Interplay Between Hydrogen Bond Formation and Multicenter π-Electron Delocalization: Intermolecular Hydrogen Bonds

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The interplay between aromatic electron delocalization and intermolecular hydrogen bonding is thoroughly investigated using multicenter delocalization analysis. The effect on the hydrogen bond strength of aromatic electron delocalization within the acceptor and donor molecules is determined by means of the interaction energies between monomers, calculated at the B3LYP/6-311++G(d,p) level of theory. This magnitude is compared to variations of multicenter electron delocalization indices and covalent hydrogen bond indices, which are shown to correlate perfectly with the relative values of the interaction energies for the different complexes studied. The multicenter electron delocalization indices and covalent bond indices have been computed using the quantum theory of atoms in molecules approach. All the hydrogen bonds are formed with oxygen as the acceptor atom; however, the atom bonded to the donor hydrogen has been either oxygen or nitrogen. The water−water complex is taken as reference, where the donor and acceptor molecular environments are modified by substituting the hydrogens and the hydroxyl group by phenol, furan, and pyrrole aromatic rings. The results here shown match perfectly with the qualitative expectations derived from the resonance model.

I. Introduction

The hydrogen bond, HB,[1] whether it is on the inter- or intramolecular level, is one of the most important interactions governing reactivity and chemical structure in fields such as (bio)chemistry and molecular biology.[1,2] A better knowledge of this phenomenon is essential for understanding and explaining the structure and behavior of a variety of molecules and their interaction with their environment.

From an electrostatic point of view, a HB is formed between a partially charged hydrogen atom and an atom Y, which possesses lone pair electrons or any electron rich source, including, for instance, also a benzene molecule. In the best-known class of hydrogen bonds, the hydrogen atom is attached to an electronegative atom such as nitrogen or oxygen. This is, however, not a strict requirement, as many molecules with C−H···O and C−H···N hydrogen bonds have already been found.[1] In the case of the first class of HBs, the HB is an electrostatic interaction between the positive end of the H−X bond dipole and the negative end of the dipole (or monopole in the case of an anion) associated with Y.[3] Due to its dipolar nature, the HB has a directional property. This means that the strength of the interaction depends on the X−H···Y angle and is the strongest when this angle approaches 180°. The atoms X and Y can approach each other because of the small size of the hydrogen atom. Also, there is a partial transfer of the hydrogen atom from the donor to the acceptor groups, which makes the HB have a greater strength than normal dipole−dipole interactions[4] such as that of the pair HCl−HCl.

SCHEME 1

However, the simple electrostatic nature of the HB does not explain many features of hydrogen bonded systems, and it is well-known that other factors such as electron delocalization, dispersion, and repulsion play a very important role in its formation.[5,6] Thus, it is accepted that the real HB holds the middle between an electrostatic and a covalent interaction. This view of a HB is summarized in the electrostatic-covalent hydrogen bond model, ECHBM.[7]

One of the most important conclusions obtained from the ECHBM is that in general the homonuclear HBs, where the acceptor and donor are the same atom, are stronger than the heteronuclear HBs because of their chemical symmetry and low difference in proton affinity, ΔPA. Thus, the valence bond resonance forms drawn in Scheme 1 are isoenergetic and mix easier when X and Y are atoms of the same element. On the other hand, heteronuclear HBs can be strengthened by adding chemical substituents that lower the ΔPA value or adding substituents that display π-electron delocalization. These latter groups can help, by resonance, the hydrogen transfer between the donor and acceptor molecules. This situation can be given at both the inter- and intramolecular level and can modify the hydrogen bond energy substantially in some particular cases.

In the intramolecular hydrogen bonds, the electron delocalization within the π-system sometimes provides the hydrogen bond with a large extra stabilization when compared to the same hydrogen bond within a localized electronic structure. These intramolecular hydrogen bonds are called resonance assisted hydrogen bonds and deserve particular attention (ref 8 and

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references therein). The most typical example of resonance assisted hydrogen bonding is the case of malonaldehyde.

On the other hand, the aromatic rings can exert a large effect on the relative strength of the intermolecular hydrogen bonds, InHBs.[8] They can either reinforce or weaken the InHB depending on the structure and relative position of the aromatic ring. For instance, its effect will be different if the ring is linked to the donor or acceptor groups and if the X or Y atoms are bonded to the aromatic ring or embedded in it. This paper aims to analyze in detail the effect of the aromatic electron delocalization on the relative strength of a series of InHBs by comparing values of multicenter electron delocalization indices[9,10] computed using the quantum theory of atoms in molecules, QTAIM,[11] before and after the hydrogen bond formation and the interaction energies obtained from quantum chemical calculations. It is shown that the qualitative ideas based on the resonance model about the effect of the electron delocalization on the relative stability of the InHBs can be replaced by quantitative measures of electron delocalization which are easily computed from the knowledge of the molecular wave function. Thus, the multicenter electron delocalization analysis provides us with a real picture of the interplay between hydrogen bonding and π-electron delocalization. A follow-up paper (part II) is devoted to the intramolecular hydrogen bonds, in particular to the study of resonance assisted hydrogen bonds.

