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# Water-Assisted Proton Transfer in the Monomer of 7-Azaindole[†]

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Ultrafast pump−probe spectroscopic studies on the hydrated 7-azaindole monomer are presented. The experiments provide evidence that excited-state proton transfer in the gas-phase hydrated 7-azaindole monomer may be possible, as predicted by theory, and can occur by means of a water proton bridge. As explained in the text, full tautomerization may not be occurring, but rather the transfer of a proton from the 7-azaindole monomer to the solvating water molecules. A calculated geometry for the structure of 7-azaindole clustered with four waters is presented and used to explain the rate increase observed in this species compared to the 7-azaindole monomer clustered with two and three waters.

## Introduction

The 7-azaindole (7Aza) molecule has proven to be an important model system for the study of proton transfer, as well as the extrapolation of these studies to matters of biological interest. Experimental research of the dimer of this species in both the gas and the condensed phase have given evidence of a rapid excited-state double proton transfer.[1−6] In addition to investigations of proton transfer in the isolated dimer, many recent studies have focused on the hydrated cluster species.[7,8] The monomer species of 7Aza is also capable of excited-state proton transfer (ESPT) in the condensed phase when assisted by solvent molecules, and the process has received much attention.

Employing recent results from both ab initio calculations and high-resolution laser-induced fluorescence spectroscopy,[9] Nakajima and co-workers have proposed configurations for 7Aza clustered with one to three waters. ESPT has been observed in studies of the dimer of 7-azaindole, as well as in the 1:1 complexes of 7Aza with acetic acid and water molecules in nonparticipating solvents.[10,11] Proton transfer in the 7Aza monomer also has been observed in bulk alcohol and water solvation environments, but at a much slower rate than in isolated systems.[12−16] This difference in time scale is likely attributable to the necessary rearrangement in the bulk solvation shell in order to obtain a favorable proton-transfer geometry with the solvent.[17]

The solvated monomer has received a great deal of attention by theoreticians who have investigated the tautomerization mechanism resulting from proton transfer by means of ab initio and direct-dynamics calculations. Results of Chaban et al. using the GAMESS program support experimental results showing that in the ground state, the normal 7-Aza species is more stable than the tautomer species by roughly 14 kcal/mol.[18] In the excited state, however, the trend reverses and the tautomer becomes more stable than the normal species by about 20 kcal/mol.[18] In addition to the formation of a more stable excited-state tautomer when compared to the normal species, the clustering of a water molecule to the monomer in the excited state results in a lower reaction barrier height having an upper limit of 6 kcal/mol.[18] Chaban et al. conclude that the addition of more than one water molecule should result in a further lowering of the activation energy for the proton transfer, so that tautomerization should be facile in the presence of water in the $S_1$ state of 7Aza.[18] It should be pointed out that proton transfer resulting in the complete tautomerization of 7Aza monomer in the gas phase, even with solvent assistance, has not been reported.[9] The pump−probe spectroscopic evidence presented in our paper leads to the conclusion that proton transfer can occur in the gas phase upon exciting 7Aza clustered with water molecules.

Smedarchina et al. also have determined that water can act as an efficient proton conduit in the proton-transfer reaction of 7Aza.[19] Their direct-dynamics calculations showed that the addition of a water molecule to the 7Aza monomer allowed the tautomerization reaction to occur. A significant finding of their study was the observation that the addition of a second water molecule also allowed the tautomerization reaction to occur at a rate similar to that for one water molecule, despite the mechanistic requirement of a triple proton transfer through the double-water bridge.[19] They also studied the effect of hydration on the tautomerization of guanine and noted an inhibitory effect on the reaction rate for two water molecules when compared to the faster, one-water bridge situation.[19] This is in marked contrast to the situation seen in 7Aza[19] and thus shows the necessity of studying many systems owing to dramatic differences that solvation can play in different ones.

