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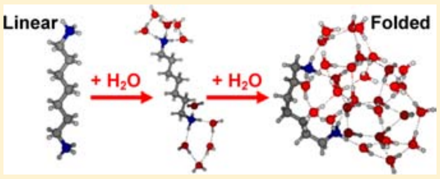
Water-Induced Folding of 1,7-Diammoniumheptane

Maria Demireva, Jeremy T. O'Brien, and Evan R. Williams*

Department of Chemistry, University of California, Berkeley 94720-1460, United States

Supporting Information



ABSTRACT: Effects of hydration on the gaseous structures of diprotonated 1,7-diaminoheptane and protonated heptylamine are investigated by infrared photodissociation (IRPD) spectroscopy and computational chemistry. IRPD spectra in the hydrogen bond stretching region (2800−3900 cm^{-1}) indicate that 1,7-diammoniumheptane is linear and that hydration occurs predominantly by alternate solvation of the two protonated amine groups for clusters with up to 10 water molecules. The relative intensities of bonded versus free hydroxyl (OH) stretches are greater in the spectra of 1,7-diammoniumheptane with more than 12 water molecules attached than the corresponding reference spectra of heptylammonium. This indicates that in the larger clusters, 1,7-diammoniumheptane adopts a more folded conformation in which the two protonated amine groups are solvated by a single water nanodrop. These results are supported by molecular dynamics simulations which show more hydrogen bonds in representative folded structures of hydrated 1,7-diammoniumheptane versus those with linear structures. These results indicate that the increase in Coulomb energy as a result of bringing the two positive charges closer together in the folded structures is compensated for by the additional hydrogen bonds that are possible when a single nanodrop solvates both protonated amine groups.

INTRODUCTION

The physical properties of molecules in solution depend on the delicate balance between intramolecular interactions and intermolecular interactions with the solvent. For example, both types of interactions are important in protein conformation, where hydrophobic groups are often in tightly packed cores to avoid exposure to water.[1,2] Intramolecular and water−ion interactions can be separated and probed in gas phase experiments, in which isolated ions or ions with a controlled number of solvent molecules attached are formed. Such studies have led to a significantly improved understanding of the role of molecular structure versus molecule−solvent interactions in a range of physical properties, including acid−base chemistry.[3,4]

Hydrated ions have been probed using a variety of different methods. The sequential hydration enthalpies and entropies for various amino acids, peptides, and other organic ions have been measured with blackbody infrared radiative dissociation (BIRD),[5−7] guided ion beam mass spectrometry,[8−10] and hydration equilibrium and high pressure mass spectrometry.[11−20] These experiments can provide information about where water binds to ions, the number of water molecules needed to stabilize the zwitterionic structures of amino acids in the gas phase, and reveal the onset of second solvent shell formation. Computational methods are often used to provide detailed structural information either independently[21−23] or in combination with experiment.[5−13] More recently, infrared photodissociation (IRPD) spectroscopy[24,25] has emerged as a powerful and sensitive technique for probing the structures and interactions of various gaseous ions[26−34] and their hydrates,[34−57] including solvation of small inorganic ions[35−50] and bioions.[52−56]

For gaseous ions that are multiply charged, Coulomb interactions can play a more significant role on molecular structure than in high dielectric solutions, such as water. For example, highly protonated gaseous ions are typically more elongated than the corresponding ions with fewer protons, and the proton transfer reactivity increases significantly with increasing charge.[58,59] The apparent gas phase basicity of singly protonated diaminoalkanes decreases with decreasing molecular length of the alkyl chain, and the reactivity can be accounted for using a simple charge model with an effective dielectric constant of 1.0 assuming an extended ion geometry for the diprotonated ion.[60,61] Similarly, measured electron binding energies for dicarboxylate dianions in photoelectron spectroscopy experiments increase with the alkyl chain length, which results from the decrease in Coulomb repulsion energy as the charge separation distance increases.[62]

The hydration of both diprotonated diaminoalkanes and dicarboxylate dianions and the effects on molecular structure have been investigated. Kebarle and co-workers measured sequential binding energies for the first four water molecules bound to diammoniumalkanes and found that these water molecules attach alternately to the two protonated amines in these linear molecules.[16−18] Protonated *n*-octylamine with 20 water molecules attached is especially abundant in evaporative cooling mass spectrometry experiments, which was attributed to the formation of a clathrate-like structure around the protonated amine group.[63] However, doubly charged 1,12-diammoniumdodecane with 40 water molecules attached is not unusually abundant, which led the authors to suggest that separate solvation of the two protonated amine groups is

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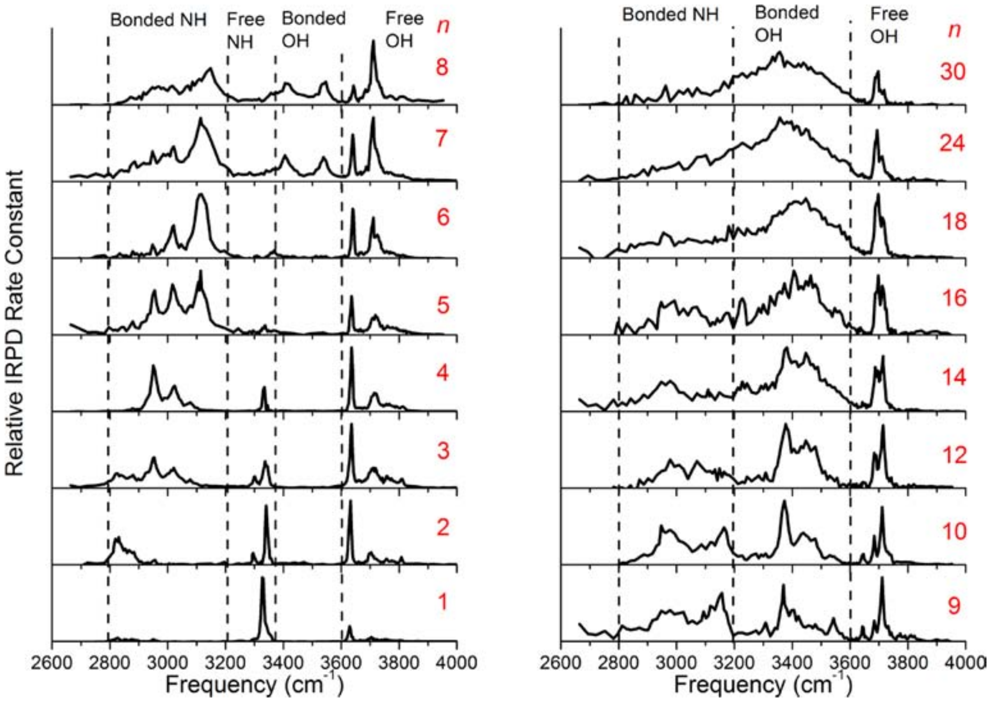

