J. Am. Chem. Soc. **2000,** *122,* 357−368

Is the Acetate Anion Stabilized by Resonance or Electrostatics? A Systematic Structural Comparison

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Received August 9, 1999

Abstract: Using ab initio MO theory, a series of isodesmic reactions was studied in which nitrogen-, oxygen-, and fluorine-containing species acted as proton donors and acceptors. Comparison of protonation and deprotonation energies suggests that approximately three-quarters of the enhanced acidity of acetic acid comes from electrostatic stabilization, while the remaining quarter results from π resonance. Similar logic shows that only one-third of the enhanced acidity of the nitrogen analogue acetamidine is electrostatic in nature, and that the remaining two-thirds derives from resonance. The primary importance of electrostatics for oxygen and of π resonance for nitrogen is further supported by the behavior of carbonic acid and guanidine. The contributions of hydroxy, amino, and fluorine substituents to the acidity and basicity of a series of alcohols and amines are well described by a simple electrostatic model with a single adjustable parameter. The model requires the electrostatic contributions of polar bonds to be additive, to be of equal magnitude but opposite sign for anions and cations, and to be strictly proportional to the electronegativity differences between the atoms comprising the bonds. Application of this model to a series of reactions lacking π bonds results in a correlation coefficient of 0.99, and indicates that on average C−F bonds contribute 15 kcal/mol, C−O bonds 9 kcal/mol, and C−N bonds 4 kcal/mol to differential acidity and basicity. Further application of the model allows an estimation of π resonance contributions to the acidity and basicity of acetic acid and a series of related compounds. These π resonance contributions are found to be much greater for nitrogen than for oxygen, and significantly greater for acidity (anions) than for basicity (cations).

Introduction

The greater acidity of carboxylic acids relative to alcohols has generally been attributed to resonance in the carboxylate anion.[1,2] The traditional resonance hypothesis postulates that the carboxylate anion is particularly stable because it is described by two equivalent resonance structures, as shown in Figure 1. Of course, a second resonance contributor can also be drawn for the corresponding carboxylic acid.[3] However, the charge separation required in this zwitterionic species raises its energy, and so there is less stabilization than with the symmetrical carboxylate anion.

During the last 15 years, however, this point of view has increasingly been questioned, and alternative electrostatic explanations have been offered. The electrostatic hypothesis states that the primary role of the carbonyl oxygen is to increase the positive charge on carbon.[4,5] The positive charge stabilizes the increase in negative charge on the adjacent hydroxy oxygen atom that occurs when a proton is lost. A schematic representation of the key electrostatic interactions is shown in Figure 1. Equivalently, one can look upon the additional positive charge at carbon as repelling the hydroxy proton in the neutral acid. Since only the difference in stability between the neutral species and the anion affects the acidity, the two perspectives are essentially the same.

Many studies have addressed the question of which of these two explanations is more correct, or whether they are equally so.[4−19] One common approach involves examining the electronic

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[3] A charge-separated resonance contributor, with no π bonds, can also be drawn (e.g., see refs 10 and 18). To a first approximation, however, this resonance structure is equally important for the neutral molecule and the anion. For the purposes of the present discussion, the resonance contribution to acidity will be understood as referring to the interplay between the more traditional resonance contributors shown in Figure 1.

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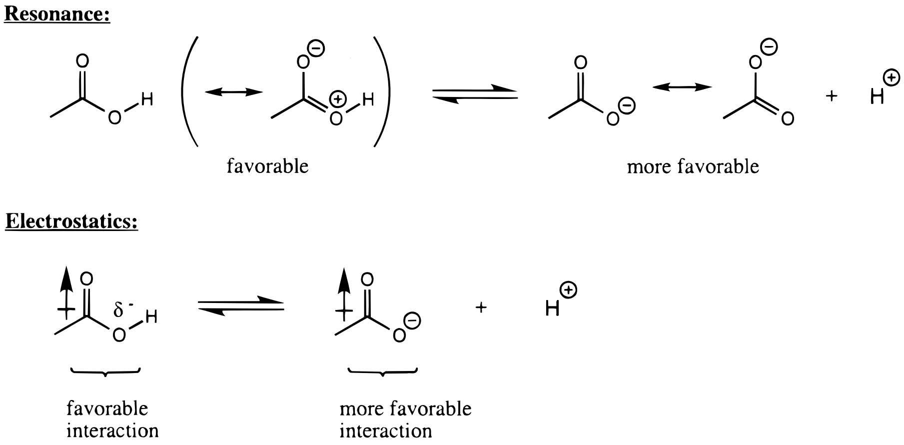

Figure 1. Resonance and electrostatic contributions to the acidity of acetic acid.

structures and physical properties of carboxylic acids and their anions directly. For instance, Siggel and Thomas first challenged the traditional point of view, and supported the alternative electrostatic explanation, based upon the behavior of the oxygen core ionization potentials during deprotonation of the acid.[4] Later, a number of computational studies confirmed this finding by demonstrating that the charge density at the carbonyl oxygen atom of a carboxylic acid changes little upon deprotonation to form the corresponding anion.[6a,7,10,18] These observations suggest that resonance is of minor importance in stabilizing the negative charge in the anion.

Others have attempted to calculate resonance energies or electronic reorganization energies directly. Ji and Thomas have computed a small electronic reorganization energy for deprotonation of a carboxylic acid, consistent with a largely electrostatic explanation.[14] Neto and Nascimento, in contrast, have used generalized multistructural wave functions to conclude that the majority of acidity enhancement results from resonance.[19] Hiberty and Byrman, on the other hand, have arrived at an intermediate position, based on resonance energies that indicate electrostatics and resonance contribute equally to the acidity of carboxylic acids.[17]

Another approach is to use comparisons between related structures to assess the relative importance of electrostatic (or inductive) and resonance contributions. Along these lines, Exner[8] has argued that the key factor leading to enhanced acidity is the stability of the carboxylate anion, not destabilization of the acid, although in fact this observation is consistent with either the resonance or the electrostatic argument.[9] Siggel, Streitweiser, and Thomas have compared the acidities of related conjugated and nonconjugated species in a manner that suggests that 80% of the acidity of acetic acid can be accounted for by electrostatic effects.[10] Dewar and Krull, however, have shown that acidity increases with chain length in a series of vinylogous formic acids, lending support to the resonance argument.[12] More recently, Bordwell and Satish have used comparisons between benzoic acid, 1,3-cyclohexanedione, and tropolone to similarly support the traditional resonance point of view.[15] In response to Dewar and Krull, Thomas has suggested that while resonance is indeed important for the vinylogs, it is not necessarily so for the parent carboxylic acids.[16] Taft and co-workers, on the other hand, have used a multiparameter fit to model the acidities of a series of related compounds, and this description suggests that two-thirds of the enhanced acidity of acetic acid results from electrostatics, and the remaining third from π delocalization.[11]

The analysis presented here follows in the second tradition, of drawing conclusions from comparisons between related structures. Energies and geometries calculated from ab initio MO theory serve as the basis of argument. Both of these properties are experimentally verifiable, and are known to be accurately reproduced by modest levels of ab initio theory for typical unstrained closed-shell organic structures such as acetic acid and acetate ion.[20] Comparisons between acetic acid and a series of related species reveal patterns that are not apparent from the isolated cases, and which offer insight into the factors that affect the acidity and basicity of hydroxy and amino groups in organic compounds.

Results

The primary data used in this study consist of calculated energy changes for a series of isodesmic reactions. The reactions themselves are listed in Schemes 1−9, and the corresponding energies are listed in Table 1. Four levels of theory were used for these calculations: CBS-4, CBS-Q, B3LYP/6-311++G(2df,p)//B3LYP/6-31+G**, and MP2/6-311++G(2df,p)//B3LYP/6-31+G**. CBS-4 and CBS-Q are compound procedures developed by Petersson and Ochterski, and have been shown to reproduce proton affinities of neutral and anionic species, among other properties, with high accuracy.[21] The latter two procedures are recommended for calculation of proton affinities by Turecek, who has found that the average between these MP2 and B3LYP energies gives excellent agreement with the highest levels of ab initio theory.[22] The energies marked “B3MP2” correspond to this average. The energies of the individual species, in hartree units, appear in Table S1 in the Supporting Information.

