Covalence and π electron delocalization influence on hydrogen bonds in proton transfer process of *o*-hydroxy aryl Schiff bases: a combined NMR and QTAIM analysis

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ABSTRACT

Within the framework of the DFT approach we studied the relationship between the chemical nature of intramolecular hydrogen bonds (HB) and NMR parameters, *J*-couplings and ^{1}H-chemical shifts (δ(^{1}H)), of atoms involved in such bonds in o-hydroxyaryl Schiff bases during the proton transfer process. For first time the shape of the dependence of the degree of covalence in HB on ^1J(N–H), ^1J(O–H), ^{2h}J(O–N), and δ(^{1}H) during the proton transfer process in *o*-hydroxyaryl Schiff bases was analyzed. Parameters obtained from Bader's theory of atoms in molecules were used to assess the dependence of covalent character in hydrogen bonds with both NMR properties. Influence of π-electronic delocalization on ^{2h}J(N–O) under the proton transfer process was investigated. ^{2h}J(O–N) in a Mannich base was also studied in order to compare results with an unsaturated system. In addition substituent effects on the phenolic ring were investigated.

Our results indicate that covalent character of HB on both sides of the transition state undergoes a smooth exponential increase as the δ(^{1}H) moves to down field. The degree of covalence of the N⋯H (O⋯H) bond increases linearly as ^1J(N–H) (^1J(O–H)) becomes more negative, even after reaching the transition state. Non-vanishing values of spin dipolar (SD) and paramagnetic spin orbital terms of ^{2h}J(O–N) show that π-electronic delocalization has a non-negligible effect on tautomeric equilibrium and give evidence of presence of the resonance assisted hydrogen bond (RAHB). Variation of SD term of ^{2h}J(O–N) follows a similar pattern as the change of the PDI aromaticity index of chelate ring.

Keywords: Hydrogen Bonds – NMR Spectroscopy – QTAIM Analysis – Resonance Assisted Hydrogen Bond – Schiff Bases.

I. INTRODUCTION

Hydrogen bonds X–H⋯Y, where X and Y are electronegative atoms are interactions that play central roles in a wide range of chemical and biological processes. Thus, they are crucial for processes such as the stabilization of biological structures, enzyme catalysis in biological environments, and also in advanced drug and materials design.[1–10] In particular, the investigation of strong and very strong intramolecular hydrogen bonds (HBs) belonging to systems where proton transfer take place are of great importance in biochemistry processes, such as enzymatic reactions where hydrogen bonding with a low barrier proton transfer have been proposed as transition states.[11–13]

Although the essential features of HBs have been extensively investigated by both theoretical and experimental analyses, there is still controversy about the nature of this type of interaction.[14–16] Several authors claim the interaction is predominantly electrostatic[2,17,18] while other characterize it as partially covalent.[19–24] According to the so-called Electrostatic–Covalent HB Model of Gilli et al., weak HBs are electrostatic interactions but become increasingly covalent if their strength increases.[25,26] Based on stabilization energy, HBs are usually classified as weak (1-4 kcal/mol), moderately strong (4–15 kcal/mol), and strong (15-40 kcal/mol).[27,28]. Another well know characteristic of a strong HB is a displacement of the ^{1}H NMR chemical shift of 16–20 ppm as well as a decrease of the IR ν(O–H) stretching frequencies up to 2560 cm^{-1}.[29–31]

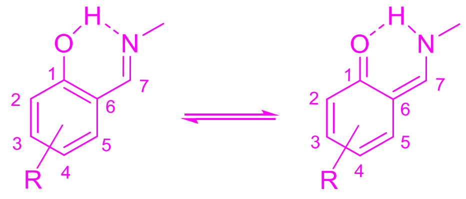


Figure 1: Tautomeric equilibrium of Schiff bases. The atomic numbering scheme for C atoms is shown in this Figure.

NMR spectroscopic parameters, *J*-couplings and magnetic shieldings, σ (or the chemical shift δ), of atoms involved in the HB, have been widely applied to provide a deeper comprehension of biological HBs, especially to understand the low barrier HBs (LBHB).[12,29,32–42] For HBs X–H⋯Y, where X and Y are O or N, it is generally believed that a decrease in ^{1}H-shielding constants relates to a shortening of HB donor–acceptor distance and an increase in the strength of such bond.[4,43,44] Indirect *J*-coupling constants through HBs have been observed in nucleic acids, proteins and carbohydrates, and its existence has been considered as proof of HB formation.[35] Some authors have suggested that *J*-couplings through HBs give evidence of the covalent character of such interaction.[45–49] In particular some studies have found that ^1J (X⋯H) presents changes in its magnitude and sign when changing the degree of covalence of the HB.[48,49] These studies have been carried out for a reduced set of small molecular systems, which do not cover the wide spectrum of existing HBs. So there are still aspects on the relationship between ^1J(X⋯H) and the covalent character of the hydrogen bonds that need to be elucidated.

A very interesting class of compounds containing strong intramolecular hydrogen bonding is Schiff bases derived from aromatic *o*-hydroxy aldehydes or ketones. These compounds have been extensively investigated due to their physical-chemical properties, such as thermochromism and photochromism, role played in catalytic biochemical processes, coordination chemistry, organic synthesis, technological applications, and design of anticancer drugs.[50–64] Some *o*-Hydroxy aryl schiff bases present a keto-enol tautomeric equilibrium [see Figure 1] which is a consequence of a proton transfer process in the intramolecular HB that gives rise to two tautomeric forms, enol–imine (or OH-) and keto–amine (or NH-).[65–68] Spectroscopic data obtained by applying different techniques such as heteronuclear NMR in both phases, FT-IR spectroscopy, X-ray and neutron diffraction, have shown that OH form predominates in solution, with a few exceptions, while in the solid state the tautomeric equilibrium is strongly shifted towards to the NH form.[68–81] Main factors determining the physicochemical properties and biological activity of these compounds are the intramolecular HB and proton transfer equilibrium.[50,51,53,54,82] Therefore, study of the proton transfer process is crucial to gain a better understanding of several physical-chemical and biological processes in which Schiff bases take part and due its potential application in technology and drug design. It has been found that the position of the proton transfer equilibrium can be modified by electronic and steric effects.[69,71,82–85].

It is known that the hydrogen atom position in an intramolecular hydrogen bridge can be inferred by analysis of δ(N) of the imine nitrogen and ^1J(N–H), if available, (quantitative assessment) or δ(C) of the carbon atom linked to the formal hydroxyl group (qualitative assessment). Nevertheless, trustworthy experimental results cannot be obtained for tautomeric protons close to the transition state (TS), because in these stages of proton transfer equilibrium, OH- and NH- tautomers may not be adequately discernible from one another owing to positional disorder. In order to cover this gap, theoretical studies must be used to obtain detailed information on the complete proton transfer path. [86] Although the chemical shift of the tautomeric proton cannot be used to decide where the proton is situated on the bridge, it can provide one with important information about the HB strength and nature.

In the present work we study for the first time the shape of the dependence of the degree of covalence in the HB on ^{1}J(N–H),^{1}J(O–H), ^{2h}J(O–N), and $\delta(^{1}H)$ during the full proton transfer process for the hydrogen bridge in *o*-hydroxy aryl Schiff bases. Furthermore, the signs of reduced coupling constants ^{1}K(N–H), ^{1}K(O–H) and ^{1}K (O–N) were monitored.

The existence of a TS along the reaction path when go from the OH- tautomer to the NH- one brings out a clear change in the nature of the intramolecular HB. One of the aims of this work is to describe the way in which *J*-couplings and $\delta(^{1}H)$ reflect these changes, that is, the shape of the functional relationship between NMR parameters and the covalent character in the HB on either side of the TS.

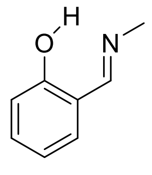
In order to find the relationship between NMR parameters and covalent character in HBs, the dependences between these spectroscopic quantities and different topological parameters provided by Bader's theory of atoms in molecules are investigated.[87–89] Substituent effects in the aromatic ring on all these properties are also analyzed.

On the other hand, six-membered rings formed by a HB and a chain of π-conjugated double bonds which links the donor and acceptor atoms, such as those containing in Schiff bases, are called quasi-aromatic chelate rings and are characterized by forming strong HBs. This type of HBs is known as resonance assisted HB (RAHB), a concept introduced by Gilli in the late 1980s.[30] According to Gilli's model the strength of the HB is influenced by the π electronic delocalization of the hetero conjugated system (H-O-C=C-C=N), which induces partial charges of opposite signs on the donor and acceptor atoms, leading to strengthening the HB.[31,90–92] In turn, changes in the strength of the HB, such as those that occur during a proton transfer process, cause a reconfiguration of the π-system. The interrelation between the strengthening of the HB and π-system delocalization is a central feature for RAHB.[93]

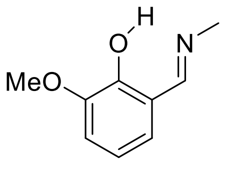
Regardless of the success of the RAHB model to elucidate different phenomena related to structural chemistry[82,94–103], some authors have raised some doubts about this original concept. They argue that the stability of these HBs is mainly originated by the features of the σ-skeleton rather than by π-electronic delocalization.[104–110] In the opposite direction, a large number of early and recent papers have found a relationship between the π-electron framework and the structural parameters engaged in RAHB that gives support to Gilli's model.[111–121]

In previous works, *J*-coupling constants have been used to elucidate the relationship between the π-conjugated system and HBs.[122–124] This was possible because the paramagnetic spin orbital (PSO) and the spin dipolar (SD) contributions to the isotropic *J*-couplings are related to the π-electronic structure of the molecules and its non-vanishing values witness the existence of conjugation through the coupling pathway.[125–129] In turn, the Fermi contact contribution is dominant in saturated molecules, since its transmission occurs mainly through the σ-framework.[130] However, when there is a π-conjugated system through the coupling pathway, the FC originates from an exchange σ-π mechanism, which implies that its transmission is also possible across the π-skeleton.[130] Thus, ^{2h}J(X-Y) might give evidence about the existence of RAHB. Previous research, where the relationship between aromaticity indices of the chelate ring and HB strength under the proton transfer process in intramolecular HB in Schiff bases have been studied, gives support to the idea that π-electron delocalization causes the tautomeric equilibrium and is one of the main factors stabilizing the NH form.[118,121] Another aim of this work is to investigate whether the SD and PSO contributions to ^{2h}J(O–N) are able to reflect the influence of the π-conjugated system on the tautomeric equilibrium during proton transfer in the intramolecular HB in *o*-hydroxy aryl Schiff bases. The effects of proton transfer process on the FC contributions are also analized. With the purpose of comparison with saturated systems, ^{2h}J(N–O) in a Mannich base which have a similar structure to Schiff Bases but present a HB without π-coupling was also investigated.

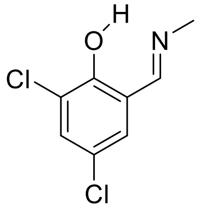
In summary the overall goal of this work is to expand the knowledge on the electronic structure and nature of intramolecular hydrogen bonds in Schiff bases and their relationship with NMR spectroscopic parameters, *J*-couplings and chemical shift, through the tautomeric equilibrium under the proton transfer process.



