

# Can larger dipoles solvate less? solute–solvent hydrogen bond and the differential solvation of phenol and phenoxy

Kaline Coutinho <sup>a</sup>, B.J. Costa Cabral <sup>b,c</sup>, Sylvio Canuto <sup>d,\*</sup>

<sup>a</sup> Universidade de Mogi das Cruzes/CIIB, CP 411, 08701-970, Mogi das Cruzes, SP, Brazil

<sup>b</sup> Departamento de Química e Bioquímica, Faculdade de Ciências da Universidade de Lisboa, 1749-016 Lisboa, Portugal

<sup>c</sup> Grupo de Física Matemática da Universidade de Lisboa, Av. Professor Gama Pinto 2, 1649-003 Lisboa, Portugal

<sup>d</sup> Instituto de Física, Universidade de São Paulo, CP 66318, 05315-970 São Paulo, SP, Brazil

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## Abstract

Quantum mechanical calculations of the dipole moments and binding energies of phenol and phenoxy radical in liquid acetonitrile and water are made using hydrogen-bonded configurations extracted from Monte Carlo simulations. We contend that the preferential solvation of phenol (the lower dipole moment solute) over phenoxy derives from the hydrogen-bond shell. The reconciliation with the usual understanding, that larger dipole solvates better, is obtained if we consider not the dipole moment of the isolated solute but, instead, the average dipole moment in solution of the solute–solvent hydrogen-bonded solvation shell.

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## 1. Introduction

In recent years the theoretical study of molecular systems in the liquid phase has attracted considerable attention. Indeed, solvent effects play a crucial role in chemistry and biochemistry [1]. The study of solvation of organic molecules is very important to understand chemical reactivity in the liquid phase. In particular, bond dissociation may lead to the formation of radicals and this is important to understand several biochemical processes. The homolytic dissociation of the OH bond in phenol (PhOH) leads to the formation of the phenoxy radical (PhO<sup>•</sup>) which is an important intermediate in green plant photosynthesis [2] and protein redox [3] reactions. This homolytic cleavage has been studied in solution both experimentally [4–6] and theoretically [7–9] and recent results are available for the standard enthalpy

of solvation [8,9]. Results [5,6,8,9] from both experiments and computer simulations conclusively assert that PhOH solvates better than PhO<sup>•</sup> in polar solvents such as acetonitrile and water. In benzene, nonpolar and nonprotic, however, the solvation enthalpies are similar. If we consider that the dipole moment of the phenoxy radical (4.1 D) is nearly three times larger than the dipole moment of phenol (1.4 D) these results imply that the system with the larger dipole moment (PhO<sup>•</sup>) solvates less than the system with the smaller dipole moment (PhOH). For instance, the hydration enthalpy of PhOH is larger by ca. 6–9 kcal/mol than the hydration enthalpy of the PhO<sup>•</sup> radical. This, of course, departs from the current view. It is normally expected that the stabilisation in a polar solvent be dominated by the dipole moment of the solute. In fact, this is at the origin of the reaction field treatments [10–12] of solvent effects. The subject of this work is to attempt a reconciliation of the theoretical and experimental results with the usual picture. We show that this can be obtained if we consider not the dipole moment of the isolated solute but, instead, the dipole

\* Corresponding author. Fax: +55 11 3091 6831.

E-mail address: [canuto@if.usp.br](mailto:canuto@if.usp.br) (S. Canuto).

moment of the hydrogen-bonded solute–solvent complex. However, it is important to mention that this reconciliation is not possible if the dipole moment of the solute–solvent system is obtained, as it is normally done, using an optimised gas phase complex. In fact, the dipole moments of the hydrogen-bonded ‘solute’ necessary for the explanation of the differential enthalpy considered here, are those obtained in the *liquid environment* and require statistical averages.

