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How Resonance Assists Hydrogen Bonding Interactions: An Energy Decomposition Analysis

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Abstract: Block-localized wave function (BLW) method, which is a variant of the *ab initio* valence bond (VB) theory, was employed to explore the nature of resonance-assisted hydrogen bonds (RAHBs) and to investigate the mechanism of synergistic interplay between π delocalization and hydrogen-bonding interactions. We examined the dimers of formic acid, formamide, 4-pyrimidinone, 2-pyridinone, 2-hydroxypyridine, and 2-hydroxycyclopenta-2,4-dien-1-one. In addition, we studied the interactions in β -diketone enols with a simplified model, namely the hydrogen bonds of 3-hydroxypropenal with both ethenol and formaldehyde. The intermolecular interaction energies, either with or without the involvement of π resonance, were decomposed into the Hitler-London energy (ΔE_{HL}), polarization energy (ΔE_{pol}), charge transfer energy (ΔE_{CT}), and electron correlation energy (ΔE_{cor}) terms. This allows for the examination of the character of hydrogen bonds and the impact of π conjugation on hydrogen bonding interactions. Although it has been proposed that resonance-assisted hydrogen bonds are accompanied with an increasing of covalency character, our analyses showed that the enhanced interactions mostly originate from the classical dipole–dipole (i.e., electrostatic) attraction, as resonance redistributes the electron density and increases the dipole moments in monomers. The covalency of hydrogen bonds, however, changes very little. This disputes the belief that RAHB is primarily covalent in nature. Accordingly, we recommend the term “resonance-assisted binding (RAB)” instead of “resonance-assisted hydrogen bonding (RHAB)” to highlight the electrostatic, which is a long-range effect, rather than the electron transfer nature of the enhanced stabilization in RAHBs.

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Key words: resonance-assisted binding; resonance-assisted hydrogen binding; electrostatic interaction; block-localized wave function

Introduction

Intermolecular and intramolecular hydrogen-bonding interactions widely exist in chemical and biological systems and play a fundamental role not only in the molecular properties and structures but also in the chemical and biological processes. A wealth of information on hydrogen bonds can be found in the literature,^{1,2} and hydrogen bonds can be probed experimentally using NMR,³ IR,⁴ and Compton profile anisotropies,⁵ and other techniques. However, there have been controversies over the essence of hydrogen bonds, notably either the pure electrostatic^{2,6} or partial covalent nature.^{5,7,8} Generally, hydrogen-bonding interactions are close to or slightly stronger than van der Waals interactions, but still fall into the category of weak interactions with a strength ranging from 2 to 10 kcal/mol, depending on the bond length and linearity.^{6,8} This view has been challenged recently as more and more strong and unconventional hydrogen bonds have been recognized.^{9–12} As a matter of fact, several types of strong hydrogen bonds have been investigated, for example, charge assisted hydrogen bonds (CAHBs),^{12,13} low barrier hydrogen bonds (LBHBs),^{14,15} dihydrogen bonds (DHBs),^{8,16} and resonance-assisted hydrogen bonds (RAHBs).^{10–12} In a CAHB, a

positive or negative charge on the proton donating or accepting group remarkably increases the strength of the hydrogen bond. LBHBs are a class of hydrogen bonds that have a low energy barrier for the proton shift from the proton donor to proton acceptor. The low barrier is usually accompanied by a very short hydrogen bond length. LBHBs are particularly important in enzymatic catalysis where a weak hydrogen bond in the initial enzyme–substrate complex can be converted to a LBHB in the transition state.^{15,17} LBHBs are assumed to be largely covalent.¹⁸ DHBs are designated as $X-H\cdots H-M$ where X is an electronegative atom such as O or N, and M is a transition metal or boron. DHBs have been found in new types of complexes, posing challenging problems in chemistry, and their strength is often larger than 10 kcal/mol.⁸ RAHB highlights the co-operativity between the π -electron delocalization and hydrogen bonds and the term was coined by Gilli and coworkers in the late 1980s, who have continued to refine their theory through a series of papers.^{10–12} In RAHB, the hydrogen bond donor and acceptor

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atoms are connected through π -conjugated double bonds. A typical example of RAHB is β -diketone enols which form intramolecular $\cdots\text{O}=\text{C}-\text{C}=\text{C}-\text{OH}\cdots$ hydrogen bonds enhanced by the resonance with O \cdots O distances as short as 2.39–2.44 Å.¹² The shortening of the hydrogen bonds is associated with a decrease of O–H vibrational frequencies and abnormal downfield ^1H NMR chemical shifts.¹¹ Heteronuclear N–H \cdots O RAHBs have a crucial role in protein folding and DNA pairing.

The goal of this work is to explore the nature of RAHB and investigate the mechanism of synergistic interplay between π delocalization and hydrogen-bonding interactions. Although, traditionally, hydrogen bonds have been thought of as predominantly electrostatic in nature, the modern view is that there is also a covalent character in hydrogen bonds which is consistent with the directionality of hydrogen bonding interactions. Gilli et al. have proposed a unified hydrogen bond theory and interpreted RAHBs with the electrostatic-covalent H-bond model (ECHBM).¹⁹ They claim that weak hydrogen bonds are electrostatic in nature but their covalent character increases as the bond strength increases. Very strong hydrogen bonds actually become three-center-four-electron covalent bonds due to the isoenergetics of valence bond (VB) resonance forms. Although Gilli and coworkers initially focused on the intramolecular hydrogen bonds as in β -diketone and β -enaminones fragments, the principle of RAHB can also be applied to intermolecular hydrogen bonds between monomers with hydrogen bonding functional groups, such as O–H \cdots O=C in carboxylic acids, carboxylate hydrates and N–H \cdots O=C in DNA, proteins and certain self-assembling systems.^{20–22} For intramolecular hydrogen bonds, the proton donor and acceptor are connected by a conjugated bridge. Resonance in this bridge allows for the acidity constants (pK_a) or proton affinities (PA) of the donor and acceptor groups matching and subsequently results in an enhanced hydrogen bond. For intermolecular hydrogen bonds, there is no such conjugated bridge between the proton donor and acceptor. But the existence of different resonance forms (structures) alters the pK_a or PA of the donor and acceptor groups and increases the strength of the hydrogen bonding, for example, in the cyclic dimers of carboxylic acids. To investigate the impact of resonance on hydrogen bonds, it is essential to quantify the π delocalization.

