Energetics of Intramolecular Hydrogen Bonding in Di-substituted Benzenes by the ortho−para Method

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The energetics of intramolecular hydrogen bonds (H-bonds) is a subject of fundamental importance in chemistry and biochemistry. In contrast with intermolecular H-bonds, whose enthalpy can be determined by experiment or accurately evaluated through a supermolecular approach, there is no general accepted procedure to determine the enthalpy of an intramolecular H-bond. In this work, different ways for assessing the energetics of intramolecular H-bonds of selected aromatic systems were applied and compared. They include the widely used conformational analysis approach (cis−trans method), a recently proposed isodesmic reaction method, and a new procedure that we designate as the ortho−para method. Energy calculations were carried out at several theory levels, including a modified complete basis set extrapolation method (CBS-QMPW1), in which the geometries are based on MPW1PW91/aug-cc-pVDZ density functional theory optimizations. The obtained results, together with a simple dipole−dipole interaction model, help to explain why the enthalpies of intramolecular H-bonds are often overestimated by the cis−trans method. The results also show that intramolecular H-bond enthalpies based on the isodesmic reaction method may be unreliable. The ortho−para method, which can be applied when accurate theoretical or experimental standard enthalpies of formation are available, is probably the best way of estimating the enthalpies of intramolecular hydrogen bonds. Finally, our results illustrate the important role played by intramolecular H-bonds in the energetics of homolytic dissociation reactions involving di-substituted benzenes.

1. Introduction

The importance of hydrogen bonds (hereafter abbreviated as H-bonds) in chemistry and biochemistry has long been recognized.[1−11] However, as noted by Jeffrey, “understanding their electronic nature appears to be more ellusive than for covalent and ionic bonds and van der Waals forces [...] because the term H-bond applies to a wider range of interactions”.[4] Although the nature of H-bonds is a controversial issue, it is generally accepted that an H-bond bond is at least as a strong as a van der Waals interaction, and that it can be described by long-range forces, which involve electrostatic, many-body induction, and dispersion contributions.[7a] Another controversial issue concerns the need to consider charge transfer as a fundamental aspect of hydrogen bonding.[7a,8] Some specific structural, energetic, vibrational, and electronic features are typical of hydrogen bonding (see, e.g., refs 5 and 7a for a detailed discussion).

There are many experimental techniques and methodologies that can be used to probe the energetics of *intermolecular* H-bonds.[2,4] For instance, equilibrium methods in solution can yield rather accurate data. A good example of this procedure is provided by an elegant study by Sousa Lopes and Thompson, where the authors report equilibrium constants of reaction 1 in tetrachloroethylene, at several temperatures, and use van’t Hoff plots to derive the reaction enthalpy and entropy (identified with the enthalpy and entropy of the H-bond between phenol and acetonitrile)[12]

$$\mathrm{PhOH\ (sln)} + \mathrm{CH_3CN\ (sln)} = \mathrm{PhOH\text{- - -}NCCH_3\ (sln)} \quad (1)$$

The available database of equilibrium constants for reactions similar to reaction 1 is fairly large. This information even allowed the calculation of empirical functional group parameters, which can be used to predict new values.[13] By contrast, the experimental data for *intramolecular* H-bonds are scarce. The reason is understandable: in most cases it will not be easy to conceive an experimental method that affords a “direct” value of the enthalpy of an intramolecular H-bond simply because that H-bond is an intrinsic feature of the ground-state structure of the molecule.[2,4,14] This has been noted before by Lampert et al., who made a detailed study of H-bonding in 2-hydroxybenzoyl compounds.[15] These authors observed good linear correlations between intramolecular H-bond energies and O−H stretching frequencies, both computed at several theoretical levels (frequency shifts are usually accepted as gauging H-bond enthalpies). Some studies have related experimental information on O−H torsional and stretching infrared band intensities relative to the amounts of conformers that were hydrogen bonded (cis) and non-hydrogen bonded (trans).[16] This relationship was based on the observation of two different infrared O−H stretching bands in *ortho*-substituted phenols, which were associated with the presence of the two conformers. By assuming that the entropy variation for the cis−trans inter-

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conversion is essentially zero, the enthalpy difference between the two conformers has been estimated from a Boltzmann distribution.[16]

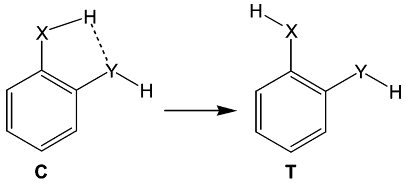
From a theoretical point of view, intramolecular and intermolecular H-bonds are of a similar nature. Intermolecular interactions are usually investigated through a supermolecular approach, where the interaction enthalpy is evaluated as the difference between the energies of a supermolecular complex and its fragments. Such an approach cannot be used to study intramolecular interactions. Consequently, some specific theoretical procedures were proposed to investigate the enthalpy of intramolecular H-bonds. The most commonly used is based on energetic conformational analysis:[9,15−25] for two conformers, which essentially differ by the presence of one intramolecular H-bond, the energy (or the enthalpy) of the bond is estimated as the difference between their energies. A second approach involves the definition of isodesmic reactions leading to bond breaking/formation related to specific intramolecular H-bonds interactions (see section 2).[21] However, the prediction of intramolecular H-bond enthalpies is still an open problem that certainly deserves further investigation.

In the present work, we report a study of intramolecular hydrogen bonding in several di-substituted benzenes. This investigation had two main objectives: first, to analyze the reliability of different approaches to estimate the enthalpy of H-bonds in those compounds; second to test a new procedure, which we believe is a significant improvement in comparison to the conformational and isodesmic approaches referred above. The obtained results are, in addition, used to discuss the importance of intramolecular H-bonds in the energetics of homolytic dissociation reactions in di-substituted benzenes.

The article is organized as follows: theoretical procedures for assessing the strength of intramolecular H-bonds are reviewed in section 2. Section 3 details the computational methods. The results are presented and discussed in section 4.

2. Theoretical Evaluation of the Intramolecular Hydrogen Bond Enthalpy in Di-substituted Benzenes

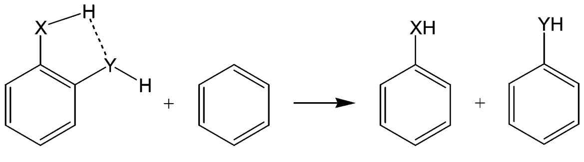
Conformational Analysis. As mentioned above, the most common approach to investigate the energetics of intramolecular H-bonds is based on conformational analysis.[9,15−25] In this approach, the enthalpy of an H-bond is assessed by comparing the energies (or enthalpies) of two conformers that differ by an intramolecular stabilizing interaction, which can be associated with a hydrogen bond. In the particular case of di-substituted benzenes, this can be defined in terms of the cis−trans method, which is illustrated in reaction 2 and can be summarized as follows. Consider, for example, the two isomeric forms of the same molecule, cis (C) and trans (T**)**. The ground-state structure (C) is stabilized by the intramolecular H-bond, whereas the trans isomer (T), where the X−H bond is rotated around the C−X bond by 180°, is not. The energy difference between them can thus be associated with the enthalpy of the intramolecular H-bond. There are, however, two options to compute the energy of T: either (1) this energy is obtained by a single point calculation of a structure identical to C, except for the 180° rotation of the X−H bond, or (2) the energy is calculated for an optimized structure of T (keeping the *trans*-conformation), i.e., it corresponds to the ground state energy of this species. In both cases the enthalpy difference between the two isomers can be assigned to the intramolecular H-bond, but the results are not necessarily the same (see below).[26] The higher value, obtained from the first alternative, which we can call the "pure" cis−trans method, reflects the "strength" or the "bond snap enthalpy" of the H-bond, since it does not involve the exothermic relaxation of the molecule to its ground state. The second approach, which is most commonly used, yields a lower value for the enthalpy of the intramolecular H-bond and, since it includes the relaxation of T, it is a true "bond dissociation enthalpy". This second approach will be adopted in the present paper.