It is readily apparent from Table 1 that the four levels of calculation agree very closely. Table 2 lists the correlation coefficients and slopes for the best fit lines relating the isodesmic reaction energies calculated via the various methods, and again the agreement is clear, since even the *lowest* correlation coefficient is 0.996. The agreement between the two best levels of theory, CBS-Q and B3MP2, is especially close, and is represented graphically by Figure S1 in the Supporting Information. The excellent accord between the various calculations lends confidence to the computational approach. Henceforth the CBS-Q energies are used for discussion except in the case of

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Table 1. Enthalpies of Isodesmic Reactions (kcal/mol)

reaction	CBS-4[a]	CBS-Q[a]	B3LYP[b]	MP2[b]	B3/MP2[c]
1.1	28.0	27.9	27.8	28.1	28.0
1.2	−6.6	−6.2	−7.2	−6.1	−6.7
1.3	38.0	37.3	37.4	37.5	37.4
1.4	−10.7	−10.7	−11.9	−10.2	−11.1
2.1	26.8	26.7	26.4	27.4	26.9
2.2	9.5	8.4	8.2	8.7	8.4
2.3	29.4	28.4	28.1	29.0	28.6
2.4	12.7	11.7	12.0	12.3	12.2
3.1	46.7	46.0	47.5	46.4	46.9
3.2	5.9	6.3	6.5	5.5	6.0
4.1	15.1	16.3	19.0	16.6	17.8
4.2	29.8	30.6	33.3	31.7	32.5
4.3	47.0	47.2	50.2	48.6	49.4
4.4	−12.8	−13.3	−13.9	−12.3	−13.1
4.5	−29.1	−29.6	−30.5	−28.1	−29.3
4.6	−46.0	−46.9	−48.5	−44.9	−46.7
5.1	10.4	10.6	10.9	10.8	10.9
5.2	19.5	20.4	20.9	21.2	21.1
5.3	24.4	24.0	24.4	24.5	24.4
6.1	5.0	4.3	4.2	4.6	4.4
6.2	6.8	6.3	6.5	6.5	6.5
6.3	11.0	10.4	10.6	10.7	10.6
7.1	6.9	4.9	4.0	3.9	3.9
7.2	7.5	7.2	7.2	7.5	7.4
7.3	8.7	8.2	8.6	8.3	8.4
8.1	21.0	22.6	23.0	22.0	22.5
9.1		12.5	10.3	9.3	9.8
9.2			18.0	16.8	17.4
9.3	18.5		24.9	24.1	24.5
9.4	−1.8		−2.8	−2.2	−2.5
9.5	−3.0		−5.7	−4.5	−5.1
9.6	−6.6		−9.0	−7.7	−8.4

[a] Enthalpy at 0 K. [b] Using the 6-311+G(2df,p) basis set, at the B3LYP/6-31+G** optimized geometry, and with the B3LYP/6-31+G** zero-point vibrational energy (scaled by 0.97) included. [c] Average of B3LYP and MP2 values.

Table 2. Comparison of Different Levels of Calculation (r^2 Values and Slopes)[a]

	CBS-4	CBS-Q	B3LYP	MP2	B3MP2
CBS-4		0.99911	0.99603	0.99805	0.99747
CBS-Q	1.004/−0.38		0.99822	0.99924	0.99919
B3LYP	1.036/−0.75	1.032/−0.37		0.99808	0.99953
MP2	1.001/+0.15	0.997/+0.53	0.965/+0.90		0.99950
B3MP2	1.019/−0.30	1.015/+0.08	0.982/+0.45	1.017/−0.46	

[a] Numbers above the diagonal are correlation coefficients (r^2). Numbers below the diagonal are slopes/intercepts.

silicon-containing species, for which CBS-Q calculations were not feasible and for which B3MP2 energies are used instead. However, none of the conclusions that follow would change in any significant manner if the CBS-4, B3LYP, or MP2 energies were used. The close correspondence between enthalpic properties calculated using these procedures and gas-phase experimental values has been amply demonstrated elsewhere.[20−22]

Discussion

Acetic Acid. The isodesmic reaction 1.1 in Scheme 1 serves as a convenient definition of the unusual acidity of acetic acid. In this reaction, acetic acid exchanges a proton with *tert*-butoxide, so that the acidity of the former is defined relative to that of *tert*-butyl alcohol. Organic chemists generally regard saturated systems as the implicit "normal" reference state, and so an alcohol seems the appropriate standard against which to judge the acidity of hydroxy compounds. Furthermore, the optimal reference alcohol should replace the oxygen atoms of acetic acid with nonpolar substituents of a similar size. Since C−C bonds are more unambiguously nonpolar than C−H bonds, and since carbon atoms are closer in size to oxygen than are hydrogen atoms, *tert*-butyl alcohol is probably the single most appropriate reference, in preference to, say, methanol or ethanol. Reaction 1.1 thus describes an exchange of C−C bonds for C−O bonds, without any potential complication resulting from a change in the number of C−H bonds.

According to this definition, acetic acid is 28.0 ± 0.2 kcal/mol more acidic than "usual", as shown in Table 1. The calculated acidity difference corresponds to the gas phase, since no account has been taken of a solution environment. For the purposes of most experimental chemists, solution acidity is the more relevant parameter. However, as here we are interested in the fundamental principles governing the stability of molecules and ions, the gas-phase values are in fact the most appropriate. The solvent quite likely complicates matters, and while solvation is clearly a topic of great interest and importance, it is nonetheless conceptually a separate issue. The most coherent approach is to consider first the gas-phase properties, and the structural principles governing these properties, and then in a subsequent step to consider the effect of the solvent.

To understand the origin of the 28 kcal/mol of "extra" acidity in acetic acid, it is desirable to decompose this quantity into a resonance contribution and an electrostatic contribution, as shown in eq 1. The coefficient of 2 appears in front of the

$$\Delta E_{\text{acidity enhancement}} = \Delta E_{\text{resonance}} + 2\Delta E_{\text{electrostatics}} \qquad (1)$$

electrostatic term to represent the separate contributions of the *two* additional C−O bonds in acetic acid compared to *tert*-butyl alcohol, one σ and one π.[23]This separation is difficult to accomplish using only information about acetic acid, since there are two variables but only a single known quantity. However, additional chemical equations can be devised that express similar contributing terms, but in different combinations.

"Acetic Base". For instance, why is CH_3CO_2H called acetic acid, and not "acetic base"? As shown in Figure 2, resonance arguments suggest that protonated acetic acid should be stabilized in exactly the same manner as acetate anion. Just as with deprotonation of the hydroxy group, protonation of the carbonyl oxygen yields a species that is described by two equivalent resonance forms, where the charge is distributed equally between the two oxygen atoms, and where the π system contains four electrons. From the simplest resonance perspective, the anionic and cationic cases are indistinguishable.[24]

However, from an electrostatic point of view, protonation of acetic acid is clearly unfavorable (Figure 2). The nearby hydroxy substituent increases the positive charge at carbon, making it more difficult to add a positively charged proton to the carbonyl oxygen than would otherwise be the case. In the case of *protonation* of acetic acid, then, one can write the following simple equation to describe the change in basicity relative to a reference carbonyl compound:

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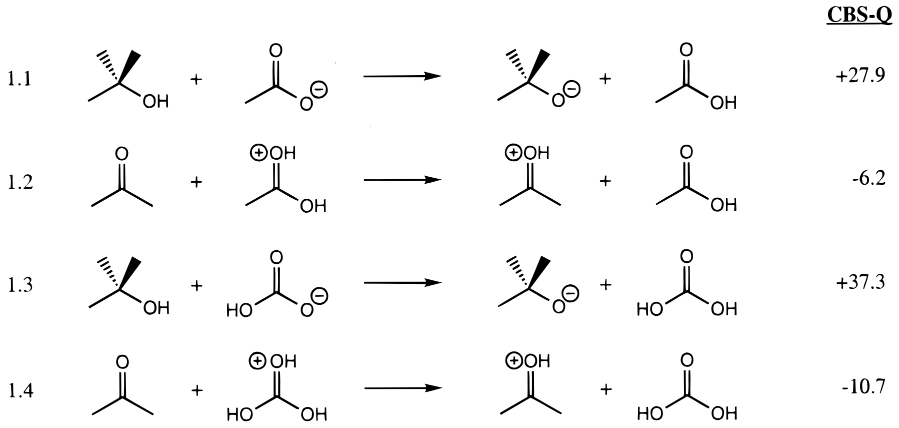
(23) If the coefficient of two for the electrostatic terms in eq 1 is omitted, the qualitative conclusions do not change substantially. However, inclusion of this coefficient provides consistency with the more detailed electrostatic model that is developed and justified later in the text.

(24) The simple resonance picture, in which delocalization is identical in the anionic and cationic cases, of course represents quite a crude approximation. It is well to bear in mind, however, that all models are simplifications, and in fact must be so to serve a useful purpose. Furthermore, this simple resonance picture, in which the energy of delocalization depends only on the number of contributing structures and their energetic similarity to each other, corresponds to both the description given in most textbooks and to the thinking of many practicing organic chemists. It also represents the point of view espoused by Wheland in his classic monograph (ref 1). A more sophisticated MO picture of delocalization would allow for differences between the anion and the cation, but presumably would still predict substantial stabilization in both cases.