In this Letter, we use the sequential Monte Carlo Quantum Mechanics methodology S-MC/QM [13–15], to obtain the dipole moments and hydrogen-binding energies of PhOH and PhO<sup>•</sup> in liquid acetonitrile (ACN), and water (W), at room temperature. These results are used to show that the differential solvation enthalpies of PhOH and PhO<sup>•</sup> are in agreement with the idea that the relevant dipole moment is not that obtained for the isolated solute systems but rather those obtained for the solute–solvent, in the hydrogen bond solvation shell, of the liquid.

## 2. Theoretical methodology

Four separate Metropolis *NpT* MC [16] simulations are performed for PhOH and PhO<sup>•</sup> radical in two solvents: water and acetonitrile. The simulated systems consist of phenol or phenoxy in 450 water (500 acetonitrile) solvent molecules at temperature of 298.15 K and pressure of 1 atm. The intermolecular interactions are described by the standard Lennard–Jones (LJ) plus Coulomb potentials. For the water molecules we use the SPC potential [17], for acetonitrile, we use the potential of Böhm et al. [18] and for the phenol and phenoxy radical that proposed by Jorgensen and Nguyen [19] with atomic charges obtained by fitting the electrostatic potential of a B3LYP/6-311++G(d,p) calculation [20,21], using the Merz–Kollman [22] procedure. For consistency, these simulations are the same as those of our solvation studies [8,9].

After thermalisation,  $50 \times 10^6$  MC steps in the case of acetonitrile and  $90 \times 10^6$  MC steps in the case of water were produced. After the MC simulation, we identify the solute–solvent hydrogen bonds (to be described later). Similar to previous studies we have calculated the auto-correlation function of the energy to sample statistically relevant configurations [14,15]. The QM calculations are performed at the B3LYP/6-31+G(d,p) level on 45 statistically uncorrelated configurations, sampled from the MC simulations, composed of a central system (phenol or phenoxy) and the solvent molecules within the hydrogen-bond solvation shell. We obtain the dipole moments and the counterpoise-corrected [23] binding energies, using the GAUSSIAN 98 [24] program. All simulations were performed with the DICE [25] Monte Carlo program.

## 3. Results and discussions

### 3.1. Identification of hydrogen bonds

We first consider the identification of the hydrogen-bonded (HB) structures between the solute and the solvent molecules obtained in the MC simulation. Fig. 1 shows the radial distribution functions between the oxygen (hydrogen) atom of phenol and the oxygen atom of water. A clear peak in the O–O distribution can be discerned ending at about 3.2 Å that is normally attributed to the hydrogen-bond shell. It cannot be assured, however, that all solvent molecules within this O–O distance are indeed associated with hydrogen bonds [26,27]. We analyse [15,28,29], in addition, the directional and energetic aspects of hydrogen bonds. We consider here that a hydrogen-bonded complex is formed between phenol and water when the distance  $R_{O-O} \leq 3.2$  Å, the angle  $\theta$  (O–OH)  $\leq 30^\circ$  and the binding energy  $\geq 3.5$  kcal/mol. These geometric conditions are obtained from the radial and angular distributions. The energetic criterion is from the pair-wise energy distribution (Fig. 2). For the specific case of phenol in water two types of hydrogen bonds can be formed. In one case, phenol is the proton acceptor (PhHO–HOH) and in the other it is the proton donor (PhOH–OH<sub>2</sub>). Phenol is both donor and acceptor of hydrogen bonds. This is the reason for the double peak seen in Fig. 2. On the average we find one HB of the type PhOH–OH<sub>2</sub> and 1.12 of PhHO–HOH. A similar analysis is made for the other simulations. For phenoxy in water, there is an average of 0.57 HB formed in the O atom of the radical. So, in the case of the phenoxy radical only 57% of the MC configurations exhibit HB. In the average, we also find that there is one HB for phenol and phenoxy in acetonitrile. Figs. 3 and 4 summarize these HB and show, in a single picture, the superposition of all the hydrogen-bonded configurations obtained in the liquid. The average quantum mechanical dipole moments and binding energies for the liquid situation

