.35, 146.15, 145.75, 145.14, 141.30, 136.10, 135.34, 133.58, 133.53, 132.74, 132.20, 131.64, 131.57, 131.52, 130.42, 130.18, 129.60, 128.82, 128.24, 128.10, 128.02, 127.18, 126.62, 126.10, 126.06, 125.91, 125.49, 125.47, 125.18, 125.06, 125.00, 124.73, 124.65, 124.63, 123.97, 123.35, 121.81, 118.41, 113.94, 76.34, 71.94, 71.69, 71.52, 70.69, 70.28, 70.17, 69.38, 68.29, 34.13, 33.86, 33.78, 33.53, 31.80, 31.67, 31.02, 30.97, 31.48, 30.68, 30.59 ppm; IR (KBr): $\tilde{\nu}$=3421, 1784, 1481, 1205, 1122 cm^{-1}; MALDI-TOF MS: m/z: 1155.6 $[M+Na]^+$, 1171.6 $[M+K]^+$; elemental analysis calcd (%) for $C_{74}H_{84}O_{10}$: C 78.41, H 7.47; found: C 78.59, H 7.53.

Compound **5a-2**: Yield 23%; m.p. 140–142°C; ^{1}H NMR: δ=8.08 (d, J= 8.9 Hz, 1H), 7.98 (d, J=8.2 Hz, 1H), 7.85 (d, J=9.0 Hz, 1H), 7.84 (d, J= 7.8 Hz, 1H), 7.52 (t, J=7.9 Hz, 1H), 7.51 (d, J=8.7 Hz, 1H), 7.39–7.06 (m, 6H), 7.13 and 7.10 (2d, J=2.0 Hz, 1H each), 7.03 and 7.02 (2s, 1H each), 6.61 and 6.60 (2s, 1H each), 6.33 and 6.31 (2s, 1H each), 6.06 (s, 1H; O*H*), 4.36 (d, J=13.8 Hz, 1H; ArC*H*$_2$Ar), 4.35 (d, J=12.5 Hz, 1H; ArC*H*$_2$Ar), 4.24 (d, J=12.8 Hz, 1H; ArC*H*$_2$Ar), 4.26 and 4.02 (2d, J= 16.5 Hz, 1H each, C*H*$_2$CO$_2$), 4.00 (d, J=12.3 Hz, 1H; ArC*H*$_2$Ar), 4.18–3.55 (m, 16H), 3.24 (d, J=13.5 Hz, 1H; ArC*H*$_2$Ar), 3.17 (d, J=12.6 Hz, 1H; ArC*H*$_2$Ar), 3.00 (d, J=13.1 Hz, 1H; ArC*H*$_2$Ar), 2.90 (d, J=13.1 Hz, 1H; ArC*H*$_2$Ar), 1.36, 1.33, 0.90, and 0.71 ppm (4s, 9H each); ^{13}C NMR: δ=168.25, 153.56, 151.96, 151.67, 150.74, 150.52, 147.45, 146.01, 145.74, 145.21, 140.95, 135.86, 135.53, 133.51, 133.49, 132.69, 132.19, 131.75, 131.72, 131.47, 130.32, 130.30, 129.22, 128.89, 128.25, 127.96, 127.92, 127.26, 126.70, 126.18, 125.98, 125.86, 125.48, 125.41, 125.08, 125.02, 124.95, 124.72, 124.60, 124.58, 123.67, 123.52, 121.80, 118.47, 114.23, 76.21, 72.11, 71.64, 71.34, 70.74, 70.33, 70.10, 69.63, 68.46, 34.15, 33.81, 33.77, 33.54, 31.78, 31.70, 31.03, 30.98, 31.39, 30.83, 30.60 ppm; IR (KBr): $\tilde{\nu}$= 3502, 1784, 1481, 1205, 1122 cm^{-1}; MALDI-TOF MS: m/z: 1155.7 $[M+Na]^+$, 1171.7 $[M+K]^+$; elemental analysis calcd (%) for $C_{74}H_{84}O_{10}$: C 78.41, H 7.47; found: C 78.44, H 7.51.

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (5c): Column chromatography (SiO_2, petroleum ether/AcOEt 5:1 then petroleum ether/acetone 9:1).

Compound **5c-1**: Yield 24%; m.p. 129–131°C; ^{1}H NMR: δ=8.00 (d, J= 8.9 Hz, 1H), 7.94 (d, J=8.2 Hz, 1H), 7.84 (d, J=8.7 Hz, 1H), 7.82 (d, J= 6.0 Hz, 1H), 7.36 (d, J=8.9 Hz, 1H), 7.49–7.15 (m, 6H), 6.99 (d, J= 8.3 Hz, 1H), 6.91–6.89 (m, 4H), 6.59 (s, 4H), 6.36 (s, 1H; O*H*), 4.85 and 4.63 (2d, J=16.8 Hz, 1H each, C*H*$_2$CO$_2$), 4.55 (d, J=12.9 Hz, 1H; ArC*H*$_2$Ar), 4.42 (d, J=12.5 Hz, 1H; ArC*H*$_2$Ar), 4.40 (d, J=12.8 Hz, 1H; ArC*H*$_2$Ar), 4.34 (d, J=12.5 Hz, 1H; ArC*H*$_2$Ar), 4.22–3.57 (m, 18H), 3.11 (d, J=14.1 Hz, 1H; ArC*H*$_2$Ar), 3.09 (d, J=12.0 Hz, 1H; ArC*H*$_2$Ar), 3.06 (d, J=13.4 Hz, 1H; ArC*H*$_2$Ar), 3.05 (d, J=12.5 Hz, 1H; ArC*H*$_2$Ar), 1.87–1.64 (m, 2H), 1.23 (s, 9H), 1.19 (s, 9H), 0.94 (s, 18H), 0.87 ppm (t, J=7.4 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=169.80, 153.52, 153.16, 153.05, 152.99, 152.31, 147.52, 145.03, 144.88, 144.45, 144.17, 134.97, 134.67, 134.32, 134.30, 133.74, 133.58, 132.95, 132.80, 132.78, 132.69, 131.98, 130.01, 129.78, 128.75, 128.14, 127.92, 126.90, 126.44, 126.12, 125.82, 125.52, 125.45, 125.30, 125.18, 124.96, 124.77, 124.68, 124.60, 124.58, 123.82, 123.14, 121.95, 118.40, 114.14, 77.30, 73.74, 72.47, 71.28, 70.44, 70.30, 70.25, 70.12, 70.04, 33.94, 33.69, 33.67, 31.58, 31.56, 31.29, 31.28, 31.17, 30.76, 23.26, 10.50 ppm; IR (KBr): $\tilde{\nu}$=3291, 1784, 1480, 1203, 1122 cm^{-1}; MALDI-TOF MS: m/z: 1197.6 $[M+Na]^+$, 1213.6 $[M+K]^+$; elemental analysis calcd (%) for $C_{77}H_{90}O_{10}$: C 78.67, H 7.72; found: C 78.45, H 7.80.

