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Distortion of Electronic Structure in Solvated Molecules: Tautomeric Equilibrium of 2-Pyridone and 2-Hydroxypridine in Water Studied by the RISM-SCF Method

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As well recognized, the electronic structure of a molecule in the solution phase is distorted from that in the gas phase. We present a new procedure that enables us to partition the electronic distortion energy caused by solvation into the energy contribution of each atom (or each moiety), with which one can evaluate the atomic-level change of electronic structure. In the present study, we combine the procedure with the RISM-SCF method that can treat solvent molecules explicitly. This method is successfully applied to the tautomerization of 2-pyridone in aqueous solution, whose equilibrium is known to show a marked solvation effect, and provides us a new detailed feature of this equilibrium. (1) As expected, electronic structures of oxygen and nitrogen atoms, which are strongly solvated, are distorted significantly. (2) However, the electronic distortion energies of the oxygen and nitrogen atoms are considerably compensated by the microscopic solvation. (3) One of the determining factors of the equilibrium is the carbon atom, with which the oxygen atom is bound, because the electronic distortion cannot be compensated by the microsolvation due to its rather inside position, and (4) the other factor is the distortion energy of the proton that directly relates to the equilibrium probably because the electronic structure changes too much to be compensated by microsolvation. These new findings lead to deep and correct understanding of this equilibrium.

1. Introduction

Study of tautomeric equilibrium of amide−imidic acid has been an important issue because it is considered relevant to biochemical processes.[1,2] For example, glycine receptor substrates are potentially involved in tautomeric phenomenon. Among various heterocyclic compounds, details of the equilibrium between 2-pyridone (PY) and 2-hydroxypyridine (HP) have been widely studied both by experimental[3,4] and by theoretical methods.[5] The equilibrium is known as a prototype reaction, particularly, to compute solvation effects on electronic structure: studies based on the dielectric continuum model and on the QM/MM[5t] strongly suggest that the equilibrium of the tautomerization in aqueous solution leans to PY, whereas HP is a slightly stable in energy in the vapor condition. Despite the capability of these dielectric continuum models to analyze the solvation energetics, they cannot provide any information on the microscopic solvation structure. Although there are several computational reports on the structures of PY/HP−water cluster, they are essentially different from the situation in the liquid phase. The RISM-SCF method, which we employ here, compiles ab initio electronic structure theory and statistical mechanics of molecular liquids. The method can provide atomic detail of solvation that is consistent with the solute electronic structure. It is of great interest to compare the present results with QM/MM, because only these two methods can treat the explicit solvent model.

Another point we focus on in this article is “distortion” of the electronic structure in the solution phase. Recently developed various molecular orbital theories including solvation effect (e.g., RISM-SCF/MCSCF, PCM, and QM/MM) reveal that the electronic structure of the solvated molecule is distorted from the gas phase one. Such distortion of electronic structure cannot be ignored and sometimes seriously affects chemical phenomena. The distortion is analyzed through various type of quantities such as electronic dipole moment, effective charges assigned on atoms. One of the measurements we have used in our previous studies is “reorganization energy”.[6,7]

$$
\begin{aligned}
E_{\mathrm{reorg}} &= E_{\mathrm{solute}} - E_{\mathrm{isolated}} \\
&= \langle \Psi | H | \Psi \rangle - \langle \Psi_0 | H | \Psi_0 \rangle \qquad (1)
\end{aligned}
$$

where E_{isolated} is the electronic energy of the isolated molecule, which can be computed with a standard ab initio method ($|\Psi_0\rangle$ is its wave function), and E_{solute} is that of solvated molecule ($|\Psi\rangle$ is its wave function). It should be noted that E_{reorg} represents the change in energy, whereas the analysis based on the multipole moment expansion provides information of the change in electronic distribution. Both of them are useful to know how much the electronic structure of the molecule is distorted, but we do not obtain any information of which atom (or moiety) dominatively contributes to the distortion of the molecule. This is in clear contrast to the situation of the RISM theory,[8,9] in which solvation free energy can be “formally” partitioned into atomic contribution.[10] It is possible, for example, to analyze which atom (or moiety) in the solute plays the most significant role in solvation. Similar analysis for the electronic distortion must be very helpful to understand the chemical processes in the solution phase. This can be achieved by using the energy partitioning technique.[11] We emphasize that such a partitioning technique on the electronic reorganization (relaxation) due to solvation is very limited,[12] although numerous ways

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to partition the solvation energy (solute−solvent interaction) have been proposed.

