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Complexation chemistry. Double- and multi-1,3-alternate-calixcrowns

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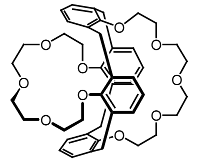
Abstract—Metal ion complexation behavior in calix[4]crown multimers (*mono*, *di*, *trimer*) have been investigated through X-ray crystallography, two-phase extraction, and ^{1}H NMR measurement. © 2003 Elsevier Science Ltd. All rights reserved.

Calix[4]arene-crown ethers or calix[4]crowns are one of the most widely investigated class of cation ligands based on calixarenes.[1] They refer to the family of macro-polycycles constructed from calix[4]arene elements and polyethylene glycolic units. They show binding properties towards alkali metal, alkaline earth metal and ammonium cations which can be tuned by selecting the most appropriate conformation of the calix[4]arene and the crown ether size. Probably the main interest in these ligands derives from their application as selective cesium extractants in radioactive waste treatment.[2] The highest selectivities towards the cesium cation have been observed for 1,3-calix[4]crowns ('1,3-' refers to the bridging of the polyethylene glycolic units onto the calix[4] skeleton) in the 1,3-alternate conformation in which the crown loops are bearing six oxygen atoms.[1] In such a molecular topology binding of cesium involves not only ether–oxygen donors but also the calixarene aromatic nuclei through cation/π interactions.[2] Interestingly, in addition to that, the 1,3-alternate conformation allows cation tunneling through the π-basic tube of the calix unit. For example, Koh et al.[3] reported that 1,3-calix[4]biscrown-5 (**1**) formed 1:1 and 1:2 (ligand/metal) complexes with alkali metal picrates in CD_2Cl_2–DMF-d_7. Cation tunneling was observed for the 1:1 complexes with K^+, Rb^+, Cs^+, and NH_4^+ as shown by the existence of two coalescence temperatures corresponding to both inter- and intramolecular metal–ligand exchange.[3] These observations lead chemists to prepare '*nano*-tubes' consisting of two or more calixarene units in the 1,3-alternate conformation.[4–6] With respect to calix[4]crowns, Asfari et al.[7] reported in 1992 the reaction of *p*-*tert*-butyl calix[4]arene with an excess of tetraethylene glycol ditosylate and K_2CO_3 leading to a double calix[4]biscrown-5 in which the two calixarenic units are crowned constraining the calix[4]crown-5 into the 1,3-alternate conformation.[7] Selectivity of complexation was observed for K^+ and Rb^+, the cation being located in the central cavity of the tritopic receptor.[7] Subsequently Kim et al.[8] synthesized three dimers **2**–**4**, two trimers among which **5**, one tetramer, and one pentamer constructed from 1,3-calix[4]crown units in the 1,3-alternate conformation and linked one to each other by crown elements. Due to the observation of extraction values higher than 100% in preliminary extraction studies 1:2 ligand/metal binuclear complexes were assumed as the extracting species in some cases: **2**·$2K^+$, **3**·$2K^+$, **3**·$2Rb^+$, **4**·$2Cs^+$, **5**·$2K^+$, **5**·$2Rb^+$, **tetramer**·$2K^+$, **tetramer**·$2Rb^+$ and **pentamer**·$2K^+$.



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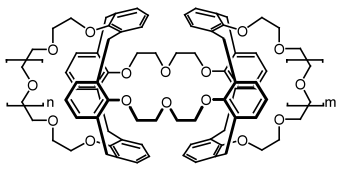
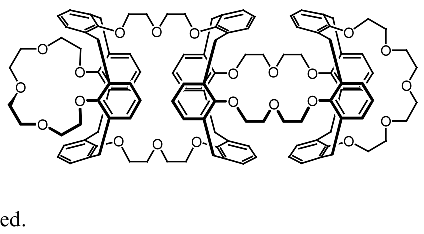


	n	m
2	1	1
3	1	2
4	2	2



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In the present paper we report the complexation behavior of ligands **1**–**5** towards potassium and cesium cations. Metal ion selectivity was observed depending on the size of the crown loop. The location of the cations was deduced from ^{1}H NMR spectrometry. We also determined the X-ray structures of ligands **2** and **4** and of the potassium complex of **2**. Complexation studies on **1**, considered as the simplest in the series, are for comparison.

