Substituent Effects on the Electronic Structure and pKₐ of Benzoic Acid

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ABSTRACT: The effects of substituents on the pKₐs of a set of 16 substituted benzoic acids have been examined using density functional theory [B3LYP/6-311G(d,p)] calculations. A variety of quantum chemical parameters were examined as indicators for the variations observed in the experimental pKₐs, including the Löwdin, Mulliken, AIM, and natural population analysis charges (Qₐ, Qₘₐ, Qₐ, and Qₐₙ) on atoms of the dissociating carboxylic acid group, the energy difference (ΔHₚₐₙₐₜ) between the carboxylic acid and its conjugate base, and the Wiberg bond index. Several of these calculated quantities yielded excellent correlations with the experimental pKₐ: ΔHₚₐₙₐₜ, r² = 0.958; Qₐ(H), r² = 0.963; Qₐ(CO₂H), r² = 0.969; Qₐ(CO₂), r² = 0.970; and Qₐ(CO₂H), r² = 0.978. The best correlation observed with the pKₐ, as expected, was from the empirical Hammett constants designed for this purpose (r² = 0.999). © 2002 Wiley Periodicals, Inc.

Key words: substituent effects; benzoic acids; acid dissociation constants (pKₐ); Hammett constants

Introduction

S ubstituent effects play a fundamental role in a variety of observed physical and chemical phenomena. For example, substituent effects influence the rates of nucleophilic substitutions and elimination reactions [1] and contribute to differences in thermal properties [2], nuclear magnetic resonance chemical shifts [3], positions of UV absorption bands [4], and the conformations of molecules. The nature and location of substituents also affect values of the acid-dissociation constants (pKₐ) [1]. Because the impact of substituents has implications in many areas of chemistry, it has long been a goal of chemists to understand how these substituents act at a molecular electronic level.

Since they were introduced in the 1930s, Hammett constants (σ) [5] have been the primary means for quantifying substituent effects. These empirical constants, which were derived from linear free-energy relationships, have been remarkably successful in their applications to a number of physi-
cochemical phenomena. Although $\sigma$ constants provide a valuable practical and heuristic tool, they cannot be expected to work in every case and sometimes yield little mechanistic insight. Recent efforts involving anilines [6–8] and phenols [8, 9] indicate that certain quantum chemical parameters might also serve as useful descriptors for understanding the physical and chemical effects of substituents.

Benzoic acid and its derivatives are chemically and biologically important molecules. Further, the $\sigma$ constants were originally formulated from ratios of the acid-dissociation constants of substituted benzoic acids relative to the acid-dissociation constant of benzoic acid itself [5]. The present work examines the applicability of quantum chemical parameters as descriptors for substituent effects on the $pK_a$s of substituted benzoic acids.

**Methods**

To determine the lowest-energy conformations for each molecule, geometry optimizations were performed at the AM1 level for several starting geometries in which one or more torsional angles were systematically varied. When multiple low-energy geometries were found for a compound, HF/6-31G(d) single-point energy calculations were performed to determine the most stable conformer. The final geometry optimization for each of the compounds was conducted at the B3LYP/6-311G(d, p) level. Vibrational frequency analyses were performed at the B3LYP/6-311G(d, p) level to ensure that minimum energy geometries had been found. The wave functions for these equilibrium geometries were used to determine Mulliken, natural, AIM, and Löwdin charges, the Wiberg bond index, and $\Delta E_{\text{prot}}$, the energy difference between the acid and its conjugate base relative to the energy difference between benzoate and benzoic acid.

The initial conformational analyses were performed with Spartan (v. 5.01) [10] software. Gaussian98 [11] was employed for the determination of the final equilibrium geometries and the calculation of nearly all of the quantum chemical descriptors. The AIMALL [12] suite of programs was used to calculate AIM charges from wave functions produced by Gaussian98. Löwdin charges were calculated with GAMESS-US [13]. It was necessary to exclude brominated compounds from the Löwdin study because the GAMESS-US 6-311G(d, p) basis set does not include bromine.