Scheme 1



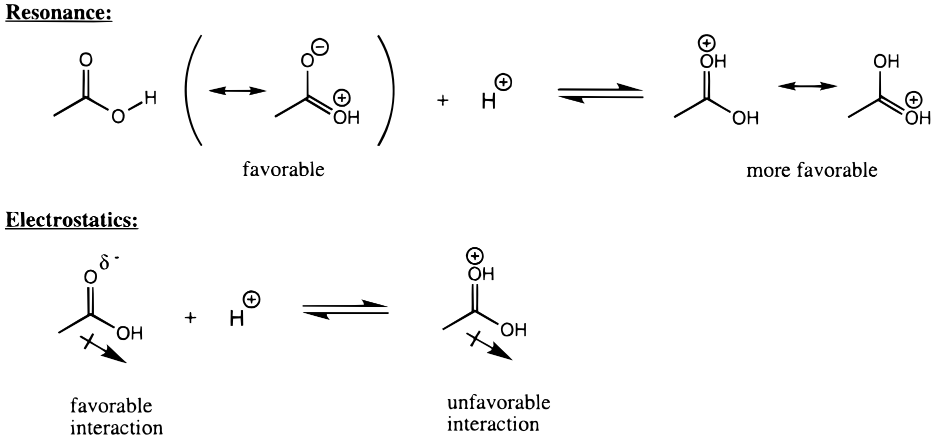


Figure 2. Resonance should enhance the basicity of acetic acid, while electrostatic effects should decrease the basicity.

$$\Delta E_{\text{basicity enhancement}} = \Delta E_{\text{resonance}} - \Delta E_{\text{electrostatics}} \qquad (2)$$

Equation 2 is written with reference to isodesmic reaction 1.2, which defines the proton affinity of acetic acid relative to acetone. Acetone represents the most logical reference compound, since protonation occurs at a carbonyl oxygen, and since, in analogy to reaction 1.1, methyl substitutes for hydroxy. The coefficient of 2 that accompanies the electrostatic term in eq 1 is absent in eq 2, because acetic acid has only one more C$-$O bond than acetone.

The same terms contribute as before for acidity, except now in opposing directions rather than in concert. The assumptions here are that (a) the resonance contributions are of the same magnitude and sign for the positively and negatively charged cases and that (b) the electrostatic contributions are of the same magnitude per C$-$O bond, but of opposite sign. These assumptions are not entirely defensible, particularly with regard to the resonance contributions. Although "pure" resonance theory depicts the cationic and anionic cases as identical, a frontier MO view of π delocalization does not.[24] However, this zeroth-order approximation establishes a useful position from which to begin.

The calculations clearly indicate that acetic acid is not, in fact, "acetic base". Protonation is 6.2 kcal/mol *less* favorable than with acetone, and so the additional hydroxy group clearly *decreases* the proton affinity of the carbonyl oxygen! This finding implies that the electrostatic effect outweighs the resonance contribution.

At this point, two equations accompany the two variables, and so solution is possible. Solving eqs 1 and 2 yields ΔE(electrostatic) = 11.4 kcal/mol per bond (22.8 kcal/mol for a C=O double bond) and ΔE(resonance) = 5.2 kcal/mol. Thus, under the assumption that resonance stabilization is comparable in the anion and the cation,[24] the enhanced acidity of acetic acid derives 80% from electrostatics and 20% from resonance. This outcome agrees closely with the results of Siggel, Streitwieser, and Thomas,[10] who concluded that resonance contributed only 20% to the acidity, and with the conclusions of Taft and co-workers,[11] who estimated the resonance contribution at 30%. The agreement with Hiberty and Byrman, who attributed 50% of the special acidity of acetic acid to resonance, is fair.[17]

Carbonic Acid. This simple model of acidity can be extended more broadly. What, for instance, is the consequence of replacing the methyl group of acetic acid with another hydroxy group? Reaction 1.3 provides the answer: the additional hydroxy group increases the acidity by another 9.4 kcal/mol. This value is a little less than half of the 22.8 kcal/mol electrostatic enhancement caused by the C=O bond in acetic acid. Such a correspondence would be expected if each individual C$-$O bond makes an approximately equal electrostatic contribution.

Furthermore, reaction 1.4 shows that the additional hydroxy group further *decreases* the proton affinity of carbonic acid relative to acetic acid, despite the fact that protonated carbonic acid has *three* equivalent resonance contributors. The additional hydroxy group thus provides not only one additional "unit" of electrostatic destabilization to the cation, but one additional "unit" of resonance stabilization as well. The 4.5 kcal/mol decrease in proton affinity thus represents the difference between the resonance and electrostatic contributions.[25] That acetic acid is the stronger base, and not carbonic acid, reflects the greater importance of electrostatics relative to resonance.

To arrive at a final set of estimates, all the information in reactions 1.1, 1.2, 1.3, and 1.4 can be combined mathematically. If the contribution to acidity or basicity of an additional resonance interaction is designated x, and the electrostatic contribution of a C−O bond is designated y, then the following equations describe the chemical transformations in reactions 1.1−1.4:

$$\begin{aligned} \Delta E(1.1) &= x + 2y \\ \Delta E(1.2) &= x - y \\ \Delta E(1.3) &= x + 3y \\ \Delta E(1.4) &= 2x + 2y \end{aligned} \tag{3}$$

Fitting the CBS-Q reaction energies to these four equations yields $x = 5.2$ kcal/mol for the contribution of a resonance interaction and $y = 11.0$ kcal/mol for the electrostatic contribution of each C−O bond.[26]

What About Nitrogen? Reactions 2.1−2.4 are the exact nitrogen analogues of reactions 1.1−1.4. Reaction 2.1 demonstrates that acetamidine is fully 26.7 kcal/mol more acidic than *tert*-butylamine. Thus, in a relative sense, acetamidine is very nearly as acidic as acetic acid. At first glance, this new information appears to contradict the importance of electrostatics established above. Nitrogen is much less electronegative than oxygen, and therefore typically bears much less negative charge. Consequently, if electrostatic factors are dominant, one might expect acetamidine to have much less strongly enhanced acidity than acetic acid. However, there is no reason to believe, a priori, that resonance contributions should be the same for nitrogen as for oxygen.

Reaction 2.2 shows that acetamidine is also a stronger base than acetone imine. Apparently, in the case of nitrogen, the resonance contribution outweighs the electrostatic contribution. This conclusion is not entirely surprising. We would have expected a weaker electrostatic contribution from nitrogen than from oxygen, since nitrogen is less electronegative. In fact, fresh application of eqs 1 and 2 to reactions 2.1 and 2.2 yields, for nitrogen, ΔE(electrostatic) = 6.1 kcal/mol per C−N bond (12.2 kcal/mol total) and ΔE(resonance) = 14.5 kcal/mol. The roles of resonance and electrostatics are reversed compared to oxygen, with resonance now contributing 60% of the effect, and electrostatics only 40%.

Reactions 2.3 and 2.4 demonstrate the effect of replacing the methyl group of acetamidine with an additional amino group, to form guanidine. Whereas the additional hydroxy group of carbonic acid increased the acidity relative to acetic acid by 9.4 kcal/mol, the additional amino group increases the acidity of guanidine relative to acetamidine by only 1.7 kcal/mol. On the other hand, the same amino group enhances the basicity by 3.3 kcal/mol. This result is qualitatively different from that for carbonic acid, where the additional hydroxy substituent decreased the basicity. With nitrogen, then, it seems abundantly clear that resonance effects are dominant over electrostatic effects.

The same mathematical manipulations that were used to obtain averaged estimates for resonance and electrostatic contributions to all four reactions in the oxygen series (eqs 3) can be applied to the nitrogen series as well. This analysis yields 13.1 kcal/mol for the resonance contribution, and 5.9 kcal/mol for the electrostatic contribution of each C−N bond, again confirming the primary importance of resonance in this series.[26,27] It is also interesting to note that the electrostatic increment, 5.9 kcal/mol, is 54% as great as with oxygen, where the increment was 11.0 kcal/mol. This ratio closely resembles that of the electronegativity[28] differences between carbon and nitrogen on one hand and carbon and oxygen on the other, $(3.4 - 2.6)/(3.0 - 2.6) = 50\%$.

Triple Bonds. With nitrogen, it is possible to consider triple bonds. Scheme 3 lists two isodesmic reactions that explore the effect of a nitrile on the acidity of an amine, and the effect of an amino group on the basicity of a nitrile. The cyano nitrogen of cyanamide is somewhat more basic than acetonitrile, as shown by reaction 3.2. In this case, resonance and inductive effects are in competition. Resonance, which favors the protonated structure, apparently exerts the stronger influence, by a margin of 6.3 kcal/mol. This value agrees closely with the difference between resonance and electrostatic contributions, 13.1 kcal/mol − 5.9 kcal/mol = 7.2 kcal/mol, expected on the basis of Scheme 2.

A cyano group dramatically increases acidity, however, as illustrated by reaction 3.1. Here, electrostatics and resonance act in concert. Two orthogonal and therefore noncompeting resonance interactions stabilize the anion. In addition, the electrostatic stabilization might reasonably be expected to be similar to that for three individual C−N single bonds. From this perspective, the 46 kcal/mol increase in acidity for cyanamide relative to *tert*-butylamine seems reasonable.

