Hydrogen Bonding Ability of Azabenzenes toward Thioacetamide, Acetamide, and Water

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Thermodynamic parameters for the hydrogen bonding interaction of azabenzenes with thioacetamide (TA) in carbon tetrachloride solution were determined using near-IR absorption spectroscopy. Pyridine (PY), pyridazine (PD), pyrimidine (PM), pyrazine (PZ), methylpyrazine (MPZ), 2,3-dimethylpyrazine (2,3-DMPZ), 2,5-dimethylpyrazine (2,5-DMPZ), and trimethylpyrazine (TMPZ) were chosen to investigate the position effect of nitrogen atoms and the substitution effect of methyl groups on the hydrogen bonding ability of azabenzenes. The standard enthalpy ($\Delta H°$) for the formation of 1:1 complexes of PY, PD, PM, and PZ with TA is −4.5, −5.4, −2.5, and −2.1 kcal/mol, respectively, which does not parallel the highest proton affinity of PY. The hydrogen bonding strength increases with the number of methyl substituents: $\Delta H° = -3.6$, −3.9, −3.7, and −4.2 kcal/mol, respectively, for MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ. The association energy of these complexes has been calculated at the B3LYP/6-311G** and B3LYP/6-31+G** levels, showing excellent agreement with the relative hydrogen bonding strength. We also calculated the association energy of 1:1 complexes of PY, PD, PM, and PZ with acetamide and water at the B3LYP/6-31+G** level. The association energy follows the same order PD > PY > PM > PZ for all three proton donors. The hydrogen bonding of two adjacent nitrogen atoms of PD may enhance the stability of the complex.

1. Introduction

Hydrogen bonding interaction has been of considerable interest because of its important role in chemical and biological processes. Tremendous studies have been therefore performed to gain insight into the characteristics of the hydrogen bond. In these studies, the hydrogen bonding ability of simple molecules as hydrogen bond donors or acceptors has been evaluated to parametrize accurate mechanical force fields for molecular modeling.

Azabenzenes that contain nitrogen atoms in an aromatic ring are known to be building blocks of oligonucleotides, pharmaceuticals, and polymers. The thermodynamic parameters for the hydrogen bonding ability of azabenzenes have been an important issue for a few decades. Joris et al. reported the correlation of the IR spectral shifts with the pK_a value of azabenzenes and with the equilibrium constants for the association of hydrogen-bonded complex with phenol.[1] Del Bene calculated the proton affinity (PA) of azabenzenes using ab initio methods.[2] Mó also performed similar ab initio calculations for the PA values.[3] Brinck et al. suggested that the experimental pK_a value of azabenzenes can be related to the molecular surface ionization energies.[4] These studies led to the finding that the relative basicity of pyridine (PY), pyridazine (PD), pyrimidine (PM), and pyrazine (PZ) is in the order PY > PD > PM > PZ.

More recently, a number of research groups focused the 1:1 complex of azabenzene with water (W) or methanol by experimental and theoretical approaches. Alagona et al. calculated the 1:1 complexes of PD, PM, and PZ with water at the SCF level with the MINI-1 and 4-31G basis sets.[5] Their interaction energies follow the order PD > PY > PM, which is inconsistent with the basicity and the proton affinity. Nobeli et al. considered the 1:1 complex with methanol using the intermolecular perturbation theory (IMPT) method and showed that the hydrogen bonding ability decreases following the order PY > PD > PM > PZ.[6] Caminati and co-workers demonstrated that the nitrogen lone pair of PD, PM, and PZ can form hydrogen bonding with water, using supersonic jet millimeter-wave absorption spectroscopy and ab initio calculation.[7−9] Cai and Peimers calculated the binding enthalpy of the hydrogen-bonded complex PY−W in the ground state and electronically excited state of PY.[10] Despite these intensive studies, the information on the strength of intermolecular hydrogen bonding is still limited and shows some controversy.

In the present work, we have investigated the hydrogen bonding ability of PY, PD, PM, and PZ toward the proton donors thioacetamide (TA), acetamide (AA), and water (W). Our group reported the evaluation of the hydrogen bonding strength for the 1:1 complex of PY and its methyl-substituted PY series with TA.[11] Here we extend the study to understand the position effect of nitrogen atoms on the hydrogen bonding ability of azabenzenes. The subsitutent effect of methyl groups on hydrogen

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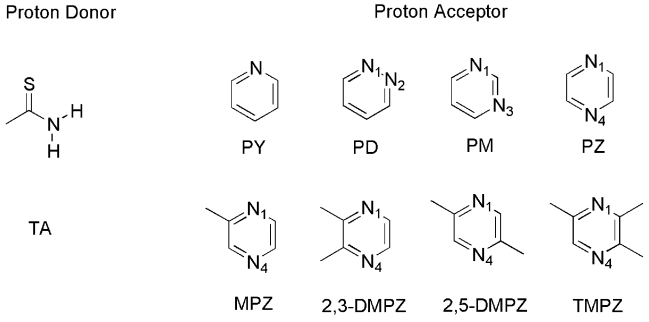

