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Proximal heteroalkylation of monoalkoxycalix[4]arenes in synthesis of inherently chiral molecules

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ABSTRACT

Proximal heteroalkylation of monoalkyl ethers of calix[4]arenes or *p*-*tert*-butylcalix[4]arenes in NaH/CH_3CN or NaOH/DMSO, respectively, was applied for synthesis of inherently chiral calixarenes with ABHH substitution pattern. The introduction by the method of (*R*)- or (*S*)-*N*-(α-phenylethyl)acetamide chiral auxiliary group gives mixtures of diastereomeric derivatives of inherently chiral calixarenes, which were separated by column chromatography. The chiral calixarenes were thoroughly characterized by ^1H, ^{13}C NMR, and X-ray diffraction methods.

1. Introduction

Calixarenes due to their unique cavity-shaped architecture and the versatility of derivatization of the upper and/or lower rim(s) are the subject of ever-increasing interest in the field of supramolecular chemistry.[1,2] The regio- and stereoselective control in the functionalization of calixarenes provides an important tool necessary to accomplish the synthesis of highly complementary and preorganized receptors for cations,[3] anions,[4] and neutral molecules.[5] Among the numerous methods of chemical modification of calixarenes the alkylation of phenolic hydroxyl groups is of great importance. In contrast to the distal dialkylation, the alkylation of two proximal hydroxyl groups is less favored. However, namely 1,2-heteroalkylated calix[4]arenes are of particular interest in as much as they possess inherent chirality caused by asymmetrical ABHH arrangement of substituents on the lower rim of the calix[4]arene macrocycle. Inherently chiral calixarenes are considered as promising host molecules for enantiorecognition and enantioseparation of chemically and/or biologically important chiral guest molecules. In this respect the development of method of 1,2-heteroalkylation is highly desirable.

Following our previous investigations[6] of chiral calixarenes we apply here the method of 1,2-heteroalkylation of monoalkoxycalix[4]arenes **1a–d** for the synthesis of inherently chiral calix[4]arenes with ABHH substitution pattern. The reaction of monopropoxy-*p*-*tert*-butylcalix[4]arene **1b** with fivefold excess of butyl bromide in NaOH/DMSO medium[7] at 65–70 °C within 7 h proceeds regioselectively and leads to the racemic mixture of 27,28-heterodialkylated calix[4]arenes **2a** and **3a** (Scheme 1). In the ^1H NMR spectrum of calixarenes **2a** and **3a** characteristic signals of axial and equatorial protons of methylene bridges appear as doublets with an average coupling constant $^2J_{HH}$=13 Hz. The distance between Ar–CH_2-*eq* and ArCH_2-*ax* resonance signals (Δδ at 1 ppm) evidences the *cone* conformation[8] of **2a** and **3a**.

Addition of Pirkle's reagent [(*S*)-2,2,2-trifluoro-1-(9-anthryl)-ethanol] to the racemic mixture splits their signals in the ^1H NMR spectrum due to the formation of two diastereomeric complexes (Fig. 1). The structures of enantiomers **2a** and **3a** in the racemic mixture were determined by X-ray methods. Suitable monocrystals were obtained by crystallization from acetonitrile. Two enantiomers are connected by the centre of the symmetry. Calixarene **3a** adopts the slightly distorted *cone* conformation (Fig. 2a). The angles between planes of opposite benzene rings of the macrocycle are close enough (49.8° and 59.7°). One molecule of acetonitrile is located inside the cavity of calixarene and is bonded with aromatic rings by the C–H···π interactions (C2S–H···π: H···C9 2.79 Å C–H···C9 168°; C2S–H···π: H···C26 2.76 Å C–H···C26 175°). In the crystal

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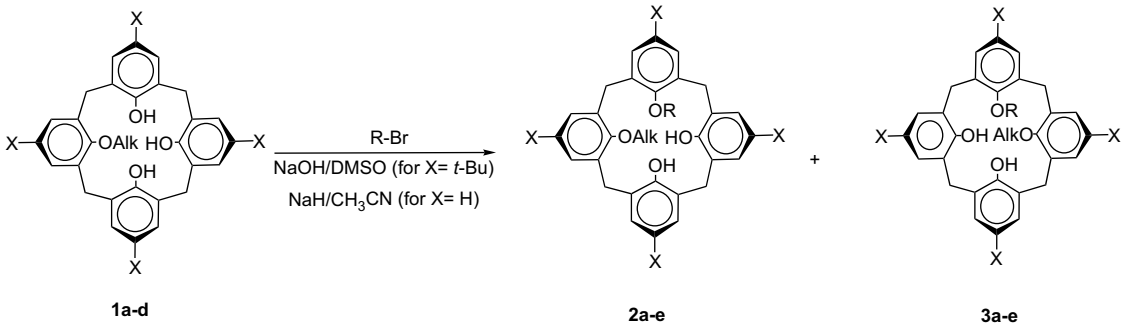

1a-d **2a-e** **3a-e**

X= *t*-Bu: Alk = Me (a), *n*-Pr (b);
X= H: Alk = Me (c), *n*-Pr (d).

X= *t*-Bu: Alk = *n*-Pr, R = *n*-Bu (a);
Alk = Me, R = (*S*)-$CH_2C(O)NHCH(Ph)CH_3$ (b);
Alk = *n*-Pr, R = (*S*)-$CH_2C(O)NHCH(Ph)CH_3$ (c);
X = H: Alk = Me, R = (*R*)-$CH_2C(O)NHCH(Ph)CH_3$ (d);
Alk = *n*-Pr, R = (*R*)-$CH_2C(O)NHCH(Ph)CH_3$ (e).

Scheme 1.

phase each enantiomer forms the stack along the [1 0 0] crystallographic direction. Enantiomers of neighboring stacks are turned relative to each other by 90° (Fig. 2b).

The reaction of monoalkoxy-*p*-*tert*-butyl-calixarenes **1a** and **1b** with twofold excess of (*S*)-*N*-(α-phenylethyl)bromoacetamide in the same conditions is also regioselective and leads to a 1:1 mixture of 1,2-heterosubstituted calixarenes **2b**,**3b** as well as **2c**,**3c**, respectively. The diastereomeric pairs **2b**,**3b** and **2c**,**3c** were resolved by column chromatography on silica gel (hexane/ethyl acetate 4:1).

The absolute configuration of diastereomer **2b** has been established by X-ray diffraction. Diffraction quality crystals of **2b** as a 1:2 solvate with methanol have been grown from methanol–water mixture. Calixarene **2b** adopts the *cone* conformation (Fig. 3a). The angles between opposite benzene ring of the macrocycle are close enough (61.1° and 55.2°, correspondingly).

The (*S*)-*N*-(α-phenylethyl)acetamide substituent at the O1 atom is oriented in such a way that it, together with one methanol molecule, locks the cavity of calixarene from the narrow rim side. The position of this substituent is also stabilized by the N1–H···O3 hydrogen bond (H···O 2.08 Å, N–H···O 163°). Methanol is bonded to the amide fragment of substituent by the O1Sb–H1Sb···O2 hydrogen bond (H···O 1.97, Å O–H···O 153°) and by the C–H···π interactions with phenyl ring (C1Sb–H···C38: H···C 2.83 Å C–H···C 131°). A second molecule of methanol is located inside the cavity of calixarene. Its location is stabilized by the C–H···π interactions between hydroxyl group of methanol and π-systems of the C15···C20 aromatic ring: (O1Sa–H···C17: H···C 2.60 Å, O–H···C 164°).

