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Resonance-Assisted Hydrogen Bonds: A Critical Examination. Structure and Stability of the Enols of *β*-Diketones and *β*-Enaminones

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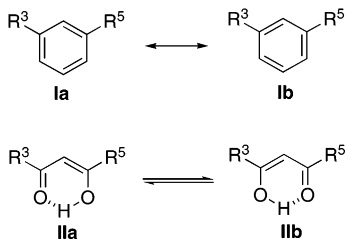
The characteristics of the intramolecular hydrogen bond (IMHB) for a series of 40 different enols of β-diketones and their nitrogen counterparts have been systematically analyzed at the B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(d,p) level of theory. In some cases, two tautomers may exist which are interconnected by a hydrogen shift through the IMHB. In tautomer **a** the HB donor group (YH) is attached to the six-membered ring, while in tautomer **b** the HB acceptor (X) is the one that is attached to the six-membered ring. We found that changing an O to a N favors the **a** tautomer when the atom is endo and the contrary when it is exo, while the presence of a double bond favors the **a** tautomers. As expected, the OH group behaves as a better HB donor than the NH_2 group and the C=NH group as a better HB acceptor than the C=O group, although the first effect clearly dominates. Accordingly, the expected IMHB strength follows the [donor, acceptor] trend: [OH, C=NH] > [OH, C=O] > [NH_2, C=NH] > [NH_2, C=O]. For all those compounds in which the functionality exhibiting the IMHB is unsaturated (**I**-type), the IMHB is much stronger than in their saturated counterparts (**II**-type). However, when the systems of the **II**-type subset, which are saturated, are constrained to have the HB donor and the HB acceptor lying in the same plane and at the same distance as in the corresponding unsaturated analogue, the IMHB is of similar or even larger strength. Hence, we conclude that, at least for this series of unsaturated compounds, the resonance-assisted hydrogen bond effect is not the primary reason behind the strength of their IMHBs, which is simply a consequence of the structure of the σ-skeleton of the system that keeps the HB donor and the HB acceptor coplanar and closer to each other.

Introduction

If one compares the resonance forms of a *meta*-substituted benzene with the two tautomers of the enol of a β-diketone, the analogy is striking.



This "visual" similitude has led some authors to propose that the intramolecular hydrogen bond (IMHB) present in structures such as **II** is stabilized by resonance (resonance-assisted hydrogen bond, RAHB) and even that these structures are aromatic.[1−10] These results are summarized in several review articles on RAHB.[11−13] One of the intrinsic difficulties in dealing with IMHBs is the impossibility of evaluating the bond energy in a precise way (although some interesting models have been proposed recently[14]), and therefore no direct energetic information on RAHB effects can be achieved. This motivated us to use other molecular properties that are sensitive to conjugation, such as magnetic properties, as a possible probe for the RAHB phenomenon. We have devoted two papers to this question. In the first one,[15] we calculated at the EOM-CCSD level the coupling constants through the hydrogen bonding of pairs of conjugated and saturated systems related to **II**. The conclusion was that neither the coupling constants nor the proton chemical shifts (GIAO/MP2) provide any evidence for the existence of RAHBs. In the second paper,[16] the work was extended to other geometries of the same compounds, confirming that the NMR properties, being a consequence of the σ-skeleton framework, do not receive significant contributions from resonance. More recent investigations from other groups[14,17,18] are in line with these conclusions, which have been also reflected in recent reviews devoted to π-electron delocalization.[19]

On the other hand, IMHBs play a fundamental role in chemistry and, for instance, are behind the enhanced basicity of many superbases,[20] such as 1,8-bis(dimethylamino)naphthalene (DMAN) (proton sponge) and related compounds, and therefore they have received much attention.[11,21−23] Maksić and co-workers have carried out an interesting design of new superbases[24−29] by replacing the NMe_2 groups in DMAN by guanidino or phosphazeno functions, which combine the possibility of forming an IMHB in the protonated species with the large intrinsic basicity of these functions due to a significant resonance stabilization of their protonated forms. However, this cationic resonance stabilization has to be clearly distinguished from a resonance stabilization of the IMHB, which, as shown before in the literature,[11] is simply not possible in some of these superbases.

