# Proton-Bridge Motions in Amine Conjugate Acid Ions Having Intramolecular Hydrogen Bonds to Hydroxyl and Amine Groups

Hou U. Ung,<sup>†</sup> Aaron R. Moehlig,<sup>†</sup> Sevana Khodagholian,<sup>†</sup> Giel Berden,<sup>‡,⊥</sup> Jos Oomens,<sup>‡,§,⊥</sup> and Thomas Hellman Morton<sup>\*,†</sup>

<sup>†</sup>Department of Chemistry, University of California, Riverside, California 92521-0403, United States <sup>‡</sup>FOM Institute for Plasmaphysics Rijnhuizen, Edisonbaan 14, NL-3439 MN Nieuwegein, The Netherlands <sup>§</sup>van't Hoff Institute for Molecular Science, University of Amsterdam, NL-1098XH, The Netherlands

**Supporting Information** 

**ABSTRACT:** Vibrational spectra of two gaseous cations having NH···O intramolecular ionic hydrogen bonds and of nine protonated di- and polyamines having NH···N internal proton bridges, recorded using IR Multiple Photon Dissociation (IRMPD) of mass-selected ions, are reported. The band positions of hydroxyl stretching frequencies do not shift when a protonated amine becomes hydrogen bonded to oxygen. In three protonated diamines, lower frequency bands ( $550-650 \text{ cm}^{-1}$ ) disappear upon isotopic substitution, as well as several bands in the  $1100-1350 \text{ cm}^{-1}$  region. By treating the internal proton bridge as a linear triatomic, theory assigns the lowest frequency



bands to N–H…N asymmetric stretches. A 2-dimensional model, based on quantization on a surface fit to points calculated using a double hybrid functional B2-P3LYP/cc-pVTZ//B3LYP/6-31G<sup>\*\*</sup>, predicts their positions accurately. In at least one case, the conjugate acid of 1,5-*cis*-bis(dimethylamino)cyclooctane, a N–H…N bend shows up in the domain predicted by DFT normal mode calculations, but in most other cases the observed bands have frequencies 20–25% lower than expected for bending vibrations. Protonated Me<sub>2</sub>NCH<sub>2</sub>CMe<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub> shows three well-resolved bands at 620, 1200, and 1320 cm<sup>-1</sup>, of which the lowest can be assigned to the asymmetric stretch. Other ions observed include doubly protonated 1,2,4,5-(Me<sub>2</sub>NCH<sub>2</sub>)<sub>4</sub>-benzene and 1,2,4-(Me<sub>2</sub>NCH<sub>2</sub>)<sub>3</sub>-benzene-5-CH<sub>2</sub>OH. Apart from the aforementioned rigid ion derived from the alicyclic diamine, the other ions enjoy greater conformational mobility, and coupling to low-frequency C–C bond torsions may account for the shift of vibrations with N–H…N character to lower frequencies. Low-barrier hydrogen bonding (LBHB) accounts for the fact that N–H…N asymmetric stretching vibrations of near linear proton bridges occur at frequencies below 650 cm<sup>-1</sup>.

The physical model dates back to antiquity: attraction of a heavenly body to a pair of neighbors causes it to hover in the middle. Aristotle makes the analogy to strategically placing a creature, both hungry and thirsty, between food and drink. Unable to decide whether to eat or to slake its thirst, the creature remains poised between the two alternatives.<sup>1</sup> The Middle Ages identified the creature as a donkey and ascribed a similar metaphor to the 14th century French philosopher Jean Buridan (although nobody has yet found that example in Buridan's extant writings).<sup>2</sup> Simply put, Buridan's Ass (*asinus Buridani*) is a donkey between a bucket of water and a bucket of oats that would perish because of its indecision.

Figure 1A depicts a political cartoon from the beginning of the 20th century, where the donkey stands between two bales of hay.<sup>3</sup> At the time, most of the American public (and many members of Congress), like the donkey, found it difficult to distinguish between the competing alternatives for where in Central America a canal might be constructed to link the Pacific and Atlantic oceans. The choices in this case are not just equally attractive, they appear identical. From a chemist's standpoint, the situation corresponds to a double-minimum potential, as Figure 1B depicts, with indistinguishable minima. The colored curves show vibrational wave functions within the double-well potential for a symmetrical linear triatomic, where the *x*-axis represents a straight cut from minimum to minimum along the asymmetric stretch coordinate of a 2-dimensional surface (where the second dimension perpendicular to the page is the symmetric stretch coordinate). As the red curve indicates, the zero-point level for a bridging H<sup>+</sup> lies above the barrier for proton transit, and the corresponding wave function looks flat over the region of the potential energy maximum. This corresponds to low-barrier hydrogen bonding (LBHB, roughly synonymous with short strong hydrogen bonding). The shape of the potential curve for proton-bound dimers of nucleobases resembles Figure

Special Issue: Peter B. Armentrout Festschrift

Received:November 21, 2012Revised:January 9, 2013Published:January 11, 2013



**Figure 1.** (A) Donkey between two bales of hay, hung up between identical alternatives.<sup>3</sup> (B) Straight cut across the 2-dimensional B2-P3LYP/cc-pVTZ//B3LYP/6-31G(d,p) potential for protonated 3,3,N,N,N',N'-hexamethyl-1,5-pentanediamine showing the positions and vibrational wave functions for the zero point and the  $\nu = 1$  level for the asymmetric N–H…N stretch.<sup>4</sup>

1B; however, the central barrier is much higher, and the proton behaves as though localized on one or the other of the partners.<sup>5</sup> LBHBs of proton-bound dimers of dialkyl ethers either have no barriers or barriers much lower than the zero point;<sup>6</sup> hence, the effects of their anharmonicity differ from what is reported herein.

# BACKGROUND

Hydrogen bonding leads to inter- and intramolecular forces, without which life on earth could not exist. This type of bonding ranges from ordinary hydrogen bonds (observed, for instance, between water molecules or between neutral DNA bases) to strong hydrogen bonds seen with ionic species. Strong hydrogen bonds (also called ionic hydrogen bonds) differ from ordinary hydrogen bonds in that electric charge is associated with either the hydrogen bond donor or the hydrogen bond acceptor, with the donor bearing a positive charge or the acceptor bearing a negative charge. If donor and acceptor bear opposite charges, the hydrogen bond is commonly called a salt bridge.

