Synthesis and Characterization of *p-tert*-Butylcalix[6]-1,4-crown-4-2,6-crown-5, *p-tert*-Butylcalix[6]-1,4-benzocrown-4-2,3-crown-5

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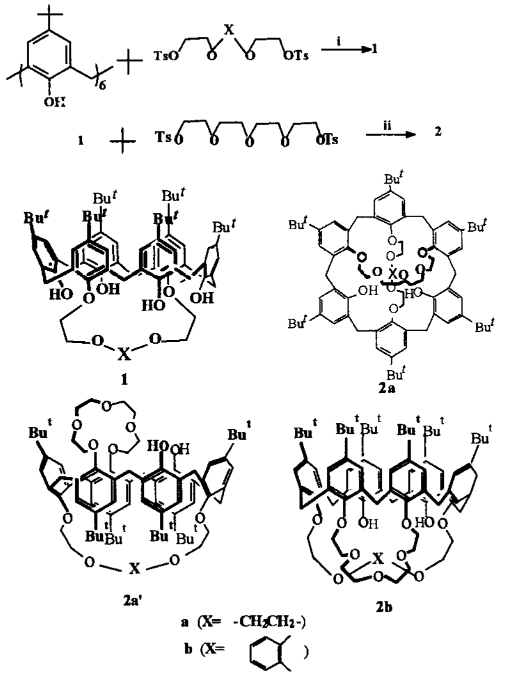
Two new types of calix[6]-bis-crowns, *p-tert*-butylcalix[6]-1,4-crown-4-2,6-crown-5 and *p-tert*-butylcalix[6]-1,4-benzocrown-4-2,3-crown-5, have been synthesized and characterized. The conformation of *p-tert*-butylcalix[6]-1,4-crown-4-2,6-crown-5 may be (**u,d,d,u,d,d**) or (**u,d,u,u,u,d**), and can not be further assigned, the latter adopts (**u,u,u,u,u,u**) conformation at room temperature.

Calixcrowns are a family of calixarenes in which the phenolic oxygens are linked via flexible poly(oxyethylene) chains intramolecularly. As they possess well preorganized structures and more rigid binding sites in comparison with calixarenes and crown ethers, they exhibited superior recognition ability toward alkali metal ions and other ions by the co-operation effect of calixarene and crown moieties. For example, the Na^+/K^+ selectivity attainable with crown ethers has been saturated at the 10^2 order, with calixarenes the selectivity can reach $10^{3.1}$, but it is $10^{5.3}$ for diethoxycalix[4]crown-4 in a partial cone conformation.[1] And also, calix[4]arene crown-6 hosts have been investigated in the sequestration and removal of radioactive ^{137}Cs from aqueous waste mixtures.[2] Therefore, much attention has been paid to the more sophisticated molecules: calix-bis-crowns. All possible types of calix[4]-bis-crowns have been synthesized,[3–9] and their recognition properties toward Cs^+, K^+ etc. have been studied.[10–14] However, in contrast to the extensive investigation on calix[4]-bis-crowns, nothing is known about calix[6]-bis-crowns until we synthesized the first calix[6]-bis-crown, *p-tert*-butylcalix[6]-1,4-2,5-bis-crown–4s[15] and meanwhile, Blanda et al. reported another example of calix[6]-bis-crowns, 1,4-diallyloxy-calix[6]-2,6-3,5-bis-crown-4s.[16] There are eight possible positional isomers of calix[6]-bis-crowns. Thus, only a small part of calix[6]-bis-crowns have been synthesized.

In this paper, we wish to report the synthesis and characterization of two new types of calix[6]-bis-crowns, *p-tert*-butylcalix[6]-1,4-crown-4-2,6-crown-5 **2a** and *p-tert*-butyl-calix-[6]-1,4-benzocrown-4-2,3-crown-5 **2b.** The new calix[6]-bis-crowns are also the first examples of calix[6]-bis-crowns with inequivalent crown loops in length. Their extraction behavior towards some picrate salts was also investigated. The synthetic route is depicted as Scheme 1:

