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Interplay between Hydrogen-Bond Formation and Multicenter π-Electron Delocalization: Intramolecular Hydrogen Bonds

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The specific case of intramolecular hydrogen bonds assisted by π-electron delocalization is thoroughly investigated using multicenter delocalization analysis. The effect of the π-electron delocalization on the intramolecular hydrogen-bond strength is determined by means of the relative molecular energies of “open” and “closed” structures, calculated at the B3LYP/6-311++G(d,p) level of theory. These relative energies are compared to variations in the multicenter electron delocalization indices and covalent hydrogen-bond indices, which are shown to correlate very well with the relative strength of the intramolecular hydrogen bonds studied. The multicenter electron delocalization indices and covalent bond indices have been computed using the quantum theory of atoms in molecules approach. The hydrogen bonds are formed with oxygen, nitrogen, or sulfur as acceptor atom, which are also the atoms considered to be bonded to the donor hydrogen. Malonaldehyde is taken as reference; the substitution of oxygen by other atoms at the acceptor and donor positions and the effect of the aromaticity have been studied. The results shown here match perfectly with the qualitative expectations derived from the resonance models. In addition, they provide a quantitative picture of the role played by the π-electron delocalization on the relative strength of intramolecular hydrogen bonds.

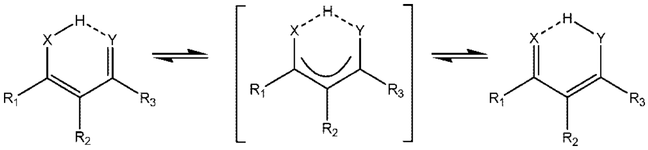
I. Introduction

This paper completes our study of the interplay between hydrogen-bond formation and multicenter π-electron delocalization, which started with the study of the intermolecular hydrogen bond.[1] The present paper addresses the intramolecular case.

There are molecular systems which display stronger intramolecular hydrogen bonds, IHBs, than the typical ones because of the resonance-assisted hydrogen-bonding effect.[2] Resonance-assisted hydrogen bonds, RAHBs, are present in many biological processes, which makes them an important topic in fields such as (bio)chemistry and molecular biology.[3,4] This effect is represented in Scheme 1 and stems from the π-electron delocalization as the mixture of two different resonance forms.

The atoms X and Y can be the same, homonuclear hydrogen bond, or different, heteronuclear hydrogen bond. The substituents can be separate groups or cyclic structures. In general, the following geometrical effects are observed:[2,3,5] the single and double carbon bonds equalize as well as the C−X and C−Y bonds; there is an elongation of the proton-donor bond distance and a decrease of the proton-acceptor bond distance (throughout the paper denoted by H−Y and H···X, respectively). These geometrical changes are a consequence of the π-electron delocalization along the X−C−C−C−Y unit. The formation of a quasi-aromatic ring between the H−X−C−C−C−Y atoms has been proposed in the literature.[2] However, due to the orthogonality of the π orbitals, responsible for the electron delocalization within the X−C−C−C−Y unit, and σ orbitals involved in the H···X bond, the H−X−C−C−C−Y ring is expected to display a very small electron delocalization.

SCHEME 1



According to valence bond theory,[6] both resonance structures represented in Scheme 1 can be described by a wave function. A linear combination of these wave functions represents the RAHB system:

$$\psi = c_1\psi_1 + c_2\psi_2 \tag{1}$$

The more effective the mixture of the separate wave functions to the RAHB-structure wave function, the greater the π-electron delocalization. It was observed that for intramolecular RAHBs, such as malonaldehyde (R_1, R_2, R_3 in Scheme 1 are all hydrogen atoms) and its derivatives, the IHB may be stronger due to other effects.[7,8] In accordance with the electrostatic covalent hydrogen-bond model,[9] ECHMB, the hydrogen-bond strength increases as the difference in protonation affinity, PA, calculated as the difference between the PA values of atoms X and Y, decreases. In this sense the substituents play a very important role. Thus, the systems containing electron-withdrawing and electron-donating substituents attached to the atom with the highest and lowest PA values, respectively, will form stronger hydrogen bonds. This is because in this way the wave functions of the different resonance structures will be more alike and thus will mix to a greater extent.

