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Synthesis and Stereochemical Configuration of Diastereomeric Inherently Chiral Calixarenes with ABCH and ABCD Type of Substitution at the Lower Rim

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Abstract—By sulfonylation of tetra(*p-tert*-butyl)-27-propoxy-25-[*N*-(1-phenylethyl)carbamoylmethoxy]calix[4]arene diastereomeric inherently chiral calixarenes with the ABCH substitution at the lower rim were synthesized and separated by column chromatography. The alkylation of these compounds afforded the corresponding calixarenes with the ABCD substitution type. The absolute configuration of compounds was established by XRD analysis.

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Calixarenes due to their unique cavity-shaped structure are capable of recognition, binding, and separation of cations, anions, and neutral organic molecules of similar properties [1]. Chiral calixarenes are especially interesting in this respect. Receptors based on these compounds can recognize and bind the optical antipodes of chiral "guest" molecules [2]. Chiral calixarenes may also be used as organic catalysts [3] or ligands in the metallocomplex catalysis [4] for asymmetric synthesis, as enantioselective sensors [5], chiral stationary phases for column chromatography [6], chiral shift reagents for NMR spectroscopy [7]. Inherently chiral calixarenes whose optical activity is due to the asymmetric position of achiral substituents on the macrocyclic matrix [8] are worth special attention. Although many examples of the synthesis of such compounds were described, mostly their racemates or diastereomeric mixtures were obtained. Only several cases were described where the optical isomers were successfully isolated in the individual state [9, 10] and their absolute configuration was established by X-ray analysis [9]. Therefore the search for efficient synthetic procedures for the preparation of individual inherently chiral calixarenes and the study of their configuration is a topical target.

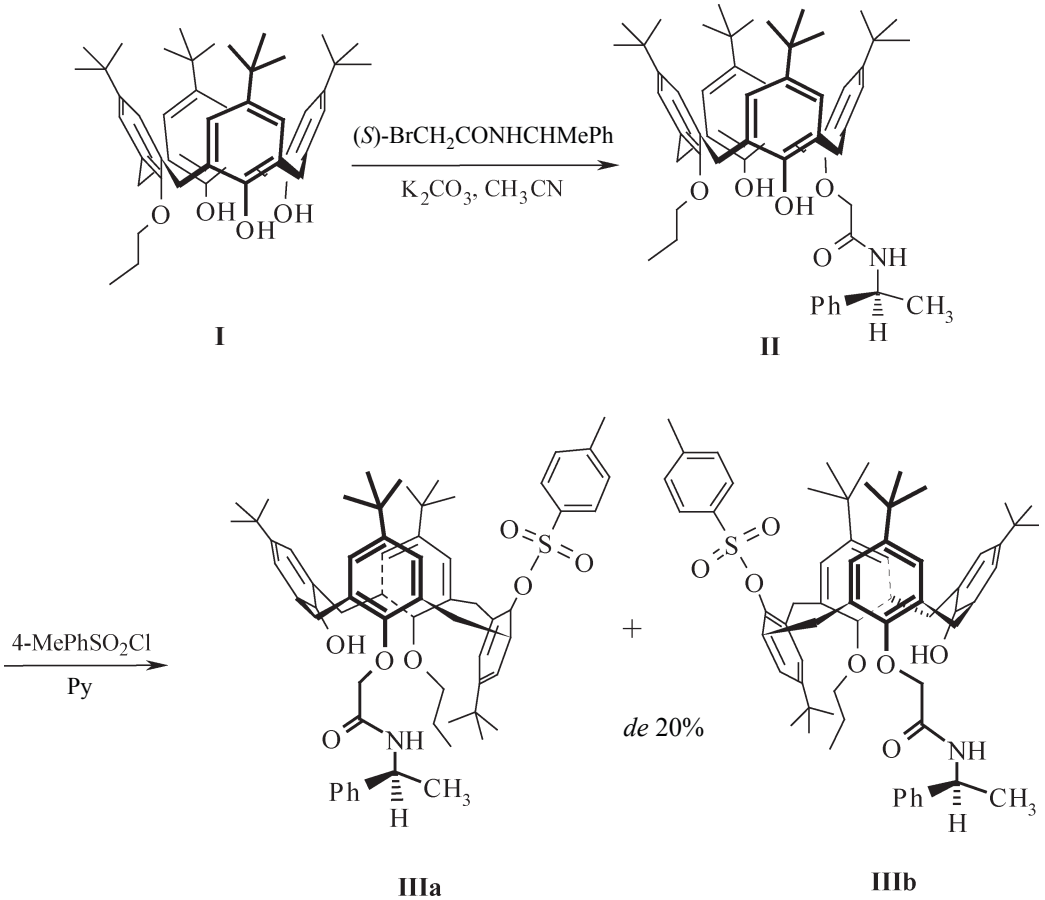
In the preceding paper [11] we reported on the synthesis and separation of diastereomeric derivatives of inherently chiral calix[4]arenes by the acylation of 27-propoxy-25-[*N*-(1-phenylethyl)carbamoylmethoxy]calix[4]arene without substituents on the upper rim of the macrocycle. In this work we synthesized diasteromeric internally chiral calix[4]arenes with *tert*-butyl groups at the upper rim and ABCH or ABCD type of substitution at the lower rin, and carried out the study of the spatial structure of compounds obtained in solution and in the crystal state.

Chiralыe calix[4]arenes **IIIa, IIIb** were obtained from 25-propoxycalix[4]arene **I** [12] in two stages (Scheme 1).

In the first stage the alkylation of the second (distal) hydroxy group of monopropoxycalixarene **I** was performed with a chiral (*S*)-*N*-(1-phenylethyl) bromoacetamide in boiling acetonitrile using K_2CO_3 as base. Tetra(*p-tert*-butyl)-27-propoxy-25-[*N*-(1-phenylethyl)carbamoylmethoxy]calix[4]arene (**II**) was isolated in spectrally pure state.