This is consistent with the findings of Maksić et al.,[27] who reported that, in the protonated forms of 1,8-bis(dimethyleth-

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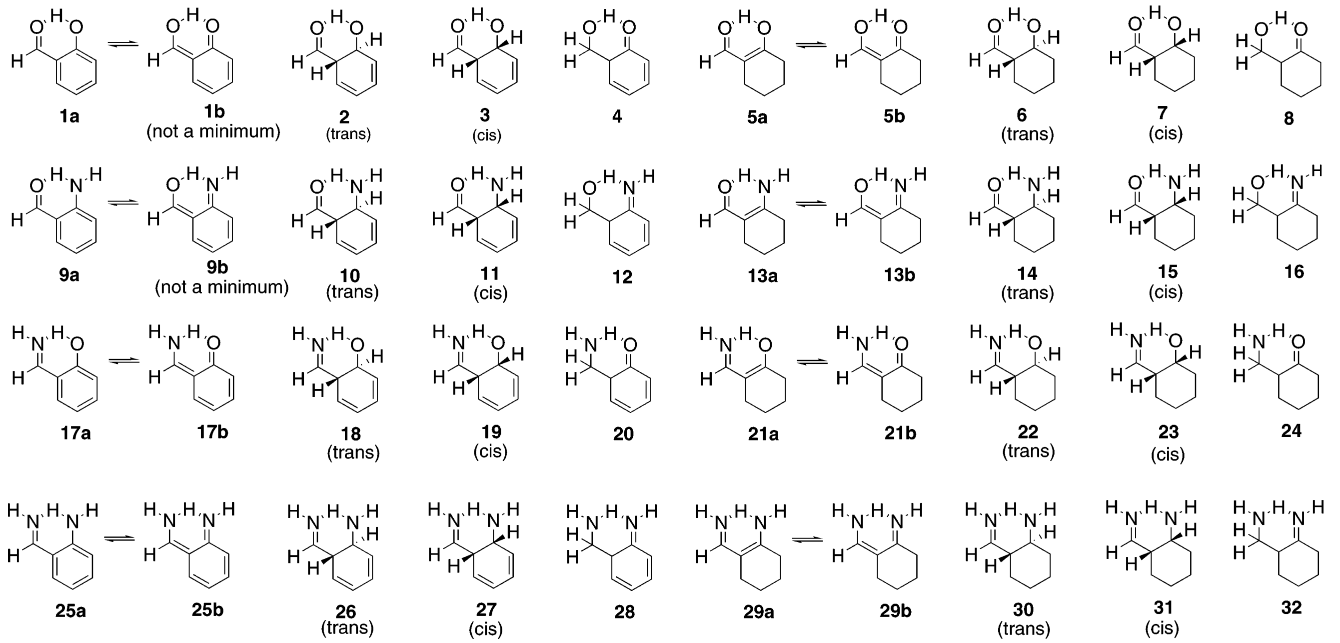
CHART 1



yleneguanidino)naphthalene and related compounds, the IMHB is not planar in both the syn and the anti conformations. On the other hand, they found, as pointed out also by Howard,[30] that steric strain also plays a significant role in the basicity of the proton sponges, although it is not possible to calculate precisely the value of the two contributions. Maksić et al. proved,[25−27] however, that the protonation of one of the guanidine groups affects the other through the IMHB. Since no RAHB is possible in these systems, this is a clear illustration of the fact that only the naphthalene moiety provides a rigid enough σ-framework favoring the aforementioned interaction.

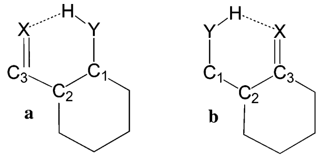
Rather interesting information on the factors affecting the strength of the IMHB in some of these protonated superbases is also provided in some of these publications,[24,26] showing, for instance, that besides the $d(\text{N}\cdots\text{N})$ and $d(\text{N}\cdots\text{H}^+)$ nonbonded contact distances, the N—H⋯N angle also plays a non-negligible role.

It then seems reasonable, in order to get some further insight into the intrinsic characteristics of this kind of IMHB, to find out how the IMHB of malonaldehyde is perturbed when the malonaldehyde moiety is fused with either saturated or conjugated six-membered rings, with different degrees of conjugation. The same question may be extended to its saturated analogue or to the corresponding nitrogen-containing systems. This will be the aim of this paper, where we present a systematic investigation of the characteristics of the IMHB in a large set of the enols of β-diketones and their nitrogen counterparts. The whole set of compounds studied is shown in Chart 1. It can be seen that, besides the derivatives that can be formed by fusing different kinds of six-membered rings to malonaldehyde or to its saturated analogue, we have also included, for the sake of completeness, similar derivatives in which one or both oxygen atoms are replaced by nitrogen.

Computational Details

Standard B3LYP density functional theory (DFT) calculations have been carried out by using the Gaussian03 series of programs.[31] The B3LYP approach includes Becke's three-parameter non-local hybrid exchange potential[32] and the non-local correlation functional of Lee, Yang, and Parr.[33] This functional has been shown to be well suited for the study of both inter- and intramolecular hydrogen bonds, provided that the basis set used in the calculations includes diffuse components.[34−39] The geometries of the systems under investigation were optimized by using a 6-311+G(d,p) basis set expansion. Harmonic vibrational frequencies were obtained at the same level of theory to classify the stationary points as local minima and to estimate the corresponding zero-point energies (ZPE), which were scaled by the empirical factor 0.9806.[40] In order to have reliable relative stabilities, the final energies were obtained at the B3LYP/6-311+G(3df,2p) level of theory.

