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A spirobiscalix[4]azacrown: synthesis and complexing properties

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ABSTRACT

The synthesis and complexation properties of a novel type of calix[4]azacrown, in which two cone calix[4]arenes are linked via a spiro C-atom incorporated into polyaminoalkylene chains are presented.

During the past decades, as a major activity in supramolecular chemistry, chemists have synthesized many types of receptors for complexing cations, anions and neutral molecules both in solution and in the solid state.[1] Since Ungaro and co-workers[2] have first reported the binding of potassium (relative to sodium and lithium) by calix[4]crown-5 ligands, the use of crown ethers covalently bound to calix[4]arenes has been studied extensively for selective extraction of complex cations.[3] Such calixcrown studies have expanded to include calix[4]arene in modified crown structures. Among them, the family of calix[4]azacrowns refers to molecules combining calix[4]arene elements and polyaminoalkylene chains attached to the calixarenes via amido functions, which may also serve as linking functions and chelating groups.[4] The amido functions come from the way they are prepared. The linkage of the azacrown unit on the calix[4]arene is often conducted by coupling diacylchloride or dimethyl- or diethylester calix derivatives with polyaminoalkylene diamino compounds to give bridged calix(aza)crowns.[4] Few reports describe their complexing properties. Calix(aza)crowns show low affinity for divalent (Be^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+})[5] and trivalent (Sc^{3+}, Y^{3+}, In^{3+}, Gd^{3+} and Bi^{3+})[5] metal cations with various stoichiometries ML, M_2L and ML_2.[6] By complexation of lanthanide ions (Eu^{3+}, Tb^{3+}, Nd^{3+}, Er^{3+} and La^{3+}), calix[4]azacrowns were used as molecular scaffolds for the generation of visible and near-infrared luminescence.[7] When the non-amido NH groups of the crown loops are protonated by HCl the resulting charged-receptors (ammonium groups as acting centres) were shown to complex anions such as Cl^-, Br^-, NO_3^- and HSO_4^-.[8] In the crystal state, some calix[4]azacrowns have been shown to form tubular architectures, in which the channels are filled by methanol.[9]

In the examples given in the literature, the calixarene unit of the calix[4]azacrowns is bridged either by one bridge (in the 1,3-disposition) or by two bridges (in the 1,2;3,4-disposition). In this Letter, we report a novel type of double-calixazacrown, spirobiscalix[4]azacrown (**5**) in which two calix[4]arenes are connected via a spiro C-atom and the two calix[4]arene moieties are in cone conformation.[10,11] Calix[4]azacrown (**3**) (considered as a half-part of **5**) was synthesized to compare the complexation properties of both ligands.

The synthesis of **3** and **5** (see Scheme 1) involves the amidation of precursor 1,3-dimethylester *p-tert*-butylcalix[4]arene (**1**) by reaction with the corresponding diamino compounds **2** and **4**.[12]

The reactions to give **3** and **5** were carried out by simple stirring at room temperature in $C_6H_5CH_3/CH_3OH$ (20/80) for 5 h and 4 d, respectively. Chromatography of the residue on silica column gave 1,3-monobridged calix[4]azacrown (**3**) (eluent: CH_2Cl_2/CH_3OH (50/50); 49% yield) and spirobiscalix[4]azacrown (**5**) (eluent: CH_2Cl_2/CH_3OH (95/5); 48% yield). **3** and **5** were fully characterized by ^1H NMR, MALDI TOF mass spectrometry and microanalysis. The formation of the amido bonds was deduced from the CON***H*** protons appearing as triplets ($J = 5.0$ Hz) at 8.68 ppm for **3** and 8.56 ppm