Herein we present gas-phase ultrafast pump−probe studies on the hydrated 7Aza monomer, and the deuterated 7Aza monomer (where only the nitrogen in the five-membered ring is deuterated) solvated with $D_2O$. In this paper we provide evidence that proton transfer is occurring in the hydrated gas-phase monomer of 7Aza, albeit not necessarily complete tautomerization. This study provides an interesting look at the effect of increasing solvation for proton transfer into a solvation shell.

## Experimental Section

Hydrated clusters of 7Aza were formed by means of supersonic expansion into a vacuum. Vapor from 7Aza (Sigma),

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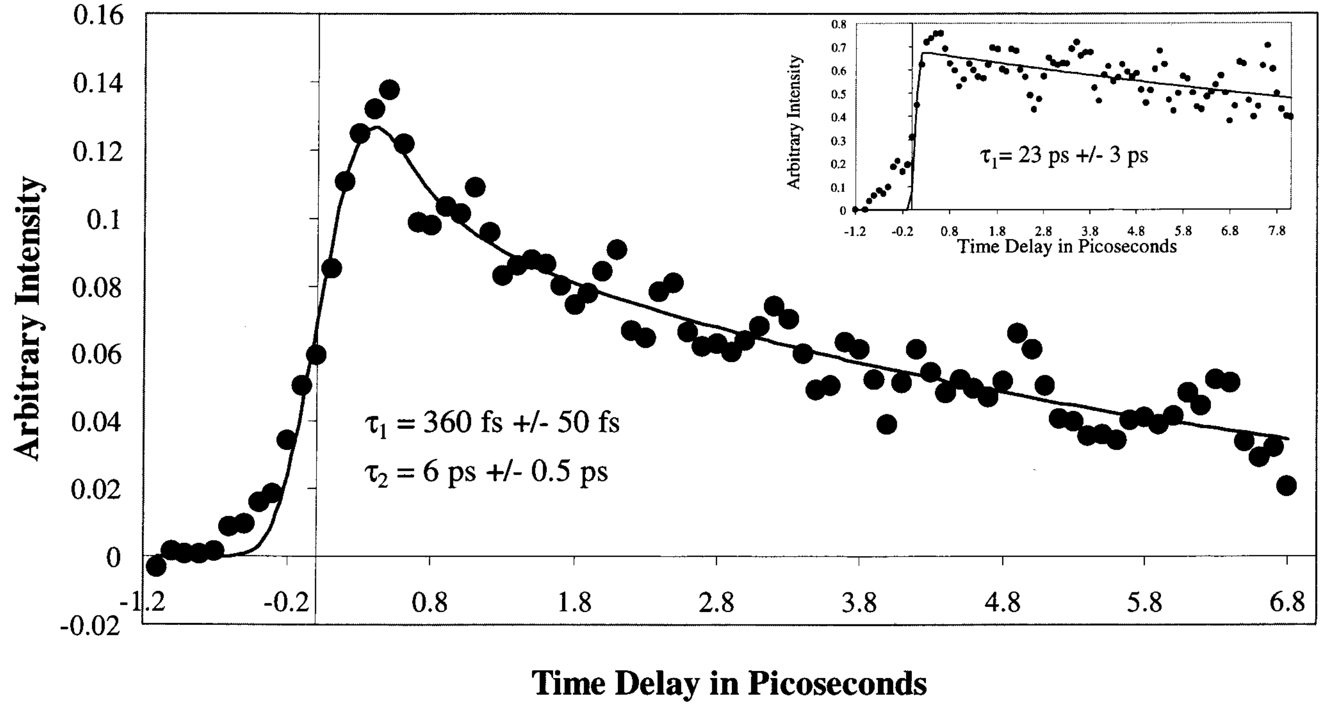

**Figure 1.** Pump−probe transient for dihydrated 7-azaindole monomer. The data were fit with a biexponential function resulting in first and second time constants of 360 ± 50 fs and 6 ± 0.5 ps, respectively. The inset shows the data for the *d*-7-azaindole monomer hydrated with two $D_2O$ molecules. The long-time component of the deuterated data yielded a time constant of 23 ± 3 ps.

