Synthesis of mono-substituted *p-tert*-butylcalix[7]arenes with reactive substituents

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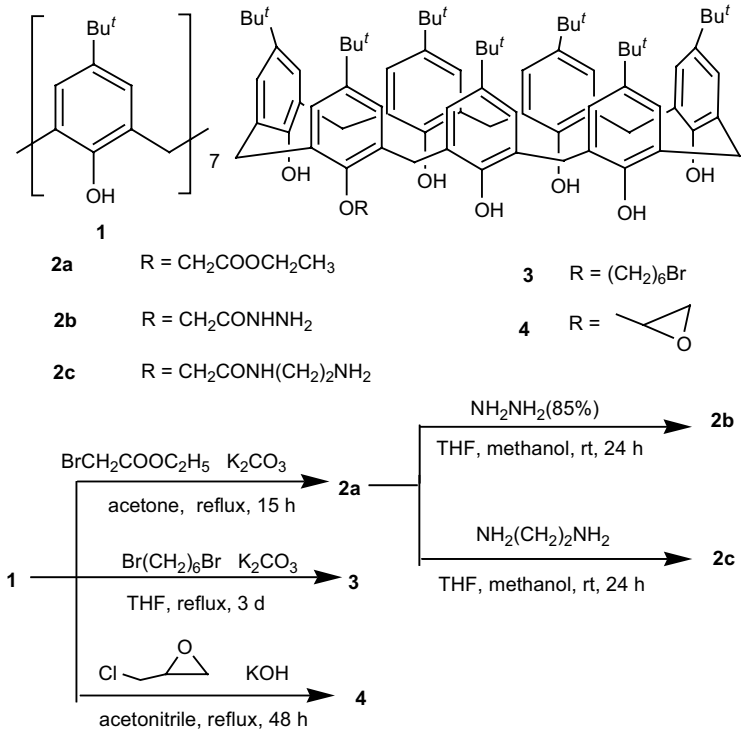
Three mono-substituted *p-tert*-butylcalix[7]arenes with various reactive substituents have been synthesised by treating *p-tert*-butylcalix[7]arene with doubly functional electrophiles. Two amino derivatives, 43-acetohydrazideoxy-*p-tert*-butylcalix[7]arene and 43-*N*-(2-aminoethyl)acetamideoxy-*p-tert*-butylcalix[7]arene were obtained by aminolysis of 43-ethoxycarbonylmethoxy-*p-tert*-butylcalix[7]arene with hydrazine hydrate or ethylene diamine in good yield.

Keywords: calixarene, *p-tert*-butylcalix[7]arene, mono-substituted, aminolysis, active terminal

Calixarenes are a family of cavity-shaped cyclic molecules in which a number of phenolic subunits are connected by methylene groups. They contain a π cavity composed of phenyl rings and a hydroxyl array to which complex organic molecules or cations, can be attached. The chemistry of even-numbered calix[n]arenes (n = 4, 6, 8) has been studied over the last 30 years,[1] but the chemistry of odd-numbered calixarenes, especially calix[7]arene has been neglected.[2-5] Little is known about mono-substituted calix[7]arenes with reactive substituents obtained from bisfunctional reagents and calix[7]arene itself. The former are key intermediates for the construction of pendant calix[7]arene polymers. The calix[7]arene polymer may exhibit some new host properties due to their high-order molecular architecture with odd numbers of phenolic rings and cooperative effect between calix[7]arene moieties. We now report the first synthesis of several mono-substituted *p-tert*-butylcalix[7]arenes with reactive groups that can be used as blocks to construct pendant calix[7]arene polymers.