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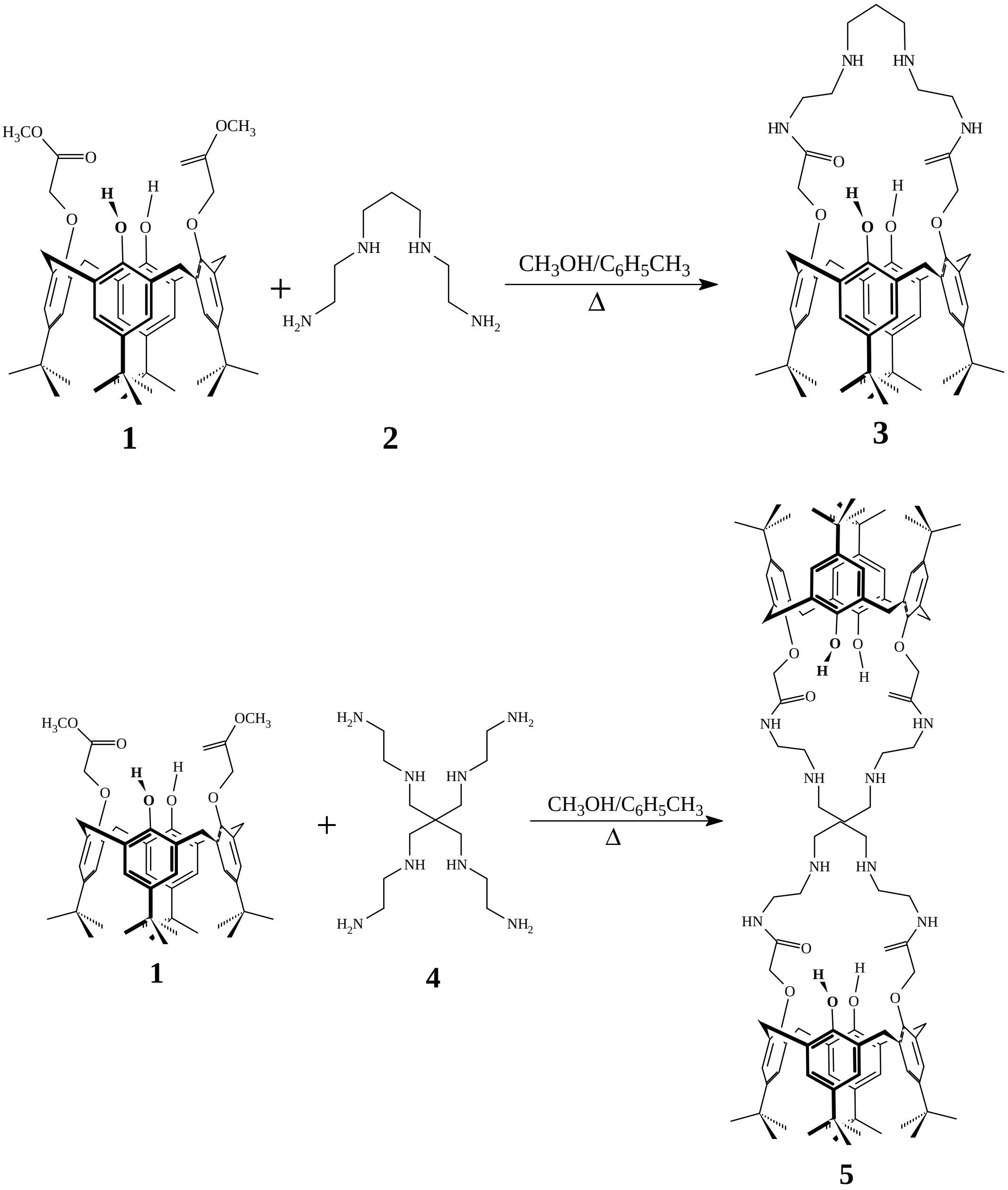
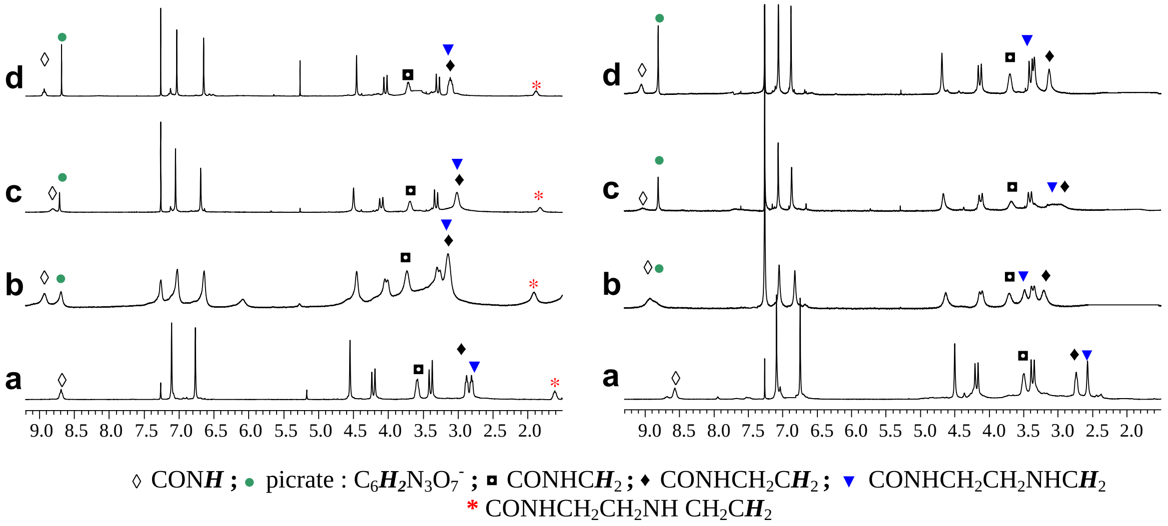


