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Theoretical Study of the Solvent Effect on Functional Group Properties and on the Charge Distribution and Acidity of Alkyl-Substituted Alcohols

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For a number of functional groups, the group electronegativity and hardness in the gas phase and in different solvents was calculated using the recently introduced self-consistent isodensity polarized continuum model (SCI-PCM). The results indicate that the groups become less electronegative and less hard with increasing dielectric constant. Using the calculated functional group properties and Sanderson's electronegativity equalization principle, charge distributions in the alkyl alcohols X−OH and their conjugated bases XO^- (with X = $-CH_3$, $-CH_2CH_3$, and $-CH(CH_3)_2$ are determined in solution. The calculated charge distributions are used in a study of the inversion of alkyl alcohol acidity from gas phase to aqueous solution. Relative acidities are calculated in the gas phase and in aqueous solution for methanol, ethanol, 2-propanol and *tert*-butanol. The experimentally observed inversion of the acidity sequences of these systems is reproduced, and special importance is assigned to the stabilization energy of the conjugate bases in both media.

I. Introduction

Group electronegativity, hardness and softness, are important concepts of practical use in structural and reactivity studies in inorganic and organic chemistry.

In the past, a lot of attention has been devoted to the group electronegativity, and a variety of scales have been proposed.[1−7] On the contrary, very few values have been published until now for the group hardness and softness.[4,5,6,8−10] Pearson obtained a series of experimental hardness values for atoms and radicals based on experimental values for the ionization energy and electron affinity.[8−10] The present authors recently presented a nonempirical computational method yielding functional group electronegativity and hardness values[6] which where used in studies on acidity of carboxylic acids,[11] alcohols and silanols,[12,13] hydrides,[14] and basicity of amines,[15,16] and amino acids[17] (for a review of these different studies, see ref 18). Other theoretical determinations of hardnesses of chemical groups are due to Komorowski et al.[4,5]

Until now, all of these calculations have been performed in the gas phase. It is however generally known that the properties of molecules can differ considerably between the gas phase and solution.[19,20] Recently some methods in the context of ab initio molecular orbital theory have been shown to be useful tools to study solvent−solute interactions. Two general approaches are commonly used: the classical ensemble treatment and quantum mechanical continuum models.[21] In the continuum methods, the solvent is treated as a continuum with a uniform dielectric constant ϵ surrounding a solute molecule which is placed in a cavity.[21] The many approaches differ in the way the cavity and the reaction field are defined. The simplest of these models is the Onsager reaction field model.[22] In this method, the solute occupies a fixed spherical cavity within the solvent field. A dipole in the solute will interact with the medium to create a dipole in the medium and the electric field exhibited by the solvent dipole will in turn interact with the molecular dipole, leading to a net stabilization. This model has the advantage of simplicity and low computing times; its principal deficiency is that a system having a zero dipole moment will exhibit no solvent effects at all and the calculations will thus give the same results as for the gas phase.

The second type of reaction field method is the polarized continuum model (PCM) proposed by Tomasi and co-workers.[21,23,24] Here the molecular cavity is defined as a union of interlocking atomic spheres, constructed using van der Waals radii. The effect of the polarization of the solvent is calculated by numerical differentiation. This model has the deficiency of much longer computing times and an arbitrary choice of the van der Waals radii to construct the cavity. Another type of reaction field is the isodensity polarized continuum model.[25−27] Here, the cavity is defined as an isodensity surface of the molecule. In this method the isodensity surface value needs to be specified (typically in the range of 0.004 to 0.001 au) instead of a set of radii for the spheres. This model has the advantage that the surface is smooth and easily integrable. The last reaction field type model is the self-consistent isodensity polarized continuum model (SCI-PCM).[25−27] In this method, one determines the electron density which minimizes the energy, including the effect of solvatation. This is however dependent on the cavity, which is in turn determined by the electron density. The effect of the solvent is thus taken into account self-consistently, thereby offering a complete coupling of the cavity and the electron density.[25−27]

In this paper, a contribution to the study of the solvent effect within DFT,[28] we will choose the SCI-PCM method as the tool to study solvent−solute interactions in view of its superiority and availability in recent quantum chemical software packages. Following the same method as in our previous work,[6,12] group electronegativities, hardnesses and softnesses were calculated for the functional groups X (with X = $-CH_3$, $-CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2F$, and $-CH_2Cl$) in gas phase ($\epsilon_r = 1$) and

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in different solvents characterized by different values for the relative dielectric constant ϵ_r such as, benzene ($\epsilon_r = 2.28$), dichloromethane ($\epsilon_r = 8.93$), pyridine ($\epsilon_r = 12.4$), acetone ($\epsilon_r = 20.7$), DMSO ($\epsilon_r = 12.4$), and water ($\epsilon_r = 78.39$). Starting from these values, the correlations between electronegativity, hardness and softness on one hand, and the Kirkwood function, $(\epsilon_r - 1)/(2\epsilon_r + 1)$[29,30] (vide infra) on the other hand are investigated.