In the case of an IHB such as that represented in Scheme 2, if the electron density of the “closed” conformation is compared

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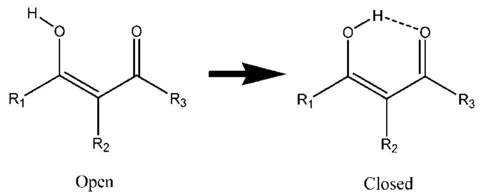
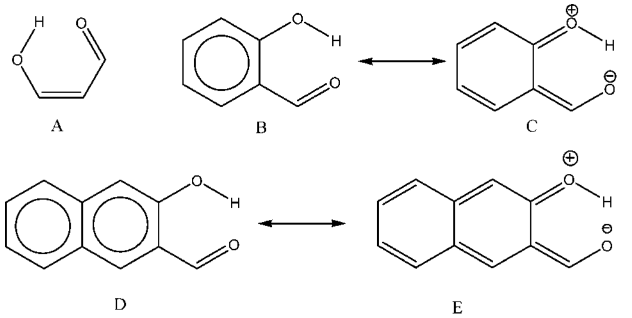
SCHEME 2



SCHEME 3



to the density of the "open" conformation using MP2 calculations and the Bader theory,[10] some trends have been observed: [11] a decrease of electron density in the hydrogen and also in the set of carbon atoms, an increase of density in both oxygens, and an overall increase of the density in the hydrogen bond. In general, a transfer of electron density is seen in the ring from the carbon bonds toward the heteroatoms and the hydrogen. It has been confirmed that this transfer depends mainly on the π-electron delocalization (it depends in smaller amount on the σ-bond delocalization) that occurs because of the formation of the quasi-ring structure. This may be considered as one of the main features of RAHB.

Little is known about systems where RAHB structures are fused to aromatic rings. The π-electron delocalization associated to the RAHB formation provokes changes in the local aromaticity of the ring. In the literature there are mentions to what happens when malonaldehyde is fused to several aromatic structures such as benzene, naphthalene, anthracene, and phenanthrene.[12] In previous works the energy difference between the "open" and "closed" forms of the RAHB is employed as a measure of the IHB strength taking malonaldehyde as the reference molecule. On the basis of the energy differences, two types of systems can be distinguished: the ones with RAHB weaker than the reference molecule and the ones with RAHB stronger. The structures B/C and D/E in Scheme 3 represent a weaker RAHB than the reference A.

The weakening of the RAHB stems from the mutual competition between the ring π-electron delocalization and the π-electron delocalization within the RAHB structure. The first one is represented by the structures B and D. Actually, these structures result from the superposition of two and three different resonance structures, respectively. On the other hand, structures C and E represent the polar resonance structures reinforcing the IHB by resonance. π electrons from the aromatic ring are involved in the RAHB structure, and therefore its aromaticity decreases. Both types of π-electron delocalization are present in all aromatic systems fused to an RAHB structure and are mutually competitive. This explains why the systems B/C and D/E have a weaker IHB than the system A.

All of these qualitative expectations are investigated in this paper for a large series of systems capable of forming RAHBs. The tools employed for this study are the atomic charges and the multicenter electron delocalization indices as well as the relative molecular energies. In this study a nice picture of the RAHB effect is provided; the multicenter electron delocalization analysis reveals the causes of the strengthening and weakening of the IHBs due to their interaction with π-electron systems. The results presented here are quantitative and allow one to predict the effect over the RAHBs of any substituent using magnitudes directly obtained from the molecular wave function. The paper is organized as follows: In the second section (section II), 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 part is devoted to the effect on the RAHB strength of different substitutions at the donor and acceptor atoms; in the second part the specific case of RAHBs involved in aromatic systems is investigated; the effect on these kinds of RAHBs of the insertion of activating and deactivating groups is discussed in the third part, whereas the hydrogen transfer process between donor and acceptor atoms in RAHB systems is presented in the fourth part. Finally, the conclusions are formulated.

II. Computational Methods

Since the formulation of multicenter electron delocalization indices, n-DIs, in the context of the quantum theory of atoms in molecules, QTAIM,[10] has been presented in previous papers,[13] we are only showing the relevant expressions employed for its calculation. Thus, eq 2 represents the n-center delocalization index, Δ_n, in terms of products of the atomic overlap integrals, $\langle i|j\rangle_A$, of spatial molecular orbitals i, j,.... $\Delta_n(A, B,..., M)$ represents the delocalized electron population among those n atoms. P represents all the nonsymmetrical permutations of the atoms A, B,..., M.

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

Expression 2 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 2 is theoretically not entirely accounted for although the wide use of eq 2 using KS orbitals has shown that the results do give chemically significant results. The values of these indices can be either positive or negative; the physical meaning of the sign is still being investigated, although it has been extensively confirmed that aromatic rings always show positive values.[13−18]

In this work we consider indices involving two, five, and six centers. The former has been proved to be a good measure of the covalent character of bonds, and so it is also called bond index.[19] The 6-DIs are employed to calculate the π-electron delocalization within the aromatic benzenoid rings and so employed as an estimate of the local aromaticity of these rings. Finally, the 5-DIs are used in this work to calculate the π-electron delocalization within the XCCCY units, providing an estimation of the RAHB effect. 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 2 inherently decreases as the number of overlap integrals increases, and the number of overlap integrals is equal to the number of centers, n.

