

## **Simple synthesis of calix[4]arenes in a *1,2-alternate* conformation**

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**Example of the synthetic procedure:**

Potassium trimethylsilanolate (4.36 g, 34.0 mmol, 5 eq.) was added to a stirred solution of **2** (5.0 g, 6.8 mmol) in 300 ml of dry THF and the reaction mixture was stirred at room temp. After 30 min, 3.32 ml (5.78 g, 34.0 mmol, 5 eq.) of propyl iodide was added and the reaction mixture was stirred at room temp. for 5 days. The reaction mixture was then poured into 250 ml of 10% aqueous HCl and solution was extracted with 4 x 40 ml of DCM. Organic layers were combined, washed subsequently with 50 ml of saturated solution of Na<sub>2</sub>SO<sub>3</sub> and 50 ml of water, and dried over MgSO<sub>4</sub>. Solvents were evaporated to dryness and the crude product was purified by column chromatography on silica gel using DCM:petroleum ether 1:10 (v:v) mixture as eluent to give 3.60 g (65 %) of **3a** as white powder.

***1,2-alternate 25,26,27,28-tetrapropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene 3a***

Isolated: 3.60 g of **3a** from 5.00 g of starting compound **2** (65 % yield) using the above-mentioned synthetic procedure.

Mp= 280-284 °C, lit<sup>[1]</sup> 279-280 °C.

<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23 °C )

0.59 (t, 12 H, *J* = 7.4 Hz, 4 × -CH<sub>3</sub>); 0.86-0.91 (m, 8 H, 4 × -CH<sub>2</sub>-); 1.30 (s, 36 H, 4 × <sup>t</sup>Bu); 3.10 (d, 2H, -CH<sub>2</sub>-, *J* = 12.4 Hz); 3.24-3.40 (m, 8 H, -OCH<sub>2</sub>); 3.86 (s, 4 H, -CH<sub>2</sub>-); 4.18 (d, 2 H, *J* = 12.1 Hz, -CH<sub>2</sub>-); 7.01 (d, 4 H, *J* = 2.2 Hz, Ar-H); 7.14 (d, 4 H, *J* = 2.2 Hz, Ar-H)

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 23 °C )

10.02; 22.32; 29.19; 31.65; 33.94; 39.20; 74.33; 125.28; 125.66; 132.00; 133.79; 143.72; 154.14

TOF MS ESI+ (CH<sub>3</sub>OH)

C<sub>56</sub>H<sub>80</sub>O<sub>4</sub> required: 816.6; found: 839.7 [M+Na]<sup>+</sup> 100%

IR (KBr pellet)

2960 (vs); 2873 (m); 1472 (m); 1210 (m)

***1,2-alternate 27,28-dibutyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene (3b)***

Isolated: 0.317 g of **3b** from 0.500 g of starting compound **2** (55 % yield) using the above-mentioned synthetic procedure with 5 equivs. of KHMDS instead of Me<sub>3</sub>SiOK.

Mp= 260 – 263 °C

<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23 °C )

0.60 (t, 6 H, *J* = 7.2 Hz, 2 × -CH<sub>3</sub>); 0.79 (t, 6 H, *J* = 7.2 Hz, 2 × -CH<sub>3</sub>); 1.06-1.13 (m, 12 H, 6 × -CH<sub>2</sub>-); 1.29 (s, 18 H, 2 × <sup>t</sup>Bu); 1.30 (s, 18 H, 2 × <sup>t</sup>Bu); 3.08 (d, 1H, -CH<sub>2</sub>-, *J* = 12.0 Hz); 3.10 (d, 1H, -CH<sub>2</sub>-, *J* = 12.0 Hz); 3.21-3.44 (m, 8 H, -OCH<sub>2</sub>); 3.85 (s, 4H, 2 × -CH<sub>2</sub>-); 4.14 (d, 1 H, *J* = 12.1 Hz, -CH<sub>2</sub>-); 4.17 (d, 1 H, *J* = 12.1 Hz, -CH<sub>2</sub>-); 6.99 (d, 2 H, *J* = 2.6 Hz, Ar-H); 7.00 (d, 2 H, *J* = 2.6 Hz, Ar-H); 7.13 (d, 2 H, *J* = 2.4 Hz, Ar-H); 7.17 (d, 2 H, *J* = 2.4 Hz, Ar-H)

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 23 °C )

9.98; 13.98; 18.95; 22.21; 29.05; 29.24; 31.01; 31.66; 33.94; 39.20; 72.49; 74.39; 125.30; 125.56; 125.66; 131.90; 132.06; 133.69; 133.87; 143.69; 154.03; 154.38

TOF MS ESI+ (CH<sub>3</sub>OH)

C<sub>58</sub>H<sub>84</sub>O<sub>4</sub> required: 844.7 ; found: 867.6 [M+Na]<sup>+</sup> 100%; 869.7 [M+K]<sup>+</sup> 10%

IR (KBr pellet)

2959 (vs); 2871 (m); 1477 (m); 1207 (m)

***1,2-alternate 27,28-dihexyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene 3c***

Isolated: 0.167 g of **3c** from 0.200 g of compound **2** (68 % yield), using the above-mentioned synthetic procedure with 5 equivs. of KHMDS instead of Me<sub>3</sub>SiOK.

