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Intramolecular Hydrogen Bonds in *ortho*-Substituted Hydroxybenzenes and in 8-Susbtituted 1-Hydroxynaphthalenes: Can a Methyl Group Be an Acceptor of Hydrogen Bonds?

Isabel Rozas,*,† Ibon Alkorta,‡ and Jose Elguero‡

Department of Chemistry, Trinity College Dublin, Dublin 2, Ireland, and Instituto de Química Médica, CSIC, Juan de la Cierva 3, 28006-Madrid, Spain

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Considering the findings of Fujii et al. showing that the cis isomer of the *o*-cresol radical cation shows a low-frequency shift of the OH stretching attributed to an intramolecular hydrogen bond with the CH_3 group and considering the studies of Knak Jensen et al. concluding that such an O−H···C interaction was not possible, the work presented in this article tries to understand if this is a consequence of the nature of the hydrogen bond acceptor (a CH_3 group) or of the five-member ring that would be formed as a result of the intramolecular interaction. Thus, we have studied *o*-cresol, 8-methyl-1-hydroxynaphthalene, 1-hydroxy-1-propene, 1-hydroxy-3-methyl-1,3-butadiene, and their derivatives in which the $-CH_3$ group has been substituted by a −F atom or by an −OH group. Taking into account interaction distances and angles, interaction energies (from isodesmic reactions), and electron density characteristics, we can conclude that, in general, a methyl group cannot behave as a hydrogen bond acceptor. In addition, we found that the formation of intramolecular hydrogen bonds driving to the formation of five-member rings is not favored even in the presence of a good acceptor. Moreover, different methods of evaluating intramolecular interaction energies have been analyzed.

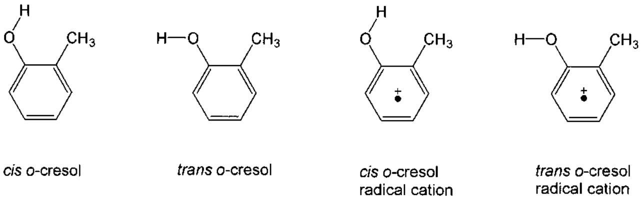
Introduction

Recently, Fujii et al.[1] presented the IR results of the cis and trans isomers of *o*-cresol and the corresponding radical cations (among other isomers of cresol and their radical cations) by using a novel experimental technique (Scheme 1). They observed that the cis isomer of the *o*-cresol radical cation shows a low-frequency shift of the OH stretching vibration relative to that of the trans, while the cis and trans neutral isomers show essentially the same frequency. Thus, they reach the conclusion that this shift is the result of an unconventional intramolecular hydrogen bond (IMHB) between the hydroxyl group and the C atom of the methyl group.

As a consequence of that paper, Knak Jensen et al.[2] have theoretically investigated the presence of this special type of IMHB in both the cation and neutral species of the cis isomer of *o*-cresol. By using ab initio geometry optimizations and the topological analysis of the electron density, they concluded that none of these approaches could support such an O−H···C interaction (forming a five-member ring), even though the calculated OH frequencies showed the same trends in frequency shifts as those observed experimentally.[1] Therefore, they suggested that the experimental frequency variation should be explained by other means.

In a previous paper,[3] we observed that the formation of an IMHB resulting in the creation of a five-member ring was not energetically favored, and therefore, those IMHB interactions, in general, were not established. However, the systems with similar HB donors and acceptors but in which an IMHB interaction resulted in the formation of a six-member ring were energetically favored.

SCHEME 1



cis o-cresol

trans o-cresol

cis o-cresol radical cation

trans o-cresol radical cation

Considering all that, a main question arises. Is the lack of evidence of an IMHB formation in the case of the cis isomer of the *o*-cresol radical cation a consequence of either the nature of the HB acceptor (a CH_3 group) or the five-member ring that would be formed as a result of the IMHB interaction? In this article, we try to answer such a question by studying *o*-cresol and some related compounds in which the $-CH_3$ group has been substituted by a −F atom (a "bad" HB acceptor[4]) or by an −OH group (the O atom can act as a "good" HB acceptor). In addition, we study some naphthol derivatives where the HB acceptor can be a $-CH_3$, −F, or −OH group and the possible IMHB interaction would result in the formation of a six-member ring. The compounds chosen as models for the study are represented in Figure 1, and they are 2-methylphenol [also known as *o*-cresol] (**1**), 2-fluorophenol (**2**), benzene-1,2-diol [also known as catechol] (**3**), 8-methyl-1-hydroxynaphthalene (**4**), 1-fluoro-8-hydroxynaphthalene (**5**), and 1,8-dihydroxynaphthalene (**6**).