Although the energy difference between the "open" and "closed" structures does not reflect the H-bond energy as good as could be expected using other more sophisticated schemes,[20] we have estimated the stability of the intramolecular hydrogen-bonded systems by using the relative molecular energies of "open" and "closed" structures, as commented in the Introduction. The optimized geometries as well as the relative molecular energies have been calculated at the B3LYP/6-311++G(d,p) level. The molecular orbitals employed in the calculation of delocalization indices have been obtained using the same level of calculation. The Gaussian03 program[21] has been used to compute the molecular energies and molecular orbitals, whereas the AIMPAC package of programs[22] has been used to compute the QTAIM atomic charges (when needed) and the atomic overlap integrals. The calculation of multicenter delocalization indices was performed using a program developed in our laboratory.

III. Results and Discussion

Before beginning the discussion of results, it must be mentioned that the hydrogen-bond interactions render small redistributions of the electron density, which in turn give rise to small values of the interaction energies. Therefore, the analysis of the electron density must be done taking into account that small variations on its associated properties are enough to explain the stability of hydrogen-bonded systems. In relation with this, previous studies performed on model unsaturated and saturated structures of malonaldehyde and its diaza counterparts with the geometry in the hydrogen-bonding region constrained to be the same reflected that OO and NN coupling constants and hydrogen chemical shifts display very small changes when going from saturated to unsaturated compounds.[23,24] The authors concluded that neither coupling constants nor chemical shifts provide any evidence for the existence of RAHBs since the changes are very small. However, looking at their results in detail one can observe that changes in coupling constants and chemical shifts in all cases point to a strengthening of the IHB in the unsaturated compounds. Moreover, the changes in the coupling constants represent the 30% and 15% of the total values of the OO and NN coupling constants in the saturated structures,[24] respectively, which should not be considered negligible.

In this section the analysis of the "open", "closed", and transition structures of several systems suitable for forming RAHBs is performed using relative energies and multicenter electron delocalization indices. The latter are shown to provide a good picture of the π-electron delocalization associated to the formation of the IHBs.

III.1. Effect of Donor and Acceptor Substitutions on the RAHB Strength. The energy profiles of several hydrogen-bonded systems, with alternation of oxygen, nitrogen, and sulfur as donor (Y) or acceptor (X) atoms are shown in Figure 1. The complementary information to the Figure 1 is collected in Table 1, where the H···X bond indices and the five-center electron delocalization indices among the atoms forming the π backbone, i.e., the XCCCY unit (see Scheme 1), are listed. Figure 1 contains valuable information about the effect of electronegativity, resonance, and aromaticity over the relative stability of the different IHBs, whereas Table 1 allows interpreting the reasons for such stability in terms of the π-electron delocalization in the system. Also, the covalent character of the IHB is given by the H···X bond indices.

Taking the energy profile of the malonaldehyde system, which is denoted as OHO profile in Figure 1, as reference we can establish the conditions for the enforcement of an IHB. Then, the substitution of an electronegative atom such as oxygen by a relatively less electronegative atom such as sulfur at the donor and acceptor positions leads to a large reduction of the stability as can be seen from the relative energies of the pairs OHO1/OHO2 and SHS1/SHS2 (12.94 and 2.75 kcal mol^{-1}, respectively). Nevertheless, it can be seen that the change in stability is not due to the substitution at the acceptor but the donor. Thus, the OHS5/OHS4 relative energy (13.50 kcal mol^{-1}) is even larger than that of OHO1/OHO2, and the OHS1/OHS2 relative energy (2.64 kcal mol^{-1}) is almost the same as that of SHS1/SHS2. At the first glance the strength of the IHB seems to confirm this idea as the stability of the IHB is largely influenced by the nature of the donor but not the acceptor.

To draw conclusions about the IHB it is important to keep in mind the electrostatic covalent hydrogen-bond model. Thus, the HB strength cannot be explained considering only the covalent character of the IHB, since it is also influenced by the electrostatic interaction which depends on the partial charge of hydrogen which is governed by the electronegativity of the donor atom. Thus, the charges obtained with the QTAIM method will be mentioned where needed.

The bond indices for the O−H···X hydrogen bonds (with X = O, N, and S) follow the trend OHO2 < OHN3 < OHS4, indicating that the covalent character increases with the substitution of oxygen by nitrogen and sulfur. This is also supported by the 5-DI values, which follow exactly the same trend, indicating the O−H···S hydrogen bond is more assisted by the π-electron system than those of O−H···N and O−H···O. However, the energy differences between the "open" and "closed" structures indicate a different trend: OHO2 < OHS4 < OHN3. The QTAIM charges for the donor atoms are O (−1.102), N (−1.149), and S (0.076). This clearly shows the importance of the electrostatic contribution to OHO2 and OHN3, whereas the charge of the sulfur atom is close to zero. This leads to stabilization of the OHO2 and OHN3 structures due to the large electrostatic interaction, whereas the OHS4 structure is hardly affected, leading to the trend given by the energy differences. It must be mentioned that the large relative energy shown by the OHS4/OHS5 pair must be largely due to the electron−electron repulsion existing between the sulfur and oxygen electron pairs, which is more important than those of the oxygen electron pairs in the OHO2/OHO1 pair and the nitrogen and oxygen electron pairs in the OHN3/OHN4 pair because of the size of sulfur.

