Gas Phase Conformations of Li$^+$, Na$^+$, K$^+$, and Cs$^+$ Complexed with 18-Crown-6

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Crown ethers have been intensely studied since their initial characterization nearly 30 years ago.[1] Much of the interest stems from their ability to selectively complex cations in solution[2] and consequently act either as cleansing agents for unwanted or dangerous ionic contaminants[3] or as possible delivery agents for transporting ionic species to specific binding sites in living tissues.[4] The prototypical systems are alkali ion "guests" in the 18-crown-6 "host". These systems have been studied at great length using molecular mechanics methods[5] and recently ab initio[6] and mixed quantum mechanics/molecular mechanics methods.[7] Of interest is the fact that binding free energies to 18-crown-6 in a variety of solvents[2,8,9] are in the order K$^+$ > Rb$^+$ > Cs$^+$ > Na$^+$ > Li$^+$, while the best theoretical estimates[6] yield "intrinsic" or gas phase binding enthalpies in the order of Li$^+$ > Na$^+$ > K$^+$ > Rb$^+$ > Cs$^+$. Clearly solvent effects play a major role in the selectivity ordering in solution, as recently documented in an extensive review.[8]

To understand how the solvent directs host/guest selectivity, it is necessary to obtain both thermodynamic and structural data in the absence of solvent. The current situation in crown ether host/guest chemistry in this regard is reminiscent of the state of affairs in the late 1960s and early 1970s, when gas phase studies finally began to yield intrinsic basicities and acidities of molecules,[10−12] resulting in a major rethinking of the factors that are responsible for these important properties.[13] Recently, gas phase studies have begun on crown ethers as well, due principally to the development of powerful mass spectrometric methods.[14] Important data have been obtained by Dearden and co-workers on the rate of association of alkali ions with various crown ethers, rates of formation of sandwich-like dimer compounds, and rates of crown switching reactions on a given metal center.[15] These studies indicate a general correlation between crown selectivity and a matching of ionic radius[16] with the crown cavity radius.[17] A recent study also suggests that gas phase chiral recognition is possible using crown ethers.[18]

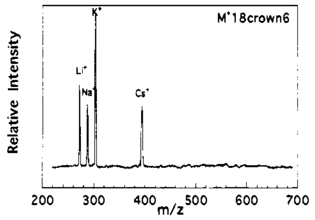

Figure 1. Mass spectrum resulting from matrix-assisted laser desorption/ionization of a mixture of alkali ion salts in sinapinic acid. Matrix peaks occurring near *m/z* = 200 are not shown.

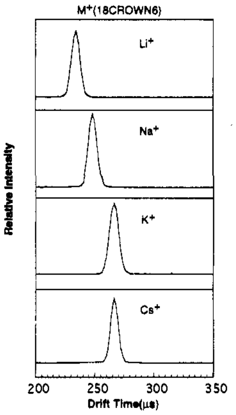

Figure 2. Arrival time distributions (ion chromatograms) for Li$^+$, Na$^+$, K$^+$, and Cs$^+$ complexed to 18-crown-6 (see text).

In this Communication, we will report the first measurements on the gas phase conformations of alkali ion/18-crown-6 inclusion complexes. In these studies, we use the recently developed ion chromatography (IC) technique,[19] which allows accurate measurement of gas phase collision cross sections of the species of interest. We have recently successfully applied IC to Na$^+$-catonized poly(ethylene glycol) (PEG) polymers,[20,21] which are functionally closely related to the crown ethers. The M$^+$/18-crown-6 ions are made in a matrix-assisted laser desorption/ionization (MALDI) ion source described elsewhere.[21] A mass spectrum from a mixture of alkali ion salts in a sinapinic acid matrix is given in Figure 1, showing clean formation of M$^+$(18-crown-6) adducts and no fragmentation. A 4 μs pulse of a mass-selected crown complex is then injected into a 4 cm long cell filled with 3 Torr of He gas at 300 K. The ions drift through the cell under the influence of a uniform but weak electric field. Upon exiting the cell, an arrival time distribution (ion chromatogram) is obtained at a detector. Such distributions for M$^+$ = Li, Na, K, and Cs are given in Figure 2.