CHART 2



It is well established that the atoms-in-molecules (AIM) theory[41] is a good tool to investigate the characteristics of inter- and intramolecular hydrogen bonds because, in general, there is a good correlation between the electron density at the corresponding hydrogen bond critical point and the strength of the interaction.[42−46] Hence, for all systems we have obtained the corresponding molecular graphs, defined by the ensemble of bond critical points (bcp's) and bond paths. These analyses will be complemented with that carried out in terms of the lengthening or shortening of the bond lengths.

Results and Discussion

As already mentioned in the Introduction, we have studied 32 systems, some of them presenting two tautomeric forms, **a** and **b**, shown in Chart 2. The total and zero-point energies of all the compounds investigated are summarized in Table S1 (Supporting Information). Geometries are available from the authors upon request. In order to simplify the presentation of our results and to make easier the comparison of one compound with another, we will designate the heteroatom of the HB acceptor group as X and that of the donor group as Y, where the X/Y atoms are O/O, O/N, N/O, and N/N.

TABLE 1: Relative Energy (ΔE, kJ mol^{-1}) of Tautomers b with Respect to the Most Stable Tautomers a

system	ΔE
5b	3.8
13b	36.9
17b	14.8
21b	18.6
25b	52.1
29b	12.2

Tautomerism. There are eight pairs of tautomers corresponding to structures **1**, **5**, **9**, **13**, **17**, **21**, **25**, and **29**. In two cases, namely **1** and **9**, the difference in stability between the two tautomers is too large, and tautomers **1b** and **9b** collapse to **1a** and **9a**, respectively. The relative stabilities of the remaining six systems are given in Table 1. These data can be analyzed using a presence/absence matrix with three parameters: the heteroatom outside the ring (X in **a** and Y in **b**) 0 if O and 1 if N, the heteroatom linked to the ring (Y in **a** and X in **b**) 0 if O and 1 if N, and the presence 1 or absence 0 of a double bond in the ring C_2-C_1 bond in **a**. A multiple regression led to the following (E_{rel} is positive when **a** is more stable than **b**):

$$E_{rel} = (5.9 \pm 2.8) - (27.1 \pm 3.4)\,\text{exo} + (36.1 \pm 2.8)\,\text{endo} + (36.6 \pm 3.4)\,\text{C=C}, \quad n = 6, \quad r^2 = 0.993$$

Changing an O to a N favors the **a** tautomer when the atom is endo (+36.1 kJ mol^{-1}) and the contrary when it is exo (−27.1 kJ mol^{-1}). The presence of a double bond favors the **a** tautomer (benzene rings in **1**, **9**, **17**, and **25**, by 36.6 kJ mol^{-1}). In the two cases where one tautomer is not a minimum, the model predicts 42.5 kJ mol^{-1} in favor of **1a** and 78.6 kJ mol^{-1} in favor of **9a**.

Strength of the IMHBs. We have summarized in Table 2 the most relevant structural parameters of all investigated IMHBs: the heteroatom internuclear distance (X···Y), the length of the IMHB itself (Y−H···X), the length of the hydrogen bond donor group (Y−H), and the lengths of the C_3=X and C_1−Y bonds. This table includes also the electron densities at the IMHB bond critical point (ρ_{bcp}) and at the ring critical point (ρ_{rcp}) associated with the cycle formed by the existence of the IMHB.

The first conspicuous fact is that there is a good logarithmic correlation between the YH···X distance and the electron density at the IMHB (see Figure 1). It is worth noting that similar logarithmic correlations had been reported in the literature for intermolecular hydrogen bonds.[43,44,47] Our results clearly indicate that the same kind of correlation is fulfilled for intramolecular hydrogen bonds. Hence, one can use either the YH···X bond length or the electron density at the IMHB critical point as a suitable index to characterize the relative strength of this weak interaction.

It is quite evident from the values in Table 2 that the IMHBs associated with unsaturated moieties (**I** in Chart 3) are much stronger than those associated with saturated moieties (**II** in Chart 3). Nevertheless, as we shall show later on, this cannot be taken as evidence of RAHB phenomena.

