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Substituent Effects on the Acidity of Weak Acids. 2. Calculated Gas-Phase Acidities of Substituted Benzoic Acids

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To investigate the origin of substituent effects on the acidity of benzoic acids, the structures of a series of substituted benzoic acids and benzoates have been calculated at the B3LYP/6-311+G* and MP2/6-311+G* theoretical levels. The vibrational frequencies were calculated using B3LYP/6-311+G* and allowed corrections for the change in zero-point energies on ionization, and the change in energy on going from 0 K (corresponding to the calculations) to 298 K. A more satisfactory agreement with the experimental values was obtained by energy calculations at the MP2/6-311++G** level using the above structures. The resulting ΔH_{acid} values agree very well with the experimental gas-phase acidities. The energies of compounds with π-electron-accepting or -releasing substituents, rotated to give the transition state geometries, provided rotational barriers that could be compared with those found for the corresponding substituted benzenes. Isodesmic reactions allowed the separate examination of the substituent effects on the energies of the acids and on the anions. Electron-withdrawing groups stabilize the benzoate anions more than they destabilize the benzoic acids. Electron-donating groups stabilize the acids and destabilize the anions by approximately equal amounts. The gas-phase acidities of *meta*- and *para*-substituted benzoic acids are linearly related. This is also found for the acidities of substituted phenylacetic acids and benzoic acids. Since direct π-electron interactions are not possible with the phenylacetic acids, this indicates that the acidities are mainly controlled by a field effect interaction between the charge distribution in the substituted benzene ring and the negative charge of the carboxylate group. The Hammett σ_M and σ_P values are also linearly related for many small substituents from NO_2 through the halogens and to OH and NH_2. Most of the other substituents fall on a line with a different slope

1. Introduction

In view of the historical importance of substituent effects on the acidity of benzoic acid,[1] it is surprising that there have been relatively few MO calculations of their acidity,[2] and even less that include the effects of electron correlation.[3] The gas-phase acidities of many substituted benzoic acids are known experimentally[4] and are particularly useful in that they avoid the problems associated with the unusual temperature dependence of the pK_a's of carboxylic acids in aqueous solution.[5] Calculations that reproduce the known gas-phase acidities of substituted benzoic acids would assist in the examination of π-electron and field effects and would provide information for some substituents that have not been examined experimentally.

These calculations would also allow the investigation of the energies of isodesmic reactions that separate the substituent and the carboxyl or carboxylate groups, as well as the effects of rotating the substituents to minimize π-electron interactions. In addition, they would allow an examination of the changes in electron density that are caused by the substituents. Further information could be obtained by comparing the acidities of substituted benzoic acids with those of the corresponding phenylacetic acids where direct π-electron interactions would be minimized.

2. Calculations

The first requirement of calculations for substituted benzoic acids is that they satisfactorily reproduce the available experimental data. Then, they could be used with some confidence in examining the origin of the substituent effects. It is important to correct for the

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(1) Hammett, L. P. *Chem. Rev.* **1935**, *11*, 125. Hammett, L. P. *Physical Organic Chemistry*; McGraw-Hill: New York, 1940.

(2) Liyuan, W.; Yu, S. J. *Photopolym. Sci. Technol.* **1999**, *12*, 331. Ponti, A.; Gamba, A. *Gazz. Chim. Ital.* **1997**, *127*, 151. Genix, P.; Jullien, H.; LeGoas, R. *J. Chemom.* **1996**, *10*, 631. Ghauri, F. Y. Blackledge, C. A.; Glen, R. C.; Sweatman, B. C.; Lindon, J. C.; Beddell, C. R.; Wilson, J. D.; Nicholson, J. K. *Biochem. Pharmacol.* **1992**, *44*, 1935. Krygowski, T. M.; Wozniak, K.; Bock, C. W.; George, P. *J. Chem. Res. (S)* **1989**, 396. Böhm, S.; Kuthan. J. *Int. J. Quantum Chem.* **1984**, *26*, 21.

(3) Koppell, I. A.; Mishima, M.; Stock, L. M.; Taft, R. W.; Topsom, R. D. *J. Phys. Org. Chem.* **1993**, *6*, 685.

(4) The data have been taken from the NIST Chemistry Webbook (www.webbook.nist.gov). The data were obtained by: (a) Yamdagni, R.; McMahon, T. B.; Kebarle, P. *J. Am. Chem. Soc.* **1974**, *96*, 4035. (b) ref 3.

(5) Cf. Christensen, J. J.; Hansen, L. D.; Izatt, R. M. *Handbook of Proton Ionization Heats and Related Quantities*; Wiley: New York, 1976.

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effects of electron correlation, and density functional theory[6] provides a computationally efficient way in order to carry out such calculations. Therefore, the energies of the acids and their ions were initially obtained by geometry optimization at the B3LYP/6-311+G* theoretical level, followed by the calculation of the vibrational frequencies at the same level.[7] This allows correction for zero-point energies and conversion of the calculated 0 K energies to 298 K. The B3LYP hybrid density functional model[8] has been found to generally give good relative energies in a wide range of systems.[6] The basis set is reasonably flexible and includes diffuse functions that are needed for anionic systems.[9]

Although there is a good linear relationship between the calculated and observed ΔH_{acid}, the calculated values are about 5 kcal/mol too small. In a related investigation,[10] it was found that added diffuse functions and polarization functions at hydrogen markedly improved agreement, and MP2 gave somewhat better agreement with experiments than B3LYP. MP2/6-311+G* optimizations were carried out for the lower energy conformers identified in the B3LYP calculations. The use of MP2/6-311++G** with MP2/6-311+G* optimized structures leads to markedly improved calculated energies.