In the present context, the term "proton bridge" designates an intramolecular strong hydrogen bond. A protonated amine having two groups bound internally by a proton bridge is a weaker Brønsted acid than an isolated ammonium ion. Under the right circumstances, addition of a proton to a molecule with an amine and a remote functional group can lead to profound changes in conformation, as eq 1 illustrates for an acyclic  $\alpha$ , $\omega$ -tertiary diamine.

$$Me_2N$$
  $X$   $NMe_2$   $H^+$   $Me_2N$   $Me_2$   $NMe_2$  (1)

Recently, Beran et al. put forth several criteria for modeling the anharmonicity of a proton-bridged ion as a linear triatomic having an LBHB:<sup>7</sup> (1) the proton must have a low barrier for transfer; (2) the two basic groups must have identical proton affinities; and (3) the geometry must be close to linear ( $\theta >$ 170°) when the molecule cyclizes upon itself as depicted by eq 1. For diamine conjugate acid ions the theoretical model treats the N–H…N symmetric and asymmetric stretches in terms of a 2-dimensional anharmonic potential and considers the remaining vibrations as harmonic. While the approach closely predicts the frequency of the asymmetric N–H…N stretch, limiting the scope to 2-dimensions does not consider the N– H…N bending vibrations.

By considering only the symmetric and asymmetric N–H…N stretches of a linear triatomic, vibrational quantization within the 2-dimensional potential surface predicts a frequency for the  $v = 0 \rightarrow v = 1$  transition of a bridging proton in a domain that agrees with bands observed in both the gaseous cation and its solid salts.<sup>7</sup> However, experiment does not permit the conclusion that all the other vibrations behave as predicted by DFT normal mode calculations. Chart 1 depicts di- and polyamine conjugate acid ions for which experimental IR absorption spectra in the fingerprint region are measured.

Chart 1. Di- and Tetraamine Conjugate Acid Ions Examined by IR Multiple Photon Dissociation (IRMPD) in the Present Study



The indicated energies in Figure 1B for the N–H…N asymmetric stretch of ion **4a** do not differ substantially from those published for the asymmetric N–H…N stretch of ion **1a**: the predicted frequencies of the  $v = 0 \rightarrow v = 1$  transition of **4a** (557 cm<sup>-1</sup>, the curve and quantization depicted in Figure 1B) and of **3a** (458 cm<sup>-1</sup>)<sup>4</sup> have values comparable to that predicted for ion **1a**, 528 cm<sup>-1.7</sup> We recently compared theory with experiment for ion **1a**, the conjugate acid of *N*,*N*,*N'*,*N'*-tetramethyl-1,4-butanediamine (the neutral diamine referred to below as tetramethylputrescine), where H<sup>+</sup> bridges intramolecularly between the two basic nitrogens.<sup>7</sup> The midpoint corresponds to a local maximum in the potential energy surface, but proton transit encounters a barrier lower than the zeropoint energy for the asymmetric stretching vibration that carries it toward one or the other potential energy minima. The local

maximum in the middle presents such a low barrier that experimental structural studies place the equilibrium position of the proton close to the midpoint.<sup>8</sup>

Contrasts between experiment and theory encourage further exploration. In the case of 1a, the conjugate acid of tetramethylputrescine, for which DFT predicts the N-H--N bond angle to be greater than 170°, one inadequacy of the reduced dimensionality model quickly becomes apparent. Distortion of the N-H...N linkage of 1a from linearity results in predicted N-H...N bending normal modes on the order of 1650 cm<sup>-1</sup>. With regard to Figure 1A, this motion corresponds to the donkey's stepping forward and backward out of the page (or up and down in the plane of the page) without approaching either bale of hay more closely. Experimentally, the only band in the 600-1800 cm<sup>-1</sup> domain affected by replacing the bridging  $H^+$  with  $D^+$  (1b vs 1a) occurs near 1200 cm<sup>-1</sup>. That outcome suggests a degree of anharmonicity for other vibrations having N-H...N character that is greater than predicted by DFT calculations that use second-order perturbation theory to apply anharmonic corrections to all the normal modes.

X-ray crystallography puts the N–N distance to be 2.66 Å for both the triflate and iodide salts of 1a, which agrees with values calculated by DFT.<sup>10</sup> Solid state NMR measures the dipolar coupling  $D_{N-H}$  in the monoprotonated triflate salt of completely deuterated tetramethylputrescine. Tetramethylputrescine- $d_{20}$  was synthesized, so that the only proton present in the salt was the bridging H<sup>+</sup>. Analysis of the residual dipolar coupling constant,  $D_{N-H}$  = 5900 Hz, places the equilibrium NH distance at 1.32 Å, about half the NN distance. The value of  $D_{\rm N-H}$  is substantially smaller than would be expected if the bridging H<sup>+</sup> were bouncing between the two potential energy minima. At the same time, as predicted by theory, an isotopically sensitive vibrational band is observed for gaseous protonated tetramethylputrescine at low frequency (530  $cm^{-1}$ , which is consistent with its having an LBHB. To what extent do other protonated amines display such a feature?

# EXPERIMENTAL SECTION

This paper makes use of IR Multiple Photon Dissociation (IRMPD) spectroscopy of gaseous cations in an FT-ICR mass spectrometer to examine vibrations of ions 3-9 in the fingerprint region and of protonated hydroxyamines 13 and 19 in the OH stretching region. Comparison of DFT-calculated IR frequencies with experimental IRMPD spectra helps to determine structural information.

IRMPD spectra were obtained at the FOM Institute for Plasma Physics Rijnhuizen, Nieuwegein, The Netherlands.<sup>11,12</sup> Ions were generated by electrospray ionization (ESI) and accumulated for several seconds before introduction into the FT-ICR cell where they were mass-isolated and subsequently irradiated for several seconds with the pulses from infrared laser sources. Absorption of IR radiation induced dissociation via loss of neutral dimethylamine. The IRMPD yield is calculated from the appearance of the  $[MH^+-NH(CH_3)_2]$  (or  $[MD^+-ND-(CH_3)_2]$  ions from deuterated samples) and concurrent disappearance of parent ions. The IRMPD spectrum is then obtained by plotting the yield as a function of infrared laser frequency.

In the fingerprint region from 300 to 1900  $\text{cm}^{-1}$ , the free electron laser for infrared experiments (FELIX) has been used as an IR source, while the OH/OD stretching region has been covered by a commercial Nd:YAG laser (Innolas, Germany)

pumped Optical Parametric Oscillator (LaserVision, USA) tunable in the range from 2350 to 3900 cm<sup>-1</sup>. To increase the on-resonance dissociation yield, ions were irradiated for several milliseconds with the output of a 30 W continuous wave (cw)  $CO_2$  laser directly after each OPO pulse.

Exact mass measurements were obtained via direct injection of aqueous methanolic solutions into the ESI source of a Waters GCT Premier Time of Flight mass spectrometer. A linear triple quadrupole mass spectrometer (Waters Quattro Ultima) was used to perform tandem MS/MS experiments on ions from an ESI source using argon collision gas at 4 and 10 V lab frame energy.

