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Theoretical study of hydrogen bonded picolinic acid-water complexes

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Quantum chemical calculations have been performed on the hydrogen bonded picolinic acid-water complexes by Hartree-Fock, second-order Moller-Plesset perturbation theory, density functional theory, and density functional theory with dispersion correction using 6-311++G(d,p) basis set. For the isolated picolinic acid moiety, four stable stationary points, corresponding to four different conformers are found at all levels of calculation. The structure with intramolecular COO–H···N hydrogen bond is found to be the most stable conformer at all levels of theory. Taking the lowest energy conformer as the starting geometry, three different conformers are predicted for the binary complexes of picolinic acid with water. Geometrical parameters, interaction energy, vibrational analysis in detail have been investigated. The intramolecular hydrogen bond is retained in two complexes while structural deformation occurs in one complex due to cleavage of the intramolecular hydrogen bond. The natural bond orbital analysis and atoms in molecules theory have been applied to understand the nature of interaction present in picolinic acid-water complexes.

Keywords: Theoretical chemistry, Density functional calculations, *Ab initio* calculations, Hydrogen bonding, Atom-in-molecule analysis, Natural bond orbitals

Importance of intermolecular interactions is well recognized in many areas of scientific research. Hydrogen bonding is one of the most important types of intermolecular interactions which play a key role in shapes, properties and functions of biomolecules. Hydrogen bonding between solute and solvent molecules containing fundamental organic functional groups is a topic of intense research in recent years[1-3].

Pyridine carboxylic acids are an important group of molecules to study non-covalent interactions such as hydrogen bonding. They have the ability to form a wide range of products containing intermolecular hydrogen bonds in the solid state to form polymeric chain[4-6]. Some of the known important interactions are O–H···N hydrogen bonds between carboxylic acids and the pyridine nitrogen atom, O–H···O hydrogen bonds between carboxylic acid groups, weak C–H···O interactions and N···H–N hydrogen bonds between neutral and zwitter ionic forms of the molecule[7]. Due to the high directionality of H-bonds[8], the stronger hydrogen bonds are formed when the donor and acceptor atoms are collinear. This influences formation of highly oriented structures.

Among pyridine carboxylic acids, picolinic acid, an isomer of nicotinic acid and isonicotinic acid is of great interest to many researchers because of its usefulness as a ligand. In human beings, it is the prime natural chelator of vital trace elements such as chromium, zinc, manganese, copper, iron and molybdenum[9-11]. Picolinic acid has been detected in several biological media such as cerebrospinal fluid, blood, human milk, pancreatic juice, and also in intestinal homogenates[12,13]. Picolinic acid is biosynthesized in liver and kidneys during the catabolism of the essential amino acid, tryptophan, and transported to the pancreas[14]. Picolinic acid and its isomers play diverse roles as reaction partners in industrial processes as well as building blocks in photovoltaic devices[15]. They are also used as model systems for environmental studies[16]. Their roles as food preservatives[17] as well as antiseptic agents in food, pharmaceutical and textile industry are well-known[18-21].

Literature of pyridine monocarboxylic acids is well enriched in both theoretical and experimental fronts. The reactivity of three isomeric pyridine monocarboxylic acids with diaazodiphenyl methane in different aprotic solvents has been studied by Vukovic *et al.*[22,23] They have reported that the reactivity is highly dependent on relative positions of the ring nitrogen and the carboxylic group. Vibrational analysis (IR and Raman spectra) of the

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three isomeric pyridine carboxylic acids is reported by Koczon's group[24]. The effect of the position of carboxylic acid group on the wave number and intensity has been discussed. The UV-vis spectra and ^{1}H and ^{13}C NMR spectra are reported for different metal complexes of picolinic acid with Fe(III), Ni(II), Zn(II), Cu(II) and Ag(I)[25]. UV-Raman spectroscopy of picolinic acid, investigated by Fang and coworkers[26], proves the existence of different molecular structures at different *p*Hs. Fourier transform microwave study of picolinic and isonicotic acid has been reported by Alonso *et al.*[27] where two different conformations of picolinic acid and one conformation of isonicotinic acid have been identified. Very recently, conformational changes of picolinic acid upon UV irradiation were investigated at low temperature matrix isolation infra red spectroscopy by Nakata *et al.*[28] According to their results, the *trans* conformer having intramolecular COO–H···N hydrogen bond is the most stable among the four conformers. They also derived the photoreaction pathways of the conformers from kinetic analysis.

In the context of cluster formation with small molecules, picolinic acid is an interesting molecule. It can act as a hydrogen donor in the form of carboxyl group as well as act as hydrogen acceptor by using the lone pair of the nitrogen atom. It also has an aromatic ring which can be another important site for complexation by acting as π-acceptor. Therefore, multifunctional behavior of picolinic acid with a small molecule such as water is a very interesting topic for investigation of noncovalent interactions. Explicit study of interaction between a multifunctional molecule such as picolinic acid and water will reveal the possibilities of formation of different structures with various energies.

Despite the potential importance of complex formation between picolinic acid and H_2O, to the best of our knowledge we could find neither theoretical nor experimental report. Study of clusters is of fundamental interest as it helps in understanding the effects of microsolvation on the properties of solute on molecular scale. It has motivated us towards theoretical prediction of picolinic acid-water hydrogen bonded complex for further study. The present work focuses on the hydrogen bonding interaction of the picolinic acid-water complex. The optimized geometries, stabilization energies and vibrational frequencies of this system are calculated using the Hartree-Fock (HF), second-order Moller-Plesset perturbation theory (MP2), density functional theory (DFT), and density functional theory with dispersion correction (DFT-D) using 6-311++G(d,p) basis set. The quantum theory of atoms in molecules (AIM) and natural bond orbital (NBO) analyses are carried out to gain more information on the nature of interaction of the complexes.