The distribution of atomic charges is of interest for the acids and their anions. There are many ways in which the charges can be calculated.[11] The Mulliken population analysis[12] fails when extended basis sets and diffuse functions are used.[13] The Natural Population Analysis[14] is not subject to these problems, but leads to exaggerated C−H bond dipoles[15] that are inconvenient in the present context. We have chosen to use the Hirshfeld charges[16] which should be ideal for calculating the changes caused by remote substituents. Here, a 3D grid is placed about the molecule in question, and the electron density is calculated at each point from the molecular wave function. A *promolecule* is constructed by placing *proatoms* (spherically symmetrical neutral atoms) at each of the nuclear positions for the real molecule. At each point on the grid, the contribution to the electron density from each of the *proatoms* is calculated, and the density of the real molecule is partitioned among its atoms in proportion to the contributions from the *proatoms*. Integration of the densities for a given atom gives the number of electrons associated with the atom.

3. Conformational Issues

With the *para*-substituted benzoic acids and anions where X = F, Cl, NH_2, CF_3, NO_2, and CN, there is only one ground state conformer. With CHO, OH, and SH as the substituent, the hydrogen may be on the same side as the OH of the acid, or on the opposite side. Not surprisingly, the difference in energy is less than 0.1 kcal/mol in each case. The corresponding anions do not have conformational problems. The substituents NH_2, NO_2, CHO, OH, and SH may also adopt rotated conformations in which there is a minimal π-electron interaction with the benzene ring, and these acids and anions also were studied, giving the rotational barriers.

It should be noted that the lowest energy anion derived from *p*-hydroxybenzoic acid appears to be *p*-carboxyphenoxide ion rather than *p*-hydroxybenzoate ion.[17] This was confirmed by our calculations that found the latter ion to have a higher energy (5.2 kcal/mol at MP2/6-311++G). Not surprisingly, the same was true for *p*-mercaptobenzoic acid, and here the benzoate ion had a higher energy than the thiophenoxide ion (8.6 kcal/mol at MP2/6-311+G*). In the tables, *p*-hydroxy and *p*-mercapto refer to the formation of the higher energy carboxylate ion.

The *p*-SH substituent is interesting in that it adopts a near-planar conformation in the acid, but rotates to a perpendicular position in the benzoate ion. This probably occurs in order to minimize the interaction between the S lone pair and the now electron rich aromatic ring and is made possible by the very low rotational barrier.

The *meta*-substituted benzoic acids present more of a problem. With benzoic acid, the substituent may be on the side of the OH group or on the opposite side. In addition, with CHO, OH, and SH, the hydrogen may be oriented toward the acid group or away from it. All of these conformers were examined. With the electron-attracting groups, the substituent preferred to be on OH side of the CO_2H group, whereas the electron-releasing substituents (NH_2, OH, SiH_3, SH) prefer to be on the C═O side of the CO_2H group. In addition, the proton of the OH and SH group prefers to point toward the CO_2H group, and in the rotational transition states, the NH_2 group prefers to point toward the CO_2H group. In all cases, the differences in energy among the conformers were small. The structures and energies of all of the conformers are available as Supporting Information.

Some of the substituents may also be rotated so as to minimize π-electron interactions, and these species also were studied to give the rotational barriers. The energies of the rotated species are available as Supporting Information.

3. Calculated Gas-Phase Acidities

The calculated acidities (ΔH_{acid}) are summarized in Table 1, and the calculated total energies are available as Supporting Information. The ΔH_{acid} are defined by the reaction HA → A^- + H^+. The calculated energies of HA and A^- were corrected for their zero-point energies and the changes in enthalpy on going to 298 K using the

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[6] Koch, W.; Holthausen, M. C. *A Chemist's Guide to Density Functional Theory*; Wiley-VCH: Weinheim, 2001.

[7] The energies and structures are available as Supporting Information.

[8] Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. Stephens, P. J.; Devlin, F. J.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

[9] Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R *J. Comput. Chem.* **1983**, *4*, 294.

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[11] Wiberg, K. B.; Rablen, P. R. *J. Comput. Chem.* **1993**, *14*, 1504.

[12] Mulliken, R. S. *J. Chem. Phys.* **1962**, *36*, 3428.

[13] With the present calculations, the Mulliken population analysis gives a negative charge at the carbonyl carbon of benzoic acid (−0.110) even though it is connected to two electronegative oxygens. The NPA charge is +0.794 and the ChelpG (Breneman, C. M.; Wiberg, K. B. *J. Comput. Chem.* **1990**, *11*, 361) charge is +0.665.

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[15] Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1986**, *84*, 2428

[16] Hirshfeld, F. L. *Theor. Chim. Acta* **1977**, *44*, 129.

[17] McMahon, T. B.; Kebarle, P. *J. Am. Chem. Soc.* **1977**, *99*, 2222.