Figure 1. Chemical structures considered in this work.

bonding ability has been examined for methylpyrazine (MPZ), 2,3-dimethylpyrazine (2,3-DMPZ), 2,5-dimethylpyrazine (2,5-DMPZ), and trimethylpyrazine (TMPZ). The azabenzenes considered here are displayed in Figure 1. The near-IR (NIR) spectroscopic technique has been employed to measure the thermodynamic parameters for the interaction of these molecules with TA in carbon tetrachloride (CCl_4) solution. We calculated the proton affinity (PA) for the series of azabenzene molecules and the association energy of the 1:1 complex of TA:azabenzene at the B3LYP/6-31+G** and B3LYP/6-311G** levels of theory. We also computed the association energy for the 1:1 complex of PY, PD, PM, and PZ with AA and W at the B3LYP/6-31+G** level.

2. Methodology

2.1. Experimental Section. The samples used here, PY (Aldrich, 99.8%), PD (Aldrich, 98%), PM (Aldrich, 99%), MPZ (Aldrich, 99+%), 2,3-DMPZ (Aldrich, 99%), 2,5-DMPZ (Aldrich, 98%), TMPZ (Aldrich, 99%), and CCl_4 (J. T. Baker, HPLC grade), were dried by adding 4 Å molecular sieves (Aldrich) without further purification. Solid TA (Aldrich, 99%) and PZ (Aldrich, 99+%) were dried at room temperature under a reduced pressure ($\sim 10^{-2}$ Torr) for 24 and 1 h, respectively. The molar concentration ratio of TA (2.72−8.0 mM) to azabenzene in CCl_4 was 1:30 for PM, MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ, 1:50 for PZ, and 1:7 for PD.

To obtain the NIR absorption spectrum of the 1:1 hydrogen-bonded complex between TA and azabenzenes in CCl_4, a Cary 5G UV−vis−NIR spectrophotometer was used (Varian Inc.). Placing a matching cell containing an equal concentration of azabenzene in the path of the reference beam eliminated the absorption due to azabenzenes and CCl_4. The sample and reference cells were placed in a multicell holder (Varian Inc.) connected to a temperature controller (Varian Inc.). The temperature range was 278−328 K, and temperature fluctuation during the measurement was less than ±0.1 K. To remove the humidity, the cell compartment was purged by nitrogen gas passing through calcium chloride. The Peak Fit (AISN Software Inc.) program was used for the nonlinear least-squares fitting of the NIR absorption band by a Gaussian−Lorentzian product function. The program terminated its iteration when χ^2 was less than 1×10^{-7}. All experiments were performed over four times.

2.2 Computational Section. Proton affinity (PA) is defined as a negative value of enthalpy change for the reaction $B(g) + H^+(g) \rightarrow BH^+(g)$, where B denotes the base. The PA value of azabenzenes was calculated at the B3LYP/6-31G* level.[12,13] Geometry optimization for the azabenzene and protonated azabenzene molecules was performed without constraints. All stationary points were confirmed as minima, indicated by the absence of imaginary frequencies. To calculate the association energy of the 1:1 TA:azabenzene complex, we first considered all plausible conformers at the HF/6-31G* level.[13] The *anti*-H and *syn*-H of TA form hydrogen bonds with the N atom of azabenzene. In the case of MPZ and TMPZ, two conformers were considered for the different hydrogen bonding acceptor sites N1 and N4 (Figure 1). The resulting HF/6-31G* complexes for TA:azabenzene were further fully optimized at the B3LYP/6-31+G** and B3LYP/6-311G** levels of theory. The basis set superposition error (BSSE) was calculated with the aid of the conventional counterpoise (CP) procedure including the influence of geometry relaxation upon the complex formation.[14] The association energies for the 1:1 complexes of PY, PD, PM, and PZ with AA and W as hydrogen bond donors were calculated at the B3LYP/6-31+G** level. All computations were carried out using the Gaussian program.[15]

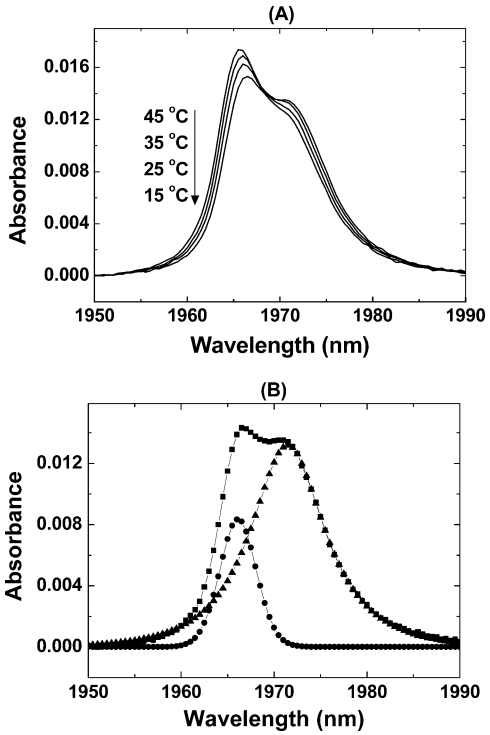

Figure 2. (A) The υ_{N-H}^{as} + amide II combination band of 7.52 mM TA with 225.6 mM PM in CCl_4 at various temperatures, showing an isosbestic point. (B) Resolved υ_{N-H}^{as}+ amide II combination band of 7.52 mM TA with 225.6 mM PM at 278 K. Filled squares (■), filled circles (●), and filled triangles (▲) represent the measured absorption spectrum, the resolved monomeric band, and the resolved hydrogen-bonded band, respectively.

