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Theoretical Studies of Substituent and Solvent Effects on Protonation Equilibria of Benzaldehydes

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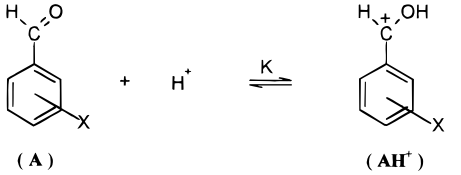
The effect of substituent on the protonation equilibria of benzaldehydes ($\mathbf{A} + H^+ \rightleftharpoons \mathbf{AH}^+$, where **A** and $\mathbf{AH}^+$ represent benzaldehyde and its protonated form) in the gas phase and in solution has been investigated theoretically at the MP2/6-31G*//MP2/6-31G* level applying two solvation (IPCM and SCIPCM) models. The absolute as well as relative $\Delta G°$ (or log K) values of the gas-phase MP2 results are in good agreement with the experimental values. All the solvation models are inadequate to reproduce experimental ρ^+ (slope of log K versus σ^+ plot) value in aqueous solution. The SCIPCM model gives the best correlation but with a much larger magnitude of ρ^+ ($=-5.29$ relative to the experimental value of $\rho^+ = -1.88$) mainly due to neglect of specific solvation (i.e., hydrogen bonding) effect. It was found that the neglect of hydrogen-bonding effect in the solvation of aldehydes (**A**) results in unduly higher equilibrium constants (K) for electron donors ($\sigma^+ < 0$); in contrast, the neglect of hydrogen bonding in the solvation of the protonated forms ($\mathbf{AH}^+$) leads to unduly lower K values for electron acceptors ($\sigma > 0$).

Introduction

Theoretical elucidation of the role of solvent in the rates and equilibria of organic reactions has become an important and growing area of research in computational chemistry. Among the solvation models currently explored, dielectric continuum reaction field methods[1] provide a simple and popular approach which has been applied quite successfully to describe a variety of physical and chemical properties in solution.[2] The first and simplest in the self-consistent reaction field (SCRF) methods is the quantum-Onsager model;[1] here a polarizable solute dipole is placed at the center of a spherical cavity and the electrostatic effects of solvent on properties of solute molecules are determined self-consistently in the presence of the solvent. Obviously, this model suffers from shortcomings due to ill-defined molecular shape by the spherical cavity. In the isodensity polarizable continuum model (IPCM),[1] the cavity mimics actual molecular shape by defining the cavity surface to follow a contour on which the solute electronic density is constant. Various different isodensity contour values have been used, but the best overall agreement with experiment has been reported with a cavity size corresponding to the 0.001 electron per cubic bohr (au) contour.[1c] In the self-consistent IPCM (SCIPCM) method,[2c,d] the isodensity molecular surface is determined self-consistently in the presence of solvent reaction field. These continuum models, however, cannot represent specific solute−solvent (e.g. hydrogen bonding) interactions. Statistical mechanical (e.g., Monte Carlo) simulations[3] with large number of solvent molecules are used to describe such specific solute−solvent interactions properly.

In a previous work, we have successfully applied the simple IPCM model to the interpretation of solvent and substituent effects on the protonation equilibria of substituted pyridines in various solvents.[4] In this paper, we report on the results of our continued work on the theoretical solvation effects based on the continuum models. We have applied the IPCM and SCIPCM models to the protonation equilibria of benzaldehydes in solution (eq 1).



(1)

In eq 1, X = p-NH$_2$, p-OCH$_3$, p-CH$_3$, m-CH$_3$, H, p-Cl, m-OCH$_3$, m-F, m-Cl, p-CHO, p-CN, and p-NO$_2$.

Calculation

The Gaussian 98 program package[5] with standard Pople-type basis sets was used throughout in this work. The geometries of both forms (**A** and $\mathbf{AH}^+$) were fully optimized at the MP2-(FC)/6-31G* level with Berny's algorithm,[6] and vibrational frequencies were calculated (unscaled) at the RHF/6-31G* level. The zero-point-corrected MP2/6-31G* electronic energy ($E°$) was converted to enthalpy ($H°$) by correcting for translational, rotational and vibrational contributions and adding RT (PV term).[7] Gibbs free energy changes, $\Delta G°$, were then obtained using the calculated entropy changes, $\Delta G^o = \Delta H^o - T\Delta S^o$. The solvation energy corrections, ΔG^o_{sol}, were applied using the isodensity polarizable continuum model (IPCM) and self-consistent IPCM (SCIPCM) models. In the polarizable continuum model (PCM)[1b] the cavity is defined as the union of a series of interlocking atomic spheres, but in the IPCM model[2] the cavity is defined as an isodensity surface of the molecule. The SCIPCM model includes the effect of solvation in the solution of the SCF problem.[2d] For the IPCM model, we have tested the effect of isodensity level by calculating both at the 0.001 and 0.0004 au levels. The isodensity level in the SCIPCM model was kept to 0.0004 au.[1c] This value of 0.0004 au cavity size has been reported to give molar volumes that are in good