Scheme 1. Synthesis of **3** and **5**.

for **5** in their ^{1}H NMR spectrum. The simplicity of the spectra also revealed the 1,3-*O*-dispostion of the bridge and the retention of the cone conformation of the calix[4]arene unit showing only one AB system pattern at 4.21 ppm (d, *J* = 14.0 Hz, 4H, AB system, ArC$\boldsymbol{H}_2$Ar) and 3.39 ppm (d, *J* = 14.0 Hz, 4H, AB system, ArC$\boldsymbol{H}_2$Ar) for **3** and 4.18 ppm (d, *J* = 14.0 Hz, 8H, ArC$\boldsymbol{H}_2$Ar) and 3.36 ppm, (d, *J* = 14.0 Hz, 8H, AB system, ArC$\boldsymbol{H}_2$Ar) for **5**. The spectra of **3** and **5** were very similar. It is noticeable that the quintuplet (*J* = 5.0 Hz) at 1.61 ppm corresponding to the central methylene protons in the azacrown loop of **3** disappeared in the spectrum of **5** (it is the spiro carbon) while the vicinal methylene triplet $CONHCH_2CH_2NHC\boldsymbol{H}_2$ (*J* = 5.0 Hz) at 2.80 ppm became a singlet at 2.57 ppm.

Preliminary complexation studies of **3** and **5** with $Fe^{2+}(Pic^-)_2$, $Zn^{2+}(Pic^-)_2$, $Cu^{2+}(Pic^-)_2$, $Co^{2+}(Pic^-)_2$, $Ni^{2+}(Pic^-)_2$ and Ag^+Pic^- were monitored by means of ^{1}H NMR. $CDCl_3$ solutions of **3** and **5** ($\sim$$10^{-3}$ moles L^{-1}) were reacted with the solid picrates (directly introduced in the NMR tube) until the spectra of the resulting solutions remained unchanged (7 days for **3** and 15 days for **5**). The formation of a complex induced changes in the ^{1}H NMR patterns with the appearance of a singlet corresponding to the extracted picrate at ~ 8.70–8.80 ppm for **3** and 8.80 ppm for **5** (noted (●) picrate: $C_6\boldsymbol{H}_2N_3O_7^-$ in Scheme 2).

The ratio of the extracted species to ligand in solution was estimated by calculating the integration ratio of the picrate proton resonances *vs* those of the aromatic protons of the ligands. Fe^{2+}, Zn^{2+} and Ag^+ induced changes of the spectrum of both ligands with the formation of the following complexes $\mathbf{3} \cdot Fe^{2+}(Pic^-)_2$, $\mathbf{3} \cdot Ag^+Pic^-$, $\mathbf{3} \cdot Zn^{2+}(Pic^-)_2$, $\mathbf{5} \cdot 2[Fe^{2+}(Pic^-)_2]$, $\mathbf{5} \cdot 2[Ag^+Pic^-]$ and $\mathbf{5} \cdot 2[Zn^{2+}(Pic^-)_2]$. One can also observe that the general pattern of **5** is maintained during the complexation in agreement with the formation of symmetrical 2:1 (metal/ligand) species, in which one metal is located in each cavity. In all cases, the largest shift was



Scheme 2. ^{1}H NMR spectra of extraction of metal picrates in CDCl$_3$. Left (a) **3**, (b) **3** with Fe^{2+}(Pic$^-$)$_2$, (c) **3** with Ag$^+$Pic$^-$, (d) **3** with Zn^{2+}(Pic$^-$)$_2$. Right (a) free **5**, (b) **5** with Fe^{2+}(Pic$^-$)$_2$, (c) **5** with Ag$^+$Pic$^-$, (d) **5** with Zn^{2+}(Pic$^-$)$_2$.

observed for the CONHCH$_2$CH$_2$NHC$\boldsymbol{H}_2$ (▼) and CONHCH$_2$C$\boldsymbol{H}_2$ (♦) allowing to conclude that the metal is near of the NH atoms of **3** and **5**. The extraction of Cu^{2+}, Co^{2+} and Ni^{2+} was evidenced by a broadening (probably because these cations are paramagnetic) of the signals of the spectra. In spite of the broadening we could evaluate 1:1 complexes in the case of **3**.