Figure 1. IRPD spectra of $NH_3^+(CH_2)_7NH_3^+ + nH_2O$ with n = 1−30. The spectral regions for free and bonded OH, and free and bonded NH stretches are indicated by the vertical dashed lines.

energetically less favorable than solvating both charge centers in a single cluster.[63] Wang and co-workers measured adiabatic electron detachment energies for sequentially hydrated dicarboxylate dianions,[64−67] and showed that these values increase with hydration extent up to 15 water molecules for the suberate dianion as a result of a decrease in Coulomb repulsion energy between the two charge sites.[65,66] However, the electron detachment energy decreased with 16 water molecules attached, which was attributed to the suberate dianion adopting a more folded conformation in which the two charge sites are closer together resulting in higher Coulomb repulsion energy.[65,66] IRPD spectroscopy has also been used to investigate the combined effects of electrostatic and solvent interactions on the conformation of the suberate dianion.[53] This elegant experiment demonstrates that the intensities of the symmetric versus asymmetric carboxylate group stretches provide clear signatures for the conformation adopted by the suberate dianion, and that about 16 water molecules are required for this dianion to adopt a folded conformation in the gas phase, consistent with conclusions from the earlier photoelectron spectroscopy experiments.[65,66]

Here, the effects of sequential hydration on the conformation of 1,7-diammoniumheptane with up to 30 water molecules attached are investigated using IRPD spectroscopy in the hydrogen bond stretching region (2800−3900 cm^{-1}). A comparison to IRPD spectra of hydrated heptylammonium used as a reference for solvation at a single protonation site indicates that a structural transition between an extended structure, in which both protonation sites are equally and separately solvated, to a folded structure, in which both protonation sites are solvated by a single nanodrop of water, occurs with 14 or more water molecules. This conclusion is supported by molecular dynamics simulations performed to investigate the average number of hydrogen bonds involved in solvating representative folded and linear conformations.

■ METHODS

Experiments. IRPD experiments were performed using a tunable optical parametric oscillator/amplifier (OPO/OPA) laser system and a 2.7 T Fourier transform ion cyclotron resonance mass spectrometer equipped with a nanoelectrospray ion source and a temperature controlled ion cell that is described in detail elsewhere.[68] Heptylamine and 1,7-diaminoheptane were obtained from Sigma Chemical Co. (St. Louis, MO) and were used without further purification. Hydrated heptylammonium and 1,7-diammoniumheptane were generated via nanoelectrospray from ∼2 mM aqueous solutions using borosilicate glass capillaries with tips pulled to an inner diameter of ∼1 μm. A potential of ∼500−700 V relative to the metal entrance capillary of the mass spectrometer was applied to a platinum wire that is in contact with the solution. Ions were introduced into the mass spectrometer via the heated entrance capillary and were guided with electrostatic lenses through five stages of differential pumping into the ion cell. The ion source parameters and trapping conditions were adjusted to optimize the signal for the clusters of interest. The ion cell is surrounded by a copper jacket that is temperature regulated with a controlled flow of liquid N_2 and thermocouples on the outside of the jacket to measure temperature.[69] All IRPD spectra were acquired at a copper jacket temperature of 133 K. Ions were accumulated in the cell for 3−6 s, during which time N_2 gas was introduced to aid with trapping and thermalizing the ions. The ions were subsequently stored for 4−12 s to allow the pressure to return to $\leq 10^{-8}$ Torr and to ensure that the ions had steady-state internal energies. The precursor ion clusters of interest were isolated using stored waveform inverse Fourier transform excitation to eject all other ions from the cell, and were irradiated using tunable infrared light produced from an OPO/OPA system (LaserVision, Bellevue, WA) pumped by the 1064 nm fundamental of a Nd:YAG laser (Continuum Surelight I-10, Santa Clara, CA) at a 10 Hz repetition rate. Irradiation times of 0.5−60 s were used so that the precursor ions were depleted by up to 60−70% of their initial intensity. The ions were subsequently detected using a MIDAS[70] data system. IRPD spectra were plotted from first-order photodissociation rate constants obtained from the abundance of the precursor and product ions after irradiation as a function of the laser frequency. These rate constants were corrected for background blackbody

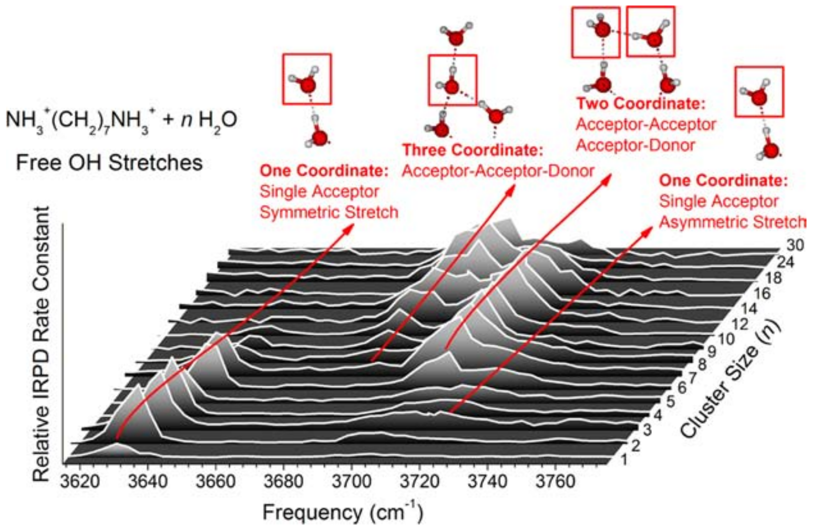

Figure 2. Expansion of the free OH stretch spectral region for $NH_3^+(CH_2)_7NH_3^+$ as a function of hydration extent. The various types of free OH stretches are identified in representative water-binding motifs.

infrared radiative dissociation and frequency dependent variations in laser power.[37,68]

Computations. Quantum chemical calculations that explore a large conformational space are impractical for heptylammonium and 1,7-diammoniumheptane with extensive hydration. Instead, an ensemble of low-energy structures was obtained from molecular dynamics simulations after initial geometry relaxation.[45] These representative structures were used to obtain the average number of hydrogen bonds in the hydrated heptylammonium and 1,7-diammoniumheptane clusters, and to determine how this number depends on the conformation of 1,7-diammoniumheptane and the extent of hydration.

