Differential Hydration of Phenol and Phenoxy Radical and the Energetics of the Phenol O−H Bond in Solution

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Monte Carlo simulations and thermodynamic perturbation theory calculations have been carried out to analyze the differential hydration of phenol (PhOH) and phenoxy radical (PhO•). The hydration enthalpy of phenol predicted by different phenol−water interaction models is in good agreement with experimental data. On the basis of the difference in the hydration enthalpy of phenol and phenoxy radical, we find that the O−H bond dissociation enthalpy in water is above the recommended experimental value for the gas phase by ca. 7 kcal/mol. This result is in agreement with photoacoustic calorimetry measurements for phenol in other polar solvents. Thermodynamic perturbation theory results for the relative hydration Gibbs energy of phenol and phenoxy radical are also reported. The structure of the solutions suggests that the differential solvation of phenol and phenoxy radical can be related to the strong character of phenol as a hydrogen bond donor in comparison with the role played by phenoxy radical as a hydrogen bond acceptor.

1. Introduction

The study of the solvation of organic molecules is very important to the understanding of chemical reactivity in the liquid phase, which plays a central role in chemistry and biochemistry.[1,2] One basic quantity that characterizes the energetics of the solvation process is the standard enthalpy of solvation of a species X from the gas phase, $\Delta H_{sln}(X,g)$. Several calorimetric techniques, including photoacoustic calorimetry,[3,4] have been used to estimate solvation enthalpies and bond dissociation enthalpies in solution. However, enthalpies of solvation of transient free radical species are still relatively scarce.[5−8] The reason is related to the limitations of the available experimental techniques to deal with transient species.[4]

The phenoxy radical (PhO•) is an important intermediate in the combustion of many aromatic compounds,[9−12] green plant photosynthesis,[13] biocatalysis,[14] and protein redox reactions.[15] Some recent works[16,17] analyzed the "hydration" of the phenoxy radical by carrying out density functional theory (DFT) calculations for PhO•−(H₂O)₁₋₄ clusters. A similar approach has been used by Chipman,[18] who carried out ab initio calculations for clusters of the *p*-aminophenoxyl radical with four water molecules.

These studies are useful because solvation is important for the understanding of the observed substituent effects on the spectra, structure, and chemistry of the phenoxy radical in water.[19] Moreover, the differential solvation of phenol and phenoxy radical can be related to the energetics of the phenol O−H homolytic bond dissociation and to chemical reactivity in solution.[6,20−22] Modeling of solvent effects by "microsolvation" in clusters has also been employed to discuss the structure and energetics of several radical species including the methoxy

radical,[23] cyclopentadienyl radicals,[24−26] and the 2,5-lutidyl radical.[27]

Statistical mechanics computer simulations can provide data on the structural and thermodynamic properties of liquids and solutions (see Dufy and Jorgensen for a recent review).[2] In addition, they also allow a detailed microscopic analysis of the solvation process. A large number of computer simulations have been performed to study the solvation of molecules[2,28−32] and charged species.[33−36]

Much less attention has been paid to the solvation of radicals.[37] This is due to the fact that interactions between radical species and the solvent molecules are not well-known and can be very specific and solvent dependent.[23]

In the present work we report Monte Carlo (MC) simulations of the hydration of phenol and phenoxy radical. We analyze the structure and thermodynamics of the solutions and the relationship between the hydration enthalpies and the energetics of the phenol O−H bond dissociation in solution, which has been extensively analyzed in a recent review work.[22]

We compare the statistical mechanics simulation results for some thermodynamical properties with those based on a previous microsolvation approach.[16] Thermodynamic perturbation theory[38−41] calculations have also been carried out to evaluate the relative hydration Gibbs energies of phenol and phenoxy radical.

2. Interaction Model and Computational Details

Monte Carlo simulations of phenol and phenoxy radical in water have been carried out in the isobaric−isothermal (NPT) ensemble[42] at $T = 25$ °C and $P = 1$ atm. The interactions between two molecules, a and b, were described by a Lennard-Jones (LJ) plus Coulomb contribution, with parameters ϵ_i, σ_i, and q_i for each atom:

$$U_{ab} = \sum_{i \in a} \sum_{j \in b} 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] + \frac{q_i q_j e^2}{r_{ij}} \quad (1)$$

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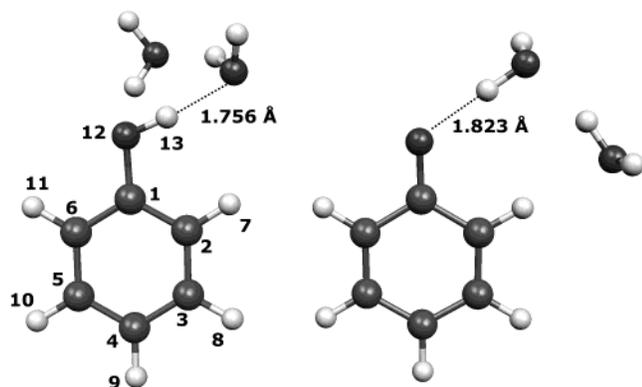*J. Phys. Chem. B, Vol. 107, No. 18, 2003* **4305**

Figure 1. Optimized structures (B3LYP/6-31G(d,p)) of clusters of phenol (left) and phenoxy radical (right) with two water molecules.

where $\epsilon_{ij} = (\epsilon_i\epsilon_j)^{1/2}$ and $\sigma_{ij} = (\sigma_i\sigma_j)^{1/2}$. The LJ parameters for the phenol molecule and phenoxy radical are those proposed by Jorgensen and Nguyen[43] for pure liquid phenol. Long-range corrections to the LJ interactions have been included. For the water molecules, the geometry and interaction parameters correspond to the SPC potential proposed by Berendsen et al.[44] In all simulations, the molecules have a rigid geometry. The geometries of phenol (planar form) and phenoxy radical were obtained from DFT optimizations. The internal rotation of the phenol O–H group, which is related to an energy barrier of 2.55 kcal/mol,[45] has not been included.

