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# Unsymmetrical Calix[4]-*bis*-crowns-6 with Unequivalent Crown Loops.

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**Abstract:** Base-catalysed reactions of calix[4]crown-6 with suitable ditosylates produced unsymmetrical calix[4]-*bis*-crowns-6 **1** and **2**. Cesium ion preferred to bind the polyether loop substituted by 1,2-phenylene or 2,3-naphthylene groups as evidenced by X-ray structure. © 1998 Elsevier Science Ltd. All rights reserved.

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1,3-Calix[4]-*bis*-crowns fixed in the 1,3-alternate conformation by the linkage of phenyl rings 1,3 and 2,4 with polyether chains have recently been shown to be selective cesium complexants when the polyether chains contain six oxygen donor atoms.[1-4] Enhanced $Cs^+/Na^+$ selectivity was obtained by introduction of 1,2-phenylene residue or 2,3-naphthyl group in the middle of the crown-6 loops. The observed better $Cs^+/Na^+$ selectivity was attributed to the replacement of *sp3* carbons by *sp2* ones in the glycol units leading to a flattening of the polyether chains.[4] This geometrical change leads to i) a stronger complexation of the cesium cation and/or ii) a weaker complexation of the sodium cation. In order to further explore the factors controlling the $Cs^+/Na^+$ selectivity in calix[4]-*bis*-crowns-6 we prepared unsymmetrical calix[4]-*bis*-crowns-6 containing both crown-6- and arylene-modified crown-6 ether loops.

We report herein the synthesis, structural characterization and complexing properties of 1,3-alternate calix[4]arene-1,3-crown-6;2,4-(1,2-phenylene)-crown-6 **1** and 1,3-alternate calix[4]arene-1,3-crown-6;2,4-(2,3-naphthylene)-crown-6 **2**. Previous studies of an unsymmetrical calix[4]arene-*bis*-crown-6 in which a 1,3-phenylene was introduced in one loop showed that the cesium ion prefers to bind the oxoethylene-crown-6 loop only.[5]

The synthesis of **1** and **2** is illustrated in Scheme 1. Calix[4]crown-6[5] was reacted with the corresponding arylene-modified pentaethyleneglycol ditosylate in the presence of potassium carbonate in refluxing acetonitrile to produce the respective calix[4]-*bis*-crown-6 **1** and **2** in good yields (see experimental[6]). The 1,3- and 2,4-polyether linkages were assigned from the $^1H$-NMR spectra which showed only a set of two triplets ($J$ = 7.5 Hz) at 6.70 ppm and 6.87 ppm, and 6.86 ppm and 6.68 ppm, for the *para* aromatic protons of the calix units in **1** and **2**, respectively. The 1,3-alternate conformations of the macrorings in **1** and **2** were assumed from the observation of respective singlets at 3.81 ppm and 3.80 ppm for the $ArCH_2Ar$ methylene protons.

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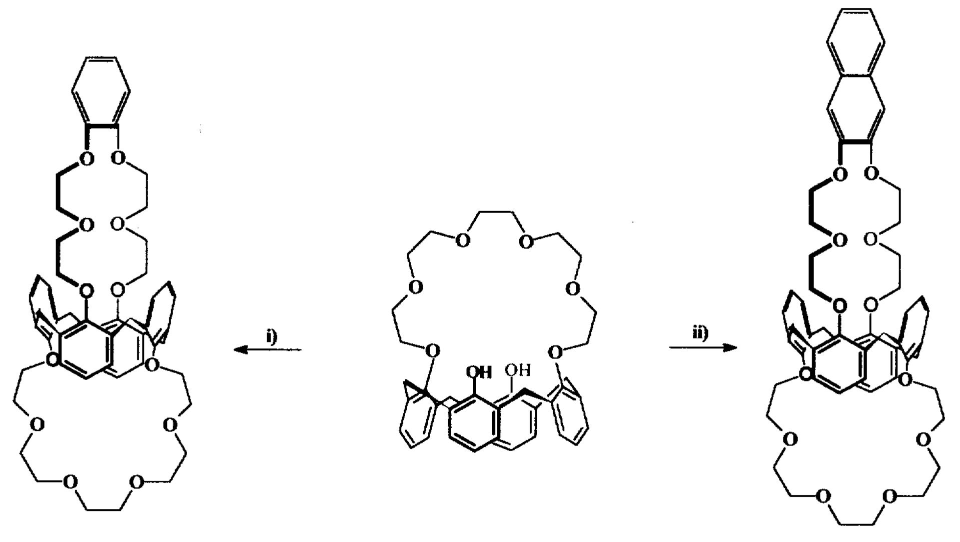

