Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2007, **17**, 330–331
Mendeleev Communications

Facile synthesis of cone *p-tert*-butylcalix[4]arene-crown conformers

Elena A. Alekseeva,* Stepan S. Basok, Alexander V. Mazepa and Andrei I. Gren

A. V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, 65080 Odessa, Ukraine. Fax: +38 0482 65 2012; e-mail: Alyeksyeyeva@rambler.ru

DOI: 10.1016/j.mencom.2007.11.010

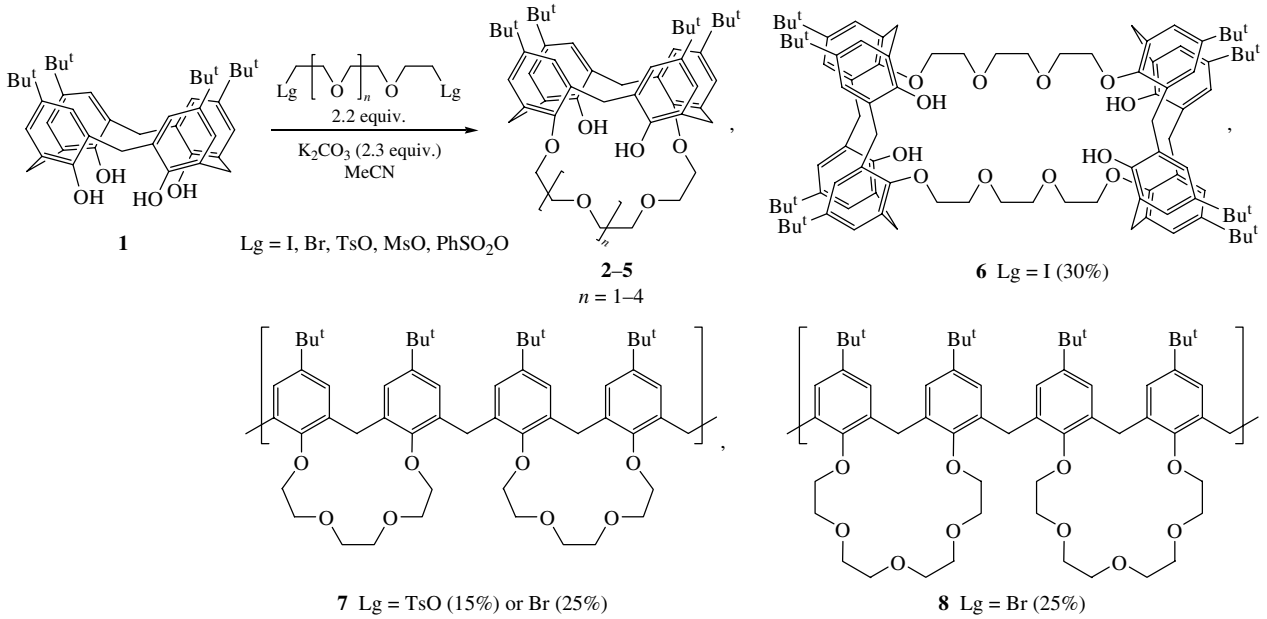
The series of *p-tert*-butylcalix[4]arene-crowns in the cone conformation was synthesised in high yields under conditions producing disubstituted calix[4]arenes in the presence of K_2CO_3 in acetonitrile; the formation of calix-bis(crown)s and doubly(calix)-doubly(crown) in these reactions was established.

Although bridging chains are the most important factors in the complexation of calixcrowns, the presence of lipophilic groups at the upper rim of a calixarene moiety also plays a relevant role in determining the selectivity.[1–7] The synthesis of cone conformers of *p-tert*-butylcalix[4]arene-crowns-5(6,7) with poly(ethylene glycol) ditosylates in refluxing benzene in the presence of Bu^{t}OK was reported previously.[8] The yields of crowned products strongly depend on the lengths of bridging fragments (15–55%). Moreover, the isolation and purification of the crude product are difficult to perform. *p-tert*-Butylcalix-[4]arene-crown-4 was usually prepared by a two-step reaction from a calixarene derivative with the residue of triethylene glycol with the tosyl group at the end of this fragment. For synthesis of biscrowned *p-tert*-butylcalix[4]arenes the either method of protected groups or alkylation of calixarene with polyethylene glycol ditosylates in the presence of a strong base (NaH) were used.[9–11]

Therefore, we studied the introduction of oligo(ethylene glycol) chains with different numbers of donor centres into the molecules of *p-tert*-butylcalix[4]arene **1** and used experimental conditions similar to the procedure leading to the disubstituted calix[4]arenes in the cone conformation in the presence of K_2CO_3 in acetonitrile.[12] At the same time, the systematic study of the leaving group effect on the reaction was carried out.