Within the set of compounds of the **I**-type, a comparison of the IMHBs in **1a**, **9a**, **17a**, and **25a** with the IMHBs in **5a**, **13a**, **21a**, and **29a**, respectively, indicates that this bond is systematically stronger in the latter set, where the six-membered ring fused to the malonaldehyde-type moiety is saturated. In contrast, when the same comparison is carried out for the **b**-type tautomers (**17b** → **21b**; **25b** → **29b**), one finds that the stronger IMHB appears when the six-membered ring fused to the malonaldehyde-type moiety is unsaturated. This could be interpreted as a result of RAHB stabilizing **5a**, **13a**, **21a**, and **29a** with respect to their analogues **1a**, **9a**, **17a**, and **25a**, and **17b** and **25b** with respect to **21b** and **29b**, respectively. However, the main problem with this idea is that cyclic delocalization is impossible from the electron distribution point of view, because the π system of the enone unit and the hydrogen bond are perfectly orthogonal.

TABLE 2: Characteristics of the IMHB of the Systems Investigated[a]

structure	ρ_{bcp}	ρ_{rcp}	X···Y	YH···X	Y−H	C_3=X	C_1−Y
1a	0.041	0.018	2.640	1.768	0.984	1.228	1.341
2	0.015	0.012	2.931	2.273	0.966	1.208	1.423
3	0.017	0.013	2.854	2.178	0.966	1.201	1.429
4	0.024	0.014	2.796	2.016	0.970	1.228	1.410
5a	0.056	0.021	2.549	1.646	0.999	1.241	1.328
5b	0.059	0.021	2.527	1.625	1.003	1.247	1.321
6	0.017	0.013	2.881	2.186	0.966	1.210	1.424
7	0.018	0.013	2.861	2.153	0.966	1.211	1.428
8	0.017	0.014	2.866	2.179	0.966	1.217	1.418
9a	0.027	0.014	2.726	1.964	1.012	1.225	1.359
10	0.011	0.010	3.023	2.413	1.015	1.206	1.469
11	0.011	0.010	2.952	2.424	1.015	1.206	1.475
12	0.030	0.015	2.780	1.964	0.976	1.288	1.409
13a	0.033	0.016	2.659	1.979	1.018	1.237	1.350
13b	0.067	0.020	2.527	1.612	1.018	1.299	1.322
14	0.012	0.011	3.055	2.411	1.014	1.208	1.464
15	0.013	0.011	2.976	2.331	1.015	1.209	1.470
16	0.023	0.015	2.818	2.088	0.969	1.276	1.417
17a	0.050	0.018	2.618	1.729	0.994	1.285	1.340
17b	0.044	0.017	2.589	1.756	1.036	1.259	1.327
18	0.021	0.014	2.859	2.137	0.969	1.269	1.420
19	0.024	0.014	2.811	2.068	0.970	1.271	1.425
20	0.013	0.011	3.012	2.345	1.016	1.227	1.444
21a	0.061	0.020	2.554	1.644	1.009	1.295	1.331
21b	0.029	0.015	2.692	1.942	1.016	1.239	1.349
22	0.023	0.014	2.832	2.088	0.969	1.272	1.422
23	0.024	0.014	2.819	2.066	0.970	1.272	1.426
24	0.012	0.011	3.001	2.408	1.015	1.215	1.466
25a	0.031	0.013	2.727	1.946	1.016	1.286	1.360
25b	0.048	0.016	2.602	1.758	1.042	1.215	1.329
26	0.014	0.011	3.007	2.366	1.016	1.269	1.469
27	0.014	0.011	2.962	2.366	1.016	1.269	1.473
28	0.014	0.011	3.075	2.367	1.017	1.287	1.448
29a	0.035	0.014	2.679	1.886	1.022	1.296	1.355
29b	0.032	0.014	2.703	1.937	1.021	1.297	1.352
30	0.014	0.011	2.988	2.333	1.016	1.271	1.468
31	0.015	0.011	2.973	2.298	1.016	1.271	1.470
32	0.013	0.011	3.012	2.345	1.016	1.227	1.444

[a] Interatomic distances (X···Y, X···H, Y−H, C_3=X, C_1−Y) are in Å. ρ_{bcp} and ρ_{rcp} are the electron densities at the IMHB bond critical point and at the ring critical point, respectively, in e au^{-3}.

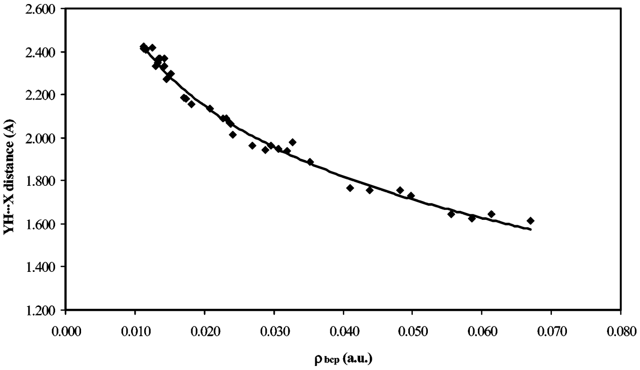
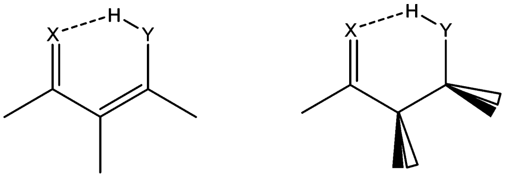