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TABLE 1: Calculated Electronic Energies (au) for the Aldehydes, A (reactant) and Protonated Aldehydes, AH$^+$ (product)

	A			**AH$^+$**		
X	gas phase	IPCM(H_2O)	SCIPCM(H_2O)	gas phase	IPCM(H_2O)	SCIPCM(H_2O)
p-NH_2	−399.681 49	−399.695 25	−399.690 56	−400.031 78	−400.121 55	−400.119 72
p-OCH_3	−458.675 87	−458.684 50	−458.583 15	−459.014 79	−459.096 92	−459.100 39
p-CH_3	−383.657 66	−383.663 47	−383.663 23	−383.987 43	−384.065 14	−384.076 85
m-CH_3	−383.657 73	−383.666 96	−383.663 13	−383.985 16	−384.079 12	−384.072 75
H	−344.486 36	−344.491 78	−344.491 82	−344.810 14	−344.898 54	−344.902 36
p-Cl	−803.518 52	−803.524 43	−803.524 06	−803.838 87	−803.952 67	−803.932 48
m-OCH_3	−458.676 13	−458.684 21	−458.682 56	−459.002 24	−459.109 37	−459.089 15
m−F	−443.504 74	−443.511 98	−443.510 46	−443.821 28	−443.919 66	−443.916 96
m-Cl	−803.517 90	−803.525 72	−803.523 26	−803.833 54	−803.941 00	−803.927 37
p-CHO	−457.513 45	−457.522 12	−457.521 39	−457.828 10	−457.912 96	−457.927 15
p-CN	−436.498 67	−436.510 23	−436.508 15	−436.807 23	−436.903 53	−436.912 82
p-NO_2	−548.494 52	−548.505 22	−548.502 84	−548.800 90	−548.893 68	−548.905 94

TABLE 2: Calculated Bond Length (d_{cc}) in the Gas Phase of A (reactant) and AH$^+$ (Product) at the MP2/6-31G* Level

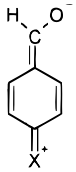
X	d_{cc}(**A**)	d_{cc}(**AH**$^+$)	$-\Delta d_{cc}{}^a$	σ^+
p-NH_2	1.470	1.382	0.088	−1.30
p-OCH_3	1.475	1.388	0.087	−0.78
p-CH_3	1.478	1.398	0.080	−0.31
m-CH_3	1.479	1.401	0.078	−0.07
H	1.480	1.403	0.077	0.00
p-Cl	1.480	1.399	0.081	0.11
m-OCH_3	1.478	1.401	0.077	0.12
m−F	1.481	1.405	0.076	0.34
m-Cl	1.482	1.406	0.076	0.37
p-CHO	1.482	1.404	0.078	0.42
p-CN	1.483	1.406	0.077	0.66
p-NO_2	1.482	1.406	0.076	0.78

[a] $\Delta d_{cc} = d_{cc}(\mathbf{AH}^+) - d_{cc}(\mathbf{A})$, where d_{cc} is the distance between carbonyl and ipso carbons. [b] The slopes (s) and correlation coefficients (*r*) of the plots of d_{cc} vs σ and σ^+ are: for $d(A)$, $s = 1.48$ with $r = 0.915(\sigma)$ and $0.964(\sigma^+)$; for $d(\mathbf{AH}^+)$, $s = 1.40$ with $r = 0.872(\sigma)$ and $r = 0.959(\sigma^+)$; and for Δd, $s = -0.08$ with $r = 0.785(\sigma)$ and $0.901(\sigma^+)$.

agreement with the experimental values.[2b] The absolute energies of the **A** and **AH**$^+$ forms in the gas phase and in the solvent (H_2O, $\epsilon = 78.4$) are summarized in Table 1. The free energy changes, $\Delta G°$, were correlated with the Hammett substituent constant, σ^+, which takes into account of the effect of direct conjugation with a strong cationic functional center in the side chain of a benzene ring.[8]

Results and Discussion

Both the aldehyde (**A**) and its protonated form (**AH**$^+$) are resonance stabilized by a π-donor para substituent.