In addition, a series of noncyclic structures has also been studied. These compounds are less rigid than the cyclic ones, and thus, the possible influence of the rigidity of the skeleton forcing the interactions of the O−H group would be partially avoided. Moreover, these linear structures can be considered as simplifications of the previous structures and can be used to test the possible utility of these compounds as models of the aromatic ones. These compounds are shown in Figure 2, and

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* Corresponding author. E-mail: rozasi@tcd.ie. FAX: +353 1 671 2826.
† Trinity College Dublin.
‡ Instituto de Química Médica.

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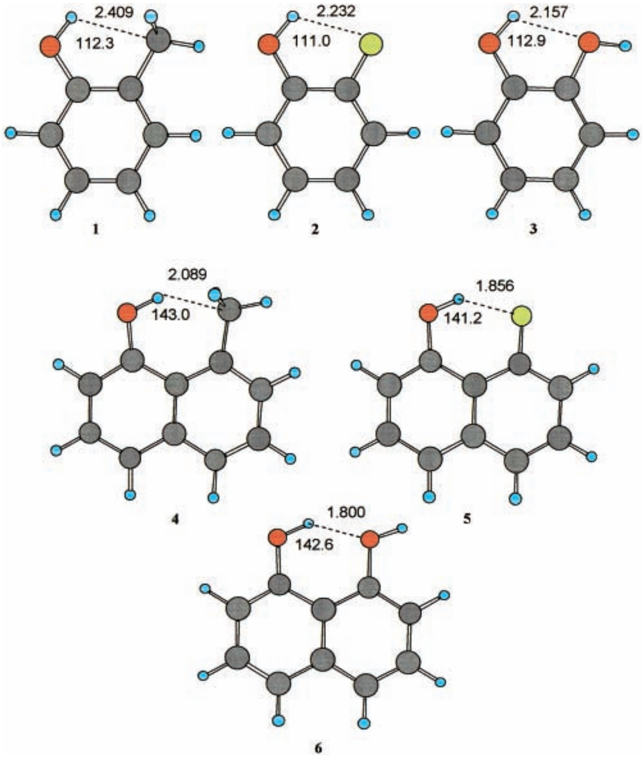


Figure 1. Optimized structures (at the B3LYP/6-31+G** level) of the phenol and naphthol derivatives **1**−**6**. The interaction distances (Å) and angles (deg) are shown.

they are (*Z*)-1-hydroxy-1-propene (**7**), (*Z*)-1-fluoro-2-hydroxyethene (**8**), (*Z*)-1,2-ethenediol (**9**), 1-hydroxy-3-methyl-1,3-butadiene (**10**), 1-fluoro-3-hydroxy-1,3-butadiene (**11**), and 1,3-dihydroxy-1,3-butadiene (**12**).

The evaluation of the interaction energy in the case of IMHB interactions has been an object of some controversy.[5] In this paper, we address different ways of evaluating such energy, and we will discuss the different approaches.

Methods

The geometries of all the compounds have been fully optimized with the program Gaussian-98[6] using the hybrid method Becke3LYP[7] with the 6-31+G**[8] basis set. In all the cases, the nature of the compounds as a potential energy minimum has been established, at the B3LYP/6-31+G** level, by verifying that all the corresponding frequencies were real.

Intramolecular hydrogen bond interaction energies, E_Is, have been calculated both by means of the corresponding isodesmic equations (Scheme 2) and as the difference between the energy of the compound with the *cis*-OH disposition (Figures 1 and 2) and that of the *trans*-OH disposition (Scheme 3). The zero-point corrected energies have been used. No scaling factor for the ZPE values has been taken into account.

The topological properties of the electron density at the bond critical points (BCPs) have been characterized using the atoms in molecules methodology (AIM)[9] with the AIMPAC program package[10] at the B3LYP/6-31+G** level. From all the criteria proposed by Koch and Popellier[11] based on the AIMs theory to establish hydrogen bonding, we have chosen the electron density at the bond critical point (ρ_{BCP}) and its Laplacian ($\nabla^2\rho_{BCP}$) as representative for this kind of interaction. In addition, since the energy density at the bond critical point (H_{BCP}) has proved to be a more sensible and appropriate index than $\nabla^2\rho_{BCP}$ to characterizing the nature of hydrogen bonds,[12] we have also used it in this study. Thus, whereas positive $\nabla^2\rho_{BCP}$ values are usually associated to ionic bonds or to HBs, H_{BCP} can become negative in some HBs, which demonstrates the real strength of those bonds. Moreover, in a previous paper,[13] we suggested that these two criteria could be used to characterize HBs. Thus, we found that weak HBs show both $\nabla^2\rho_{BCP}$ and $H_{BCP} > 0$ and medium HBs show $\nabla^2\rho_{BCP} > 0$ and $H_{BCP} < 0$, while strong HBs show both $\nabla^2\rho_{BCP}$ and $H_{BCP} < 0$.