Computational Methods

Calculations were performed using the Firefly QC package[29], which is partially based on the GAMESS (US)[30] source code. The geometries of the isolated picolinic acid, water moieties and their various binary complexes were fully optimized using HF, DFT using Becke's three parameter hybrid functional in conjunction with Lee, Yang and Parr's correlation functional (B3LYP), DFT-D[31] and also at MP2 level employing split valence 6-311++G(d, p) basis set. Analytic vibrational frequencies were calculated at the same level, as used for geometry optimizations to further ascertain the nature of minima. The zero point energies were computed using the harmonic vibrational frequencies. The stabilization energies between the partners in each complex at the energetic minimum were calculated using the super-molecule method. According to this method, stabilization energy (ΔE) is the difference between the electronic energy of the complex and the combined energies of the isolated monomer component as given in equation (1),

$$\Delta E = E_{\text{complex}} - \Sigma\, E_{\text{component}} \qquad \text{...(1)}$$

where E_{complex} and $E_{\text{component}}$ are optimized energies of hydrogen bonded complex and each isolated component molecules, respectively. The interaction energy is corrected for zero point vibrational energy (ZPE). Since we used the incomplete basis set, the results are contaminated with basis set superposition error (BSSE). In the complex, each of the monomer moieties may use the basis set of the other, resulting in overestimation of interaction energy. Hence, the stabilization energy was corrected for BSSE using the counterpoise method of Boys and Bernardi[32]. Final interaction energies were calculated based on both ZPE and BSSE corrections. The theory of atoms in molecules method (AIM) was used to investigate the electronic densities and intermolecular hydrogen bonding interactions of all the binary complexes of picolinic acid with H_2O. Bader's AIM theory is based on topological analysis of ρ and $\nabla^2\rho$. According to the topological analysis of electron density in AIM theory, ρ is used to describe the strength of the bond whereas the $\nabla^2\rho$ describes the characteristics of the bond. If $\nabla^2\rho < 0$ then the bond is taken as covalent bond and if $\nabla^2\rho > 0$, it is referred as a closed cell interaction and is characteristic of the ionic bond, hydrogen bond or van der Waals interaction. There is a set of criteria for ρ and $\nabla^2\rho$ at bond critical points (BCPs) for the hydrogen bonds proposed by Popelier[33-34]. However, the criteria proposed are exceeded by those of the reported hydrogen bonding interactions. The wave functions computed at B3LYP/6-311++G(d,p) level of theory were used to calculate the electron density $\rho(r)$ and Laplacian of $\rho(r)$ at the bond critical points. Furthermore, to evaluate the direction and magnitude of the donor-acceptor interactions, the natural bond orbital (NBO) analyses for all of the complexes were performed using NBO 5.0 program[35] linked to the Firefly package. NBO analysis is an appropriate method to investigate hyperconjugative interactions in the case of intermolecular and intramolecular hydrogen bonded complexes. Donor-acceptor interaction strength between filled orbital of the donor (ϕ_i) and the empty orbital of the acceptor (ϕ_j) was determined by second order perturbation energy ($\Delta E_{ij}^{(2)}$) calculated using Eq. (2),

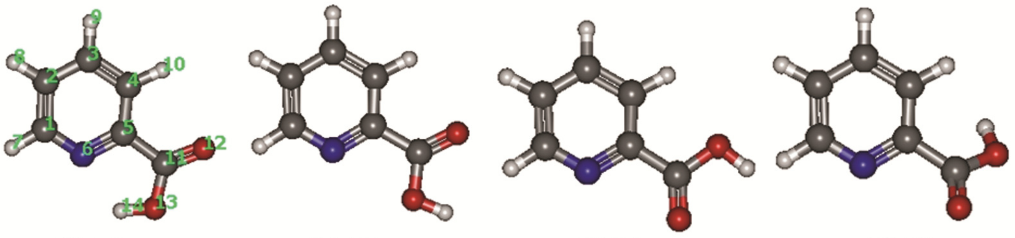
$$\Delta E_{ij}^{(2)} = 2\frac{<\phi_i|F_{ij}|\phi_j>^2}{\varepsilon_i - \varepsilon_j} \qquad \ldots(2)$$

where ε_i and ε_j are NBO energies and F_{ij} is Fock matrix element between ith and jth NBO orbitals. Both AIM and NBO analyses were performed at B3LYP/6-311++G(d,p) level. The topological properties of the electron densities for the complexes at the bond critical points were calculated using the AIMALL program[36]. Visualization of the molecules was done by using Gabedit[37] and Macmolplt software[38].