Compound **5c-2**: Yield 22%; m.p. 130–132°C; ^{1}H NMR: δ=7.99 (d, J= 8.9 Hz, 1H), 7.94 (d, J=8.2 Hz, 1H), 7.84 (d, J=8.8 Hz, 2H), 7.50–7.13 (m, 7H), 7.04 (d, J=8.4 Hz, 1H), 6.81 (s, 2H), 6.77–6.65 (m, 6H), 5.95 (s, 1H; O*H*), 4.58 (s, 2H; C*H*$_2$CO$_2$), 4.40 (d, J=13.6 Hz, 1H; ArC*H*$_2$Ar), 4.36 (d, J=13.4 Hz, 1H; ArC*H*$_2$Ar), 4.33 (d, J=12.5 Hz, 1H; ArC*H*$_2$Ar), 4.11 (d, J=13.0 Hz, 1H; ArC*H*$_2$Ar), 4.10–3.43 (m, 18H), 3.09 (d, J= 12.5 Hz, 1H; ArC*H*$_2$Ar), 3.07 (d, J=12.5 Hz, 1H; ArC*H*$_2$Ar), 2.95 (d, J= 12.9 Hz, 1H; ArC*H*$_2$Ar), 2.93 (d, J=13.0 Hz, 1H; ArC*H*$_2$Ar), 1.95 (m, 2H), 1.14, 1.11, 1.04, and 1.00 (4s, 9H each), 0.95 ppm (t, J=7.4 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=169.31, 153.42, 153.40, 153.15, 152.01, 151.94, 147.69, 145.07, 144.69, 144.56, 144.21, 134.23, 134.12, 133.95, 133.83, 133.63, 133.48, 133.34, 133.27, 133.04, 132.12, 130.26, 130.13, 128.86, 128.16, 127.85, 127.16, 126.59, 126.05, 125.88, 125.33, 125.17, 125.09, 125.07, 124.96, 124.95, 124.86, 124.80, 124.71, 124.69, 123.71, 123.45, 121.87, 118.58, 114.31, 77.15, 73.33, 73.19, 71.11, 70.57, 70.51, 70.40, 70.15, 33.86, 33.78, 33.73, 31.48, 31.37, 31.60, 31.09, 30.62, 23.15, 10.59 ppm; IR (KBr): $\tilde{\nu}$=3445, 1785, 1480, 1203, 1121 cm^{-1}; MALDI-TOF MS: m/z: 1197.5 $[M+Na]^+$, 1213.4 $[M+K]^+$; elemental analysis calcd (%) for $C_{77}H_{90}O_{10}$: C 78.67, H 7.72; found: C 78.49, H 7.78.

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-4-benzyloxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (5d): Column chromatography (SiO_2, petroleum ether/AcOEt 5:1 then petroleum ether/acetone 10:1).

Compound **5d-1**: Yield 31%; m.p. 133–135°C; ^{1}H NMR: δ=8.01 (d, J= 8.9 Hz, 1H), 7.95 (d, J=8.2 Hz, 1H), 7.82 (d, J=8.9 Hz, 1H), 7.81 (d, J= 7.7 Hz, 1H), 7.50–7.02 (m, 13H), 6.91–6.89 (m, 4H), 6.58–6.55 (m, 4H), 6.14 (s, 1H; O*H*), 4.78 and 4.72 (2d, J=11.0 Hz, 1H each), 4.73 and 4.57 (2d, J=16.9 Hz, 1H each, C*H*$_2$CO$_2$), 4.42 (d, J=12.9 Hz, 1H; ArC*H*$_2$Ar), 4.39 (d, J=12.4 Hz, 1H; ArC*H*$_2$Ar), 4.29 (d, J=13.8 Hz, 1H; ArC*H*$_2$Ar), 4.25 (d, J=13.0 Hz, 1H; ArC*H*$_2$Ar), 4.06–3.41 (m, 16H), 3.07 (d, J= 12.7 Hz, 1H; ArC*H*$_2$Ar), 3.01 (d, J=12.9 Hz, 2H; ArC*H*$_2$Ar), 2.93 (d, J= 12.9 Hz, 1H; ArC*H*$_2$Ar), 1.24, 1.19, 0.94, and 0.92 ppm (4s, 9H each); ^{13}C NMR: δ=170.09, 153.63, 152.96, 152.75, 152.36, 152.20, 147.62, 144.99, 144.85, 144.44, 144.42, 137.97, 134.93, 134.66, 134.60, 134.13, 133.73, 133.54, 132.99, 132.87, 132.80, 132.61, 132.00, 130.09, 129.96, 129.70, 129.68, 128.81, 128.13, 128.11, 127.95, 127.63, 127.00, 126.53, 126.00, 125.90, 125.48, 125.36, 125.20, 125.18, 124.90, 124.75, 124.67, 124.60, 123.74, 123.27, 121.87, 118.49, 114.19, 73.76, 72.49, 71.10, 70.35, 70.27, 70.21, 70.15, 70.03, 69.89, 33.94, 33.67, 33.65, 31.67, 31.47, 30.71, 31.60, 31.56, 31.23 ppm; IR (KBr): $\tilde{\nu}$=3524, 1783, 1479, 1204, 1121 cm^{-1}; MALDI-TOF MS: m/z: 1245.2 $[M+Na]^+$; elemental analysis calcd (%) for $C_{81}H_{90}O_{10}$: C 79.51, H 7.41; found: C 79.69, H 7.52.