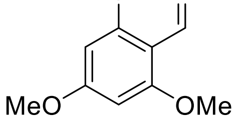
(*E*)-2-((methylimino) methyl)phenol (**I**)



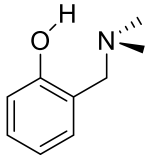
(*E*)-2-methoxy-6-((methylimino) methyl)phenol (**II**)



(*E*)-2,4-dichloro-6-((methylimino) methyl)phenol (**III**)



(*E*)-3,5-dimethoxy-2-((methylimino) methyl)phenol (**IV**)



2-((dimethylamino)methyl) phenol (**V**)

Figure 2: Schematic structure of molecular systems analyzed in this study

II. COMPUTATIONAL DETAILS

Geometry Optimization

In order to obtain the proton transfer reaction path for selected Schiff bases a one dimensional relaxed potential energy surface (PES) scan was carried out starting on the optimized geometry of the OH tautomeric form by varying the N–H distance from 1.81 to 0.95 Å with steps of 0.02 Å. At each point of the scan process the N-H distance was fixed with full optimization of the remainder structural parameters.

With the aim of comparison, in the case of the selected Mannich base (Figure 2.V), the proton transfer process was simulated in a similar way starting from its optimized geometry with the proton bonded to the oxygen atom, but with atoms belonging to the hydrogen bond and the methylene carbon that joins the nitrogen atom to the aromatic ring restricted to be in the same plane as the phenyl group. This comparison procedure is similar to that followed by Filarowski in a previous work.[121]

Geometry optimizations were performed within the framework of the DFT theory[131] using the B3LYP functional[132] with dispersion corrections as developed by Grimme[133134], B3LYP-D3(BJ) combined with the 6-311++G(d,p)[135] basis sets with the Gaussian 16 program package.[136]

NMR parameters

The theory underlying the NMR parameters and of several computational methods to evaluating them has been outlined widely in the literature.[130,137–139] However, it should be emphasized that both parameters, *J*-coupligns and nuclear magnetic shieldings, strongly depend on the electronic environment of the nuclei in molecular systems.

According to nonrelativistic Ramsey's theory the scalar nuclear magnetic shielding is given as the sum of a diamagnetic and a paramagnetic contribution which do not depend on the spin of electrons.[140,141] The diamagnetic term arises from spherical charge distributions, whereas the paramagnetic term originates in non-spherical charges distributions from p or higher angular momentum electrons. NMR experiments do not routinely measure nuclear magnetic shieldings, instead what is obtained is the chemical shift as the change of resonance frequency of a given nucleus respect to a reference compound.

In this work ^{1}H nuclear magnetic shielding values, $\sigma(^1\mathrm{H})$, were converted to chemical shifts using the relationship: $\delta(^1\mathrm{H}) = \sigma(^1\mathrm{H})^{\mathrm{TMS}} - \sigma(^1\mathrm{H})$, where $\sigma(^1\mathrm{H})^{\mathrm{TMS}}$ is the nuclear magnetic shielding of the hydrogen atom in TMS calculated at the same theoretical level as σ (^{1}H).

Ramsey's expression of scalar *J*-coupling[142] between nuclei M and N is given as the sum of four components: the Fermi contact (FC) and the spin-dipolar (SD), which originate from the interaction of the nuclear magnetic moments with the spin of the electrons; the diamagnetic spin orbital (DSO) and the paramagnetic spin orbital (PSO), which arise form interaction of the nuclear spins with the orbital angular momentum of the electrons.

It is a known fact that FC term is by far the major contribution in saturated molecules, since its transmission occurs mainly through the σ-framework.[130] The SD and PSO coupling mechanisms are associated to the π-electronic structure of the molecular systems. Therefore, when there are double or triple bonds through the coupling pathway those terms acquire important values that can be even larger than those of the FC term.[122,123,125–129]

With the aim to compare coupling constants between hydrogen bonds with different donors and acceptors, they have been transformed to reduced coupling constants K which are independent of the sign and magnitude of the gyromagnetic ratios:

$$K(M-N)=\frac{4\pi^2}{h\gamma_M\gamma_N}J(M-N) \qquad (1)$$

where γ_M and γ_N are the gyromagnetic ratios of nucleus M and N and h is Planck's constant. NMR spectroscopic parameters were calculated within the framework of the DFT theory at the B3LYP/cc-pVTZ[143144] level of approach using the Gaussian 16 program package. Nuclear magnetic shielding constants were obtained using the GIAO approximation to guarantee gauge-invariant values.[145–147]

Obtained results of *J*-coupling and ^{1}H nuclear magnetic shielding constants for atoms involved in hydrogen bonds similar to those studied in this work, using our selected theoretical approach, have shown to be in good agreement with experimental results and the best *ab initio* methods.[86,122,148,149]

QTAIM calculations

Bader's quantum theory of atoms in molecules (QTAIM) approach[87,88] has been widely applied to the study of the strength and covalent character of HB.[111,150–157] According to this topological theory, when two neighboring atoms are chemically linked or if there is a weak interaction between them, a bond critical point (BCP) arise. Previous works have been shown that electron density ρ and Laplacian of electron density $\nabla^2\rho$ at the HB critical points H⋯Y as well as total electronic energy density H_C and its components (kinetic energy G_C and potential energy V_C) at BCPs are good descriptors of the strength and covalence of HBs.[154,155] At BCP this quantities are connected through the next local virial theorem in atomic units

$$\frac{1}{4}\nabla^2\rho_{BCP} = 2G_{c_{BCP}} + V_{c_{BCP}} \quad , \qquad\qquad H_C = G_C + V_c \qquad (2)$$

In this work, BCPs were analyzed using Bader's theory to obtain further details about the nature of HB in the investigated systems. The optimized geometries of Schiff bases in different steps of the proton transfer process were employed to obtain wavefunctions and charge densities at B3LYP/6-311++G(d,p) level as implemented in the Gaussian program. The resulting data were used to perform topological analysis of charge density in the context of QTAIM approach with the help of Multiwfn software.[158]

For quantitative estimation of π-electronic delocalization in the chelate ring para-delocalization index (PDI)[159] based on the calculation of delocalization indices (DI) were computed in the framework of QTAIM approach. This aromaticity index has turn into one of the most suitable ways to describe the degree of electron delocalization in aromatic system. PDI is obtained as an average of all DI[160,161] of para-related atoms in the ring.

The DI between atoms A and B, δ(A,B), is obtained by the double integration of the exchange-correlation density ($\Gamma_{XC}(\vec{r}_1,\vec{r}_2)$) over the space occupied by atoms M and N:

$$\delta(M,N) = -2\int_M \int_N \Gamma_{XC}(\vec{r}_1,\vec{r}_2)\, d\vec{r}_1 d\vec{r}_2 \qquad (3)$$

When only single-determinant closed-shell wave functions are implied, equation (3) can be rewritten as:

$$\delta(M,N) = 4\sum_{ij}^{N/2} S_{ij}(M)S_{ij}(N) \qquad (4)$$

The sums in equation (4) run over all the N/2 occupied molecular orbitals and $S_{ij}(M)$ is the overlap between molecular orbitals i and j within the basin of atom M.

The PDI index for the investigated system were obtained with the Multiwfn program from wave functions calculated at B3LYP/ 6-311++ G(d,p) level as mentioned above**.**

III. RESULTS AND DISCUSSION

A. POTENTIAL CURVES AND OPTIMIZED GEOMETRIES

Structural features of compounds analyzed in this work are shown in Figure 2, whereas, the potential energy curves that allow a more wisely comprehension of HBs properties along the proton transfer pathway in the intramolecular HB for the selected Schiff bases (compounds **I-IV** in Figure 2) are shown in Figure 3. Such curves describe the relative energies of the molecular structures at different steps of the proton transfer process as a function of the NH distance and were obtained as outlined in Computational Details section.

In all cases, potential energy curves present two minima, a global minimum, where OH tautomer is observed, and a local minimum where NH tautomer is located. The proton transfer barrier for compounds **I-IV** range from 6.15 to 3.97 Kcal/mol and decrease following the order **I**> **II**> **III**> **IV**, whereas the energy gap between two potential minima for the same compounds vary from 4.51 to 0.97 Kcal/mol and decrease in the same order as the transfer energy barriers. Our theoretical results are in good agreement with those reported for various o-hydroxy aryl Schiff bases in previous works, where it was found that energy differences between the OH and NH tautomers and potential barrier heights are less than 5 and 6.5 kcal, respectively.[83,118,121,162]

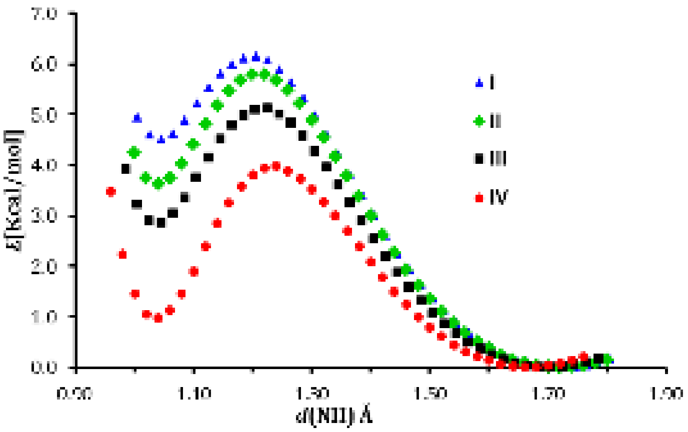


Figure 3: Potential energy curves for proton transfer reaction in studied Schiff bases (Figure 2.I-IV). In all cases the global minimum with respect to which the relative energy is calculated corresponds to OH tautomer.

Shapes of the potential energy curves reflect the effect of the substituents in the aromatic ring on proton-transfer barrier. Thus, the OCH3 moiety in position 2, (compound **II**), reduces the height of the potential barrier very slightly and does not affect significantly the proton transfer process. Two chlorine atoms in positions 2 and 4 decrease the height of the potential barrier to a somewhat larger extent and cause a moderate shift of the equilibrium towards the NH form. This fact results from the decreasing charge density on the oxygen atom due to electron-withdrawing properties of Cl substituents, which makes the proton more acidic. The decrease in the potential barrier is even more pronounced when electron-donating OCH3 substituents are introduced at positions 3 and 5 (compound **IV**). The OCH3 groups in these positions increase the charge density on the nitrogen atom rising up its basicity and therefore favoring a more effective proton transfer from oxygen to nitrogen.

The effects of the substituents in the ring on the tautomeric equilibrium found from our theoretical results are in good agreement with those found from experimental values of NMR parameters obtained by Rozwadowski et al.[69] and by Schilf et al.[71,73] Experimental measurements of NMR parameters obtained in chloroform solution at different temperatures gave evidence that compounds **I** and **II** do not present proton transfer tautomeric equilibrium and only exist as OH forms, whereas for compounds **III** and **IV** these measurements allowed to demonstrate that such proton transfer equilibrium is present. From our theoretical results, proton transfer barriers for compound **III** and **IV** are 5.11 and 3.96 Kcal/mol, respectively, whereas the energy gap between two potential minima for the same compounds are 2.86 and 0.97 kcal/mol, respectively. From aforesaid, intra molecular hydrogen bonds in compounds **III** and **IV** might be regarded as LBHBs. This is in agreement with conclusions found in references [83,118,162–164] where some Schiff bases containing HBs regarded as LBHBs were investigated. It should be taken into account that the height of the proton transfer potential barriers calculated in the gas phase for this type of compounds is somewhat higher than that observed in environments with a permittivity larger than one, as explained in ref [162].

