

The Interaction of Carbonyl Groups with Substituents

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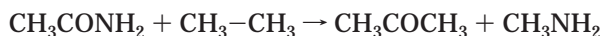
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1. Introduction

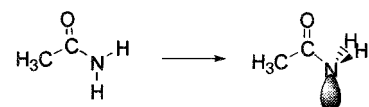
The carbonyl group is probably the most important functional group in organic chemistry, and its properties are strongly affected by substituents. This Account will be concerned with the modes of interaction between carbonyl groups and substituents, and how these interactions are manifested in the properties of the compounds containing this group. A comparison will be made between carbonyl groups and related groups, such as thio-carbonyl.

The interaction of carbonyl groups with substituents has usually been described in terms of π electron interactions such as "amide resonance". However, substituents may affect carbonyl groups in several different ways. They may withdraw or donate electron density via the σ bond, depending on their electronegativity. One of the important features of the carbonyl group is the difference in electronegativity between carbon and oxygen, which leads to both σ and π electron transfer from C to O and to a positively charged carbon. As a result, substituents that have lone pairs may also transfer π electron density to the electron-deficient carbon. Finally, if the atom of the substituent that is attached to the carbonyl group bears a partial charge, it will lead to a Coulombic interaction with the positively charged carbon. All of these modes of interaction have been found.

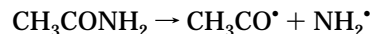
There are three basic ways in which the energetics of the interaction of a carbonyl group with a substituent may be examined. The first makes use of a group-transfer reaction such as



Here, the reaction is used to separate the carbonyl group and its substituent, and the energy change provides a measure of the magnitude of the interaction. A second way makes use of rotational barriers such as



This process removes the normal π interaction between the substituent and the carbonyl group but does not affect the σ interactions. Thus, the group-transfer energy and the rotational barrier may well be different. A third way is to examine the bond dissociation energy:



This should provide information similar to the group-transfer energy.

Although considerable experimental data are available, it is not possible to make detailed comparisons using only experimental data. They must be supplemented by theoretical calculations. Fortunately, recently developed model chemistries such as G2¹ and CBS-Q² are able to reproduce heats of formation and bond dissociation energies with an rms deviation of only ± 1 kcal/mol.³ This is comparable to the uncertainties in many of the experimental measurements. Thus, it becomes practical to combine experimental and theoretical energies in order to provide a more complete picture of the nature of interactions with carbonyl groups.

2. Group-Transfer Energies

Group-transfer energies for the reaction of acetyl derivatives and formyl derivatives have been examined using the G2 energies (Table 1).⁴ Experimental data are available for only some of the compounds, and in these cases the rms deviation between the observed and calculated energy changes is 1.0 kcal/mol,⁴ which is about the same as the experimental uncertainty. Thus, it seems appropriate to use just the G2 energies so that a consistent set of data may be obtained. It is useful to compare the group-

Table 1. Group Separation Energy Changes and Rotational Barriers for Formyl and Acetyl Derivatives

R		X		R		X	
X	GSE	$\Delta H\pi$	$\Delta H\sigma$	X	GSE	$\Delta H\pi$	$\Delta H\sigma$
R = H							
F	+15.0	0.0	+15.0	SH	+5.4	+8.8	-4.5
OH	+22.3	+11.5	+10.8	PH ₂	-4.9	0.0	-4.9
NH ₂	+20.5	+16.0	+4.5	SiH ₃	-14.1	0.0	-14.1
Cl	+5.1	0.0	+5.1				
R = CH ₃							
F	+16.7	0.0	+16.7	SH	+6.1	+8.1	-2.0
OH	+22.7	+11.5	+11.2	PH ₂	-3.9	0.0	-3.9
NH ₂	+19.3	+13.9	+5.4	SiH ₃	-12.7	0.0	-12.7
Cl	+6.8	0.0	+6.8				
R = H, Thiocarbonyl Derivatives							
F	+4.7	0.0	+4.7	SH	+5.2	+10.2	-5.0
OH	+25.7	+12.3	+3.5	PH ₂	-2.2	0.0	-2.2
NH ₂	+18.4	+18.0	+0.5	SiH ₃	-7.4	0.0	-7.4
Cl	+0.1	0.0	+0.1				

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Table 2. Group Separation Energy Changes and Rotational Barriers for Modified Formyl Derivatives

$$\text{H}-\text{C}(=\text{Y})-\text{X} + \text{H}_3\text{C}-\text{CH}_3 \longrightarrow \text{H}-\text{C}(=\text{Y})-\text{CH}_3 + \text{H}_3\text{C}-\text{X}$$

