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A Tribenzo Modified 1,3-Calix[4]-*bis*-crown-6: A Highly Selective Receptor for Cesium

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Abstract: It is reported the synthesis of calix[4]-*bis*-(tribenzo)crown-6 **1** consisting of a calix[4]arene fixed in the 1,3-alternate conformation by the 1,3- and 2,4-bridges made of two modified polyether chains in which the three central ethylene links have been replaced by three 1,2-phenylenes. Ligand **1** complex cesium cation and not sodium one.

Keywords: Calixarenes, crown-ethers, cesium, complexation, molecular recognition.

1,3-Calix[4]-*bis*-crowns refers to calixcrown-type receptors in which the calix[4]unit is maintained in the 1,3-alternate conformation by the linkages of phenyl rings 1,3 and 2,4 with polyether chains. They 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 one 1,2-arylene residue in the middle of the crown-6 loops. This was attributed to the replacement of sp3 carbons by sp2 ones in the glycol units leading to a flattening of the polyether chains. This geometrical change was accounted for i) a higher complexation of the cesium cation and/or ii) a lower complexation of the sodium cation. Such a preference was subsequently evidenced when unsymmetrical 1,3-calix[4]-*bis*-crown-6 containing one crown-6 loop and a 1,2-arylene modified crown-6 was shown to complex the cesium cation in the modified chain and the sodium in the crown-6.[5] Two recent publications report that introduction of two 1,2-phenylene residues in a symmetrical manner in the glycolic chains of calix[4]-*bis*-crown-6[6] and a related calix[4]-*mono*-crown-6[7] in the 1,3-alternate conformation lead to enhanced Cs^+/Na^+ selectivity compared to the 1,2-arylene analogues. Despite these last results no choice on assumptions i) or ii) was done by the different authors.

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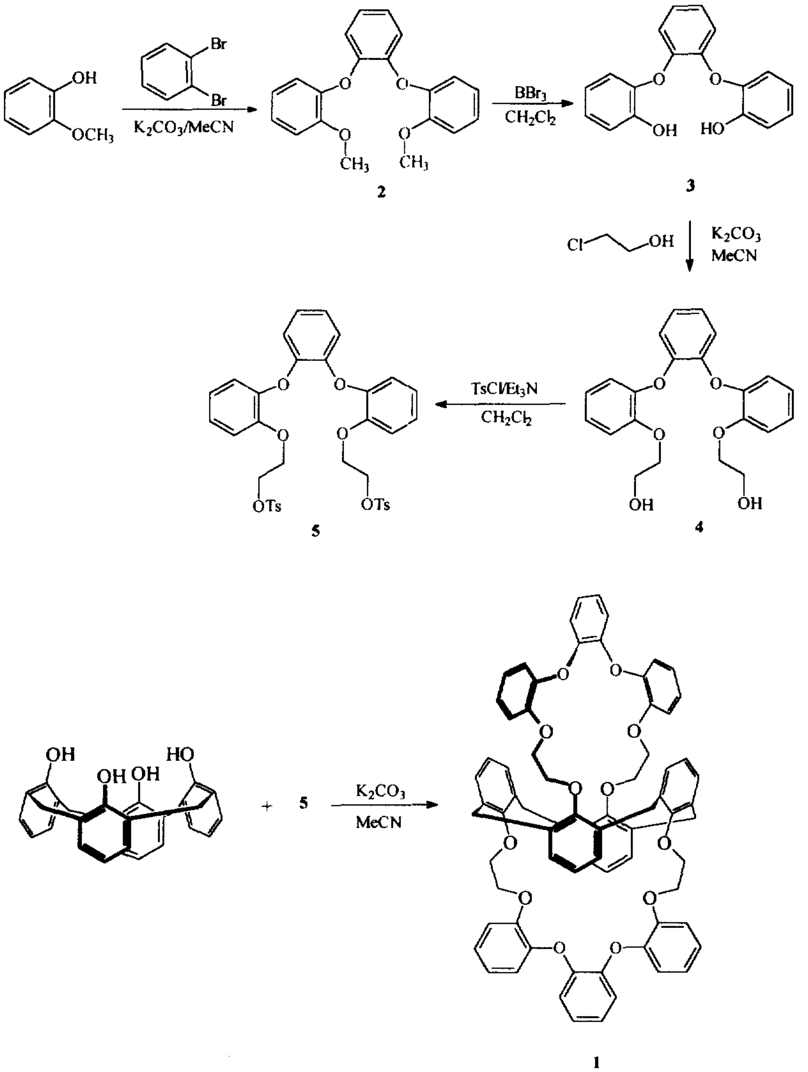
We report herein the synthesis, characterization, and preliminary complexing properties of 1,3-alternate calix[4]-*bis*-(tribenzo)crown-6 **1** consisting of a calix[4]arene fixed in the 1,3-alternate conformation by the 1,3- and 2,4-bridges made of two modified polyether chains in which the three central ethylene links have been replaced by three fused 1,2-phenylenes. Ligand **1** was shown to complex cesium and not sodium.

The synthesis of ligand **1** is presented in Scheme 1.