Geometries obtained for the two tautomeric forms fits well with experimental measurements. Bond distances C1–O and C7–N are geometric parameters that best characterize the structural form of compounds. Our results show when proton is transferred from the OH tautomer to the NH, the C1–O distance for compound **I** changes from 1.341 to 1.265 Å, respectively, while the C7–N distance changes from 1.280 Å to 1.318 Å, respectively. These values are in line with tendencies found by experimental measurements. For example, from X-ray studies it was found that C1–O and C7–N distances for the OH tautomer are 1.346 and 1.270 Å[165], respectively, while for the NH tautomer they are 1.286 and 1.309 Å[166] , respectively. Changes in C1–O and C7–N bond distances for compounds **II**, **III** and **IV** when comparing OH- and NH-forms follow a similar pattern (see Table SII in the Supporting Information)

It should be noted that trends observed in bond distance variations throughout the proton transfer process show that modifications in HB features bring out a reconfiguration of π-conjugated double bonds system.

B. RELATIONSHIPS BETWEEN NMR PARAMETERS AND COVALENCE OF HYDROGEN BONDS

1. ^{1}H Chemical Shifts

Our theoretical value for $\sigma(^1\text{H})$ in TMS is 31.67 ppm. This result is in very good agreement with the gas phase experimental value of 30.84 ppm reported in reference [167].

Theoretical values of $\delta(^1\text{H})$ and corresponding N–H distance, d(NH), during the proton transfer process for hydrogen-bonded protons in the selected Schiff bases are shown in Figure 4 and Tables SI and SIV in the Supporting Information. Calculated results show that shapes of functional dependencies of $\delta(^1\text{H})$ on d(NH) are not affected by the substituent on the ring. It means that these substituents influence in a similar way the electron density closest to the hydrogen nucleus. In all cases $\delta(^1\text{H})$ reaches its maximum value around 23.7 ppm for a N–H distance close to 1.24 Å, region where the TS appear. In that location, the N–O length has its minimum value of 2.4 Å. Since the acceptor distance from the donor could be associated with the strength of the HB, it indicates that TS has the strongest HB. The strengthening of HBs when the formation of the TS occurs has been proposed as a feature of LBHBs.[11,32,40,83,85,118,162–164] Furthermore, N–O distances of the two stable tautomeric forms are very close (see Figure S1 and Table SI in the Supporting Information), which means that their HB strengths should not differ significantly.

Calculated values of $\delta(^1\text{H})$ for OH forms of compounds **I**, **II** and **III** are 13.32, 13.37 and 13.82 ppm, respectively, whereas experimental results in chloroform solution for the same compounds are 13.50, 13.85 and 14.48 ppm.[69] In the case of compound **IV**, our calculated $\delta(^1\text{H})$ value for the NH form is 14.08 ppm, while the experimental value in dichloromethane solution is 14.58 ppm.[69] Therefore, theoretical results (which correspond to the gas phase) are very close to the experimental ones and, though there might be quantitative improvements upon inclusion of solvent effects, the trends of $\delta(^1\text{H})$ as a function of the molecular structure are very well reproduced.

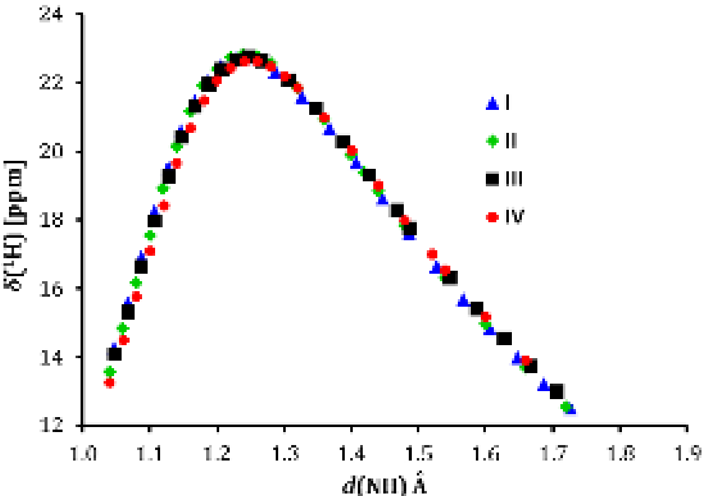


Figure 4: Variations of ^1H NMR chemical shifts with the N-H distance during proton transfer process for hydrogen-bonded protons in the studied Schiff bases (Figure 2.I-IV).

To find out the relationship between NMR parameters and HB properties, such parameters were related to topological and energetic descriptors provided by Bader's AIM theory.

It is known that the electron density, ρ_{BCP}, its Laplacian $\nabla^2\rho_{BCP}$ and total electron energy density, H_C, at BCP are very useful tools to describe the covalent character and the relative strength of hydrogen bonds. A relatively large value of ρ_{BCP} and a large negative Laplacian reveals electronic charge concentration along the relevant bond path and are observed for the shared interactions (covalent bonds). Whereas, small and positive small values of ρ_{BCP} and its Laplacian $\nabla^2\rho_{BCP}$ reflect electronic charge depletion along the relevant bond path, and are conditions for appearance of bonds with partial covalent character. A negative total energy density at the BCP value emerges as a consequence of accumulated stabilizing electronic charge and indicates that potential energy density is predominant. Bonds with a covalent or partially covalent character have a value of H_C at BCP which is less than zero. Regarding the strength of hydrogen bonds, it is generally accepted that both H_C and $\nabla^2\rho_{BCP}$ are positive for weak or medium HB, both are negative for very strong HB, whereas for strong HBs, $H_C<0$ and Laplacian $\nabla^2\rho_{BCP}>0$.[155]

Variations of ρ, $\nabla^2\rho$ and H_C at BCPs of N–H and O–H bond along the proton transfer path are shown in Figure 5, Figure S2 and Table SIII in the Supporting Information. Values obtained from topological parameters and total energy densities exhibit an exponential dependence on the related bond lengths similar to that found in previous studies where the proton transfer process for different Schiff bases was investigated.[85,118] This exponential behavior has been attributed to the existence of HBs.[85,150,168,169] In fact, a more detailed analysis from Figure S3 in the Supporting Information corresponding to compound **III**, allows to distinguish two well differentiated behaviors of H_C(N–H) at BCPs of N–H interaction as a function of d(NH). In the first part of the reaction path, when the proton is transferred from the OH form to the TS, an exponential dependence is observed. During the next stage of the proton transfer process, from the TS to the stable NH form, such dependence has linear characteristic. This clearly shows that the exponential character of curves in Figure 5.c is determined by the presence of HB interactions. Furthermore, this differentiated behavior on either side of the TS reflects the change in the nature of the N atom within the HB, in the first part is an acceptor and in the second one becomes a donor.

It should be noted that shapes of the functional dependencies of ρ, $\nabla^2\rho$ and H_C at the critical point on the bond distances are independent of electronic effects of substituents in the ring.

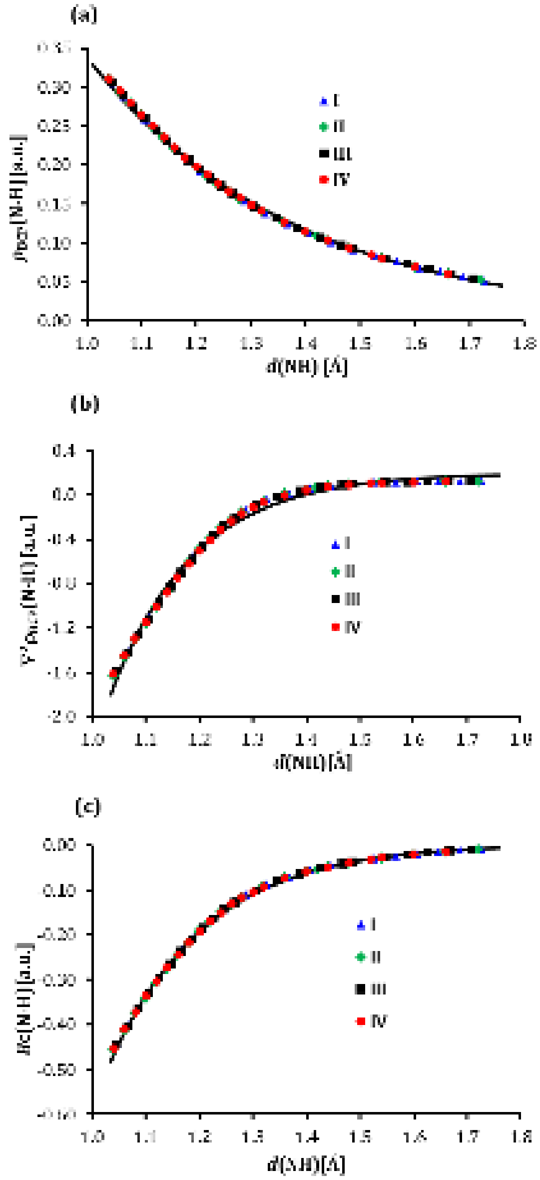


Figure 5: (a) Variations of electron densities, (b) Laplacians of electron density and (c) total electron energies at BCP of N-H bond against amine bond elongation for selected Schiff bases (Figure 2.I-IV). Correlations are expressed as: (a) ρ_{BCP}(N-H) =4.8469 exp[-2.662d(NH)], R^2=0.9986; (b) $\nabla^2\rho_{BCP}$(N-H) = 0.1968 - 1.5038 × 10^3 exp[-6.399d(NH)], R^2=0.9982 (c) H_C(N-H) =0.0027 - 140.2421 exp[-5.476d(NH)], R^2=0.9995.

Hydrogen bonds X–H···Y for which $\nabla^2\rho$ at bond critical point of H···Y bond path is less than zero, are considered shared-electron or covalent HBs. In such situations the hydrogen has shared-electron interactions with both donor and acceptor atoms, (since $\nabla^2\rho_{BCP}$(N–H) < 0 and

$\nabla^2\rho_{BCP}$(O–H) <0) . Donor atom is considered to be the one for which $\nabla^2\rho$ is most negative when its values are compared at the BCP of the X–H and Y–H bonds.

Total electronic energy density values show that HBs of all the studied compounds have some degree of covalent character (Figure 5.c and Table SIII). More precisely, for N–H distances between 1.73 and 137 Å HBs have a partial covalent character. Next, when N–H changes from 1.36 to 1.22 Å , hydrogen bonding turn into a shared electron interaction. After that, for N–H distances between 1.20 and .104 Å, nitrogen atom has already become the hydrogen donor, and the N–H bond is purely covalent, (Tables SI and SIII at Supporting Information).

In the following section, unless stated otherwise, only results obtained for compound **III** will be discussed, since conclusions obtained are similar to those of the rest of Schiff bases here studied (see the Supporting Information). We now centered on examination of the relationship between covalence of hydrogen bonds and ^{1}H NMR chemical shift. The dependence of the total electron energy density at BCP of N ⋯ H and O ⋯ H bond before and after reaching the transition state upon the $\delta(^1H)$ is shown in Figure 6. It can be seen that degree of covalence obtained for N ⋯ H bond increases exponentially as ^{1}H NMR signal is shifted to downfield within the range from OH form to the zone where the TS appears (from left to right in Figure 6.a). For $\delta(^1H)$ values between 13.82 and 21.14 ppm the HB has a partial covalent character (H_C(N–H)<0 and $\nabla^2\rho_{BCP}$(N–H)> 0). Thereafter, when $\delta(^1H)$ changes from 22.10 to 23.24 ppm, hydrogen bonding is a shared electron interaction and the hydrogen atom is covalently bonded to both N and O. After $\delta(^1H)$ reaches its maximum value, the N atom becomes donor and O acceptor. From there, the degree of covalence of the O ⋯ H bond decreases exponentially as ^{1}H NMR signal is shifted to upfield until the stable NH form arises (from right to left in Figure 6.b). Shapes of curves showing an exponential behavior are not exactly the same, due to asymmetry of the HB.

