Effect of Chain Length and Heteroatom Position on Ammonium Ion Binding in Nitrogen-containing 'Lariat' Ethers

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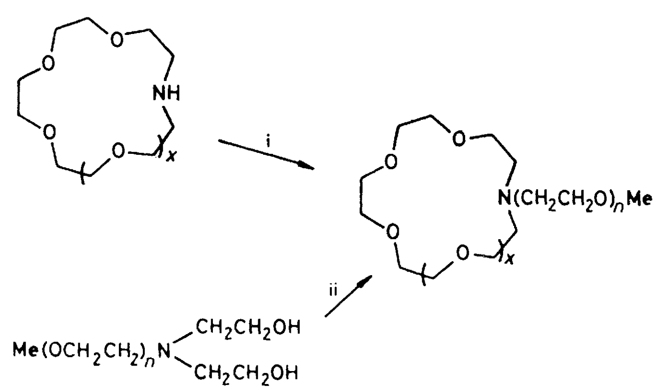
Macrocyclic polyethers having polyethyleneoxy-sidechains extending from a nitrogen pivot bind ammonium ions quite strongly when an 18-membered ring and a two-oxygen sidechain are present; a 15-membered ring and other chain lengths give inferior binding.

During the past decade, considerable attention has been given to the interaction between macrocyclic (crown) polyethers and ammonium ions. Pedersen first observed such an interaction nearly 15 years ago,[1] and more recently, several studies of macrocycle–NH_4^+ binding have appeared.[2] Numerous reports have dealt with substituted ammonium ions (*e.g.* t-butylammonium)[3] and a number of papers record the remarkable interactions between bis-ammonium salts and bis-crowns.[4] We have previously reported that lariat ethers constructed using nitrogen as a pivot atom, exhibit considerably enhanced alkali metal cation binding[5] when compared with monocyclic ethers without sidechains.[6] We now report that 18-membered-ring nitrogen lariat ethers strongly bind NH_4^+ whereas the 15-membered ring analogues bind weakly, even when the latter's sidechains are lengthy. Further, the second, rather than the first, oxygen in the 18-membered ring's ethyleneoxy-sidechain affords maximal binding. The stability constant (K_S) is, to our knowledge, the largest yet reported for an uncharged, single-nitrogen monocycle.†

N-Methylmonoaza-15-crown-5 and -18-crown-6 were obtained by methylation of the secondary amines which, in turn, are available by hydrogenolytic debenzylation of the corresponding *N*-benzyl crowns[7] (Scheme 1, route i). The lariat ethers with three or fewer ethyleneoxy-units in the sidechains were obtained as illustrated in Scheme 1, route ii, as previously described.[5] Those compounds having longer sidechains were prepared according to route i. Note that the compounds with the longest sidechains (x = 1,2; n = 8) were prepared from an oligomeric mixture with average molecular weight indicating an average chain length of 8.[8]



Scheme 1. *Conditions and reagents:* i, x = 1,2; n = 0,4,5,8; Me_2SO_4 or $Me(OCH_2CH_2)_nOSO_2C_6H_4Me$-*p*, Na_2CO_3, ii, x = 1,2; n = 1,2,3; m = 3,4; NaH, tetrahydrofuran, *p*-$MeC_6H_4SO_2$-$(OCH_2CH_2)_mOSO_2C_6H_4Me$-*p*.

The tetrahedral ammonium cation presumably binds to three of the available six heteroatoms in the 18-membered rings,[9] but probably binds to only two such sites in the 15-membered rings. The smaller ring size leads to the expected lower binding. In the case of the 18-membered ring compounds, one of the four NH_4^+ hydrogens presumably protrudes upward from the centre of, and perpendicular to, the mean plane of the heteroatoms. An examination of Corey–Pauling–Koltun space-filling molecular models suggests that the ethyleneoxy-chain can overlay the ring and the sidechain heteroatoms can provide an additional hydrogen bond acceptor. It is this secondary interaction, further binding the complexed cation which suggested the name 'lariat'. This binding arrangement could therefore be called the 'lariat conformation'. It is

† Lehn and his coworkers have reported extremely strong binding of NH_4^+ by a variety of structures but these values are for a spherand (ref. 2d), a macrocycle containing ionizable sidechains (ref. 2b), and a triazacrown (ref. 2f). In the latter case, the stability constant (K_S) is reported in 9:1 MeOH–water and is for the methylammonium cation rather than NH_4^+. The two former K_S values were measured in aqueous solution.

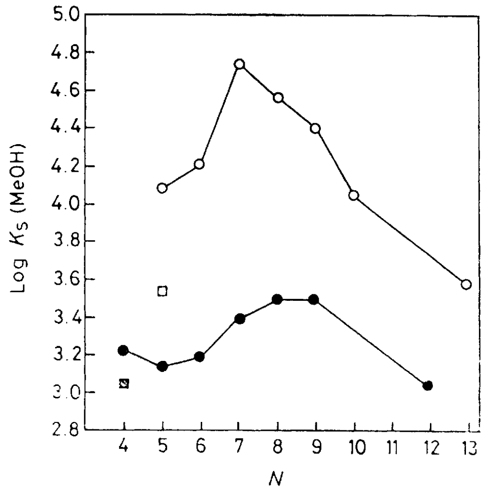


Figure 1. Ammonium ion binding by nitrogen-containing lariat ethers. N = total number of oxygen atoms in the compounds. ○ 18-membered rings, ● 15-membered rings, □ monoaza-18-crown-6, ■ monoaza-15-crown-5. Binding constants (stability constants, K_S) were determined in MeOH solution at 25 ± 1.0 °C as previously described (ref. 5).

further suggested by an examination of these models that the second rather than the first oxygen is in the best position to accommodate the complexed NH_4^+ ion. The binding constants graphed in Figure 1 confirm this expectation.

The stability constants thus give important structural information on the NH_4^+ complex. The binding data for the structurally demanding NH_4^+ ion show unequivocally that the flexible sidechain participates in binding as envisioned in the original design. These conclusions are reinforced by the very low K_S values for the 15-membered ring compounds which gradually increase as the sidechain lengthens. In this case, three-point ring binding is sterically prohibited and both ring and sidechain are probably used as hydrogen bond receptors, although less successfully than the 'properly' sized and organized 18-membered ring.

The existence of a peak in each set of data suggests that, beyond a certain point, the long chain becomes a hindrance rather than an asset. This may be owing to hydrogen bonding between it and the medium, reducing sidechain flexibility, or coiling of the chain over the ring may be responsible. We have observed the same phenomenon with Na^+ cations.[8]

We thank the National Institutes of Health for support of this work.

Received, 19th October 1981; Com. 1227

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