

Electrospray Ionization of a Novel Sodium Ion Binding Molecule

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The design and use of aryl macrocycles such as cyclophanes, cryptophanes and collarenes to bind small organic molecules in a host-guest relationship has been a well investigated field of study¹. In these studies, the importance of noncovalent forces such as hydrogen bonding and the hydrophobic effect have always been recognized, and some success in optimizing these forces has been achieved. Only more recently has the cation- π interaction been proposed as a major participant in host-guest binding. Much of this research has been dedicated towards organic cations such as acetylcholine and other quaternary amines.² Although there is a rapidly growing understanding of the importance of alkali metal cation- π interactions in biological systems,³ relatively few attempts to coordinate alkali metal cations with aryl macrocycles have been reported.⁴ Towards that goal, we have successfully synthesized a new cyclophane which we believe coordinates a sodium cation in a host-guest relationship exclusively through cation- π interactions.

1,6,13,18-Tetraoxa[6.6]paracyclophane-3,15-diyne, or pyxophane, features a central cavity, bordered by two benzene rings and two rigid acetylenic spacers. This central cavity has a size of 2.1Å by 3.6Å, and is surrounded by π electrons. This distance suggests that a sodium cation, with a diameter of 1.98Å, should easily be able to fit into the host molecule. The advantage of mass spectrometry as a tool for determining whether pyxophane selectively binds Na⁺ is that the host-guest complex is ionic and stable in solution. Electrospray Ionization Mass Spectrometry (ESI MS) was selected for this series of experiments because it is compatible with a wide variety of experimental solvent systems, and because the ionization process is of a low energy, allowing the detection of noncovalently bound complexes which might dissociate under more energetic conditions.

The ultimate goal of these experiments was to determine not just whether pyxophane can bind metal cations, but also to try to determine how these cations bind to the pyxophane molecule. In other words, do the cations have a nonspecific affinity for the π electron system, perhaps binding to the outside of the molecule, or can the central cavity of the pyxophane molecule be occupied by a metal cation of the appropriate size, such as Na⁺?

In the first experiment, Na⁺, Rb⁺, Cs⁺ and K⁺ were compared with respect to their ability to bind to pyxophane. The cation that produced the most intense signal for the pyxophane/cation complex was Na⁺. Cs⁺ also produced a significant

complex ion, but Rb⁺ gave only a very weak signal. K⁺ did not produce a measurable complex ion under these conditions, even though it is closest in size to the Na⁺ ion.

Another observation is the formation of complexes of one metal cation with two pyxophane molecules, or [2(pyxophane)+M]⁺. This dimer is observed with Na⁺, Rb⁺, and Cs⁺, although the intensity of the signal for this dimer varies considerably between these metal cations. In the case of Na⁺, the dimer signal is much smaller (approximately 10%) than that of the simple complex. For Rb⁺ and Cs⁺, the signal for the dimer is higher compared to the monomer signal, although the intensities in general are much lower. This implies that the complexation of Rb⁺ and Cs⁺ with pyxophane, while generally not as strong as for Na⁺, are more likely to produce dimers. The presence of these dimers may be consistent with an external (*exo*) location for the metal cation, allowing the cation to coordinate with either the π systems or the lone electron pairs of the oxygens of two pyxophane molecules at the same time. This dimerization seems to be more effective for the larger metal cations, Rb⁺ and Cs⁺. It is possible that the lower relative intensity of the dimer signal for Na⁺ is due to it occupying the central cavity of the pyxophane molecule, and being less accessible for dimer formation.

In the second experiment, molecules with similar functionality to pyxophane (anisole and phenetole), but without the central cavity, did not show any significant affinity for the sodium cation under the same experimental conditions as were used for pyxophane. This implies that the very high affinity of Na⁺ for pyxophane is to some degree dependent on the structure of the pyxophane molecule. Other metal cations were not tested, but Cs⁺ and Rb⁺ might be expected to have some affinity for anisole and/or phenetole.

References

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