Compound **II** is well soluble both in polar (e.g.,

Scheme 1.



methanol) and nonpolar (hexane) solvents. The structure was proved using ^{1}H NMR spectroscopy. Under the effect of the asymmetric carbon atom in the (*S*)-*N*-(1-phenylethyl)amide fragment of the molecule the bridging protons (Ar–CH_2–Ar) (8 pair of doublets which partially overlapped), and also the protons OCH_2 of the propyl group (multiplet at 3.81–3.93 ppm), methylene protons of the residue $OCH_2C(O)NHCH(Me)Ph$ (two doublets at 4.47 and 4.53 ppm), and the protons of the hydroxy groups became diastereotopic. Even the protons of the aromatic rings located on the other side of the macrocycle became nonequivalent. They appeared as multiplets instead of two singlets and two doublets. The values of spin-spin coupling constants of 13.2–13.4 Hz for the bridging protons and the difference of ~0.8 ppm between the chemical shifts of the axial and equatorial protons confirm the cone conformation of calixarene **II** [13].

In the next stage the sulfonylation of calix[4]arene **II** was performed with *p*-toluenesulfonyl chloride in anhydrous pyridine where the latter simultaneously served as a base. Under these conditions only one phenol group reacted giving diastereomers **IIIa** and **IIIb** possessing two symmetry elements each: the carbon atom of the phenylethylamide residue and the ABCH asymmetrically substituted macrocyclic frame.

The mixture of diastereomers **IIIa** and **IIIb** was isolated in 92% yield, their ratio was determined from the integral intensity of the signals of the methyl groups belonging to the *p*-toluyl fragment at 2.19 and 2.05 ppm. This ratio was 3 : 2 (diastereomeric excess, *de* 20%) and it was independent of the reaction temperature.

The attempt to separate diastereomers **IIIa** and **IIIb** by crystallization led only to the formation of the racemic mixture both in the solution and in the crystalline state. The diastereomers were separated by column chromatography and were isolated in the yields 26% (**IIIa**) and 38% (**IIIb**). The analysis of the ^{1}H NMR spectra of the diastereomers confirmed the asymmetric substitution of the macrocyclic frame. All the bridging methylene protons are different and give rise to 4 pairs of doublets. Also four singlets are observed originating from

the *tert*-butyl groups. The prochiral protons OCH_2 of the propyl group appear as two multiplets, and the methylene protons of the amide residue are observed as two doublets. The ^1H NMR spectra of different diastereomers possess a number of distinguishing features. For instance, the signals $\delta(CH_3)$ and $\delta(CH_2)$ of the propyl group of calixarene **IIIa** are shifted upfield as compared with the spectrum of calixarene **IIIb** ($\Delta\delta$ 0.3 ppm) that may be attributed to the shielding of these protons by the benzene ring of the phenylethylamide group.

The NMR data show that calixarenes **IIIa** and **IIIb** are present in the partial cone conformation. The difference in the chemical shifts for axial and equatorial protons in two pairs of $ArCH_2Ar$ doublets lies in the range 0.54–1.13 ppm (1.13, 1.05, 0.54, 0.55) and corresponds to the *syn*-orientation of the neighboring benzene rings. For two other pairs of doublets this difference is less than 0.5 ppm (0.44, 0.40, 0.13, 0.04), characteristic of the *anti*-orientation of the adjacent benzene rings [14]. In the ^{13}C NMR spectra of calixarenes the pairs of signals 32.72, 32.73 ppm (**IIIa**) and 32.36, 32.57 ppm (**IIIb**) correspond to the carbon atoms of the methylene bridges between two *syn*-oriented benzene rings, and the pairs of signals 38.97, 38.99 ppm (**IIIa**) and 38.61, 38.73 ppm (**IIIb**), to the carbon atoms of the methylene bridges between two *anti*-oriented benzene rings [14].

The absolute configuration of diastereomers **IIIa** and **IIIb** was established by X-ray method. In the crystal of the racemate both diastereomers are located in the asymmetric part of the unit cell (Fig. 1). The diastereomers are distinguished by the sequence of substituents location on the macrocyclic frame. In compound **IIIa** the substituents HO, PrO, $TolSO_2O$, $Ph(Me)CHNHC(O)CH_2O$ are placed clockwise (Fig. 2), in diastereomer **IIIb**, counterclockwise (Fig. 3) (view from above).

Both diastereomers in pure form and in the racemate have the partial cone conformation. The geometrical characteristics of the macrocycle are very similar. The benzene ring with the toluenesulfoxide substituent is turned upside down, and the aromatic ring of the substituent enters the macrocyclic cavity. A slight difference is observed in the conformation of the (*S*)-*N*-(1-phenylethyl)amide residue. In the individual structures **IIIa**, **IIIb** this substituent is so oriented that it closes the calixarene cavity from the bottom side. The intramolecular hydrogen bond N^1–H···O^1 [H···O 2.31 Å, N–H···O 172° (**IIIa**), H···O 2.38 Å, N–H···O 173° (**IIIb**)] stabilizes this position of the substituent. In the crystal of racemate **IIIa**, **IIIb** containing

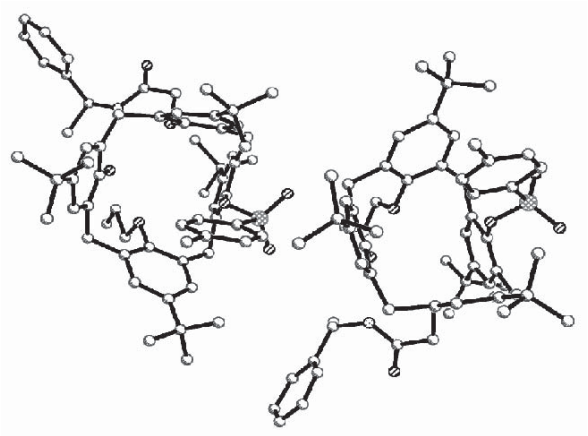


Fig. 1. Molecular structure of diastereomers in the crystal of racemate **IIIa, IIIb**.