Figure 1. Logarithmic correlation ($R_{YH\cdots X} = -0.4744 \ln(\rho_{bcp}) + 0.2926$, $r^2 = 0.988$) between the IMHB length (YH···X) and the electron density at the corresponding bond critical point (ρ_{bcp}).

CHART 3



I **II**

TABLE 3: Relative Stability (ΔE, kJ mol^{-1}) of the *Cis* Conformer of II-Type Compounds with Respect to the Most Stable *Trans* Conformer

compound	ΔE
3	6.8[a]
7	3.3[b]
11	7.2[c]
15	2.6[d]
19	7.0[e]
23	2.8[f]
27	8.0[g]
31	5.6[h]

[a] Relative to **2**. [b] Relative to **6**. [c] Relative to **10**. [d] Relative to **14**. [e] Relative to **18**. [f] Relative to **22**. [g] Relative to **26**. [h] Relative to **30**.

The observed relative strength can be easily understood if one takes into account that the hydrogen atom involved in the IMHB is more acidic in **5a**, **13a**, **21a**, and **29a** than in **1a**, **9a**, **17a**, and **25a**, respectively. As a matter of fact, in the second set of compounds C_1 belongs to an aromatic system, while in the first set it participates in a C═C double bond. This implies that C_1 is intrinsically more electronegative in **5a**, **13a**, **21a**, and **29a** than in **1a**, **9a**, **17a**, and **25a**, rendering the corresponding heteroatom directly attached to it also intrinsically more electronegative. This is consistent with a larger net positive charge on the corresponding acidic hydrogens, as evaluated using both Mulliken and NBO partition techniques. The situation is completely different when the series of **b**-type tautomers is considered. In this case, as mentioned above, the comparison has to be restricted to only two couples, because the **1b** and **9b** are not stationary points of the potential energy surface. Using arguments similar to those employed above, one should expect the heteroatom acting as the hydrogen bond acceptor to be less basic, i.e., a poorer proton acceptor in **21b** and **29b** than in **17b** and **25b**, respectively. The reason is the same as that mentioned before. Now C3 is the atom that we have to look at. In **17b** and **25b** it belongs to a conjugated six-membered ring, while in **21b** and **29b** it should be intrinsically more electronegative since it is attached to a C═C double bond. Accordingly, the proton acceptors (carbonyl oxygen or imino nitrogen) in these latter two compounds should be poorer electron donors than the corresponding ones in **17b** and **25b**. It is worth noting that, in these six couples, which present the same kind of IMHB within each couple, the relative strength of the IMHB is reflected in the electron density at the ring critical point. In other words, this density is larger for **5a**, **13a**, **21a**, and **29a** than for **1a**, **9a**, **17a**, and **25a**, respectively. Similarly, it is larger for **17b** and **25b** than for **21b** and **29b**, respectively.

Let us analyze now the IMHB within the **II**-type subset of compounds. First, it should be mentioned that, according to our estimates, the *trans* conformer is systematically more stable than the corresponding *cis* (see Table 3). Although the stability differences are not very large, it can be easily seen that these compounds may be grouped in two different sets: those in which the *trans*−*cis* energy gap is typically around 7 kJ mol^{-1}, and those in which it is typically around 3 kJ mol^{-1}. The second subset corresponds to those **II**-type derivatives in which the six-membered ring is saturated and therefore more flexible that the conjugated six-membered ring present in the first subset of compounds.

Although in all these compounds, as reflected in the YH···X distances and in the electron densities at the IMHB critical point, the IMHB is rather weak, it is worth noting that it is systematically stronger in the *cis* derivatives, likely reflecting a more favorable orientation of the HB donor group with respect to the HB acceptor.

The subset of compounds **4**, **8**, **12**, **16**, **20**, **24**, **28**, and **32** has in common that the HB donor group is attached to an alkyl chain which is, in turn, bound to a saturated C atom of the six-membered ring, while the HB acceptor is directly bonded to the six-membered ring. All these systems exhibit a weak IMHB, reflecting the unfavorable orientation of the donor group with respect to the acceptor one. The fact that the CH_2−YH group is bonded to a saturated C atom of the six-membered ring forces this group to be above or below the plane of the ring (in the case of six-membered conjugated rings) and above or below the plane that contains the C═X group. Hence, in the most stable conformation, the Y···X distance is necessarily too large to lead to a strong IMHB. Within this subset, the presence or absence of conjugation within the six-membered ring does not have a systematic influence on the strength of the IMHB. As a matter of fact, while the IMHB in **4** and **12**, which contain a conjugated six-membered ring, is stronger than in the analogues with a saturated six-membered ring, namely **8** and **16**, for **20** and **28** it is the other way around, and they have an IMHB weaker than the one in their analogues **24** and **32**, which contain a saturated six-membered ring.