Y	X = NH ₂			X = OH			X = F		
	GSE	ΔHπ	ΔHσ	GSE	ΔHπ	ΔHσ	GSE	ΔHπ	ΔHσ
NH	+13.1	+10.2	+2.9	+15.6	+9.6	+6.0	+9.0	0.0	+9.0
CH ₂	+6.1	+5.1	+1.3	+6.3	+4.0	+2.3	+2.4	0.0	+2.4
PH	+10.7	+11.2	-0.5	+6.2	+6.4	-0.2	-0.8	0.0	-0.8
SiH ₂	+3.9	+5.3	-1.4	-0.1	+3.0	-3.1	-5.1	0.0	-5.1

transfer energies with the rotational barriers, and they are also given in Table 1 as ΔHπ. An examination of the table shows that the group-transfer energies are often larger than the rotational barriers. The latter are well known experimentally for *N,N*-dimethylformamide and *N,N*-dimethylacetamide, and here there is a very good agreement between the calculated and experimental barriers.⁵ The same is true for formamide.⁶ Less precise experimental information is available for acetic and formic acids,⁷ but the calculated values are in good agreement with the experiments in these cases.

The gas-phase rotational barrier for *N,N*-dimethylthioamide has been determined and has been found to be larger than that for *N,N*-dimethylformamide.⁸ In solution, the barriers for thioamides are uniformly larger than those for the corresponding amide.⁹ The calculated values reproduce this trend.¹⁰ Thus, it seems appropriate also to use the G2-calculated rotational barriers for the whole set of compounds.

In the table, the group separation energies are given as GSE and correspond to the total interaction between the substituent, X, and the unsaturated center, C=Y. The rotational barriers for the C–X bond are a measure of the π interaction and are given as ΔHπ. The difference between the GSE and the barrier must involve the σ system and is designated as ΔHσ. It can be seen that this term is large when the attached atom has high electronegativity and changes sign when the substituent is less electronegative than carbon.

Additional information may be obtained by examining related compounds in which C=O is replaced by C=S, C=NH, C=PH, C=CH₂, and C=SiH₂. This would show how the electronegativity of the atom doubly bonded to carbon affects the interaction energy. This series has been examined for the formyl derivatives where the substituents are NH₂, OH, and F (Table 2).⁹

The origin of the rotational barriers will be considered below, and here we shall concentrate on the ΔHσ values. It should be noted that evidence from bond dissociation energies (see below) shows that fluorine and chlorine are not π donors with respect to the carbonyl carbon, and therefore the group separation energies for acetyl fluoride and acetyl chloride may be equated with ΔHσ. An examination of the data shows that the maximum values of ΔHσ are found when the groups attached to the carbonyl carbon are much more electronegative than carbon. Thus, the largest value is found when Y = O and X = F. As the electronegativity of the substituent X decreases, ΔHσ also

Table 3. G2 Bond Dissociation Energies

X	CH ₃ X	CH ₂ =CHX	HC(O)X	CH ₃ COX	HCSX
CH ₃	88.3	100.4	83.4	83.5	87.2
NH ₂ (gs)	83.8	101.8	98.9	97.8	100.6
NH ₂ (ts)		96.8	82.9	83.9	82.6
OH(g)	91.5	109.9	108.9	109.5	106.2
OH(ts)		105.9	97.5	97.9	94.0
F	110.6	121.5	120.7	122.5	114.2
SiH ₃	87.3	96.0	68.9	69.8	78.8
PH ₂	70.2	81.0	60.3	61.5	66.9
SH(g)	73.0	84.6	73.5	74.3	77.1
SH(ts)		83.9	64.7	66.2	66.9
Cl	82.9	92.5	83.1	84.9	81.9

decreases, and when the substituent is less electronegative than carbon, as with SiH₃ and PH₂, the sign of ΔHσ is reversed. Similarly, when Y is less electronegative than oxygen, smaller values of ΔHσ are found, and when Y = SiH₂ and X = F, it changes sign and is -5 kcal/mol.

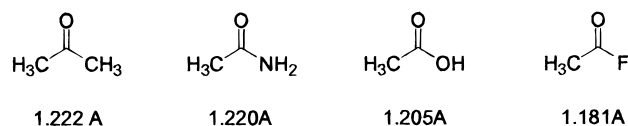
It is clear that electronegativity is the determining factor. Acetyl fluoride is strongly polarized in the sense O⁻-C⁺-F⁻. This will lead to strong electrostatic stabilization and the largest value of ΔHσ. As either Y or X become less electronegative, the bond polarization decreases, and ΔHσ decreases. Finally, with electropositive substituents that will donate electron density to carbon, the stabilization inherent in the carbonyl group is reduced, and the sign of ΔHσ is reversed.

