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LOWER RIM SILYL SUBSTITUTED CALIX[8]ARENES

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ABSTRACT. New lower rim silyl substituted calix[8]arenes have been synthesized by reaction of the parent *p-tert*-butylcalix[8]arene with *n*-BuLi at low temperature followed by addition of trimethylchlorosilane/(3-chloropropyl)-trimethoxysilane when octakis-(trimethylsilyl)calix[8]arene (**3**)/octakis-(*n*-propyl-trimetoxisilan)calix[8]arene (**4**) is obtained. The new calixarene derivative **4** has been characterized by NMR and IR spectroscopy.

Keywords**:** *calix[8]arene, octakis-(n-propyl-trimetoxisilan)calix[8]arene.*

INTRODUCTION

Functionalization of calix[n]arenes is an important way in getting useful products for many areas of research and applications [1, 2, 3].

The most accessed positions for functionalizations of the parent calixarenes are the phenolic -OH groups of the lower rim or the *p*- position of the aromatic rings (upper rim) [4,5]. *Tert*-butylcalix[n]arenes (n = 4,6,8) can be functionalized at the upper rim either by removal of the *tert*-butyl groups thus forming calix[n]arenes which can be then halogenated (see references [6] and [7] for bromination), or directly by reactions of nitration or sulfonation [6,7]. The first step in all the processes is however the protection of -OH groups by *o*-methylation or acetylation [8,9].

Larger calixarenes have been successfully modified at the lower rim with ethers or esters formation leading to new host molecules by the introduction of additional functional groups [10]. These functionalizations allow a degree of control on the calixarene conformations and also on the hindrance of ring inversion since voluminous groups attached to the oxygen atoms increase the barrier to conformational inversion in calix[8]arenes compared with calix[4]arenes [11].

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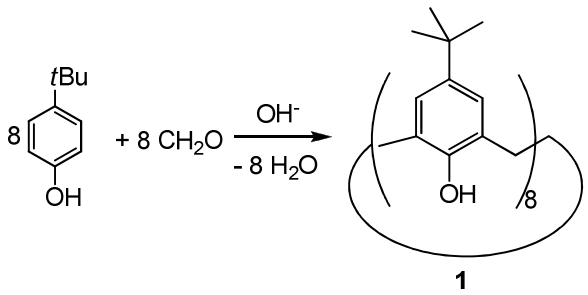
In view of their potential to bind to inorganic substrates, calixarenes functionalized with organosilyl groups are promising precursors for new hybrid organic/inorganic materials.

Literature data show that trimethylsilylated-*tert*-butylcalix[n]arenes are obtained from the brominated derivative of the corresponding calixarene, by lithiation with an excess of *tert*-butyllithium followed by silylation with excess chlorotrimethylsilane [12]. In case of calix[4]arenes, a *tetra*-trimethylsilylated product was obtained by this method, however only tri-trimethylsilylated and di-trimethylsilylated derivatives were reported for calix[6]arene and calix[8]arene respectively [12]. A fully substituted *tert*-octylcalix[8]arene octakis-(trimethylsilyl) ether was obtained by reaction of *p-tert*-octyl-calix[8]arene with N-O-bis[(trimethylsilyl)oxy]acetamide in solution of acetonitrile [12].

Herein we present a new method based on the lithiation of calix[8]arenes for the synthesis of octakis-(trimethylsilyl) ether of *tert*-butylcalix[8]arene. This protocol has been also applied for obtaining the new silyl substituted octakis(*n*-propyl-trimethoxisilan)calix[8]arene.

RESULTS AND DISCUSSIONS

The parent *p-tert*-butylcalix[8]arene has been obtained by the method described in literature [13] (Scheme 1).



