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Calcium cation complexation by lariat ether receptors having arene-terminated sidearms

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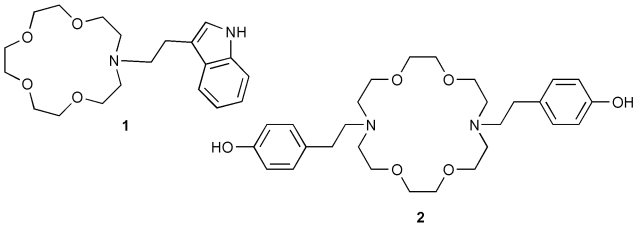
The first reported calcium azalariat complex has an arene terminated sidearm that behaves differently from an otherwise identical indole-sidearmed complex; twin phenolic sidearms on a diaza-18-crown-6 lead to an infinite, H-bonded network.

The abundance of Na^+ and K^+ in living systems begs the question of their interactions with amino acid sidechains in proteins.[1] The importance of interactions between Na^+ and K^+ and the aromatic sidechains of phenylalanine (benzene), tyrosine (phenol), and tryptophan (indole) has proved difficult to document experimentally.[2] The search for Na^+– and K^+–arene interactions was conducted as early as the 1980s by mass spectrometry,[3–7] database analyses,[8] computational,[9–11] and solid state structural studies.[12,13] We have used lariat ether receptor systems to obtain clear structural evidence for cation–π interactions between Na^+ or K^+ and benzene,[14] phenol,[15] or indole.[16] These host molecules show quite different behavior when complexing Ca^{2+}.

Two receptor molecules, **1** and **2**,[15] were prepared for the studies described here. Thus, aza-15-crown-5 was treated with 3-(2-bromoethyl)indole and Na_2CO_3 (CH_3CN, Δ, 48 h) to afford **1** as a yellow oil (93%).[17] Cation complexes of these receptors were obtained by dissolving the host and an equivalent of salt in either acetonitrile or ethanol. Slow evaporation, usually over days at ambient temperature, afforded crystals. The complexes reported here are **1**·$NaBPh_4$ (mp 177–178 °C), **1**·CaI_2 (mp 163–165 °C), and **2**·CaI_2 (mp 310 °C, decomp.). To our knowledge, only one diazacrown–calcium[18] and one calcium cryptate[19] have been reported although numerous calcium-containing structures are known.[20]



1

2

When **1** complexes Na^+, its sidearm is positioned to interact as an apical π-donor for ring-bound Na^+. The 15-crown-5 framework is somewhat congested and even 'appropriately sized' cations such as Na^+ and Ca^{2+} perch, rather than nest, in the macrocycle. The structure of **1**·$NaBPh_4$ is shown at the left in Fig. 1.† The anion does not interact with the cation complex and is not shown. Except for the remarkable Na^+–arene interaction, the structure[17] is typical of lariat ether complexes.[21]

The complex **1**·CaI_2·$(H_2O)_5$ is shown in Fig. 1 (right).† Its structure is of special interest because of its contrast with **1**·$NaBPh_4$ and because it is, to our knowledge, the first azacrown calcium complex X-ray structure reported. The calcium ion is coordinated by four oxygen atoms (average Ca–O distance ($d_{Ca–O}$) = 2.49 Å) and one nitrogen ($d_{Ca–N}$ = 2.64 Å). Three of five total water molecules are metal ion donors (average distance = 2.42 Å) making Ca^{2+} octacoordinate. This is the expected coordination number for most Ca^{2+} complexes. The sidearm clearly plays no coordinating role and Ca^{2+} is ~1.1 Å above the mean plane of the macroring heteroatoms. The two non-calcium-coordinated water molecules are part of a network that interacts with the iodide counterions. In particular, the uppermost water shown in Fig. 1 bridges both iodide ions approximately equidistantly ($d_{I–O}$ ~3.6 Å). The I–O–I angle is ~122° and the closest through-space I···I distance is >6 Å.

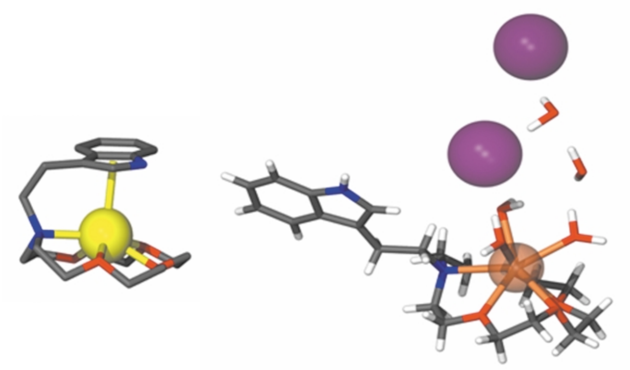


Fig. 1 Left: solid state structure of **1**·$NaBPh_4$ (anion omitted for clarity). Right, solid state structure of **1**·CaI_2·$(H_2O)_5$.

