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Research Communication

Synthesis of an Unsymmetrically Doubly Bridged Calix[4]arene in the 1,3-Alternate Conformation

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Abstract. We report the synthesis of the first calix[4]arene constrained to a 1,3-alternate conformation by one crown ether and one di-aza-benzo crown ether bridgings. Preliminary binding properties are also given.

Key words: Bridged calix[4]arenes, 1,3-alternate conformation, crown-ether, di-aza-benzo-crown ether.

Calixarenes, and calix[4]arenes in particular, have been chemically transformed into a large variety of derivatives designed for the selective binding of various metal ions [1, 2]. Among these derivatives, calix[4]arenes have been constrained to a 1,3-alternate conformation by doubly bridging thus producing globular ligands presenting very rigid cavities with specific complexing properties. For example, 1,3-calix[4]arenes doubly-bridged at the 'upper rim' with xylyl units have been shown to be good ionophores due to π-donor participation in the complexation of cations [3]. At the same time, evidence has been presented for metal-tunneling through the calixarene cavity in these receptors [3]. The reaction of calix[4]arenes with various polyethylene ditosylates afforded a series of 1,3-calix[4]-*bis*-crowns in which the glycolic chains are attached at the 'lower rim' of calix[4]arenes in a 1,3-alternate conformation (see Chart I with $X_1 = X_2$ = crown ether element) [4–7]. Depending on the nature of the crown ether, these receptors have been shown to be selective carriers of Cs through supported liquid membranes [4]. Similarly, 1,3-calix[4]-*bis*-(di-aza-benzo) crown ethers (see Chart I with $X_1 = X_2$ = di-aza-benzo crown element) have been described which are able to complex ammonium cation with an inter- or intramolecular cation-exchange [8].

All those doubly bridged 1,3-calix[4]arenes described in the literature are symmetrical, presenting two equivalent coordination sites. This paper reports on the synthesis and complexing properties of hybrid 1,3-calix[4]-*mono*-(di-aza-

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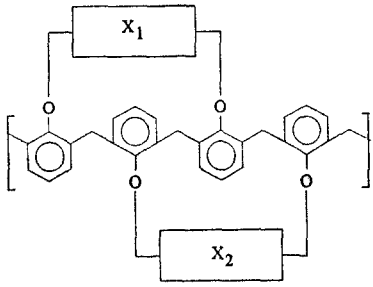
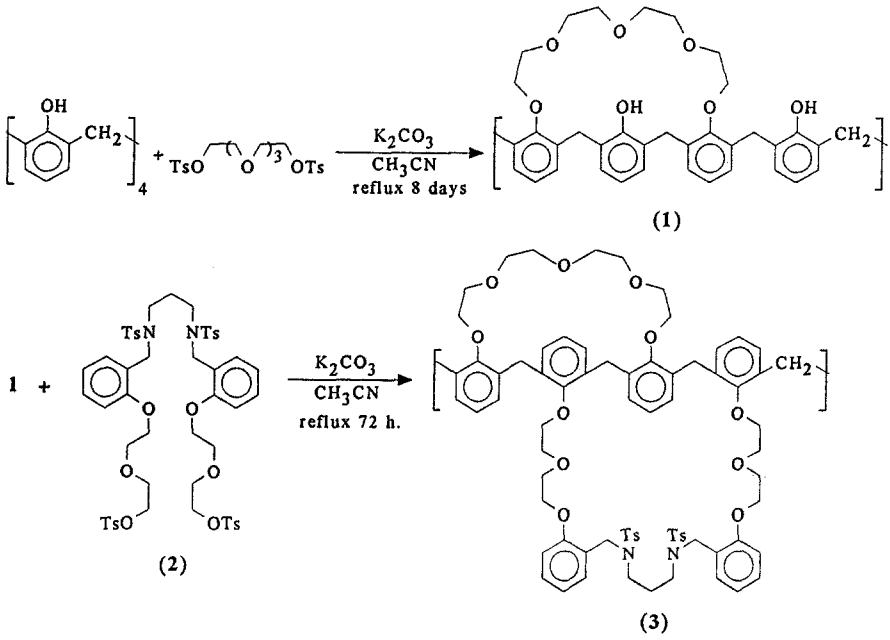


Chart I.

benzo)crown-*mono*-crown-5 (**3**) (see Chart I with X_1 = crown ether and X_2 = di-aza-benzo crown elements).