If this argument is correct, it should be possible to find stabilization with reversed bond polarities. The latter may be reversed by making Y = SiH₂ and X = SiH₃, leading to the charge distribution Si⁺-C⁻-Si⁺. The reaction



is calculated to be endothermic by +5.2 kcal/mol. Since one would not expect any π interactions in this case, the energy change may be assigned to ΔHσ, and the compound with two silicons is stabilized electrostatically. The effect is smaller than that found with the first-row substituents, and this must, at least in part, be due to the longer bond lengths to the second-row substituents.

If electrostatic effects are involved, the C=O bond length should decrease as the electronegativity of X increases. The lengths for some acetyl derivatives are¹¹



and the expected change in bond length is found.

3. Bond Dissociation Energies

One of the more fundamental ways in which the energetics of the interaction of a substituent with a carbonyl group may be examined is via the use of bond dissociation energies. Some experimental data are available,¹² but not the complete set that are needed for this study. Therefore, we shall make use of the G2-calculated dissociation energies, and they are given in Table 3. The rms error

between the calculated and the available experimental BDEs for this set of compounds is 1.0 kcal/mol, which is close to the experimental error.³

The relationship between the BDEs is more easily seen in a series of plots (Figure 1). To have a reference plot that does not involve electronegative atoms in the base group, Figure 1a compares the BDEs for vinyl and methyl derivatives. There are small π interaction energies in the vinyl derivatives in which $X = \text{NH}_2$, OH, and SH. These interactions may be minimized by examining the compounds in which the groups have been rotated by about 90° (i.e., the C–X bond rotational transition states). It can be seen that there is a good linear relationship between the vinyl (unconjugated) and methyl dissociation energies ($r^2 = 0.98$), and the slope of the line is close to unity (1.02). It is interesting to note that the vinyl derivative BDEs are uniformly 12 kcal/mol greater than those for the methyl derivatives. This may be attributed to the stronger bonds formed using sp^2 -hybridized orbitals than sp^3 orbitals.¹³

As would be expected, the acetyl and formyl derivative BDEs are linearly related with a unit slope (Figure 1b). The relationship between the acetyl and methyl BDEs is shown in Figure 1c. Here, the closed circles for the acetyl derivatives correspond to PH_2 , SH (unconj), Cl, NH_2 (unconj), OH (unconj), and F, and the line is drawn through these points. These substituents were chosen to define the line since they should have similar hybridization and correspond mainly to an increase in electronegativity. It is interesting to note that the points for acetone and, especially, acetylsilane, fall off the line. The line has $r^2 = 0.99$, and the slope is 1.52.

What is the origin of the large slope when the comparison with the vinyl derivatives gave a slope close to unity? And, why does SiH_3 as the substituent fall so far from the line? The electrostatic factors discussed above provide an explanation for both of these questions. Consider the conversion of acetone to acetyl fluoride. In acetone, the carbonyl group is polarized in the sense $\text{C}^+ - \text{O}^-$ for both the σ and π systems, resulting in a fairly large positive charge at the carbonyl carbon. With methyl fluoride, the 20 kcal/mol increase in BDE as compared to that of ethane may largely be attributed to the electronegativity of the fluorine, which leads to bond polarization in the sense $\text{C}^+ - \text{F}^-$. This results in internal electrostatic stabilization, leading to a stronger bond. With acetone, the replacement of a methyl group by fluorine leads to charge withdrawal from the carbonyl carbon by the fluorine, a negative charge at fluorine, and an increased positive charge at the carbon. The C–F bond in acetyl fluoride is strengthened in the same fashion as with methyl fluoride, but at the same time the increased positive charge at carbon increases the electrostatic interaction with the negatively charged carbonyl oxygen. Thus, the replacement of methyl by fluorine leads to stabilization of both the C–F bond and the C=O bond, making the acetyl derivative more susceptible to electronegative substituents than are the methyl derivatives.

The destabilization of acetylsilane has a similar origin. The silicon of the SiH_3 group has a positive charge since

