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Synthesis, Structure and Selective Upper Rim Functionalization of Long Chained Alkoxythiacalix[4]arenes

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Abstract

The synthesis and X-ray structure investigation of the *cone* shaped monodecyloxythiacalix[4]arene, as well as the introduction of the reactive bromide or chloromethyl groups on it's upper rim are described. Preparation of the amphiphilic derivative of thiacalixarene bearing three hydrophilic diethoxyphosphoryl groups at the upper rim and lipophilic decyloxy group at the lower rim is presented.

Introduction

Thiacalix[4]arenes, as the new members of the well-known calix[4]arene family [1], have been intensively studied during the last decade [2–6]. The presence of four bridging sulfur atoms in the thiacalix[4]arene macrocyclic skeleton, instead of four methylene groups in the classical calix[4]arenes, increases the size of the molecular cavity and enables supplementary modification of the macrocyclic skeleton by the oxidation of the sulfur atoms [4, 7–9].

Calixarenes possessing long chain alkyl groups are promising platforms in the design of self-assembled systems such as: Langmuir or Langmuir–Blodgett films; nanoparticles; biomembrane modifiers etc. [1].

Some examples of the lower rim total or partial alkylation of thiacalix[4]arenes **1a,b** with methyl-, ethyl-, propyl- or butyl haloids are described in the literature [6, 10–13]. However, there is no example of the thiacalixarene lower rim functionalization with the long chain alkyl substituents.

In this article we describe the syntheses and structural examinations of the long chain (C_{10}, C_{12}) O-substituted thiacalix[4]arenes which can be used as the suitable platforms for the design of self-assembled systems. Regioselective functionalization of the *cone* shaped monodecyloxythiacalix[4]arene upper rim with three bromide, chloromethyl or diethoxyphosphoryl groups is presented.

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Experimental

Synthesis of **2a**, **2b** *and* **2c**

Decylbromide (8.91 g, 40.32 mmol, 8.40 ml) was added to a suspension of **1a** (1.00 g, 2.02 mmol) and K_2CO_3 (5.57 g, 40.40 mmol) in dry acetone (40 ml). The reaction mixture was refluxed at stirring for 40 h. About 1 N HCl was added to the mixture (pH < 7). Water layer was washed with chloroform (3×30 ml). The combined organic layers were dried over Na_2SO_4 and evaporated. Isopropyl alcohol (10 ml) was added and the crystalline residue was filtered, washed with isopropyl alcohol (2×5 ml) and dried for 2 h under vacuum (0.01 mmHg) at 50 °C. Compound **2a** (0.53 g, 25%) was obtained as a colorless crystalline product. Mp 75–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (t, 12H, J = 6.7 Hz, CH_3), 1.08 (m, 16H, $(CH_2)_2$–CH_3), 1.14–1.38 (m, 48H, $(CH_2)_6$–$(CH_2)_2$–CH_3), 3.86 (t, 8H, J = 6.6 Hz, O–CH_2), 6.81 (t, 4H, J = 7.7 Hz, H-arom.), 7.34 (d, 8H, J = 7.7 Hz, H-arom.); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.13 (s, CH_3), 22.73 (s, CH_2–CH_3), 25.75 (s, CH_2–CH_2–CH_3), 28.94 (s, CH_2–$(CH_2)_2$–CH_3), 29.50 (s, CH_2–$(CH_2)_3$–CH_3), 29.75 (s, $(CH_2)_3$–$(CH_2)_4$–CH_3), 32.01 (s, CH_2–$(CH_2)_7$–CH_3), 69.14 (s, O–CH_2), 122.67 (s, C-arom.), 128.86 (s, C-arom.), 131.59 (s, C-arom.), 159.84 (s, C-arom.). Anal. calcd for $C_{64}H_{96}O_4S_4$, %: C, 72.68; H, 9.15; S, 12.13. Found, %: C, 72.61; H, 8.88; S, 11.85.