In the next step, Sanderson's electronegativity equalization principle[31,32] using the calculated functional group properties will be used to study the charge distribution in molecules of the type X$-$OH and the corresponding conjugate bases X$-$O$^-$: the charge transfer $\Delta N_{OH}(\epsilon)$ to OH in X$-$OH and $\Delta N_O(\epsilon)$ to O in X$-$O$^-$ is calculated in the gas phase and in solution along the lines given in ref 12 and compared with ab initio calculations.

Finally, we will study the change in the acidity of alkyl-substituted alcohols when passing from the gas phase to aqueous solution.

II. Theory and Computational Details

II.1. Group Electronegativity, Hardness, and Softness. The electronegativity χ, identified by Parr et al. with the negative of the chemical potential μ, is defined as[33]

$$\mu = -\chi = \left(\frac{\partial E}{\partial N}\right)_{v(\underline{r})} \tag{1}$$

with E the energy of the system, N the number of electrons, and $v(\mathrm{r})$ the external (i.e., due to the nuclei) potential. The hardness, defined by Parr and Pearson,[34] is given by

$$\eta = {}^1/_2\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\underline{r})} \tag{2}$$

Finally, the global softness is defined as[35]

$$S = \frac{1}{2\eta} \tag{3}$$

Assuming a quadratic relationship between the energy and the number of electrons, one obtains from (1) Mulliken's formula[36] for the electronegativity

$$\chi \approx \frac{\mathrm{IE} + \mathrm{EA}}{2} \tag{4}$$

with IE and EA the vertical ionization energy and electron affinity respectively.

Upon the introduction of a SCRF model the energy of the neutral system, cation and anion will become a function of the dielectric constant ϵ of the solvent so that (4) can be generalized to

$$\chi(\epsilon) \approx \frac{\mathrm{IE}(\epsilon) + \mathrm{EA}(\epsilon)}{2} \tag{5}$$

with its obvious counterparts

$$\eta(\epsilon) \approx \frac{\mathrm{IE}(\epsilon) - \mathrm{EA}(\epsilon)}{2} \tag{6}$$

and

$$S(\epsilon) \approx \frac{1}{\mathrm{IE}(\epsilon) - \mathrm{EA}(\epsilon)} \tag{7}$$

where IE(ϵ) and EA(ϵ) are the vertical ionization energy and electron affinity in a dielectric medium characterized by the dielectric constant ϵ, yielding solvent dependent group properties. We propose to use expressions (5), (6), and (7) as working equations to calculate the group electronegativity, hardness, and softness in a solvent. Following our previously designed methodology,[6] this necessitates the calculation of the energies of the neutral (N_0 electron system), the cation ($N_0 - 1$ electron system) and the anion ($N_0 + 1$ electron system) for a group (e.g., the CH_3 group), taken as the corresponding radical at the geometry the group usually adopts in a molecule. In order to obtain this geometry of a functional group X in a molecule, the following methodology was adopted. The structure of H$-$X was optimized at the Hartree Fock level with the 6-31+G* basis set in the gas phase and in the different solvents. Finally, the functional group X geometry is obtained by breaking the H$-$X bond.

II.2. Application to Charge Distributions in Alkyl Alcohols and Their Conjugate Bases. A very simple method to determine the molecular charge distribution was the use of the electronegativity equalisation principle already formulated by Sanderson.[31,32] It can be shown that the electronegativity of a functional group in a molecule depends on the change in number of electrons ΔN_X of this group upon molecule formation by the approximate relation[37]

$$\chi_X = \chi_X^0 - 2\eta_X^0 \Delta N_X \tag{8}$$

where χ_X^0 and η_X^0 is the electronegativity and the hardness of the isolated functional group X and ΔN_X is the charge transfer to or away from X. If one applies this relation for the group X and the OH group in XOH and for X and O in XO$^-$, one can calculate the charge transfer $\Delta N_{X_1}(\epsilon)$ to X in XOH and $\Delta N_{X_2}(\epsilon)$ to X in XO$^-$ in a medium with a dielectric constant ϵ. These charge transfers, which might deviate significantly from gas phase calculated charge transfers as the charge distributions of polar compounds are often altered significantly in the presence of a solvent reaction field,[38] thus become

$$\Delta N_{X_1}(\epsilon) = \frac{\chi_X^0(\epsilon) - \chi_{OH}^0(\epsilon)}{2(\eta_X^0(\epsilon) + \eta_{OH}^0(\epsilon))} \tag{9}$$

$$\Delta N_{X_2}(\epsilon) = \frac{\chi_X^0(\epsilon) - \chi_O^0(\epsilon)}{2(\eta_X^0(\epsilon) + \eta_O^0(\epsilon))} + \frac{\eta_O^0(\epsilon)}{\eta_X^0(\epsilon) + \eta_O^0(\epsilon)} \tag{10}$$