The Ca–O bond distances[20] and the perching of the cation over the macroring are both typical of the few known $[15\text{-crown-5}\cdot Ca]^{2+}$ complexes. A search of the Cambridge Structural Database (CSD) revealed no aza-15-crown-5 complex and only six 15-crown-5 complexes, two of which are benzo-15-crown-5 derivatives. The average Ca(II)–O distance for the four 15-crown-5 complexes (FUYCIL,[22] JAWQUT,[23] RABQOA,[24] and VIFBOB[25]) is 2.51 Å. The value we observed was 2.49 Å. No Ca^{2+}–macroring-N distance is available for a crown complex in the CSD but the structure of an $[18\text{-crown-6}\cdot Ca\cdot(NH_3)_3]^{2+}$ structure shows average $H_3N \rightarrow Ca$ distances of 2.51 Å. The NH_3 molecules are arrayed two on one side and one on the other. Calcium cation is above the calculated mean donor plane by ~1.18 Å in the four Ca·15-crown-5 complexes. This corresponds closely to 1.13 Å observed for **1**·CaI_2·$(H_2O)_5$.

The contrast between the complexes of **2** with Na^+ and either Ca^{2+} or K^+ is dramatic (see Fig. 2). Of these three complexes, **2**·KI is the most remarkable owing to its previously reported apical π-interaction.[26] Iodide is excluded from the solvation sphere of **2**·KI and one phenolic hydroxyl is H-bonded to it. Previously reported,[26] non-π-complexed **2**·NaI is shown in panel a. The average Na^+–O and Na^+–N bonds are 2.39 and 2.56 Å, respectively. The conformation appears to be defined by the formation of a hydrogen bond involving both phenolic hydroxyls. The O···I···O distances are 3.48 and 3.50 Å (O–I–O angle = 108.3°).

The structure of **2**·CaI_2·$(H_2O)_2$ is shown in panel c and its dimer appears in panel d. The latter is actually a fragment of an infinite network. The average Ca^{2+}–O bond length is 2.46 Å, longer than the Na^+–O (2.39 Å) bonds in **2**·NaI. The Na^+–N

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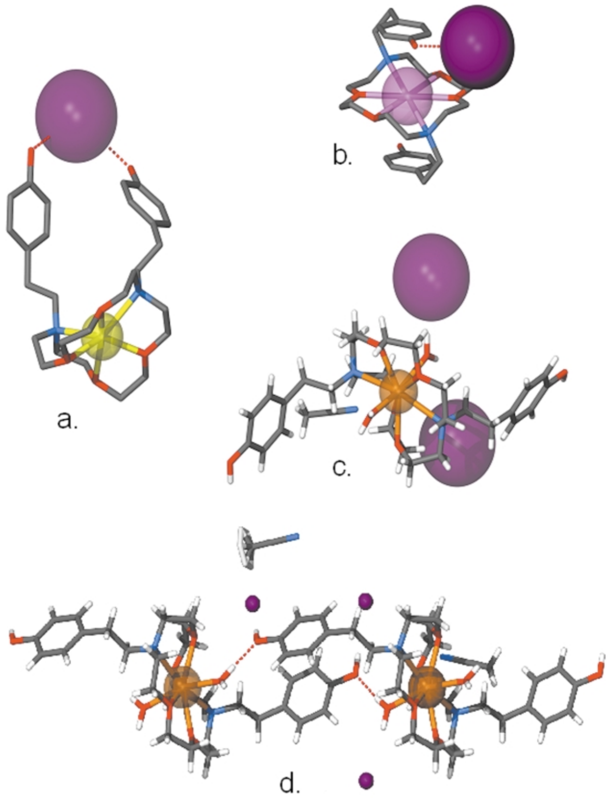

Fig. 2 Solid state structures of a. **2**·NaI, b. **2**·KI, c. **2**·$CaI_2 \cdot (H_2O)_2$. d. Dimer fragment of **2**·$CaI_2 \cdot (H_2O)_2$.

distance in **2**·NaI (2.56 Å) is shorter than the distances (2.76 Å) observed in **2**·$CaI \cdot (H_2O)_2$. The seventh and eighth coordination sites are occupied by apical water molecules (average distance 2.37 Å, O–Ca–O angle 159.1°). The apical water molecules play a critical role in organizing the network (panel d of Fig. 2). The water to phenol hydroxyl H-bond ($d_{O\cdots O}$) is 2.86 Å and nearly linear (171.4°). The iodide ions do not interact directly with ring-bound Ca^{2+}. Both I···Ca distances are > 5.4 Å and the I^- ions are more than 8 Å apart. The arenes are separated by about 4 Å but they are out of parallel by about 15°. Assuming an arene half-thickness of 1.8 Å,[27] the two phenol rings are not in intimate contact.

We report here the first examples of azacrown complexes of calcium cation. In contrast to the situation with K^+, the phenolic rings do not serve as σ-donors. In that respect they are more like the Na^+ complex. Instead, however, they form an infinite H-bonded network that relies on the phenolic hydroxyls and coordinated water and to which the iodide ions appear largely irrelevant.

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Notes and references

† *Crystal data*: for **1**·$CaI(H_2O)_5$: $C_{20}H_{40}CaI_2N_2O_9$, a = 9.8848(12), b = 12.7563(16), c = 12.3719(16) Å, β = 110.326(2)°, monoclinic, space group $P2_1$. For **2**·$CaI_2 \cdot (H_2O)_2$: $C_{30}H_{49}CaI_2N_3O_8$, a = 32.992(3), b = 17.5027(15), c = 12.9431(11) Å, orthorhombic, space group *Cmca*. CCDC reference numbers 189638 and 189639. See http://www.rsc.org/suppdata/cc/b2/b204311b/ for crystallographic data in CIF or other electronic format.

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