In all cases, a narrow, monomodal arrival time distribution is observed. These results immediately indicate that in each complex only a single structure, or set of very similar structures, occurs, since the many collisions with He, while transiting the cell, result in spatial and temporal separation of isomers with

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(1) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495; 7017.

(2) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J.; Seu, D. *Chem. Rev.* **1985**, *85*, 271.

(3) Horwitz, E. P.; Dietz, M. L.; Fisher, D. E. *Solvent Extr. Ion Exch.* **1991**, *9*, 1. Tang, T.; Wai, C. M. *Anal. Chem.* **1986**, *58*, 3233.

(4) Kozak, R. W.; Waldman, T. A.; Atcher, R. W.; Gansow, O. A. *Trends Biotechnol.* **1985**, *4*, 259.

(5) Wipff, G.; Wiener, P.; Kollman, P. *J. Am. Chem. Soc.* **1982**, *104*, 3249. Dang, L. X.; Kollman, P. *J. Am. Chem. Soc.* **1990**, *112*, 5716.

(6) Glendening, E. D.; Feller, D.; Thompson, M. A. *J. Am. Chem. Soc.* **1994**, *116*, 10657.

(7) Thompson, M. A.; Glendening, E. D.; Feller, D. *J. Phys. Chem.* **1994**, *98*, 10465.

(8) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1991**, *91*, 1721.

(9) Not all solvents have the ordering given here. For example, Na$^+$ and K$^+$ are reversed in the order in acetonitrile: DeJong, F.; Reinhardt, D. N. *Adv. Phys. Org. Chem.* **1980**, *17*, 279.

(10) Brauman, J. I.; Blair, L. K. *J. Am. Chem. Soc.* **1968**, *90*, 5636.

(11) Bowers, M. T.; Aue, D. H.; Webb, H. M.; McIver, R. T. *J. Am. Chem. Soc.* **1971**, *93*, 4314.

(12) Briggs, J. P.; Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1972**, *94*, 5138.

(13) Aue, D.; Bowers, M. Stabilities of Positive Ions from Equilibrium Gas-Phase Basistity Measurements. In *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic: New York, 1979; Vol. II, pp 1−51. Aue, D. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1976**, *98*, 318.

(14) *Accs. Chem. Res.* **1994**, *27*, Issue No. 11.

(15) (a) Zhang, H.; Chu, I.-H.; Leming, S.; Dearden, D. V. *J. Am. Chem. Soc.* **1991**, *113*, 7415. (b) Chu, I.-H.; Zhang, H.; Dearden, D. V. *J. Am. Chem. Soc.* **1993**, *115*, 5736.

(16) Shannon, R. D. *Acta Crystallogr., Sect. A* **1976**, *32*, 751.

(17) Dalley, N. K. In *Synthetic Multidentate Macrocyclic Compounds*; Izatt, R. M., Christensen, J. J., Eds.; Academic: New York, 1978; pp 207−243.

(18) Chu, I.-H.; Dearden, D. V.; Bradshaw, J. S.; Huszthy, P.; Izatt, R. M. *J. Am. Chem. Soc.* **1993**, *115*, 4318.

(19) Bowers, M. T.; Kemper, P. R.; von Helden, G.; van Koppen, P. A. M. *Science* **1993**, *260*, 1446. Kemper, P. R.; Bowers, M. T. *J. Phys. Chem.* **1991**, *95*, 5134.

(20) von Helden, G.; Wyttenbach, T.; Bowers, M. T. *Science* **1995**, *267*, 1483.

(21) von Helden, G.; Wyttenbach, T.; Bowers, M. T. *Int. J. Mass Spectrom. Ion Processes*, in press.