The $\delta(^1H)$ values range characterizing partially covalent bonds and shared electron interactions reported here are in good agreement with those obtained in a previous work by Arnold[32], where model compounds containing short, strong HBs involved in enzyme catalysis, and also low-barrier HBs were studied. According to that study (and references therein), partially covalent hydrogen bond have $\delta(^1H)$ values in the 15-20 ppm range, while shared-electron LBHB hydrogen bond present $\delta(^1H)$ between 20 and 21 ppm. Therefore, in the case of *o*-hydroxyaryl Schiff bases, large values of ^{1}H chemical shift, as well as corresponding N–O distances less than 2.60 Å support the idea that their intramolecular HBs might be regarded as LBHB, as suggested in references [83,84,162,163].

Furthermore, in reference [32] the range of *H*c values found to characterize mentioned kind of hydrogen bonding interactions were -0.011 to -0.188 a.u, which is very in nice agreement with our calculated *H*c values. In fact, though in Figure 6 only Hc values above than -0.160 au were represented, from Table SIII in the supporting information it can be seen that hydrogen bonds become shared electron interaction for *H*c(N-H) values between -0.081 and -0.187 a.u. It should be mentioned that although in Arnold's work intermolecular hydrogen bonds were studied, an exponential behavior of *H*c with δ (^{1}H) was found similar to that reported here for intramolecular hydrogen bonds.

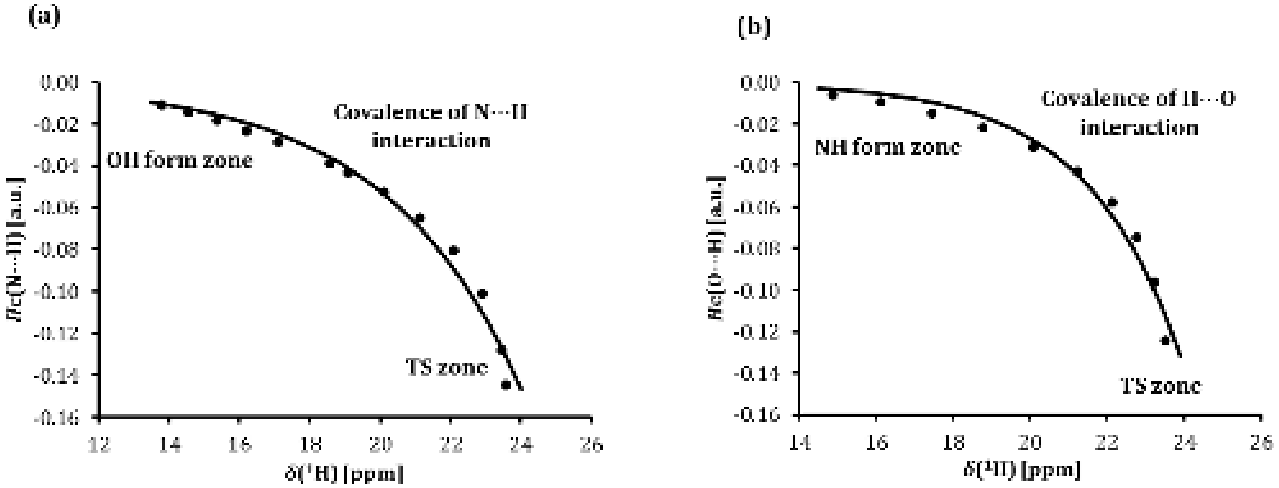


Figure 6: Dependencies of total electron energies at BCP of N···H and O···H bonds (a) before and (b) after reaching the TS with ^{1}H NMR chemical shifts for the proton transferred from O to N for compound **III** (Figure 2): (a) Hc(N···H)=-2.969 × 10^{-4} exp[0.2584δ(H)], R^2=0.9908; (b) Hc(O···H)=-7.9605 × 10^{-5} exp[0.4064δ(H)], R^2=0.9878.

2. *J*-Couplings

Detection of *J*-couplings through HBs has been taken as evidence of some degree of covalence of such interaction.[45–49] In fact, there is some controversy on this topic, since some research has shown that transmission of *J*-coupling through HBs can be measured when the degree of covalence of these bonds is very small or even if is not present.[32,130] On the other hand some studies, where small set of molecules were included, have suggested that *J*-coupling across intramolecular Hbs exhibit drastic variations on its magnitude and sign when changing the degree of covalence in the HB.[48,49]

To get a wide understanding on this issue, we evaluated the relationship between the degree of covalence in HBs and *J*-couplings, ^1J(X–H), (X = N, O), along the proton transfer path. In order to compare coupling constants through HBs with different proton donors and proton acceptors, they have been converted to reduced coupling constants K which are independent of the sign and magnitude of the gyromagnetic ratios (eq. 1)

In the following, J-couplings and corresponding reduced constants for compound **III** will be analyzed. Conclusions obtained are also valid for the others Schiff bases included in this study since, as shown in a previous work[86], ^1J(N–H) for this type of molecular systems mainly depends on N–H distance. A similar conclusion is obtained when analyzing ^1J(O–H) as a function of d(OH) or d(NH), as can be seen in Table SIV and in Figure S4 in the Supporting Information.

Theoretical calculations of ^1J(N–H),^1J(O–H) and corresponding reduced coupling constants for different steps during the proton transfer process for compound **III** are shown in the Table SIV in the Supporting Information. Since the magnetogyric ratio of ^{1}H is positive and that of ^{15}N and ^{17}O are negative, all J-couplings and corresponding reduced coupling constants across HBs have opposite signs. ^1J(N-H) values found for the stable OH and NH forms, as well as the range of values throughout the proton transfer process are similar to those reported in reference [86], where various Schiff bases were investigated and a good agreement with experimental values was found.

It must be pointed out that J-coupling constants involving oxygen atoms present difficulties to be obtained experimentally because the magnetic isotope of oxygen, that is, ^{17}O has an I = 5/2 that implies a quadrupole moment which causes the broadening of NMR signal. Despite this, for water and for alcohols, it has been possible to obtain experimental values of ^1J(O–H) in the range of -73 to -83 Hz.[170] As can be seen in Table SIV, our theoretical values obtained for the tautomeric OH form are in the same order.

We now turn to the analysis of the relationship between the degree of covalence of HBs and J-couplings. Variations of Hc(N–H) at BCP of amine bond as a function of ^1J(N-H) on either side of the TS are shown in Figure 7. In the first part of the proton transfer reaction, where the OH form predominates and there is a hydrogen bond N···H interaction, the dependence of Hc(N-H) with ^1J (N–H) is linear (Figure 7.a). While in the second part, where the N-H bond is purely covalent, the change of Hc(N-H) as a function of ^1J(N–H) acquires an exponential character (Figure 7.b). However, inspection of variation of Hc(N-H) throughout the total proton transfer process, (see Figure S5 in the Supporting Information), starting in the region of OH form and ending up when the NH form is reached shows that the behavior of Hc(N-H) in the region where TS appears is still linear. That is, the change of Hc(N-H) to an exponential behavior occurs after reaching the TS, which determine the shape of the curve shown in Figure 7.b

No drastic change in the degree of covalence is observed when ^{1}J(N–H) undergoes a sign change at d(NH) ~1.55 Å. When ^{1}J(N–H) suffers a sign change $\nabla^2\rho$ (N–H)> 0 and $\nabla^2\rho$(O–H) <0, therefore the change of sign of ^{1}J(N–H) does not indicate that N modifies its nature from a proton acceptor to become a proton donor. This change occurs in later steps of the proton transfer process for an NH distance of about 1.24 Å and a ^{1}J(N–H) value around -33 Hz.

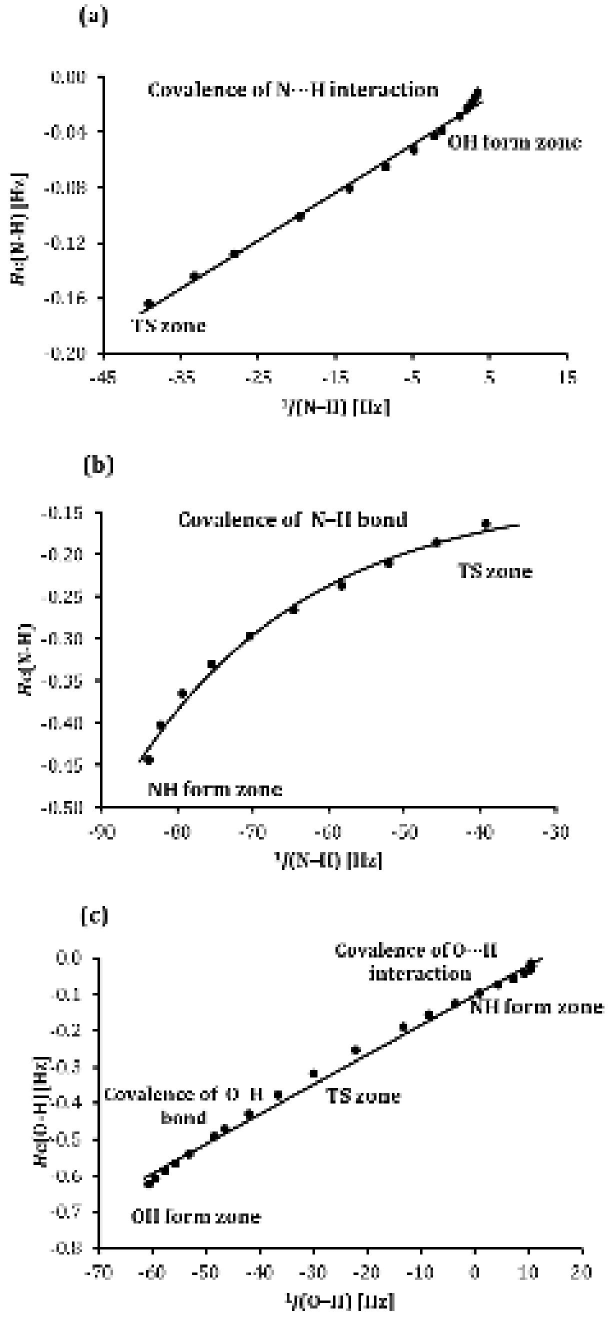


Figure 7: Variation of total electron energies at BCP of NH and OH bonds with: nitrogen-proton one bond coupling constants (a) before and (b) after reaching the TS, and (c) with oxygen-proton one bond coupling constants through the full proton transfer path. Results were obtained from the hydrogen bond of compound **III** (Figure 2). Correlations are

expressed as: (a) Hc(N⋯H) = -0.0035 ^{1}J(N–H) + 0.0316, R^2 = 0.9936; (b) Hc(N–H)=-0.1271 – 8.6166 × 10^{-3} exp[-0.042514 ^{1}J(N-H)], R^2=0.9909; (c) Hc(O—H) = -0.0082 ^{1}J(O–H) - 0.0993, R^2 = 0.9959

When ^{1}J(N–H) value decreases from 3.5 Hz to -8.35 Hz the HB N⋯H has a partial covalent character. Next, while ^{1}J(N–H) changes from -13.16 to -45.70 Hz, hydrogen bonding turn into a shared electron interaction. Afterwards, N atom has already become the hydrogen donor and the covalent character of N–H bond continues to increase linearly until ^{1}J(N–H) takes a value of about -60 Hz. From there, the functional dependence of ^{1}J(N–H) with d(NH) is exponential up to the stable NH form is reached.