In particular, this paper deals with the effect on the InHB strength of the insertion of different aromatic rings in the acceptor and donor molecules. The O−H interaction is the object of our study, and the water dimer is taken as reference. The paper is organized as follows: In the second section, multicenter delocalization indices are briefly reviewed and the computational details are presented. The Results and Discussion section (section III) is partitioned into four different parts: the first two parts are devoted to the effect on the InHB strength of the aromatic electron delocalization in the donor and acceptor molecules, respectively; in the third part, the cooperativity effect between the aromatic electron delocalization in donor and acceptor molecules is investigated, and the insertion of activating and deactivating groups in the aromatic rings is discussed in the fourth part. Finally, the conclusions are formulated.

It should be noted that the use of multicenter indices to characterize dihydrogen bonds was very recently studied by Giambiagi and Bultinck.[12] It was found there that there is a very good correlation between the size of the multicenter indices on the one hand and the interaction energies on the other. So, a further aim of the present paper is to see whether such good correlation appears in general.

II. Computational Details

Since the derivation of the multicenter delocalization indices, n-DIs, in the context of the QTAIM, has been presented in a previous paper,[10] we only show the relevant expressions employed for its calculation. Thus, eq 1 represents the n-center delocalization index, Δ_n, in terms of products of the atomic overlap integrals, $\langle i|j\rangle_A$, given in eq 2, where Ω_A represents the atomic domain of the atom A and ϕ_i and ϕ_j are molecular orbitals. $\Delta_n(A, B, ..., M)$ characterizes the delocalized electron population among those n atoms. The summation over all P accounts for all symmetry unique permutations of the atoms A, B, ..., M.

$$\Delta_n(A, B, ..., M) = 4n\sum_{P}\sum_{i,j,k,\,...,\,m}^{N/2}\langle i|j\rangle_A\langle j|k\rangle_B...\langle m|i\rangle_M \qquad (1)$$

$$\langle i|j\rangle_A = \int_{\Omega_A}\varphi_i(\vec{r})\,\varphi_j(\vec{r})\,\mathrm{d}r \qquad (2)$$

The expression 1 is strictly valid for monodeterminant wave functions of closed shell systems, the molecular orbitals (MOs) employed can be based on Hartree−Fock or Kohn−Sham (KS) density functional theory. Nevertheless, it has to be noticed that, in the KS formalism, the monodeterminant wave function is just an effective one-particle approximation to the real one which reproduces the exact electron density of the interacting system. So, eq 1 is theoretically not entirely accounted for, although the wide use of eq 1 using KS orbitals has shown that the results do give chemically significant results. The values of these indices can be either positive or negative, and the physical meaning of the sign is still being investigated, nevertheless it has been extensively confirmed in different kinds of aromatic systems that aromatic rings always show positive values.[9,10,13–16]

In this work, we are concerned with the indices involving two, five, and six centers. The former has been proven to be a good measure of the covalent character of the bonds, and so it is also called bond index.[17] The 5-DIs are employed to calculate the π-electron delocalization within the pyrrol and furan rings, whereas the 6-DIs are employed to calculate the π-electron delocalization within the phenyl rings. They are estimators of the local aromaticity of these rings.[13] It must be mentioned that relative values of the n-DIs cannot be directly compared for different values of n, since the value of each term of the summation in eq 1 inherently decreases as the number of overlap integrals in the product increases with the number of centers n.

The relative strength of the InHBs has been quantified using the interaction energies, E_{int}. The E_{int} values were corrected for basis set superposition error, BSSE, using the counterpoise method.[18] The optimized geometries as well as the molecular energies have been calculated at the B3LYP/6-311++G(d,p) level. The molecular orbitals employed in the calculation of multicenter delocalization indices have been obtained using the same level of calculation. The Gaussian03 program[19] has been used to compute the molecular energies and molecular orbitals, whereas the AIMPAC package of programs[20] has been used to compute the atomic overlap integrals. The calculation of multicenter delocalization indices was performed using a program developed in our laboratory.

III. Results and Discussion

First, it must be mentioned that hydrogen bond interactions entail only small redistributions of the electron density when compared to other strong covalent bonds. This is reflected in the small values of the intermolecular interaction energies. Therefore, the relative stability of different hydrogen bonded systems is related to quite small differences in the electron density properties.

The structures and nomenclature employed for the monomers and complexes studied are shown in Figure 1. The values of E_{int} and the main geometrical parameters involved in the InHB formation are collected in Table 1. On the other hand, Table 2 lists the bond indices calculated for the most relevant bonds involved in the InHB formation, whereas Table 3 collects the multicenter electron delocalization indices of the aromatic rings in the monomers and complexes.