Mp= 181-184 °C

<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23 °C )

0.59 (t, 6 H, *J* = 7.2 Hz, 2 × -CH<sub>3</sub>); 0.83 (t, 6 H, *J* = 7.2 Hz, 2 × -CH<sub>3</sub>); 1.30 (brs, 36 H, 4 × <sup>t</sup>Bu); 1.08-1.16 (m, 8 H, 4 × -CH<sub>2</sub>-); 1.20-1.28 (m, 12 H, 6 × -CH<sub>2</sub>-); 3.09 (d, 1H, -CH<sub>2</sub>-, *J* = 12.2 Hz); 3.11 (d, 1H, -CH<sub>2</sub>-, *J* = 12.2 Hz); 3.21-3.44 (m, 8 H, -OCH<sub>2</sub>); 3.86 (bs, 4 H, -CH<sub>2</sub>-); 4.14 (d, 1 H, *J* = 12.1 Hz, -CH<sub>2</sub>-); 4.18 (d, 1 H, *J* = 12.1 Hz, -CH<sub>2</sub>-); 6.99 (d, 2 H, *J* = 2.6 Hz, Ar-H); 7.00 (d, 2 H, *J* = 2.6 Hz, Ar-H); 7.14 (d, 2 H, *J* = 2.4 Hz, Ar-H); 7.17 (d, 2 H, *J* = 2.4 Hz, Ar-H)

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 23 °C )

9.98; 14.00; 22.21; 22.81; 25.50; 29.09; 29.22; 31.67; 33.93; 39.21; 72.79; 74.38; 125.29; 125.53; 125.64; 131.89; 132.06; 133.70; 133.86; 143.68; 143.71; 154.00; 154.35

TOF MS ESI+ (CH<sub>3</sub>OH)

C<sub>62</sub>H<sub>92</sub>O<sub>4</sub> required: 900.7; found: 923.8 [M+Na]<sup>+</sup> 100%, 939.8 [M+K]<sup>+</sup> 12%

IR (KBr pellet)

2958 (vs); 2929 (s); 1470 (m); 1208 (m)

**1,2-alternate 27,28-dibenzyloxy-25,26-dipropoxy-5,11,17,23-tetra-*tert*-butylcalix[4]arene (3d)**

Isolated: 0.202 g of **3d** from 0.300 g of compound **2** (54% yield), using the above-mentioned synthetic procedure with 5 equivs. of KHMDS instead of Me<sub>3</sub>SiOK.

Mp= 216 - 220 °C

<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23 °C )

0.60 (brs, 6 H, 2 × -CH<sub>3</sub>); 0.93 (brs, 4 H, -CH<sub>2</sub>-); 1.16 (s, 18 H, 2 × <sup>t</sup>Bu); 1.32 (s, 18 H, 2 × <sup>t</sup>Bu); 3.02 (d, 1H, -CH<sub>2</sub>-, *J* = 12.4 Hz); 3.13 (d, 1H, -CH<sub>2</sub>-, *J* = 12.4 Hz); 3.18-3.24 (m, 4 H, -OCH<sub>2</sub>); 3.70 and 3.72 (2 × d, 4 H, *J* = 12.4 Hz, -CH<sub>2</sub>-); 4.11 (d, 1 H, *J* = 12.4 Hz, -CH<sub>2</sub>-); 4.17 (d, 1 H, *J* = 12.6 Hz, -CH<sub>2</sub>-); 4.47 (s, 4 H, -O-CH<sub>2</sub>-Ph); 6.71 (d, 4 H, *J* = 7.4 Hz, *o*-Ph-H); 6.76 (d, 2 H, *J* = 2.2 Hz, Ar-H); 6.95 (t, 4 H, *J* = 7.6 Hz, *m*-Ph-H); 7.01 (d, 2 H, *J* = 2.2 Hz, Ar-H); 7.08 (t, 2 H, *J* = 7.6 Hz, *p*-Ph-H); 7.13 (d, 2 H, *J* = 2.4 Hz, Ar-H); 7.25 (d, 2 H, *J* = 2.4 Hz, Ar-H)

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 25 °C )

10.00; 21.70; 29.41; 30.07; 31.48; 31.68; 33.86; 33.98; 38.82; 74.31; 75.11; 125.16; 125.58; 125.81; 125.94; 126.42; 127.09; 127.79; 132.17; 132.58; 133.53; 134.33; 138.64; 144.03; 144.18; 153.91; 154.55

TOF MS ESI+ (CH<sub>3</sub>OH)

C<sub>64</sub>H<sub>80</sub>O<sub>4</sub> required: 912.6; found: 935.7 [M+Na]<sup>+</sup> 100%; 951.7 [M+K]<sup>+</sup> 3%

IR (KBr pellet)

2960 (vs); 2871 (m); 1480 (m); 1201 (m)