Results and discussion

Reaction of **1**[6] with doubly functional electrophiles in the presence of a base afforded mono-substituted calix[7]arenes. Treatment of **1** with ethyl bromoacetate in the presence of K_2CO_3 in refluxing acetone gave 43-ethoxycarbonylmethoxy-*p-tert*-butylcalix[7]arene **2a** in 56% yield after column chromatography (Table 1, entry 1). **2a** was subjected to aminolysis in a mixed solvent composed of THF and methanol at room temperature with hydrazine hydrate or 1,2-diaminoethane to afford 43-acetohydrazideoxy-*p-tert*-butylcalix[7]arene **2b** and 43-*N*-(2-aminoethyl)acetamideoxy-*p-tert*-butylcalix[7]-arene **2c** respectively. The yields were more than 65% (entries 2, 3). Reaction of **1** with 1,6-dibromohexane in refluxing THF in the presence of K_2CO_3 gave 43-(ω-bromohexyloxy)-*p-tert*-butylcalix[7]arene **3** in 31% yield after column chromatography and recrystallisation from chloroform/ethanol (entry 4). Using epichlorohydrin as an electrophile and KOH as a base in MeCN at reflux temperature, 43-methyloxyoxirane-*p-tert*-butylcalix[7]arene **4** was obtained in 16% yield (entry 5).



Scheme 1 Synthesis of mono-substituted *p-tert*-butylcalix[7]arenes with active terminals **2**, **3** and **4**.

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Table 1 Mono-substituted *p-tert*-butylcalix[7]arenes with active terminal

Entry	Compound	Solvent	Temp	Time	Yield/%
1	**2a**	Acetone	Reflux	15 h	56
2	**2b**	THF + methanol	r.t.	24 h	72[a]
3	**2c**	THF + methanol	r.t.	24 h	65[a]
4	**3**	THF	Reflux	72 h	31
5	**4**	Acetonitrile	Reflux	48 h	16

[a]The yields of **2b** and **2c** were calculated from **2a**.

The structure of these singly *O*-substituted *p-tert*-butylcalix[7]arenes was deduced from ESI-MS, IR, elemental analysis and ^{1}H NMR spectra.[2,7,8] Taking **3** as an example, ESI-MS and elemental analysis showed it was a singly *O*-substituted *p-tert*-butylcalix[7]arene. The signals of the *tert*-butyl protons appeared at δ = 1.23, 1.25, 1.27, 1.29 ppm in a ratio of 2 : 2 : 1 : 2 and hydroxyl protons appeared at δ = 8.98, 9.64 and 10.09 ppm in a 2 : 2 : 2 ratio assigning as s, d_1 and d_2 respectively in Fig. 1 were in agreement with singly *O*-substituted pattern. The singly *O*-substituted derivatives have no defined conformation as indicated by the broad peaks of methylene protons due to the "*tert*-butyl through the annulus" inversion. Because substitution breaks the lower rim circular hydrogen bond, the conformational mobility of singly *O*-substituted *p-tert*-butylcalix[7]arenes is even higher than that of calix[7]arene **1** itself.[5]

Conclusions

In conclusion, we have synthesised several of mono-substituted *p-tert*-butylcalix[7]arenes with reactive substituents from *p-tert*-butylcalix[7]arene. Another two amino-terminal derivatives **2b** and **2c** were obtained in more than 65% yields from ethoxycarbonylmethyloxy *p-tert*-butylcalix[7]arene **2a** through aminolysis with hydrazine or diamine. These singly *O*-substituted derivatives can be considered as useful building blocks for constructing pendant calix[7]arene polymers, which can be used in supramolecular chemistry.

Experimental

General

Satisfactory microanalytical and spectral data were obtained for all new compounds. The ^{1}H NMR spectra were recorded at 300 MHz on Varian Mercury-VX300 spectrometer. The chemical shifts were recorded in parts per million (ppm) with TMS as the internal reference. ESI mass spectra were determined using Finnigan LCQ Advantage mass spectrometer. IR spectra were obtained on Nicolet NEXUS670 FTIR spectrometer. Elemental analyses were performed with Yanaco MT-5.

