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Heats of Reduction of Carbonyl Compounds

Kenneth B. Wiberg*,[1a] and Mark A. Murcko[1b]

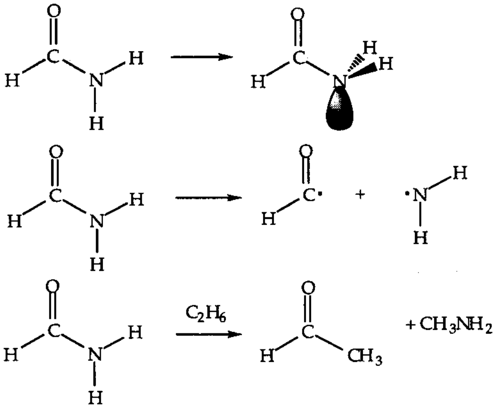
Department of Chemistry, Yale University, New Haven, CT 06520 and
Vertex Pharmaceuticals, 130 Waverly St., Cambridge MA 02139

Abstract: The heats of reduction of a series of compounds having C=C, C=O and C=S bonds have been calculated at the G2 theoretical level. The energy changes are related to the electronegativity, charge and π-donor ability of the substituents, and to the properties of the double bonds. © 1997 Elsevier Science Ltd.

INTRODUCTION

The carbonyl group is probably the most important functional group in organic and biochemistry. Substituents can affect this group in several ways: via π-interactions, inductive effects and electrostatic effects. These effects often lead to important differences in properties and reactivity.

Substituent effects at carbonyl groups have been examined via (a) the calculation of rotational barriers that indicate π-interactions, (b) calculations of bond dissociation energies that give the strength of the bonds, and (c) group transfer reactions that give a measure of the stabilization of the carbonyl group by a substituent relative to a methyl group.[2,3] They are illustrated below with an amino group as the substituent:



Each of these measures a somewhat different interaction, and none of the interactions are "pure" for there always are additional interactions to be considered. For example, the rotational barrier measures mainly the π-interaction with the carbonyl group, but there may also be some intramolecular interactions between the substituent and the σ-bonds in the rotated form. Therefore, it is helpful to have a number of different measures of the interaction so that they may be compared.

The heats of reduction of the carbonyl group to an alcohol would provide additional information.[4] Here, it would be necessary to have some related reactions for a comparison. We have carried out a theoretical study of the reduction of a series of carbonyl compounds, as well as the corresponding compounds having a carbon-carbon double bond and a carbon-sulfur double bond. In the former case, the double bond is non-polar, in contrast to the carbonyl group. The C=O and C=S groups share some common characteristics, but there is a large difference in polarity of the two groups. A comparison of the substituent effects on the three types of double bonds should help in sorting out the origin of the effects.

Table 1. Experimental heats of formation

Compound	$\Delta H_f(298K)$	$\Delta H_f(0K)$	$\Delta H_{redn}(0K)^a$
$CH_2=CH_2$	12.5±0.1	14.5	-30.8±0.2 (-30.5)
CH_3-CH_3	-20.0±0.1	-16.3	
$CH_3CH=CH_2$	4.8±0.2	8.4	-28.1±0.2 (-27.9)
$CH_3CH_2CH_3$	-25.0±0.1	-19.7	
$(CH_3)_2C=CH_2$	-4.0±0.2	1.1	-26.3±0.3 (-26.1)
$(CH_3)_2CHCH_3$	-32.1±0.2	-25.2	
$CH_2=CHCH=CH_2$	26.3±0.2	29.8	-24.7±0.3 (-24.2)
$CH_3CH_2CH=CH_2$	0.0±0.2	5.1	
$H_2C=O$	-26.1±0.1	-25.1	-20.5±0.2 (-18.6)
CH_3OH	-48.2±0.1	-45.6	
CH_3CHO	-39.7±0.1	-37.3	-14.6±0.2 (-13.3)
C_2H_5OH	-56.2±0.1	-51.9	
$(CH_3)_2C=O$	-51.9±0.2	-48.1	-11.3±0.2 (-10.1)
$(CH_3)_2CHOH$	-65.2±0.1	-59.4	
$CH_2=CHOH$	-29.8±2.0	-27.1	-24.8±2.0 (-24.5)

a. Values in parentheses are calculated values (Table 4).