Both the E_{int} and the H−X bond index are employed as a measure of the InHB strength throughout this section. As can be seen in Figure 2, these two quantities show a good linear

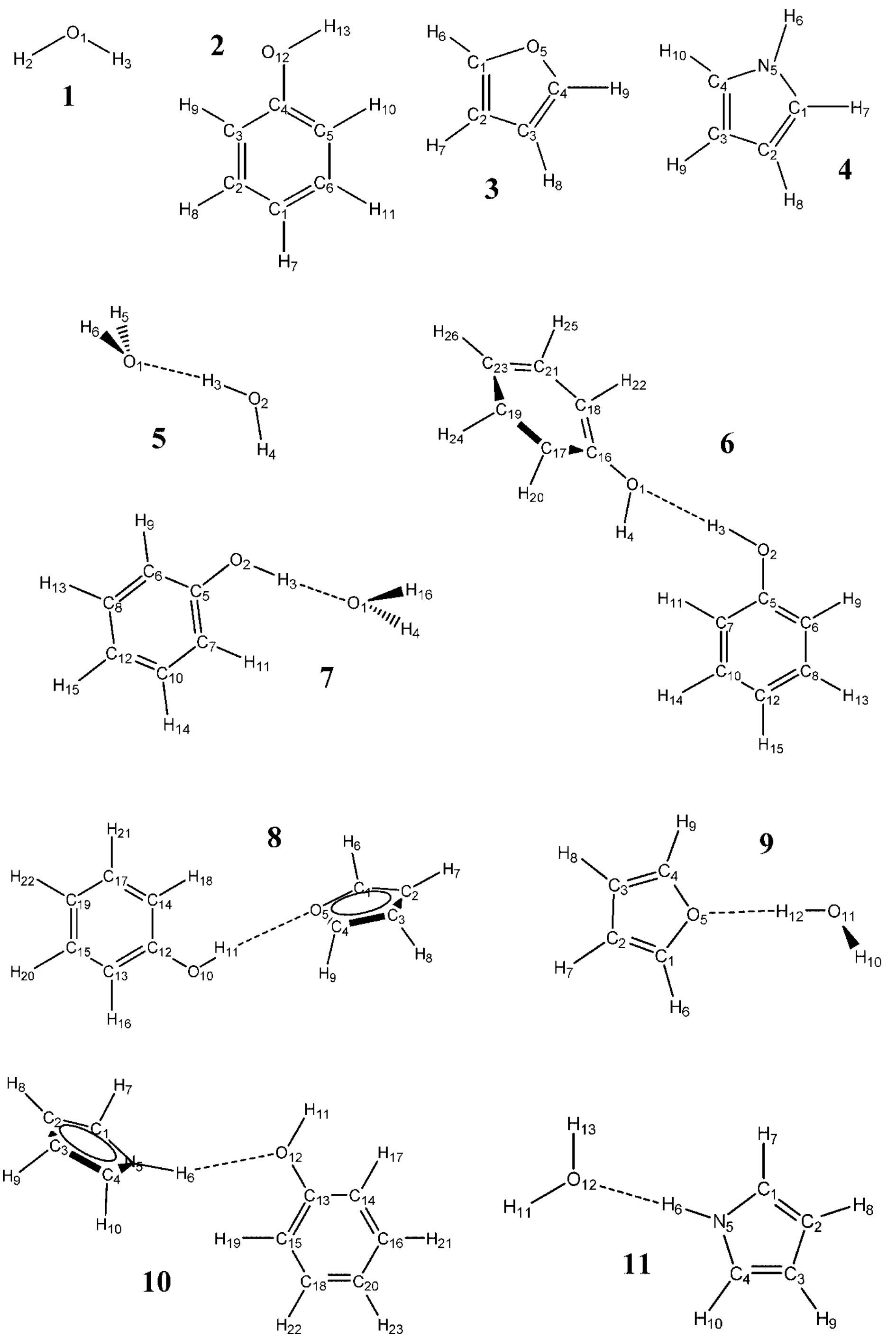


Figure 1. Structures of the monomers and intermolecular H-bonded complexes together with the atom numbering. The dotted lines indicate the intermolecular hydrogen bond. The structures are numbered as follows: (1) water; (2) phenol; (3) furan; (4) pyrrol; (5) water−water complex; (6) phenol−phenol complex; (7) water−phenol complex; (8) phenol−furan complex; (9) water−furan complex; (10) phenol−pyrrol complex; and (11) water−pyrrol complex.

correlation, which supports the use of the H−X bond index as an estimator of the InHB strength. Particular discussions about every complex are done in the following subsections.