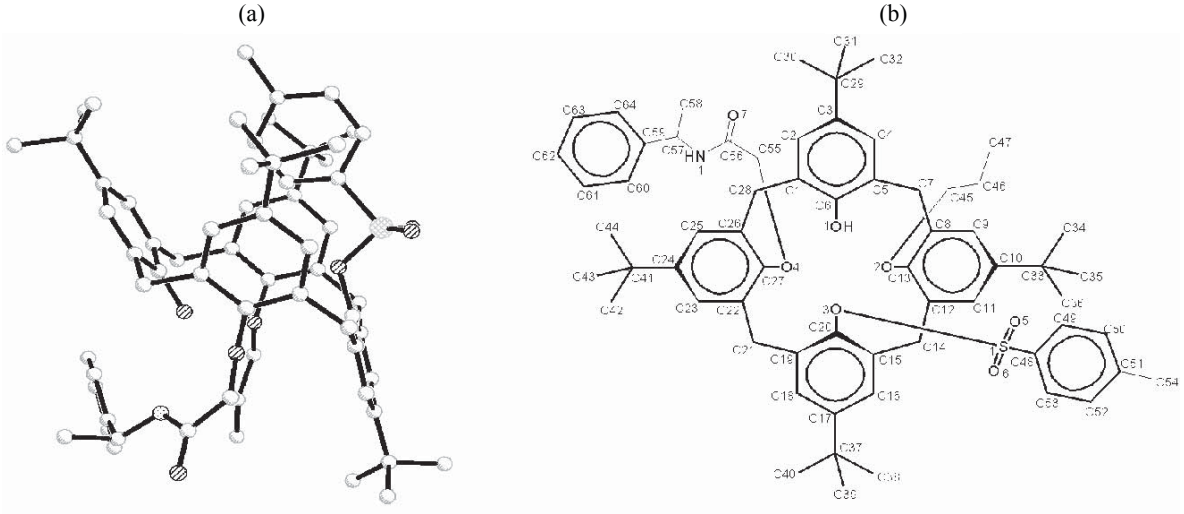


Fig. 2. Molecular structure of diastereomer **IIIa** (a) and numeration of nonhydrogen atoms (b).

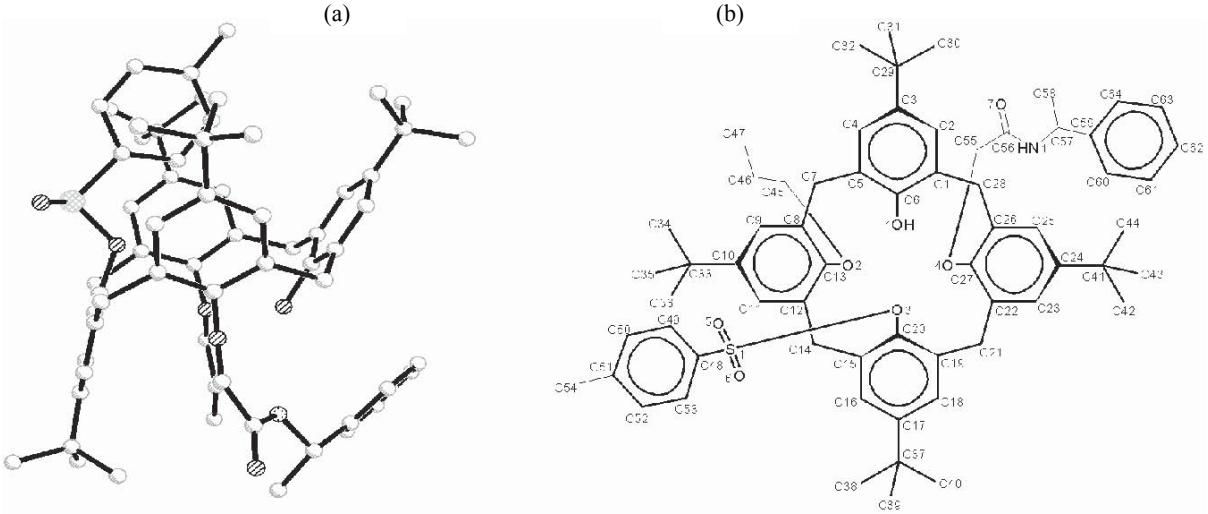


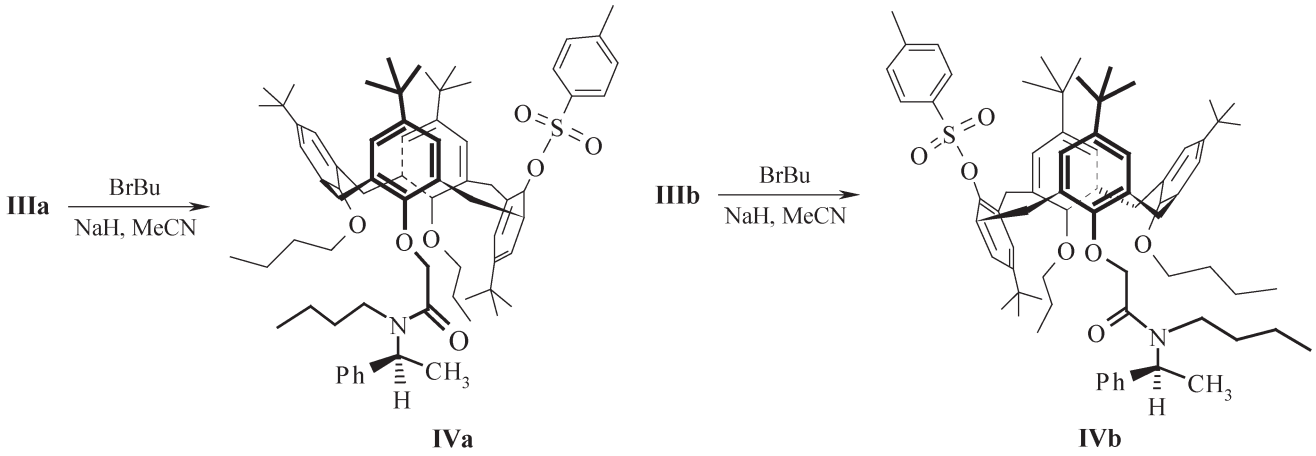
Fig. 3. Molecular structure of diastereomer **IIIb** (a) and numeration of nonhydrogen atoms (b).