TABLE 1. Gas-Phase Acidities of Substituted Benzoic Acids

a. Ground State Conformers

	para			*meta*		
X	B3L calcd[a]	MP2 calcd[b]	obsd[c]	B3L calcd	MP2 calcd	obsd
H	335.1	339.7	340.0	335.1	339.7	340.0
Me	336.3	340.6	341.0	335.8	340.3	341.0
NH_2	339.7	342.7	343.4	336.8	341.1	341.9
OH	336.2	340.2	*d*	333.3	338.0	339.0 (d)
F	331.8	336.6	337.0	330.7	335.6	336.5
SiH_3	331.8	336.7		332.2	337.1	
SH	332.7	336.0		331.6	337.2	
Cl	330.4	335.7	335.5	329.7	335.0	335.6
CF_3	326.2	332.0	332.3	327.2	332.2	332.6
CHO	326.4	332.5	332.8	327.0	332.4	
CN	324.0	329.8	327.8	324.8	329.9	328.9
NO_2	322.1	329.0	328.1	323.8	329.4	329.5

b. C−X Rotational Transition State Conformers, MP2/6-311++G**

X	*para*-calcd	$\Delta\Delta H^e$	*meta*-calcd	$\Delta\Delta H^e$
NH_2	339.8	2.9	338.6	2.5
OH	338.7	1.5	338.2	−0.2
CHO	334.6	−2.1	334.0	−1.5
NO_2	329.9	−0.9	329.4	0.0

[a] 6-311+G* basis set. [b] 6-311++G** basis set. [c] Data from ref 4 + 7.4 kcal/mol to convert ΔG_{acid} to ΔH_{acid} for the *meta*-substituted acids, or +7.0 kcal/mol for the *para*-substituted acids. [d] *p*-Methoxybenzoic acid, ΔH_{acid} = 340.8 kcal/mol; *m*-methoxybenzoic acid, ΔH_{acid} = 339.8 kcal/mol. [e] Change in acidity on rotating about the Ar−X bond.

B3LYP calculated vibrational frequencies. The proton has an electronic energy of zero, but at 298 K it has translational enthalpy and a Δ(pV) term which sum to 1.5 kcal/mol. When several conformers of a given substituted benzoic acid or benzoate ion are possible, the acidity derived from the lowest energy conformers is reported in the table.

The experimental ΔG_{acid} were taken from the NIST chemistry webbook[4] and were converted to ΔH_{acid} using the average $T\Delta S$ value of 7.4 kcal/mol for *meta*-substituted benzoic acids, and 7.0 kcal/mol for *para*-substituted benzoic acids.[18,19] There is a generally good correlation between the B3LYP calculated and the observed acidities (Figure 1), but the calculated values are about 5 kcal/mol too small. The MP2/6-311++G** calculated acidities give a significantly better agreement (Figure 1) with an rms deviation of 0.8 kcal/mol. This is quite satisfactory since the uncertainty in the relative acidities of these closely related acids is about ±0.5 kcal/mol.[20]

It has been noted that the acidities of benzoic acids substituted by electron-withdrawing substituents are almost the same for *meta*- and *para*-substitution.[21] This is further explored with additional substituents in Figure 2 using the available experimental data. Methoxy was included rather than hydroxy in view of the problem with *p*-hydroxybenzoic acid noted above. There is a good correlation with a slope of 0.87.

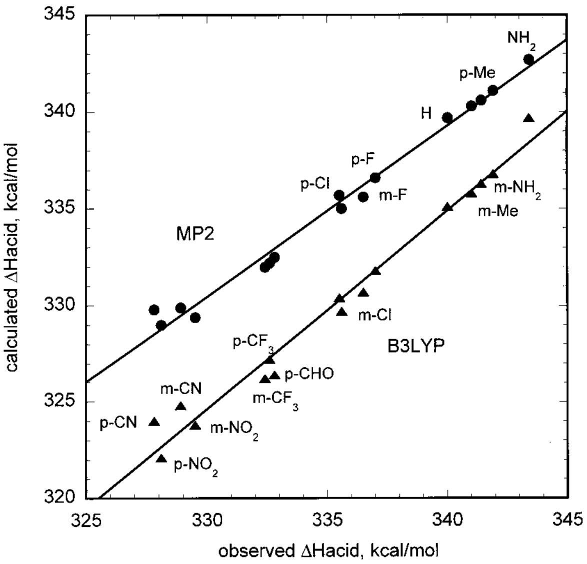

FIGURE 1. Relationship between the calculated B3LYP/6-311+G* and MP2/6-311++G** ΔH_{acid} and the observed gas-phase values.

Since experimental data for only a limited number of substituents are available, Figure 3 shows the relationship using the calculated acidities for a full set of both electron-releasing and electron-accepting substituents. There is a fairly good linear relationship with a slope of

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(18) Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl 1.

(19) With many *para*-substituted benzoic acids, the benzoate ions have C_{2v} symmetry, and either of the two benzoate oxygens may be protonated to give the acid, leading to an RT ln 2 free energy term (0.4 kcal/mol). Because of the negligible difference in energy between the two rotationally distinct acids in the other cases, this will be approximately correct. The *meta*-substituted benzoates do - not have this symmetry. (Cf. Eberson, L. In *The Chemistry of Carboxylic Acids and Esters*; Patai, S., Ed.; Interscience, London, 1969; p 219.) A more detailed treatment would include correction for the large amplitude torsional modes and for the higher energy *m*-benzoic acid conformers. However, these terms would be expected to be significantly smaller than the experimental uncertainty, and the considerable additional computational effort did not appear to be warranted.

(20) The uncertainty in Δ*G* from a direct comparison of two acids in the gas phase is about ±0.2 kcal/mol. For acids derived from a ladder of acidities, the uncertainty will be larger, and ±0.5 kcal/mol would appear to be a reasonable value. There is also some uncertainty in the TΔS correction term.[19]

(21) Decouzon, M.; Exner, O.; Gal, J. F.; Maria, P. C. *J. Phys. Org. Chem.* **1994**, *7*, 615.