Our purposes here are to clarify details of solvation structure and to discuss its coupling with the electronic structure in the tautomerization between PY and HP. Our intention here is to present a new analysis method with combination of RISM-SCF[13,14] and an energy partitioning scheme, and to a provide new and deep understanding of the electronic structure of the solvated molecule.

2. Computational Methods

The RISM-SCF method compiles ab initio electronic structure theory and statistical mechanical theory of the molecular liquid. The total energy of the system is defined as the sum of electronic energy of the solute (E_{solute}) and excess chemical potential, i.e., solvation free energy, $\Delta\mu_{\mathrm{HNC}}$, where HNC stands for hypernetted-chain.

$$\mathscr{A} = E_{\mathrm{solute}} + \Delta\mu_{\mathrm{HNC}} \tag{2}$$

Because the electronic structure of the solute and the solvation structure around it are determined in a self-consistent manner, the wave function of the solute molecule is distorted from that in the isolated state. As shown in eq 1, the energy difference between the solute in the isolated state (E_{isolated}) and that in the solvent (E_{solute}) is a quantity to measure the contribution from "solvation effects" in the electronic structure. Equation 2 can be thus rewritten as follows,

$$\mathscr{A} = E_{\mathrm{isolated}} + E_{\mathrm{reorg}} + \Delta\mu_{\mathrm{HNC}} \tag{3}$$

The last term, the solvation free energy $\Delta\mu_{\mathrm{HNC}}$,[15] is "formally" expressed as a sum of the site−site contributions, and we can decompose it into the contribution from each atom (α) in the solute.

$$\Delta\mu_{\mathrm{HNC}} = \sum_{\alpha} \Delta\mu^{\alpha}_{\mathrm{HNC}} \tag{4}$$

It must be noted that $\Delta\mu^{\alpha}_{\mathrm{HNC}}$ is not the same as the solvation free energy of an atom α isolated in the solvent, because the correlation functions in $\Delta\mu_{\mathrm{HNC}}$ also depend on the other atoms in the solute. The electronic distortion energy, E_{reorg}, can be partitioned into atomic contributions in a similar manner. The electronic energy of the composing atoms can be "formally" defined by using a similar procedure to the Mulliken charge population analysis (EDA), developed by Nakai.[11] In the case of Hartree−Fock method, the total energy of the solute molecule ($E = E_{\mathrm{isolated}}$ or E_{solute}) is given as follows:

$$E = \frac{1}{2}\sum_{A}\sum_{B\neq A}\frac{Z_A Z_B}{R_{AB}} + \sum_{\mu,\nu} P_{\nu\mu}\left\{\left\langle \mu \left| -\frac{1}{2}\nabla^2 \right| \nu \right\rangle + \left\langle \mu \left| \sum_{A}\frac{Z_A}{r_A} \right| \nu \right\rangle + \frac{1}{2}G_{\mu\nu}\right\} \tag{5}$$

where $P_{\nu\mu}$ is a density matrix and $\mu \equiv \chi_\mu$ and $\nu \equiv \chi_\nu$ are atomic orbitals (AOs). Other notations used here have the usual meanings. Partitioning the first term in the right-hand side of the equation into atomic contributions is trivial.

$$E^{\alpha}_{\mathrm{NN}} = \frac{1}{2}\sum_{B\neq\alpha}\frac{Z_\alpha Z_B}{R_{\alpha B}} \tag{6}$$

Because summation in the other three terms runs over AO indices, contribution from atom $\alpha(E^{\alpha})$ can be defined by dividing the trace into each atom, which is analogous to the Mulliken gross charge population.

TABLE 1: Lennard Jones Parameters for PY/HP[a]

	σ/Å	ϵ/kcal mol^{-1}
C	3.75	0.11
N	3.25	0.17
O	2.96	0.21
H	1.78	0.02

$$E^{\alpha}_{\mathrm{T}} = \sum_{\nu\in\alpha}\sum_{\mu} P_{\nu\mu}\left\langle \mu \left| -\frac{1}{2}\nabla^2 \right| \nu \right\rangle \tag{7}$$

$$E^{\alpha}_{\mathrm{ee}} = \frac{1}{2}\sum_{\nu\in\alpha}\sum_{\mu} P_{\nu\mu} G_{\mu\nu} \tag{8}$$

