



Nitro derivatives of 1,3-calix[4]arene bis-crown-6. Synthesis, structure and complexing properties.

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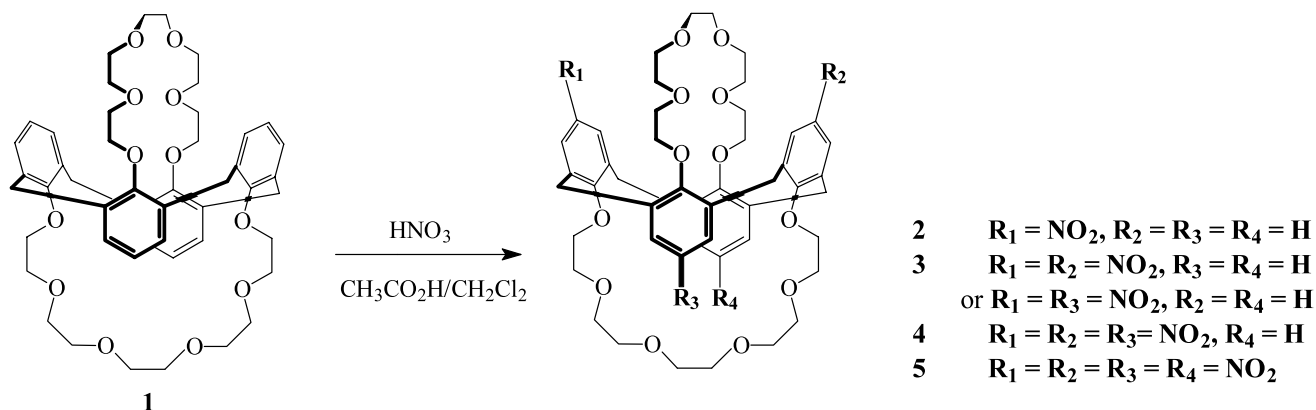
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Abstract—The synthesis of nitro derivatives of 1,3-calix[4]arene bis-crown-6 is reported. The X-ray structure of one of them is given. The complexation of cesium cation is presented and shows the role of the nitro groups for the complexation to occur. © 2001 Published by Elsevier Science Ltd.

Calix[4]arene bis-crowns refer to the family of macrotricycles constructed from one calix[4]arene and two polyethylene glycol chains.^{1,2} The polyether chains are usually attached via the phenolic oxygens of the calixarene unit.^{1,2} 1,3-Calix[4]arene bis-crowns are constrained to the 1,3-*alternate* conformation by the 1,3- and 2,4-bridges.^{1,2} Their shape is globular, with polyether chains defining two possible sites for cation coordination.^{1,2} In particular, the 1,3-calix[4]arene bis (crown 6) (**1**) containing six oxygen donor atoms was shown to be a potential extractant for the selective removal of cesium cation from radioactive liquid

nuclear waste. Degradation products of calixcrown **1** are to be expected during the extraction process. The behavior of **1** under irradiation has been recently investigated.³ The analysis by electrospray ionization mass spectrometry (ES/MS) of irradiated organic phases showed that **1** can form nitro derivatives when the irradiation was performed in the presence of nitric acid.³ Molecular Dynamics (MD) simulations showed that the addition of one nitro group does not significantly modify the behavior of **1** towards alkali cations, indicating that the exceptional selectivity towards Cs⁺ is maintained after nitration.³



Scheme 1. Synthesis of ligands 2–5.

Keywords: calixarenes; nitro calixarenes; cesium complexation.

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In the present note we report the synthesis of nitro derivatives **2–5**. Their complexation behaviors towards the cesium cation were investigated by ^1H NMR. Compounds **2–5** were prepared according to Scheme 1.

