Protonation-Induced Conformational Changes of *N,N,N′,N′*-Tetramethylethylenediamine. Importance of Strong N–H$^+$···N Hydrogen Bonding

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The effect of protonation on the conformation of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) has been studied by Raman spectroscopy and ab initio theory. TMEDA and $TMEDAH_2^{2+}$ molecules assume predominantly the *trans* NC–CN conformation in aqueous solution, while a large number of $TMEDAH^+$ molecules assume the *gauche* NC–CN conformation, as stabilized by strong intramolecular 1,4-N–H$^+$···N hydrogen bonding.

Hydrogen bonding plays an important role in life processes and displays great variety both in the energetics of the bonds and in their structural features in biological molecules.[1] In previous papers,[2,3] the existence of strong intramolecular 1,4-N–H$^+$···O hydrogen bonding has been reported for protonated 2-(*N,N*-dimethylamino)ethanol ($DMAEH^+$). The molecules of $DMAEH^+$ assume predominantly the $G^{\mp}G^{\pm}t$ conformation (G, *gauche*; t or T, *trans*) around the H$^+$N–C–C–OH bonds in aqueous solution, indicating that intramolecular 1,4-N–H$^+$···O hydrogen bonding is stronger than intermolecular O–H···O hydrogen bonding. The ab initio calculations by the HF/6-31G** and MP2/6-31G* methods indicated that intramolecular 1,4-N–H$^+$···O hydrogen bonding is more than twice stronger than intramolecular 1,4-N···H–O hydrogen bonding. For *N,N,N′,N′*-tetramethylethylenediamine (TMEDA), intramolecular 1,4-N–H$^+$···N hydrogen bonding is possible for the monoprotonated species ($TMEDAH^+$), and $(CH_3)_2N\cdots N(CH_3)_2$ and $(CH_3)_2NH^+\cdots H^+N(CH_3)_2$ repulsions are possible for TMEDA and the diprotonated species ($TMEDAH_2^{2+}$), respectively. In the present work, we have studied the effect of protonation on the conformation of TMEDA by Raman spectroscopy and ab initio theory, aiming at elucidating the existence and the strength of intramolecular 1,4-N–H$^+$···N hydrogen bonding.

The Raman spectra were measured for the liquid state, the 30% aqueous solution, and the HCl solution of TMEDA and for the solid state of ammonium salts $[TMEDAH_2]SO_4$ and $[TMEDAH_2]Cl_2$. The protonated state was determined on the basis of the titration curve. The ab initio molecular orbital calculations by the HF/6-31G** method were performed for possible conformers of TMEDA, $TMEDAH^+$, and $TMEDAH_2^{2+}$.[4] The relative energies of the conformers and their dipole moments are given in Table 1, where hydrogen bonding involved is indicated for the relevant conformers. The results of calculations show that for TMEDA the stable conformers are $G^{\pm}TG^{\pm}$, $G^{\pm}TG^{\mp}$, $G^{\mp}G^{\pm}G^{\mp}$, $G^{\mp}G^{\pm}G^{\pm}$, and $G^{\pm}TT$ with respect to the LN–C–C–NL bonds, where L denotes the lone pair of nitrogen. For $TMEDAH^+$, the most stable conformer is $G^{\mp}G^{\pm}G^{\mp}$ with respect to the H$^+$N–C–C–NL bonds, as shown in Figure 1, which is far more stable than others. The high stability of this conformer is explained by strong intramolecular 1,4-N–H$^+$···N hydrogen bonding, as supported by the calculated non-bonded distance 2.10 Å, which is much shorter than the sum of the van der Waals radii of hydrogen and nitrogen 2.70 Å, and the calculated partial charges $N^{-0.60}$–$H^{+0.39}\cdots N^{-0.66}$ in *e* units. The calculations showed that the conformers of $TMEDAH_2^{2+}$ with the *gauche* H$^+$NC–CNH$^+$ conformation were not optimized because of the electrostatic $(CH_3)_2NH^+\cdots H^+N(CH_3)_2$ repulsion.

