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Is the Hydrogen Atomic Charge Representative of the Acidity of Parasubstituted Phenols?

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A theoretical analysis is presented concerning the study of the influence of the substituent X on the acidity of a set of parasubstituted phenols $X-C_6H_4OH$. Linear correlation analyses between calculated Gibbs free energy changes on dissociation of parasubstituted phenols in the gas phase ($\Delta G°$), the hydrogen atom charge of $X-C_6H_4OH$ (q_H), and the electronegativity of the fragment $X-C_6H_4O$ ($\chi_{XC_6H_4O}$) show that acidity is related to q_H and $\chi_{XC_6H_4O}$. When the electronegativity increases, the hydrogen atom charge and the acidity of the parasubstituted phenols increase as well. These results suggest that there is no direct interaction between the X substituent and the hydrogen atom; the effect is primarily due to the interaction of X with the C_6H_4O group. The substituent does transmit its effect through the π system of the benzene ring, and q_H shows the effect of the electronegativity of the fragment $X-C_6H_4O$ on the hydrogen atom. Analytical equations obtained from density functional theory (DFT) and the hard and soft acids and bases principle (HSAB) provide guidelines to obtain a quantitative description of the fit parameters in the linear correlation equations. The results obtained suggest that q_H is representative of the gas-phase acidity of parasubstituted phenols.

Introduction

Acidity and basicity play important roles in determining the chemical reactivity of organic compounds. Several organic reactions begin with steps that involve reagent protonation or deprotonation.[1] In the elimination (E2) and substitution (S_N2) reactions of alkyl halides, the elimination−substitution ratio ($E2/S_N2$) depends on the basicity of the nucleophile.[2] In particular, the reaction between *p*-nitrophenethyl bromide and parasubstituted phenolates shows that the ($E2/S_N2$) ratio increases when the phenol acidity decreases (phenolate basicity increases).[3]

The influence of the substituent on the acidity of benzene compounds has been explained, in general, in terms of resonance and inductive effects.[4] Although a substituent on a benzene ring is expected to interact by the two mechanisms, the simple linearity of many $\sigma\rho$ relationships might seem to imply the existence of a single interaction mechanism.[5] For example, in the benzoic acid ionization where the σ scale is widely applicable, it has been suggested that the substituent effect is primarily inductive, due to the fact that there is no direct resonance interaction between the substituent and the reaction center.[6] In the ionization of *p*-nitrophenol, where correlation with the σ scale is not observed, it has been suggested that the nitro substituent can come into direct resonance interaction with the π system of the benzene ring and the reaction center; in these cases the balance of inductive and resonance contributions of the substituent is significantly different from that in the benzoic acid system, as the resonance interaction will become more important.[6]

A quantitative understanding of the acidity substituent effect is of general interest.[7] However, analytical equations for acidity substituent effects remain absent, and the extra-thermodynamic equations often found are simple linear Gibbs free energy relationships.[8,9] In the Hammett equation, for example, $\log(\{K_a^X\}/\{K_a^H\}) = \rho\sigma$, the assumption is that within a particular class of acids, the substituents produce free energy changes which are linearly additive.[10,11]

Recently we were working with a simple linear regression analysis to predict the effect of substituents on the reactivity of parasubstituted phenolate anions.[12] The reaction between *p*-nitrophenethyl bromide, $NO_2C_6H_4CH_2CH_2Br$, and a set of parasubstituted phenolates $XC_6H_4O^-$ yielded elimination (E2) and substitution (S_N2) products.[3] The linear regression analysis between equilibrium (pK_a) and kinetic ($E2/S_N2$ ratio) parameters showed that phenol acidity is related to the $E2/S_N2$ ratio. The extent of charge dispersal in the parasubstituted phenolate anions was considered to be the key to understanding the gas-phase acidity orders. The parasubstituted phenols XC_6H_4O-H, with highly delocalized conjugate base anions (resonance stabilized by an electron-accepting substituent), were relatively strong acids in the gas phase, whereas those whose conjugate base anions were strongly localized behaved as weak acids in the gas phase. Because the effects of the substituents on the acidity of phenols were largely determined by effects in the phenolate anions[12−16] and because there was a close correspondence between the positive charge carried by the phenolic hydrogen atom (q_H) and the pK_a values of the phenols,[12] the objective of this paper is to show that the substituent influence should be described in terms of the properties of phenol (bond polarization $XC_6H_4O^{\delta-}-H^{\delta+}$ and bond dissociation XC_6H_4O-H) and phenolate anion (anion stabilization $XC_6H_4O^-$). To our knowledge, no study has been presented so far in this regard.