In the crystal phase, the molecules of **2b** form infinite chains along the [1 0 1] crystallographic direction in which the substituent at the O1 atom locks also the wide rim of the neighboring calixarene molecule.

The attempts to grow a diffraction quality crystal of diastereomer **3b** weren't successful. The structures of diastereomers **2b** and **3b** were optimized by M05-2X/cc-pvdz method using geometry of molecule in crystalline state as starting point for **2b** and the approximate geometry for **3b**. According to the M05-2X/cc-pvdz calculation molecule **2b** posses the same conformation in vacuo. However diastereomer **3b** in vacuo differs from **2b** by the orientation of methoxy and phenylethylacetamide group **3b**. Calixarene **3b** differs from **2b** by the location of the substituents on the macrocycle rim. The quantum-chemical calculations demonstrate that calixarene **2b** is 0.83 kcal/mol more stable than its isomer **3b**.

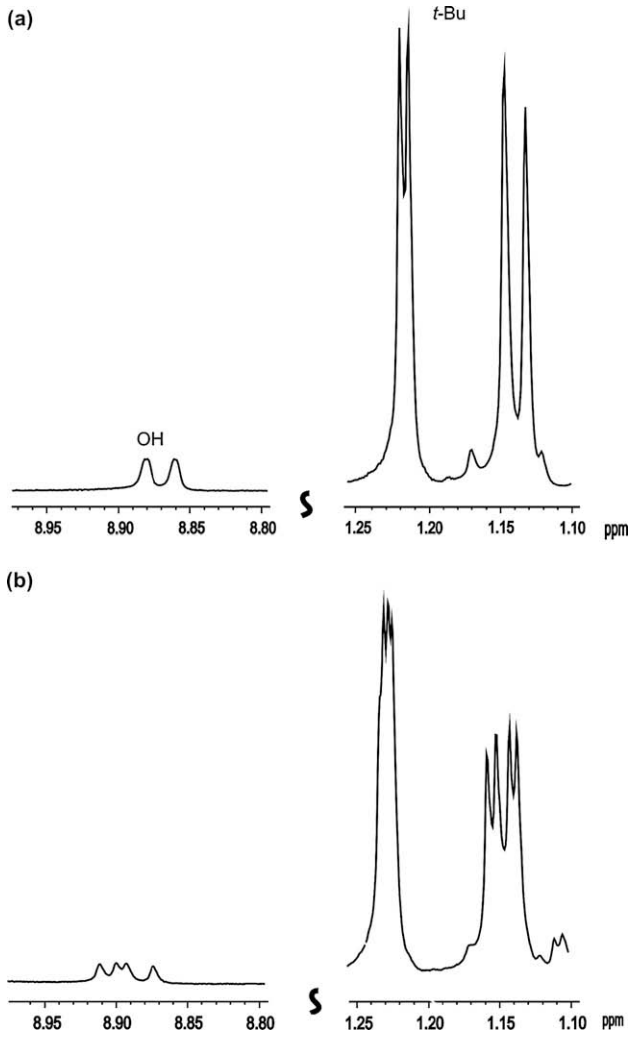

Figure 1. Signals of *t*-Bu and OH groups in the ^{1}H NMR spectrum ($CDCl_3$) of the racemic mixture of **2a** and **3a** before (a) and after (b) Pirkle's reagent addition.

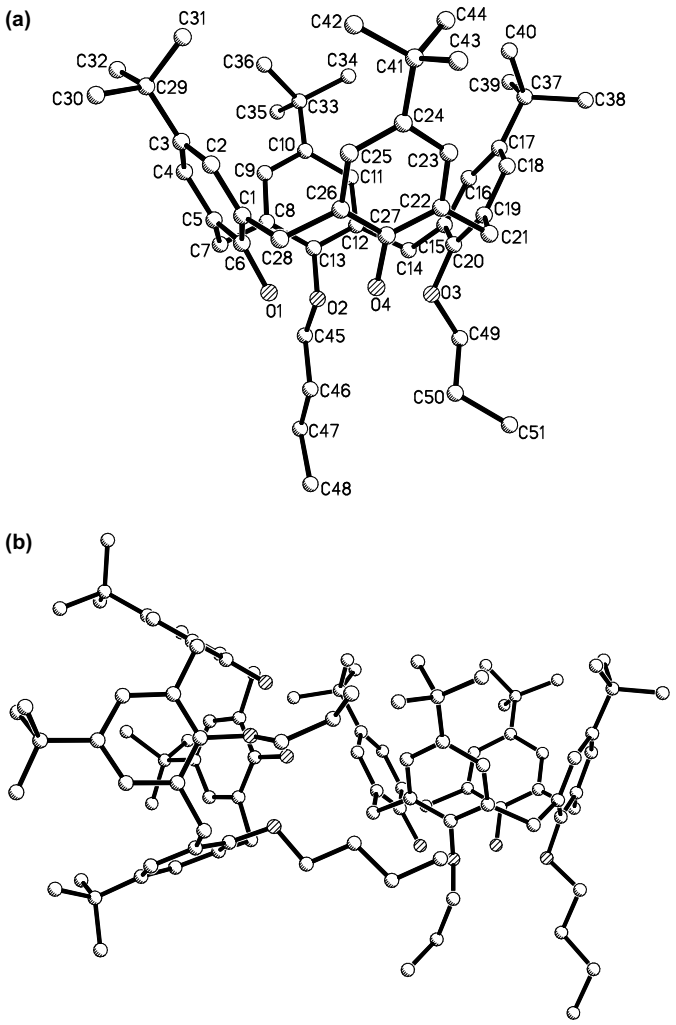

Figure 2. X-ray molecular structure of calixarene **3a** (a) and packing of enantiomers **2a** and **3a** (b).

The methylene bridge signals of diastereomers **2b** and **3b** in the ^{13}C NMR spectra at 31–32 ppm indicate the *cone* conformation[9] for both compounds in $CDCl_3$ solution. Significant differences between the ^{1}H NMR spectra of the diastereomers are observed (Fig. 4). In calixarene **2b** protons of $ArCH_2Ar$ groups occur as four pairs of doublets between 3.31 and 4.41 ppm. One of the doublets of the axial protons of calixarene **2b** is shielded by the benzene ring of phenylethylamide residue (Fig. 4). The intramolecular hydrogen bonding between NH protons and O3 atom of the neighboring hydroxyl group observed in the crystalline state takes place in solution as well, proved by considerable deshielding of the NH proton (9.36 ppm). To compare, the NH proton of (*S*)-*N*-(α-phenylethyl)bromoacetamide isn't hydrogen bonded and appears at 6.74 ppm (intramolecular hydrogen bonding doesn't occur in this case). The *p-tert*-butyl groups of diastereomer **2b** appear as four singlets at 1.26, 1.22, 1.20, and 1.11 ppm with integral intensity 9H for each signal, while in the spectrum of diastereomer **3b** three signals occur at high field (1.13, 1.22, and 1.25 ppm) with intensities 9H, 18H, and 9H. The biggest difference between chemical shifts is observed for OMe signals. The singlet for the methoxy group of diastereomer **3b** lies, as usual, in the section of axial protons (4.01 ppm),[10] while the mentioned signal of **2b** moves to the equatorial signals section (3.52 ppm). It is seen from the X-ray structure (Fig. 3a) and calculated one (Fig. 3b) that OMe protons of calixarene **2b** are shielded by the benzene ring of the phenylethylamide residue. The methoxy protons of diastereomer **3b** are not affected by the phenylethylamide residue.