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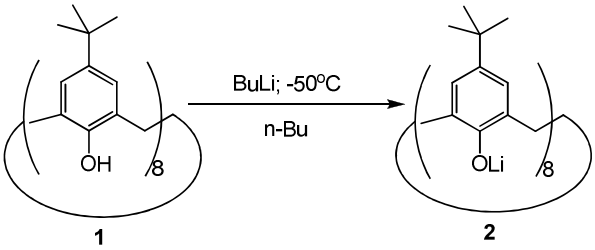
Scheme 1

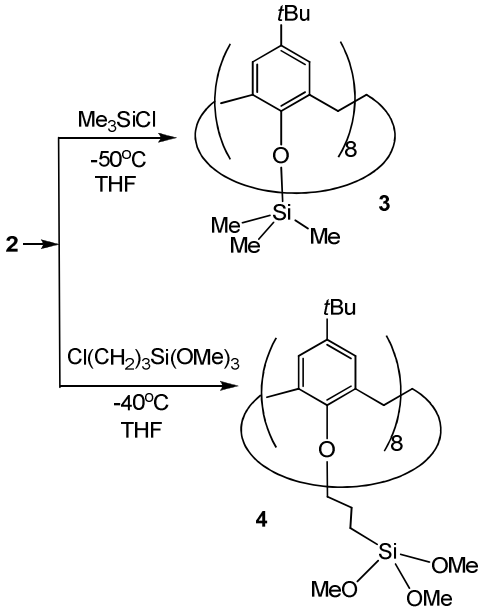
^{1}H NMR spectrum of **1** shows a specific signal at 9.66 ppm due to the presence of the –OH groups. Two nonequivalent doublet signals in the 3 – 4,5 ppm range are assigned to the two nonequivalent (*endo* and *exo*) protons of the methylene bridges [14,15].

The new silyls substituted derivatives **3** and **4** were obtained via the lithium intermediate **2** which is stable under inert atmosphere until 0 ^{o}C (Scheme 2). The reaction is complete after 2 hours of stirring at a temperature ranging from -50 to -20 ^{o}C.



Scheme 2

Lithium derivative **2** is added at -50 °C to a solution (THF) containing excess trimethylchlorosilane or (3-chloropropyl)trimethoxysilane and the corresponding **3** or **4** lower rim silyl substituted calix[8]arenes are formed (**Scheme 3**).



Scheme 3

Calix[8]arenes **3** and **4** were characterized by multinuclear NMR, and IR spectroscopy.

In the ^{1}H NMR spectra of **3** and **4,** the singlet signal corresponding to -OH groups of the parent calixarene is missing, proving the full substitution at the oxygen atoms. Furthermore, in the aliphatic range of spectrum, the characteristic signals for O-Si*Me*$_3$ (2.19 ppm) and -O-(*CH*$_2$)$_3$-Si(OMe)$_3$ (1.30 ppm for -C<u>H</u>$_2$-Si(OMe)$_3$,1.90 ppm for -CH$_2$-C<u>H</u>$_2$-CH$_2$-, 3.53 ppm for -O-C<u>H</u>$_2$-, and 3.57 ppm for Si-(O-C<u>H</u>$_3$)$_3$) protons were observed. **3** and **4** derivatives show a

broadened signal for the bridge methylene protons, as opposed to the sharp AB system observed for the parent compound. This has been evidenced in the case of other similar substituted compounds as well [12] and it is no doubt due to a greater flexibility of the substituted calixarene basket. A PM3 energy profile calculation with Spartan06 [16] for a monosubstituted calixarene[8]arene (Figure 1) shows a barrier for the inversion of the methylene group, accompanied by a corresponding rotation of the arene ring, of less then 15 kcal/mol, comparable with the experimentally determined barriers of interconversion of various calix[4,8] arenes [10]. The calculated overall barrier is even smaller when two vicinal oxygen atoms are substituted with $SiMe_3$ groups (Figure 2), so the observed pattern of the bridging methylene groups in the NMR spectra of **3** and **4** has also some theoretical support.