The conjugate bases of 1 (tetramethylputrescine) and of 2 (N,N,N',N'-tetramethyl-1,3-propanediamine) are commercially available. The conjugate base of 3, N,N,N',N'-tetramethyl-1,5-pentanediamine (tetramethylcadaverine), was prepared by Eschweiler–Clark methylation of commercially available cadaverine.<sup>13</sup> The conjugate base of 4, 3,3-N,N,N',N'-hexamethylpentane-1,5-diamine (hexamethylcadaverine), has been previously reported.<sup>8,14</sup>

Synthesis of the conjugate base of **6** was accomplished starting from *cis*-1,5-cyclooctanediol via *cis*-1,5-diaminocyclooctane.<sup>15</sup> *cis*-1,5-Ditosyloxycyclooctane, prepared following the Corey and Block procedure,<sup>16</sup> as shown in Scheme 1, was

Scheme 1. Preparation of N,N,N',N'-Tetramethyl-*cis*-1,5diaminocyclooctane Starting from the Ditosylate of *cis*-1,5-Cyclooctanediol Followed by Eschweiler-Clarke Methylation



converted to the corresponding bisazide, reduced with LiAlH<sub>4</sub>, and permethylated using formaldehyde/formic acid via the Eschweiler–Clark procedure.<sup>17</sup> The product was then purified by distillation at reduced pressure: bp 95–97° (0.1 Torr); <sup>1</sup>H NMR (300 MHz, CHCl<sub>3</sub>)  $\delta$  2.47 (2H m)  $\delta$  2.2 (12H s) 1.3–1.9 (12H m); APCI-ESI MS MH<sup>+</sup>, 199.2177 (calcd 199.2169).

Tetrakis(dimethylaminomethyl)benzene (the conjugate base of 7) was prepared as described by Schindlbauer.<sup>18,19</sup> Each side of the ring bears a strong resemblance to tetramethylputrescine, except that two sp<sup>2</sup> centers intervene between the *ortho*-Me<sub>2</sub>NCH<sub>2</sub> groups. The neutral tetraamide (14) was synthesized following Schindlbauer first by converting the tetracarboxylic acid to tetraamide, followed by reduction with LiAlH<sub>4</sub>. In our hands the first step did not give pure 14 but a mixture with triamide carboxylic acid (15), as Scheme 2 shows.

A mixture of ions 7a and 8a, as well as mono- and diprotonated triamine alcohol (12 and 13), gave the ESI-MS shown in Figure 2. This mixture of products does not present a problem for IRMPD experiments because ions with individual m/z values are isolated in the FT- ICR prior to IRMPD. The diprotonated ion 13 is believed to be the smallest doubly charged ion yet observed by ESI without the support of solvent clusters.

The conjugate base of ion **5**, 2,2-*N*,*N*,*N*',*N*'-hexamethylpentane-1,5-diamine, was prepared by converting the commercially Scheme 2. Synthesis of a Mixture of the Tetraamine (Conjugate Base of 7 and 8) and the Triamine Alcohol (Conjugate Base of 12 and 13) Starting from Pyromellitic Acid



Figure 2. ESI-MS spectrum of a mixture containing mono- and diprotonated ions from LiAlH<sub>4</sub> reduction of a mixture containing 14 and 15.

available 2,2-dimethylglutaric acid to its bisdimethylamide by means of the Schindlbauer procedure.<sup>18</sup> The crude product, which contained both the desired 2,2-N,N,N',N'-hexamethylpentanedioic diamide as well as the half amide/half acid shown to the left in eq 2, was reduced using lithium aluminum hydride without further purification. Because the conjugate acid ions of the two products to the right were easily separated by mass spectrometry prior to IRMPD spectroscopy, this mixture was used without further purification. ESI-MS Exact Mass: MH<sup>+</sup>, 187.2182 (calcd 187.2169).



*N*,*N*-3,3-tetramethyl-5-amino-1-pentanol (18) was prepared from the commercially available 3,3-dimethylglutaric anhydride as outlined in eq 3. The anhydride was treated with excess dimethylamine in methanol, and after removal of solvent, the resulting dimethylammonium salt of the half acid/half amide was reduced with lithium aluminum hydride. ESI of a methanolic solution of 18 afforded the MH<sup>+</sup> ion 19, while ESI of a solution in deuterated methanol afforded the doubly deuterated ion 20. ESI-MS Exact Mass: MH<sup>+</sup>, 160.1695 (calcd 160.1696).



# COMPUTATIONAL

Anharmonic calculations on ions 1, 3, and 4 were performed by treating the N-H...N linkage via reduced dimensionality as though it were a linear triatomic using a potential surface produced by interpolating points calculated using the B2-P3LYP/cc-pVTZ double hybrid functional on geometries optimized at B3LYP/6-31G(d,p).7 This 2-dimensional analysis makes different predictions for the N-H…N asymmetric stretching frequency than do conventional anharmonic B3LYP/6-31G\*\* density functional (DFT) calculations using a pruned (99 590) grid (int = grid = ultrafine).<sup>9,10</sup> The anharmonic DFT calculation at 6-31G\*\* predicts a vibrationally averaged N-H…N bond angle for 1 of 172.2° and bending modes at 1598 and 1640 cm<sup>-1</sup>. The inadequacy of a secondorder perturbation approach for the N-H...N asymmetric stretch is exemplified by comparing the frequency predicted for the  $v = 0 \rightarrow v = 2$  transition, 850 cm<sup>-1</sup>, with that predicted for the  $v = 0 \rightarrow v = 1$  transition, 961 cm<sup>-1</sup>. This absurdity illustrates the limitations of using derivatives of the Hessian matrix in such cases.

DFT calculations on **3** predict a more linear vibrationally averaged N–H···N bond angle (177.1°), with anharmonic N– H···N DFT bending frequencies (1616 and 1629 cm<sup>-1</sup>) having slightly lower values than those predicted for **1**. The asymmetric N–H···N stretching frequencies calculated using second-order perturbation theory,<sup>9</sup> 1061 cm<sup>-1</sup> for  $v = 0 \rightarrow v =$ 1 and 1076 cm<sup>-1</sup> for  $v = 0 \rightarrow v = 2$ , disagree with those calculated using reduced dimensionality. Symmetric and asymmetric NH···N stretches for **3** and **4** predicted using the reduced dimensionality treatment as a linear triatomic<sup>4,14</sup> give a calculated  $v = 0 \rightarrow v = 1$  asymmetric stretch transition for ion **3a** (458 cm<sup>-1</sup>), much lower than predicted by anharmonic DFT, while the  $v = 0 \rightarrow v = 2$  asymmetric stretch transition, 1707 cm<sup>-1</sup>, has a much higher value.

# RESULTS

The proton-bridged ions in Chart 1 contain strong hydrogen bonds that are symmetrical (1–4, 6, 7, 9) or nearly so. Unimolecular transfer of the hydrogen from one nitrogen to the other gives a chemically equivalent structure (or one that is close in energy) without major changes in molecular conformation. As a prelude to presenting the IRMPD of these ions in the fingerprint region, studies of the ions containing NH…O intramolecular strong hydrogen bonds in the 2500–3600 cm<sup>-1</sup> domain shown in Chart 2 warrant discussion. Those proton bridges are highly unsymmetrical, because oxygen has such a low basicity relative to nitrogen that proton transfer does not yield a stable structure in the absence of a profound conformational change.