Effect of the Aromatic Electron Delocalization in the Donor Molecule. The interaction energy of two water molecules (structure 5) leads to a stabilization of -5.42 kcal mol^{-1}. As expected, the interaction causes an increase in the H−Y bond distance compared to the monomer. The same trend is seen in the phenol−water interaction (structure 7) where the H−Y bond is longer in comparison to the isolated phenol. The E_{int} values show that the phenol−water interaction is ~0.9 kcal mol^{-1} stronger than the water−water interaction, which is also reflected in a shorter H−X bond distance. The H−Y bond indices match the bond distances and their values are smaller in the complexes for both water and phenol. Also, the value of the H−X bond index is higher in complex 7 than in complex 5, and that of C−O in phenol increases in the complex, supporting the observation of a stronger InHB in structure 7. As for the 6-DIs, it can be seen that the multicenter electron delocalization in the phenyl ring of phenol decreases in the complex. The reinforcement of the InHB when water is replaced by phenol is supported by the possibility for the π-electrons to delocalize in the aromatic phenol ring, as shown in Scheme 2. It has to be noticed that these electron movements are just a representation

TABLE 1: Interaction Energy, E_{int}, and Main Geometrical Parameters Involved in the Intermolecular Hydrogen Bond (InHB)[a]

structure[b]	E_{int}[c]	H−X	H−Y[d]	XHY
5	−5.42	1.934	0.970	175.1
6	−4.84	1.916	0.971	173.7
7	−6.29	1.880	0.972	175.0
8	−3.72	1.978	0.968	172.8
9	−2.94	2.046	0.966	173.4
10	−3.79	2.040	1.012	178.7
11	−4.90	1.984	1.013	179.9

[a] Energies in kcal mol^{-1}, distances in Å, and angles in degrees. [b] Structures given in Figure 1. [c] Energies corrected from the BSSE. [d] The H−Y bond distances of the monomers are 0.962, 0.963, and 1.006 Å for, respectively, water, phenol, and pyrrol.

TABLE 2: Bond Indices for the Relevant Bonds of the Monomers and Complexes of Figure 1

		H−Y		C−X/C−Y	
structure[a]	H−X	atoms[a]		atoms[a]	
1		1−2	0.7167		
2		12−13	0.6701	4−12	0.9298
3				1−5	0.9770
4		5−6	0.8078	1−5	1.1152
5	0.0752	2−3	0.601		
6	0.0688	2−3	0.5646	2−5	0.9440
6	0.0688	1−4	0.6515	1−16	0.9013
7	0.0785	2−3	0.5547	2−5	0.9472
8	0.0591			1−5	0.9505
8	0.0591	10−11	0.5803	10−12	0.9406
9	0.0539	11−12	0.6291	1−5	0.9552
10	0.0618	5−6	0.7284	1−5	1.1230
10	0.0618	11−12	0.6563	12−13	0.9077
11	0.0684	5−6	0.7164	1−5	1.1269

[a] Nomenclature and atom numbering given in Figure 1.

TABLE 3: Five-Center and Six-Center Delocalization Indices for the Aromatic Rings in the Monomers and Complexes of Figure 1

structure[a]	molecule	$10^2\Delta_5$	$10^2\Delta_6$
2			2.349
3		1.849	
4		2.777	
6	donor		2.311
6	acceptor		2.403
7			2.308
8	donor		2.319
8	acceptor	1.490	
9		1.552	
10	donor	2.818	
10	acceptor		2.392
11		2.861	

[a] Nomenclature given in Figure 1.

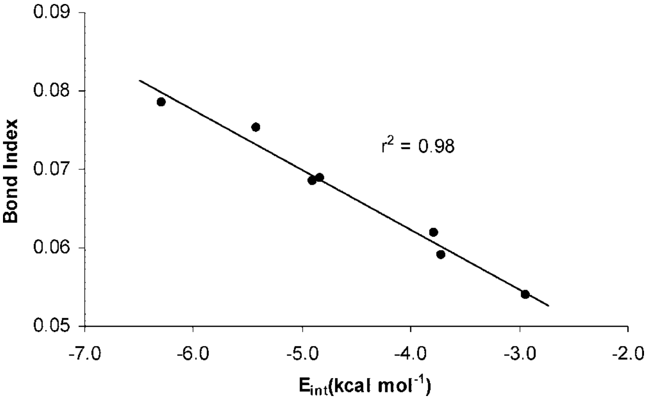
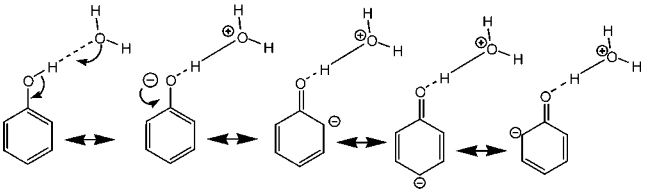
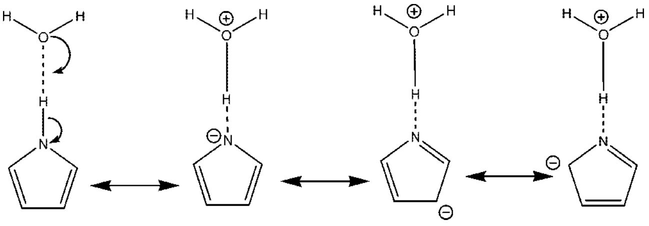


Figure 2. Correlation between the E_{int} and the H−O bond indices for the series of intermolecular H-bonded systems studied.