Computationally, one appropriate method to understand the nature of hydrogen bonds in a physically meaningful way is to divide the interaction energy into various components such as electrostatic, exchange, dispersion, relaxation, etc.^{23,24} Although a certain arbitrariness is inevitable in energy decomposition schemes, consensus can be drawn from the analysis of a group of complexes. An alternative approach is to examine changes in other molecular properties such as charge and momentum distributions.²⁵ These methods, however, are applicable to the study of intermolecular interactions but not the resonance effect, which is an intramolecular phenomenon. The concept of resonance came up when one Lewis (resonance) structure was not enough to describe a conjugated system. According to the original definition of Pauling and Wheland,^{6,26–28} resonance effect can be measured with resonance energy, which is “obtained by subtracting the actual energy of the molecule in question from that of the most stable contributing structure.”²⁷ Thus, the question

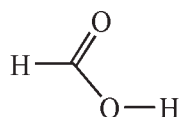
now is how to derive the wave function and its energy for the most stable resonance structure such as the Kekulé structure for benzene. Because of the delocalization nature of molecular orbitals (MOs), the MO theory is unable to provide solutions to the above question. Indirectly, various isodesmic and homodesmotic model reactions have been devised to estimate the resonance (and aromaticity) energies without resorting to the explicit wave functions of resonance structures.^{29,30} But these kinds of model reactions rely on the choice of reference molecules and other effects in the reference systems, such as strain, hyperconjugation, Coulomb repulsion imbalance (especially in charged systems), and uncompensated van der Waals attractions, which have not been recognized, and wide deviations in the results have been observed.³¹

The best way to study the resonance effect is *ab initio* VB methods, where each resonance structure is represented by a Heitler-London-Slater-Pauling (HLSP) wave function.^{6,28} *Ab initio* VB theory has been rejuvenated in the past two decades,³² even though its further broad application will require a significant reduction in its computational demands. Alternatively, the recently proposed block-localized wave function (BLW) method, which can be regarded as a variant of the *ab initio* VB theory, preserves the characteristics and advantages of both the VB and molecular orbital (MO) theory,^{33–35} and thus provides a practical means to compute the conventional Pauling-Wheland resonance energy. In the BLW method, the wave function of a resonance structure is defined with a Slater determinant and block-localized MOs, which are expanded only in a fraction of the overall basis space. Moreover, based on the BLW method, an energy decomposition approach (BLW-ED) has been proposed to analyze the nature of intermolecular interactions in terms of electrostatic, Pauli repulsion, polarization, and charge-transfer effects, etc.^{24,36–38} Compared with other energy decomposition schemes, an unique characteristic of the BLW-ED method is the construction of an intermediate diabatic state, where charge transfer among interacting monomers is quenched and the wave function is self-consistently optimized. This kind of intermediate diabatic state actually corresponds to a resonance structure (often the most stable) within the conventional resonance theory. In such a way, a physical separation of polarization and charge transfer effects are feasible and insights into the nature of hydrogen bonding interactions can be gained. It is also worthwhile to point out that most of the energy decomposition schemes are solely based on the analysis of adiabatic (delocalized) state wave function. In the BLW-ED method, basis set superposition error (BSSE)³⁹ is considered in the computational algorithm and is attributed to the CT energy.²⁴ The method has been applied to a variety of systems, including cation- π , acid-base complexes, and DNA base pairs, and has shown limited basis set dependence from 6-31G(d) to 6-311+G(d,p) and cc-pVTZ.^{22,24,36–38}

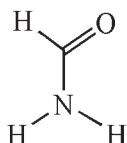
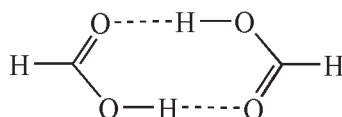
In this work, we employed both BLW and BLW-ED to study the impact of resonance on hydrogen bonds. Our focus is on the hydrogen bonds involving the amide and carboxylic acid functional groups, either of which can act as proton donor and acceptor.⁹ Acetic acid, for example, can form intermolecularly hydrogen-bonded dimers in CCl_4 solvent, with an association constant of $K_\text{assoc} = 2370 \text{ M}^{-1}$ at 24°C .⁴⁰ Thus, first of all we will examine the dimers of formic acid (1) and formamide (2).

Other systems to be studied include 4-pyrimidinone (3), 2-pyridinone (4), 2-hydroxypyridine (5), and 2-hydroxycyclopenta-2,4-dien-1-one (6) as shown in Figure 1. Finally we will study the interactions in β -diketone enols, with a simplified model, the

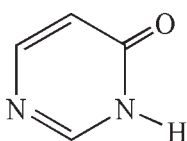
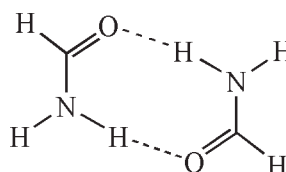
interaction of 3-hydroxypropenal (7) with both formaldehyde (8) and ethanol (9) (see Fig. 2). In all the above-mentioned complexes, there are two equivalent hydrogen bonds linking the monomers together.



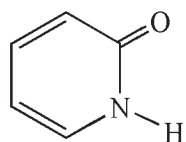
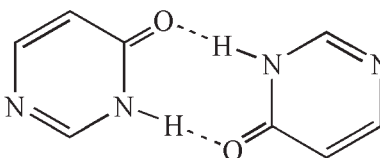
(a) Formic acid monomer (1) and dimer



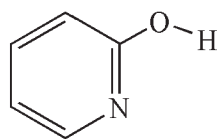
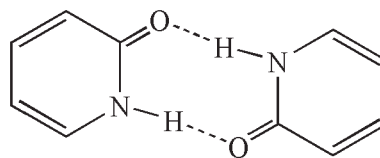
(b) Formamide monomer (2) and dimer



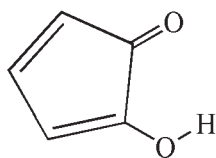
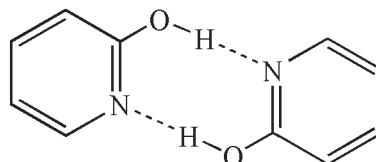
(c) 4-pyrimidinone monomer (3) and dimer



(d) 2-pyridinone monomer (4) and dimer



(e) 2-hydroxypyridine monomer (5) and dimer



(f) 2-hydroxycyclopenta-2,4-dien-1-one monomer (6) and dimer

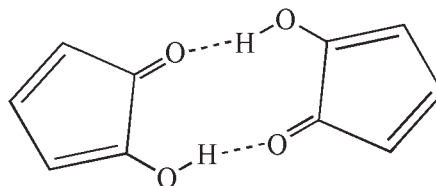
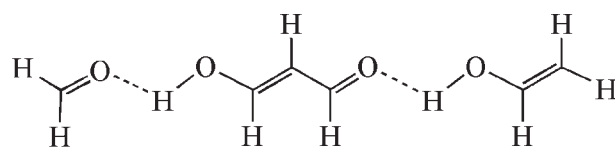


Figure 1. Illustration of the hydrogen bond interacting systems with resonance in monomers.



formaldehyde (8) 3-hydroxypropenal (7) ethenol (9)

Figure 2. Model to simulate the resonance-assisted hydrogen bonds in β -diketone enols.