The Role of the Different HB Donor and Acceptor Groups. The whole set of compounds considered in our scrutiny is large enough that we may extract some useful trends as far as the role of the different HB donor and acceptor groups may have in determining the strength of the IMHB. In this set (arranged in columns in Chart 1), there are 18 different couples of compounds, namely **1a/9a**, **17a/25a**, **2/10**, **18/26**, **3/11**, **19/27**, **4/20**, **12/28**, **5a/13a**, **21a/25a**, **5b/21b**, **13b/29b**, **6/14**, **22/30**, **7/15**, **23/31**, **8/24**, and **16/32**, which differ only in the nature of the HB donor, being either an OH or an NH_2 group. Inspection of the YH···X distances or of the electron density at the corresponding bcp clearly indicates that, as expected, due to the larger $Y^{\delta-}-H^{\delta+}$ polarity, the OH···X IMHBs are systematically stronger than the NH···X IMHBs. Similarly, it is possible to identify 19 different couples, namely **1a/17a**, **9a/25a**, **17b/25b**, **2/18**, **10/26**, **3/19**, **11/27**, **4/12**, **20/28**, **5a/21a**, **13a/29a**, **5b/13b**, **21b/29b**, **6/22**, **14/30**, **7/23**, **15/31**, **8/16**, and **24/32**, which differ only in the nature of the HB acceptor, being either a carbonyl oxygen (C═O) or an imino nitrogen (C═NH). From the values in Table 2, it is obvious that the IMHBs in which the imino group is the HB acceptor are stronger than those in which the acceptor is the carbonyl group, likely reflecting the fact that the intrinsic basicity of a C═NH group is slightly larger than that of a carbonyl group.[48] The only exception to this general behavior out of a total of 19 couples is for the couple **24/32**, for which the IMHB in **24** is predicted to be slightly stronger than that in **32**. However, this is not significant because, in this particular case, the interaction is so weak that the difference in the YH···X distances (0.008 Å) between these two compounds leads to a negligibly small change in the energy (0.024 kJ mol^{-1}).

It is also worth noting that the reinforcement of the HB when a C═O acceptor group is replaced by a C═NH acceptor group

TABLE 4: Hydrogen Bond Lengths ($R_{YH\cdots X}$, in Å) and Electron Density at the Corresponding bcp (ρ_{bcp}, in e au^{-3}) for I-Type Compounds and Their II-Type Analogues When Their Structures Have Been Constrained (See Text)

I-type compounds			constrained **II**-type analogues			
system	Y—H···X	ρ_{bcp}	system	Y—H···X	ρ_{bcp}	ΔE^a
1a	1.768	0.041	**2**	1.767	0.041	91.6
5a	1.646	0.055	**6**	1.665	0.051	90.4
9a	1.964	0.027	**10**	1.866	0.033	92.9
13a	1.979	0.033	**14**	1.800	0.038	93.3
17a	1.729	0.050	**18**	1.731	0.049	89.9
21a	1.644	0.061	**22**	1.659	0.058	90.8
25a	1.946	0.031	**26**	1.853	0.038	96.6
29a	1.886	0.035	**30**	1.828	0.040	97.1

[a] ΔE is the energy difference (in kJ mol^{-1}) between the constrained structures and the corresponding equilibrium ones.

is quantitatively smaller, in terms of both lengths and electron densities at the bcp, than the reinforcement achieved when an NH_2 donor group is replaced by an OH donor group. This means that the expected IMHB strength should follow the following [donor, acceptor] trend: [OH, C=NH] > [OH, C=O] > [NH_2, C=NH] > [NH_2, C=O], as is indeed the case for the 38 species investigated with the same non-significant exception we have mentioned above.