**Crystallographic data:**



**Compound 3a:** C<sub>56</sub>H<sub>80</sub>O<sub>4</sub>, M = 817.20 g.mol<sup>-1</sup>, triclinic system, space group P-1, *a* = 9.771(4) Å, *b* = 13.056(5) Å, *c* = 20.194(10) Å, α = 79.31(4)°, β = 80.22(5)°, γ = 84.12(5)°, Z = 2, V = 2488.0(19) Å<sup>3</sup>, D<sub>c</sub> = 1.091 g.cm<sup>-3</sup>, μ(Cu-Kα) = 0.506 mm<sup>-1</sup>, crystal dimensions of 0.06 x 0.18 x 0.32 mm. Data were collected at 150(2) K on a Xcalibur PX diffractometer with graphite monochromated Cu Kα radiation. The structure was solved by direct methods<sup>[1]</sup> using the SHELX suite of programs<sup>[2]</sup> and anisotropically refined by full-matrix least-squares on F<sup>2</sup> values to final *R* = 0.1125 and *R*<sub>w</sub> = 0.3084 using 9889 independent reflections (*θ*<sub>max</sub> = 77.92°) and 615 parameters. The positions of disordered groups were found from the electron density maps. Disordered fragments were then placed in appropriate

positions, and all distances between neighbouring atoms and angles were fixed. Site occupancies were refined for the different parts with the same thermal parameters for the same atoms in the various fragments. At the end of refinement, site occupancies were fixed and hydrogen atoms were placed in calculated positions. The structure was deposited into the CCD under CCDC number 666975.