Variations of Hc(O–H) as a function of ^{1}J(O–H) under the proton transfer process are depicted in Figure 7.c. In this case, Hc(O-H) behavior as a function of ^{1}J(O–H) is linear along the entire proton transfer path. It is observed that ^{1}J(O–H) sign change from negative to positive occurs at a very close O–H distance (~1.29 Å) at which $\nabla^2\rho_{\mathrm{BCP}}$(O–H) changes its sign in the same way (~1.33 Å). That is, the change of sign of ^{1}J(O–H) occurs at the limit of the region in which the hydrogen bond is a shared electron interaction. This change is not accompanied by an abrupt modification in the covalent character of the O–H bond but by a linearly gradual one.

As can be seen from results shown in Tables SIII and SIV when ^{1}J(O–H) changes from -60 to -36 Hz, the O–H bond has a full covalent character. After that, when the HB has features of a shared electron interaction, ^{1}J(O–H) changes from -29.95 to 0.99 Hz. From there, ^{1}J(O–H) values continues linearly increase to about 10 Hz when the stable NH form is reached.

Concerning to reduced coupling constants, our results show that if ^{1}K(X–H) has a positive value then X–H bond is fully covalent or has some degree of covalent character. However, a negative ^{1}K(X–H) value does not exclude the possibility that the X–H bond has a certain degree of covalent character.

Regarding the J-coupling between O and N atoms, values for the OH and NH forms are 8.47 and 10.47 Hz, respectively. Those values are in the same range of that obtained for azamalonaldehyde using equation-of-motion coupled cluster singles and doubles calculations in the CI-like approximation in reference. [123] Furthermore, the observed functional dependence of ^{2h}J(O–N) with d(NH) (Figure S6) follows a similar pattern to that found when the relationship between $\delta(^{1}H)$ and d(NH) was analyzed (Figure 4). In fact, the correlation between ^{2h}J(O–N) and $\delta(^{1}H)$ through the proton transfer process is linear (see Figure S7). Therefore it is not surprising that the dependence of the total energy density at the bond critical points of N ⋯ H and O ⋯ H before and after reaching the TS, respectively, with ${}^{2h}J$(N–O) has an exponential character (Figure S8). Inspection of values listed in Tables SIII and SIV reveal that within range of the ${}^{2h}J$(O–N) values comprehended between 8.5 and 16.7 Hz, the hydrogen bond is partially covalent. While for values of ${}^{2h}J$(O–N) between 17.9 and 18.5 Hz the hydrogen bond is a shared electron interaction. Furthermore, since magnetogyric ratios of both O and N are negative, ${}^{2h}J$(O–N) and ${}^{2h}K$(O–N) have equal signs. Therefore, throughout the entire proton transfer process ${}^{2h}K$(O–N) has a positive sign. Similar values of sign of ${}^{2h}K$(O–N) were reported in previous works where a series of neutral and charged intermolecular hydrogen bonds were investigated.[171]

These findings provide clues that can be used to estimate the degree of covalence in OH ⋯ N HBs from the values of ${}^{1}J$(N–H), ${}^{1}J$(O–H) and ${}^{2h}J$(O–N) in Schiff bases and other molecular systems with similar neutral intramolecular hydrogen bonds.

C. INFLUENCE OF π-DELOCALIZATION WITHIN CHELATE RING ON ${}^{2h}J$(O–N)

Although the concept of RAHB has been criticized, several authors have suggested that in the case of Schiff bases, π electron delocalization in the conjugated system joining the donor and acceptor leads to the strengthening of the HB, it is one of the driving forces of the proton transfer process and has an important influence on the stabilization of the NH tautomeric form.

At this stage of our study we investigated whether the different terms of the spin-spin coupling constant across X-H⋯Y intramolecular HB, ${}^{2h}J$(X–Y), give evidence for the existence of some degree of interrelation between hydrogen bonding and π-electron delocalization in the conjugated chain that links proton donor and proton acceptor atoms.

In previous works[122,123] where molecular systems containing intramolecular HBs connected to a π conjugated system were studied, it was found that the FC term of the ${}^{2h}J$(X–Y) accounts for the transmission of the coupling through the σ-electronic framework, being its value mainly determined by interactions evolving the bonding orbital σ(X–H) and one of the lone pairs of the acceptor atom.[124] In turn SD and PSO terms of ${}^{2h}J$(X–Y) coupling have non-negligible values when the transmission of the coupling also takes place through the π conjugated double bond system, as observed in the case of the ${}^{2h}J$(O–O) coupling in malonaldehyde.[122–124] Therefore, ${}^{2h}J$(X–Y) coupling is a valid tool to obtain proofs for the existence or absence of RAHB. Here it is assumed that relatively non-negligible values of SD and PSO contributions to ${}^{2h}J$(O–N) give evidence of the existence of an interrelation between the properties of the HB and the π conjugated double bond system.

More specifically, the relative value of the sum of SD and PSO terms of ${}^{2h}J$(O–N) is considered to be a measure of degree of influence of π-electron delocalization in the conjugated system on the characteristics of the O-H···N/ N-H···O hydrogen bond.

Our goal is analyze the behavior of *J*-coupling through HBs in Shiff bases as well as in systems with a similar σ structure but containing hydrogen bonds that are not part of a quasi-aromatic ring. Therefore we perform a comparison of ${}^{2h}J$(O–N) values of the Schiff base without substituents on the ring (compound **I**) and the Mannich base showed in Figure 2.V.

With the purpose to reduce differences in the sigma skeleton of both molecules, during the optimization of Mannich base structures, atoms belonging to the HB and the methylene carbon that joins the nitrogen atom to the aromatic ring were restricted to be in the same plane as the phenyl group. Although in order to obtain structures not very far from those that appear in nature, an equal distance *d*(ON) for compounds **I** and **V** was not fixed in the course of optimization process, as explained in the Computational Details section.

Calculated *J*-couplings values for model compounds **I** and **V** corresponding to selected structures with similar values of *d*(NO) throughout the proton transfer process are given in Table I. This selection criterion was used because it is well known that the FC coupling mechanism strongly depends on the donor-acceptor distance. The DSO term is not included since for all compounds investigated here is negligible (see Table SV in the Supporting Information). Results show that the SD and PSO terms are negligible for compound **V**, while for compound **I** the sum of these non-contact terms amounts up to 25% of the total *J*-coupling. These results indicate that the SD and PSO contributions of ${}^{2h}J$(N–O) detect a non-negligible influence of the π conjugated double bond system on the HB in *o*-hydroxy aryl Schiff bases. As will be discussed later, the relative importance of the noncontact terms undergoes changes throughout the proton transfer process.

Table I: Hydrogen bond length (d(ON) in Å), total O–N two bond coupling constant through HB, ^{2h}J(O-N), and their Ramsey contributions (in Hz) for Mannich and Schiff bases without substituents in the ring,(compounds **V** and **I** in Figure 2, respectively) for selected steps during the proton transfer process. For Schiff base the per cent of sum of SD and PSO terms respect to the total and the impact of π system on ^{2h}J(O-N) (%$J_{\pi\ \mathrm{impact}}$,eq. 4) are also listed.[a]

Mannich_Base (V)					**Schiff Base (I)**						
***d*(ON)**	**FC**	**SD**	**PSO**	**Total**	***d*(ON)**	**FC**	**SD**	**PSO**	**Total**	**% (SD+PSO)**	**% *J* π impact**
2.62	5.12	0.15	-0.04	5.25	2.62	6.29	0.63	1.08	8.03	21.34	34.64
2.59	5.68	0.16	-0.05	5.81	2.60	6.99	0.66	1.15	8.82	20.55	34.11
2.56	6.26	0.17	-0.05	6.40	2.57	7.75	0.69	1.23	9.69	19.84	33.96
2.54	6.92	0.18	-0.06	7.06	2.54	8.57	0.72	1.32	10.63	19.22	33.59
2.51	7.59	0.19	-0.06	7.75	2.51	9.45	0.76	1.42	11.64	18.70	33.45
2.49	8.28	0.20	-0.07	8.44	2.49	10.37	0.80	1.52	12.71	18.28	33.61
2.46	8.97	0.21	-0.07	9.14	2.47	11.33	0.84	1.64	13.83	17.96	33.93
2.44	9.64	0.23	-0.07	9.82	2.44	12.31	0.89	1.77	14.99	17.78	34.50
2.42	10.26	0.24	-0.07	10.45	2.42	13.27	0.95	1.91	16.16	17.73	35.31
2.41	10.79	0.25	-0.07	10.99	2.41	14.17	1.02	2.07	17.28	17.88	36.38
2.39	11.43	0.26	-0.06	11.65	2.39	15.40	1.19	2.41	19.01	18.92	38.71
2.40	10.96	0.26	-0.05	11.19	2.40	15.13	1.35	2.65	19.15	20.88	41.53
2.41	10.38	0.25	-0.04	10.61	2.41	14.65	1.41	2.70	18.78	21.90	43.47
2.42	9.67	0.23	-0.03	9.89	2.43	14.02	1.46	2.74	18.24	23.03	45.76
2.44	8.82	0.21	-0.02	9.03	2.44	13.26	1.51	2.74	17.53	24.29	48.50

[a] Computed at B3LYP/cc-pVTZ.

Turn out to the contact term, it is known that its most important forms of transmission are through interactions involving the bonding orbital σ(X – H), the anti-bonding orbital σ*(X - H) and a lone pair of the acceptor atom LP(Y).[130] In a previous work[118] where a NBO analysis was performed during the proton transfer process in a salicylidenaniline, it was found that an increase of π-electronic delocalization of the quasiaromatic ring when the proton is transferred from the OH form to the NH form cause a decrease in electronic population of LP orbital on N and an increase in population of non-Lewis type valence orbital (LP*) on the transferred proton. From such results, authors inferred that LP orbital on N atom and phenyl ring give electronic charge to setting up π delocalization in the quasi-aromatic ring. Therefore, if π electron delocalization in the conjugate chain modifies electron density of LP(Y) in a singular way, FC term should reflect these changes. In fact, although results in Table I show that FC term is dominant in both analyzed compounds, it is observed that its value is systematically higher in the Schiff base, for similar O–N distance values. This difference might be attributed to the impact of the π system on the σ structure through which FC term is transmitted.