In the same conditions, compound **2b** (68%) was obtained as a colorless crystalline product. Mp 165–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, 12H,

J = 6.7 Hz, CH_3), 0.99 (m, 8H, CH_2–CH_3), 1.00–1.40 (m, 92H, $(CH_2)_7$–CH_2–CH_3 and C(CH_3)$_3$), 3.82 (t, 8H, J = 6.6 Hz, O–CH_2), 7.31 (s, 8H, H-arom.); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.07 (s, CH_3), 22.69 (s, CH_2–CH_3), 25.88 (s, CH_2–CH_2–CH_3), 29.00 (s, CH_2–$(CH_2)_2$–CH_3), 29.30 (s, CH_2–$(CH_2)_3$–CH_3), 29.63 (s, CH_2–$(CH_2)_4$–CH_3), 29.75 (s, CH_2–$(CH_2)_5$–CH_3), 29.97 (s, CH_2–$(CH_2)_6$–CH_3), 31.38 (s, C(CH_3)$_3$), 31.93 (s, CH_2–$(CH_2)_7$–CH_3), 34.19 (s, $C(CH_3)_3$), 68.87 (s, O–CH_2), 127.65 (s, C-arom.), 128.10 (s, C-arom.), 145.28 (s, C-arom.), 157.22 (s, C-arom.). Anal. calcd for $C_{80}H_{128}O_4S_4$, %: C, 74.94; H, 10.06; S, 10.00. Found, %: C, 74.90; H, 10.12; S, 10.08.

In the same conditions, compound **2c** (70%) was obtained as a colorless crystalline product. Mp 160–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, 12H, J = 6.9 Hz, CH_3), 0.94–1.40 (m, 116H, $(CH_2)_{10}$–CH_3 and C(CH_3)$_3$), 3.81 (t, 8H, J = 7.3 Hz, O–CH_2), 7.30 (s, 8H, H-arom.). Anal. calcd for $C_{88}H_{144}O_4S_4$, %: C, 75.80; H, 10.41; S, 9.20. Found, %: C, 75.64; H, 10.37; S, 9.08.

X-ray crystallography data of **2a**, **2b** *and* **3**

Intensity data for the compounds **2a**, **2b** and **3** were collected at 200 K on a Bruker SMART-APEX diffractometer using $Mo_{K\alpha}$ radiation (λ = 0.7107 Å). Lorentz and polarization corrections were applied and diffracted data were also corrected for absorption using the SADABS program. The structures were solved by the direct methods and Fourier techniques. Structure solution and refinement were based on $|F|^2$. All non-hydrogen atoms were refined with anisotropic displacement parameters. The H atoms of the C–H groups were fixed in the calculated positions. The hydrogen atoms of the hydroxyl groups in three were located via difference Fourier map inspection and refined with riding coordinates and isotropic thermal parameters based upon the corresponding O atoms [U(H) = 1.2 Ueq (O)]. All crystallographic calculations were conducted with the SHELXTL 6.10 program package. The crystallographic data for the crystal structures has been deposited at the Cambridge Crystallographic Data Center and allocated the deposition numbers.

Crystal data for **2a**

Empirical formula $C_{64}H_{96}O_4S_4$, M = 1057.65 g mol^{-1}, triclinic, space group P-1, a = 13.724(2), b = 14.226(2), c = 19.299(2) Å, α = 106.712(3), β = 93.563(2), γ = 118.832(2) deg, U = 3071.7(6) Å^3, Z = 2, d_{calc} = 1.144 g cm^{-3}, μ = 0.199 mm^{-1}, F(000) = 1152, $2\theta_{max}$ = 48.32° ($-15 \le h \le 15$, $-16 \le k \le 16$, $-21 \le l \le 22$). Final residuals (for 653 parameters) were: $R1$ = 0.0773, $wR2$ = 0.1509 for 5091 reflections with $I > 2\sigma(I)$ and $R1$ = 0.1511, $wR2$ = 0.1836, GooF = 1.007 for all 9572 data (R_{int} = 0.0679). Residual electron density was 0.293 and −0.304 e Å^{-3}. CCDC 610205.

Crystal data for **2b**

Empirical formula $C_{80}H_{128}O_4S_4$, M = 1282.06 g mol^{-1}, monoclinic, space group $P2(1)/n$, a = 10.542(1), b = 41.885(3), c = 18.743(2) Å, β = 104.638(2) deg, U = 8007.7(10) Å^3, Z = 4, d_{calc} = 1.063 g cm^{-3}, μ = 0.163 mm^{-1}, F(000) = 2816, $2\theta_{max}$ = 50.14° ($-12 \le h \le 12$, $-49 \le k \le 38$, $-21 \le l \le 22$). Final residuals (for 809 parameters) were $R1$ = 0.0896, $wR2$ = 0.2030 for 6794 reflections with $I > 2\sigma(I)$ and $R1$ = 0.1821, $wR2$ = 0.2491, GooF = 1.022 for all 14166 data (R_{int} = 0.0913). Residual electron density was 0.404 and −0.327 e Å^{-3}. CCDC 610206.