(2)

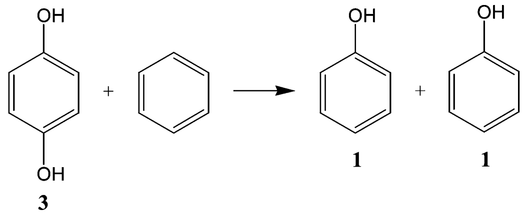
The reliability of the cis−trans method to estimate the energetics of intramolecular hydrogen bonding is a controversial issue in the literature.[18,19,21] Some criticism has been raised because the energetic stabilization of C includes several contributions, such as the balance between attractive and repulsive terms, sterical constraints of the benzene ring, conjugation, and other interactions, making it difficult to attribute only to the H-bond the energy difference between the two conformers.[21] There is also some indication, which is based on the comparison between theoretical calculations [17,19,21] and experimental information,[17] that the intramolecular H-bond enthalpy in catechol, evaluated by the cis−trans method, is overestimated.

Isodesmic Reaction. In this method, an isodesmic reaction associated with an intramolecular H-bond breaking/formation, such as reaction 3, is used to estimate the H-bond strength.



(3)

The idea behind this approach, which has been recently applied to catechol (**2**),[21] is that the XH- - -Y hydrogen bond enthalpy can be identified with the enthalpy of the isodesmic reaction 3. However, if this were exact, then the isodesmic reaction 4 should be thermoneutral.



(4)

For hydroquinone (**3**) our most accurate theoretical calculations predict that $\Delta_r H_4° = -4.3$ kJ mol^{-1} (larger deviations from thermoneutrality are obtained for the equivalent reaction involving radicals; see section 4). It can be argued that the exothermicity of reaction 4 indicates that the introduction of a *para*-OH group in phenol has a destabilizing effect.[27,28] If one assumes that the electronic effects of the *ortho*- and *para*-OH substituent on the energetics are comparable, then the enthalpy of reaction 3 (for X = Y = OH) cannot be exclusively assigned to the cleavage of the intramolecular H-bond.

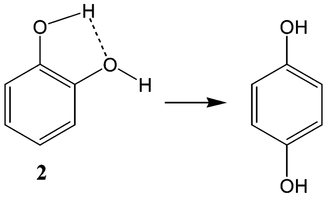
ortho−para Approach. Although the isodesmic approach may provide a different route to assess intramolecular H-bond strengths, we believe that it can be significantly improved.

TABLE 1: Intramolecular H-Bond Enthalpies (kJ mol^{-1}) Based on Different Methods and on Several Theory Levels[a]

	method								
	cis−trans			isodesmic			ortho-para		
compound	DFT[b]	CBS-4M	CBS-QMPW1	DFT[b]	CBS-4M	CBS-QMPW1	DFT[b]	CBS-4M	CBS-QMPW1
				Cathecol					
2	15.5	17.3	16.9	0.4	4.1	5.3	8.6	9.6	9.6
2r	37.3	33.9	35.7	39.5	31.8	38.9	26.5	22.2	25.1
Δ	21.8	16.6	18.8	39.1	27.7	33.6	17.9	12.6	15.5
				ortho-Benzenedithiol					
2	3.8	0.0	3.5	−1.8	2.6	4.5	0.6	5.5	5.5
2r	10.0	4.3	5.9	13.4	8.1	13.0	6.1	2.0	6.6
Δ	6.2	4.3	2.4	15.2	5.5	8.5	5.5	−3.5	1.1
				ortho-Benzenediamine					
2				−2.4	−4.7	5.1	8.7	3.9	10.8
2r				28.4	29.1	30.4	16.1	15.3	30.8
Δ				30.8	33.8	25.3	7.4	11.4	20.0
				ortho-Methoxyphenol					
2	16.8	19.1	18.6	2.1	6.2	7.4	9.8	11.8	11.6

[a] Δ represents the difference between the intramolecular H-bond enthalpy in the radical and in the corresponding parent molecule. [b] DFT calculations at the MPW1PW91/aug-cc-pVDZ level.

Taking into consideration the fact that reaction 4 is not thermoneutral, a better way of estimating the enthalpy of the intramolecular H-bond in catechol is through $\Delta_r H_3^\circ - \Delta_r H_4^\circ$. This difference represents the enthalpy of reaction 5 and in this particular case, only the energies of catechol (**2**) and hydroquinone (**3**) are required.



2 **3**

(5)

It is worth stressing the main difference between this approach and the cis−trans method of reaction 2 (X = Y = O). The repulsive interactions between the oxygen atoms, as well as the O−H dipole−dipole interactions, are significant in catechol (**2**) and negligible in hydroquinone (**3**).

3. Computational Details

Density functional theory (DFT) geometry optimizations were carried with the Barone and Adamos's Becke style one parameter functional, using a modified Perdew−Wang exchange (MPW1)[29] and Perdew−Wang 91 correlation,[30] a combination represented by MPW1PW91.[31] Total energies (E) were obtained from eq 6,[32] where V_{NN} is the nuclear−nuclear interaction, H^{CORE} is a monoelectronic contribution to the total energy, including electron kinetic and electron−nuclear interaction energies, and V_{ee} is the Coulombic interaction between the electrons

$$E = V_{NN} + H^{CORE} + V_{ee} + E_X[\rho] + E_C[\rho] \qquad (6)$$

The terms $E_X[\rho]$ and $E_C[\rho]$ represent respectively the exchange and correlation energy functionals of the electronic density ρ. The geometries were fully optimized with the Dunning double-ζ correlation consistent basis set, including diffuse functions (aug-cc-pVDZ).[33] Vibrational frequency analysis was used to confirm that stationary points were minimum energy structures and to calculate zero-point energy (ZPE) corrections. Harmonic frequencies were not scaled.[34]

Several theoretical works on the energetics of homolytic bond dissociation indicated that, in general, DFT methods, which can be based in different representations of the $E_{XC}[\rho] = E_X[\rho] + E_C[\rho]$ exchange correlation functional, systematically underestimate homolytic bond dissociation enthalpies.[35] On the other hand, it is known that DFT predicts structural properties in very good agreement with experiment.[36] Therefore, we decided to evaluate total energies by using DFT-optimized geometries.[36] A composite quantum mechanical approach based on the complete basis set extrapolation CBS-QB3[36−38] was adopted. The main difference between the present approach and the standard CBS-QB3[36] method is that in our approach the geometries are optimized at the MPW1PW91/aug-cc-pVDZ level, and no frequency scaling was used, whereas the CBS-QB3 is based on B3LYP/6-31G† optimizations, and the frequencies are scaled by 0.91844.[36] We designate the present approach as CBS-QMPW1. A strong reason to select the MPW1PW91 functional is that it provides a correct description of the structure and energetics of hydrogen bond systems.[31]

A complete basis set procedure (CBS-4M)[39] was also applied to calculate the energies of all of the molecules involved in the present study. This composite method was used because it represents a compromise between accuracy and computational effort, mainly for large molecular systems. CBS-4M calculations are based on geometry optimizations at the HF/3-21G* level, which can lead to some discrepancies with experimental geometries.

