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Resonance and field/inductive substituent effects on the gas-phase acidities of *para*-substituted phenols: a direct approach employing density functional theory

Josiah B. Barbour and Joel M. Karty*

Department of Chemistry, Elon University, 2625 Campus Box, Elon, North Carolina 27244, USA

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ABSTRACT: Relative gas-phase acidities of *para*-substituted phenols (**1**, Sub—C_6H_4—OH) and their ω-substituted *para*-alkylphenol analogs [**2**, Sub—$(CH_2)_n$—C_6H_4—OH] were calculated at the B3LYP/6–31+G* and AM1 levels of theory. The acidity of a substituted molecule of **2** is compared with that of the unsubstituted molecule of **2** to determine the field/inductive effect of the substituent on the acidity of **2**. This field/inductive effect was extrapolated to $n = 0$, yielding the field/inductive effect of the substituent on the acidity of **1**. The derived field/inductive effect in **1** was subtracted from the difference in acidity between **1** and phenol in order to determine the resonance effect of the substituent on the acidity of **1**. Our results are compared with the field/inductive and resonance substituent parameters empirically derived from previous experimental solution studies. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: *para*-substituted phenols; gas-phase acidity; field/inductive effect; resonance effect; density functional theory

INTRODUCTION

Resonance and field/inductive substituent effects on the thermodynamics and kinetics of chemical reactions have long been of interest to chemists.[1] These substituent effects continue to be a topic of lively discussion, largely because it is non-trivial to separate resonance effects from field/inductive effects.[2] Recent studies have therefore turned to quantum theoretical calculations, examining those effects by taking into account quantities that are parametric with each effect. Those parametric quantities have included the Mulliken population at the reaction center, in which the reaction center is adjacent to a *para*-substituted phenyl ring (both delocalized and localized rings),[3] charge density redistribution in model systems[2,4,5] and charge flux in substituted benzene.[6] However, each of those parametric quantities is an indirect measure of the resonance and field/inductive effects on the thermodynamics of chemical reactions. Furthermore, there is no guarantee that effects on charge density can be directly correlated with effects on thermochemistry. To our knowledge, there has been no systematic computational study in which resonance and field/inductive effects on thermochemistry have been obtained in a direct fashion. In this paper, we present a methodology to do so.

Traditionally, resonance and field/inductive parameters are obtained by employing what are effectively extensions of the Hammett equation,[7] illustrated in the equation

$$\log(k/k_0) = \rho\sigma \tag{1}$$

where k is either a rate or equilibrium constant involving a substituted reactant, k_0 is for the unsubstituted reactant, σ is an intrinsic substituent parameter describing the ability of that substituent to effect a change in k and ρ is a reaction's sensitivity to that substituent effect.

In one extension of the Hammett equation, Taft and co-workers proposed[8,9] the relationship

$$\log(k/k_0) = \rho_I\sigma_I + \rho_R\sigma_R \tag{2}$$

where the first term on the right-hand side describes the field/inductive effect and the second term describes the resonance effect. They proposed that one of four types of σ_R parameters is necessary [σ_R^-, σ_R^+, σ_R^0 or σ_R(BA)], depending on the demand for electrons within the particular reaction.

Swain and Lupton,[10] however, suggested that the different resonance parameters were unnecessary, and that σ itself could be taken as a sum of the field/inductive and resonance effects, according to the equations

$$\sigma = fF + rR \tag{3a}$$

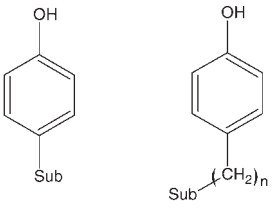
**Correspondence to:* J. M. Karty, Department of Chemistry, Elon University, 2625 Campus Box, Elon, North Carolina 27244, USA.
E-mail: jkarty@elon.edu
Contact/grant sponsor: Research Corporation; *Contact/grant number:* CC5978.
Contact/grant sponsor: Elon University.

$$\log(k/k_0) = \rho(fF + rR) \quad (3b)$$

where F and R are constants for a given substituent, regardless of the reaction in which they are involved or of the reaction conditions. The weighting factors, f and r, are constant with regard to a specific reaction and reaction conditions, and are independent of the substituent involved.

