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# Solvent Effect on Hydrogen-Bonded Acetic Acid...Arginine/Imidazole/ Phenol Dyads

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**Research Article** 

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## Abstract

The hydrogen bond plays a vital role in structural arrangement, intermediate state stabilization, and biological activity of certain enzymatic reactions. The hybrid B3LYP functional was employed with 6-311++G(d, p) basis set for the exploration about the solvent effect on hydrogen-bonded acetic acid...arginine, acetic acid...imidazole, acetic acid...phenol dyads, as well as the Tyr...Asp...Arg triads. The difference of two hydrogen bonds lengths in every dyad is enlarged in diethyl ether solvent as compared to that in gas phase. The increasing of solvent dielectric constant enhances the isomers' relative stability owing to the interaction between the polar conformer and the polarity solvent molecules. While the proton transfer barrier reduces. The linear relationship between dipole moment and stability can be utilized to estimate the stability modification by measuring the alteration of dipole moment of the dyad.

**Keywords:** Hydrogen bond; Density functional theory; Solvent effect; Potential energy surface; Proton transfer

#### Introduction

Hydrogen bond, which is ubiquitous in chemistry, biology, and materials, plays a fundamental role in many aspects of molecular science. According to the bond energy between a donor group (XH) and an acceptor (Y) (Both X and Y are electronegative atoms), the hydrogen bonds are classified into three types:

(i) weak or conventional with the interaction ranges from 2.4 to 12 kcal/mol;

(ii) strong or low-barrier with the coupling between 12 and 24 kcal/mol;

(iii) very strong or single-well with over 24 kcal/mol interaction [1].

The hydrogen bond plays a vital role in structural arrangement, intermediate state stabilization, material function, and biological activity of certain enzymatic reactions. Especially, the successive hydrogen bonds constitute the channel for proton transfer. Generation or breakage of a hydrogen bond can produce significant changes in the kinetics or mechanism of an enzymatic reaction. The nature of the hydrogen bond in solution is of particular interest and has been probed extensively utilizing various experimental and theoretical methods [2-6].

It is reported that a strongly hydrogen bonded tyrosine residue within the active site of enzyme ketosteroid isomerase facilitates quantum proton delocalization, which dramatically stabilizes the deprotonation of the tyrosine residue, resulting in a very large isotope effect on its acidity [7]. Where, the heavy-atom distances in hydrogen-bonds are slightly longer (~ 2.6 Å) than those typically associated with low-barrier hydrogen bonds (LBHB) [1,8,9], which have been characterized in a variety of systems [10-13]. To simulate the electron and proton transfer behavior in photosystem, the phenolimidazole-base triads have been employed with a special emphasis on solvent effect [14]. The hydrogen-bonded triads have been observed in exoglucanase [15,16]. The hydrogen bonds have been observed in a number of enzymes, and play a vital role in the substrate recognition, the generation of enzyme-substrate complex, the detailed reaction mechanism, as well as the formation and delivering of the product [17,18].

To reveal the role of these hydrogen bonds in the enzyme, it is necessary to recognize the characteristic of this network.

The hydrogen bonded dyads, generated by acetic acid and one of phenol, imidazole, and arginine, as well as the Tyr...Asp...Arg triads are explored. Section 2 presents the computational details. The solvent effects on geometry structure, proton transfer mechanism, IR spectra, and the relative stability are compared. The results and discussion are collected in Section 3. Section 4 shows the conclusion.

## **Computational Details**

The well-developed density functional theory (DFT) with the Becke three parameterized Lee-Yang-Parr (B3LYP) exchange correlation functionals has been proven to be successful in describing large free radicals and hydrogen bonded complexes [14,19,20]. All calculations were performed employing B3LYP functional with the 6-311++G(d, p) basis set using a suite of Gaussian 09 programs [21]. At the same level, the vibrational frequency calculations were carried out to confirm the optimized stationary points to be local minima or transition states on the potential energy surfaces (PES). Solvent effect on geometry structure, IR spectra, and the energy profile for proton transfer was compared employing the integral equation formalism polarizable contimuum model (PCM) within the framework of the self-consistent reaction field theory (SCRF), which was well-developed and accepted in treating solvent effects of molecular properties. The solvent effects were estimated using the diethylether and water solvents with the dielectric constant of 4.2 and 78.4. The variations of geometrical structure, IR spectra, and the proton transfer energy profile upon reduction and oxidation are also detected [22-24].