^{1}H NMR studies

The formation of mononuclear 1:1 and binuclear 1:2 (ligand:metal) complexes with K^+ and Cs^+ was evidenced by using ^{1}H NMR.[9] The changes of the chemical shifts $\Delta\delta$ (given in ppm) of free ligand **1** (Fig. 1A) in $CDCl_3$ upon addition of K^+Pic^- are shown in Fig. 1. In the presence of an excess of K^+Pic^- (Fig. 1B), the ethylene glycolic protons H_a–H_d of the crown-5 loops shifted downfield indicating that these oxygen atoms bind the K^+ ion more strongly than other oxygen atoms of the linkers. The triplet of aromatic protons at 6.94 (H_i, *para*) is split into two triplets at 6.95 and 7.01 ppm (Fig. 1B) corresponding to empty and filled cavities. The observation that only 1:1 species are formed even in the presence of an excess of K^+Pic^- can be attributed to the presence of the first potassium in one cavity preventing the second cation from entering by electrostatic repulsion. Such a repulsion has already been invoked during the complexation of cesium by related 1,3-calix[4]biscrown-6.[10]

The changes of the chemical shifts of free ligand **2** (Fig. 2A) in $CDCl_3$ upon addition of K^+Pic^- are shown in Fig. 2. In the presence of an excess of K^+Pic^- (Fig. 2B), the ethylene glycolic protons H_a–H_d of the crown-5 loops shifted downfield by $\Delta\delta = 0.70$, 0.63, 0.13, and 0.13 ppm, respectively, indicating that these oxygen atoms bind the K^+ ion more strongly than other oxygen atoms of the linkers. 7.05 (H_k, *para*) ppm were shifted to 7.17 ($\Delta\delta = 0.12$) and 7.19 ($\Delta\delta = 0.14$) ppm, respectively. In addition, the two doublets of aromatic protons at 7.11 (H_j, *meta*) and 7.21 (H_l, *meta*) ppm were shifted to 7.30 ($\Delta\delta = 0.19$) and 7.36 ($\Delta\delta = 0.15$) ppm, respectively, indicating that the *meta*- and *para*-carbons of two pairs of inverted benzene rings are involved in cation-π interactions. The integral ratio between the aromatic protons of the picrate anion and the aromatic protons of **2** indicated the presence of a 1:2 complex. Addition of 1.5 equiv. of K^+Pic^- (Fig. 2C) lead to a complicated spectrum corresponding to a mixture of ligand **2**, mononuclear complex **2**·K^+, and binuclear complex **2**·$2K^+$.

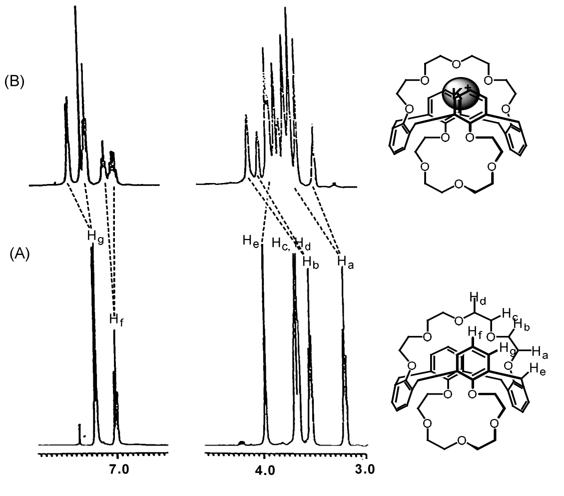


Figure 1. ^{1}H NMR spectra of (A): free ligand **1** and (B): **1**·K^+.