The geometries have been optimized with Becke's three-parameter hybrid method (B3)[46] with the Lee, Yang, and Parr (LYP)[47] correlation (B3LYP) and the 6-31G(d,p) basis set.[48]

Three different models have represented the Coulomb interactions between phenol and water. The first two correspond to phenol charge distributions proposed, respectively, by Jorgensen and Nguyen[43] and by Mooney et al.[45] In the third model the atomic charges have been fitted to the electrostatic potential by using the Merz–Kollman–Singh[49,50] procedure. To take into account the polarization of the solute charges by the solvent molecules, the solute charges have been estimated in small clusters of phenol and phenoxy radical with two water molecules (see Figure 1) with SPC charges. By using this method, the phenoxy radical charge distribution is slightly asymmetric, but we have verified that it leads to essentially equivalent solute–solvent interactions if a symmetrized charge distribution is used. The charges were calculated at the B3LYP/6-311++G(d,p) level with B3LYP/6-31G(d,p)-optimized geometries. We note that the LJ parameters of Jorgensen and Nguyen[43] and Mooney et al.[45] are identical with the exception of ϵ for the phenol oxygen. The interaction parameters are reported in Table 1.

In the present model the effective dipole moment of phenol in the presence of two water molecules is 2.10 D, in very good agreement with the value reported by Jorgensen and Nguyen[43] (2.11 D), but higher than the effective dipole moment proposed by Mooney et al. (1.89 D)[45] for the liquid phase, which was based on the Onsager self-consistent reaction field. The gas-phase dipole moment at the B3LYP/6-311++G(d,p)//B3LYP/6-31G(d,p) level is 1.44 D, in excellent agreement with experiment (1.4 D)[51] and other theoretical results.[52] In addition, we have verified that our model leads to liquid properties of pure liquid phenol in very good agreement with experiment and other theoretical models.[43,45]

In the simulations a cubic cell with periodic boundary conditions has been used. The simulated systems include one solute molecule (phenol or phenoxy radical) and 200 and 450 water molecules (N_w). For each value of N_w, the interactions

TABLE 1: Lennard-Jones Parameters and Charge Distribution for Phenol (PhOH) and Phenoxy Radical (PhO•)

phenol and phenoxy	ϵ^a (kcal/mol)	σ^a (Å)	q^b (au) PhOH	q^b (au) PhO•
C1	0.070	3.550	0.5667	0.6020
C2	0.070	3.550	−0.4090	0.2384
C3	0.070	3.550	−0.0214	−0.1010
C4	0.070	3.550	−0.2304	−0.1317
C5	0.070	3.550	−0.0952	−0.1010
C6	0.070	3.550	−0.2910	−0.2384
H7	0.030	2.420	0.1900	0.1241
H8	0.030	2.420	0.1157	0.1313
H9	0.030	2.420	0.1394	0.1397
H10	0.030	2.420	0.1281	0.1313
H11	0.030	2.420	0.1680	0.1241
O12	0.170 or 0.155^c	3.070	−0.7613	−0.4420
H13	0.0	0.0	0.5004	
SPC water^d				
O	0.155	3.165	−0.820	
H1, H2	0.0	0.0	0.410	

^{a} Lennard-Jones parameters from Jorgensen and Nguyen.[43] ^{b} Atomic charges are Merz−Kollman charges from B3LYP/6-311++G(d,p) calculations. ^{c} Parameter ϵ for the phenol oxygen from Mooney et al.[45] ^{d} SPC parameters for water from Berendsen et al.[44]

TABLE 2: Thermodynamic Properties of Pure Water, Phenol−Water, and Phenoxy Radical−Water Solutions from NPT Monte Carlo Simulations at $T = 25°$ C and $P = 1$ atm^a

N_w	200	450
R_c (Å)	8.9	11.6
	Pure Water	
ρ^*	1.059 ± 0.018	1.058 ± 0.011
H_{ss}^*	−2168.1 ± 1.5	−4869.6 ± 0.9
	Phenol−Water	
ρ	1.047 ± 0.010	1.060 ± 0.019
	1.048 ± 0.015^c	
	1.048 ± 0.020^d	
E_{sx}	−33.00 ± 0.10	−34.26 ± 0.10
	−29.48 ± 0.20^c	
	−27.04 ± 0.25^d	
H_{ss}	−2152.3 ± 1.4 (15.8 ± 1.2)	−4853.4 ± 0.8 (16.2 ± 1.2)
	−2155.1 ± 1.8^c (13.0 ± 1.8)	
	−2155.4 ± 1.8^d (12.7 ± 1.8)	
ΔH_{hyd}(PhOH,g)^b	−17.8 ± 1.5	−18.6 ± 1.1
	−17.1 ± 2.5^c	
	−14.9 ± 3.1^d	
	Phenoxy−Water	
ρ	1.048 ± 0.010	1.059 ± 0.012
E_{sx}	−19.96 ± 0.10	−20.46 ± 0.08
H_{ss}	−2156.0 ± 1.2 (12.1 ± 1.2)	−4859.1 ± 0.6 (10.5 ± 1.2)
ΔH_{hyd}(PhO•,g)	−8.5 ± 1.6	−10.6 ± 1.1

^{a} N_w is the number of water molecules. R_c is the cutoff radius for the interactions between the solute (X) and the solvent (S). $H_{ss} = E_{ss} + PV$ is the enthalpy (kcal/mol) of the water in the solution, and $H_{ss}^* = E_{ss}^* + PV^*$ is the enthalpy of pure liquid water, where E_{ss}^* and V^* are the energy and volume of pure liquid water. ρ^* and ρ are, respectively, the densities (g/cm³) of pure liquid water and the solution. $\Delta H_{hyd}(X,g) = E_{sx} + (H_{ss} - H_{ss}^*) - RT$ is the hydration enthalpy from the gas phase of the solute species X. Values in parentheses are the relaxation enthalpies (ΔH_R). ^{b} Experimental values for ΔH_{hyd}(PhOH,g) are −13.6 kcal/mol[59] and −13.8 ± 0.2 kcal/mol.[16] ^{c} Potential model of phenol from Mooney et al.[45] ^{d} Potential model of phenol from Jorgensen and Nguyen.[43]

have been truncated at a different cutoff distance R_c, which is reported in Table 2. The initial configuration has been generated randomly. The maximum displacement of the molecules has been self-adjusted to give an acceptance ratio around 50%. Attempts were made to change the volume every 1000 steps. Each step involves the attempt to move one molecule of the system. At least 10^8 steps have been carried out for equilibration.