Compound **5d-2**: Yield 33%; m.p. 123–125°C; ^{1}H NMR: δ=7.95 (d, J= 8.9 Hz, 1H), 7.94 (d, J=8.0 Hz, 1H), 7.85 (d, J=8.8 Hz, 1H), 7.83 (d, J= 8.2 Hz, 1H), 7.51–6.92 (m, 13H), 6.89 (s, 2H; Ar*H*), 6.90 and 6.88 (2d, J=2.4 Hz, 1H each), 6.61 and 6.56 (2d, J=2.3 Hz, 1H each), 6.59 (s, 2H), 4.90 and 4.69 (2d, J=10.8 Hz, 1H each), 4.72 and 4.60 (2d, J=

15.7 Hz, 1H each, CH_2CO_2), 4.40 (d, J=13.7 Hz, 1H; ArCH_2Ar), 4.36 (d, J=13.0 Hz, 1H; ArCH_2Ar), 4.23 (d, J=12.4 Hz, 1H; ArCH_2Ar), 4.20 (d, J=13.0 Hz, 1H; ArCH_2Ar), 3.98–3.19 (m, 16H), 3.05 (d, J=12.7 Hz, 1H; ArCH_2Ar), 3.00 (d, J=13.5 Hz, 1H; ArCH_2Ar), 2.98 (d, J=12.8 Hz, 1H; ArCH_2Ar), 2.95 (d, J=13.7 Hz, 1H; ArCH_2Ar), 1.25, 1.17, 0.95, and 0.94 ppm (4s, 9H each); ^{13}C NMR: δ=169.80, 153.71, 152.73, 152.36, 152.03, 151.99, 147.74, 145.32, 144.78, 144.48, 138.16, 134.77, 134.65, 134.59, 134.56, 133.64, 133.43, 133.12, 133.05, 132.89, 132.58, 132.11, 130.38, 130.15, 129.96, 129.94, 128.86, 128.23, 128.21, 128.14, 127.85, 127.69, 127.19, 126.68, 126.08, 125.79, 125.37, 125.35, 125.13, 125.11, 124.89, 124.80, 124.70, 124.68, 123.53, 123.51, 121.78, 118.57, 114.33, 73.85, 72.75, 70.72, 70.52, 70.38, 69.91, 69.86, 69.72, 33.99, 33.91, 33.69, 33.68, 31.67, 31.38, 31.05, 30.62, 31.60, 31.54, 31.26 ppm; IR (KBr): $\tilde{\nu}$=3420, 1784, 1479, 1203 cm^{-1}; MALDI-TOF MS: m/z: 1245.1 $[M+Na]^+$; elemental analysis calcd (%) for $C_{81}H_{90}O_{10}\cdot 0.5\,H_2O$: C 78.93, H 7.44; found: C 78.98, H 7.57.

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, cone conformer (5e): Column chromatography (SiO_2, petroleum ether/AcOEt 5:1 then petroleum ether/acetone 10:1).

Compound **5e-1**: Yield 26%; m.p. 113–115°C; ^{1}H NMR: δ=8.01 (d, J=8.9 Hz, 1H), 7.95 (d, J=8.3 Hz, 1H), 7.86 (d, J=8.4 Hz, 1H), 7.84 (d, J=5.8 Hz, 1H), 7.47 (t, J=7.2 Hz, 1H), 7.45 (d, J=9.0 Hz, 1H), 7.33–7.29 (m, 4H), 7.18 (t, J=8.0 Hz, 1H), 7.01 (d, J=8.4 Hz, 1H), 6.89–6.61 (m, 8H), 4.58 (ABq, J=16.2 Hz, 2H; CH_2CO_2), 4.60 (d, J=12.9 Hz, 1H; ArCH_2Ar), 4.43 (d, J=12.5 Hz, 1H; ArCH_2Ar), 4.34 (d, J=12.5 Hz, 1H; ArCH_2Ar), 4.26 (d, J=12.8 Hz, 1H; ArCH_2Ar), 4.17–3.49 (m, 22H), 3.11 (d, J=12.4 Hz, 1H; ArCH_2Ar), 3.09 (d, J=13.7 Hz, 1H; ArCH_2Ar), 3.04 (d, J=14.2 Hz, 1H; ArCH_2Ar), 3.01 (d, J=12.7 Hz, 1H; ArCH_2Ar), 1.84–1.61 (m, 2H), 1.18, 1.16, 0.98, and 0.96 (4s, 9H each), 0.88 ppm (t, J=7.5 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=169.27, 153.29, 153.26, 153.05, 152.94, 152.25, 147.46, 145.13, 144.89, 144.47, 144.31, 134.78, 134.54, 134.31, 133.91, 133.77, 133.55, 133.16, 133.14, 132.99, 132.70, 131.99, 130.04, 129.68, 128.73, 128.19, 127.94, 126.92, 126.58, 126.10, 125.87, 125.55, 125.44, 125.19, 125.17, 124.92, 124.84, 124.82, 124.75, 124.62, 123.63, 123.24, 122.18, 118.23, 114.09, 77.32, 77.25, 73.03, 71.79, 70.91, 70.70, 70.60, 70.42, 70.31, 69.97, 69.83, 33.94, 33.74, 33.71, 31.55, 31.33, 31.19, 31.07, 23.39, 10.44 ppm; IR (KBr): $\tilde{\nu}$=3292, 1784, 1480, 1203, 1122 cm^{-1}; MALDI-TOF MS: m/z: 1241.3 $[M+Na]^+$, 1257.2 $[M+K]^+$; elemental analysis calcd (%) for $C_{79}H_{94}O_{11}$: C 77.80, H 7.77; found: C 77.87, H 7.91.

Compound **5e-2**: Yield 22%; m.p. 113–115°C; ^{1}H NMR: δ=8.05 (d, J=8.9 Hz, 1H), 7.98 (d, J=8.2 Hz, 1H), 7.87 (d, J=9.1 Hz, 1H), 7.86 (d, J=6.5 Hz, 1H), 7.54–7.25 (m, 6H), 7.18 (t, J=7.2 Hz, 1H), 7.05 (d, J=8.4 Hz, 1H), 6.82 and 6.81 (2s, 1H each), 6.76–6.69 (m, 6H), 4.44 (ABq, J=16.5 Hz, 2H; OCH_2CO_2), 4.49 (d, J=12.4 Hz, 1H; ArCH_2Ar), 4.36 (d, J=12.4 Hz, 1H; ArCH_2Ar), 4.33 (d, J=12.7 Hz, 1H; ArCH_2Ar), 4.16 (d, J=12.7 Hz, 1H; ArCH_2Ar), 4.12–3.59 (m, 22H), 3.11 (d, J=12.6 Hz, 2H; ArCH_2Ar), 2.98 (d, J=13.3 Hz, 1H; ArCH_2Ar), 2.94 (d, J=13.2 Hz, 1H; ArCH_2Ar), 1.90 (m, 2H; $CH_2CH_2CH_3$), 1.12, 1.11, 1.08, and 1.04 (4s, 9H each), 0.93 ppm (t, J=7.4 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=168.9, 153.5, 153.3, 153.2, 152.1, 152.0, 147.5, 145.0, 144.7, 144.6, 144.2, 134.0, 133.9, 133.7, 133.6, 133.5, 133.4, 133.3, 133.2, 132.0, 130.1, 130.0, 128.8, 128.2, 128.1, 127.9, 127.8, 127.1, 126.5, 126.0, 125.9, 125.8, 125.2, 125.1, 125.0, 124.9, 124.8, 124.7, 124.6, 123.9, 123.5, 123.3, 121.8, 118.5, 114.1, 72.73, 72.62, 70.80, 70.74, 70.62, 70.57, 70.49, 70.38, 70.15, 69.87, 33.75, 33.67, 33.50, 31.50, 31.36, 31.31, 31.11, 30.95, 30.86, 23.11, 10.35 ppm; IR (KBr): $\tilde{\nu}$=3291, 1785, 1480, 1203, 1121 cm^{-1}; MALDI-TOF MS: m/z: 1241.2 $[M+Na]^+$, 1257.2 $[M+K]^+$; elemental analysis calcd (%) for $C_{79}H_{94}O_{11}$: C 77.80, H 7.77; found: C 77.85, H 7.83.