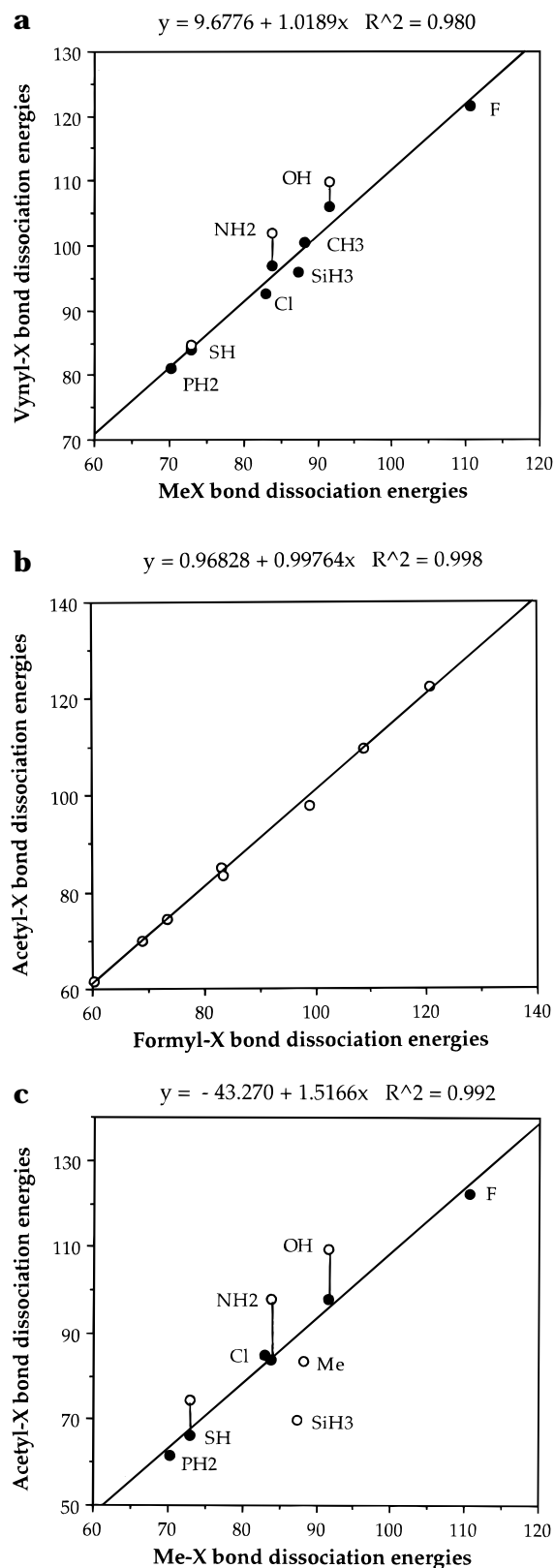
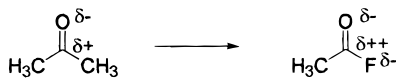


FIGURE 1. (a) Comparison of the bond dissociation energies of vinyl compounds with the corresponding methyl derivatives. For $X = \text{SH}$, NH_2 , and OH, the open circles give the observed BDEs, and the closed circles give the values corrected for the rotational barriers. (b) Comparison of acetyl and formyl derivative BDEs. (c) Comparison between the BDEs of acetyl and methyl derivatives.



the hydrogens are more electronegative than silicon. Now, when it is attached to the carbonyl carbon, two atoms with positive charges are joined, leading to electrostatic destabilization. Similar destabilization would be expected with other substituents having positive charges on the atom attached to the carbonyl oxygen, and it is known that $\text{CH}_3\text{-COCN}$, CH_3CONO_2 , and CH_3COCF_3 all are destabilized in this fashion.⁴

The deviation from the line for the methyl group is probably due to its different hybridization. The carbon forms its bond to the carbonyl group using an sp^3 orbital, whereas the other substituents make use of orbitals with higher p character so that the lone pair(s) may make use of orbitals with relatively high s character.

4. Rotational Barriers

The C–X rotational barriers in amides, thioamides, and carboxylic acids have received much attention. However, an analysis of these barriers might best begin by considering a set of vinyl derivatives. Here, the electronegativity factors that complicate interaction of substituents with carbonyl groups are minimized.

Vinylamine has a small rotational barrier of about 5 kcal/mol, and similar but somewhat smaller barriers are found with vinyl alcohol and vinylthiol.⁴ Rotational barriers involving π donor substituents are usually associated with changes in electron distribution, and an examination of these distributions can provide valuable clues to the origin of the barriers. The change in charge distribution on rotation may be examined by using high-quality ab initio wave functions to calculate a 3-D array ("cube") of electron density about both the planar vinyl derivative and the $\sim 90^\circ$ transition state. One is subtracted from the other, and the difference is presented as a 3-D plot. The difference also may be integrated to give the total change in electron density.

The change on rotation for vinylthiol is shown in Figure 2, where the change in electron density due to the SH group has been deleted. Here, the C–S bond is long enough that both carbons of the vinyl group may be examined without interference from the electron density associated with the hydrogen that moves during the rotation. It can be seen that the terminal methylene group has increased π density in the planar form. However, the other carbon has reduced π density. Thus, it appears that the main role of the sulfur is to polarize the C=C bond when the lone pair on sulfur is aligned with the π orbital of the double bond. This will lead to a stabilizing interaction between the sulfur lone pair electrons and the positively charged end of the double bond.