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$\sigma$</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H (benzoic acid)</td>
<td>0</td>
<td>4.19</td>
</tr>
<tr>
<td>m-bromo</td>
<td>0.39</td>
<td>3.81</td>
</tr>
<tr>
<td>m-chloro</td>
<td>0.37</td>
<td>3.83</td>
</tr>
<tr>
<td>m-cyano</td>
<td>0.56</td>
<td>3.60</td>
</tr>
<tr>
<td>m-fluoro</td>
<td>0.34</td>
<td>3.87</td>
</tr>
<tr>
<td>m-hydroxy</td>
<td>0.12</td>
<td>4.08</td>
</tr>
<tr>
<td>m-methoxy</td>
<td>0.12</td>
<td>4.09</td>
</tr>
<tr>
<td>m-methyl</td>
<td>−0.07</td>
<td>4.27</td>
</tr>
<tr>
<td>m-nitro</td>
<td>0.71</td>
<td>3.49</td>
</tr>
<tr>
<td>p-bromo</td>
<td>0.23</td>
<td>3.97</td>
</tr>
<tr>
<td>p-chloro</td>
<td>0.23</td>
<td>3.98</td>
</tr>
<tr>
<td>p-cyano</td>
<td>0.66</td>
<td>3.55</td>
</tr>
<tr>
<td>p-fluoro</td>
<td>0.06</td>
<td>4.14</td>
</tr>
<tr>
<td>p-hydroxy</td>
<td>−0.37</td>
<td>3.57</td>
</tr>
<tr>
<td>p-methoxy</td>
<td>−0.27</td>
<td>3.47</td>
</tr>
<tr>
<td>p-methyl</td>
<td>−0.17</td>
<td>4.37</td>
</tr>
<tr>
<td>p-nitro</td>
<td>0.78</td>
<td>3.43</td>
</tr>
</tbody>
</table>

Hammett constants were taken from the compilation by Hansch et al. [14]. The values for experimental $pK_a$s were taken from Albert and Serjeant [15]. This compilation did not include $pK_a$ values for $m$-amino and $p$-amino benzoic acids, although experimental values for these compounds are reported elsewhere [16]. Because the latter $pK_a$ values were from a separate source, the amino-substituted compounds were not included in the regression analyses. Instead, the regression equations have been used to predict the $pK_a$s for these amino compounds.

**Results**

**HAMMETT CONSTANTS**

The values for the $\sigma$ constants employed here, as well as the experimental $pK_a$s, are given in Table I. The empirical Hammett $\sigma$ constants, as expected, exhibited a strong correlation with the experimental $pK_a$ values of this series of benzoic acids:

$$pK_a = -1.005(\pm 0.011)\sigma + 4.200(\pm 0.004)$$

$$n = 17, r^2 = 0.9985, s = 0.0126, F = 8788,$$

where $n$ is the number of compounds, $r$ is the correlation coefficient, $s$ is the standard deviation, and $F$ is the Fisher ratio. The regression is illus-
trated in Figure 1. There were no outliers in this set. The \( r^2 = 0.9998 \) showed a correlation that was only slightly better than the \textit{meta} compounds \( (r^2 = 0.9971) \).

\section*{ATOMIC CHARGES}

Although the atomic charge on an atom in a molecule is not a proper quantum chemical observable, the atomic charge concept has proven to be a valuable tool for the explanation of a variety of chemical phenomena. Several methods have been developed, both empirical and quantum mechanical, for the determination of atomic charge. The usefulness of the values obtained for these charges depends upon both the particular scheme employed for their calculation and the application under consideration [8].

Four separate types of charges have been included in the present study: Mulliken charges \( (Q_M) \) [17–20], Löwdin charges \( (Q_L) \) [21], natural population analysis charges \( (Q_N) \) [22], and AIM charges \( (Q_A) \) [23]. These charges were calculated for the acidic hydrogen (H) and the entire carboxylic acid group (COOH) for each of the neutral benzoic acid species. Charges on the oxygen \( (O^-) \) from which the proton was abstracted and the charge on the whole carboxylate group \( (COO^-) \) were determined for the corresponding conjugate bases. The results of these charge calculations are summarized in Tables II–V.