Over the years, such extensions of the Hammett equation have been met with substantial scrutiny. One of the main reasons is that, as with the Hammett equation itself, these models are purely empirical, having no theoretical basis.[1,5,6] Instead, the field/inductive and resonance parameters have been derived by fitting experimental thermodynamic and kinetic values (and later, other experimental values, such as NMR chemical shifts[11] and IR band intensities[12]) to their respective equations [e.g. Eqns (2) and (3)]. Furthermore, there has been disagreement as to the appropriate model. The Swain–Lupton model, specifically, was heavily criticized by a number of workers,[13–15] who cast doubt on critical assumptions and also the statistical methods that were used. Swain wrote a paper in rebuttal.[16]

In this work, we studied resonance and field/inductive effects on the gas-phase acidities of *para*-substituted phenols (**1**) [note: σ_R^- is therefore the resonance parameter used in Eqn (2)]. This was accomplished by calculating gas-phase acidities of ω-substituted *para*-alkyl phenols (**2**), which enabled us to obtain each effect in a direct fashion (i.e. in units of energy), without the need for an intermediate parameter, as described below. We compared our calculated field/inductive effects with both F and σ_I, and compared our calculated resonance effects wtih both R and σ_R^-.



1 **2**

METHODOLOGY

Relative gas-phase acidities are calculated for **1**, as well as their counterparts **2**, up to $n = 6$. Any acidity difference between **1** and phenol (Sub = H) is expected to be a result of both field/inductive and resonance effects of the substituent. Any acidity difference between **2** and the corresponding (same n) unsubstituted (Sub = H) *para*-alkylphenol, however, is expected to be a result of only the field/inductive effect of the substituent. This is because the sp^3 hybridization of the center(s) separating the substituent from the phenyl ring largely destroys the substituent's resonance effects on the acidity of the phenolic proton.[1] Therefore, extrapolation of the field/inductive effects to $n = 0$ should provide the field/inductive effects on the acidity difference between **1** and phenol. Resonance effects should account for the remainder of the acidity difference.[17,18]

This methodology is similar to that employed by Siggel *et al.*[18] to obtain a measure of the resonance and inductive effects on the acidity enhancement of carboxylic acids over alcohols. Their study took advantage of the fact that for alcohols of the form YOH, where Y is a substituent only capable of field/inductive effects, the insertion of a CH_2 group attenuates the field/inductive effects by a factor of about 2.6.[19] Therefore, Siggel *et al.* multiplied the field/inductive contribution of the $CH_3C{=}O$ group in hydroxyacetone [$CH_3C(=O)CH_2OH$] by 2.6 to determine the field/inductive contribution by the $CH_3C{=}O$ group in acetic acid.

Our methodology presented here is also related to that employed previously by our group to determine the contribution by resonance and field/inductive effects toward the acidity enhancement of formic acid over methanol,[17] and toward the enhanced acidity and hydride abstraction enthalpy of propene over propane.[20] In those studies, we calculated the appropriate thermochemical values of hypothetical vinylogs[21] (where 1–3 vinyl units were inserted between the substituent and the reaction center) of the respective parent molecules—that is, of formic acid and methanol in the first study and of propene and propane in the second (we define the nth vinylog as the species in which n vinyl groups have been inserted between the reaction center and the substituent, with the *E*-configuration at all double bonds). We also calculated the appropriate thermochemical values of vinylogs of formic acid and propene under conformational constraints that essentially remove contribution by resonance effects. Comparisons among the calculated thermochemistries of those vinylogs allowed us, directly and independently, to arrive at the contributions by resonance and field/inductive effects in the vinylogs of formic acid and propene. Both effects were extrapolated to zero inserted vinyl units to obtain the resonance and field/inductive effects in formic acid and propene. The independent extrapolations were consistent with one another, which helped to substantiate our methodology. Furthermore, the results from that study were in excellent quantitative agreement with those of a number of other workers.[18,21,22]