Methodologies

Block-Localized Wave Function Method

Lewis first introduced dot diagrams to explain the chemical bonding in molecules or ions 90 years ago.⁴¹ In the Lewis structures, valence electrons are paired to show the bonding patterns of molecules, and each bonding pair of electrons are localized to either two bonding atoms or one atom. When it was found that a single Lewis structure (or resonance structure) cannot rationally explain the molecular geometries and properties with delocalized π electrons, the concept of resonance was introduced with a set of resonance structures to describe a conjugated system.^{6,28} Theoretically, each resonance structure is characterized by a HLSP wave function, and the actual wave function of a system is a superposition of all possible HLSP functions. For instance, for a resonance structure K for a system of $2n$ ($S = 0$) electrons can be expressed as

$$\begin{aligned}\Phi_k &= N_k \hat{A} \left\{ \phi_1(1) \phi_2(2) \cdots \phi_N(N) \right. \\ &\quad \times \prod_{(ij)} 2^{1/2} [\alpha(i)\beta(j) - \beta(i)\alpha(j)] \prod_k \alpha(k) \left. \right\} \\ &= N_k \hat{A} (\varphi_{1,2} \varphi_{3,4} \cdots \varphi_{2n-1,2n})\end{aligned}\quad (1)$$

where N_K is the normalization constant, \hat{A} is the antisymmetrizer and $\varphi_{i,j}$ is simply a bond function corresponding to the bond between orbitals χ_i and χ_j which are nonorthogonal

$$\varphi_{i,j} = \hat{A} \{ \phi_i \phi_j [\alpha(i)\beta(j) - \beta(i)\alpha(j)] \}. \quad (2)$$

Since eq. (1) can be expanded into 2^n Slater determinants, the computational demanding related to HLSP functions increases dramatically with the increasing of the number of electrons involved in the *ab initio* VB calculations. But this can be greatly lessened by using doubly occupied MO-like localized orbitals as bond functions.⁴² In this way, the VB wave function as shown in eq. (1) is simplified to a single Slater determinant, but the bond orbitals remain nonorthogonal.⁴³ The partial use of doubly occupied MOs in the VB wave function [eq. (1)] leads to the generalized VB (GVB) method,⁴⁴ which retains the VB form for one or a few focused bonds (perfect pairs) but accommodates the rest of the electrons with orthogonal and doubly occupied MOs.

The BLW method is a further extension and generalization of the idea of localized bond functions with the intention to sig-

nificantly simplify the computational efforts involved in HLSP wave functions.^{33–35} The basic assumption in the BLW method is that the overall electrons and primitive basis functions can be partitioned into k subgroups, depending on the targeted resonance structure or in more general, the diabatic state. The i th subspace consists of $\{\chi_{i\mu}, \mu = 1, 2, \dots, m_i\}$ basis functions and accommodates n_i electrons. Obviously, for a resonance structure every two electrons form a subspace. However, here we generalize the definition of resonance structures, and a subspace may include much more than two electrons (e.g., a monomer in a dimer). The MOs for the i th subspace $\{\varphi_{ij}, j = 1, 2, \dots, m_i\}$ are expanded in terms of $\{\chi_{i\mu}\}$ only

$$\varphi_{ij} = \sum_{\mu=1}^{m_i} C_{ij\mu} \chi_{i\mu} \quad (3)$$

and thus are block-localized. The final BLW function at the HF level is expressed by a Slater determinant

$$\Phi^{\text{BLW}} = M(N!)^{-1/2} \det \left| \varphi_{11}^2 \varphi_{12}^2 \cdots \varphi_{1\frac{n_1}{2}}^2 \varphi_{21}^2 \cdots \varphi_{i1}^2 \cdots \varphi_{i\frac{n_i}{2}}^2 \cdots \varphi_{k\frac{n_k}{2}}^2 \right| \quad (4)$$

where M is the normalization constant. The block-localized MOs in the same subspace are subject to the orthogonality constraint, such as those in conventional MO methods, while those belonging to different subspaces are free to overlap, such as those in VB methods. The energy of the localized wave function is determined as the expectation value of the Hamiltonian \mathbf{H} , which is given as follows:

$$E^{\text{BLW}} = \langle \Phi^{\text{BLW}} | \mathbf{H} | \Phi^{\text{BLW}} \rangle = \sum_{\mu=1}^m \sum_{\nu=1}^m d_{\mu\nu} h_{\mu\nu} + \sum_{\mu=1}^m \sum_{\nu=1}^m d_{\mu\nu} F_{\mu\nu}. \quad (5)$$

In eq. (5), $h_{\mu\nu}$ and $F_{\mu\nu}$ are, respectively, elements of the usual one-electron and the Fock matrices, and $d_{\mu\nu}$ is an element of the density matrix, \mathbf{D} , which is evaluated by using eq. (6).

$$\mathbf{D} = \mathbf{C}(\mathbf{C}^+ \mathbf{S} \mathbf{C})^{-1} \mathbf{C}^+ \quad (6)$$

where \mathbf{S} is the overlap matrix of the basis functions.

Since the present BLW method is established at the HF level, and the HF wave function refers to the real state where all electrons are free to delocalize in the whole system, the energy difference between the HF and BLW wave functions can be generally defined as the electron delocalization energy, which measures intramolecular resonance and hyperconjugation effects or even intermolecular charge-transfer effect. The self-consistent optimization of the block-localized orbitals can be accomplished using successive Jacobi rotation as we initially adopted,³³ or preferably using the algorithm of Gianinetti et al.⁴⁵ We have implemented the algorithm of Gianinetti et al. into our BLW code and ported the code to the GAMESS software,⁴⁶ which has the capability of geometrical optimizations.³⁴

BLW Energy Decomposition Approach

To probe the nature of intermolecular interactions among a few monomers, we can define a BLW where each block corresponds to a monomer, and subsequently decomposes the interaction energy into a set of physically meaningful contributions. In the BLW-ED approach, the binding energy ΔE_B between two monomers A and B at the HF level is defined as the sum of deformation energy ΔE_{def} and the intermolecular interaction energy ΔE_{int}

$$\Delta E_B = \Delta E_{\text{def}} + \Delta E_{\text{int}}. \quad (7)$$

The deformation energy refers to the energetic cost to deform the monomers from their separated optimal structures to the distorted geometries in the optimal structure of dimer AB. The interaction energy ΔE_{int} is the energy difference between the dimer (whose wave function is Ψ_{AB}) and the sum of the individual energies of monomers (whose wave functions are $\Psi_{A(0)}$ and $\Psi_{B(0)}$) with the correction of the basis set superposition error (BSSE)³⁹ and consists of the Heitler-London energy (ΔE_{HL}), polarization energy (ΔE_{pol}), and charge transfer energy (ΔE_{CT}) terms

$$\begin{aligned} \Delta E_{\text{int}} &= E(\Psi_{AB}) - E(\Psi_A^0) - E(\Psi_B^0) + \text{BSSE} \\ &= \Delta E_{\text{HL}} + \Delta E_{\text{pol}} + \Delta E_{\text{CT}}. \end{aligned} \quad (8)$$

The derivation of these individual energy terms is based on the construction of the initial BLW function for the dimer Ψ_{AB}^{BLW0} as well as its self-consistent form Ψ_{AB}^{BLW} as

$$\Psi_{AB}^{\text{BLW0}} = \hat{A}(\Psi_A^0 \Psi_B^0) \quad (9a)$$

$$\Psi_{AB}^{\text{BLW}} = \hat{A}(\Psi_A \Psi_B). \quad (9b)$$

Once the initial and optimal BLW's are defined, the energy terms in eq. (8) can be subsequently expressed as

$$\Delta E_{\text{HL}} = E(\Psi_{AB}^{\text{BLW0}}) - E(\Psi_A^0) - E(\Psi_B^0) \quad (10a)$$

$$\Delta E_{\text{pol}} = E(\Psi_{AB}^{\text{BLW}}) - E(\Psi_{AB}^{\text{BLW0}}) \quad (10b)$$

$$\Delta E_{\text{CT}} = E(\Psi_{AB}^{\text{HF}}) - E(\Psi_{AB}^{\text{BLW}}) + \text{BSSE}. \quad (10c)$$