For the electron−nucleus interaction term, we use the following expression (see Appendix):

$$E^{\alpha}_{\mathrm{eN}} = \frac{1}{2}\sum_{\nu\in\alpha}\sum_{\mu} P_{\nu\mu}\left\langle \mu \left| \sum_{A}\frac{Z_A}{r_A} \right| \nu \right\rangle + \frac{1}{2}\sum_{\nu}\sum_{\mu} P_{\nu\mu}\left\langle \mu \left| \frac{Z_\alpha}{r_\alpha} \right| \nu \right\rangle \tag{9}$$

The energy partitioned on atom α is then given by

$$E^{\alpha} = E^{\alpha}_{\mathrm{NN}} + E^{\alpha}_{\mathrm{T}} + E^{\alpha}_{\mathrm{eN}} + E^{\alpha}_{\mathrm{ee}} \tag{10}$$

EDA has successfully applied to various chemical reactions.[11] We compute the total energy of molecules in gas and solution phases, in which the partitioned energies are, respectively, defined as follows:

$$E_{\mathrm{solute}} = \sum_{\alpha} E^{\alpha}_{\mathrm{solute}}$$

$$E_{\mathrm{isolated}} = \sum_{\alpha} E^{\alpha}_{\mathrm{isolated}} \tag{11}$$

The difference between these energies correspond to partitioned reorganization energy.

$$E_{\mathrm{reorg}} = \sum_{\alpha} E^{\alpha}_{\mathrm{reorg}} = \sum_{\alpha}(E^{\alpha}_{\mathrm{solute}} - E^{\alpha}_{\mathrm{isolated}}) \tag{12}$$

This quantity represents how much the local (atomic level) electronic structure of the solute is affected by solvation. Note that $E^{\alpha}_{\mathrm{reorg}}$ consists of two types of contributions: one is from electric polarization within atom α, the other is from electron movement between atoms. (One might regard that it is analogous to the combination of "polarization" and "charge transfer" in the Morokuma analysis, although we consider interatomic interaction in this work.) Hence, E_{reorg} can be related not only to the polarization of each atom but also to the change in number of electron assigned in the atom.

The electronic wave functions of solvated PY and HP were computed on the basis of the RHF method with triple-ζ basis sets augmented by a p-polarization function on the hydrogen atom and d-polarization functions on all the heavy atoms.[16] It has been already reported that computation by the Hartree−Fock method can achieve good accuracy in the present system and the electron correlation effect does not play significant roles.[5c] In the RISM theory, PY and HP are modeled with all atom-type interactions including fourteen sites, whose Lennard-Jones parameters were taken from the literature[17] and summarized in Table 1. The SPC-like water[6] was employed to

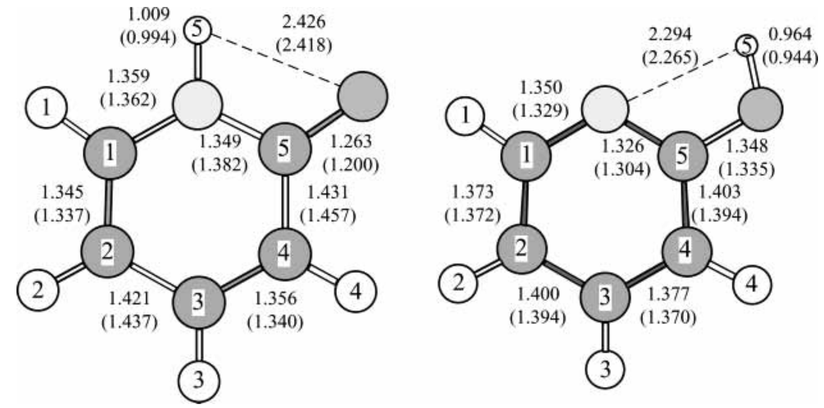

Figure 1. Selected geometrical parameters and atomic labeling in PY and HP.

TABLE 2: Energy Components and Dipole Moments

	energy components/kcal mol^{-1}					
	gas phase	aqueous solution			dipole moments/Debye	
	E_{isolated}	E_{reorg}	$\Delta\mu_{\text{HNC}}$	A	gas phase	aqueous soln
HP	−0.7	6.4	7.7	13.4	1.50	3.16
PY	0.0[a]	20.3	−16.7	3.6	4.67	9.44
Δ(HP−PY)	−0.7	−13.9	24.4	9.7		

[a] −321.66925 hartree.

describe the solvent. All the van der Waals interactions between solute and solvent are determined by means of the standard combination rule. The density of water is assumed to be 0.033337 molecule/Å^3 at 298.15 K.

