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Synthesis of *p-tert*-butylcalix[6]-1,4-2,5-bis-crowns

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Abstract

The synthesis and complexation properties of the first example of *p-tert*-butylcalix[6]-1,4-2,5-bis-crowns are reported. Their complexation abilities and selectivities are different from that of analogous calix[6]crown. Compound **2b** exhibits high complexation selectivity towards *n*-$PrNH_3^+$.

Calixcrowns are a family of macropolycyclic molecules in which the subunits of calixarene and crown ethers are combined through the bridging of phenolic oxygen atoms of the calixarene by polyoxyethylene chains. The first member of this family was reported by Alfieri et al. as early as 1983.[1] As calixcrowns possess well preorganized structures and more rigid binding sites in comparison with calixarenes and crown ethers, they exhibited superior recognition ability toward alkali metal cations. 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.[2] Therefore, much attention has been paid to more sophisticated molecules: calixa-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] Two types of calix[8]-bis-crowns have also been reported.[15,16] However, no paper concerning the synthesis of calix[6]-bis-crowns has appeared to date. Even for calix[6]crowns, only 1,4-*p-tert*-butylcalix[6]crown-5 and 1,4-calixa[6]crown-5[17] as well as 1,3-*p-tert*-butylcalix[6]crown-3[18] have been synthesized.

In this paper, we wish to report the synthesis of the first calix[6]-bis-crowns: *p-tert*-butylcalix[6]-1,4-2,5-bis-crown-4 **2a** and *p-tert*-butylcalix[6]-1,4-crown-4-2,5-benzocrown-4 **2b** as well as their extraction abilities toward some cations. The synthetic route is depicted in Scheme 1.

Reacting *p-tert*-butylcalix[6]arenes with triethylene glycol ditosylates or 1,2-bistosyloxyethoxybenzene in the presence of 9 equiv. of K_2CO_3 in toluene for 36 h under a nitrogen atmosphere, gave 1,4-*p-tert*-butylcalix[6]crown-4 **1a** and 1,4-*p-tert*-butylcalix[6]benzocrown-4 **1b**.[19] To the DMF solution of **1**, NaH was added at room temperature, followed by 1.2 equiv. of triethylene glycol ditosylate with stirring at 70°C for 7 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

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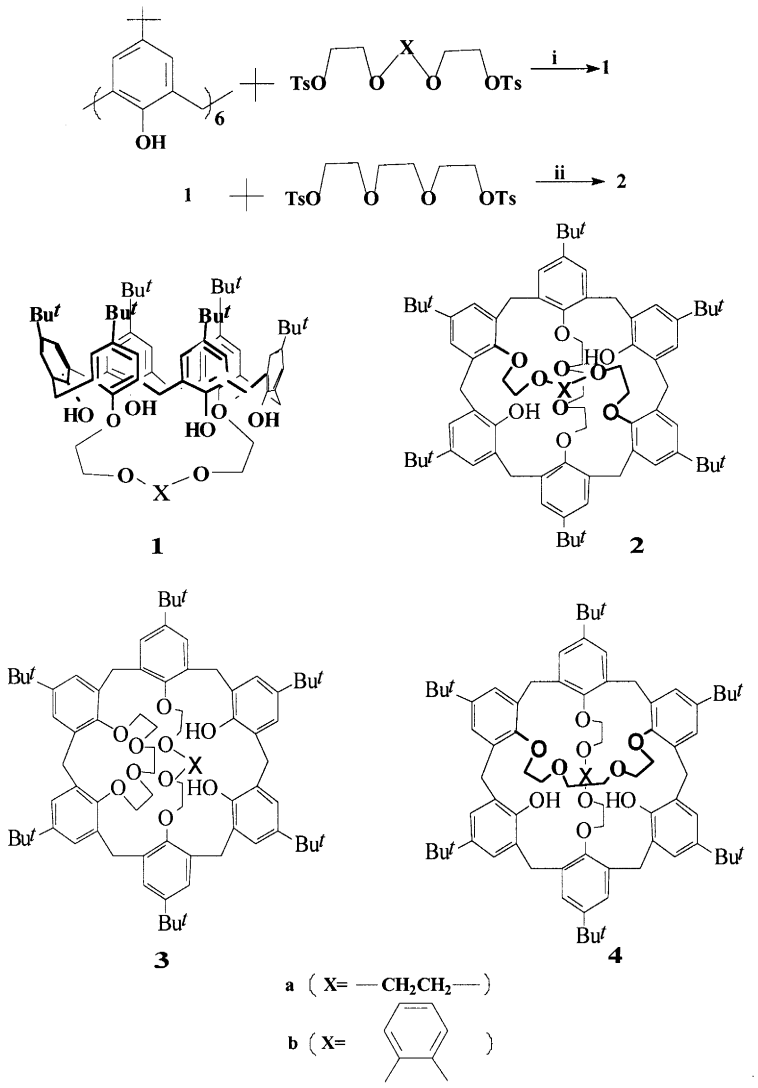

Scheme 1. *Reagents and conditions*: (i) K_2CO_3, toluene, reflux, 36 h; (ii) NaH/DMF, 70°C, 7 h

acetate. After purification by column chromatography, the *p-tert*-butylcalix[6]-1,4-2,5-bis-crowns-4 **2a** and *p-tert*-butylcalix[6]-1,4-crown-4-2,5-benzocrown-4 **2b** were isolated as white solids in 66% yield, m.p. 322–324°C and in 70% yield, m.p. 308–310°C, respectively.