As was shown,[7] alkylation of *p-tert*-butyl depleted calix[4]arenes in NaOH/DMSO medium isn't regioselective and gives mainly tetraalkylated derivatives. The alkylation of monoalkoxycalix[4]arenes **1c**,**d** with (*R*)-*N*-(α-phenylethyl)bromoacetamide in the NaH/CH_3CN medium at room temperature proceeds regioselectively and gives proximally heterosubstituted calixarenes **2d**,**e** and **3d**,**e**. The diastereomers **2d**, **3d** as well as **2e**, **3e** have been separated by column chromatography on silica gel (hexane/ethyl acetate 3:1).

The alkyl substituents of (*R*)-*N*-(α-phenylethyl)bromoacetamide derivatives **3d**,**e** are shielded by benzene ring of phenylethylamide residue. As a result OMe and OPr signals of **3d**,**e** are shifted to high field (see Experimental) in comparison with analogous signals of diastereomers **3b**,**c** bearing (*S*)-*N*-(α-phenylethyl)amide residue.

The X-ray diffraction study demonstrates that asymmetric part of unit cell of crystals **2e** contains two conformers A and B having slightly different geometrical parameters. Alkyl substituents of both molecules are not affected by the benzene ring of the phenylethylamide residue (Fig. 5). The angles between two opposite aromatic rings are 50.3° and 76.8° for molecule A and 42.6° and 88.4° for B.

The substituent at the O1 atom is oriented in such a way that it locks the cavity of the calixarene from the narrow rim side. The N1–H···O5 intramolecular hydrogen bond (H···O 2.22 Å A,

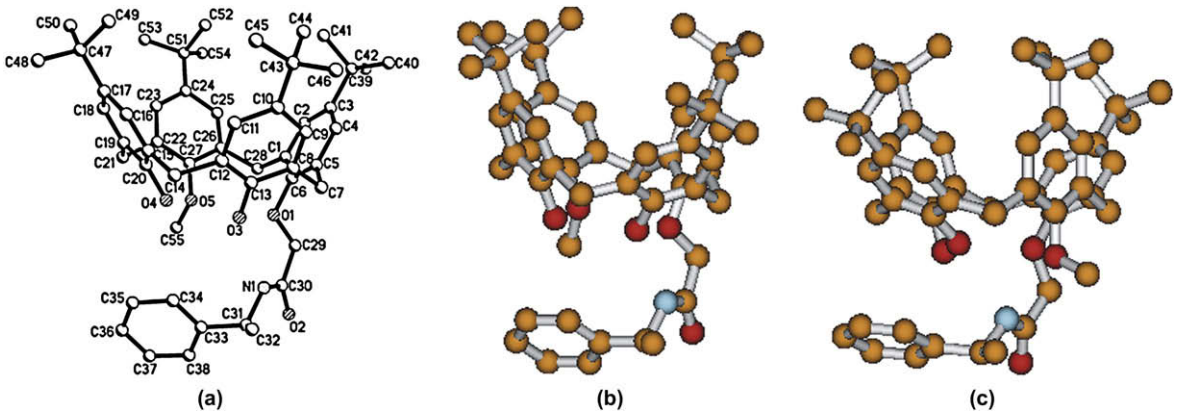

Figure 3. X-ray molecular structure of calixarene **2b** (a). Molecular structure of **2b** (b) and **3b** (c) optimized by M05-2X/cc-pvdz method.

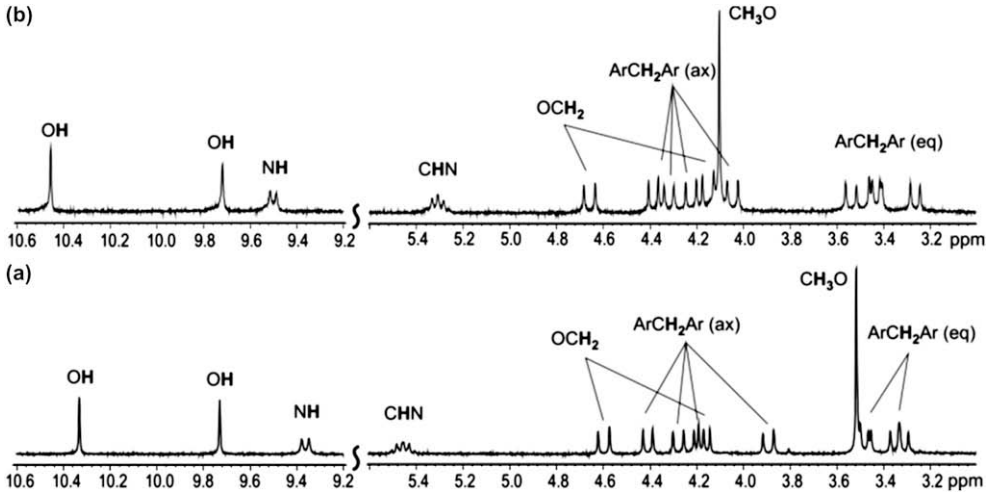

Figure 4. Representative sections of ^{1}H NMR spectra of diastereomers **2b** (a) and **3b** (b) in $CDCl_3$ at 298 K.

2.58 Å B, N–H···O 171° A, 173° B) stabilizes the position of this substituent.

In the crystal phase both A and B molecules of calixarene **2e** form infinite chains along [0 1 0] crystallographic directions (Fig. 6). The self-assembly of molecule A is driven by intermolecular C–H··· π interactions C39–H···C2′ (−*x*, 0.5+*y*, −1−*z*) (H···C: 2.79 Å, C–H···C 152°; C41–H41a···C(9)′ (*x*, *y*, *z*−1): H···C 2.87 Å, C-H···C 141°; C41–H41a···C10′ (*x*, *y*, *z*−1): H···C 2.82 Å, C–H···C 169°; C41–H41a···C11′ (*x*, *y*, *z*−1): H···C 2.82 Å, C–H···C 153°; C(41)–H41a··· C12′ (*x*, *y*, *z*−1): H···C 2.90 Å, C–H···C 126°; C41–H41b···C20′ (*x*, *y*, *z*−1): H···C 2.85 Å, C–H···C 137°; C41–H41c···C5′ (*x*, *y*, *z*−1): H···C 2.86 Å C–H···C 142° in the infinite chains). Accordingly, molecules B are assembled by the following C–H···π interactions: C40–H···C3′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.86 Å, C–H···C 125°; C41–H41e···C(15)′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.81 Å, C–H···C 131°; C41–H41e···C16′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.79 Å, C–H···C 141°; C41–H41e···C17′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.79 Å, C–H···C 160°; C41–H41e···C18′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.83 Å, C–H···C 168°; C41–H41e···C19′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.87 Å, C–H···C 149°; C41–H41e···C20′ (−2−*x*, 0.5+*y*, −*z*): H···C 2.81 Å, C–H···C 135°.

2. Conclusions

The developed regioselective reaction of monoalkyl ethers of *p-tert*-butylcalix[4]arenes or calix[4]arenes in NaOH/DMSO or NaH/CH_3CN medium, respectively, is a good tool for the synthesis of inherently chiral calixarene backbones with ABHH substitution pattern.