Hence, following ref.[123], the global impact of π system on ^{2h}J(O–N) through HB in the Schiff base (**I**), taking as a reference without RAHB the Mannich base (**V**) might be rationalized as:

$$\% J_{\pi\ impact} = \frac{{}^{2h}J(O-N)_{Schiff\ base} - {}^{2h}J(O-N)_{Mannich\ base}}{{}^{2h}J(O-N)_{Schiff\ base}} \times 100 \quad \text{(eq. 4)}$$

Therefore, from theoretical calculations, the impact of π electronic delocalization on ${}^{2h}J$(O-N) through hydrogen bond can be up to 45% (see Table I)

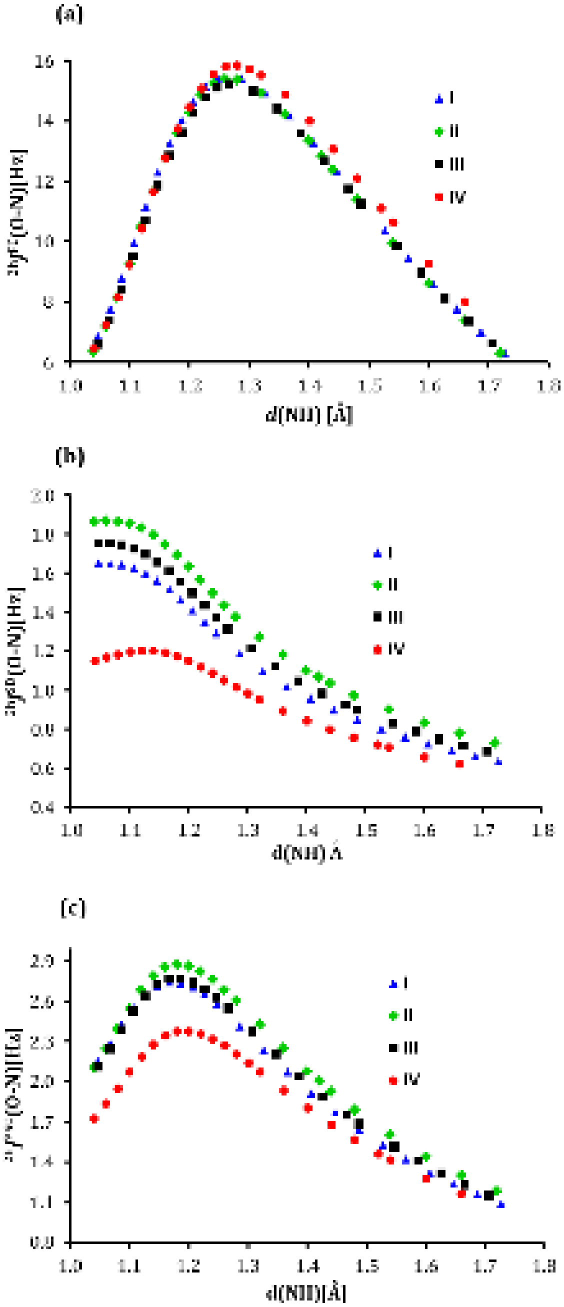


Figure 8: Variations of (a) FC , (b) SD and (c) PSO terms of oxygen-nitrogen *J*-coupling with N–H distance for selected Schiff bases (Figure 2.I-IV)

The analysis now focuses on the behavior of the ${}^{2h}J$(O–N) coupling mechanisms throughout the proton transfer process for the selected Schiff bases. Theoretical calculations of different non-negligible ${}^{2h}J$(O–N) terms as a function of N–H distance for compounds **I-IV** are shown in

Figure 8. In all cases FC term is dominant and determines the shape of the dependence of total ^{2h}J(O–N) on d(NH) (Figure 8.a and S9). FC term increases continuously until the transition state is reached and then decreases up to the stable form NH appears. The contact term shows to be not very sensitive to the electronic effect of the substituents on the ring and is mainly determined by the O–N distance. Although in the case of compound **IV**, during the first part of the reaction (up to the TS zone), the electronic effect of methoxy substituents at positions 3 and 5 causes a slight increase in the FC value (around 1Hz) compared to the other compounds, for similar values of NH and ON distances. The global trend of FC term as a function of N–H distance, is similar to that observed for $\delta(^1H)$.

The dependencies of SD and PSO terms (Figures 8.b and 8.c) on d(NH) during the proton transfer process reveal that both terms are sensitive to the electronic effect of substituents. For similar d(NH) of analyzed compounds, relative SD and PSO values show the following relationship: $\mathbf{IV} \lesssim \mathbf{I} \lesssim \mathbf{III} \lesssim \mathbf{II}$. Both non-contact terms increase continuously up to a d(NH) around 1.14 Å, that is, after reaching the transition state. Thereafter SD values remain almost constant while PSO values decrease slightly until the stable NH form appears. The small difference in the behavior of SD and PSO terms can be attributed to the larger weight that contributions from lone pairs of the proton donor and proton acceptor atoms have on PSO values.

The effect of substituents on SD and PSO values can be explained from the effect of such groups on π-electron delocalization of chelate ring. One of the most useful tools to describe the degree of delocalization of conjugated systems is the para delocalization index , PDI. The dependence of PDI of chelate rings for compounds **I**-**IV** as a function of N–H distance is shown in Figure 9.a. The PDIs behavior is very similar to that observed for the SD term, although the spin dipolar coupling mechanism shows to be slightly more able of differentiating the effect of substituents. The functional relationship that best describes the dependence between the SD term and PDI is smoothly quadratic with an $R^2 \sim 1$, (Figure 9.b). Theoretical calculations of both non-contact terms, as well as of PDIs, show that π electronic delocalization within chelate ring is larger in NH tautomer than in OH form, for all Schiff bases here investigated. A similar behavior of π electron delocalization was found in previous studies where aromaticity of various Schiff bases was studied throughout the proton transfer process.[118,121]

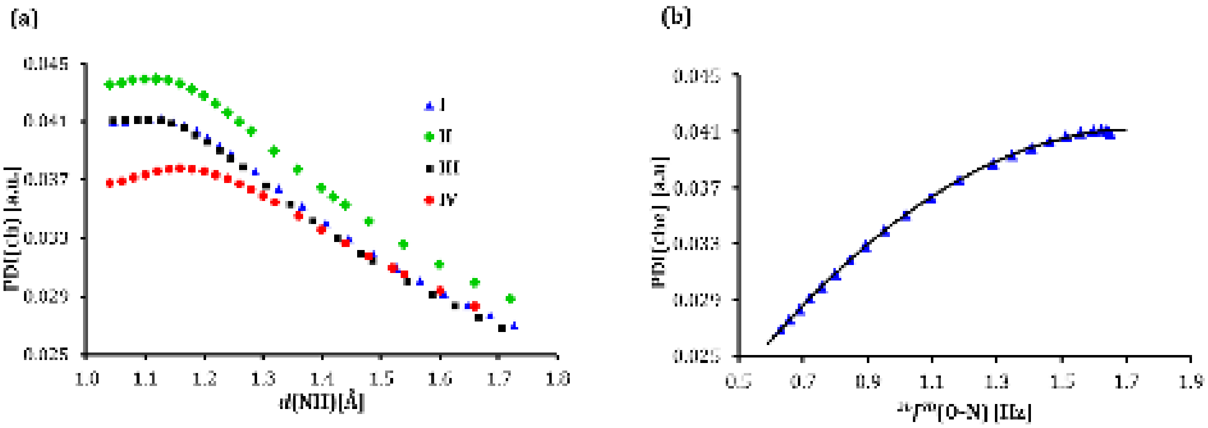


Figure 9: (a) Variations of PDIs for chelate ring against N-H bond elongation for selected Schiff bases (Figure 2.I-IV), (b) Relationship between PDIs of chelate ring and SD terms of oxygen-nitrogen J-coupling for compound **III** (Figure 2): PDI(che) = -0.0115 $^{2h}J^{SD}$(O-N)^2 + 0.04 $^{2h}J^{SD}$(O-N) + 0.0062, R^2 = 0.9998

IV. CONCLUSIONS

Our main results provide new and valuable insights concerning two aspects of HBs in proton transfer process of *o*-hydroxyaryl Schiff bases: one of them is related to the covalent character of HBs in connection with NMR observables, *J*-couplings and ^{1}H chemical shifts, and the other one addresses the impact of π electron delocalization on such HBs and its manifestation through the *J*-coupling between the donor and acceptor. To evaluate the relationship between hydrogen bonds properties and NMR parameters, topological and energetic descriptors provided by Bader's AIM theory were calculated.

With regard to the relationship between covalence of hydrogen bonds and NMR properties, we found that the degree of covalence in hydrogen bonds N ···H and O···H on either side of the transition state as a function of δ (^{1}H) increases exponentially as the ^{1}H NMR signal moves to down field. Though, shapes of the curves showing an exponential behavior are not exactly the same, due to the asymmetry of the hydrogen bond. Our results show that for δ(^{1}H) values variations between ~13.5 and ~21.5 ppm the intramolecular hydrogen bond has an increasing partial covalent character. Whereas when δ(^{1}H) changes from ~22.1 to ~23.2 ppm, hydrogen bonding is a shared electron interaction and the hydrogen atom is covalently bonded to both N and O. We have observed that that the degree of covalence of N···H and O···H bonds increases in a continuous and linearly way as ^1J(N–H) and ^1J(O–H) becomes more negative, even after reaching the transition state. This dependence becomes exponential for

^{1}J(N–H) values corresponding to structures close to the stable NH form. No drastic change in the degree of covalence is observed when ^{1}J(X–H) undergoes a sign change, with X=O,N. When ^{1}J(N–H) value decreases from ~3 Hz to ~(-8.5) Hz the hydrogen bond N⋯H has a partial covalent character, whereas for ^{1}J(N–H) values within the range ~(-13) Hz ≤ J(NH)≤ ~(-46) Hz hydrogen bonding turn into a shared electron interaction. More negative ^{1}J(N–H) values correspond to a fully covalent N-H bond. These results provide a valuable guide to relate the magnitudes of NMR observables (measured routinely in the laboratory) with characteristics of hydrogen bonds that determine the biochemical and technological applications of these interesting systems. Furthermore, our results show that if reduced coupling constant ^{1}K(XH) has a positive value then X–H bond is fully covalent or has some degree of covalent character. However, a negative ^{1}K(X–H) value does not exclude the possibility that the X–H bond has a certain degree of covalent character. We also found that the dependence of the degree of covalence in hydrogen bonds N ⋯H and O⋯H before and after reaching the TS, respectively, with ^{2h}J(N–O) has an exponential character. Which is in line with the fact that correlation between ^{2h}J(O–N) and $\delta(^{1}H)$ through the proton transfer process reported here is linear.

Concerning π electron delocalization influence on HBs, the non-vanishing values of SD and PSO terms of ^{2h}J(O–N) in Schiff bases show that π-electronic delocalization in the chelate ring has a relatively non negligible effect on tautomeric equilibrium and give evidence of the presence with some extension of the so called resonance assisted hydrogen bond . Besides, when comparing values of the FC term of ^{2h}J(O–N) of a Schiff base and of a Mannich base with alike structures for similar d(ON) values, the FC term is systematically higher for the Schiff basis. It means that the FC contribution to ^{2h}J(O–N) reflects the impact of π structure on the σ backbone during proton transfer process in Schiff bases. Our theoretical calculations show that the global impact of π system on ^{2h}J(O–N) through hydrogen bond in Schiff bases, taking as a reference without RAHB a Mannich base with similar structure can be up to 40% of its value.

Furthermore, our findings showed that shapes of the functional dependencies with NH bond distance of the NMR parameters $\delta(^{1}H)$, ^{1}J(O–H), $^{2h}J^{FC}$(O–N), and the AIM theory descriptors ρ, $\nabla^{2}\rho$ and Hc at BCP of HB interactions are independent of the electronic effects of the substituents on the ring. Unlike it, the dependencies of SD and PSO terms of ^{2h}J(O–N) on d(NH) during the proton transfer process reveal that both terms are sensitive to those effects. Moreover, our calculated potential energy curves predict an effect of the substituents in the aromatic ring on the proton transfer barrier, and therefore on the position of the tautomeric equilibrium, similar to that estimated from experimental measurements of NMR spectrocopic parameters.

SUPPLEMENTARY MATERIAL

Additional numerical values and figures for *J*-couplings and chemical shifts, electron density, Laplacian of electron density, and total electronic energy density. Distances between atoms involved in the hydrogen bond and C1–O and C7-N bond lengths.

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DATA AVAILABILITY

The data that supports the findings of this study are available within the article [and its supplementary material].