### Compound 3d

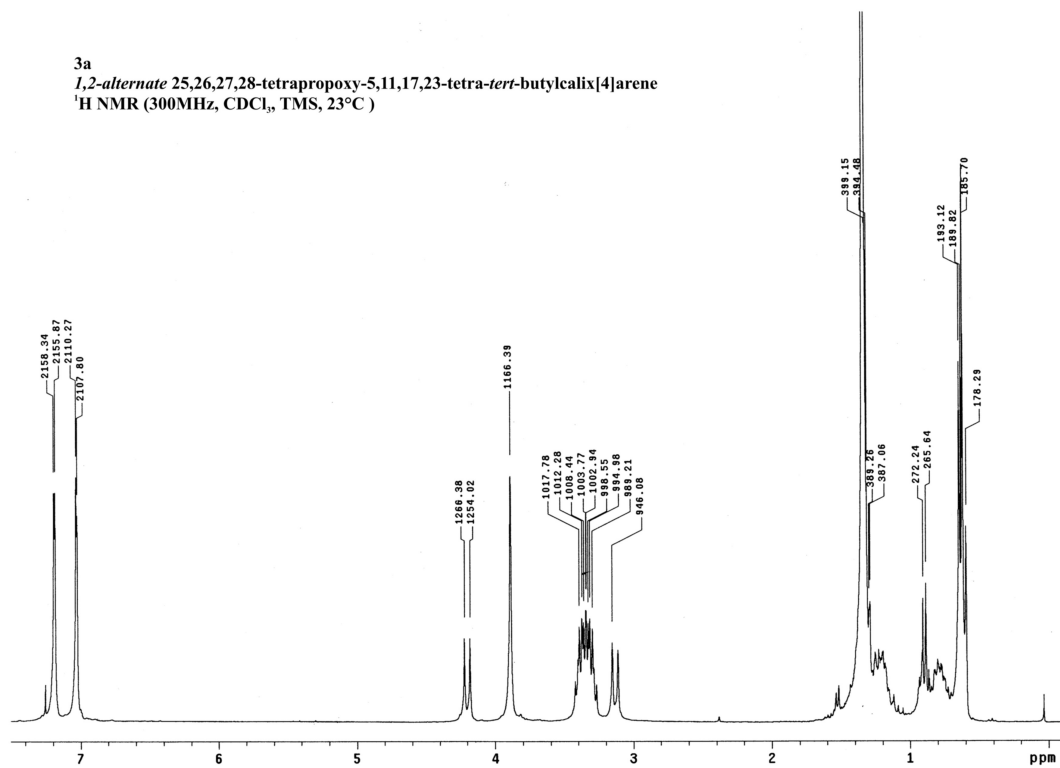


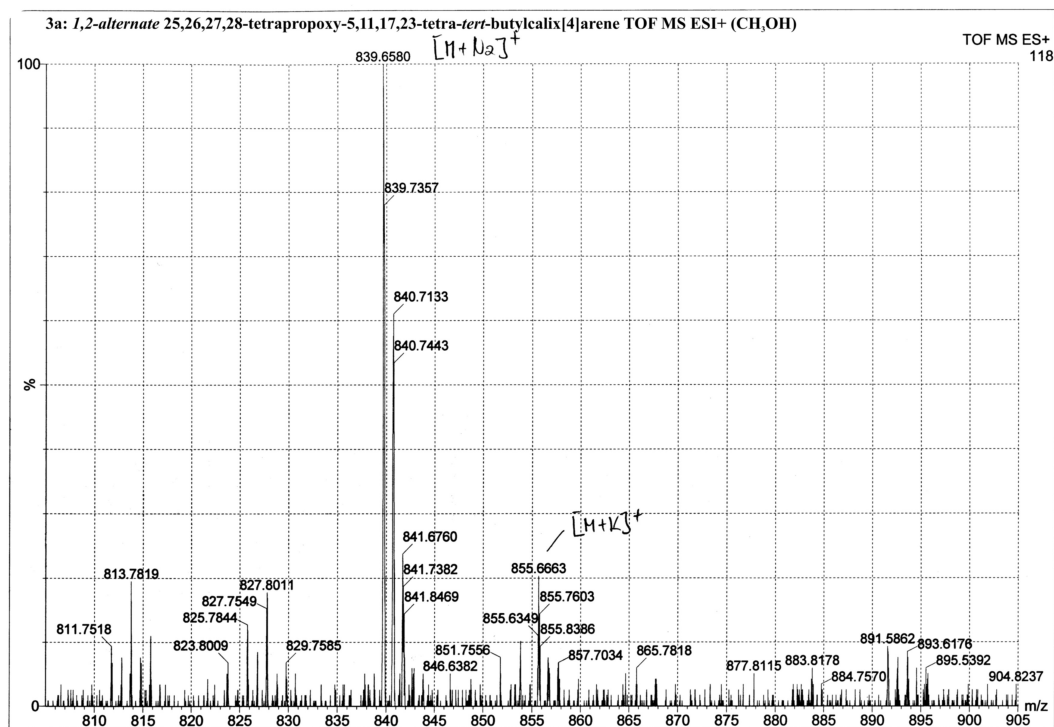
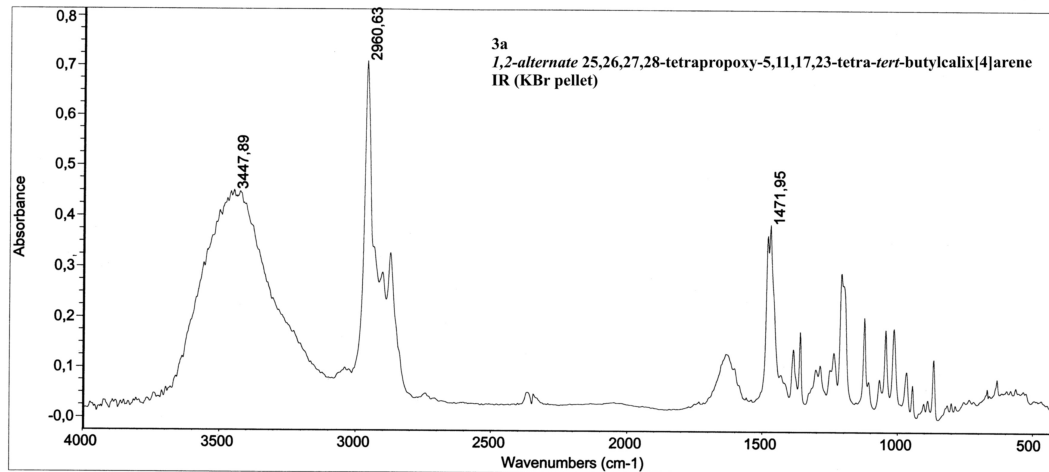
$C_{64}H_{77}O_4$ ,  $M = 910.26 \text{ g.mol}^{-1}$ , monoclinic system, space group  $P2_1/c$ ,  $a = 14.957(2) \text{ \AA}$ ,  $b = 20.196(2) \text{ \AA}$ ,  $c = 19.100(2) \text{ \AA}$ ,  $\beta = 106.679(9)^\circ$ ,  $Z = 4$ ,  $V = 5526.6(9) \text{ \AA}^3$ ,  $D_c = 1.097 \text{ g.cm}^{-3}$ ,  $\mu(\text{Cu-K}\alpha) = 0.509 \text{ mm}^{-1}$ , crystal dimensions of  $0.06 \times 0.15 \times 0.28 \text{ mm}$ . Data were collected at  $150(2) \text{ K}$  on a Xcalibur PX diffractometer with graphite monochromated Cu  $K\alpha$  radiation. The structure was solved by direct methods<sup>[1]</sup> using the SHELX suite of programs<sup>[2]</sup> and anisotropically refined by full-matrix least-squares on  $F^2$  values to final  $R = 0.0807$  and  $R_w = 0.2212$  using 11474 independent reflections ( $\theta_{max} = 76.66^\circ$ ) and 603 parameters. The positions of disordered groups were found from the electron density maps. Disordered fragments were then placed in appropriate positions, and all distances between neighbouring atoms and angles were fixed. Site occupancies were refined for the different parts with the same thermal parameters for the same atoms in the various fragments. At the end of refinement, site occupancies were fixed and hydrogen atoms were placed in calculated positions. The structure was deposited into the CCD under CCDC number 666976.