In this context, we have calculated the phenol/phenolate Gibbs free energy change ($\Delta G°$) in a set of parasubstituted phenols XC_6H_4OH in the gas phase. $\Delta G°$ describes the acidity of the substituted phenol and therefore is sensitive to the substituent effect. Great quantitative agreement between experimental and calculated data was obtained. Linear variations between $\Delta G°$, the hydrogen atom charge (q_H), and the electronegativity of the fragment $X-C_6H_4O$ ($\chi_{XC_6H_4O}$) were obtained; when the electronegativity of the $X-C_6H_4O$ fragment increases, the hydrogen atom charge q_H and the acidity of the parasubstituted phenols XC_6H_4OH increase as well. To understand the nature of the parameters involved in determining the acid strength of parasubstituted phenols XC_6H_4OH, the phenol/phenolate Gibbs

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TABLE 1: Absolute Gas-Phase Acidity $\Delta G°$ of the Parasubstituted Phenols (All Values Are in Kilocalories per Mole)

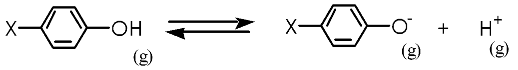
X	$\Delta G^\circ_{\text{calcd1}}$ [a]	$\Delta G^\circ_{\text{exptl}}$ [b]	$\lvert\Delta G^\circ_{\text{calcd1}} - \Delta G^\circ_{\text{exptl}}\rvert$
CF_3	325.1	331.1	5.6
CH_2CH_3	339.8	343.6	3.8
CH_3	340.9	344.1	3.2
CHO	321.6	327.2	5.6
Cl	332.6	337.1	4.5
CN	320.9	326.4	5.5
$COOCH_3$	326.1	331.3	5.2
COOH	324.2	333.2	9.0
F	336.2	340.7	4.5
H	339.4	343.0	3.6
i-Pr	339.5	343.1	3.6
NH_2	343.2	346.3	3.1
NO_2	314.6	322.1	7.5
OCH_3	340.2	344.2	4.0
OH	340.3	344.2	3.9
t-Bu	339.4	342.4	3.0

[a] Values obtained through the equation $\Delta G^\circ_{\text{acid}} = G^\circ(XC_6H_4O^-) + G^\circ(H^+) - G^\circ(XC_6H_4OH)$. The gap $G^\circ(XC_6H_4O^-) - G^\circ(XC_6H_4OH)$ and $G^\circ(H^+)$ were obtained by means of a vibrational calculation and statistical thermodynamics, respectively, $G^\circ(H^+) = -6.26$ kcal/mol. [b] Experimental values obtained from ref 22.

energy gap was described in terms of bond polarization $XC_6H_4O^{\delta-}{-}H^{\delta+}$, bond dissociation $XC_6H_4O{-}H$, and anion stabilization $XC_6H_4O^-$. An extra-thermodynamic equation was obtained and then was developed in terms of the density functional theory (DFT)[17] and the hard and soft acids and bases principle (HSAB).[18]

Results and Discussion

The ground-state structures and energies of 16 parasubstituted phenols XC_6H_4OH and 16 parasubstituted phenolates $XC_6H_4O^-$ were calculated at the B3LYP/6-31+G** level by means of GAUSSIAN 98.[19] The dissociation reaction of the substituted phenols XC_6H_4OH is represented in the gas phase by eq 1:



(1),

the absolute gas-phase acidity $\Delta G^\circ_{\text{acid}}$ is given by

$$\Delta G^\circ_{\text{acid}} = G^\circ(XC_6H_4O^-) + G^\circ(H^+) - G^\circ(XC_6H_4OH) \quad (2)$$

