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1- and 2-Naphthylmethyl sidearms of isomeric bibracchial lariat ethers significantly affect alkali metal cation complexation

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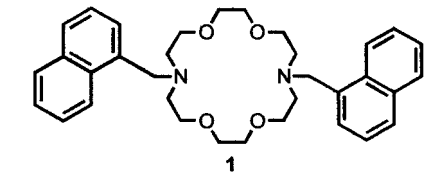
Derivatives of 4,13-diaza-18-crown-6 having benzyl or isomeric naphthylmethyl sidearms have significantly different solid state structures and show differences in cation complexation strengths.

During the more than three decades since Pedersen reported the first crown ethers,[1] these remarkable cation binders have been studied in exquisite detail. Numerous structural studies have established their conformations when unbound or when complexed by a variety of alkali and alkaline earth metal cations as well as by numerous other cationic and even neutral species. The now well-established chemistry of macrocycles[2] is exhibiting utility in the development of supramolecular systems.[3] As more complicated structures are designed, unanticipated properties occasionally emerge. Understanding such unusual effects is critical for achieving the desired properties in supramolecular structures that incorporate crowns as modules. We have recently reported the first definitive evidence for arene participation in the complexation of sodium and potassium cations.[4] In a second study, the indolylethyl sidearms[4] that bound Na^+ or K^+ were replaced by 9-anthrylmethyl.[5] In the latter case,[5] the intercession of C–H···O hydrogen bonding affected complexation geometry and cation binding strength. We now report the results of a study involving isomeric aromatic sidearms and the effect they have on complexation geometry and cation binding strength.

N,*N*′-Bis(1-naphthylmethyl)-4,13-diaza-18-crown-6, **1**, and its isomer *N*,*N*′-bis(2-naphthylmethyl)-4,13-diaza-18-crown-6, **2**, were prepared by alkylation (48 h reflux) of diaza-18-crown-6[6] using either 1-chloro- or 2-bromomethylnaphthalene in $CH_3CH_2CH_2CN$ in the presence of KI and Na_2CO_3. Compound **2** was obtained as a thick yellow oil that crystallized from hexanes and then EtOH to give light yellow prisms (76%, mp 92–93 °C).[7]



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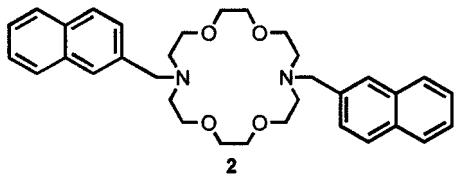

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Kubo and coworkers have recently reported the preparation of **1** as part of a program to develop fluorescent cation sensors.[8] The fluorescent properties of **1** allowed them to determine cation complexation constants. They reported that log K_s values in anhydrous MeOH for Na^+ and K^+ complexation by **1** were 2.09 and 3.27, respectively. This compares with binding constants determined for *N*,*N*′-dibenzyl-4,13-diaza-18-crown-6 (**3**) as follows: log K_s (Na^+) = 2.68 and log K_s (K^+) = 3.38. There is a 1.3-fold difference in the K^+ binding constant but a larger, ~4-fold, difference in the Na^+ binding constant. We have independently determined the binding constant for **1** and find log K_s (Na^+) to be 2.32 ± 0.26. While this 1.7-fold difference is more in line with related compounds, K_s is still lower than expected. A complexation constant determination for previously unreported **2** gave a log K_s value of 2.68 ± 0.10. For calibration, **3** was re-examined and log K_s (Na^+) was found to be 2.71, identical within experimental error to the previously reported value (see above) and to the binding constant for **2**.

Although the complexation constant differences are not major, the variation between isomers **1** and **2** is striking. We thus determined the solid state structures of the two Na^+ complexes in the hope that differences observed there might help to account for the binding variation. The structures of **1**·Na^+ and **2**·Na^+ are shown in Fig. 1(*b*),(*d*). Kubo and coworkers have reported the structure **1** in the absence of any cation (not shown).[8a] The previously unreported structure of **3**·NaI is shown in Fig. 1(*a*). For comparison, the structure we reported a number of years ago for **3**·KSCN is shown in Fig. 1(*c*).[9]

It is worth noting at the outset that the reported structure[8a] of uncomplexed **1** (not shown) is similar to many other unbound 18-membered macrocycles. The conformation of **1** is planar and the methylene groups adjacent to each macroring nitrogen atom are rotated inward in a typical free macrocycle conformation. The naphthyl groups are clearly turned away from the macroring. Kubo comments that 'the naphthalene ring of [**1**] is close to the N atom of the crown ether; the distance between C1 and N1 is 2.505 Å, shorter than the sum (3.05 Å) of their van der