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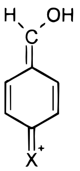


II

The bond length (d_{cc}) between the carbonyl (C_α) and ipso (C_{ip}) carbons depends on the extent of resonance delocalization as evident from the bond lengths, d_{cc}, summarized in Table 2.

The plots of d_{cc}(**A**), d_{cc}(**AH**$^+$), and Δd_{cc} ($=d_{cc}(\mathbf{AH}^+) - d_{cc}(\mathbf{A})$) against σ and σ^+ gave the slopes[9] and correlation coefficients (*r*) as listed in Table 2. We note that the bond length, d_{cc}, is better correlated with σ^+ than with σ as expected from the resonance delocalization of the π-donors.[9] The negative value of Δd (<0) indicates that the delocalization is stronger in the protonated form (**AH**$^+$).

The energetics are summarized in Table 3. The gas-phase experimental values are available for 11 compounds, which are given in Table 3. The free energy change in solution (ΔG^o_{aq}) is obtained by adding the solvation free energy change (ΔG^o_{sol}) to the gas-phase free energy change (ΔG^o_g) (eq 2).

$$\Delta G^o_{aq} = \Delta G^o_g + \Delta G^o_{sol} \tag{2}$$

$$\begin{aligned}\Delta G^o_{sol} &= G^o_s(\mathbf{AH}^+) - [G^o_s(\mathbf{A}) + G^o_s(\mathrm{H}^+)] \\ &= [G^o_s(\mathbf{AH}^+) - G^o_s(\mathbf{A})] - (-260.9) \\ &= \Delta G^o_s + 260.9 \end{aligned} \tag{3}$$

The ΔG^o_{sol} value in turn is obtained by subtracting the experimental ion solvation[4] free energy of H$^+$ ($G^o_s = -260.9$ kcal mol^{-1})[10] from the difference in the calculated solvation free energy between **AH**$^+$ and **A** ($\Delta G^o_s = G^o_s(\mathbf{AH}^+) - G^o_s(\mathbf{A})$), eq 3.[4] The dissection of solvation energies into G^o_s(**A**) and G^o_s(**AH**$^+$) is shown for the SCIPCM model in Table 4. The experimental ΔG^o_{aq} values are reported for seven compounds which are presented in Table 4.

Reference to Table 3 reveals that the MP2 results of the gas-phase free energies are in satisfactory agreement with the experimental values.[10] For X = H, the MP2 ΔG^o_g value is higher by 4.0 kcal mol^{-1} than the experimental value. The comparison of our 11 MP2 gas-phase values with those corresponding experimental values (Table 3) shows that the errors (all positive) range from 4.0 kcal mol^{-1} (X = H) to 8.9 kcal mol^{-1} (X = *m*-CH_3) with overall average of 5.2 kcal mol^{-1}, $\delta\Delta G^o_g$ [$=\Delta G^o_g(\mathrm{MP2}) - \Delta G^o_g(\mathrm{expt})$] = 5.2 kcal mol^{-1}. The Hammett plots using σ^+ constants according to eq 4 are shown in Figures 1 and 2. Agreement between the MP2 and experimental Hammett ρ^+ values is excellent: $\rho^+_{(expt)} = -9.21 \pm 0.67$ with correlation coefficient of $r = 0.977$[11] and $\rho^+_{(MP2)} = -9.40 \pm 0.52$ with $r = 0.985$ at 298 K. In fact, the plot of $\delta\Delta G^o_g$(MP2) against $\delta\Delta G^o_g$(expt) in Figure 3 exhibits a good linear correlation with the slope of 1.06 ± 0.04 and $r = 0.995$. The intercept is also near zero with -0.83 ± 0.20 kcal mol^{-1} (the range of $\delta\Delta G^o_g$ is ca. 20 kcal mol^{-1}). This means that the absolute errors of our MP2 results are persistent throughout the compounds, i.e., substituent changes do not influence the magnitude of error.

$$\log(K_X/K_H)\ (=-\delta\Delta G°/2.303RT) = \rho^+\sigma^+ \tag{4}$$

The performances of the solvation models in reproducing the solvation energies are not satisfactory. The best value of ΔG^o_{aq} for X = H is obtained by the SCIPCM model. The SCIPCM free energy change in water for X = H ($\Delta G^o_{aq} = +18.36$ kcal