3. Results and Discussion

3.1. Optimized Structures in the Gas and Aqueous Solution Phases. Molecular geometries of PY and HP are optimized in both the gas and aqueous solution phase under a constraint of planar C_s symmetry. Results for selected parameters of geometry and atomic labels are shown in Figure 1. The gas-phase structural data obtained for PY and HP show reasonable agreement with microwave spectroscopy experiments;[3] the C−O bond length in PY (1.200 Å) and in HP (1.335 Å) are quite close to the experimental data (1.203 and 1.336 Å, respectively), and the bond lengths for the key atom in the tautomerization, H_5−nitrogen (0.994 Å), and H_5−oxygen (0.944 Å) are slightly shorter than the experimental results (1.005 and 0.960 Å). The discrepancy between the computed bond length and the experimental measurements are satisfactorily small in any case (less than 0.03 Å). As shown in the figure, all the optimized bonds tend to be stretched in aqueous solution, but they are not deviated so much from those in the gas phase. One of the most significant deviations in the geometry occurs in the C═O bond of PY, although the change of the bond length is only 0.06 Å.

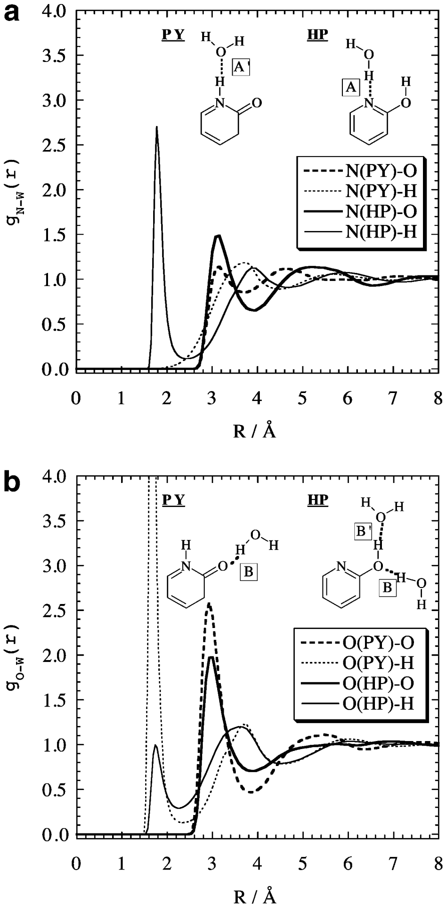

Figure 2. Radial distribution function of the solvent water molecule (a) around the nitrogen atom and (b) around the oxygen atom.

Total energies of these structures in both the gas (E_{isolate}) and aqueous solution phases are listed in Table 2. HP is lower in energy than PY in the gas phase, but this energetic relationship is reversed by aqueous solution. This tendency shows agreement with the previous studies based on the dielectric continuum model[5d,h,i,m] and on QM/MM.[5t] The total free energy difference of 9.7 kcal/mol is much greater than that obtained by the QM/MM method (5.7 kcal/mol). E_{reorg} in PY is more than 20 kcal/mol, suggesting that the electronic structure in aqueous solution is remarkably deviated from that in an isolated molecule. At the same time, a large amount of stabilization (ca. 17 kcal/mol) is gained by the solvation. The quantitative disagreement in the free energy difference between the QM/MM and the present computation can be attributed to the difference of electronic Hamiltonian: the QM/MM computation is based on the semiempirical AM1 method, whereas the present study uses the ab initio method. Another source is the difference of solvation strength. Unfortunately, radial distribution functions are not shown in ref 5t, and we cannot compare the solvation numbers. But the reorganization energy in the QM/MM system (denoted ΔG_{pol} in the ref 5t) is much smaller than that in the present system. These differences between the two methods are a common tendency, and details are discussed elsewhere.[19]

3.2. Solvation Structure. The solvation structure is described in terms of a set of pair correlation functions (PCFs) in the present theory. Shown in Figure 2a,b are the PCFs of solvent water molecules around nitrogen atom in PY and HP and those around oxygen atom in PY and HP, respectively. The sharp peak located around 2 Å in Figure 2a (see thin solid line in the figure) corresponds to a hydrogen bonding between the lone pair of the nitrogen in HP and the water hydrogen. This hydrogen bonding is schematically depicted as A in the right-upper side of the figure. This peak virtually disappears in PY (bold-solid line in the figure). This is because the newly formed H_5-N bond excludes solvent water in this region. Instead of that, another type of hydrogen bonding between H_5 and O (water) appears, as illustrated in A′ in the figure; actually, the N−O peak at 3.0 Å (bold dashed line) and the N−H peak at 3.8 Å (thin dashed line) confirm this interaction. (Note that the PCF around H_5 is not shown here). Although the first peak position of N−O(water) PCFs is observed around 3.0 Å in both PY and HP (bold solid and dashed lines), they are due to different types of hydrogen bonding, i.e., A and A′. This difference in the oxygen atom between PY and HP is more clearly shown by remarkable PCFs around the solute oxygen atoms in PY and HP (Figure 2b). Peaks around 2 Å (O−H) (thin solid and dashed lines in the figure) and those around 3 Å (O−O) (bold solid and dashed lines) obviously indicate formation of strong hydrogen bonding. By analyzing them, we found that the PCF of the O−O pair around 3 Å in HP is attributed to a superposition of two types of bonding, namely, B and B′ depicted in the figure. B is considered dominant in the PY isomer and much stronger than that in HP because of its peak height.