Table 1. Relative energies of conformers of TMEDA, $TMEDAH^+$, and $TMEDAH_2^{2+}$ calculated by the HF/6-31G** method

Compound	Conformer[a]	Relative energy kJ mol^{-1}	Dipole moment D	Hydrogen bonding[b]
TMEDA	G$^{\pm}$TG$^{\pm}$	0.00	0.8	
	G$^{\pm}$TG$^{\mp}$	0.24	0.0	
	G$^{\mp}$G$^{\pm}$G$^{\mp}$	1.26	0.9	C–H···N (2)
	G$^{\mp}$G$^{\pm}$G$^{\pm}$	2.94	1.0	C–H···N (1)
	G$^{\pm}$TT	4.41	1.3	
	G$^{\mp}$G$^{\pm}$T	6.42	1.3	C–H···N (1)
	TTT	9.79	0.0	
$TMEDAH^+$	**G**$^{\mp}$G$^{\pm}$G$^{\mp}$	0.00		N–H$^+$···N (1)
	TG$^{\pm}$G$^{\mp}$	25.60		C–H···N (1)
	G$^{\pm}$TG$^{\mp}$	33.96		
	G$^{\pm}$TG$^{\pm}$	35.07		
	TTG$^{\pm}$	39.57		
	G$^{\pm}$TT	43.27		
	G$^{\mp}$G$^{\pm}$T	44.11		
	TTT	48.52		
$TMEDAH_2^{2+}$	**G**$^{\pm}$T**G**$^{\pm}$	0.00		
	G$^{\pm}$T**G**$^{\mp}$	2.08		
	G$^{\pm}$T**T**	5.80		
	TT**T**	11.53		

[a] The bold letter indicates the conformation around the H$^+$N–CC bond.
[b] C–H···N, weak intramolecular 1,5-C–H···N hydrogen bonding;[5] N–H$^+$···N, strong intramolecular 1,4-N–H$^+$···N hydrogen bonding. The number of hydrogen bonding involved is given in parentheses.

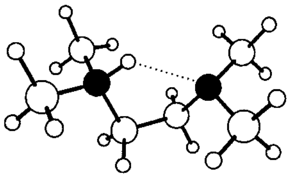

Figure 1. Molecular structure of the $G^{\mp}G^{\pm}G^{\mp}$ conformer of $TMEDAH^+$ optimized by the HF/6-31G** method. A dotted line indicates strong intramolecular 1,4-N–H$^+$···N hydrogen bonding.

Figure 2 shows the Raman spectra of solid $[TMEDAH_2]SO_4$ and $[TMEDAH_2]Cl_2$, and the calculated spectra for $G^{\mp}G^{\pm}G^{\mp}$ of $[TMEDAH_2]SO_4$ and $G^{\pm}TG^{\mp}$ of $[TMEDAH_2]Cl_2$. These results show that $TMEDAH_2^{2+}$ assumes $G^{\mp}G^{\pm}G^{\mp}$ in $[TMEDAH_2]SO_4$ and $G^{\pm}TG^{\mp}$ in $[TMEDAH_2]Cl_2$. Comparison with the calculated energies (Table 1) indicates that these conformers are stabilized primarily by intermolecular interactions in crystals. The molec-

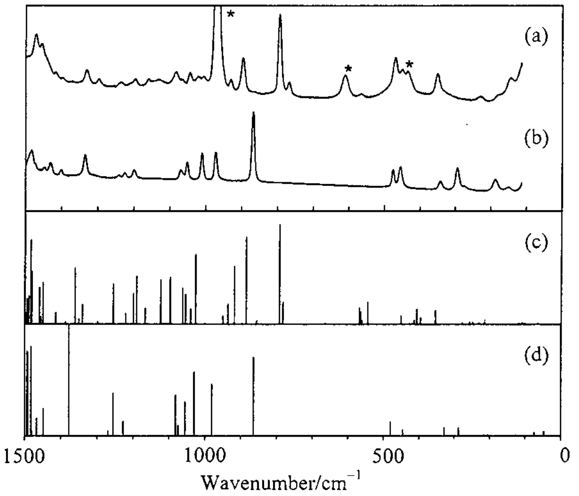

Figure 2. Raman spectra of ammonium salts: (a) solid $[TMEDAH_2]SO_4$ and (b) solid $[TMEDAH_2]Cl_2$, and calculated spectra for (c) $G^{\mp}G^{\pm}G^{\mp}$ of $[TMEDAH_2]SO_4$ and (d) $G^{\pm}TG^{\mp}$ of $[TMEDAH_2]Cl_2$. The asterisk indicates the bands due to sulfate ion. The calculated wavenumbers were scaled by a factor of 0.92.