Results and Discussion

Geometries, energies and frequencies

Picolinic acid can have two different conformations, *trans* and *cis* around the C-COOH bond and OC-OH bonds, which results in a total of four conformations. The conformer, PA-T1, is the structure where the oxygen atom of C=O group is at *trans* position with respect to the N atom in the pyridine ring, while the –OH group is also in *trans* position against the C=O group. This conformer is stabilized by formation of an intramolecular COOH...N hydrogen bond. The second conformer PA-T2 is also characterized by the presence of *trans* conformation of C=O group against ring nitrogen atom but the conformation of –OH group is *cis* with respect to the C=O group. In the third conformer PA-C1, the conformation of both C=O group and –OH group is *cis* with respect to ring N atom and carboxylic C=O group, respectively. The fourth conformer, PA-C2, is characterized by the *cis* conformation of C=O group against pyridine ring nitrogen atom, while –OH group is *trans* with respect to the C=O group. Among these four conformers, the structure PA-C2 is non-planar to avoid the steric hindrance between the two hydrogen atoms, one of which is the –OH group and the other is in the –CH group of the pyridine ring. We have considered these four conformers for the study of picolinic acid monomer. Full geometry optimization for all the conformations have been performed along with analytic vibrational frequency calculations using HF, DFT, DFT-D and MP2 methods using 6-311++G(d, p) basis set which shows that all are true minima in the potential energy surface. B3LYP method is a suitable tool to study such hydrogen bonded complexes at lower computational cost and can be used in this case to give reliable results. The optimized structures at B3LYP level are shown in Fig. 1. The calculated geometry of the structures at other computational methods is similar to that of B3LYP method. Henceforth, the discussion of the picolinic acid-water complex is considered at this level unless and otherwise mentioned. The ZPE corrected relative energies of the conformers calculated at various computational methods are listed in Table 1 and optimized geometrical parameters are listed in Table 2, where the numbering of atoms is as denoted in Fig. 1. From Table 1 it can be seen that the order of relative stability is PA-T1>PA-T2>PA-C1>PA-C2 at all levels of theory. The most stable PA-T1 conformer is the global minimum in this case. This is in contrast to the general trend that carboxylic acids follow, in which the *trans* conformation is less stable than the *cis* conformation because of the repulsion of lone pairs in the two O atoms in the –COOH group. There are a few reports regarding stability of carboxylic acid conformers for example, formic acid[39], acetic acid[40], propionic acid[41], benzoic acid[42], and 2-chlorobenzoic acid[43] where it is shown that, the *trans* conformer is destabilized due to lone pair repulsion. Moreover, the



PA-T1 PA-T2 PAC1 PAC2

Fig. 1—Optimized structures of picolinic acid conformers at B3LYP/6-311++G(d,p) level.

Table 1—ZPE corrected relative energies of various conformers of picolinic acid

Level	Relative energy (kJ/mol)			
	PA-T1	PA-T2	PA-C1	PA-C2
HF	0.0	7.9	13.8	46.6
B3LYP	0.0	13.4	18.3	47.0
DFT-D	0.0	16.0	20.9	45.2
MP2	0.0	14.9	18.7	45.8

Table 2—Geometrical parameters calculated for the conformer PA-T1 at various computational methods. [Bond length (*r*) in Å and bond angle (Θ) and torsional angle (τ) in degrees][a].

Parameter	HF	B3LYP	DFT-D	MP2
r(C1-C2)	1.385	1.394	1.399	1.398
r(C2-C3)	1.383	1.393	1.398	1.399
r(C3-C4)	1.383	1.391	1.396	1.395
r(C4-C5)	1.383	1.393	1.398	1.398
r(C5-N6)	1.320	1.339	1.346	1.346
r(C1-N6)	1.318	1.334	1.340	1.343
r(C5-C11)	1.510	1.511	1.514	1.509
r(C11-O12)	1.179	1.203	1.210	1.209
r(C11-O13)	1.316	1.340	1.350	1.342
r(O13-H14)	0.948	0.978	0.985	0.977
r(N6-H14)	2.076	1.997	1.969	1.977
r(H10-O12)	2.561	2.602	2.620	2.586
Θ(N6-H14-O13)	116.87	120.47	122.18	122.37
Θ(C11-O13-H14)	109.53	106.68	105.46	105.25
Θ(C11-C5-N6)	116.24	115.74	115.55	115.64
Θ(C5-C11-O12)	122.36	123.17	123.45	122.85
Θ(C5-C11-O13)	114.69	113.70	113.34	113.79
Θ(C11-O13-H14)	109.53	106.68	105.46	105.25
Θ(C4-C5-C11)	120.14	120.79	120.95	120.42
τ(H14-O13-C11-O12)	179.99	179.99	179.99	179.99
τ(H14-O13-C11-C5)	-0.00	-0.01	-0.00	-0.00
τ(O12-C11-C5-N6)	-179.99	-179.99	-179.99	-179.99
τ(O13-C11-C5-N6)	0.00	0.01	0.00	0.00

[a]Numbering of carbon atoms is given in Fig. 1.

trans conformer returns to the more stable *cis* conformer through hydrogen atom tunneling. In the case of 2-chlorobenzoic acid, the *trans* conformer is so unstable that it cannot exist even at low temperature argon matrix in spite of the intramolecular hydrogen bond stabilization. Picolinic acid is an exception to this trend. It is reasonable to understand the stability of PA-T1 as it involves the intramolecular COOH...N hydrogen bond, giving a cyclic structure which aids the stability. The most unstable conformer PA-C2 ((47 kJ mol^{-1}) is due to its non-planar structure. PA-C1 and PA-T2 are less stable by 18.3 and 13.4 kJ/mol, respectively at B3LYP/6-311++G(d, p) level of theory. The result is in good agreement with the previous studies[24,28]. At DFT-D computational level, the stability of all conformers except PA-C2 increases compared to other levels.