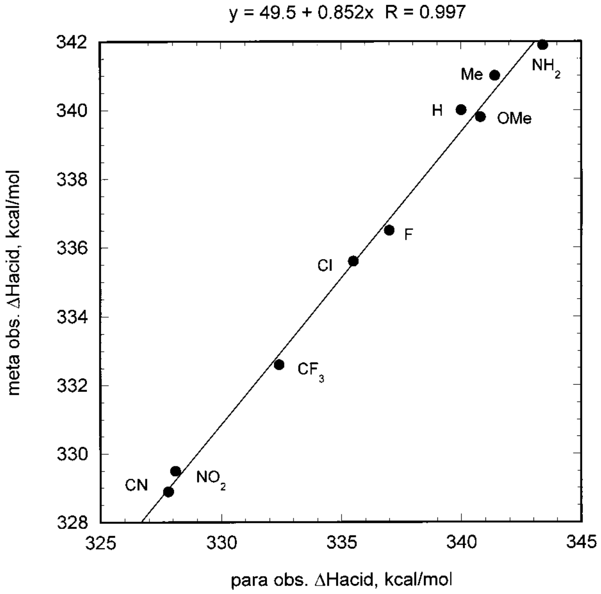


FIGURE 2. Relationship between the experimental gas-phase acidities for *meta*- and *para*-substituted benzoic acids.

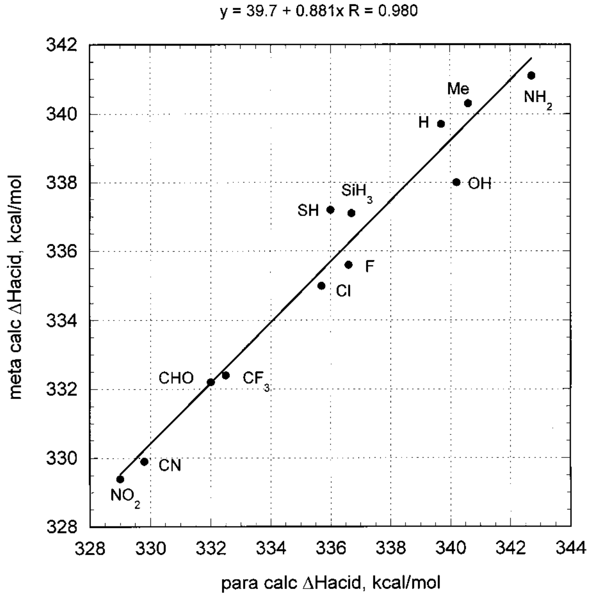


FIGURE 3. Relationship between the calculated gas-phase acidities of *meta*- and *para*-substituted benzoic acids.

0.88. It would be possible to obtain a somewhat better correlation using just the electron-withdrawing groups and those having lone pairs, but it is not clear that this is warranted.

The correlation indicates that the origin of the substituent effect must be in large measure related at the *meta*- and *para*-positions, and that it is attenuated by ~20% at the *meta*-position as compared to *para*. This is contrary to the frequently expressed viewpoint that both resonance and field/inductive effects are found at the *para*-position but only the latter is important at the *meta*-position.[20] The equation representing the correlation in Figure 2 indicates that the acidities of the *meta*- and *para*-substituted acids should be equal for $\Delta H_{\mathrm{acid}} = 326$, which is just between the acids with strong electron withdrawing substituents and the other acids. Thus, with electron releasing groups, the *meta*-substituted acids have the greater acidity, and with strong electron withdrawing substituents the *para*-substituted acids have the greater acidity.

4. Analysis of Substituent Effects

The substituent effects will be examined in several different ways in order to separate the effects on the acids vs their anions, and to separate the field and π-electron effects.[22] Four approaches will be used:

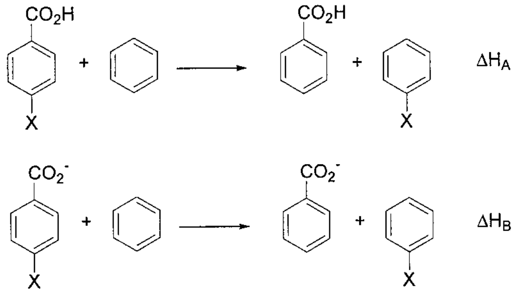
a. Isodesmic reactions will be used to separate the substituent and the carboxyl or carboxylate groups by attaching them to different benzene rings. This will allow the total substituent effect to be evaluated for each species.

b. A comparison of the Ar−X rotational barriers for substituted benzenes, benzoic acids and benzoate ions will give a measure of the π-electron interactions in the latter species.

c. The “classical” comparison of the acidities of *para*-substituted benzoic acids and 4-substituted bicyclo[2.2.2]-octane-1-carboxylic acids[23] will be extended to a wider range of substituents than is possible using just experimental data. The difference between the acidities of the two series of acids may be attributed to π-electron effects.

d. Another useful comparison is between benzoic and phenylacetic acids. Here, the CH_2 group in the latter disrupts π-electron interactions between the benzene ring and the carboxylic/carboxylate groups, but still retains the interaction between the substituent and the aromatic ring.

4.1. Separation of Substituent Effects into Those for Acids vs Anions. When a substituent leads to an increase in acidity, it may be due to either the stabilization of the benzoate anion or the destabilization of the benzoic acid. These interactions may be separately studied by the use of the following isodesmic reactions:



Here, the interaction between the substituent on the carboxyl or carboxylic acid group is removed by placing the two groups on separate benzene rings. The MP2/6-311++G** reaction energies are summarized in Table 2.