For the particular case of catechol, ab initio calculations at the Hartree−Fock (HF) level,[40] second-order Møller-Pleset perturbation theory (MP2)[41] with the frozen core (FC) approximation, and coupled cluster with both single and double substitutions (CCSD)[42,43] levels were also carried out. All the calculations were performed with the Gaussian-98 Program.[44]

4. Results and Discussion

4.1. Intramolecular Hydrogen Bonding. The theoretical results obtained from the three different approaches (cis−trans, isodesmic, and ortho−para) used to evaluate the intramolecular H-bond enthalpies in di-substituted benzenes and in the respective radical species are summarized in Table 1. These and other calculated reaction enthalpies relevant for the discussion are given in Table 2. Total energies for di-substituted benzenes from DFT (MPW1PW91/aug-cc-pVDZ), CBS-4M, and CBS-QMPW1 calculations are provided as supplementary information.

TABLE 2: Reaction Enthalpies at 298 K Calculated at the MPW1PW91/aug-cc-pVDZ, CBS-4M, and CBS-QMPW1

	$\Delta_r H^o$/kJ mol^{-1}			
reaction[a]	MPW1PW91	CBS-4M	CBS-QMPW1	obs.[b]
		Catechol		
2 + C_6H_6 → **1** + **1**	0.4	4.1	5.3	H-bond, isodesmic reaction
3 + C_6H_6 → **1** + **1**	−8.2	−5.5	−4.3	
2r + C_6H_6 → **1r** + **1**	39.5	31.8	38.9	H-bond, isodesmic reaction
3r + C_6H_6 → **1r** + **1**	13.0	9.6	13.8	
2 → **3**	8.6	9.6	9.6	H-bond, ortho−para
2r → **3r**	26.5	22.2	25.1	H-bond, ortho−para
3 → **2′**	6.9	7.7	7.3	
2 → **2′**	15.5	17.3	16.9	H-bond, cis−trans
2r → **2′r**	37.3	33.9	35.7	H-bond, cis−trans
		ortho-Benzenedithiol		
2 + C_6H_6 → **1** + **1**	−1.8	2.6	4.5	H-bond, isodesmic reaction
3 + C_6H_6 → **1** + **1**	−2.4	−3.0	−1.0	
2r + C_6H_6 → **1r** + **1**	13.4	8.1	13.0	H-bond, isodesmic reaction
3r + C_6H_6 → **1r** + **1**	7.3	6.1	6.4	
2 → **3**	0.6	5.5	5.5	H-bond, ortho−para
2r → **3r**	6.1	2.0	6.6	H-bond, ortho−para
3 → **2′**	3.2	−5.5	−2.0	
2 → **2′**	3.8	0.0	3.5	H-bond, cis−trans
2r → **2′r**	10.0	4.3	5.9	H-bond, cis−trans
		ortho-Benzenediamine		
2 + C_6H_6 → **1** + **1**	−2.4	−4.7	5.1	H-bond, isodesmic reaction
3 + C_6H_6 → **1** + **1**	−11.1	−8.6	−5.7	
2r + C_6H_6 → **1r** + **1**	28.4	29.1	30.4	H-bond, isodesmic reaction
3r + C_6H_6 → **1r** + **1**	12.3	13.7	−0.4	
2 → **3**	8.7	3.9	10.8	H-bond, ortho−para
2r → **3r**	16.1	15.3	30.8	H-bond, ortho−para
		ortho-Xylene		
2 + C_6H_6 → **1** + **1**	−1.1	−1.1	1.9	isodesmic reaction
3 + C_6H_6 → **1** + **1**	−0.8	−2.9	−0.1	
2r + C_6H_6 → **1r** + **1**	−1.2	−0.3	1.8	isodesmic reaction
3r + C_6H_6 → **1r** + **1**	0.6	0.1	1.2	
2 → **3**	−0.3	1.8	2.0	ortho−para
2r → **3r**	−1.8	−0.4	0.6	ortho−para
		ortho-Methoxyphenol		
2 + C_6H_6 → PhOH + **1**	2.1	6.2	7.4	H-bond, isodesmic reaction
3 + C_6H_6 → PhOH + **1**	−7.7	−5.6	−4.2	
2r + C_6H_6 → **1r** + **1**	7.0	3.6	8.3	isodesmic reaction
3r + C_6H_6 → **1r** + **1**	14.4	11.9	15.5	
2 → **3**	9.8	11.8	11.6	H-bond, ortho−para
2r → **3r**	−7.3	−8.3	−7.2	ortho−para
3 → **2′**	7.0	7.3	7.0	
2 → **2′**	16.8	19.1	18.6	H-bond, cis−trans
2r → **2′r**	1.2	1.4	0.9	cis−trans

[a] For each family, the molecules are identically numbered, e.g., PhOH, PhSH, $PhNH_2$, and $PhCH_3$ are denoted by **1** and their radicals by **1r**. [b] Indicates when the enthalpy refers to the intramolecular H-bond and names the corresponding method.

Catechol. Results for the energetics of the intramolecular H-bond in cathecol predicted by the cis−trans method and calculated at several theory levels are collected in Table 3.

The importance of electronic correlation effects on intramolecular H-bond enthalpies can be assessed by comparing HF with MP2 and CCSD results, which indicate that, by using the cc-pVDZ basis set, correlation effects reduce the strength of the intramolecular H-bond in cathecol by less than 2 kJ mol^{-1} (see Table 3). We observe some significant dependence of the results on the basis set. In particular, the introduction of diffuse functions contributes to reduce the enthalpy of the H-bond. By using the aug-cc-pVDZ basis set, a very good agreement between MPW1PW91 (15.5 kJ mol^{-1}) and MP2 (15.3 kJ mol^{-1}) results is observed. This agreement supports the reliability of our present approach to investigate hydrogen bonding in di-substituted benzenes, which is mainly based on MPW1PW91 optimizations. In addition, we note that the cathecol intramolecular H-bond predicted by the CBS-QMPW1 level (16.9 kJ mol^{-1}) is in perfect agreement with the standard CBS-QB3 procedure. In general, the present results also concur with other theoretical predictions reported in the literature (Table 3).[19−24,45]

As observed in Table 1, the DFT prediction for the intramolecular H-bond in catechol based on the isodesmic approach (0.4 kJ mol^{-1}) is significantly lower than the results based on the cis−trans (15.5 kJ mol^{-1}) and ortho−para (8.6 kJ mol^{-1}) methods. A similar trend is observed for CBS-4M and CBS-QMPW1 predictions. We note that the H-bond enthalpy results based on the ortho−para method are in very good agreement with experimental information (9.5 kJ mol^{-1}),[16] which was based on the relative population of cis and trans conformers derived from infrared O−H relative intensities.[16] Therefore, it appears that the isodesmic procedure is not adequate to evaluate intramolecular H-bond strengths in catechol. The origin of the discrepancies with other approaches and experimental information should be related with the enthalpy of reaction 4, which is not thermoneutral.