A detailed study of hydrogen bond interaction between water and PA-T1 is reported herein, and PA-T1 conformation is described as PA in the complex system. Association of one molecule of picolinic acid with one molecule of water leads to the formation of three 1:1 clusters which are denoted as PA-W1, PA-W2 and PA-W3 (Fig. 2). Among the three binary complexes of picolinic acid and water, PA-W1 and PA-W2 are cyclic in nature, whereas PA-W3 is an open structure. The intramolecular O–H···N hydrogen bond of the monomer is retained in PA-W1 and PA-W3 complexes, while in PA-W2 it is broken by the interacting water molecule. Therefore, serious structural deformation occurs in complex PA-W2, which lowers its stability drastically. The complex PA-W1 is characterized by the presence of C–H···O hydrogen bond involving C–H group, which is *ortho* to the carboxylic acid group with the lone pair of electrons on water molecule and O–H···O hydrogen bond wherein the carboxylic oxygen acts as an acceptor to one of the OH groups of water moiety. The O–H group of carboxylic acid moiety is also

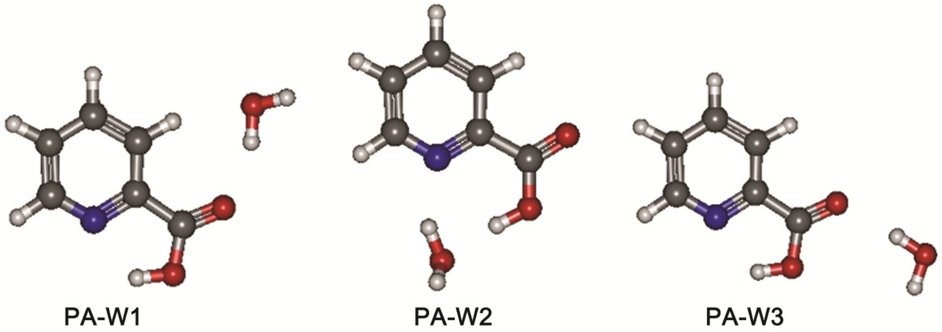


Fig. 2—Optimized structures of various binary complexes of picolinic acid-water at B3LYP/6-311++G(d,p) level.

involved in intramolecular O–H···N hydrogen bond with the ring nitrogen atom. The complex, PA-W2, is characterized by the presence of O–H···N and O–H···O hydrogen bonds wherein the water molecule serves as both a donor and an acceptor, respectively. In this case, the intramolecular O–H···N hydrogen bond with the ring nitrogen atom is broken by the interacting water molecule. The complex, PA-W3, involves O–H···O hydrogen bond where OH group of water moiety acts as the donor to the carboxylic oxygen. This complex is also characterized by the presence of intramolecular O–H···N hydrogen bond with the ring nitrogen atom, similar to the complex PA-W1.

The aromatic ring of the picolinic acid moiety is also considered for a complexation site. We tried several times to optimize the π-bonded water complex of picolinic acid. However, we were unsuccessful in obtaining a π-bonded picolinic acid water complex. Each time, the input geometry was minimized into PA-W1 structure. From this, it may be inferred that the PA-WI is the global minimum structure in this case. Theoretical calculations reported earlier suggested that the low electrostatic potential on the nitrogen atom in the pyridine ring facilitates the formation of stable van der Waals σ_N type complexes with polar molecules rather than forming π-bonded complex[44,45]. In the case of picolinic acid-water complex, pyridine ring nitrogen atom remains the most probable site of interaction with the polar water molecule.

Stabilization energies of the binary complexes of picolinic acid with water are listed in Table 3. According to the order of stability, PA-W1> PA-W3>PA-W2 at HF, B3LYP and MP2 methods in which the dispersion term is excluded. The calculation at DFT-D method indicates the order of stability: as PA-W1>PA-W2>PA-W3. The complex, PA-W1, is most stable in all levels of calculation while stabilization energy of PA-W2 complex increases at DFT-D method, making it more stable than the PA-W3 complex. From Table 3 it is evident that the value of stabilization energy is higher at DFT-D method compared to other methods due to inclusion of the dispersion term. Lowest stability of PA-W2 complex at B3LYP method may be due to the cleavage of intramolecular O–H···N hydrogen bond by the interacting water molecule, which leads to structural deformation. Similar situation is observed in the case of tryptophan-water and adrenaline-water complexes where structural deformation leads to lowering of stability in one of the complexes[46,47]. Various structural parameters of the hydrogen bonded binary complexes of picolinic acid and water are

Table 3—Stabilization energies (kJ/mol) and different correction terms for various binary complexes of picolinic acid with water

		PA-W1	PA-W2	PA-W3
Δ*E* (uncorr)	HF	25.28	14.37	20.35
	B3LYP	29.73	22.84	22.68
	DFT-D	31.91	28.82	24.91
	MP2	32.58	25.33	25.21
Δ*E* (ZPE)	HF	18.14	9.98	14.52
	B3LYP	21.89	14.71	16.62
	DFT-D	24.24	20.75	18.81
	MP2	24.59	15.43	17.49
Δ*E* (BSSE)	HF	23.49	11.55	18.80
	B3LYP	27.22	19.69	20.87
	DFT-D	29.05	24.48	22.36
	MP2	25.09	14.16	18.06
Δ*E* (ZPE+BSSE)	HF	16.35	7.16	12.97
	B3LYP	19.38	11.56	14.81
	DFT-D	21.38	16.41	16.26
	MP2	17.10	4.26	10.34