The same trend is found for the NHS profile; the NHS4/NHS3 relative energy (3.68 kcal mol^{-1}) is close to that of SHS1/SHS2 and OHS1/OHS2, showing that substitution at the acceptor position does not change the stability significantly. However, the bond index as well as the 5-DI displays larger values when the acceptor is sulfur, followed by nitrogen and oxygen, which is the opposite trend to the electronegativity. The covalent effect seems to compensate for the electrostatic effect in this case. As a general rule, the 5-DI is always larger for the "closed" structures, which confirms that the π-system assists the IHB formation in the three cases.

At this point, it has been confirmed that the π-electron delocalization within the XCCCY unit can increase the stability of the hydrogen-bonded structures; in other words, it can reinforce the IHB. However, there are some conformations where the IHB may be destabilized by resonance instead of stabilized. This possibility is generalized for all the RAHBs considered in this work and shown in Scheme 4, where the destabilized structure has an acceptor atom X which displays a single bond with the carbon atom and the donor Y has a double bond. In this situation the π-electron delocalization between the carbon atoms and the acceptor and donor is clearly hindered.

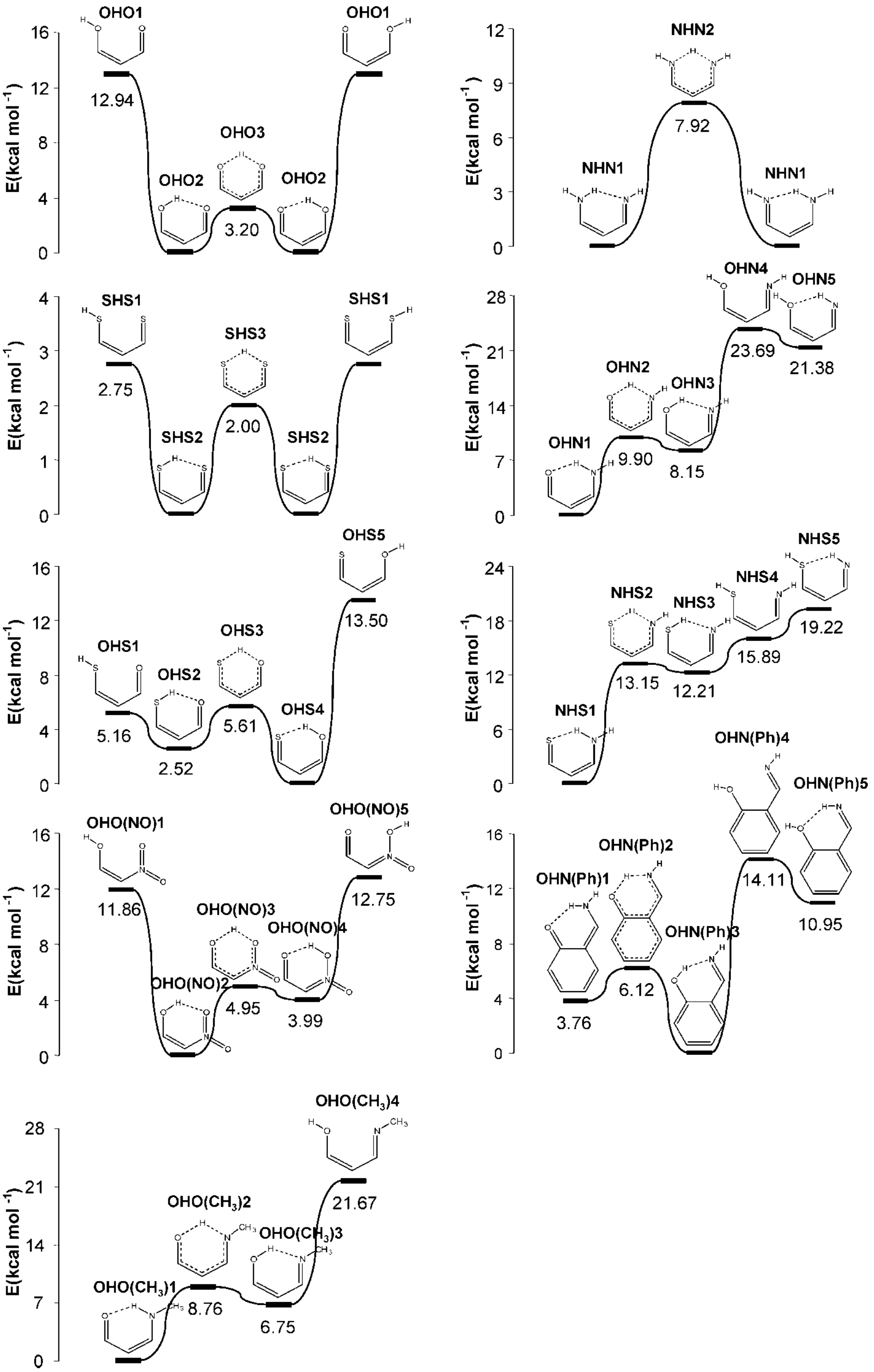


Figure 1. Energy profile and nomenclature of several structures suitable for forming RAHB.

Thus, the question is, are the IHBs in these structures destabilized by the π-system? The answer is yes. Looking at the relative energies of the pairs OHN4/OHN5 (2.31 kcal mol^{-1}) and NHS4/NHS5 (-3.33 kcal mol^{-1}) it can be stated that the IHB in the OHN5 and NHS5 structures is weaker than those of OHN3 and NHS3, respectively. Moreover, the substitution of oxygen by sulfur at the acceptor position comes out with larger relative destabilization. This can be attributed to the large electron delocalization associated to the sulfur systems, which now weakens the IHB instead of reinforcing it. There is no compensation between electrostatic