where the charge conservation relations (i.e., $\Delta N_{X_1}(\epsilon) + \Delta N_{OH}(\epsilon) = 0$ and $\Delta N_{X_2}(\epsilon) + \Delta N_O(\epsilon) = 1$) have been used. It is easily seen that the charge transfer $\Delta N_{OH}(\epsilon)$ to OH in XOH and $\Delta N_O(\epsilon)$ to O in XO$^-$ is equal to

$$\Delta N_{OH}(\epsilon) = -\frac{\chi_X^0(\epsilon) - \chi_{OH}^0(\epsilon)}{2(\eta_X^0(\epsilon) + \eta_{OH}^0(\epsilon))} \tag{11}$$

$$\Delta N_O(\epsilon) = 1 - \frac{\chi_X^0(\epsilon) - \chi_O^0(\epsilon)}{2(\eta_X^0(\epsilon) + \eta_O^0(\epsilon))} - \frac{\eta_O^0(\epsilon)}{\eta_X^0(\epsilon) + \eta_O^0(\epsilon)} \tag{12}$$

These charge transfers can also be calculated using ab initio methods when using the following relation

$$\Delta N_A = N_A - N_A^0 \tag{13}$$

TABLE 1: Group Electronegativity χ_X for X = FCH_2, $ClCH_2$, CH_3, CH_2CH_3, and $CH(CH_3)_2$ Calculated in the Gas Phase and Different Solvents Characterized by Their Relative Dielectric Constants ϵ_r (All Values are in eV)

	ϵ_r	χ_{FCH_2}	χ_{ClCH_2}	χ_{CH_3}	$\chi_{CH_2CH_3}$	$\chi_{CH(CH_3)_2}$
gas phase	1.0	4.637	4.783	4.406	3.726	3.295
benzene	2.28	4.077	4.315	3.855	3.280	2.877
CH_2Cl_2	8.93	3.713	4.017	3.542	3.017	2.636
pyridine	12.4	3.673	3.986	3.510	2.991	2.615
acetone	20.70	3.630	3.952	3.478	2.962	2.583
DMSO	46.68	3.592	3.923	3.450	2.938	2.568
H_2O	78.39	3.579	3.914	3.440	2.931	2.561

where N_A and N_A^0 are the number of electrons in the functional group in the molecule and in the isolated group, respectively.

All calculations were performed with the Gaussian 94[39] program on the CRAY J-916/8-1024 computer of the Brussels Free Universities computer center combined with the UniChem software package[40] on a Silicon Graphics ONYX Extreme workstation. In the case of the alcohol molecules and their conjugate bases, all structures have been optimized in the gas phase and in different solvents at Hartree−Fock level using a 6-31+G* basis set. Starting from these gas phase equilibrium structures (radicals and alcohols), all molecular properties such as the total energies and the charges of these systems were calculated at the Hartree−Fock level using a 6-31+G* basis set in the gas phase and in different solvents using the SCI-PCM method, using a 0.001 au isodensity surface.

III. Results and Discussion

III.1. Functional Group Properties. Tables 1 and 2 list the group electronegativities, hardnesses, and softnesses in different solvents for the groups mentioned in the introduction. The electronegativity χ_X and the hardness η_X decrease when going from the gas phase to solution for all the groups considered. Moreover, these properties continue to decrease when the dielectric constant of the medium increases thus giving rise to an increase of the group softness S_X. The evolution of the group properties as a function of an increasing dielectric constant can be analyzed via a plot of the energy of the functional group as a with respect to its number of electrons N (at constant external potential), as shown in Figure 1 for the methyl group. As can be seen, a decrease of the electronic energy E of the anionic and cationic forms occurs, when the relative dielectric constant of the medium increases from 1 to 78.3, while the electronic energy E for the neutral form is almost constant. This result is also in agreement with the experimental and theoretical results indicating that charged systems are solvated to a much larger extent than the neutral systems.[38] As a consequence, the ionization energy decreases and the electron affinity energy EA increases with increasing dielectric constant. These trends in the ionization energy and the electron affinity explain the decrease for the group values χ_X and η_X if we take into account that the change in ionization energy is always larger than the change in electron affinity, since the former are always higher than the latter.[41] To confirm this effect we compared the slope of IE and EA when passing from the gas phase to different solvents. We therefore calculated the differences for the ionization energy ΔIE and electron affinity ΔEA by the following equations

$$\Delta \mathrm{IE} = \mathrm{IE}_{gas} - \mathrm{IE}_{sol} \tag{14}$$

$$\Delta \mathrm{EA} = \mathrm{EA}_{gas} - \mathrm{EA}_{sol} \tag{15}$$

where IE_{gas}, IE_{sol}, EA_{gas}, and EA_{sol}, are the ionization energy and the electron affinity in the gas phase and in different solvents for a given system. In Figure 2 we have plotted the absolute values of ΔIE and ΔEA values, again for the methyl group, against the Kirkwood function, $(\epsilon_r - 1)/(2\epsilon_r + 1)$. This figure indeed confirms that the absolute value for the difference (14) is indeed larger than (15), confirming that the electronegativity and the hardness decrease when the dielectric constant of the solvent increases.