\section*{Mulliken Charges}

The Mulliken charges performed well for this series of compounds (Table II), in contrast to their weak performance for a series of anilines studied earlier [7]. Among the Mulliken charges examined, the charge on the entire carboxylate group correlated most favorably with the experimental \( pK_a \):

\[
pK_a = -20.08(\pm 1.26)Q_M(COO^-) - 8.687(\pm 0.794)
\]

\( n = 17, r^2 = 0.9444, s = 0.0828, F = 255. \)

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Substituent} & \textbf{\( Q_M(H) \)} & \textbf{\( Q_M(COOH) \)} & \textbf{\( Q_M(O^-) \)} & \textbf{\( Q_M(COO^-) \)} \\
\hline
H (benzoic acid) & 0.2539 & 0.0071 & -0.4909 & -0.6485 \\
m-bromo & 0.2580 & 0.0398 & -0.4808 & -0.6169 \\
m-chloro & 0.2581 & 0.0396 & -0.4820 & -0.6206 \\
m-cyano & 0.2615 & 0.0502 & -0.4777 & -0.6117 \\
m-fluoro & 0.2570 & 0.0383 & -0.4859 & -0.6299 \\
m-hydroxy & 0.2540 & 0.0259 & -0.4877 & -0.6395 \\
m-methoxy & 0.2529 & 0.0215 & -0.4880 & -0.6364 \\
m-methyl & 0.2529 & 0.0190 & -0.4909 & -0.6461 \\
p-bromo & 0.2571 & 0.0321 & -0.4856 & -0.6297 \\
p-chloro & 0.2572 & 0.0185 & -0.4862 & -0.6304 \\
p-cyano & 0.2610 & 0.0341 & -0.4797 & -0.6145 \\
p-fluoro & 0.2560 & 0.0114 & -0.4896 & -0.6404 \\
p-hydroxy & 0.2523 & 0.0074 & -0.4921 & -0.6520 \\
p-methoxy & 0.2514 & 0.0047 & -0.4924 & -0.6512 \\
p-methyl & 0.2525 & 0.0131 & -0.4912 & -0.6508 \\
p-nitro & 0.2619 & 0.0577 & -0.4775 & -0.6058 \\
\hline
\end{tabular}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Substituent} & \textbf{\( Q_L(H) \)} & \textbf{\( Q_L(COOH) \)} & \textbf{\( Q_L(O^-) \)} & \textbf{\( Q_L(COO^-) \)} \\
\hline
H (benzoic acid) & 0.1135 & -0.0533 & -0.3699 & -0.8018 \\
m-bromo & 0.1166 & -0.0388 & -0.3595 & -0.7879 \\
m-chloro & 0.1187 & -0.0328 & -0.3561 & -0.7825 \\
m-cyano & 0.1158 & -0.0385 & -0.3621 & -0.7901 \\
m-fluoro & 0.1150 & -0.0471 & -0.3637 & -0.7956 \\
m-hydroxy & 0.1145 & -0.0497 & -0.3640 & -0.7977 \\
m-methoxy & 0.1136 & -0.0549 & -0.3696 & -0.8021 \\
m-methyl & 0.1195 & -0.0303 & -0.3527 & -0.7798 \\
p-bromo & 0.1156 & -0.0459 & -0.3645 & -0.7907 \\
p-chloro & 0.1182 & -0.0312 & -0.3567 & -0.7768 \\
p-cyano & 0.1149 & -0.0526 & -0.3688 & -0.7986 \\
p-fluoro & 0.1127 & -0.0667 & -0.3726 & -0.8076 \\
p-hydroxy & 0.1123 & -0.0688 & -0.3729 & -0.8076 \\
p-methoxy & 0.1126 & -0.0597 & -0.3713 & -0.8046 \\
p-methyl & 0.1191 & -0.0254 & -0.3540 & -0.7719 \\
p-nitro & 0.9631 & 0.9776 & 0.9569 & 0.9698 \\
\hline
\end{tabular}
\end{table}
The results (Fig. 2) demonstrate that benzoic acids substituted with electron-withdrawing groups (EWGs) have lower pKa values than those with electron-donating groups (EDGs). EWGs increase the delocalization of the negative charge that results from acid dissociation, thereby stabilizing the anionic conjugate base. EDGs decrease this delocalization, allowing less stabilization of the anionic species. The para compounds ($r^2 = 0.9538$) and meta compounds ($r^2 = 0.9562$) exhibited similar correlations for this set.