43-ethoxycarbonylmethoxy-p-tert-butylcalix[7]arene (**2a**): A suspension of *p-tert*-butylcalix[7]arene **1** (2.27 g, 2 mmol) and K_2CO_3 (0.276 g, 2 mmol) was stirred in refluxing acetone (120 ml) for 1 h. Then ethyl bromoacetate (0.4 g, 2.4 mmol) was added and stirring was continued for an additional 15 h. After removal of the solvent under vacuum, the residue was extracted with $CHCl_3$ (50 ml). After filtration, the organic layer was washed with 0.1 N HCl (40 ml), H_2O (2 × 20 ml), and dried over $MgSO_4$. After filtration and concentration, the residue was subjected to column chromatography on silica gel using CH_2Cl_2–petroleum ether (60–90°C) (1 : 1 v/v) as an eluent to afford **2a** (1.37 g, 56% yield) as a white powder. ESI-MS *m/z*, 1220.8 $[M]^-$; ^{1}H NMR (300 MHz, TMS, $CDCl_3$, 298 K) δ 1.24 (s, *t*-Bu, 36H), 1.25 (s, *t*-Bu, 9H), 1.30 (s, *t*-Bu, 18H), 1.46 (t, CH_2CH_3, 3H), 3.68–4.02 (m, $ArCH_2Ar$, 14H), 4.27 (br, OCH_2CH_3, 2H), 4.40 (s, OCH_2CO, 2H), 7.08 (s, Ar*H*, 2H), 7.13 (s, Ar*H*, 2H), 7.16 (s, Ar*H*, 2H), 7.19 (s, Ar*H*, 8H), 8.57 (s, ArO*H*, 2H), 9.79 (s, ArO*H*, 2H), 10.24 (s, ArO*H*, 2H) ppm; IR (KBr, cm^{-1}) 1750.2 (s, C=O). Anal. Calcd. for $C_{81}H_{104}O_9$ (1220.8): C, 79.63; H, 8.58. Found: C, 79.51; H, 8.63.

43-(6-bromohexyloxy)-p-tert-butylcalix[7]arene (**3**): A suspension of *p-tert*-butylcalix[7]arene **1** (2.27 g, 2 mmol) and K_2CO_3 (0.82 g, 6 mmol) was stirred in refluxing THF (120 ml) for 1 h. Then 1,6-dibromohexane (0.6 g, 2.4 mmol) was added and the reaction mixture was stirred for an additional 72 h. After removal of the solvent under vacuum, 50 ml of $CHCl_3$ was added and stirred for 1 h. The organic layer was washed with 0.1 N HCl (40 ml), H_2O (2 × 20 ml), and dried over $MgSO_4$. After filtration and concentration, the residue was subjected to column chromatography on silica gel using CH_2Cl_2–petroleum ether (60–90°C) (1: 4 v/v) as the eluent. Compound **3** was obtained as a white powder (0.80 g, 31% yield) after recrystallisation from chloroform/ethanol. ESI-MS *m/z*, 1297.7 $[M + 1]^-$; ^{1}H NMR (300 MHz, TMS, $CDCl_3$, 298 K) δ1.23 (s, *t*-Bu, 18H), 1.25 (s, *t*-Bu, 18H), 1.27 (s, *t*-Bu, 9H), 1.29 (s, *t*-Bu, 18H), 1.56 (br, $(CH_2)_2(CH_2)_2(CH_2)_2$, 4H), 1.75 (br, $CH_2CH_2(CH_2)_4Br$, 2H), 1.86 (br, $O(CH_2)_4CH_2CH_2$, 2H), 2.80 (br, CH_2Br, 2H), 3.58–4.10 (m, $ArCH_2Ar$, 14H), 4.15 (br, OCH_2, 2H), 7.06 (s, Ar*H*, 2H), 7.14 (s, Ar*H*, 2H),7.16 (s, Ar*H*, 2H), 7.19 (s, Ar*H*, 8H), 8.98 (s, ArO*H*, 2H), 9.64 (s, ArO*H*, 2H), 10.09 (s, ArO*H*, 2H) ppm. Anal. Calcd. for $C_{83}H_{109}BrO_7$ (1296.7): C, 76.76; H, 8.46. Found: C, 76.72; H, 8.48.