Fluorinated Alcohols. If each C−O bond makes a 11.0 kcal/mol electrostatic contribution to acidity and basicity, and each C−N bond contributes 5.9 kcal/mol, what is predicted for fluorine? Linear extrapolation based on the electronegativity differences suggests that each C−F bond should increase the acidity and decrease the basicity by 20 kcal/mol. Reactions 4.1−4.6 show that this prediction is fairly accurate.

Electrostatic considerations can easily explain the enhancement of acidity brought about by fluorination of an alcohol, but in principle hyperconjugation can do so as well.[29−31] As shown in Figure 3, the lone pairs on oxygen are able to donate into the adjacent σ^*_{CF} orbitals. While such interactions can occur

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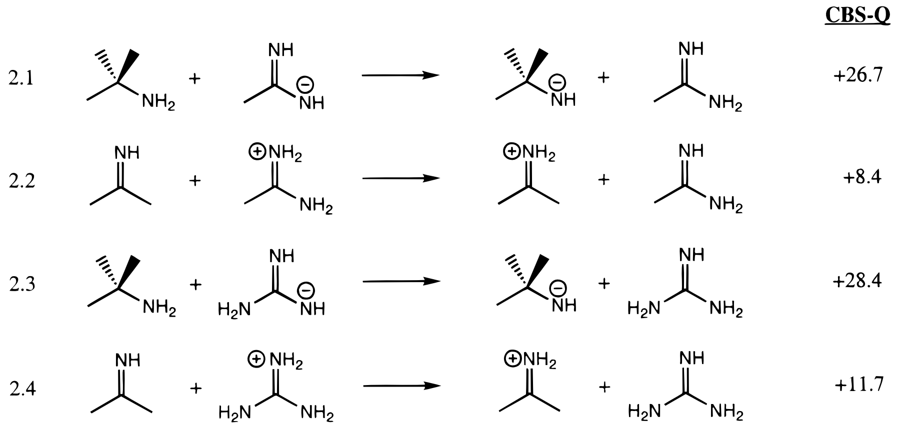
[25] Reactions 1.1 and 1.2 yield estimates of the electrostatic and resonance contributions that differ by 11.4 kcal/mol − 5.2 kcal/mol = 6.2 kcal/mol. The close numerical agreement of this value with the difference in calculated proton affinity between acetic acid and carbonic acid, 4.5 kcal/mol, is very encouraging, as it suggests internal consistency of the model.

[26] This set of four equations in two unknowns is of course overdetermined, even though two of the equations are in fact not linearly independent of each other, and two others are nearly so. The values for x and y reported in the text represent averages obtained by graphical solution of the system of equations. The graphical solutions are provided as Figures S2 and S3 in the Supporting Information.

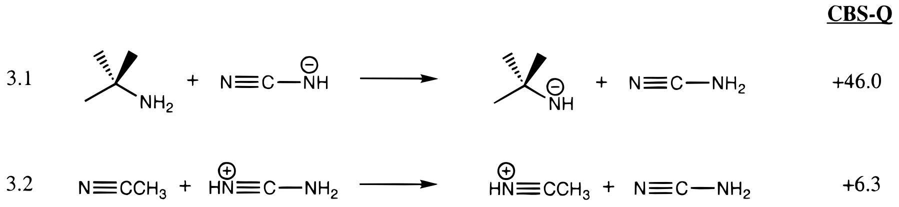
[27] The estimates of resonance and electrostatic contributions derived from eqs 3 and all four of the reactions in Scheme 2 differ somewhat from those obtained using eqs 1 and 2 and only reactions 2.1 and 2.2. In particular, including all four reactions reduces the resonance estimate from 14.5 kcal/mol to 13.1 kcal/mol, although the electrostatic estimate remains essentially constant at 6.0 ± 0.2 kcal/mol per C−N bond. This difference probably arises because multiple resonance contributions do not accumulate in a strictly linear fashion. As a result, consideration of the doubly resonance stabilized guanidinium ion reduces the average stabilization attributed to a resonance contributor. The observation of nonadditivity is hardly surprising, since a saturation effect is expected as additional resonance structures are included, i.e., adding a third equivalent resonance structure when two are already present yields less of an advantage than adding a second when only one structure was available before. Alternatively, from a molecular orbital point of view, the two nitrogen lone pairs compete to donate into the protonated carbonyl π^* orbital, and neither can do so as effectively as it could if it were the only lone pair present.

[28] Allred−Rochow electronegativity values are used throughout this paper: Allred, A. L.; Rochow, E. R. *J. Inorg. Nucl. Chem.* **1958**, *5*, 264−268.

Scheme 2



Scheme 3



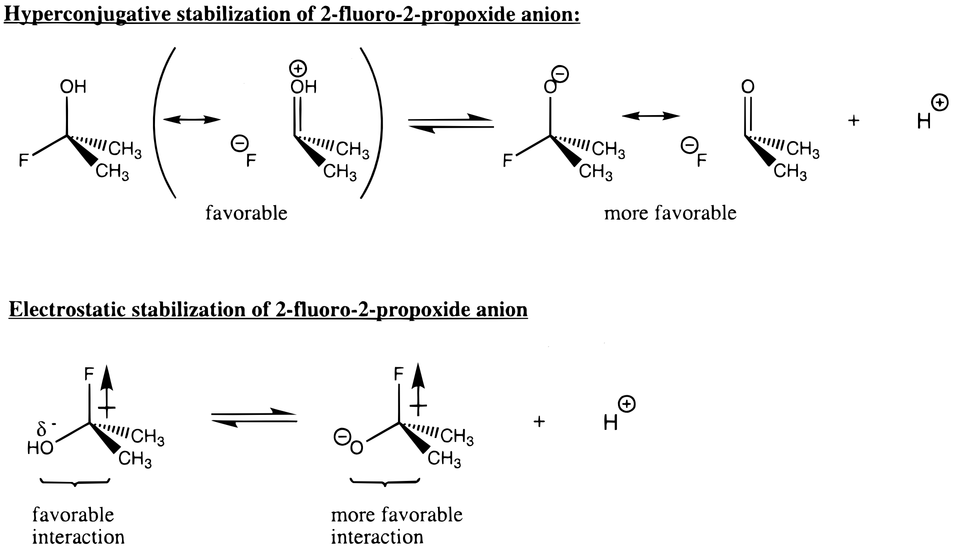


Figure 3. Hyperconjugative and electrostatic explanations for the acidity of 2-fluoro-2-propanol.

both in the neutral alcohol and in the corresponding anion, they would certainly be stronger in the anion, and could thus account for the enhanced acidity of the alcohol. Furthermore, protonation of the alcohol would be expected to inhibit hyperconjugation, and so the decreased basicity of fluorinated alcohols can also be explained by hyperconjugation.

There is in fact some geometric and spectroscopic, as well as theoretical, evidence to support the role of hyperconjugation.[32,33] The hyperconjugative argument predicts that the C−F bonds should lengthen in the anion compared to the neutral alcohol, as the result of increased donation into the C−F antibonding orbitals, and that the C−O bond should correspondingly shorten. Table 3 shows that these changes do indeed take place, and are in fact quite pronounced. These geometric effects have been observed and studied previously, both by experimental and by computational means, including X-ray crystallography.[33] Interestingly, the most dramatic lengthening of a C−F bond occurs in the monofluoro species, and the effect

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(29) (a) Roberts, J. D.; Webb, R. L.; McElhill, E. A. *J. Am. Chem. Soc.* **1950**, *72*, 408−411. (b) Streitwieser, A., Jr.; Holtz, D.; Ziegler, G. R.; Stoffer, J. O.; Brokaw, M. L.; Guibé, F. *J. Am. Chem. Soc.* **1976**, *98*, 5229−5234. (c) Sleigh, J. H.; Stephens, R.; Tatlow, J. C. *J. Chem. Soc., Chem. Commun.* **1979**, 921−922. (d) Schleyer, P. v. R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141−1150. (e) Friedman, D. S.; Francl, M. M.; Allen, L. C. *Tetrahedron* **1985**, *41*, 499−506.

(30) (a) Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1497−1513. (b) Schneider, W. F.; Nance, B. I.; Wallington, T. J. *J. Am. Chem. Soc.* **1995**, *117*, 478−485.

(31) (a) Holtz, D. *Chem. Rev.* **1971**, *71*, 139−145. (b) Holtz, D. *Prog. Phys. Org. Chem.* **1971**, *8*, 1−74.

(32) (a) Francisco, J. S.; Williams, I. H. *Chem. Phys.* **1985**, *98*, 105−114. (b) Grein, F.; Lawlor, L. J. *Theor. Chim. Acta* **1983**, *63*, 161−175. (c) Francisco, J. S.; Williams, I. H. *Mol. Phys.* **1984**, *52*, 743−748. (d) Dewar, M. J. S.; Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 784−790. (e) Ault, B. S. *J. Phys. Chem.* **1980**, *84*, 3448−3450. Oberhammer, however, favors an electrostatic argument in the related fluorinated methane series of compounds: (f) Oberhammer, H. *J. Mol. Struct.* **1975**, *28*, 349−357. (g) Typke, V.; Dakkouri, M.; Oberhammer, H. *J. Mol. Struct.* **1978**, *44*, 85−96.