3. Results and Discussion

3.1. Thermodynamic Parameters for the 1:1 Complex between TA and Azabenzenes. Our previous works showed that the υ_{N-H}^{as}+ amide II combination band of TA is appropriate to obtain the thermodynamic parameters of intermolecular hydrogen bonding interaction because of its large absorption coefficient and little interference from other peaks.[11,16] Figure 2A shows the υ_{N-H}^{as}+ amide II combination band of 7.52 mM TA with 225.6 mM PM as a function of temperature in the range 288−318 K. The spectra show an isosbestic point, implying that only two species, monomeric and hydrogen-bonded TA, are in equilibrium. The band can be resolved into two bands whose peak is at 1965 nm (5089 cm^{-1}) and 1971 nm (5074 cm^{-1}) as shown in Figure 2B. The two bands are assigned to the monomeric TA and the hydrogen-bonded TA, respectively. Each of the monomeric and the hydrogen-bonded

TABLE 1: Equilibrium Constants and Thermodynamic Parameters for the Hydrogen Bonding Formation of TA with PY, PD, PM, PZ, MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ in CCl_4

	equilibrium constant (M^{-1})							
acceptors	278 K	288 K	298 K	308 K	318 K	328 K	$\Delta H°$ (kcal/mol)	$\Delta S°$ (cal/mol K)
PY[a]		18.1 ± 0.9	13. 9 ± 0.7	11. 3 ± 0.6	8.6 ± 0.4		−4.5 ± 0.1	−9.9 ± 0.2
PD	147.6 ± 5.2	111.9 ± 1.5	81. 3 ± 1.6	59. 4 ± 2.1	46.0 ± 0.9	33.3 ± 0.8	−5.4 ± 0.1	−9.5 ± 0.2
PM	12.1 ± 0.5	11.3 ± 0.4	9.6 ± 0.5	8.6 ± 0.2	7.6 ± 0.2	6.1 ± 0.3	−2.5 ± 0.1	−4.0 ± 0.4
PZ	6.7 ± 0.3	6.2 ± 0.1	5.6 ± 0.4	5.0 ± 0.3	4.4 ± 0.2	3.8 ± 0.1	−2.1 ± 0.1	−3.7 ± 0.3
MPZ	13.0 ± 1.7	10.1 ± 1.0	8.2 ± 0.7	7.1 ± 0.3	5.7 ± 0.2	4.8 ± 0.1	−3.6 ± 0.2	−8.0 ± 0.7
2,3-DMPZ	13.9 ± 0.7	10.9 ± 0.5	8.6 ± 0.4	6.8 ± 0.4	5.6 ± 0.4	4.8 ± 0.3	−3.9 ± 0.2	−8.8 ± 0.5
2,5-DMPZ	15.2 ± 0.5	12.0 ± 0.8	9.7 ± 1.0	8.0 ± 0.4	6.6 ± 0.4	5.5 ± 0.2	−3.7 ± 0.2	−7.8 ± 0.6
TMPZ	16.2 ± 0.7	12.4 ± 0.7	9.4 ± 0.5	7.8 ± 0.2	6.2 ± 0.2	5.2 ± 0.2	−4.2 ± 0.2	−9.5 ± 0.8

[a] Reference 11.

TABLE 2: Total Electric Energy (E_{elec}) and Zero-Point Energy (ZPE) of Azabenzenes (B) and Their Protonated Form (BH^+), and Proton Affinity (^{theo}PA) Calculated at B3LYP/6-31+G Level**

molecule (B)	E_{elec} of B[a] (hartrees)	ZPE of B (hartrees)	E_{elec} of BH^+ (hartrees)	ZPE of BH^+ (hartrees)	^{theo}PA (kcal/mol)	^{exp}PA[b] (kcal/mol)
PY	−248.284 973	0.089 037	−248.656 978	0.103 258	215.5	220.8
PD	−264.211 222	0.076 366	−264.562 455	0.090 866	211.3	215.6
PM	−264.246 442	0.077 283	−264.586 871	0.090 857	205.1	210.5
PZ	−264.240 185	0.077 05	−264.576 297	0.090 792	202.3	209.0
MPZ[b]	−303.534 372	0.104 593	−303.879 113	0.118 217	207.8	
MPZ[d]			−303.877 827	0.118 235	207.0	
2,3-DMPZ	−342.827 186	0.132 546	−343.178 479	0.146 063	212.0	
2,5-DMPZ	−342.828 305	0.132 122	−343.179 587	0.145 715	211.9	
TMPZ[c]	−382.121 151	0.159 958	−382.479 501	0.173 333	216.5	
TMPZ[d]			−382.478 502	0.173 364	215.8	

[a] Total electric energies and zero-point energies are in hartrees. [b] Experimental PA values, ref 20. [c] Protonated at N1 position. [d] Protonated at N4 position.