2,3-epoxypropoxy-p-tert-butylcalix[7]arene (**4**): A suspension of *p-tert*-butylcalix[7]arene **1** (2.27 g, 2 mmol) and KOH (0.12 g, 2.2 mmol) was stirred in refluxing MeCN for 1 h. Then epichlorohydrin (0.48 g, 5 mmol) was added and the reaction mixture was stirred for 48 h. After removal of the solvent under vacuum, 50 ml of $CHCl_3$ was added and stirred for 1 h. The organic layer was washed with 0.1 N HCl (25 ml), H_2O (2 × 20 ml), and dried over $MgSO_4$. After filtration and concentration, the residue was subjected to column chromatography on silica gel using CH_2Cl_2–petroleum ether (60–90°C) (3 : 1 v/v) as an eluent to afford **4** (0.38 g, 16% yield) as a white powder. ESI-MS *m/z*, 1191.7$[M + 1]^-$; ^{1}H NMR (300 MHz, TMS, $CDCl_3$, 298 K) δ 1.27 (s, *t*-Bu, 63H), 3.49 (br, CH_2CHCH_2, 3H), 3.88 (s, $ArCH_2Ar$, 8H), 3.94 (s, $ArCH_2Ar$, 2H), 4.04 (s, $ArCH_2Ar$, 4H), 4.25 (br, OCH_2, 2H), 7.10 (s, Ar*H*, 2H), 7.16 (s, Ar*H*, 8H),7.18 (s, Ar*H*, 4H), 8.49 (s, ArO*H*, 2H), 9.69 (s, ArO*H*, 2H), 10.18 (s, ArO*H*, 2H) ppm. Anal. Calcd. for $C_{80}H_{102}O_8$ (1190.8): C, 80.63; H, 8.63. Found: C, 80.58; H, 8.70.

Hydrazinocarbonylmethoxy-p-tert-butylcalix[7]arene (**2b**) *and aminoethylaminocarbonylmethoxy-p-tert-butylcalix[7]arene* (**2c**): A suspension of 0.61 g (0.5 mmol) of **2a** was stirred in a mixed solvent composed of 15 ml THF and 20 ml methanol. Then hydrazine

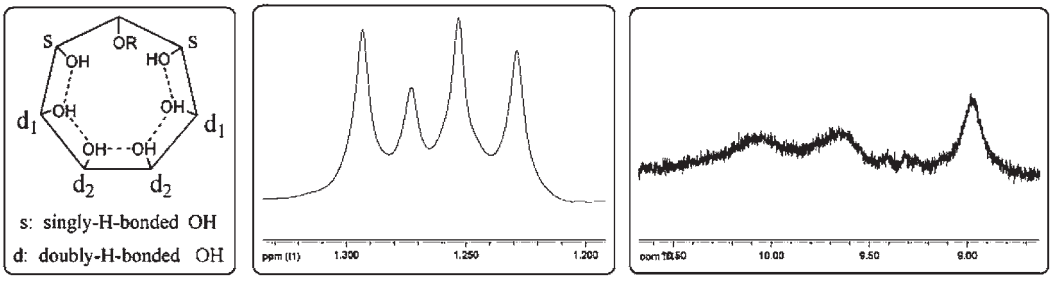

Fig. 1 "Semicircular" H-bond of mono-substituted *p-tert*-butylcalix[7]arenes, and ^{1}H NMR chemical shift of *t*-Bu and OH groups of compound **3**.