Molecular dynamics simulations for hydrated heptylammonium and 1,7-diammoniumheptane clusters were performed using Impact 5.7 (Schrödinger, LLC, Portland, OR) with the OPLS2005 force field to obtain 5000 structures for each cluster size. The temperature of the canonical ensemble was 133 K (the copper jacket temperature in the experiments), and the simulations were performed for 10 ns using a 1 fs time-step and saving a structure every 2 ps. For 1,7-diammoniumheptane with clusters containing more than 12 water molecules, both linear and folded starting structures were considered. Energies, vibrational frequencies, and intensities for structures of 1,7-diammoniumheptane with up to 10 water molecules were calculated with B3LYP using the 6-31+G** basis set (see Supporting Information).

■ RESULTS AND DISCUSSION

IRPD spectra of 1,7-diammoniumheptane with up to 30 water molecules attached were measured in the hydrogen bond stretching region between 2800 and 3900 cm^{-1} and these spectra are shown in Figure 1. 1,7-Diammoniumheptane has two protonated amine groups where hydration is favorable[16] and these groups are separated by a hydrophobic alkane chain. Each protonated amine group has three hydrogen atoms available to hydrogen bond with a total of six water molecules, which constitute the first solvation shell around each charge site.

$NH_3^+(CH_2)_7NH_3^+$ + nH_2O with n = 1−6. For 1,7-diammoniumheptane with one water molecule attached, there is an intense peak at ~3328 cm^{-1} and a less intense band at ~3629 cm^{-1} (Figure 1). There are also much lower intensity bands around 2800−3000 and 3700−3800 cm^{-1}. The most intense band (~3328 cm^{-1}) can be assigned to free amine hydrogen (NH) stretches. Only one of the amine hydrogen atoms is hydrogen bonded to a water molecule, leaving five free amine hydrogens whose stretches contribute to this band. Bonded NH bands will be red-shifted from the free NH stretches[49] and can be identified between 2800 and 3000 cm^{-1}. These bands have significantly lower intensity, in part because only one of the amine hydrogens is bonded for n = 1, and in part because a lower photon energy results in a slower dissociation rate. Carbon−hydrogen stretches from the alkane chain should appear in this same region; however, these bands are typically weak.[68] The hydroxyl group (OH) stretches from water molecules will appear in the frequency range ~3100−3900 cm^{-1}.[35−37] Bands above 3600 cm^{-1} correspond to OH groups that are not involved in a hydrogen bond, that is, free OH stretches. The band at ~3629 cm^{-1} in the spectrum of the single hydrate corresponds to the symmetric free OH stretch of a single-acceptor (one-coordinate) water molecule. The broader and much lower intensity OH features observed at ~3700−3800 cm^{-1} are similar to features observed for $NH_4^+(H_2O)_n$ with n = 2−4, which were attributed to the K rotationally coupled asymmetric stretches of a single-acceptor water molecule.[49] These free OH stretches become more intense with increasing number of water molecules attached.

The intensity of the free NH stretches decreases relative to the intensity of the bonded NH stretches with increased hydration extent (Figure 1). For 1,7-diammoniumheptane with two and three water molecules attached, there are two distinct peaks at ~3293 and ~3340 cm^{-1} in the free NH stretch region. Only the band at ~3340 cm^{-1} is observed for n = 4, and the relative intensity of this band for n = 5 and 6 is substantially reduced. The decrease in the free NH stretch intensity for n = 1−6 indicates that hydration of 1,7-diammoniumheptane occurs primarily by water molecule binding to the amine hydrogens rather than formation of a second solvent shell. This is further supported by the absence of bands in the spectral region ~3200−3600 cm^{-1}, which would correspond to bonded OH stretches that result from hydrogen bonding between water molecules.

Solvation of 1,7-diammoniumheptane with an even number of water molecules can occur either symmetrically with both protonated amine groups solvated by an equal number of water molecules, or asymmetrically with one protonated amine group binding more water molecules than the other. Changes in the bonded NH features as a function of cluster size provide information on whether symmetric or asymmetric binding is favored for $n = 2$–6. For 1,7-diammoniumheptane with two water molecules, there is a broad feature in the hydrogen bonded NH region with bands at ~2820 and ~2870 cm^{-1}. Three additional sharper bands emerge at ~2950, ~3020, and ~3080 cm^{-1} for $n = 3$ and only these three bands persist and are sharper for $n = 4$ (Figure 1). These results suggest that the bonded NH feature at ~2800–2900 cm^{-1} in the IRPD spectra for $n = 1$–3 arises from the binding of a single water molecule to a protonated amine group and the additional bands observed at ~2900–3100 cm^{-1} for $n = 3$ and 4 correspond to hydrogen bonded NH stretches that result from two water molecules binding to a protonated amine group. On the basis of these trends in the hydrogen bonded NH features, symmetric binding is favored in the dominant conformer for $n = 2$ and 4. The bonded NH stretches shift to higher frequencies with increased solvation of the protonated amine group. This results from the weakening of the individual charge–dipole interactions between the water molecules and the amine group hydrogen atoms with increasing number of water molecules attached. Thus, the new band that emerges at ~3110 cm^{-1} for 1,7-diammoniumheptane with five water molecules is consistent with a structure where one of the protonated amine groups is completely solvated by three water molecules and the other amine group has two water molecules attached. This band becomes more intense relative to the other bonded NH stretches for $n = 6$, indicating that symmetric binding with both amine groups solvated by three water molecules is also favored in the predominant structure of this cluster size.

$NH_3^+(CH_2)_7NH_3^+ + nH_2O$ with $n = 7$–14. In the IRPD spectra for $n > 6$, new bands emerge in both the free and bonded OH stretch region (~3100–3900 cm^{-1}). Some of the water–water binding configurations that arise with increased hydration extent can be identified from bands that appear in the free OH stretch region. An expansion of this region as a function of cluster size is shown in Figure 2. The peak that emerges at ~3710 cm^{-1} for $n = 6$ and persists for larger cluster sizes is assigned to the free OH stretch of a two-coordinated water molecule[50] that is either involved in donating and accepting one hydrogen bond or in accepting two hydrogen bonds (Figure 2). The appearance of this band already at $n = 6$ indicates the presence of a conformer where a water molecule hydrogen bonds to two water molecules rather than the amine hydrogen to fill the first solvation shell around each protonated amine group. Both the absence of any significant free NH stretches and bonded OH bands suggest that this is a minor conformer. An additional band at ~3684 cm^{-1} is observed prominently for $n = 9$ and is due to the free OH stretch for three-coordinated water.[50] The relative intensity of this band increases with increased hydration, and by 14 water molecules, its relative intensity is similar to that of the free OH stretch for two-coordinated water. In contrast, the relative intensity for the symmetric free OH stretch of one-coordinated water at ~3630 cm^{-1} decreases in intensity with increased hydration for $n = 6$–10, and this band is not observed in the IRPD spectra of larger clusters. With increasing hydration, water molecules become involved in extensive hydrogen-bonding networks, as indicated by the appearance of free OH stretches for two- and three-coordinated water molecules, and concomitant disappearance of single acceptor water molecules.