EXPERIMENTAL

AM1 calculations were performed using PC Spartan Pro (Wavefunction), and density functional theory (DFT) calculations were performed at the B3LYP/6–31+G* level, using Gaussian 98W.[23] The AM1 acidity of each molecule of **1** and **2** was computed by subtracting the

calculated heat of formation of the optimized neutral acid from the sum of the calculated heats of formation of the proton and the optimized anion:

$$HA \rightarrow H^+ + A^- \quad (4)$$

DFT acidities for the parent acids **1** were computed by subtracting the enthalpy of the optimized acid from the sum of the enthalpies of the proton and optimized anion. The DFT acidity of each molecule of **2** was computed by subtracting the uncorrected energy of the acid from that of the anion; all thermal corrections should effectively cancel out in our extrapolations (see Discussion).

In order to avoid complications with steric effects, the alkyl groups in **2**, connecting the substituent to the benzene ring, were each in the all-*trans* conformation. Furthermore, the orientation of each substituent in the acid of **2** was the same as in the anion. Therefore, in computing acidity, any steric effects that might be introduced in the acid should cancel with the steric effects in the anion.

With increased n in **2**, convergence of our DFT calculations became increasingly difficult owing to the additional heavy atoms, and also the additional flexibility of the species. For this reason, we limited our studies to substituents that had few, if any, internal rotational degrees of freedom. Also, we made a simplifying assumption for Sub = CO_2CH_3 that the resonance and field/inductive effects are the same as Sub = CO_2H. Furthermore, on a number of species in which difficulty in convergence persisted, we employed the quadratically convergent SCF method within Gaussian.

RESULTS

Table 1 contains calculated and available experimental[24] gas-phase acidities of substituted phenols. Table 1 also contains the calculated field/inductive and resonance effects of the corresponding substituents, along with their Swain and Taft substituent parameters. Table 2 contains the DFT calculated energies and acidities of **2**. Figure 1 is a plot of the AM1-calculated relative acidities against the experimental relative acidities. Figure 2 is a plot of the calculated relative DFT acidities against the experimental relative acidities. The DFT-calculated field/inductive effect is plotted against the Swain F parameter and the Taft σ_I parameter in Figs 3 and 4, respectively. The DFT-calculated resonance effect is plotted against the Swain R parameter and the Taft σ_R^- parameter in Figs 5 and 6, respectively.

DISCUSSION

The field/inductive effect of each substituent in **2**, for a given value of n, was computed as the difference in

Table 1. Field/inductive and resonance effects on acidities and the Swain and Taft parameters

Sub	$\Delta H°_{acid}$(kcal mol^{-1})						Field/inductive effect[b] (kcal mol^{-1})		Swain F parameter[c]	Taft σ_I parameter[d]	Resonance effect[b] (kcal mol^{-1})		Swain R parameter[c]	Taft σ_R^- parameter[e]
	Absolute			Relative										
	Expt[a]	AM1	DFT	Expt	AM1	DFT	AM1	DFT			AM1	DFT		
NH_2	354.5	296.5	354.7	4.2	0.3	3.8	3.6	2.9	0.38	0.14	−3.9	−6.6	−2.52	−0.28
OH	350.4	294.0	352.9	0.1	−2.2	1.9	5.7	5.8	0.46	0.26	−3.5	−7.6	−1.89	−0.28
H	350.3	296.2	351.0	0	0	0	0	0	0	0	0	0	0	0
CH_3	350.3	295.5	352.2	0	−0.7	1.2	1.3	0.1	−0.01	−0.02	−0.6	−1.3	−0.41	0.03
F	346.8	290.3	347.5	−3.5	−5.9	−3.4	7.9	8.9	0.74	0.50	−2.0	−5.4	−0.60	−0.25
Cl	343.7	288.9	344.0	−6.6	−7.3	−7.0	9.6	13.4	0.72	0.46	−2.3	−6.4	−0.24	−0.12
CF_3	337.0	280.0	336.9	−13.3	−16.2	−14.1	12.6	9.8	0.64	0.45	3.7	4.2	0.76	0.07
CO_2H	337.2	280.5	335.3	−13.1	−15.7	−15.7	9.3	6.7	0.47[f]	0.30[f]	6.4	9.0	0.67[f]	0.16[f]
$COCH_3$	335.5	282.0	335.4	−14.8	−14.2	−15.6	8.0	7.5	0.50	0.28	6.2	8.1	0.9	0.17
CN	332.2	280.4	332.0	−18.1	−15.8	−19.0	11.4	15.3	0.90	0.58	4.4	3.7	0.71	0.10
NO_2	327.8	269.5	325.3	−22.5	−26.7	−25.7	20.8	17.1	1	0.65	5.9	8.5	1	0.18