both diastereomers the amide substituent does not close the calixarene cavity from the bottom side. The benzene ring of this substituent is turned to the outside, and the macrocycle cavity is closed from the bottom side by the sulfoxide group of the contiguous molecule. Owing to this interaction of a pair of diastereomers in the racemate crystal endless chains form along the crysatallographic direction [0 0 1]. Diastereomer **IIIa** in contrast to **IIIb** exists in the crystalline phase as a solvate with methanol in the ratio 1 : 3.

Individual diastereomers **IIIa** and **IIIb** were used in the synthesis of diasteromeric calixarenes with the ABCD substitution type. In their alkylation with butyl bromide in acetonitrile in the presence of sodium hydride as a base not only the fourth hydroxy group of calixarene reacted, but also the amide group of the chiral substituent resulting in the formation of compounds **IVa, IVb** respectively (Scheme 2).

The structure of tetra-substituted calix[4]arenes **IVa, IVb** was confirmed by the spectral data. In the mass spectra of compounds **IV** the main peak corresponds to the molecular ion (*m/z* 1118.6), and the peak of *m/z* 1062.4 (50%) belongs to the fragment after the elimination of the butyl group from the amide nitrogen atom. The large number of substituents and the presence of the chiral and prochiral centers considerably complicates the NMR spectra leading to the splitting and broadening of the signals. Therefore we carried out the study of the temperature dependence of the ^{1}H NMR spectra. Only at 100°C in DMSO the signals became sufficiently clear for the identification. According to the spectral data, the molecule remains in the partial cone conformation.

Scheme 2.



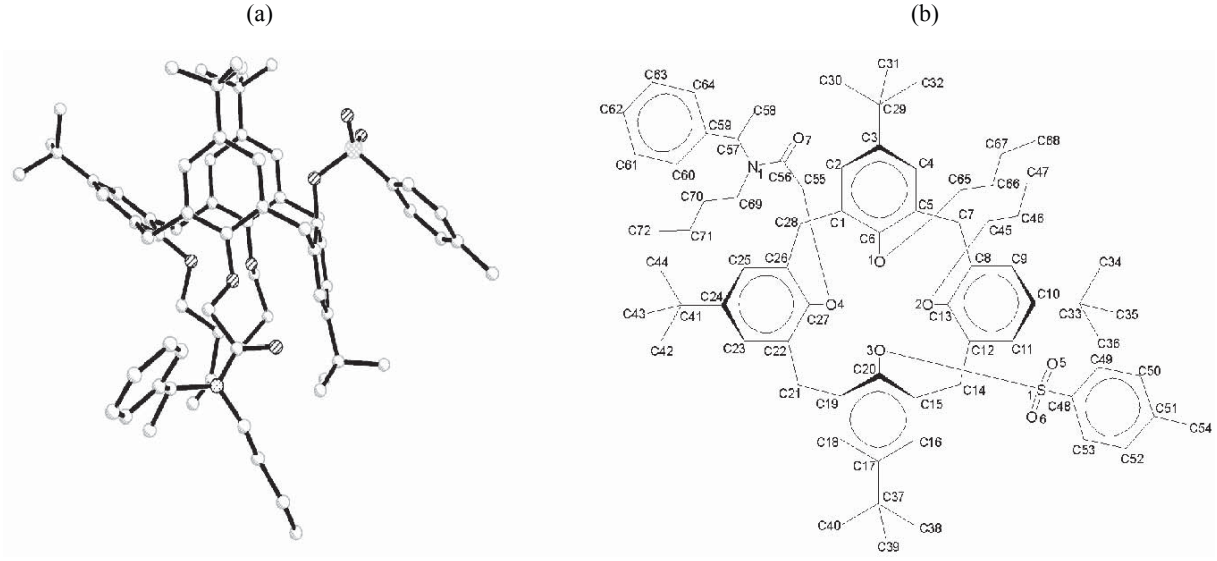


Fig. 4. Molecular structure of compound **IVa** (a) and the numeration of nonhydrogen atoms (b).

The NMR spectra of diastereomers **IVa, IVb** have close parameters. The difference is observed only in the signals corresponding to the dissimilar position of the chiral amide group with respect to the calixarene phenyl rings. The final proof of the structure of molecules was obtained by X-ray analysis (Fig. 4).

The molecule of compound **IVa**, like that of compound **III**, exists in the partial cone conformation where the benzene ring of the macrocycle bearing the toluenesulfoxide substituent is turned upside down. But unlike the structure of compound **III** the aromatic ring of the substituent does not enter into the calixarene cavity. This results in a significant change in the macrocycle conformation. The angle between the aromatic rings neighboring to the turned one decreases from 45–55° in molecule **III** to 7° in molecule **IV**a resulting in the deformation of the macrocycle. The presence of substituents in all aromatic rings causes the change in the orientation of the substituent containing the amide fragment. Its flat amide fragment is turned with respect to the aromatic ring of the macrocycle by 52.3(4)° (torsion angle $C^{55}O^{4}C^{27}C^{26}$). The butyl group attached to the nitrogen atom has the *anti*-conformation [torsion angles $N^{1}C^{69}C^{70}C^{71}$ –176.1(3)°, $C^{69}C^{70}C^{71}C^{72}$ 180.0(3)°]. The methyl group of this substituent is fixed in the *+ac* conformation with respect to the bond C^{56}–N^{1} [torsion angle $C^{56}N^{1}C^{57}C^{58}$ 121.2(3)°], and the phenyl ring is located in the *–ac* orientation with respect to the bond C^{56}–N^{1} and is turned with respect to the bond N^{1}–C^{57} [torsion angles $C^{56}N^{1}C^{57}C^{59}$ –110.2(3)°, $N^{1}C^{57}C^{59}C^{60}$ 45.4(4)°].