(33) Farnham, W. B.; Smart, B. E.; Middleton, W. J.; Calabrese, J. C.; Dixon, D. A. *J. Am. Chem. Soc.* **1985**, *107*, 4565−4567.

Table 3. Calculated Bond Lengths (Å)[a]

	C−O bond			C−X bond(s)[c,d]			C−C bond(s)[d]		
species[b]	anion	neutral	cation	anion	neutral	cation	anion	neutral	cation
$C(CH_3)_3OH$	1.3444	1.4443	1.7145				1.5722	1.5304 N	1.5095 Y
								1.5362 Y	1.5084 N
								1.5362 Y	1.5084 N
$C(CH_3)_2FOH$	1.2584	1.3939	1.6651	1.7467	1.4276 Y	1.3450 Y	1.5422	1.5170 N	1.4972 N
								1.5231 N	1.4972 N
$C(CH_3)F_2OH$	1.2349	1.3620	1.6456	1.5211	1.3871 Y	1.3167 Y	1.5326	1.5059 N	1.4863 N
					1.3871 Y	1.3148 N			
CF_3OH	1.2225	1.3474	1.5682	1.4426	1.3347 N	1.2951 N			
					1.3578 Y	1.2951 N			
					1.3578 Y	1.3013 Y			
$C(CH_3)_2(SiH_3)OH$	1.3436	1.4467	1.6898	1.9652	1.9236 N	1.9517 N	1.5599	1.5357 Y	1.5117 Y
								1.5357 Y	1.5107 N
$C(CH_3)(SiH_3)_2OH$	1.3558	1.4592	1.6495	1.9343	1.9189 Y	1.9455 N	1.5564	1.5386 Y	1.5190 Y
					1.9157 N	1.9455 N			
$C(SiH_3)_3OH$	1.3734	1.4724	1.6368	1.9103	1.9096 N	1.9358 Y			
					1.9114 Y	1.9384 N			
					1.9114 Y	1.9380 N			

[a] From B3LYP/6-31+G** geometry optimization. [b] Parent species; bond lengths are shown for the alcohol and for its protonated (cationic) and deprotonated (anionic) forms. [c] X refers to F or Si, as appropriate. [d] Y after a bond length indicates that the bond *is* in conjugation with (i.e., oriented anti to) a lone pair on oxygen; N indicates that the bond is *not* in conjugation with any lone pair on oxygen. Notations are not made for the anions, since all the C−X bonds are equivalent and all the C−C bonds are equivalent (all *are* in conjugation with lone pairs).

decreases markedly as the degree of fluorine substitution increases. The C−F bond length increases by 0.32 Å in 2-fluoro-2-propanol, but by only 0.09 Å, on average, in trifluoromethanol. To a lesser extent, the same observation holds true for the C−O bond, which shortens upon deprotonation by 0.14 Å in 2-fluoro-2-propanol but by only 0.12 Å in trifluoromethanol.

However, an electrostatic argument[31] can also be given for why the C−F bonds should lengthen and the C−O bonds shorten in the anions: the increased negative charge on oxygen repels the negatively charged fluorine atoms and attracts the positively charged carbon atom. Furthermore, one can even rationalize the variation in the degree of lengthening of C−F bonds along the series. As the number of attached fluorine atoms increases, so does the positive charge on carbon, so that the repulsive effect of the negatively charged oxygen is increasingly counteracted.

Furthermore, Table 3 shows that the C−O bond of *tert*-butyl alcohol shortens by 0.10 Å upon deprotonation, only slightly less than it does in the fluorinated species. The C−C bonds lengthen, too, although only by about 0.03 Å. Consequently, the relationship between bond lengths and stabilization is not entirely clear.

Further complicating matters, the difference in length between C−F bonds that are and are not in conjugation with (oriented anti to) oxygen lone pairs in the neutral alcohols is only 0.00−0.02 Å. This variation is far less than the changes of 0.05−0.08 Å observed on going from the neutral alcohols to the protonated forms. These observations suggest that the majority of the geometric changes are the result of electrostatic factors, which do not depend on orientation, rather than hyperconjugation.

The acidity and basicity of fluorinated alcohols can thus be rationalized either by electrostatic or by hyperconjugative arguments. However, the reactions in Schemes 1−4 in aggregate demonstrate that, in the absence of π delocalization, polar bonds very generally make contributions to acidity and basicity that are additive, that are proportional to the electronegativity differences between the atoms, and that are positive or negative depending on whether an anion or a cation is formed. This behavior is highly consistent with an electrostatic model. First, an electrostatic contribution by a polar C−X bond, where X is an electronegative element, would certainly be repulsive for formation of a cation (basicity) and attractive for formation of an anion (acidity). Second, the linear dependence on the electronegativity difference between C and X is exactly what an electrostatic model would predict.

The predicted additivity of electrostatic contributions to the acidity and basicity of fluorinated alcohols depends on a corresponding linearity in the atomic charge at carbon. If the atomic charge on fluorine were to remain essentially the same in the mono-, di-, and trifluorinated alcohols, then the corresponding charge on carbon would linearly depend on the number of attached fluorine atoms. Since the electrostatic effect scales with the charge at carbon, this constancy of atomic charge at fluorine would imply additivity in the electrostatic contributions of the C−F bonds. It has in fact been shown that the charge on fluorine remains essentially constant in the related series of compounds fluoromethane, difluoromethane, trifluoromethane, and tetrafluoromethane.[34] Thus good evidence exists to support the hypothesis that electrostatic contributions from C−F bonds should be additive.

Atomic charges are subject to a great deal of debate, as no single, unambiguously correct definition of atomic charge exists. Furthermore, the magnitudes of calculated atomic charges often vary a great deal depending on which of several popular definitions is used. However, the constancy of fluorine atomic charges in the fluoromethane series holds true for a variety of definitions of atomic charge, and so would seem to reflect an underlying reality.[35]

A Simple Model for the Electrostatic Contributions of Polar Bonds to Acidity and Basicity. As described above, the constancy of atomic charge on fluorine leads to additivity of the expected electrostatic contributions of the C−F bonds. The actual observation of a highly linear relationship is thus highly consistent with an electrostatic origin. Ab initio calculations suggest that oxygen behaves similarly, even to the extent that a C═O bond withdraws the same amount of charge density from

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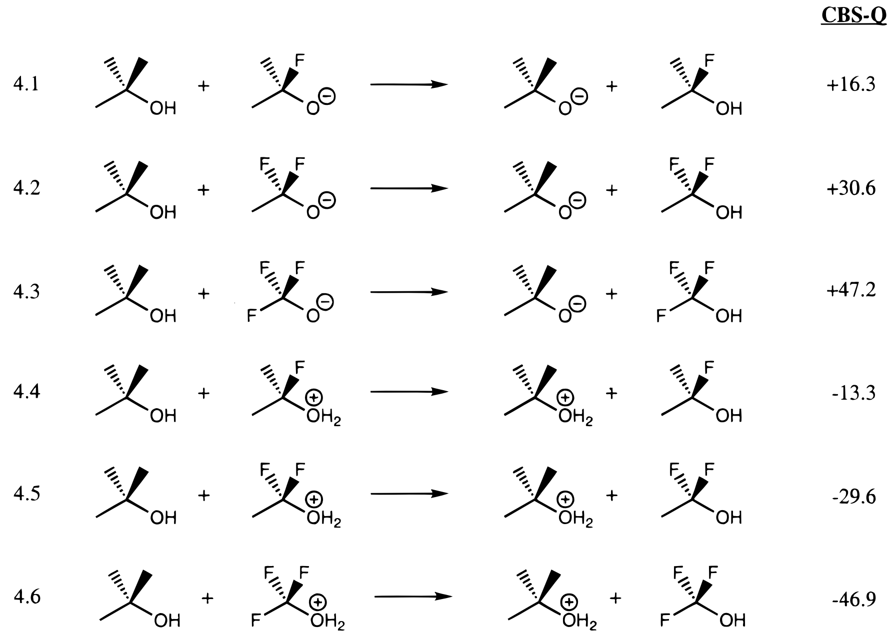
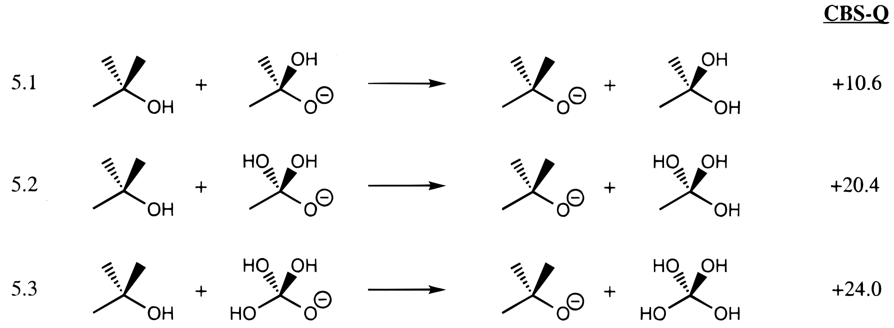
(34) Wiberg, K. B.; Rablen, P. R. *J. Am. Chem. Soc.* **1993**, *115*, 614−625.