Reacting *p-tert*-butyl-calix[6]arene with triethylene glycol ditosylates or 1,2-bistosyloxyethoxybenzene in the presence of 9 equivs of K_2CO_3 in toluene for 24 h under a nitrogen atmosphere, 1,4-*p-tert*-butylcalix[6]crown-4 **1a** and 1,4-*p-tert*-butylcalix [6]benzocrown-4 **1b** were obtained in 40 and 55% yield, respectively.[15] To the DMF solution of **1**, NaH was added at room temperature, followed by 1.2 equivs of tetraethylene glycol ditosylates with stirring at 60 °C for 12 h. The excess of NaH was quenched by addition of a minimal quantity of methanol (**caution!**). Distilling off the solvent, the residue was treated with HCl(10%, v/v) and then extracted with ethyl acetate. After purification by column chromatography, *p-tert*-butylcalix[6]-1,4-crown-4-2,6-crown-5 **2a** and *p-tert*-butylcalix[6]-1,4-benzocrown-4-2,3-crown-5 **2b** were isolated as white solids in 32% yield, mp 314-316 °C and in 46% yield, mp 283–285 °C, respectively.



Scheme 1. Reagents and conditions: (i)K_2CO_3, toluene, reflux, 24 h; (ii) NaH/DMF, 60 °C, 12 h.

Two compounds gave satisfactory elemental analysis results and exhibited the expected molecular ion peaks. The structures of these compounds were also confirmed by NMR spectra.[18] In the NMR spectrum of **2a,** four singlets for the *tert*-butyl groups (1:2:2:1), three pairs of doublets (one is mixed with ethylene protons) (1:1:1) for methylene protons and a singlet for hydroxyl protons can be assigned. This is in good accordance with the structure of *p-tert*-butylcalix[6]-1,4-crown-4-2,6-crown-5 **2a** and not in accordance with other structures such as *p-tert*-butylcalix[6]-1,4-crown-4-2,5-crown-5 or *p-tert*-butylcalix[6]-1,4-crown-4-2,3-crown-5, which should have three singlets for the *tert*-butyl groups (1:1:1). However, as the (**u,d,d,u,d,d**) **2a'** and (**u,d,u,u,u,d**) **2a"** conformations will give similar NMR data for methylene protons, it is not possible to further assigned, although we believe that the former is more plausible. In the NMR spectrum of **2b**, three singlets for the *p-tert*-butyl groups (1:1:1), four pairs of doublets (one is mixed with ethylene protons) (1:2:2:1) for methylene protons, a singlet for hydroxyl protons can be assigned. This is consistent with the structure of *p-tert*-butylcalix[6]-1,4-benzocrown-4-2,3-crown-5 and not with other structures such as *p-tert*-butylcalix[6]-1,4-benzocrown-4-2,6-crown-5, which should have four singlets for *p-tert*-butyl (1:2:2:1) or *p-tert*-butylcalix[6]-1,4-benzocrown-4-2,5-crown-5 which should have three pairs doublets (1:1:1) for methylene protons. The cone (**u,u,u,u,u,u**) conformation of **2b** at room temperature is easily deduced from the methylene protons in calixarene skeleton showing four pairs of doublets in a ratio of 1:2:2:1.

Examination of the CPK molecular models reveals that compounds **2a**, **2b** are well preorganized for binding cations. 1,4-*p-tert*-Butylcalix[6]crown-4 **1a** and 1,4-*p-tert*-butylcalix-[6]-benzocrown-4 **1b** are used as reference compounds. Percentage extraction of hosts **2a**, **2b** towards several picrate salts from water into $CHCl_3$ at 25 °C are summarized in Table 1. Comparing with compounds **1a** and **1b**, the extraction level of *p-tert*-butylcalix[6]-1,4-benzocrown-4-2,3-crown-5 (**2b**) is much higher, this can be attributed to the beneficial influence of a second bridging subunit generally increases the rigidity of calix[6]arene framework and compound **2b** adopts a cone conformation at the room temperature. Besides, the seletivity towards the alkali metal ions for compounds **2a** and **2b** is also different for that of compounds **1a** and **1b**. This may be attributed to two polyethylene glycol chains co-operation effect.