EXPERIMENTAL

Melting points were measured on a Boëtius heating block. ^{1}H NMR spectra were registered on a spectrometer Varian VXR-300 (299.943 MHz), ^{13}C NMR spectra, on a spectrometer Varian Gemini-2000 (100.607 MHz), external reference TMS. IR spectra were recorded on a spectrophotometer M-80. The reactions were carried out in anhydrous solvents under an argon atmosphere. The column chromatography was performed on silica gel purchased from Acros Organics (0.035–0.070 mm, pore diameter 6 nm).

5,11,17,23-Tetra(*p-tert*-butyl)-25,27-dihydroxy-28-propoxy-26-[*N*-(1-phenylethyl)carbamoylmethoxy] calix[4]arene (II). To a solution of 1 g (1.447 mmol) of propoxycalix[4]arene **I** in 40 ml of acetonitrile was added 0.120 g (0.868 mmol) of K_2CO_3 , and the mixture was strirred for 1 h at 70°C. Then 0.368 g (1.52 mmol) of bromoacetic acid (*S*)-*N*-(1-phenylethyl)amide was added. The reaction mixture was boiled for 16–18 h, the solvent was distilled off in a vacuum of a water-jet pump. The residue was dissolved in 10 ml of chloroform and washed with 25 ml of 1% solution of hydrochloric acid. The water layer was extracted with chloroform (2 × 5 ml). The organic extracts were washed with 10 ml of brine and dried with Na_2SO_4. Chloroform was distilled off in a vacuum. To remove the residual water twice 5 ml of benzene was added, and the solvent was evaporated in a vacuum. Yield 1.23 g (96%), mp 93–95°C. IR spectrum (KBr), ν, cm^{-1}: 3330 br (OH···OAlk), 1685 m (C=O).

^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 s [18H, 2 (*t*-Bu)], 0.98 t (3H, $OCH_2CH_2C\underline{H}_3$, ^3J 7.4 Hz), 1.30 s (9H, *t*-Bu), 1.31 s (9H, *t*-Bu), 1.65 d (3H, $CHC\underline{H}_3$, ^3J 7.2 Hz), 1.79 m (2H, $OCH_2C\underline{H}_2CH_3$), 3.28 d [1H, $ArC\underline{H}_2$ (H^e), ^2J 13.3 Hz], 3.35 d [3H, $ArC\underline{H}_2$($3H^e$), ^2J 13.3 Hz], 3.87 m (2H, $OC\underline{H}_2CH_2CH_3$), 4.14 d [1H, $ArC\underline{H}_2$ ($1H^a$), ^2J 13.3 Hz], 4.21 d [2H, $2ArC\underline{H}_2$ ($2H^a$), ^2J 13.3 Hz], 4.24 d [1H, $ArC\underline{H}_2$ ($1H^a$), ^2J 13.3 Hz], 4.48 d (1H, $OC\underline{H}_2CO$, ^2J 15.0 Hz), 4.53 d (1H, $OC\underline{H}_2CO$, ^2J 15.0 Hz), 5.29 m (1H, CH), 6.76 m ($4H_{arom}$), 7.05 m ($6H_{arom}$), 7.24 m ($3H_{arom}$), 7.43 s (1H, OH), 7.45 s (1H, OH), 8.77 d (1H, NH, ^3J 8.2 Hz). Found, %: C 80.07; H 8.36; N 1.75. $C_{57}H_{73}NO_5$. Calculated, %: C 80.34; H 8.63; N 1.64. According to ^{1}H NMR spectrum the compound was pure for further syntheses.

The sulfonylation of calix[4]arene II with 4-toluenesulfonyl chloride. A solution of 1 g (1.17 mmol) of calix[4]arene **II** in 15 ml of anhydrous pyridine was stirred for 1 h at room temperature, 1.3 g (6.82 mmol) of 4-toluenesulfonyl chloride was added, and the mixture was stirred for 30 min at room temperature till complete dissolution, then it was heated for 25 h at 90–100°C (the solution became dark-brown). The solvent was distilled off in a vacuum (at the bath temperature 90°C). To the brown oily residue was added 100 ml of cold 10% solution of hydrochloric acid, the mixture was stirred for 15 min and left standing for 24 h at 5–10°C. The separated precipitate was filtered off, washed with water, and dried in air. The yield of the diastereomeric mixture as a grey powder was 1.08 g (92%). The diastereomers were separated by column chromatography, eluent ethyl acetate–hexane, 1 : 6.