**1** **2**

i) TsO($CH_2CH_2O)_2$-1,2-phenylene-($OCH_2CH_2)_2$OTs, $K_2CO_3$, $CH_3CN$, reflux
ii) TsO($CH_2CH_2O)_2$-2,3-naphthyl-($OCH_2CH_2)_2$OTs, $K_2CO_3$, $CH_3CN$, reflux

**Scheme 1.** Synthesis of **1** and **2**.

The molecular geometries of **1** and **2** were confirmed by the determination of their crystal structures[7] which are consistent with the connectivity of the glycolic chains as formulated above. Both molecules complex two acetonitrile molecules (one in each loop), which is a common occurrence with such compounds.[8] The crown conformations can be described by the sequence of *gauche* O-C-C-O torsion angles, identical in **1** and **2**: $g^+g^-g^+g^-g^+$ for the crown-6 moieties and $g^+g^-Og^+g^-$ for the substituted crowns (with no anomalies on C-O-C-C anti angles). All the ether oxygen lone pairs are directed towards the crown centre predisposed to complex cations.

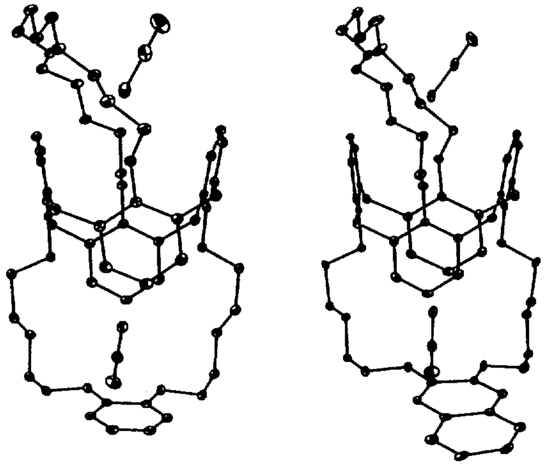

**Figure 1.** Molecular structures of **1**.$3CH_3CN$ (left) and **2**.$3CH_3CN.CHCl_3$ (right). Uncomplexed solvent molecules are omitted.

Reactions of chloroform solutions of **1** and **2** with excess solid sodium and cesium picrates for 24 h resulted in the formation of solutions of complexes **1.Na**$^+$, **1.Cs**$^+$, **2.Na**$^+$, and **2.Cs**$^+$ of 1:1 stoichiometries (as judged by integration of the $^1$H-NMR spectra). Changes in both ligands spectra resulting from complexation were readily discerned in the well-resolved resonances attributed to the glycolic and aromatic hydrogen atoms. In the case of ligand **1** all these signals, however, are significantly shifted, so that although it is clear that only one product was formed, it was not obvious to determine where the cations were actually bound. Although the spectra of **2.Na**$^+$, and **2.Cs**$^+$ were not fully readable, they were indicative of the location of the cations. Important downfield-shifts were observed for the signals (from 7.72-7.66 ppm to 7.55-7.51 ppm for $H_4$ and $H_{11}$, from 7.36-7.32 ppm to 7.15-7.11 ppm for $H_6$ and $H_9$, and from 7.22 ppm to 6.96 ppm for $H_7$ and $H_8$) of the aromatic protons of the naphthylene group allowed us to localize the cesium in the modified glycolic chain. These signals remained unchanged in the spectra of **1.Na**$^+$ when compared to spectrum of **1**. It was therefore assumed the sodium cation to be included in the oxoethylene crown-6. We have been able to obtain single crystals of **1**.$CsNO_3$ complex **3** suitable for the determination of its structure by X-ray crystallography (Figure 2).[7] The cesium was found to be located in the modified crown loop. The features of cesium coordination were identical to those already described for related systems.[11] The crown conformations corresponded to the sequences $g^+g^-Og^+g^-$ for the substituted crowns (with an *anti* angle transformed into a *gauche* one) for the cesium-complexing crown and $g^+g^-g^+g^-g^+$ for the crown-6. The former one has not yet been observed in analogous molecules.[11]