Bands with significant intensity also begin to appear in the bonded OH stretch region for 1,7-diammoniumheptane with seven water molecules at ~3405 and ~3538 cm^{-1}, signifying the onset of second solvent shell formation. The band near 3540 cm^{-1} corresponds to a four-membered ring[48,49] structure formed by the amine group and three water molecules, where two acceptor–donor water molecules each accept a hydrogen from the amine group and donate a hydrogen bond to a third water molecule (acceptor–acceptor). The emergence of this band at $n = 7$ for 1,7-diammoniumheptane correlates well with previous results[48,49] for $CH_3NH_3^+(H_2O)_4$ and $NH_4^+(H_2O)_5$, indicating that formation of this ring structure occurs for clusters with one water molecule in excess of the number required to fill the first solvation shell around the protonated amine groups or ammonium ion. The bonded OH feature around 3400 cm^{-1} in the IRPD spectrum for 1,7-diammoniumheptane with seven water molecules likely arises from a conformer where the second solvent shell water molecule binds to only one of the inner shell water molecules. With increasing cluster size, the hydrogen bonded OH region becomes more complex. For cluster sizes with $n = 8$–14, a distinct band at ~3369 cm^{-1} and a broader feature at ~3452 cm^{-1} are identifiable. However, it becomes increasingly more difficult to resolve individual bands for $n \geq 16$.

The bonded NH features provide less structural information for $n > 6$; these bands become significantly broader with fewer distinguishable peaks. The absolute intensities of these bands increase with cluster size, reaching a plateau for clusters with more than 10 water molecules. However, the relative intensities of these bands compared to those for the bonded and free OH stretches decrease with increasing hydration for $n > 6$, consistent with both protonated amine groups predominantly solvated by $n = 6$.

$NH_3^+(CH_2)_7NH_3^+ + nH_2O$ with $n = 16$–30. Many isomers with different hydrogen bonding configurations become likely for the larger 1,7-diammoniumheptane clusters, consistent with the disappearance of distinct peaks in the bonded OH region for $n \geq 16$. The bonded OH stretch intensity increases significantly relative to the intensity of the bands for the free OH stretches with increased hydration, indicating that an increasing number of water molecules are involved in hydrogen bonding with other water molecules. This is further supported by the increase in the intensity of the free OH stretch for three-coordinated water relative to that of two-coordinated water with increasing cluster size (Figure 2).

Increased solvation of the protonated amine groups should lead to a decrease in the Coulomb repulsion, making it more energetically favorable for 1,7-diammoniumheptane to adopt a folded conformation at larger cluster sizes, with the two charged amine groups more effectively solvated by a single water nanodrop. Previous results for microsolvated suberate dianion, that is, two carboxylate groups separated by a six-carbon alkane chain, showed that this dianion adopts a folded conformation with about 16 water molecules attached.[53,66] The relative intensities of the symmetric (~1390 cm^{-1}) and asymmetric (~1570 cm^{-1}) stretches for the two carboxylate groups measured by IRPD spectroscopy were used as signatures for solvent-mediated folding.[53] Here, an indication of a change in the structure of 1,7-diammoniumheptane with increased hydration is obtained by comparing the IRPD spectra for hydrated 1,7-diammoniumheptane with spectra for hydrated heptylammonium, a reference ion that has only one protonated amine group. The IRPD spectra of 1,7-diammoniumheptane

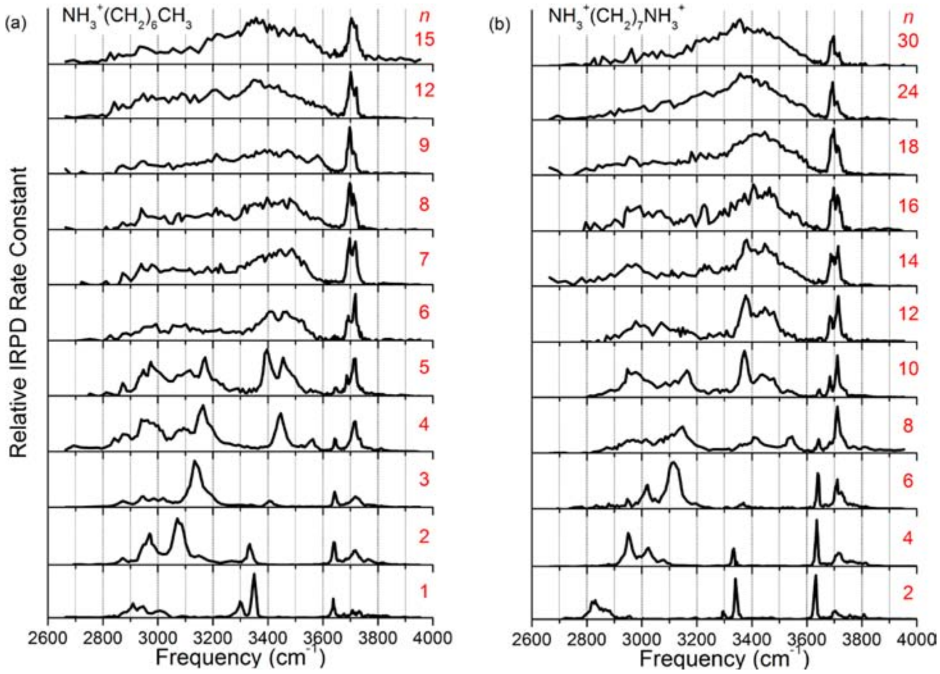

Figure 3. IRPD spectra of (a) $NH_3^+(CH_2)_6CH_3$ + nH_2O with n = 1−15 compared with (b) corresponding IRPD spectra for hydrated 1,7-diammoniumheptane.

with an even number of water molecules should closely resemble the spectra for hydrated heptylammonium if sequential hydration of 1,7-diammoniumheptane occurs by alternately solvating the two protonated amine groups in a linear structure.

Comparisons of Hydrated $NH_3^+(CH_2)_7NH_3^+$ and $NH_3^+(CH_2)_6CH_3$. IRPD spectra were measured for heptylammonium with 1−15 water molecules attached and are compared to the corresponding spectra for hydrated 1,7-diammoniumheptane with twice the number of water molecules attached (Figure 3). There are similar features in the IRPD spectra of both ions. However, there are notable differences in the frequencies and relative intensities of some of the bands. For example, there are differences in the frequencies of the bonded NH bands in the spectra of hydrated heptylammonium and 1,7-diammoniumheptane that likely arise from differences in the charge state of these ions. The bonded NH stretch frequencies for 1,7-diammoniumheptane with two, four, and six water molecules are slightly red-shifted from those for heptylammonium with one to three water molecules, respectively (Figure 3), consistent with slightly stronger charge−dipole interactions between the water molecules and the hydrogen atoms on the diprotonated ions.