**Loewdin Charges**

The Loewdin charge on the carboxylic acid group proved to be an extremely effective quantum chemical parameter for the description of benzoic acid pKa values (Figs. 3 and 4 and Table III). $Q_L$(COOH) correlated with pKa almost as well as the Hammett $\sigma$ constants:

$$pK_a = -26.68(\pm1.12)Q_L$(COOH) + 2.76(\pm0.05)$$

$$n = 15, \ r^2 = 0.9776, \ s = 0.0560, \ F = 567.$$
There were no apparent outliers in the set. The correlations resulting from the \( r^2 = 0.9863 \) and the \( r^2 = 0.9733 \) were nearly identical.

There was also a strong correlation between the \( \text{Lo} \ddot{\text{w}} \text{din} \) charge on the acidic hydrogen and the \( pK_a \):

\[
pK_a = -144.3(\pm 7.8)Q_1(H) + 20.7(\pm 0.9) \]
\[ n = 15, \ r^2 = 0.9631, \ s = 0.0719, \ F = 339. \]

More acidic hydrogens are in general involved in more highly polarized bonds. The charge on the hydrogen atom can serve as an indicator of the degree of this polarization. The plot of benzoic acid \( pK_a \) vs \( Q_1(H) \) in Figure 4 shows that compounds with more positively charged hydrogens in the acid functional group have lower \( pK_a \) values.

**Natural Population Analysis Charges**

Of the four atom and group natural population analysis charges calculated, \( Q_n(COOH) \) showed the strongest correlation with \( pK_a \) (Table III). (This was also the case for the Löwdin charges.) In fact, the regression equation for \( Q_n(COOH) \) was nearly identical to that for \( Q_L(COOH) \):

\[
pK_a = -27.94(\pm 1.29)Q_n(COOH) + 4.15(\pm 0.02) \]
\[ n = 17, \ r^2 = 0.9689, \ s = 0.0620, \ F = 467. \]

This correlation is illustrated in Figure 5.

**AIM Charges**

Due to difficulties in numerical integration, AIM charges could only be confidently determined for the acidic hydrogen atom and the entire carboxylic acid group (Table V). The regression (Fig. 6) for \( Q_A(H) \) reaffirmed that hydrogens with a more positive charge are more acidic:

\[
pK_a = -112.5(\pm 8.9)Q_A(H) + 69.5(\pm 5.2) \]
\[ n = 17, \ r^2 = 0.9134, \ s = 0.1034, \ F = 158. \]

This correlation was not as strong as those obtained for other methods of charge determination. The values of \( Q_A(COOH) \) and \( pK_a \) were even less well correlated \( (r^2 = 0.8698) \).

**RELATIVE PROTON TRANSFER ENERGIES**

A measure of the acidity of the substituted benzoic acids relative to benzoic acid can be obtained...
by the examination of the energetics of the isodesmic reaction shown in Structure 1. The zero-point energies, thermal corrections, and entropies should be similar for the reactants and the products. Consequently, the difference in energies of the products and reactants provides a reasonable approximation to the enthalpy change $\Delta H_{\text{prot}}$ for the reaction and hence to the change in Gibbs energy of the reaction, $\Delta G_{\text{prot}}$. Compounds involved in reactions for which $\Delta G_{\text{prot}}$ is negative should be less acidic than benzoic acid. The $pK_s$ for compounds taking part in reactions with a positive $\Delta G_{\text{prot}}$ should be lower than that of benzoic acid.

The $\Delta E_{\text{prot}}$ values obtained for reactions with each of the substituted benzoic acids (Table VI) support these assumptions. The values for $\Delta E_{\text{prot}}$ correlated well with experimental benzoic acid $pK_s$ (Fig. 7):

\[
\text{pK}_s = -0.066(\pm 0.004)\Delta E_{\text{prot}} + 4.249(\pm 0.023)
\]

\[n = 17, r^2 = 0.9582, s = 0.0718, F = 344.\]

Obviously, the good agreement for these gas-phase calculations with the aqueous $pK_s$ trends demonstrates that the solvation effects are moderately constant for these substituted benzoic acids.