The reaction of **1** with 2.2 equiv. of oligo(oxa)alkane diiodides containing from two to five oxygen atoms in the presence of 2.3 equiv. of K_2CO_3 in refluxing acetonitrile produced 1,3-*p-tert*-butylcalix[4]crowns-4(5–7) **2–5** in a cone conformation in 60–85% yields. The unexpected result was found with the use of 1,8-diiodo-3,6-dioxaoctane when doubly-(calix[4]arene)-doubly(crown-4) **6** was isolated in > 30% yield. The ^{1}H NMR spectrum of **2** indicated that the calixarene units are in a cone conformation and linked by distal glycol chains in 1,3–1,3-positions: one AB system from the methylene protons of the macrocycles, two singlets from *tert*-butyl protons and two singlets from the protons of aromatic rings with 1:1. The interaction of *p-tert*-butylcalix[4]arene with 1,11-diiodo-3,6,9-trioxaundecane leads to a mixture of the desired product and a small amount of calix[4]arene-crown-5 with the residue of 11-iodo-3,6,9-trioxaundecane.

The change of the iodide ion by the tosyloxy group results in the formation of crowned compounds in 70–95% yields. In case of using the ditosylates of triethylene glycol, 1,2-bridged *p-tert*-butylcalix[4]arene-bis(crown-4) **7** was formed as a by-product in 15% yield, instead of interaction with bromides of 3,6-dioxaoctane or 3,6,9-trioxaundecane, when 1,2-calix[4]-arene-bis(crown-4) and bis(crown-5) **8** were formed in almost 25% yields.



1 **2–5** **6** Lg = I (30%)

7 Lg = TsO (15%) or Br (25%) **8** Lg = Br (25%)

Scheme 1

Table 1 Yields of calixcrowns **2**–**5**.

Lg	Yields of calixcrowns (%)			
	2	**3**	**4**	**5**
I	60	85	85	85
TsO	70–75	90	90	95
Br	70	70	87	90
MsO or $PhSO_3$	65–70	**3** + **4** + **5**: 60–65		

However, the reaction between H-calix[4]arene **9** and diiodides of oligo(oxa)alkanes or ditosylates of oligo(ethylene glycols) yielded only calix[4]arene-crown-4(5,6) ethers **10**–**12** (65–75%).

Thereupon, the alkylation of calixarene **1** with mesylates and phenylsulfonates of oligo(ethylene glycols) resulted in only crowned compounds but with a large amount of unconverted *p-tert*-butylcalix[4]arene (about 30–35%) (Scheme 1, Table 1).

All calix[4]arene-crown ethers were isolated by simple recrystallization from alcohols without column chromatography or HPLC.†

Thus, the method proposed for the preparation of *p-tert*-butylcalix[4]crowns in a cone conformation leads to desired products in good yields. We found that the formation of calixbis(crown) and doubly(calix)-doubly(crown) as by-products depends on the structure of the bridging chain and the nature of the leaving group in the alkylating agent. In the interaction of calix[4]arene with diiodides of oligo(oxa)alkanes or ditosylates of oligo(ethylene glycols), only the calixarene-crowns were formed.

† ^{1}H NMR spectra were recorded on a Varian VXR-300 (300 MHz) spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard. Mass spectra were recorded on MX-1321 and VG 70-70EQ spectrometers; FAB mass spectra were measured on a VG 70-70EQ mass spectrometer using *m*-nitrobenzyl alcohol as a matrix.

General procedure for the calixarene-crowns: a suspension of *p-tert*-butylcalix[4]arene **1** (4 mmol, 2.96 g) or calix[4]arene **9** (4 mmol, 1.69 g) and K_2CO_3 (9.2 mmol, 1.27 g) in dry MeCN (80 ml) was stirred for 30 min; then, the solution of a corresponding alkylation agent (8.8 mmol) in 50 ml of MeCN was added dropwise for 45 min. After stirring for 12–14 (in case of the iodide ion), 8–12 (tosyloxy or bromide ion) or 18–20 h (mesyl or phenylsulfonate), the reaction was stopped; the inorganic precipitate was filtered off; the solution was vacuum concentrated to leave a residue, which was dissolved in $CHCl_3$, washed with 10% HCl and water and then dried over $MgSO_4$. The evaporation of the solvent afforded a white solid crude product, which was purified by crystallization from alcohols. The doubly crowned compounds were isolated from the crude mixture by trituration in hot hexane or heptane and then purified by recrystallization from alcohol–water. Monocrowned calixarenes were purified by recrystallization from methanol or ethanol.