The Gibbs free energies G° (XC_6H_4OH) and G° $(XC_6H_4O^-)$ were obtained by means of a vibrational calculation using GAUSSIAN 98.[19] The Gibbs free energy $G^\circ(H^+)$ was obtained considering the translational energy of the proton, using statistical thermodynamic relations.[20] In agreement with previous calculations,[21] good values of $\Delta G^\circ_{\text{acid}}$ were obtained. The calculated $\Delta G^\circ_{\text{calcd1}}$ values underestimate the $\Delta G^\circ_{\text{exptl}}$ values by 9 to 3 kcal/mol.[22] From Table 1 we can observe that the acidity of the phenol is altered by adding a substituent X in the para position; the electronic influence of the substituent X can be exerted at the reaction center OH and/or at the base structure C_6H_4, where X and OH are bonded. We propose that the electronic influence of the substituent X should be assessed in one of the following fragments: X, XC_6H_4, or XC_6H_4O. If x_i is the electronic property of each fragment, the criterion for deciding whether the variable has been correctly identified is simple: the plot of $\Delta G^\circ_{\text{acid}}$ versus x_i must be linear over the range of substituents to which the extra-thermodynamics relationship applies. The two-parameter linear model was used:[23,24]

$$\Delta G^\circ = a_0 + a_1 x_1 \quad (3)$$

In eq 3 a_0 and a_1 are the fitted constants. The electronic properties of the fragments x_i considered in this study were the hydrogen atom charge q_H, the chemical potential μ, and the hardness η.[17] The DFT global properties μ and η represent the system as a whole, and they have the same value everywhere in the molecule. The chemical potential μ represents the change in energy E with the number of electrons N, $\mu = (\partial E/\partial N)_\nu$, and it is identified as the negative of the electronegativity χ ($\mu = -\chi$).[25] Pearson's chemical hardness, η, is the change in the chemical potential μ with the number of electrons (N), $\eta = (\partial\mu/\partial N)_\nu$ (the chemical softness is the inverse of the hardness $S = \eta^{-1}$).[17,26] The derivatives can be evaluated under a finite differences scheme[25−27] as $\mu = {}^1/_2(I + A)$ and $\eta = {}^1/_2(I - A)$, where I is the ionization potential and A is the electron affinity. The structures and energies of the XC_6H_4O, XC_6H_4, and X fragments were calculated at the B3LYP/6-31+G** ground geometry of the XC_6H_4OH by means of GAUSSIAN 98.[19] The I and A values of the structures were calculated from the energies of the oxidized and reduced (cation and anion) species at the geometry of the neutral for all of the fragments and parasubstituted phenols. There was no spin contamination for the doublet open shell structures calculated at the UB3LYP/6-31+G** level. Table 2 shows the hydrogen atom charge (q_H) and the DFT global properties of the XC_6H_4O, XC_6H_4, and X fragments and the parasubstituted phenols XC_6H_4OH.

Table 3 shows the results of a simple linear regression analysis between the $\Delta G^\circ_{\text{exptl}}$ values and the q_H of the XC_6H_4-OH and the DFT global properties of the XC_6H_4O, XC_6H_4, and X fragments and the XC_6H_4OH. In general q_H, $\mu_{XC_6H_4OH}$, and $\mu_{XC_6H_4O}$ yield correlation coefficients $R^2 \geq 0.90$. On the other hand, $\eta_{XC_6H_4}$, $\mu_{XC_6H_4}$, η_X, and μ_X yield correlation coefficients $R^2 \leq 0.87$. The correlation analysis shows that the acidity of the parasubstituted phenols depends on the positive hydrogen net charge q_H and the fragment electronegativity $\chi_{XC_6H_4O}$ ($\chi_{XC_6H_4O} = -\mu_{XC_6H_4O}$). The acidity has no linear dependence on the X and XC_6H_4 fragment properties μ_X, η_X, $\mu_{XC_6H_4}$, and $\eta_{XC_6H_4}$ (there is a significant linear correlation with $\mu_{XC_6H_4}$). The results suggest that the effect is primarily due to the interaction of X with the C_6H_4O structure. If the substituent perturbation is included in the XC_6H_4O fragment, then the substituent does transmit its effect through the π system of the benzene ring, and q_H should show the effect of the electronegativity of the fragment $\chi_{XC_6H_4O}$ on the hydrogen atom. For this reason, there is no linear regression with the σ scale, mentioned before; the substituent X behaves as a part of the XC_6H_4O fragment.