Scheme 1. Synthesis of **1**

The synthesis began by reacting 2-methoxyphenol with 0.5 equiv of 1,2-bromobenzene in the presence of K_2CO_3 in refluxing acetonitrile for 4 days to produce 2,2'-(1,2-phenylenedioxy)diphenol *bis*(methyl ether) **2** as a yellow solid (mp 102-104 °C) in 30 % yield. Dimethoxy **2** was reacted with 4.0 equivs of BBr_3 in CH_2Cl_2 at – 60 °C for 10 h to give demethylated 2,2'-(1,2-phenylenedioxy)diphenol **3** as a white solid (90-91 °C) in 88 % yield. Diphenol **3** was di-alkylated into diethylene triphenol **4** with 4 equivs of 2-chloroethanol in the presence of K_2CO_3 in refluxing acetonitrile during 3 days. Product **4** was isolated in 62 % yield as a white solid (mp 115-116 °C). Compound **4** was transformed into ditosylate derivative **5** by reaction with 2.0 equivs of tosyl chloride in the presence of NEt_3 in CH_2Cl_2 for 48 h. Ditosylate **5** was obtained in 60 % yield. The final step to **1** was performed according to well established procedures from preparation of a number of calixcrowns.[2] Calix[4]arene[8] was reacted with 2.0 equivs of ditosylate **5** in the presence of 20.0 equivs of K_2CO_3 in refluxing acetonitrile for 14 days. Calix[4]-*bis*-(tribenzo)crown-6 **1** was obtained as a white solid melting at 151-152 °C. It is to be noticed that the formation of two macrocyclic, polyether units on the calix[4]arene base occured in acceptable 30 % yield without the need for special reaction conditions such as the use of high dilution.

Calix[4]-*bis*-(tribenzo)crown-6 **1** was fully characterized by ^{1}H-NMR, FAB spectrometry and elemental analysis. It was deduced to be in the *1,3-alternate* conformation from its ^{1}H-NMR spectrum which showed a singlet at 3.72 ppm for the $ArCH_2Ar$ methylene protons in the macroring. In this conformation **1** presents a special arrangement: one glycolic chain connects two opposite oxygen atoms while the second enforces the calix[4]arene to adopt the 1,3-alternate conformation by linking the two remaining oxygen atoms. The simplicity of the polyether chains methylene resonnance in particular indicated that the chains must be conformationally mobile on the NMR time scale, so that the ligand may be regarded as having effective D_{2h} symmetry. This is also reflected by the presence of only one doublet at 6.69 ppm with J=7.0 Hz for the Ar*H meta* and one triplet at 6.55 ppm with J=7.0 Hz for the Ar*H para* protons of the calix[4] unit.

Extended reaction of chloroform solution of **1** with an excess of cesium picrate for 24 h at rt resulted in the formation of a solution of a complex of 1:1 stoichiometry (as determined by integration of the ^{1}H-NMR spectrum). This range of time is generally used in similar complexation evaluation for related calix[4]arene *bis* crowns previously studied.[5] Changes in the ligand spectrum resulting from complexation are most readily discerned in the well-resolved resonances attributable to the aromatic hydrogen atoms *para* to the calixarene phenolic oxygen atoms and to the OCH_2CH_2O group. This was indicative of the presence of an *endo* complex within the oxygen atoms array in the polyether loop. However, we were unable to really evidence the precise location of the cesium in the loop. In a separate experiment, a chloroform solution of **1** was reacted with an excess of sodium picrate in the same conditions of time and temperature as for cesium picrate. A very weak signal of the picrate was discerned in the ^{1}H-NMR spectrum of the solution. This behaviour is quite different from previous findings on related systems in which 1:1 ligand-metal ratio can be reached. This was indicative of a stronger preference of ligand **1** for the cesium cation and no complexation of the sodium.

The present results along with precedent ones from literature[1-7] indicate that the changes of sp3 oxygen atoms by sp2 ones disfavours the complexation of the sodium cation in these systems.

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8. **General:** Mps, capillaries under nitrogen, Büchi 500. Chromatography, SiO_2 column with Kieselgel Merck (Art. 11567). ^{1}H-NMR in $CDCl_3$, Bruker SY200 (δ in ppm, *J* in Hz), FAB(+), VG-Analytical ZAB HF. Elemental analysis were performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg. **Preparation of 1:** calix[4]arene (0.425 g; 1.00 mmol), K_2CO_3 (1.380 g; 10.00 mmol), ditosylate **5** (0.691 g; 1.00 mmol), and acetonitrile (100 mL) were refluxed for 7 days. Then the same quantities of K_2CO_3 and ditosylate **5** were added to and were refluxed for 7 additionnal days. The solvents were evaporated. The residue was solubilized in CH_2Cl_2 and acidified with 1 N HCl to pH ~ 1. The organic phase was dried over Na_2SO_4 and concentrated. Calix[4]-*bis*-(tribenzo)crown-6 **1** (0.340 g) was obtained pure, as a white solid melting at 151-152 °C, after chromatography on silica column with a mixture 90:10 CH_2Cl_2-acetone as eluent. ^{1}H-NMR (200 MHz, $CDCl_3$) 7.22-6.94 (m, 24H, tribenzo Ar*H*), 6.69 (d, *J*=7.0, 8H, calix Ar*H* meta), 6.55 (t, 4H, *J*=7.0, calix Ar*H* para), 3.72 (s, 8H, $ArCH_2Ar$), 3.21-3.17 (m, 16H, OCH_2CH_2O). FAB(+) MS, m/z 1116..52. *Anal. Calcd.* For $C_{72}H_{60}O_{12}$: C, 77.40; H, 5.41. *Found.* C, 77.12; H, 5.49. **Yield 30 %.**