The Heitler-London energy ΔE_{HL} is defined as the energy change by bringing monomers together without disturbing their individual electron densities, while the polarization energy ΔE_{pol} corresponds to the redistribution of electron density within each monomer due to the electric field imposed by the other monomer. This is an energy-lowering step for the complex, but there is no penetration of electrons between the monomers. The extension of electron movements from block-localized orbitals to the whole complex further stabilizes the complex, and this energy variation is denoted as the charge transfer energy ΔE_{CT} . In this step, the BSSE is also introduced, and thus the correction is completely assigned to the charge transfer energy term. It should be noted that ΔE_{HL} is a sum of electrostatic and Pauli exchange repulsion energies. Since the exchange of electrons is a quantum mechanical effect and classical force field approaches have difficulties to formulate the exchange energy separately, here we simply use ΔE_{HL} . The electron correlation contribution ΔE_{cor} , which is mostly responsible for the dispersion phenomenon, can be estimated by the comparison between the interaction energies calculated at the HF level and higher, such as the MP2 level. Thus, overall the binding energy $\Delta E_B(\text{MP2})$ at the MP2 level is decomposed into deformation energy (ΔE_{def}), Heitler-London energy (ΔE_{HL}), polarization energy (ΔE_{pol}), charge transfer energy (ΔE_{CT}), and correlation energy (ΔE_{cor})

$$\Delta E_B(\text{MP2}) = \Delta E_{\text{def}} + \Delta E_{\text{HL}} + \Delta E_{\text{pol}} + \Delta E_{\text{CT}} + \Delta E_{\text{cor}}. \quad (11)$$

Computational Strategy to Study RAHB

To quantify the resonance effect on the hydrogen bonding interactions in the RAHB systems shown in Figures 1 and 2, we conducted two kinds of energy decomposition analyses. The first kind involves the resonance and all monomers are delocalized. The second kind concerns the interaction between two resonance structures where the π delocalization effect is quenched. The latter kind of energy decomposition analyses was conducted at the optimal dimer geometries and involved only three energy terms, namely ΔE_{HL} , ΔE_{pol} , and ΔE_{CT} . The comparison between the two kinds of computations uniquely measures the influence of resonance on the intermolecular interactions and reveals the nature of RAHBs. All systems studied here involve two equivalent hydrogen bonds. Unless specified, all geometries are optimized

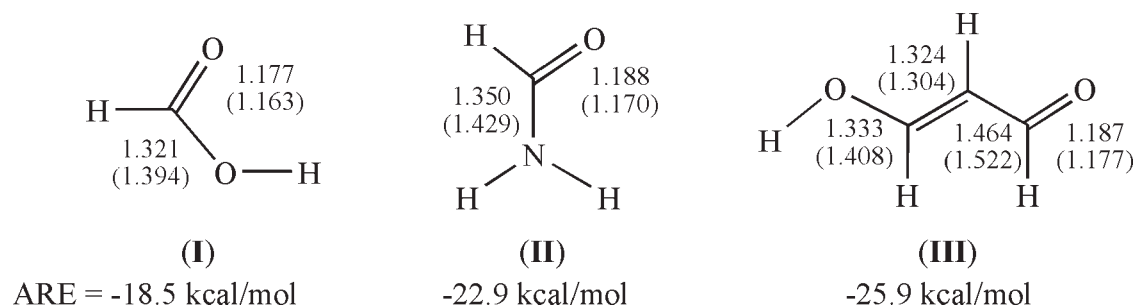


Figure 3. Comparison between the optimal delocalized (HF) and localized (BLW, in parentheses) structures (in Angstrom) with adiabatic resonance energies.

at the MP2/6-311 + G(d,p) level of theory with the Gaussian 03 software,⁴⁷ and BLW or BLW-ED calculations are performed with an in-house code ported to the GAMESS package.⁴⁶

Results and Discussion

Resonance Effect

To gain a detailed insight into the resonance effect, first of all we investigated the three linear conjugated systems, namely formic acid (1), formamide (2), and 3-hydroxypropenal (7), whose geometries are optimized with both the HF and BLW methods. There are two types of resonance energies, depending on the geometries employed. The vertical resonance energy (VRE) is the energy difference between the delocalized (HF) wave function and the localized (BLW) wave function at the same geometry, whereas the adiabatic resonance energy (ARE) is the energy difference between the optimal ground state and the optimal resonance structure. The difference between VRE and ARE reflects the compression energy for the σ frame. Figure 3 shows the optimal geometries and the AREs for the three linear monomers.

Similar to what we have observed and discussed before,^{34,48} the comparison between delocalized and localized geometries confirms that π conjugation results in the shortening of single bonds and the lengthening of double bonds. This is consistent with our qualitative picture that the electron delocalization from the lone oxygen or nitrogen pair in the hydroxyl or amine group to the carbonyl π anti-bond leads to the enhancement of the C—X (X=O, N) bond strength with partial double-bond character and the weakening of the carbonyl bond. Because of the high bond force constant in double bonds, the variation of double bond lengths is much less significant than that of single bond lengths when the π conjugation is turned off. For example, resonance only slightly elongates the carbonyl bonds in the three systems by 0.014, 0.018, and 0.010 Å, and the CC double bond in 7 by 0.020 Å, but remarkably shortens the single bonds by around 0.07 Å in all cases.

It is expected that the π electronic delocalization will increase with the decreasing of the electronegativity of the substitute group attached to the carbonyl group in HCOX (X=OH, NH₂, CHCHOH). Indeed, we find that the resonance magnitude increases in the order of $1 < 2 < 7$. With the increasing movement of π electron to the carbonyl group side, the dipole moment will also increase (see Table 3). This redistribution of

electron density can be visualized by the electron density difference (EDD) between HF and BLW wave functions, as shown in Figure 4a for the case of 7, where the black color indicates the increasing of electron density due to the conjugation effect and the gray refers to the loss of electrons. Clearly, the π electron movement mainly occurs from the hydroxyl group in the left to the carbonyl oxygen in the right, and the resonance can be schematically illustrated by an arrow diagram as shown in Figure 4b. However, Figure 4a also reveals that part of the π resonance effect will be offset by the σ polarization in the reverse direction. For instance, the carbonyl oxygen loses, while the hydroxyl oxygen gains σ electron density. Since the σ electrons (lone pairs of oxygen) are mostly responsible for the hydrogen bonding if the hydrogen bond is covalent in nature, π electron delocalization towards the carbonyl oxygen does not mean that the latter could enhance its role as a proton acceptor. Of course, the net result is the shifting of electron density from the hydroxyl group side to the carbonyl group (Fig. 4b). For instance, Mulliken population analysis indicates that the charge on the carbonyl oxygen increases from -0.346 to -0.380 e because of π resonance, while the charge on the hydroxyl oxygen significantly reduces from -0.407 to -0.277 e. Notably, the positive charge on the hydroxyl hydrogen changes very little, from 0.262 to 0.278 e. As a consequence, the dipole moment of the system has been remarkably altered, from 4.285 Debye in the optimal localized (resonance) structure to 5.589 Debye in the optimal delocalized structure. This will favor the classical electrostatic attraction if monomers approach in appropriate orientations.