TABLE 3: Relative Free Energy Change ($\delta\Delta G^o = \Delta G^o(X) - \Delta G^o(H)$ in kcal mol^{-1}) and Solvation Energy Change ($\delta\Delta G^o_{sol}$ in kcal mol^{-1})

	gas phase (exptl)[b]	gas phase (MP2)		IPCM(H_2O)		SCIPCM(H_2O)	
X	$\delta\Delta G^o_g$	$\delta\Delta G^o_g$	$\delta\Delta E^o_g$	$\delta\Delta G^o_{aq}$	$\delta\Delta G^o_{sol}$	$\delta\Delta G^o_{aq}$	$\delta\Delta G^o_{sol}$
p-NH_2		−16.15	−16.64	−11.77	4.38	−11.21	4.94
p-OCH_3	−10.20	−9.40	−9.51	−3.45	5.95	−4.1	5.30
p-CH_3	−4.50	−4.29	−3.76	2.66	6.95	−0.27	4.02
m-CH_3	−2.80	−1.88	−2.30	−2.98	−1.10	0.99	2.87
H	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	(−192.10)[a]	(−188.10)[a]	(−203.17)	(20.73)[a]	(208.83)	(18.36)[a]	(206.46)
						(9.68)[b]	
p-Cl	0.60	2.08	2.15	−13.55	−15.63	1.48	−0.60
m-OCH_3	−2.70	−2.52	−2.21	−7.61	−5.09	1.42	3.94
m−F	4.00	4.45	4.53	−0.66	−5.11	2.44	−2.01
m-Cl	3.20	5.00	5.10	−5.45	−10.45	3.94	−1.06
p-CHO	5.00	5.47	5.72	8.73	3.26	2.75	−2.72
p-CN	8.10	9.34	9.55	8.23	−1.11	3.47	−5.87
p-NO_2	8.70	10.78	10.92	10.97	0.55	4.53	−6.25
						(11.53)[b]	

[a] The absolute values (ΔG^o_g) for X = H are shown in parentheses. $\Delta G^o_g = G^o_g(\mathbf{AH}^+) - G^o_g(\mathbf{A}) - G^o_g(H^+)$ where $G^o_g(H^+)$ (=−6.28 kcal mol^{-1}) is calculated using statistical thermodynamic relationship. [b] Experimental value, ref 9.

TABLE 4: Dissection of Free Energy Change (kcal mol^{-1}) in Aqueous Solution by the SCIPCM Model: $\Delta G^o_{aq} = \Delta G^o_g + \Delta G^o_{sol}$, and $\Delta G^o_{sol} = G^o_s(AH^+) - [G^o_s(A) + G^o_s(H^+)] = G^o_s(AH^+) - G^o_s(A) - (-260.9) = \Delta G^o_s + 260.9$

X	ΔG^o_g[a]	ΔG^o_{aq}[b]	ΔG^o_{sol}[c]	ΔG^o_s[d]	$G^o_s(\mathbf{A})$[e]	$G^o_s(\mathbf{AH}^+)$[f]
p-NH_2	−204.25	7.15	211.40	−49.50	−5.69	−55.19
p-OCH_3	−197.50	14.26	211.76	−49.14	−4.57	−53.17
		(7.56)[g]				
p-CH_3	−192.39	18.09	210.48	−50.42	−5.69	−56.11
		(8.62)				
m-CH_3	−185.98	19.35	209.33	−51.57	−3.39	−54.96
		(9.63)				
H	−188.10	18.36	206.46	−54.44	−3.43	−57.87
	(−192.10)[g]	(9.68)				
p-Cl	−186.02	19.84	205.86	−55.04	−3.71	−58.75
		(9.90)				
m-OCH_3	−190.62	19.78	210.40	−50.50	−4.04	−54.54
m−F	−183.65	20.80	204.45	−56.45	−3.59	−60.04
m-Cl	−183.10	22.30	205.40	−55.50	−3.37	−58.87
		(10.48)				
p-CHO	−182.63	21.11	203.74	−57.16	−4.99	−62.15
p-CN	−178.76	21.83	200.59	−60.31	−5.95	−66.26
p-NO_2	−177.68	22.53	200.21	−60.69	−5.22	−65.91
		(11.53)				

[a] The gas phase free energy change. [b] The free energy change in aqueous solution. [c] The solvation free energy change. [d] The solvation energy difference: $\Delta G^o_s = G^o_s(\mathbf{AH}^+) - G^o_s(\mathbf{A})$. [e] The solvation energy of benzaldehydes (**A**). [f] The solvation energy of the protonated benzaldehydes ($\mathbf{AH}^+$). [g] Experimental values are in parentheses; refs 9 and 10.