Calixcrown **1** was reacted with 100% HNO_3 at 0°C for 2.5 h in a 1:2 mixture of 100% $\text{CH}_3\text{CO}_2\text{H}/\text{CH}_2\text{Cl}_2$.⁴ After evaporation of the solvents the residue was chromatographed on silica with a mixture of 8:2 dichloromethane-acetone as eluent. All the products were identified by ^1H NMR, FAB (+) mass spectrometry and microanalysis. The tetra- (**5**), tri- (**4**), di- (**3**) and mono-nitro (**2**) 1,3-calix[4]arene bis-crown-6 were eluted in this order seemingly following the order of polarity of the eluted molecule. The mononitration of **1** that occurs is evidenced by the presence of one singlet at 8.04 ppm for the $p\text{-NO}_2\text{-ArH}$, and two triplets at 6.88 and 6.86 ppm with $J=7.0$ Hz, in an integration ratio of 2:1 for the calix-Ar- H_{para} in its ^1H NMR spectrum. The presence of the nitro group also induces the differentiation of the two crown ether loops and two triplets at 3.86 ppm and 3.82 ppm with $J=7.0$ Hz for the $\text{ArOCH}_2\text{CH}_2\text{O}$ attached directly to the phenolic units plus two triplets at 3.35 and 3.27 ppm with $J=6.0$ Hz for $\text{OCH}_2\text{CH}_2\text{O}$ are observed. No choice is made on the assignment of the triplets to one or the other loop. The ^1H NMR of the trinitro derivative **4** presented two singlets at 8.08 and 8.06 ppm corresponding to $p\text{-NO}_2\text{-ArH}$. A doublet at 7.16 ppm with $J=7.0$ Hz was attributed to the calixAr H_{meta} protons and the triplet at 6.98 ppm with $J=7.0$ Hz to Ar H_{para} . The higher symmetrical structure of the tetranitro compound **5** is shown by its simple pattern. Four singlets at 8.10, 3.97, 3.53 and 3.49 ppm are found for $p\text{-NO}_2\text{-ArH}$, $\text{OCH}_2\text{CH}_2\text{O}$, Ar CH_2Ar , and $\text{OCH}_2\text{CH}_2\text{O}$, respectively. Two triplets are also observed at 3.74 and 3.39 ppm with $J=6.0$ Hz for Ar $\text{OCH}_2\text{CH}_2\text{O}$ and $\text{OCH}_2\text{CH}_2\text{O}$. Whereas the structures of **2**, **4** and **5** are easily assigned because the positions of the nitro groups are obvious, we are unable to choose between the two possible isomeric structures of **3**. The structure of the tetranitro derivative **5** is confirmed by X-ray diffraction (Fig. 1).⁵

In the solid state, molecule **5** does not possess any symmetry element. The conformation of the calixarene structure is less symmetrical than for previously studied calix[4]arene bis-crown-6.² The dihedral angles between the four aromatic rings and the mean plane defined by the four methylenic carbon atoms (rms deviation 0.03 Å) are 71.2(1), 58.5(1), 51.4(1) and 72.2(1)°. Two adjacent aromatic rings (i.e. associated to each of the two ether chains) are more tilted towards the mean plane than the two other ones and the calixarene is farther from a pseudo- S_4 symmetry than usual. The nitro groups are coplanar with the attached aromatic rings (the rms deviations of the mean planes don't exceed 0.09 Å). The two crown ether loops are roughly orthogonal to the mean plane defined by the methylenic bridges: the dihedral angles between the mean O_6 planes and this reference plane are 85.0(1) and 84.8(1)°. The conformations of the crown ethers, characterized by the sequences of O–C–C–O torsion angles $ag^-g^+g^-a$ and $g^+g^+g^-a$ for the two crowns, respectively

(g =gauche, a =anti) are unusual.⁷ As a consequence, all the oxygen atoms lone pairs are not directed towards the crown centre. The nitro groups thus appear to strongly modify the usual calixcrown conformation and a decrease in the preorganization towards cesium complexation can be expected.

Preliminary complexations of **2–5** with cesium cations were done by means of ^1H NMR. CDCl_3 solutions of **2–5** were reacted at room temperature with solid cesium picrate (Cs^+Pic^-).⁴ Only mononitro ligand **2** showed 100% extraction after 6 h, while very low yields of extraction were observed for **3** (8% E) and **4** (2% E) and no extraction was observed for **5** even after 48 h. The decrease of extraction power with the increase in the number of nitro groups may come from either a steric effect similar to that of *tert*-butyl groups² preventing the cesium to enter the crown ether or a desactivation of the oxygen donor atoms as already observed in the case of benzocrown ethers substituted with electron-attractive nitro groups.⁸ In the ^1H NMR spectrum of **2**· Cs^+Pic^- the Ar H_{pic} protons of the picrate appeared as a singlet at 8.88 ppm. A singlet at 8.08 ppm for $p\text{-NO}_2\text{-ArH}$, a doublet at 7.20 ppm and a triplet at 6.96 ppm $J=8.0$ Hz for calix-Ar H_{meta} and calix-Ar- H_{para} , respectively, are also detected. The integration ratio between the picrate singlet and the singlet of $p\text{-NO}_2\text{-ArH}_{meta}$ is 1:1, indicating the formation of a 1:1 complex. The simplicity of the spectrum also indicates that the cesium cation is located in only one cavity. The small difference in the shifts of the singlets for $p\text{-NO}_2\text{-ArH}$ between the free ligand **2** and the complex **2**· Cs^+Pic^- seems to indicate that the cesium is not located close to these protons but rather in the opposite crown cavity. This assumption has been confirmed by MD calculations showing the greater effect is due to the repulsion between the nitrate anion and the NO_2 polar group.