(35) (a) Wiberg, K. B.; Rablen, P. R. *J. Comput. Chem.* **1993**, *14*, 1504−1518. (b) Salzner, U.; Schleyer, P. v. R. *Chem. Phys. Lett.* **1992**, *190*, 401−406.

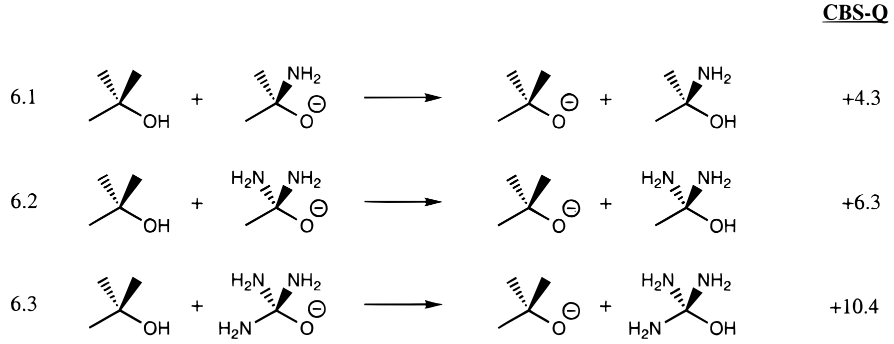
Scheme 4



Scheme 5



Scheme 6



carbon as do two C−O bonds. For instance, a carbonyl oxygen typically bears a charge quite similar to that of an ether or alcohol oxygen. Similarly, the charge on the carbon of an aldehyde or ketone generally is very similar to that in the corresponding hydrate.[36] One might reasonably expect nitrogen to behave in a similar fashion as well.

Thus there is good reason to suspect that the electrostatic contributions of polar bonds to acidity and basicity should quite generally be additive in nature, as well as proportional to the polarity of the bonds. This hypothesis suggests the reactions in Schemes 5−7. These reactions systematically explore the effect of C−O and C−N σ bonds on acidity and basicity, in a manner analogous to that used for fluorine in Scheme 4. If the understanding of electrostatic contributions given above holds merit, then the acidity enhancements should be described quantitatively by the mathematical expression in eq 4, in which a summation is performed over the adjacent polar bonds. The contribution of each bond depends only on a sign *S* that reflects whether a cation or an anion is being generated; the polarity of the bond, as defined by the difference in electronegativity[28] between the atoms involved; and a constant, *C*.

$$\Delta E_{\text{electrostatic}} = S*C*\sum_{\text{bonds}}(\chi_i - \chi_j) \qquad (4)$$

Equation 4 thus describes mathematically the observation that

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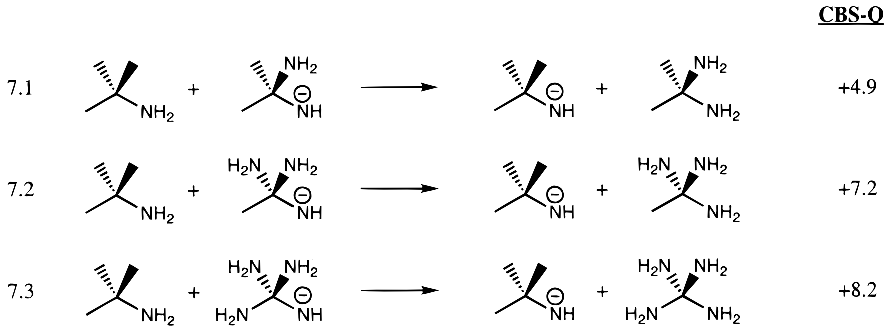
[36] Morgan, K. M. Thermochemistry of Carbonyl Compounds: Hydrate, Hemiacetal and Acetal Formation Reactions. Ph.D. Thesis, Department of Chemistry, Yale University, 1994; pp 58−66.

Scheme 7



polar bonds tend to make contributions to acidity and basicity that are additive and that are proportional to bond polarity. The implied linear additivity of substituent effects bears some resemblance to the classic linear free energy relationships pioneered by Hammett and others.[37]

Table 4 provides the results of applying this equation to the isodesmic reactions in Schemes 1−9. The constant *C* is the only adjustable parameter in the model. If *C* is set to 1, plotting the energies of the isodesmic reactions against the right-hand side of eq 4 yields the linear relationship appearing in Figure 4.[38] The best-fit line, characterized by a correlation coefficient of $r^2 = 0.99$, is drawn through the filled circles. These data points correspond to the reactions in Schemes 4−7, which contain only σ bonds. The slope of the best fit line, 11.0 kcal/mol, represents the optimal value for the constant *C* in eq 4. The simple-minded approach to electrostatic contributions represented by eq 4 thus yields remarkably accurate predictions for systems comprised only of σ bonds! The unfilled circles in Figure 4 do not fall on the line, but these data points correspond to the reactions in Schemes 1−3 and 8, which contain π bonds as well as σ bonds.

As discussed earlier in connection with the acidity of fluorinated alcohols, the contributions of polar σ-bonds to acidity and basicity can be accounted for either by electrostatics or by hyperconjugation, or by a combination of the two. However, for the hyperconjugative explanation, a series of coincidences would seem necessary to account for the all of the observed linearity, whereas this behavior naturally falls out of the electrostatic model, perhaps making the latter argument more succinct. For instance, that a single constant *C* of 11.0 kcal/mol should describe so well the effects of all three elements nitrogen, oxygen, and fluorine, and also the effects on both acidity and basicity, is precisely what one would expect for electrostatic contributions. It is not obvious that hyperconjugation should so exactly yield the same behavior.

Furthermore, the electrostatic contributions to acidity and basicity estimated using two quite different approaches agree closely. Analysis of Schemes 4−7, which contain only σ bonds, led to eq 4 and Figure 4, and thereby to predicted electrostatic contributions of 8.8 and 4.4 kcal/mol for each C−O and C−N bond, respectively. Earlier, however, quite different comparisons were made between the unsaturated species in Schemes 1 and 2. Whereas the substitution patterns in Schemes 4−7 affected acidity and basicity in the same manner, except for sign, the substitutions in Schemes 1 and 2 affected acidity and basicity very differently. The electrostatic and resonance contributions could reasonably be predicted to act in concert with respect to some structural perturbations, but in competition with respect to others. Consequently, the differences between how acidity and basicity were affected by structural changes facilitated deconvolution of the electrostatic and resonance contributions. This different line of reasoning led to estimates of 11.0 and 5.9 kcal/mol for C−O and C−N bonds, respectively. These figures are in fairly close agreement with the corresponding values 8.8 and 4.4 kcal/mol derived from eq 4. Furthermore, it makes sense

Table 4. Comparison of Reaction Energies to Estimates from the Electrostatic Model (kcal/mol)

reaction	electro.[a]	reson.[b]	total[c]	prediction[d]	CBS-Q[e]	diff.[f]
1.1	$+2a$	$+x$	$2a + x$	+17.6	+27.9	+10.3
1.2	$-a$	$+x$	$x - a$	−8.8	−6.2	+2.6
1.3	$+3a$	$+x$	$3a + x$	+26.4	+37.3	+10.9
1.4	$-2a$	$+2x$	$2x - 2a$	−17.6	−10.7	+6.9
2.1	$+2b$	$+y$	$2b + y$	+8.8	+26.7	+17.9
2.2	$-b$	$+y$	$y - b$	−4.4	+8.4	+12.8
2.3	$+3b$	$+y$	$3b + y$	+13.2	+28.4	+15.2
2.4	$-2b$	$+2y$	$2y - 2b$	−8.8	+11.7	+20.5
3.1	$+3b$	$+2y$	$3b + 2y$	+13.2	+46.0	+32.8
3.2	$-b$	$+y$	$y - b$	−4.4	+6.3	+10.7
4.1	$+c$	0	c	+15.4	+16.3	*+0.9*
4.2	$+2c$	0	$2c$	+30.8	+30.6	*−0.2*
4.3	$+3c$	0	$3c$	+46.2	+47.2	*+1.0*
4.4	$-c$	0	$-c$	−15.4	−13.3	*+2.1*
4.5	$-2c$	0	$-2c$	−30.8	−29.6	*+1.2*
4.6	$-3c$	0	$-3c$	−46.2	−46.9	*−0.7*
5.1	$+a$	0	a	+8.8	+10.6	*+1.8*
5.2	$+2a$	0	$2a$	+17.6	+20.4	*+2.8*
5.3	$+3a$	0	$3a$	+26.4	+24.0	*−2.4*
6.1	$+b$	0	b	+4.4	+4.3	*−0.1*
6.2	$+2b$	0	$2b$	+8.8	+6.3	*−2.5*
6.3	$+3b$	0	$3b$	+13.2	+10.4	*−2.8*
7.1	$+b$	0	b	+4.4	+4.9	*+0.5*
7.2	$+2b$	0	$2b$	+8.8	+7.2	*−1.6*
7.3	$+3b$	0	$3b$	+13.2	+8.2	*−5.0*
8.1	0	$+z$	z	0.0	+22.6	+22.6
9.1	$+d$	0	d	−7.7	(+9.8)	(+17.5)
9.2	$+2d$	0	$2d$	−15.4	(+17.4)	(+32.8)
9.3	$+3d$	0	$3d$	−23.1	(+24.5)	(+47.6)
9.4	$-d$	0	$-d$	+7.7	(−2.5)	(−10.2)
9.5	$-2d$	0	$-2d$	+15.4	(−5.1)	(−20.5)
9.6	$-3d$	0	$-3d$	+23.1	(−8.4)	(−31.5)