and covalent contributions anymore, and the difference on stability of the IHB in both systems is more than 4.5 kcal mol^{-1}. The values of the H$\cdots$X bond index in OHN5 and NHS5 are clearly smaller than those of OHN3 and NHS3. The 5-DIs are also very small and decrease substantially with respect to the "open" structures, OHN4 and NHS4. It must be noticed that even though the destabilization of the IHB in NHS5 is clear, the structure represents a minimum in the global potential energy surface, PES.

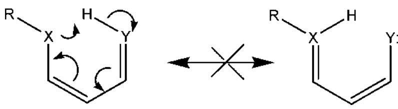
The effect of linking different substituents to the acceptor atom has also been investigated. The effects of nitrogen methylation on the OHN system and the substitution of C=O by N(O)=O in the OHO system are represented in Figure 1 (the OHN(CH_3) and OHO(NO) energy profiles, respectively). The OHN(CH_3)4/OHN(CH_3)3 relative energy (14.92 kcal mol^{-1}) is about 0.6 kcal mol^{-1} lower than that of OHN4/OHN3, indicating the small but destabilizing effect of methylation. The IHB bond index and 5-DI are also lower in OHN(CH_3)3 with

TABLE 1: H···X Bond Indices and 5-DI Values for the XCCCY Unit in All the Conformations Shown in Figure 1

conformation	Δ_2(H···X)	$10^2\ \Delta_5$	conformation	Δ_2(H···X)	$10^2\ \Delta_5$
OHO1		0.2150	NHS1	0.1248	2.2043
OHO2	0.1207	0.6741	NHS2	0.2920[a] 0.6520[b]	1.6522
OHO3	0.3108	1.1920	NHS3	0.1521	0.9876
NHN1	0.0932	1.2725	NHS4		0.7420
NHN2	0.3483	2.0685	NHS5	0.0598	0.4469
SHS1		1.8812	OHO(NO)1		0.2839
SHS2	0.2036	2.2926	OHO(NO)2	0.1021	0.4702
SHS3	0.5137	3.1115	OHO(NO)3	0.2860[c] 0.3289[d]	0.6530
OHN1	0.0753	1.0720	OHO(NO)4	0.1652	0.4269
OHN2	0.3445[c] 0.3078[a]	1.4427	OHO(NO)5		0.1568
OHN3	0.1451	0.8348	OHN(Ph)1	0.1162	0.7739
OHN4			OHN(Ph)2	0.2823[c] 0.3879[a]	0.7388
OHN5	0.0440	0.1588	OHN(Ph)3	0.1281	0.2886
OHS1		0.6571	OHN(Ph)4		0.1396
OHS2	0.1140	0.7928	OHN(Ph)5	0.0533	0.0675
OHS3	0.3222[c] 0.5661[b]	1.7270	OHN(CH_3)1	0.0870	1.2108
OHS4	0.1697	1.5150	OHN(CH_3)2	0.3449[c] 0.3135[a]	1.348
OHS5		0.8826	OHN(CH_3)3	0.1424	0.7187
			OHN(CH_3)4		0.2972

[a] H···N. [b] H···S. [c] H···O. [d] H···O(NO).