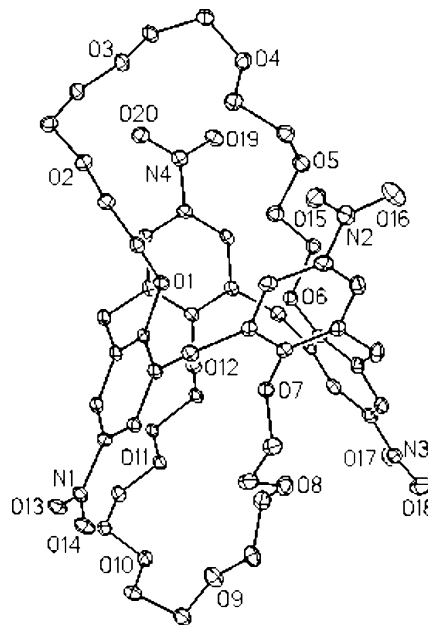


Figure 1. Crystal structure of **5**. Hydrogen atoms are omitted for clarity.

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- Analytical procedures.** Melting points (mps) were taken on a Büchi 500 apparatus in capillaries sealed under nitrogen. Elemental analyses were carried out at the Service de Microanalyse of the Institut de Chimie de Strasbourg. ^1H NMR spectra were recorded at 200 MHz on a Bruker SY 200 spectrometer. Chemical shifts are given on a δ scale in ppm from TMS. The FAB(+) mass spectra was obtained on a VG-Analytical ZAB apparatus. All chemicals were reagent grade and used without further purification. 1,3-calix[4]bis-crown-6 (**1**) was prepared as described in literature.¹
Preparation of nitro derivatives 2–5. 1,3-Calix[4]bis-crown-6 (**1**) (0.828 g; 1.00 mmol) was dissolved in a mixture of dichloromethane (40 mL), acetic acid 100% (20 mL). After cooling at 0°C, HNO_3 99.5% (10 mL) was added. After stirring 2.5 h, the reaction was quenched with water. The mixture was extracted with dichloromethane. The organic layer was dried over Na_2SO_4 . The solvents were evaporated to dryness. Tlc plates showed the presence of five spots (UV light) at R_f s=0.34 (starting material), 0.39, 0.54, 0.71, and 0.79, respectively (8:2 dichloromethane–acetone as eluent). The residue was separated on a 50 g silica column (Geduran Kieselgel SiO_2 60 (40–63 μm)) with the same eluent. **Mononitrocalix[4]biscrown-6 (2)** (0.220 g; 25%). White solid ($>275^\circ\text{C}$). ^1H NMR (CDCl_3): 8.04 (s, 2H, $p\text{-NO}_2\text{-ArH}$), 7.22–7.08 (m, 4H, calix-Ar- H_{meta}), 7.09 (d, $J=7.0$ Hz, 2H, calix-Ar- H_{meta}), 6.88 (t, $J=7.0$ Hz, 2H, calix-Ar- H_{para}), 6.86 (t, $J=7.0$ Hz, 1H, calix-Ar- H_{para}), 3.86 (t, $J=7.0$ Hz, 4H, $\text{ArOCH}_2\text{CH}_2\text{O}$), 3.82 (t, $J=7.0$ Hz, 4H, $\text{ArOCH}_2\text{CH}_2\text{O}$), 3.70 (s, 4H, ArCH_2Ar), 3.65 (s, 4H, ArCH_2Ar), 3.64–3.58 (m, 16H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.35 (t, $J=6.0$ Hz, 4H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.27 (t, $J=6.0$ Hz, 4H, $\text{OCH}_2\text{CH}_2\text{O}$). FAB(+) MS, m/z 874.5. Anal calcd for $\text{C}_{48}\text{H}_{59}\text{O}_{14}\text{N}$: C, 65.96 H, 6.80. Found C, 65.84 H, 6.91.
Dinitrocalix[4]biscrown-6 (3) (0.101 g; 11%). White solid ($>275^\circ\text{C}$). ^1H NMR (CDCl_3): 8.04 (s, 4H, $p\text{-NO}_2\text{-ArH}$), 7.16–7.10 (m, 4H, calixAr H_{meta}), 6.97–6.89 (m, 2H, Ar H_{para}), 3.91–3.25 (m, 48H, all CH_2). FAB(+) MS, m/z 919.3. Anal calcd for $\text{C}_{48}\text{H}_{58}\text{O}_{16}\text{N}_2$: C, 62.73 H, 6.36. Found C, 62.89 H, 6.22.