**Bond Order**

Bond orders for the O—H bond in the carboxylic acid group have been calculated in the form of

**TABLE VI**

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$E$ (acid)</th>
<th>$E$ (conjugate base)</th>
<th>$\Delta E$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H (benzoic acid)</td>
<td>-420.9374</td>
<td>-420.3730</td>
<td>0.0000</td>
</tr>
<tr>
<td>m-bromo</td>
<td>-2994.4784</td>
<td>-2993.9243</td>
<td>0.0013</td>
</tr>
<tr>
<td>m-chloro</td>
<td>-880.5579</td>
<td>-880.0035</td>
<td>0.0044</td>
</tr>
<tr>
<td>m-cyano</td>
<td>-513.1991</td>
<td>-512.6518</td>
<td>0.0019</td>
</tr>
<tr>
<td>m-fluoro</td>
<td>-520.2003</td>
<td>-519.6424</td>
<td>0.0059</td>
</tr>
<tr>
<td>m-hydroxy</td>
<td>-496.1807</td>
<td>-495.6186</td>
<td>0.0021</td>
</tr>
<tr>
<td>m-methoxy</td>
<td>-535.4908</td>
<td>-534.9272</td>
<td>0.0036</td>
</tr>
<tr>
<td>m-methyl</td>
<td>-460.2652</td>
<td>-459.6998</td>
<td>0.0054</td>
</tr>
<tr>
<td>m-nitro</td>
<td>-625.4882</td>
<td>-624.9418</td>
<td>0.0064</td>
</tr>
<tr>
<td>p-bromo</td>
<td>-2994.4791</td>
<td>-2993.9238</td>
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</tr>
<tr>
<td>p-chloro</td>
<td>-880.5609</td>
<td>-880.0032</td>
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<td>p-cyano</td>
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<tr>
<td>p-fluoro</td>
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<td>p-hydroxy</td>
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<td>p-methoxy</td>
<td>-535.4924</td>
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<td>-0.0038</td>
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<tr>
<td>p-methyl</td>
<td>-460.2657</td>
<td>-459.6995</td>
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</tr>
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<td>p-nitro</td>
<td>-625.4876</td>
<td>-624.9437</td>
<td>0.0206</td>
</tr>
<tr>
<td>$r^2$</td>
<td>0.9582</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Wiberg bond indices for each of the benzoic acid species (Table VII). A positive correlation was obtained between bond order and $p_K_a$:

$$p_K_a = 163.2(\pm 11.1)BI - 117.8(\pm 8.3)$$

$n = 17$, $r^2 = 0.9353$, $s = 0.0893$, $F = 217$.

The relationship between bond order and $p_K_a$ is illustrated in Figure 8. Bond orders are a measure of the strength of a chemical bond. The results show that the acid-dissociation constants for benzoic acids are proportional to the strength of the bond between hydrogen and oxygen in the carboxylic acid group. Note that small differences in the bond index correspond to fairly substantial changes in the $p_K_a$.

### TABLE VIII
Experimental and predicted $p_K_a$ values for amino-substituted benzoic acids.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$m$-amino</th>
<th>$p$-amino</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment Value</td>
<td>4.78</td>
<td>4.874</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>-0.16</td>
<td>-0.66</td>
</tr>
<tr>
<td>$Q_M$(COOH)</td>
<td>-0.6472</td>
<td>-0.6593</td>
</tr>
<tr>
<td>$Q_H$(COOH)</td>
<td>-0.7994</td>
<td>-0.8119</td>
</tr>
<tr>
<td>$Q_M$(COO$^-$)</td>
<td>-0.7709</td>
<td>-0.7771</td>
</tr>
<tr>
<td>$\Delta E_{prot}$ (kcal/mol)</td>
<td>-1.9573</td>
<td>-4.8061</td>
</tr>
<tr>
<td>Wiberg bond index</td>
<td>0.7490</td>
<td>0.7505</td>
</tr>
<tr>
<td>Average of QM parameters</td>
<td>4.38</td>
<td>4.68</td>
</tr>
</tbody>
</table>