The magnitude of resonance in aromatic rings will be significantly increased in comparison with linear systems because of the strong coupling (or aromaticity⁴⁹) from isoenergetic resonance structures, but the general features are similar to those in 3-hydroxypropenal. Figure 5 shows the EDD maps in 2-pyridinone (4) and 2-hydroxypyridine (5).

Strengths of Hydrogen Bonds

Table 1 compiled the optimal hydrogen bond lengths and binding energies in the complexes. Computations confirm the collinearity of the donor and acceptor groups. From first look, there is no obvious correlation between the hydrogen bond lengths and the binding energies. But we note that there are three types of hydrogen bonds in the seven complexes, namely homonuclear (O—H...O) and heteronuclear (N—H...O and O—H...N) bonds.

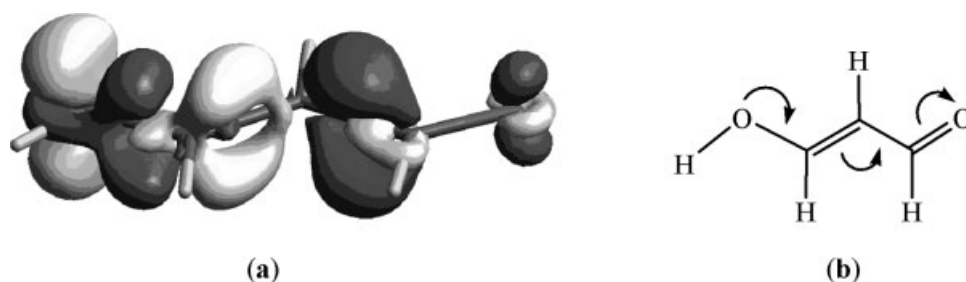


Figure 4. (a) Electron density difference (EDD) map showing the resonance in 3-hydroxypropenal (isodensity 3×10^{-3} au); (b) schematic diagram showing the movement of electron density.

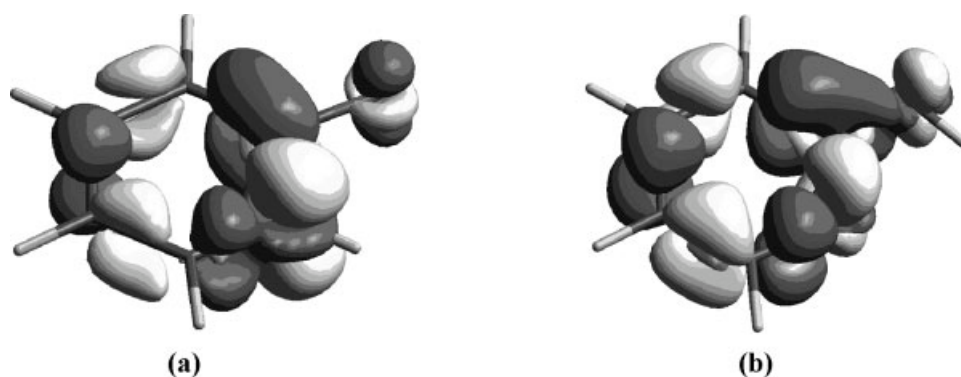


Figure 5. Electron density difference (EDD) map showing the resonance in (a) 2-pyridinone; (b) 2-hydroxypyridine (isodensity 5×10^{-3} au).

Correlations can be sorted out for the same type of hydrogen bonds. For example, dimers of 2, 3, and 4 involves the type of N—H...O hydrogen bonding, whose strength is reversely proportional to the hydrogen bond length $R(\text{N}\cdots\text{O})$. The importance of electron correlation to the geometries and binding energies in hydrogen-bonding (and other weakly interacting) systems has been well recognized. For instance, studies on DNA base pairs by Šponer et al. with large basis sets reveal a significant basis set effect on the geometries, and the hydrogen bond lengths optimized at the RI-MP2/cc-pVTZ level are much shorter than crystal structural data and computational results at either MP2/6-311G** or HF/cc-pVTZ level, suggesting a larger dispersion effect in these systems than previously thought.²¹ In our cases, the binding energies are underestimated to some extent. For example, binding energy for the formic acid dimer is -14.0 kcal/mol at the MP2/aug-cc-pVDZ level,¹³ compared with -11.6 kcal/mol at the present MP2/6-311 + G(d,p) level. The discrepancy almost completely results from the electron correlation (dispersion) effect as we found that the HF binding energies are very similar (-11.6 vs. -11.7 kcal/mol) at the geometries optimized at the MP2 level with either 6-311 + G(d,p) or aug-cc-pVDZ. Although 6-311 + G(d,p) uses slightly fewer basis functions than aug-cc-pVDZ,^{30,50} and the former leads to lower calculated energies and usually better molecular structures than the latter,⁵¹ the MP2/aug-cc-pVDZ level recovers much more correlation energies than the MP2/6-311 + G(d,p) level. As our focus is on the change of the binding energy with the deactivation of

π resonance, i.e., the difference between the complexation energies in a pair of delocalized and “artificially” localized monomers, the underestimation of the electron correlation effect should have a very limited impact on our final results and discussion.

To probe the nature of the hydrogen bonds, we broke down the binding energies into physically meaningful contributions from deformation, Heitler-London, polarization, charge transfer, and dispersion (MP2 electron correlation) terms. The energetic data are compiled in Table 2. In general, we found a good correlation between the deformation energies and binding energies, as increasing the binding energy tends to distort the geometries of monomers more. The examination of individual energy contributions reveals that both the polarization and charge transfer effects in general make the most significant contributions to the hydrogen bonding. Our previous studies have shown large magnitudes of the Pauli exchange and electrostatic interaction in opposite roles.³⁶ The repulsive Pauli energy and attractive electrostatic energy in the present cases are largely cancelled out, resulting in a small value of the Heitler-London energy term. Except the dimer of 5, the electrostatic attraction apparently outweighs the exchange repulsion as ΔE_{HL} values are negative. This can be well interpreted in terms of the orientations of the dipole moments of the monomers. In all cases apart from 5 in Figure 1, the dipole moments approximately orient from down to up for the left-side monomers, as the up carbonyl group is a π electron-acceptor group, while the down amine or hydroxyl

Table 1. Optimal Hydrogen Bond Lengths and Strengths at the MP2/6-311 + G(d,p) level.

| Complex | $R(\text{X}-\text{H})$ (Å) | $R(\text{Y}\cdots\text{H})$ (Å) | $R(\text{X}\cdots\text{Y})$ (Å) | $\angle\text{XHY}$ (°) | ΔE_{b} (kcal/mol) |
|--------------------|----------------------------|---------------------------------|---------------------------------|------------------------|----------------------------------|
| 1+1 | 0.990 | 1.727 | 2.717 | 178.3 | −11.6 |
| 2+2 | 1.023 | 1.904 | 2.921 | 172.4 | −11.5 |
| 3+3 | 1.042 | 1.726 | 2.767 | 177.5 | −17.2 |
| 4+4 | 1.044 | 1.702 | 2.746 | 179.9 | −18.3 |
| 5+5 | 0.999 | 1.741 | 2.737 | 174.0 | −14.1 |
| 6+6 | 0.973 | 1.918 | 2.839 | 157.0 | −6.9 |
| 8+7+9 ^a | 0.973(0.974) | 1.811 (1.798) | 2.784 (2.767) | 179.8 (173.0) | −14.4 |

^aParameters in parenthesis refer to the right-side hydrogen bond between 7 and 9 in Fig. 2.