The synthesis of (**3**) is depicted in Scheme 1. By means of a procedure described by us [9] calix[4]arene was condensed with 1 equiv. of tetraethylene glycol ditosylate in the presence of K_2CO_3 in refluxing acetonitrile for 8 days [10]. Calixcrown-5 (**1**) was obtained pure by chromatography on silica with 95/5 CH_2Cl_2/acetone as eluent. The yield was 27%. The structure of (**1**) was ascertained by its analytical data: the *distal* 1,3-capping and the cone conformation of (**1**) was deduced from the presence of an AB system for the methylene protons in the calixarene ring. The closely related 1,3-capped *p-tert*-butylcalix[4]crown-6 [11] and calix[4]crown-4 [5] have been described elsewhere. In a second step calixcrown (**1**) was treated with 1 equiv. of the tetrakis *O*, *N*-tosylated compound (**2**) [8] in the presence of K_2CO_3 in refluxing acetonitrile for 2 days [10]. Product (**3**) was obtained pure in 20% yield by chromatography on silica with 90/5/5 CH_2Cl_2/CH_3OH/acetone as eluent. During this condensation the capping by the di-aza-benzo crown chains enforces the 1,3-alternate conformation on calixcrown (**1**) as reflected by the ^{1}H-NMR spectrum of (**3**). One observes a singlet at 3.86 ppm for the methylene protons $ArCH_2Ar$ in (**3**). The detection of one singlet at 2.41 ppm for the methyl of the *N*-tosyl indicated the symmetry of (**3**).

Ligand (**3**) was observed to extract potassium picrate, K^+Pic^-, and ammonium picrate, $NH_4^+Pic^-$. ^{1}H-NMR indicated the formation of a 1 : 1 complex as deduced from the integration ratio between the picrate proton singlet and the CH_3 signal of the tosyl residue and mass spectrometry in both cases [12]. The $ArOCH_2$ signal of the two cavities shifted from 3.13 ppm in (**3**) to 3.56 and 3.51 ppm in (**3**)–$\mathbf{K^+Pic^-}$ and (**3**)–$\mathbf{NH_4^+Pic^-}$, respectively. The signal of the *meta* aromatic protons shifted from 7.00 ppm in (**3**) to 7.23 ppm in (**3**)–$\mathbf{K^+Pic^-}$ and (**3**)–$\mathbf{NH_4^+Pic^-}$. One deduces the cation to be located near the phenolic *O*-donor atoms and in the center of the calix[4]arene. However we were unable to choose which loop the metal cation was located in. In a previous work [8] we have observed the corresponding signals to coalesce due to an inter- or intramolecular cation-exchange in the 1 : 1 complexes **$NH_4^+Pic^-$-1,3-calix[4]-bis-(di-aza-benzo) crown ethers** ($X_1 = X_2$ = di-aza-benzo crown). In contrast to these observations, the absence of coalescence in the ^{1}H-



Scheme I.

NMR spectra of the (3)–K^+Pic^- and (3)–$NH_4^+Pic^-$ complexes are indicative of stronger complexes prevented from cation-ligand exchange and in which the cation is tightly located. One can assume that the role of the crown ether chain is to preorganize the ligand for better complexation and/or to more tightly bind the cations.

Our objectives are: (a) to replace the crown ether chain by an alkyl chain of the same length to evaluate its coordination role; (b) to remove the tosyl groups to provide calixarenic ligands having both hard and soft coordinating sites.

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10. *Preparation of* (**1**): In a 1000 mL 2-necked round bottom flask, a solution of calix[4]arene (4.245 g, 10.00 mmoles) and potassium carbonate (1.451 g. 10.50 mmoles) in acetonitrile (700 mL) was stirred at r. t. overnight. A solution of tetraethylene glycol ditosylate (5.026 g, 10.00 mmoles) in acetonitrile (20 mL) was added in one time and refluxed for 8 days. After evaporation to dryness under reduced pressure, the residue was dissolved in chloroform and the potassium carbonate neutralised with 1N HCl. The organic layer was dried over Na_2SO_4 and concentrated to obtain a yellow solid (6.571 g). Pure product (**1**) (1.556 g, 27%) was obtained as a white solid after chromatography (SiO_2, Bio-Rad, Bio Sil 40–63, CH_2Cl_2/acetone 95/5). Mp. 263–264 °C. ^{1}H-NMR ($CDCl_3$, 200 MHz, 25 °C): δ 3.37 and 4.43 (AB system, J = 13 Hz, 8H, CH_2), 3.86 (t, J = 4.8 Hz, 4H, CH_2), 3.96 (t, J = 4.8 Hz, 4H, CH_2), 4.10 (s, 8H, CH_2), 6.67–7.10 (m, 12H, arom.), 7.74 (s, 2H, OH). Positive ion FAB, m/z = 582.2 (M^+, 100%). *Found*: H 6.47, C 74.26, *Calcd.* for $C_{36}H_{38}O_7$: H 6.57, C 74.21.