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-4-benzyloxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, cone conformer (5f): Column chromatography (SiO_2, petroleum ether/AcOEt 5:1 then petroleum ether/acetone 10:1).

Compound **5f-1**: Yield 20%; m.p. 112–114°C; ^{1}H NMR: δ=8.03 (d, J=8.9 Hz, 1H), 7.96 (d, J=8.2 Hz, 1H), 7.85 (d, J=8.7 Hz, 1H), 7.82 (d, J=5.8 Hz, 1H), 7.51–7.03 (m, 13H), 6.89 and 6.88 (2s, 1H each), 6.85 (s, 2H), 6.62 and 6.57 (2d, J=2.3 Hz, 1H each), 6.59 (s, 2H), 6.16 (s, 1H; OH), 4.75 (ABq, J=11.0 Hz, 2H; OCH_2Ph), 4.46 (ABq, J=17.2 Hz, 2H; OCH_2CO_2), 4.48 (d, J=14.5 Hz, 1H; ArCH_2Ar), 4.40 (d, J=11.1 Hz, 1H; ArCH_2Ar), 4.27 (d, J=12.5 Hz, 1H; ArCH_2Ar), 4.10 (d, J=12.8 Hz, 1H; ArCH_2Ar), 4.15–3.39 (m, 20H), 3.07 (d, J=13.6 Hz, 1H; ArCH_2Ar), 3.03 (d, J=13.6 Hz, 1H; ArCH_2Ar), 2.96 (d, J=13.1 Hz, 1H; ArCH_2Ar), 2.90 (d, J=12.9 Hz, 1H; ArCH_2Ar), 1.20, 1.17, 0.96, and 0.95 ppm (4s, 9H each); ^{13}C NMR: δ=169.54, 153.51, 152.80, 152.77, 152.38, 152.11, 147.49, 145.00, 144.82, 144.55, 144.45, 137.84, 134.70, 134.50, 134.10, 134.05, 133.68, 133.47, 133.04, 132.98, 132.01, 130.17, 129.92, 129.73, 129.72, 128.75, 128.18, 128.15, 128.13, 127.93, 127.75, 127.03, 126.62, 125.96, 125.94, 125.43, 125.41, 125.17, 125.03, 124.88, 124.84, 124.75, 124.67, 124.56, 123.55, 123.33, 122.03, 118.28, 114.07, 72.96, 72.11, 70.85, 70.63, 70.49, 70.45, 70.27, 70.17, 69.99, 69.80, 33.90, 33.69, 33.68, 31.53, 31.52, 31.26, 31.11, 31.04 ppm; IR (KBr): $\tilde{\nu}$=3365, 1784, 1479, 1203 cm^{-1}; MALDI-TOF MS: m/z: 1289.0 $[M+Na]^+$; elemental analysis calcd (%) for $C_{83}H_{94}O_{11}$: C 78.64, H 7.47; found: C 78.81, H 7.62.

Compound **5f-2**: Yield 16%; m.p. 104–106°C; ^{1}H NMR: δ=8.03 (d, J=8.9 Hz, 1H), 7.97 (d, J=8.3 Hz, 1H), 7.85 (d, J=8.6 Hz, 2H), 7.53–7.15 (m, 12H), 7.04 (d, J=8.4 Hz, 1H), 6.87 (s, 3H), 6.82 (d, J=1.7 Hz, 1H), 6.64 and 6.62 (2s, 2H each), 4.83 (ABq, J=11.0 Hz, 2H; OCH_2Ph), 4.44 (ABq, J=16.6 Hz, 2H; OCH_2CO_2), 4.46 (d, J=12.6 Hz, 1H; ArCH_2Ar), 4.38 (d, J=12.8 Hz, 1H; ArCH_2Ar), 4.22 (d, J=12.9 Hz, 1H; ArCH_2Ar), 4.20 (d, J=12.3 Hz, 1H; ArCH_2Ar), 4.06–3.36 (m, 20H), 3.08 (d, J=12.6 Hz, 1H; ArCH_2Ar), 3.00 (d, J=12.8 Hz, 1H; ArCH_2Ar), 2.99 (d, J=11.8 Hz, 1H; ArCH_2Ar), 2.95 (d, J=12.8 Hz, 1H; ArCH_2Ar), 1.20, 1.16, 0.99, and 0.98 ppm (4s, 9H each); ^{13}C NMR: δ=169.21, 153.48, 152.81, 152.52, 152.49, 152.16, 147.53, 145.11, 144.76, 144.56, 144.52, 138.07, 134.56, 134.45, 134.08, 133.87, 133.58, 133.44, 133.41, 133.23, 132.96, 132.90, 132.01, 130.25, 129.99, 129.87, 129.85, 128.78, 128.20, 128.14, 128.12, 127.94, 127.69, 127.04, 126.52, 126.02, 125.94, 125.44, 125.38, 125.11, 125.00, 124.88, 124.85, 124.72, 124.67, 123.53, 123.30, 121.95, 118.57, 114.14, 73.02, 72.14, 70.91, 70.73, 70.49, 70.37, 70.26, 69.53, 33.91, 33.89, 33.73, 33.71, 31.53, 31.50, 31.29, 31.02, 30.91, 29.70 ppm; IR (KBr): $\tilde{\nu}$=3284, 1784, 1479, 1203 cm^{-1}; MALDI-TOF MS: m/z: 1289.2 $[M+Na]^+$; elemental analysis calcd (%) for $C_{83}H_{94}O_{11}$: C 78.64, H 7.47; found: C 78.25, H 7.57.