Another relevant issue concerns the difference between the cis−trans and ortho−para procedures. In the case of catechol

TABLE 3: Enthalpy of the Intramolecular H-Bond in Catechol Predicted by the cis−trans Method

theory level	ΔH/kJ mol^{-1} [a]	ref
HF/cc-pVDZ	17.8	this work
MP2(FC)/cc-pVDZ	16.5	this work
CCSD/cc-pVDZ	16.6[b]	this work
MP2(FC)/aug-cc-pVDZ	15.3[b]	this work
MPW1PW91/cc-pVDZ	19.5	this work
MPW1PW91/aug-cc-pVDZ	15.5	45
B3LYP/6-31G(d,p)	17.2	23, 24
UB3LYP/6-31+G(,3pd)	21.2	20
B3LYP/6-31+G(d,p)	17.5[c]	21
B3LYP/6-311G(d)	18.9[c]	19
(RO)B3LYP/6-311+G(2d,2p)// B3LYP/6-31G(d)//B3LYP/6-31G(d)	15.9	22
CBS-4M	17.3	45
CBS-QMPW1	16.9	this work
CBS-QB3	16.9	this work

[a] T = 298.15 K, except when indicated otherwise. The results involved the structure optimization of the trans conformer. [b] Single-point energy calculation. Geometry optimized at the MP2(FC)/cc-pVDZ level. [c] T = 0 K.

it amounts to 7.3 kJ mol^{-1} (CBS-QMPW1). As mentioned above, it is difficult to define a "true" H-bond enthalpy. For this purpose, a simplified approach can be helpful. By using charges fitted to the electrostatic potential (ESP charges),[46] the O−H dipole−dipole interactions for the cis (**2**) and trans (**2′**) configurations of cathecol were evaluated. The atomic charges were obtained at the MPW1PW91/aug-cc-pVDZ level and the dipoles were calculated by taking as origin the midpoint of the O−H bond. Deviations from neutrality of the O−H groups make the dipoles origin dependent. However, it was verified that the electrostatic energy *difference* between the conformers can be correctly represented by a dipole−dipole interaction model. The results for the dipoles are 2.43 and 2.35 D for the cis (**2**) and 2.0 D for the trans conformer (**2′**), leading to an attractive dipole−dipole interaction $E_{dd}(2) = -16.6$ kJ mol^{-1} in catechol, and a repulsive interaction $E_{dd}(2') = 10.6$ kJ mol^{-1} in the *trans*-conformer. On the other hand, the attractive interaction in hydroquinone (**3**) is close to zero (−0.4 kJ mol^{-1}), due to the large distance between the dipoles (see Figure 1). Let us assume that hydrogen bonding in cathecol can be described by a very simple model involving, basically, the interaction between the O−H groups. The model includes Lennard-Jones (LJ) interactions representing short-range repulsion and dispersion contributions and the dipole−dipole interaction. The energy corresponding to the interaction between the O−H groups for the conformer X can be written as

$$E_{OH}(X) = E_{LJ}(X) + E_{dd}(X) \tag{7}$$

Thus, the energy difference between the trans (**2′**) and cis (**2**) conformers, $\Delta E(2 \rightarrow 2') = E(2') - E(2)$, can be approximated by

$$\begin{aligned}\Delta E(2 \rightarrow 2') &\cong E_{LJ}(2') - E_{LJ}(2) + E_{dd}(2') - E_{dd}(2) \\ &= E_{LJ}(O{-}O)_{2'} + E_{dd}(2') - [E_{LJ}(O{-}O)_2 + \\ &\qquad E_{LJ}(H{-}{-}{-}O) + E_{dd}(2)]\end{aligned} \tag{8}$$

E_{LJ}(O−O) is the LJ interaction between the oxygen atoms and E_{LJ}(H- - -O) denotes the LJ interaction between the hydrogen of the OH donor group and the oxygen atom of the OH acceptor group. By using Lennard-Jones parameters for phenol,[47] E_{LJ}(H- - -O) is neglected [47a] and $\Delta E(2 \rightarrow 2')$ is estimated as 28.8 kJ mol^{-1}. This value is 11.9 kJ mol^{-1} above our best cis−trans result based on the CBS-QMPW1 procedure (Table 1). However, it is difficult to identify $\Delta E(2 \rightarrow 2')$ with the H-bond strength in cathecol (**2**) because the interaction between the dipoles in (**2′**) is included and the E_{LJ}(O−O) contributions nearly cancel out. The H-bond strength should be associated with the interaction between the OH groups in the geometry of **2**. A reasonable estimate for the O- - -H bond breaking is given by

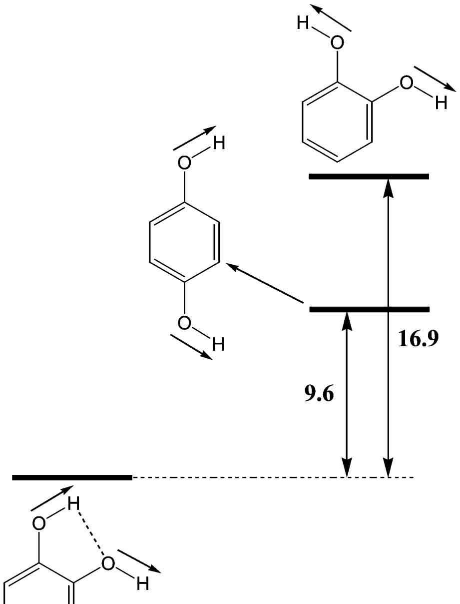


Figure 1. Relative energies (kJ mol^{-1}) of catechol (cis and trans conformers) and hydroquinone. The trans conformer is destabilized due to the repulsive interaction of the O−H bond dipole moments. Values from the CBS-QMPW1 calculations.

$$\Delta E_{HB} \cong -[E_{LJ}(O{-}O)_2 + E_{dd}(2)] \tag{9}$$

By using DFT optimized structures we find $\Delta E_{HB} \cong 8.3$ kJ mol^{-1}. Therefore, a procedure based on quantum mechanical energy differences for evaluating the H-bond strength in cathechol (**2**) should include the interactions defined in eq 9. This is accomplished by the ortho−para method. The interactions between the oxygen atoms and also between the O−H dipoles in hydroquinone (**3**) are clearly negligible. When the ortho−para method is applied for estimating the energy difference between cathecol (**2**) and hydroquinone (**3**)**,** the H-bond enthalpy in cathecol is 8.6 kJ mol^{-1} (DFT) and 9.6 kJ mol^{-1} (CBS-4M and CBS-QMPW1). These results are in good agreement with ΔE_{HB} from the simplified model. However, more important than stressing the agreement (which is very dependent on the LJ parameters), we observe that the model can be useful to understand why the ortho−para method is possibly the most reliable procedure to estimate intramolecular H-bond enthalpies.