3.3. Energy Partitioning in Solvated Molecule. Distortion of electronic structure must be related to the change of effective charge assigned to each atom. The partitioned energies given in eq 11, $E^{\alpha}_{\text{isolated}}$ and $E^{\alpha}_{\text{solute}}$, on (a) carbon and (b) hydrogen atoms are plotted in Figure 3 as functions of the effective charge. We examined four types of computations for PY and HP, respectively: gas-phase computation with the optimized structure in the gas phase (G_g), gas-phase computation with the optimized structure in the aqueous solution phase (G_s), and computations in aqueous solution with these two optimized structures (S_g and S_s). The results for the five carbon atoms (C_1-C_5) and five hydrogens (H_1-H_5) are shown in Figure 3. An obvious correlation is found in each atom except for several points that deviate from the linear relationship. The deviation is observed at $|e| = +0.3$ to $+0.4$ around -37.88 hartrees. These points correspond to C_5 in PY. The reason is easily understood in terms that the C_5 atom stands between aromatic and carbonyl characters and are different from the other four aromatic carbon atoms. Another interesting feature in the figure is the universality of the electronic distortion: the same relationship between the atomic local distortion energy and the Mulliken charge is seen in both isomers and both in the gas and aqueous solution phases. In other words, the distortion of the electronic structure is governed by the inherent character of atoms even when the molecule is solvated. Also, one can notice that the slope of the relation is regarded as the electronegativity of the atoms. The least-squares fitting of the lines yields the slope of 3.1 for carbon (3.9 if the deviated four points are ignored), which is related to Mulliken's estimated value (5.6). The slope for the hydrogen atom (5.5) is also close to Mulliken's value (7.2). The quantity is universal and is not affected by solvation.

Our next focus is how much each atom contributes to the distortion in electronic structure induced by the tautomerization. The following quantity is introduced to analyze the effect.

$$\Delta E^{\alpha}_{\text{isolated}} = E^{\alpha}_{\text{isolated}}(\text{HP}) - E^{\alpha}_{\text{isolated}}(\text{PY}) \qquad (13)$$

$$\Delta E^{\alpha}_{\text{solute}} = E^{\alpha}_{\text{solute}}(\text{HP}) - E^{\alpha}_{\text{solute}}(\text{PY}) \qquad (14)$$

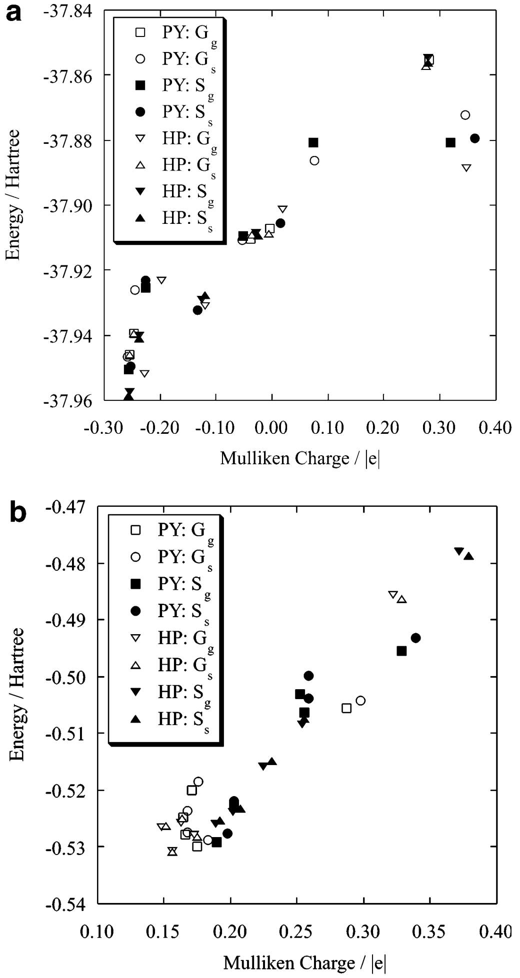

Figure 3. Relationship between the Mulliken charge and local energy evaluated by EDA: (a) all carbon atoms; (b) all hydrogen atoms.