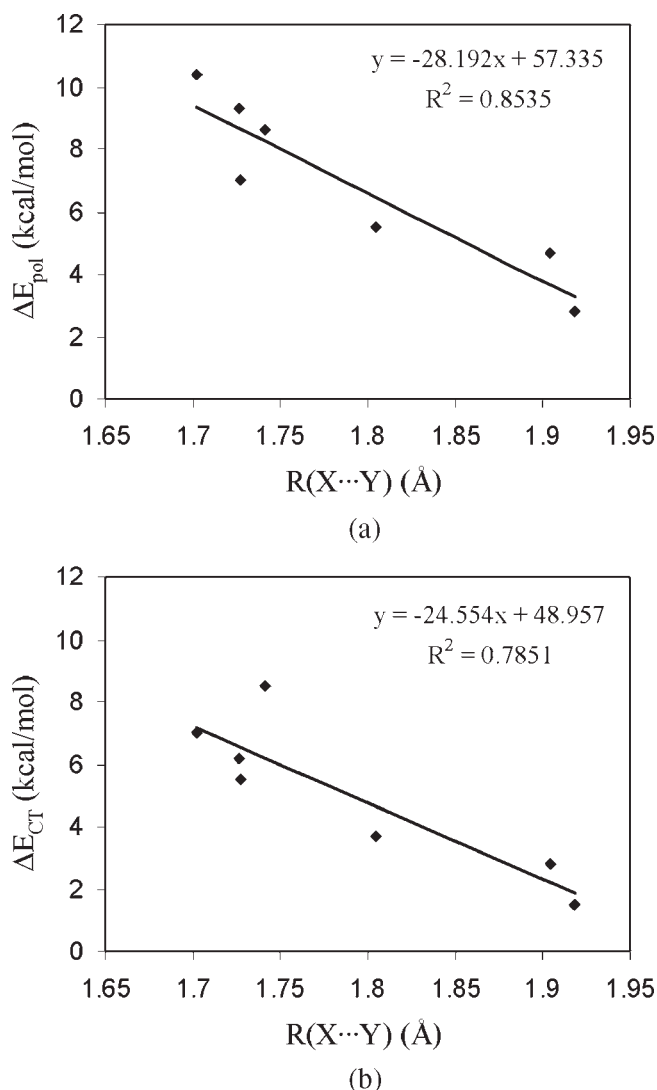
Table 2. Energy Contributions to the Binding Energies With or Without the Assistance of Resonance (kcal/mol).

| Complex | Type of HB ^a | ΔE_{def} | ΔE_{HL} | ΔE_{pol} | ΔE_{CT} | ΔE_{cor} | ΔE_{b} |
|---------|-------------------------|-------------------------|------------------------|-------------------------|------------------------|-------------------------|-----------------------|
| 1+1 | RA | 2.8 | -1.9 | -7.0 | -5.5 | 0.0 | -11.6 |
| | Non-RA | | 2.2 | -5.6 | -4.7 | | -5.3 |
| | Difference | | 4.1 | 1.4 | 0.8 | | 6.3 |
| 2+2 | RA | 2.0 | -4.8 | -4.7 | -2.8 | -1.1 | -11.5 |
| | Non-RA | | -0.1 | -3.2 | -2.2 | | -4.7 |
| | Difference | | 4.7 | 1.5 | 0.6 | | 6.8 |
| 3+3 | RA | 4.5 | -4.2 | -9.3 | -6.2 | -2.0 | -17.2 |
| | Non-RA | | 3.9 | -6.6 | -4.7 | | -4.9 |
| | Difference | | 8.1 | 2.7 | 1.5 | | 12.3 |
| 4+4 | RA | 5.1 | -2.5 | -10.4 | -7.0 | -3.5 | -18.3 |
| | Non-RA | | 7.3 | -7.0 | -5.2 | | -3.3 |
| | Difference | | 9.8 | 3.4 | 1.8 | | 15.0 |
| 5+5 | RA | 3.5 | 4.8 | -8.6 | -8.5 | -5.3 | -14.1 |
| | Non-RA | | 4.7 | -8.2 | -8.1 | | -13.4 |
| | Difference | | -0.1 | 0.4 | 0.4 | | 0.7 |
| 6+6 | RA | 0.6 | -3.4 | -2.8 | -1.5 | 0.2 | -6.9 |
| | Non-RA | | -1.4 | -2.3 | -1.2 | | -4.1 |
| | Difference | | 2.0 | 0.5 | 0.3 | | 2.8 |
| 8+7+9 | RA | 2.0 | -6.0 | -5.5 | -3.7 | -1.2 | -14.4 |
| | Non-RA | | -3.1 | -4.5 | -3.2 | | -10.0 |
| | Difference | | 2.9 | 1.0 | 0.5 | | 4.4 |

^aRA refers to the energy analysis between delocalized monomers and Non-RA refers to the interaction between the most stable resonance structures.

groups are π electron-donor groups. Thus, when they form dimers, the dipole moments of the monomers are in antiparallel in the interfacial region, leading to favorable classical dipole-dipole (electrostatic) attractions. Conversely, such kind of favorable attractions does not exist in the dimer of 5, as the dipole moment directs from left to right, and the subsequent head to head interaction in the dimer destabilizes the complex.

Similar to Lewis acid-base complexes, the covalence in hydrogen bond can be measured by the magnitude of charge transfer effect, as the bond is formed by the interaction between an occupied donor orbital and virtual acceptor orbital. But unlike strong Lewis acid-base complexes, such as BH_3NH_3 , where the charge transfer energy is comparable to the overall interaction energy,^{36,37,52} in present pairs we observed a relatively weak charge transfer interaction which accounts for around 20–48% of the overall interaction (excluding the structural deformation energy). This is comparable to the DNA base pairs²² and indicates a low covalence in these hydrogen bonds. Charge transfer effect is a short-range interaction and decays exponentially with the distance. Thus, we expect that the charge transfer stabilization energy heavily depends on the hydrogen bond length. Polarization effect, which is induced by the mutual influence of two monomers, has the electrostatic nature. In our current cases, polarization contributes the largest stabilizing energy to the binding between dimers and accounts for about 34–45% of the total interaction energies. Figure 6 plots the correlation between the hydrogen bond lengths and polarization or charge transfer energies. Approximately with the shortening of a hydrogen bond

**Figure 6.** Correlation between the hydrogen bond lengths and (a) polarization energies or (b) charge transfer energies.

length, both polarization and charge transfer stabilization energies increase. As there are three different types of hydrogen bonds, better correlations can be anticipated for the same type of

Table 3. Comparison of the Dipole Moments (μ , in Debye) in the Delocalized and Localized States and the Vertical Resonance Energies (VRE, in kcal/mol) in monomers.