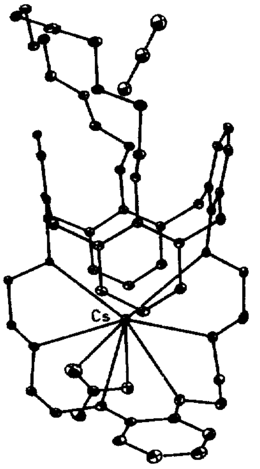

**Figure 2.** Molecular structure of **3**.$2CH_3CN$. Solvent molecules are omitted.

In the light of the behaviour of the 'symmetrical' analogues of **1** and **2**, we interpreted the formation of a 1:1 complex as indicative of an ability to bind Cs$^+$ within the oxoethylene-crown-6 cavity with stronger binding to the 1,2-arylene-linked polyether arms than in the unmodified crowns-6. In addition to the geometrical changes due to the introduction of 1,2-arylenes in the oxoethylene crown loops, one can also assume the preference for the cesium cation to be attributed to electronic variations in the modified polyethereal frame. These are to be investigated by theoretical means and will be published in due course.

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6. **General:** Mps, capillaries under nitrogen, Büchi 500. Chromatography, $SiO_2$ columns with Kieselgel Merck (Art. 11567). $^1$H-NMR in $CDCl_3$, Bruker SY200 ($\delta$ in ppm, $J$ in Hz), FAB(+), VG-Analytical ZAB HF. Elemental analyses performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg.

   **Preparation of 1:** Calix[4]crown-6 (6.26 g, 10.00 mmol), $K_2CO_3$ (13.83 g, 100.00 mmol) and $CH_3CN$ (500 mL) were stirred for 2 h at room temperature under $N_2$. 1,2-Phenylene modified pentaethylene glycol ditosylate[2] (6.54 g, 11.00 mmol) was added. After refluxing for 14 days solvents were evaporated to dryness and the residue was dissolved in $CH_2Cl_2$. The solution was acidified (1N HCl). The organic layer was dried ($Na_2SO_4$), filtered and evaporated to dryness. Chromatography ($SiO_2$, 95:5 $CH_2Cl_2$/acetone as eluent) afforded **1** as a white solid (5.52 g, 63 %). M. p. 161-162 °C. $^1$H-NMR (200 MHz, $CDCl_3$) 7.12 (d, $J$ = 7.5, 4 $\mathrm{Ar}H$ in meta position), 7.07 (d, $J$ = 7.5, 4 $\mathrm{Ar}H$ in meta position), 7.00 (s, 4$H$ phenylene), 6.87 (t, $J$ = 7.5, 4 $\mathrm{Ar}H$ in para position), 6.70 (t, $J$ = 7.5, 4 $\mathrm{Ar}H$ in para position), 4.14 (t, J = 4.5, 2 $\mathrm{ArOC}H_2$), 3.81 (s, 4 $\mathrm{ArC}H_2\mathrm{Ar}$), 3.72 (s, $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$), 3.70-3.35 (m, 7 $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$). *Anal. Calcd.* For $C_{52}H_{60}O_{12}$: C, 71.21; H, 6.90. *Found.* C, 71.11; H, 6.82.