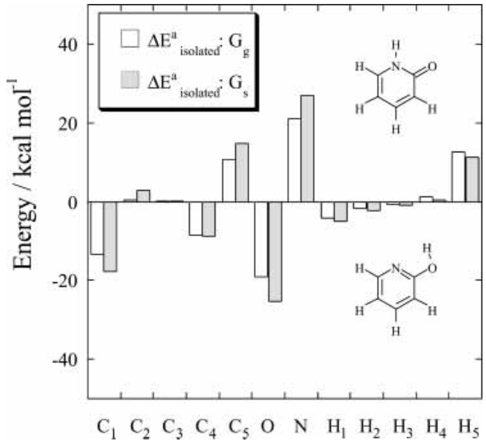

Figure 4. Energy distortion at the atomic level: energy difference between PY and HP of the isolated (gas phase) molecule.

If $\Delta E^{\alpha}_{X} > 0$, the energy contribution of atom α stabilizes PY more than HP, whereas $\Delta E^{\alpha}_{X} < 0$ indicates that the energy contribution of atom α stabilizes HP more than PY. Figure 4 shows ΔE^{α}_{X} of the isolated molecule in two different geometrical structures, namely, the optimized structure in gas phase (G_g) and that in aqueous solution (G_s). Striking changes in electronic structure on the tautomerization are found in the oxygen and nitrogen atoms, and these changes are not strongly affected by the geometrical change between G_g and G_s. For example, the electronic structure in the nitrogen atom yields much less contribution in the PY isomer in both geometries. A more important feature is that the nitrogen atom stabilizes the

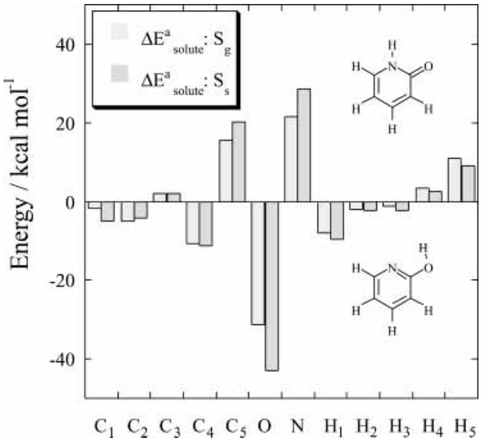

Figure 5. Energy distortion at the atomic level: energy difference between PY and HP of the molecule in aqueous solution.

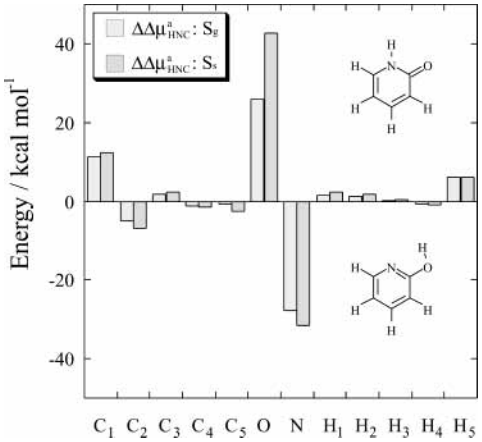

Figure 6. Solvation free energy at the atomic level: energy difference between PY and HP of the molecule in aqueous solution.

PY form but the oxygen atom stabilizes the HP form more. The same plot for the electronic structure in aqueous solution is given in Figure 5. The changes in aqueous solution occur with the same tendency as that in the gas phase, but somewhat enhanced. For example, the energy contribution of the oxygen atom stabilizes the HP form much more than the PY form. This is because the PY isomer contains strong hydrogen bonding at the oxygen site (aforementioned as type A), which makes the distortion in the oxygen atom greater than that of the gas phase. It is also interesting that contributions from the C_1 atom, which connects to the nitrogen atom, show significant change upon transferring from the gas phase to aqueous solution.