## **Results and Discussion**

The acetic acid...arginine (AA), acetic acid...imidazole (AI),

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Received September 23, 2016; Accepted October 05, 2016; Published October 10, 2016

Citation: Shihai Y, Kang W, Sun L (2016) Solvent Effect on Hydrogen-Bonded Acetic Acid...Arginine/Imidazole/Phenol Dyads. Med Chem (Los Angeles) 6: 604-610. doi:10.4172/2161-0444.1000405

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acetic acid...phenol (**AP**) dyads, as well as the Tyr...Asp...Arg (**TAA**) triads in gas phase and diethylether solvent were explored. Here, the methyl-guanidine is employed as a model for arginine. The primary geometrical parameters optimized in gas phase, as well as those obtained in diethylether solvent (labeled with italic character) are presented in Figure 1. The IR spectra of these complexes in gas phase and solvent are collected in Figures 2 and 3 denotes the one-dimensional (1D) potential energy surface of **AA** dyad in gas phase, as well as in the diethylether and water solvents. The corresponding 2D potential energy surfaces of **AA** and **AP** in gas phase and diethylether solvent are described in Figures 4 and 5, respectively. The variation of relative energy along with the dipole moment when the environment changes from gas phase into diethylether solvent is shown in Figure 6.

### **Geometrical structure**

Three conformations (AA1 ~ AA3) are determined according to two protons location for the acetic acid...arginine (AA) dyad. In AA1, the O<sup>e2</sup>...HN<sup>n2</sup> hydrogen bond distance is 2.914 Å (Table 1), longer than that of O<sup>e1</sup>H...N<sup>n1</sup> (2.649 Å), which carries the characteristic of low barrier hydrogen bond (LBHB). The protons positions are opposite in AA2 as compared with those in AA1. The O<sup>e1</sup>...HN<sup>n1</sup> and O<sup>e2</sup>H...N<sup>n2</sup> hydrogen bonds distances are 2.888 and 2.627 Å, respectively (Figure 1). Thus, the distance of OH...N is shorter than that of O...HN. As indicates that the larger the electronegativity of the atom covalently bonded with hydrogen is, the stronger the hydrogen bond is. Two fragments coupling through hydrogen bonds in AA1 and AA2, where two moieties remain neutral. The coupling between two fragments of AA3 varies into cation...anion electrostatic interaction. Both protons locate at nitrogen site in AA3, with short O...HN distances (2.587 and 2.636 Å) and bearing the LBHB features. Two isomers are optimized for the acetic acid...imidazole (AI) dyad, AI1 and AI2. The bare nitrogen of the imidazole fragment acts as the hydrogen bond acceptor in both of them. No proton transferred AI conformer is found. The N...HO bond is a little longer by ~0.1 Å than those in AA dyads. While, the CH...O coupling is weak, as is manifested by the longer distance of H...O (Table 2).

In the first isomer of acetic acid...phenol dyad, **AP1**, the hydroxyl group acts as both the proton donor and acceptor, with the O<sup>n</sup>H...  $O^{\epsilon_1}$  and  $O^{\epsilon_2}H...O^{\eta}$  distances of 2.729 and 2.788 Å, respectively. The electronegativity of O<sup>n</sup> should be larger than O<sup>ε2</sup>, as reflects the electron withdrawing property of benzene ring. The hydroxyl group of phenol fragment in this conformer, similar to OH in water, acts as the bridge during the proton relay from O<sup>ε2</sup>H to O<sup>ε1</sup>. Besides, the proton transferred conformer is same with **AP1**, and they are antipode. When  $O^{\eta}$  and the adjacent CH group serving as the hydrogen bond acceptor and donor, respectively, the AP2 structure is generated, with longer O<sup>ε2</sup>H...O<sup>η</sup>/ CH...O<sup>ε1</sup> distances (2.832/3.470 Å). Only one state is determined for gaseous hydrogen bonded neutral Tyr...Asp...Arg triad TAA1), where three residues are all neutral. The hydrogen bond between Tyr and Asp is longer by 0.10 Å than that between Asp and Arg. The optimized CO distance in neutral triads (1.360 Å) is in good agreement with that calculated for phenol (1.370 Å).14 It was pointed out that the CO bond length was dominated by the n value in  $sp^n$  hybridization of oxygen and carbon atoms of the phenolic CO sigma bond.