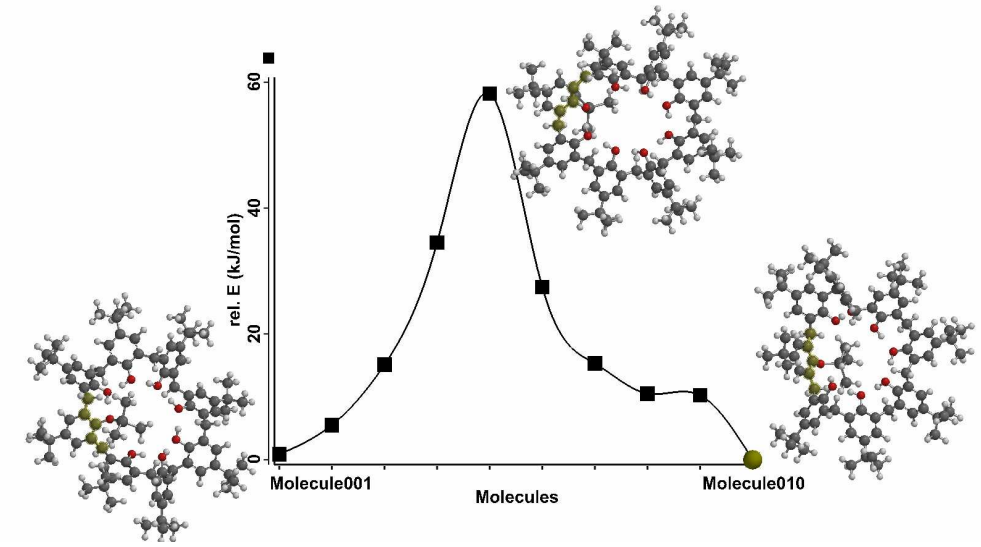


Figure 1. A plot of the PM3 calculated energies against the HC…CH (marked) dihedral angle for the monosubstituted calix[8]arene.

The complete substitution at the lower rim has also been evidenced by the IR spectra of **3** and **4** where the band corresponding to the –OH stretching vibration at 3280 cm^{-1} [17, 18] is no longer present.

Furthermore, in the 3000-2800 cm^{-1} range, the characteristic C-H stretching vibrations for the -Me groups of the -$SiMe_3$ fragment appear as sharp bands. In addition, an intense band corresponding to the -O-Si- stretching vibration evidenced at 1148 cm^{-1} for **3** and 1013 cm^{-1} for **4** [18]. Most probably the substituents in **3** are oriented alternatively up and down relative to the mean plane of **1**, (Figure 3) an arrangement which minimizes the repusions between the $SiMe_3$ groups and also maximizes the π...HC interactions between the arene fragments and the silyl substituents.

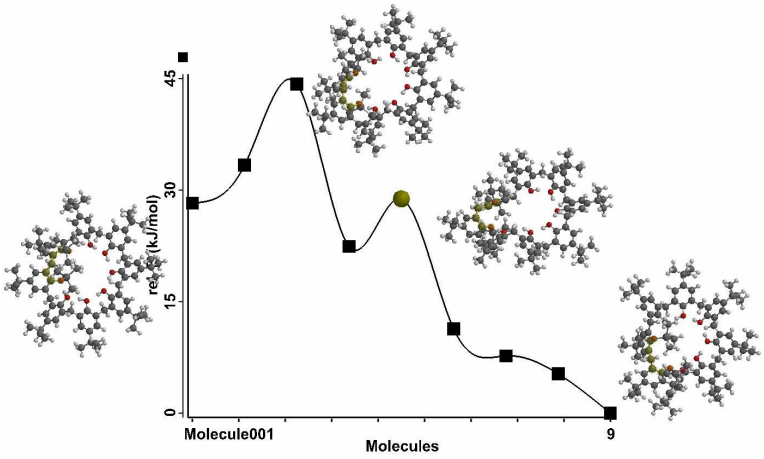


Figure 2. A plot of the PM3 calculated energies against the HC…CH (marked) dihedral angle for a vicinal disubstituted calix[8]arene.