Analysis of the Possible RAHB Effect. As indicated in preceding sections, when the functionality exhibiting the IMHB is unsaturated (**I**-type), the IMHB is much stronger than in corresponding analogues of the **II**-type, shown in Chart 3, where this functionality is saturated. Is this a consequence of the so-called RAHB phenomenon? Or, as already pointed out in previous publications,[15,16] is this primarily a consequence of the characteristics of the σ-skeleton of the system? In an attempt to answer these questions, we have chosen a series of compounds, all belonging to the **II** series and covering all possible HB donor/HB acceptor combinations, with saturated or conjugated nature of the six-membered ring. These compounds are **2[OH,C=O,*c*]**, **6[OH,C=O,*s*]**, **10[NH$_2$,C=O,*c*]**, **14[NH$_2$,C=O,*s*]**, **18[OH,C=NH,*c*]**, **22[OH,C=NH,*s*]**, **26[NH$_2$,C=NH,*c*]**, and **30[NH$_2$,C=NH,*s*]**, where the symbols within the brackets identify the HB donor, the HB acceptor, and the nature of the six-membered ring (*c* = conjugated, *s* = saturated). The geometries of these compounds were optimized by imposing the heteroatom distance (X···Y) to be equal to that of its corresponding analogue within the **I** series of compounds (**1a**, **5a, 9a**, **13a**, **17a**, **21a**, **25a**, and **29a**, respectively) and forcing the $XC_3C_2C_1YH$ fragment to lie in the same plane. The remaining structural parameters were fully optimized at the B3LYP/6-311+G(d,p) level. In this way, we ensure that the **I**-type and the corresponding **II**-type analogues have their HB donor and HB acceptor in comparable arrangements to form the IMHB. In Table 4, we have summarized the results obtained. It can be observed that now the IMHBs in both **I**- and **II**-type series of compounds are, in most cases, of identical strength. Even for some particular **II**-type systems, namely **10**, **14**, **26**, and **30**, the IMHB is stronger than in their **I**-type analogues, **9a**, **13a**, **25a**, and **29a**, respectively. What is quite obvious is that the enormous enhancement of the IMHB in these **II**-type compounds has no relation whatsoever with any RAHB phenomenon, since they are completely saturated systems. The obvious conclusion is that the strength of the IMHB in the analogues of the **I**-type series is not a consequence of resonance stabilization but is a consequence of the favorable orientation and coplanarity of the HB donor and the HB acceptor groups; in other words, it is a simple consequence of the characteristics of the σ-skeleton of the system. It is also evident that neither coplanarity nor a favorable orientation of these two groups is possible for saturated compounds, and this favorable structural arrangement can be attained only at a very high energetic cost, higher than the energy gained when a strong IMHB is formed. In other words, although in the aforementioned systems the IMHB becomes much stronger when the appropriate geometrical restrictions are imposed than in the equilibrium conformation, the energy of this constrained structure is, on average, 92 kJ mol^{-1} higher (see Table 4). As a matter of fact, as illustrated in Figure 2, taking compounds **2** and **6** as suitable examples, when the aforementioned geometry restrictions are imposed, mainly the coplanarity of HB donor and acceptor, the geometry of the six-membered ring becomes significantly distorted in order to alleviate the structural tension that this geometry restriction introduces.

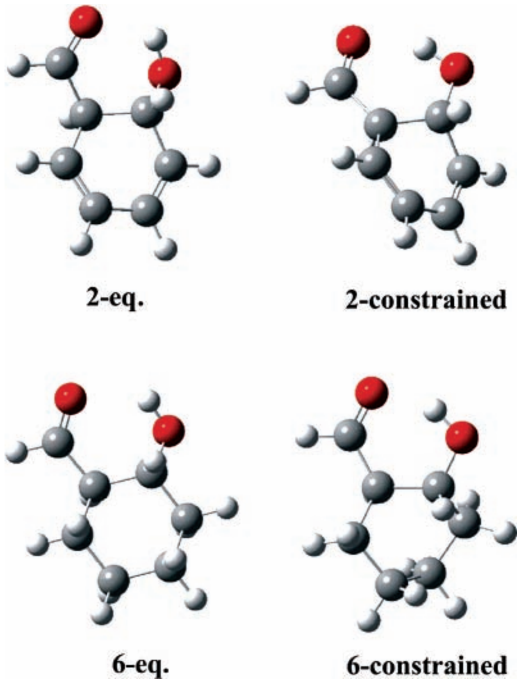


Figure 2. Comparison between the equilibrium geometries of **2** and **6** when the HB donor and acceptor are constrained to lie in the same plane and at a distance equal to that in **1a** and **5a**, respectively.

We do not deny that IMHBs are much stronger in unsaturated than in saturated compounds, as is clearly reflected not only in the bond distances but also in the ^{1}H NMR chemical shifts and other molecular properties, but we emphasize that our results for a large set of enolic forms of β-diketones and their nitrogen-containing analogues do not uphold the RAHB model. Furthermore, these conclusions are consistent with the fact that initial RAHB ideas were launched for the interpretation of crystal structures, where, as pointed out by Dannenberg et al.,[49] short H-bonding interactions could be explained simply by an increase in the electric field felt by each molecule due to the polarization of the neighbors and not to RAHB effects. They are also in line with the fact that many compounds closely related to malonaldehyde, the paradigmatic example of RAHB, show no significant evidence of electronic delocalization when the anisotropy of the induced current density (AICD)[50] is evaluated. They are also not in contradiction with a very recent analysis carried out by Beck and Mó[51] using the block-localized wave function (BLW) method in the framework of the valence bond theory, which shows that the connection between resonance and binding energies is unclear and that “most of the ‘extra’ binding energies compared with conventional hydrogen bonds without the assistance of resonance come from electrostatic attraction”.