The solvent effect on geometry structure is explored employing the diethylether solvent. The corresponding parameters are gathered together with those obtained in gas phase in Figure 1. Based on the initial structure utilized in gas phase optimization, all stationary





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	AA1			AA2	AA3		
	Gas	Diethylether	Gas	Diethylether	Gas	Diethylether	
O <sup>ℓ1</sup> H/N <sup>η1</sup> H	1.032	1.058	1.024	1.022	1.098	1.056	
O <sup>ε1</sup> N <sup>η1</sup>	2.649	2.592	2.888	2.918	2.587	2.700	
O <sup>ε2</sup> H/N <sup>η2</sup> H	1.023	1.021	1.040	1.075	1.075	1.051	
Ο <sup>ε2</sup> Ν <sup>η2</sup>	2.914	2.948	2.627	2.565	2.636	2.722	

Table 1: Primary geometrical parameters (Å) of acetic acid...arginine isomers optimized at B3LYP/6-311++G(d, p) basis set level.

	Al1		Al2			AP1		AP2	
	Gas	Diethylether	Gas	Diethylether		Gas	Diethylether	Gas	Diethylether
(C)HO	2.415	2.664	2.575	2.847	O <sup>n</sup> H	0.977	0.977	0.963	0.965
OH	1.009	1.022	1.006	1.019	HO <sup>ε1</sup>	2.729	2.747	2.432	2.553
NO	2.726	2.676	2.737	2.686	HO <sup>2</sup>	0.982	0.982	0.980	0.982
					O <sup>η</sup> Ο <sup>ε2</sup>	2.788	2.798	2.832	2.806

Table 2: Primary geometrical parameters (Å) of acetic acid...imidazole and acetic acid...phenol isomers optimized at B3LYP/6-311++G(d, p) basis set level.

states are determined in diethylether solvent. Furthermore, another conformer (**TAA2**) with the proton transferred from Asp to Arg is appended. The O<sup>¬</sup>H...O<sup>ε1</sup> distance in **TAA2** is shorter as compared to the corresponding length in **TAA1** by ~0.1 Å. This indicates that the coupling between Tyr and Asp is strengthened along with this proton transfer. As compared with the length optimized in gas phase, the longer hydrogen bond lengthens while the shorter one shortens in diethylether solvent. In other words, the difference between two hydrogen bonds is enlarged in diethylether solvent. The gap of hydrogen bonds lengths is enhanced further with the increase of dielectric constants.

## IR spectra

As a good facility, the IR spectra have been employed to determine the geometry structure because the variation of conformer can be reflected directly by the shift of IR spectra. The IR spectra of the selected dyads calculated in gas phase and diethylether solvent are presented in Figure 2. The difference of IR spectra in fingerprint region for three gaseous **AA** conformers is slight. Significant distinction is observed for the spectra with strong signals over 2000 cm<sup>-1</sup>. Two signals appear at 2571.6 and 3373.8 cm<sup>-1</sup> for conformer **AA1**. They are assigned as the O<sup>e1</sup>H...N<sup>η1</sup> and O<sup>e2</sup>...HN<sup>η2</sup> hydrogen bonds stretching, respectively. In **AA2**, the spectra with distinct signal locate at 2443.3 and 3351.3 cm<sup>-1</sup> are assigned as the O<sup>e2</sup>H...N<sup>η2</sup> and O<sup>e1</sup>...HN<sup>η1</sup> stretching modes, respectively. Two strong signals are observed in the IR spectra of gaseous conformer **AA3** at 2168.9 and 2530.3 cm<sup>-1</sup>. The assignments were given as the O<sup>e1</sup>...HN<sup>η1</sup> and O<sup>e2</sup>...H N<sup>η2</sup> hydrogen bonds stretching, respectively.