The substituent effects on the carboxylic acids (ΔH_a) are generally quite small, with small stabilizing effects of π-electron-releasing substituents and small destabilizing effects of π-electron-attracting substituents. This

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[22] For a detailed analysis of the separation of the various components of the substituent effects, see Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1 and March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: NY, 1992; pp 278−286.

[23] Roberts, J. D.; Moreland, W. T. *J. Am. Chem. Soc.* **1953**, *75*, 2176 and ref 22.

TABLE 2. Isodesmic Reaction Energies, kcal/mol

	ground state				rotational TS			
	para		meta		para		meta	
X	acid	anion	acid	anion	acid	anion	acid	anion
H	0.0	0.0	0.0	0.0				
Me	−0.2	0.7	−0.2	0.5				
NH_2	−1.2	1.8	−0.8	0.6	−0.2	−0.1	−0.2	−1.2
OH	−0.5	0.0	−0.6	−2.3	−0.1	−1.0	0.2	−1.3
F	0.2	−2.9	0.5	−3.5				
SiH_3	0.1	−2.9	0.1	−2.4				
SH	0.3	−4.0	0.8	−3.3				
Cl	0.1	−4.0	0.5	−4.2				
CF_3	0.9	−6.7	1.1	−6.4				
CHO	0.9	−6.4	0.9	−6.4	0.6	−4.4	0.6	−5.1
CN	1.0	−8.9	1.5	−8.2				
NO_2	1.0	−9.7	1.5	−8.8	1.0	−8.8	1.2	−9.1

TABLE 3. Ar−X Rotational Barriers (Δ*H*, 25° C)

	calcd		
X	B3LYP[a]	MP2[b]	obsd[22]
NH_2	4.8	3.9	
OH	2.9	2.1	3.5
NO_2	5.1	2.8	2.8
CHO	7.9	6.3	4.6

[a] B3LYP/6-311+G*. [b] MP2/6-311++G**//MP2/6-311+G*.

TABLE 4. Benzoic Acid Ar−X Rotational Barriers, kcal/mol

	para		meta	
X	acid	anion	acid	anion
a. Calculated Barriers				
NH_2	5.0	2.1	4.5	2.1
OH	2.6	1.1	2.9	3.1
NO_2	2.8	3.7	2.6	2.5
CHO	6.0	8.3	6.1	7.7
b. Change in Barrier with Respect to Ar−X				
NH_2	1.1	−1.8	0.6	−1.8
OH	0.5	−1.0	0.8	1.0
NO_2	0.0	0.9	−0.2	−0.3
CHO	−0.3	2.0	−0.2	1.4

should be expected since the carboxylic acid carbon is somewhat electron deficient and can be stabilized by substituents such as NH_2 that can donate π-electrons to the ring, and destabilized by groups such as NO_2 that will decrease the electron density in the ring.

The main effect of substituents is found with the carboxylate anions. Here, the substituent effects are opposite to those for the acids, with electron-withdrawing substituents stabilizing the carboxylate group. The larger effect is expected since in the carboxylate ions there is a full negative charge that may be stabilized by the effect of the substituents.

4.2. Rotational Barriers. The examination of substituent effects given above provide a measure of the total effect, but does not distinguish between π- and σ-electron components. One way in which to gain such information is to examine the Ar−X rotational barriers. By rotating NH_2, OH, CHO, and NO_2 groups by ~90° to give the rotational transition states, the π-electron component is effectively eliminated. Thus, if the rotational barrier of a substituted benzoic acid is greater than that for the corresponding substituted benzene, the difference may be attributed to an extra π-interaction.

The calculated rotational barriers for the substituted benzenes are given in Table 3. These barriers have been studied by Head-Gordon et al.[24] at the MP2/6-311G**//HF/6-31G* level. Our MP2/6-311++G** calculated barriers are in somewhat better agreement with the experimental values. Any errors in the calculated rotational barriers should also appear in the following calculations and should approximately cancel.

The calculated rotational barriers for the substituted benzoic acids are given in Table 4 which also includes the changes in barriers with respect to the parent Ar−X compound. With the benzoic acids, the barrier is increased by the electron-donating substituents whereas the electron-withdrawing substituents have little effect. The changes are generally larger with the anions. Here, the amino substituent decreases the barrier by 1.8 kcal/mol at *both* the *meta*- and *para*-positions, indicating that it destabilizes these benzoate anions. The formyl group leads to large rotational barriers for benzaldehyde as well as the benzoate anions. Here, the anion is stabilized by 2.0 kcal/mol by a *p*-CHO group and by 1.4 kcal/mol by a *m*-CHO group. Hydroxy is unusual in that it destabilizes the *para*-substituted benzoate and stabilizes the *meta*-substituted anion. The nitro group has a relatively small effect on the rotational barriers, but it does give 0.9 kcal/mol stabilization for *p*-nitrobenzoate.

The acidities of the acids with rotated Ar−X bonds so as to minimize π-electron effects were calculated and are given in Table 1b. It is interesting to note that the *meta*- and *para*-substituted compounds now have essentially the same calculated acidities. The change in acidity on rotating about the Ar−X bond is also given, and for the π-substituted compounds, the changes correspond to common expectation. Amino gives the largest decrease in acidity for the ground-state acid, which is followed by OH. Both CHO and NO_2 give significant increases in acidity of the ground-state acid, which is lost when the Ar−X bond is rotated.