The changes on rotation for vinylamine and vinyl alcohol are shown in Figure 3. Again, the terminal methylene group gains π density in the planar forms. However, the short C–N and C–O distances make it difficult to

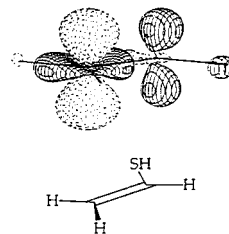


FIGURE 2. Change in electron density distribution on rotation about the C–S bond of vinylthiol.

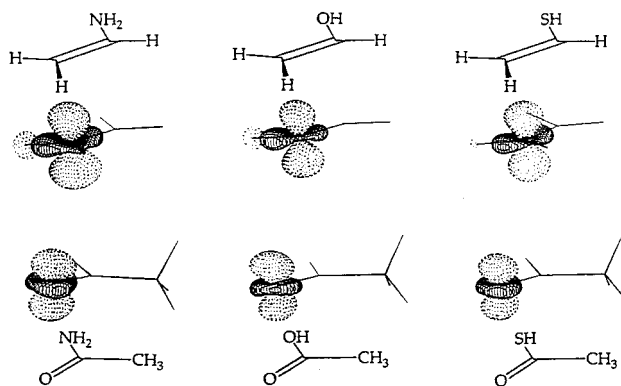


FIGURE 3. Change in electron density distribution on rotation about the C–N bond of vinylamine and formamide, and the C–O bond of vinyl alcohol and formic acid.

separate the changes in electron density due to the rotated group, and therefore it was not possible to examine the other carbon. Thus, in addition to the polarization mechanism found with vinylthiol, it is possible that some charge transfer from N or O to the terminal methylene carbon may occur.

The rotational barriers for amides and carboxylic acids may now be considered. Charge density difference plots are shown in Figure 3. It might first be noted that the changes in π density at the methylene carbon of vinylamine and for the oxygen of formamide are about the same, despite the 3-fold difference in rotational barrier. A similar observation may be made for vinyl alcohol and formic acid. Thus, it appears unlikely that the charge transfer to the carbonyl oxygen of the amides and carboxylic acids can be the main source of the rotational barriers.

The origin of the rotational barrier in amides has received much discussion.¹⁴ Before examining the origin, it seems appropriate to list the observations that have been made concerning the barrier. First, amides tend to be planar but have a relatively low barrier for amino group wagging. The calculated out-of-plane distortion potentials for *N,N*-dimethylformamide and *N,N*-dimethylthioformamide are shown in Figure 4.⁷ In the case of the amide, the potential near the minimum is very flat, and distortions of up to 10° are possible without significantly increasing the energy.

Second, the barrier to rotation about the C–N bond is on the order of 16–20 kcal/mol and is increased on going to polar solvents.^{7,8–15} Thioamides have somewhat larger rotational barriers and stiffer out-of-plane bending po-

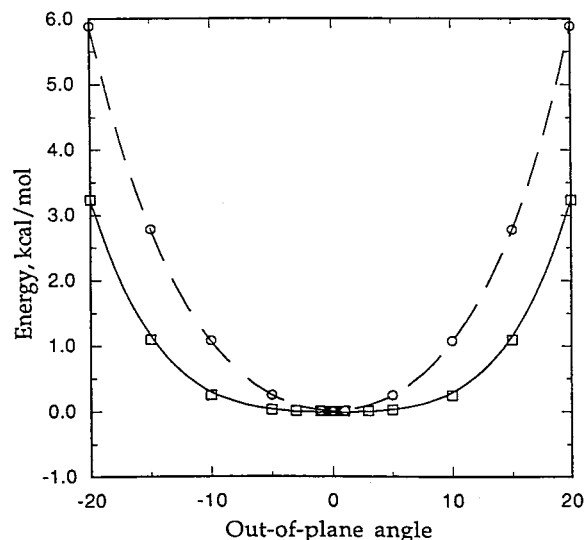


FIGURE 4. Change in potential energy for the out-of-plane wagging mode of the NH_2 groups of formamide (solid line) and thioformamide (dashed line).

tential than amides.^{7,8} Third, amides are less basic than amines and are protonated at oxygen rather than nitrogen.¹⁶

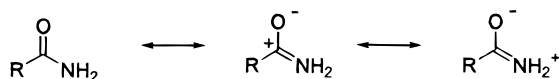
Additional information may be obtained from theoretical calculations. On rotation from the planar form to the rotational transition state, the $\text{C}=\text{O}$ bond shortens only slightly (0.01 Å), whereas the $\text{C}-\text{N}$ bond lengthens considerably (0.08 Å). Experimental data support these calculations.¹⁴ The electron population at oxygen changes only slightly on rotation from the planar form to the rotational transition state. With thioamides, on the other hand, the charge transfer from N to S is considerably larger.