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, partial cone conformer (5h): First the crude product was purified by column chromatography (SiO_2, petroleum ether/AcOEt 4:1) and then the diastereomeric mixture was subjected to preparative TLC ($CHCl_3$/AcOEt 5:1) to give **5h-1** and **5h-2** as white solids.

Compound **5h-1**: Yield 24%; m.p. 118–120°C; ^{1}H NMR: δ=7.99 (d, J=8.9 Hz, 1H), 7.93 (d, J=8.2 Hz, 1H), 7.88 (d, J=8.8 Hz, 1H), 7.86 (d, J=7.9 Hz, 1H), 7.43 (d, J=8.9 Hz, 1H), 7.47–6.98 (m, 7H), 7.06 (s, 2H), 7.01 (s, 2H), 6.87 (s, 2H), 6.69 and 6.67 (2d, J=2.4 Hz, 1H each), 4.70 (d, J=13.3 Hz, 1H; ArCH_2Ar), 4.34 (2d, J=16.6 Hz, 2H; OCH_2CO_2), 4.25 (d, J=12.1 Hz, 1H; ArCH_2Ar), 4.09–3.59 (m, 20H), 3.06 (d, J=12.5 Hz, 1H; ArCH_2Ar), 2.98 (d, J=13.4 Hz, 1H; ArCH_2Ar), 2.72 (t, J=7.5 Hz, 2H; $CH_2CH_2CH_3$), 1.41, 1.30, 1.09, and 1.04 (4s, 9H each), 0.88–0.76 (m, 2H; $CH_2CH_2CH_3$), 0.41 ppm (t, J=7.5 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=169.12, 154.89, 153.81, 153.52, 153.14, 152.46, 146.94, 145.18, 144.53, 144.05, 143.23, 135.38, 135.39, 133.86, 133.60, 133.24, 133.06, 133.03, 132.40, 132.23, 132.08, 131.69, 130.31, 129.54, 128.60, 128.19, 128.17, 127.96, 126.74, 126.72, 126.68, 126.51, 126.35, 126.05, 125.91, 125.88, 125.73, 125.55, 125.17, 125.03, 124.20, 123.12, 122.12, 118.05, 113.79, 73.78, 73.07, 71.61, 70.87, 70.60, 70.50, 70.22, 70.11, 69.38, 69.18, 38.18, 38.16, 31.89, 30.66, 34.04, 33.76, 33.75, 32.10, 31.64, 31.32, 23.46, 9.93 ppm; IR (KBr): $\tilde{\nu}$=3249, 1785, 1479, 1203, 1120 cm^{-1}; MALDI-TOF MS: m/z: 1197.2 $[M+Na]^+$, 1213.2 $[M+K]^+$. HRMS $[M+NH_4]^+$: calcd. (%) for $C_{77}H_{94}O_{10}N$: 1192.6872; found: 1192.6850.

Compound **5h-2**: Yield 24%; m.p. 132–135°C; ^{1}H NMR: δ=8.05 (d, J=8.9 Hz, 1H), 7.96 (d, J=8.2 Hz, 1H), 7.83 (d, J=7.8 Hz, 1H), 7.76 (d, J=8.8 Hz, 1H), 7.52 (d, J=8.9 Hz, 1H), 7.50–7.03 (m, 7H), 7.29 and 7.21 (2d, J=2.4 Hz, 1H each), 7.06 and 7.03 (2d, J=2.5 Hz, 1H each), 6.83 (d, J=2.5 Hz, 1H), 6.79 (d, J=2.5 Hz, 1H), 6.54 (d, J=2.4 Hz, 1H), 6.44 (d, J=2.4 Hz, 1H), 4.33 and 3.70 (2d, J=15.8 Hz, 1H each, OCH_2CO_2), 4.24 (d, J=12.6 Hz, 1H; ArCH_2Ar), 4.08–3.40 (m, 23H), 3.01 (d, J=12.8 Hz,

1H; ArCH_2Ar), 2.63 (d, J=13.3 Hz, 1H; ArCH_2Ar), 1.77–1.64 (m, 2H; $CH_2CH_2CH_3$), 1.40, 1.38, 1.02, and 1.00 (4s, 9H each), 0.83 ppm (t, J=7.5 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=167.37, 154.91, 153.49, 153.16, 152.75, 152.33, 147.33, 144.80, 144.41, 143.76, 143.25, 135.97, 134.79, 133.65, 133.54, 132.76, 132.43, 132.36, 132.02, 131.81, 131.69, 131.67, 130.02, 129.68, 128.71, 128.16, 127.95, 127.92, 127.90, 126.92, 126.51, 126.11, 126.02, 126.00, 125.89, 125.86, 125.61, 125.31, 125.30, 124.58, 124.30, 123.24, 121.89, 118.77, 114.48, 74.24, 72.97, 71.71, 70.57, 70.55, 70.51, 70.47, 70.37, 69.64, 69.56, 37.79, 37.25, 31.26, 31.17, 34.08, 34.05, 33.69, 31.84, 31.75, 31.40, 31.34, 23.97, 10.38 ppm; IR (KBr): $\tilde{\nu}$=3238, 1786, 1479, 1202, 1120 cm^{-1}; MALDI-TOF MS: m/z: 1197.4 $[M+Na]^+$, 1213.4 $[M+K]^+$. HRMS $[M+NH_4]^+$: calcd. (%) for $C_{77}H_{94}O_{10}N$: 1192.6872; found: 1192.6916.

3-({[(*S*)-2′-Hydroxybinaphthyloxycarbonyl]methyl}oxy)-4-propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-6, partial cone conformer (5i): First the crude product was purified by column chromatography (SiO_2, petroleum ether/AcOEt 4:1) and then the diastereomeric mixture was subjected to preparative TLC ($CHCl_3$/AcOEt 5:1) to give **5i-1** and **5i-2** as white solids.