Crystal data for **3**

Empirical formula $C_{34}H_{36}O_4S_4$, M = 636.87 g mol^{-1}, monoclinic, space group $P2(1)/c$, a = 12.1997(13), b = 13.5203(15), c = 19.1770(20) Å, β = 94.302(2) deg, U = 3154.3(6) Å^3, Z = 4, d_{calc} = 1.341 g cm^{-3}, μ = 0.339 mm^{-1}, F(000) = 1344, $2\theta_{max}$ = 50.06° ($-11 \le h \le 14$, $-14 \le k \le 16$, $-22 \le l \le 22$). Final residuals (for 380 parameters) were $R1$ = 0.0528, $wR2$ = 0.1178 for 3767 reflections with $I > 2\sigma(I)$ and $R1$ = 0.0849, $wR2$ = 0.1330, GooF = 1.033 for all 5565 data (R_{int} = 0.0480). Residual electron density was 0.421 and −0.340 e Å^{-3}. CCDC 610207.

Synthesis of **3**

Decylbromide (3.56 g, 16.13 mmol, 3.34 ml) was added to the suspension of **1a** (2.00 g, 4.03 mmol) and K_2CO_3 (0.83 g, 6.05 mmol) in dry acetone (120 ml). The reaction mixture was refluxed for 100 h at stirring. About 1 N HCl was added to the mixture (pH < 7). Water layer was washed with chloroform (3×50 ml). The combined organic fractions were dried over Na_2SO_4 and evaporated. Diethyl ether (20 ml) was added and the crystalline residue was filtered, washed with diethyl ether (3×5 ml) and dried for 1 h under vacuum (0.01 mmHg) at 100 °C. Compound **3** (1.53 g, 60%) was obtained as a colorless crystalline product. Mp 135–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.19–1.58 (m, 12H, $(CH_2)_6$–CH_3), 1.64 (m, 2H, CH_2–$(CH_2)_6$–CH_3), 2.16 (m, 2H, CH_2–$(CH_2)_7$–CH_3), 4.33 (t, 2H, J = 7.0 Hz, O–CH_2), 6.62 (t, 1H, J = 7.6 Hz, H-arom.), 6.73 (t, 2H, J = 7.6 Hz, H-arom.), 6.88 (t, 1H, J = 7.6 Hz, H-arom.), 7.43 (d, 2H, J = 7.6 Hz, H-arom.), 7.51 (d, 2H, J = 7.6 Hz, H-arom.), 7.62 (d, 4H, J = 7.6 Hz, H-arom.), 8.76 (s, 3H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.13 (s, CH_3), 22.71 (s, CH_2–CH_3), 25.73 (s, CH_2–CH_2–CH_3), 29.41 (s, $(CH_2)_2$–$(CH_2)_2$–CH_3), 29.62 (s, $(CH_2)_3$–$(CH_2)_4$–CH_3), 31.94 (s, CH_2–$(CH_2)_7$–CH_3), 78.92 (s, O–CH_2), 120.35 (s, C-arom.), 120.70 (s, C-arom.), 121.18 (s, C-arom.), 121.42 (s, C-arom.), 126.05 (s, C-arom.), 128.77 (s, C-arom.), 137.84 (s, C-arom.), 138.27 (s, C-arom.), 138.51 (s, C-arom.), 139.13 (s, C-arom.), 157.92 (s, C-arom.), 158.87 (s, C-arom.), 160.13 (s, C-arom.). Anal. calcd for $C_{34}H_{36}O_4S_4$, %: C, 64.12; H, 5.70; S, 20.14. Found, %:

C, 63.79; H, 5.73; S, 19.68. MS (FAB) *m/z* 637.0 ([M^+]); *m/z* 660.0 ([M + Na^+]).