Table1. Percentage extraction (%E) of picrate salts from water into $CHCl_3$ at 25 °C [a]

Host	%E						
	Li^+	Na^+	K^+	Cs^+	*n*-$PrNH_3^+$	$Me_2NH_2^+$	$Et_2NH_2^+$
2a	3.4	6.9	5.9	16.2	12.8	11.4	12.1
2b	6.3	11.2	19.5	42.4	14.1	13.6	16.5
1a	2.6	6.5	4.5	----	2.5	3.7	5.3
1b	1.2	3.9	4.1	----	2.9	3.8	5.6

Arithmetic mean of several experiments-standard deviation on the mean: $\sigma_{N-1} \leq 1$.

[a] 1.00 ml of 0.0025 mol dm^{-3} receptor solution in $CHCl_3$ was shaken (10 min) with 1.00 ml of 0.005 mol dm^{-3} picrate salt solution in H_2O and the percentage extraction was measured from the resulting absorbance at 380 nm. The definition of E%, experimental procedure, *etc* are the same as in the literature.[17]

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18 ^1H NMR (300 MHz, $CDCl_3$): **2a.**1.17(s, 9H, $C(CH_3)_3$), 1.24(s, 18H, $C(CH_3)_3$), 1.26(s, 18H, $C(CH_3)_3$), 1.32(s, 9H, $C(CH_3)_3$), 2.35(t, 4H, *J* = 9.0 Hz, OCH_2CH_2), 2.70(d, 2H, *J* = 10.8 Hz, OCH_2CH_2), 2.88(q, 4H, *J* = 10.5 Hz, $COCH_2CH_2$), 3.16(q, 4H, *J* = 10.5 Hz, OCH_2CH_2), 3.31(t, 4H, *J* = 9.0 Hz, OCH_2CH_2), 3.44(d, 2H, *J* = 10.2Hz, $ArCH_2Ar$), 3.53–3.64(m, 12H, OCH_2CH_2 and $ArCH_2Ar$), 3.87(d, 2H, *J* = 10.2 Hz, $ArCH_2Ar$), 4.08(d, 2H, *J* = 13.5 Hz, $ArCH_2Ar$), 4.17(d, 2H, *J* = 13.5 Hz, $ArCH_2Ar$), 4.47(d, 2H, *J* = 17.7 Hz, $ArCH_2Ar$), 6.54(d, 2H, *J* = 2.7 Hz, ArH), 6.72 (d, 4H, *J* = 2.7 Hz, ArH), 6.95(d, 4H, *J* = 2.7 Hz, ArH), 7.14(s, 2H, ArOH), 7.34(d, 2H, *J* = 2.7 Hz, ArH). MS(FAB): 1,244 (M^+, 20%). Anal. Calcd for $C_{80}H_{108}O_{11}$: C, 77.13; H, 8.74%. Found: C, 77.15; H, 8.71%.

2b. 1.16(s, 18H, $C(CH_3)_3$), 1.22(s, 18H, $C(CH_3)_3$), 1.26(s, 18H, $C(CH_3)_3$), 2.44(t, 2H, *J* = 9.0 Hz, OCH_2CH_2), 2.73(q, 4H, *J* = 10.2 Hz, OCH_2CH_2), 2.92(q, 4H, *J* = 10.2 Hz, OCH_2CH_2), 3.11(t, 4H, *J* = 9.0 Hz, OCH_2CH_2), 3.26-3.59(m, 11H, OCH_2CH_2 and $ArCH_2Ar$), 3.82(d, 1H, *J* = 10.2 Hz, $ArCH_2Ar$), 3.90(d, 1H, *J* = 10.2 Hz, $ArCH_2Ar$), 4.03(d, 2H, *J* = 17.4 Hz, $ArCH_2Ar$), 4.14(d, 2H, *J* = 13.8 Hz, $ArCH_2Ar$), 4.19(d, 1H, *J* = 12.9 Hz, $ArCH_2Ar$), 4.34(d, 2H, *J* = 13.8 Hz, $ArCH_2Ar$), 4.43(d, 2H, *J* = 17.4 Hz, $ArCH_2Ar$), 6.44(s, 4H, ArH), 6.62(d, 4H, *J* = 2.7 Hz), 7.05(d, 4H, *J* = 2.7 Hz, ArH), 7.36(d, 4H, *J* = 2.7 Hz, ArH), 8.15(s, 2H, ArOH). MS(FAB): 1,293 (MH^+, 10%). Anal. Calcd for $C_{84}H_{108}O_{11}$: C, 77.98;H, 8.41%. Found: C, 77.95; H,8.45%.