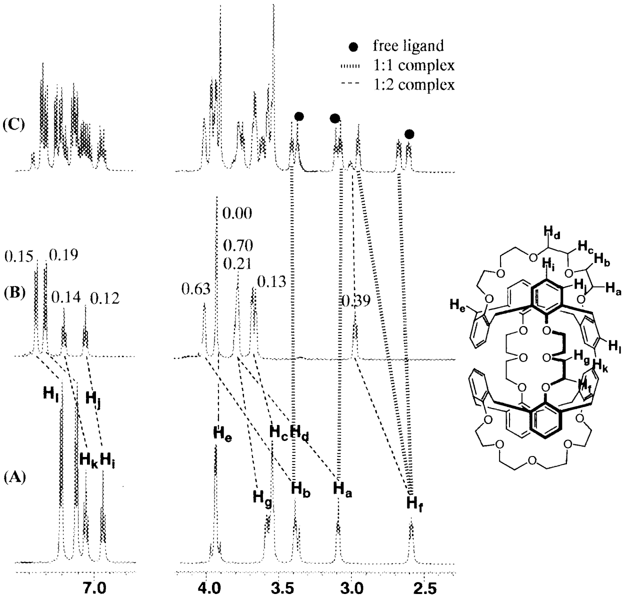


Figure 2. ^{1}H NMR spectra of (A): free ligand **2**; (B): **1**·$2K^+$ and (C): **1**+1.5 equiv. of K^+Pic^-. The numbers denote chemical shift change upon K^+ ion complexation.

The same species were observed even upon addition of only 0.5 equiv. of K^+Pic^- showing that the two crown-5 loops of **2** are acting in an independent manner. In contradiction to ligand **1** the formation of distinct 1:1 and 1:2 complexes were observed. This is in agreement with a distance which is shorter between the two 1,3-calix-crown-5 cavities in **1** than in **2** leading to two independent cavities in **2** with an easier formation of the 1:2 complex. Kim et al. previously reported the X-ray structure of the binuclear complex between 1,3-calix[4]crown-5;crown-6 and two K^+. The K_1–K_2 distance is 6.892 Å.[11]

Figure 3 shows the changes of chemical shifts of hybrid **3** (having both crown-5 and crown-6 loops: Fig. 3A). Upon addition of an excess of K^+Pic^-, only was observed the formation of the 1:1 complex (Fig. 3B). The spectrum of **3**·K^+ showed that the triplet corresponding to H_k is shifted downfield by $\Delta\delta = 0.32$ larger than that of H_n ($\Delta\delta = 0.10$). In addition, considering two sets of *para*-carbon hydrogen atoms (H_o and H_s)

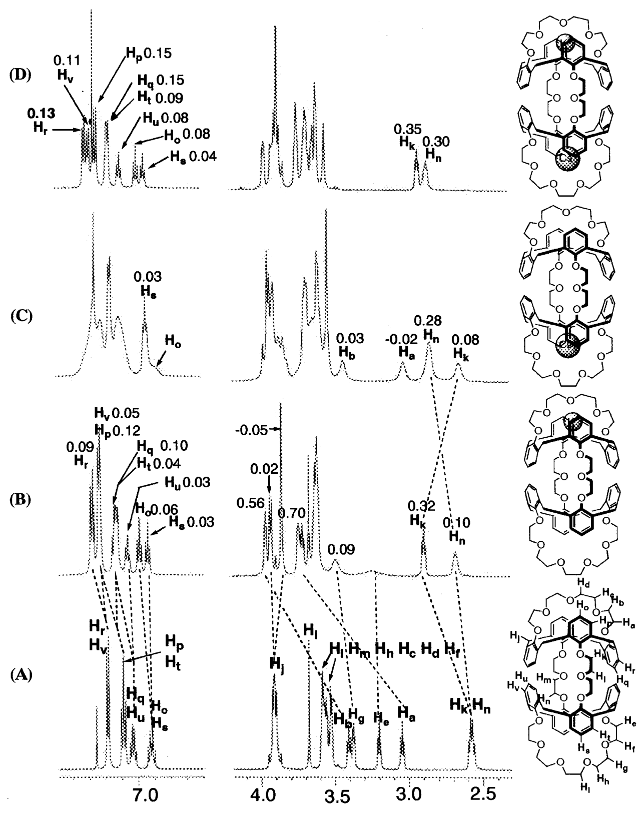


Figure 3. ^{1}H NMR spectra of (A): free ligand **3** only; (B): **3**·K$^+$; (C): **3**·Cs$^+$; (D): **3**·K$^+$·Cs$^+$. The numbers denote chemical shift change upon K$^+$ and Cs$^+$ complexation.

and *meta*-carbon hydrogen atoms (H$_p$ and H$_t$) related to the π-metal complexation, H$_o$ and H$_p$ (towards crown-5) shifted more downfield than H$_s$ and H$_t$ (towards crown-6). This indicated that the K$^+$ is encapsulated in crown-5 loop. Mass data ($m/z=1387.5$) and integration ratio between the picrate protons (δ) and the aromatic protons of **3** in the ^{1}H NMR supported this assumption of the formation of a 1/1 complex.