### TABLE IX
Correlations among selected parameters.

<table>
<thead>
<tr>
<th>$p_K_a$</th>
<th>$Q_M$(H)</th>
<th>$Q_H$(H)</th>
<th>$Q_M$(COOH)</th>
<th>$Q_H$(COOH)</th>
<th>$Q_M$(COO$^-$)</th>
<th>$Q_H$(COO$^-$)</th>
<th>$\Delta E_{prot}$</th>
<th>$\Delta E_{prot}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0000</td>
<td>0.9924</td>
<td>0.9883</td>
<td>0.9857</td>
<td>0.9879</td>
<td>0.9854</td>
<td>0.9834</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>0.9901</td>
<td>0.9863</td>
<td>0.9851</td>
<td>0.9832</td>
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<td>0.9852</td>
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<td>1.0000</td>
</tr>
<tr>
<td>0.9794</td>
<td>0.9841</td>
<td>0.9828</td>
<td>0.9814</td>
<td>0.9861</td>
<td>0.9834</td>
<td>0.9834</td>
<td>1.0000</td>
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</tr>
<tr>
<td>0.9687</td>
<td>0.9828</td>
<td>0.9803</td>
<td>0.9804</td>
<td>0.9851</td>
<td>0.9854</td>
<td>0.9834</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>0.9580</td>
<td>0.9841</td>
<td>0.9794</td>
<td>0.9784</td>
<td>0.9861</td>
<td>0.9834</td>
<td>0.9834</td>
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<td>1.0000</td>
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<tr>
<td>0.9473</td>
<td>0.9828</td>
<td>0.9784</td>
<td>0.9814</td>
<td>0.9879</td>
<td>0.9851</td>
<td>0.9834</td>
<td>1.0000</td>
<td>1.0000</td>
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<tr>
<td>0.9366</td>
<td>0.9841</td>
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<td>0.9828</td>
<td>0.9851</td>
<td>0.9851</td>
<td>0.9834</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>0.9259</td>
<td>0.9828</td>
<td>0.9794</td>
<td>0.9814</td>
<td>0.9861</td>
<td>0.9852</td>
<td>0.9834</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

**FIGURE 8.** Correlation between $p_K_a$ and the O–H Wiberg bond index.
AMINO-SUBSTITUTED COMPOUNDS

As noted earlier, experimental $pK_a$ values for $m$-amino and $p$-aminobenzoic acid were not included in the source [15] employed for the $pK_a$s of the other compounds, and as a precaution these compounds were not included in the regression analyses. Regression equations from several of the quantum chemical parameters described above have been used to predict the $pK_a$s of the amino-substituted compounds (Table VIII).

The average value for the $pK_a$ of $m$-aminobenzoic, as predicted by the quantum chemical parameters, was 4.38. Further, the $pK_a$ value for $m$-aminobenzoic acid as predicted by the Hammett constant is 4.36, essentially identical to the value predicted by the quantum models. The Handbook of Chemistry and Physics [16] lists an experimental value of 4.78 for the $m$-aminobenzoic acid. Models can sometimes call attention to the presence of questionable or erroneous reported experimental values [24], and we suggest that the reported $pK_a$ value for $m$-aminobenzoic acid warrants reexamination.

In contrast, the quantum chemical parameters (on average) predict the $pK_a$ of $p$-aminobenzoic acid to be 4.80. This is consistent with the reported experimental value of 4.874 [16]. The Hammett constant for $p$-aminobenzoic acid predicts its $pK_a$ to be 4.86.

The correlations among selected parameters and the $pK_a$ are shown in Table IX.

Conclusions

This study of benzoic acids, along with previous studies of anilines [6, 7] and phenols [9], demonstrates that quantum chemical parameters can be used successfully to account for substituent effects. In addition to their ability to quantitatively relate the electronic properties of substituents to their physicochemical effects, an attractive feature of quantum chemical parameters is that they are both flexible and interpretable. Such models can also call attention to questionable experimental values reported in the literature, and encourage a reexamination of the experiments in such cases.

References

10. Spartan 5.1. Wavefunction Inc.; Irvine, CA.
12. Keith, T. AIMALL; Yale University: New Haven, CT.