generated by heating 7Aza in a glass sample holder to a temperature of ∼150 °C, was expanded into vacuum with 20 psi of helium backing gas. Hydration was accomplished by passing the helium through an external cell containing water at room temperature prior to introduction into the 7Aza sample holder. Preparation of the *N*′-deuterated derivative of 7Aza, *d*-7-azaindole, was accomplished using the method reported by Zewail.[4] The deuterated 7Aza was introduced into the gas phase by the same methods used for the nondeuterated species. Hydration with heavy water was accomplished by addition of $D_2O$ (Isotec, Inc., 99.9% pure) into the external cell.

Generated clusters were interrogated by pump−probe spectroscopy followed by detection with a reflectron time-of-flight mass spectrometer. The laser pulses used for the pump−probe experiments were generated with a colliding pulse mode-locked ring dye laser. Employing Rhodamine 590 tetrafluoroborate in the gain jet of the dye laser, with DODCI as a saturable absorber, followed by 4 stages of Nd:Yag pumped amplification using sulforhodamine 640, we are able to obtain 1.5 mJ amplified light pulses of 150 ± 50 fs duration with centers of 612−620 nm depending on the tuning of the oscillator cavity. Second-harmonic pulses are generated by focusing 50% of the amplified beam into a BBO nonlinear crystal. In the experiments presented herein, the pump pulse used to excite the molecules is the second harmonic from the CPM, with the fundamental laser pulse acting as the probe beam to ionize the clusters. The pump and probe beams are delayed in time with respect to each other using a delay stage and are subsequently collinearly recombined and focused into the mass spectrometer by means of a 40 cm lens to interact with the generated clusters.

## Results and Discussion

All hydrated monomer clusters $7Aza(H_2O)_n$ with $n = 1-4$ were generated and observed with our mass spectrometer, but owing to the wavelength restrictions of our current laser setup, only the species with $n = 2-4$ could be studied in the $S_1$ excited state by means of pump−probe spectroscopy. Studies by Nakajima et al. have experimentally determined the 0−0 transition for the $S_1$ excited states of the first three hydrated 7Aza.[9] Those values are 299.93 nm (33 340.4 $\text{cm}^{-1}$) for one water clustered to the monomer, 306.45 nm (32 632.1 $\text{cm}^{-1}$) for two waters, and 307.18 nm (32 554.3 $\text{cm}^{-1}$) for three waters.[9] The value for four waters was not determined, but likely lies very close to the value for three waters. In light of these requisite excitation energies, we only report data for two, three, and four waters clustered to the 7Aza monomer.

Tautomerization for the hydrated 7-azaindole monomer has been observed directly in solution. Chou and co-workers studied the 7-azaindole monomer in solutions of ethyl ether and *p*-dioxane.[11] In both solvents, the “normal” 7-azaindole monomer exhibits a fluorescence band in the range of 350 nm. Upon the addition of water to both solvents, a red-shifted fluorescence band on the order of 530 nm appears. The red-shifted band is attributed to the formation of a water-catalyzed 7-azaindole tautomer. It should be noted that in bulk water the tautomer band is not present; rather, only a red-shifted “normal” band at 385 nm is observed. Interpretation of our mass spectrometric ultrafast pump−probe data is made in light of observations in the gas phase and the condensed phase and in theoretical calculations[9,11,18,19]

The transient pump−probe signal, as depicted in Figures 1−3, is generated from the raw data by plotting the integrated peak intensity for the mass of interest with respect to delay time between the pump and probe lasers. The generated transient data directly correlates to the ionization efficiency for the particular mass studied. As noted by Zewail in studies of the 7-azaindole dimer,[1] one is observing a change in the ionization cross section for the mass of interest as the molecules evolve on the potential energy surface. Photoelectron spectroscopy studies performed by Lopez-Marten et al. have in fact proven that the tautomer of the 7-azaindole dimer has a much lower ionization cross section than the normal dimer.[20] In this way, molecules