2: mp 262–264 °C. ^{1}H NMR, δ: 0.95 (s, 18H, Bu^t), 1.29 (s, 18H, Bu^t), 3.27 (d, 4H, $ArCH_2Ar$, *J* 13.53 Hz), 4.00–4.15 (m, 12H, OCH_2CH_2O), 4.37 (d, 4H, $ArCH_2Ar$, *J* 13.53 Hz), 6.79 (s, 4H, ArH), 7.05 (s, 4H, ArH), 7.39 (s, 2H, OH). FAB-MS, *m/z*: 763 $(M + H)^+$. Found (%): C, 78.78; H, 8.81. Calc. for $C_{50}H_{66}O_6$ (%): C, 78.70; H, 8.72.

3: mp 250–252 °C. ^{1}H NMR, δ: 0.94 (s, 18H, Bu^t), 1.34 (s, 18H, Bu^t), 3.35 (d, 4H, $ArCH_2Ar$, *J* 13.0 Hz), 3.80–4.15 (m, 16H, OCH_2CH_2O), 4.43 (d, 4H, $ArCH_2Ar$, *J* 13.0 Hz), 6.8 (s, 4H, ArH), 7.15 (s, 4H, ArH), 7.20 (s, 2H, OH). FAB-MS, *m/z*: 807 $(M + H)^+$. Found (%): C, 77.31; H, 8.80. Calc. for $C_{52}H_{70}O_7$ (%): C, 77.38; H, 8.74.

4: mp 240–242 °C. ^{1}H NMR, δ: 0.85 (s, 18H, Bu^t), 1.25 (s, 18H, Bu^t), 3.20 (d, 4H, $ArCH_2Ar$, *J* 13.2 Hz), 3.65–4.10 (m, 20H, OCH_2CH_2O), 4.31 (d, 4H, $ArCH_2Ar$, *J* 13.2 Hz), 6.75 (s, 4H, ArH), 6.98 (s, 4H, ArH), 7.00 (s, 2H, OH). FAB-MS, *m/z*: 851 $(M + H)^+$. Found (%): C, 76.12; H, 8.81. Calc. for $C_{54}H_{74}O_8$ (%): C, 76.20; H, 8.76.

References

1 C. Alfieri, E. Dradi, A. Pochini, R. Ungaro and G. D. Adreetti, *J. Chem. Soc., Chem. Commun*., 1983, 1075.
2 P. J. Dijkstra, J. A. Brunink, K.-E. Bugge, D. N. Reinhoudt, S. Harkema, R. Ungaro, F. Ugozzoli and E. Ghidini, *J. Am. Chem. Soc*., 1989, **111**, 7567.
3 V. Lamare, J.-F. Dozol, F. Ugozzoli, A. Casnati and R. Ungaro, *Eur. J. Org. Chem*., 1998, 1559.
4 T. Jin, *J. Chem. Soc., Perkin Trans. 2*, 2002, 151.
5 B. Pipoosananakaton, M. Sukwattanasinitt, N. Jaiboon, N. Chaichit and Th. Tuntulani, *Tetrahedron Lett*., 2000, **41**, 9095.
6 A. P. Marchand, H.-S. Chong, T. P. Kumar, Z. Huang, S. Alihodzic, W. H. Watson and K. Ejsmont, *Tetrahedron*, 2002, **58**, 10205.
7 Z. Asfari, S. Wenger and J. Vicens, *Supramol. Sci.*, 1994, **1**, 103.
8 J. Dozol, H. Rouquette, R. Ungaro and A. Casnati, *US Patent*, 5926687, B01D, 1999.
9 Y. He, Y. Xiao, L. Meng, Zh. Zeng, Z. Wu and Ch.-T. Wu, *Tetrahedron Lett*., 2002, **43**, 6249.
10 H. Yamamoto, T. Sakaki and S. Shinkai, *Chem. Lett*., 1994, 469.
11 A. Arduini, A. Casnati, L. Dodi, A. Pochini and R. Ungaro, *J. Chem. Soc., Chem. Commun*., 1990, 1597.
12 K. Iwamoto, K. Araki and S. Shinkai, *Tetrahedron*, 1991, **47**, 4325.

Received: 2nd April 2007; Com. 07/2901

5: mp 235–236 °C. ^{1}H NMR δ: 0.80 (s, 18H, Bu^t), 1.21 (s, 18H, Bu^t), 3.40 (d, 4H, $ArCH_2Ar$, *J* 13.5 Hz), 3.70–4.21 (m, 24H, OCH_2CH_2O), 4.45 (d, 4H, $ArCH_2Ar$, *J* 13.5 Hz), 6.84 (s, 4H, ArH), 7.10 (s, 4H, ArH), 7.30 (s, 2H, OH). FAB-MS, *m/z*: 895 $(M + H)^+$. Found (%): C, 75.07; H, 8.84. Calc. for $C_{56}H_{78}O_9$ (%): C, 75.13; H, 8.78.