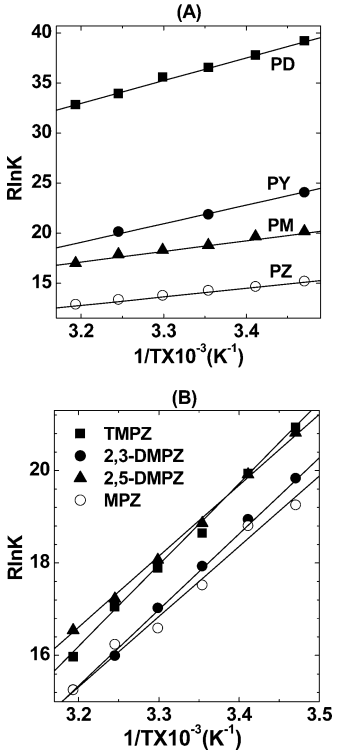

Figure 3. Plot of $R \ln K$ vs $1/T$ for 1:1 complex formation of TA with (A) PY, PD, PM, and PZ and (B) MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ.

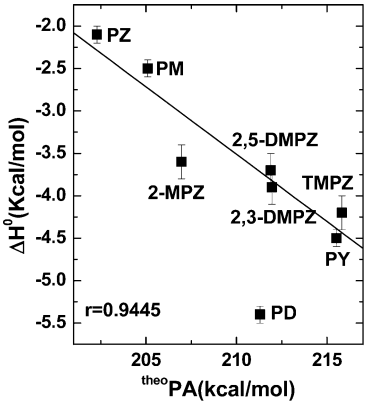

Figure 4. Plot of correlation between standard enthalpy change ($\Delta H°$) for formation of hydrogen-bonded TA:azabenzene complexes and PA (^{theo}PA) values calculated at B3LYP/6-31G* level. The line corresponds to a linear fit for the data excluding PD.

TA absorption bands is well fitted by a Gaussian−Lorentzian product function. The detailed procedure of data analysis was reported in our previous works.[16d]

Since TA and azabenzene form a 1:1 complex, the equilibrium of hydrogen-bonded complex formation and its equilibrium constants (K) could be expressed by the following equations:

$$\text{TA} + \text{acceptor} \rightleftharpoons \text{TA:acceptor} \qquad (1)$$

$$K = C_{1:1}/(C_{\text{mono}}C_{\text{free}}), \qquad C_{1:1}/C_{\text{mono}} = C_{\text{free}}K$$

Here, $C_{1:1}$ is the concentration of the hydrogen-bonded TA, C_{mono} is the concentration of monomeric TA, and C_{free} is the concentration of the free proton acceptors. As an approximation, the concentration was used instead of the activity. The ratio of $C_{1:1}$ to C_{mono} is obtained directly from the area of the two resolved bands, because the integrated absorption coefficients of the two bands are the same. The linear fit of the $C_{1:1}/C_{\text{mono}}$ vs C_{free} plot yields the equilibrium constant (K).

Table 1 contains the equilibrium constants for the formation of hydrogen-bonded 1:1 TA:azabenzene complexes at the