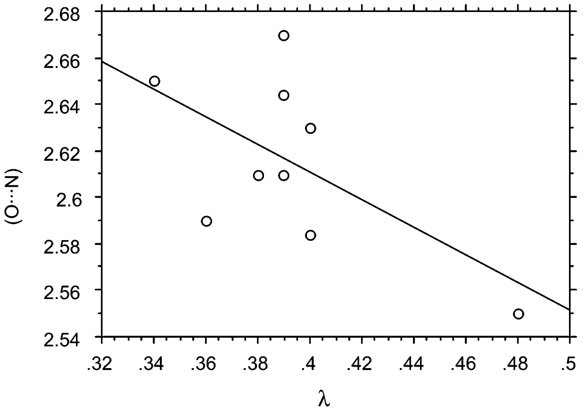


Figure 3. Correlation between the O···N distance and the delocalization parameter (λ) as defined in ref 52 for a set of β-enaminones (values taken from Table 4 of ref 52).

It is also worth noting that our finding that the enhanced strength of the IHMB is primarily a consequence of the structure of the σ-skeleton of the system and not a consequence of a RAHB effect would explain the absolute lack of correlation between the delocalization parameter (λ) defined in ref 52 and the distance between the heteroatoms participating in the IMHB in β-enaminones (see Figure 3).[52] Finally, in line with our conclusions, Sorensen et al.,[53] in a very recent study on the IMHBs in 2-acetyl-1,8-dihydroxy-3,6-dimethylnaphthalene, concluded that the RAHB mechanism may not play so strong a role in the corresponding keto–enol fragments and that short, strong HBs can exist without being stabilized by resonance.

Conclusions

The characteristics of the IMHB have been systematically analyzed for a series of 40 different enols of β-diketones and their nitrogen counterparts. As is the case for intermolecular hydrogen bonds,[43,44,47] also for the intramolecular hydrogen bonds investigated, a logarithmic correlation exists between the IMHB length and the electron density at the corresponding bond critical point.

In some cases, two tautomers may exist which are interconnected by a hydrogen shift through the IMHB. In tautomer **a** the HB donor group (YH) is attached to the six-membered ring, while in tautomer **b** the HB acceptor (X) is the one that is attached to the six-membered ring. We found that changing an O to a N favors the **a** tautomer when the atom is endo and the contrary when it is exo, while the presence of a double bond favors the **a** tautomers.

All those compounds in which the functionality exhibiting the IMHB is unsaturated (**I**-type) exhibit a much stronger IMHB than their saturated counterparts (**II**-type). Among the former, the IMHB is stronger for tautomers **a** than for tautomers **b** if the six-membered ring fused to the functionality that presents the IMHB is conjugated. Conversely, the IMHB is stronger for tautomers **b** if the six-membered ring is saturated.

Within the **II**-type subset of compounds, the *trans* conformers are systematically slightly more stable than the *cis* ones, although in the latter the IMHB is slightly stronger. The *cis*/*trans* energy gap depends on the nature, conjugated or saturated, of the six-membered ring attached to the functionality that exhibits the IMHB.

As expected, the OH group behaves as a better HB donor than the NH_2, and the C=NH group as a better HB acceptor than the C=O group, although the first effect clearly dominates. Accordingly, the expected IMHB strength follows the [donor, acceptor] trend: [OH, C=NH] > [OH, C=O] > [NH_2, C=NH] > [NH_2, C=O].

For all those compounds in which the functionality exhibiting the IMHB is unsaturated (**I**-type), the IMHB is much stronger than in their saturated counterparts (**II**-type). However, when the systems of the **II**-type subset, which are saturated, are constrained to have the HB donor and the HB acceptor lying in the same plane and at the same distance as in the corresponding unsaturated analogue, the IMHB is of similar or even larger strength. Hence, we conclude that, at least for this series of unsaturated compounds, the resonance-assisted hydrogen bond (RAHB) effect is not the primary reason behind the strength of their IMHBs, which is simply a consequence of the structure of the σ-skeleton of the system that keeps the HB donor and the HB acceptor coplanar and closer to each other.

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Supporting Information Available: Zero-point energies and total energies. This material is available free of charge via the Internet at http://pubs.acs.org.

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