0002-7863/95/1517-10159$09.00/0

Table 1. Collision Cross Sections in Å^2 of M$^+$(18-Crown-6) with He

M$^+$	experiment[a]	molecular mechanics[b,d]	ab initio[c,d]
Li$^+$	95.0	94.8	92.3
Na$^+$	100.2	101.4	99.1
K$^+$	105.0	105.7	104.4
Cs$^+$	104.7	105.4	106.5

[a] Absolute experimental uncertainty is about 2%, but relative values are much more accurate. [b] This work used the AMBER suite of programs (ref 24) as described in the text. Parameters for H, C, O, and He are from ref 21, and parameters for Li$^+$, Na$^+$, K$^+$, and Cs$^+$ are from ref 25. [c] Reference 6 [d] The three-dimensional collision cross sections were determined from theoretical structures using Monte Carlo methods (ref 23) and were converged to 1%.

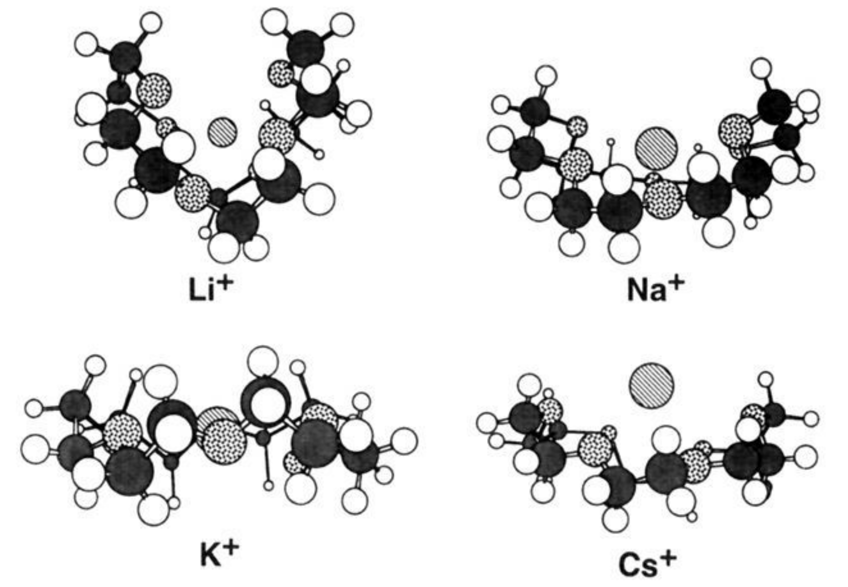

Figure 3. Conformations generated by molecular mechanics for Li$^+$, Na$^+$, K$^+$, and Cs$^+$ complexed to 18-crown-6 that yield the cross sections given in Table 1. Only the side view is shown. In all cases, the alkali ion is located on an axis running through the center of the crown cavity but perpendicular to the plane of the free crown. The alkali ion has the diagonal striping, oxygens are speckled, carbons are darkly shaded, and hydrogens are open.

different collision cross sections. Since the experimental conditions were identical for all four systems, the data also indicate that Li$^+$(18-crown-6) goes through the cell most quickly, followed by Na$^+$(18-crown-6), with K$^+$ and Cs$^+$ complexes slower but with nearly equivalent drift times. Hence, the Li$^+$ complex is most compact, followed by Na$^+$(18-crown-6); the K$^+$ and Cs$^+$ complexes are least compact.

To obtain structural information, the data are quantified by determining accurate mobilities in He, K_0, which are inversely proportional to the collision cross section in the hard-sphere limit.[21,22] Candidate structures are then obtained from theoretical models for comparison with experimental cross sections. Using our work on Na$^+$PEG$_n$ systems as a guide,[20,21] we used the Amber molecular mechanics force field[23] to generate trial structures which were subjected to extensive annealing to find the global minimum for each of the complexes. Monte Carlo methods[24] were then applied to obtain cross sections. We used no adjustable parameters in this process.

The experimental and model cross sections are compared in Table 1, and the actual structures of the complexes are given in Figure 3. We have also calculated cross sections from the ab initio results of Glendening et al.[6] and included these in Table 1 as well. It is apparent from Table 1 that the agreement between experiment and both the molecular mechanics and ab initio predictions is excellent. Since the errors in both the experimental and Monte Carlo modeling of the cross sections are of the order of 1−2%, clearly the almost perfect agreement is fortuitous. What is important is the fact the model nearly exactly matches the trend in cross sections as M changes. The relative values of the cross sections are very accurately determined, and the 10% change from M = Li to M = K, Cs is far outside of experimental error.