listed in Table 4. Structural parameters of hydrogen bonded complexes provide useful information to judge the nature of hydrogen bonds. It is well known that the hydrogen bond formation is associated with the elongation of the proton donating X–H bond (except the special case of blue shifted hydrogen bonds where X–H bond shortens) as well as the shortening of H···Y bond. Therefore, the length of X–H and H···Y bond is a measure of the strength of interaction. The longer X–H bond and shorter H···Y bond denote stronger interaction and vice versa. From Table 4, it is seen that for C–H···O interaction of PA-W1, C–H acting as the H-donor, is the weakest one due to the longest $R_{\text{H–Y}}$ (2.246 Å) and almost unchanged $\Delta R_{\text{X–H}}$ value. The hydrogen bonds involving C–H, N–H and O–H as hydrogen bond donors, which are encountered in the binary complexes, have positive $\Delta R_{\text{X–H}}$ values and are red shifted hydrogen bonds. The largest $\Delta R_{\text{X–H}}$ value (0.017 Å) is found in O–H···N interaction of PA-W2 complex which seems to be a strong interaction. The short H···Y distance (1.899 Å) further confirms it to be a strong intermolecular hydrogen bonding interaction. Again, the shortest H···Y distance (1.764 Å) is found for the O–H···O interaction in PA-W2 complex, which also appears to be a strong interaction although its $\Delta R_{\text{X–H}}$ value (0.007 Å) is not very large. The breakage of the intramolecular O–H···N hydrogen bond and formation of intermolecular hydrogen bond by the interacting water molecule leads to a smaller $\Delta R_{\text{X–H}}$ value. However, measuring the strength of hydrogen bonding interaction on the basis of the length of H···Y distance is only approximate even in the case of homogeneous X–H···Y system. Estimation of strength of hydrogen bond directly on the basis of $R_{\text{H···Y}}$ is not possible for a heterogeneous system containing hydrogen bonds that differ in the type of H-donor and/or H-acceptor. To overcome the above difficulties, a hydrogen bond parameter $\delta R_{\text{H···Y}}$ is used which allows one to compare interactions and estimate their strength even in the case of heterogeneous system. $\delta R_{\text{H···Y}}$ is defined as[48] in Eq. (3),

$$\delta R_{\text{H···Y}} = R_{\text{H}}^{\text{VDW}} + R_{\text{Y}}^{\text{VDW}} - R_{\text{H···Y}} \qquad \ldots(3)$$

where $R_{\text{H}}^{\text{VDW}}$ and $R_{\text{Y}}^{\text{VDW}}$ are van der Waals radii of H and Y atoms[49], respectively, and $R_{\text{H···Y}}$ is the distance between the H-donor and the H-acceptor. From Table 4, it can be seen that the largest value of $\delta R_{\text{H···Y}}$ is found to be 0.956 Å in the complex PA-W2 for O–H···O and the second largest value of $\delta R_{\text{H···Y}}$ is 0.851 Å for O–H···N interaction in the same complex. It is worth mentioning that the $\delta R_{\text{H···Y}}$ (0.474 Å) of the C–H···O interaction in PA-W1 complex is the smallest one, which implies that it is the weakest hydrogen bonding interaction in the presently studied complex. In this case, the $R_{\text{H···Y}}$ is close to the sum of van der Waals radii of H and Y atoms. Hence, from the structural viewpoint, the interaction between the C–H and O atom is very weak and is regarded as the mixture of

Table 4—Structural parameters, vibrational frequencies and intensity of H-bonds in picolinic acid-water complexes calculated at B3LYP/6-311++G(d,p) level

Complex	H-bond	$R_{\text{X-H}}$ (Å)	$\Delta R_{\text{X-H}}$ [a] (Å)	$R_{\text{H···Y}}$ (Å)	$\delta R_{\text{H···Y}}$ (Å)	∠X–H···Y (deg.)	$\nu_{\text{X-H}}$ [b] (cm^{-1})	$\Delta\nu_{\text{X-H}}$ (cm^{-1})
PA-W1	O–H···O	0.971	+0.009	1.916	0.804	159.92	3686(7.78)	-123^{s}, -231^{as}
	O–H···N	0.980	+0.002	1.957	0.793	121.14	3540(4.87)	-44
	C–H···O	1.083	+0.001	2.246	0.474	161.51	3194(0.26)	-16
PA-W2	O–H···O	0.985	+0.007	1.764	0.956	173.80	3401(11.34)	-183
	O–H···N	0.979	+0.017	1.899	0.851	148.77	3543(23.55)	-266^{s}, -374^{as}
PA-W3	O–H···O	0.969	+0.007	1.995	0.725	175.74	3727(10.07)	-82^{s}, -190^{as}
	O–H···N	0.979	+0.001	1.992	0.758	120.20	3563(4.71)	-21
PA-T1	H14···N6	1.997			0.753			
	C4–H10	1.082					3211(0.04)	
	O13–H14	0.978					3584(3.98)	
WATER	O–H	0.962					3809^{s},3917^{as}	

[a] $\Delta R_{\text{X-H}} = R_{\text{X-H}}$ (complex) - $R_{\text{X-H}}$ (free monomer).

[b] The values in parenthesis are corresponding intensity of the IR frequency.

hydrogen bonding interaction and van der Waals interaction. The $\delta R_{H\cdots Y}$ of the intramolecular O–H···N hydrogen bond in the binary complexes, PA-W1 and PA-W3, is found to be larger than that of the picolinic acid monomer, which suggests that the intramolecular O–H···N hydrogen bond is strengthened in these complexes.