| Species | $\mu(\text{HF})$ | $\mu(\text{BLW})$ | VRE |
|---------|------------------|-------------------|--------|
| 1 | 2.00 | 1.33 | -22.6 |
| 2 | 4.56 | 3.67 | -27.9 |
| 3 | 3.28 | 2.32 | -82.2 |
| 4 | 5.39 | 4.31 | -82.9 |
| 5 | 1.37 | 1.87 | -101.4 |
| 6 | 2.46 | 2.92 | -43.1 |
| 7 | 6.10 | 4.87 | -33.0 |

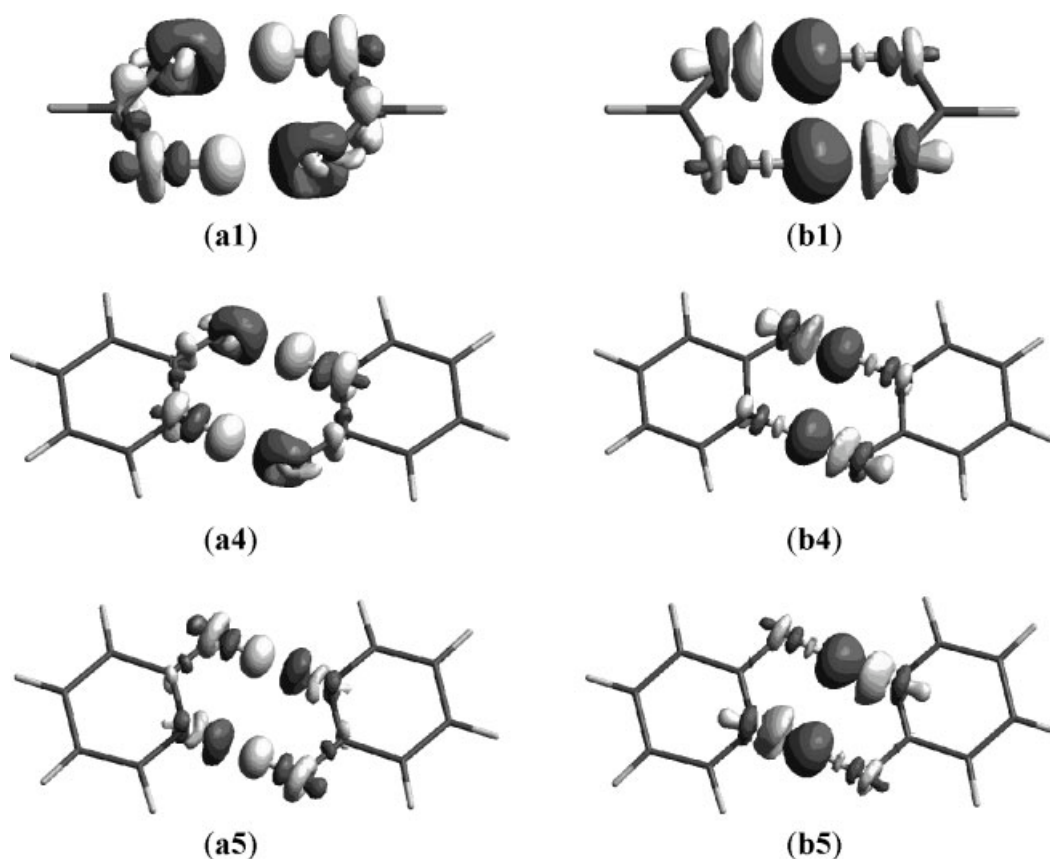


Figure 7. Electron density difference (EDD) maps show (a) the polarization effect in the dimers of 1, 4, and 5 (isodensity 4×10^{-3} au) and (b) the charge transfer effect in the dimers of 1, 4, and 5 (isodensity 1×10^{-4} au).

hydrogen bonds. Again this can be verified by the dimers of 2, 3, and 4 of the same type of N—H···O hydrogen bonds. The correlation (dispersion) energy term is closely related to the resonance magnitude (Table 3), suggesting that this part of energy mainly comes from the delocalized π electrons.

The covalent nature of hydrogen bonds can be illustrated with the frontier orbitals (HOMOs and LUMOs) of both the proton donor and acceptor. Alternatively, we can plot electron density difference (EDD) maps which can intuitively demonstrate the electron movement due to either the polarization or charge transfer effect between the proton donor and acceptor. Since the BLW defines a diabatic state where the electron flow among monomers is forbidden, the difference between the electron densities of the delocalized HF wave function Ψ_{AB} and localized BLW Ψ_{AB}^{BLW} solely reflects the electron transfer between the monomers A and B. On the other hand, the polarization effect can be visualized by the electron density difference between optimal Ψ_{AB}^{BLW} and initial Ψ_{AB}^{BLW0} . Figure 7 exemplifies the polarization and charge transfer effects in the dimers of 1, 4, and 5.

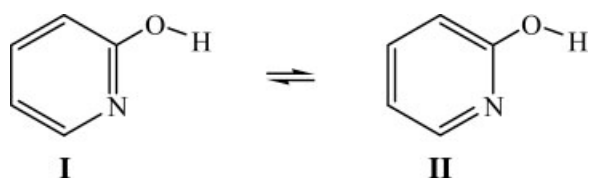
The initial survey of the EDD maps in Figure 7 suggests that both polarization and charge transfer are essentially local effects. As resonance involves the whole systems, the localization of the polarization and charge transfer effects related to the hydrogen

bonds somewhat challenges the claim that resonance assists hydrogen bonding interactions. In other words, it seems that resonance plays an indirect and secondary role in the hydrogen bonding. In the interface between two monomers, we observe the X—H (X=O, N) bond polarization from hydrogen to oxygen or nitrogen in all monomers (Fig. 7a), whereas proton acceptors gain electron density from adjacent bonding atoms to prepare for the formation of hydrogen bonds, which makes these acceptors lose electron density to the protons (Fig. 7b). This charge shift confirms the sort of covalence nature of hydrogen bonds in the dimers.

Resonance Effect on the Strengths of Hydrogen Bonds

The above energy analysis confirms the partial covalent nature in RAHBs, but the connection between resonance and binding energies is still unclear. The ideal solution to quantify the impact of π resonance on the hydrogen bonding interactions in the focused complexes is to analyze the hydrogen bonds by switching off the resonance effect. To achieve this, we first need identify the most stable resonance structure of each monomer, followed by studying the hydrogen bonds between two localized resonance structures. Defining the most stable resonance structures for species 1–9 is straightforward by following Wheland's

rules,²⁸ except 2-hydroxypyridine 5 which has two comparable Kekulé-like structures



Either **I** or **II** can be uniquely defined with one BLW. At the geometry in the optimal complex, **I** is much more stable than **II** by 101.4 kcal/mol. The preference of **I** over **II** can actually be inferred from the geometry whose aromatic ring has alternating bond lengths.