Average values have been calculated over $(8-18) \times 10^8$ additional steps. We remark that such a very large number of steps are necessary to get a reliable estimation of the solvent relaxation energy (see section 3.A.2). The DFT calculations have been carried out with the Gaussian-98 program.[53] The Monte Carlo simulations have been performed with the DICE program.[54]

We are also reporting results for the hydration enthalpy of the hydrogen atom by assuming that it can be represented by a classical LJ particle, and that quantum effects are negligible at $T = 298$ K.[55] We have carried out NPT simulations with two sets of LJ parameters to model the interactions between the hydrogen atom and the SPC water. In the first, $\epsilon = 0.030$ kcal/mol and $\sigma = 2.420$ Å (see Table 1). In the second, the LJ parameters for fluid hydrogen reported by Buch[56] ($\epsilon = 0.0675$ kcal/mol and $\sigma = 3.06$ Å) have been used.

3. Results and Discussion

A. Thermodynamics. *1. Hydration Enthalpy of Phenol and Phenoxy Radical.* H_{sx} and $H_{ss}*$ will represent, respectively, the total enthalpies of the solution (with one solute molecule) and pure liquid water, for systems with N_w water molecules. They are defined as

$$H_{sx} = E_{sx} + E_{ss} + PV \quad (2)$$

and

$$H_{ss}* = E_{ss}* + PV* \quad (3)$$

where E_{sx} is the solute−solvent energy, E_{ss} is the solvent−solvent energy, $E_{ss}*$ is the solvent−solvent energy in the pure liquid, and $V*$ and V are, respectively, the volumes of the pure liquid and solution. The hydration enthalpy from the gas phase of the solute species X = (PhOH, PhO•) can be calculated as

$$\Delta H_{hyd}(X,g) = H_{sx} - H_{ss}* - RT \quad (4)$$

$$= E_{sx} + (E_{ss} - E_{ss}*) + P(V - V*) - RT \quad (5)$$

$$= E_{sx} + \Delta H_R - RT \quad (6)$$

where

$$\Delta H_R = \Delta E_R + P\Delta V_R = H_{ss} - H_{ss}* \quad (7)$$

is the contribution of the solvation relaxation to the enthalpy, given by the solvent relaxation energy $\Delta E_R = E_{ss} - E_{ss}*$ and the solvent relaxation volume $P\Delta V_R = P(V - V*)$, which is negligible under normal conditions.

The estimation of solvation enthalpies from expression 6 is difficult due to the slow convergence of the solvent relaxation energy $\Delta E_R = E_{ss} - E_{ss}*$, which is calculated as the difference between two large fluctuating numbers.[57,58] However, by carrying out very long simulations, it is possible to get reliable values, as discussed below.

Table 2 reports thermodynamic data from the simulations of pure liquid water and solutions. The experimental hydration enthalpy for phenol, $\Delta H_{hyd}(PhOH,g)$, has been reported by Cabani et al. (−13.6 kcal/mol)[59] and by Guedes et al. (−13.8 ± 0.2 kcal/mol).[16] The theoretical results obtained here range from −14.9 ± 3.1 to −18.6 kcal/mol depending on the theoretical model used. Using the models of Jorgensen and Nguyen[43] and Mooney et al.,[45] we obtain −14.9 ± 3.1 and −17.1 ± 2.5 kcal/mol, respectively. The result using our model that fits the charge to the electrostatic potential is −17.8 ± 1.5

kcal/mol for a solvation in 200 water molecules and −18.6 ± 1.1 kcal/mol in 450 waters. Overall, the results for ΔH_{hyd}-(PhOH,g) are in satisfactory agreement with experiment. One possible reason for the deviation from the experimental result is the approximation used that the phenol molecule has a rigid O−H group. As shown in Table 2, the hydration enthalpy of phenoxy radical, $\Delta H_{hyd}(PhO•,g)$, is −10.6 ± 1.1 kcal/mol ($N_w = 450$). No experimental result seems to be available for comparison. We are thus predicting that the enthalpy of solvation for the phenoxy radical $\Delta H_{hyd}(PhO•,g)$ is about 8 kcal/mol higher than the enthalpy of solvation for the phenol molecule ΔH_{hyd}-(PhOH,g). The results of Table 2 also give information on the contribution of the solvation relaxation to the enthalpy. The total relaxation ΔH_R is calculated as 16.2 ± 1.2 kcal/mol for the phenol and 10.5 ± 1.2 kcal/mol for the phenoxy. Thus, the relaxation not only is sizable for the individual cases but also contributes 5.7 kcal/mol for the differential hydration.

2. Comparison with a Microsolvation Approach. It is interesting to compare the hydration enthalpy $\Delta H_{hyd}(X,g)$ with the enthalpy ΔH_r of the following reaction in the gas phase, $[X-(H_2O)_{N_w}] \rightarrow X + (H_2O)_{N_w}$, from a previous study based on a microsolvation approach.[16] X represents the solute (phenol or phenoxy radical), and N_w is the number of water molecules in the cluster. For phenol, good agreement between the present results and the microsolvation approach is observed for the $[PhOH-(H_2O)_3]$ cluster ($\Delta H_r = -14.1$ kcal/mol obtained using B3LYP/D95V(d,p)).[16] However, the results depend on the cluster size. For instance, in the case of $[PhOH-(H_2O)_6]$, $\Delta H_r = -9.65$ kcal/mol, which is 4.1 kcal/mol above the experimental result (−13.8 ± 0.2 kcal/mol). For the phenoxy radical case, the results for the microsolvation show a strong dependence on the cluster size and it is difficult to attribute a correspondence between $\Delta H_{hyd}(PhO•,g)$ and ΔH_r, although for $[PhO•-(H_2O)_2]$, $\Delta H_r = -10.8$ kcal/mol (B3LYP/D95V(d,p)), in good agreement with the calculated value for $\Delta H_{hyd}(PhO•,g)$. The dependence of the results on the cluster size observed in the microsolvation approach (mainly for phenoxy radical) suggests that extrapolations to liquid-state solvation should be carried out with caution.