Similarly, there are differences in the symmetric free OH stretch frequency in the spectra of hydrated heptylammonium and 1,7-diammoniumheptane. This frequency is plotted as function of hydration extent for heptylammonium and 1,7-diammoniumheptane in Figure 4. The frequency of the symmetric free OH stretch for 1,7-diammoniumheptane shifts from ~3629 cm^{-1} for n = 1 to ~3646 cm^{-1} for n = 10 (Figure 4). For heptylammonium, the frequency of this band shifts from ~3637 cm^{-1} for n = 1 to ~3647 cm^{-1} for n = 5, and is consistently higher than the frequency observed for the corresponding hydrated 1,7-diammoniumheptane as a result of the higher charge state of the latter ion. This frequency difference between hydrated heptylammonium and 1,7-diammoniumheptane is reduced with increased solvation, indicating that the water molecules effectively solvate the additional charge on 1,7-diammoniumheptane. The data for heptylammonium are consistent with IRPD spectroscopy results for $NH_4^+(H_2O)_n$, which show the frequency of the symmetric stretch increasing from ~3636 cm^{-1} for n = 1 to ~3648 cm^{-1} for n = 7.[49]

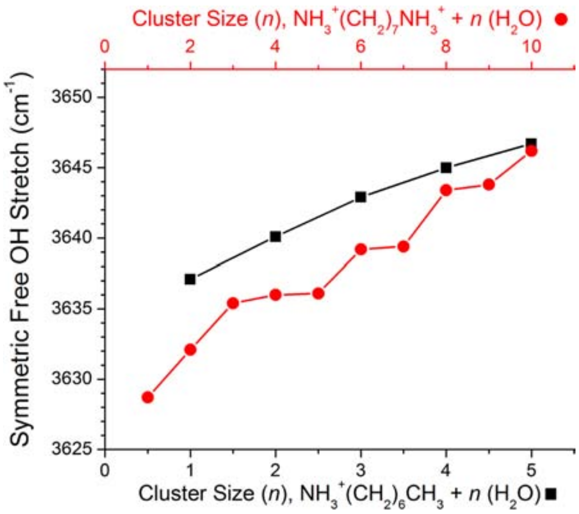

Figure 4. Comparison of the symmetric free OH stretch frequency for heptylammonium (squares) and 1,7-diammoniumheptane (circles) as a function of hydration extent, n.

The frequency of the symmetric free OH stretch for hydrated 1,7-diammoniumheptane changes in two water molecule steps for $n > 3$. This trend is consistent with water molecule binding occurring alternately between the two protonated amine groups with increased hydration extent, thereby affecting the symmetric free OH stretch frequency only after addition of every two water molecules. Symmetric solvation of diprotonated diamines for up to four water molecules attached was indicated from water binding energy measurements.[16−18] Our experimental results indicate that water molecules solvate the two protonated amine groups in a largely symmetrical way for up to at least 10 water molecules attached. Calculated IR spectra and relative energies at the B3LYP/6-31+G** level of theory for various structures of 1,7-diammoniumheptane with up to 10 water molecules (Supporting Information) also support symmetrical binding to the two protonated amine groups. Structures with asymmetric binding are higher in energy by ~3 kcal/mol for $n = 2$, but become more competitive with increasing cluster size, and for $n = 8$, an asymmetric structure (5 and 3 water molecules) is comparable in energy (within 1 kcal/mol) to the lowest energy symmetric structure. For $n = 8$, the calculated spectrum for the symmetric structure matches better with the experimental spectrum suggesting that symmetric binding is favored in these experiments at least up to this cluster size. It becomes more difficult to determine computationally all possible isomers with increased hydration extent, and thus, only a few representative structures are considered for 1,7-diammoniumheptane with 10 water molecules attached. An asymmetric structure with 6 and 4 water molecules is calculated to be isoenergetic with the lowest energy symmetric structure and its spectrum agrees equally well with the experimental spectrum as the calculated spectrum for the symmetric structure. However, an asymmetric structure with 7 and 3 water molecules is calculated to be 4 kcal/mol higher in energy. This suggests that only symmetric and asymmetric structures with 6 and 4 water molecules likely contribute to the experimental spectrum of 1,7-diammoniumheptane with 10 water molecules attached.

Bonded versus Free OH Intensity. The intensities of the hydrogen bonded and free OH stretches can be used as a measure of the relative number of hydrogen bonds in the hydrated heptylammonium and 1,7-diammoniumheptane clusters. The ratio of the intensities for bonded to free OH stretches is compared for heptylammonium and 1,7-diammoniumheptane at corresponding cluster sizes in Figure 5. The ratios for 1,7-diammoniumheptane overlap with those for heptylammonium at small cluster sizes, that is, up to about 6 and 12 water molecules for heptylammonium and 1,7-diammoniumheptane, respectively. These ratios should be similar if solvation of the protonated amine groups occurs independently. The ratios for hydrated heptylammonium and 1,7-diammoniumheptane diverge for clusters with $n \geq 7$ and 14 respectively, with the ratio for 1,7-diammoniumheptane consistently larger than that of heptylammonium. The deviation in the ratios observed for these larger clusters suggests that water molecules can more optimally hydrogen bond with 1,7-diammoniumheptane as a result of this dication adopting a more folded conformation where both protonated amine groups are solvated by a single water nanodrop which makes possible maximum hydrogen bonding. Evidence for this is also indicated by molecular dynamics simulations.

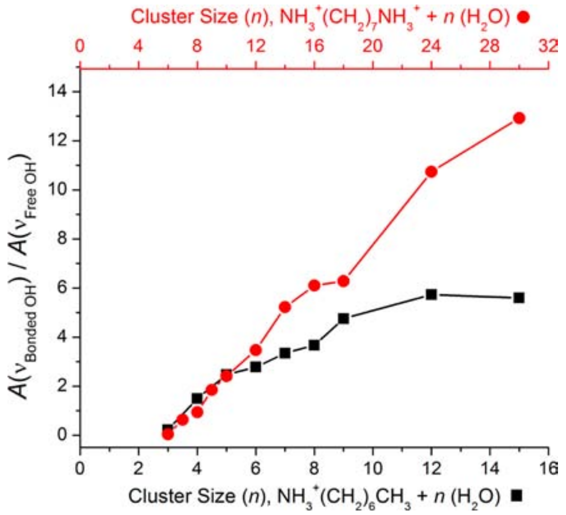

Figure 5. Ratios of the intensities for bonded to free OH stretches for heptylammonium (squares) and 1,7-diammoniumheptane (circles) as a function of hydration extent, *n*.