SCHEME 2



SCHEME 3

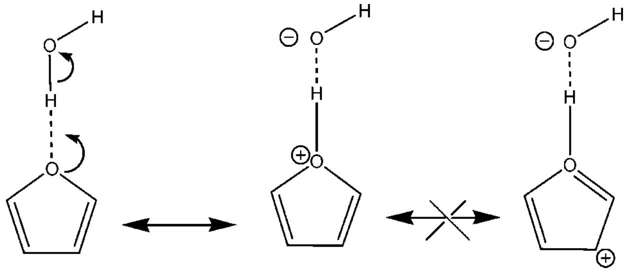


of the effect which does not imply real charge transfer between atoms. In fact it has been extensively shown with QTAIM that global evolution of atomic charges along hydrogen bond formation does not keep in line with the charges displayed by resonance forms.[21–24] These studies have shown that the stabilization gained by the complex comes from a redistribution of electron density where the hydrogens of the acceptor molecule lose electron population, as well as the hydrogen atom in the InHB, which is collected by the rest of the donor molecule. The acceptor atom always displays an increase of electron density in the complex with regard to the isolated monomer. Although the bulk of the interaction energy comes from this electron redistribution, the electron movement proposed in Scheme 2 explains the extra stability of structure 7 in comparison to structure 5. This implies a partial rupture of the ring π-electron delocalization as is confirmed by the lower 6-DI of the phenol ring (2.308 au) in comparison to the phenol monomer (2.349 au). This shows that the multicenter indices effectively support the resonance model. However, the formal charges represented by this model cannot be compared to the atomic charges but are just employed as a qualitative picture of the electron delocalization.

The pyrrole−water complex has the same behavior as the phenol−water complex. The H−Y bond distance increases in the complex. A look at the bond indices shows that the strength of the CY bonds increases slightly, whereas the H−Y bond weakens in the complex. This can be explained by the pyrrole molecule acting as a proton donor, thereby weakening the H−Y bond, while there is a delocalization from the water oxygen toward the hydrogen atom. This latter effect is supported by the electron delocalization in the pyrrole ring as can be seen in Scheme 3.

An important observation is that the 5-DI in the pyrrole ring of the pyrrole−water complex possesses a higher value than the pyrrole monomer. The pyrrole monomer is described by just one Kékule structure, but three additional resonant forms can be drawn for the pyrrole in structure 11 with the nitrogen atom acting as pyrimidinic nitrogen. These three additional forms are obviously extreme cases where fixed charges have no physical meaning, but they indicate how electron density is delocalized among atoms. Thus, the nitrogen is "less bonded"

SCHEME 4

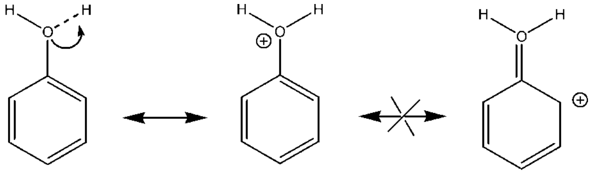


to exocyclic atoms in the complex than when isolated, and therefore, its electron density is more involved in the ring current when it is incorporated in the complex increasing the pyrrole ring 5-DI. Unfortunately, we cannot compare directly structures 5 and 11, since the substitution of oxygen by nitrogen at the donor implies an extra effect which is independent of the π-electron delocalization.

Effect of the Aromatic Electron Delocalization in the Acceptor Molecule. The furan—water complex (structure 9) shows a significantly smaller interaction energy than those of the water—water, phenol—water, and pyrrole—water complexes. There is stabilization of complex 9 due to the InHB, but it is not as strong as it is in complexes 5, 7, and 11. This is confirmed by the H—X distance which is quite longer than the H—X distance in the others. In addition, the C—X bond index decreases in the complex in comparison to the monomer, the H—Y bond that belongs to water experiences a decrease in its bond index, while the other H—O bond in water has an increase in its bond index. All this leads to the conclusion that in complex 9 the delocalization is, as expected for a HB, directed from the oxygen in the furan ring toward the hydrogen from water. However, the formation of the InHB is not enhanced by the electron delocalization in the aromatic ring, since it implies the formation of four bonds on the oxygen atom (see Scheme 4), which is obviously disfavored.