CDCl$_3$ solutions of **3** · Fe^{2+}(Pic$^-$)$_2$, **3** · Ag$^+$Pic$^-$, **3** · Zn^{2+}(Pic$^-$)$_2$, **5** · 2[Fe^{2+}(Pic$^-$)$_2$], **5** · 2Ag$^+$Pic$^-$ and **5** · 2[Zn^{2+}(Pic$^-$)$_2$] complexes were directly submitted to mass spectrometry technique. For **3**:**3** + Zn^{2+} ($m/z = 953.490$) and for **5**:**5** + Ag$^+$ ($m/z = 1870.30$), **5** + 2Ag$^+$ ($m/z = 1978.17$) and **5** + Ag$^+$ + Pic$^-$ ($m/z = 2098.39$) could be registered, the others giving the mass of the free ligands. The results confirmed the stoichiometry of the observed complexes by ^{1}H NMR. The detection of free ligands can be due to complexes with low stability.

To sum up, in this Letter we have presented the synthesis and metal complexing properties of a novel a C-spirobiscalix[4]azacrown (**5**). Comparison with 'half-partner' **3** shows that the complexation of soft cations occurs in the azacrown unit via chelation of the NH amino functions. Monoazacrown **3** gave mononuclear species, while C-spirobiscalix[4]azacrown (**5**) gave binuclear species. Times of complexation by **5** were longer than those of **3** leading to the conclusion that the second cation has more difficulty to enter the second cavity of **5** probably because it is prevented from entering by the presence of the first either by positive charge repulsion or by cation-induced conformational changes.