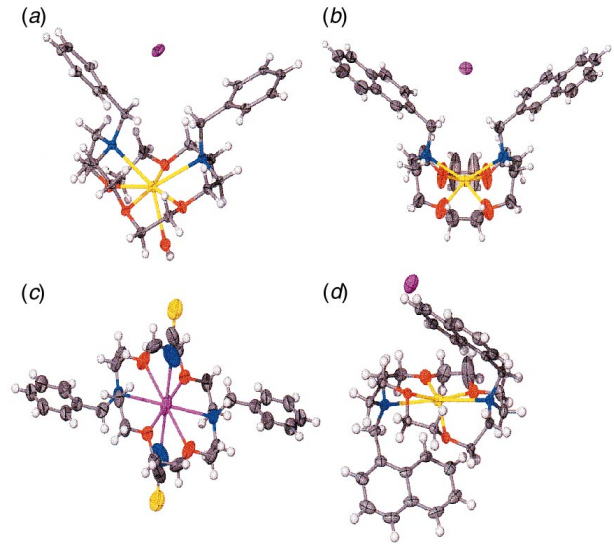

Fig. 1 (*a*) Structure of dibenzyl sodium complex, **3**·NaI. (*b*) Structure of bis(2-naphthyl) sodium complex, **2**·NaI. (*c*) Structure of **3**·KSCN (see ref. 9). (*d*) Structure of bis(1-naphthyl) sodium complex, **1**·NaI.

Waals radii.'[8a] The authors note only that intramolecular charge transfer between these atoms may be favorable.

The structures of **2** and **3** complexing NaI are both unusual but identical in essential features. In both cases the macrocycle is bowed upward with the nitrogen atoms at the peaks. This contraction reduced the N↔N separation from ~5.5–6 Å to ~4.5 Å. Likewise, the sidearm methylenes are separated by 4.02 Å and the sidearm methylene hydrogens across the ring from each other are separated by 2.76 Å and 3.41 Å, respectively. The *syn* 2-naphthyl residues mirror each other through a symmetry plane that intersects Na^+ and I^-. The bowed macroring conformation is also observed for the bis(benzyl)crown complex, **3**·NaI.

The **3**·NaI complex [Fig. 1(*a*)] differs significantly from the structure of **3**·KSCN [Fig. 1*c*)]. In the latter, the macrocycle is in the expected D_{3d} conformation, the M^+–O and M^+–N contacts are as expected, and the apical positions are occupied by SCN anions. In fact, the structure of **3**·KSCN is typical of 18-membered ring crown complexes that lack sidearms.

In contrast to the situation with **2**·NaI [Fig. 1(*b*)], the isomeric complex **1**·NaI [Fig. 1(*d*)] has an *anti*, rather than *syn*, arrangement of the 1-naphthyl sidearms. Although the macroring is far from planar, the N↔N separation is a more typical 5.9 Å. One of the naphthalene α-hydrogens is separated from the nearest macroring oxygen atom by only 2.67 Å (C···O distance = 3.56 Å). The adjacent β-hydrogen is 2.99 Å from the adjacent macroring nitrogen atom and that C–H is only 3.31 Å from iodide. These close contacts suggest significant C–H···X hydrogen bonding interactions.[10] The presence of C–H···O contacts in complexes of **1** and their absence in complexes of **2** may help to account for differences in cation binding strengths observed for these isomeric host molecules. The arene-sidearm to ring C–H···O contacts observed for **1** correspond well with those noted for the structurally related anthrylmethyl derivative previously reported.[5]

The dibenzyl- and dinaphthyldiaza-18-crown-6 derivatives reveal unexpected complex structures. The **1**·NaI complex does not appear to be stabilized by π-stacking interactions but rather by a variety of C–H···X contacts that define sidearm and, in turn, macroring conformation. The **1**·NaI complex exhibits the geometry noted above and **1** also exhibits reduced cation binding affinity, a pattern observed in previous studies from this laboratory.[5,11] Two factors may contribute to the decreased binding ability of **1** compared to **2** or **3**. First, complexes of **1** may require more complete desolvation of the cation than do complexes of **2** or **3** because of the 1-naphthyl sidearms' steric requirements compared to either benzyl or 2-naphthyl. Second, the C–H···O interactions that we observe in the complex of **1** may be able to organize the naphthyl sidearms over the macrocycle in the unbound state, therefore blocking access by the cation. It seems reasonable that both cation binding and release may be directly affected by these sidearm interactions. Our previous study of the 9-anthrylmethyl sidearmed compound,[5] which is closely related to **1**, shows a similar result for a similar geometrical situation. Ultimately, resolution of the contributory factors will require a thermodynamic study so that entropic and enthalpic contributions to ΔG and, in turn, to K_s can be appreciated. For now, it is important to note that such significant differences in conformational and binding behavior occur with isomeric host molecules.

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