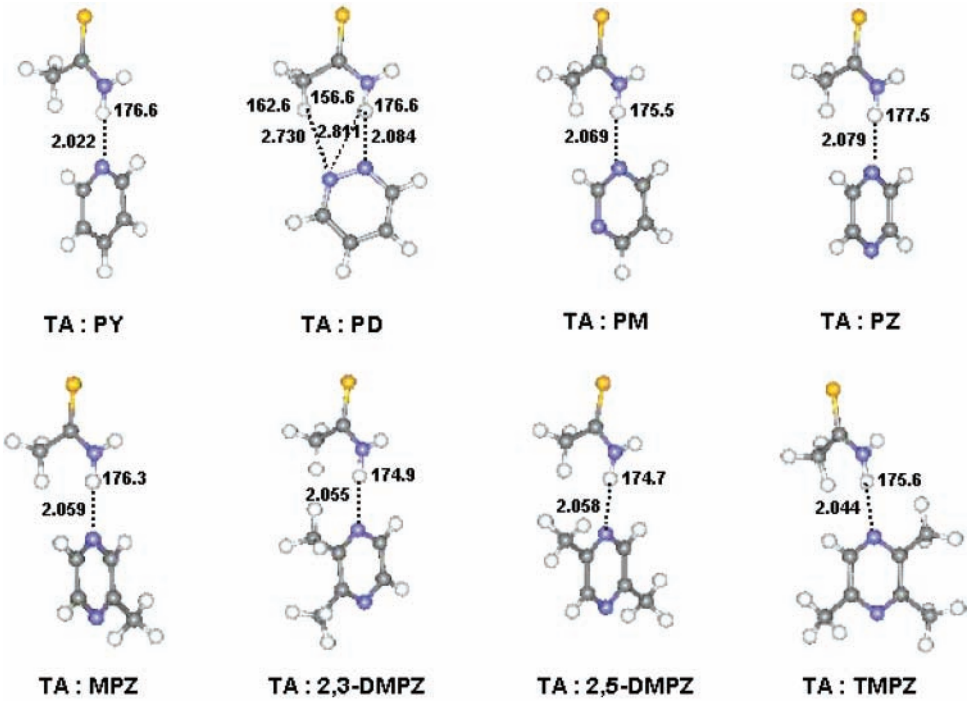

Figure 5. Equilibrium structure of TA:azabenzene complexes formed via *anti*-H of TA, calculated at B3LYP/6-31+G** level. The hydrogen bond distances (in angstroms) and angles (in degrees) are displayed.

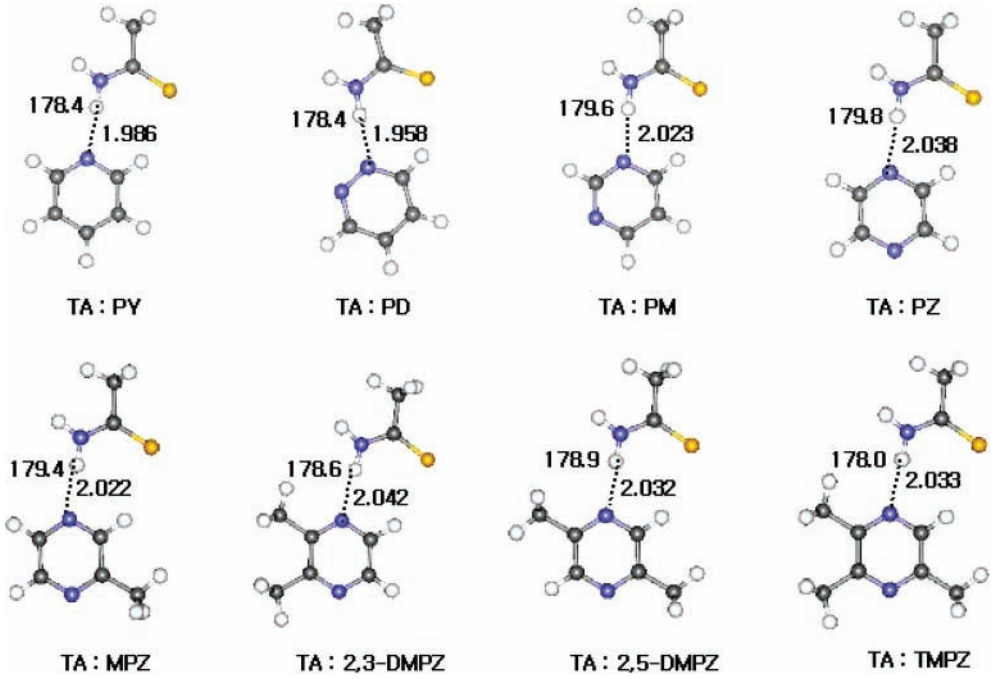

Figure 6. Equilibrium structure of TA:azabenzene complexes formed via *syn*-H of TA, calculated at B3LYP/6-31+G** level. The hydrogen bond distances (in angstroms) and angles (in degrees) are displayed.

temperatures 278, 288, 298, 308, 318, and 328 K. The thermodynamic parameters of $\Delta H°$ and $\Delta S°$ for the hydrogen bonding interaction can be evaluated by using the van't Hoff equation, $(\ln K)/\mathrm{d}(1/T) = -\Delta H°/R$. Figure 3 shows a plot of $R \ln K$ vs $1/T$, which fit well to the linear function. The respective $\Delta H°$ values are -4.5 ± 0.1, -5.4 ± 0.2, -2.5 ± 0.1, and -2.1 ± 0.2 kcal/mol for PY, PD, PM, and PZ. The $\Delta H°$ value of PD is higher by 0.9 kcal/mol than that of PY. PM and PZ have the much lower values of $\angle\Delta H°$ than PY by 2.0 and 2.4 kcal/mol, respectively.

The $\Delta H°$ values are -3.6 ± 0.2, -3.9 ± 0.2, -3.7 ± 0.2, and 4.2 ± 0.2 kcal/mol, respectively for MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ. The substitution of the first methyl group enhances the $-\Delta H°$ value by 1.5 kcal/mol. Further methyl substitution increases the $-\Delta H°$ value by about 0.3 kcal/mol per methyl group. In the methyl-substituted PY series, the substitution of one methyl group increases the $-\Delta H°$ value by about 0.5 kcal/mol on average.[11] Therefore, the result reveals that the methyl substituent effect on the hydrogen bonding ability of azabenzene can depend on the molecule.