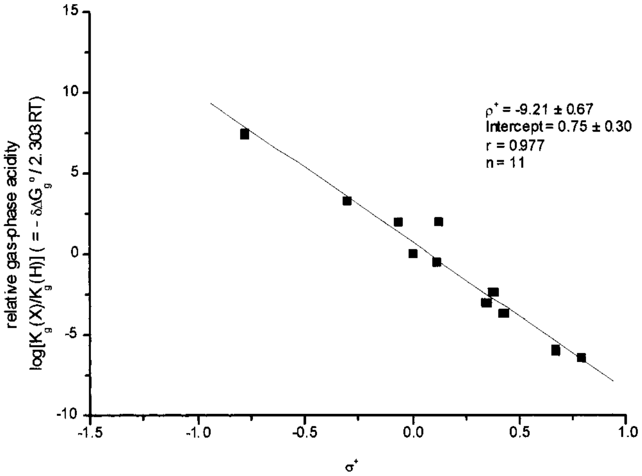


Figure 1. Plot of relative experimental gas-phase acidity, $\log[K_g(X)/K_g(H)]$, vs σ^+.

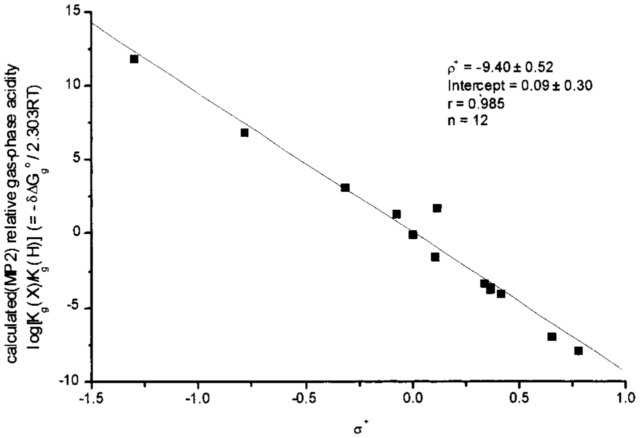


Figure 2. Plot of calculated (MP2) relative gas-phase acidity, $\log[K_g(X)/K_g(H)]$, vs σ^+.

mol^{-1}) is higher than the experimental value (9.68 kcal mol^{-1})[12] by ca. 8.7 kcal mol^{-1}. In contrast, the IPCM model gives a value that is twice as much higher (11.1 kcal mol^{-1}) than this. Since the error in the theoretical (MP2) estimate of ΔG^o_g for X = H is +4.0 kcal mol^{-1} and that of ΔG^o_{aq} for X = H is +8.7 kcal mol^{-1}, the error in the theoretical estimate of ΔG^o_{sol} value should be +4.7 kcal mol^{-1} by the SCIPCM model. The average error of our SCIPCM ΔG^o_{aq} (Table 4) values for seven compounds (for which experimental values are reported) is 9.6 kcal mol^{-1}: $\delta\Delta G^o_{aq}$ [$=\Delta G^o_{aq}$(SCIPCM) $- \Delta G^o_{aq}$(expt)] = 9.6 kcal mol^{-1}. Since this error is partly transmitted (eq 2) from the gas-phase values (+5.2 kcal mol^{-1}), the error due to theoretical estimate of solvation free energies by the SCIPCM model is 9.6 − 5.2 = 4.4 kcal mol^{-1} for the average of seven compounds. The errors in the solvation free energies are actually smaller than those in the gas-phase ΔG^o_g values. This should be considered as quite good theoretical solvation energy estimates, albeit we neglected nonelectrostatic components, e.g., cavitation and dispersion energies which were within our error limit of ca. 4 kcal mol^{-1}.[13b] For example, for X = H the nonelectrostatic components were 1.62 and 1.43 kcal mol^{-1} for the **A** and $\mathbf{AH}^+$ forms, respectively, so that the difference between the two is 0.2 kcal mol^{-1}.