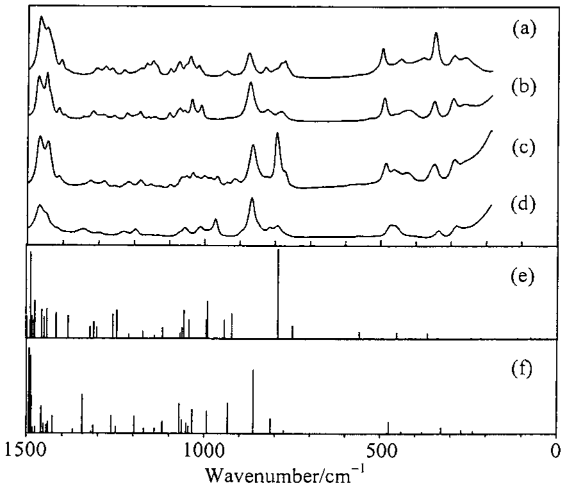

Figure 3. Raman spectra (a) in the liquid state of TMEDA, and in the 30% aqueous solution (b) at pH 11.8 (TMEDA), (c) at pH 7.8 ($TMEDAH^+$), and (d) at pH 3.2 ($TMEDAH_2^{2+}$), and the calculated spectra for (e) $G^{\mp}G^{\pm}G^{\mp}$ and (f) $G^{\pm}TG^{\mp}$ of $TMEDAH^+$. The calculated wavenumbers were scaled by a factor of 0.92.

ular structures of $[TMEDAH_2]SO_4$[6] and $[TMEDAH_2]Br_2$[7] were determined by X-ray diffraction, with $TMEDAH_2^{2+}$ in $G^{\mp}G^{\pm}G^{\mp}$ and $G^{\pm}TG^{\mp}$, respectively. Thus, the strong Raman bands at 794 and 870 cm^{-1} assigned to the NC_3 symmetric stretching vibration are due to the molecules with the *gauche* and *trans* NC–CN conformations, respectively, as supported by normal coordinate calculations.

Figure 3 shows the Raman spectra in the liquid state of TMEDA, and in the 30% aqueous solution at pH 11.8 (TMEDA), at pH 7.8 ($TMEDAH^+$), and at pH 3.2 ($TMEDAH_2^{2+}$), and the calculated spectra for $G^{\mp}G^{\pm}G^{\mp}$ and $G^{\pm}TG^{\mp}$ of $TMEDAH^+$. In the spectra for pH 11.8 and 3.2, strong bands are observed at 873 and 863 cm^{-1}, respectively, while in the spectrum for pH 7.8 two strong bands are observed at 793 and 865 cm^{-1}. Thus, the TMEDA and $TMEDAH_2^{2+}$ molecules assume predominantly the *trans* NC–CN conformation in aqueous solution, while a large number of $TMEDAH^+$ molecules assume the *gauche* NC–CN conformation ($G^{\mp}G^{\pm}G^{\mp}$), indicating the existence of strong intramolecular 1,4-N–H$^+$···N hydrogen bonding. For $TMEDAH^+$, the calculated Raman scattering activities of the bands at 793 cm^{-1} ($G^{\mp}G^{\pm}G^{\mp}$) and 865 cm^{-1} ($G^{\pm}TG^{\mp}$) are 20.1 and 16.8 Å^4 amu^{-1}, respectively. At pH 7.8 ($TMEDAH^+$), the number of molecules with the *gauche* NC–CN conformation is nearly the same as that of the molecules with the *trans* NC–CN conformation, in contrast with the $DMAEH^+$ molecules which assume predominantly the *gauche* NC–CO conformation.[2] This result shows that intramolecular 1,4-N–H$^+$···N hydrogen bonding is likely to be rather weaker than intramolecular 1,4-N–H$^+$···O hydrogen bonding.

The relative intensity of the band at 774 cm^{-1} in the liquid state is stronger than that at 784 cm^{-1} in aqueous solution. The population of the conformers in the liquid state is consistent with the calculated relative energies of the conformers of TMEDA given in Table 1. In aqueous solution, the TMEDA molecules assume predominantly the *trans* NC–CN conformation. This result is not explained by the effect of dielectric properties of solvent, because the dipole moment of $G^{\pm}TG^{\mp}$ is zero and the dipole moments of $G^{\pm}TG^{\pm}$ and $G^{\mp}G^{\pm}G^{\mp}$ are similar to each other (Table 1). It is likely that the formation of hydrogen bonding between the nitrogen atoms of TMEDA and water molecules stabilizes the *trans* NC–CN conformation rather than the *gauche* NC–CN conformation. The calculations showed that the molecules of $TMEDAH_2^{2+}$ prefer the *trans* NC–CN conformation to the *gauche* conformation, the latter being destabilized by the electrostatic repulsion between the two $(CH_3)_2NH^+$ groups.

In conclusion, the interconversion, depending on pH, between strong intramolecular 1,4-N–H$^+$···N hydrogen bonding and $(CH_3)_2N$···$N(CH_3)_2$ or $(CH_3)_2NH^+$···$H^+N(CH_3)_2$ repulsion is certainly one of the important structural factors in biological molecules such as polyamines.

References and Notes

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