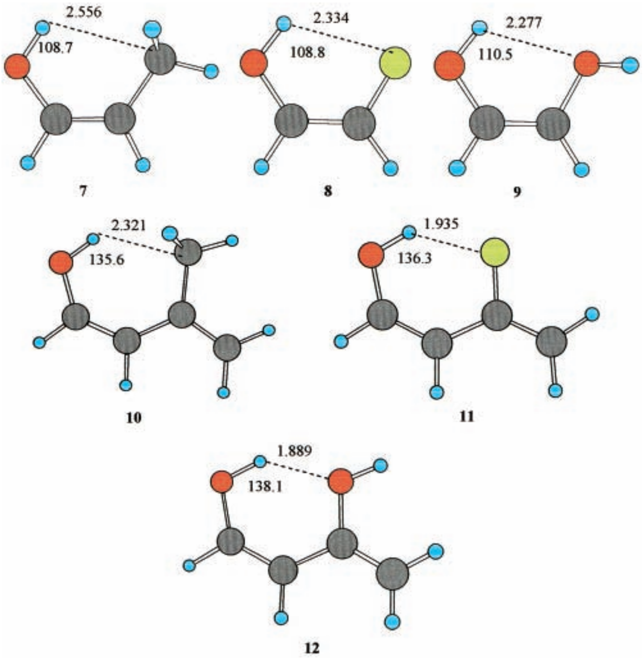


Figure 2. Optimized structures (at the B3LYP/6-31+G** level) of the hydroxyethene and hydroxy-1,3-butadiene derivatives **7** to **12**. The interaction distances (Å) and angles (deg) are shown.

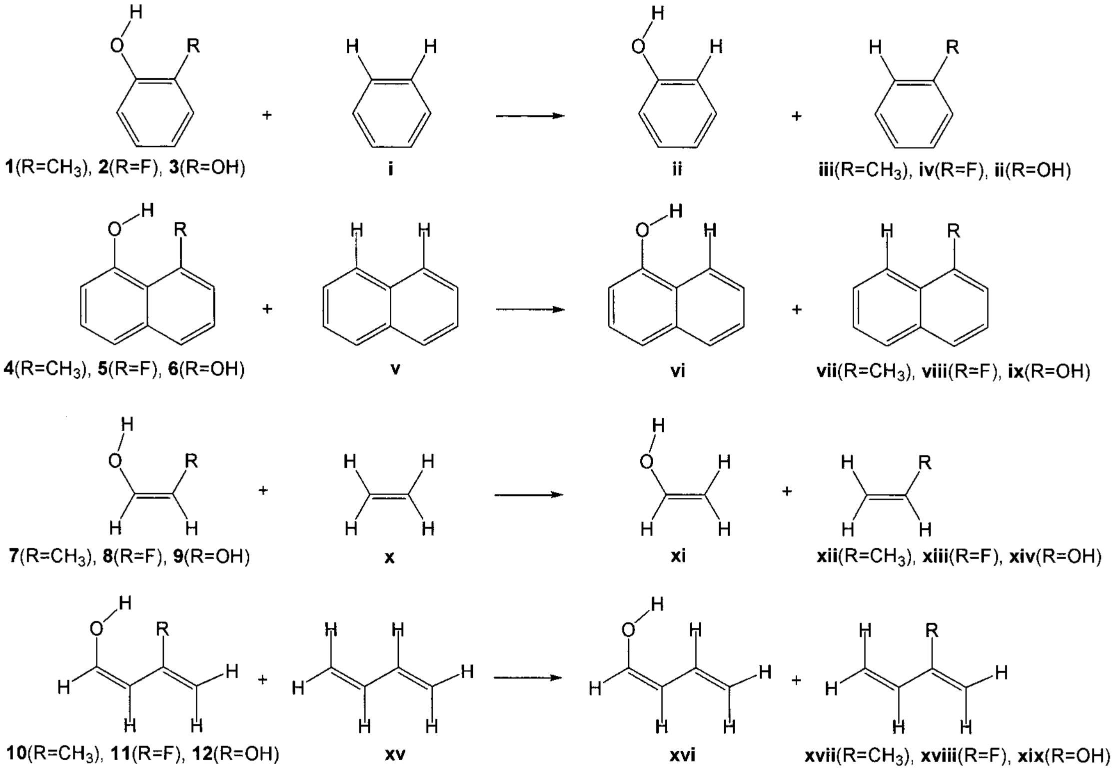
In addition, it has been demonstrated that the formation of an O−H···X HB results in a red shifting of the OH frequency. Considering the experimental IR results obtained by Fujii et al.[1] for cresol and other experimental data on OH frequencies, the theoretical (and experimental when found) OH stretching of all the compounds studied have been analyzed.