3. Experimental

3.1. General

Melting points were determined on a Boëtius apparatus and are uncorrected. All the reactions were carried out in anhydrous solvents, which were freshly distilled prior to use. Column chromatography was carried out using Acros Organics silica gel (0.04–0.06 mm, pore diameter 6 nm). IR spectra were recorded on M 80 spectrometer. The ^{1}H NMR spectra were recorded on a Varian VXR-300 spectrometer with frequency 300 MHz (TMS as internal standard). ^{13}C NMR spectra were recorded on a Varian

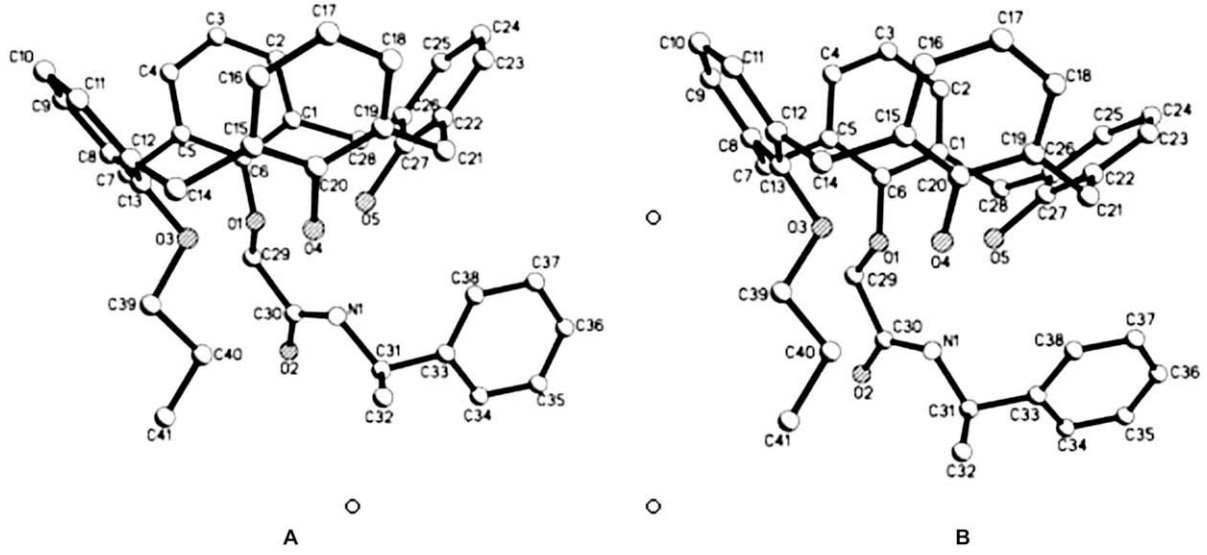

Figure 5. X-ray molecular structure of conformers A and B of calixarene **2e**.

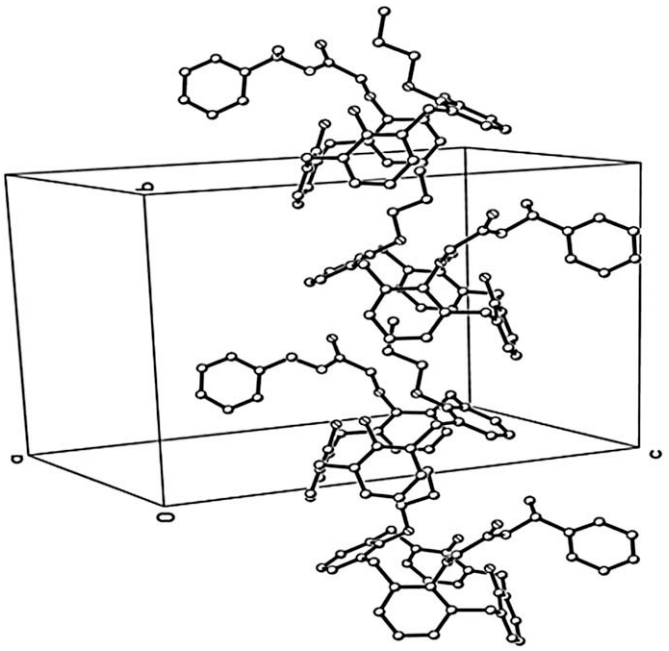

Figure 6. The infinite chains formed by molecules A of **2e**.

GEMINI 2000 spectrometer with frequency 100 MHz (TMS as internal standard). Optical rotations were measured using Perkin–Elmer Polarimeter 341. Monoalkoxycalixarenes **1a–c** were obtained according to the literature.[11]

3.2. 5,11,17,23-Tetra-*p*-*tert*-butyl-25,26-dihydroxy-27-butoxy-28-propoxycalix[4]arene[12] 2a and 5,11,17,23-tetra-*p*-*tert*-butyl-25,26-dihydroxy-27-propoxy-28-butoxycalix[4]arene 3a (racemic mixture)

The mixture of calix[4]arene **1b** (1.00 g, 1.45 mmol), sodium hydroxide (1.6 ml of 13 M solution of NaOH, 20.8 mmol), and DMSO (10 ml) was warmed to 60 °C. Alkyl bromide (0.93 g, 7.25 mmol) was added and the mixture was stirred at 65–70 °C for 7 h. After cooling to 20 °C, 5% solution of HCl (100 ml) was added to the reaction mixture. After stirring at ambient temperature for 2 h, the white precipitate was filtered off, washed with water (2×20 ml), dried in the open air, and crystallized from acetonitrile. Yield 82%.

Mp 86–87 °C. IR (KBr, ν/cm^{-1}): 3370 (OH···OAlk), 3190 (OH···OH). ^{1}H NMR ($CDCl_3$), δ: 1.04 (t, 3H, $OCH_2CH_2CH_2CH_3$, J^3_{H-H}=7.4 Hz), 1.12 (s, 9H, *t*-Bu), 1.13 (s+t, 12H, *t*-Bu+$OCH_2CH_2CH_3$), 1.19 (s, 9H, *t*-Bu), 1.20 (s, 9H, *t*-Bu), 1.57 (m, 2H, $OCH_2CH_2CH_2CH_3$), 2.09 (m, 4H, $OCH_2CH_2CH_3$+$OCH_2CH_2CH_2CH_3$), 3.32 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.3 Hz), 3.35 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.36 (d, 2H, Ar–CH_2-eq, J^2_{H-H}=12.9 Hz), 3.88 (m, 2H, $OCH_2CH_2CH_2CH_3$), 4.06 (m, 2H, $OCH_2CH_2CH_3$), 4.30 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.9 Hz), 4.31 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.9 Hz), 4.33 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.3 Hz), 4.47 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 6.93–7.05 (m, 8H, ArH), 8.81 (s, 1H, OH), 8.83 (s, 1H, OH). ^{13}C NMR ($CDCl_3$), δ: 10.50, 14.19, 19.41, 23.42, 30.69, 31.38, 31.39, 31.59, 31.60, 32.22, 32.41, 32.57, 32.59, 33.98, 34.17, 34.18, 76.40, 78.06, 124.76, 124.78, 125.17, 125.18, 125.63, 125.65, 125.70, 128.54, 128.61, 128.92, 128.99, 133.32, 133.38, 133.85, 133.94, 142.75, 142.80, 146.59, 146.62, 148.65, 148.73, 151.19, 151.22. Calcd, %: C 81.99, H 9.44. $C_{51}H_{70}O_4$ found, %: C 81.64, H 9.62.