Synthesis of **4**

NBS (0.84 g, 4.72 mmol) was added to the suspension of **3** (1.00 g, 1.57 mmol) in dry acetone (75 ml). The reaction mixture was stirred for 4 h at r.t. The crystalline residue was filtered, washed with acetone (2×5 ml) and diethyl ether (2×5 ml) and dried for 1 h under vacuum (0.01 mmHg) at 100 °C. Compound **4** (1.23 g, 90%) was obtained as a colorless crystalline product. (The use of methyl ethyl ketone as the solvent resulted in a lower yield, 50%). Mp 190–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 6.8 Hz, *CH_3*), 1.20–1.40 (m, 10H, *$(CH_2)_5$*–CH_3), 1.47 (m, 2H, *CH_2*–$(CH_2)_5$–CH_3), 1.60 (m, 2H, *CH_2*–$(CH_2)_6$–CH_3), 2.13 (m, 2H, *CH_2*–$(CH_2)_7$–CH_3), 4.30 (t, 2H, J = 7.1 Hz, O–*CH_2*), 7.00 (t, 1H, J = 7.8 Hz, H-arom.), 7.53 (s, 2H, H-arom.), 7.57 (d, 2H, J = 7.9 Hz, H-arom.), 7.74 (d, 2H, J = 2.2 Hz, H-arom.), 7.77 (d, 2H, J = 2.2 Hz, H-arom.), 8.44 (s, 1H, *OH*), 8.60 (s, 2H, *OH*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.08 (s, *CH_3*), 22.69 (s, *CH_2*–CH_3), 25.73 (s, *CH_2*–CH_2–CH_3), 29.37 (s, *$(CH_2)_2$*–$(CH_2)_2$–CH_3), 29.61 (s, *$(CH_2)_3$*–$(CH_2)_4$–CH_3), 31.94 (s, *CH_2*–$(CH_2)_7$–CH_3), 79.15 (s, O–*CH_2*), 110.97 (s, C-arom.), 111.80 (s, C-arom.), 121.84 (s, C-arom.), 122.43 (s, C-arom.), 122.77 (s, C-arom.), 126.69 (s, C-arom.), 128.05 (s, C-arom.), 139.46 (s, C-arom.), 139.73 (s, C-arom.), 139.99 (s, C-arom.), 140.52 (s, C-arom.), 157.22 (s, C-arom.), 157.92 (s, C-arom.), 160.01 (s, C-arom.). Anal. calcd for $C_{34}H_{33}Br_3O_4S_4$, %: C, 46.75; H, 3.81; Br, 27.44; S, 14.68. Found, %: C, 46.90; H, 4.03; Br, 27.83; S, 15.21. MS (FAB) *m/z* 876.0 ([M^+]); m/z 896.8 ([M + Na^+]).

Synthesis of **5**

$SnCl_4$ (1.64 g, 6.29 mmol, 0.74 ml) and methyl chloromethyl ether (1.01 g, 12.58 mmol, 0.96 ml) were added to the solution of **3** (0.20 g, 0.31 mmol) in dry chloroform (20 ml). The reaction mixture was stirred for 24 h at r.t. Distilled water (40 ml) was added to the mixture. Water layer was washed with chloroform (2×20 ml). The combined chloroform layers were washed with water (1×20 ml), dried over Na_2SO_4 and evaporated. Obtained colorless oil was dissolved in chloroform (3 ml). Hexane (40 ml) was added and the solid impurity was filtered-off. The solution was evaporated and the procedure was repeated. Obtained residue was dried for 1 h under vacuum (0.01 mmHg) at 100 °C. Compound **5** (0.10 g, 41%) was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 6.8 Hz, *CH_3*), 1.16–1.54 (m, 12H, *$(CH_2)_6$*–CH_3), 1.62 (m, 2H, *CH_2*–$(CH_2)_6$–CH_3), 2.14 (m, 2H, *CH_2*–$(CH_2)_7$–CH_3), 4.33 (t, 2H, J = 7.1 Hz, O–*CH_2*), 4.36 (s, 2H, *CH_2Cl*), 4.47 (s, 4H, *CH_2Cl*), 6.96 (t, 1H, J = 7.9 Hz, H-arom.), 7.50 (s, 2H, H-arom.), 7.58 (d, 2H, J = 7.7 Hz, H-arom.), 7.65 (d, 2H, J = 2.1 Hz, H-arom.), 7.68 (d, 2H, J = 2.1 Hz, H-arom.), 8.81 (s, 1H, *OH*), 8.86 (s, 2H, *OH*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.15 (s, *CH_3*), 22.71 (s, *CH_2*–CH_3), 25.72 (s, *CH_2*–CH_2–CH_3), 29.39 (s, *CH_2*–$(CH_2)_2$–CH_3), 29.61 (s, *$(CH_2)_2$*–$(CH_2)_3$–CH_3), 29.69 (s, *$(CH_2)_2$*–$(CH_2)_5$–CH_3), 31.93 (s, *CH_2*–$(CH_2)_7$–CH_3), 44.91 (s, *CH_2Cl*), 45.02 (s, *CH_2Cl*), 79.09 (s, O–*CH_2*), 120.65 (s, C-arom.), 121.15 (s, C-arom.), 121.40 (s, C-arom.), 126.40 (s, C-arom.), 128.44 (s, C-arom.), 129.76 (s, C-arom.), 130.49 (s, C-arom.), 138.13 (s, C-arom.), 138.43 (s, C-arom.), 138.89 (s, C-arom.), 139.52 (s, C-arom.), 158.07 (s, C-arom.), 158.89 (s, C-arom.), 160.20 (s, C-arom.).