Results and Discussion

Geometry. The optimized geometries of the aromatic and open derivatives in their cis orientation are gathered in Figures 1 and 2, respectively. In the case of the phenol derivatives (**1**, **2** and **3**), which would form a five-member ring by the creation of a HB between the OH group and the ortho substituent, the (O)H···X (X= C, F, O) distances obtained are compatible with a HB [d(H···X) < 2.5 Å]. The calculated O−H···X angles are smaller than 120.0°, and that is not favorable for the formation of a IMHB interaction (angles acceptable in a HB are usually between 180 and 120°). However, all the naphthol derivatives (**4**, **5** and **6**), which form a six-member ring through a IMHB interaction between the OH group and the substituent in position 8, show (O)H···X distances (remarkably short, between 1.8 and 2.09 Å) and O−H···X angles (>140°) in agreement with the formation of a HB interaction.

In the case of the nonaromatic derivatives, all the hydroxyethene derivatives **7**, **8**, and **9** (forming a five-member ring by a IMHB interaction) show calculated (O)H···X distances smaller than 2.5 Å but O−H···X angles that are not compatible with the formation of a HB interaction (<120°). Furthermore, the three hydroxybuta-1,3-dienes (**10**, **11**, and **12**) exhibit (O)H···X distances and O−H···X angles (>135°) in agreement with the formation of a HB interaction.

SCHEME 2



SCHEME 3

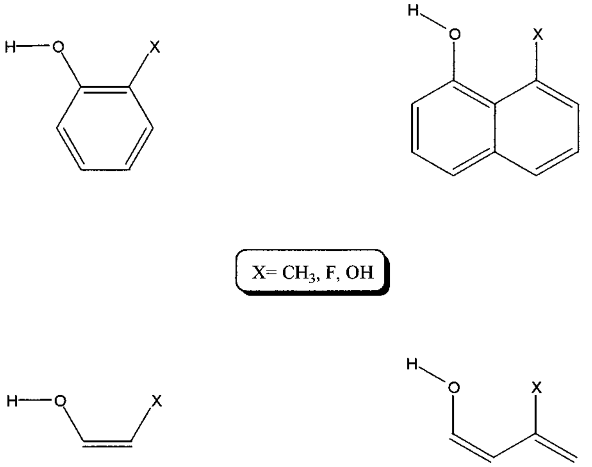


TABLE 1: Total Energies, Including the ZPE Correction (E_T(ZPE), au) and HB Interaction Energies Calculated from the Corresponding Isodesmic Reactions showed in Figure 4 (E_I(ID), kcal mol^{-1}), and Relative Energies Estimated from the Difference in Energy between the *cis*-OH and *trans*-OH Isomers (E_I(*ct*), kcal mol^{-1}) for Compounds 1−12 Computed at the B3LYP/6-31+G Level**

compound	E_T(ZPE)	E_I(ID)	E_I(ct)
1	−346.682544	0.35	0.50
2	−406.637017	0.90	−2.87
3	−382.611768	−0.46	−4.19
4	−500.277546	4.02	1.81
5	−560.241712	−0.98	−3.93
6	−536.217184	−2.39	−6.60
7	−193.062341	0.35	−0.73
8	−253.013342	3.43	−3.33
9	−228.987118	2.73	−4.11
10	−270.435781	1.85	−0.03
11	−330.400399	−2.84	−5.49
12	−306.375352	−4.23	−7.74

Energy. The interaction energy of an HB can be easily calculated as the difference between the energy of the complex and that of the isolated molecules.[14] However, in the case of IMHBs, such an approach cannot be followed, and until now there, has been no direct way to calculate the stabilization energy of an IMHB.

Several approaches have been followed to evaluate this kind of intramolecular stabilization. One possible approach is that of the isodesmic reactions that are "... transformations in which the numbers of bonds of each formal type are conserved and only the relationships among the bonds are altered...".[15] The isodesmic reactions used for the present study are shown in Scheme 2. It can be seen that the only feature not present in the right-hand side of the equations are the IMHBs, and therefore, the energy balance of these equation would yield the stabilization energy due to these interactions (E_I(ID) in Table 1). Thus, all the structures involved in these isodesmic reactions (compounds **i-xix**) were optimized at the B3LYP/6-31+G** level (see Table 2) and the energy balance calculated. From the values reported in Table 1 compounds **1**, **2**, **4**, **7**, **8**, **9**, and **10** show positive E_I(ID)s, meaning that the (O)H···X interaction is a repulsive interaction.