Preparation of (**3**): In a 250 mL 2-necked round bottom flask, a solution of (**1**) (1.165 g, 2.00 mmoles) and potassium carbonate (1.382 g, 10.10 mmoles) in acetonitrile (150 mL) was stirred at r. t. for 4 h. A solution of (**2**) (2.159 g, 2.00 mmoles) in acetonitrile (15 mL) was added dropwise and refluxed for 2 days. After evaporation to dryness under reduced pressure, the residue was dissolved in chloroform and the potassium carbonate neutralised with 1N HCl. The organic layer was dried over Na_2SO_4 and concentrated to obtain a beige solid (3.019 g). Pure product (**3**) (0.525 g, 20%) was obtained as a white solid after chromatography (SiO_2, Bio-Rad, Bio Sil 40–63, CH_2Cl_2/MeOH/acetone 90/5/5). Mp. 92–93 °C. ^{1}H-NMR ($CDCl_3$, 200 MHz, 25 °C): δ 1.50–1.57 (m, 2H, CH_2), 2.41 (s, 6H, CH_3), 2.98 (t, J = 6.9 Hz, 4H, CH_2), 3.13 (t, J = 5.00 Hz, 8H, CH_2), 3.39–3.93 (m, 24H, CH_2), 3.86 (s, 8H, CH_2), 4.25 (s, 4H, CH_2), 6.75–7.64 (m, 28H, arom.). Positive ion FAB, m/z = 1317.4 (M^+, 58%), 1161.4 (M^+—$C_7H_7O_2S_1$, 100%). *Found*: H 6.37, C 68.13; *Calcd.* for $C_{75}H_{84}O_{15}N_2S_2$: H 6.43, C. 68.37.

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12. *Preparation of the 1 : 1 complex* (**3**)–$\mathbf{K^+Pic^-}$: ligand (**3**) (0.015 g, 0.011 mmoles) and solid potassium picrate (0.016 g, 0.057 mmoles) were stirred for 24 h. The unreacted K^+Pic^- was filtered off and the filtrate evaporated to dryness to give a yellow solid. Mp = 120–121 °C. Quantitatively yield. ^{1}H-NMR ($CDCl_3$, 200 MHz, 25 °C): δ 1.25 (s large, 2H, CH_2), 2.41 (s, 6H, CH_3), 2.95 (t, J = 6.9 Hz, 4H, CH_2), 3.56 (t, J = 5.00 Hz, 8H, CH_2), 3.66–4.10 (m, 24H, CH_2), 3.80 (s, 8H, CH_2), 4.28 (s, 4H, CH_2), 6.71–7.62 (m, 28H, arom.), 8.79 (s, 2H, arom.). Positive ion FAB, m/z = 1355.0 ($M^+ + K^+$, 100%). *Found*: H 5.70, C 61.30; *Calcd.* for $C_{81}H_{86}O_{22}N_5S_2K_1$: H 5.47, C 61.39.

Preparation of the 1 : 1 complex (**3**)–$\mathbf{NH_4^+Pic^-}$: ligand (**3**) (0.015 g, 0.011 mmoles); ammonium picrate (0.015 g, 0.057 mmoles); 2 h. Mp = 85–86 °C. Quantitative yield. ^{1}H-NMR ($CDCl_3$, 200 MHz, 25 °C): δ 1.36 (s large, 2H, CH_2), 2.41 (s, 6H, CH_3), 2.95 (t, J = 6.9 Hz, 4H, CH_2), 3.51 (t, J = 5.00 Hz, 8H, CH_2), 3.67–4.10 (m, 24H, CH_2), 3.82 (s, 8H, CH_2), 4.28 (s, 4H, CH_2), 6.69–7.61 (m, 28H, arom.), 8.79 (s, 2H, arom.). Positive ion FAB, m/z = 1334.7 ($M^+ + NH_4^+$, 34%). *Found*: H 5.88, C 60.16; *Calcd.* for $C_{81}H_{90}O_{22}N_6S_2 \cdot 3H_2O$: H 5.98, C 60.14.