Molecular Dynamics Simulations. The number of hydrogen bonds in hydrated linear and folded structures of 1,7-diammoniumheptane was investigated using molecular dynamics. The ratio between the number of hydrogen bonded and nonbonded hydrogen atoms of water was obtained for 5000 representative structures. The average value of this ratio as a function of cluster size is shown in Figure 6a for heptylammonium and 1,7-diammoniumheptane. The range of values indicated corresponds to one standard deviation in the average value. For 1,7-diammoniumheptane with $n \geq 14$, both linear and folded starting structures were considered in the molecular dynamics simulations. During the 10 ns long molecular dynamics simulations, the linear structures for 1,7-diammoniumheptane remained linear and the folded structures (except for $n = 14$) remained folded. The results from the molecular dynamics modeling indicate that the number of hydrogen bonds in the folded 1,7-diammoniumheptane structures (closed circles) is higher than that for linear structures (open circles) for $n > 14$. In contrast, the relative number of hydrogen bonds for hydrated heptylammonium (closed squares) is similar to that for hydrated 1,7-diammoniumheptane with linear conformations (open circles). These results are consistent with the experimental data in Figure 5 and further support that the differences in the observed experimental ratios between hydrated heptylammmonium and 1,7-diammoniumheptane arise from a change in the conformation of 1,7-diammoniumheptane from a linear to folded structure.

The distance between the two amine group nitrogen atoms (N−N distance) for 1,7-diammoniumheptane is used to characterize the extent of folding in these structures and this average distance is shown in Figure 6b. The average distance for linear structures decreases slightly as a function of hydration extent from 10.1 to 10.0 Å for 1,7-diammoniumheptane with 6 and 30 water molecules, respectively. This effect is attributed to the decreasing Coulomb repulsion with increasing hydration extent. For folded structures, the N−N distance decreases more significantly with increased hydration from 7.7 to 6.3 Å for $n = 16$ and 30, respectively. The large range of values for $n = 14$ is due to the large spread in the distance as the initially folded structure became unfolded during the course of the simulation.

The Coulomb repulsion energy between the two protonated amine groups can be approximated for the modeled structures using the following expression[60]

$$\text{Coulomb Energy} = \frac{q^2}{4\pi\epsilon_0\epsilon_r r_{\text{N-N}}} \qquad (1)$$

where q is the elementary charge, ϵ_0 is the vacuum permittivity constant, ϵ_r is the intrinsic dielectric polarizability with a value

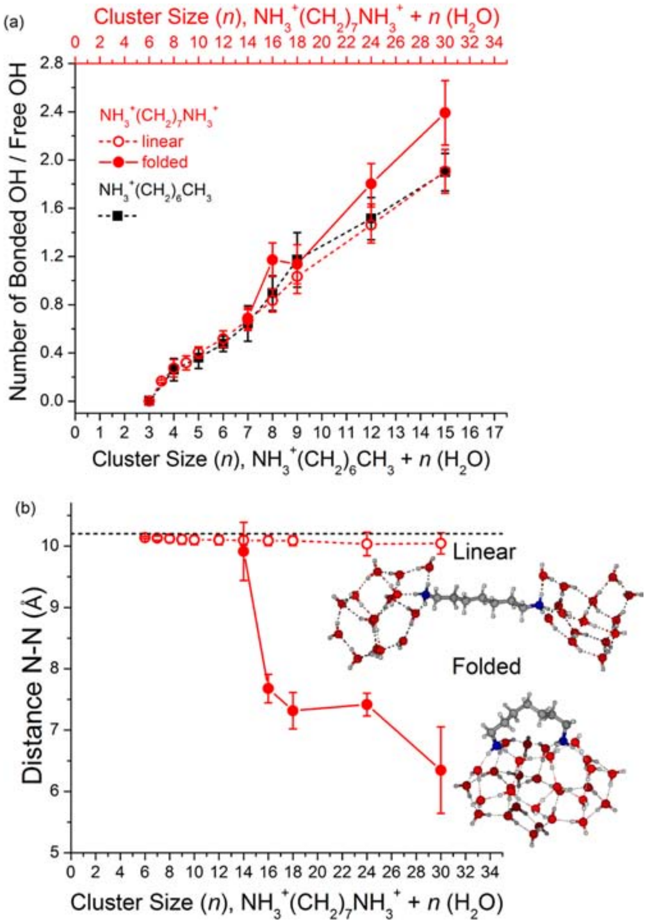

Figure 6. (a) Average ratio of the number of bonded to free OH stretches for heptylammonium (squares) and 1,7-diammoniumheptane (circles) as a function of cluster size, n, obtained from 5000 structures generated by molecular dynamics simulations. The range of values indicated corresponds to one standard deviation in the average ratio. In addition to a linear starting structure, a folded starting structure is considered in the molecular dynamics simulations for 1,7-diammoniumheptane with $n > 12$. Ratios obtained for a folded and linear starting structure for 1,7-diammoniumheptane are shown as closed and open circles, respectively. (b) The average distance between the two amine group nitrogen atoms of hydrated 1,7-diammoniumheptane is plotted as a function of hydration extent, n, for 5000 structures obtained from molecular dynamics simulations. The range of values indicated corresponds to one standard deviation. The average distance between the two amine group nitrogen atoms for both linear (open circles) and folded (closed circles) starting structures is shown for 1,7-diammoniumheptane with $n > 12$.

of 1.0 (in the absence of solvent) for 1,7-diammoniumheptane,[60] and r_{N-N} is the distance between the amine group nitrogen atoms. The increase in Coulomb energy upon folding for $n = 16$ and 30 is 11 ± 1 and 20 ± 7 kcal mol^{-1}, respectively, not taking into account the effect of water on ϵ_r. The energy gained from additional hydrogen bonds formed in the clusters of the folded structures is 13 ± 7 and 14 ± 10 kcal mol^{-1}, respectively, assuming an energy of ~5.0 kcal mol^{-1} (approximately half of the heat of vaporization for bulk water[71]) for each hydrogen bond. Assuming that the effects of water on ϵ_r further reduce the Coulomb energy, this crude approximation indicates that the increase in Coulomb energy as a result of folding can be compensated by the additional hydrogen bonds that form between the water molecules upon solvating the folded structure of 1,7-diammoniumheptane.