The values obtained for the hydroxybenzene derivatives indicate that only a IMHB interaction would be possible in the case of the catechol **3**, in which a weak O−H···O−H bonding interaction occurs (−0.46 kcal.mol^{-1}). In the case of the 1-hydroxynaphthalene derivatives, both compounds with F and OH groups as HB acceptors show negative interaction energies, indicating the formation of a bonding interaction. The isodesmic energies obtained for the hydroxyethene derivatives are always positive; thus, no IMHB can be considered. Finally, the 1-hydroxy-1,3-butadiene derivatives with F or OH as possible HB acceptors show negative isodesmic energies showing the formation of a bonding interaction. It should be noted that in all the cases in which CH_3 would be the IMHB acceptor, the interaction energies obtained are positive.

Another approach widely used to define IMHB energies is considering the difference between the bridging intramolecular system (here denoted as *cis*-OH isomers) and that obtained after rotating the OH group 180° around the C−O bond (here denoted as *trans*-OH isomers). To evaluate the E_Is using this approach, the corresponding *trans*-OH isomers of all the compounds studied (see Scheme 3) were optimized (see Table 3) at the same level of calculation used for the *cis*-OH isomers (B3LYP/6-31+G**). According to this approximation, the difference in energy between the *cis*-OH and *trans*-OH isomers (denoted as E_I(ct) in Table 1) will denote the stabilization ($E_I(ct) < 0$) or destabilization ($E_I(ct) > 0$) energy due to the possible IMHB present in the cis isomers. Thus, by looking at the E_I(ct) values, we observed that in most cases the *cis*-OH isomer is more stable than the *trans*-OH one. Exceptions are those structures with a CH_3 group, compounds **1** and **4** in which the *trans*-OH is more stable, and compounds **7** and **10** in which both are almost equally or slightly more stable the *cis*-OH isomer. These exceptions are quite interesting because it seems that the H···C interaction is even less favored than that between the lone pairs of the O atoms and the two H atoms of the methyl groups.

Both methods of evaluating the intramolecular interaction energy provide similar positive or negative interaction energies in most of the cases except in compounds **2**, **7**, **8**, **9**, and **10**. In the cases in which similar attractive or repulsive interactions are suggested, the cis/trans approach seems to favor the energy of the cis isomers (see Table 1). Even though the values obtained for compounds **7** and **10** are different in the sign of the interaction energy, the difference between them is only of 1 or 2 kcal.mol^{-1}. However, in the case of *o*-fluorophenol (**2**), 1-fluoro-2-hydroxyethene (**8**), and 1,2-ethenediol (**9**), whereas the isodesmic method proposes repulsive interactions, the cis/trans approach suggests attractive ones with a difference of 4, 6, and 7 kcal.mol^{-1} respectively.

To compare these two methods of evaluating the intramolecular interaction energy and to evaluate which one describes this energy better, several correlations with different parameters were performed. From all those intended, a correlation between E_I(ct) and the OH IR frequency was found [$E_I(ct) = (0.050 \pm 0.006)\,\nu_{IR}$, $n = 12$, $r^2 = 0.87$]. However, this correlation is not very relevant because the IR data comes from each of the cis or trans rotamers and it is not a surprise that they would be related to the difference between their corresponding energies. When comparing E_I(ID) versus E_I(ct) in the 12 cases studied, $r^2 = 0.73$ results. However, a graphical representation of this correlation (Figure 3) shows that when excluding compounds **8** and **9**, better statistical parameters are obtained [$E_I(ID) = (1.673 \pm 0.685)E_I(ct)$, $n = 12$, $r^2 = 0.85$]. These two compounds (1-fluoro-2-hydroxyethene and 1,2-ethenediol) are the ones showing the largest difference in the values of both E_Is (around 6 to 7 kcal.mol^{-1}; see Table 1). In the case of the isodesmic energies, the values obtained in both cases are extremely repulsive (+3.43 and +2.73), but no explanation could be found for such a large repulsion, which was not observed in related structures (see in Table 1 compounds **2** and **3**, **5** and **6**, and **11** and **12**).

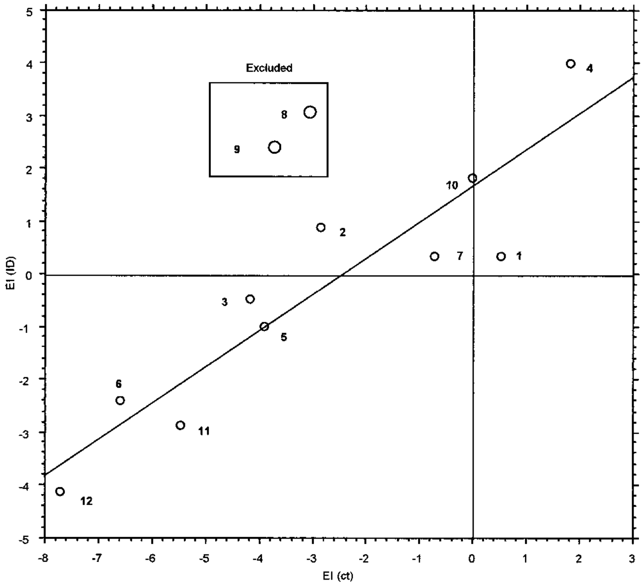


Figure 3. Graphical representation of the correlation found between E_I(ID) vs E_I(ct).