hydrate (2.94 g, 50 mmol) or diaminoethane (3 g, 50 mmol) was added and the mixture was stirred for 24 h at room temperature. After removal of the solvent under vacuum, the residue was subjected to column chromatography on silica gel using CH_2Cl_2–acetone (for **2b**: 25 : 1 v/v and for **2c**: 10 : 1 v/v) as the eluent to afford **2b** (0.43 g, 72% yield) or **2c** (0.40 g, 65% yield) as slight yellow powder. For compound **2b**: ESI-MS *m/z*, 1246.1 $[M + CH_3OH\text{-}2]^-$; ^{1}H NMR (300 MHz, TMS, $CDCl_3$, 298 K) δ 1.22 (s, *t*-Bu, 9H), 1.25 (s, *t*-Bu, 9H), 1.26 (s, *t*-Bu, 36H), 1.31 (s, *t*-Bu, 9H), 3.59–4.42 (m, ArC*H*$_2$Ar, 14H), 4.47 (br, NHN*H*$_2$, 2H), 4.54 (s, OC*H*$_2$, 2H), 7.11 (s, Ar*H*, 2H), 7.16 (s, Ar*H*, 2H), 7.18 (s, Ar*H*, 8H), 7.23 (s, Ar*H*, 2H), 8.16 (s, ArO*H*, 2H), 9.50 (s, ArO*H*, 2H), 9.78 (s, N*H*NH$_2$, 1H), 10.33 (s, ArO*H*, 2H) ppm; IR (KBr, cm^{-1}) 1684.5 (s, C=O). Anal. Calcd. for $C_{79}H_{102}N_2O_8$ (1206.8): C, 78.57; H, 8.51; N, 2.32. Found: C, 78.52; H, 8.53; N, 2.29. For compound **2c**: ESI-MS *m/z*, 1234.6 $[M]^+$; ^{1}H NMR (300 MHz, TMS, $CDCl_3$, 298 K) δ 1.19 (s, *t*-Bu, 18H), 1.24 (s, *t*-Bu, 9H), 1.27 (s, *t*-Bu, 18H), 1.44 (s, *t*-Bu, 18H), 2.18 (s, CH$_2$N*H*$_2$, 2H), 3.10 (d, C*H*$_2$NH$_2$, 2H), 3.30 (d, NHC*H*$_2$, 2H), 3.38–4.20 (m, ArC*H*$_2$Ar, 14H), 4.30 (d, OC*H*$_2$, 2H), 6.55 (s, CON*H*, 1H), 7.00 (s, Ar*H*, 2H), 7.11 (s, Ar*H*, 8H), 7.24 (s, Ar*H*, 2H), 7.32 (s, Ar*H*, 2H), 8.19 (s, ArO*H*, 2H), 9.53 (s, ArO*H*, 2H), 10.08 (s, ArO*H*, 2H) ppm; IR (KBr, cm^{-1}) 1665.0 (s, C=O). Anal. Calcd. for $C_{81}H_{106}N_2O_8$ (1234.8): C, 78.73; H, 8.65; N, 2.27. Found: C, 78.69; H, 8.67; N, 2.26.

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References

1 For general reviews on calixarenes, see: (a) C.D. Gutsche, *Calixarenes*, J.F. Stoddart, Ed.; RSC Monographs in Supramolecular Chemistry, Royal Society of Chemistry; Cambridge, 1989; (b) C.D. Gutsche, *Calixarenes Revisited*, J.F. Stoddart, Ed.; RSC Monographs in Supramolecular Chemistry, Royal Society of Chemistry; Cambridge, 1998; (c) Z. Asfari, V. Böhmer, J. Harrowfield and J. Vicens, *Calixarenes 2001*; Kluwer Academic: Dordrecht, 2001; pp 89-109. (d) V. Böhmer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 713.
2 M. Martino, L. Gregoli, C. Gaeta and P. Neri, *Org. Lett*., 2002, **4**, 1531.
3 M. Martino, C. Gaeta, L. Gregoli and P. Neri, *Tetrahedron Lett*., 2002, **43**, 9521.
4 Z.Y. Luo, S.L. Gong, C.L. Zhang, Q. Zheng and Y.Y. Chen, *Synlett*, 2006, 795.
5 M. Martino and P. Neri, *Mini-Rev. Org. Chem*., 2004, **1**, 219.
6 D.R. Stewart and C.D. Gutsche, *J. Am. Chem. Soc.*, 1999, **121**, 4136.
7 F. Cunsolo, G.M.L. Consoli, M. Piattelli and P. Neri, *J. Org. Chem*., 1998, **63**, 6852.
8 H. Otsuka, K. Araki and S. Shinkai, *J. Org. Chem*., 1994, **59,** 1542.