3.2. Proton Affinity (PA). It is known that PA could reflect the hydrogen bonding ability or basicity for certain molecules.[17−19] Table 2 lists the PA value of azabenzenes considered here. The PA value follows the order PY > PD > PM > PZ, which is

TABLE 3: Association Energy of Hydrogen-Bonded 1:1 Complexes of TA:Azabenzene at B3LYP/6-31+G and B3LYP/6-311G** Levels of Theory**

	E_{assn}[a] (kcal/mol)		E_{assn}[b] (kcal/mol)	
acceptors	anti	syn	anti	syn
PY	−7.18 (−8.61)[c]	−7.35 (−8.40)	−6.79 (−6.91)	−6.95 (−7.07)
PD	−7.42 (−8.91)	−8.99 (−9.85)	−7.00 (−7.37)	−8.46 (−8.66)
PM	−5.89 (−7.26)	−7.25 (−8.20)	−5.53 (−5.66)	−6.83 (−6.96)
PZ	−5.62 (−6.95)	−6.59 (−7.56)	−5.29 (−5.46)	−6.18 (−6.33)
MPZ[d]	−5.65 (−7.15)	−6.35 (−7.39)	−5.29 (−5.44)	−5.94 (−6.11)
MPZ[e]	−6.04 (−7.39)	−6.85 (−7.84)	−5.67 (−5.84)	−6.42 (−6.59)
2,3-DMPZ	−5.94 (−7.45)	−6.15 (−7.00)	−5.58 (−5.67)	−5.75 (−5.78)
2,5-DMPZ	−6.03 (−7.53)	−6.60 (−7.63)	−5.64 (−5.83)	−6.18 (−6.34)
TMPZ[d]	−5.64 (−7.35)	−5.44 (−6.79)	−5.22 (−5.32)	−4.97 (−5.03)
TMPZ[e]	−6.33 (−7.82)	−6.41 (−7.26)	−5.91 (−6.04)	−5.98 (−6.00)

[a] Without BSSE. [b] With BSSE. [c] Calculated at the B3LYP/6-311G** level in parentheses. [d] At N1 position. [e] At N4 position.

consistent with the experimental PA values.[20] However, the PA values are not correlated with the experimental result that the hydrogen bond strength ($-\Delta H°$) of PD is higher than that of PY. The calculated PA value increases with the number of methyl groups, showing a good agreement with the $-\Delta H°$ value. In MPZ and TMPZ, the N1 atom is the more favorable protonation site than the N4 atom. Figure 4 shows a good linear correlation between the PA and $-\Delta H°$ values. However, PD exhibits a significant deviation from the linear correlation.

Del Bene explained why the PA value follows the order PD > PM > PZ, in terms of the nonbonding orbital energy calculated using the 4-31G basis set.[2] Increasing the nonbonding orbital energy of the base correlates with increasing PA. The interaction between two nonbonding orbital electron pairs on the nitrogen atoms results in a destabilization of the nonbonding orbital over both nitrogen atoms. The unstable nonbonding orbital for PD is probably due to the strong interaction of adjacent 2p orbitals. Mó suggested that the extra stabilization of the protonated form via intramolecular hydrogen bonding would result in a higher PA value of PD than those of PM and PZ.[3]

3.3. Association Energies and Structures of 1:1 Complexes of TA:Azabenzene. We calculated the association energies for the 1:1 TA:azabenzene complexes for two different hydrogen bond donor sites (*anti*-H and *syn*-H) of TA in the gas phase. The results were compared with the experimental value $-\Delta H°$ using a plausible assumption that the nonpolar solvent CCl_4 would not influence the hydrogen bonding interaction between TA and azabenzenes. Figure 5 shows the equilibrium structures and selected geometric parameters of azabenzene complex formed via *anti*-H of TA calculated at the B3LYP/6-31+G** level. The aromatic ring of PY, PM, PZ, and the methyl-substituted PZ derivatives is nearly perpendicular to the plane of TA. In contrast, PD forms a planar structure with TA and thus can have three hydrogen bonds involving in N−H···N1, N−H···N2, and C−H···N2. We found that the planar structure is more stable than the perpendicular structure by −0.21 kcal/mol. Although the C−H···N2 bond can be weak, this interaction may contribute to forming the planar structure of TA−PD complex. These cooperative interactions would stabilize the complex, resulting in a better hydrogen bonding ability of PD than that of PY. Figure 6 shows the equilibrium structures and selected geometric parameters for the complex formed via *syn*-H of TA. The equilibrium structure is planar irrespective of the molecules, which would result from the C−H···S interaction.