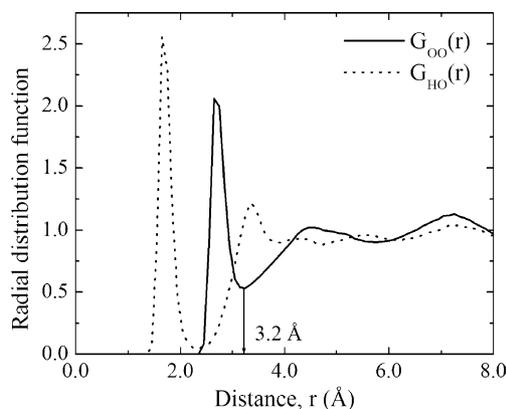


Fig. 1. Radial distribution functions between the oxygen (hydrogen) atom of phenol and the oxygen atom of water.

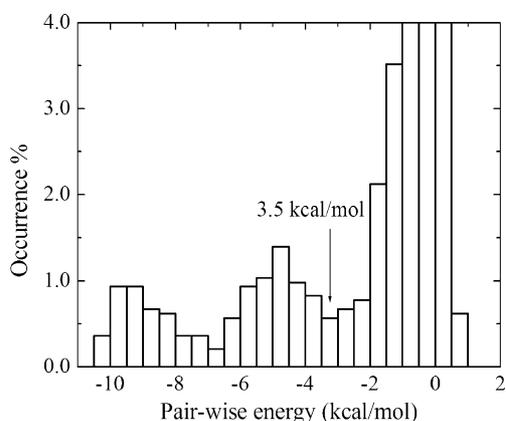


Fig. 2. Histogram of the pair-wise interaction energy between phenol and water obtained from the simulation.

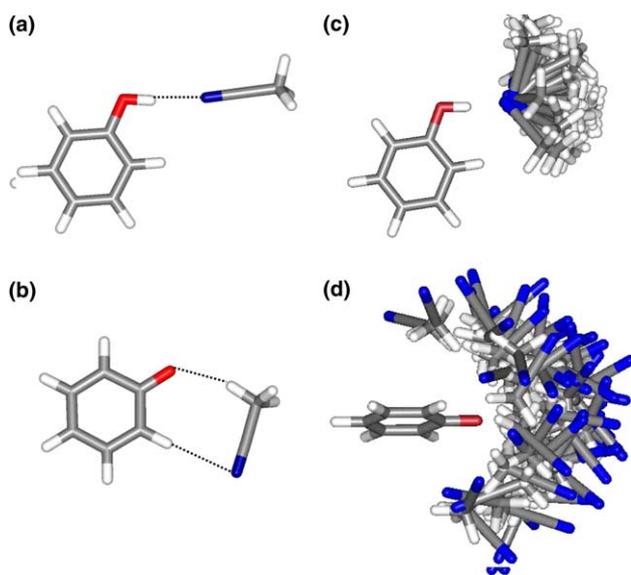


Fig. 3. Superposition of configurations of the hydrogen bonds formed by (c) phenol and (d) phenoxy in liquid acetonitrile. (a) and (b) are geometry-optimised structures.

are obtained using these structures. For comparison, it is also shown the corresponding geometry-optimised HB.

### 3.2. Quantum mechanical results

Figs. 3c, 3d, 4c and 4d illustrate very clearly the configuration space spanned by the hydrogen-bonded solvent molecules. In some cases (e.g. phenol in acetonitrile, Fig. 3a and c) the liquid provides an ensemble of structures similar to the gas phase. The calculated dipole moment for the optimised PhOH-ACN (Fig. 3a) is 6.85 D. In comparison (see Table 1), using the liquid configurations (Fig. 3c) the calculated average dipole moment is  $6.42 \pm 0.56$  D. For PhO-ACN, however, the minimum-energy structure cannot represent the liquid at room temperature (Fig. 3b and d). The average dipole