Synthesis of **6**

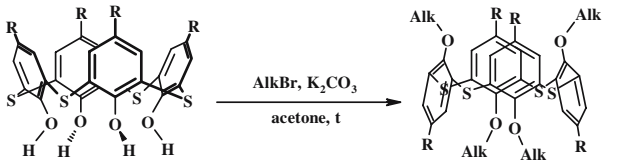
Triethyl phosphite (0.34 g, 2.05 mmol, 0.35 ml) was added to the solution of **5** (0.10 g, 0.13 mmol) in dry chloroform (10 ml). The reaction mixture was stirred for 4 h at r.t. The solvent was evaporated under vacuum (10 mmHg) at r.t. Hexane (10 ml) was added to the residue and the mixture was stirred for 1 h. The hexane layer was poured out. The procedure was repeated twice. The obtained residue was dried for 1 h under vacuum (0.01 Hgmm) at 100 °C. Compound **6** (0.10 g, 71%) was obtained as a colorless glassy product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 6.5 Hz, *CH_3*), 1.13 (t, 6H, J = 7.0 Hz, O–CH_2–*CH_3*), 1.18–1.54 (m, 24H, *$(CH_2)_6$*–CH_3 and O–CH_2–*CH_3*), 1.62 (m, 2H, *CH_2*–$(CH_2)_6$–CH_3), 2.15 (m, 2H, *CH_2*–$(CH_2)_7$–CH_3), 2.85 (d, 2H, ^2J = 21.7 Hz, *CH_2*–P), 2.99 (d, 4H, ^2J = 21.4 Hz, *CH_2*–P), 3.80–4.17 (m, 12H, *CH_2*–O–P), 4.33 (t, 2H, J = 7.3 Hz, O–*CH_2*), 6.90 (t, 1H, J = 7.8 Hz, H-arom.), 7.40 (s, 2H, H-arom.), 7.47–7.66 (m, 6H, H-arom.), 8.74 (s, 3H, *OH*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.04 (s, *CH_3*), 16.28 (s, O–CH_2–*CH_3*), 22.59 (s, *CH_2*–CH_3), 25.64 (s, *CH_2*–CH_2–CH_3), 29.24 (s, *CH_2*–$(CH_2)_2$–CH_3), 29.32 (s, *CH_2*–$(CH_2)_3$–CH_3), 29.49 (s, *$(CH_2)_2$*–$(CH_2)_4$–CH_3), 29.60 (s, *CH_2*–$(CH_2)_6$–CH_3), 31.82 (s, *CH_2*–$(CH_2)_7$–CH_3), 32.16 (d, ^1J = 141.0 Hz, *CH_2*–P), 62.09 (d, ^2J = 6.4 Hz, *CH_2*–O–P), 78.91 (s, O–*CH_2*), 120.49 (s, C-arom.), 121.11 (s, C-arom. (two types)), 123.57 (d, ^2J = 8.9 Hz, *C-arom.*–CH_2–P), 124.37 (d, ^2J = 8.7 Hz, *C-arom.*–CH_2–P), 125.96 (s, C-arom.), 128.64 (s, C-arom.), 138.76 (d, ^3J = 6.2 Hz, *C-arom.*–CH_2–P), 139.09–139.33 (m, *C-arom.* (two types)), 139.63 (d, ^3J = 6.2 Hz, *C-arom.*–CH_2–P), 156.82 (s, C-arom.), 157.66 (s, C-arom.), 160.14 (s, C-arom.). ^{31}P NMR (121 MHz, $CDCl_3$): δ 26.4.