5,11,17,23-Tetra(*p-tert*-butyl)-25-hydroxy-27-[(4-methylphenyl)sulfonyloxy]-28-propoxy-26-[*N*-(1-phenylethyl)carbamoylmethoxy]calix[4]arene (IIIa). Yield 0.31 g (26%), mp 138–139°C (MeOH), R_f 0.12. IR spectrum (KBr), ν, cm^{-1}: 3330 br (OH), 1680 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.55 t (3H, $C\underline{H}_3CH_2CH_2O$, ^3J 7.4 Hz), 0.69 s (9H, *t*-Bu), 0.76 s (9H, *t*-Bu), 1.34 s (9H, *t*-Bu), 1.41 s (9H, *t*-Bu), 1.49 d [3H, $C\underline{H}_3$(Ph)CHNH, ^3J 6.8 Hz], 1.56–1.84 m (2H, $CH_3C\underline{H}_2CH_2O$), 2.14 s (3H, $C\underline{H}_3ArSO_2$), 3.22 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 12.4 Hz], 3.40 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 13.6 Hz] + 3.38–3.49 m (1H, $CH_3CH_2C\underline{H}_2O$), 3.66–3.74 m (1H, $CH_3CH_2C\underline{H}_2O$), 3.74 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 16.1 Hz)] 3.75 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 15.8 Hz], 3.84 d [1H, $ArC\underline{H}_2$ ($1H^a$), ^2J 13.6 Hz], 3.87 d [1H, NHC(O)$C\underline{H}_2$, ^2J 15.6 Hz], 4.15 d [1H, $ArC\underline{H}_2$ ($1H^a$), ^2J 15.8 Hz], 4.33 d [1H, $ArC\underline{H}_2$ ($1H^a$), ^2J 16.1 Hz], 4.40 d [1H, $ArC\underline{H}_2$ ($1H^a$), ^2J 12.4 Hz], 4.76 d [1H, NHC(O)$C\underline{H}_2$, ^2J 15.6 Hz], 5.08–5.20 m [1H, CH_3(Ph)C$\underline{H}$NH], 6.24 d (2H, $ArSO_2$, ^3J 8.4 Hz), 6.43 d (2H, $ArSO_2$, ^3J 8.4 Hz), 6.81 s ($2H_{arom}$), 6.85 s ($2H_{arom}$), 7.13 d ($1H_{arom}$, ^4J 2.2 Hz), 7.17 d ($1H_{arom}$, ^4J 2.2 Hz), 7.20–7.32 m [7H, $2H_{arom}$ + 5H, CH_3(Ph)CHNH], 8.03 s (1H, OH), 8.66 d (1H, NH, ^3J 7.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 10.05, 21.36, 21.89, 22.54, 30.96, 31.04, 31.71, 32.12, 32.72, 32.73, 33.86, 34.03, 34.28, 34.50, 38.97, 38.99, 49.12, 72.19, 75.60, 124.36, 125.45, 126.61, 126.21, 126.58, 126.65, 126.75, 126.93, 127.08, 127.33, 127.43, 128.24, 128.28, 128.99, 130.13, 131.68, 131.83, 132.42, 132.48, 134.38, 134.94, 135.16, 142.49, 142.71, 143.32, 143.61, 145.79, 147.23, 149.01, 149.53, 150.12, 153.59, 169.65. Found, %: C 76.67; H 7.25; N 1.56; S 3.30. $C_{64}H_{79}NO_7S$. Calculated, %: C 76.38; H 7.91; N 1.39; S 3.19.

5,11,17,23-Tetra(*p-tert*-butyl)-25-hydroxy-27-[(4-methylphenyl)sulfonyloxy]-26-propoxy-28-[*N*-(1-phenylethyl)carbamoylmethoxy]calix[4]arene (IIIb). Yield 0.45 g (38%), mp 73–75°C (MeOH–H_2O), R_f 0.08. IR spectrum (KBr), ν, cm^{-1}: 3330 br (OH), 1680 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.73 s (9H, *t*-Bu), 0.83 s (9H, *t*-Bu), 0.89 t (3H, $C\underline{H}_3CH_2CH_2O$, ^3J 7.4 Hz), 1.30–1.44 s (9H, *t*-Bu) + + s (9H, *t*-Bu) + m (2H, $CH_3C\underline{H}_2CH_2O$), 1.47 d [3H, $C\underline{H}_3$(Ph)CHNH, ^3J 6.8 Hz], 2.20 d (3H, $C\underline{H}_3ArSO_2$), 2.99 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 12.7 Hz], 3.39 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 13.7 Hz], 3.57–3.70 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 15.8 Hz] + m (1H, $CH_3CH_2C\underline{H}_2O$), 3.71–3.81 d [1H, $ArC\underline{H}_2$ ($1H^e$), ^2J 15.8 Hz] + d [1H, NHC(O)$C\underline{H}_2$, ^2J 14.9 Hz], 3.83–4.00 2 d [2H, $2ArC\underline{H}_2$ ($2H^a$), ^2J 13.7, 15.8 Hz] + m (1H, $CH_3CH_2C\underline{H}_2O$), 4.09 d [1H, $ArC\underline{H}_2$($1H^a$), ^2J 12.7 Hz], 4.25 d [1H, $ArCH_2$ ($1H^a$), ^2J 15.8 Hz], 4.69 d [1H, NHC(O)$C\underline{H}_2$, ^2J 14.9 Hz], 5.07–5.19 m [1H, CH_3(Ph)C$\underline{H}$NH], 6.53 d (2H, $ArSO_2$, ^3J 8.0 Hz), 6.61 d (2H, $ArSO_2$, ^3J 8.0 Hz), 6.73 s ($1H_{arom}$), 6.77 s ($1H_{arom}$), 6.85 s ($1H_{arom}$), 6.92 s ($1H_{arom}$), 7.01–7.36 m [7H, $2H_{arom}$ + 5H, CH_3(Ph)CHNH], 7.54 s (1H, OH), 8.52 d (1H, NH, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 10.21, 21.48, 22.12, 23.24, 31.05, 31.14, 31.82, 32.08, 32.36, 32.57, 33.90, 34.12, 34.24, 34.57, 38.61, 38.73, 48.83, 71.99, 75.99, 124.26, 125.48, 125.85, 126.34, 126.64, 126.75, 126.79, 126.82, 127.02, 127.11, 127.82, 128.24, 129.14, 129.93, 131.56, 131.59, 132.24, 132.26, 134.39, 134.82, 135.19, 142.51, 143.26, 143.27, 143.44, 144.02, 145.77, 147.24, 148.77, 149.53, 150.39, 153.03, 168.94. Found, %: C 76.58; H 8.13;

N 1.33; S 3.10. $C_{64}H_{79}NO_7S$. Calculated, %: C 76.38; H 7.91; N 1.39; S 3.19.