The Hammett plots based on the free energy changes in solution, $-\delta\Delta G^o_{aq}/1.364$ vs σ^+ (eq 4), are presented in Figure

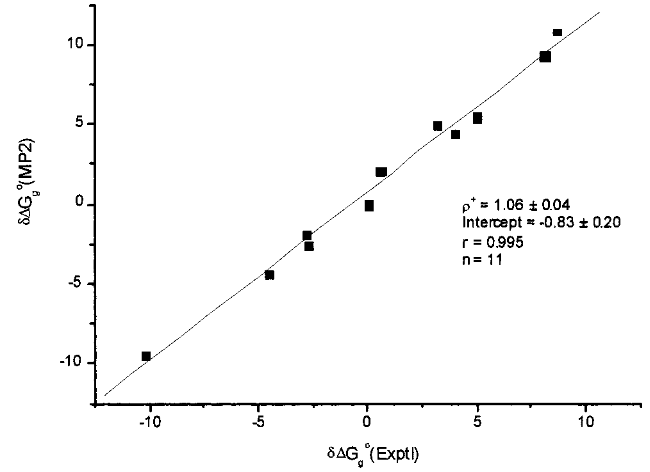


Figure 3. Plot of calculated, [$\delta\Delta G_g°$(MP2)], vs experimental relative gas-phase free energy changes, [$\delta\Delta G_g°$(exptl)].

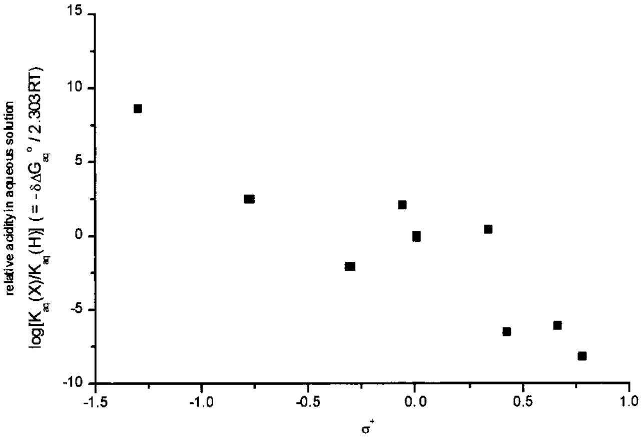


Figure 4. Plot of calculated (IPCM model at the isodensity level of 0.001 au) relative acidity in aqueous solution, log[K_{aq}(X)/K_{aq}(H)], vs σ^+. (A similar plot is obtained at the isodensity level of 0.0004 au. Refer to Supporting Information.)

4. Quite strikingly, the IPCM models (at the isodensity levels of both 0.001 au and 0.0004 au) give unsatisfactory linear correlations with particularly large positive deviations in various solvents (CH_3CN, CH_2Cl_2, and H_2O; The plots in the former two solvents are shown in Supporting Information) for the electron-withdrawing groups ($\sigma_x > 0$). Under strong polarization of the protonated forms (**AH**$^+$) by the electron-acceptor groups, the electrostatic solute−solvent interaction should be high and result in a contraction of the cavity which is not reflected in the IPCM model [IPCM model uses fixed isodensity level (0.001 or 0.0004 au)] and lead to underestimation of such interaction energies (vide infra). However, such cavity size changes for charged species are taken into account self-consistently in the SCIPCM method. The linear correlation is satisfactory *only for the SCIPCM model* with $\rho^+ = -5.29 \pm 0.43$ and $r = 0.968$ in water as shown in Figure 5. The magnitude of the ρ^+(SCIPCM) in water is, however, unduly larger than the corresponding experimental ρ^+ ($=-1.88$)[14] in water. But this is not unexpected, since in the continuum solvation model (all the models used in the present work) the specific solvation (e.g., hydrogen bond) effect is neglected.[1] Solvents such as benzene derivatives and many chlorides and bromides have high polarizability or a large quadrupole moment[15] and the solvent effect becomes larger than expected based on the dielectric constant.[2b] For water, this type of effect will be absent and the hydrogen bond effect will be the main component that is neglected in the continuum model.

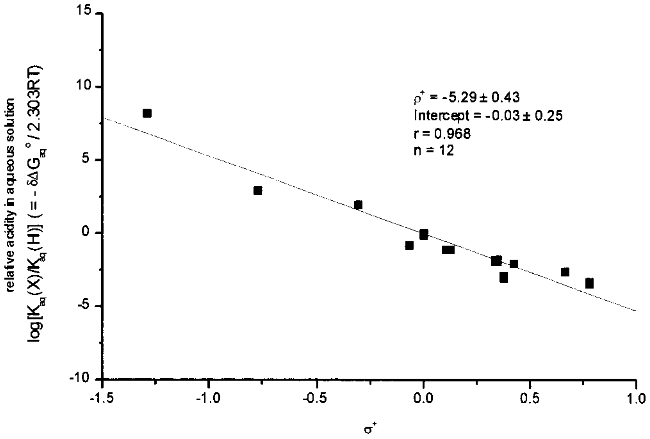
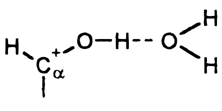


Figure 5. Plot of calculated (SCIPCM model) relative acidity in aqueous solution, log[K_{aq}(X)/K_{aq}(H)] vs σ^+.