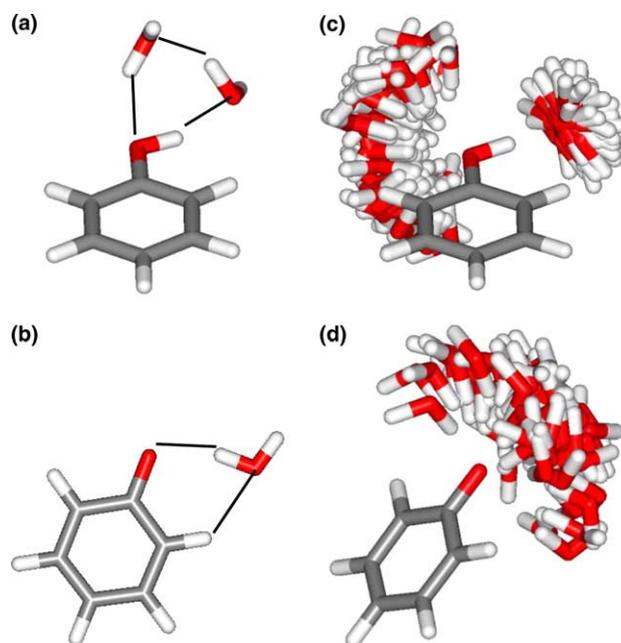


Fig. 4. Superposition of configurations of the hydrogen bonds formed by (c) phenol and (d) phenoxy in liquid water. (a) and (b) are geometry-optimised structures.

Table 1

Calculated hydrogen-bond distances, counterpoise-corrected binding energies and dipole moments for the hydrogen-bonded complexes

	$R_{A-H}$ (Å)	$E_B^{CP}$ (kcal/mol)	$\mu$ (D)
PhOH			1.41
PhOH-ACN (optimised)	1.989	5.01	6.85
PhOH-ACN (liquid)	$1.88 \pm 0.19$	$3.68 \pm 1.27$	$6.42 \pm 0.56$
PhO <sup>•</sup>			4.08
PhO <sup>•</sup> -ACN (optimised)	2.268	3.03	3.28
PhO <sup>•</sup> -ACN (liquid)	$2.55 \pm 0.22$	$1.68 \pm 0.67$	$6.95 \pm 1.84$
PhHO-H <sub>2</sub> O (optimised)	1.761	11.22	1.00
PhOH-OH <sub>2</sub> (optimised)	1.825		
PhHO-H <sub>2</sub> O (liquid)	$1.72 \pm 0.12$	$7.10 \pm 1.59$	$5.48 \pm 0.87$
PhOH-OH <sub>2</sub> (liquid)	$1.85 \pm 0.16$		
PhO <sup>•</sup> -H <sub>2</sub> O (optimised)	1.927	6.45	3.38
PhO <sup>•</sup> -H <sub>2</sub> O (liquid)	$1.97 \pm 0.17$	$2.01 \pm 1.07$	$5.33 \pm 0.92$

Liquid results are averages of configurations sampled from the Monte Carlo simulations. For PhOH in water two hydrogen bonds are considered. See text and Figs. 3 and 4.

moments are substantially different. In the liquid case, the average value is  $6.95 \pm 1.84$  D, whereas the geometry-optimised gives a dipole moment of 3.28 D. The similarity of the numerical values of the dipole moments of PhOH-ACN and PhO-ACN, in the liquid situation, corroborates the idea that for large distances the solvent molecules are subjected to the dipole moment of the 'solute' that is now considered to be the solute-solvent hydrogen-bond shell, leading to equivalent solvation enthalpies.

Now we turn to the more interesting case of PhOH and PhO<sup>•</sup> in water. The enthalpy in this case favours

the phenol hydration by ca. 6–9 kcal/mol. Comparing the geometry-optimised structures of PhOH–W<sub>2</sub> and PhO<sup>•</sup>–W clusters (Fig. 4a and b) with the structures of the liquid simulations (Fig. 4c and d), clearly indicates that some gas phase local minima are not necessarily present in solution. This can be explained by noting that in the liquid, the interactions between the solvent molecules compete with the solute–solvent interactions. This result makes it difficult to establish a correspondence between geometry-optimised structures and liquid state configurations. Moreover, it stresses the importance of the statistical analysis of hydrogen bonds in liquids.