When the dyads are dipped into the diethylether solvent, the frequency of the OH...N stretching mode in **AA1** and **AA2** is redshifted significantly, approaching to 2000 cm<sup>-1</sup>. The effect on O...HN hydrogen bond is slight. Two O...HN stretching modes are blueshifted and approach to each other in **AA3** structure as compared to those in gas phase. The OH...N stretching mode in **AI1** and **AI2** is red shifted when the system changes from gas phase into diethylether solvent. On the contrary, the influence brought by solvent dielectric constant on the spectra of **AP** is slight (Figure 2).

The CO stretching mode of gaseous **TAA1** is assigned at 1292.3 cm<sup>-1</sup>, which is blue-shifted slightly as compared with the CO stretching in AP1 and AP2 by 21 and 50 cm<sup>-1</sup>, respectively. The CO stretching of **TAA1** red-shifts to 1281.6 cm<sup>-1</sup> in diethylether solvent. The OH...O and OH...N stretching modes connecting three fragments are assigned in gas phase at 3570.6 and 2962.4 cm<sup>-1</sup>, respectively. The OH...N mode red-shifts distinctly in diethylether solvent to 2502.2 cm<sup>-1</sup>, while the

solvent effect on OH...O stretching is slight. These two stretching modes of **TAA2** are assigned at 2775.0 cm<sup>-1</sup> for OH...O hydrogen bond and 3241.6 cm<sup>-1</sup> for O...HN hydrogen bond, respectively.

## Potential energy surfaces

The potential energy surfaces (PESs) for proton transfer of **AA** system in gas phase, diethylether, and water solvent were determined (Figure 3). Taken the energy of the most stable structure in every phase as zero point, the lines are described as the relationship between the relative energy and two O...H distances.

In gas phase, the most stable structure is AA1, the other two conformers are higher in energy by 1.4 (AA2) and 2.1 (AA3) kcal/ mol, respectively. AA1, the predominant conformer in gas phase, corresponds to the left minima points on black and red lines at  $\sim 1.05$  Å of O...H distance  $(R_{O...H})$ . AA2 and AA3 refer to the right local minima on red and black lines, respectively, approaching 1.55 Å of O...H distance. The transition state, locating between AA1 and AA2/AA3, is determined with the energy higher than AA1 by 1.5/2.3 kcal/mol. For the backward reaction, the barrier for the inversion of configuration from AA3 to AA1/AA2 is very low. In diethylether solvent, the energy of conformer AA3 is the lowest around O...H distance of 1.65 Å. Relatively, AA1 and AA2 are higher in energy by 3.3 and 4.3 kcal/ mol, respectively near 1.05 Å of R<sub>0...H</sub>. The energy barrier varing from high-energy conform AA1/AA2 to low-energy structure AA3 is 0.3/0.0 kcal/mol, decreasing as compared with the barrier in gas phase. The principal conformation corresponds to conformer AA3.

The increasing of solvent dielectric constant enhances the stability of polar conformer. Similar phenomenon has been observed in hydrogenbonded water chains [19]. As contributes mainly to the interaction between the polar conformer and the polarity solvent molecules. The larger the solvent dielectric constant is, the stronger the interaction is. Here, the potential energy surfaces in water solvent are also explored in order to inspect the dielectric constant effect on proton transfer. When the dielectric constant increases furthermore along with the solvent variation from diethylether to water, the minimum at left side near 1.05 Å of  $R_{0...H}$  disappears, and the double-well PES converts into the single-well PES. No matter where the protons locate initially, both of which transfer to the Arg moiety after optimization.