   **Preparation of 2:** similar to **1** with: calix[4]crown-6 (3.13 g, 5.00 mmol), $K_2CO_3$ (6.93 g, 50.00 mmol) and 2,3-naphthylene modified pentaethylene glycol ditosylate[2] (3.23 g, 5.00 mmol), $CH_3CN$ (600 mL). Chromatography ($SiO_2$, 95:5 $CH_2Cl_2$/acetone as eluent) afforded **2** as a white solid (2.45 g, %). M. p. 178-179 °C. $^1$H-NMR (200 MHz, $CDCl_3$) 7.72-7.66 (m, $H_4$ and $H_{11}$ naphthylene), 7.36-7.32 (m, $H_6$ and $H_9$ naphthylene), 7.22 (s, $H_7$ and $H_8$ naphthylene), 7.14 (d, $J$ = 7.5, 4 $\mathrm{Ar}H$ in meta position), 7.10 (d, $J$ = 7.5, 4 $\mathrm{Ar}H$ in meta position), 6.86 (t, $J$ = 7.5, 4 $\mathrm{Ar}H$ in para position), 6.68 (t, $J$ = 7.5, 4 $\mathrm{Ar}H$ in para position), 4.26 (t, J = 4.5, 2 $\mathrm{ArOC}H_2$), 3.84 (t, J = 4.5, 2 $\mathrm{ArOC}H_2$), 3.80 (s, 4 $\mathrm{ArC}H_2\mathrm{Ar}$), 3.72 (s, $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$), 3.70-3.35 (m, 6 $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$). *Anal. Calcd.* For $C_{56}H_{62}O_{12}$: C, 72.55; H, 6.74. *Found.* C, 72.42; H, 6.81.
7. **Crystal data for 1**.$3CH_3CN$: $C_{58}H_{69}N_3O_{12}$, $Mr$ = 1000.16, monoclinic, space group $P21/c$, $a$ = 17.4718(8), $b$ = 16.0820(6), $c$ = 20.9259(10) Å, $\beta$ = 111.117(2)°, $V$ = 5485(2) Å$^3$, $Z$ = 4, $D_c$ = 1.211 g.cm$^{-3}$, $\mu$ = 0.085 mm$^{-1}$, $F$(000) = 2136, data collected at 293 K, 12009 unique reflections used, $R$ = 0.046, $R_w$ = 0.083, $S$ = 1.012.

   **Crystal data for 2**.$3CH_3CN.CHCl_3$: $C_{63}H_{72}Cl_3N_3O_{12}$, $Mr$ = 1169.59, monoclinic, space group $P21/c$, $a$ = 13.0519(5), $b$ = 20.4239(13), $c$ = 22.4713(14) Å, $\beta$ = 89.820(2)°, $V$ = 5990(2) Å$^3$, $Z$ = 4, $D_c$ = 1.297 g.cm$^{-3}$, $\mu$ = 0.217 mm$^{-1}$, $F$(000) = 2472, data collected at 123 K, 6174 unique reflections used, $R$ = 0.076, $R_w$ = 0.205, $S$ = 1.291.

   **Preparation of 3:** compound **1** (0.33 mmol) was reacted with $CsNO_3$ (0.33 mmol) in 1:1 $CHCl_3/CH_3CN$ (10 mL) at room temperature for 8 h. Slow evaporation yielded single-crystals suitable for X-ray crystallography.

   **Crystal data for 3**.$2CH_3CN$: $C_{56}H_{66}CsN_3O_{15}$, $Mr$ = 1154.03, monoclinic, space group $P21/n$, $a$ = 16.0619(5), $b$ = 15.6748(6), $c$ = 21.5857(6) Å, $\beta$ = 92.594(2)°, $V$ = 5429(2) Å$^3$, $Z$ = 4, $D_c$ = 1.412 g.cm$^{-3}$, $\mu$ = 0.752 mm$^{-1}$, $F$(000) = 2392, data collected at 293 K, 10578 unique reflections used, $R$ = 0.050, $R_w$ = 0.125, $S$ = 1.144.

   **Data collection and refinement:** data collected on a Nonius Kappa-CCD diffractometer using graphite monochromated Mo$K\alpha$ radiation and processed with the HKL package.[8] Structures solved by direct methods with SHELXS-86[9] (**1** and **2**) or by the heavy atom method (**3**) and refined on $F^2$ with SHELXTL.[10] Molecular drawings done with SHELXTL.
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