The dipole moments obtained for the minimum-energy hydrogen-bonded structures give unreasonable results to represent the liquid situation. In the minimum-energy case, the total dipole moment calculated here for PhOH–W<sub>2</sub> is only 1.0 D (Fig. 4a). This is in agreement with the geometry-optimised value of 1.1 D obtained previously [30]. To minimize the total energy, the two water molecules, that are bound to PhOH are also hydrogen-bonded to one another. This situation is more difficult in the liquid case because the two water molecules interact also with the bulk water molecules, as seen in Fig. 4c. In this case the dipole moment of PhOH–W<sub>2</sub> is  $5.48 \pm 0.87$  D, a value that is considerably larger than the dipole moments of the isolated gas phase PhOH and the geometry-optimised PhOH–W<sub>2</sub>. Interesting enough, this value is now very close to the calculated average dipole moment of PhO<sup>•</sup>–W,  $5.33 \pm 0.92$  D. We should mention that all calculated values are statistically converged, as in previous works [14,15,28].

### 3.3. Differential solvation of phenol and phenoxy

The solvation enthalpy [8,9] of the gas-phase solute species X (PhOH or PhO<sup>•</sup>) is given by

$$\Delta_{\text{sln}}H^0(\text{X}, \text{g}) = E_{\text{SX}} + \Delta H_{\text{R}} - RT, \quad (1)$$

where,  $E_{\text{SX}}$  is the solute–solvent energy, and  $\Delta H_{\text{R}} = H_{\text{SS}} - H_{\text{SS}}^*$  is the solvent relaxation enthalpy due to the presence of PhOH or PhO<sup>•</sup>. The differential solvation enthalpy between phenol and phenoxy is simply

$$\Delta_{\text{sln}}H^0(\text{PhOH}, \text{g}) - \Delta_{\text{sln}}H^0(\text{PhO}^{\bullet}, \text{g}) = \Delta E_{\text{SX}} + \Delta \Delta H_{\text{R}}. \quad (2)$$

The solvent relaxation,  $\Delta H_{\text{R}}$ , may be sizeable both for phenol and phenoxy but the differential relaxation enthalpy  $\Delta \Delta H_{\text{R}}$  nearly cancels. For instance, in acetonitrile the  $\Delta H_{\text{R}}$  values for PhOH and PhO<sup>•</sup> are calculated [9] as  $12.2 \pm 1.2$  and  $11.3 \pm 1.1$  kcal/mol, respectively. Hence, the most important quantity in Eq. (2) is the difference in solute–solvent interaction energy  $\Delta E_{\text{SX}}$  that has two main contributions (see Fig. 5). One is the long-range interaction that is dominated by the dipole