[a] Obtained from Ref. 25.
[b] Calculated using the methodology outlined in the text.
[c] Obtained from Ref. 27.
[d] Average of values listed in Ref. 30.
[e] Obtained from Ref. 30.
[f] Parameters for CO_2H were taken to be the same as for CO_2CH_3.

Table 2. DFT-calculated energies and acidities (B3LYP/6–31+G*) of **2**

	$n=2$			$n=4$			$n=6$		
Sub	Acid (a.u.)	Anion (a.u.)	Acidity (kcal mol^{-1})	Acid (a.u.)	Anion (a.u.)	Acidity (kcal mol^{-1})	Acid (a.u.)	Anion (a.u.)	Acidity (kcal mol^{-1})
NH_2	−441.458 775	−440.901 625	349.6	−520.087 783	−519.529 849	350.1	−598.717 240	−598.158 784	350.4
OH	−461.324 735	−460.769 894	348.2	−539.953 845	−539.397 143	349.3	−618.583 309	−618.025 435	350.1
H	−386.112 463	−385.552 470	351.4	−464.742 238	−464.182 440	351.3	−543.371 612	−542.812 051	351.1
CH_3	−425.427 535	−424.867 703	351.3	−504.056 982	−503.497 361	351.2	−582.686 413	−582.126 861	351.1
F	−485.352 289	−484.800 527	346.2	−563.981 422	−563.426 317	348.3	−642.610 965	−642.054 152	349.4
Cl	−845.709 810	−845.161 027	344.4	−924.338 949	−923.784 776	347.7	−1002.968 524	−1002.411 988	349.2
CF_3	−723.176 602	−722.626 353	345.3	−801.806 585	−801.252 418	347.7	−880.435 799	−879.879 874	348.8
CO_2H	−574.689 928	−574.135 491	347.9	−653.319 699	−652.762 708	349.5	−731.949 141	−731.391 068	350.2
$COCH_3$	−538.760 089	−538.206 085	347.6	−617.389 506	−616.832 704	349.4	−696.017 762	−695.460 069	349.5
CN	−478.3554 887	−477.809 203	342.8	−556.985 209	−556.433 114	346.4	−635.614 862	−635.059 626	348.4
NO_2	−590.622 474	−590.080 418	340.1	−669.251 529	−668.702 362	344.6	−747.881 300	−747.329 091	346.5

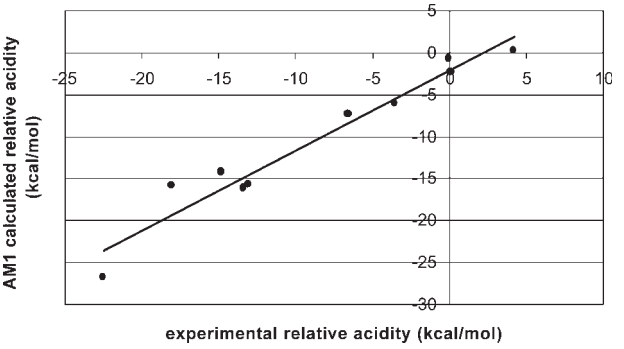


Figure 1. Plot of calculated relative acidities at the AM1 level against experimental relative acidities. Linear regression yields a slope of 0.9517 ± 0.0796, a *y*-intercept of -2.103 ± 0.966 and $R^2 = 0.9471$