Figure 3 shows also a linear dependence of enthalpy of formation with the number of $SiMe_3$ substituents.

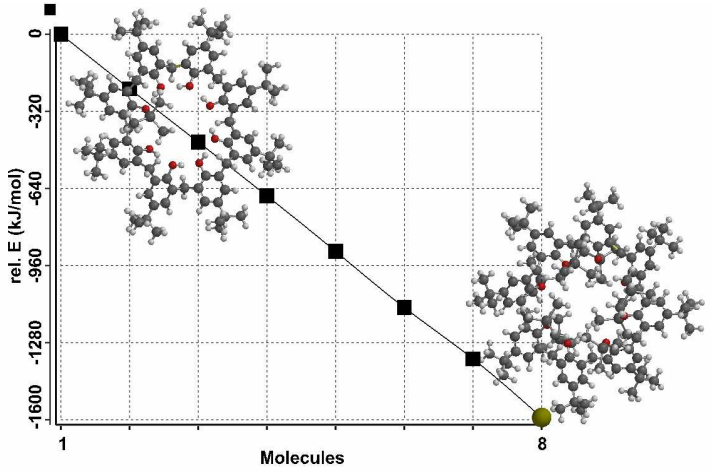


Figure 3. Variation of the PM3 calculated enthalpy of formation of $SiMe_3$ substituted calix[8]arenes. Only structures of the monosubstituted and fully substituted calixarenes are displayed.

CONCLUSIONS

Lithiation of the parent calix[8]arene followed by addition of the appropriate halogeno-alkoxisilane proves to be a convenient way to prepare lower rim fully substituted calix[8]arenes.

EXPERIMENTAL SECTION

All experiments were carried out in flame-dried glassware under argon atmosphere by using high-vacuum-line techniques. Solvents were dried and freshly purified with SPS-5MB system. NMR spectra were recorded (with $CDCl_3$ as solvent) with a Bruker Avance 300 spectrometer at the following frequencies: ^{1}H, 300.13 MHz; ^{13}C, 75.47 MHz (reference TMS). IR spectra were recorded with a Vector 22 Bruker spectrometer by direct introduction method and a Jasco FT/IR Specord 600 spectometer in KBr pills. Melting points were determined with a Wild Leitz-Biomed apparatus. Me_3SiCl, $Cl\text{-}(CH_2)_3\text{-}Si(OMe_3)_3$, and BuLi were purchased from Merck.

p-tert-butyl-calix[8]arene 1

p-tert-butylcalix[8]arene was obtained according to the literature data [13]. *p-tert*-butylphenol (50 g; 0,33 mol), *para*formaldehyde (17.5 g, 0,58 mol), sodium hydroxide (2,5 ml, 10 N) were dissolved in a mixture of xylenes (300 ml) at room temperature. This suspension was stirred for 4 h at reflux temperature and the water was eliminated through a Dean Stark trap. Solvents and volatile products were removed in vacuo, and the white precipitate formed was filtered and washed with water and acetone. Recrystallization from chloroform (100 ml) afforded pure **1**.

Yield: 46.1 g (85 %). M.p. 405–410 ℃.

^{1}H NMR: δ = 9.66 ppm (s, 1H, OH), 7.17 ppm (s, 2H, H-5, ArH), 3.53 ppm (d, 2H, CH_2), 1.25 ppm (s, 9H, $C(CH_3)_3$).