The results for the *meta*-substituted compounds are interesting. Here, amino still gives a fairly large acidity decreasing π-electron effect for the ground state acid, and the formyl group gives a fairly large acidity increasing π-electron effect for the ground-state acid which is lost on rotating about the Ar−X bond. Thus, even with the *meta*-substituted acids, there are significant π-electron effects.

4.3. Comparison between Benzoic and Bicyclo[2.2.2]octane-1-carboxylic Acids. The relative acidities of the 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids have been used to define a field effect parameter, *F*.[21] This quantity for the gas phase, which is the difference of the calculated acidities, corrected for the small difference in distance between substituent and the carboxyl group as compared to benzoate ion, is given in Table 5. Subtracting it from the calculated relative acidities of the *para*-substituted benzoic acids gives *R*, the "resonance" term. Both have the units of kcal/mol.

As expected, the largest negative *R* term is found with NH_2 as the substituent, and this is followed in order by OH, Me, Cl, and F. The largest positive *R* value is found with CHO as the substituent, and this is followed by NO_2,

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[24] Head-Gordon, M.; Pople, J. A. *J. Phys. Chem.* **1993**, *97*, 1147.

TABLE 5. Separation of Field and π-Effects

	BC[2.2.2] acids		benzoic acids		
X	ΔH_{acid}	$F = 0.96 \times \Delta H_{rel}$	ΔH_{acid}	ΔH_{rel}	$R = \Delta H_{rel} - F$
H	343.5	0.0	339.7	0.0	0.0
Me	343.1	0.4	340.6	−0.9	−1.3
NH_2	342.8	0.7	342.7	−3.0	−3.7
OH	340.6	2.8	340.2	−0.5	−3.3
F	338.8	4.5	336.6	3.1	−1.4
SiH_3	341.1	2.3	336.7	3.0	0.7
SH	340.5	2.9	336.0	3.7	0.8
Cl	338.5	4.8	336.7	3.0	−1.8
CF_3	337.5	5.8	332.0	7.7	1.9
CN	334.9	8.3	332.5	7.2	−1.1
CHO	337.5	5.8	329.8	9.9	4.1
NO_2	334.8	8.4	329.0	10.7	2.3
Benzoic Acids with Rotated C−X Bonds					
NH_2	342.8	0.7	339.8	-0.1	−0.8
OH	340.6	2.8	338.7	1.0	−1.8
CHO	337.5	5.8	334.6	5.1	−0.7
NO_2	334.8	8.4	329.9	9.8	1.3

TABLE 6. Calculated Dipole Moments (MP2/6-311++G)**

X	Ar−X	BC[2.2.2]-X
H	0.000	0.000
CH_3	−0.412	0.153
NH_2	−0.897	0.694
OH	0.337	1.490
F	1.978	2.797
SiH_3	0.862	1.226
SH	1.475	2.092
Cl	1.995	3.216
CF_3	3.323	3.529
CHO	3.483	3.271
CN	5.082	4.936
NO_2	5.458	5.292
NH_2 (rot)	0.018	
OH (rot)	0.621	
CHO (rot)	2.716	
NO_2 (rot)	5.009	

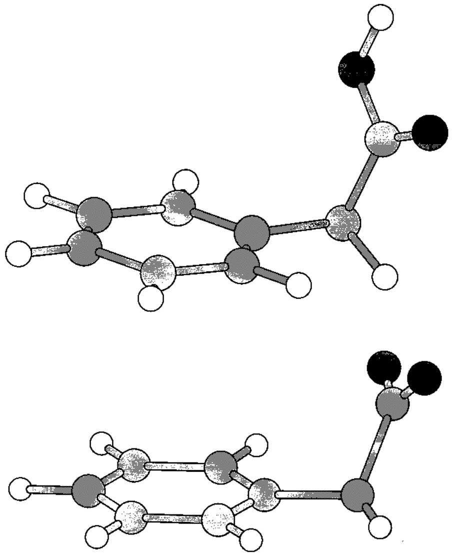

FIGURE 4. Low energy conformers of phenylacetic acid and phenylacetate ion.

CF_3, SH, and SiH_3. It is interesting that CN gives a negative *R* value.

The rotational barriers and the comparison with the bicyclooctane acids clearly show that π-electron effects are important in determining the acidity of substituted benzoic acids. However, the detailed mechanism of how these effects operate is not well defined by these data.

4.4. Comparison between Benzoic and Phenylacetic Acids. The classical separation of σ and π substituent effects described above misses one important difference between the benzene and bicyclo[2.2.2]octane systems. In the latter, the C−X bond dipoles are essentially localized, as can be seen in the small changes in charges at adjacent atoms and the very good correspondence between the calculated dipoles in the bicyclo[1.1.1]pentane and bicyclo[2.2.2]octane systems.[10] However, with substituted benzenes, the substituents lead to changes in electron distribution throughout the ring,[25] and as a result, the dipole moments are not localized in the C−X bonds. This can be seen in a comparison between the bicyclooctyl−X and Ar−X dipoles (Table 6) and between the charge distribution in the substituted bicyclooctane acids and anions[10] and the corresponding benzoic acids and anions (Table S3, Supporting Information).

The differences for the π-electron-releasing substituents is quite striking. With the bicyclooctylamine, the C−N dipole has the sense $C^+{-}N^-$ resulting from the greater electronegativity of N as compared to C. With aniline, the sign is reversed, and this must result from π-electron donation to the benzene ring leading to a dipole in the sense $Ar^-{-}N^+$.