The neutral product from eq 3 above,  $(CH_3)_2NCH_2CH_2C-(CH_3)_2CH_2CH_2OH$  (18), gives a protonated parent ion (19)

Chart 2. Proton-Bridged Amino Alcohols Investigated by IRMPD Spectroscopy



in the gas phase. The inset in Figure 3 reproduces the OH band observed in its IRMPD spectrum. The two ionic decomposition



Figure 3. IRMPD spectra of ion 13 and of ion 19 (inset) using 5 ns OPO laser pulses followed by 23 ms pulses from a cw  $CO_2$  laser. Losses of both HNMe<sub>2</sub> and HNMe<sub>2</sub> plus water were monitored for the spectrum of 13. Losses of HNMe<sub>2</sub> and of water were monitored for the spectrum of 19.

pathways used to monitor the IRMPD spectrum of the ion in Figure 3—loss of neutral dimethylamine and loss of water in a 4:1 ratio—each gives the same peak profile, showing a band maximum close to  $3650 \text{ cm}^{-1}$ . For comparison, the published gas-phase IR absorption spectrum of a neutral isomer of **18**,  $(CH_3CH_2)_2NCH_2CH_2CH_2CH_2CH_2OH$ , displays the band from its free OH at nearly the same frequency,  $3660 \text{ cm}^{-1.20}$  The *O*,*N*-dideuterated ion **20** (prepared by ESI in CH<sub>3</sub>OD) decomposes exclusively via D<sub>2</sub>O loss, which makes the IRMPD spectrum much more difficult to record and which shows no absorption bands.

Another experiment confirms that acting as a hydrogen-bond acceptor does not alter the OH stretching frequency of cations possessing N-H<sup>+</sup>...OH intramolecular bonds. Scanning the IRMPD of the doubly protonated ion 13 over the domain accessible to the OPO laser (Figure 3) reveals only an OH stretch at 3650 cm<sup>-1</sup>. IRMPD does not produce any observable singly charged fragments. Monitoring both doubly charged fragment ions—from loss of dimethylamine (m/z 118) and from subsequent loss of water (m/z 109, plausibly the same structure as drawn for ion 11 below)—as a function of OPO wavelength demonstrates that, as in the case of 19, the OH stretch of the ion occurs at nearly the same frequency as does that of the neutral reference compound.

With regard to protonated diamines, bands disappear with deuterium substitution. This may be due to a diminution of intensity as well as a shift of frequency. Figure 4 reproduces the IRMPD spectra of 3a and 3b. One band (indicated by the black arrow in Figure 4) vanishes upon replacement of H<sup>+</sup> with D<sup>+</sup>. Otherwise, the spectrum of 3b exhibits the same bands as 3a and matches peaks in the calculated anhamonic DFT spectra



**Figure 4.** IRMPD spectra of **3a** (black) vs **3b** (red) in the region from 350 to 1900 cm<sup>-1</sup> for **4a** and **5a** below. The black arrow indicates a band that disappears when bridging  $D^+$  replaces  $H^+$ . The expected isotopic shift of the band indicated by the arrow would bring it into a region obscured by more intense absorptions.

(see Supporting Information). The disappearance of the 1340  $\text{cm}^{-1}$  band upon deuteration raises the question as to whether it possesses NH···N bending character.

Unfortunately, the IRMPD spectrum of ion 3a in the 300– 600 cm<sup>-1</sup> domain (shown as the ×5 magnification at the far left) is too weak and noisy for a useful comparison with that of the deuterated analogue 3b. The only feature below 600 cm<sup>-1</sup> is a broad band centered around 475 cm<sup>-1</sup> with a full width at half-maximum of approximately 125 cm<sup>-1</sup>. This band corresponds to the superposition of the four most intense peaks predicted for that domain by an anharmonic normal mode calculation (436, 445, 484, and 503 cm<sup>-1</sup>) as well as to the band calculated for a 2-dimensional potential for the N– H…N asymmetric stretch.

Because the N–H…N asymmetric stretch and the NN stretch predicted for **3a** appear to overlap with other bands, the IRMPDs of the 3,3-dimethyl homologue, ions **4a**  $(m/z \ 187)$  and **4b**  $(m/z \ 188)$ , were examined. This *gem*-dimethyl substitution lowers the calculated barrier to proton transit.<sup>14</sup> The conjugate acid ions give the spectra reproduced in Figures 5 and 6.

The broad absorption in the  $560-680 \text{ cm}^{-1}$  domain is assigned to a single band. The effect of replacing the bridging H<sup>+</sup> (in black) with D<sup>+</sup> (in red) is even more pronounced than for 1: the broad band around  $600 \text{ cm}^{-1}$  vanishes upon insertion of the heavier isotope. The solid black arrow in Figure 6 indicates the position computed from the 2-dimensional potential energy surface for the N–H…N asymmetric stretch in Figure 1B. As in the case of ion 1b, the N–D…N asymmetric stretch is predicted to be outside of the domain of the free electron laser scan, as the solid red arrow indicates. Just as in ion 3a, a weak band near 1350 cm<sup>-1</sup> also disappears upon deuteration. Again, much more intense bands obscure the region where an isotopically shifted band might have been expected.

Ion **5a** has a similar carbon backbone as **4a**, but the repositioning of the pair of methyl groups at the 2-position alters the relative basicities of the two nitrogens. Figure 7 shows IRMPD spectra comparing ion **5a** vs **5b**. Three bands disappear when the bridging  $H^+$  is replaced with a bridging  $D^+$  (620,



**Figure 5.** IRMPD spectra of 3,3-*N*,*N*,*N*',*N*'-hexamethylcadaverine (HMC) conjugate acid ions (black trace with bridging  $H^+$  **4a**; red trace with bridging  $D^+$  **4b**) in the 550–1800 cm<sup>-1</sup> wavelength domain.



Figure 6. IRMPD spectra of 3,3-N,N,N',N'-hexamethylcadaverine conjugate acid ions in the long-wavelength domain. Arrows correspond to frequencies calculated from the 2-dimensional surface in Figure 1B: dashed arrows for NN stretches (black for 4a and red for 4b); the black solid arrow for the asymmetric N-H…N stretch predicted for 4a; and the red solid arrow for the position of the asymmetric N-D…N stretch of 4b, which is not observed experimentally.