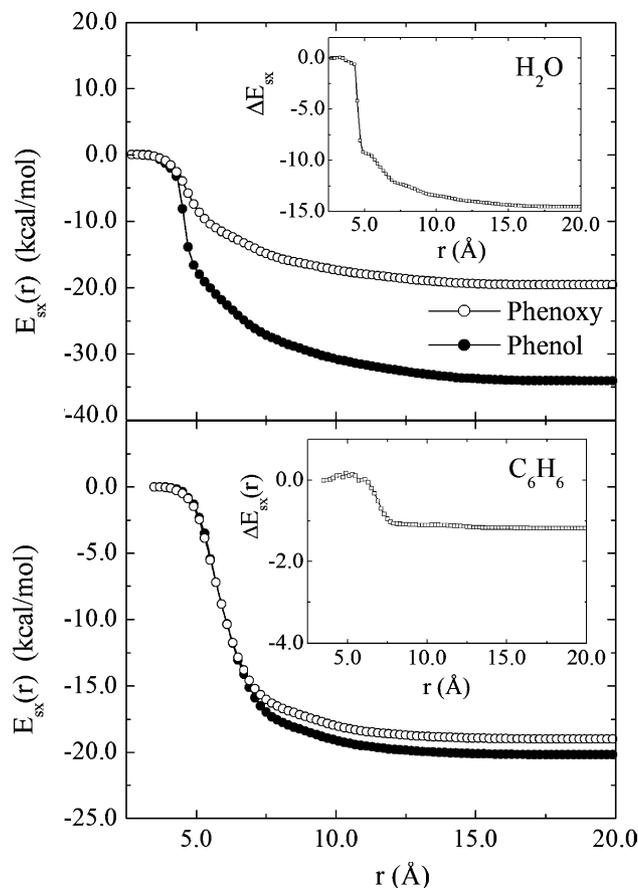


Fig. 5. Average solute–solvent energy of phenol and phenoxy in water and benzene, as a function of the centre-of-mass distance from the solute. The insets show the differential solute–solvent  $\Delta E_{\text{SX}}(r)$  energy.

moment of the ‘solute’. Now we consider that for the outer solvent molecules the solute is the hydrogen-bond shell, phenol–water and phenoxy–water. The dipole moments of the phenol–water ( $5.48 \pm 0.87$  D) and phenoxy–water ( $5.33 \pm 0.92$  D) hydrogen-bonded ‘solutes’ are numerically equivalent, and large, explaining the long-range but similar behaviour of the solute–solvent interaction (Fig. 5). This, considered alone, would lead to the preliminary conclusion that phenol and phenoxy hydrates equivalently. The distinction, leading to the correct qualitative result that phenol hydrates better, is obtained considering now the short-range part of the  $\Delta E_{\text{SX}}$  interaction. As Table 1 shows the counterpoise-corrected hydrogen binding energy is larger for PhOH ( $7.10 \pm 1.59$  kcal/mol) compared to PhO<sup>•</sup> ( $2.01 \pm 1.07$  kcal/mol), in water. This originates from two aspects. First, phenol is both a proton donor and proton acceptor of hydrogen bond, thus making two hydrogen bonds. Second, the phenoxy radical is a weak hydrogen-bond acceptor making only 0.57 hydrogen bonds. The difference in hydrogen bond solute–solvent interaction is 5.09 kcal/mol. This is a substantial contribution to the differential hydration energy based on Monte Carlo simulations [8], which is between 6 and 9 kcal/mol.

The results above lead to the conclusion that hydrogen bonds play a crucial role in the differential solvation enthalpy of phenol and phenoxy radical in protic and polar solvents. A quite similar reasoning can be made for acetonitrile but the magnitudes involved are smaller. The differential solvation energy in acetonitrile [9] amounts to less than 2.0 kcal/mol. Before concluding, we should discuss the differential solvation in benzene. As this solvent cannot form hydrogen bonds a special consideration is needed. Fig. 5 shows the behaviour of the differential solute–solvent interaction energy  $\Delta E_{SX}$ . The long-range values of  $E_{SX}$  are the same for phenol and phenoxy because benzene polarises very little, even by the large dipole moment of phenoxy. The differential solvation, in this case, is given predominantly by the solute–solvent interaction in the first solvation shell ( $R \leq 7.5 \text{ \AA}$ ).

#### 4. Summary and conclusions

Considering the solute–solvent hydrogen-bonded complexes in the liquid situation a qualitative and semi-quantitative description of the solvent effects on the O–H bond cleavage  $\text{PhOH} \rightarrow \text{PhO}^\bullet + \text{H}^\bullet$  in solution was presented. The usual view that the solute with the larger dipole moment has a higher solvation enthalpy in a polar solvent is recuperated. We contend that the preferential solvation of phenol (the lower dipole moment solute) over phenoxy derives from the hydrogen-bonded shell. The reconciliation with the usual understanding is obtained if we consider not the dipole moment of the isolated solute but, instead, the average dipole moment in solution of the solute–solvent hydrogen bonded solvation shell.

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