3.3. Reaction of monoalkoxycalixarenes 1a,b with (*S*)-*N*-(α-phenylethyl)bromoacetamide

3.3.1. General procedure

The mixture of monoalkoxycalix[4]arenes **1a**,**b** (1.0 mmol), sodium hydroxide (40% water solution, 3.53 ml, 50.05 mmol), and DMSO (25 ml) was warmed to 60 °C. Then (*S*)-*N*-(α-phenylethyl)bromoacetamide (2.0 mmol) was added and the mixture was stirred under inert atmosphere at 60 °C for 6 h. The reaction was monitored by TLC (hexane/ethyl acetate 4:1). After cooling to room temperature the reaction mixture was acidified with 10% hydrochloric acid to pH=4–5; then the mixture was extracted with CH_2Cl_2 (50 ml). The organic phase was washed with water (2×30 ml) and dried over Na_2SO_4 and concentrated. The oiled residue was refluxed with methanol (10 ml) for 1 h. After cooling to room temperature water (1.5 ml) was added while stirring vigorously. The white precipitate was filtered off and dried in the open air. Diastereomeric mixtures **2b**,**3b** and **2c**,**3c** were separated by column chromatography on silica gel (hexane/ethyl acetate 4:1). Further details are given for the individual compounds.

*3.3.2. 5,11,17,23-Tetra-p-tert-butyl-25,26-dihydroxy-27-N-(α-phenylethyl)aminocarbonyl-28-methoxycalix[4]arene **2b***

The first fraction. Yield 25%. Mp 132–136 °C (decomp.). $[\alpha]_D^{20}$ −11.6 (*c* 0.005 M, CH_3OH). ^{1}H NMR ($CDCl_3$), δ: 1.11 (s, 9H, *t*-Bu), 1.20 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.26 (s, 9H, *t*-Bu), 1.68 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=7.2 Hz), 3.31 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.35 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.47 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.4 Hz), 3.50 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.4 Hz), 3.52 (s, 3H, OCH_3), 3.89 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.4 Hz), 4.17 (d, 1H, Ar–CH_2-eq, $J_{H-H}{}^2$=14.6 Hz), 4.19 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 4.28 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.4 Hz), 4.41 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.59 (d, 1H, OCH_2C(O), J^2_{H-H}=14.6 Hz), 5.45 (dq, 1H, NH–C*H*(CH_3)Ph, J^3_{H-H}=7.2 Hz, J^3_{H-H}=9.3 Hz), 6.91 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 6.94 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 6.97 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 6.99 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.06 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.13 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.15 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.20 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.29 (t, 1H, *p*-Ph, J^3_{H-H}=7.5 Hz), 7.43 (t, 2H, *m*-Ph, J^3_{H-H}=7.5 Hz), 7.67 (d, 2H, *o*-Ph, J^3_{H-H}=7.5 Hz), 9.36 (d, 1H, NH, J^3_{H-H}=9.3 Hz), 9.73 (s, 1H, OH), 10.33 (s, 1H, OH). ^{13}C NMR ($CDCl_3$), δ: 21.97, 31.55, 31.70, 31.90, 31.97, 32.52, 33.60, 33.72, 34.31, 34.45, 34.47, 34.65, 34.90, 35.11, 48.78, 62.53, 74.80, 125.39, 125.55, 125.80, 125.85, 126.06, 126.58, 127.07, 127.08, 127.16, 127.19, 127.40, 127.44, 128.94, 129.05, 130.28, 132.07, 133.06, 133.54, 134.79, 142.84, 143.76, 144.28, 147.07, 148.16, 148.49, 149.69, 150.43, 151.13. Calcd, %: C 80.16, H 8.44, N 1.70. $C_{55}H_{69}NO_5$ found, %: C 79.98, H 8.60, N 1.80.

*3.3.3. 5,11,17,23-Tetra-p-tert-butyl-25,26-dihydroxy-27-methoxy-28-N-(α-phenylethyl)aminocarbonylcalix[4]arene **3b***

The second fraction. Yield 23%. Mp 124–129 °C (decomp.). $[\alpha]_D^{20}$ 41.4 (*c* 0.005 M, CH_3OH). ^{1}H NMR ($CDCl_3$), δ: 1.13 (s, 9H, *t*-Bu), 1.22 (s, 18H, *t*-Bu), 1.25 (s, 9H, *t*-Bu), 1.78 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=7.2 Hz), 3.26 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.5 Hz), 3.42 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.5 Hz), 3.44 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.7 Hz), 3.53 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=14.0 Hz), 4.04 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.7 Hz), 4.10 (s, 3H, OCH_3), 4.15 (d, 1H, OCH_2C(O), J^2_{H-H}=14.3 Hz), 4.22 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.7 Hz), 4.32 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.5 Hz), 4.38 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.5 Hz), 4.66 (d, 1H, OCH_2C(O)J^2_{H-H}=14.3 Hz), 5.31 (m, 1H, NH–C*H*(CH_3)Ph, J^3_{H-H}=7.2, 7.8 Hz), 6.93 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 6.95 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 6.99 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.02 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.06 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.11 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.13 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.23 (m partly overlapped, 1H, ArH, J^4_{H-H}=2.5 Hz, and 1H, *p*-Ph), 7.30 (t, 2H, *m*-Ph, J^3_{H-H}=7.5 Hz), 7.50 (d, 2H, *o*-Ph, J^3_{H-H}=7.5 Hz), 9.50 (d, 1H, NH, J^3_{H-H}=7.8 Hz), 9.72 (s, 1H, OH), 10.45 (s, 1H, OH). ^{13}C NMR

($CDCl_3$), δ: 23.03, 31.56, 31.71, 31.83, 31.88, 31.96, 32.55, 33.65, 34.30, 34.44, 34.48, 34.69, 34.90, 35.11, 49.46, 62.81, 74.68, 77.47, 125.30, 125.61, 125.86, 126.14, 126.61, 126.67, 127.06, 127.13, 127.15, 127.19, 127.45, 128.70, 129.09, 130.16, 132.21, 133.10, 133.70, 134.82, 142.81, 143.90, 144.21, 147.12, 148.05, 148.64, 149.55, 150.40, 151.13, 168.95.

3.3.4. 5,11,17,23-Tetra-p-tert-butyl-25,26-dihydroxy-27-N-(α-phenylethyl)aminocarbonyl-28-propoxycalix[4]arene ***2c***