The harmonic vibrational frequencies with intensities and their shifts upon formation of hydrogen bonding in picolinic acid-water complexes are also listed in Table 4. Conventionally, it is assumed that formation of hydrogen bonds weakens X–H bond. Therefore, red shift in X–H stretching vibrational frequency is considered as an important fingerprint of hydrogen bond. The strength of the hydrogen bond depends on the frequency shift value. The larger the shift value, the stronger is the hydrogen bond. From Table 4, it can be seen that the two largest red shifts of frequency occur in the complex PA-W2 indicating these two as the strongest interactions. The red shifts of O–H···N interaction are larger than the O–H···O interaction suggesting that the former interaction is stronger than the latter. However, in the case of the complexes, PA-W1 and PA-W3, the situation is reverse as the red shift of O–H···O interaction is higher than that in the O–H···N interaction, suggesting that the O–H···O interaction makes more contribution towards the interaction energy of the complexes. The negative $\Delta\nu_{X\text{-}H}$ values of the intramolecular O–H···N hydrogen bond in the complexes, PA-W1 and PA-W3, indicate that they are strengthened during the formation of the binary complexes with water. There is excellent correlation between H-bond enthalpy (ΔH) and H-bond distance ($R_{H\cdots B}$) for the computed picolinic acid-water complexes. A well established empirical relationship exists between the hydrogen bond distance ($R_{H\cdots B}$) and energy (enthalpy in the gas phase) given by Rozenberg *et al.*[50] (Eq. 4),

$$-\Delta H = 0.134R^{-3.05} \text{ (with } R \text{ in nm)} \quad \ldots(4)$$

A very good correlation (R^2 value of 0.99) is obtained between $R_{H\cdots B}$ and $-\Delta H$ (calculated using Eq. (3)) in the case of picolinic acid-water complexes. The correlation plot of $R_{H\cdots B}$ and $-\Delta H$ is depicted in Fig. 3.

AIM analysis

AIM is a powerful tool to investigate hydrogen bonding interactions. The characteristics of critical points provide useful information on the nature of interactions. Therefore, to characterize the interaction within the picolinic acid-water system, several basic parameters at bond critical point (BCP) such as electron density (ρ), Laplacian of electron density ($\nabla^2\rho$), kinetic energy density (G_c), potential energy density (V_c) and total electron energy density (H_c) from Bader's theory of AIM were calculated. The corresponding results are listed in Table 5. AIM calculations were done using the wave functions computed at the B3LYP/6-311++G** level of theory for both the monomer and the binary complexes. The molecular graphs for monomer and hydrogen bonded complexes are shown in Fig. 4. Popelier[33,34] proposed a set of criteria for the existence of hydrogen bonding from AIM calculations. The criteria provide a basis to distinguish hydrogen bonding interactions from van der Waals interactions which have been proved to be valid for conventional as well as non-conventional hydrogen bonds. The proposed range of electron density (ρ) at BCP is 0.002–0.035 a.u. for hydrogen bonds and for all closed shell interactions including ionic bonds, hydrogen bonds and van der Waals interactions, $\nabla^2\rho$ is positive and within the range of 0.024–0.139 a.u. Therefore, both ρ and $\nabla^2\rho$ at BCP are good measures of the strength of hydrogen bonds. Popelier has also proposed some criteria on the strength of hydrogen bonds, which are: for weak and medium strength hydrogen bonds, $\nabla^2\rho > 0$ and $H_c > 0$; for strong hydrogen bonds $\nabla^2\rho > 0$ and $H_c < 0$; for very strong hydrogen bonds $\nabla^2\rho < 0$ and $H_c < 0$. From this classification, it is well understood that weak hydrogen bonds eventually merge with weaker van der Waals interactions, while strong hydrogen bonds merge with covalent and polar bonds at the other end of the continuum. The molecular graphs of monomer picolinic acid PA-T show two ring critical points, one for the benzene ring and the other for the ring formed

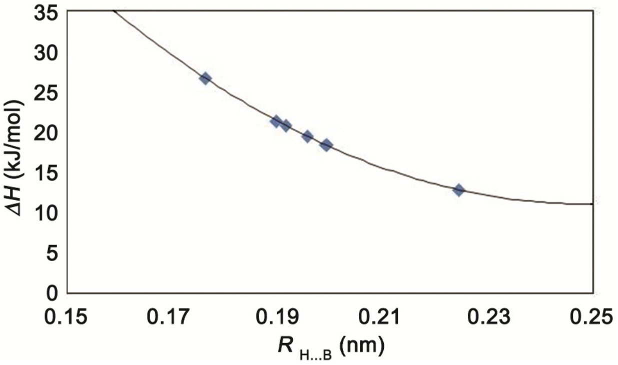
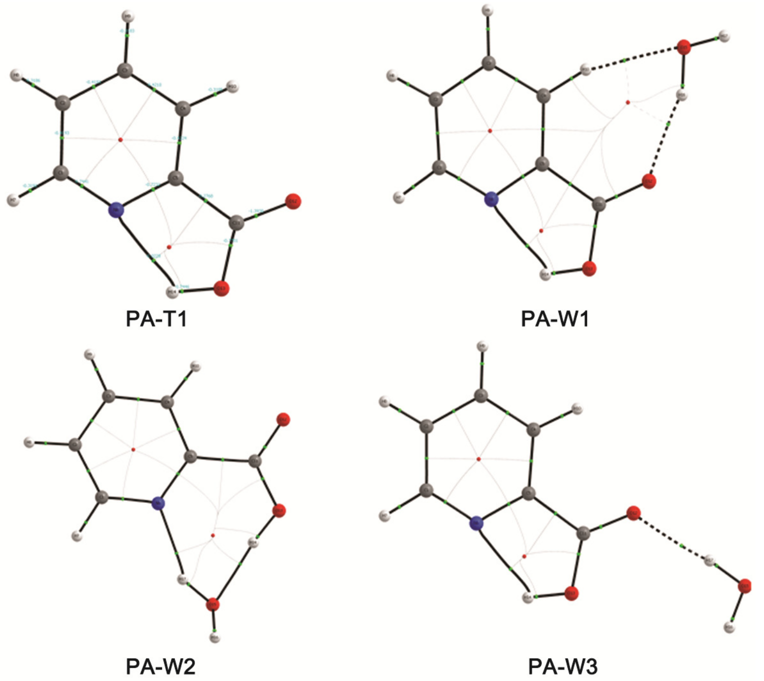


Fig. 3—Correlation of H-bond enthalpy (ΔH) and H-bond distance ($R_{H\cdots B}$) of the calculated picolinic acid-water complexes.