1200, and 1320 cm<sup>-1</sup>). The 620 cm<sup>-1</sup> band is assigned to the N–H…N asymmetric stretch, analogous to 1a/b and 4a/b. The bands at 1200 and 1320 cm<sup>-1</sup> also have N–H…N character since they also vanish upon deuteration and occur around the same domain as the previous examples (1a vs 1b, 2a vs 2b, 3a vs 3b, and 4a vs 4b). While the isotopic shift might have been expected to bring the N–D…N asymmetric stretch of 5b into a comparatively uncongested domain of Figure 7, the 620 cm<sup>-1</sup> band of 4a simply vanishes upon deuteration.

Figure 8 shows the IRMPD spectra of more rigid cyclic ions, the conjugate acids of N,N,N',N'-tetramethyl-*cis*-1,5-diaminocyclooctane (abbreviated Me<sub>4</sub>DACO), which has the two dimethylamino groups situated on a cyclooctane ring. Comparison of IRMPD spectra of the protonated (red, **6a**) and deuterated (black, **6b**) ions from **6** shows a band around 1650 cm<sup>-1</sup> in **6a**, assigned as the N–H…N bending mode, which disappears upon deuteration in **6b**, in the domain close



Article

Figure 7. IRMPD spectra of 5a (black) vs 5b (red) in the 300–1700 cm<sup>-1</sup> domain.



Figure 8. IRMPD spectra of ions 6a (red) vs 6b (black) in the 600–1800 cm<sup>-1</sup> domain.

to the B3LYP/6-31G<sup>\*\*</sup> normal mode N–H…N bending frequencies (1635 and 1648 cm<sup>-1</sup> unscaled). By contrast, the aforementioned examples of more conformationally mobile, linear diamines showed isotopically sensitive bands in the 1100–1350 cm<sup>-1</sup> domain.

Protonated tetraamines have also been examined. Ion 7a is calculated to have an equilibrium N–H…N bond angle of  $165^{\circ}$  and should have amine groups of equal basicity, but it deviates further from linearity than do ions 1a-6a. The diprotonated analog 8a is calculated to have an equilibrium N–H…N bond angle of  $165^{\circ}$  on one side and an N–H…N bond angle of  $162^{\circ}$  on the other side. 8a can exist as two tautomers. The tautomer with the charges farthest away from each other (8a) is calculated to be more stable by 0.2 kcal/mol when compared to tautomer 8c shown in eq 4. Although the H<sup>+</sup> can transfer rapidly from one nitrogen to the other, having the H<sup>+</sup> on one dimethylamine group causes the amine groups on the opposite side of the molecule to differ slightly in basicity.



DFT (B3LYP/cc-pVTZ) provides an estimate of the thermochemistry of a variety of unimolecular decomposition pathways. For a monoprotonated tetraamine to dissociate via

loss of neutral dimethylamine, it first has to break the strong hydrogen bond and rotate about the C–C bond before an internal nucleophilic displacement can take place, a net reaction that DFT predicts (eq 5) to be endothermic.



DFT predicts the dissociation of the doubly protonated tetraamine 8a to produce two singly charged daughter ions (10 via loss of protonated dimethylamine) exothermically. Expulsion of one or two neutral dimethylamines, in which both charges remain on the daughter ions (9a and 11), is expected to be even more endothermic than eq 5, as shown in eq 6. As noted above, the diprotonated triamine alcohol 13 loses dimethylamine and water in sequence to yield a doubly charged ion, for which 11 depicts the most plausible structure.

On one hand, the first step, loss of neutral dimethylamine to produce ion 9a, which has an equilibrium N–H…N bond angle of 162°, is calculated to have  $\Delta H = 16$  kcal/mol. On the other hand, if the ejected neutral dimethylamine was somehow to shuttle to the other side and remove the intramolecularly bound proton, that dissociation pathway to yield 10 plus protonated dimethylamine would be exothermic,  $\Delta H = -16$  kcal/mol.



Tandem MS/MS experiments using a linear triple quadrupole mass spectrometer at 4 V and at 10 V lab frame energy show doubly charged ions as the predominant decomposition products. Figure 9 reproduces the fragmentation pattern of **8a** 



Figure 9. (A) Spectra from collisionally activated dissociation of 8a by collisions with Ar gas. (B) Blowup of the high mass region. Values of m/z and of measured intensities above each peak.

after collisions with Ar gas at 4 V lab frame energy. The collisionally activated dissociation (CAD) of 7a produces ion 10, as predicted. The dissociation of 8a gives doubly charged dissociation products to a much greater extent than singly charged daughter ions. The doubly charged daughter ions 9a and 11 have intensities roughly 2 orders of magnitude greater than the singly charged fragment 10. Contrary to expectation on the basis of net thermochemistry, formation of doubly charged fragments takes place more often than the formation of

singly charged fragments. As noted above, the same holds true for decomposition of the doubly protonated ion 13.

Similarly, IR irradiation of mass-selected, doubly charged parent ions principally yields doubly charged fragments resulting from loss of neutral dimethylamine. Comparison of the singly charged ions 7a (black) and 7b (red) IRMPD spectra shows the profiles to be nearly identical (Figure 10), except for



**Figure 10.** IRMPD spectra of protonated tetrakis-(dimethylaminomethyl)benzene (7a black) vs deuteronated tetrakis-(dimethylaminomethyl)benzene (7b red) in the 750–1800 cm<sup>-1</sup> domain. Arrow indicates the position of a shoulder in the protonated ion that is not seen in the deuteronated ion.

a 2-fold difference in intensity. DFT predicts both N–H···N bending vibrations to occur near 1600 cm<sup>-1</sup>. A small shoulder around 1500 cm<sup>-1</sup>, which disappears upon deuteration, could be a bending mode associated with the bridging proton, which is not clearly resolved. The amine groups in the neutral precursor 14 ought to have equal basicities; therefore, the major difference between ion 7a and ion 1a is the bond angle and degree of conformational mobility. The bond angle in 7a is 6° farther away from linearity than ion 1a. Were the IR spectrum to be examined below 600 cm<sup>-1</sup>, one would expect to observe an N–H···N asymmetric stretch at lower frequency.

The IRMPD spectra of doubly charged ions 8a and 8b tell a different story (Figure 11). Isotopic replacement affects at least six bands. Two of these bands could represent the pair of N–H…N asymmetric stretches, while the other bands might correspond to the four N–H…N bending modes. All of these bands vanish upon isotopic replacement. They occur in the domain similar to that of the aforementioned ion 2a.

Figure 12 reproduces the IRMPD spectra of doubly charged ions **9a** and **9b**. DFT predicts that the neutral dimethylamino groups of the singly charged analogue **10** have equal basicity, and calculations predict an equilibrium N–H…N bond angle for **9** of 161°. Replacing the bridging proton of **9a** with deuterium results in the disappearance of a large, broad band near 1175 cm<sup>-1</sup>, perhaps flanked by smaller bands on either side. This band (or superposition of bands) occurs in the same domain as one of the bands seen for ion **1a** but cannot yet be definitively assigned.