The simple π electron "resonance" model



does not provide an adequate description of amide stabilization. It suggests that the π electron transfer is largely between nitrogen and oxygen, whereas it is largely between nitrogen and carbon. On the basis of this model, one might expect that the changes in $\text{C}=\text{O}$ and $\text{C}-\text{N}$ bond lengths might be comparable, although in opposite directions. In fact, the $\text{C}-\text{N}$ bond length change is much larger than that for the $\text{C}=\text{O}$ bond. Finally, it does not provide a ready explanation of the difference between amides and thioamides.

This description may be improved by adding the carbonyl dipolar structure, which is very important for amides:



The π electron interaction involves mainly the latter two structures, corresponding to the transfer of π electron density from nitrogen to carbon. On the other hand, the

dipolar structure is relatively unimportant for thioamides, and as a result, transfer of π electron density from the nitrogen now involves the sulfur.

All of the above observations are easily accommodated using a frontier MO (FMO) model.¹⁷ In amides, the high electronegativity of oxygen leads to a $\text{C}=\text{O}$ π MO that has its largest coefficient at oxygen. As a result, the empty π^* $\text{C}=\text{O}$ MO has its largest coefficient at carbon. π electron transfer from N to the carbonyl group will mainly lead to an increase in π electron density at carbon. With thioamides, the S and C have similar electronegativities, and therefore the $\text{C}=\text{S}$ π MO coefficients will be similar. The same will be true for the π^* MO (but with opposite signs). Now, π charge transfer from N to the $\text{C}=\text{S}$ group will lead to an increase in the π population at both C and S.

This is not, however, the full story. Resonance arguments are concerned with π electrons, but there usually also are changes in the σ system. One of the simplest is σ/π polarization, in which the σ electrons move in the opposite direction from the π electrons in order to minimize electron repulsion.¹⁸ The σ and π systems are orthogonal and, therefore, do not interact directly. But σ and π electrons still repel each other and try to find an arrangement in which this repulsion is minimized. This can be seen for acetamide in Figure 3, where the loss of π electron density on rotation (dashed contours) is compensated by a gain in σ density (solid contours).

In the case of amides, an additional factor is the change in hybridization at nitrogen on rotation. In the planar form, it adopts sp^2 hybridization with approximately 120° bond angles and places the lone pair in a p orbital. On rotation, the N adopts a pyramidal arrangement similar to that of amines with an $\text{H}-\text{N}-\text{H}$ bond angle of about 106° . Here, the lone pair is placed in an orbital with high s character in order to stabilize it. As a result, for the $\text{C}-\text{N}$ bond the planar N uses an sp^2 orbital, and in the transition state it uses an orbital with high p character and smaller electronegativity. This leads to a smaller σ electron withdrawal by nitrogen in the transition-state structure. Thus, as the N donates π electron density to the carbon in the planar amide, it also withdraws σ electron density from the nitrogen.

5. Effect of Carbonyl Groups on Acidity

It is known that, in the gas phase, formic acid is 40 kcal/mol more acidic than methanol and that the enol of malonaldehyde is more acidic than vinyl alcohol.¹⁹ The increases in acidity are clearly associated with the carbonyl group. How does this group lead to an increase in acidity?

The question has received much study, and two principal mechanisms have been proposed. First, one may recognize that the carbonyl group is strongly polarized in the sense C^+-O^- for both the σ and π systems. The positive charge at the carbonyl carbon will stabilize the developing negative charge in the anion:



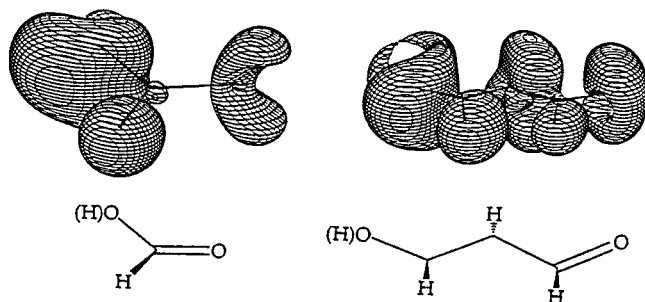
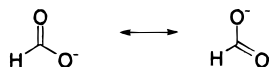


FIGURE 5. Change in electron density distribution on the ionization of formic acid and of malonaldehyde enol.