Results and discussion

The exhaustive alkylation of thiacalixarenes **1a,b** with 20-fold excess of decyl or dodecyl bromides (Scheme 1) was achieved by reflux in acetone in the presence of the excess of potassium carbonate. The tetralkylated thiacalixarenes **2a**–**c** (*1,3-alternate*) were obtained as the colorless crystalline products (25–70% yield).

In solutions the *1,3-alternate* conformation is characterized by the high field resonance of –CH_2 protons (δ

3.81–3.86 ppm) in the ^{1}H NMR spectra ($CDCl_3$, 25 °C) according to the shielding effect of two neighboring benzene rings [11, 13].



1a,b

2a R = H; Alk = $C_{10}H_{21}$
2b R = *t*-Bu; Alk = $C_{10}H_{21}$
2c R = *t*-Bu; Alk = $C_{12}H_{25}$

Scheme 1.

Single crystals of **2a** and **2b** were obtained by the crystallization from *n*-hexane and their structure was solved by X-ray diffraction. The molecular structures (Figures 1a and 2a) confirm that both molecules, in the solid state, are in the *1,3-alternate* conformation. The average C–S distances in **2a** and **2b** are 1.77 Å with average C–S–C angles of 108.8° and 107.2°, respectively. In both structures, the geometry of the macrocycles is highly symmetrical, the distances between the *para*-carbons of the aromatics rings are 7.47 Å, 7.61 Å for **2a** and 7.18 Å, 7.38 Å for **2b**.

For **2a**, with regard to the aliphatic chains, they are symmetrically elongated with all dihedral angles in the range of 172.0–180.0°. In the case of **2b**, the chains show lower symmetry: only one chain is elongated (dihedral angles 169.0–180.0°). The packing of **2a** and **2b** are shown in Figures 1b and 2b, respectively. The structures are stabilized exclusively

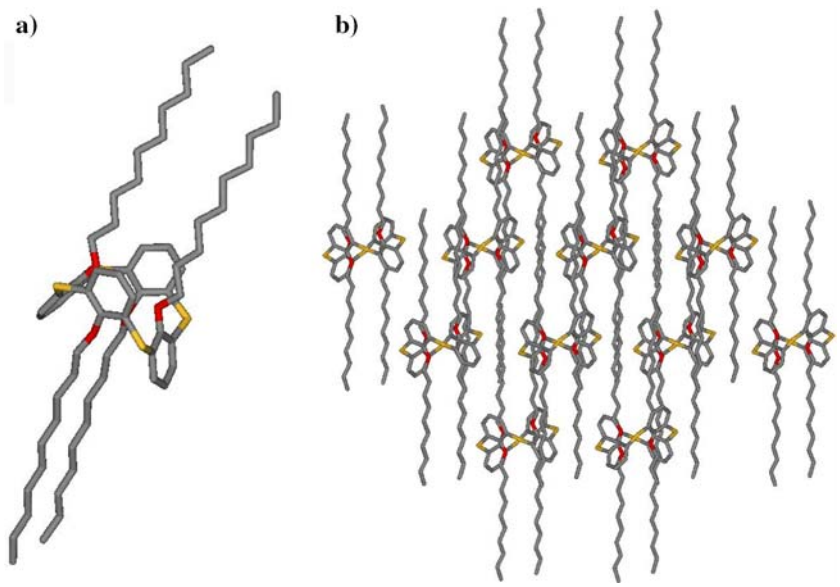


Figure 1. (a) Molecular structure of tetradecyloxythiacalix[4]arene **2a**; (b) View of the packing of **2a**.