### Literature

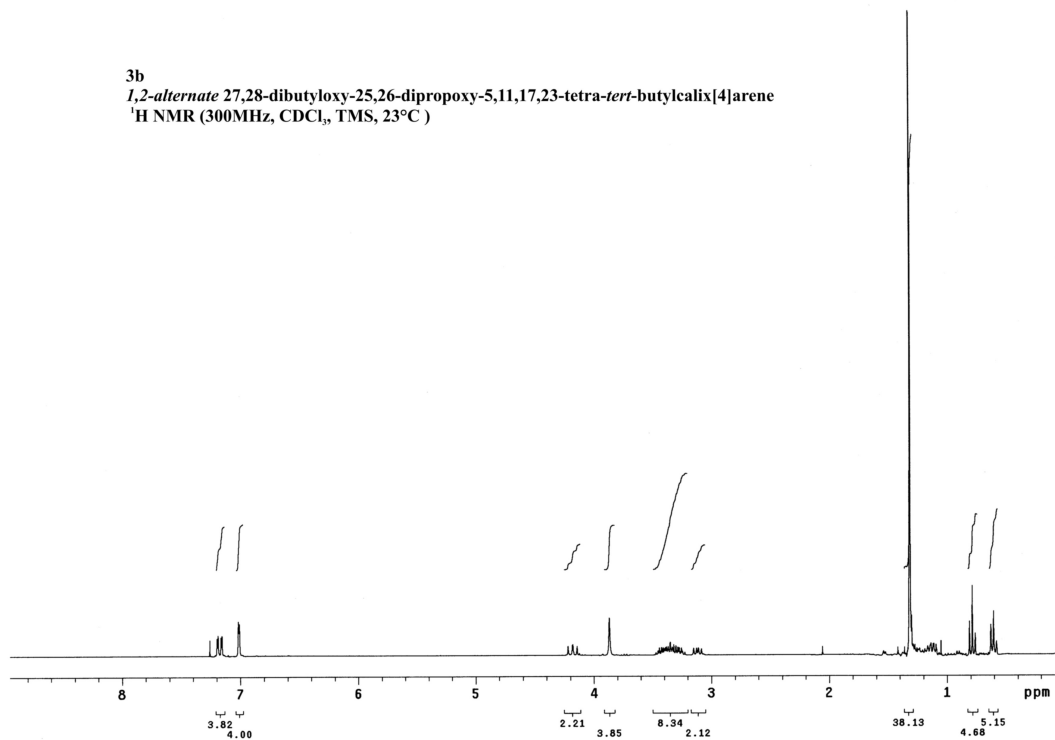
- [1] K. Iwamoto, K. Fujimoto, T. Matsuda and S. Shinkai, *Tetrahedron Lett.* 1990, 31, 7169
- [2] A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Crystallogr.* 1999, **32**, 115.
- [3] (a) G. M. Sheldrick, *Acta Crystallogr. Sec. A* 1990, **46**, 467. (b) G. M. Sheldrick, *Acta Crystallogr. Sec. A* 1993, **49** (Suppl.), C53.

**3a**  
*1,2-alternate 25,26,27,28-tetrapropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene*  
<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23°C)