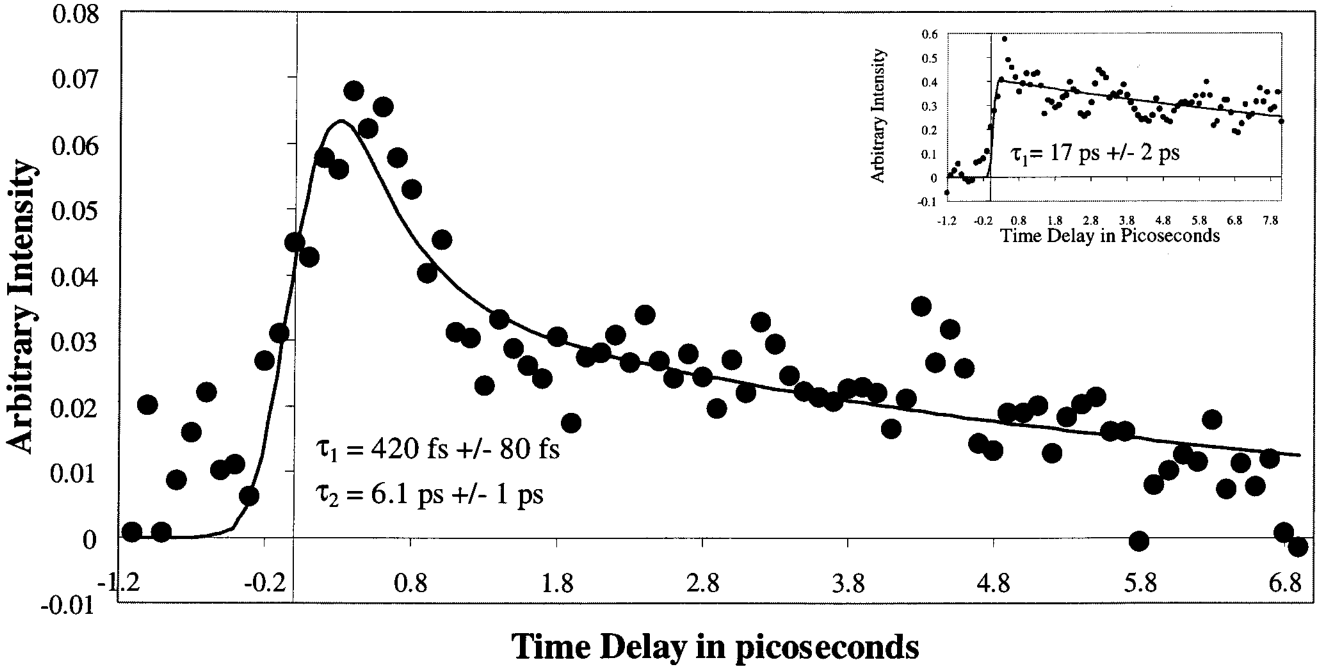

**Figure 2.** Pump–probe transient for the 7-azaindole monomer clustered with three waters. The data were fit with a biexponential function yielding time constants of 420 ± 80 fs and 6.1 ± 1 ps. The inset shows the data for *d*-7-Aza$(D_2O)_3$. The long-time component of the deuterated data was fit with a time constant of 17 ± 2 ps.