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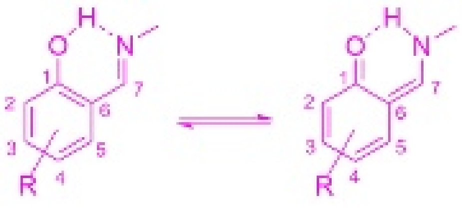
H
O
N
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6
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R
4
H
O
N
1
7
2
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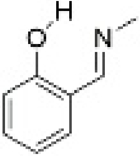
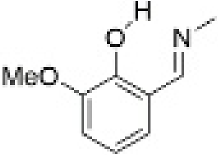
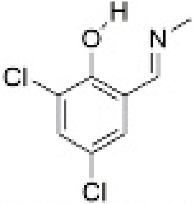
3
5
R
4



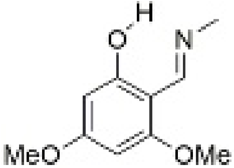
(*E*)-2-((methylimino)
methyl)phenol (**I**)



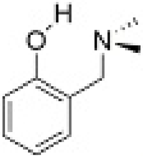
(*E*)-2-methoxy-6-((methylimino)
methyl)phenol (**II**)



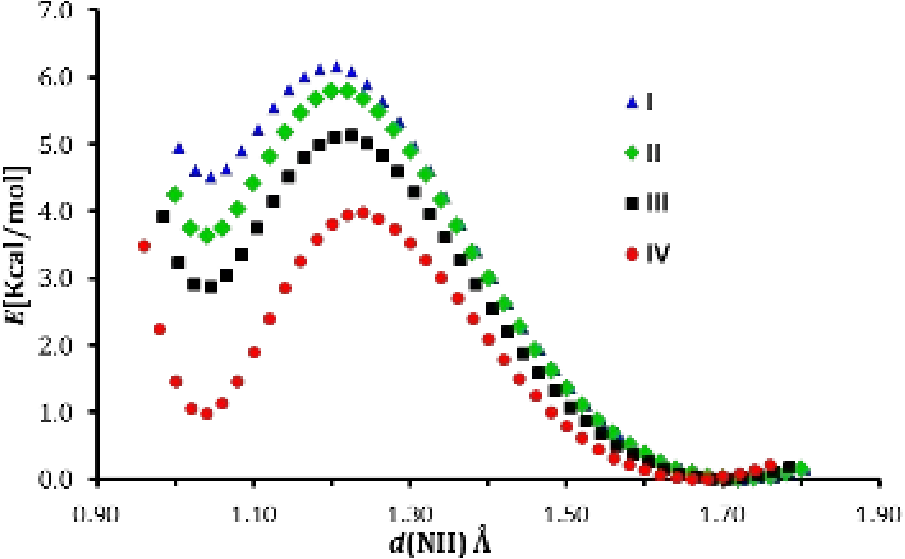
(*E*)-2,4-dichloro-6-((methylimino)
methyl)phenol (**III**)

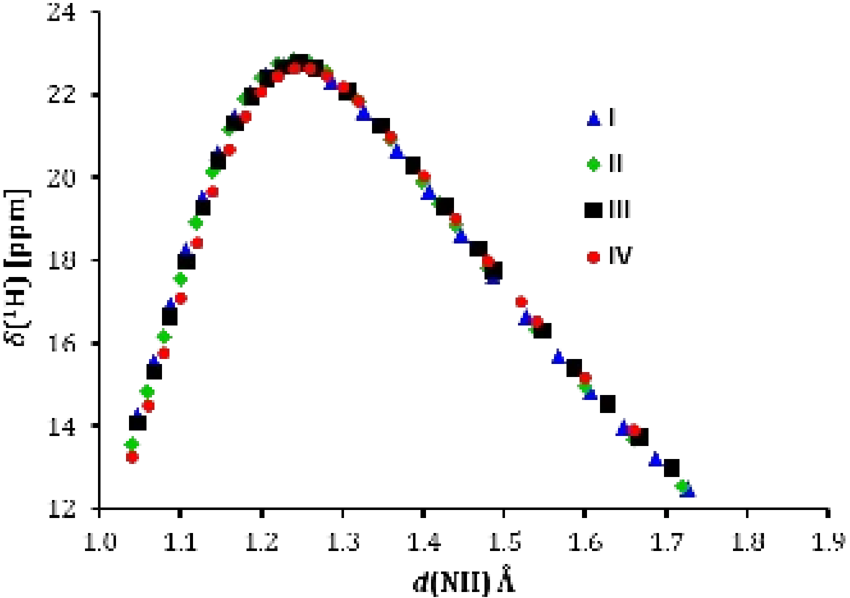


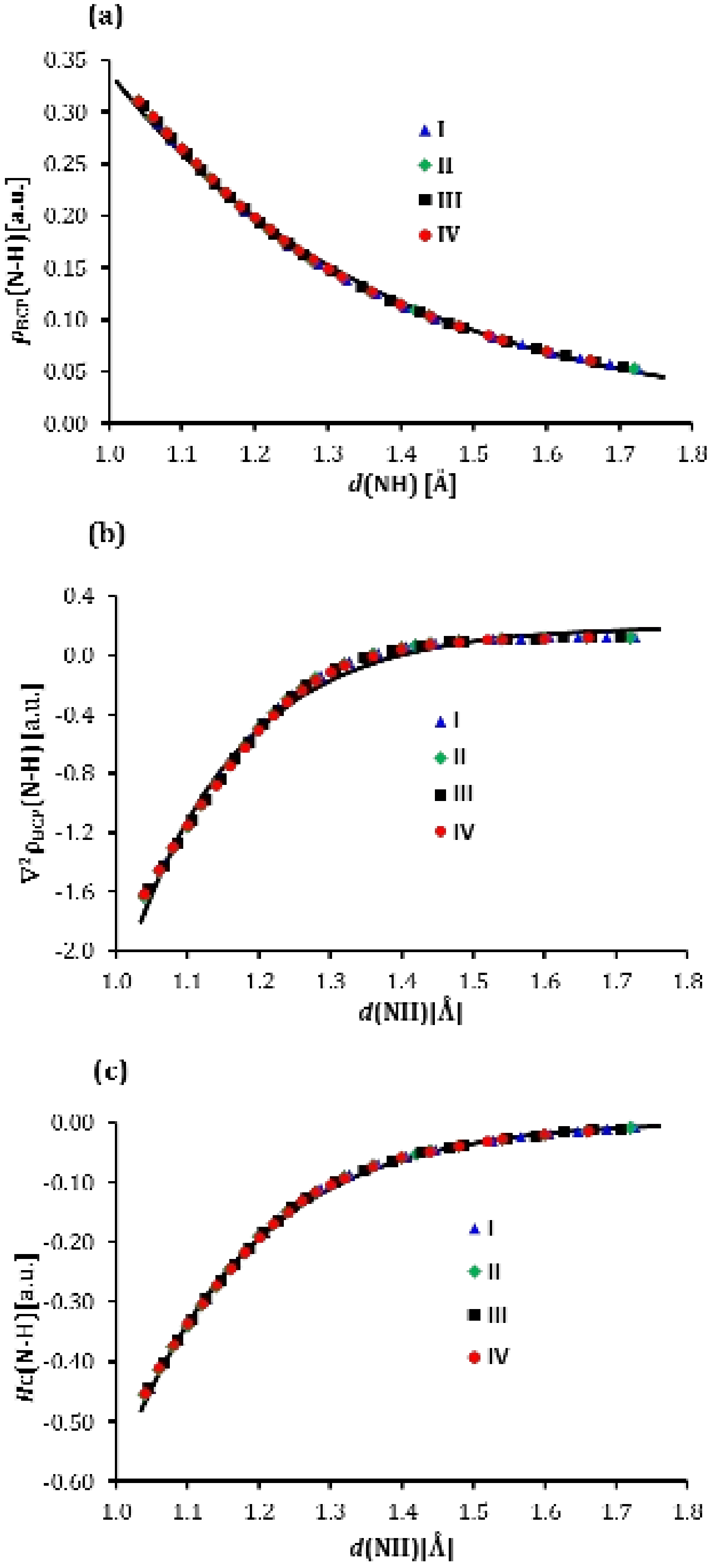
(*E*)-3,5-dimethoxy-2-((methylimino)
methyl)phenol (**IV**)