On the other hand, addition of an excess of Cs$^+$Pic$^-$ provided a different result showing that Cs$^+$ is located in the crown-6 loop where H$_n$ shifted downfield but not H$_k$. We observed the mononuclear **3**·Cs$^+$ with mass spectrum ($m/z=1481.6$). Upon addition of K$^+$Pic$^-$ and Cs$^+$Pic$^-$ together, both H$_k$ and H$_n$ signals shifted downfield by 0.35 and 0.30 ppm, respectively, as shown in Figure 3D. We assumed therefore that in the formation of heterobinuclear complex **3**·K$^+$·Cs$^+$, H$_o$ and H$_p$ signals in crown-5 showed the changes larger than those of H$_s$ and H$_t$ in crown-6 upon addition of each metal ion indicating that binding ability of crown-5 towards K$^+$ ion is somewhat stronger than that of crown-6 towards Cs$^+$ ion.

Very similar observations were made during the complexation studies of Cs$^+$Pic$^-$ by ligand **4**. They are presented in Figure 4. We also noticed that ligand **2** did not react with Cs$^+$Pic$^-$ while ligand **4** did not with K$^+$Pic$^-$ showing the selective complexation behavior of the ligands (Fig. 4). In addition, we have observed a 1:2 complex of calix[4]crown-5 trimer **5** with potassium ion in ^{1}H NMR spectra as shown in Figure 5. Two potassium ions were entrapped in both the end-crown loops, but not in the internal polyether chains.

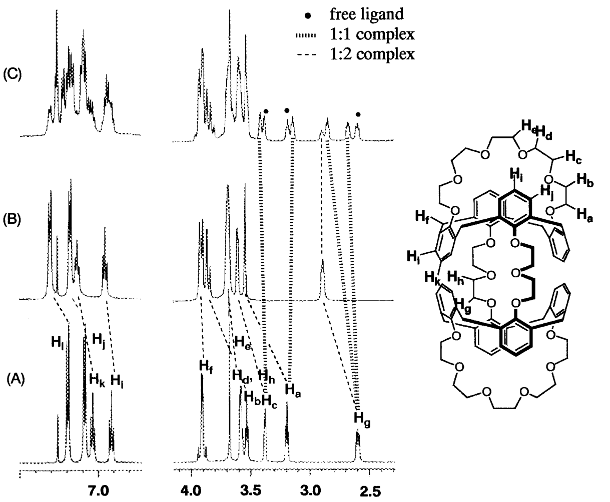


Figure 4. ^{1}H NMR spectra of (A): free ligand **4**; (B): **4**·2Cs$^+$ and (C): **4**+1.5 equiv. of Cs$^+$Pic$^-$.

X-Ray crystal studies

Single crystals of **2** and **4** suitable for X-ray crystallography were prepared by slow evaporation of methanol/chloroform solutions. The X-ray crystal structures gave evidence of the 1,3-alternate conformation of the **2** and **4** and are shown in Figure 6. Compounds **2** and **4** were commonly crystallized in the monoclinic space groups $P2_1/c$ and each possesses an inversion center at the center of the compounds.[12] So the asymmetric unit consists of a half of the compound. The calix[4]arene moieties in both cases are in the saddle-shaped 1,3-alternate conformations: the aromatic rings are tilted up (B and D) and down (A and C) alternately related to the α-C$_4$ core. The α-C$_4$ core forms a square plane, and the average displacements of the core atoms from the mean plane are 0.03 Å for **2** and 0.004 Å for **4**. The