Compound **5i-1**: Yield 31%; m.p. 127–129°C; ^{1}H NMR: δ=8.01 (d, J=8.9 Hz, 1H), 7.94 (d, J=8.2 Hz, 1H), 7.87 (d, J=8.9 Hz, 1H), 7.85 (d, J=7.9 Hz, 1H), 7.49–6.97 (m, 8H), 7.23 and 7.09 (2d, J=2.4 Hz, 1H each), 7.06 and 7.02 (2d, J=2.4 Hz, 1H each), 6.88 and 6.70 (2d, J=2.4 Hz, 1H each), 6.86 and 6.68 (2d, J=2.4 Hz, 1H each), 4.49 (d, J=12.9 Hz, 1H; ArCH_2Ar), 4.34 (d, J=12.4 Hz, 1H; ArCH_2Ar), 4.25 (ABq, J=16.5 Hz, 2H; CH_2CO$_2$), 4.19–3.43 (m, 24H), 3.04 (d, J=12.6 Hz, 1H; ArCH_2Ar), 2.92 (d, J=13.1 Hz, 1H; ArCH_2Ar), 2.58–2.51 (m, 2H; CH_2CH$_2$CH$_3$), 1.39, 1.31, 1.07, and 1.06 (4s, 9H each), 0.86–0.79 (m, 2H), 0.31 ppm (t, J=7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=168.97, 154.93, 153.69, 153.24, 152.75, 152.19, 147.14, 145.37, 144.58, 144.17, 143.44, 135.65, 135.32, 133.72, 133.58, 133.36, 133.27, 132.77, 132.72, 132.48, 132.14, 131.94, 130.32, 129.89, 128.71, 128.20, 127.99, 127.77, 127.04, 126.96, 126.59, 126.57, 126.28, 126.26, 125.94, 125.88, 125.57, 125.38, 125.31, 124.89, 123.85, 123.25, 121.98, 118.11, 113.73, 73.71, 71.90, 70.68, 70.52, 70.42, 70.34, 70.18, 70.09, 69.81, 69.68, 69.23, 38.32, 38.11, 30.59, 34.07, 34.03, 33.78, 31.99, 31.65, 31.30, 23.36, 9.79 ppm; IR (KBr): $\tilde{\nu}$=3274, 1784, 1479, 1203, 1120 cm^{-1}; MALDI-TOF MS: m/z: 1241.5 $[M+Na]^+$, 1257.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{79}H_{94}O_{11}$: C 77.80, H 7.77; found: C 77.69, H 7.90.

Compound **5i-2**: Yield 31%; m.p. 128–130°C; ^{1}H NMR: δ=8.05 (d, J=8.9 Hz, 1H), 7.97 (d, J=8.2 Hz, 1H), 7.83 (d, J=5.7 Hz, 1H), 7.80 (d, J=8.7 Hz, 1H), 7.50 (d, J=8.9 Hz, 1H), 7.53–7.01 (m, 9H), 7.08 and 7.05 (2d, J=2.4 Hz, 1H each), 6.85 and 6.61 (2d, J=2.4 Hz, 1H each), 6.80 and 6.51 (2d, J=2.4 Hz, 1H each), 4.32 (d, 1H; J=14.2 Hz, ArCH_2Ar), 4.27 and 3.85 (2d, J=16.2 Hz, 1H each, CH_2CO$_2$), 4.15–3.20 (m, 27H), 3.01 (d, J=12.8 Hz, 1H; ArCH_2Ar), 2.78 (d, J=12.9 Hz, 1H; ArCH_2Ar), 1.69–1.56 (m, 2H), 1.38, 1.36, 1.04, and 1.01 (4s, 9H each), 0.71 ppm (t, J=7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=167.98, 155.04, 153.53, 152.93, 152.80, 152.16, 147.42, 145.09, 144.32, 143.91, 143.38, 135.59, 135.42, 133.56, 133.47, 133.01, 132.77, 132.57, 132.13, 132.09, 131.79, 131.75, 130.13, 129.95, 128.77, 128.22, 127.97, 127.95, 127.46, 127.08, 126.57, 126.24, 126.10, 126.08, 126.02, 125.84, 125.50, 125.26, 125.24, 124.58, 123.73, 123.31, 121.95, 118.51, 114.17, 73.98, 71.98, 70.82, 70.62, 70.41, 70.37, 70.32, 70.25, 69.90, 69.55, 38.04, 37.41, 31.08, 30.82, 34.10, 34.02, 33.72, 33.71, 31.84, 31.72, 31.37, 31.32, 23.80, 10.18 ppm; IR (KBr): $\tilde{\nu}$=3275, 1784, 1479, 1203, 1120 cm^{-1}; MALDI-TOF MS: m/z: 1241.4 $[M+Na]^+$, 1257.3 $[M+K]^+$; elemental analysis calcd (%) for $C_{79}H_{94}O_{11}$: C 77.80, H 7.77; found: C 77.86, H 7.79.

Hydrolysis of compounds 5: general procedure for the preparation of optically pure enantiomers 4: Compound **5–1** or **5–2** (0.08 mmol) in THF (10 mL) was refluxed with aqueous 10% tetramethylammonium hydroxide solution (5.0 equiv, 0.44 mL) for 12 h. After removal of the solvent, 10% HCl (10 mL) was added. The aqueous solution was extracted with CH_2Cl_2 (2×10 mL), And then the organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography (SiO_2, petroleum ether/AcOEt 3:1 to 1:1) to give enantiomerically pure compound **4–1** or **4–2** as a white solid without recrystallization. The relative spectroscopic data were identical to those of the racemates **4**.

Compound **4a-1**: Yield 0.055 g, 80%; m.p. 127–129°C; $[\alpha]_D^{25}$=−16 (c=0.5 in $CHCl_3$). Compound **4a-2**: Yield 0.057 g, 82%; m.p. 127–129°C; $[\alpha]_D^{25}$=+16 (c=0.5 in $CHCl_3$).

Compound **4c-1**: Yield 0.057 g, 78%; m.p. 116–118°C; $[\alpha]_D^{25}$=+8 (c=0.5 in $CHCl_3$). Compound **4c-2**: Yield 0.052 g, 72%; m.p. 116–118°C; $[\alpha]_D^{25}$=−8 (c=0.5 in $CHCl_3$).

Compound **4d-1**: Yield 0.059 g, 77%; m.p. 109–111°C; $[\alpha]_D^{25}$=−8 (c=0.5 in $CHCl_3$). Compound **4d-2**: Yield 0.063 g, 82%; m.p. 109–111°C; $[\alpha]_D^{25}$=+8 (c=0.5 in $CHCl_3$).

Compound **4e-1**: Yield 0.063 g, 83%; m.p. 93–95°C; $[\alpha]_D^{25}$=−4 (c=0.5 in $CHCl_3$). Compound **4e-2**: Yield 0.057 g, 75%; m.p. 93–95°C; $[\alpha]_D^{25}$=+4 (c=0.5 in $CHCl_3$).