To further examine this question, we shall consider the solute−solvent interaction energy using quantum mechanical calculations of the solute and all solvent molecules within the first solvation shell. We have thus selected 20 statistically uncorrelated[29] MC configurations, separated by 10^5 steps. By selecting uncorrelated configurations, it is possible to evaluate converged statistical averages with a relatively small number of structures.[29] These configurations were then used to carry out single-point energy DFT (B3LYP/6-31G(d,p)) calculations for the selected 20 clusters composed of one solute molecule (phenol or phenoxy radical) and the 32 water molecules lying in the first coordination shell. From the total energies we have obtained the average solute−solvent interaction energies E_{sx}.[60] Counterpoise correction to BSSE[61] has been included in all cases. First, the convergence of E_{sx} evaluated over 20 uncorrelated configurations is demonstrated in Figure 2. As can be seen in the case of phenol the average value obtained for E_{sx} over these 20 statistically uncorrelated configurations is −15.6 ± 0.92 kcal/mol. For the phenoxy radical, E_{sx} is −10.0 ± 1.21 kcal/mol. Although these DFT calculations include only the solvent molecules in the first coordination shell, it is common practice to assume that the interaction with the solvent molecules beyond this shell will represent only a small correction to E_{sx}. These solute−solvent energies are considerably smaller than the classical result for the bulk (Table 2). For a better comparison, the E_{sx} energy calculated using the classical
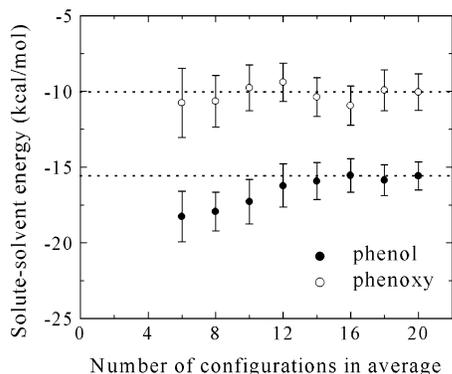
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Figure 2. Solute−solvent energy (E_{sx}, kcal/mol) for uncorrelated configurations including 1 solute and 32 water molecules in the first coordination shell.
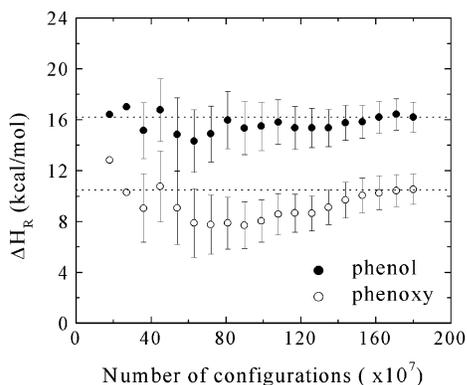

Figure 3. Convergence of the solvent relaxation ΔH_R as a function of the number of configurations included in the average value.

potential of the simulation, in these same 20 configurations with the first coordination shell, is -25.03 ± 0.76 kcal/mol for the phenol and -12.89 ± 0.73 kcal/mol for the phenoxy. In the classical result, therefore, not considering the outer solvation shells gives a total E_{sx} energy cost of ∼8 kcal/mol for the phenol and ∼7 kcal/mol for the phenoxy. Use of the quantum mechanical results of microsolvation calculations to estimate solvation enthalpy assumes that the solvation relaxation ΔH_R is negligible, and in this case E_{sx} would give a good estimate (eq 6) of the solvation energy in the liquid case. The values obtained here for ΔH_R are, however, not negligible. It thus seems that the use of the microsolvation model in this case cannot give good results for the independent cases of phenol and phenoxy. However, it might be noted that even the differential hydration could not be well described. The computed differences between E_{sx} of phenol and phenoxy radical from the DFT calculations (5.6 kcal/ mol) and the results obtained using the classical potential (12.1 kcal/mol) are not in close agreement. The difference between $\Delta\Delta H_{hyd}(X,g)$ and ΔE_{sx} is the difference in solvent relaxations $\Delta\Delta H_R$ of phenol and phenoxy, which is not zero. This difference in ΔH_R between phenol and phenoxy using the classical model is 5.7 kcal/mol ($N_w = 450$), 3.7 kcal/ mol ($N_w = 200$), and 3.0 kcal/mol ($N_w = 32$) for the first coordination shell. This is indicative that a large part of the solvent relaxation contribution to the differential hydration comes from the first coordination shell. The convergence of ΔH_R is shown in Figure 3 and illustrates the computational effort. As can be seen, a very long simulation (18×10^8 MC steps) is necessary to obtain converged numerical results. In the case of phenol in 450 water molecules the converged average value, as reported in Table 2, is 16.2 ± 1.2 kcal/mol, and that of phenoxy is 10.5 ± 1.2 kcal/mol.

3. Phenol O−H Bond Dissociation Enthalpy in Water. The difference in the solvation enthalpies of phenol and phenoxy radical are very important to analyze the energetics of the O−H bond.[6,22] If D(PhO−H) and D_w(PhO−H) represent, respectively, the bond dissociation enthalpies (BDEs) of phenol in the gas phase and in water, a route to estimate D_w(PhO−H), starting from gas-phase data, is based on the relation[21,22]

$$D(\text{PhO−H}) = D_w(\text{PhO−H}) + \Delta H_{hyd}(\text{PhOH,g}) - \Delta H_{hyd}(\text{PhO}^\bullet,\text{g}) - \Delta H_{hyd}(\text{H}^\bullet,\text{g}) \quad (8)$$

which can be derived from a thermochemical cycle involving solution and gas-phase enthalpies related to the phenol O−H homolytic bond dissociation.[22] $\Delta H_{hyd}(\text{H}^\bullet,\text{g})$, representing the enthalpy of solvation of the hydrogen atom, has never been experimentally determined. We have carried out NPT Monte Carlo simulations to evaluate $\Delta H_{hyd}(\text{H}^\bullet,\text{g})$ in SPC water. Using the two theoretical models described in section 2, we predict that $\Delta H_{hyd}(\text{H}^\bullet,\text{g})$ is -0.91 ± 0.38 and -1.43 ± 0.38 kcal/mol (Buch parameters[56]). These results are in very good agreement with the experimental enthalpy of hydration of H_2 ($\Delta H_{hyd}(H_2,g) = -0.96$ kcal/mol) proposed by Wilhelm[62] and supports the usual assumption that $\Delta H_{hyd}(\text{H}^\bullet,\text{g})$ is similar to $\Delta H_{hyd}(H_2,g)$.[63] In this case of hydrogen hydration the solvent relaxation, as expected, is calculated to be negligible. The importance of relation 8 is that many bond dissociation enthalpies have been measured in the gas phase although most of the chemistry to which they apply occurs in solution. Relation 8 involves the difference in the hydration enthalpies of phenol and phenoxy radical, $\Delta\Delta H_{hyd} = \Delta H_{hyd}(\text{PhOH,g}) - \Delta H_{hyd}(\text{PhO}^\bullet,\text{g})$. Several techniques were proposed to determine BDEs in solution,[22] and various experimental works analyzed the solvent effects on homolytic bond dissociation enthalpies.[5,6,20−22]