Octakis-(trimethylsilyl)-*p-tert*-butyl-calix[8]arene 3

4.24 ml of a solution of *n*BuLi (1.6 M in hexane, 6.78 mmol) mmol) was added dropwise, at –80 ℃, to a solution of *p-tert*-butyl-calix[8]arene (1 g, 0.77 mmol) in THF (40 ml). The solution turned yellow and was stirred at this temperature for an additional hour. The lithium compound was then transferred to Me_3SiCl (0.9 ml, 7.04 mmol, d = 0.85 g/ml) in THF (20 ml) cooled at –80 ℃. After 2 hours of stirring the mixture was allowed to warm to room temperature. Solvents and volatile products were removed in vacuo, and the residue was dissolved in pentane (20 ml) to filter out the lithium salts. Recrystallization from chloroform (100 ml) afforded pure **3**

Yield: 0.81 g (62 %). M.p. 316 - 322 ℃.

^{1}H NMR: δ = 1.10, 1.27 ppm (m, 9H, $C(CH_3)_3$), 2.19 ppm (s, 9H -O-SiMe_3) 3.85 ppm (broad m, $^{2}J_{HH}$ = 12,85 Hz, 2H, CH_2), 6.92 ppm (broad s, 2H, H arom.).

IR: 2904-2869 cm^{-1} (ν_a $SiMe_3$), 1148 cm^{-1} (ν_a -O-Si-)

Octakis-(*n*-propyl-trimethoxysilane)-*p-tert*-butyl-calix[8]arene 4

4.5 ml of a solution of *n*BuLi (1.6 M in hexane, 7.2 mmol) was added dropwise, at –80 ℃, to a solution of *p-tert*-butyl-calix[8]arene (1 g, 0.77 mmol) in THF (40 ml). The solution turned yellow and was stirred at this temperature

for an additional hour. The lithium compound was then transferred to a solution of 3-chloropropyl-trimetoxysilane (1.30 ml, 7.09 mmol, d = 1.09 g/ml) in THF (20 ml) cooled at –40 ℃. The orange solution was allowed to warm to room temperature. Solvents and volatile products were removed in vacuo, and the residue was dissolved into pentane (20 ml). Lithium salts were filtered out; compound **4** crystallized as a brick-colored solid after 4 – 5 h at – 4 ℃ under argon atmosphere.
Yield: 1.13 g (56 %). M.p. 422 ℃ (decomposition).
^{1}H NMR: δ = 0.80 ppm (dd, 2H, -C$\underline{H}_2$-Si(OMe)$_3$), 1.30 ppm (m, 9H, *t*-Bu), 1.90 ppm (q, 2H, -CH$_2$-C$\underline{H}_2$-CH$_2$-), 3.53 ppm (t, 2H, -O-C$\underline{H}_2$-), 3.57 ppm (s, 9H, -Si-(O-C$\underline{H}_3$)$_3$), 7.15 ppm (m, 2H, H arom).
^{13}C RMN: δ = 6.63 ppm (s, -$\underline{C}$H$_2$-Si(OMe)$_3$), 8.03 ppm (s, -CH$_2$-$\underline{C}$H$_2$-CH$_2$-), 26.21 ppm (s, -$\underline{C}$-(CH$_3$)$_3$), 31.66 ppm (s, -C-($\underline{C}$H$_3$)$_3$), 33.77 ppm (s, -Ph-$\underline{C}$H$_2$-Ph-), 47.14 ppm (s, -Ar-O-$\underline{C}$H$_2$-) 50.44 ppm (s, -(O-$\underline{C}$H$_3$)$_3$), 122-126 ppm (m, *meta* $\underline{C}$), 126-132 ppm (m, ipso $\underline{C}$), 135-145 ppm (m, *para* $\underline{C}$).
IR: 1013 cm^{-1} (ν_a *Si-O*Me)