To obtain an analytical equation for the relationship between the gas-phase acidity and the hydrogen atomic charge, $\Delta G°$ can be calculated as $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$.[28] In general, a thermochemical cycle is used for calculating $\Delta H°$; the cycle involves the following steps:[4,22]

$$XC_6H_4OH \rightarrow XC_6H_4O^\circ + H^\circ \qquad DH^\circ(XC_6H_4O{-}H) \quad (4)$$

$$H^\circ \rightarrow H^+ + e^- \qquad I_H \quad (5)$$

$$XC_6H_4O^\circ + e^- \rightarrow XC_6H_4O^- \qquad -A_{XC_6H_4O} \quad (6)$$

$$XC_6H_4OH \rightarrow XC_6H_4O^- + H^+ \qquad \Delta H^\circ = DH^\circ(XC_6H_4O{-}H) + I_H - A_{XC_6H_4O} \quad (7)$$

$\Delta S°$ can be evaluated using statistical thermodynamics.[29]

TABLE 2: Calculated Values for q_H and the DFT-Based Electronic Properties μ and η for Parasubstituted Phenols and Their Fragments (μ and η Values Are in Electronvolts)

X	q_H[a]	$\mu_{XC_6H_4OH}$ ($\eta_{XC_6H_4OH}$)[b]	$\mu_{XC_6H_4O}$ ($\eta_{XC_6H_4O}$)[b]	$\mu_{XC_6H_4}$ ($\eta_{XC_6H_4}$)[b]	μ_X (η_X)[b]
CF_3	0.358	−4.18 (4.84)	−6.26 (3.48)	−5.77 (4.38)	−7.01 (5.41)
CH_2CH_3	0.350	−3.59 (4.48)	−5.39 (3.34)	−5.11 (4.19)	−4.83 (4.84)
CH_3	0.350	−3.55 (4.57)	−5.40 (3.40)	−5.12 (4.23)	−5.69 (5.30)
CHO	0.358	−4.44 (4.42)	−6.25 (2.71)	−5.69 (4.19)	−5.17 (5.01)
Cl	0.353	−3.77 (4.63)	−5.75 (3.45)	−5.60 (4.28)	−9.46 (5.74)
CN	0.357	−4.29 (4.62)	−6.31 (3.30)	−5.94 (4.27)	−9.59 (5.57)
$COOCH_3$	0.357	−4.11 (4.52)	−6.00 (3.29)	−5.49 (4.19)	−5.79 (4.67)
COOH	0.358	−4.25 (4.54)	−6.15 (3.33)	−5.61 (4.23)	−6.30 (4.85)
F	0.352	−3.82 (4.71)	−5.75 (3.53)	−5.56 (4.39)	−12.46 (8.95)
H	0.351	−3.68 (4.78)	−5.68 (3.54)	−5.22 (4.31)	−7.18 (6.43)
i-Pr	0.351	−3.58 (4.46)	−5.36 (3.31)	−5.09 (4.16)	−4.40 (4.48)
NH_2	0.348	−3.18 (4.19)	−4.87 (3.24)	−4.92 (4.11)	−6.72 (6.07)
NO_2	0.362	−5.02 (4.28)	−6.65 (3.34)	−6.10 (4.30)	−7.52 (5.15)
OCH_3	0.350	−3.36 (4.33)	−5.11 (3.28)	−5.17 (4.27)	−7.06 (5.81)
OH	0.351	−3.51 (4.40)	−5.25 (3.38)	−5.28 (4.31)	−9.06 (7.30)
t-Bu	0.351	−3.57 (4.43)	−5.35 (3.28)	−5.07 (4.14)	−4.27 (4.16)

[a] Obtained from a Mulliken population analysis. [b] Calculated through the equations $\mu = {}^1/_2(I + A)$ and $\eta = {}^1/_2(I - A)$.