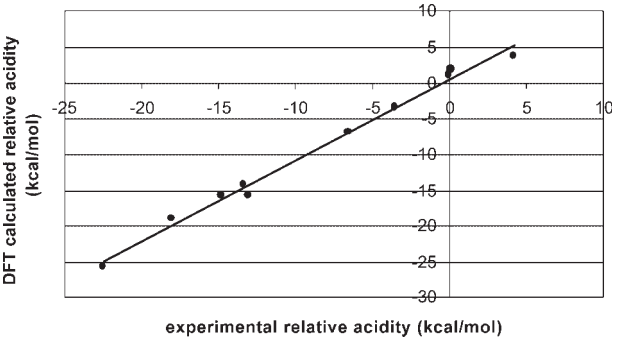


Figure 2. Plot of calculated relative acidities at the B3LYP/6–31+G* level of theory against experimental relative acidities. Linear regression yields a slope of 1.1315 ± 0.0382, a *y*-intercept of 0.552 ± 0.464 and $R^2 = 0.991$

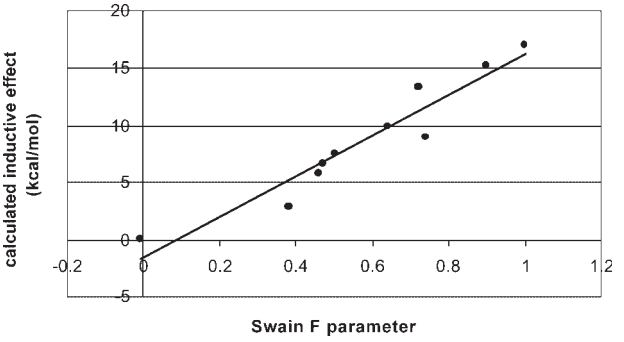


Figure 3. Plot of DFT-calculated inductive effects on *para*-substituted phenols versus the Swain *F* parameter. Linear regression yields a slope of 17.8 ± 2.0, a *y*-intercept of -1.5 ± 1.3, and $R^2 = 0.9121$

acidity between a substituted (Sub ≠ H) molecule of **2** and the corresponding (same *n*) unsubstituted (Sub = H) molecule of **2**. This field/inductive effect was then extrapolated to $n = 0$ to determine the field/inductive effect in the parent molecule, **1**. In our extrapolations, data were fit to a decaying exponential function, following observations made by Bianchi *et al.*[25]

For each extrapolation, the inclusion of all data points (all values of $n > 0$) yielded correlation coefficients that

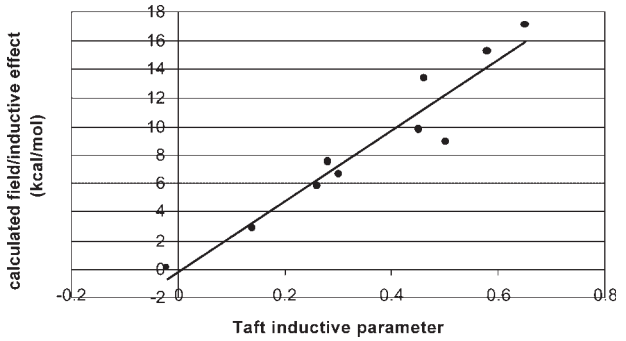


Figure 4. Plot of DFT-calculated field/inductive effects on the acidity of *para*-substituted phenols against the Taft σ_I parameter. Linear regression yields a slope of 24.9 ± 2.7, a *y*-intercept of -0.2 ± 1.1 and $R^2 = 0.9169$

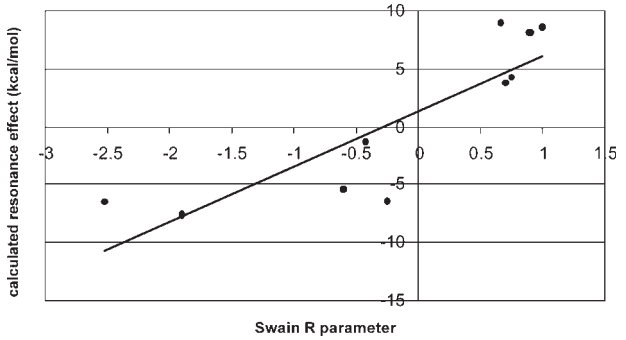


Figure 5. Plot of DFT-calculated resonance effects on the acidity of *para*-substituted phenols against the Swain *R* parameter. Linear regression yields a slope of 4.8 ± 1.0, a *y*-intercept of 1.4 ± 1.2 and $R^2 = 0.7393$