Some authors[5,21] provided evidence that, in some cases, BDEs in solution can be identified with the gas-phase values because solvent effects are expected to be small. However, photoacoustic calorimetric measurements by Wayner et al.[6] indicated that the magnitude of the phenol BDEs is dependent on the solvent where the measurements have been made. These authors also provided evidence that this behavior can be related to the differential solvation of reactants and products. From Table 2 and by using the present model, the difference in the hydration enthalpies of phenol and phenoxy radical ($\Delta\Delta H_{hyd}$) is -8.2 ± 2.2 kcal/mol ($N_w = 450$). By using the Mooney et al.[45] and the Jorgensen and Nguyen[43] models, $\Delta\Delta H_{hyd}$ values are -8.5 ± 3.6 and -6.3 ± 4.5 kcal/mol, respectively. These results support the view that the solvation enthalpies $\Delta H_{sln}(\text{PhOH,g})$ and $\Delta H_{sln}(\text{PhO}^\bullet,\text{g})$ are not the same in solvents which can form hydrogen bonds to phenol.[6] This can be explained by the different solute−solvent interactions of phenol and phenoxy radical with water and solvent relaxation contributions (see the previous section). It is difficult to generalize this conclusion to other systems, including substituted phenols and other polar solvents. The specific character of the interactions between the solvated species and the solvent, as well as the solvent relaxation enthalpy, should be appropriately taken into account.

The recommended value for the PhO−H bond dissociation energy D(PhO−H) is 88.74 ± 0.55 kcal/mol.[22] On the basis of expression 8, we are predicting that D_w(PhO−H) is above the gas-phase value by ca. 7 kcal/mol. This difference between D_w(PhO−H) and D(PhO−H) is comparable to the experimental value for phenol in other polar solvents, for example, phenol in acetonitrile (5.6 kcal/mol).[6,22]

4. Relative Hydration Free Energy of Phenol and Phenoxy Radical. We have used thermodynamic perturbation theory[38−41]

TABLE 3: Gibbs Energy Differences (kcal/mol) for Phenol ↔ Phenoxy Radical Interconversion in SPC Water at 25 °C

λ_i	λ_j	$\Delta G_{hyd}(i \rightarrow j)$	$\Delta G_{hyd}(j \rightarrow i)$
0.00	0.125	3.18 ± 0.05	-2.91 ± 0.15
0.125	0.250	1.41 ± 0.12	-1.67 ± 0.02
0.250	0.375	1.23 ± 0.02	-0.92 ± 0.02
0.375	0.500	0.54 ± 0.03	-0.78 ± 0.09
0.500	0.625	0.39 ± 0.06	-0.47 ± 0.02
0.625	0.750	0.20 ± 0.01	0.01 ± 0.04
0.750	0.875	-0.44 ± 0.03	0.15 ± 0.04
0.875	1.00	-0.51 ± 0.05	0.69 ± 0.09
total		6.00 ± 0.37	-5.90 ± 0.47

to evaluate the relative hydration Gibbs energy of phenol and phenoxy radical. The method is based on the following relation for the Gibbs energy difference between systems i and j:

$$G_j - G_i = -k_B T \ln \langle \exp[-(H_j - H_i)/k_B T] \rangle_i \qquad (9)$$

where the average corresponds to sampling using system i.

If ξ denotes a geometric or potential function parameter, a coupling parameter λ connecting systems i and j can be defined as

$$\xi(\lambda) = \xi_i + \lambda(\xi_j - \xi_i) \qquad (10)$$

The connection between systems i and j is then possible by mutating one system to another as λ goes from 0 to 1. In our simulations phenol is mutated into phenoxy radical by scaling the charges reported in Table 3 according to expression 10. It has been assumed that the geometry and the LJ parameters of the solutes are not modified during the mutation. This assumption means that the main difference between the solvation of phenol and phenoxy radical in water should be related to electrostatic interactions. It is important to note that the hydrogen atom of the phenol O−H group is represented in the simulation only by the Coulomb charge (see Table 1). Therefore, the H atom vanishes when the charge becomes zero. Free energy differences during the mutation are reported in Table 3. The hysteresis of the results is quite small, reflecting that the $\Delta\lambda$ values are adequate. The $\lambda_i \rightarrow \lambda_j$ and $\lambda_j \rightarrow \lambda_i$ results lead to total ΔG_{hyd} values of 6.0 ± 0.37 and -5.9 ± 0.47 kcal/ mol, respectively.

B. Structure. Figure 4 shows the phenol−water ($\lambda = 0$) and phenoxy radical−water ($\lambda = 1$) center-of-mass (cm−cm) radial distribution function (RDF). The phenol−water RDF is characterized by the presence of a small shoulder between 3 and 4 Å and by a peak (1.2 at $r = 5.1$ Å) reflecting the organization of the water molecules around the phenol O−H group. Both the shoulder and the peak disappear when λ increases. Integration of this function up to the first minimum (0.93 at 6.2 Å) yields 32 molecules, which is the number of water molecules in the phenol first coordination shell. The phenoxy radical−water cm−cm RDF ($\lambda = 1$) has a maximum (1.53) at $r = 4.9$ Å. Integration up to the first minimum (0.83 at 6.2 Å) yields 32 water molecules, which is the same coordination number of phenol. Figure 4 also shows the RDF of the mutating phenol molecule for different values of λ. When $\lambda = 0.25$, this function is already similar to the phenoxy radical−water RDF ($\lambda = 1$), indicating that a small change in the charge distribution can disrupt the organization of the water molecule around the O−H group.