Alkylation of calix[4]arenes IIIa, IIIb with butyl bromide. A solution of 0.25 g (0.25 mmol) of calix[4]-arene **IIIa, IIIb** in 3 ml of anhydrous acetonitrile was added dropwise to a dispersion of 0.04 g (1.00 mmol) of sodium hydride in 4 ml of acetonitrile at room temperature stirring with a rate preventing vigorous foaming. After the addition of all solution the reaction mixture was stirred for 30 min at 40°C, to the dispersion 0.17 g (0.13 ml, 1.24 mmol) of butyl bromide in 3 ml of acetonitrile was added, and the reaction mixture was boiled over 4–5 h. The solvent was evaporated, the residue was dissolved in 5 ml of chloroform, the solution was washed with 10% hydrochloric acid solution till acidic reaction (2 × 2 ml), dried with Na_2SO_4, and evaporated. We obtained 0.26 g (92%) of yellow solid substance that was purified by column chromatography, eluent hexane–ethyl acetate, 6 : 1.

5,11,17,23-Tetra(*p-tert*-butyl)-26-[*N*-butyl-(1-phenylethyl)carbamoylmethoxy]-25-butoxy-27-[(4-methylphenyl)sulfonyloxy]-28-propoxycalix[4]arene (IVa). Yield 0.17 g (60%), mp 140–141°C (MeOH), R_f 0.40. IR spectrum (KBr), ν, cm^{-1}: 1670 (C=O). ^{1}H NMR spectrum (DMSO-d_6, 100°C), δ, ppm: 0.74 t (3H, $C\underline{H}_3CH_2CH_2CH_2N$, ^3J 7.2 Hz), 0.82 t (3H, $C\underline{H}_3CH_2CH_2CH_2O$, ^3J 7.4 Hz), 1.00 s (9H, *t*-Bu), 1.01 s (9H, *t*-Bu) + t (3H, $C\underline{H}_3CH_2CH_2O$, ^3J 7.4 Hz), 1.07–1.22 m (6H, $CH_3C\underline{H}_2C\underline{H}_2CH_2N$ + $CH_3C\underline{H}_2CH_2CH_2O$), 1.33 s (9H, *t*-Bu), 1.43 s (9H, *t*-Bu), 1.46 d [3H, $C\underline{H}_3$(Ph)CHNH, ^3J 7.0 Hz], 1.45–1.54 m (2H, $CH_3CH_2C\underline{H}_2CH_2O$), 1.76–1.89 m (2H, $CH_3C\underline{H}_2CH_2O$), 2.45 s (3H, $C\underline{H}_3ArSO_2$), 2.86–3.00 m (2H, $CH_3CH_2CH_2C\underline{H}_2N$), 3.03 d [2H, $2ArC\underline{H}_2$ (2H^e), ^2J 12.7 Hz], 3.32 d [1H, $ArC\underline{H}_2$ (1H^e), ^2J 13.6 Hz], 3.43–3.73 m [1H, $ArC\underline{H}_2$ (1H^e) + 1H, $ArC\underline{H}_2$ (1H^a) + 2H, $CH_3CH_2C\underline{H}_2O$ + 2H, $CH_3CH_2CH_2C\underline{H}_2O$], 3.88 d [1H, $ArC\underline{H}_2$ (1H^a), ^2J 13.6 Hz], 4.05 d [1H, $ArC\underline{H}_2$ (1H^a), ^2J 12.7 Hz], 4.12 d [1H, $ArC\underline{H}_2$ (1H^a), ^2J 12.7 Hz], 4.36 d [1H, $NHC(O)C\underline{H}_2$, ^2J 13.6 Hz], 4.49 d [1H, $NHC(O)C\underline{H}_2$, ^2J 13.6 Hz], 5.36–5.50 m [1H, CH_3(Ph)C$\underline{H}$NH], 6.53 br.s (2H$_{arom}$), 6.72 d (1H$_{arom}$, ^4J 2.5 Hz), 6.80 d (1H$_{arom}$, ^4J 2.5 Hz), 7.09 d (1H$_{arom}$, ^4J 2.4 Hz), 7.10 d (1H$_{arom}$, ^4J 2.4 Hz), 7.23–7.34 m [6H, 2H$_{arom}$ + 4H, $CH_3(\underline{Ph})CHNH$], 7.47 d (2H, $ArSO_2$, ^3J 8.3 Hz), 7.59 d [1H, $CH_3(\underline{Ph})CHNH$, ^3J 2.5 Hz], 7.69 d (2H, $ArSO_2$, ^3J 8.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 1118.7 (100) $[M]^+$, 1062.6 (50) $[M - Bu]^+$. Found, %: C 76.97; H 8.25; N 1.56; S 2.50. $C_{72}H_{95}NO_7S$. Calculated, %: C 77.31; H 8.56; N 1.25; S 2.87. *M* 1118.6.