The first fraction. Yield 24%. Mp 124–127 °C (decomp.). $[\alpha]_D^{20}$ 9.0 (*c* 0.006 M, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ: 0.62 (t, 3H, $OCH_2CH_2CH_3$, J^3_{H-H}=7.5 Hz), 1.12 (s, 9H, *t*-Bu), 1.20 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.25 (m overlapped, 2H, $OCH_2CH_2CH_3$), 1.26 (s, 9H, *t*-Bu), 1.62 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=6.8 Hz), 3.30 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.36 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.47 (d, 1H, Ar-CH_2-eq, J^2_{H-H}=13.7 Hz), 3.47 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.7 Hz), 3.65 and 3.86 (two m, 1H each, diastereotopic $OCH_2CH_2CH_3$), 3.92 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.4 Hz), 4.07 (d, 1H, OCH_2C(O), J^2_{H-H}=14.9 Hz), 4.27 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.30 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.7 Hz), 4.44 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.69 (d, 1H, OCH_2C(O), J^2_{H-H}=14.9 Hz), 5.41 (dq, 1H, NH–C*H*(CH_3)Ph, J^3_{H-H}=6.8, 8.7 Hz), 6.96 (m, 4H, ArH), 7.05 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.12 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.16 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.22 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.28 (t, 1H, *p*-Ph, J^3_{H-H}=7.5 Hz), 7.40 (t, 2H, *m*-Ph, J^3_{H-H}=7.5 Hz), 7.65 (d, 2H, *o*-Ph, J^3_{H-H}=7.5 Hz), 9.59 (d, 1H, NH, J^3_{H-H}=8.7 Hz), 9.72 (s, 1H, OH), 10.30 (s, 1H, OH). ^{13}C NMR ($CDCl_3$), δ: 9.81, 22.08, 22.62, 30.57, 31.07, 31.22, 31.42, 31.48, 32.53, 33.27, 33.52, 33.83, 33.96, 34.14, 48.58, 74.31, 78.65, 124.81, 125.01, 125.41, 125.43, 125.50, 126.23, 126.31, 126.67, 126.76, 126.89, 126.93, 128.21, 128.29, 130.04, 131.24, 132.81, 132.86, 134.60, 142.31, 143.10, 143.31, 146.41, 147.74, 147.90, 149.19, 149.29, 150.72, 168.04.

3.3.5. 5,11,17,23-Tetra-p-tert-butyl-25,26-dihydroxy-27-propoxy-28-N-(α-phenylethyl)aminocarbonylcalix[4]arene ***3c***

The second fraction. Yield 25%. Mp 192–196 °C (decomp.). $[\alpha]_D^{20}$ 15.7 (*c* 0.006 M, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ: 1.12 (s, 9H, *t*-Bu), 1.19 (t partly overlapped, 3H, $OCH_2CH_2CH_3$, J^3_{H-H}=7.5 Hz), 1.21 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.25 (s, 9H, *t*-Bu), 1.72 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=7.2 Hz), 2.17 (m, 2H, $OCH_2CH_2CH_3$), 3.22 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.42 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.44 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.7 Hz), 3.53 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.4 Hz), 3.90 (m, 1H, $OCH_2CH_2CH_3$), 4.03 (d, 1H, OCH_2C(O), J^2_{H-H}=14.9 Hz), 4.04 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.4 Hz), 4.18 (m, 1H, $OCH_2CH_2CH_3$), 4.22 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.7 Hz), 4.36 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.37 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.71 (d, 1H, OCH_2C(O), J^2_{H-H}=14.9 Hz), 5.26 (m, 1H, NH–C*H*(CH_3)Ph), 6.95 (dd, 2H, ArH, J^4_{H-H}=2.2 Hz), 6.99 (dd, 2H, ArH, J^4_{H-H}=2.2, 2.5 Hz), 7.06 (d, 1H, ArH, J^4_{H-H}=2.2 Hz), 7.10 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.13 (d, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.19 (m partly overlapped, 1H, *p*-Ph), 7.24 (d partly overlapped, 1H, ArH, J^4_{H-H}=2.5 Hz), 7.25 (m partly overlapped, 2H, *m*-Ph), 7.44 (d, 2H, *o*-Ph, J^3_{H-H}=7.5 Hz), 9.73 and 9.75 (partly overlapped d and s, respectively, 2H, NH, OH, J^3_{H-H}=8.1 Hz), 10.40 (s, 1H, OH). ^{13}C NMR ($CDCl_3$), δ: 10.50, 22.18, 23.19, 30.55, 31.08, 31.23, 31.41, 31.47, 32.55, 33.18, 33.49, 33.82, 33.94, 33.96, 34.17, 48.95, 74.40, 78.84, 124.75, 124.99, 125.41, 125.50, 126.02, 126.26, 126.31, 126.50, 126.63, 126.97, 128.11, 128.13, 129.90, 131.26, 132.85, 132.90, 134.65, 142.31, 143.22, 143.96, 146.43, 147.76, 147.87, 149.08, 149.32, 150.60, 168.42. Calcd, %: C 80.34, H 8.63. $C_{57}H_{73}NO_5$, found, %: C 80.47, H 8.73.

3.4. Reaction of monoalkoxycalixarens 1c,d with (*R*)-*N*-(α-phenylethyl)bromoacetamide

3.4.1. General procedure

A solution of monoalkoxycalix[4]arene **1c**,**d** (2.69 mmol) in acetonitrile (100 ml) was stirred with NaH (60% dispersion in mineral oil, 0.36 g, 8.88 mmol) at room temperature for 16 h. Then (*R*)-*N*-(α-phenylethyl)bromoacetamide (0.68 g, 2.79 mmol) was added and the reaction mixture was stirred at room temperature for 24 h. The solution of 5% HCl (10 ml) was added to the reaction mixture and acetonitrile was removed under reduced pressure. Water (50 ml) was added to the remaining solid, the product was extracted with $CHCl_3$ (2×25 ml), washed with water, brined, and dried over Na_2SO_4. The solvent was removed in vacuo. The crude product was subjected to the column chromatography.

3.4.2. 25,26-Dihydroxy-27-methoxy-28-N-(α-phenylethyl)-aminocarbonylcalix[4]arene ***2d***

The second fraction. Yield 0.35 g (22%). Mp=158–159 °C. ^{1}H NMR ($CDCl_3$), δ: 1.81 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=6.8 Hz), 3.30 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.45 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.5 Hz), 3.48 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.56 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.8 Hz), 4.06 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.5 Hz), 4.15 (s, 3H, OCH_3), 4.16 (d, 1H, OCH_2C(O), J^2_{H-H}=14.5 Hz), 4.20 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.8 Hz), 4.35 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.37 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.67 (d, 1H, OCH_2C(O), J^2_{H-H}=14.5 Hz), 5.35 (m, 1H, NH–C*H*(CH_3)Ph), 6.64–6.82 (m, 4H, ArH), 6.92–7.11 (m, 8H, ArH), 7.19–7.31(m, 4H, ArH), 7.51 (m, 1H, ArH), 9.43 (d, 1H, NH, J^3_{H-H}=8.1 Hz), 9.56 (s, 1H, OH), 10.07 (s, 1H, OH). Calcd, %: C 78.11, H 6.22, N 2.34. $C_{39}H_{37}NO_5$, found, %: C 77.76, H 6.32, N 2.38.

3.4.3. 25,26-Dihydroxy-27-N-(α-phenylethyl)aminocarbonyl-28-methoxycalix[4]arene ***3d***

The first fraction. Yield 0.37 g (23%). Mp=114–115 °C. ^{1}H NMR ($CDCl_3$), δ: 1.7 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=6.8 Hz), 3.37 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.6 Hz), 3.41 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.6 Hz), 3.48 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.6 Hz), 3.50 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.3 Hz), 3.57 (s, 3H, OCH_3), 3.90 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.3 Hz), 4.18 (d, 1H, OCH_2C(O), J^2_{H-H}=14.1 Hz), 4.24 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.6 Hz), 4.26 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.6 Hz), 4.42 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.6 Hz), 4.61 (d, 1H, OCH_2C(O), J^2_{H-H}=14.1 Hz), 5.47 (m, 1H, NH–C*H*(CH_3)Ph), 6.67–6.77 (m, 4H, ArH), 6.91–7.11 (m, 9H, ArH), 7.18 (d, 2H, ArH, J^3_{H-H}=7.3 Hz), 7.46 (d, 1H, ArH, J^3_{H-H}=7.3 Hz), 7.68 (d, 1H, ArH, J^3_{H-H}=7.3 Hz), 9.21 (d, 1H, NH, J^3_{H-H}=8.7 Hz), 9.55 (s, 1H, OH), 9.88 (s, 1H, OH). Calcd, %: C 78.11, H 6.22, N 2.34. $C_{39}H_{37}NO_5$, found, %: C 77.23, H 6.44, N 2.41.