Compound **4f-1**: Yield 0.06 g, 75%; m.p. 91–93°C; $[\alpha]_D^{25}$=−20 (c=0.5 in $CHCl_3$). Compound **4f-2**: Yield 0.06 g, 75%; m.p. 91–93°C; $[\alpha]_D^{25}$=+20 (c=0.5 in $CHCl_3$).

Compound **4h-1**: Yield 0.062 g, 85%; m.p. 122–124°C; $[\alpha]_D^{25}$=−32 (c=0.5 in $CHCl_3$). Compound **4h-2**: Yield 0.059 g, 81%; m.p. 122–124°C; $[\alpha]_D^{25}$=+32 (c=0.5 in $CHCl_3$).

Compound **4i-1**: Yield 0.061 g, 80%; m.p. 112–114°C; $[\alpha]_D^{25}$=−40 (c=0.5 in $CHCl_3$). Compound **4i-2**: Yield 0.062 g, 82%; m.p. 112–114°C; $[\alpha]_D^{25}$=+40 (c=0.5 in $CHCl_3$).

3-Propoxy-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, cone conformer (6): A stirred mixture of **2a** (1.7 g, 2.1 mmol), *n*-propyl iodide (246 μL, 1.2 equiv), and Cs_2CO_3 (0.822 g, 1.2 equiv) in DMF (80 mL) was heated at 60°C for 6 h. Then 10% HCl (2.5 mL) was added to quench the reaction. After removal of the solvent under reduced pressure, the residue was partitioned between water and CH_2Cl_2. The organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography (SiO_2, petroleum ether/acetone 20:1) to give **6** as a white solid. Yield 46%; m.p. 236–238°C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ=7.14 (s, 2H), 7.07 and 7.06 (2d, J=2.3 Hz, 1H each), 6.53 (s, 2H), 6.46 (s, 2H), 5.99 (s, 1H; OH), 4.47 (d, J=13.4 Hz, 1H; ArCH_2Ar), 4.47 (d, J=13.4 Hz, 1H; ArCH_2Ar), 4.38 (d, J=13.7 Hz, 1H; ArCH_2Ar), 4.37 (d, J=13.0 Hz, 1H; ArCH_2Ar), 4.34 (d, J=12.7 Hz, 1H; ArCH_2Ar), 4.56–3.64 (m, 18H), 3.23 (d, J=14.1 Hz, 2H; ArCH_2Ar), 3.18 (d, J=14.4 Hz, 2H; ArCH_2Ar), 2.06–1.85 (m, 2H), 1.34, 1.33, 0.83, and 0.78 (4s, 9H each), 1.12 ppm (t, J=7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=153.62, 151.76, 151.24, 150.86, 145.80, 145.49, 144.88, 141.06, 136.01, 135.89, 132.26, 131.93, 131.87, 131.79, 129.02, 128.79, 125.74, 125.58, 125.13, 125.00, 124.98, 124.75, 124.72, 124.61, 77.85, 76.12, 72.08, 71.61, 71.15, 70.52, 69.98, 69.78, 68.38, 34.15, 33.82, 33.68, 33.60, 31.78, 31.68, 31.04, 31.03, 31.05, 30.96, 30.87, 23.44, 11.04 ppm; IR (KBr): $\tilde{\nu}$=3546, 1483, 1203, 1120 cm^{-1}; MALDI-TOF MS: m/z: 871.4 $[M+Na]^+$, 887.4 $[M+K]^+$; elemental analysis calcd (%) for $C_{55}H_{76}O_7$: C 77.79, H 9.02; found: C 77.77, H 9.08.

3-Propoxy-4-{[(ethoxycarbonyl)methyl]oxy}-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, partial cone conformer (7): Compound **6** (0.671 g, 0.79 mmol), ethyl bromoacetate (879 μL, 10 equiv), and Cs_2CO_3 (2.58 g, 10 equiv) in DMF (60 mL) were stirred at 70°C for 2 d. Then 10% HCl (6.5 mL) was added to quench the reaction. After removal of the solvent under reduced pressure, the residue was partitioned between water (50 mL) and CH_2Cl_2 (2×50 mL). The organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was purified by column chromatography (SiO_2, petroleum ether/ethyl acetate 10:1) to give **7** as a white solid. Yield 42%; m.p. 238–240°C; ^{1}H NMR: δ=7.25 and 7.22 (2d, J=2.6 Hz, 1H each), 7.07 and 7.06 (2d, J=2.5 Hz, 1H each), 7.03 and 7.00 (2d, J=2.5 Hz, 1H each), 6.55 (s, 2H), 4.28 (ABq, J=15.0 Hz, 2H; CH_2CO$_2$), 4.30 (d, J=12.3 Hz, 1H; ArCH_2Ar), 4.20 (q, J=7.2 Hz, 2H; CO$_2$CH_2CH$_3$), 4.06–3.50 (m, 21H), 4.10 (d, J=12.6 Hz, 1H; ArCH_2Ar), 3.98 (d, J=13.2 Hz, 1H; ArCH_2Ar), 3.06 (d, J=12.8 Hz, 1H; ArCH_2Ar), 3.04 (d, J=12.7 Hz, 1H; ArCH_2Ar), 1.90 (m, 2H), 1.44, 1.33, 1.03, and 1.02 (4s, 9H each), 1.29 (t, J=7.2 Hz, 3H; CO$_2$CH$_2$CH_3), 0.98 ppm (t, J=7.5 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ=169.68, 155.08, 153.72, 153.56, 153.40, 144.88, 144.00, 143.70, 143.54, 135.90, 135.21, 132.65, 132.47, 132.33, 132.20, 131.46, 131.44, 128.25, 127.87, 126.07, 125.68, 125.49,

125.41, 125.39, 125.26, 76.31, 73.22, 71.60, 71.11, 70.94, 70.77, 70.15, 69.94, 69.05, 60.71, 37.40, 37.37, 30.96, 34.04, 33.68, 33.66, 31.76, 31.69, 31.35, 23.69, 14.22, 10.55 ppm; IR (KBr): $\tilde{\nu}$ = 1763, 1479, 1201, 1122 cm^{-1}; MALDI-TOF MS: *m*/*z*: 957.5 $[M+Na]^+$, 973.5 $[M+K]^+$; elemental analysis calcd (%) for $C_{59}H_{82}O_9$: C 75.77, H 8.84; found: C 75.80, H 8.89.