Two of the synthesized compounds gave satisfactory elemental analysis results and exhibited the expected molecular ion peaks. The structures of these compounds were also confirmed by NMR spectra.[20] In the NMR spectrum of **2a**, two singlets for the *tert*-butyl groups (2:1), a pair of doublets (one overlaps with ethylene protons) and one singlet for methylene bridges (2:1), and a singlet for hydroxy protons can be assigned. This is in good accordance with the structure of *p-tert*-butylcalix[6]-1,4-2,5-bis-crowns **2a** and not in accordance with other structures such as *p-tert*-butylcalix[6]-1,4-2,3-bis-crowns **3a** or *p-tert*-butylcalix[6]-1,4-2,6-bis-crowns **4a** which should have three singlets for the *tert*-butyl groups (1:1:1) as shown in Scheme 1. As **2a** and **2b** are synthesized by the same method, it is reasonable to assume that they possess similar structures. This is supported by their NMR spectra. In the NMR

Table 1
Percentage extraction (%E) of picrate salts from water into $CHCl_3$ at 25°C.[a] Arithmetic mean of several experiments–standard deviation on the mean: $ó_{N-1} < 1$

Host	*%E*						
	Li^+	Na^+	K^+	NH_4^+	*n*-$PrNH_3^+$	$Me_2NH_2^+$	$Et_2NH_2^+$
2a	1.4	5.2	18.9	16.2	4.8	6.4	12.1
2b	0.3	1.2	9.5	12.4	24.1	3.6	6.5
1a	2.6	6.5	4.5	3.6	2.5	3.7	5.3
1b	1.2	3.9	4.1	4.0	2.9	3.8	5.6

[a]1.00 ml of 0.0025 mol dm^{-3} receptor solution in $CHCl_3$ was shaken(10min) with 1.00ml of 0.005 mol dm^{-3} picrate salt solution in H_2O and the percentage extraction was measured from the resulting absorbance at 380nm.

spectrum of **2b**, three singlets for the *tert*-butyl groups (1:1:1), three pairs of doublets (a pair of doublets overlaps with ethylene protons) for methylene bridges, and a singlet for the hydroxy protons can be distinguished. This is also consistent with the structure of **2b** and not with **3b** which should have four pairs of doublets for methylene bridges at least or **4b** which should have four singlets for *tert*-butyl groups. It is noteworthy that although the conformations of **2a** and **2b** are difficult to define, they are different from cone or 1,2,3-alternate conformations which have been studied thoroughly.

The percentage extraction of hosts **2a** and **2b** as well as **1a** and **1b** toward some picrate salts are shown in Table 1, the extraction abilities of **2a** toward the tested cations are higher than that of **2b** except for *n*-$PrNH_3^+$. The host **2b** shows very high selectivity toward *n*-$PrNH_3^+$. To the best of our knowledge, this is the most effective ionophore for *n*-$PrNH_3^+$ reported in calixarene chemistry. Compared to **1a** and **1b**, the extraction levels of **2a** and **2b** toward K^+, NH_4^+, *n*-$PrNH_3^+$ etc. are much higher, but the reverse phenomena are observed for small alkali metal cations, i.e. Li^+ and Na^+.

Acknowledgements

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20. ^{1}H NMR (250 MHz, $CDCl_3$): **2a**: 1.16 (s, 36H, $ArC(CH_3)_3$), 1.33 (s, 18H, $ArC(CH_3)_3$), 2.86 (t, 4H, J=9.0 Hz, OCH_2CH_2), 3.25 (q, 4H, J=10.5 Hz, OCH_2CH_2), 3.34–3.50 (m, 16H, OCH_2CH_2 and $ArCH_2Ar$), 3.8 (q, 4H, J=10.5 Hz, OCH_2CH_2), 4.07 (s, 4H, $ArCH_2Ar$), 4.39 (d, 4H, J=15.0 Hz, $ArCH_2Ar$), 6.91 (s, 4H, ArH), 7.03 (s, 2H, ArOH), 7.04 (s, 4H, ArH), 7.11 (s, 4H, ArH). MS (FAB): 1239 (MK^+, 100%), 1200 (M^+, 20%). Anal calcd for $C_{78}H_{104}O_{10}$: C, 77.96; H, 8.72; found: C, 78.10; H, 8.60; **2b**: 1.14 (s, 18H, $ArC_3(CH_3)$), 1.25 (s, 18H, $ArC(CH_3)_3$), 1.28 (s, 18H, $ArC(CH_3)_3$), 2.44 (t, 2H, J=9.7Hz, OCH_2CH_2), 2.74 (q, 2H, J=7.1 Hz, OCH_2CH_2), 3.15 (q, 2H, J=7.1 Hz, OCH_2CH_2), 3.26–3.86 (m, 18H, OCH_2CH_2 and $ArCH_2Ar$), 3.99 (d, 2H, J=17.4 Hz, $ArCH_2Ar$), 4.19 (d, 2H, J=13.5 Hz, $ArCH_2Ar$), 4.23 (d, 2H, J=13.5 Hz, $ArCH_2Ar$), 4.64 (d, 2H, J=17.4 Hz, $ArCH_2Ar$), 6.54 (t, 4H, J=2.4 Hz, ArH), 6.72 (t, 4H, J=2.4 Hz, ArH), 6.95 (d, 2H, J=2.5 Hz, ArH), 7.04 (s, 2H, ArOH), 7.10 (d, 2H, J=2.5 Hz, ArH), 7.17 (d, 2H, J=2.5 Hz, Ar), 7.24 (d, 2H, J=2.5 Hz, ArH). MS (FAB): 1287 (MK^+, 100%), 1248 (M^+, 20%). Anal. calcd for $C_{82}H_{104}O_{10}$: C, 78.81; H, 8.39; found: C, 78.85; H, 8.4.