SCHEME 4



respect to the OHN3, but the difference is small. On the other hand, the substitution of the carbonyl group by the nitro group as acceptor comes out with a small destabilization (around 1 kcal mol^{-1}), as can be derived from the comparison of the OHO(NO)1/OHO(NO)2 and OHO1/OHO2 relative energies. Here the IHB bond index and 5-DI values are slightly smaller in the less stable structure, the OHO(NO)2.

The effect is different when the substitution affects the donor atom. Thus, the OHO(NO)5/OHO(NO)4 relative energy (8.76 kcal mol^{-1}) is quite smaller than that of OHO1/OHO2, but the H···X bond index is larger in the OHO(NO)4. This system also displays a smaller value of 5-DI, which indicates that even though the π-electron delocalization decreases, the covalent character of the IHB increases. That can be explained by the fact that the π-electron delocalization in the OHO(NO) structures extends to six atoms instead of five (the OCCN(O)O unit) and probably the electron density in this unit is drawn away from the IHB toward the N=O bond with the oxygen atom situated outside the ring.

It must be pointed out that Wojtulewski and Grabowski reported values of the CC bond equalization by calculating the difference between the C−C and C=C distances at the same level of theory for a set of nine structures included in our study.[25] Their results are consistent with the 5-DI values collected in Table 1, so the largest π-delocalized structures are the SHS2, NHS1, and OHS4 according to both studies. Moreover, we have also found a linear correlation between the CC bond equalization and the 5-DI values for the nine structures. Although the regression coefficient for this linear correlation is not good (r = 0.8), it can be considered acceptable since the CC bond equalization does not include the bond distances between the carbons and the heteroatoms, whereas the 5-DI also includes the heteroatoms in the calculation.

III.2. Effect of the Aromaticity on the RAHB Strength. The OHN(Ph)1 and OHN1 are hydrogen-bond structures that deserve closer scrutiny. The OHN1 conformation is the most stable OHN structure due to its strong RAHB. On the contrary, the OHN(Ph)1 conformation is not the most stable OHN(Ph) structure. As one can see the electron delocalization within the ring is hindered in this conformation; the 6-DI values (multiplied by 10^2) for the phenyl ring are 0.8276 and 1.8173 in the OHN(Ph)1 and OHN(Ph)3 conformations, respectively. Even though the RAHB is stronger (look at the 5-DI values in Table 1) the energetic cost resulting from the loss of aromaticity is revealed to be more important. Thus, the OHN(Ph)3 conformation is the most stable because the aromatic character of the phenyl ring is not affected by the electron delocalization in the RAHB. The effect of the aromaticity over the relative stability of an RAHB is noticeable for other conformations. Thus, the OHN(Ph)4/OHN(Ph)3 relative energy (14.11 kcal mol^{-1}) as given in Figure 1 is more than 1 kcal mol^{-1} lower than the OHN4/OHN3 relative energy. The H···X bond index decreases with the presence of the aromatic ring, and the decrease is much more noticeable for the 5-DI index (see Table 1).

On the other hand, it is interesting to look at what happens for an IHB that is destabilized by resonance when the ethylene group is part of an aromatic ring. As can be derived from the OHN(Ph)4/OHN(Ph)5 and OHN4/OHN5 relative energies (respectively, 3.16 and 2.31 kcal mol^{-1}), the IHB is stabilized when the ethylene is part of an aromatic ring. However, this result is not surprising since the ethylene is less available to take part in the IHB because of its participation in the ring electron delocalization.

Other examples of destabilized RAHBs due to aromaticity are shown in Figure 2. The relative stabilization of the RAHB decreases about 2 kcal mol^{-1} in the OHO and OHS systems, whereas it decreases about 1 kcal mol^{-1} in the OHO(NO) system when the ethylene group is part of an aromatic ring. The H···X bond indices and 5-DIs are also smaller. The effect of the aromaticity over the stability of the RAHBs is even larger when the aromatic system is the naphthalene group instead of the phenyl group. Thus, a larger decrease in the relative energy is found as well as the H···X bond index and 5-DI values when the phenyl ring is replaced by naphthalene.

The differences in the 6-DIs between the "closed" and "open" conformations are shown in Figure 3. If an RAHB system is part of an aromatic cycle, the formation of the IHB will induce a decrease of the electron delocalization in the aromatic cycle. The 6-DI values shown in Figure 3 confirm this. The particular

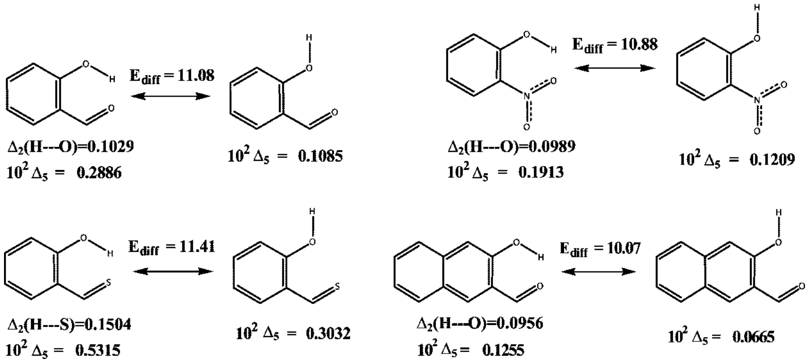


Figure 2. Relative energies, E_{diff}, H···X bond indices, and 5-DI values of the XCCCY unit, for the "open" and "closed" conformations in several structures suitable for forming RAHB and containing aromatic systems.