If one accepts the ortho−para method as the best way to evaluate the energetics of intramolecular H-bonds, then we should compare our theoretical predictions with experimental data for these isomers. Nevertheless, one should bear in mind that experimental data are not necessarily accurate. Take, for instance, the case under discussion, the comparison between catechol and hydroquinone, i.e., $\Delta_r H^\circ_5 = \Delta_f H^\circ(3) - \Delta_f H^\circ(2)$. The standard enthalpies of formation of gaseous **2** and **3** recommended in Pedley's compillation[48] are −267.5 ± 1.9 and −265.3 ± 2.3 kJ mol^{-1}, respectively, implying that the energy of the intramolecular H-bond in catechol is 2.2 ± 3.0 kJ mol^{-1},

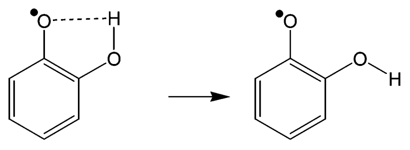
TABLE 4: Experimental Thermochemical Data (at 298 K, in kJ mol^{-1}) for Catechol and Hydroquinone

molecule	$\Delta_f H^o$(cr/l)	$\Delta_{sub} H^o$	$\Delta_f H^o$(g)	ref
C_6H_6, l	49.0 ± 0.5		82.6 ± 0.7	48
PhOH, cr (**1**)	−165.1 ± 0.7		−96.4 ± 0.9	48
1,2-$C_6H_4(OH)_2$, cr (**2**)	−354.1 ± 1.1		−267.5 ± 1.9	48,49
	−355.1 ± 1.6			50
		86.6 ± 1.6		51
		89.7 ± 0.5		50
		87.5 ± 0.3		52
		87.7 ± 2.4		53
selected	*−354.6 ± 1.0*	*87.7 ± 2.4*	*−266.9 ± 2.6*	
1,4-$C_6H_4(OH)_2$, cr (**3**)	−364.5 ± 1.5		−265.3 ± 2.3	48
	−369.3 ± 0.9			54
	−362.8 ± 1.0			55
	−393.7 ± 1.2			56
	−365.9 ± 0.9			57
		99.2 ± 1.7		56
		94.1 ± 0.5		52
		105.0 ± 0.8		50
		103.2		53,58
		104.8		53,59
		104.1		53,56
		103.3 ± 3.0		53
selected	*−369.3 ± 0.9*	*103.3 ± 3.0*	*−266.0 ± 3.1*	

i.e., about 7 kJ mol^{-1} weaker than the one found through computation. However, a different selection of experimental data (Table 4)[48−59] leads to higher (10.7 ± 2.6 kJ mol^{-1})[50,51,55] or even to negative values (−10.8 ± 1.6 kJ mol^{-1}).[49,50,52,54] These results suggest that the standard enthalpies of formation of gaseous catechol and hydroquinone should be redetermined and stress the interest of performing theoretical calculations to evaluate intramolecular H-bonds in these compounds.

There is another procedure to assess the energetics of intramolecular H-bonds, based on group additivity schemes.[60−62] These methods consider that the value of the enthalpy of formation of a molecule is the sum of a number of contributions, each one defined for a given molecular fragment (an atom, a bond, or a group). By assuming transferability, i.e., that the contribution of each fragment to the molecular property of interest will always be the same in any other molecule, an enthalpy of formation can be estimated by a sum of those group contributions (or "terms"). For many organic molecules, the agreement with experimental data is excellent, so that when discrepancies are found they can be assigned to effects such as steric repulsion, strain, and hydrogen bonding.[63] However, the results from this procedure are often questionable because they depend on the values assigned to the several group terms and to a number of corrections. For instance, in the case of catechol, the method used by Pilcher leads to −271.4±1.5 kJ mol $^{-1}$ for the enthalpy of formation in the ideal gas state (an empirical 4 kJ mol^{-1} correction due to the steric repulsion of the ortho groups was included),[63] which is 4 kJ mol^{-1} lower than the experimental value recommended in Pedley's tables (−267.5±1.9 kJ mol $^{-1}$).[48] The set of group terms defined in the THERM program[62] yields −267.8 kJ mol^{-1} (a 7 kJ mol^{-1} correction due to steric repulsion of the ortho groups was included). These repulsive ortho corrections imply that catechol has no intramolecular H-bond since it is less stable (by 4 or 7 kJ mol^{-1}) than hydroquinone. Incidentally, if the ortho correction were neglected, the result would be very similar to the one derived from the ortho−para method. This confirms that the group additivity method needs to be used with caution.

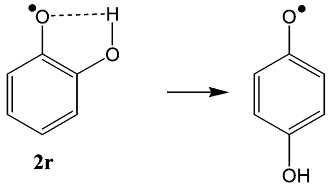
The above discussion for the cis−trans and the ortho−para methods can be extended to radicals. The analysis of intramolecular H-bond in radical species is very important to understand the energetics of homolytic bond dissociation of the parent molecules. In a recent work,[45] we have calculated the enthalpy of reaction 10 as 37.3 kJ mol^{-1} (DFT) and 33.9 kJ mol^{-1} (CBS-4M) and concluded that the intramolecular H-bond in the radical **2r** is 21.8 kJ mol^{-1} (DFT) or 16.6 kJ mol^{-1} (CBS-4M) stronger than in the parent catechol.



2r **2'r**

(10)

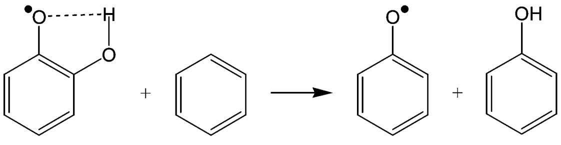
On the other hand, the ortho−para method (reaction 11) leads to 26.5 kJ mol^{-1} (DFT), 22.2 kJ mol^{-1} (CBS-4M), or 25.1 kJ mol^{-1} (CBS-QMPW1). When these values are compared with the ones obtained for the parent compounds (reaction 5), one concludes that the intramolecular H-bond in the radical species is 17.9 kJ mol^{-1} (DFT), 12.6 kJ mol^{-1} (CBS-4M), or 15.5 kJ mol^{-1} (CBS-QMPW1) stronger than in catechol (see Table 1).



2r **3r**

(11)

It is also interesting to note that the isodesmic reaction method (which underestimates the H-bond in catechol), yields a very high value for the H-bond in the radical: the enthalpy of reaction 12 is calculated as 39.5 kJ mol^{-1} (DFT), 31.8 kJ mol^{-1} (CBS-4M), and 38.9 kJ mol^{-1} (CBS-QMPW1). This overestimate is caused by the extra resonance stabilization of **2r**, due to the presence of the strong electron donor OH group, which of course does not occur in **1r**. Note that this effect is canceled when the ortho−para method is used.



2r **1r** **1**

(12)

ortho-Benzenedithiol. The previous study was repeated for the equivalent thiol compounds, and the results are displayed in Tables 1 and 2. The molecules were numbered as for the phenol analogues, e.g., PhSH (**1**), PhS (**1r**), etc.