[a] Predicted electrostatic contribution from eq 4. Electronegativity differences: $a = \chi_O - \chi_C$; $b = \chi_N - \chi_C$; $c = \chi_F - \chi_C$; $d = \chi_{Si} - \chi_C$ ($\chi_{Si} = 1.9$; $\chi_C = 2.6$; $\chi_N = 3.0$; $\chi_O = 3.4$; $\chi_F = 4.0$). [b] Resonance contribution: *x*, O/O; *y*, N/N; *z*, C/C. [c] Total prediction for isodesmic reaction energy (sum of preceding two columns). [d] Electrostatic prediction derived from eq 4, using $C = 11.0$ kcal/mol. [e] CBS-Q isodesmic reaction energy (repeated from Table 1); numbers in parentheses are B3/MP2 values instead of CBS-Q. [f] Difference between observed reaction energy and electrostatic prediction, which can perhaps be attributed to resonance. Numbers in parentheses are derived from the B3/MP2 calculated reaction energies instead of the CBS-Q reaction energies. Values in italics correspond to cases where π resonance is absent and the value of the difference is expected to be close to zero.

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(37) (a) Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96−103. (b) Topsom, R. D. *Prog. Phys. Org. Chem.* **1976**, *12*, 1−20. (c) Wells, P. R. *Linear Free Energy Relationships*; Academic Press: New York, 1968.

(38) The plot in Figure 4 was generated using eq 4 with the value of *C* already set to 11.0 kcal/mol. However, the plot would of course look the same with *C* set to 1, except that the slope would be approximately 11.0 kcal/mol instead of very close to 1.0 kcal/mol.

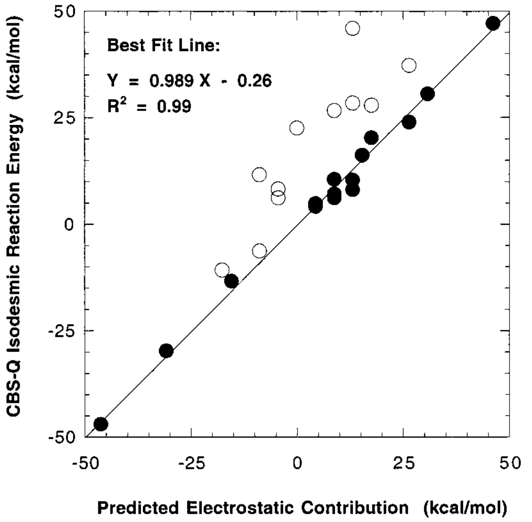


Figure 4. Comparison between the CBS-Q calculated energies of the isodesmic reactions in Schemes 1−7 and the electrostatic contributions predicted by eq 4 with the constant C set to 11.0 kcal/mol. The filled circles represent the reactions in Schemes 4−7, which contain only σ bonds. The unfilled circles represent the reactions in Schemes 1−3 and 8, which contain both π and σ bonds. The best fit line is drawn through the filled circles, and has the following equation: E(CBS-Q) = 0.989 × E(eq 4) − 0.26 kcal/mol; $r^2 = 0.99$.

that the electrostatic contributions are slightly greater in the unsaturated systems, where the bond distances are slightly shorter and the bond angles are somewhat wider (approximately 120° instead of approximately 109.5°).

Nonetheless, there is quite likely no way to make a definitive breakdown between electrostatic and σ-hyperconjugative effects. All one can say with certainty is that the contributions of polar bonds, *excluding π resonance contributions*, are additive, proportional to the electronegativity difference between the atoms, and have a sign that is determined by whether an anion or a cation is being formed.

Estimates of π Resonance Contributions. Having developed a model for the electrostatic contributions to acidity and basicity differences, it is now possible to estimate the π resonance contributions by subtracting the predicted electrostatic component from the total. Graphically, these π resonance contributions are the vertical distances separating the data points in Figure 4 from the line. This subtraction has been carried out in the rightmost column of Table 4. A sharp distinction exists between those species that have π systems and those that do not. The resonance contributions for reactions involving only species with no π bonds are written in italics, and with the exception of the silicon-containing cases in Scheme 9 (discussed below), all are close to zero. This behavior is expected if eq 4 properly accounts for the electrostatic σ contributions it was parametrized to describe. The greatest deviation occurs for reaction 7.3 in Scheme 7, where tetraaminomethane acts as an acid. The large number of intramolecular hydrogen bonds possible in this species and in its conjugate base perhaps lead to this discrepancy. In all other cases, the total reaction energy lies within 3.0 kcal/mol of the electrostatic prediction.

For those reactions where π systems are present, on the other hand, the residual energies are universally positive, and generally quite large. The smallest value, 2.6 kcal/mol, occurs for acetic acid acting as a base. The next smallest value, 6.9 kcal/mol, corresponds to carbonic acid acting as a base. For every remaining reaction with a π system, the apparent π contribution is greater than 10 kcal/mol. Figure 4 illustrates the distinction between systems with and without π bonds graphically. Reactions with only σ bonds (filled circles) fall on the line, while reactions with π systems (open circles) fall well above the line.

According to Table 4, electrostatic factors are responsible for roughly two-thirds (17.6 kcal/mol) of the enhanced acidity of acetic acid, while resonance accounts for the remaining third (10.3 kcal/mol). On the other hand, consideration of *only* the reactions in Scheme 1, via eqs 3, earlier yielded a ratio of 4:1. The more broadly defined electrostatic model represented in Table 4 thus suggests a more even balance between electrostatic and resonance contributions than does Scheme 1 in isolation. However, both approaches clearly identify electrostatics as the predominant cause of the acidity of acetic acid.

Closer examination of the π contributions for the reactions in Schemes 1−3 reveals some interesting trends. First, π resonance interactions are clearly much weaker for oxygen substituents than for nitrogen substituents. Averaging the values in Table 4 corresponding to the reactions in Scheme 1 yields 6.1 kcal/mol as the average contribution of a single oxygen π resonance interaction. For the nitrogen-containing molecules in Schemes 2 and 3, on the other hand, the average π resonance contribution is 13.7 kcal/mol. The much greater importance of resonance when nitrogen is the substituent perhaps results from the higher energy and correspondingly greater donor ability of a nitrogen lone pair compared to an oxygen lone pair. The trend observed here suggests that carbon substituents should yield the strongest resonance interactions of all. Indeed, the energy of 22.6 kcal/mol calculated for the isodesmic reaction in Scheme 8 supports this hypothesis.

Furthermore, these averages hide a substantial difference in the behavior of anions and cations. For the oxygen-containing species in Scheme 1, the average π resonance contribution to acidity is 10.6 kcal/mol, while the average contribution to basicity is only 3.2 kcal/mol. Some part of the difference undoubtedly results from the fact that the cationic average includes a molecule where two interactions compete (protonated carbonic acid), whereas the anionic average does not. Even so, it is clear that the resonance contributions to basicity are less than half as strong as the resonance contributions to acidity.

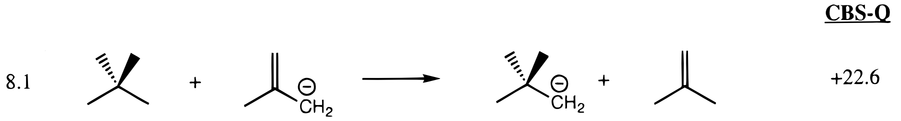
The discrepancy between anionic and cationic stabilization is not as great for nitrogen as for oxygen, but is still substantial. Averaging the reactions in Schemes 2 and 3 yields π resonance contributions of 16.5 and 11.0 kcal/mol for acidity and basicity, respectively.