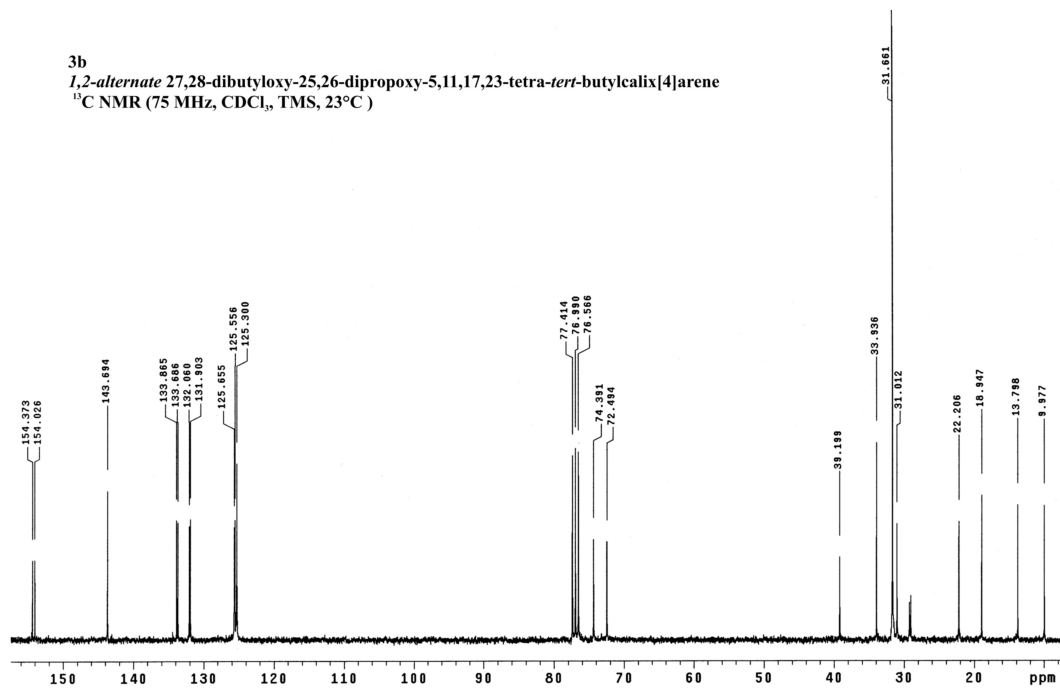




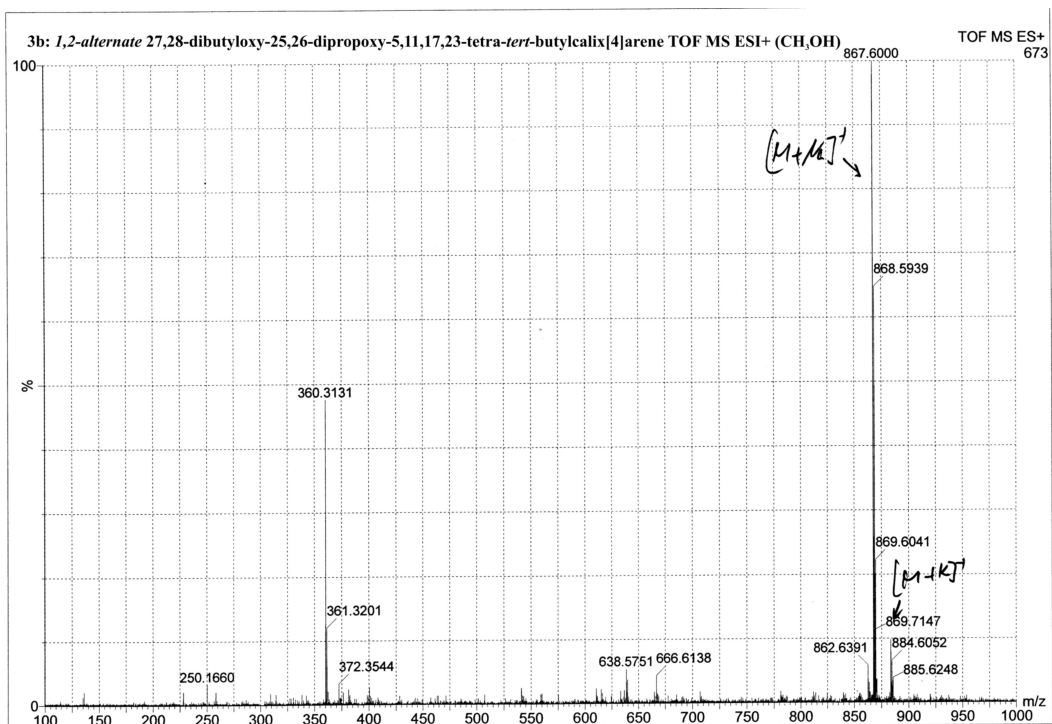
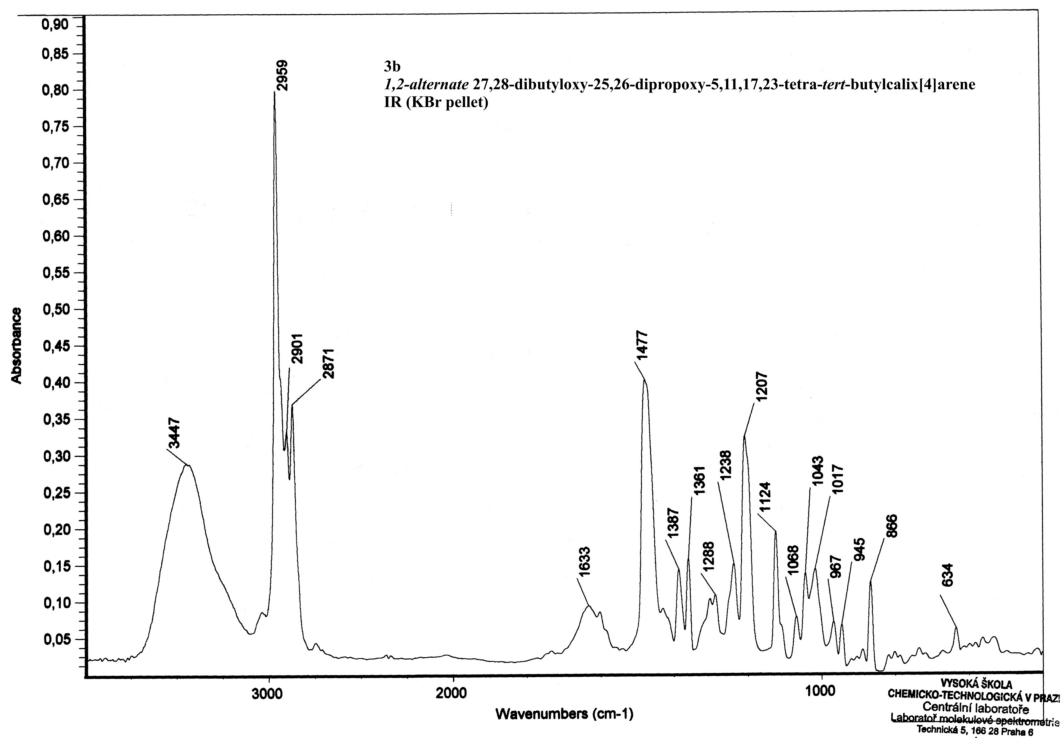
**3b**  
*1,2-alternate 27,28-dibutyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene*  