Figure 6 shows the solvation free energy difference between two isomers.

$$\Delta\Delta\mu^{\alpha}_{\mathrm{HNC}} = \Delta\mu^{\alpha}_{\mathrm{HNC}}(\mathrm{HP}) - \Delta\mu^{\alpha}_{\mathrm{HNC}}(\mathrm{PY}) \qquad (15)$$

Like the discussion on ΔE^{α}, $\Delta\Delta\mu^{\alpha}_{\mathrm{HNC}} > 0$ denotes atom α in PY gains greater stabilization in energy by the solvation, whereas $\Delta\Delta\mu^{\alpha}_{\mathrm{HNC}} < 0$ denotes atom α in HP gains greater stabilization in energy by the solvation. The figure clearly shows that the oxygen atom in PY and the nitrogen atom in HP receive great stabilization and that the other atoms contribute little relative stability to the PY and HP isomers. In other words, the electronic structure change by the PY and HP tautomerization is local and mainly determined by the O and N atoms. These results are consistent with the above-mentioned solvation structure analysis, in which strong hydrogen bonding of these atoms is found.

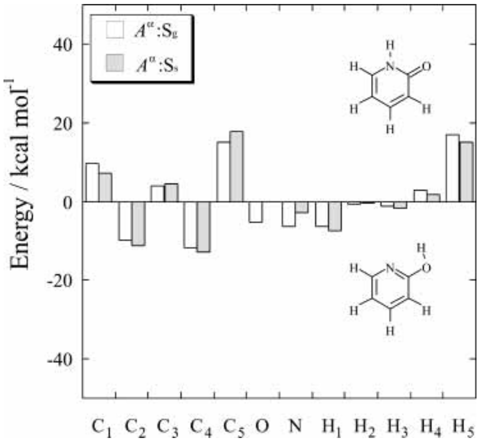

Figure 7. Total energy at the atomic level: energy difference between PY and HP of the molecule in aqueous solution.

In aqueous solution the local energy ($\mathcal{A}^{\alpha}$) is defined as the sum of the contribution from the electronic energy ($E^{\alpha}_{\mathrm{solute}}$) and the solvation energy $\Delta\mu^{\alpha}_{\mathrm{HNC}}$,

$$\mathcal{A}^{\alpha} = E^{\alpha}_{\mathrm{solute}} + \Delta\mu^{\alpha}_{\mathrm{HNC}} = E^{\alpha}_{\mathrm{isolated}} + E^{\alpha}_{\mathrm{reorg}} + \Delta\mu^{\alpha}_{\mathrm{HNC}} \qquad (16)$$

and

$$\mathcal{A} = \sum_{\alpha} \mathcal{A}^{\alpha} \qquad (17)$$

Figure 7 illustrates $\mathcal{A}^{\alpha}$. Apparently, great distortion in electronic energy and great stabilization in energy by the solvation are canceled out in oxygen and nitrogen atoms. Contribution from the other atoms becomes rather greater, whereas all the difference is less than 20.0 kcal/mol. Here, our attention is drawn to two interesting aspects for the solvation of the present HP−PY system as follows, first, the solvation free energies themselves are gained at two heteroatoms, but the electronic structures of these atoms are strongly distorted simultaneously. The energetically preferable solvation should cause a penalty in electronic structure because the electronic structure of the solute and the solvation structure are determined in a self-consistent manner in the present RISM-SCF treatment. The second aspect is the solvation effect on the energy difference of tautomerization. In the gas phase, the energy difference of the two isomers is mainly attributed to the oxygen and nitrogen atoms. However, in aqueous solution, the situation is drastically changed if one considers the whole solvation system containing the solute and solvent. Contributions from $E^{\alpha}_{\mathrm{solute}}$ and $\Delta\mu^{\alpha}$ compensate each other at oxygen and nitrogen and are not great any more. The role of various atoms such as carbon and hydrogen atoms become rather important in aqueous solution. It is of great interest that the contribution from the shifting hydrogen atom (H_5) becomes important in aqueous solution when we see the solvation at the local, atomic level description. Contribution from C_5 is also remarkable. This is because the atom does not play any significant role in the solvation process and the electronic distortion between HP and PY in the gas phase is directly related to the situation in aqueous solution, which is shown in Figure 7.

4. Concluding Remarks

We present a new combination of RISM-SCF and an energy partitioning scheme to clarify the distortion of electronic structure by solvation. Analysis of the interplay between the electronic structure and microscopic solvation can be realized by this procedure. Though a combination of the energy partitioning and other solvation theories such as PCM is possible, such a combination cannot touch details of the interplay because a continuum model does not provide a microscopic picture of solvation. The combination of RISM-SCF and the energy partitioning presented in this article can provide a new way to understand the solvation.