3-Propoxy-4-[(carboxymethyl)oxy]-*p*-*tert*-butylcalix[4]arene-(1,2)-crown-5, partial cone conformer (8): Compound **7** (0.14 g, 0.15 mmol) in THF (20 mL) was refluxed with aqueous 10% tetramethylammonium hydroxide solution (682 μL, 5 equiv) for 12 h. After removal of the solvent, 10% HCl (20 mL) was added. The aqueous solution was extracted with CH_2Cl_2 (2×20 mL) and then the organic layer was dried with Na_2SO_4 and the solvent evaporated. The residue was crystallized from CH_2Cl_2/CH_3OH to give **8** as a white solid. Yield 84%; m.p. 143–145 °C (CH_2Cl_2/CH_3OH); ^{1}H NMR: δ = 7.72 (s, 1H; CO_2H), 7.26 (s, 2H), 7.13 and 7.11 (2d, J = 2.4 Hz, 1H each), 6.90 and 6.89 (2d, J = 2.3 Hz, 1H each), 6.74 (s, 2H), 4.38 (d, J = 12.3 Hz, 1H; ArCH_2Ar), 4.19 (d, J = 12.4 Hz, 1H; ArCH_2Ar), 4.07–3.54 (m, 24H), 3.16 (d, J = 12.5 Hz, 1H; ArCH_2Ar), 3.14 (d, J = 12.4 Hz, 1H; ArCH_2Ar), 1.92–1.72 (m, 2H), 1.45 and 1.31 (2s, 9H each), 1.09 (s, 18H), 0.95 ppm (t, J = 7.2 Hz, 3H; $CH_2CH_2CH_3$); ^{13}C NMR: δ = 168.46, 153.59, 153.31, 152.79, 150.83, 145.97, 145.88, 145.44, 145.17, 135.28, 134.82, 134.25, 133.85, 133.11, 132.82, 131.62, 131.55, 127.84, 127.49, 126.92, 126.88, 125.50, 125.37, 124.31, 124.08, 75.98, 72.76, 71.91, 71.40, 70.92, 70.87, 70.29, 70.22, 69.03, 66.25, 38.28, 31.01, 30.58, 34.25, 34.12, 33.84, 33.83, 31.70, 31.58, 31.09, 23.40, 10.48 ppm; IR (KBr): $\tilde{\nu}$ = 3406, 1759, 1479, 1202, 1122 cm^{-1}; MALDI-TOF MS: *m*/*z*: 929.4 $[M+Na]^+$, 945.4 $[M+K]^+$; elemental analysis calcd (%) for $C_{57}H_{78}O_9$: C 75.46, H 8.67; found: C 75.25, H 8.55.

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[1] For reviews on inherently chiral calixarenes and related compounds, see: a) V. Böhmer, D. Kraft, M. Tabatabai, *J. Incl. Phenom. Mol. Recogn.* **1994**, *19*, 17–39; b) H. Otsuka, S. Shinkai, *Supramol. Sci.* **1996**, *3*, 189–205; c) M. Vysotsky, C. Schmidt, V. Böhmer, *Adv. Supramol. Chem.* **2000**, *7*, 139–233.

[2] a) S. Shinkai, T. Arimura, H. Kawabata, H. Murakami, K. Araki, K. Iwamoto, T. Matsuda, *J. Chem. Soc. Chem. Commun.* **1990**, 1743–1744; b) K. Iwamoto, A. Yanagi, T. Arimura, T. Matsuda, S. Shinkai, *Chem. Lett.* **1990**, 1901–1904; c) S. Shinkai, T. Arimura, H. Kawabata, H. Murakami, K. Iwamoto, *J. Chem. Soc. Perkin Trans. 1* **1991**, 2429–2434; d) S. Pappalardo, S. Caccamese, L. Giunta, *Tetrahedron Lett.* **1991**, *32*, 7747–7750; e) K. Iwamoto, H. Shimizu, K. Araki, S. Shinkai, *J. Am. Chem. Soc.* **1993**, *115*, 3997–4006 (*Corrigendum*: **1993**, *115*, 12228); f) G. Ferguson, J. F. Gallagher, L. Giunta, P. Neri, S. Pappalardo, M. Parisi, *J. Org. Chem.* **1994**, *59*, 42–53; g) F. Arnaud-Neu, S. Caccamese, S. Fuangswasdi, S. Pappalardo, M. F. Parisi, A. Petringa, G. Principato, *J. Org. Chem.* **1997**, *62*, 8041–8048; h) T. Jin, K. Monde, *Chem. Commun.* **1998**, 1357–1358; i) S. Caccamese, A. Bottino, F. Cunsolo, S. Parlato, P. Neri, *Tetrahedron: Asymmetry* **2000**, *11*, 3103–3112; j) D. Hesek, Y. Inoue, M. G. B. Drew, P. D. Beer, G. A. Hembury, H. Ishida, F. Aoki, *Org. Lett.* **2000**, *2*, 2237–2240.

[3] a) B. Xu, P. J. Carroll, T. M. Swager, *Angew. Chem.* **1996**, *108*, 2238–2242; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2094–2097; b) M. A. Tairov, M. O. Vysotsky, O. I. Kalchenko, V. V. Pirozhenko, V. I. Kalchenko, *J. Chem. Soc. Perkin Trans. 1* **2002**, 1405–1411.

[4] a) C. Dieleman, S. Steyer, C. Jeunesse, D. Matt, *J. Chem. Soc. Dalton Trans.* **2001**, 2508–2517; b) F. Narumi, W. Yamabuki, T. Hattori, H. Kameyama, S. Miyano, *Chem. Lett.* **2003**, *32*, 320–321.

[5] Y. D. Cao, J. Luo, Q. Y. Zheng, C. F. Chen, M. X. Wang, Z. T. Huang, *J. Org. Chem.* **2004**, *69*, 206–208.

[6] A. Arduini, A. Casnati, M. Fabbi, P. Minari, A. Pochini, A. R. Sicuri, R. Ungaro, *Supramol. Chem.* **1993**, *1*, 235–246.

[7] C. Jaime, J. de Mendoza, P. Prados, P. M. Nieto, C. Sanchez, *J. Org. Chem.* **1991**, *56*, 3372–3377.

[8] S. Caccamese, A. Notti, S. Pappalardo, M. F. Parisi, G. Principato, *Tetrahedron* **1999**, *55*, 5505–5514.

[9] S. Shimizu, A. Moriyama, K. Kito, Y. Sasaki, *J. Org. Chem.* **2003**, *68*, 2187–2194.

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