If we are interested in the interaction between the substituted benzene rings and the carboxylic or carboxylate groups, a good comparison might be between substituted benzoic acids and the corresponding phenylacetic acids. In the phenylacetic acids, the CH_2 group separates the ring from the carboxylic or carboxylate groups, but retains the field effect of the substituents on the aromatic ring. The phenylacetic acids and phenylacetate ions were studied in the same ways as the benzoic acids: B3LYP/6-311+G* geometry optimizations including a calculation of the vibrational frequencies. The lower energy conformers have the $CH_2{-}CO_2$ bond approximately perpendicular to the aromatic ring (Figure 4). These conformers were reoptimized at the MP2/6-311+G* level followed by MP2/6-311++G** calculations using the MP2 geometries. The calculated acidities are summarized in Table 7, and they are compared with the benzoic acids in Figure 5.

There is a remarkably good linear relationship between the acidities of the benzoic and phenylacetic acids, including the acids with rotated C−X groups and the *meta*-substituted acids. With the phenylacetic acids, the interaction that causes the substituent effect must be a field effect involving the interaction of the distributed charges in the benzene ring with the carboxylate group of the phenylacetate anions. Since the benzoic acid acidities are linear related to those for the phenylacetic acid, it seems reasonable to conclude that the same mechanism is involved. The slope in Figure 6 is 0.82 indicating a slightly smaller susceptibility to substituent

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[25] Wiberg, K. B.; Rablen, P. R. *J. Org. Chem.* **1998**, *63*, 3722.

TABLE 7. Acidity of Substituted Phenylacetic Acids

	para			*meta*	
X	B3L calcd	MP2 calcd	obsd	B3L calcd	MP2 calcd
H	335.1	339.7	340.2	335.1	339.7
Me	336.3	342.0		335.4	341.2
NH_2	337.0	342.5		335.8	341.2
OH	335.2	340.6		332.6	338.6
F	332.2	338.1		331.6	337.7
SiH_3	332.1	338.2			
SH	331.9	337.8			
Cl	331.0	337.4		331.0	337.3
CF_3	328.3	334.8			
CHO	327.1	334.6			
CN	325.3	332.2		326.5	332.8
NO_2	322.9	331.4		325.4	332.3

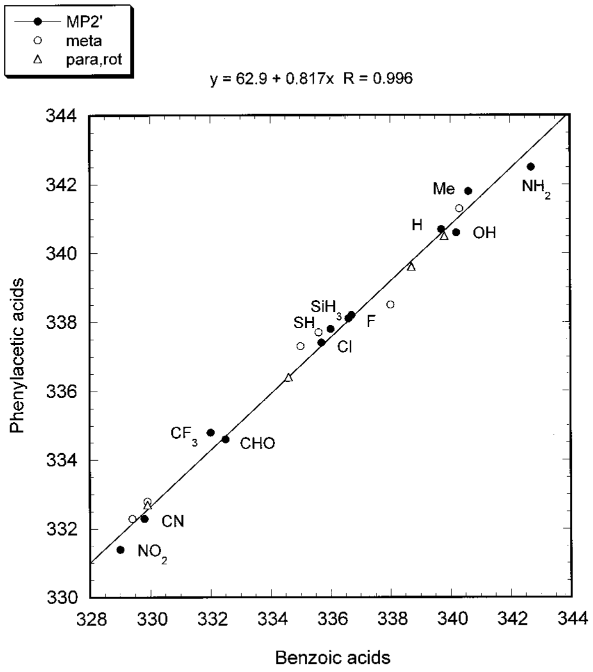


FIGURE 5. Relationship between the calculated gas-phase acidities of phenylacetic and benzoic acids. The correlation line was derived from the *para*-substituted acids (solid circles). The *meta*-substituted acids (open circles) are substituted by NO_2, CN, F, OH, NH_2, and Me, and the Ar−X rotated *para*-substituted acids (open triangles) are substituted by NO_2, CHO, OH, and NH_2.

effects for the phenylacetic acids, and that is just what should be expected since the carboxylate group of the phenylacetates is further from the benzene ring than in the benzoates, and the field effect decreases as the square of the distance.[26]

The conclusion that the field effect is the major component of the substituent effect for benzoic acids also accounts for the relationship between the *meta*- and *para*-substituted benzoic acids. A given substituent will lead to a redistribution of charge in the benzene ring, and the carboxylate group interacts with the resulting charge distribution. It is slightly more effective when the substituent is para to the carboxylate group than when it is in the meta position because of the small difference in the overall charge distribution.

As an example, the changes in charge distribution with respect to benzoate ion at the carbons in *p*-aminobenzoate ion and *m*-aminobenzoate ion are:

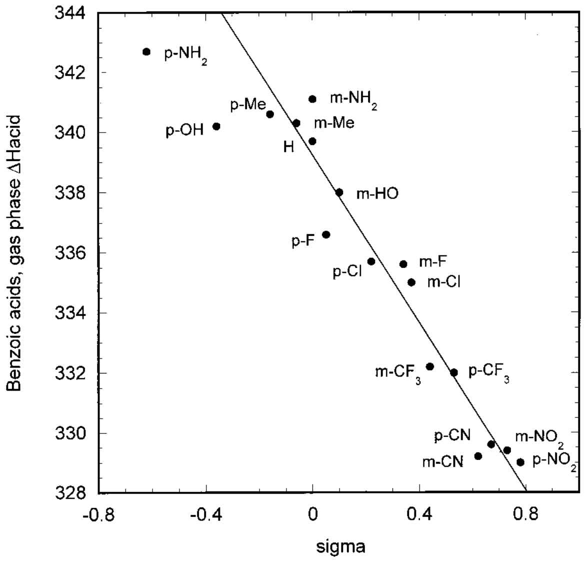
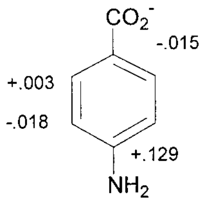
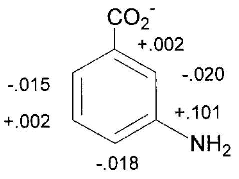


FIGURE 6. Relationship between the acidities of substituted benzoic acids in the gas phase and in aqueous solution (σ-values).