Table 1 gives the available experimental data for the compounds in this study[5] and the derived heats of reduction. It can be seen that there are relatively few data, and so a study of this type requires the calculation of most of the energies of interest. They have been calculated at the G2 theoretical level devised by Pople, et. al.[6] that reproduces the experimental data for a large number of organic compounds with only a ±1 kcal/mol deviation.[7] It is effectively QCISD(T)/6-311+G(3df,2p) plus corrections for the zero-point energy and a higher level correction. When dealing with closely related compounds, the errors would be expected to be even smaller. The G2 energies of the unsaturated compounds are given in Table 2. In some cases it is of interest to try to separate σ and π effects, and therefore the rotational barriers were calculated where appropriate (designated as TS in the Table). The G2 energies for the corresponding saturated compound are given in Table 3. Finally, the heats of reduction obtained using these date are given in Table 4.

It is now possible to make comparisons with the available experimental data. The latter are given in Table 1, and the calculated heats of reduction are given in parentheses. It can be seen that the heats of reduction of C=C groups are very well reproduced at this level of theory. In the case of the C=O groups, the calculated values are high by about 1 kcal/mol

Table 2. G2 Calculated energies of unsaturated compounds

X_1	X_2	$X_1X_2C=CH_2$	$X_1X_2C=O$	$X_1X_2C=S$
H	H	-78.41593	-114.33888	-436.93369
CH_3	H	-117.64502	-153.57683	-476.16827
CH_3	CH_3	-156.87635	-192.81358	-515.40286
NH_2	H	-133.69129	-169.64548	-492.23362
NH_2,TS	H	-133.68317	-169.61993	-492.20488
HO	H	-153.55902	-189.51630	-512.09731
HO,TS	H	-153.55267	-189.49804	-512.07789
F	H	-177.57213	-213.52406	-536.09908
SiH_3	H	-368.66650	-404.58118	-727.18326
PH_2	H	-419.91821	-455.84411	-778.43992
SH	H	-476.16174	-512.10293	-834.69411
SH,TS	H	-476.16063	-512.08895	-834.67790
Cl	H	-537.56830	-573.50789	-896.09139
CN	H	-170.53398	-206.44764	-529.04606
$CH=CH_2$	H	-155.66431	-191.59265	-514.18790

Table 3. G2 Calculated energies of saturated compounds

X_1	X_2	$X_1X_2CH\text{-}CH_3$	$X_1X_2CH\text{-}OH$	$X_1X_2CH\text{-}SH$
H	H	-79.63090	-115.53489	-438.14847
CH_3	H	-118.85578	-154.76444 (t)	-477.37437 (t)
			-154.76428 (g)	-477.37528 (g)
CH_3	CH_3	-158.08431	-193.99608 (C_s)	-516.60462 (C_s)
			-193.99646 (C_1)	-516.60441 (C_1)
NH_2	H	-134.89458 (C_s)	-170.81107 (g)	-493.41586 (g)
		-134.89455 (C_1)	-170.81068 (t)	-493.41406 (t)
HO	H	-154.76444 (t)	-190.67992[a]	-513.28274[a]
		-154.76428 (g)		
F	H	-178.78491	-214.70200 (g)	-537.30052 (g)
			-214.69162 (t)[b]	-537.29467 (t)
SiH_3	H	-369.87822 (C_{3v})	-405.77915 (t)	-728.39689 (t)
PH_2	H	-421.13056 (C_s)	-457.03497	-779.64830
SH	H	-477.37437 (t)	-513.28274[a]	-835.89049[a]
		-477.37528 (g)		
Cl	H	-538.78236	-574.69156 (g)	-897.29603 (g)
			-574.68067 (t)	-897.29266 (t)
CN	H	-171.74721	-207.64750	-530.25968
$CH=CH_2$	H	-156.86927	-192.77737 [c]	-515.38970 (-g)
			-192.77679 [d]	-515.38785 (t)
				-515.38818 (g)

a. +sc,+sc b. rotational transition state. c. CCCO = 120°, CCOH = -60°. d. CCCO = 0°, CCOH = 60°.

indicating a systematic error associated with the G2 model. One might reasonably expect this to be about constant throughout the series that was studied.