Figure 5 shows configurations from the simulations of phenol and phenoxy radical in water. The snapshots include 32 water molecules in the first coordination shell. Hydrogen bonding between the phenol O−H group (left panel) and the water
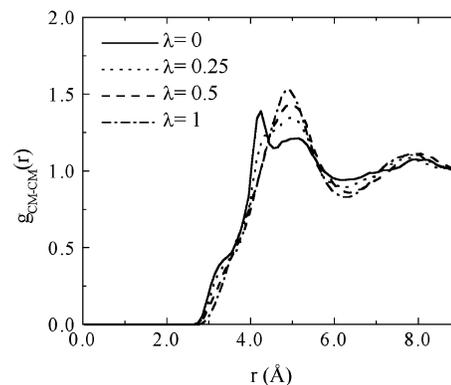

Figure 4. Phenol−water and phenoxy radical−water center-of-mass radial distribution function as a function of the mutating parameter λ from phenol ($\lambda = 0$) to phenoxy radical ($\lambda = 1$). Integration of these functions up to the first minimum (6.2 Å) yields 32 water molecules which define the first coordination shell.

molecules as well as between the phenoxy radical oxygen (right panel) and the water hydrogen is illustrated. Figure 6 reports $g_{H_x-O_w}(r)$ that represents the partial radial distribution functions describing the correlations between the mutating H atom of phenol and the oxygen atoms of water. The first maximum of this function (2.5 at $r = 1.65$ Å) when $\lambda = 0$ reflects the hydrogen bond formation between the hydrogen in the phenol O−H group and the water molecules. This maximum shows an interesting behavior as a function of λ. It is shifted to the right and drops quickly to zero when λ increases. For $\lambda = 0.5$ this function is similar to $g_{O_x-O_w}(r)$ shown in Figure 7. This can be explained by observing that, for the phenoxy radical species, the correlations between this (virtual) site and the water oxygen reflects the interactions between the phenoxy radical oxygen and the water oxygen. Moreover, the strong dependence of $g_{H_x-O_w}$ on λ illustrates how the hydrogen bond donor properties of the hydroxyl group are modified when we move away from phenol ($\lambda = 1$).

Figure 7 shows $g_{O_x-O_w}(r)$. When $\lambda = 0$, this function describes the correlations between the oxygen atom in the phenol O−H group and the oxygen atoms of water. This function exhibits a first maximum (2.0 at $r = 2.65$ Å). Integration up to the first minimum (0.5 at $r = 3.2$ Å) yields 3.0, which is the average number of water molecules in close interaction with the phenol O−H group. When λ increases, the local order around the O−H group is significantly modified. The maximum of $g_{O_x-O_w}(r)$ is reduced and shifted to the right. When $\lambda = 1$, this function exhibits a first maximum (1.05 at $r = 3.15$ Å). Integration up to the first minimum (0.84 at $r = 4.55$ Å) yields 10.0. The behavior of this function when the solute mutates from phenol to phenoxy radical indicates that the differential solvation of these species involves some reorganization around the solute oxygen atom. One specific feature characterizing this reorganization is a significant increase of the average distance between the solute and the water oxygen atoms when we move from phenol to phenoxy radical.

Figure 8 shows $g_{O_x-H_w}(r)$ that describes hydrogen bonding related to the acceptor character of the solute oxygen. When $\lambda = 0$, this function shows a sharp peak (1.2 at $r = 1.75$ Å), which is related to the hydrogen bonding in phenol. Integration up to the first minimum (0.15 at $r = 2.45$ Å) yields 1.6, which is the average number of water hydrogen atoms closer to the phenol oxygen. When λ increases, this peak is reduced and shifted to the right (0.5 at $r = 1.9$ Å for $\lambda = 1$). Integration up to the first minimum (0.4 at $r = 2.45$ Å) yields 1.3, which is the average
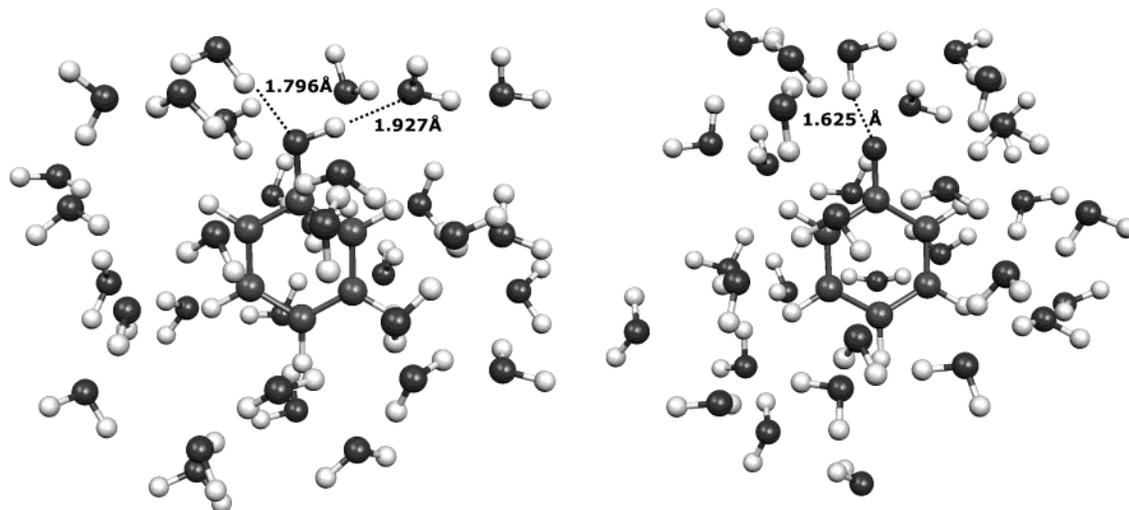
Hydration of Phenol and Phenoxy Radical

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Figure 5. Configurations from the simulation of phenol (left) and phenoxy radical (right) in water. Typical hydrogen bonding between the solutes and the water molecules is indicated.
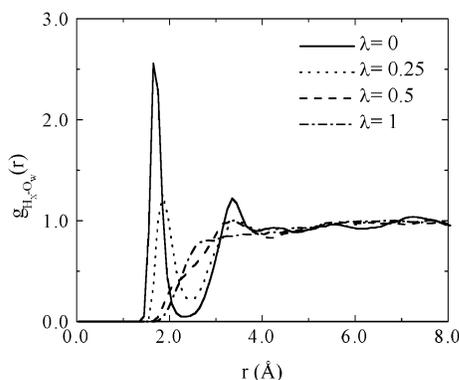

Figure 6. Solute−solvent $g_{H_x-O_w}(r)$ radial distribution function between the mutating hydrogen and the water oxygen as a function of λ.
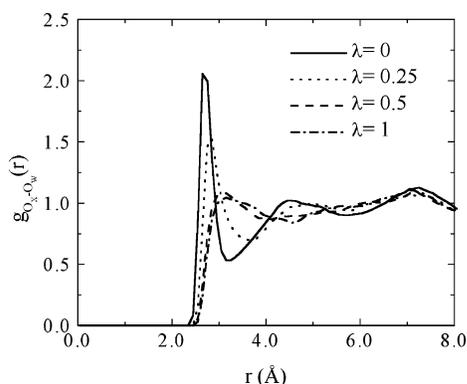

Figure 8. Solute−solvent $g_{O_x-H_w}(r)$ radial distribution function between the mutating oxygen and the water hydrogen as a function of λ.