TABLE 2: Total Energies, Including the ZPE Correction (E_T(ZPE), au) Calculated for the Compounds (i−xix) Involved in the Corresponding Isodesmic Reactions Shown in Figure 4 at the B3LYP/6-31+G Level**

compound	E_T(ZPE)	compound	E_T(ZPE)
i	−232.16795	**xi**	−153.77102
ii	−307.38950	**xii**	−117.84053
iii	−271.46156	**xiii**	−177.79645
iv	−331.41690	**xiv**	−153.76910
v	−385.77213	**xv**	−155.92559
vi	−460.99187	**xvi**	−231.14589
vii	−425.06421	**xvii**	−195.21842
viii	−485.02041	**xviii**	−255.17556
ix	−460.99364	**xix**	−231.14830
x	−78.54866		

TABLE 3: Total Energies, Including the ZPE Correction (E_T(ZPE), au) Calculated for the *trans*-OH Isomers of Compounds 1−12 at the B3LYP/6-31+G Level**

compound	E_T(ZPE)	compound	E_T(ZPE)
1-t	−346.683348	**7-t**	−193.061181
2-t	−406.632438	**8-t**	−253.008037
3-t	−382.605087	**9-t**	−228.980563
4-t	−500.280427	**10-t**	−270.435727
5-t	−560.235450	**11-t**	−330.391652
6-t	−536.206663	**12-t**	−306.363018

Electron Density Analysis. The topological analysis of the electron density of all the systems show that only compounds **3**, **4**, **5**, **6**, **10**, **11**, and **12** exhibit a bond critical point (BCP) between the H atom of the OH group (HB donor) and the corresponding HB acceptor, O(H), in the case of compounds **3**, **6**, and **12**, F in the case of compounds **5** and **11**, and, interestingly, C(H_3) in the case of compounds **4** and **10**. The electron density at those BCPs the Laplacian of that electron density and the energy density at those BCPs are gathered in Table 4. In all the cases, the ρ_{BCP}s are on the order of 10^{-2}, in agreement with a HB interaction, and the values of $\nabla^2\rho_{BCP}$ and H_{BCP} would correspond to weak HBs according to our own classification (both positive values).[13]

However, the presence of a BCP between a H atom and an acceptor one, with the characteristics already mentioned of electron density in such a point, cannot be taken as an absolute indicator of a bonding interaction and more particularly of a HB. In the systems studied in this article, only those with F and OH as acceptors and only in the cases in which a six-member ring is formed by means of the H···X interaction show a bonding interaction that could be described as a IMHB because only in those cases negative interaction energies are obtained (see Table 1) and an appropriate BCP is found. Compound **3** exhibits the same situation; despite the fact that the interaction between the H and the acceptor (an OH) will form a five-member ring, the interaction energy is negative (though very small). This indicates a weak IMHB.

TABLE 4: Electron Density (ρ_{BCP}, e/au^3), Laplacian ($\nabla^2\rho_{BCP}$, e/au^5), and Energy Density (H_{BCP}, hartree/au^3) Calculated at the Bond Critical Points of the Possible IMHBs Formed in Compounds 1−12 with the B3LYP/6-31+G Method[a]**

compound	ρ_{BCP}	$\nabla^2\rho_{BCP}$	H_{BCP}	d(H$\cdots$X)	a(O−H$\cdots$X)
1	−	−	−	2.409	112.3
2	−	−	−	2.232	111.0
3	0.017	0.080	0.002	2.157	112.9
4	0.022	0.074	0.001	2.089	143.0
5	0.028	0.095	−0.002	1.856	141.2
6	0.034	0.117	0.001	1.800	142.6
7	−	−	−	2.556	108.7
8	−	−	−	2.334	108.0
9	−	−	−	2.277	110.5
10	0.014	0.052	0.002	2.321	135.6
11	0.024	0.081	−0.001	1.935	136.3
12	0.028	0.094	0.000	1.889	138.1

[a] The distance (Å) and angle (deg) of such interactions are also included.

In the cases of compounds **4** and **10** in which a six-member ring would be formed but the HB acceptor is a methyl group, the finding of a BCP with the appropriate characteristics is only an indication of a certain amount of electron density found between the H and C atoms. But the positive interaction energy values found indicate a repulsive interaction, which, obviously, is not a HB.