TABLE 3: Correlation Equation for the Parasubstituted Phenols Involving q_H or a Single DFT-Based Electronic Property (x_i): $\Delta G° = a_0 + a_1x_1$ ($\Delta G°$ Values Are in Kilocalories per Mole)[a]

fragment	x_1	a_1	a_0	R^2
XC_6H_4OH	q_H	−1926.34	1018.56	0.96
	$\mu_{XC_6H_4OH}$	15.70	398.24	0.92
	$\eta_{X_6H_4OH}$	−4.93	359.74	0.01
XC_6H_4O	$\mu_{XC_6H_4O}$	14.59	420.97	0.90
	$\eta_{XC_6H_4O}$	13.93	291.31	0.11
XC_6H_4	$\mu_{XC_6H_4}$	20.90	450.74	0.87
	$\eta_{XC_6H_4}$	−20.09	422.72	0.04
X	μ_X	0.38	340.19	0.01
	η_X	1.69	328.01	0.07

[a] $\Delta G°_{exptl}$ values were used for the linear regression analysis.

There is an expression for the interaction energy ΔE_{int} between two chemical species A + B → A − B in terms of the chemical potential (μ_A, μ_B) and the hardness (η_A, η_B).[30] The equation $\Delta E_{int} = \Delta E_\nu + \Delta E_\mu$ was obtained by dividing the total interaction energy in two steps, the charge-transfer process between A and B at constant nuclear positions ΔE_ν, and the electronic density reshuffling at constant chemical potential ΔE_μ.[30] Because the DH° (A − B) term can be approximated by $-\Delta E_{int}$, the expression $\Delta E_{int} = \Delta E_\nu + \Delta E_\mu$ provides a formula to estimate the bond strength DH° (A − B).[31] $\Delta H°$ can be approximated as

$$\Delta H° \approx -\Delta E_\nu - \Delta E_\mu + I_H - A_{XC_6H_4O} \tag{8}$$

$\Delta H°$ is expressed in terms of the $XC_6H_4O^{\delta-}{-}H^{\delta+}$ bond polarization energy (ΔE_ν), the $XC_6H_4O{-}H$ bond stabilization energy (ΔE_μ), the anion stabilization energy ($A_{XC_6H_4O}$), and a constant value (I_H).

It is interesting to observe from eq 8 that the ($I_H - A_{XC_6H_4O} - \Delta E_\nu$) term is an energy charge-transfer term, and it corresponds to the energy required to transfer $1 - \Delta N_\nu$ electrons from H to XC_6H_4O (ΔN_ν is the contribution of the charge transferred between A and B at constant nuclear positions).[18] In the dissociation reaction, the H atom increases its positive net charge from q_H to +1. Reed has studied the influence of the atomic charge on the proton affinity and has shown that the charging energy for the proton affinity reaction is the energy needed to transfer the amount of charge which would bring the conjugate base fragment and the hydrogen to the charges that they would carry in the products.[32] The relationship between q_H and ΔN_ν can be stated as $q_H = \Delta N_\nu + \Delta N_\mu$, where ΔN_μ is the charge shifted in the electronic density reshuffling at constant chemical potential.

By substitution of the local expressions[33,34] $\Delta E_\nu = -(\mu_H - \mu_{XC_6H_4O})^2/2(\eta_H^- + \eta_O^+)$ and $\Delta E_\mu = -\lambda(\eta_H^-\,\eta_O^+)/2(\eta_H^- + \eta_O^+)$ into eq 8 we obtain

$$\Delta H° = \frac{(\mu_H - \mu_{XC_6H_4O})^2}{2(\eta_H^- + \eta_O^+)} + \frac{\lambda(\eta_H^-\,\eta_O^+)}{2(\eta_H^- + \eta_O^+)} + I_H - A_{XC_6H_4O} \tag{9}$$