Another important observation is the remarkable decrease of the 5-DI for the furan ring in the furan—water complex with respect to the isolated furan. In the complex, furan acts as acceptor and the formal H—O bond reduces the electron delocalization within the ring as represented by the central resonance structure in Scheme 4. It must be remarked that the effect of the InHB formation on phenol in complex 7 is completely different from the effect on furan in complex 9, even though both diminish the electron delocalization within the ring. This is because the phenol acts as a donor whereas the furan acts as an acceptor and also the heteroatom in phenol is not incorporated in the ring structure whereas it is in the furan. In the case of the water—phenol complex, the multicenter electron delocalization increases in the unit formed by the phenyl ring and the hydroxyl oxygen with respect to the isolated phenol as it is represented in Scheme 2, which is supported by the 7-DI value that increases 1.7×10^{-4} au in the complex (it must be remarked that the absolute values of the n-DI indices decrease with the number of centers involved, that is why this value is smaller than the variation of the 6-DI for the phenyl ring, which is -4.1×10^{-4} au). The extension of the electron delocalization from the phenyl ring to the exocyclic oxygen atom also reduces the multicenter electron delocalization within the ring. This reduction of the electron delocalization within the phenol and furan rings in the hydrogen bonded systems is also confirmed by the values of the component perpendicular to the ring plane of the nucleus independent chemical shift[25] calculated at 1 Å above the ring critical points, NICS$_{zz}$(1), which were proved to be the best NICS indices for planar aromatic hydrocarbons.[26] The absolute values of the NICS$_{zz}$(1) decrease 0.70 and 0.64 for complexes 7 and 9 with respect to the isolated phenol and furan, respectively.

SCHEME 5



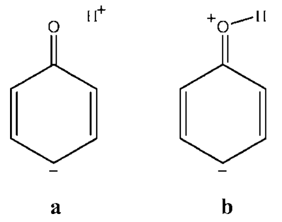
Cooperativity Between the Aromatic Electron Delocalization in the Donor and Acceptor Molecules. In this subsection, the interplay between the aromatic electron delocalization in the donor and acceptor molecules through the HB bridge is investigated. The E_{int} of the phenol—phenol complex (structure 6) is ~1.45 kcal mol^{-1} less stable than that of the phenol—water complex (structure 7). Also, the H—X bond distance increases and the bond index decreases. The same behavior is displayed by the pyrrole—phenol complex (structure 10), which is ~1.11 kcal mol^{-1} less stable than that of the pyrrole—water complex (structure 11). These observations indicate a noncooperativity between the electron delocalization at the donor and acceptor molecules and then the destabilization of the InHB when water is replaced by phenol as the acceptor molecule. The furan—phenol complex (structure 8) however is more stable than the furan—water complex (structure 9) by ~0.78 kcal mol^{-1}. Also, the InHB distance decreases and the bond index increases, indicating a cooperativity effect between the electron delocalization in the donor and acceptor molecules which provides an additional stabilization of the InHB when water is replaced by phenol as the acceptor molecule.

The cooperativity/noncooperativity effect is reflected on the electron delocalization of the aromatic rings from the acceptor molecules. Thus, the extension of the electron conjugation from the aromatic ring of the acceptor to the aromatic ring of the donor in structures 6 and 10 is disfavored. As can be seen in Scheme 5, the right top resonance structure where the positive charge is delocalized throughout the ring implies the formation of oxygen with four bonds. Therefore, the electron delocalization of the acceptor phenol is kept on the ring, and moreover, it is enhanced with respect to the isolated phenol (see the 6-DI values in Table 3). This is because the electron delocalization between the hydroxyl oxygen and the aromatic ring is disrupted by the hydrogen bond formation as represented by the central resonance structure of Scheme 5. On the other hand, the electron delocalization within the furan ring of structure 8 decreases with respect to both structure 9 and the isolated furan (see the 5-DI values in Table 3). In this case, the extension of the electron conjugation from acceptor to donor is favored, which results in a decrease of the electron delocalization within the furan ring.

Effect of the Insertion of Activating/Deactivating Groups in the Aromatic Rings. To further check the ability of multicenter electron delocalization analysis to explain the interplay between hydrogen bond formation and electron delocalization, we have taken the phenol—phenol complex (structure 6) and performed substitutions on the phenyl ring with activating/deactivating groups ($-NH_2$ and $-NO_2$). These groups are expected to delocalize electrons throughout the phenyl ring and then modify the effect of the electron delocalization on the InHB.

First of all, it is important to analyze the effect of activating/deactivating groups from a qualitative point of view. The

SCHEME 6



insertion of these groups affects the acceptor and donor molecules in a different way. One must keep in mind the conclusions derived from the study of the phenol−phenol complex; the π-electron delocalization in the donor phenol reinforces the hydrogen bond because it enhances the hydrogen transfer capability of the donor oxygen, whereas the π-electron delocalization in the acceptor phenol weakens the hydrogen bond because it decreases the nucleophilic character of the acceptor oxygen. This is reflected in the negative and positive changes of the 6-DI values after the hydrogen bond formation for the donor and acceptor rings, respectively. In other words, in the case of the donor phenol, the reinforcement of the hydrogen bond comes from the enhancement of the hydrogen transfer capability, which is represented by the polar resonance structure (a) in Scheme 6 (only shown in para position). On the contrary, in the case of the acceptor phenol, the reinforcement of the hydrogen bond comes from the mitigation of the electron delocalization between the oxygen and the phenyl ring, which is represented by the polar resonance structure (b) in Scheme 6 (also shown in para position).