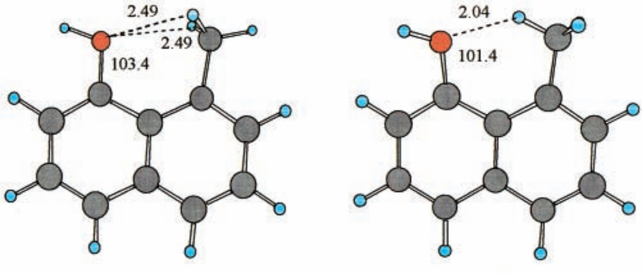
O−H Distances and Vibrational Frequencies. Before 1965, the most important methods for the study of HB were spectroscopic and, in particular IR, Raman and NMR spectroscopies. The shift to lower frequencies of the IR X−H stretching band reflecting the weakening of such a bond as a result of the HB formation was a major indicator. At present and more in particular in the case of O−H derivatives, IR spectroscopy continues being a technique widely used to study the possible formation of HBs. Examples are not only the work already mentioned of Fujii[1] but also those of Gerhards on catechol[16] and on resorcinol and hydroquinone.[17] Also, computational studies have been performed to evaluate the IR frequencies and shifts associated to the formation of a HB. That has been the case in the previously mentioned work by Knak Jensen[2] and also the study of Trindle on the *o*-cresol radical cation.[18] It has to be mentioned that experimental shifts to higher frequencies associated with the formation of a HB have been recently reported.[19]

The O−H stretching vibrations, calculated for all the compounds studied in this work (cis and trans isomers) at the B3-LYP/6-31+G** level of theory, are collected in Table 5. The corresponding experimental values are also included, except for compounds **5**, **7**, **8**, **10**, **11**, and **12**, which, to our knowledge, have neither been prepared nor for which experimental data can be found. For those compounds in which an IMHB is expected considering the interaction energies [E_I(ID)] and electron density characteristics, a shift to lower frequencies is found when comparing the trans isomer with the cis one, that is, when the IMHB is formed. These shifts can be small like in the case of compounds **3** and **5** (−40 and −20 cm^{-1}, respectively), in agreement with the small interaction energies computed (−0.46 and −0.98 kcal mol^{-1}, respectively). On the contrary, large shifts are obtained for compounds **6**, **11**, and **12** (−103, −94, and −165 cm^{-1}, respectively), in agreement also with the interaction energies calculated (−2.39, −2.84, and −4.23 kcal mol^{-1}, respectively). Thus, the larger the shift is to lower frequencies, the stronger the IMHB formed is [shift = (38 ± 3)E_I(ID), n = 5, r^2 = 0.976].

TABLE 5: O−H Stretching Vibrations (cm^{-1}) and Distances (Å) Calculated for Compounds 1−12 with the B3LYP/6-31+G Method[a]**

compound	ν_{exp}	$\nu_{B3LYP/6-31G**}$	d(O−H)
1	3655[20] 3620[21]/3613[22] 3610−3540[23] 3645[24]/3628[25]	3839 (+11)	0.965
1-t	3655[20]	3828	0.966
2	3634−3495[26] 3591[27]/3616[25]	3803 (−27)	0.968
2-t		3830	0.966
3	3700−3200[28]/3566[29] 3620−3575[30]/3567[31] 3554−3300[32] 3617−3568[33]/3554[34]	3790 (−40)	0.969
3-t		3830	0.965
4	3600[35]	3879 (+55)	0.962
4-t		3824	0.966
5	−	3799 (−20)	0.968
5-t	−	3819	0.967
6	3153[36]	3714 (−103)	0.971
6-t		3817	0.966
7	−	3812 (−55)	0.967
7-t	−	3867	0.964
8	−	3791 (−77)	0.969
8-t	−	3868	0.964
9	3280[37]	3773 (−95)	0.971
9-t	−	3868	0.963
10	−	3832 (−30)	0.966
10-t	−	3862	0.964
11	−	3761 (−94)	0.971
11-t	−	3855	0.964
12	−	3690 (−165)	0.975
12-t	−	3855	0.964

[a] When found, experimental frequencies were included. The frequency shifts between cis and trans isomers appear between parentheses.



4-t **4-tt**

Figure 4. Optimized structures of the trans rotamers of compound **4** (**4-t** and **4-tt**).

Curiously, in those compounds showing a BCP but with positive interaction energies (compounds **4** and **10**), the shifts in the OH frequencies calculated do not follow the same trend. Thus, whereas the shift for compound **4** is to higher frequencies (+55 cm^{-1}), the shift for compound **10** goes to lower frequencies (−30 cm^{-1}). For the particular case of *o*-cresol (**1**), as it happens to the naphthalene analogue **4**, the shift is to higher frequencies (+11 cm^{-1}).