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REFERENCES

1. C. D. Gutsche, J. A. Levine, *J.Am.Chem.Soc.*, **1982**, *104*, 2652.
2. Z. Asfari, V. Bohmer, J. Harrowfield, J. Vicens, *Calixarenes 2001*, Kluwer Academic Publishers, **2001**, chapter 5.
3. P. Jose, S. Menon, *Bioinorg. Chem. Appl*., **2007**, ID 65815, 1.
4. J. W. Cornforth, E. D. Morgan, K. T. Potts, R. J. W. Rees, *Tetrahedron*, **1973**, *29*, 1659.
5. D. Gutsche, *Calixarenes: An introduction, 2nd edition,* RSC, Thomas Graham House, Science Park, Milton Road, Cambridge, UK, **2008**, chapter 2.
6. S. Seiji, K. Hirosuke, A. Takashi, M. Tsutomu, S. Hirosi, M. Osamu, *J. Chem. Soc. Perkin Trans. 1*, **1989**, *5*, 1073.
7. A. Arduini, A. Casnati, *Macrocycle Synth*., **1996**, 145.
8. C. D. Gutsche, L. G. Lin, *Tetrahedron*, **1986**, *42*, 1633.
9. C. D. Gutsche, B. Dhawan, K. H. No, R. Muthukrishnam, *J. Am. Chem. Soc.*, **1981**, *103*, 3782.
10. C.D.Gutsche, L. J. Bauer, *J. Am. Chem. Soc*., **1985**, *107*, 6052.
11. C. D. Gutsche, L. J. Bauer, *J. Am. Chem. Soc.*,**1985**, *107*, 6059.

12. F. Billo, R. M. Musau, A. Whiting, *ARKIVOC*, **2006**, *10*, 199.

13. J. H. Munch, C. D. Gutsche, *Org*. *Synth*., **1990**, *68*, 243.

14. G. Ferguson, J. F. Gallagher, M. A. McKervey, E. Madigan, *J. Chem. Soc. Perkin Trans 1*, **1996**, 599.

15. C. D. Gutsche, *Calixarenes Revisited*, The Royal Society of Chemistry, Thomas Graham House, UK, **1998**, chapter 3.

16. Spartan'06 Wavefunction, Inc. Irvine, CA, Except for molecular mechanics and semi-empirical models, the calculation methods used in Spartan have been documented in: Y. Shao, L.F. Molnar, Y. Jung, J. Kussmann, C. Ochsenfeld, S.T. Brown, A.T.B. Gilbert, L.V. Slipchenko, S.V. Levchenko, D.P. O'Neill, R.A. DiStasio Jr., R.C. Lochan, T. Wang, G.J.O. Beran, N.A. Besley, J.M. Herbert, C.Y. Lin, T. Van Voorhis, S.H. Chien, A. Sodt, R.P. Steele, V.A. Rassolov, P.E. Maslen, P.P. Korambath, R.D. Adamson, B. Austin, J. Baker, E.F.C. Byrd, H. Dachsel, R.J. Doerksen, A. Dreuw, B.D. Dunietz, A.D. Dutoi, T.R. Furlani, S.R. Gwaltney, A. Heyden, S. Hirata, C-P. Hsu, G. Kedziora, R.Z. Khalliulin, P. Klunzinger, A.M. Lee, M.S. Lee, W.Z. Liang, I. Lotan, N. Nair, B. Peters, E.I. Proynov, P.A. Pieniazek, Y.M. Rhee, J. Ritchie, E. Rosta, C.D. Sherrill, A.C. Simmonett, J.E. Subotnik, H.L. Woodcock III, W. Zhang, A.T. Bell, A.K. Chakraborty, D.M. Chipman, F.J. Keil, A.Warshel, W.J. Hehre, H.F. Schaefer, J. Kong, A.I. Krylov, P.M.W. Gill and M. Head-Gordon, *Phys. Chem. Chem. Phys*., **2006**, *8*, 3172.

17. G. Ferguson, J. F. Gallagher, M. A. Mckervey, E.Madigan, *J. Chem. Soc. Perkin Trans 1*, **1996,** *599*.

18. P. J. Launer, *Infrared Analysis of Organosilicon Compounds: Spectra-Structure Correlation*, B. Arkles, G. L. Larson (eds), Petrarch Systems (section 8), **1987**.