The condensed hardness values η_H^- and η_O^+ represent the atomic hardness involved in the process when the O−H bond is broken. They reflect how the electronic density in the H and O atoms may respond to the electronic perturbations resulting from removal and addition of charges in the H and O atoms, respectively. The η_O^+ value is obtained from $\eta_O^+ = \eta_{XC_6H_4O}/f_O^+$, where f_O^+ is the condensed version of the fukui function for nucleophilic attack, $f^+(r) = (\partial\rho(r)/\partial N)_\nu{}^+$. The integration of $f^+(r)$ in the neighborhood of the O atom can be approximated by using the gross population q_O for the O atom in the X−C_6H_4O neutral and anion species: $f_O^+ = q_O(X{-}C_6H_4O^-) - q_O(X{-}C_6H_4O°)$.[35,36] The η_H^- value corresponds to the global hardness of the free H atom; the experimental value is $\eta_H^- = 6.43$ eV.[18] The λ parameter is a constant related with an *effective number of valence electrons* that participate in the interaction between H and X−C_6H_4O. It bears information on the system $XC_6H_4O{-}H$ when H and X−C_6H_4O are far away from each other and when the $XC_6H_4O{-}H$ system is at equilibrium.[30,37] The results obtained in some organic reactions as 1,3-dipolar cycloadditons,[38] and the addition of singlet carbenes to alkenes,[39] yielded λ values equal to 1. Using the local expression $\Delta N_\nu = (\mu_H - \mu_{XC_6H_4O})/2(\eta_H^- + \eta_O^+)$ and eq 9 in $\Delta G° = \Delta H° - T\Delta S°$, $\Delta G°$ can be expressed as

$$\Delta G° \approx [c_0 + \Delta N_\mu(c_2\Delta N_\mu - c_1)] + (c_1 - 2c_2\Delta N_\mu)q_H + c_2q_H^2 \tag{10}$$

where $c_0 = I_H - A_{XC_6H_4O} - T\Delta S$, $c_1 = \lambda(\eta_H^-\,\eta_O^+)/(\mu_H - \mu_{XC_6H_4O})$, and $c_2 = 2(\eta_H^- + \eta_O^+)$. It is interesting to observe in eq 10 that $\Delta G°$ becomes a quadratic function of q_H. Ickowsky and Margrave have suggested an energy formulation of a neutral atom as a quadratic function of the charge carried by the atom: $-E_q = aq + {}^1/_2bq^2$, where *a* and *b* are empirical constants obtained from spectroscopic data.[40] Table 4 shows the calculated values η_O^+, $T\Delta S°$, and $A_{XC_6H_4O}$ for the X−C_6H_4O species; these

TABLE 4: Electron Affinity (A), Entropy ($\Delta S°$), and the Oxygen Condensed Hardness (η_{O}^{+}) Values for the XC_6H_4O Species[a]

X	$A_{XC_6H_4O}$[b]	$T\Delta S°$[c]	ΔN_μ[d]	η_{O}^{+}[e]
CF_3	64.3	7.6	0.360	250.0
CH_2CH_3	47.2	7.4	0.354	333.3
CH_3	46.4	7.3	0.355	333.3
CHO	81.8	7.4	0.361	200.0
Cl	55.4	7.6	0.358	250.0
CN	69.7	7.5	0.361	166.7
$COOCH_3$	62.6	7.5	0.359	333.3
COOH	65.2	7.5	0.360	333.3
F	51.2	7.5	0.358	200.0
H	49.2	7.5	0.355	166.7
i-Pr	47.4	7.5	0.354	333.3
NH_2	37.6	7.9	0.355	250.0
NO_2	76.4	7.3	0.365	142.9
OCH_3	42.2	7.9	0.356	333.3
OH	43.1	8.6	0.357	250.0
t-Bu	47.7	7.5	0.354	500.0

[a] Values of the charge shifted in the electronic density reshuffling at constant chemical potential (ΔN_μ) (A and $\Delta S°$ values in kcal/mol and η_{O}^{+} values in eV). [b] Obtained through the equation $A = E(N) - E(N + 1)$. [c] $\Delta S°$ was obtained by means of a vibrational calculation using GAUSSIAN 98. [d] Calculated through the equations $q_H = \Delta N_\nu + \Delta N_\mu$ and $\Delta N_\nu = -(\mu_H - \mu_{XC_6H_4O})/2(\eta_{H}^{-} + \eta_{O}^{+})$. [e] Calculated through the equation $\eta_{O}^{+} = \eta_{XC_6H_4O}/f_{O}^{+}$.