The global minimum structures given in Figure 3 for the four complexes are revealing. As expected, all alkali ions are centered on the crown cavity axis. However, only for K$^+$ is the complex quasi-planar. The small Li$^+$ ion moves well out of the plane along the axis and induces substantial distortion in the crown in order to better coordinate with the partially negatively charged oxygen atoms. This process is repeated, but the distortion is smaller for the larger Na$^+$ ion. Finally, Cs$^+$ is too large for the crown cavity and is forced out of plane, with the crown distorting to maximize coordination. This dramatic structural change with ion size is responsible for the 10% change in cross section from Li$^+$ to K$^+$, Cs$^+$ and explains a number of additional observed phenomena.

For example, Li$^+$ and Na$^+$ do not form M$^+$L$_2$ sandwich compounds for L = 18-crown-6, but Cs$^+$ readily does, and K$^+$ does so very slowly.[15b] Clearly, only for K$^+$ and Cs$^+$ is the alkali ion accessible to a second ligand. The different ordering of binding energies in solution and in the gas phase is also consistent with these structures. In the gas phase, Li$^+$ is bound the strongest,[6] reflecting its relatively high charge density and its ability to intimately associate with all six oxygen atoms. A monotonic trend leading to the weakest binding for Cs$^+$ reasonably flows from increasing ion size. In solution, since Li$^+$ is essentially fully solvated by the crown, it benefits only in a minor way from further solvation, in spite of the fact that it has the largest solvation energy of any of the alkali ions. The same holds to a lesser extent for Na$^+$. Hence, these two systems have the weakest binding energies in solution. Conversely, K$^+$ and Cs$^+$ are exposed and can benefit from solvation. In fact, theory suggests that water as a solvent displaces the K$^+$ ion an average of 0.25 Å from the crown center of mass, resulting in coordination with two water molecules in its first solvation shell.[7] In this system, the average K$^+$−O distance is essentially equal for all eight O atoms (six on the crown and two on the water molecules). Consequently, in water solution, K$^+$ is bound most strongly of the alkali ions to 18-crown-6. What is most important, however, is the fact the K$^+$ ion is still primarily solvated by the crown in competition with water as a solvent. This makes sense because K$^+$ is bound much more strongly to small ethers than to H$_2$O due to the contribution of larger dispersion forces for the ethers.[26] Similar reasoning applies for the remaining alkali ions.[27]

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(22) Mason, E. A.; McDaniel, E. *Transport Properties of Ions in Gases*; Wiley: New York, 1988.

(23) von Helden, G.; Hsu, M.-T.; Gotts, N. G.; Bowers, M. T. *J. Phys. Chem.* **1993**, *97*, 8182.

(24) Pearlman, D. A.; Case, D. A.; Caldwell, J. C.; Seibel, G. L.; Singh, U. C.; Weiner, P.; Kollman, P. A. *AMBER 4.0*, University of California; San Francisco, CA, 1991.

(25) Grootenhuis, P. D. J.; Kollman, P. A. *J. Am. Chem. Soc.* **1989**, *111*, 2152.

(26) Davidson, W. R.; Kebarle, P. *J. Am. Chem. Soc.* **1976**, *98*, 6133.

(27) The alkali ion/crown/water system is complex, and the exact conformation of the system centered around the crown is not precisely known for any system and may well be fluxional in nature at 300 K. What is known is that alkali ions strongly prefer association with small ethers (to water) in the gas phase, and there is no reason to believe this tendency will not carry over to water solutions. Theory indicates that solvating K$^+$(18-crown-6) in H$_2$O has very little effect on the K$^+$/crown structure. If one considers the complete thermodynamic cycle for this process, this is the expected result. Consequently, it is expected that similar results will hold for other alkali ions, even though detailed thermodynamics are not yet available for them. Hence, it is expected the gas phase structures determined here will be modified only to a small extent when injected into solution. This point remains to be proven, however.