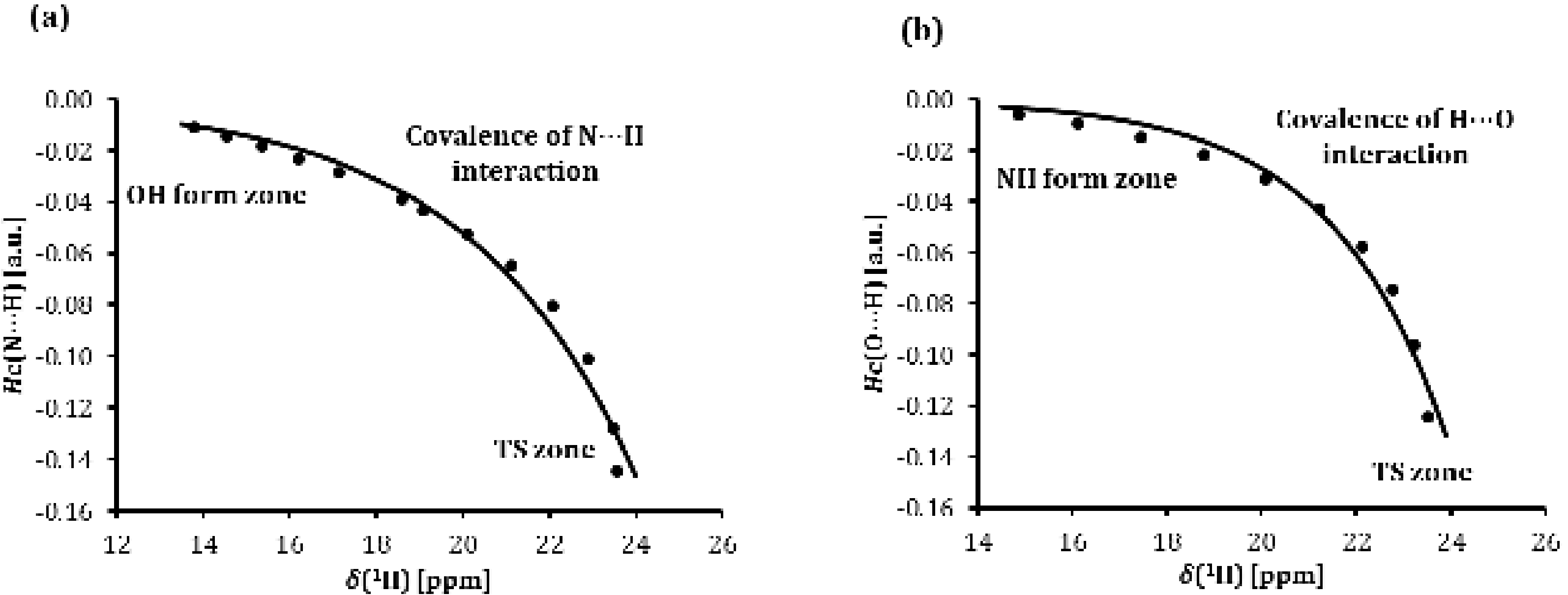


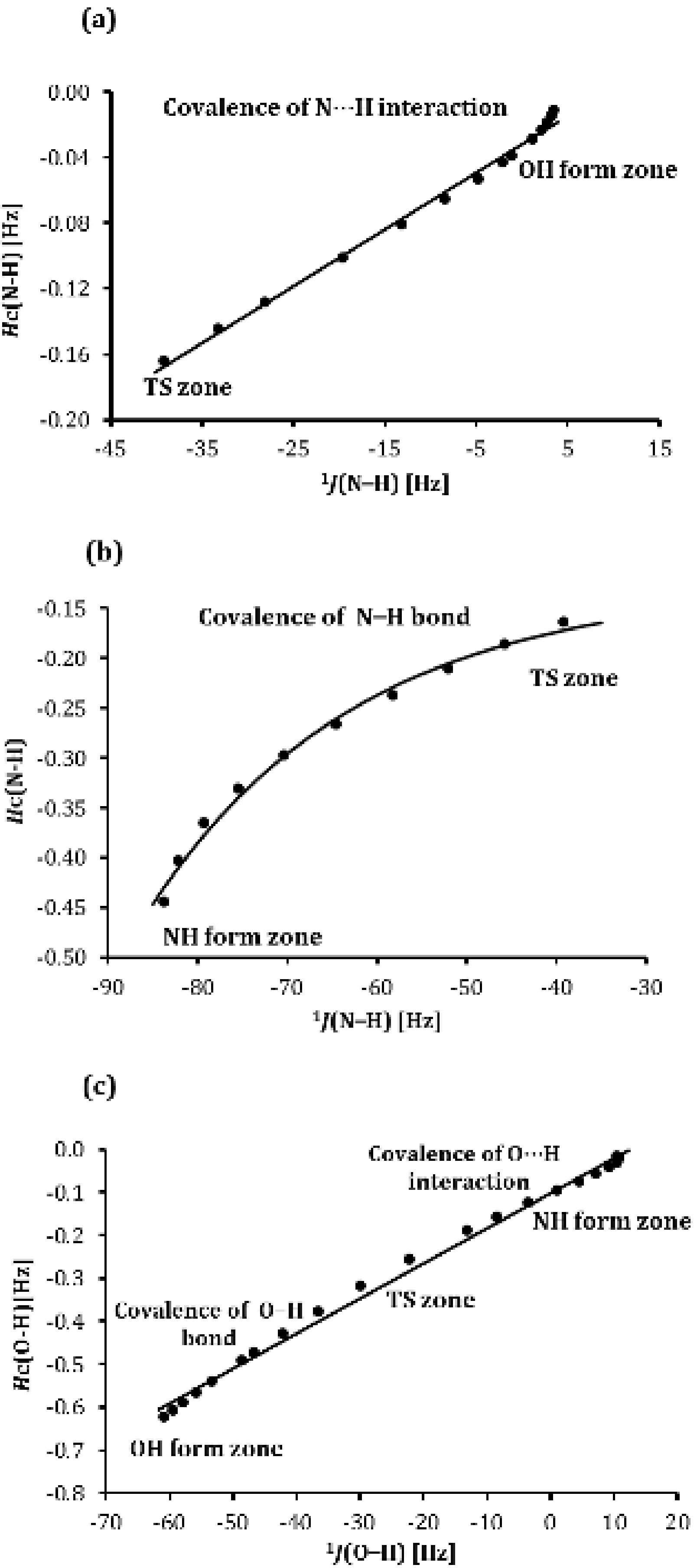
2-((dimethylamino)methyl)
phenol (**V**)

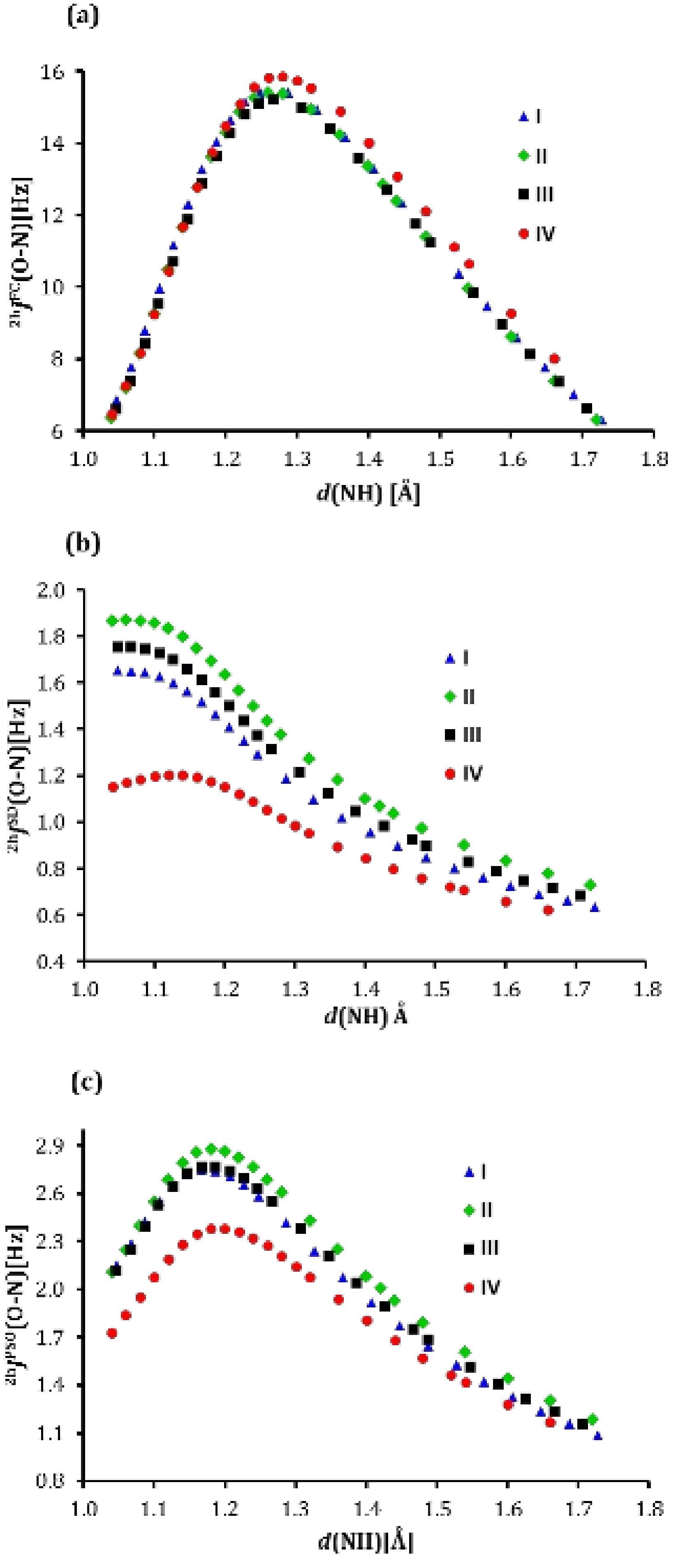

7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
E[Kcal/mol]
0.90
1.10
1.30
1.50
1.70
1.90
d(NII) Å
I
II
III
IV

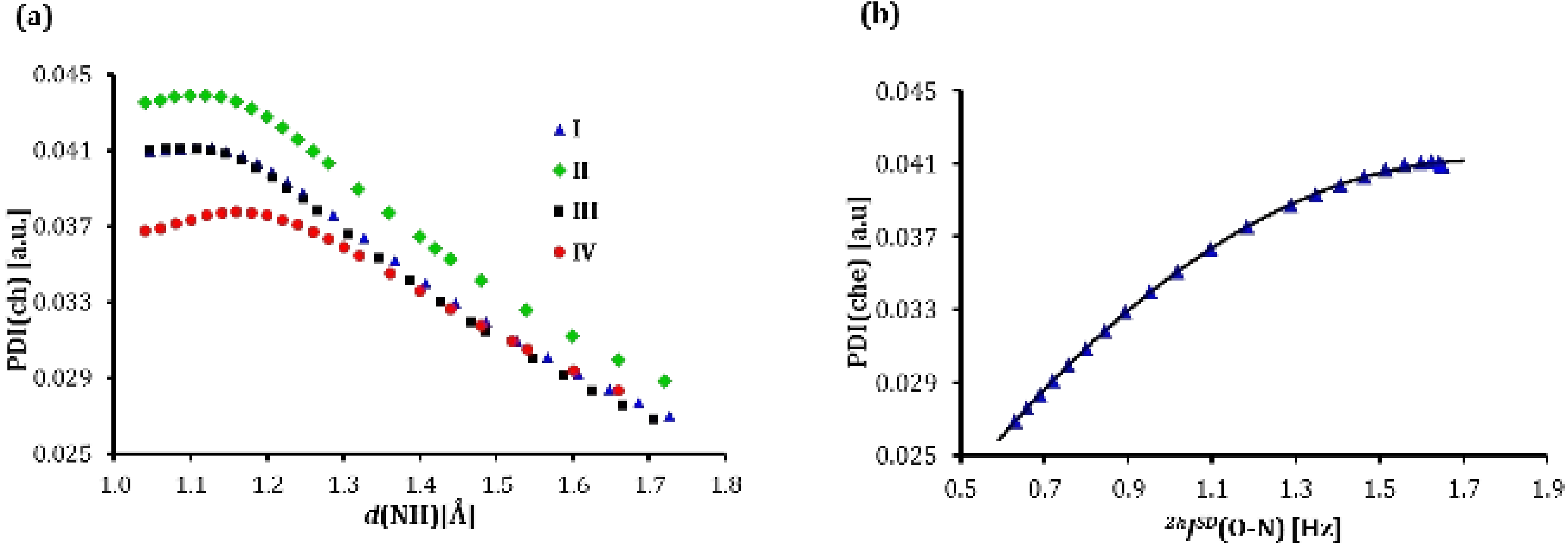

24
22
20
18
16
14
12
δ(¹H) [ppm]
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
d(NH) Å
▲ I
◆ II
■ III
● IV


(a)
ρBCP(N-H) [a.u.]
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH) [Å]
I
II
III
IV
(b)
∇²ρBCP(N-H) [a.u.]
0.4
0.0
-0.4
-0.8
-1.2
-1.6
-2.0
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH) [Å]
I
II
III
IV
(c)
HC(N-H) [a.u.]
0.00
-0.10
-0.20
-0.30
-0.40
-0.50
-0.60
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH) [Å]
I
II
III
IV


(a)
Hc(N···H) [a.u.]
0.00
-0.02
-0.04
-0.06
-0.08
-0.10
-0.12
-0.14
-0.16
12
14
16
18
20
22
24
26
δ(¹H) [ppm]
Covalence of N···H
interaction
OH form zone
TS zone
(b)
Hc(O···H) [a.u.]
0.00
-0.02
-0.04
-0.06
-0.08
-0.10
-0.12
-0.14
-0.16
14
16
18
20
22
24
26
δ(¹H) [ppm]
Covalence of H···O
interaction
NH form zone
TS zone


(a)
Covalence of N···H interaction
OH form zone
TS zone
Hc(N-H) [Hz]
0.00
-0.04
-0.08
-0.12
-0.16
-0.20
-45
-35
-25
-15
-5
5
15
^1J(N–H) [Hz]
(b)
Covalence of N–H bond
TS zone
NH form zone
Hc(N-H)
-0.15
-0.20
-0.25
-0.30
-0.35
-0.40
-0.45
-0.50
-90
-80
-70
-60
-50
-40
-30
^1J(N–H) [Hz]
(c)
Covalence of O···H interaction
NH form zone
TS zone
Covalence of O–H bond
OH form zone
Hc(O-H) [Hz]
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-70
-60
-50
-40
-30
-20
-10
0
10
20
^1J(O–H) [Hz]

(a)
16
14
12
10
8
6
²ʰJᶠᶜ(O-N)[Hz]
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH) [Å]
I
II
III
IV
(b)
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
²ʰJˢᴰ(O-N)[Hz]
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH) Å
I
II
III
IV
(c)
2.9
2.6
2.3
2.0
1.7
1.4
1.1
0.8
²ʰJᴾˢᴼ(O-N)[Hz]
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH)[Å]
I
II
III
IV


(a)
0.045
0.041
0.037
0.033
0.029
0.025
PDI(ch) [a.u.]
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
d(NH) [Å]
▲ I
◆ II
■ III
● IV
(b)
0.045
0.041
0.037
0.033
0.029
0.025
PDI(che) [a.u]
0.5
0.7
0.9
1.1
1.3
1.5
1.7
1.9
$^{2h}J^{SD}$(O-N) [Hz]