values and the experimental values $I_H = 313.8$ kcal/mol and $\mu_H = -7.18$ eV can be used to evaluate the c_0, c_1, and $\mathbf{c}_2$ constants. Table 4 also shows the ΔN_μ values calculated from equation $q_H = \Delta N_\nu + \Delta N_\mu$. Table 5 shows the calculated values $\Delta G°_{calcd2}$ using eq 10 with λ=1. Good values of $\Delta G°_{calcd2}$ were obtained, the $\Delta G°_{calcd2}$ values underestimate the $\Delta G°_{exp}$ values by 5.50 to 30.96 kcal/mol. At this point, it would be interesting to obtain the λ values for which $\Delta G°_{calcd2} = \Delta G°_{exptl}$. Table 5 shows the calculated λ values obtained by substitution of the $\Delta G°_{exptl}$ into eq 10; they are >1. The λ value trends for the parasubstituted phenols in the gas phase are $\lambda_{electron-acceptor} > \lambda_H > \lambda_{electron-releasing}$:

$$\lambda_{CHO} > \lambda_{NO_2} > \lambda_{COOH} > \lambda_{CN} > \lambda_{CF_3} > \lambda_{COOCH_3} = \lambda_H > \lambda_{Cl} = \lambda_F > \lambda_{Me} = \lambda_{Et} = \lambda_{i-Pr} > \lambda_{OH} = \lambda_{t-Bu} > \lambda_{OCH_3} > \lambda_{NH_2}$$

To see if there is a relationship between the λ values and the substituent constant σ^- (the Hammet constant that takes into account the resonance interaction between the substituent and the substrate),[2] we made a linear correlation analysis. The result obtained suggests that there is no linear relationship between λ and σ^- ($R^2 = 0.64$). However, a simple regression analysis shows that there are linear relationships between σ^- and q_H; $\sigma^- = 98.125q_H - 34.393$ ($R^2 = 0.97$) and ΔN_μ and σ^-; $\sigma^- = 124.1\Delta N_\mu - 44.105$ ($R^2 = 0.93$). Haeberlein and Brinck have found a close linear relationship between σ^- and the electrostatic potential (V_{min}).[16] A multiple-regression analysis shows that there is a relationship between σ^-, q_H, and ΔN_μ: $\sigma^- = 18.292\Delta N_\mu + 84.419q_H - 36.093$ ($R^2 = 0.97$); when q_H and ΔN_μ increase, σ^- increases as well. Table 5 shows the experimental σ^- values obtained by Fujio, McIver, and Taft for a set of 10 parasubstituted phenols in the gas phase used by us in the linear regression analysis.[22]

To obtain an analytical relationship between σ^-, q_H, and ΔN_μ, we use eq 10 and the expression $\sigma^- = -(\log e/\rho RT)(\Delta G°_X - \Delta G°_H)$ obtained through the equations $\Delta G° = -RT \ln K_a$ and $\rho\sigma^- = \log(K_a{}^H/K_a{}^X)$. The substituent constant σ^- can be expressed in terms of ΔN_μ and q_H by the following equation:

$$\sigma^- \approx \frac{-\log e}{\rho RT}\{[c_0 + \Delta N_\mu(c_2\Delta N_\mu - c_1) + (c_1 - 2c_2\Delta N_\mu)q_H + c_2{q_H}^2]_X - [c_0 + \Delta N_\mu(c_2\Delta N_\mu - c_1) + (c_1 - 2c_2\Delta N_\mu)q_H + c_2{q_H}^2]_H\} \quad (11)$$

Table 5 shows the σ^- values calculated with eq 11, and the experimental values obtained by Fujio, McIver, and Taft for a set of 10 parasubstituted phenols in the gas phase.[22] The calculated σ^- values underestimate the experimental σ^- values by 0.02−0.22 except for the CHO substituent, which is overestimated by 0.4. The calculated σ^- value trends are $\sigma^-_{electron-acceptor} > \sigma^-_H > \sigma^-_{electron-releasing}$. If the calculated λ values are used in eq 11, $\sigma^-_{calcd} = \sigma^-_{exptl}$ (see Table 5).