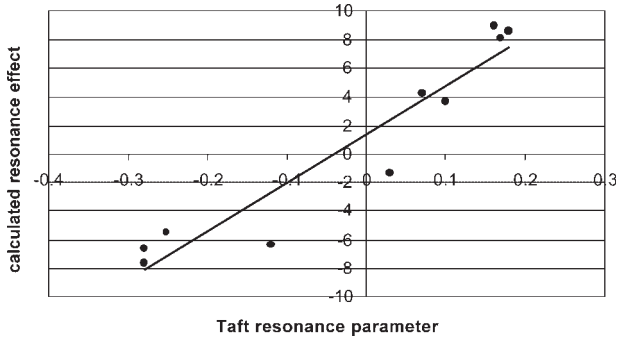


Figure 6. Plot of DFT-calculated resonance effects on the acidity of *para*-substituted phenols against the Taft σ_R^- parameter. Linear regression yields a slope of 33.8 ± 4.0, a *y*-intercept of 1.4 ± 0.7 and $R^2 = 0.911$

were not acceptable. This is because for odd values of *n*, the C—Sub single bond is at a significant angle relative to the plane of the benzene ring (Fig. 7), whereas in **1**, the C—Sub bond is parallel to the plane of the ring. Therefore, in our extrapolations, the field/inductive effects in **2**, where $n =$ odd, are not expected to map smoothly into those in **1**. On the other hand, for even values of *n*, the C—Sub bond is parallel with the plane of the benzene ring. As a consequence, there is expected to be a smooth

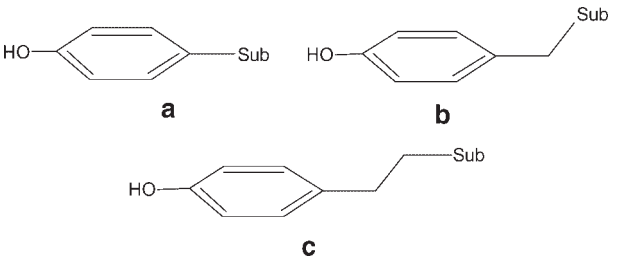


Figure 7. (a) Molecule of **1**, explicitly showing the C—Sub bond in the plane of the benzene ring. (b) A representative molecule of **2** with $n =$ odd (in this case, $n = 1$). The C—Sub bond is at a significant angle with respect to the plane of the benzene ring. (c) A representative molecule of **2** with $n =$ even (in this case, $n = 2$). The C—Sub bond is parallel to the plane of the benzene ring

transition from the field/inductive effects in **2** to those in **1**. In support of this, for all extrapolations using only even values of *n*, it is noted that the smallest correlation coefficient is 0.996, at both the DFT and the AM1 levels of theory. Therefore, each of our extrapolated field/inductive effects to $n = 0$ (Table 1) are those obtained using only even values of *n*.

The resonance effects in **1** were computed once the extrapolated field/inductive effects were obtained. The difference in acidity between a substituted molecule of **1** and the unsubstituted molecule of **1** is taken to be the sum of the field/inductive and resonance effects in **1** [Eqns (2) and (3)]. Polarizability effects were assumed to be negligible, given the large distance between the substituent and the reaction center and given the significant polarizability already present in the unsubstituted ring.[4,26] Therefore, the field/inductive effect was subtracted from the acidity difference to yield the resonance effect on the acidity.

Although there are very few experimental gas-phase acidities with which to compare our calculated acidities of **2**, we believe that our DFT results are reliable, for a number of reasons. First, there is excellent agreement between the DFT-calculated and experimental gas-phase absolute acidities of the parent acids (Table 1, Fig. 2). This suggests that our DFT calculations are sufficiently sensitive to both resonance and field/inductive effects.