3.4.4. 25,26-Dihydroxy-27-propoxy-28-N-(α-phenylethyl)-aminocarbonylcalix[4]arene ***2e***

The second fraction. Yield 0.44 g (26%). Mp=239–240 °C. ^{1}H NMR ($CDCl_3$), δ: 1.21 (t, 3H, $CH_3CH_2CH_2O$, J^3_{H-H}=7.5 Hz), 1.75 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=6.9 Hz), 2.22 (m, 2H, $CH_3CH_2CH_2O$), 3.25 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.6 Hz), 3.45 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.6 Hz), 3.48 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.6 Hz), 3.55 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.6 Hz), 3.96 (m, 1H, $OCH_2CH_2CH_3$), 4.03 (d, 1H, OCH_2C(O), J^2_{H-H}=14.9 Hz), 4.05 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.6 Hz), 4.16–4.24 (d+m, 2H, Ar–CH_2-ax+$OCH_2CH_2CH_3$, J^2_{H-H}=13.6 Hz), 4.34 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.6 Hz), 4.43 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.6 Hz), 4.74 (d, 1H, OCH_2C(O), J^2_{H-H}=14.9 Hz), 5.31 (m, 1H, NH–C*H*(CH_3)Ph), 6.64–6.77 (m, 3H, ArH), 6.90–7.08 (m, 8H, ArH), 7.16–7.24 (m, 4H, ArH), 7.45 (m, 2H, ArH), 9.56 (s, 1H, OH), 9.61 (d, 1H, NH, J^3_{H-H}=7.8 Hz), 10.06 (s, 1H, OH). ^{13}C NMR ($CDCl_3$), δ: 10.64, 22.31, 23.48, 30.03, 32.01, 32.16, 32.63, 49.09, 74.74, 77.20, 79.28, 120.57, 121.57, 121.68, 124.98, 126.01, 126.28, 126.87, 127.23, 127.98, 128.14, 128.17, 128.36, 128.45, 128.50, 128.85, 128.99, 129.42, 129.63, 129.88, 130.24, 133.12, 133.92, 133.94, 135.55, 143.84, 149.44, 151.40, 151.74, 153.06, 168.26. Calcd, %: C 78.44, H 6.58, N 2.23. $C_{41}H_{41}NO_5$, found, %: C 78.12; H 6.96; N 2.46.

Table 1
The crystallographic data and experimental parameters for compounds **2a**, **2b**, and **2e**

Parameter	2a	2b	2e
Unit cell dimensions			
a, Å	12.8943(3)	10.9610(5)	11.0494(5)
b, Å	23.1705(6)	19.3356(6)	15.2553(7)
c, Å	17.8863(5)	12.8943(6)	20.620(2)
β, °	103.838(3)	112.236(5)	102.185(5)
V, Å^3	5188.7(2)	2529.6(2)	3399.4(3)
F(000)	1796	964	1336
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1$	$P2_1$
Z	4	2	4
μ, mm^{-1}	0.065	0.075	0.080
D_{calcd}, g/cm^3	1.058	1.166	1.227
$2\Theta_{max}$, grad	50	55	50
Measured reflections	25,869	12,494	16,800
Independent reflections	8875	7458	11,149
R_{int}	0.042	0.024	0.077
Reflections with $F>4\sigma(F)$	4389	5250	3747
Parameters	663	603	851
$R1$	0.087	0.063	0.045
$wR2$	0.257	0.174	0.048
S	0.927	0.979	0.584

3.4.5. 25,26-Dihydroxy-27-N-(α-phenylethyl)aminocarbonyl-28-propoxycalix[4]arene ***3e***

The first fraction. Yield 0.36 g (21%). Mp=208–209 °C. ^{1}H NMR ($CDCl_3$), δ: 0.68 (t, 3H, $CH_3CH_2CH_2O$, J^3_{H-H}=7.8 Hz), 1.52 (m, 2H, $CH_3CH_2CH_2O$), 1.63 (d, 3H, NH–CH(CH_3)Ph, J^3_{H-H}=7.0 Hz), 3.36 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.4 Hz), 3.43 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=12.6 Hz), 3.48 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.6 Hz), 3.49 (d, 1H, Ar–CH_2-eq, J^2_{H-H}=13.7 Hz), 3.72 (m, 1H, $OCH_2CH_2CH_3$), 3.90 (m, 1H, $OCH_2CH_2CH_3$), 3.93 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.7 Hz), 4.09 (d, 1H, OCH_2C(O), J^2_{H-H}=15.1 Hz), 4.27 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=13.6 Hz), 4.33 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.4 Hz), 4.46 (d, 1H, Ar–CH_2-ax, J^2_{H-H}=12.6 Hz), 4.72 (d, 1H, OCH_2C(O), J^2_{H-H}=15.1 Hz), 5.42 (m, 1H, NH–$CH(CH_3)$Ph), 6.65–6.78 (m, 3H, ArH), 6.90 (t, 1H, ArH, J^3_{H-H}=7.7 Hz), 6.98–7.10 (m, 7H, ArH), 7.21 (d, 1H, J^3_{H-H}=7.7 Hz, ArH), 7.33 (d, 1H, J^3_{H-H}=7.7 Hz, ArH), 7.44 (t, 2H, J^3_{H-H}=7.7 Hz, ArH), 7.65 (d, 2H, J^3_{H-H}=7.7 Hz, ArH), 9.47 (d, 1H, NH, J^3_{H-H}=9.0 Hz), 9.55 (s, 1H, OH), 9.90 (s, 1H, OH). ^{13}C NMR ($CDCl_3$), δ: 9.98, 22.08, 22.84, 29.92, 31.93, 32.18, 32.55, 48.74, 74.52, 79.03, 120.56, 121.53, 124.97, 125.86, 126.87, 127.10, 127.23, 128.01, 128.10, 128.47, 128.55, 128.68, 128.84, 129.25, 129.47, 129.82, 130.30, 133.01, 133.79, 133.88, 135.40, 143.24, 149.43, 151.43, 151.53, 152.99, 167.92. Calcd, %: C 78.44; H 6.58; N 2.23. $C_{41}H_{41}NO_5$, found, %: C 78.51; H 7.20; N 2.13.

3.5. The X-ray diffraction study

All experiments were carried out on the 'Xcalibur-3' diffractometer (graphite monochromated Mo Kα radiation, CCD detector, ω-scanning) at 100 K. The structures were solved by direct method using SHELXTL package.[13]

The positions of hydrogen atoms were calculated geometrically and refined by 'riding' model with $U_{iso}=nU_{eq}$ of non-hydrogen atom bonded with given hydrogen atom (n=1.5 for methyl and hydroxyl groups and n=1.2 for other hydrogen atoms). The crystallographic data and experimental parameters are listed in Table 1. The absolute configuration of the chiral centers in molecules **2b**, **2e** was determined using the known absolute configuration of phenylethylamide fragment as marker. Structures were refined within anisotropic approximation for non-hydrogen atoms. The restrictions on the bond lengths (Csp^3–Csp^3 1.54 Å, Csp^3–Csp 1.46 Å, Nsp–Csp 1.13 Å) in the disordered fragment were applied in the refinement of structure **2a**. The final atomic coordinates and crystallographic data for molecules **2a**, **2b**, and **2e** have been deposited to the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 711387 for **2a**, CCDC 711385 for **2b**, and CCDC 711386 for **2e**.