<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23°C)



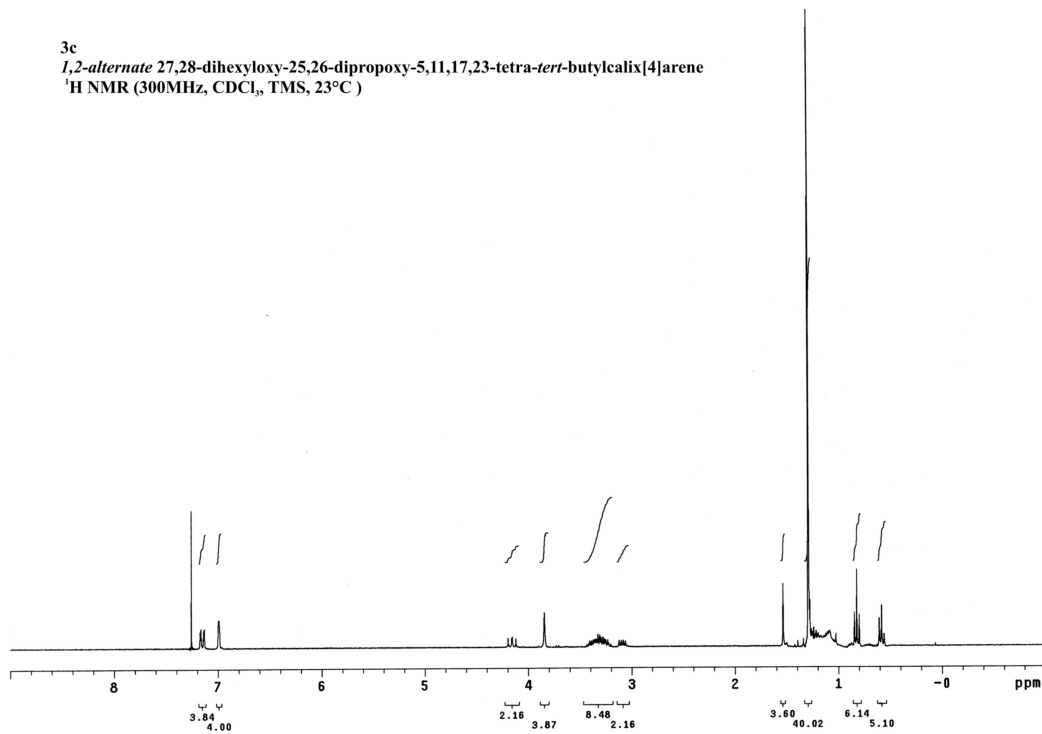
**3b**  
*1,2-alternate 27,28-dibutyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene*  
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 23°C)