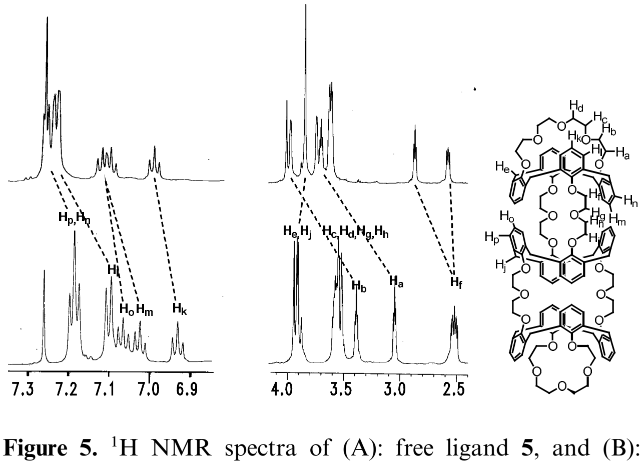
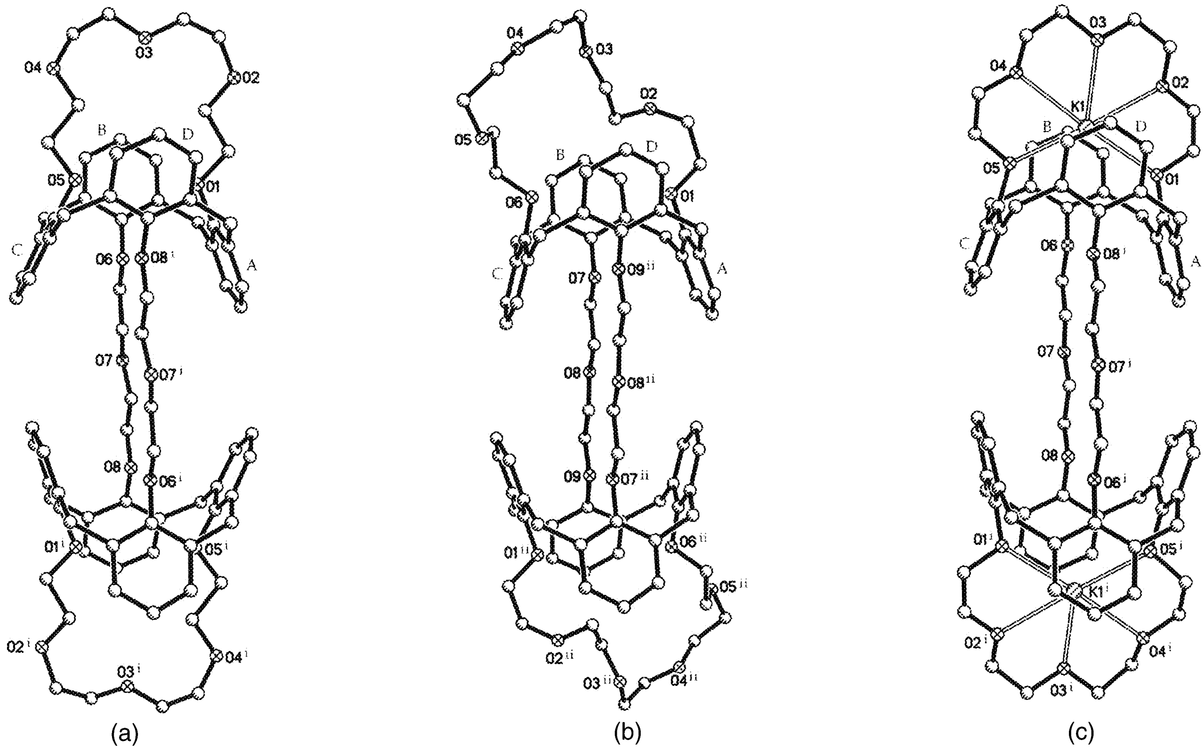


Figure 5. ^{1}H NMR spectra of (A): free ligand **5**, and (B): **5**·2K$^+$.