Symmetry will lead to equalization of the charges at the two oxygens and of the two C–O bond lengths in the anion. Here, it is interesting to note that the proton that is lost has only about 0.5 electron as a result of being attached to an electronegative oxygen, and so there is not so much negative charge to be distributed in the anion. Both oxygens of formic acid have relatively large negative charges, and so there will not be such a large change on going to the anion. In addition, the relative locations of the H and the two O's are unchanged on going from the acid to the anion; only the carbon moves so as to be equidistant from the oxygens.²⁰

The other mechanism is that described by a resonance interaction in the carboxylate ion:



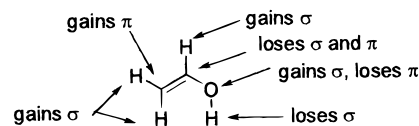
The energetic stabilization that results from this interaction has generally been considered to be the main explanation for the enhanced acidity of carboxylic acids.²¹

Charge density difference plots provide a means for examining the charge shifts that occur on going from a carboxylic acid to its anion, and from the enol of a 1,3-dicarbonyl compound to its enolate ion.¹⁷ Some of these plots are shown in Figure 5.

One striking feature of the charge shifts on going from formic acid to formate ion is the similarity of the charge shifts to the carbonyl oxygen and to the carbon-bound hydrogen that is in the nodal plane of the π system. Integration of the regions in the figure and also examination of electron populations calculated using either the Weinhold–Reed natural population analysis (NPA)²² or Bader's theory of atoms in molecules (AIM)²³ show that both atoms gain about 0.15 electron on going to the anion.¹⁷ This shows the importance of the changes in the σ system that are not taken into account by the resonance formulation.

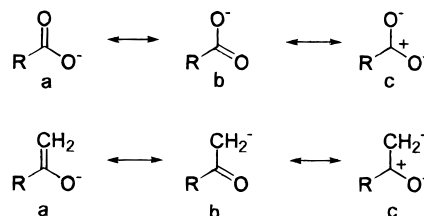
Malonaldehyde enol is another weak acid that has received considerable attention. In the gas phase, it is about 10 kcal/mol less acidic than formic acid. An examination of the change in electron density on going from the enol to the anion (Figure 5) shows a remarkable similarity to that for formic acid. Again, considerable electron density is found at the hydrogens that are in the nodal plane of the π system.

A detailed examination of the factors that lead vinyl alcohol to be more acidic than methanol found the following changes in electron density on ionization:



These changes follow in a logical pattern starting with the oxygen. The proton that is lost has only σ density, which is transferred to the oxygen. The repulsion between the increased oxygen σ density and its π electrons leads to donation of π density to the π^* orbital of the double bond, a loss of π density at the oxygen, and a gain in π density at the terminal carbon. It may also be described classically in terms of the greater polarizability of π bonds: the π electrons of the double bond are polarized by the increased charge at oxygen to make one end more positive and the other more negative. The hydrogens at the terminal carbon gain σ density, again via σ/π polarization at the carbon. Similar changes in charge are found with the vinyllogues of vinyl alcohol.

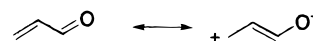
These results, as well as other calculations,²⁴ indicate that, if a resonance formalism is used for the π systems of these compounds, it must include the carbonyl polarized structures, c.



In addition to the changes in the π system, there are also very important changes in the σ system that contribute to the stabilization of the anions.

6. Interaction of Carbonyl Groups with C–C Double Bonds

The interaction of carbon–carbon double bonds with carbonyl groups is easily observed in processes such as the Michael addition. This is often attributed to a resonance interaction of the type



However, stabilization of the ground state in this fashion can only lead to a reduction in reactivity. The fact that addition of nucleophiles to enones occurs so readily, in contrast to ordinary carbon–carbon double bonds, means that the stabilizing effect of the oxygen must be larger in the transition state than in the enone.

There is little evidence for significant ground-state stabilization of enones. An examination of the charge distribution in acrolein on rotation about the central carbon–carbon bond found little change.²⁵

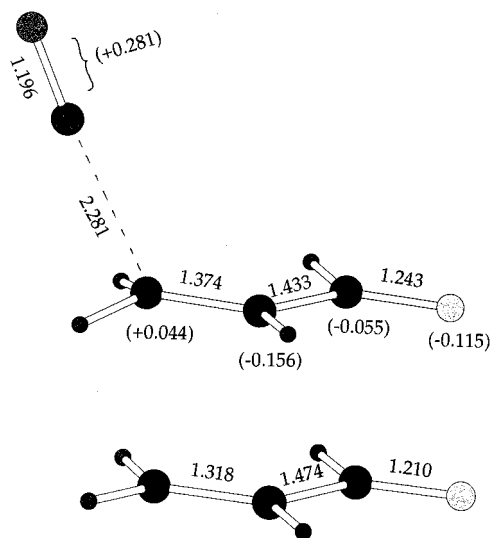


FIGURE 6. Structure of the transition state for cyanide addition to acrolein. The changes in the NPA electron populations on going from acrolein to the transition state are given in parentheses. The hydrogens are combined with the carbons in calculating the populations.