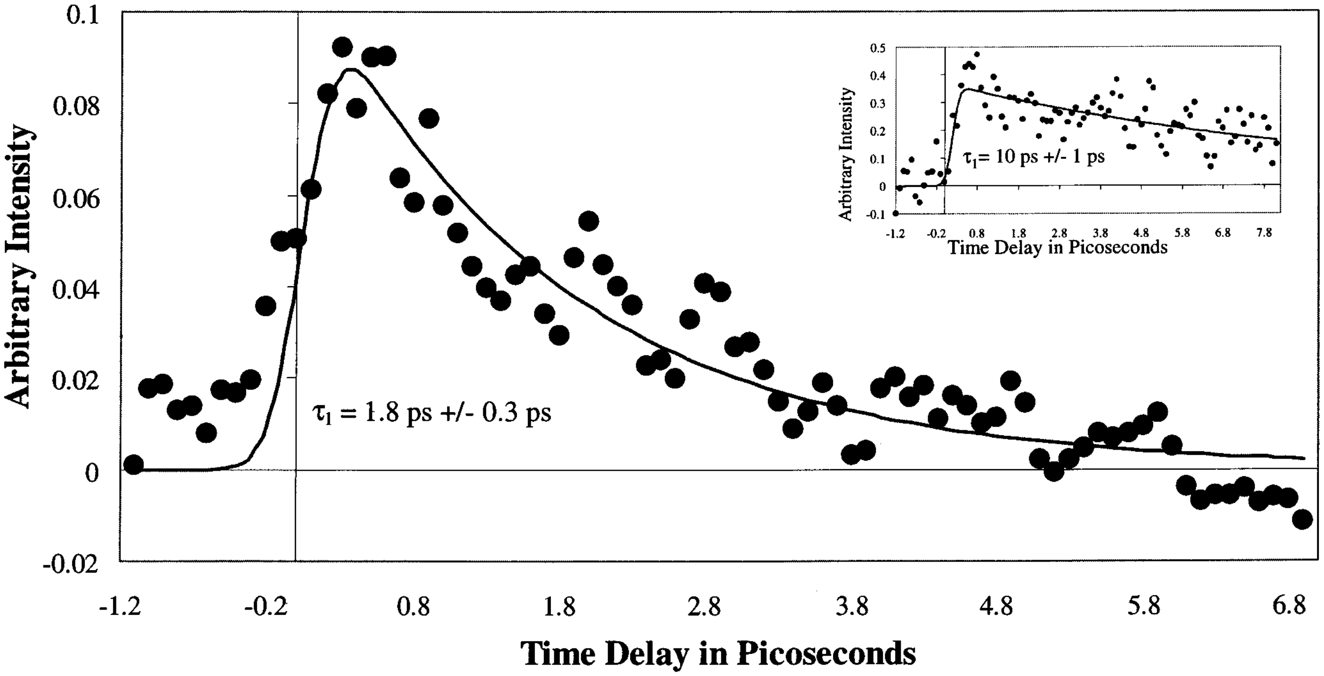

**Figure 3.** Pump–probe transient for 7-azaindole solvated with four water molecules. The data were best fit with a single-exponential yielding a time of 1.8 ± 0.3 ps. The inset shows the deuterated data for *d*-7-Aza$(D_2O)_4$. The long-time component of the deuterated data was fit with a time of 10 ± 1 ps.

having different ionization cross sections will yield a transient signal that can be fit by an appropriate series of functions to yield the time dynamics for the proton-transfer reaction.

The pump–probe data obtained for the hydrated 7Aza clusters and the deuterated 7Aza clustered with $D_2O$ is presented in Figures 1–3. Figure 1 shows the data for the species 7Aza-$(H_2O)_2$ and corresponding time constants obtained using the fitting method described above. The doubly hydrated species was best fit with a biexponential function yielding a fast first time constant of 360 ± 50 fs, and a second time constant of 6.0 ± 0.5 ps. The inset to Figure 1 depicts the data obtained for the deuterated 7Aza monomer clustered with two heavy waters, *d*-7-Aza$(D_2O)_2$. It should be noted that the overall signal intensity decreased dramatically in the deuterated studies as a result of the large number of additional hydrated structures present owing to mixing of the deuterated species with light species. This unfortunate consequence of the deuteration experiments resulted in the lower quality data shown in the insets in Figures 1–3. As a result of the lower data quality, we only attempted to fit the long time character of the deuterated data. Nevertheless, the deuterated data definitively depicts a process with a much longer lifetime, thus representing a definite isotope effect. For the long-time component, the data shows a fit with a single-exponential function yielding a lifetime of 23 ± 3 ps. This large isotope effect strongly suggests that tunneling is present, and as a result that our data represents the occurrence of a proton-transfer process.[22] Figure 2 shows the data for the triply hydrated monomer 7-Aza$(H_2O)_3$. Again in this case the data was best fit using a biexponential function yielding a first time of 420 ± 80 fs and a second time of 6.1 ± 1 ps. Figure 2 also contains an inset showing the data for *d*-7-Aza$(D_2O)_3$. The deuterated data is presented along with a data fit showing a time of 17 ± 2 ps. Once again the deuterated data displays an isotope effect reflecting that a proton transfer is likely occurring. The data for the species 7-Aza$(H_2O)_4$ is presented in Figure 3. As can be seen in Figure 3, the monomer species clustered with four waters exhibits a proton-transfer process much faster than that for two and three waters clustered to the 7Aza monomer. The data for four waters was best fit with a single exponential yielding a time of 1.8 ± 0.3 ps. The inset showing the data for the deuterated case *d*-7-Aza$(D_2O)_4$ also exhibits a corresponding faster time of 10 ± 1 ps when compared with the deuterated data for two and three heavy waters.