Whereas there is additional negative charge at the ipso carbon of the *p*-aminobenzoate, there are significant negative charges at both *ortho*-positions of *m*-aminobenzoate. The distance between the *ortho*-positions and the carboxylate oxygens is somewhat greater than that for the *para*-position, but there are two negatively charged *ortho*-carbons in the *meta*-anion, and only one negatively charged ipso position in the *para*-anion. Thus the effects should be similar in the two series.

5. Relation between Gas Phase and Solution Acidities. Are the gas-phase acidities related to the acidities measured in aqueous solution? This is examined in Figure 6. There is a fair correlation between the calculated acidities of the substituted benzoic acids and the solution values of σ.[27] Not surprisingly the *p*-NH_2 and *p*-OH substituents fall well off the correlation line. These are groups that would be especially affected by hydrogen bonding in aqueous solutions. The correlation with the observed acidities is essentially the same.

In view of the above correlations, one might then ask if the *meta*- and *para*-σ constants are related. This is examined in Figure 7 that includes some substituents that were not included in the above calculations. It can be seen that many substituents including amino, the halogens, and the electron-withdrawing groups give a fair linear relationship, and that other substituents such as Me, t-Bu, H, and CF_3 fall near a line with a different slope. Most of the substituents in the former group will be significantly hydrogen bonded in water, and this may

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(26) Bjerrum, N. *Z. Physik. Chem.* **1923**, *106*, 219.

(27) The σ values were taken from Shorter, J. *Pure Appl. Chem.* **1994**, *66*, 2451; **1997**, *69*, 2497.

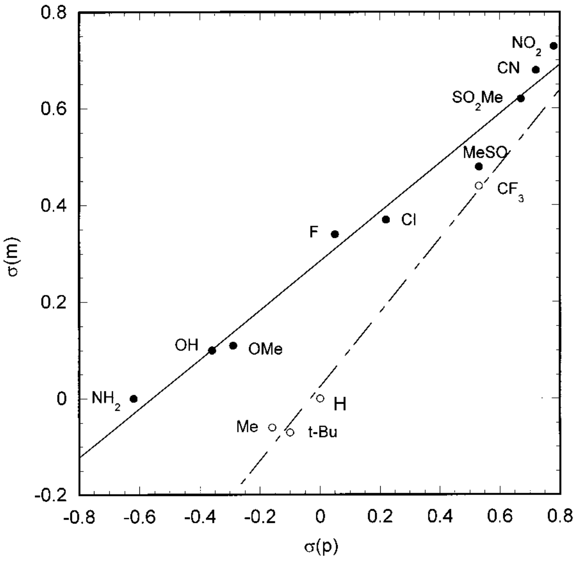

FIGURE 7. Relationship between σ_M and σ_P.

help explain the difference between the two groups of substituents.

6. Summary. The acidities of the substituted benzoic acids are well reproduced by MP2/6-311++G** calculations with corrections for differences in zero-point energies and for the change in enthalpy on going from 0 K to 298 K. The calculations could then be used to examine the origin of the substituent effects.

The acidities of the *meta*- and *para*-substituted acids are correlated with a slope of 0.88. This indicates a strong relationship between the substituent effects at the two positions. The *meta*-substituted acids are more acidic than their *para*-substituted counterparts for electron-releasing substituents, and the reverse is true for strong electron-withdrawing substituents. The origin of the *meta*-substituent effect can be seen in the charge distributions. Whereas a *para*-substituent places a charge at the ipso position, a *meta*-substituent places charges at both *ortho* positions.

A key observation is the good correlation between the acidities of benzoic and phenylacetic acids. Since in the latter case only the field effect will be operative, it suggests that this is also the case for the benzoic acids. The field effect is a Coulombic interaction between the distributed charge in the substituted benzene ring and the carboxylate group.

The gas-phase acidities of the substituted benzoic acids, with the exception of *p*-NH_2 and *p*-OH, are fairly well correlated with σ. The correlation between σ_M and σ_P also was examined, and for a group of substituents from NH_2 and HO through the halogens to NO_2, there was a linear relationship. The other substituents, which are less likely to have hydrogen bonding with the solvent, fell near a separate correlation line. The significance of this observation requires further study.

Calculations. The ab initio calculations were carried out using Gaussian-99,[28] and the Hirshfeld charges were calculated using Hirshd.[29]

Acknowledgment. This investigation was supported by the National Science Foundation.

Supporting Information Available: Tables of structures and energies of benzoic acids and benzoates, MP2 calculated energies, charge distributions, and MP2 calculated atomic coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortis, J. V.; Baboul, A. G.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.;. Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T. A.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian 99, Development Version (Rev. B) Gaussian, Inc., Pittsburgh, PA, 1998.

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