In principle, two conclusions can be derived from this qualitative analysis: the insertion of deactivating groups such as $-NO_2$ is expected to reinforce the hydrogen bond when it is carried out on the donor phenol but weaken it when it is carried out on the acceptor phenol, whereas the opposite is expected for activating groups such as $-NH_2$.

Our quantitative study starts with the calculation of the interaction energies for the complexes formed by substituted phenol monomers. These values are collected in Table 4, where good agreement with the qualitative expectations is demonstrated. Thus, the interaction energy increases with regard to the phenol−phenol complex when $-NO_2$ and $-NH_2$ are inserted in the donor and acceptor molecules, respectively. On the contrary, the interaction energy decreases when the substitution is reversed. Also, it is remarkable that the larger E_{int} value corresponds to the substitution of both $-NO_2$ and $-NH_2$ in the donor and acceptor molecules, respectively, indicating additivity between the effects of activating and deactivating groups. As a surprising result, which contradicts the resonance model, the substitutions in para and meta positions do not show very different results. As one can see in Table 4, the extra stabilization provided by the substituents is only a bit larger in para positions than in meta positions, whereas the destabilization is quite similar in both cases. These results evidence the drawbacks of using a qualitative model such the resonance model to explain the electronic effects of activating/deactivating groups. This model does not predict the extra stabilization given by the meta substitutions but only the para and ortho substitutions. It must be clarified that the ortho substitution has not been studied here because of the additional intramolecular interactions that such substitutions carry in, which would screen the hydrogen bonding effect.

In terms of bond indices, the values calculated for the InHBs reflect a perfect linear correlation with the E_{int} values (see Figure 3). On the other hand, the 6-DI appears to be a very sensitive quantity. Comparing the values in the complexes with those of the isolated monomers, one finds that they always decrease for the donor molecule and increase for the acceptor molecule, as previously found in the phenol−phenol complex. The validity of the qualitative model explained above is confirmed when comparing the complexes formed by a substituted phenol and phenol with the phenol−phenol complex. It is found that the decrease in the donor ring electron delocalization, which corresponds to the enhancement of the hydrogen transfer capability, is larger in the substituted donor phenols for the more stable complexes, whereas it is smaller for the less stable ones. On the other hand, the increase in the acceptor ring electron delocalization, which corresponds to the mitigation of the nucleophilic character of the oxygen, is smaller in the substituted acceptor phenols for the more stable complexes, whereas it is larger for the less stable ones. The most significant example is the complex formed with paranitrophenol and paraaminophenol as donor and acceptor molecules, respectively, which displays the largest decrease and the smallest increase of the electron delocalization in the donor and acceptor aromatic rings, respectively.

TABLE 4: Interaction Energy, Hydrogen Bond Index, and Values of the Six-Center Delocalization Index for the Phenyl Ring in Donor and Acceptor Molecules for the Hydrogen Bonded Complexes Formed by Several Substituted Phenol Molecules[a]

substituted molecule	inserted group	position[b]	E_{int}	H−X	$10^2\Delta\Delta_6^{\text{donor}c}$	$10^2\Delta\Delta_6^{\text{acceptor}c}$
donor	$-NO_2$	para	−6.37	0.0773	−0.0704	0.0685
		meta	−6.00	0.0751	−0.0541	0.0659
	$-NH_2$	para	−4.44	0.0671	−0.0147	0.0510
		meta	−4.51	0.0683	−0.0175	0.0513
acceptor	$-NO_2$	para	−3.33	0.0621	−0.0252	0.0713
		meta	−3.34	0.0617	−0.0226	0.0573
	$-NH_2$	para	−5.42	0.0721	−0.0414	0.0217
		meta	−5.25	0.0712	−0.0433	0.0232
donor	$-NO_2$	para	−7.21	0.0815	−0.0802	0.0209
acceptor	$-NH_2$	para	−7.21	0.0815	−0.0802	0.0209
structure6			−4.84	0.0688	−0.0380	0.0540

[a] E_{int} values are given in kcal mol^{-1}, and remaining values are given in au. The corresponding values for the unsubstituted phenol−phenol complex are also included for comparison. [b] With respect to the hydroxyl group. [c] Values relative to that of the isolated monomer.

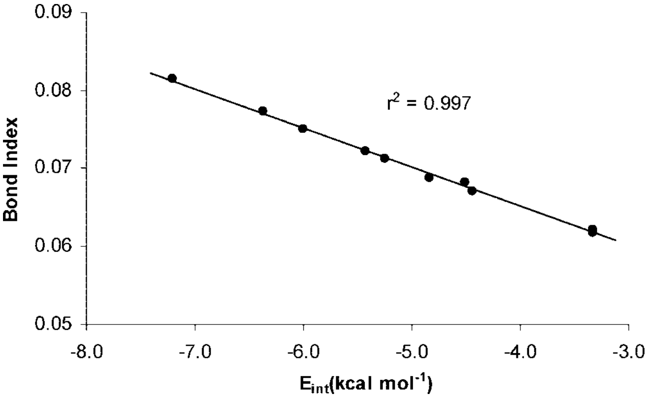


Figure 3. Correlation between the E_{int} values and the H−O bond indices for the series of H-bonded systems collected in Table 4.