Table 4. G2 calculated heats of reduction[a]

X_1	X_2	$X_1X_2C{=}CH_2$	$X_1X_2C{=}O$	$X_1X_2C{=}S$
H	H	-30.5	-18.6	-30.4
CH_3	H	-27.9	-13.3	-25.5
CH_3	CH_3	-26.1	-10.4	-22.2
NH_2	H	-23.2	0.5	-10.0
NH_2,TS	H	-28.3	-15.5	-28.0
HO	H	-24.5	1.7	-12.0
HO,TS	H	-28.5	-9.7	-24.2
F	H	-29.1	-7.3	-22.0
SiH_3	H	-28.5	-19.8	-29.7
PH_2	H	-28.9	-15.4	-26.4
SH	H	-29.0	-8.4	-18.8
SH,TS	H	-30.3	-17.2	-31.6
Cl	H	-29.9	-10.9	-24.0
CN	H	-29.4	-21.0	-29.7
$CH{=}CH_2$	H	-24.2	-11.5	-22.2

a. The G2 energy of H_2 is -1.16636 H.

CONFORMATIONS OF COMPOUNDS.

In many cases, the compounds of interest may exist in several conformations, and it was important to determine which had the lower energy. The conformations of the vinyl derivatives along with their rotational transition states have been studied previously.[2] Acrolein and thioacrolein are known to prefer the transoid conformation.[8] With acetaldehyde, acetone and their thio derivatives, the preferred conformation is known to have a methyl hydrogen eclipsed with the carbonyl or thiocarbonyl group.[9] The conformations and rotational transition states for the formyl and thioformyl derivatives have been studied.[3]

The reduction products have a larger number of possible conformers. Ethanol was found to prefer the trans orientation of the hydroxy group, whereas ethanethiol preferred the gauche orientation of the SH group. Isopropyl alcohol preferred the C_1 (gauche) conformer and isopropylthiol preferred the C_s conformer. Ethylamine had essentially no conformational preference whereas with the phosphine the C_s structure was preferred. With the isopropyl group, the C_1 structure was preferred with the amine, and there was little conformational preference for the phosphine. These results agree with the HF/6-31G* conformational preferences we reported previously.[10]

The compounds with amino or PH_2 groups and hydroxy or thiol groups have a number of possible conformers. The lower energy forms at the HF/6-31G* level had the hydrogens of the amino or PH_2 group anti with respect to the hydrogens of the CH_2 group. The hydroxy group preferred to be gauche in these compounds, and the SH group prefers a gauche position with the amino group as the other substituent, and the anti position with the PH_2 group as the other substituent.

The compounds having two hydroxy or thiol groups, or one of each, were assumed to adopt the preferred anomeric conformation, +sc,+sc.[11]

REDUCTION OF CARBON-CARBON DOUBLE BONDS.

The calculated heats of reduction are in very good agreement with the experimental data (Table 1). The well known, but not well understood, stabilization of carbon-carbon double bonds by methyl groups[12] is reproduced. In the present context, the set of compounds in which one hydrogen of ethylene has been replaced is of special interest. The calculated heats of reduction when the π-interaction with the double bond has been eliminated by rotation of the substituents having lone pairs are as follows:

$H_3CCH=CH_2$	-27.9	$H_3SiCH=CH_2$	-28.5
$H_2NCH=CH_2$	-28.3	$H_2PCH=CH_2$	-28.9
$HOCH=CH_2$	-28.5	$HSCH=CH_2$	-29.6
$FCH=CH_2$	-29.1	$ClCH=CH_2$	-29.9