Table 5—Topological parameters at the bond critical points (BCP) for various hydrogen bonded complexes calculated at B3LYP/6-311++G(d,p) level

Complex	Interaction	ρ (a.u.)	$\nabla^2\rho$ (a.u.)	G_c (a.u.)	$-V_c$ (a.u.)	$-(G_c/V_c)$ (a.u.)	H (a.u.)
PA-W1	C4-H10···O15	0.0125	0.0471	0.0097	0.0076	1.276	0.0021
	O15-H16···O12	0.0247	0.0972	0.0216	0.0189	1.143	0.0027
	O13-H14···N6	0.0314	0.1042	0.0258	0.0256	1.008	0.0002
PA-W2	O13-H14···O15	0.0379	0.1194	0.0313	0.0328	0.954	-0.0015
	O15-H17···N6	0.0345	0.0970	0.0256	0.0269	0.952	-0.0013
PA-W3	O15-H17···O12	0.0209	0.0796	0.0240	0.0147	1.633	0.0093
	O13-H14···N6	0.0291	0.0994	0.0173	0.0231	0.749	-0.0058
PA4	N6···H14	0.0287	0.0989	0.0238	0.0228	0.104	0.0010



PA-T1 PA-W1

PA-W2 PA-W3

Fig. 4—Molecular graphs of various H-bonded picolinic acid-water complexes. (Small green and red dots represent the bond critical point and ring critical point respectively).

by the intramolecular O–H···N interaction. Among the three binary complexes, the structure PA-W1 has one extra ring critical point as compared to the monomer picolinic moiety due to the formation of a cyclic structure with the interacting water molecule. From Table 5, it can be seen that charge density and their Laplacian at the bond critical points are well within the range specified for the existence of hydrogen bond in the present studied complexes. The only value that does not match with the specified range is the value of ρ for O–H···O interaction in the case of complex PA-W2. Here, the value of ρ (0.0379 a.u.) is beyond the upper limit of the range. Moreover, this interaction has negative H_c and positive $\nabla^2\rho$ values, which signify that a partial covalent character is attained for O–H···O interaction in this complex. Even O–H···N interaction in this complex has negative H_c and positive $\nabla^2\rho$ values, which indicates it to be a strong hydrogen bond. Again, in the complex PA-W3, the intramolecular O–H···N interaction shows a positive $\nabla^2\rho$ value accompanied by very high negative H_c value (-0.058 a.u.) compared to that of the picolinic acid monomer. Therefore, O–H···N interactions in both PA-W2 and PA-W3 are the strongest interactions among all other interactions present in these complexes. In the complex PA-W1, for the H-bond involving C–H as the hydrogen bond donor, both ρ (0.0125) and $\nabla^2\rho$ (0.0471) values are close to the lower limits of the criteria proposed by Popelier and these values are the lowest among all the interactions studied here. It clearly indicates that the C–H···O interaction is the weakest one and can be thought of as the combination of hydrogen bonding interaction and van der Waals interaction. For such extreme cases, existence of BCP is not the sole criteria to indicate a weak hydrogen bond; application of NBO analysis is very much necessary. C-H is a weak donor; hence the bond strength of C–H···O interaction will be much lower than that of the other conformer which is also supported by our NBO calculation.

A linear relationship is found between $\delta R_{\mathrm{H}\cdots\mathrm{Y}}$ and topological parameters (electron density and Laplacian of electron density) from AIM calculation of the hydrogen bonded complexes. The correlation plot between $\delta R_{\mathrm{H}\cdots\mathrm{Y}}$ and $\nabla^2\rho$ is shown in Fig. 5 and plot of $\delta R_{\mathrm{H}\cdots\mathrm{Y}}$ and ρ is depicted in Fig. 6. It is evident that a better correlation exists between $\delta R_{\mathrm{H}\cdots\mathrm{Y}}$ and $\nabla^2\rho$.

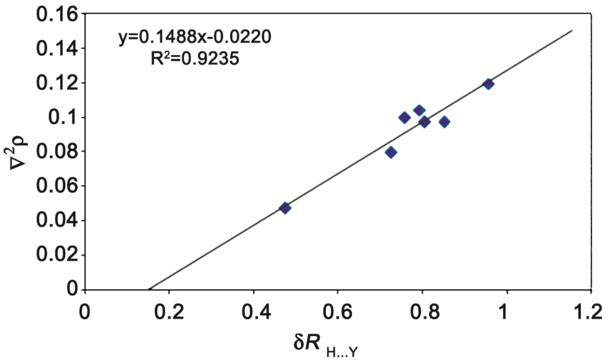


Fig. 5—Correlation between $\delta R_{\mathrm{H}\cdots\mathrm{Y}}$ and Laplacian of electron density ($\nabla^2\rho$) of H-bonded complexes of picolinic acid-water.