■ CONCLUSIONS

These results for hydrated 1,7-diammoniumheptane demonstrate that the number of water molecules needed to stabilize the folded conformation of a dication in the gas phase can be determined with IRPD spectroscopy by comparing the IRPD spectra of the hydrated dication with those of a reference monocation, which serves as a model for the separate solvation of each charge site. In a folded conformation, the two charge sites of the dication are solvated by a single water nanodrop, which results in an increase in the number of hydrogen bonds formed compared to the separate solvation of each charge site in a linear conformation. The increase in the number of hydrogen bonds is reflected in the relative IR intensity of the bonded to free OH stretch bands in the IRPD spectra, and a conformational change from linear to folded in the dication is indicated by an increase in the relative bonded to free OH intensities compared with those for the monocation.

Although folding of 1,7-diammoniumheptane requires about the same number of water molecules (~14) as the suberate dianion,[53] different stabilizing forces are responsible for the water-induced change in conformation of these two oppositely charged ions. For the suberate dianion, the stability of the folded structure was attributed to additional ion−water molecule bonds, rather than water−water hydrogen bonds.[53] This contrasts with the results for 1,7-diammoniumheptane, where the first solvent shell around each protonated amine group is completed with a total of 6 water molecules attached and therefore no additional ion−water molecule bonds are formed for larger hydrates. Instead the increase in Coulomb energy that results from bringing the two charge sites together in the folded configurations is compensated by additional water−water hydrogen bonds that are formed. These differences in solvation of multiply protonated and deprotonated functional groups can have implications in the hydration and structure of biomolecules, such as proteins, that have both protonated and deprotanated basic and acidic residues.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Calculated structures, relative energies, and spectra for 1,7-diammoniumheptane with 1−10 water molecules attached. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

williams@cchem.berkeley.edu

Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Levy, Y.; Onuchic, J. N. *Annu. Rev. Biophys. Biomol. Struct.* **2006**, *35*, 389−415.

(2) Pratt, L. R.; Pohorille, A. *Chem. Rev.* **2002**, *102*, 2671−2692.

(3) Moylan, C. R.; Brauman, J. I. *Annu. Rev. Phys. Chem.* **1983**, *34*, 187−215.

(4) Brauman, J. I.; Riveros, J. M.; Blair, L. K. *J. Am. Chem. Soc.* **1971**, *93*, 3914−3916.

(5) Lemoff, A. S.; Bush, M. F.; Wu, C. C.; Williams, E. R. *J. Am. Chem. Soc.* **2005**, *127*, 10276−10286.

(6) Lemoff, A. S.; Bush, M. F.; Williams, E. R. *J. Am. Chem. Soc.* **2003**, *125*, 13576−13584.

(7) Lemoff, A. S.; Bush, M. F.; O'Brien, J. T.; Williams, E. R. *J. Phys. Chem. A* **2006**, *110*, 8433−8442.

(8) Ye, S. J.; Moision, R. M.; Armentrout, P. B. *Int. J. Mass Spectrom.* **2005**, *240*, 233−248.

(9) Ye, S. J.; Moision, R. M.; Armentrout, P. B. *Int. J. Mass Spectrom.* **2006**, *253*, 288−304.

(10) Ye, S. J.; Armentrout, P. B. *Phys. Chem. Chem. Phys.* **2010**, *12*, 13419−13433.

(11) Wyttenbach, T.; Bowers, M. T. *Chem. Phys. Lett.* **2009**, *480*, 1−16.

(12) Kohtani, M.; Jarrold, M. F. *J. Am. Chem. Soc.* **2002**, *124*, 11148−11158.

(13) Gao, B.; Wyttenbach, T.; Bowers, M. T. *J. Am. Chem. Soc.* **2009**, *131*, 4695−4701.

(14) Wincel, H. *Chem. Phys. Lett.* **2007**, *439*, 157−161.

(15) Wincel, H. *Int. J. Mass Spectrom.* **2006**, *251*, 23−31.

(16) Blades, A. T.; Klassen, J. S.; Kebarle, P. *J. Am. Chem. Soc.* **1996**, *118*, 12437−12442.

(17) Klassen, J. S.; Blades, A. T.; Kebarle, P. *J. Phys. Chem.* **1995**, *99*, 15509−15517.

(18) Klassen, J. S.; Blades, A. T.; Kebarle, P. *J. Am. Chem. Soc.* **1994**, *116*, 12075−12076.

(19) Meot-Ner (Mautner), M. *Int. J. Mass Spectrom.* **2003**, *227*, 525−554.

(20) Gilligan, J. J.; Lampe, F. W.; Nguyen, V. Q.; Vieira, N. E.; Yergey, A. L. *J. Phys. Chem. A* **2003**, *107*, 3687−3691.

(21) Ding, Y.; Krogh-Jespersen, K. *J. Comput. Chem.* **1996**, *17*, 338−349.

(22) Hwang, T. K.; Eom, G. Y.; Choi, M. S.; Jang, S. W.; Kim, J. Y.; Lee, S.; Lee, Y.; Kim, B. *J. Phys. Chem. B* **2011**, *115*, 10147−10153.

(23) Kim, K. Y.; Cho, U. I.; Boo, D. W. *Bull. Korean Chem. Soc.* **2001**, *22*, 597−604.

(24) Eyler, J. R. *Mass Spectrom. Rev.* **2009**, *28*, 448−467.

(25) Polfer, N. C.; Oomens, J. *Mass Spectrom. Rev.* **2009**, *28*, 468−494.

(26) Rodgers, M. T.; Armentrout, P. B.; Oomens, J.; Steill, J. D. *J. Phys. Chem. A* **2008**, *112*, 2258−2267.

(27) Kapota, C.; Lemaire, J.; Maître, P.; Ohanessian, G. *J. Am. Chem. Soc.* **2004**, *126*, 1836−1842.

(28) Forbes, M. W.; Bush, M. F.; Polfer, N. C.; Oomens, J.; Dunbar, R. C.; Williams, E. R.; Jockusch, R. A. *J. Phys. Chem. A* **2007**, *111*, 11759−11770.

(29) Drayss, M. K.; Blunk, D.; Oomens, J.; Schäfer, M. *J. Phys. Chem. A* **2008**, *112*, 11972−11974.

(30) Polfer, N. C.; Paizs, B.; Snoek, L. C.; Compagnon, I.; Suhai, S.; Meijer, G.; von Helden, G.; Oomens, J. *J. Am. Chem. Soc.* **2005**, *127*, 8571−8579.

(31) Prell, J. S.; Demireva, M.; Oomens, J.; Williams, E. R. *J. Am. Chem. Soc.* **2009**, *131*, 1232−1242.

(32) Grégoire, G.; Gaigeot, M. P.; Marinica, D. C.; Lemaire, J.; Schermann, J. P.; Desfrançois, C. *Phys. Chem. Chem. Phys.* **2007**, *9*, 3082−3097.