In the remaining part of this work we will use the Kirkwood function when studying the evolution of a given quantity as a function of the dielectric constant. When looking at the Hamiltonian in the SCRF model the Kirkwood function, $(\epsilon_r - 1)/(2\epsilon_r + 1)$ appears in natural way.[21] This function appears when considering the free energy of solvatation ΔG_{solv} of a dipole in a continuous dielectric with a relative dielectric constant ϵ_r via the eq[29,30]

$$\Delta G_{solv} = -\frac{\mu^2}{r^3}\left(\frac{\epsilon_r - 1}{2\epsilon_r + 1}\right) \tag{16}$$

with μ is the permanent dipole moment of the solute and r is the radius of the molecule containing the dipole: from now on, the index r for the relative dielectric constant will be omitted (this index r will also be dropped in the Figures).

In the graphs presented in Figures 3 and 4 we have plotted the group electronegativities and softness versus the Kirkwood function. A linear correlation is obtained.

III.2. Application to Molecular Charge Distributions in Akyl Alcohols and their Conjugate Bases. This parts attempts a study of the charge distribution in molecules XOH and in their ions XO^- in gas phase and in different solvents (X being equal to $-CH_3$, $-CH_2CH_3$, and $-CH(CH_3)_2$) applying an electronegativity equalization scheme with functional groups, and using equation (11) and (12) as working equations to calculate the charge transfer $\Delta N_{OH}(\epsilon)$ to OH in XOH and $\Delta N_O(\epsilon)$ to O in XO^- in the gas phase and in a dielectric medium. The evolution in the calculated charge transfer $\Delta N_{OH}(\epsilon)$ when going from the gas phase to a solvent is given in Table 3. It can be seen that in gas phase the charge transfer to OH in X−OH increases as the alkyl group size increases; this results is in agreement with our previous results,[12] pointing out the increasing charge capacity with increasing alkyl group size. Moreover, we find that the degree of charge transfer from X to OH increases with increasing relative dielectric constant. The correlation between the the charge transfer to OH in CH_3OH, CH_3CH_2OH, and $(CH_3)_2CHOH$ and the Kirkwood function is given in Figure 5.

In the next step we have calculated the charge transfer $\Delta N_O(\epsilon)$ to O in XO^- using the same methodology. The calculated results are also given in Table 3. As can be seen, the solvent reaction field also has a strong influence on the electronic structure and charge distribution in XO^- for all these groups. The correlation between the Kirkwood function and the charge transfer to O in CH_3O^-, $CH_3CH_2O^-$, and $(CH_3)_2CHO^-$ is also given in Figure 5.

Finally, the charge transfer in XOH obtained via ab initio calculations (Mulliken charges) was plotted against the results from electronegativity equalization calculations (Figure 6). A satisfying correlation is obtained. It is clear that the combination of the electronegativity equalization principle with calculated group properties and the SCI-PCM method seems to be a useful tool to study the effect of the solvent on the molecular charge distribution.

This methodology will now be used to study the evolution of acidity for alkyl substituted alcohols when passing from the gas phase to the aqueous solution.

TABLE 2: Group Hardness η and Softness S for $-FCH_2$, $-ClCH_2$, $-CH_3$, $-$ CH_2CH_3, and $-CH(CH_3)_2$ Calculated in Gas Phase and Solvents Characterized by Different Relative Dielectric Constants ϵ_r (All Values Are in eV (Hardness) or 10^{-2} eV^{-1} (Softness))

		FCH_2		$ClCH_2$		CH_3		CH_2CH_3		$CH(CH_3)_2$	
	ϵ_r	η	S	η	S	η	S	η	S	η	S
gas phase	1.0	5.882	8.501	5.354	9.338	5.673	8.814	5.359	9.330	5.075	9.852
benzene	2.28	4.079	12.258	3.760	13.297	3.877	12.896	3.762	13.292	3.624	13.797
CH_2Cl_2	8.93	2.936	17.027	2.770	18.052	2.771	18.041	2.763	18.098	2.709	18.453
pyridine	12.4	2.805	17.730	2.656	18.725	2.646	18.787	2.649	18.780	2.611	19.076
acetone	20.70	2.698	18.531	2.566	19.486	2.547	19.633	2.557	19.553	2.523	19.820
DMSO	46.68	2.594	19.273	2.478	20.176	2.450	20.404	2.469	20.255	2.442	20.477
H_2O	78.39	2.560	19.528	2.450	20.410	2.419	20.671	2.440	20.494	2.415	20.703

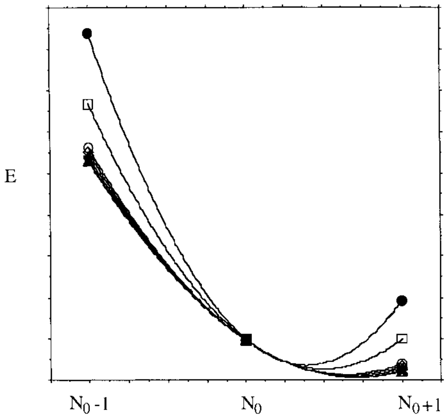

Figure 1. The evolution of the total energy E vs the number of electrons N for the CH_3 radical (●) gas phase, (□) benzene, (○) dichloromethane, (◇) pyridine, (+) acetone, (×) DMSO and (△) aqueous solution, respectively). N_0 denotes the number of electrons of the neutral system.