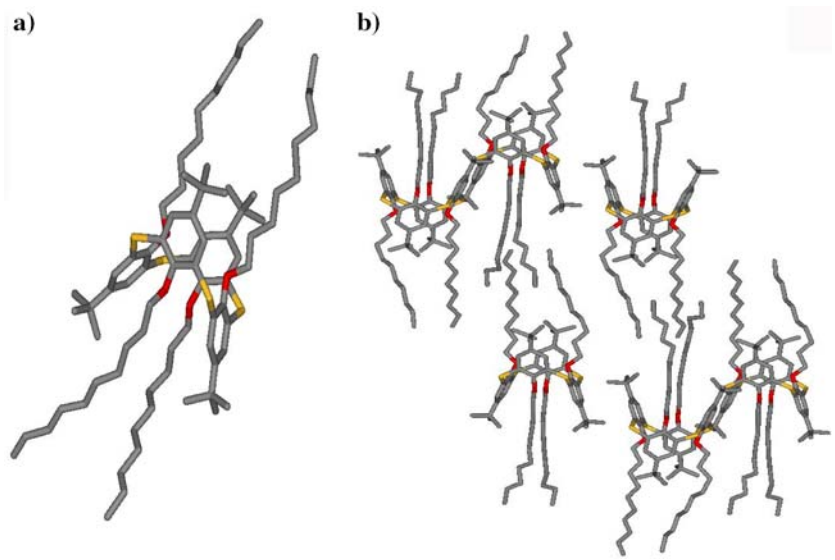


Figure 2. (a) Molecular structure of tetra-*tert*-butyl-tetradecyloxythiacalix[4]arene **2b**; (b) View of the packing of **2b**.

Table 1. Products distribution for the decylaltion of thiacalix[4]arene **1a** ($C_{10}H_{21}Br$, K_2CO_3, acetone)

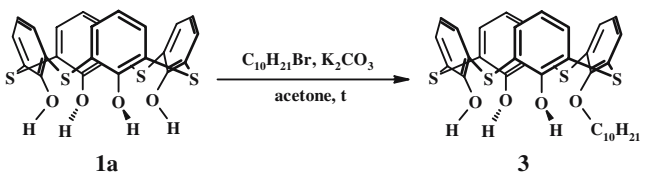
No.	*n*-$C_{10}H_{21}Br$ Ratio (mol/mol **1a**)	K_2CO_3	Volume of the solvent (acetone), (ml/g **1a**)	Time (h)	Products distribution (%)[a]		
					Mono-**3**	Tetra-**2a**	Parent-**1a**
1	20	20	40	40	45	55(25[b])	0
2	20	0.5	40	50	0	0	100
3	20	20	40	5	10	0	90
4	2	1	60	50	60	0	40
5	2	1	60	100	85	0	15
6	3	1.5	60	100	90	10	0
7	4	1.5	60	100	95(60[b])	5	0

[a]Determined by the ^{1}H NMR method.
[b]Yield of the isolated product.

by Van der Waals forces (all intermolecular distances are above 4.30 Å).

The alkylation process with the long chained alkyl bromides is slower in comparison to the alkylation by the lower (C_1–C_4) alkyl bromides [6, 10–14]. This regularity was successfully used for the selective lower rim decylation of thiacalix[4]arene.

Varying of the reaction conditions (Table 1), resulted in obtaining of monodecyloxythiacalix[4]arene **3** in satisfactory yield (60%) as a colorless crystalline product (Scheme 2).



Scheme 2.

Monodecyloxythiacalix[4]arene **3**, due to the circular system of the intramolecular hydrogen bonds O–H···O at the lower rim, keeps the initial *cone* conformation [4].

The ^{1}H NMR spectra of compound **3** (*cone* conformer) have signals of the characteristic protons of the –CH_2 fragments in the rather low field (δ 4.33 ppm) in comparison with the *1,3-alternate* conformer **2a** (δ 3.86 ppm). The same low field shifts are observed for some further methylen fragments of the decyloxy group (see experimental), which is completely correlated with the theory of the shielding and deshielding effects [11, 13]. Finally the *cone* conformation of **3** was confirmed by X-ray crystallography (Figure 3a, b).

Suitable crystals for X-ray diffraction of **3** were grown from *n*-hexane. In contrast to **2a** and **2b**, **3** is presented in the *cone* conformation. Hydrogen bonds between the phenolic units (distances between oxygen atoms are: 2.82 Å, 2.86 Å, 2.89 Å and 2.93 Å) reinforce the *flattened cone* conformation with angles between the opposite aromatic rings of 113.4° and 31.0° and *para*-carbon-*para*-carbon distances of 10.23 Å and 6.88 Å. The single alkyl chain is bent back across the lower rim of the macrocycle.

The packing represented in Figure 3b, shows that the structural motif is an interdigitated dimer with an interdigitation angle of 167.3°. This is close to the angle of 158.8° seen in the ubiquitous dimeric structural motif of calix[4]arene *bis*-dihydroxyphosphonic acid [15]. The macrocyclic dimers are arranged in layers, (interlayer distance 12.20 Å) separated by the folded alkyl chains.

The *cone* conformation of **3** gives a possibility to design amphiphilic derivatives by functionalyzation of the upper rim with hydrophilic groups. The reactive bromide or chloromethyl groups were introduced for this aim [16].