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12. General: All reagents and solvents for synthesis were commercial and used without further purification. All the reactions were performed under a N$_2$ atmosphere. TLC's were carried out on Silica gel 60 F$_{254}$ (Merck 1.05554.0001). SiO$_2$ (Geduran 1.11567) was used for column chromatography. ^{1}H NMR spectra were recorded at 300 K, unless otherwise stated, using a 300 MHz Bruker SY 200. Shifts (δ) are referenced relative to the internal reference standard, tetramethylsilane (TMS). Coupling constants *J* are given in Hertz. MALDI TOF mass spectra were measured on a Biflex Bruker. Melting points were measured using an electrothermal Buchi 535 melting point (Mp) apparatus and are reported uncorrected. Elemental analyses were carried out at the Service de Microanalyse de l'ULP à Strasbourg. 1,3-Dimethylester *p*-*tert*-butylcalix[4]arene (**1**) was prepared according to the literature.[13] *N*,*N*′-bis(2-aminoethyl)-1,3-propanediamine (**2**) was prepared by the reported procedure,[14] then it was purified by distillation at 142-145 C/8 mm Hg. Cobalt complex, [*Trans*-Cl$_2$Co(**4**)CoCl$_2$-*trans*]Cl$_2$·4H$_2$O was prepared as described elsewhere.[15] *Preparation of* **3**. 1,3-Dimethylester *p*-*tert*-butyl calix[4]arene (**1**) (600 mg, 0.75 mmol) and *N*,*N*′-bis(2-aminoethyl)propyldiamine (**2**) (240 mg, 1.49 mmol) in C$_6$H$_5$CH$_3$/CH$_3$OH 1/4 (15 mL) were stirred for 5 h at room temperature. The solvents were evaporated and the residue was chromatographed on a silica column using CH$_2$Cl$_2$/CH$_3$OH 50/50 as eluent. Pure **3** was obtained as a white solid (328 mg, 49%). Mp = 154–155 C. ^{1}H NMR (300 MHz) δ (ppm): 8.68 (t, $J = 5.0$ Hz, 2H, CON$\boldsymbol{H}$), 7.10 (s, 4H, Ar$\boldsymbol{H}$), 6.76 (s, 4H, Ar$\boldsymbol{H}$), 4.54 (s, 4H, ArOC$\boldsymbol{H}_2$), 4.21 (d, $J = 14.0$ Hz, 4H, AB system, ArC$\boldsymbol{H}_2$Ar), 3.58 (t, $J = 5.0$ Hz, 4H, CONHC$\boldsymbol{H}_2$), 3.39 (d, $J = 14.0$ Hz, 4H, AB system, ArC$\boldsymbol{H}_2$Ar) 2.87 (t, $J = 5.0$ Hz, 4H, CONHCH$_2$C$\boldsymbol{H}_2$), 2.80 (t, $J = 5.0$ Hz, 4H, CONHCH$_2$CH$_2$NHC$\boldsymbol{H}_2$), 1.61 (quint., $J = 5.0$ Hz, 4H, CONHCH$_2$CH$_2$NH CH$_2$C$\boldsymbol{H}_2$) 1.30 (s, 18H, C(C$\boldsymbol{H}_3$)$_3$), 0.93 (s, 18H, C(C$\boldsymbol{H}_3$)$_3$). $M_w = 889.24$ calcd for C$_{55}$H$_{76}$N$_4$O$_6$. MALDI-TOF: $m/z = 889.62$. Anal. Calcd: C, 74.28; H, 8.61. Found C, 74.17; H, 8.23. *Preparation of* **4**. Cobalt complex, [*trans*-Cl$_2$Co(**4**)CoCl$_2$-*trans*]Cl$_2$·4H$_2$O (2.81 g, 4.0 mmol), was dissolved in water (200 mL) and Zn powder (5.00 g, 76.5 mmol) was added before adding 2 mol L^{-1} HCl (100 mL) dropwise with stirring. The pale pink solution was adsorbed onto Dowex 50W-x2 (H$^+$ form) after filtering off the unreacted Zn, and was washed with water (200 mL) and 0.5 mol L^{-1} HCl (200 mL), then this was eluted with 4 mol L^{-1} HCl. The eluate was evaporated to dryness under reduced pressure and was dissolved in water (100 mL). This was slowly passed through Dowex 1X (OH$^-$ form) and the resin was washed with water (200 mL). The eluate was evaporated to give yellow oil under reduced pressure. Yield 80%. ^{1}H NMR (300 MHz) δ (ppm): 2.75 (t, $J = 5.5$ Hz, 8H, NHCH$_2$C$\boldsymbol{H}_2$NH$_2$), 2.61 (t, $J = 5.5$ Hz, 8H, NHC$\boldsymbol{H}_2$CH$_2$NH$_2$), 2.55 (s, 8H, CC$\boldsymbol{H}_2$NH), 1.56 (br s, 8H, N$\boldsymbol{H}_2$). *Preparation of* **5**. 1,3-Dimethylester *p*-*tert*-butyl calix[4]arene (**1**) (400 mg, 0.50 mmol) and C-spirooctaamine **4** (76 mg, 0.25 mmol) in C$_6$H$_5$CH$_3$/CH$_3$OH 1/4 (15 mL) were stirred for 4 days at room temperature. The solvents were evaporated and the residue was chromatographed on a silica column using CH$_2$Cl$_2$/CH$_3$OH 95/5 as eluent. Pure **5** was a white solid (166 mg, 48%). Mp = 253–255 C. ^{1}H NMR (300 MHz) δ (ppm): 8.56 (t, $J = 5.0$ Hz, 4H, CON$\boldsymbol{H}$),

7.08 (s, 8H, Ar$\boldsymbol{H}$), 6.74 (s, 8H, Ar$\boldsymbol{H}$), 4.49 (s, 8H, ArOC$\boldsymbol{H}_2$), 4.18 (d, $J = 14.0$ Hz, 8H, AB system, ArC$\boldsymbol{H}_2$Ar), 3.49 (t, $J = 5.0$ Hz, 8H, CONHC$\boldsymbol{H}_2$), 3.36 (d, $J = 14.0$ Hz, 8H, AB system, ArC$\boldsymbol{H}_2$Ar), 2.73 (t, $J = 5.0$ Hz, 8H, CONHCH$_2$C$\boldsymbol{H}_2$), 2.57 (s, 8H, CONHCH$_2$CH$_2$NHC$\boldsymbol{H}_2$), 1.28 (s, 36H, C(C$\boldsymbol{H}_3$)$_3$), 0.92 (s, 36H, C(C$\boldsymbol{H}_3$)$_3$). $M_w = 1762.43$ g calcd for $C_{109}H_{148}N_8O_{12}$. MALDI-TOF: $m/z = 1762.01$. Anal. Calcd.: C, 74.28, H, 8.46. Found C, 74.39; H, 8.23.

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