For example, water molecule will stabilize the aldehyde with a π-donor substituent (**I**) by donating hydrogen bond to the carbonyl oxygen. The lack of this stabilizing effect in **I** will be only partially compensated for by the lack of hydrogen bond acceptor effect in **II** (vide infra) so that the net neglect of hydrogen bond donor effect will result in an unduly larger log *K* value for the π-electron donors. This will, of course, lead to a steeper negative slope, i.e., the larger negative ρ^+ value than the experimental ρ^+ in which such effect is properly accounted for. For the electron acceptor substituent, the π-polarization effect should be negligible in the aldehydes (**A**), but the cationic charge on the carbonyl carbon, C_α, will be strengthened and consequently the strong C_α^+ charge will induce water a weak hydrogen bond acceptor effect, **III**. The neglect of this hydrogen bond acceptor effect of water for the **AH**$^+$ forms substituted with strong electron-withdrawing groups (X = *p*-CN, *p*-NO_2, etc.) should result in a small decrease in the log *K* value. This, in turn, should also lead to a steeper slope for a linear plot of log *K* against σ^+ in the continuum models. This latter effect is, however, expected to be smaller than that caused by the neglect of hydrogen bond donor effect of water for the aldehydes, **A**, substituted with a π-donor. The unduly higher log *K* values for π-donor substituents become evident when we plot the solvation energy component of log *K* (log K_{sol}) against σ^+, as shown in Figure 6. We note that the π-donors exhibit strong positive deviations from an approximate linear correlation between log K_{sol} and σ^+. Estimation of the experimental log K_{aq} value for X = *p*-NH_2 ($\sigma^+ = -1.30$) by extrapolation using the experimental ρ^+($=-1.88$)[14] gives −4.7. The SCIPCM//MP2/6-31G* value of −0.6 for X = *p*-NH_2 is higher than the estimated experimental value by 4.1, Δ log K_{aq} = log K_{aq}(theor) − log K_{aq}(exptl) = +4.1. On the other hand, for X = *p*-NO_2 the theoretical value of log K_{aq} ($=-12.2$) is lower than the experimental value (−8.5)[12] by 3.7 (Δ log $K_{aq} = -3.7$). It has been shown that for the primary and secondary amines the effect of water as a hydrogen bond donor is stronger than that as an acceptor with ca. −6 and −2 to −3 kcal mol^{-1}, respectively.[16] In order to account for the specific hydrogen bond effect theoretically we have to resort to statistical mechanical simulations of solvent, e.g., the Monte Carlo simulation.[3,17]



III

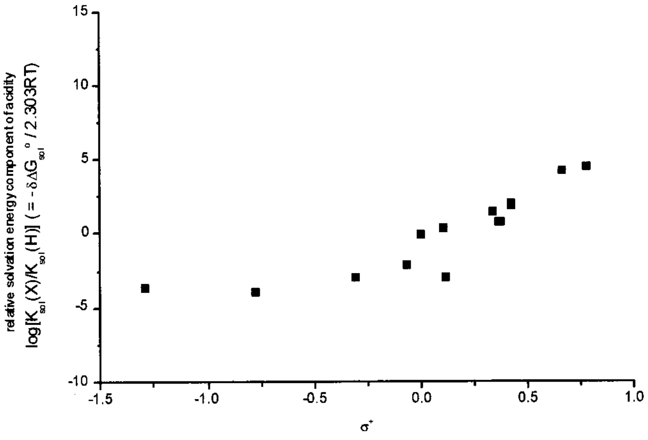


Figure 6. Plot of calculated (SCIPCM model) relative solvation energy component of acidity, $\log[K_{aq}(X)/K_{aq}(H)]$ vs σ^+.