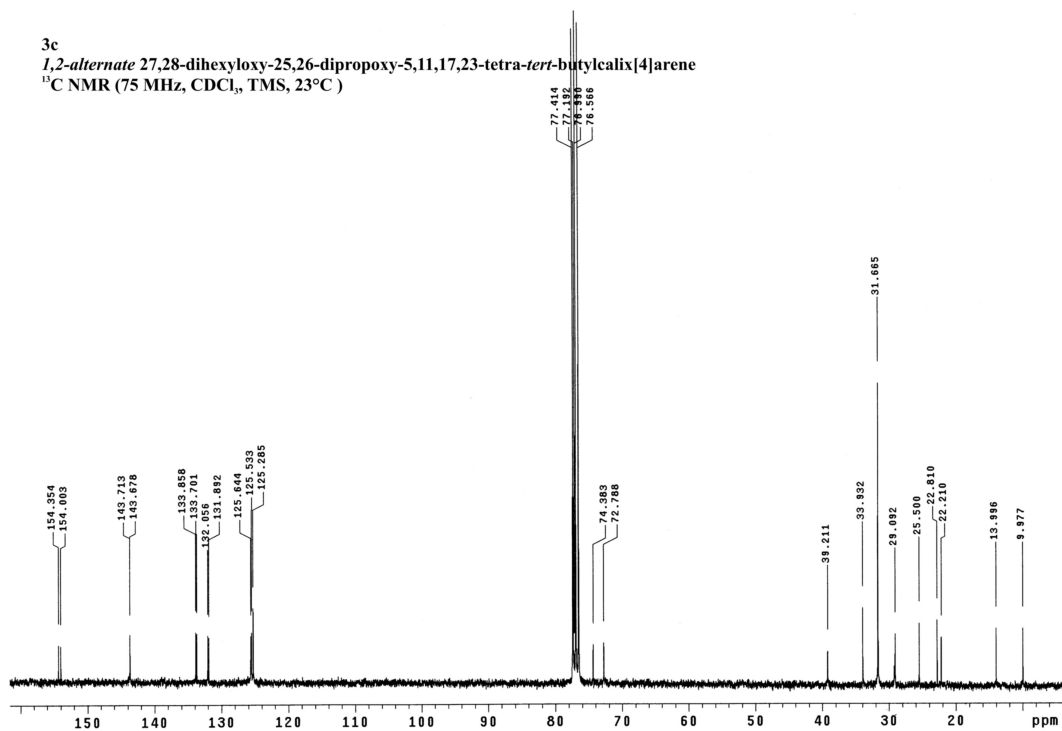


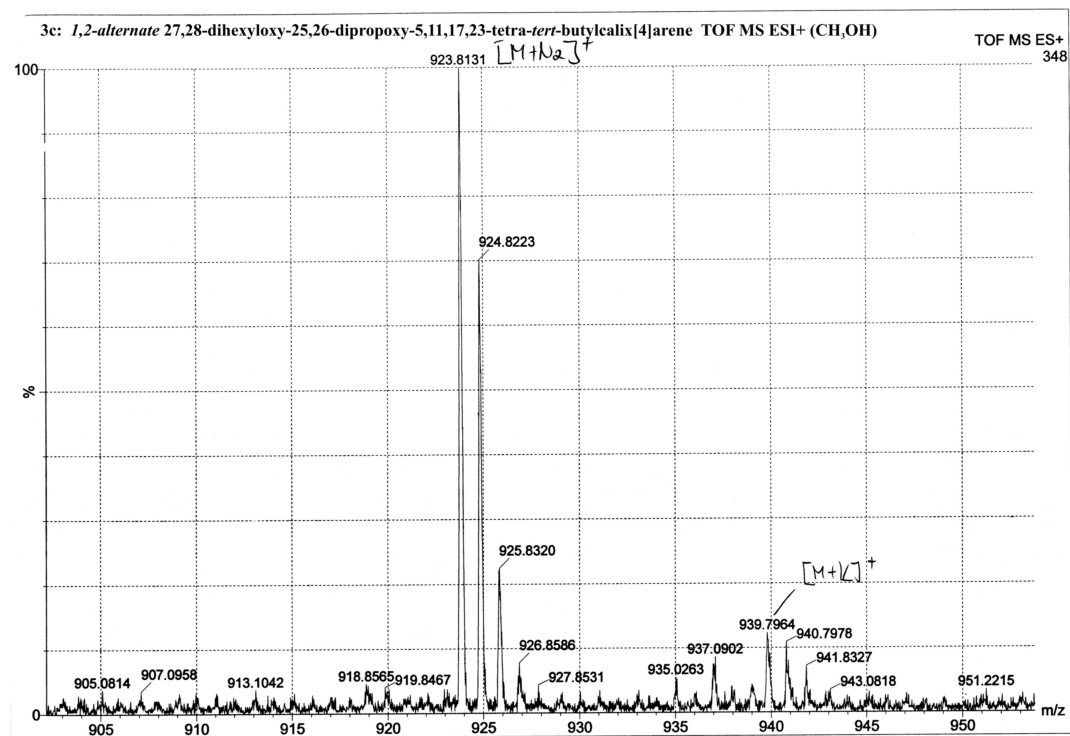
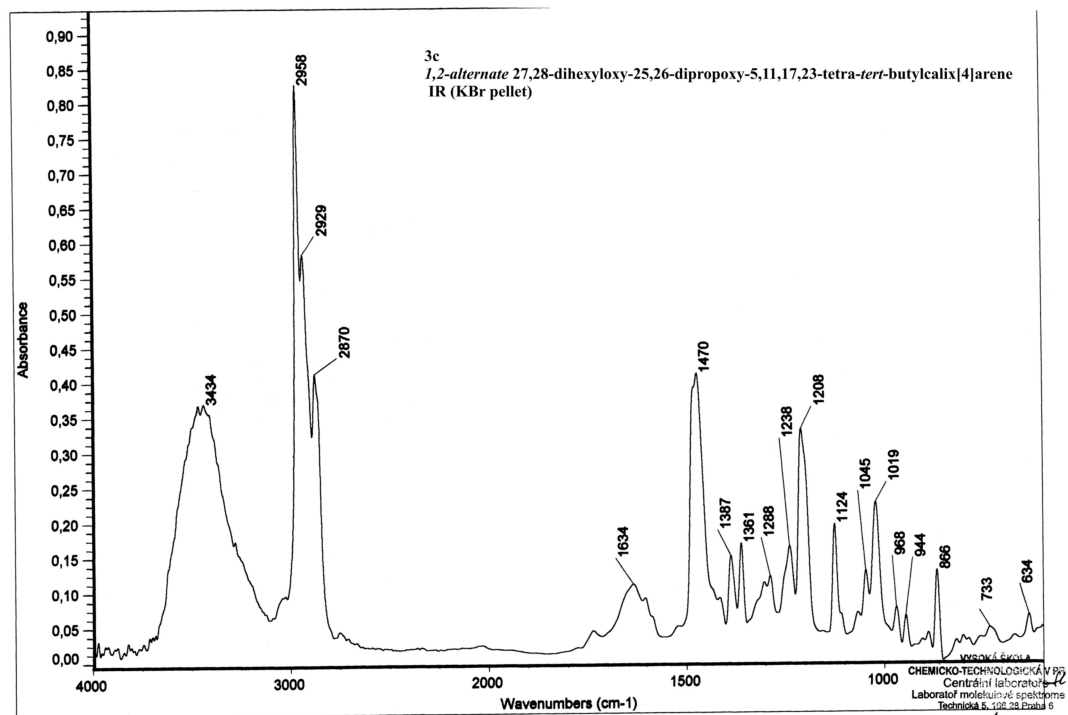


**3c**  
*1,2-alternate 27,28-dihexyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene*  
<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23°C)

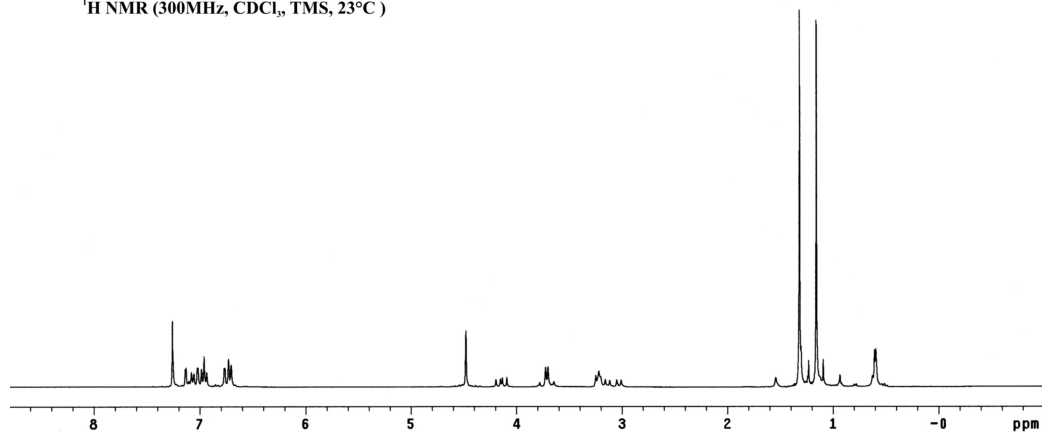


**3c**  
*1,2-alternate 27,28-dihexyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene*  
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 23°C)





**3d**  
*1,2-alternate 27,28- dibenzyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene*  
<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>, TMS, 23°C)



**3d: 1,2-alternate 27,28- dibenzyloxy-25,26-dipropoxy-5,11,17,23-tetra-tert-butylcalix[4]arene** <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS, 23°C)