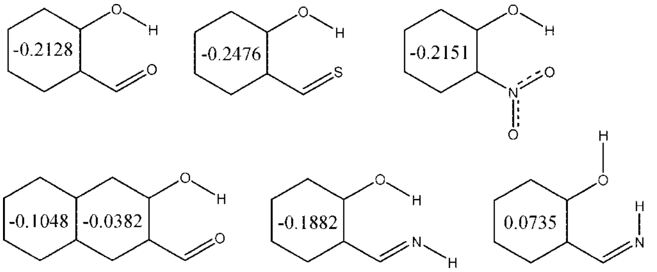


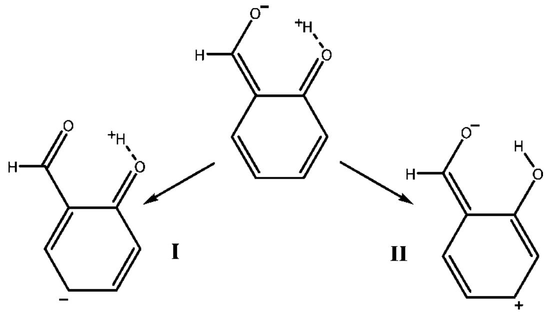
Figure 3. Variations of the 6-DI in the aromatic rings fused to the RAHB structure. The displayed 6-DI values are the difference between the "closed" and "open" conformations and are multiplied by 10^2.

TABLE 2: Relative Energies, 6-DIs, and 5-DIs for the "Open" and "Closed" Structures of 2-Hydroxy-4-amino-benzaldehyde (1), 2-Hydroxy-5-amino-benzaldehyde (2), 2-Hydroxy-4-nitro-benzaldehyde (3), and 2-Hydroxy-5-nitro-benzaldehyde (4)[a]

molecule	ΔE/kcal mol^{-1}	$10^2\Delta\Delta_6$	$10^2\Delta\Delta_5$	r(H···O)/Å	Δ_2(H···O)
1	−12.42	−0.2072	0.1011	1.743	0.1084
2	−10.89	−0.1868	0.1143	1.784	0.0989
3	−10.32	−0.1592	0.1161	1.773	0.0993
4	−11.14	−0.1764	0.1121	1.752	0.1034

[a] The H···O distances and bond indices are shown for the "closed" structures. The relative energies are shown in kcal mol^{-1}, and the bond distances are in angstroms.

SCHEME 5



case of the naphthalene group deserves mention; it can be seen that the outer ring experiences a larger decrease in the electron delocalization than the inner ring. This indicates that the effect of the RAHB on the aromatic system extends to remote rings, even to larger degree than that of the fused ring. This fact can be qualitatively explained using the Clar's aromatic sextet theory,[26] where the larger local aromaticity is assigned to rings displaying π-sextets in the Clar structure (Clar's rule), this structure being the Kekulé resonance structure that displays more π-sextets. In the case of naphthalene both rings display a π-sextet in the two symmetrical Clar structures. However, the RAHB favors one of these structures, concretely the one having the π-sextet on the inner ring (this is also the one drawn in Figure 2), which makes this ring more aromatic. It must be noticed that recently very good agreement has been shown between n-DIs and the local aromaticity indices calculated with the chemical graph theory,[27] which are the quantitative expression of the Clar's rule.[28]

On the other hand, when the IHB is destabilized by resonance as in OHN(Ph)5 the electron delocalization in the aromatic ring increases, which is accompanied by a decrease of the 5-DI values in the XCCCY unit with respect to the "open" structure, OHN(Ph)4, as can be seen in Table 1.