The presented findings raise a question about what the observed times represent. If full tautomerization were occurring in the hydrated 7-azaindole monomer, a process yielding two time constants as in the case for one and two waters would imply that a stepwise proton-transfer process is occurring. In this case as well, a single time constant as seen in the four-water scenario would imply that the proton is being transferred in a single concerted step through the proton wire. Another possibility in the single time constant scenario is that the first proton step has become too fast to be observed with the laser pulse widths employed in these experiments. If one considers the possibility that a full proton transfer resulting in tautomerization is not occurring, one must consider the effects of increasing solvation on the transferred proton. For instance, in this case, it makes a great deal of sense that the proton-transfer process is more favorable upon the addition of four waters owing to the increased ability of the transferred proton to become stabilized. Also, any possible effects of solvation on the barriers to transfer must be considered. In this case the observation of time constants would correspond to the evolution of the transferred proton through the water network. Once again there is the possibility that the process occurring with four waters solvated to the monomer is actually a two-step process, but we are unable to observe the first step owing to laser pulse width restrictions.

The structure of the monomer with four waters could perhaps give a clue as to why a drastic change is seen compared to the doubly and triply hydrated species. Unfortunately, to our knowledge, structures have only been published for one, two, and three waters clustered to the monomer. In light of this, we have performed a calculation to gain some insight into the possible structure for the 7Aza$(H_2O)_4$ in order to assist in the discussion and interpretation of our data. The generated structure, as seen in Figure 4, was calculated using Gaussian 98 with a Hartree−Fock level of theory and a 6-31G basis set.[22] All calculations were performed on the Pennsylvania State University's IBM RS/6000 SP high-performance computers. As a means of comparison, calculations were also performed for one, two, and three waters using the same theory and basis set in order to compare with current literature values. The bond lengths obtained for one, two, and three waters matched almost exactly those values reported by Nakajima et al. for the lowest energy species obtained in their calculations.[9] In light of this, we believe that the structure we report for four waters is sufficiently accurate to aid us in interpreting our data.

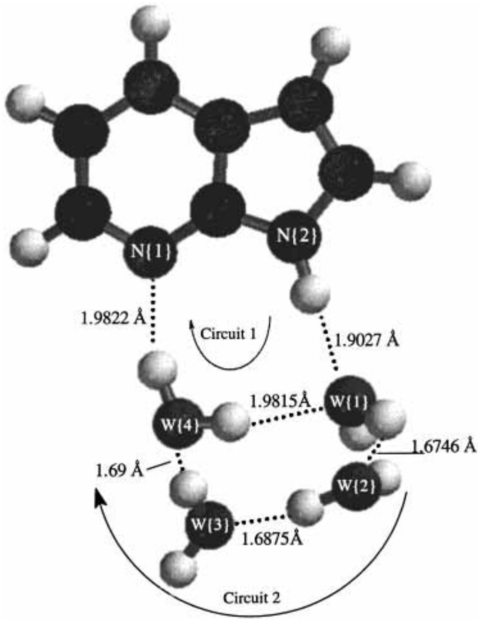

**Figure 4.** Calculated structure of the 7-azaindole monomer solvated with four water molecules generated with Gaussian 98 using HF/6-31G.[22] Hydrogen bonds are depicted with a dashed line, and individual hydrogen bond lengths are given in angstroms.