In general, the trend in the results is similar to the one observed for catechol. As expected, the differences between the predictions from the three methods are now smaller because the S−H- - -S intramolecular hydrogen bond is weaker. The S−H group dipole moments (∼1.2 D) lead to a repulsive dipole−dipole interaction of only 1.9 kJ mol^{-1} for **2′** and an attractive interaction of −1.3 kJ mol^{-1} for the cis conformer **2**, which are significantly smaller than the interactions for the phenol analogues. Our best estimate for the S- - -H bond enthalpy in *ortho*-benzenethiol (based on the ortho−para approach) is 5.5 kJ mol^{-1} (CBS-QMPW1). DFT based on the isodesmic reaction method predicts that the enthalpy of this bond is negative (−1.8 kJ mol^{-1}). However, the CBS-QMPW1 value (4.5 kJ mol^{-1}) is similar to our best estimate based on the ortho−para method. We are not aware of LJ parameters for benzenethiols. By using parameters for sulfur reported by Pastorino and Gamba,[47b] $\Delta E(2 \rightarrow 2')$ is estimated as 7.3 kJ mol^{-1}, which is not in very good agreement with the cis−trans results reported in Table 1. The calculation based on the model described above (eq 9) leads to $\Delta E_{HB} \cong -2.4$ kJ mol^{-1}, indicating that the LJ parameters for sulfur are not adequate to represent the small interaction in benzenedithiol.

H-bond enthalpies for benzenedithiol radicals are also reported in Table 1. In keeping with the results for cathecol, all calculations (with the noticeable exception of the CBS-4M results for the ortho−para method) predict that the H-bond enthalpy in the radical is higher than in the parent compounds. Note also that, with the exception of the isodesmic method, DFT calculations yield similar differences between the H-bond enthalpies in the radical and in the parent compound: 6.2 kJ mol^{-1} (cis−trans) and 5.5 kJ mol^{-1} (ortho−para). The DFT result based on the isodesmic reaction method (15.2 kJ mol^{-1}) seems to overestimate that difference. Finally, accepting that the best value for the H-bond enthalpy in the radical is the ortho−para result from the CBS-QMPW1 method (6.6 kJ mol^{-1}), it appears that the isodesmic method prediction (13.0 kJ mol^{-1}) is significantly overestimated.

To our knowledge, there are no experimental values for the standard enthalpies of formation of *ortho*- and *para*-benzenedithiol. The THERM program[62] estimates that the gas-phase standard enthalpy of formation for both ortho and para isomers is 141.9 kJ mol^{-1}, which means that the intramolecular H-bond enthalpy in *ortho*-benzenedithiol is negligible. By combining this value with the experimental data for gaseous PhSH and C_6H_6, 111.3 ± 1.3 and 82.6 ± 0.7 kJ mol^{-1} (Table 4) respectively, the enthalpy of the isodesmic reaction 3 (see Table 2) for $X = Y = S$ is calculated as −1.9 kJ mol^{-1}, which is quite similar to the DFT result and 6 kJ mol^{-1} lower than the CBS-QMPW1 prediction.

ortho-Benzenediamine. The molecules were numbered as in the previous cases, e.g., $PhNH_2$ (**1**), PhNH (**1r**), etc. For obvious reasons, the cis−trans method cannot be used in the case of *ortho*-benzenediamine. The isodesmic reaction method yields a negative value for the intramolecular H-bond enthalpy when DFT and CBS-4M calculations are used (−2.4 and −4.7 kJ mol^{-1}, respectively).

The differences between the H-bond enthalpy in the radical and in the parent compound (Δ) are also presented in Table 1. The isodesmic method predicts that Δ is 30.8 kJ mol^{-1} (DFT), 33.8 kJ mol^{-1} (CBS-4M), and 25.3 kJ mol^{-1} (CBS-QMPW1). From the ortho−para method these differences are much smaller, 7.4 kJ mol^{-1} (DFT), 11.4 kJ mol^{-1} (CBS-4M), and 20.0 kJ mol^{-1} (CBS-QMPW1), suggesting once again that the isodesmic reaction method tends to overestimate the enthalpy of the intramolecular H-bond in the radical (**2r**).

The enthalpies of formation of benzenediamines are only known in the solid phase. However, the group additivity method gives 91.1 kJ mol^{-1} for both the ortho and para isomers in the gas state.[62] This value, together with the enthalpies of formation of gaseous aniline (87.1 ± 1.1 kJ mol^{-1}) and benzene (Table 4), yield 0.5 kJ mol^{-1} for the enthalpies of reactions 3 ($X = Y = NH$) and 4 (O replaced by NH). Our best estimates (CBS-QMPW1) are 5.1 kJ mol^{-1} (isodesmic reaction) and 10.8 kJ mol^{-1} (ortho−para method), which are only in fair agreement with the results based on the group additivity scheme.

ortho-Xylene. There is clearly no intramolecular H-bond in *ortho*-xylene, but the calculations were carried out because in this case the experimental data are quite reliable and can be used to discuss the accuracy of the theoretical methods. The absence of any significant interaction between the methyl groups is confirmed by the values in Table 2 (the energy differences between ortho and para conformers are quite small). CBS-QMPW1 predictions for the enthalpies of reactions 3 ($X = Y = CH_2$) and 4 (O replaced by CH_2) are 1.9 and −0.1 kJ mol^{-1}, respectively. Using the experimental enthalpies of formation of gaseous *ortho*- and *para*-xylene, respectively 19.1 ± 1.0 and 18.1 ± 1.0 kJ mol^{-1},[48] together with the enthalpies of formation of benzene (Table 4) and toluene (50.5 ± 0.5 kJ mol^{-1}) in the gas state,[48] one obtains −0.7 ± 1.4 and 0.3 ± 1.4 kJ mol^{-1} for the enthalpies of the same reactions, respectively, showing good agreement with the theoretical results (Table 2). The additivity scheme yields 19.3 and 18.0 kJ mol^{-1} for the enthalpies of formation of the gaseous ortho and para isomers, respectively (a positive ortho correction, 1.26 kJ mol^{-1}, was used, reflecting the small repulsive interaction of the methyl groups),[57] yielding 1.3 kJ mol^{-1} for the enthalpy of reaction 5. This is in very good agreement with the calculated CBS-QMPW1 result, 2.0 kJ mol^{-1}.