Conclusions

The present analysis allows us to explain the dissociation reaction of the parasubstituted phenols XC_6H_4OH in the gas-phase $XC_6H_4OH_{(g)} \rightarrow XC_6H_4O^-_{(g)} + H^+_{(g)}$, in terms of DFT and the local HSAB principle. The simple linear regression analysis obtained between the phenol/phenolate Gibbs energy gap and the hydrogen atom charge q_H suggests that there is an important

TABLE 5: Parasubstituted Phenols Absolute Gas-Phase Acidity $\Delta G°$ and the Substituent Constants σ^- ($\Delta G°$ Values Are in Kilocalories per Mole; $T = 298.15$ K and $\rho = 14.66$)

X	$\Delta G°_{calcd2(\lambda=1)}$[a]	$\lvert\Delta G°_{calcd2(\lambda=1)} - \Delta G°_{exptl}\rvert$[b]	$\lambda_{(\Delta G°_{calc2} = \Delta G°_{exp})}$[c]	σ^-[d]	σ^-[e] (σ^-)[f]
CF_3	314.4	16.7	1.23	0.59	0.53 (0.59)
CH_2CH_3	331.9	11.7	1.16		−0.12 (−0.03)
CH_3	332.8	11.3	1.16	−0.06	−0.15 (−0.06)
CHO	296.2	31.0	1.43	0.79	1.19 (0.79)
Cl	323.1	14.0	1.19	0.30	0.21 (0.30)
CN	308.2	18.2	1.25	0.83	0.75 (0.83)
$COOCH_3$	316.6	14.7	1.20	0.59	0.44 (0.59)
COOH	313.7	19.5	1.27		0.55 (0.49)
F	326.9	13.8	1.19	0.12	0.07 (0.12)
H	328.8	14.2	1.20	0.00	0.00 (0.00)
i-Pr	331.8	11.3	1.16		−0.11 (−0.01)
NH_2	340.8	5.5	1.08	−0.17	−0.44 (−0.17)
NO_2	300.9	21.2	1.30	1.04	1.02 (1.04)
OCH_3	336.3	7.9	1.11	−0.06	−0.28 (−0.06)
OH	334.3	9.9	1.14		−0.20 (−0.06)
t-Bu	331.9	10.5	1.14		−0.11 (0.03)

[a] Calculated through eq 10 with $\lambda = 1$. [b] Experimental values obtained through ref 22. [c] Calculated λ values. [d] Values obtained by Fujio, McIver, and Taft.[22] [e] Values obtained through eq 11 with $\lambda = 1$. [f] Values obtained through eq 11 with calculated λ values.

extra-thermodynamic relationship between $\Delta G°$ and q_H. The equation obtained from DFT and the local HSAB principle $\Delta G° \approx [c_0 + \Delta N_\mu(c_2\Delta N_\mu - c_1)] + (c_1 - 2c_2\Delta N_\mu)q_H + c_2q_H^2$ was developed in terms of the $XC_6H_4O^{\delta-}{-}H^{\delta+}$ bond polarization, the $XC_6H_4O{-}H$ bond energy, and the $XC_6H_4O^-$ anion stabilization. The results obtained suggest that the hydrogen atom charge q_H is representative of the parasubstituted phenols' acidity. The calculated λ values were obtained for the parasubstituted phenols using the $\Delta G°_{exptl}$ values, they are higher than one, and the trends are $\lambda_{electron-acceptor} > \lambda_H > \lambda_{electron-releasing}$. A multiple-regression analysis shows that there is a relationship between σ^-, q_H, and ΔN_μ. The equation obtained from DFT and the local HSAB principle shows that the calculated σ^- value trends are $\sigma^-_{electron-acceptor} > \sigma^-_H > \sigma^-_{electron-releasing}$. In general, the analysis suggests that there is no direct interaction between the substituent and the hydrogen atom; the effect is primarily due to the interaction of the substituent with the C_6H_4O group. The substituent transmits its effect through the π system of the benzene ring, and q_H shows the effect of the electronegativity of the fragment $X{-}C_6H_4O$ on the hydrogen atom. The analytical equations obtained from DFT and the local HSAB principle provide guidelines to obtain a quantitative description of the fit parameters in the linear correlation equations.

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