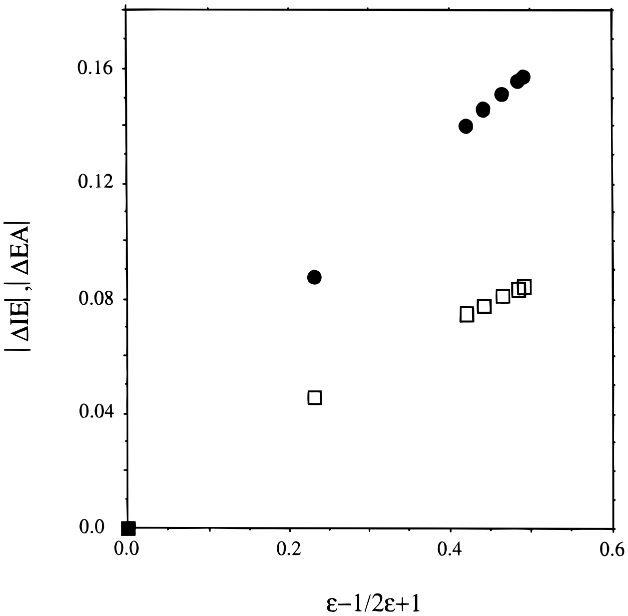

Figure 2. Evolution of IE and EA (absolute values, au) vs $((\epsilon - 1)/(2\epsilon + 1))$ (●) represents ΔIE and (□) represents ΔEA) in the case of CH_3.

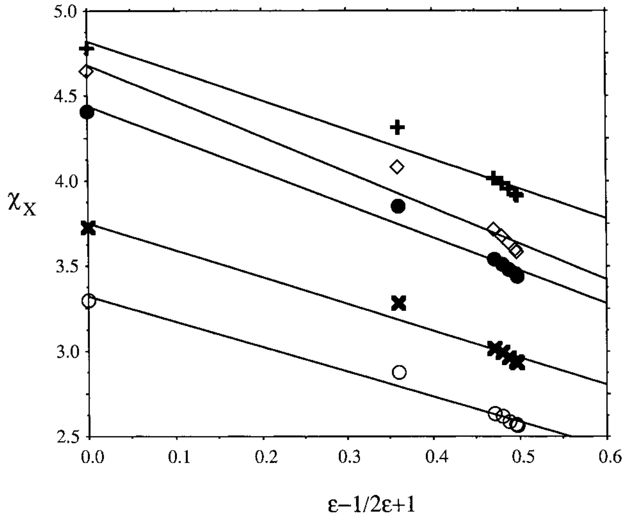

Figure 3. Correlation between the group electronegativity χ_X and the Kirkwood function $((\epsilon - 1)/(2\epsilon + 1))$ for X = (●) CH_3, (×) CH_2CH_3, (○) $CH(CH_3)_2$, (◇) CH_2F, and (+) CH_2Cl.

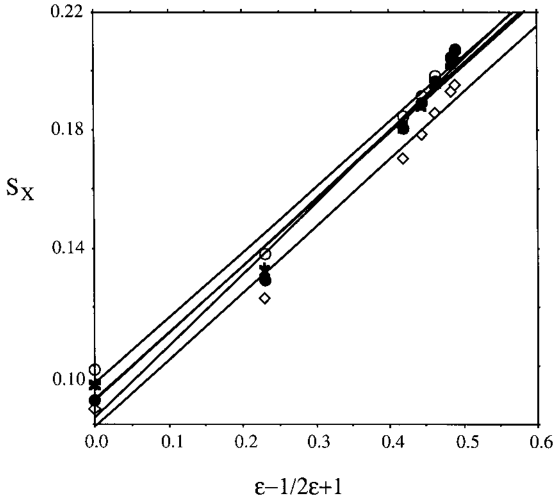

Figure 4. Correlation between the group softness S_X (eV^{-1}) and the Kirkwood function $((\epsilon - 1)/(2\epsilon + 1))$ for X = (●) CH_3, (×) CH_2CH_3, (○) $CH(CH_3)_2$, (◇) CH_2F, and (+) CH_2Cl.