We conclude that only the SCIPCM model reproduces adequately the relative continuum solvent effect on the equilibrium constant (on log K) for the protonation equilibria of benzaldehydes in water. In order to reproduce the relative solvent effect correctly, however, theoretical account for the specific solvation effect is essential.[17]

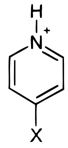
In the IPCM model, the solute−solvent boundary isodensity surface is defined using the gas-phase molecular wave functions. The increased solute−solvent interaction of charged species leads to a contraction of the cavity, and the solvation free energies of the protonated forms (**AH**$^+$) are underestimated[14] by the IPCM model. The IPCM model strongly underestimates the $\Delta G_s{}^o$ value for X = NO$_2$ [$\delta\Delta G^o{}_s = \Delta G^o{}_s$(SCIPCM) − $\Delta G^o{}_s$(IPCM) is −9.2 kcal mol^{-1}].

The SCIPCM model, however, uses the isodensity surface determined self-consistently in the presence of the polarizable medium[2a] and is shown to give sensitive variation of cavity sizes depending on the substituent X so that the calculated relative solvation energy seems to represent the correct relative value.

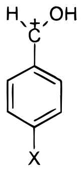
In the SCIPCM method, cavity contraction due to the increased cationic charge is reflected on the cavity size defined by an isodensity surface of the solute determined self-consistently. The cavitation and dispersion energies are small[13] but they are also related to the size and surface area of the cavity.[1b] Thus, their contributions are partly accounted for in the SCIPCM model.

Activation free energies for the Menshutkin reaction of CH$_3$Br with pyridine in cyclohexane ($\Delta G^\ddagger = 28.1$ kcal mol^{-1}) and di-*n*-butyl ether ($\Delta G^\ddagger = 24.5$ kcal mol^{-1}) calculated using the SCIPCM model[2b] were in remarkably good agreement with the experimental values ($\Delta G^\ddagger = 27.6$ and 25.6 kcal mol^{-1}, respectively). Thus, we believe that the SCIPCM model works well for the equilibria and activation processes involving delocalized charges in aprotic solvents and also in water when the water molecule does not act as a hydrogen bond donor.[4] Recently, we found that geometry optimization of reactants and transition states involved in various acyl transfer reactions in solution by the SCIPCM model leads to very little improvement in the calculated solvation free energy changes.[18] For example, the solvation free energy changes, $\Delta G^\ddagger{}_s$, involved in the chloride exchange reactions HCOCl + Cl$^-$ and CH$_3$COCl + Cl$^-$ were 14.32 and 13.82 kcal mol^{-1}, respectively, at the SCIPCM/B3LYP/6-31+G*//B3LYP/6-31+G* level, but they were 14.31 and 13.98 kcal mol^{-1} at the SCIPCM/B3LYP/6-31+G*//SCIPCM/B3LYP/6-31+G* level, respectively.

Another interesting aspect of the linear Hammett plots of log K vs σ^+ in the gas phase and in water (by SCIPCM model) is that the π-donor effect of strong π-acceptor substituents[4,19,20] is absent in the protonation equilibria of benzaldehydes. It is absent both in the gas phase and in aqueous solution. It has been shown that the strong π-acceptors (e.g., X = *p*-CN, *p*-NO$_2$, etc.) exhibit substantial positive deviations from the otherwise linear Hammett plots of log K vs σ, for the protonation equilibria of pyridines.[4]



IV



AH$^+$

The absence of this effect in the protonation equilibria of benzaldehydes may be ascribed to the weaker cationic charge on the functional center, C$_\alpha$, due to (i) the presence of a π-electron donor substituent, OH, and (ii) the longer distance (there is an extra C−C bond) between C$_\alpha$ and substituent in **AH**$^+$ compared to the strong cationic charge on the azonium ion in the protonated pyridines. The electron-attracting power of the azonium ion ($\sigma_p = 2.63$)[21] is stronger than that ($\sigma_p = 0.78$) of the strongest electron acceptor group, X = *p*-NO$_2$, by more than 3 times, which reverses electronic effect of *p*-NO$_2$ group from π-electron withdrawing to π-electron donating in the protonation equilibria of pyridines.[4] However, the 2pπ orbital on N in **IV** is occupied, whereas that on C$_\alpha$ in **AH**$^+$ is empty. This is why log K is correlated with σ in **IV**, but with σ^+ in **AH**$^+$.

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Supporting Information Available: Tables of free energy change by the IPCM model, and electronic energy, thermal correction term, and entropy values for aldehydes and protonated aldehydes; log K_{aq} vs σ^+ plot for the IPCM model. This material is available free of charge via the Internet at http://pubs.acs.org.

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