6: mp 156 °C. ^{1}H NMR, δ: 1.20 (s, 36H, Bu^t), 1.23 (s, 36H, Bu^t), 3.34 (d, 8H, $ArCH_2Ar$, *J* 12.3 Hz), 3.93 (s, 8H, OCH_2CH_2O), 4.14–4.23 (m, 16H, OCH_2CH_2O), 4.37 (d, 8H, $ArCH_2Ar$, *J* 12.3 Hz), 7.00 (s, 8H, ArH), 7.09 (s, 8H, ArH), 8.50 (s, 4H, OH). FAB-MS, *m/z*: 1521 $(M + H)^+$. Found (%): C, 78.62; H, 8.77. Calc. for $C_{100}H_{132}O_{12}$ (%): C, 78.70; H, 8.72.

7: mp 184–186 °C. ^{1}H NMR, δ: 1.19 (s, 18H, Bu^t), 1.20 (s, 18H, Bu^t), 3.18 (d, 2H, $ArCH_2Ar$, *J* 14 Hz), 3.34 (d, 2H, $ArCH_2Ar$, *J* 14 Hz), 3.98 (s, 8H, OCH_2CH_2O), 4.16–4.21 (m, 16H, OCH_2CH_2O), 4.40 (d, 2H, $ArCH_2Ar$, *J* 14 Hz), 4.65 (d, 2H, $ArCH_2Ar$, *J* 14 Hz), 7.00 (s, 4H, ArH), 7.09 (s, 4H, ArH). FAB-MS, *m/z*: 876 $(M + H)^+$. Found (%): C, 76.60; H, 8.78. Calc. for $C_{56}H_{76}O_8$ (%): C, 76.68; H, 8.73.

8: mp 195–197 °C. ^{1}H NMR, δ: 1.17 (s, 18H, Bu^t), 1.19 (s, 18H, Bu^t), 3.20 (d, 2H, $ArCH_2Ar$, *J* 14.2 Hz), 3.60 (d, 2H, $ArCH_2Ar$, *J* 14.2 Hz), 3.70–4.30 (m, 32H, OCH_2CH_2O), 4.50 (d, 2H, $ArCH_2Ar$, *J* 14.7 Hz), 4.75 (d, 2H, $ArCH_2Ar$, *J* 14.7 Hz), 6.87 (s, 4H, ArH), 7.00 (s, 4H, ArH). FAB-MS, *m/z*: 966 $(M + H)^+$. Found (%): C, 74.58; H, 8.82. Calc. for $C_{60}H_{84}O_{10}$ (%): C, 74.65; H, 8.77.

10: mp 381–382 °C. ^{1}H NMR, δ: 3.32 (d, 4H, $ArCH_2Ar$, *J* 12.48 Hz), 3.91 (s, 4H, OCH_2CH_2O), 4.20–4.28 (m, 8H, OCH_2CH_2O), 4.40 (d, 4H, $ArCH_2Ar$, *J* 12.48 Hz), 6.60 (t, 2H, ArH, *J* 7.3 Hz), 6.85 (t, 2H, ArH, *J* 7.3 Hz), 7.04 (d, 4H, ArH, *J* 7.5 Hz), 7.08 (d, 4H, ArH, *J* 7.5 Hz), 8.84 (s, 2H, OH). FAB-MS, *m/z*: 539 $(M + H)^+$.

11: mp 268 °C. ^{1}H NMR, δ: 3.35 (d, 4H, $ArCH_2Ar$, *J* 13.2 Hz), 3.80–4.15 (m, 16H, OCH_2CH_2O), 4.43 (d, 4H, $ArCH_2Ar$, *J* 13.2 Hz), 6.68 (t, 2H, ArH, *J* 7.5 Hz), 6.75 (t, 2H, ArH, *J* 7.5 Hz), 6.95 (d, 4H, ArH, *J* 7.5 Hz), 7.04 (d, 4H, ArH, *J* 7.5 Hz), 7.87 (s, 2H, OH). FAB-MS, *m/z*: 584 $(M + H)^+$.

12: mp 230–232 °C. ^{1}H NMR, δ: 3.38 (d, 4H, $ArCH_2Ar$, *J* 13.4 Hz), 3.80 (s, 4H, OCH_2CH_2O), 3.85–3.94 (m, 4H, OCH_2CH_2O), 4.00–4.10 (m, 12H, OCH_2CH_2O), 4.43 (d, 4H, $ArCH_2Ar$, *J* 13.4 Hz), 6.65 (t, 2H, ArH, *J* 7.5 Hz), 6.72 (t, 2H, ArH, *J* 7.5 Hz), 6.88 (d, 4H, ArH, *J* 7.5 Hz), 7.04 (d, 4H, ArH, *J* 7.5 Hz), 7.52 (s, 2H, OH). FAB-MS, *m/z*: 627 $(M + H)^+$.