The expression $\Delta(\Delta N_X(\epsilon))$, defined as the charge transfer to the alkyl group upon deprotonation,

$$\Delta(\Delta N_X(\epsilon)) = \Delta N_{X_1}(\epsilon) - \Delta N_{X_2}(\epsilon) \tag{17}$$

and which can considered as the ability of the alkyl groups to stabilize the negative charge in the process of deprotonation, was calculated for the alkyl alcohols. Using the reasonable approximation $\chi_{OH} \approx \chi_O$ and $\eta_{OH} \approx \eta_O$,[12] this charge transfer can be written as (cf. (9) and (10)):

$$\Delta(\Delta N_X(\epsilon)) = \frac{\eta_O^0(\epsilon)}{\eta_X^0(\epsilon) + \eta_O^0(\epsilon)} \tag{18}$$

Table 4 summarizes the calculated charge transfer $\Delta(\Delta N_X(\epsilon))$ for the different alkyl groups (CH_3, CH_3CH_2 and $CH(CH_3)_2$) of the alcohol in the gas phase and in solvent. The correlation between the charge transfer and Kirkwood function is shown

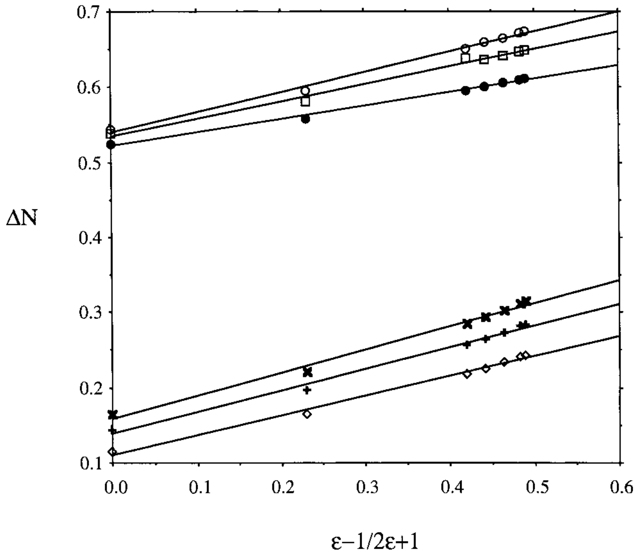

Figure 5. Correlation between the charge transfers ΔN to OH in XOH (bottom curves) and to O in XO^- (upper curves) and the Kirkwood function $((\epsilon - 1)/(2\epsilon + 1))$ (◇) CH_3OH, (+) CH_3CH_2OH, (×) $(CH_3)_2CHOH$, (○) CH_3O^-, (□) $CH_3CH_2O^-$, and (●) $(CH_3)_2CHO^-$).

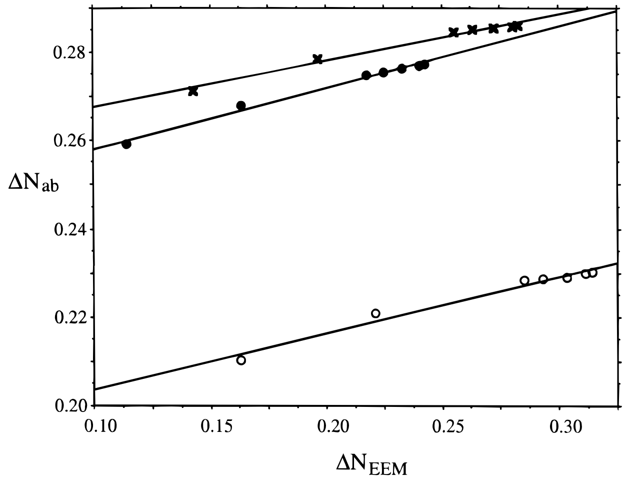

Figure 6. Correlation between the charge transfer ΔN_{OH} to OH in XOH calculated with the electronegativity equalization method ΔN_{EEM} and using ab initio Mulliken charges ΔN_{ab}. ((●) CH_3OH, (◇) CH_3CH_3OH, (+) and (+) $(CH_3)_2CHOH$).

TABLE 3: Charge Transfers ΔN_{OH} to OH in XOH and ΔN_O to O in XO^- with X = CH_3, CH_2CH_3, and $CH(CH_3)_2$ Calculated in the Gas Phase and in Different Solvents Characterized by Their Relative Dielectric Constants ϵ_r (All Values Are in au)

		X					
		CH_3		CH_2CH_3		$CH(CH_3)_2$	
	ϵ_r	ΔN_{OH}	ΔN_O	ΔN_{OH}	ΔN_O	ΔN_{OH}	ΔN_O
gas phase	1.0	0.1144	0.5248	0.1431	0.5382	0.1630	0.5443
benzene	2.28	0.1636	0.5583	0.1964	0.5813	0.2213	0.5955
CH_2Cl_2	8.93	0.2175	0.5961	0.2555	0.6281	0.2856	0.6499
pyridine	12.4	0.2257	0.6011	0.2643	0.6354	0.2937	0.6583
acetone	20.70	0.2329	0.6054	0.2724	0.6409	0.3032	0.6651
DMSO	46.68	0.2404	0.6094	0.2804	0.6461	0.3112	0.6707
H_2O	78.39	0.2409	0.6114	0.2830	0.6484	0.3140	0.6734

in Figure 7. This plot shows, as seen previously, that in the gas phase the charge transfer to the oxygen atom decreases from methanol to 2-propanol. The stabilization for the conjugate base goes in the same direction. This result agrees with the theoretical results obtained by our group and the experimental results that explain the increase of the stabilization for the conjugate base by a increase in the polarisability for the alkyl groups. In aqueous solution we find an inversion of $\Delta(\Delta N_X(\epsilon))$ between the methyl, ethyl, and isopropyl groups yielding an inversion in the stabilization of the conjugate base for the alkyl groups.