Table 1 summarizes frequencies (to the nearest  $10 \text{ cm}^{-1}$ ) of experimentally observed bands of protonated di- and polyamines that disappear upon replacement of bridging H<sup>+</sup> with bridging D<sup>+</sup>. In some cases (1, 4, 5), low-frequency bands are observed, which bring to mind the 375 cm<sup>-1</sup> band of the



Figure 11. IRMPD spectra of diprotonated tetrakis-(dimethylaminomethyl)benzene (8a, black) vs dideuteronated tetrakis(dimethylaminomethyl)benzene (8b, red) in the 500–1800 cm<sup>-1</sup> wavelength domain.



Figure 12. IRMPD spectra of doubly charged ions 9a (black) vs 9b (red) in the 800-1600 cm<sup>-1</sup> domain.

Table 1. Experimental IRMPD Bands That Disappear When Bridging  $D^+$  Replaces Bridging  $H^+$  in Diamine (1–6b) and Tetraamine (7–9) Conjugate Acid Ions<sup>*a*</sup>

cation	equilbrium $\theta$	band frequencies (cm <sup>-1</sup> )
1	171°	530, 1200
2	155°	1200, 1300, 1360
3	177°	1340
4	178°	600 (broad), 1350
5	184°, 187°	620, 1200, 1320
6	$172^{\circ}$	1660
7	166°	1540 (shoulder)
8	162°, 165°	1110, 1140, 1160, 1200, 1230, 1300
9	161°	1170 (w/smaller bands on both sides?)
<sup>a</sup> Values of	equilibrium N–H	N bond angles $ heta$ from B3LYP/6-31G*

geometry optimizations do not change at B3LYP/cc-pVTZ.

proton-bound dimer of ammonia  $(N_2H_7^+)$ , which is assigned to the asymmetric stretch of the bridging nitrogen (and which has a shoulder indicative of a closely spaced combination band).<sup>21</sup> In all cases, though, isotopically sensitive vibrations occur at higher frequencies, too.

# DISCUSSION

Used here, the term "proton bridge" refers to an intramolecular strong hydrogen bond. When the barrier for internal H<sup>+</sup> transit becomes low enough, low-barrier hydrogen bonding (LBHB) contributes to the stability of a proton bridge by virtue of a diminished zero-point energy.<sup>22</sup> Typically, attention has focused on low- frequency stretching vibrations. The N–H…N asymmetric stretch of ion 1a (predicted by anharmonic DFT calculations to occur at 961 cm<sup>-1</sup>) appears experimentally around 530 cm<sup>-1.7</sup> The spectra reported here suggest that, in many cases, other vibrational modes with N–H…N character occur at frequencies much lower than predicted by anharmonic DFT for N–H…N bends.

Figure 3 demonstrates that the frequency of an OH stretch remains unaffected when a protonated amino group forms a proton bridge to the oxygen. In other words, the hydroxylic proton does not change the force constant for its stretching vibration significantly. Available theory cannot yet explain all of the band positions observed in the diamine experiments reported here, but correlations can be drawn among the experimental results.

The singly charged diamine conjugate acids whose N–H…N bond angles do not deviate too greatly from linearity include ions 1, 3, 4, 5, and 6 (for which the equilibrium bond angle has a value of  $\theta$  = 172.5°). Ions 1, 4, 5, and perhaps 3 exhibit low-frequency IRMPD bands in well-separated regions that vanish upon deuterium substitution. Reduced dimensionality calculations (e.g., Figure 1B) and vibrational spectra of crystalline salts<sup>7</sup> assign these bands (<650 cm<sup>-1</sup>) to N–H…N asymmetric stretches. This leaves the assignment of higher-frequency bands (1100–1350 cm<sup>-1</sup>) to other vibrations having N–H…N character.

The contrast between cations 1-4 and ion 6 indicates a more complicated situation than modeling the N-H…N simply as a triatomic would suggest. All of these ions should exist as single tautomers. On one hand, the comparatively rigid bicyclic ion formed by proton bridging in 6 exhibits an isotopically sensitive band at 1660 cm<sup>-1</sup> consistent with the DFT-calculated position for an N-H…N bend. Similarly, the degenerate N-H…N bends of the proton-bound dimer of ammonia give rise to a peak in that same region, not far from the peak predicted by a normal mode calculation.<sup>21</sup> On the other hand, the ions containing conformationally mobile chains (which retain flexibility upon cyclization to 7- and 8-membered rings) display bands at frequencies 20-25% lower than predicted by anharmonic DFT for bending vibrations. This leads to the hypothesis that the 1100–1350  $\text{cm}^{-1}$  bands in 1a and 3a–5a involve coupling with C–C torsions.

In ion 1a, the band around 1200 cm<sup>-1</sup> virtually disappears from the IRMPD spectrum upon replacement of the exchangeable H<sup>+</sup> by D<sup>+,7</sup> The change in mass of the bridging hydrogen should not only displace this band to lower frequency (where other bands might obscure it) but might also diminish its intensity. Consequently, the 1200 cm<sup>-1</sup> vibration must involve a substantial contribution from the bridging proton to its reduced mass. The adjacent band near 1250 cm<sup>-1</sup>, which does not move upon deuteration, probably corresponds to CH<sub>3</sub> rocking motions calculated at 1158 cm<sup>-1</sup> by anharmonic DFT.<sup>7</sup> It would have been tempting to surmise that a shoulder around 1600 cm<sup>-1</sup> in the IRMPD spectrum comes from N–H…N bending vibrations, but the fact that the shoulder does not change upon deuteration argues against such an assignment.<sup>7</sup>

#### The Journal of Physical Chemistry A

Similarly, anharmonic DFT calculations (see Supporting Information) predict that N-H...N bending vibrations in 3a ought to occur around 1600 cm<sup>-1</sup>. As in 1a/1b, the shoulder around 1600 cm<sup>-1</sup> does not shift upon replacing the bridging  $H^+$  with  $D^+$ , so it again seems unlikely that this feature corresponds to a vibration in which the bridging proton moves. The only major peak that disappears upon deuteration at the bridging position of 3 occurs around 1340 cm<sup>-1</sup>. DFT anharmonic IR spectra match the experimental IRMPD spectrum, apart from the motions of the bridging proton. As noted above, assignment of the 1340 cm<sup>-1</sup> band of 3a to coupling of a vibration with N-H...N character with torsions parallels the rationale outlined above. Other than that, both isotopomers exhibit the same bands above 700 cm<sup>-1</sup> in Figure 4 (except for the broad shoulder above  $1500 \text{ cm}^{-1}$ , which is more intense for the deuterated analogue 3b).

In 4a vs 4b, two bands vanish upon deuteration. The disappearance of the band around 1350 cm<sup>-1</sup> in a domain similar to the previous examples (1a-3a) implies N-H…N character (possibly coupled with torsions). The lower frequency domain region from 300 to 650 cm<sup>-1</sup> shows a broad feature, which disappears upon replacement of the bridging H<sup>+</sup> with D<sup>+</sup>, centered around 600 cm<sup>-1</sup>, assigned to the N-H…N asymmetric stretch (Figures 5 and 6).

