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Gas Phase Ion−Molecule Equilibria Involving Ions Produced by Electrospray. Hydration of Doubly Protonated Diamines

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Electrospray[1] (ES) affords the production of ions in the gas phase, such as doubly and triply charged transition metal and alkaline earth ion−ligand complexes,[2] multiply protonated peptides and proteins,[3] doubly charged anions like SO_4^{2-} and HPO_4^{2-}, and multiply deprotonated nucleic acids,[5] which are of paramount importance in solution chemistry and biochemistry, but which could not be obtained in the gas phase prior to the development of ES.

We will describe here apparatus with which ion−molecule equilibria,[6] involving electrospray-produced ions, can be measured. Ion equilibria are the main source of gas phase ion thermochemistry.[6−8] The major difficulty with ES is the high pressure, $\sim$1 atm, at which the ions are generated, and the presence of solvent vapor. Accurate mass spectrometric determinations of ion equilibria at such high pressures are difficult.[2] Pressures in the Torr range, *i.e.*, under conditions used in previous work with conventional gas phase ions,[6] are preferable.

A reaction chamber operating in the Torr range, to which ES ions from 1 atm were transferred via a capillary, was described recently.[9] This design was not successful for equilibria measurements because the capillary was coaxial with the ion sampling orifice. The new successful design, where the capillary is at right angles to the orifice axis, OR, is shown in Figure 1.

Gas expanding out of a capillary into a low-pressure region forms a supersonic jet which preserves its integrity over a considerable distance.[10] In the previous[9] coaxial design, the jet transported the ions in the direction of the orifice, and this led to high sensitivity; however, the composition of the gas surrounding the ions could not be controlled accurately. In the present design, the ions are deflected out of the jet by an electric field imposed by electrodes D and IN. Some of the ions drift into the reaction chamber, RC, through the 4 mm diameter orifice in IN. A reagent gas mixture consisting of a bath gas, $\sim$10 Torr of N_2, and known partial pressures of water vapor, in the 1−80 mTorr range, flows through the reaction chamber and exits into the main volume through the orifice in IN. The effluent of the capillary, CAP, and the reagent gas are pumped out through the pumping lead, PL.

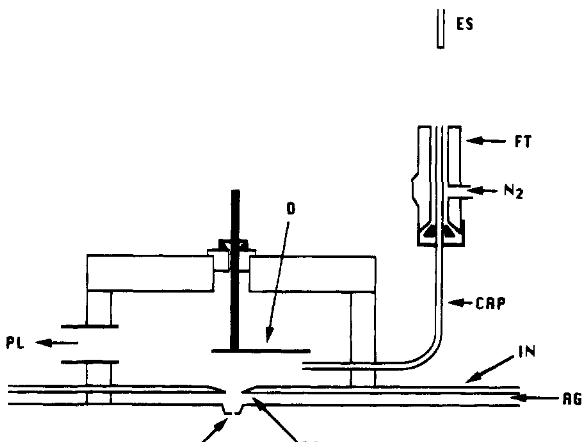

Figure 1. The capillary tip, ES, at $\sim$5 kV produces spray, some of which is sucked in by the capillary, CAP, $\sim$150 V, 5 cm long, 0.4 mm i.d. Ions deflected out of the gas jet by the deflector, D, $\sim$150 V, drift to the interface plate, IN, 110 V, and enter the reaction chamber, RC. Reagent gas, RG, is supplied to RC at 85 mL/min at STP. The orifice, OR, 100 μm diameter, 100 V, allows ions to enter the vacuum of the quadrupole mass spectrometer. PL, pumping lead. Purified N_2 flow at 2 L/min at STP in FT, 700 V, reduces the amount of air and solvent vapor entering CAP. The gas phase ions M^+ and M^{2+} generated in the spray of the ES capillary were obtained from 10^{-5}−10^{-4} mol/L solutions of soluble salts MX or MX_2 in methanol at solution flow rates between 1 and 3 μL/min.

The equilibria, eq 1, establish in RC. The relative equilibrium concentrations of the ions are determined by measuring, with a quadrupole mass spectrometer, the relative ion intensities of ions escaping through the orifice, OR. In general the sensitivity of ion detection was very good. The total intensity of the ion hydrates was in the 10^5 ion counts/s region.

$$M^{Z+}(H_2O)_{n-1} + H_2O = M^{Z+}(H_2O)_n \qquad (1)$$

The equilibrium expression $K_{n-1,n}$ requires that a plot of the ion intensity ratio (I_n/I_{n-1}) versus the partial pressure of H_2O leads to a straight line which goes through the origin. Experiments in which the H_2O pressure was changed from 1 to 70 mTorr in five or six steps led to excellent plots with correlation coefficients generally better than $R = 0.997$. The slope of the plots led to $K_{n-1,n}$. The free energy was obtained from the relationship $\Delta G°_{n-1,n} = -RT \ln K_{n-1,n}$. Determinations involving the hydration of several ions, H_3O^+, Na^+, and K^+, whose $\Delta G°_{n-1,n}$ had been measured previously by other methods, were found to be in good agreement with the previous work.[6,7] A full documentation of the experimental method will be provided elsewhere.[11]

The $\Delta G°_{n-1,n}$ values of the present work are shown in Table 1. The $-\Delta G°_{n-1,n}$ values for ammonia or protonated amines have been found to decrease as n increases.[6,7,13] This is the case also for the *n*-propyl- and *n*-octylammonium ions (see Table 1), where for the propyl ion $-\Delta G°_{1,2} = 6.7$ kcal/mol and $-\Delta G°_{2,3} = 4.8$ kcal/mol. Such decreases are easily rationalized. The strong hydrogen-bonding interactions are primarily electrostatic, and the interaction of each protic hydrogen on the