Table 3 lists the calculated association energy (E_{assn}) without BSSE and with BSSE at the B3LYP/6-31+G** and B3LYP/6-311G** levels. The complex formed via *syn*-H of TA is more energetically stable than that formed via *anti*-H. Remarkably,

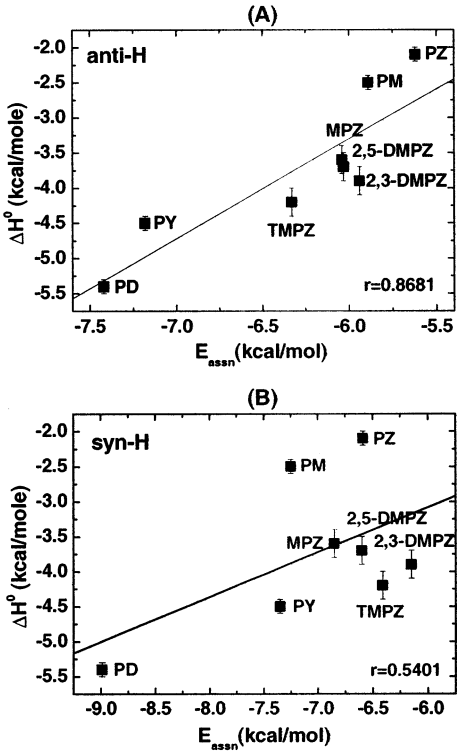

Figure 7. Plot of $\Delta H°$ value vs association energy (B3LYP/6-31+G** without BSSE) of 1:1 TA:azabenzene complex formed via (A) *anti*-H and (B) *syn*-H of TA.

the E_{assn} value of PD:*anti*-H (or *syn*-H) TA is higher than that of *anti*-H (or *syn*-H) PY, which is consistent with the experimental results. For MPZ and TMPZ, TA forms more stable complexes with the N4 atom than with the N1 atom. It is probably related to the steric hindrance of the methyl group toward the H of TA.[11] Parts A and B of Figure 7 show the plot of $-\Delta H°$ vs E_{assn} calculated at the B3LYP/6-31+G** level without BSSE for *anti*-H and *syn*-H of TA, respectively. The E_{assn} value for *anti*-H of TA shows a better correlation with the $-\Delta H°$ value than that for *syn*-H of TA. This trend is also found at the B3LYP/6-31+G** when BSSE is included and also at the B3LYP/6-311G** level. It suggests that *azabenzenes may form a hydrogen bond with TA via anti-H rather than syn-H.* The results are supported by our NMR data showing that TA forms a more stable hydrogen-bonded complex via *anti*-H with a series of acetamides, e.g., *N*,*N*-dimethylacetamide, *N*,*N*-diethylacetamide, and *N*,*N*-diisopropylacetamide.[16d,e] Therefore, we suggested that the conformer of TA:azabenzene complex via *anti*-H would be more favorable although the calculations predict a more stable conformer for *syn*-H.

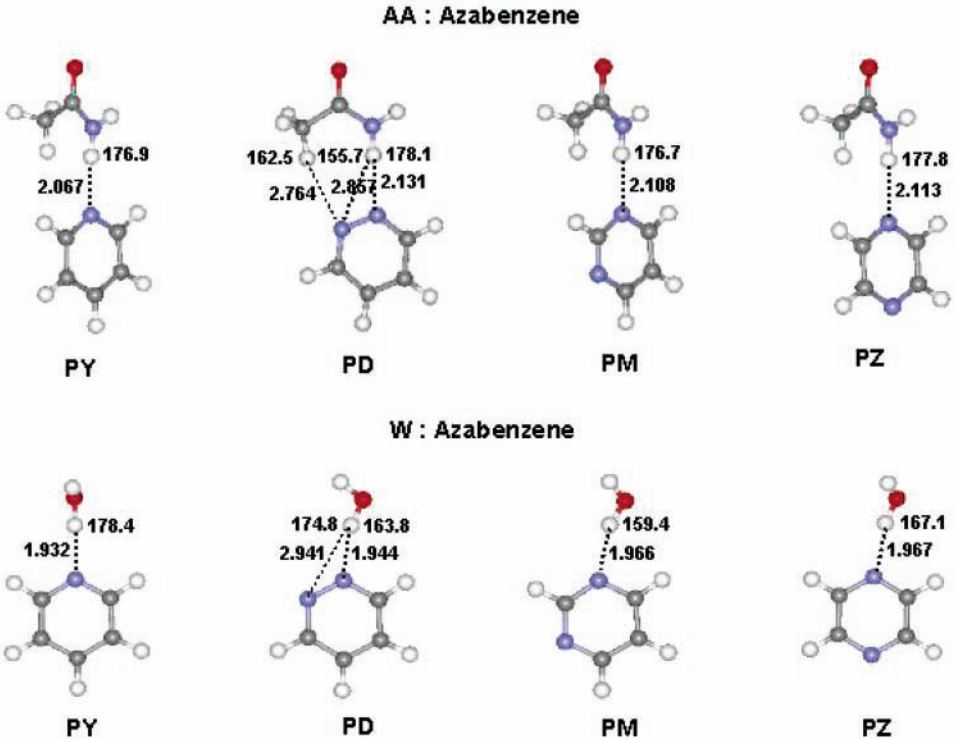

Figure 8. Equilibrium structure of AA:azabenzene formed via *anti*-H of TA and W:azabenzene calculated at B3LYP/6-31+G** level. The hydrogen bond distances (in angstroms) and angles (in degrees) are displayed.