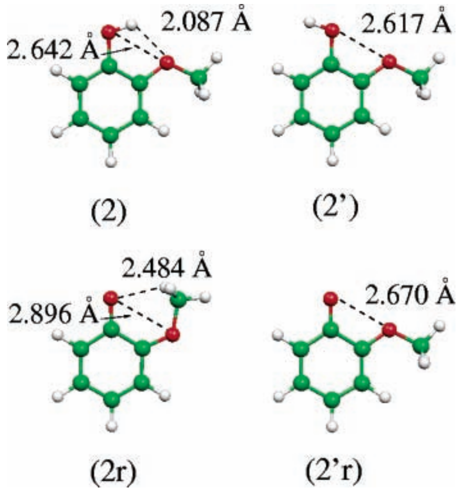


Figure 2. Molecular structures of *ortho*-methoxyphenol and of the corresponding radical species, calculated at the MPW1PW91/aug-cc-pVDZ level.

ortho-Methoxyphenol. The molecules were also numbered as in the previous cases, e.g., $C_6H_5OCH_3$ (**1**), C_6H_5O (**1r**), 2-$CH_3OC_6H_4OH$ (**2**), 2-$CH_3OC_6H_4O$ (**2r**), etc. As observed in Tables 1 and 2, the results from all of the methods are rather similar (within ca. 2 kJ mol^{-1}) to those obtained for catechol, i.e., the cis−trans method overestimates and the isodesmic reaction method underestimates the enthalpy of the intramolecular H-bond. The main difference from catechol is that the *ortho*-methoxyphenoxy radical has no intramolecular H-bond, and therefore, for instance, the reaction $\mathbf{2r} \rightarrow \mathbf{2'r}$ (see Figure 2) is nearly thermoneutral (0.9 kJ mol^{-1} at the CBS-QMPW1 level). In addition, the *para*-methoxyphenoxy radical (**3r**) is more stable than the ortho conformer (**2r**) by 7.2 kJ mol^{-1}, and there is a large and negative difference (−18.8 kJ mol^{-1}) between the enthalpies of the reactions $\mathbf{2r} \rightarrow \mathbf{3r}$ and $\mathbf{2} \rightarrow \mathbf{3}$. This is of course due to the absence of H-bond. A possible repulsive interaction between the methyl group and the oxygen atom in the *ortho*-methoxyphenoxy radical (**2r**) is ruled out on the basis that the reaction $\mathbf{2r} \rightarrow \mathbf{2'r}$ is endothermic.

Experimental data for the standard enthalpies of formation of gaseous **2** (−246.1 ± 1.9 kJ mol^{-1}) and **3** (−229.7 ± 1.8 kJ mol^{-1}) have only recently become available.[64] These data, together with the enthalpies of formation of benzene, phenol (Table 4), and anisole in the gas state (−67.9 ± 0.8 kJ mol^{-1}),[48] lead to −0.8 ± 2.4 and −17.2 ± 2.6 kJ mol^{-1} for the enthalpies

TABLE 5: DFT Frequencies and Structural Data for Di-substituted Benzenes[a]

catechol	ν(O−H)	r(O−H)	r(O−O)	r(O- - -H)
2	3830	0.964	2.676	2.138
2′	3878	0.961	2.648	
Δ	48	−0.003		
2r	3554	0.981	2.608	1.982
2′r	3852	0.963	2.696	
Δ	302	−0.018		
ortho-benzenedithiol	ν(S−H)	r(S−H)	r(S−S)	r(S- - -H)
2	2674	1.356	3.212	2.711
2′	2723	1.351	3.109	
Δ	51	−0.005		
2r	2530	1.369	3.304	2.343
2′r	2689	1.356	3.148	
Δ	160	−0.013		
ortho-methoxyphenol	ν(O−H)	r(O−H)	r(O−O)	r(O- - -H)
2	3817	0.965	2.642	2.087
2′	3877	0.961	2.617	
Δ	60	−0.004		

[a] MPW1PW91/aug-cc-pVDZ results. Unscaled harmonic frequencies in cm^{-1} and distances in Å.

of reactions 3 (X = O, YH = OCH_3) and 4 (with OCH_3 substituted for one OH group). These values, particularly the one involving the *para*-isomer (**3**) are in some disagreement with those computed at the CBS-QMPW1 level (Table 2), 7.4 and −4.2 kJ mol^{-1}, respectively. However, when the above experimental enthalpies of formation are used to evaluate the enthalpy of the intramolecular H-bond in **3** by the ortho−para method, the value obtained, 16.4 ± 2.6 kJ mol^{-1} is in better agreement with the one in Table 1 (11.6 kJ mol^{-1}).

The ortho−para method can also be applied using the B3LYP theoretical values reported by Matos et al. with two different basis sets.[64] One obtains 10.9 or 10.5 kJ mol^{-1}, in accord with our results. The same authors report the enthalpy of the intramolecular H-bond in *ortho*-methoxyphenol as 20.1 kJ mol^{-1}. This value was derived from the cis−trans method and it is close to the DFT (16.8 kJ mol^{-1}), CBS-4M (19.1 kJ mol^{-1}), and CBS-QMPW1 (18.6 kJ mol^{-1}) results reported in Table 1.

4.2. Vibrational Properties and Structure. The relationship between intermolecular interactions and vibrational frequency shifts is of great interest to discuss the nature of the interactions and has been widely exploited to investigate intermolecular H-bond formation. Usually, intermolecular H-bond strengths can be correlated with frequency shifts and structural changes.[2,4−6]

Frequencies associated with the vibrational stretching of the hydrogen bonding donor groups in di-substituted benzenes are reported in Table 5. The formation of the O- - -H bond in catechol, which corresponds to reaction 2, is characterized by a 48 cm^{-1} red shift of the O−H donor stretching frequency. For the radical species, a much stronger red shift (302 cm^{-1}) is calculated, reflecting the increase of the O- - -H bond strength in the radical. Comparison between the r(O- - -H) distances in the H-bonded catechol and respective radical species shows a 0.16 Å reduction. For *ortho*-benzenedithiol, smaller frequency shifts are observed, which are related to smaller H-bond strengths in comparison with catechol. However, the r(S- - -H) in the *ortho*-benzenedithiol radical is reduced by 0.37 Å in comparison with its parent species.

The O−H frequency shift associated with reaction 2 for *ortho*-methoxyphenol is 60 cm^{-1}, quite close to the one observed in cathecol. Interestingly, a ∼60 cm^{-1} blue shift of the C−H stretching vibrational frequencies of the methyl group in the radical (**2r**) relative to *ortho*-methoxyphenol (**2**) is observed. Blue shift of X−H stretch frequency in hydrogen bonded X−H···Y complexes is associated with improper intermolecular H-bond and has been the subject of several investigations (see ref 11 for a review). We stress, however, that the C−H blue shift presently observed involves an *intramolecular* H-bond in a radical species. As noted above, the *ortho*-methoxyphenoxy radical has no intramolecular H-bond (see Figure 2).