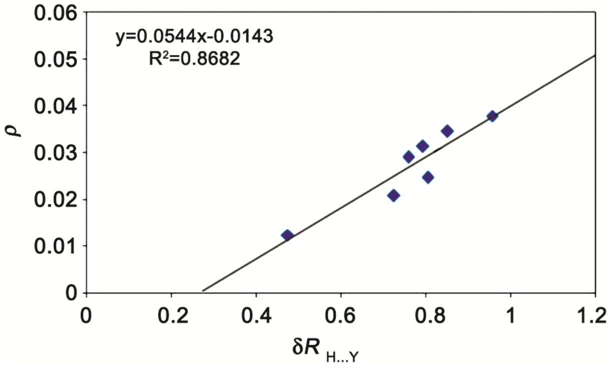


Fig. 6—Correlation between $\delta R_{\mathrm{H}\cdots\mathrm{Y}}$ and electron density (ρ) of H-bonded complexes of picolinic acid-water.

NBO analysis

AIM analysis provides relevant information on the strength of hydrogen bonds, but it does not indicate anything about the electron delocalization or charge transfer between donor and acceptor centers in a hydrogen bonded complex. Generally, a certain amount of charge transfer from H-acceptor to H-donor is one of the important characteristics associated with hydrogen bonded complexes. To evaluate the direction and magnitude of the donor-acceptor interactions, the natural bond orbital (NBO)[51,52] analysis for all the complexes along with the monomer picolinic acid has been performed using NBO 5.0 at B3LYP/6-311++G(d, p) level. The results of NBO analysis are listed in Table 6. The NBO analysis is an effective tool to estimate the overlap between the lone pair orbital of Y and the anti-bonding orbital of the X–H bond of the X–H···Y hydrogen-bonded complex. The second-order perturbative energy, *E*(2), which is proportional to the extent of overlap between the donor and acceptor orbitals, is a measure of the strength of the hydrogen bond[53]. *E*(2) is calculated by second order perturbation analysis of the Fock matrix and associated with a charge transfer interaction between the relevant donor and acceptor orbital. The hydrogen bond formation leads to an increase of the occupancy of the σ^*_{XH} antibonding orbital and hence the X–H bond gets weakened and elongated. As a result frequency shift ($\Delta\nu_{\mathrm{X-H}}$) in stretching frequency of the hydrogen bonded complexes is red shifted compared to the monomer. From Table 6, it is evident that the O–H···O interaction in PA-W2 complex has the highest *E*(2) value of 74.94 kJ/mol, indicating it to be the strongest interaction. This result is commensurate with our AIM calculation. Again *E*(2) value O–H···N interaction in the same complex is the second highest

Table 6—Second-order perturbation energies, *E*(2), of H-bonded picolinic acid-water complexes calculated at B3LYP/6-311++G(d,p) level

Complex	Type of interaction	Donor NBO	Acceptor NBO	Δ*E*(2) (kJ/mol)
PA-W1	O···H–O	LP(O12)	σ* (O15-H16)	17.20
	N···H–O	LP(N6)	σ* (O13-H14)	30.79
	O···H–C	LP(O15)	σ* (C4-H10)	9.83
PA-W2	O···H–O	LP(O15)	σ* (O13-H14)	74.94
	N···H–O	LP(N6)	σ* (O15-H17)	52.22
PA-W3	O···H–O	LP(O12)	σ* (O15-H17)	15.23
	N···H–O	LP(N6)	σ* (O13-H14)	25.90
PA-T1	N6···H14	LP(N6)	σ* (O13-H14)	24.73

value. Therefore in the PA-W2 complex, strong charge transfer interaction is responsible for both the O–H···O and O–H···N hydrogen bonding interactions. Such strong charge transfer effect suggests a partial covalent character of these bonds, which is consistent with our AIM calculation. The O–H···N interactions in both PA-W1 and PA-W3 complexes are stronger than the O–H···O interactions. The *E*(2) values of intramolecular O–H···N interactions in both PA-W1 and PA-W3 complexes are larger than that of the picolinic acid monomer. This indicates that strong charge transfer effect occurred in these complexes due to the intermolecular hydrogen bond, which in turn suggests that there exists a certain amount of cooperative effect between the intramolecular O–H···N hydrogen bond and intermolecular hydrogen bond in these complexes. In the PA-W1 complex, the *E*(2) value of C–H···O interaction is the lowest (9.83 kJ/mol) among all the interactions present. Due to smaller *E*(2) values, weaker charge transfer occurred, which indicates that the major contribution to the hydrogen bond is from non-charge transfer interactions rather than from the charge transfer interactions.

Conclusions

Quantum chemical calculations have been carried out to study the interactions between 1:1 picolinic acid-water complexes. Geometries, energies, IR vibrational analysis, AIM and NBO analysis of the hydrogen bonded complexes have been investigated. Three monohydrated complexes have been identified and reported for the first time. Bond lengths, angles and interaction energy have been calculated using HF, B3LYP, DFT-D and MP2 methods. Harmonic vibrational frequency analysis confirms that these complexes are minima on the potential energy surface at all levels of computations. Among the three hydrated picolinic acid complexes, the structures PA-W1 and PA-W3 retain intramolecular O–H···N interactions upon hydration. The complex PA-W1, containing three different types of hydrogen bonding, is the most stable among the three structures. The AIM and NBO calculations suggest that both the O–H···N and O–H···O interactions in PA-W2 complex have a partial covalent character. Regardless of the strong hydrogen bonding, the stability of PA-W2 is weakened by the structural deformation. Both hydrogen bonding interaction and structural deformation play important roles in the relative stabilities of the complexes. The theoretical IR analysis shows that all the complexes have classical hydrogen bonding with red shifted stretching frequency. The variety of hydrogen bonding motifs in the studied complexes may be helpful to understand the hydrogen bonding interaction between picolinic acid and other small molecules.

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