It is illuminating to examine how the localization of π electrons can influence the redistribution of electrons as we discussed previously. Table 3 compared the dipole moments in the delocalized and localized states as well as the vertical resonance energies (VREs). Species with aromatic rings (3–5) exhibit very high resonance energies, in accord with their extraordinary stability or aromaticity.⁴⁹ However, we are interested in the redistribution of electron density due to resonance, as delocalization significantly changes the dipole moments which will subsequently

influence the interaction between monomers. With the resonance of π electrons turned off, we conducted the energy analysis and results on the nonresonance-assisted hydrogen bonds (non-RAHBs) are listed in Table 2. Compared with RAHBs, there is a reduction of the binding energies in non-RAHBs with different extent. Interestingly, the reduction dominantly results from the Heitler-London energy (65–71%), and secondly from the polarization effect (18–23%). For dimers of 3 and 4 which have the strongest RAHBs in our cases, we observed a change of the Heitler-London energy by as high as 8.1 and 9.8 kcal/mol. Since we maintain the geometries unchanged, we believe the Heitler-London energy variation is overwhelmingly due to the electrostatic interaction, which can be further traced down to the change of the dipole moments of the monomers. In all cases, however, the charge transfer energy varies very little. This offers a strong proof that the nature of resonance-assisted hydrogen bonding (RAHB) is in essence the resonance-enhanced electrostatic attraction and polarization effect, as the covalence in hydrogen bonds has only slight changes with the deactivation of resonance.

Among the systems studied in this work, there is an abnormal case, namely the dimer of 5, which exhibits the negligible energy change in binding with the resonance switched off. To find out the origin, we plotted the magnitudes and orientations

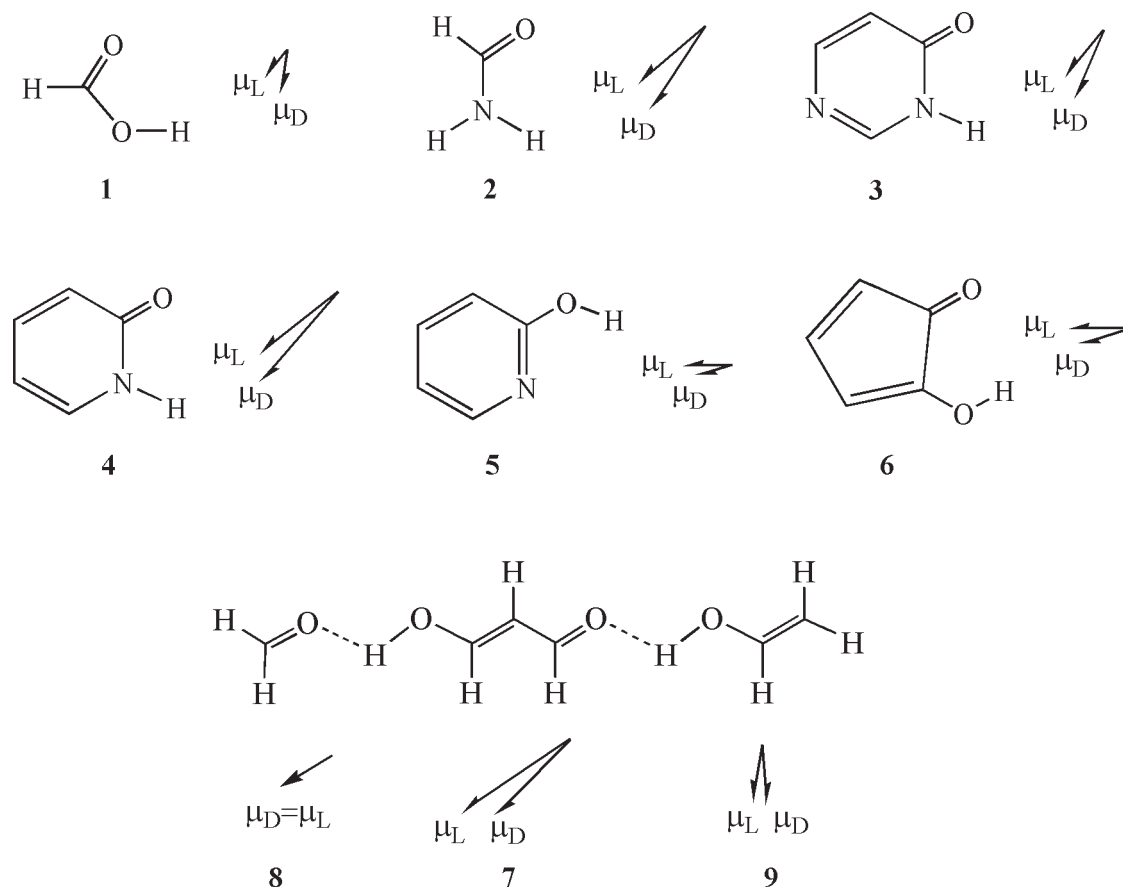


Figure 8. Magnitudes and orientations of the dipole moments in species 1–9 with the π resonance switched on (μ_D) and off (μ_L).

of the dipole moments in monomers with the resonance turned on (μ_D) and off (μ_L). For species 1–4, the π resonance not only increases the magnitude of their individual dipole moments, but also adjusts the orientations of dipole moments (μ_D) in a way (from top to down) that an antiparallel dimer would benefit from enhanced dipole–dipole electrostatic attractions. For 5 and 6, however, the dipole moments point from right to left and the π resonance only slightly modulates the unfavorable head to head orientation of dipole moments in their dimers. In addition, their magnitudes of dipole moments reduce with the π resonance turned on. All these “abnormalities” make the dimers of 5 and 6 experience the least binding energy changes (0.7 and 2.8 kcal/mol, respectively) in the complexes shown in Figure 1. We note that there is the least polarization effect in the dimer of 6, which is closely correlated to its very low resonance energy compared with the rest of the three ring systems 3–5. This suggests a low aromaticity in 6. Unfavorable dipole–dipole orientations also appear in the trimer $8 + 7 + 9$, and lead to a relatively weak resonance assistance in its binding (Fig. 8).

Conclusion

In this work, we employed the BLW method, which is a variant of the *ab initio* VB theory, to investigate the nature of RAHB. The computational strategy includes the hydrogen bonding energy decomposition analyses with or without the assistance of resonance. Over the years there have been constant controversies regarding the nature of hydrogen bonds. Although all experimental and theoretical studies confirm the directionality of hydrogen bonds, in accord with the definition of covalent bonds, a widespread belief is that hydrogen bonds are predominantly electrostatic in nature. Our study shows that there is indeed considerable covalence nature in the hydrogen bonds in a series of dimers where the hydrogen bond donors and acceptors are linked by conjugated bonds in monomers, particularly for the dimers of formic acid (1), 4-pyrimidinone (3), 2-pyridinone (4), and 2-hydroxypyridine (5), whose hydrogen bonds are short. However, most of the “extra” binding energies compared with conventional hydrogen bonds without the assistance of resonance come from the electrostatic attraction. With the deactivation of π conjugation, the charge transfer energy changes the least compared with the Heitler-London and polarization energies. Further analyses show that the strong binding in the RAHBs results from favorable dipole–dipole electrostatic interaction between the monomers, which is assisted by the π electron delocalization. Thus, we recommend the term “resonance-assisted binding” instead of “resonance-assisted hydrogen bonding (RHAB)” to reinforce the electrostatic rather than covalent nature of the enhanced stabilization in the hydrogen bonds linked by conjugated bonds.

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