3.6. Quantum-chemical calculations

The molecular structures of **2b** and **3b** were fully optimized using M05-2X[14] theory with the aug-cc-pVDZ basis set[15] in the NWChem5.1 program.[16]

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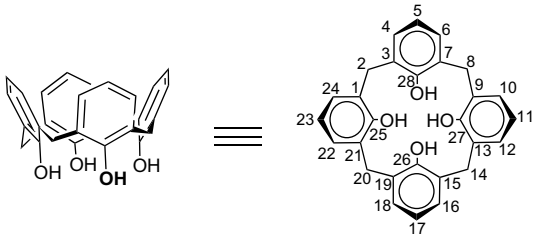
References and notes

1. *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J. M., Vicens, J., Eds.; Kluwer Academic: Dordrecht, 2001.
2. Gutsche, C. D. Calixarenes Revisited. In *Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1998.
3. (a) Yoon, K.; Kim, K. *J. Org. Chem.* **2005**, *70*, 427–432; (b) He, H.; Mortellaro, M. A.; Leiner, M. J. P.; Fraatz, R. J.; Tusa, J. K. *J. Am. Chem. Soc.* **2003**, *125*, 1468–1469; (c) Kim, J. S.; Noh, K. H.; Lee, S. H.; Kim, S. K.; Yoon, J. *J. Org. Chem.* **2003**, *68*, 597–600; (d) Chen, Q.-Y.; Chen, C.-F. *Tetrahedron Lett.* **2005**, *46*, 165–168.
4. (a) Lee, J. Y.; Kim, S. K.; Jung, J. H.; Kim, J. S. *J. Org. Chem.* **2005**, *70*, 1463–1466; (b) Tomapatanaget, B.; Tuntulani, T.; Chailapakul, O. *Org. Lett.* **2003**, *5*, 1539–1542; (c) Sansone, F.; Baldini, L.; Casnati, A.; Lazzaroto, M.; Ugozzli, F.; Ungaro, R. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *99*, 4842–4847; (d) Sdira, S. B.; Felix, C. P.; Giudicelli, M.-B. A.; Siegle-Ferrand, P. F.; Perrin, M.; Lamartine, R. J. *J. Org. Chem.* **2003**, *68*, 6632–6638; (e) Miao, R.; Zheng, Q.-Y.; Chen, C.-F.; Huang, Z.-T. *Tetrahedron Lett.* **2004**, *45*, 4959–4962; (f) Miao, R.; Zheng, Q.-Y.; Chen, C.-F.; Huang, Z.-T. *Tetrahedron Lett.* **2005**, *46*, 2155–2158.
5. (a) Sénèque, O.; Rager, M.-N.; Giorgi, M.; Reinaud, O. *J. Am. Chem. Soc.* **2000**, *122*, 6183–6189; (b) Pinkhassik, E.; Sidorov, V.; Stibor, I. *J. Org. Chem.* **1998**, *63*, 9644–9651; (c) Arduini, A.; Secchi, A.; Pochini, A. *J. Org. Chem.* **2000**, *65*, 9085–9091.
6. (a) Boyko, V. I.; Shivanyuk, A.; Pirozhenko, V. V.; Zubatyuk, R. I.; Shishkin, O. V.; Kalchenko, V. I. *Tetrahedron Lett.* **2006**, *47*, 7775–7778; (b) Yakovenko, A. V.; Boyko, V. I.; Danylyuk, O.; Suwinska, K.; Lipkowski, J.; Kalchenko, V. I. *Org. Lett.* **2007**, *9*, 1183–1185; (c) Boyko, V. I.; Yakovenko, A. V.; MatvieievYu, I.; Kalchenko, O. I.; Shishkin, O. V.; Shishkina, S. V.; Kalchenko, V. I. *Tetrahedron* **2008**, *64*, 7567–7573.
7. Boyko, V. I.; Podoprigorina, A. A.; Yakovenko, A. V.; Pirozhenko, V. V.; Kalchenko, V. I. *J. Inclusion Phenom.* **2004**, *50*, 193–197.
8. (a) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713–745; (b) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955–4962.
9. Margans, J. O.; de Mendoza, J.; Pons, M.; Prados, P. *J. Org. Chem.* **1997**, *62*, 4518–4520.
10. Casnati, A.; Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R. *Tetrahedron* **1991**, *47*, 2221–2228.
11. Shu, C.-M.; Chung, W.-S.; Wu, S.-H.; Ho, Z.-C.; Lin, L.-G. *J. Org. Chem.* **1999**, *64*, 2673–2679.



12. The carbon atoms of the macrocyclic skeleton of the *cone*-shaped inherently chiral calixarenes described are numbered in a clockwise manner.
13. Sheldrick, G. M. *SHELXTL PLUS. PC Version* A system of computer programs for the determination of crystal structure from X-ray diffraction data. Rev.5.1; 1998.
14. Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 5656–5667.
15. (a) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007–1024; (b) Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1994**, *100*, 2975–2989; (c) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007–1024; (d) Kendall, R. A.; Dunning, T. H., Jr.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796–6807; (e) Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1993**, *98*, 1358–1372; (f) Wilson, A. K.; Woon, D. E.; Peterson, K. A.; Dunning, T. H., Jr. *J. Chem. Phys.* **1999**, *110*, 7667–7677.
16. Straatsma, T. P.; Aprà, E.; Windus, T. L.; Bylaska, E. J.; de Jong, W.; Hirata, S.; Valiev, M.; Hackler, M.; Pollack, L.; Harrison, R.; Dupuis, M.; Smith, D. M. A.; Nieplocha, J.; Tipparaju, V.; Krishnan, M.; Auer, A. A.; Brown, E.; Cisneros, G.; Fann, G.; Früchtl,

H.; Garza, J.; Hirao, K.; Kendall, R.; Nichols, J.; Tsemekhman, K.; Wolinski, K.; Anchell, J.; Bernholdt, D.; Borowski, P.; Clark, T.; Clerc, D.; Dachsel, H.; Deegan, M.; Dyall, K.; Elwood, D.; Glendening, E.; Gutowski, M.; Hess, A.; Jaffe, J.; Johnson, B.; Ju, J.; Kobayashi, R.; Kutteh, R.; Lin, Z.; Littlefield, R.; Long, X.; Meng, B.; Nakajima, T.; Niu, S.; Rosing, M.; Sandrone, G.; Stave, M.; Taylor, H.; Thomas, G.; van Lenthe, J.; Wong, A.; Zhang, Z. *NWChem* A Computational Chemistry Package for Parallel Computers, Version 4.6; Pacific Northwest National Laboratory: Richland, Washington 99352-0999, USA, 2004; High Performance Computational Chemistry: an Overview of NWChem a Distributed Parallel Application Kendall, R. A.; Aprà, E.; Bernholdt, D. E.; Bylaska, E. J.; Dupuis, M.; Fann, G. I.; Harrison, R. J.; Ju, J.; Nichols, J. A.; Nieplocha, J.; Straatsma, T. P.; Windus, T. L.; Wong, A. T. *Comput. Phys. Commun.* **2000**, *128*, 260–283.