Second, it appears that any errors introduced in the calculated acidities of **2** are largely canceled out in our extrapolation methods. The reason for this is that we extrapolate *differences* in acidity, rather than absolute acidity, and the reference acid, unsubstituted phenol, is structurally very similar to the substituted acids. The significant cancellation of errors is evidenced by the very good agreement between our DFT results and our AM1 results (Table 1). The AM1-calculated absolute acidities are in significant disagreement with experiment, but the extrapolations using the AM1 calculated acidities of **2** yield similar resonance and inductive effects to our extrapolations using the DFT calculated acidities.

A third reason why we believe our DFT results are reliable is that in our previous study on formic acid,[17] we showed that our DFT calculations were in excellent agreement with those from the G2 level of theory.

Finally, our results are in general in qualitative agreement with resonance and inductive parameters from solution, and are consistent with intuition. For example, our results indicate that field/inductive effects increase in the order $CH_3 < NH_2 < OH < F$, which is the same as the order of electronegativity of the atom directly bonded to the phenyl ring (i.e. C, N, O and F). Furthermore, the NO_2 group has the greatest contribution from both field/inductive and resonance effects. In addition, the F, OH, NH_2 and Cl substituents appear to decrease the acidity via resonance, consistent with resonance structures that can be drawn involving the lone pairs of electrons on the heteroatoms. Notably, our methodology suggests that the CF_3 group enhances the acidity of phenol via resonance by 4.2 kcal mol^{-1} (1 kcal = 4.184 kJ), in qualitative agreement with calculations by Janesko *et al.*[3] Swain *et al.* argue that this is a reflection of fluoride hyperconjugation.[27]

There are, however, some discrepancies between our results and the parameters derived from solution. Our results suggest that the field/inductive effect of Cl is greater than that of F (13.4 and 8.9 kcal mol^{-1}, respectively), whereas both the Taft and the Swain–Lupton parameters suggest the reverse order (Table 1). Furthermore, one would expect F to have a greater field/inductive effect than Cl, given the greater electronegativity of F than of Cl. Although we do not fully understand the nature of this disagreement, we believe that it may be due, in part, to the fact that our numbers are derived from gas phase acidities, whereas both the Taft and the Swain parameters were obtained from solution values. Support for this assertion comes from Janesko *et al.*,[3] who argue that in solution, the field/inductive effect is strongly attenuated by the solvent. They suggest that this is the reason for the anomalously large field/inductive effects in the gas phase for fully charged substituents such as NH_3^+. Furthermore, such a reversal on going from gas phase to solution phase is not surprising. Early work by Brauman and Blair[28] showed that the order of gas-phase acidities of small aliphatic alcohols is reversed from that in solution.

We attempted to test this hypothesis by carrying out the same calculations on **2**, with F and Cl as substituents, using a polarized continuum model within the Gaussian software package to account for solvent effects from water. However, the difference between the experimental aqueous acidity of *p*-fluorophenol and *p*-chlorophenol is only 0.57 p*K* units,[29] or about 0.8 kcal mol^{-1}. As argued in our previous paper on the acidity of formic acid, our methodology is reliable to within about 1–2 kcal mol^{-1}. Therefore, our methodology is not sufficiently precise for solution studies.

Another discrepancy between our results and those from solution is the prediction that the resonance effect by the NH_2 substituent is less than that by the OH substituent (6.6 and 7.6 kcal mol^{-1}, respectively). Both of the solution resonance parameters, on the other hand, suggest that the NH_2 substituent should have a greater effect via resonance. This is in agreement with intuition, since the less electronegative nitrogen atom is expected to be a better electron donor via resonance.