On the other hand, stabilization in the transition state for the Michael addition would be expected since some negative charge can be transferred to the carbonyl oxygen. The MP2/6-31G* optimized geometry for the transition state for the addition of cyanide ion to acrolein is shown in Figure 6, along with the corresponding structure for acrolein. The bond lengths are given along with the change in electron population on going from acrolein to the transition state, as calculated using the NPA method. The C=C and C=O bonds lengthen, the C-C bond shortens, and 0.28 e is transferred from the cyanide ion to the aldehyde in the transition state.

It is interesting that the carbon that is attacked by cyanide ion loses electron population. This is not an artifact of the calculation since the AIM populations lead to the same result. It appears that the negatively charged cyanide ion polarizes the C=C bond and shifts electron density to the adjacent carbon. It also should be noted that much of the negative charge appears at C2, and that the oxygen gains less electron density. This is probably a result of the relative high negative charge at oxygen in acrolein itself, which makes it difficult to accept additional electron density.

7. Addition to Carbonyl Groups—Hydrate Formation

Another characteristic of some carbonyl groups is the addition of molecules such as water or hydrogen cyanide, and again this reaction is strongly affected by substituents. The hydration reaction has been extensively studied, and it is known that formaldehyde is essentially completely hydrated in aqueous solution, acetaldehyde is about 10% hydrated, and acetone is only about 1% hydrated.²⁶ The replacement of the methyl group in acetaldehyde with a strongly electron withdrawing group such as CF₃ or CCl₃ again leads to complete hydration. Strained molecules

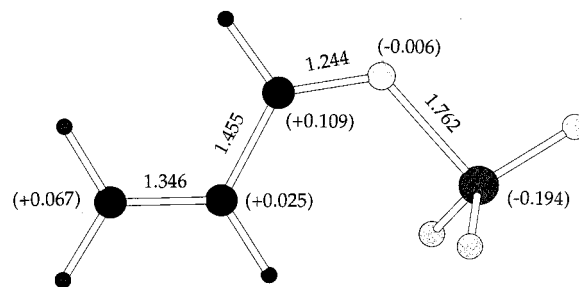


FIGURE 7. Structure of the acrolein-BF₃ complex. The changes in the NPA electron populations on going from acrolein to the complex are shown in parentheses. The hydrogens are combined with the carbons in calculating the populations.

such as cyclopropanone also lead to almost complete hydration.²⁷

Structural effects on hydration equilibria have been examined in some detail both experimentally and theoretically.²⁸ It was found that hemiacetal formation is favored over hydration by 4–5 kcal/mol, and the conversion of hemiacetals to acetals leads to a further 4–5 kcal/mol stabilization. This appears to be a general effect of replacing OH by OR.

The factors that contribute to the stabilization or destabilization of a carbonyl group and of a *gem*-diol group were examined. It was found that alkyl substitution stabilizes a carbonyl group, and that the effect of such groups on the *gem*-diol was considerably smaller. The CF₃ and CCl₃ groups act by destabilizing the carbonyl group more than the *gem*-diol. The differences in the reactions of cyclopropanone through cyclohexanone reflected the combined effects of strain and bond eclipsing.

The origin of the destabilization of a carbonyl group by CF₃ is clear. As noted above, the positively charged carbon of this group will have a repulsive electrostatic interaction with the positively charged carbon of the carbonyl group, leading to an increase in energy. A methyl group will stabilize a carbonyl group by 7 kcal/mol,²⁹ considerably larger than the 3 kcal/mol stabilization of a carbon-carbon double bond. What is the origin of this stabilization? It appears that the methyl C-H bonds will donate electron density to the electron-deficient carbonyl carbon (hyperconjugation).

8. Interaction of Carbonyl Groups with Lewis Acids

Lewis acids often lead to an increase in the reactivity of α,β -unsaturated carbonyl compounds, and Lewis acid catalysis has been found to be very effective in accelerating the rates of some Diels-Alder reactions.³⁰ The structure of the benzaldehyde-BF₃ complex has been studied both experimentally and theoretically.³¹ The calculated structure of the complex of acrolein with BF₃ is shown in Figure 7, and the changes in electron population with respect to acrolein are shown in parentheses. It can be seen that there is a significant decrease in electron population at the terminal methylene group, and that about 0.2 e is transferred from the aldehyde to BF₃. At the same time, the terminal double bond has increased in length by 0.03

Å, while the central C–C bond has shortened by 0.02 Å. The increased polarization is presumably at least in part responsible for the increased reactivity, although transition-state effects may also be important.

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