(33) Mino, W. K. J.; Gulyuz, K.; Wang, D.; Stedwell, C. N.; Polfer, N. C. *J. Phys. Chem. Lett.* **2011**, *2*, 299−304.

(34) Burt, M. B.; Decker, S. G. A.; Atkins, C. G.; Rowsell, M.; Peremans, A.; Fridgen, T. D. *J. Phys. Chem. B* **2011**, *115*, 11506−11518.

(35) Shin, J. W.; Hammer, N. I.; Diken, E. G.; Johnson, M. A.; Walters, R. S.; Jaeger, T. D.; Duncan, M. A.; Christie, R. A.; Jordan, K. D. *Science* **2004**, *304*, 1137−1140.

(36) Miyazaki, M.; Fujii, A.; Ebata, T.; Mikami, N. *Science* **2004**, *304*, 1134−1137.

(37) Bush, M. F.; Saykally, R. J.; Williams, E. R. *J. Am. Chem. Soc.* **2008**, *130*, 15482−15489.

(38) Mizuse, K.; Fujii, A.; Mikami, N. *J. Chem. Phys.* **2007**, *126*, 231101−231104.

(39) Headrick, J. M.; Diken, E. G.; Walters, R. S.; Hammer, N. I.; Christie, R. A.; Cui, J.; Myshakin, E. M.; Duncan, M. A.; Johnson, M. A.; Jordan, K. D. *Science* **2005**, *308*, 1765−1769.

(40) Miller, D. J.; Lisy, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 15393−15404.

(41) Walters, R. S.; Pillai, E. D.; Duncan, M. A. *J. Am. Chem. Soc.* **2005**, *127*, 16599−16610.

(42) Vaden, T. D.; Lisy, J. M.; Carnegie, P. D.; Pillai, E. D.; Duncan, M. A. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3078−3082.

(43) Ayotte, P.; Bailey, C. G.; Weddle, G. H.; Johnson, M. A. *J. Phys. Chem. A* **1998**, *102*, 3067−3071.

(44) Sinha, R. K.; Nicol, E.; Steinmetz, V.; Maître, P. *J. Am. Soc. Mass Spectrom.* **2010**, *21*, 758−772.

(45) Prell, J. S.; O'Brien, J. T.; Williams, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 4810−4818.

(46) Cooper, T. E.; O'Brien, J. T.; Williams, E. R.; Armentrout, P. B. *J. Phys. Chem. A* **2010**, *114*, 12646−12655.

(47) O'Brien, J. T.; Williams, E. R. *J. Phys. Chem. A* **2008**, *112*, 5893−5901.

(48) Wang, Y. S.; Chang, H. C.; Jiang, J. C.; Lin, S. H.; Lee, Y. T.; Chang, H. C. *J. Am. Chem. Soc.* **1998**, *120*, 8777−8788.

(49) Chang, H. C.; Wang, Y. S.; Lee, Y. T.; Chang, H. C. *Int. J. Mass Spectrom.* **1998**, *179/180*, 91−102.

(50) Wang, Y. S.; Jiang, J. C.; Cheng, C. L.; Lin, S. H.; Lee, Y. T.; Chang, H. C. *J. Chem. Phys.* **1997**, *107*, 9695−9698.

(51) Asmis, K. R.; Neumark, D. M. *Acc. Chem. Res.* **2012**, *45*, 43−52.

(52) Kamariotis, A.; Boyarkin, O. V.; Mercier, S. R.; Beck, R. D.; Bush, M. F.; Williams, E. R.; Rizzo, T. R. *J. Am. Chem. Soc.* **2006**, *128*, 905−916.

(53) Wende, T.; Wanko, M.; Jiang, L.; Meijer, G.; Asmis, K. R.; Rubio, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 3807−3810.

(54) Prell, J. S.; Chang, T. M.; O'Brien, J. T.; Williams, E. R. *J. Am. Chem. Soc.* **2010**, *132*, 7811−7819.

(55) Prell, J. S.; Correra, T. C.; Chang, T. M.; Biles, J. A.; Williams, E. R. *J. Am. Chem. Soc.* **2010**, *132*, 14733−14735.

(56) Bush, M. F.; Prell, J. S.; Saykally, R. J.; Williams, E. R. *J. Am. Chem. Soc.* **2007**, *129*, 13544−13553.

(57) Miller, D. J.; Lisy, J. M. *J. Phys. Chem. A* **2007**, *111*, 12409−12416.

(58) Jarrold, M. F. *Annu. Rev. Phys. Chem.* **2000**, *51*, 179−207.

(59) Williams, E. R. *J. Mass Spectrom.* **1996**, *31*, 831−842.

(60) Gross, D. S.; Rodriguez-Cruz, S. E.; Bock, S.; Williams, E. R. *J. Phys. Chem.* **1995**, *99*, 4034−4038.

(61) Gronert, S. *Int. J. Mass Spectrom.* **1999**, *185/186/187*, 351−357.

(62) Wang, L. S.; Ding, C. F.; Wang, X. B.; Nicholas, J. B. *Phys. Rev. Lett.* **1998**, *81*, 2667−2670.

(63) Lee, S. W.; Freivogel, P.; Schindler, T.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1998**, *120*, 11758−11765.

(64) Ding, C. F.; Wang, X. B.; Wang, L. S. *J. Phys. Chem. A* **1998**, *102*, 8633−8636.

(65) Wang, X. B.; Yang, J.; Wang, L. S. *J. Phys. Chem. A* **2008**, *112*, 172−175.

(66) Yang, X.; Fu, Y. J.; Wang, X. B.; Slavíček, P.; Mucha, M.; Jungwirth, P.; Wang, L. S. *J. Am. Chem. Soc.* **2004**, *126*, 876−883.

(67) Minofar, B.; Mucha, M.; Jungwirth, P.; Yang, X.; Fu, Y. J.; Wang, X. B.; Wang, L. S. *J. Am. Chem. Soc.* **2004**, *126*, 11691−11698.

(68) Bush, M. F.; O'Brien, J. T.; Prell, J. S.; Saykally, R. J.; Williams, E. R. *J. Am. Chem. Soc.* **2007**, *129*, 1612−1622.

(69) Wong, R. L.; Paech, K.; Williams, E. R. *Int. J. Mass Spectrom.* **2004**, *232*, 59−66.

(70) Senko, M. W.; Canterbury, J. D.; Guan, S. H.; Marshall, A. G. *Rapid Commun. Mass Spectrom.* **1996**, *10*, 1839−1844.
(71) Marsh, K. N. *Recommended Reference Materials for the Realization of Physiochemical Properties*; Blackwell Scientific Publications: Oxford, 1987.