TABLE 4: Association Energy (kcal/mol) of 1:1 Complex of PY, PD, PM, and PZ with Different Hydrogen Bond Donors Calculated at B3LYP/6-31+G Level**

	PY	PD	PM	PZ
TA[a]	−7.18[b] (−6.79)[c]	−7.42 (−7.00)	−5.89 (−5.53)	−5.62 (−5.29)
AA[a]	−6.25 (−5.90)	−6.40 (−6.00)	−5.18 (−4.82)	−4.96 (−4.56)
water	−6.95 (−6.44)	−7.20 (−6.61)	−6.19 (−5.70)	−5.87 (−5.40)
water[d]	−6.03	−6.14	−5.38	

[a] *anti*-H. [b] Without BSSE. [c] With BSSE. [d] Reference 9.

3.4. Comparison of Hydrogen Bond Donor Ability of TA, AA, and W. The experimental $-\Delta H°$ and the theoretical E_{assn} values indicate consistently that PD is a stronger hydrogen bond acceptor than PY when TA is the hydrogen bond donor. Now we question if this novelty is limited to only TA. We therefore computed the association energies of 1:1 complexes for PY, PD, PM, and PZ with other proton donors AA and W. Since our results imply that the conformer of TA:azabenzene complex via *anti*-H would be more favorable, we focused only on the anti forms of AA with azabenzenes.

To evaluate the hydrogen bonding strength between AA and azabenzene, the plausible conformers via *anti*-H of AA were examined at the HF/3-21G level and fully optimized at the B3LYP/6-31+G** level. For W:azabenzene complex, the structure optimization at the B3LYP/6-31+G** level were started from the available experimental and theoretical geometries.[6−8] The equilibrium structures of the complex with AA and W are displayed in Figure 8. The present structure corresponds to the lowest energy minimum that would be suitable to understanding the hydrogen bonding ability of azabenzenes. The association energy of azabenzenes with AA and W, calculated at the B3LYP/6-31+G** level, is summarized in Table 4, showing the same order PD > PY > PM > PZ as that of TA. The structure of AA:PD and W:PD is also planar, similar to the TA:PD complex. This implies that cooperative interaction would also stabilize the hydrogen-bonded complexes with AA and W. It is noteworthy that the E_{assn} value of AA is always lower than that of TA for all four azabenzenes. This result is consistent with the recent theoretical studies revealing that formamide is a weaker hydrogen donor than thioamide.[21] Interestingly, the E_{assn} value of W is lower than that of TA for PY and PD, but is higher for PM and PZ. Further study would be necessary to explain such unique behavior of water as a hydrogen bond donor.

4. Conclusion

The intermolecular hydrogen bonding strength has been studied experimentally and theoretically for a series of azabenzenes: PY, PD, PM, PZ, MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ. The $-\Delta H°$ value for the formation of hydrogen-bonded 1:1 TA:azabenzene complex in CCl_4 has been measured using the temperature-dependent NIR spectrum of TA. The $\Delta H°$ values for PY, PD, PM, and PZ are −4.5, −5.4, −2.5, and −2.1 kcal/mol, respectively, following the order PD > PY > PM > PZ. The $\Delta H°$ values are −3.6, −3.9, −3.7, and −4.2 kcal/mol, respectively, for MPZ, 2,3-DMPZ, 2,5-DMPZ, and TMPZ, showing an increase with the number of methyl groups. The PA value has been calculated at the B3LYP/6-31G* level, which can be linearly correlated with the relative hydrogen bonding strength ($-\Delta H°$). However, it cannot predict the highest hydrogen bonding strength of PD. The association energy of the 1:1 TA:azabenzene complex has been calculated at the B3LYP/6-31+G** level without and with BSSE correction, showing an excellent consistency with the hydrogen bonding strength. The association energy for the complex formed via *anti*-H of TA has a better linear correlation with the experimental $\Delta H°$ value, suggesting that the azabenzene molecules may form hydrogen bonding via the *anti*-H of TA. We also calculated the association energy of AA and W for PD, PY, PM, and PZ, showing that it follows the same order as that of TA. We suggest that a bifurcated hydrogen bonding of PD toward the protons of TA, AA, and W would enhance the stability of the complex.

Supporting Information Available: Tables S1 and S2 listing the Cartesian coordinates of the B3LYP/6-31+G** optimized structure of azabenzenes with TA, AA, and W; Table S3 listing the binding energy of the hydrogen-bonded 1:1 complex of azabenzenes with *anti*-H of TA at the B3LYP/6-31+G** and B3LYP/6-311G** levels of theory; Table S4 listing the binding energy of azabenzenes with *anti*-H of AA and W at the B3LYP/6-31+G** level. This material is available free of charge via the Internet at http://pubs.acs.org.

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