Considering the possibility of full tautomerization, one can look at Figure 4 and envision two possible circuits for the proton from N{2} to follow when undergoing proton transfer. The first circuit would follow a path from N{2} through water{1} and water{4} to reach N{1}. Transfer through the first circuit would require rearrangement of water{1} and {4} to effect a circuit conducive to proton transfer. While this is entirely possible, and one should not envision a static structure in such a dynamic solvent as water, our fast single-step transfer data for four waters would lead one to conclude that this rearrangement is probably not occurring. Therefore it seems likely that if the water molecules are acting as a proton bridge in the tautomerization of 7Aza, they are doing so by means of a complete circuit from N{2} to water{1} to water{2} to water{3} to water{4} and finally to N{1}. In this case the circuit in the water proton bridge would probably occur through a proton displacement process rather than the scenario where an individual proton is passed from water molecule to water molecule. The unique aspect of this circuit lies perhaps in the individual hydrogen bond lengths between the water molecules. All three of the water-to-water hydrogen bonds in the circuit are significantly shorter than the water-to-7Aza hydrogen bonds, and the water{1}-to-water{4} hydrogen bond in the present structure. They are also found to be considerably shorter than all of the hydrogen bonds calculated by Nakajima et al. for 7Aza clustered with one to three waters. Thus the nature of the water molecule circuit could be the reason for the efficient concerted proton bridge as observed in our pump−probe data for 7Aza$(H_2O)_4$.

If one considers the other possible scenario where proton transfer is not resulting in a full tautomerization of the hydrated monomer, then Figure 4 can also be instructive. In this case the faster transfer time seen in Figure 3 would likely result from the stronger solvation capabilities of the four-water group as evidenced by the shorter hydrogen bonds demonstrated in the calculation.

We do not believe that the proton-transfer anomaly occurring with the clustering of four waters to 7Aza is necessarily specific to water. Experiments are currently underway in our laboratory to investigate the dynamics of 7Aza with ammonia clusters. Preliminary results suggest that a switch from a sequential to a concerted process also occurs at the onset of four ammonia molecules. Interestingly, the reaction also appears to be concerted for five ammonia molecules clustered to 7Aza, so perhaps it is the establishment of a four-member proton bridge ring that allows the efficient transfer to occur. Further investigations on ammonia are underway and will be reported in a subsequent paper.

## Conclusions

In this paper we have presented ultrafast pump−probe spectroscopic evidence suggesting the occurrence of excited-state proton transfer in gas-phase clusters of hydrated 7Aza monomer. The proton transfer appears to take place by means of a proton bridge formed by the network of clustered water molecules. The transfer for the complex with two and three waters occurs in a stepwise fashion on the order of 6 ps, while the system with four waters undergoes proton transfer in a concerted fashion on a time scale of about 1.8 ps. The rapid increase in reaction rates between three and four waters clustered to the 7Aza monomer is likely due to the formation of an efficient proton bridge as evidenced by the shorter hydrogen bonds calculated between water molecules in the water tetramer as shown in Figure 4. While deuteration studies provide proof that proton transfer is occurring, it cannot be determined conclusively from the current experiments that the proton-transfer results in a complete tautomerization of the 7Aza monomer. Despite evidence for tautomerization in the bulk and prediction by theory, spectroscopic evidence does not support a complete tautomerization reaction in the gas phase for the 7Aza monomer.[9] Despite this, the studies presented here show the interesting effects of increasing solvation on the proton-transfer processes in the 7Aza monomer.

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