(a) (b) (c)

Figure 6. X-Ray crystal structures of (a) **2**; (b) **4** and (c) **2**·2K+2ClO$_4^-$.

conformation of the rims in **2** and **4**, which connect two opposite xylyl rings differs from each other due to the difference of flexibility. In **2**, for example, the ether ring spans causing a sequence of *trans–gauche–gauche–trans* torsion angles of –O–C–C–O– (beginning from O1 to O5), whereas those of **4** are all *gauche* arrangement. The diameters for the cavity formed by the rim are approximately 3.90–5.79 Å for **2** (O1···O3 4.870(6), O1···O4 5.790(6) and O1···O5 3.899(5) Å) and 4.59–7.16 Å for **4** (O1···O3 5.371(4), O1···O4 7.160(4), O1···O5 3.783(4) and O1···O6 4.586(4) Å). It is clearly observed that two calix[4]arene units are interconnected by two parallel O$_3$-ether linkages via bridgehead aromatic carbons in B and D. In both compounds, the linking O$_3$-ether moieties are fully stretched with all *trans* conformations to separate the calix[4]arene unit as far apart as possible to minimize the repulsive force. The distances between the α-C$_4$ cores for **2** and **4** are 9.333(7) and 9.149(2) Å, respectively. The reaction of **2** with excess of KClO$_4$ in CHCl$_3$ afforded a colorless crystalline product. Figure 6(C) shows the dinuclear complex, **2**·2K$^+$·2ClO$_4^-$. Each K$^+$ is encapsulated in each 1,3-calix[4]crown-5 cavity of **2** like in peanut-shell. Upon complexation, the O$_5$-ether rim unit became quite rigid and changed into all *gauche* arrangement. Each K$^+$ is coordinated to the five oxygen atoms in the loop. The distances between K$^+$ and oxygen atoms range from 2.705(4) to 2.827(5) Å. Cation-π interactions (K$^+$···C (*meta* in D); 3.387(7) and 3.356(7) Å, K$^+$···C (*para* in D); 3.261(7) Å) were observed as an extra stabilization source of the complex. The distance between two K$^+$ is 14.564(4) Å. This distance is to compare with the K$_1$–K$_2$ distance of 6.892 Å for related 1,3-calix[4]crown-5;crown-6.[11] Since it was not observed K$^+$ encapsulated in the spacer between the two calix[4]crown-5 units of **2**, one can also assume that electrostatic interactions between the oxygen donor atoms of the crown ether ring and the metal cation plays a major role for entrapping metal ion and that the cation-π interaction plays a minor role.

Acknowledgements

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9. Experimental. Ligands **1**[2] and **2**–**5**[8] were prepared as previously reported. Complexation studies were carried out by the use of ^{1}H NMR on 400 MHz (Bruker). Chemical shifts are reported in ppm from TMS. $CDCl_3$ solutions of **1**–**5** were reacted either with a number of equivalents of salts picrates (K^+Pic^- or Cs^+Pic^-) or with an excess of these salts. FAB+ mass spectra were obtained from JEOL-JMS-HX 110A/110A High Resolution Tandem Mass Spectrometry in Korea Basic Science in Daejon, Korea. Single crystals of **2** and **4** suitable for X-ray crystallography were prepared by slow evaporation of methanol/chloroform solution. Single crystals of **2**·$2K^+ \cdot 2ClO_4^-$ was obtained crystallisation in methanol. For X-ray crystallography, data were collected on a Siemens Smart CCD area-detector diffractometer equipped with a graphite monochromated Mo K_α ($\lambda = 0.71073$ Å) radiation source at room temperature.
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12. Crystal data. **2**: $C_{82}H_{90}C_{16}O_{16}$; 0.4×0.4×0.5 mm; monoclinic; $P2_1/c$; $Z=2$; calculated density = 1.308 g cm^{-3}; R_1 ($I>2\sigma(I)$) = 0.0826. **3**: $C_{84}H_{96}O_{18}$; 0.2×0.4×0.4 mm; monoclinic; $P2_1/c$; $Z=2$; calculated density = 1.290 g cm^{-3}; R_1 ($I>2\sigma(I)$) = 0.0680. **2**·$2K^+ClO_4^-$: $C_{82}H_{98}Cl_2K_2O_{27}$; 0.1×0.2×0.4 mm; monoclinic; P-1; $Z=1$; calculated density = 1.352 g cm^{-3}; R_1 ($I>2\sigma(I)$) = 0.0930.