The substituent induced changes are quite small, and the heats of reduction become slightly more exothermic with increasing electronegativity of the substituent. This corresponds to increasing the energy of the double bond relative to the single bond, and is the expected effect of changing from an sp^3 to an sp^2 hybridized orbital in the bond to the substituent. According to Bent's rule,[13] electronegative groups prefer to be bonded to an orbital with high p character. Thus the lower p character of the sp^2 orbitals leads to destabilization. It is interesting that the second row substituents uniformly give ~1 kcal/mol more exothermic reactiuons and the first row substituents. These data provide a basis for comparison with the C=O and C=S double bonds.

As expected, a vinyl substituent led to stabilization of the C=C bond, and led to a less exothermic reduction (-24.2 kcal/mol). However, a cyano group led to a relatively exothermic reduction (-29.4 kcal/mol) consistent with an electron withdrawing group that does not give a significant π-interaction.

SUBSTITUENT EFFECTS AT CARBONYL GROUPS

The stabilization of the carbonyl group by methyl groups is reproduced by the calculations. The origin of this stabilization will be examined below. The effect of replacing a hydrogen of formaldehyde by a substituent will first be examined, again using the rotated forms for the substituent that have lone pairs so as to minimize π-interactions. The heats of reduction are:

$H_3CCH=O$	-13.3	$H_3SiCH=O$	-19.8
$H_2NCH=O$	-15.5	$H_2PCH=O$	-15.4
$HOCH=O$	-9.7	$HSCH=O$	-17.2
$FCH=O$	-7.3	$ClCH=O$	-10.9

Here, electronegative substituents make the reduction less exothermic, indicating that the carbonyl group is stabilized relative to the saturated product. This is the opposite of what was found for carbon-carbon double bonds, and the magnitude of the effect is considerably larger. A methyl group appears to stabilize a carbonyl by more than an amino group (excluding the π stabilization by the latter). In addition, groups that are electropositive with respect to carbon (e.g. SiH_3, CN) lead to more exothermic reactions, indicating destabilization of the carbonyl group.

These changes are in good agreement with our conclusions derived from bond dissociation energies and group transfer reactions. The energy changes in the above list are largely electrostatic in origin. The carbonyl group is strongly polarized in the sense C^+-O^-. When the atom of a substituent that is bonded to the carbon bears a positive charge, as with a SiH_3 group, there is electrostatic repulsion leading to an increase in energy. This is also the case with the CN group, which gives the most exothermic reaction. On the other hand, an electron withdrawing group such as F will withdraw electron density from the carbon, making it more positive than in formaldehyde. This serves to strengthen the carbonyl group, thus stabilizing it. The electrostatic interaction is seen in the C=O bond length that is significantly shorter in formyl fluoride than in formaldehyde.[14]

A vinyl group as the substituent does lead to a less exothermic reduction, but the effect is small, only 2 kcal/mol with respect to a methyl group.

CARBON-SULFUR DOUBLE BONDS

The stabilization of the carbon-sulfur double bond by methyl groups is somewhat greater than for C=C, but less than for C=O. The monosubstituted compounds for which the π-interaction has been eliminated give the following heats of reduction:

$H_3CCH{=}S$	-25.5	$H_3SiCH{=}S$	-29.7
$H_2NCH{=}S$	-28.0	$H_2PCH{=}S$	-26.4
HOCH=S	-24.2	HSCH=S	-29.0
FCH=S	-22.0	ClCH=S	-24.0

With the first row substituents, the trend is the same as that found with the carbonyl group, with electronegative substituents giving less exothermic reductions. Thus, these groups stabilize the C=S group, but to a much smaller extent than a C=O group. The same trend is seen with the second row substituents, except for PH_2 which appears to be anomalous. This is also the one case where the gauche and syn arrangements for the SH group in the reduction product had the same energy, whereas in the other cases, both OH and SH preferred the gauche position.