The tautomerization of 2-pyridone in aqueous solution is examined to illustrate the method. There are remarkable contributions to the solvation free energy by hydrogen bonding at nitrogen and oxygen atoms. This is solvation phenomena *around* these heteroatoms. At the same time, the electronic structure *within* these atoms is strongly distorted from that in the gas phase. Contributions from $E^{\alpha}_{\mathrm{solute}}$ and $\Delta\mu^{\alpha}$ compensate each other at oxygen and nitrogen and are not great any more. It has been possible to discuss specific sites of solvation, namely, which atoms of the solute molecule mainly contribute to the solvation. However, if we look at the solvation as a combined event of such solvent coordination and the change of electronic structure in solute molecule, these atoms with specific solvation may receive strong distortion in electronic structure, and the importance of other atoms is enhanced. In the present studied tautomerization, contributions from shifting hydrogen (H_5) and from carbon atoms that connect to the heteroatoms are important.

We believe a localized character of solvation with atomic level introduced in this article could help deeper understanding of solvation processes.

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Appendix

The electron−nucleus interaction term consists of two center for electron (A and B) and one center for nuclei (C).

$$E_{\mathrm{eN}} = \sum_{\mu,\nu} P_{\nu\mu} \left\langle \mu \left| \sum_{C} \frac{Z_{\mathrm{C}}}{r_{\mathrm{C}}} \right| \nu \right\rangle = \sum_{\mathrm{A,B,C}} \left\{ \sum_{\mu\in\mathrm{A}} \sum_{\nu\in\mathrm{B}} P_{\nu\mu} \left\langle \mu \left| \frac{Z_{\mathrm{C}}}{r_{\mathrm{C}}} \right| \nu \right\rangle \right\} \tag{18}$$

Ichikawa et al. suggested[18] that these integrals are classified to one- and two-center components.

$$E_{\mathrm{eN}} = \sum_{X} \langle V_{\mathrm{eN}} \rangle_{\mathrm{X}} + \sum_{\mathrm{X>Y}} \langle V_{\mathrm{eN}} \rangle_{\mathrm{X-Y}} \tag{19}$$

and

$$\langle V_{\mathrm{eN}} \rangle_{\mathrm{X}} = \sum_{\mu\in\mathrm{X}} \sum_{\nu} P_{\nu\mu} \left\langle \mu \left| \frac{Z_{\mathrm{X}}}{r_{\mathrm{X}}} \right| \nu \right\rangle$$

$$\langle V_{\mathrm{eN}} \rangle_{\mathrm{XY}} = \sum_{\mu\in\mathrm{X}} \sum_{\nu} P_{\nu\mu} \left\langle \mu \left| \frac{Z_{\mathrm{Y}}}{r_{\mathrm{Y}}} \right| \nu \right\rangle + \sum_{\mu\in\mathrm{Y}} \sum_{\nu} P_{\nu\mu} \left\langle \mu \left| \frac{Z_{\mathrm{X}}}{r_{\mathrm{X}}} \right| \nu \right\rangle \tag{20}$$

We define the one-center (atomic) contribution by partitioning the two-center components into two (X and Y) one-center components

$$E^{\mathrm{X}}_{\mathrm{eN}} = \langle V_{\mathrm{eN}} \rangle_{\mathrm{X}} + \frac{1}{2} \sum_{\mathrm{Y}\neq\mathrm{X}} \langle V_{\mathrm{eN}} \rangle_{\mathrm{XY}} \tag{21}$$

which gives eq 9. The expression is equivalent to the energy density analysis (EDA).[11] It is noted that other definitions are also possible. For example,

$$E^{\mathrm{X}}_{\mathrm{eN}} = \begin{cases} \displaystyle\sum_{\mu\in\mathrm{X}} \sum_{\nu} P_{\nu\mu} \left\langle \mu \left| \sum_{\mathrm{A}} \frac{Z_{\mathrm{A}}}{r_{\mathrm{A}}} \right| \nu \right\rangle & \text{(model A)} \\ \displaystyle\sum_{\mu} \sum_{\nu} P_{\nu\mu} \left\langle \mu \left| \frac{Z_{\mathrm{X}}}{r_{\mathrm{X}}} \right| \nu \right\rangle & \text{(model B)} \end{cases} \tag{22}$$

Contribution from all the nuclei is averaged in model A, whereas that from electrons is averaged in model B. We examined all these models and found that models A and B are not adequate to represent the partitioning energy because of their ill-balanced treatment on the nuclei and electrons.

References and Notes

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