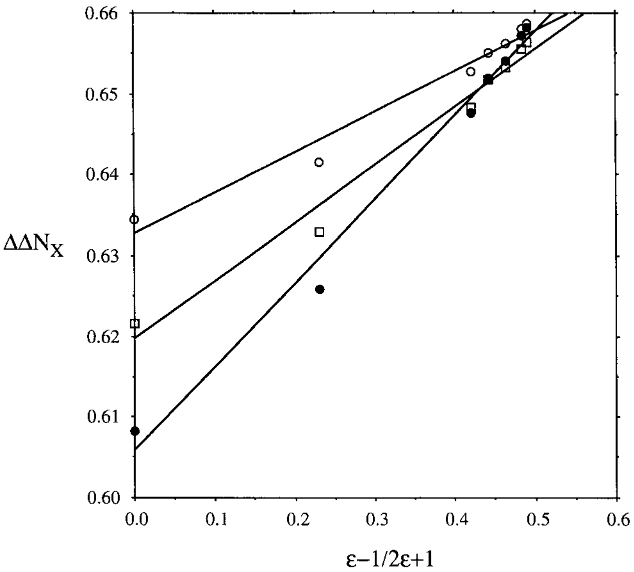

Figure 7. Plot of $\Delta(\Delta N_X)$ vs the Kirkwood function $((\epsilon - 1)/(2\epsilon + 1))$. (●) CH_3OH, (×) CH_3CH_3OH, and (○) $(CH_3)_2CHOH$).

TABLE 4: Charge Transfer $\Delta\Delta(N_X)$ with X = CH_3, CH_2CH_3, and $CH(CH_3)_2$ Calculated in the Gas Phase and in Different Solvents Characterized by Their Relative Dielectric Constants ϵ_r (All Values are in au)

	ϵ_r	$\Delta\Delta(N_{CH_3})$	$\Delta\Delta(N_{CH_3CH_2})$	$\Delta\Delta(N_{CH(CH_3)_2})$
gas phase	1.0	0.6081	0.6216	0.6343
benzene	2.28	0.6269	0.6339	0.6425
CH_2Cl_2	8.93	0.6476	0.6483	0.6527
pyridine	12.4	0.6510	0.6507	0.6540
acetone	20.70	0.6540	0.6531	0.6561
DMSO	46.68	0.6571	0.6554	0.6579
H_2O	78.39	0.6582	0.6562	0.6586

III.3. Acidity of Alkyl-Substituted Alcohols in the Gas Phase and in Aqueous Solution. In aqueous solution a number of acidity or basicity sequences are inverted as compared to the gas phase.[19,20] The series formed by methanol, ethanol, 2-propanol, and *tert*-butanol is a representative example of this phenomenon.[19] The aqueous solution acidity of these alcohols decreases when going from methanol to *tert*-butanol, in accordance with the electron donating properties of alkyl groups. In the gas phase, however, the acidity sequence is inverted, thus assigning electron-withdrawing properties to the alkyl groups.

The theoretical study of the inversion of the alkyl substituted alcohol acidity scales from the gas phase to aqueous solution has been the subject of various papers (see, e.g., refs 12 and 42); the inversion is explained by the decrease in the electrostatic solute−solvent interaction energy when the charge distribution is stabilized.

In this study, we will try to confirm this effect by considering the relative strengths of acidity (relative to methanol) in the gas phase ($\Delta(\Delta E_g)$) and aqueous solution ($\Delta(\Delta E_{aq})$) for CH_3OH, CH_3CH_2OH, $(CH_3)_2CHOH$, and $(CH_3)_3COH$. By taking CH_3OH as a reference, the calculation of the hydration energy of the proton can be avoided. The free energy calculations for CH_3OH, CH_3CH_2OH, $(CH_3)_2CHOH$, and $(CH_3)_3COH$ and each conjugate base were carried out in the gas phase and in aqueous solution again using the SCI-PCM methodology.

TABLE 5: Calculated Deprotonation Energies of the Alkyl Alcohols in the Gas Phase and in Aqueous Solution with CH_3OH as a Reference[a]

compounds	ΔE_g(Kcal/mol)	ΔE_{aq}(Kcal/mol)	ΔE_{sa}(Kcal/mol)	ΔE_{sb}(Kcal/mol)
CH_3OH	0	0	−6.59	−64.55
CH_3CH_2OH	−2.14	1.34	−6.06	−60.58
$(CH_3)_2CHOH$	−4.41	3.41	−6.39	−56.57
$(CH_3)_3COH$	−5.33	5.09	−5.82	−53.42

[a] Also listed are the solvatation energies of the acids (ΔE_{sa}) and bases (ΔE_{sb}).