5,11,17,23-Tetra(*p-tert*-butyl)-28-[*N*-butyl-(1-phenylethyl)carbamoylmethoxy]-25-butoxy-27-[(4-methylphenyl)sulfonyloxy]-26-propoxycalix[4]arene (IVb). Yield 0.18 g (63%), mp 112–113°C (MeOH–H_2O), R_f 0.45. IR spectrum (KBr), ν, cm^{-1}: 1670 (C=O). ^{1}H NMR spectrum (DMSO-d_6, 90°C), δ, ppm: 0.75 t (3H, $C\underline{H}_3CH_2CH_2CH_2N$, ^3J 7.2 Hz), 0.82 t (3H, $C\underline{H}_3CH_2CH_2CH_2O$, ^3J 7.4 Hz), 1.00 s (9H, *t*-Bu), 1.006 t (3H, $C\underline{H}_3CH_2CH_2O$, ^3J 7.4 Hz), 1.007 s (9H, *t*-Bu), 1.07–1.22 m (6H, $CH_3C\underline{H}_2C\underline{H}_2CH_2N$ + $CH_3C\underline{H}_2CH_2CH_2O$), 1.33 s (9H, *t*-Bu), 1.42 s (9H, *t*-Bu), 1.49 d [3H, $C\underline{H}_3$(Ph)CHNH, ^3J 7.0 Hz], 1.42–1.55 m (2H, $CH_3CH_2C\underline{H}_2CH_2O$), 1.76–1.90 m (2H, $CH_3C\underline{H}_2CH_2O$), 2.44 s (3H, $C\underline{H}_3ArSO_2$), 2.86–3.00 m (2H, $CH_3CH_2CH_2C\underline{H}_2N$), 3.03 d [2H, $2ArC\underline{H}_2$ (2H^e), ^2J 12.8 Hz], 3.30 d [1H, $2ArC\underline{H}_2$ (1H^e), ^2J 13.6 Hz], 3.43–3.74 m [1H, $ArC\underline{H}_2$ (1H^e) + 1H, $ArC\underline{H}_2$ (1H^a) + 2H, $CH_3CH_2C\underline{H}_2O$ + 2H, $CH_3CH_2CH_2C\underline{H}_2O$], 3.88 d [1H, $ArC\underline{H}_2$ (1H^a), ^2J 13.6 Hz], 4.05 d [1H, $ArC\underline{H}_2$ (1H^a), ^2J 12.8 Hz], 4.09 d [1H, $ArC\underline{H}_2$ (1H^a), ^2J 12.8 Hz], 4.38 d [1H, $NHC(O)C\underline{H}_2$, ^2J 13.4 Hz], 4.45 d [1H, $NHC(O)C\underline{H}_2$, ^2J 13.4 Hz], 5.33–5.48 m [1H, CH_3(Ph)C$\underline{H}$NH], 6.52 d (1H$_{arom}$, ^4J 2.5 Hz), 6.53 d (1H$_{arom}$, ^4J 2.5 Hz), 6.71 d (1H$_{arom}$, ^4J 2.5 Hz), 6.81 d (1H$_{arom}$, ^4J 2.5 Hz), 7.09 s (2H$_{arom}$), 7.23–7.32 m [6H, 2H$_{arom}$ + 4H, $CH_3(\underline{Ph})CHNH$], 7.47 d (2H, $ArSO_2$, ^3J 8.3 Hz), 7.61 d [1H, $CH_3(\underline{Ph})CHNH$, ^3J 2.5 Hz], 7.69 d (2H, $\underline{Ar}SO_2$, ^3J 8.3 Hz). Found, %: C 77.17; H 8.37; N 1.13; S 2.52. M^+ 1118.8. $C_{72}H_{95}NO_7S$. Calculated, %: C 77.31; H 8.56; N 1.25; S 2.87. *M* 1118.6.

X-ray diffraction experiment was carried out on an automatic diffractometer Xcalibur 3 (monochromated MoK_α radiation, CCD-detector, ω-scanning). The structures were solved by the direct method with the use of program package SHELXTL [15]. The configuration of diastereomers for all molecules was determined according to the known configuration of the chiral center on the atom C^{57} that did not change in the course of reactions. The restriction of bond lengths (C_{sp^3}–C_{sp^3} 1.54, C_{sp^3}–O 1.43 Å) was introduced in the refining of the position of the propyl and *tert*-butyl substituents with respect to the solvating methanol molecules in **IIIa** structure. The positions of hydrogen atoms were revealed from the difference synthesis of the electron density and were refined in the rider model with $U_{iso} = nU_{eq}$ (n = 1.5 for methyl and hydroxy groups, 1.2 for the other hydrogen atoms). In structure **IIIb** the hydrogen atoms involved into the hydrogen bonds formation were

Parameters	**IIIa, IIIb** (racemate)	**IIIa**	**IIIb**	**IVa**
Unit cell parameters				
a, Å	17.0672(6)	13.411(2)	13.1552(3)	9.8984(5)
b, Å	18.7837(6)	15.138(2)	15.0305(3)	13.6458(9)
c, Å	19.5752(8)	31.353(4)	28.6873(5)	13.9768(7)
α, deg	90	90	90	62.279(6)
β, deg	115.117(5)	90	90	74.448(4)
γ, deg	90	90	90	82.148(5)
V, Å^3	5682.1(4)	6365(1)	5672.3(2)	1609.8(2)
F(000)	2168	2384	2168	606
Crystal system	Monoclinic	Rhombic	Rhombic	Triclinic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$	P1
Z	4	4	4	1
T, K	100	100	100	100
μ, mm^{-1}	0.110	0.107	0.110	0.104
d_{calc}, g cm^{-3}	1.176	1.150	1.178	1.154
$2\Theta_{max}$, deg	50	50	60	60
Measured reflections	37298	35710	34685	16847
Independent reflections	19063	10891	16227	12414
R_{int}	0.084	0.164	0.060	0.043
Reflections with $F > 4\sigma(F)$	10523	5374	10740	9157
Refined parameters	1315	719	681	747
R_1	0.065	0.094	0.068	0.061
wR_2	0.135	0.178	0.110	0.129
S	0.911	0.907	0.951	0.983
CCDC number	816612	816610	816611	816613

refined in the isotropic approximation. Crystallographic data and the experimental parameters are presented in the table. The final atomic coordinates, geometric parameters, and crystallographic data are deposited in the Cambridge Crystallographic Data Centre, 11 Union Road, Cambridge, CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk). The registration data are given in the table.

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