An even clearer differentiation appears in the bands that disappear in going from **5a** to **5b**. The dimethylamino groups in the neutral diamine are not equivalent (and therefore have different basicities); hence, the mass-selected ion contains a mixture of a pair of tautomers with a low barrier ( $\Delta E^{\rm el} = 1.4$  kcal/mol going from the more stable tautomer) between them. Three prominent bands in **5a** disappear upon deuteration, as Table 1 summarizes. Except for the band at 620 cm<sup>-1</sup> these appear in the same domains as seen for previous examples (1a-4a). The 620 cm<sup>-1</sup> band corresponds to an N-H…N asymmetric stretch that interconverts the two tautomers, by analogy to low-frequency bands observed for 1a and 4a that are also predicted by theory.

Connecting the dimethylaminomethyl groups to a benzene ring, as in the singly charged ion 7a, increases the rigidity of the system relative to 1-5, but not as much as does the cyclooctane ring system in 6. The isotopically sensitive band of 6a near  $1650 \text{ cm}^{-1}$  occurs not far from the DFT-calculated normal-mode frequencies for in-plane and out-of-plane N-H…N bends

If such an assignment is correct, stretching vibrations occur at lower frequencies than the corresponding bending vibrations. This is the case for the proton-bound dimer of ammonia,<sup>21</sup> and it may be characteristic of near-linear LBHBs. For cases where the N–H···N bond angle deviates substantially from linearity ( $\theta \le 165^{\circ}$ ), such as 2 or the doubly protonated ion 8a (which has nonequivalent nitrogens, as eq 4 summarizes), several peaks show up in the 1100–1350 cm<sup>-1</sup> region, suggestive of strong coupling between stretching and bending modes. The question remains as to the relative contributions of indistinguishability and nonlinearity to the separation between stretching and bending vibrations.

The equilibrium N–H···N bond angles in ion **5a** deviate from linearity by 4–7° as compared to 15-18° in ion **8a**, depending on the tautomers. The clear difference between **5a**/ **5b** and **8a**/**8b**, where **5a** shows a 620 cm<sup>-1</sup> band assigned to the asymmetric N–H···N stretch, results more from deviation of the N–H···N geometry from linearity in **8a** rather than from the slight difference in nitrogen basicity. It seems reasonable to infer that making the nitrogens distinguishable does not exert as great an effect on the observed spectra as does having an N–H…N bond angle  $\theta \leq 165^{\circ}$ .

The doubly charged ion 9a remains somewhat of an enigma. IRMPD spectroscopy of this ion shows a strong band near  $1175 \text{ cm}^{-1}$  (as well as perhaps a half dozen other, much smaller absorptions between 1080 and 1280 cm<sup>-1</sup>) that disappears upon deuteration. Because the proton bridge renders 9a quite inflexible, a bending mode ought to appear around  $1500 \text{ cm}^{-1}$ , but no isotopically sensitive band can be seen there. Nonlinearity and coupling between N-H-N stretching and other motions may shift bending vibrations to lower frequencies than normal mode calculations predict. In any event, rapid transit of H<sup>+</sup> should render the proton-bridged nitrogens equivalent, which suggests a situation similar to that of ion 2a, where proton bridging creates a 6-membered ring. Ion 2a exhibits three bands with equal intensity that vanish upon deuteration, but a single major absorption of 9a occurs in that same domain. The analogy between the singly charged ion 2a and the doubly charged ion 9a (where the proton bridge creates a 7-membered ring having a pair of  $sp^2$  centers) requires further examination.

# CONCLUSIONS

The experiments reported here address properties of intramolecular ionic hydrogen bonds. Gaseous cations containing  $N-H\cdots OH$  proton bridges exhibit the same OH stretching frequencies as do neutral analogues in the gas phase. The conjugate acid ions of acyclic diamines typically exhibit more than one isotopically sensitive band.

Which has a greater impact on vibrational frequencies associated with intramolecular low-barrier hydrogen bonds (LBHBs): having a bond angle close to linearity or having nitrogens that become equivalent as a result of proton transit? The N-H…N vibrations of seven protonated di- and polyamines have here been investigated in the gas phase along with two cases (1a/1b and 2a/2b) previously studied. Of the protonated di- and polyamines, the conjugate acid ions of all five open-chain diamines (1a-5a) show bands in the 1100-1350 cm<sup>-1</sup> domain that disappear when H<sup>+</sup> is exchanged with D<sup>+</sup>. Comparing ion 6a and  $H_3N\cdots H^+\cdots NH_3$  with the protonated open-chain diamines shows that, while N-H-N bending frequencies of the former pair of examples agree with normal mode calculations, the latter do not appear in the domain predicted by theory. It seems possible that coupling of the bending motions of the proton bridge with torsions of the mobile methylene chain shifts bands to lower frequencies. Anharmonic corrections to normal mode DFT calculations using second-order perturbation theory<sup>9,10</sup> do not account for this shift.

The conjugate base of ion **5** has nitrogens of unequal basicity, but the clean separation among the three bands of **5a** that disappear upon replacement of H<sup>+</sup> with D<sup>+</sup> represents a clear separation of the N–H…N asymmetric stretch from other isotopically sensitive vibrations. The bond angle  $\theta$  of **5** has a value that deviates from linearity by <10°. In contrast, diprotonated ion **8a** has  $\theta$  < 165° and displays at least six bands, ranging from 1180 to 1300 cm<sup>-1</sup>, all believed to be associated with the motion of the bridging proton, although they have yet to be assigned.

The asymmetric stretch of  $H_3N\cdots H^+\cdots NH_3$  has previously been reported to occur near 375 cm<sup>-1.21</sup> Comparison of that value with the IRMPD of ions 1a, 4a, and 5a (having assigned asymmetric stretches observed at 530, 600, and 620 cm<sup>-1</sup>, respectively) shows bands not far from that region of the IR. The nine di- and polyamine conjugate acid ions have different N–H…N bond angles ( $\theta$ ), and two of them show slight differences between basicities of the dimethylamino groups. Having a bond angle close to linearity seems to be more important than possessing nitrogens with identical basicities.

DFT suggests that the protonated di- and polyamines described here all fall under the rubric of LBHBs. Experimental and theoretical studies have characterized ion **1a** as possessing an LBHB, based on IRMPD, comparison of solid-phase NMR with X-ray crystallography, inelastic neutron scattering, and pressure-dependent Raman spectroscopy.<sup>7,8</sup> The spectroscopic signatures of the protonated ions presented here bear resemblance to the vibrational structure of **1a**. Hence, it seems probable that all of these positive ions also contain LBHBs. Negatively charged LBHBs have been reported in proteins, observed by neutron diffraction, in which H<sup>+</sup> sits between a phenoxide anion (an ionized Tyr residue) and a carboxylic acid.<sup>23</sup> On the basis of the IRMPD of **5a**, it appears that positively charged LBHBs also do not require that the double-well potential be absolutely symmetrical.