Using reaction 19, the theoretical (relative to methanol) acidity $\Delta(\Delta E_g)$ of the alkyl substituted alcohols in gas phase is found via eq 20:

$$XOH(g) + CH_3O^-(g) \rightleftarrows XO^-(g) + CH_3OH(g) \quad (19)$$

with

$$\Delta(\Delta E_g) = E(XO^-(g)) + E(CH_3OH(g)) - E(XOH(g)) - E(CH_3O^-(g)) \quad (20)$$

In this equation, $E(XOH(g))$, $E(XO^-(g))$, $E(CH_3OH(g))$, and $E(CH_3O^-(g))$ are the energies in gas phase for the alcohols XOH, conjugate bases XO^-, and methanol and its conjugate base, respectively. Using (21) and (22), we find the theoretical (relative to methanol) acidity of alkyl-substituted alcohols in solution $\Delta(\Delta E_{aq})$:

$$XOH(aq) + CH_3O^-(aq) \rightleftarrows XO^-(aq) + CH_3OH(aq) \quad (21)$$

$$\Delta(\Delta E_{aq}) = E(XO^-(aq)) + E(CH_3OH(aq)) - E(XOH(aq)) - E(CH_3O^-(aq)) \quad (22)$$

where $E(XOH(aq))$, $E(XO^-(aq))$, $E(CH_3OH(aq))$, and $E(CH_3O^-(aq))$ are the energies in solution for the alcohol XOH, its conjugate base XO^- and methanol and its conjugate base, respectively. The HF/6-31+G* calculated results of the relative energy changes upon proton release in the gas phase and in aqueous solution are given in Table 5. As can be seen in this table, the order in the strength of the alkyl-substituted alcohols in the gas phase is $(CH_3)_3COH > (CH_3)_2CHOH > CH_3CH_2OH > CH_3OH$. In aqueous solution, the reversed order of acidity is seen. We finally calculated the solvation energy of all the structures in order to study the solvation influence on both the acid and conjugate base form of a given acid−base equilibrium. We therefore calculated the solvation energy ΔE_{sa} for the acidic form and ΔE_{sb} for the basic form using the equation

$$\Delta E_s = E_{aq} - E_g \quad (23)$$

where E_{aq} and E_g represent the energy of the system in aqueous solution and gas phase respectively. These stabilization energies can be connected to the acid−base equilibria in the gas phase and solution via the following cycle:

$$\begin{tikzcd}
XOH(g) + CH_3O^-(g) \arrow[r, shift left, "\Delta(\Delta E_g)"] \arrow[d, "\Delta E_{sa}"] & XO^-(g) + CH_3OH(g) \arrow[l, shift left] \arrow[d, "\Delta E_{sb}"] \\
XOH(aq) + CH_3O^-(aq) \arrow[r, shift left, "\Delta(\Delta E_{aq})"] & XO^-(aq) + CH_3OH(aq) \arrow[l, shift left]
\end{tikzcd}$$

The results show that the basic form is solvated to a much larger extent than the acidic form, as is shown in Table 5 ($-\Delta E_{sb}$ is much larger than $-\Delta E_{sa}$). The charged systems are indeed more stabilized than the neutral systems, and the conjugate bases play the crucial role in determining the acidity and basicity for a system in the aqueous solution.[18]

The main contribution to the change in the acidity sequence in solution is the electrostatic component of the solvation energy of the basic form; the charge delocalization caused by the substitution of hydrogen atoms by methyl groups can be used to understand the acidity order in the gas phase. Indeed in the gas phase, when passing from methanol to *tert*-butanol, the alkyl groups stabilize the conjugate base, giving the following sequence for the acidity: $(CH_3)_3COH > (CH_3)_2CHOH > CH_3CH_2OH > CH_3OH$. In aqueous solution, we have the same effect as in the gas phase, but this effect is dominated by the solvation energy of the conjugate base, which decreases from methanol to *tert*-butanol. Consequently, the sequence for the acidity is $CH_3OH > CH_3CH_2OH > (CH_3)_2CHOH > (CH_3)_3COH$.

IV. Conclusions

In this paper, the SCI-PCM method was used for the calculation of functional group electronegativities, hardnesses and softnesses in solution for the $-CH_3$, $-CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2F$, and $-CH_2Cl$ functional groups. Both the electronegativity and hardness of these groups was found to decrease upon increasing dielectric constant of the solvent.

The charge transfer to the above mentioned alkyl groups in the alcohols XOH and their conjugate bases ion XO^- was calculated in the gas phase and in different solvents using Sanderson's electronegativity equalization principle at the functional group resolution and were compared with results from ab initio molecular orbital calculations. The charge transfer in these molecules was seen to increase when the dielectric constant of the solvent increases. The charge distributions of these molecular systems were used in a study of the inversion of the alkyl alcohol acidities when going from gas phase to aqueous solution. In a final part, the SCI-PCM methodology was used to calculate the relative acidities of methanol, ethanol, isopropanol, and *tert*-butanol in the gas phase and in aqueous solution. An inversion of the acidity scale was observed, an important parameter being the stabilization energy of the conjugate base in aqueous solution.

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