4.3. Intramolecular Hydrogen Bonding and the Energetics of the Homolytic Bond Dissociation. As discussed elsewhere,[65] the difference between the enthalpies of the intramolecular H-bond in a radical (R) and in the parent closed-shell molecule (RH) may have a significant impact on the R−H bond dissociation enthalpy, i.e., the enthalpy of reaction 13

$$\mathrm{RH\ (g)} \rightarrow \mathrm{R^{\bullet}\ (g)} + \mathrm{H^{\bullet}\ (g)} \qquad (13)$$

The computed enthalpies of reaction 13 for the di-substituted benzenes addressed in the present study, together with selected experimental data,[28,45,66−70] are collected in Table 6. One major, although not unexpected, conclusion concerns the good general agreement between CSB-QMPW1 and CBS-4M predictions and experimental information. Although CBS-QB3 calculations were not carried out for all reactions in Table 6, it may be instructive to assess the relative accuracy of CBS-QB3 and CBS-QMPW1 methods. CBS-QB3 calculations predict that *DH*°(R−H) of phenol and thiophenol are 362.0 and 336.8 kJ mol^{-1}, respectively. These values are quite similar to the CBS-QMPW1 results (363.6 and 338.4 kJ mol^{-1}). Therefore, these results indicate that CBS-QMPW1 and CBS-QB3 predict quite similar bond dissociation enthalpies for the compounds of Table 6. On the other hand, in keeping with early studies, we note that DFT calculations underestimate homolytic bond dissociation enthalpies.[35,45]

The impact of the difference between the enthalpy of the intramolecular H-bond in the radical and the parent compound on catechol *DH*°(O−H) is significant. Although the electronic effects of the electron donor OH group in the radical stabilization are similar in catechol and hydroquinone,[71] *DH*°(O−H) in catechol is about 17.8 kJ mol^{-1} (DFT), 12.6 kJ mol^{-1} (CBS-4M), and 15.5 kJ mol^{-1} (CBS-QMPW1) lower than hydroquinone. This conclusion does not hold if the experimental *DH*°(O−H) of hydroquinone is accepted but this value is probably a low limit.[45]

The case of *ortho*-methoxyphenol provides an interesting comparison with catechol. As stated above, there is no intramolecular H-bond stabilizing the corresponding radical. Therefore, *DH*°(O−H) is determined by two opposing effects: the strong electron donor *ortho*-methoxy group stabilizes the radical, decreasing the bond dissociation enthalpy, but the intramolecular H-bond stabilizes the parent compound, increasing *DH*°(O−H). These effects are of similar magnitude and the energy differences between the parent and the radical species in phenol and *ortho*-methoxyphenol are almost identical. Therefore, *DH*°(O−H) of *ortho*-methoxyphenol is quite close to the one computed for phenol. In the case of *para*-methoxyphenol, where there is no intramolecular H-bond, the methoxy group stabilizes the radical, yielding a decrease of the O−H bond dissociation enthalpy (about 20 kJ mol^{-1} lower than in phenol).

The experimental values for the methoxyphenols shown in Table 6 rely on the selected value for phenol (Table 6) and on experimental data reported by de Heer et al.,[70] which show that *DH*°(O−H) in the ortho isomer is 1.7 kJ mol^{-1} higher than in

TABLE 6: Theoretical and Experimental Bond Dissociation Enthalpies at $T = 298$ K

molecule	$DH^o(R-H)$/kJ mol^{-1} MPW1PW91	CBS-4M	CBS-QMPW1	exp.
PhO−H	346.8	375.4	363.6	371.3 ± 2.3[a]
1,2-$C_6H_4(OH)O-H$	307.8	347.6	330.1	345 ± 5[b]
1,4-$C_6H_4(OH)O-H$	325.6	360.2	345.6	344 ± 10[c]
PhS−H	313.7	336.3	338.4	349.4 ± 4.5[d]
1,2-$C_6H_4(SH)S-H$	298.5	330.8	329.8	
1,4-$C_6H_4(SH)S-H$	304.0	327.2	331.0	
PhNH−H	364.0	377.1	381.9	377[e], 373[f]
1,2-$C_6H_4(NH_2)NH-H$	333.2	343.3	356.6	
1,4-$C_6H_4(NH_2)NH-H$	340.6	354.7	376.6	360[f]
$PhCH_2-H$	355.6	375.4	379.1	375 ± 5[g]
1,2-$C_6H_4(CH_3)CH_2-H$	355.7	374.5	379.1	
1,4-$C_6H_4(CH_3)CH_2-H$	354.2	372.3	377.7	
2-$CH_3OC_6H_4O-H$	341.8	377.9	362.7	373 ± 6[h]
4-$CH_3OC_6H_4O-H$	324.7	357.9	343.9	351 ± 6[h]

[a] Reference 28. A selection of literature data. [b] Reference 45. [c] Reference 28. As discussed in ref 45, this value is probably a low limit. [d] Reference 66. See text. [e] Reference 68. [f] Reference 69. [g] Reference 67. A selection of literature data. [h] Calculated from data in ref 70. See text.

phenol and that in the para isomer is 20.5 kJ mol^{-1} lower than phenol. This last value is in good agreement with the theoretical results.

The discussion for the N−H bond dissociation enthalpies in the diamines is similar to one made for catechol and hydroquinone: the difference between the enthalpy of the intramolecular H-bond in *ortho*-benzenediamine and in its radical lead to a $DH°(N-H)$ that is about 20 kJ mol^{-1} (CBS-QMPW1) lower than the value found for the para isomer.

Finally, the weak intramolecular H-bonds in *ortho*-benzenedithiol and its radical justify that $DH°(S-H)$ in this compound is similar to the value in the para isomer. Both are also close to the S−H bond dissociation enthalpy in PhSH, due to the small stabilization of the radical by the weak electron donor SH group.

A significant discrepancy between theoretical results based on the CBS methods and experimental data is observed for $DH°(PhS-H)$ in Table 6. In this case, calculations at the G3(MP2) level led to 346.8 kJ mol^{-1}, in keeping with the selected experimental value,[66] and also with the value recommended by McMillen and Golden.[72] However, the controversy around the “best” $DH°(PhS-H)$ value still persists. An estimate by Bordwell et al.,[73] based on the so-called “electrochemical method”, is 331 kJ mol^{-1}, close to the CBS-4M and the CBS-QMPW1 results in Table 6. Moreover, recent theoretical calculations at the B3LYP/6-311G(d,p)//(RO)B3LYP/6-311++G(2df,2p) level afforded $DH°(PhS-H) = 332.6 \pm 4.0$ kJ mol^{-1} ($T = 298$ K),[74] also in good agreement with the “low” value.

5. Conclusions

Different theoretical procedures for assessing intramolecular H-bond strengths were applied to di-substituted benzenes. They include conformational analysis, a recent method based on isodesmic reactions, and a new approach that we designate as the ortho−para method. By using an accurate quantum mechanical procedure for the calculation of total energies, which is very similar to the CBS-QB3 method, we have provided evidence that the widely used cis−trans method overestimates intramolecular H-bond enthalpies in di-substituted benzenes.

The enthalpies of intramolecular H-bonds in di-substituted aromatic compounds can be easily obtained by comparing the ground-state energies of the ortho and para isomers or, when reliable standard enthalpies of formation are available, from the difference $\Delta_f H°(\text{para}) - \Delta_f H°(\text{ortho})$. A simple interaction model was then proposed to explain this finding. In addition, our predictions for H-bond strengths based on the ortho−para method seem to be supported by indirect experimental information. This approach should be preferred to the cis−trans method, and also to a recently proposed procedure that makes use of an isodesmic reaction, which usually underestimates the intramolecular H-bond strengths for closed-shell molecules and overestimates them for the corresponding radicals.

The choice between the ortho−para and the cis−trans method to evaluate the *difference* between the enthalpies of intramolecular H-bonds in a radical species and in its parent compound is less important than for predicting their individual values: both procedures lead to comparable results.

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Supporting Information Available: Table showing the total energies calculated at the MPW1PW91/aug-cc-pVDZ, CBS-4M, and CBS-QMPW1 levels. This material is available free of charge via the Internet at http://pubs.acs.org.

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