To determine the proton transfer mechanism of these two protons (concerted or stepwise), the 2-dimentional potential energy surfaces in gas phase and diethylether solvent were determined (Figure 4). Three minima can be observed on top-left corner, top-right corner, and bottom-right corner in plot (a), corresponding to AA1, AA3, and AA2, Citation: Shihai Y, Kang W, Sun L (2016) Solvent Effect on Hydrogen-Bonded Acetic Acid...Arginine/Imidazole/Phenol Dyads. Med Chem (Los Angeles) 6: 604-610. doi:10.4172/2161-0444.1000405



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Figure 3: The 1-D potential energy surface of acetic acid...arginine (AA) dyad in gas phase (G), diethylether (D), and water solvent (W). Arginine is simplified with a model of methyl guanidine. The energy of the most stable structure in gas phase is taken as the zero point.





respectively. The barriers from **AA3** to **AA1** and from **AA3** to **AA2** are relatively low as compared with that from **AA2** to **AA1** (5.8 kcal/mol). Therefore, these two protons transfer according to the one-by-one mechanism. The 2-dimentional PESs obtained in diethylether solvent (plot b) show obviously that **AA3** corresponds to the minimum point.

The 2D PESs of acetic acid...phenol dyad in gas phase, diethylether, and water solvent shown in Figure 5 illustrate that there are two minima points, locating at bottom-left corner and top-right corner, respectively. Two protons transfer synergetically along the red dotted line, which represents the minimum energy path. Along with the increasing of solvent dielectric, the barrier of this double proton transfer decreases gradually from ~22.5 kcal/mol in gas phase to 19.2 kcal/mol in diethylether and 18.9 kcal/mol in water.

#### **Dipole Moment**

The dipole moment reflects the electrical polarity of a system. The variation of solvent dielectric constant induces the shift of dipole moment. The complexes, shown in Figure 1, were optimized in gas phase and diethylether solvent. A good linear relationship is found between the shift of the dipole moment and the variation of the relative energy (Figure 6). Such as **AA1**, the relative energy and the dipole moment in gas phase are 0.0 kcal/mol and 4.2 Debye, respectively. When **AA1** is put into the diethylether solvent, the relative energy decreases by 5.9 kcal/mol and the dipole moment increases to 5.5 Debye. Therefore, the variation of relative energy is 5.9 kcal/mol, and the alteration of the dipole moment 1.3 Debye. Thus, this relationship can be utilized to estimate the stability modification by measuring the alteration of dipole moment.

#### Conclusion

The calculations were carried out at B3LYP/6-311++G(d,p) level employing the polarizable contimuum model (PCM) to illustrate the solvent effect on hydrogen bonds. The difference between two hydrogen bonds distance is enlarged in diethylether solvent as compared to those in gas phase. The solvent effect on IR spectra is distinctive. The potential energy surfaces for the proton transfer of acetic acid... arginine complex in gas phase and diethylether solvent are determined. The protons transfer according to the stepwise mechanism. While, the proton transfer mechanism of acid...phenol dyad was based on the



Figure 6: The variation of energy and the dipole moment when the system changes from gas phase to diethylether solvent. The energy refers to the difference of the dyad in gas phase and diethylether solvent.

concerted mechanism. The increasing of solvent dielectric constant enhances the isomers' relative stability and reduces of energy barrier for proton transfer. The dipole moment can be taken as an index to judge the variation of stability.

#### Acknowledgements

This work is supported by National Nature Science Foundation of China (Grant No. 21203227, 21103080) and the Research Foundation for Talented Scholars of the Qing.