IV. Concluding remarks

The interplay between the aromatic electron delocalization and the intermolecular hydrogen bonding has been thoroughly investigated using multicenter delocalization analysis. It has been quantitatively described the role played by the aromatic electron delocalization over the relative stability of intramolecular hydrogen bonded systems. As a general conclusion, the hydrogen bond is reinforced when the effect of the aromatic electron delocalization is to favor the proton transfer ability of the donor molecule and to enhance the nucleophilic character of the acceptor molecule; both situations can be effectively quantified by means of multicenter electron delocalization indices. It is proven that even small effects over the hydrogen bond strength as those associated with the aromatic ring substitutions are accounted for by multicenter electron delocalization analysis.

The results shown here match perfectly with the qualitative expectations derived from the resonance model. This, together with previous results of atomic charges, reveals that the partial charges drawn with this model are just a qualitative picture of the electron delocalization but do not represent the "real" electron density redistributions associated to the hydrogen bond formation.

As a further result, it has been found that the interaction energies in the complexes and the hydrogen bond indices show a good linear correlation at least for systems with oxygen as the acceptor atom. This supports the use of the hydrogen bond index as an estimator of the InHB strength.

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References and Notes

(1) Jeffrey, G. A. *An Introduction to Hydrogen Bonding*; Oxford University Press: New York, Oxford, 1997.

(2) Jeffrey, G. A.; Saenger, W. *Hydrogen bonding in Biological Structures*; Springer-Verlag: Berlin, New York, Heidelberg, 1991.

(3) Perrin, C. L.; Nielson, J. B. *Annu. Rev. Phys. Chem.* **1997**, *48*, 511.

(4) Szalewicz, K.; Jeziorski, B. *Molecular Interactions*; Wiley: Chichester, 1995.

(5) Sing, U. C.; Kollman, P. A. *J. Chem. Phys.* **1985**, *83*, 4033.

(6) Spackman, M. A. *J. Chem. Phys.* **1986**, *85*, 6587.

(7) Gilli, G.; Gilli, P. *J. Mol. Struct.* **2000**, *552*, 1.

(8) Sobczyk, L.; Grabowski, S. J.; Krygowski, T. M. *Chem. Rev.* **2005**, *105*, 3513.

(9) Bultinck, P.; Michel, R.; Ponec, R.; Van Gheluwe, B.; Carbó-Dorca, R.; Popelier, P. *J. Phys. Chem. A* **2006**, *110*, 7642.

(10) Mandado, M.; González-Moa, M. J.; Mosquera, R. A. *J. Comput. Chem.* **2007**, *28*, 127.

(11) Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Oxford University Press: Oxford, 1990.

(12) Giambiagi, M.; Bultinck, P. *J. Braz. Chem. Soc.* **2008**, *19*, 263.

(13) Mandado, M.; Otero, N.; Mosquera, R. A. *Tetrahedron* **2006**, *62*, 12204.

(14) Mandado, M.; Krishtal, A.; Van Alsenoy, C.; Bultinck, P.; Hermida-Ramon, J. M. *J. Phys. Chem. A* **2007**, *111*, 11885.

(15) Caramori, G. F.; de Oliveira, K. T.; Galembeck, S. E.; Bultinck, P.; Constantino, M. G. *J. Org. Chem.* **2007**, *72*, 76.

(16) Ponec, R.; Bultinck, P.; Gallegos-Saliner, A. *J. Phys. Chem. A* **2005**, *109*, 6606.

(17) Angyan, J. G.; Loos, M.; Mayer, I. *J. Phys. Chem.* **1994**, *98*, 5244.

(18) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1978**, *19*, 553.

(19) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.

(20) *AIMPAC: A suite of programs for the Theory of Atoms in Molecules*; Bader R. F. W.; McMaster University: Hamilton, Ont., Canada. Contact: bader@mcmail.cis.mcmaster.ca.

(21) Vila, A.; Mosquera, R. A.; Hermida-Ramón, J. M. *J. Mol. Struct. (THEOCHEM)* **2001**, *541*, 149.

(22) Vila, A.; Mosquera, R. A. *Chem. Phys.* **2003**, *291*, 73.

(23) Mandado, M.; Graña, A. M.; Mosquera, R. A. *Phys. Chem. Chem. Phys.* **2004**, *6*, 4391.

(24) Mandado, M.; Mosquera, R. A.; Van Alsenoy, C. *Tetrahedron* **2006**, *62*, 4243.

(25) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317.

(26) Fallah-Bagher-Shaidaei, H.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 863.

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