# ASSOCIATED CONTENT

# **S** Supporting Information

Predicted anharmonic IR absorption spectrum of **3a** compared with the IRMPD spectrum and comparisons of experimental IRMPD spectra with scaled harmonic spectra calculated at B3LYP/cc-pVTZ for ions **7a/b**, **8a/b**, and **9a/b**, along with B3LYP/cc-pVTZ geometries. This material is available free of charge via the Internet at http://pubs.acs.org.

# AUTHOR INFORMATION

#### **Corresponding Author**

\*E-mail: morton@citrus.ucr.edu.

#### **Present Address**

<sup>⊥</sup>Institute for Molecules and Materials, FELIX facility, Radboud University Nijmegen, Toernooiveld 7, 6525 ED Nijmegen, The Netherlands.

# Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

Dedicated to Peter Armentrout on the occasion of his 60th birthday. The authors are grateful to Prof. G.O. Beran, Prof. L.J. Mueller, and Ms. Kelly Theel for communicating results of their theoretical calculations; to Prof. Bruno Figadère of the Faculté de Pharmacie, Universite Paris-Sud XI, Châtenay-Malabry for material and advice; and to Dr. Audrey Solgadi of that Fac for assistance with CAD experiments. We would also like to acknowledge the assistance of Dr. J. D. Steill, as well as of the FELIX staff, in particular Drs A. F. G. van der Meer and B. Redlich. This work was supported by the Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) and by NSF Grant CHE-0848517 (T.H.M.).

# REFERENCES

(1) Aristotle On the Heavens II.xiii.295b.31-34.

(2) Zupko, J. John Buridan. Portrait of a Fourteenth-Century Arts Master; University of Notre Dame Press: Notre Dame, Indiana, 2003, p 400. (3) Excerpt from *Harper's Weekly* circa 1900 in McCullough, D. *The Path Between the Seas. The Creation of the Panama Canal 1870–1914;* Simon & Schuster: New York, 1977; p 297.

(4) Beran, G. J. O.; Mueller, L.; Theel, K., unpublished results.

(5) (a) Hud, N. V.; Morton, T. H. J. Phys. Chem. A 2007, 111, 3369– 3377. (b) Rajabi, K.; Theel, K.; Gillis, E. A. L.; Beran, G.; Fridgen, T. D. J. Phys. Chem. A 2009, 113, 8099–8107. (c) Engelhart, A. E.; Hud, N. V.; Morton, T. H. Chem. Commun. 2009, 647–649.

(6) (a) Moore, D. T.; Oomens, J.; van der Meer, L.; von Helden, G.; Meijer, G.; Valle, J.; Marshall, A. G.; Eyler, J. R. *ChemPhysChem* 2004, *5*, 740–743. (b) Fridgen, T. D.; MacAleese, L.; Maitre, P.; McMahon, T. B.; Boissel, P.; Lemaire, J. *Phys. Chem. Chem. Phys.* 2005, *7*, 2747– 2755. (c) Li, X.; Moore, D. T.; Iyengar, S. *J. Chem. Phys.* 2008, *128*, 184308. (d) Li, X.; Oomens, J.; Eyler, J. R.; Moore, D. T.; Iyengar, S. S. *J. Chem. Phys.* 2010, *132*, 244301.

(7) Beran, G. J. O.; Chronister, E. L.; Daemen, L. L.; Moehlig, A. R.; Mueller, L. J.; Oomens, J.; Rice, A.; Santiago-Dieppa, D. R.; Tham, F. S.; Theel, K.; Yaghmaei, S.; Morton, T. H. *Phys. Chem. Chem. Phys.* **2011**, *13*, 20380–20392.

(8) Neugebauer, J.; Hess, B. A. J. Chem. Phys. 2003, 118, 7215-7225.
(9) (a) Barone, V. Chem. Phys. Lett. 2004, 383, 528-532. (b) Barone, V. J. Chem. Phys. 2005, 122, 14108-14110. (c) Hanson-Heine, M. W. D.; George, M. W.; Besley, N. A. J. Phys. Chem. A 2012, 116, 4417-4425.

(10) Yaghmaei, S.; Khodagholian, S.; Kaiser, J. M.; Tham, F. S.; Mueller, L. J.; Morton, T. H. *J. Am. Chem. Soc.* **2008**, *130*, 7836–7838. (11) Oepts, D.; Van Der Meer, A. F. G.; Van Amersfoort, P. W.

Infrared Phys. Technol. **1995**, 36, 297–308.

(12) (a) Polfer, N. C.; Oomens, J. Phys. Chem. Chem. Phys. 2007, 9, 3804–3817. (b) Polfer, N. C. Chem. Soc. Rev. 2011, 40, 2211–2221.

(13) Pluth, M. D.; Bergman, R. G.; Raymond, K. N. J. Am. Chem. Soc. 2008, 130, 6362-6366.

(14) Khodagholian, S. Ph.D. Thesis, University of California, Riverside, 2010.

(15) Poutsma, J. C.; Andriole, E. J.; Sissung, T.; Morton, T. H. Chem. Commun. 2003, 2040–2041.

(16) Corey, E. J.; Block, E. J. Org. Chem. 1966, 31, 1663-1668.

(17) Moehlig, A. R. Ph.D. Thesis, University of California, Riverside,

2011. Current address: Adams State University, Alamosa, CO 81101.

(18) Schindlbauer, H. Monatsh. Chem. 1968, 99, 1799–1807.

(19) Schindlbauer, H. Monatsh. Chem. 1969, 100, 1413–1422.

(20) Stein, S.E. Infrared Spectra. In NIST Chemistry WebBook, NIST Standard Reference Database Number 69; Linstrom, P.J., Mallard, W.G., Ed.; National Institute of Standards and Technology: Gaithersburg MD, 20899, http://webbook.nist.gov.

(21) (a) Asmis, K. R.; Yang, Y.; Santambrogio, G.; Brummer, M.; Roscioli, J. R.; McCunn, L. R.; Johnson, M. A.; Kühn, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 8691–8694. (b) Yang, Y.; Kühn, O.; Santambrogio, G.; Goebbert, D. J.; Asmis, K. R. J. Chem. Phys. **2008**, *129*, 224302– 224308.

(22) Kreevoy, M. M.; Liang, T. M. J. Am. Chem. Soc. 1980, 102, 3315-3322.

(23) Yamaguchi, S.; Kamikubo, H.; Kurihara, K.; Kuroki, R.; Niimura, N.; Shimizu, N.; Yamazaki, Y.; Kataoka, M. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 440–444.