Carbon−nitrogen triple bonds in general behave somewhat differently from the corresponding double bonds. The reactions in Scheme 3 indicate that the resonance contributions to acidity (i.e., for anions) are greater for C≡N bonds than for C═N bonds, while the contributions to basicity are smaller than for C═N bonds.

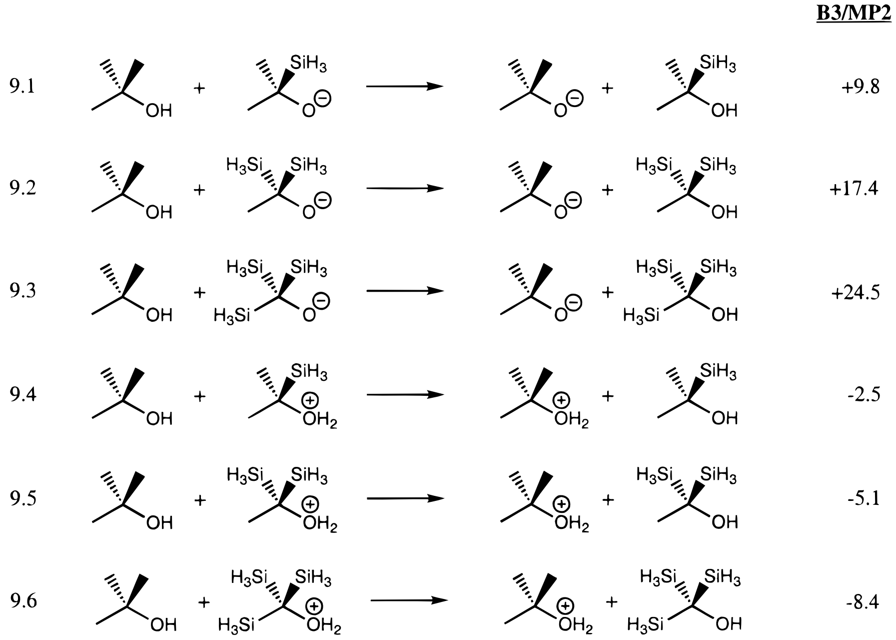
The Anomalous Case of Silicon. Scheme 9 shows reactions analogous to those in Schemes 4−6, but with silyl substituents. On the basis of electrostatic reasoning, it was expected that silicon would enhance the basicity and decrease the acidity, opposite to the effect of nitrogen, oxygen, and fluorine. However, the calculated reaction energies contradict this prediction. In fact, much the opposite occurs: silicon strongly enhances the acidity of an alcohol, and moderately decreases the basicity.

Silicon thus does not follow the model developed for electrostatic contributions of first-row atoms. One possible explanation for the observed enhancement of acidity is that the lone pairs of the anionic oxygens are able to donate hyperconjugatively into the C−Si bonds. Although the polarity of C−Si bonds is not in the direction that would be optimal for such

Scheme 8



Scheme 9



donation, the relatively low-lying σ^* orbital of the C–Si bond makes the suggestion plausible. However, as shown in Table 3, the changes in the C–Si bond lengths upon going from the neutral alcohols to the corresponding anions are very small, in fact no larger than the changes observed for the C–C bonds of the reference compound *tert*-butyl alcohol on going to the *tert*-butoxide anion. Since the hyperconjugative argument would clearly predict greater bond lengthening than is observed, hyperconjugation seems an unlikely explanation for the enhanced acidity. The observation that oxygen lone pairs apparently do not prefer orientations anti to the C–Si bonds in the silyl alcohols further speaks against the presence of important hyperconjugative donation into the C–Si bonds.

A second possibility is that the carbon–silicon bonds stabilize the negative charge by virtue of their high polarizability, similar to the way in which carbon–sulfur bonds stabilize the negative charge in dithiane anions. This explanation seems quite reasonable, except that one would probably expect polarizability to stabilize positive charge as well as negative charge. However, reactions 9.4–9.6 show that silyl substituents in fact modestly decrease the basicity of an alcohol.

Summary

The fact that acetic acid is not an unusually strong base suggests that the majority of its acidity derives from electrostatic stabilization of the acetate anion by the polar C=O bond. The fact that carbonic acid is more acidic, but less basic, than acetic acid further supports this conclusion. On the other hand, that acetamidine exhibits enhanced basicity as well as enhanced acidity suggests that resonance provides the majority of the special stabilization of its conjugate acid and conjugate base. In agreement with this premise, the additional amino group of guanidine further enhances both acidity and basicity with respect to acetamidine. Quantitative application of the above logic leads to the conclusion that approximately three-quarters of the enhanced acidity of acetic acid is electrostatic in nature, and that the remaining quarter results from π resonance stabilization. On the other hand, only about one-third of the enhanced acidity of acetamidine is electrostatic, while the remaining two-thirds results from resonance.[39]

The contributions of hydroxy, amino, and fluorine substituents to the acidity and basicity of alcohols and amines are very well described by a simple electrostatic model with a single adjustable parameter. The model treats the electrostatic contributions of polar bonds as additive, and requires that they be of equal magnitude but opposite sign for anions and cations. The model further requires that each polar bond contributes in a manner that is strictly proportional to the electronegativity difference between the atoms comprising the bond. Application of this model to a series of molecules lacking π bonds yields a correlation coefficient r^2 of 0.99 and a slope of 11.0 kcal/mol. The value of the slope indicates that C–F bonds contribute 15.4 kcal/mol, C–O bonds 8.8 kcal/mol, and C–N bonds 4.4 kcal/mol to differential acidity and basicity.

Application of the electrostatic model permits the estimation of resonance effects by subtraction. This approach suggests that resonance interactions are much weaker for oxygen substituents than for nitrogen substituents, the former averaging 6.1 kcal/mol, compared to 13.7 kcal/mol for the latter. Resonance contributions for carbon are estimated at 22.6 kcal/mol, and thus follow the same trend of increasing as electronegativity decreases.

Furthermore, resonance contributions are consistently smaller for cationic stabilization than for anionic stabilization. In the case of oxygen, resonance interactions contribute 10.6 kcal/mol on average to acidity, but only 3.2 kcal/mol on average to basicity. The divergence for nitrogen is smaller but still

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(39) These rough estimates were obtained by averaging two sets of results: those obtained from the analyses of Schemes 1 and 2, using eqs 3, and those obtained from Table 4, using the electrostatic model represented by eq 4 and Figure 4.

significant, with resonance contributing 16.5 kcal/mol to acidity but only 11.0 kcal/mol to basicity.

The reaction energies also indicate that resonance contributions are not at all additive when two different lone pairs donate into the same acceptor orbital. Instead, the second interaction contributes much less than the first. With $C\equiv N$ bonds, the resonance contributions to acidity are stronger than for $C=N$ bonds, while the contributions to basicity are weaker than for $C=N$ bonds.

Finally, silyl-substituted alcohols behave in a manner almost opposite to that predicted by the electrostatic model. The strong enhancement of acidity, and weak inhibition of basicity, caused by silyl substitution does not appear to result from hyperconjugative interactions either. Polarizability of the silicon atom can be invoked to explain the acidity, although not the basicity.

Calculations

The Gaussian 94[40] and Gaussian 98[41] packages were used to carry out all ab initio calculations. Standard Pople-type basis sets were employed.[20] For molecules with rotatable bonds, all possible rotamers were calculated at the HF/3-21G* level of theory. The lowest-energy conformer was then carried through to higher level calculations.[42] All structures were verified as minima via HF/6-31G* frequency calculations (i.e., no imaginary frequencies). CBS-4 and CBS-Q calculations were carried out using the corresponding keywords. B3LYP/6-31+G** geometry optimizations and frequency calculations were also performed, followed by B3LYP/6-311+G(2df,p) and MP2/6-311+G(2df,p) single-point calculations. Table S1 in the Supporting Information tabulates the CBS-4,[21] CBS-Q,[21] B3LYP,[43] and MP2[44] energies. The CBS-4 and CBS-Q values include zero-point energy (ZPE) corrections by definition. The B3LYP, MP2, and B3MP2 energies in Schemes 1−9 include ZPE's calculated at B3LYP/6-31+G** and scaled by 0.97.[45]

Acknowledgment. Financial support for this work was provided by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by a New Faculty Startup Grant from the Camille and Henry Dreyfus Foundation. Gratitude is expressed to the Department of Chemistry of the University of Washington for use of their computer facilities during a sabbatical leave, and to the research group of Professor Weston Borden in particular for generously hosting this sabbatical and providing a stimulating research environment. The author also thanks Kenneth Wiberg of Yale University for stimulating discussions and for many fruitful collaborations over the past decade which have been instrumental to the development of the ideas presented in this paper.

Supporting Information Available: Energies in hartrees (Table S1); plot comparing CBS-Q and B3LYP/MP2 calculated reaction energies (Figure S1); graphical solutions to eqs 3 using data from Schemes 1 and 2 (Figures S2 and S3); B3LYP/6-31+G** optimized geometries in **Z**-matrix form (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA9928475

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