Trinitrocalix[4]biscrown-6 (4) (0.077 g; 8%). White solid ($>275^\circ\text{C}$). ^1H NMR (CDCl_3): 8.08 (s, 4H, $p\text{-NO}_2\text{-ArH}$), 8.06 (s, 2H, $p\text{-NO}_2\text{-ArH}$), 7.16 (d, $J=7.0$ Hz, 2H, calixAr H_{meta}), 6.98 (t, $J=7.0$ Hz, 1H, Ar H_{para}), 3.95–3.25 (m, 48H, all CH_2). FAB(+) MS, m/z 1005.6 ($\text{M}^+ + \text{Na}^+ + \text{H}_2\text{O}$). Anal calcd for $\text{C}_{48}\text{H}_{57}\text{O}_{18}\text{N}_3$: C, 59.81 H, 5.96. Found C, 59.93 H, 5.87.
Tetra-nitrocalix[4]biscrown-6 (5) (0.050 g; 5%). White solid ($>275^\circ\text{C}$). ^1H NMR (CDCl_3): 8.10 (s, 8H, $p\text{-NO}_2\text{-ArH}$), 3.97 (s, 8H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.74 (t, $J=6.0$ Hz, 8H, $\text{ArOCH}_2\text{CH}_2\text{O}$), 3.53 (s, 8H, ArCH_2Ar), 3.49 (s, 16H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.39 (t, $J=6.0$ Hz, 8H, $\text{OCH}_2\text{CH}_2\text{O}$). FAB(+) MS, m/z 1009.3. Anal calcd for $\text{C}_{48}\text{H}_{56}\text{O}_{20}\text{N}_4$: C, 57.14 H, 5.59. Found C, 57.29 H, 5.48.
Reaction of 2–5 with solid cesium picrate. Ligands **2–5** (~ 0.010 g) and solid cesium picrate (0.010 g) were mixed and stirred in deuterated chloroform (2.5 mL). ^1H NMR spectra were run after various reaction times with **2** (6 h), **3** (48 h), **4** (48 h), and **5** (48 h) and filtration of the heterogeneous mixtures. **2-Cs $^+$ Pic $^-$** : ^1H NMR (CDCl_3): 8.88 (s, 2H, Ar H_{pic}), 8.08 (s, 2H, $p\text{-NO}_2\text{-ArH}$), 7.20 (d, $J=8.0$ Hz, 6H, calix-Ar- H_{meta}), 6.96 (t, $J=8.0$ Hz, 3H, calix-Ar- H_{para}), 3.96–3.57 (m, 48H, all CH_2). Very low intensity singlets at 8.87 and 8.88 ppm due to Ar H_{pic} appeared for **3** and **4**. No new peak appeared for **5**.
5. Crystal structure of 5. Single crystals were obtained by recrystallization from $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$. The data were collected on a Nonius Kappa-CCD area detector diffractometer using graphite-monochromated Mo-K α radiation (0.71073 Å). The structure was solved by direct methods and subsequent Fourier-difference synthesis and refined by full-matrix least-squares on F^2 with SHELXTL.⁶ No absorption correction was done. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced at calculated positions as riding atoms with a displacement parameter equal to 1.2 times that of the parent atom. $R_1=0.121$, $wR_2=0.330$, $S=0.999$ for 7877 unique reflections ($R_{\text{int}}=0.059$) and 650 parameters. Crystal data have been deposited with the Cambridge Crystallographic Data Centre, under reference CCDC: 157567. Crystal data for **5**: $\text{C}_{48}\text{H}_{56}\text{N}_4\text{O}_{20}$, $M=1008.97$, triclinic, space group $P-1$, $a=12.3805(10)$, $b=12.8377(10)$, $c=15.6828(9)$ Å, $\alpha=76.520(5)$, $\beta=77.888(4)$, $\gamma=77.802(3)^\circ$, $V=2335.1(3)$ Å 3 , $Z=2$, $D_c=1.435$ g cm $^{-3}$, $\mu=0.113$ mm $^{-1}$, $F(000)=1064$, $T=123(2)$ K.
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