This apparent anomaly can be explained, at least in part, by examining the geometries of both the NH_2 and OH substituents in the phenoxide anions. In the optimized geometry of the anion of *p*-aminophenol, the conformation of the NH_2 group is such that the H—N—H angle is bisected by the plane of the ring. Therefore, the lone pair of electrons on the nitrogen atom is confined to the plane of the ring, which should preclude its involvement in resonance with the extended π-system. On the other hand, the energy-minimized structure of the *p*-hydroxyphenol anion is entirely planar. As a result, the two lone pairs of electrons should retain the appropriate symmetry that allows it to interact with the π-system of the ring.

In order to compare our results quantitatively with the empirical results from solution, we plotted our DFT-calculated resonance and field/inductive effects against the resonance and field/inductive parameters from both Swain and Taft (Figs 3–6). Our calculated field/inductive effects scaled fairly linearly (Figs 3 and 4) with both the Swain and the Taft field/inductive parameters: $R^2 = 0.912$ and 0.917, respectively. Our calculated resonance effects also appear to scale linearly (Fig. 6) with the Taft resonance parameters, as the value for R^2 is 0.911. However, there is substantial scatter in the plot of our calculated resonance effects against the Swain resonance parameters (Fig. 5); the value of R^2 is 0.739.

In order to evaluate the slopes in Figs 3–6, linear least-squares fits of the experimental gas-phase acidities (this is similar to the linear regression performed by Taft *et al.*[26]) were performed using the Swain–Lupton substituent parameters and also the Taft parameters [Eqns (2) and (3)]. The slope in Fig. 3 is $\rho f_{calc} = 17.8 \pm 2.0$, and a linear least-squares fit of the experimental acidities to Eqn (3) yields $\rho f_{expt} = 12.3 \pm 2.5$. The slope in Fig. 4 is $\rho_{I,calc} = 24.9 \pm 2.7$, and a linear least-squares fit of experimental acidities to Eqn (2) yields $\rho_{I,expt} = 22.4 \pm 1.8$. The slope in Fig. 5 is $\rho r_{calc} = 4.8 \pm 1.0$, and the linear least-squares fit of experimental acidities to Eqn (3) yields $\rho r_{expt} = 4.4 \pm 0.6$. Finally, the slope in Fig. 6 is $\rho_{R,calc} = 33.8 \pm 4.0$, and the linear least-squares fit of experimental acidities to Eqn (2) yields $\rho_{R,expt} = 31.7 \pm 2.2$.

The linear least-squares fit of experimental acidities is in agreement with the slopes in Figs 4–6. However, it is in significant disagreement with Fig. 3. This, in combination with the substantially smaller R^2 value in Fig. 5 than in Fig. 6, may suggest that the Taft parameters are more appropriate than the Swain parameters. However, it is difficult to use our gas-phase results to comment, with

certainty, on the appropriateness of each set of solution parameters. This is especially true given the apparent reversal of trends between solution and the gas phase, as seen with the field/inductive effects of F versus Cl and the resonance effects of NH_2 versus OH.

As a final note, it is worth discussing our AM1 results. As mentioned earlier, they are in very good agreement with our results from DFT calculations. The average difference between field/inductive effects derived from the two different levels of theory is 2.0 kcal mol^{-1}, the largest difference being 3.8 kcal mol^{-1}. The respective values for resonance effects are 2.3 and 4.1 kcal mol^{-1}. This is particularly noteworthy, given the computational time required for some of the larger molecules of **2**, using moderately high-level DFT calculations. Whereas, for example, calculating the substituent effects of NO_2 consumed about 2 weeks of CPU time with our DFT calculations, the same calculations at the AM1 level of theory required only minutes. Therefore, employing the AM1 level of theory may be attractive towards obtaining reasonably accurate field/inductive and resonance effects of additional substituents on the acidity of phenol, and also on other reactions.

CONCLUSIONS

Resonance and field/inductive effects on the acidity of *para*-substituted phenols were determined for a variety of substituents. These effects were obtained for each substituent by extrapolating the field/inductive effect on the acidity of ω-substituted *p*-alkylphenols to $n = 0$, and assuming that the total substituent effect is the sum of the field/inductive and resonance effects. Our calculated field/inductive effects agree somewhat better with the Taft σ_I and σ_R^- parameters than with the Swain *F* and *R* parameters.

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