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Table 1. Free Energy Changes, $\Delta G°_{n-1,n}$, from Equilibria Measurements[a]

	$(n-1,n)$				
ion	(1,2)	(2,3)	(3,4)	(4,5)	(5,6)
$(CH_3CH_2CH_2NH_3^+)$	6.7	4.8			
$(CH_3(CH_2)_7NH_3^+)$	6.4	5.0			
$NH_3(CH_2)_6NH_3^{2+}$		8.3	7.4	6.2	5.6
$NH_3(CH_2)_8NH_3^{2+}$		8.0	7.2	6.1	5.5
$NH_3(CH_2)_{10}NH_3^{2+}$		7.7	6.9	5.9	5.3
$NH_3(CH_2)_{12}NH_3^{2+}$		7.4	6.7	5.8	5.2

[a] $-\Delta G°_{n-1,n}$ values for hydration reactions, eq 1, in kcal/mol. Standard state, 1 atm. $T = 290$ °K.

amine with a water molecule reduces the protic character of the remaining hydrogens.

Once all protic hydrogens have been used up, a somewhat larger bond energy drop is observed because the incoming water molecule must form a "secondary" hydrogen bond to "inner shell" water molecules.[6,12,13] For the alkylamines, Table 1, the inner shell is complete with three water molecules, and our inability to observe the (3,4) equilibrium is probably due to the weaker bonding expected for the fourth, outer shell water molecule.

For the diprotonated diamines equilibria are observed for (2,3) up to (5,6), Table 1. The $-\Delta G°_{2,3}$ values are some 3 kcal/mol higher than was the case for the singly protonated amines. In the gas phase the diprotonated amines will be stretched out so as to minimize the Coulombic repulsion between the two charges. The hydration of this system to a certain extent resembles the hydration of two separate protonated amino groups. The higher exoergicity for the diammonium ions is thus partly a consequence of the fact that there are "two" ions to be solvated and the water molecules distribute themselves between them. This model is also supported by the observed changes of the $\Delta G°_{n-1,n}$ values for the diammonium ions with increasing n. Typically the changes are $-(\Delta G°_{2,3} - \Delta G°_{3,4}) = 0.8$ kcal/mol, $-(\Delta G°_{3,4} - \Delta G°_{4,5}) = 1.1$ kcal/mol, and $-(\Delta G°_{4,5} - \Delta G°_{5,6}) = 0.6$ kcal/mol. This special pattern is consistent with the following buildup of hydrates. The first two water molecules go one each on the two ammonium groups. The third and fourth do the same. Since the third and fourth molecules occupy similar positions, the drop of bond energy, 0.8 kcal/mol, is small. The fifth water molecule faces a tripling up on one of the ammonium ions, and this leads to a large drop, 1.1 kcal/mol, while the sixth enters a similar triple position on the other ammonium group, and the drop is small, 0.6 kcal/mol. Plots of the $\Delta G°_{n-1,n}$ values for the diamines versus the carbon chain lengths are shown in Figure 2. The large decrease of bonding between $-\Delta G°_{3,4}$ and $-\Delta G°_{4,5}$, discussed above, is readily noticeable in the figure since it occurs for all diammonium ions.

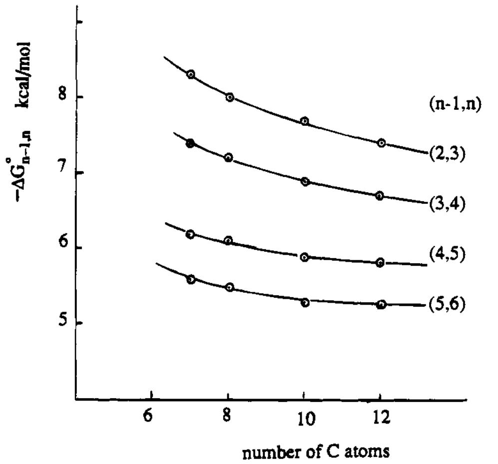

Figure 2. Measured $\Delta G°_{n-1,n}$ for diprotonated alkyl diamines versus number of carbon atoms in the alkyl chain.

The $-\Delta G°_{n-1,n}$ for a given n, such as $-\Delta G°_{2,3}$, decreases significantly as the length of the carbon chain is increased. This means that the presence of a positive charge at the other end of the molecule has a significant hydration bond strengthening effect even when the carbon chain involves seven and more carbon atoms. As expected, the effect is largest for the lowest hydrate, $-\Delta G°_{2,3}$, and weakest for $-\Delta G°_{5,6}$, where the charge on each ionic terminus has been partially dispersed over some three water molecules. A rapid increase of $-\Delta G°_{n-1,n}$ when the number of carbon atoms is decreased below seven is indicated by the data. Unfortunately we were unable to get determinations for shorter chains because the abundances of the observed doubly relative to singly protonated ions decreased very rapidly for shorter chain lengths.

The work presented above demonstrates that consistent experimental results which can be readily interpreted can be obtained for these interesting new ions. We have extended the studies to the hydration of cyclized monoprotonated diamines[14] and to some singly and doubly protonated di- and tripeptides. Preliminary results indicate that the hydration patterns can reveal structural features of the polyprotonated peptides. We are confident that the simple device described will be able to provide valuable thermochemical data not only of ions of general chemical interest but also for the biologically important ions which have created such excitement in analytical electrospray mass spectrometry.

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