III.3. Effect of Activating and Deactivating Groups on the RAHB Strength. In this section the effect of introducing activating/deactivating groups into the phenyl ring is investigated. The reference system chosen is 2-hydroxy-benzaldehyde, and the activating and deactivating groups are the amino and nitro groups, respectively. These groups have been introduced in meta and para positions with regard to the hydroxyl group. In Table 2 the relative energies of "open" (nonbonded) and "closed" (hydrogen-bonded) structures are shown. As can be seen in the table, the effect of activating and deactivating groups is different. Thus, whereas the amino group reinforces the IHB in the meta position and weakens it in para, the nitro group causes the opposite effect. The values of the H···O distance and bond index indicate the same behavior. A qualitative explanation can be found in Scheme 5; the reinforcement or weakening of the IHB comes through the stabilization or destabilization of a resonance form with formal negative and positive charges placed on the acceptor oxygen and donor hydrogen atoms, respectively. This resonance form gives rise to two different forms where the donor character of the hydrogen and the acceptor character of the oxygen are enhanced (structures I and II, respectively), leaving negative and positive charges in the phenyl ring which are placed on the para and meta positions, respectively. Therefore, a group which stabilizes or destabilizes one of these resonance forms reinforces or weakens the IHB. In this case, the activating amino group stabilizes the structure II, when inserted in the meta position, and destabilizes structure I, when inserted in the para position. The opposite happens for the nitro group.

Looking at the structures in Scheme 5 one deduces that the electron delocalization within the phenyl ring and within the OCCCO unit decreases due to the presence of these resonance forms. Thus, they should decrease more when the groups stabilize the forms than when the groups destabilize. In other words, reinforced IHBs should reflect larger π-localization and vice versa. The relative values of 6-DIs for the phenyl rings and 5-DIs for the OCCCO units are collected in Table 2 and confirm the expectations given above. These results prove that the multicenter delocalization analysis is a very sensitive method which is able to reflect very small changes in the molecular environment such as ring substitutions.

III.4. The Donor−Acceptor Proton Transfer Process. As can be seen in Figure 1, there are two types of transition states (TSs): those where the donor and acceptor atoms are the same (symmetric transition states), such as the OHO3, the SHS3, and the NHN2 structures, and those where the donor and acceptor atoms are different (asymmetric transition states), which are all the other systems.

In the symmetric TSs, the energy profile is the same on both sides. The geometric properties such as bond distance and angles will equalize between the two symmetric halves of the molecule. The 5-DIs values for these TSs always possess the highest values in comparison to the "closed" and "open" conformations.

The asymmetric TSs show a more diverse range of energy profiles. They display large 5-DI values for the OHN, OHS, OHO(NO), and the OHN(CH_3) systems; the remaining systems also show significant 5-DI values though. The same can be said for the H···X bond indices, which possess the largest value when compared to the other conformations. These are indicators that the proton transfer from the donor to the acceptor atoms in systems with symmetric or asymmetric TSs happens by a concerted mechanism which is assisted by the π-electron system (the ability of multicenter electron delocalization analysis to predict concerted reaction mechanisms has been also proven in pericyclic reactions[29]). During this "one-step" process, the TS displays the largest π-electron delocalization within the XCCCY unit and also a significant σ-electron delocalization within the XHY unit, as confirmed by the 3-DI values. However, the π-electron delocalization within the XCCCY unit and the σ-electron delocalization within the XHY unit take place independently since the values of the 6-DI for the HXCCCY unit are negligible. For instance, the largest values are displayed by the SHS3 structures, and they are 3.1115, −9.3029, and 0.1864 for the 5-DI, 3-DI, and 6-DI indices, respectively (these values are multiplied by 10^2).

Finally, the asymmetric TSs always connect two RAHB structures which have different relative stabilities. For example, OHS3 connects the structures OHS2 and OHS4. It is observed that these TSs are shifted to the least stable RAHB in all cases. For instance, the H···S bond has a larger bond index (0.5661) than the H···O bond (0.3222) in the structure OHS3.

IV. Concluding Remarks

The interplay between the multicenter electron delocalization and the intramolecular hydrogen bonding has been thoroughly investigated using multicenter electron delocalization analysis. The role played by the π-electron delocalization on the relative stability of RAHBs has been determined. As a general conclusion the hydrogen bond is reinforced when the direction of the electron delocalization favors the proton transfer from the donor to the acceptor molecule; this situation can be effectively quantified by means of multicenter electron delocalization indices. On the contrary, it has been shown that there exist systems where the IHB is destabilized by resonance when the π-electron delocalization between the carbon atoms and the acceptor and donor is hindered.

The largest resonant stabilization occurs in systems where the sulfur atom acts as acceptor. Nevertheless, systems with O or N as acceptor compensate their less resonant stabilization with a larger electrostatic interaction, the resulting order of stability being O < S < N for the systems studied here.

In the specific case of RAHBs also involved in aromatic electron delocalization it has been demonstrated that there is mutual competition between the ring π-electron delocalization and the π-electron delocalization within the RAHB structure, which decreases the stability of the hydrogen bond. It has been 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 here shown match perfectly with the qualitative expectations derived from the resonance model. This, together with the previous results obtained for intermolecular hydrogen bonds, supports the statement that the resonance model provides an appropriate qualitative picture of the electron delocalization upon hydrogen-bond formation even though the formal charges drawn with this model cannot be employed to predict electron density redistributions.

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