Figure 7. Solute−solvent $g_{O_x-O_w}(r)$ radial distribution function between the mutating oxygen and the water oxygen as a function of λ.

number of water hydrogen atoms closer to the phenoxy radical oxygen. This result indicates that the hydrogen bond acceptor role played by the phenoxy radical is less important than the role played as a hydrogen bond donor by phenol (see Figure 6). For larger distances and $\lambda = 1$, $g_{O_x-H_w}(r)$ is almost structureless and exhibits a wide shoulder with a maximum value of 0.9 at $r = 4.75$ Å.

We have verified that the solvent−solvent RDFs are not modified by the presence of the solutes. This is in agreement with thermodynamic results indicating that solvation of phenol or phenoxy radical in water occurs without a significant reorganization of the solvent, beyond the first solvation shell.
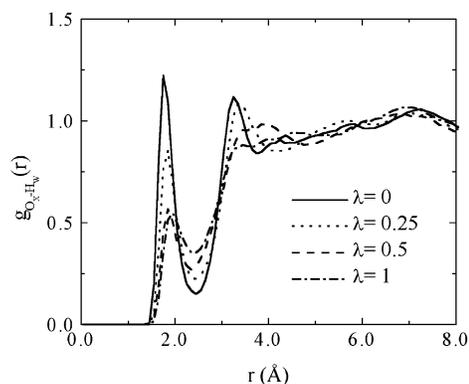
4. Conclusions

Monte Carlo simulations and thermodynamic perturbation theory calculations have been carried out to analyze the differential hydration of phenol and phenoxy radical. The theoretical hydration enthalpy of phenol is in good agreement with experimental data.[16,59]

We predict that the difference in the hydration enthalpy of phenol and phenoxy radical ranges from 6.4 to 9.3 kcal/mol, and we explain that this difference reflects the role played by phenol as a hydrogen bond donor in water that is more important than the one played by phenoxy radical as a hydrogen bond acceptor. This result contradicts the assumption adopted by some experimental works that the difference in the hydration enthalpy of phenol and phenoxy radical is not significant.[5] Consequently, our results provide additional theoretical support to the view[6] that solvent effects are indeed important to estimate with accuracy the O−H bond dissociation enthalpy in a hydrogen bond donor or acceptor solvent. Comparison with a previous study based on clusters of phenol and phenoxy radical with water[16] illustrates some limitations of the microsolvation approach to obtain estimates of hydration enthalpy because of its strong dependence on the number of water molecules and for not allowing for the sizable contribution of solvent relaxation.

The analysis of the structure of the solutions has provided some evidence that the changes related to the differential hydration of phenol and phenoxy radical are essentially driven by electrostatic interactions. A small modification of the solute

charge distribution when we move from phenol to phenoxy radical disrupts the organization around the O−H group and modifies the hydrogen bond donor properties of the mutating hydroxyl group. However, this reorganization is apparently local, and our results indicate that the solvation of both phenol and phenoxy radical occurs with a significant reorganization of the solvent in the first coordination shell.

References and Notes

(1) Cornell, W. D.; Cieplak, P.; Bayly, C. I.; Merz, K. M.; Ferguson, D. M.; Spellmayer, D. C.; Fox, T.; Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 5179.

(2) Dufy, E. M.; Jorgensen, W. L. *J. Am. Chem. Soc.* **2000**, *122*, 2878.

(3) Laarhoven, L. J. J.; Mulder, P.; Wayner, D. D. M. *Acc. Chem. Res.* **1999**, *32*, 342.

(4) Santos, R. M. B.; Muralha, V. S. F.; Correia, C. F.; Simões, J. A. M. *J. Am. Chem. Soc.* **2001**, *123*, 12670.

(5) Kanabus-Kaminska, J. M.; Gilbert, B. C.; Griller, D. J. *J. Am. Chem. Soc.* **1989**, *111*, 3311.

(6) Wayner, D. D. M.; Lusztyk, E.; Pagé, D.; Ingold, K. U.; Mulder, P.; Laarhoven, L. J. J.; Aldrich, H. S. *J. Am. Chem. Soc.* **1995**, *117*, 8737.

(7) de Heer, M. I.; Korth, H.-G.; Mulder, P. J. *J. Org. Chem.* **1999**, *64*, 6969.

(8) Santos, R. M. B.; Lagoa, A. L. C.; Simões, J. A. M. *J. Chem. Thermodyn.* **1999**, *31*, 1483.

(9) Platz, J.; Nielsen, O. J.; Wallington, T. J.; Ball, J. C.; Hurley, M. D.; Straccia, A. M.; Schneider, W. F. *J. Phys. Chem. A* **1998**, *102*, 7964.

(10) Sibener, S. J.; Buss, R. J.; Casavecchia, P.; Hirooka, T.; Lee, Y. T. *J. Chem. Phys.* **1980**, *72*, 4341.

(11) Liu, R.; Morokuma, K.; Mebel, A. M.; Lin, M. C. *J. Phys. Chem.* **1996**, *100*, 9314.

(12) Lin, C.-Y.; Lin, M. C. *J. Phys. Chem.* **1986**, *90*, 425.

(13) Weaver, E. C. *Annu. Rev. Plant. Physiol.* **1968**, *19*, 283.

(14) Itoh, S.; Taki, M.; Fukuzumi, S. *Coord. Chem. Rev.* **2000**, *198*, 3.

(15) Kagan, V. E.; Tyurina, Y. Y. *Ann. N. Y. Acad. Sci.* **1998**, 854.