Case of 8-Methyl-1-hydroxynaphthalene (4). The particular case of compound **4**, in which, despite the repulsive intramolecular interaction energy computed, a shift of the OH vibration to higher frequencies was found, was studied more in detail. Thus, another possible situation was considered, that in which a C−H of the methyl group in position 8 would be forming a IMHB with the O(H) in position 1 producing a six-member ring. This possible C−H$\cdots$O(H) interaction could be responsible of the frequency shift observed for the O−H bond. The two possible situations are represented in Figure 4 by the optimized structures of rotamers **4-t** and **4-tt**. The computations at B3LYP/6-31+G** showed that rotamer **4-t** was a minimum in the potential energy, whereas the **4-tt** isomer showed an imaginary frequency. In both cases, the interaction energy calculated from the corresponding isodesmic equations was positive (3.32 and 3.98 kcal mol^{-1} respectively), showing a nonbonding interaction. BCPs were found for both structures. In the case of **4-t**, two symmetric BCPs ($\rho_{BCP} = 0.014$, $\nabla^2\rho_{BCP} = 0.062$, and $H_{BCP} = 0.002$, au) were found between each one of the C−H and the O(H) and in the case of **4-tt**, one BCP ($\rho_{BCP} = 0.022$, $\nabla^2\rho_{BCP} = 0.080$, and $H_{BCP} = 0.001$, au) was found between the C−H and the O(H). The distances between the (C)H and the O(H) atom were 2.493 Å for each of the H atoms in **4-t** and 2.041 Å for the **4-tt** rotamer. Finally, the O−H distances and frequencies were 0.966 Å and 3824 cm^{-1} for **4-t** and 0.962 Å and 3820 cm^{-1} for **4-tt**. Compared with isomer **4** (3879 cm^{-1}), these vibrations result shifted to lower frequencies by 55 and 59 cm^{-1}.

Now, considering that in **4-t** and **4-tt** the possible HB donor is the CH_3 group, we should compare the shifts of the C−H frequencies with respect to compound **4**. In the case of compound **4-t**, because the possible HB donors are the two*o*-methyl H atoms out of the plane, we should compare both the symmetric and antisymmetric frequencies that affect those H atoms. Thus, compound **4** shows the symmetric frequency at 3009 and the antisymmetric at 3064 cm^{-1}, whereas **4-t** has the symmetric vibration at 3053 and the antisymmetric one at 3120 cm^{-1}. This means that shifts of $+44$ cm^{-1} are observed in both cases. In the case of the **4-tt** isomer, the vibrations to be compared are those of the C−H on the aromatic plane. Thus, for compound **4**, this vibration appears at 3117 cm^{-1}, whereas for compound **4-tt**, this C−H vibration appears at 3234 cm^{-1}, meaning a shift of $+117$ cm^{-1} to higher frequencies.

Considering all these results in terms of isodesmic interaction energies, electron density characteristics and vibrational frequencies it can be concluded that the CH_3 group, which, in some cases, has been considered as a weak HB donor; in this particular case, it does not act as a HB donor to form any IMHB with the OH group of compound **4**.

Conclusions

Answering the question formulated in the Title and Introduction and taking into account HB distances and angles, interaction energies (from isodesmic reactions), and electron density characteristics, we can conclude that, in general, the methyl group cannot behave as a HB acceptor, even though in the case in which a six-member ring is formed, as in compounds **4** and **10**, a BCP between the OH and methyl groups is obtained, the calculated interaction energy (by both isodesmic and cis/trans approaches) being positive or null indicating repulsive interactions. The formation of such as BCPs can be explained by the atomic congestion in a spatial region due to the rigidity of the systems considered. In addition, the formation of IMHB driving to the formation of five-member rings (compounds **1**-**3** and **7**-**9**) seems not to be favored even if the HB acceptor is a good acceptor. Only in the case of 1,2-dihydroxybenzene (**3**) does a IMHB seem to be formed between both OH groups but with a very small interaction energy (E_I(ID) $= -0.46$ kcal.mol^{-1}) and with electron density characteristics in agreement with weak HBs (small ρ_{BCP}, and positive $\nabla^2\rho_{BCP}$ and H_{BCP} values).

In terms of the method used to evaluate the intramolecular interaction energy, it seems that the isodesmic reactions provide more reasonable results than the cis/trans approach. This latter method overestimates these energies and suggests attractive interactions in cases where electron density analysis shows no BCPs between the (O)H and the HB acceptor. Thus, we can reach the conclusion that the E_I(ct) only reflects which rotamer is more stable and, therefore, it cannot be used to measure the IMHB interaction energy which seems to be better evaluated by the E_I(ID)s.

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