#### References

- Frey PA, Whitt SA, Tobin JB (1994) A low-barrier hydrogen bond in the catalytic triad of serine proteases Science. Science-New York Then Washington 264: 1927-1930.
- Perrin CL, Nielson JB (1997) Strong hydrogen bonds in chemistry and biology. Annu Rev Phys Chem 48: 511-544.
- Li P, Wang W, Sun Q, Li Z, Du A, et al. (2013) Insights into the Mechanism of the Reaction between Tetrachloro-p-Benzoquinone and Hydrogen Peroxide and their Implications in the Catalytic Role of Water Molecules in Producing the Hydroxyl Radial. Chem phy chem 14: 2737-2743.
- Li P, Ma Z, Wang W, Song R, Zhai Y, et al. (2011) Theoretical studies on the electron capture properties of the H2SO4- HOO<sup>-</sup> complex and its implications as an alternative source of HOOH. Physical Chemistry Chemical Physics 13: 5931-5939.
- Li P, Ma Z, Wang W, Zhai Y, Sun H, et al. (2011) Theoretical studies on the coupling interactions in H2SO4- HOO<sup>-</sup>(H2O) n (n= 0–2) clusters: toward understanding the role of water molecules in the uptake of HOO<sup>-</sup> radical by sulfuric acid aerosols. Physical Chemistry Chemical Physics 13: 941-953.
- Li P, Shen Z, Wang W, Ma Z, Bi S, et al. (2010) The capture of 'H and' OH radicals by vitamin C and implications for the new source for the formation of the anion free radical. Physical Chemistry Chemical Physics 12: 5256-5267.
- Wang L, Fried SD, Boxer SG, Markland TE (2014) Quantum delocalization of protons in the hydrogen-bond network of an enzyme active site. Proceedings of the National Academy of Sciences 111: 18454-18459.
- Cleland WW, Kreevoy MM (1994) Low-barrier hydrogen bonds and enzymic catalysis. Science-New York Then Washington.
- Zhao Q, Abeygunawardana C, Talalay P, Mildvan AS (1996) NMR evidence for the participation of a low-barrier hydrogen bond in the mechanism of delta 5-3-ketosteroid isomerase. Proceedings of the National Academy of Sciences 93: 8220-8224.
- Ash EL, Sudmeier JL, De Fabo EC, Bachovchin WW (1997) A low-barrier hydrogen bond in the catalytic triad of serine proteases. Theory versus experiment Science 278: 1128-1132.
- Kim KS, Oh KS, Lee JY (2000) Catalytic role of enzymes: Short strong H-bondinduced partial proton shuttles and charge redistributions. Proceedings of the National Academy of Sciences 97: 6373-6378.
- Pan YP, McAllister MA (1997) The low barrier hydrogen bond in enzymatic catalysis. Journal of Biological Chemistry. J Am Chem Soc 119: 7561.
- 13. Smallwood CJ, McAllister MA (1997) J Am Chem Soc 119: 11277.
- Yan S, Kang S, Hayashi T, Mukamel S, Lee JY (2010) Computational studies on electron and proton transfer in phenol-imidazole-base triads. Journal of computational chemistry 31: 393-402.
- Yan S, Li T, Yao L (2011) Mutational effects on the catalytic mechanism of cellobiohydrolase I from Trichoderma reesei. The Journal of Physical Chemistry B 115: 4982-4989.
- Zhang Y, Yan S, Yao L (2013) A mechanistic study of Trichoderma reesei Cel7B catalyzed glycosidic bond cleavage. The Journal of Physical Chemistry B 117: 8714-8722.
- Lupas AN, Ponting CP, Russell RB (2001) On the evolution of protein folds: are similar motifs in different protein folds the result of convergence, insertion, or relics of an ancient peptide world. Journal of structural biology 134: 191-203.
- 18. Nigro CA, Aimaretti S (2002) J Mol Biol 320: 303.
- Kim SK, Bok JH, Bartsch RA, Lee JY, Kim JS (2005) A fluoride-selective PCT chemosensor based on formation of a static pyrene excimer. Organic letters 7: 4839-4842.

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- Yan S, Zhang L, Cukier RI, Bu Y (2007) Exploration on Regulating Factors for Proton Transfer along Hydrogen-Bonded Water Chains. Chem Phys Chem 8: 944-954.
- 21. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, et al. (2010) Gaussian 09. rev B 01 Gaussian Inc., Wallingford CT.
- Miertuš S, Scrocco E, Tomasi J (1981) Electrostatic interaction of a solute with a continuum. A direct utilization of AB initio molecular potentials for the prevision of solvent effects. Chemical Physics 55: 117-129.
- Miertus S, Tomasi J (1982) Approximate evaluations of the electrostatic free energy and internal energy changes in solution processes. Chemical physics 65: 239-245.
- Cossi M, Barone V, Cammi R, Tomasi J (1996) Ab initio study of solvated molecules: a new implementation of the polarizable continuum model. Chemical Physics Letters 255: 327-335.