(16) Guedes, R. C.; Cabral, B. J. C.; Simões, J. A. M.; Diogo, H. P. *J. Phys. Chem. A* **2000**, *104*, 6062.

(17) Couto, P. C.; Guedes, R. C.; Cabral, B. J. C.; Simões, J. A. M. *Int. J. Quantum Chem.* **2002**, *86*, 297.

(18) Chipman, D. M. *J. Phys. Chem. A* **1999**, *103*, 11181.

(19) Tripathi, G. N. R. *J. Phys. Chem. A* **1998**, *102*, 2388.

(20) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 1229.

(21) Bordwell, F. G.; Wei-Zhang, L. *J. Am. Chem. Soc.* **1996**, *118*, 10819.

(22) Santos, R. M. B.; Simões, J. A. M. *J. Phys. Chem. Ref. Data* **1998**, *27*, 707.

(23) Fernandez, J. A.; Yao, J.; Bernstein, E. R. *J. Chem. Phys.* **1997**, *107*, 3363.

(24) Fernandez, J. A.; Yao, J.; Bernstein, E. R. *J. Chem. Phys.* **1999**, *110*, 5159.

(25) Yao, J.; Fernandez, J. A.; Bernstein, E. R. *J. Chem. Phys.* **1999**, *110*, 5174.

(26) Fernandez, J. A.; Yao, J.; Bernstein, E. R. *J. Chem. Phys.* **1999**, *110*, 5183.

(27) Bray, J. A.; Bernstein, E. R. *J. Phys. Chem. A* **1999**, *103*, 2214.

(28) Urahata, S.; Canuto, S. *Chem. Phys. Lett.* **1999**, *313*, 235.

(29) Coutinho, K.; Canuto S.; Zerner, M. C. *J. Chem. Phys.* **2000**, *112*, 9874.

(30) Coutinho, K.; Canuto S. *J. Chem. Phys.* **2000**, *113*, 9132.

(31) de Almeida, K. J.; Coutinho, K.; de Almeida, W. B.; Rocha, W. R.; Canuto, S. *Phys. Chem. Chem. Phys.* **2001**, *3*, 1583.

(32) Hernández-Cobos, J.; Mackie, A. D.; Vega, L. F. *J. Chem. Phys.* **2001**, *114*, 7527.

(33) Nguyen, M. T.; Raspoet, G.; Vanquickenborne, L. G. *J. Phys. Chem. A* **1997**, *101*, 7379.

(34) Mejías, J. A.; Lago, S. *J. Chem. Phys.* **2000**, *113*, 7306.

(35) Sprik, M. *J. Phys.: Condens. Matter* **1996**, *8*, 9405.

(36) Laidig, K. E.; Speers, P.; Streitwieser, A. *Coord. Chem. Rev.* **2000**, *197*, 125.

(37) Mohr, M.; Marx, D.; Parrinello, M.; Zipse, H. *Chem.−Eur. J.* **2000**, *6*, 4009.

(38) Kirkwood, J. G. *J. Chem. Phys.* **1935**, *3*, 300.

(39) Zwanzig, R. W. *J. Chem. Phys.* **1954**, *22*, 1420.

(40) Jorgensen, W. L.; Ravimohan, C. *J. Chem. Phys.* **1985**, *83*, 3050.

(41) Straatsma, T. P.; McCammon, J. A. *J. Chem. Phys.* **1989**, *90*, 3300.

(42) Allen, M. P.; Tildesley, D. J. *Computer Simulation of Liquids*; Clarendon: New York, 1987.

(43) Jorgensen, W. L.; Nguyen, T. B. *J. Comput. Chem.* **1993**, *14*, 195.

(44) Berendsen, H. J. C.; Postma, J. P. M.; van Gusteren, W. F.; Hermans, J. In *Intermolecular Forces*; Pullman, B., Ed.; Reidel: Dordrecht, The Netherlands, 1981; p 331.

(45) Mooney, D. A.; Müller-Plathe, F.; Kremer, K. *Chem. Phys. Lett.* **1998**, *294*, 135.

(46) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(47) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(48) Petersson, G. A.; Bennett, A.; Tensfeldt, T. G.; Al-Laham, M. A.; Shirley, W. A.; Mantzaris, J. *J. Chem. Phys.* **1988**, *89*, 2193.

(49) Singh, U. C.; Kollman, P. A. *J. Comput. Chem.* **1984**, *5*, 129.

(50) Besler, B. H.; Merz, K. M., Jr.; Kollman, P. A. *J. Comput. Chem.* **1990**, *11*, 431.

(51) McClenman, A. L. *Tables of experimental dipole moments*; Freeman: San Franciso, CA, 1963; Vol. 1.

(52) Cabral, B. J. C.; Fonseca, R. G. B.; Simões, J. A. M. *Chem. Phys. Lett.* **1996**, *258*, 436.

(53) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*; Gaussian, Inc.: Pittsburgh, PA, 1998.

(54) Coutinho, K.; Canuto, S. *DICE: A general Monte Carlo program for liquid simulation*; University of São Paulo: São Paulo, Brazil, 2000.

(55) Wang, Q.; Karl Jonhson, J.; Broughton, J. Q. *Mol. Phys.* **1996**, *89*, 1105.

(56) Buch, V. *J. Chem. Phys.* **1994**, *100*, 7610.

(57) Levchuk, V. N.; Sheykhet, I. I.; Simkin, B. Ya. *Chem. Phys. Lett.* **1991**, *185*, 339.

(58) Lazaridis, T. *J. Phys. Chem. B* **2000**, *104*, 4964.

(59) Cabani, S.; Gianni, P.; Mollica, V.; Lepori, L. *J. Solution Chem.* **1981**, *10*, 563.

(60) E_{sx} has been calculated as $E_{sx} = E_t − E_w − E_x$, where E_t is the total energy of the system with the solute X (phenol or phenoxy radical) and the 32 water molecules in the first coordination shell, E_w is the energy of the 32 water molecules in the same configurations, and E_x is the energy of the solute X. Counterpoise corrections to BSSE have been included by adding to the basis set of X the basis set of the water molecules in the cluster.

(61) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.

(62) Wilhelm, E.; Battino, R.; Wilcock, R. J. *Chem. Rev.* **1977**, *77*, 219.

(63) Parker, V. D. *J. Am. Chem. Soc.* **1993**, *114*, 7458; **1993**, *115*, 1201.