The regioselective bromination of trihydroxy-monodecyloxythiacalix[4]arene **3** at the *para*-position of the non-alkylated phenolic rings with NBS in the acetone solution (Scheme 3) gives trihydroxy-monodecyloxy-tribromothiacalix[4]arene **4** in 90% yield as a colorless crystalline substance.

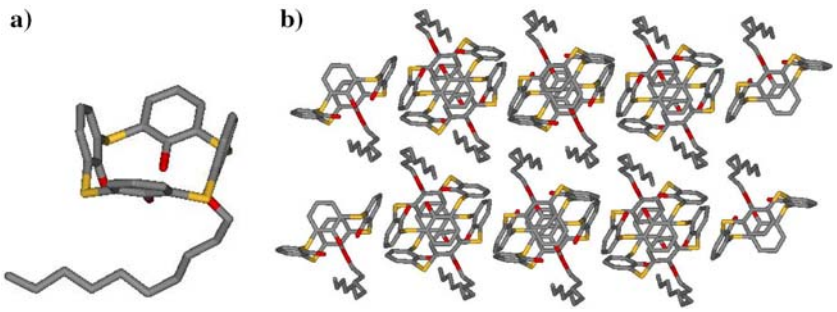
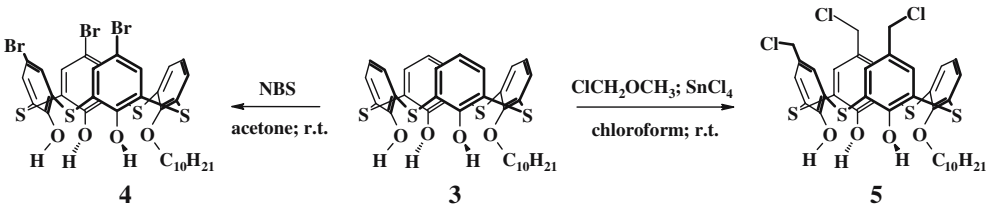


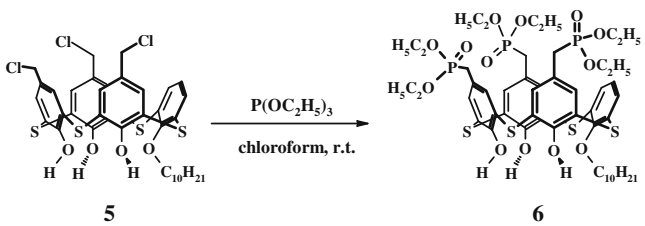
Figure 3. (a) Molecular structure of monodecyloxythiacalix[4]arene **3**; (b) View of the packing of **3**.



Scheme 3.

Three chloromethyl groups were selectively introduced into the same *para*-positions by the reaction of **3** with an excess of methyl chloromethyl ether and tin tetrachloride in the chloroform solution (Scheme 3). Trihydroxy-monodecyloxy-trichloromethylthiacalix[4]arene **5** was obtained in 41% yield as a colorless oil.

These functionalities allow further modification of the macrocycle upper rim by the bromine (catalytic) or chlorine replacement with different nucleophilic groups [17–20]. For example, the Arbuzov reaction of chloromethylthiacalix[4]arene **5** with triethyl phosphite in the chloroform solution leads to chlorine atoms substitution with the hydrophilic diethoxyphosphoryl groups. The amphiphilic triphosphorylated derivative was obtained in a good yield (71%) as a colorless glassy product (Scheme 4).



Scheme 4.

The ^{1}H NMR spectra of **4–6** confirms the *cone* conformation. The signals of the decyloxy group are situated in rather low field: O–CH_2–CH_2–CH_2 (δ 1.60–1.64 ppm); O–CH_2–CH_2 (δ 2.13–2.16 ppm); O–CH_2 (δ 4.30–4.33 ppm).

Conclusion

In conclusion, we have described the first efficient methods of the synthesis of the *cone* shaped monodecyloxythiacalix[4]arene **3** and its upper rim tribromo- and trichloromethyl-derivatives **4** and **5**. It was shown that monodecyloxy-trichloromethylthiacalix[4]arene **5** is convenient starting material for the synthesis of the amphiphilic thiacalix[4]arene derivatives. The preparation of tetrakis-decyl(dodecyl)oxythiacalix[4]arenes **2a–c** in *1,3-alternate* conformation is also presented.

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