ROTATIONAL BARRIERS

In the above, the primary emphasis as been on the substituent effects found with the σ-systems. Another important effect is the interaction of the lone pairs of the substituents with the double bonds. To a first approximation, this is given by the rotational barriers, and these barriers have been calculated where X = NH_2, OH and SH (Table 5). The PH_2 group shows no π-interactions, and generally adopts a conformation which will minimize the interaction of the lone pair with the double bond.[15] Why does S give a π-interaction whereas P does not? The bond angles at both P and S are close to 90° and suggest that the σ-bonds are formed using largely p-orbitals. The lone pair at P is then in an orbital with high s-character, and it will not interact with an adjacent double bonds. The same is true for one of the lone pairs at S, but the other lone pair will be in a p-orbital that can interact with the double bonds.

Table 5. Rotational barriers, kcal/mol

X	XHC=CH$_2$	XHC=O	XHC=S
NH$_2$	5.1	16.0	18.0
OH	4.0	11.4	12.2
SH	0.7	8.8	10.2

The C-X rotational barriers for the vinyl compounds are much smaller than those for the carbonyl derivatives, despite the fact that the amount of charge transfer from X to the terminal atom of the double bond is essentially the same for the two groups of compounds.[3] This indicates that charge transfer to oxygen is not the major factor controlling the rotational barrier in amides, carboxylic acids and their sulfur analogs. The strong polarization of the C=O group in the sense C^+-O^- for both the σ and π systems leads to an electron deficient carbon to which π-density from the X group may be donated. This may also be stated in terms of frontier MO (FMO) theory. The bonding C=O π MO will have its largest coefficient at oxygen because of its high electronegativity with respect to carbon. As a result, the π^* MO, into which the N lone pair electrons may be donated, will have its largest coefficient at carbon, and thus the main π charge transfer from nitrogen to the carbonyl group will be to the carbon. In addition, the hybridization at nitrogen will change from ~sp^2 in the planar amide to ~sp^3 in the rotated form, as may be seen in the change in the bond angles at N (~120° in the planar form and ~107° in the rotated form). Thus, the nitrogen has larger s character and a greater electronegativity in the planar form, and there will be σ donation from carbon to nitrogen to offset the π donation from nitrogen to carbon.

The lower basicity of the lone pair electrons at O and S as compared to N leads to the reduced rotational barriers for formic acid and thioformic acid.

The rotational barrier increases on going from the carbonyl to the thiocarbonyl compounds, and at the same time, the amount of charge transfer from nitrogen in a thioamide to sulfur is much greater than the corresponding charge transfer in the amides.[3] Here, the C=S bond is much less polarized than C=O, and in fact the electronegativities of carbon and sulfur are very similar. Since the sulfur is large and almost neutral, it is relatively easy to transfer charge to it. In an FMO description, the bonding π MO for the C=S group will have similar coefficients at C and S, and the same will be true for the π^* MO. Thus, π-charge transfer from the amide nitrogen will be to both the carbon and the sulfur.

METHYL SUBSTITUENT EFFECTS

One of the more interesting of the substituent effects at double bonds is the stabilization afforded by alkyl groups. The conformational preference for acetaldehyde, i.e. with a methyl hydrogen eclipsed with the carbonyl group, is not difficult to explain, remembering that the rotational barrier is only 1 kcal/mol, or one-third that found in ethane. In the latter case, the main geometrical change found on rotating about the C-C bond is an increase in the C-C bond length by 0.014Å.[16] An examination of the electron densities associated with the C-H localized bond orbitals of ethane (Figure 1) shows why this is the case. There will be a repulsive interaction in the eclipsed form that can best be relieved by stretching the C-C bond. The same will be true for the high energy rotamer of acetaldehyde that has a methyl hydrogen eclipsed with the aldehyde C-H bond. Here, the C-C bond length increases by 0.007Å.[17] Since there is only one CH/CH interaction, it is not surprising that it is one-third that found in ethane. Similar considerations explain the 1 kcal/mol rotational barrier found with methanol and the approximately 2 kcal/mol barrier for methylamine[18]

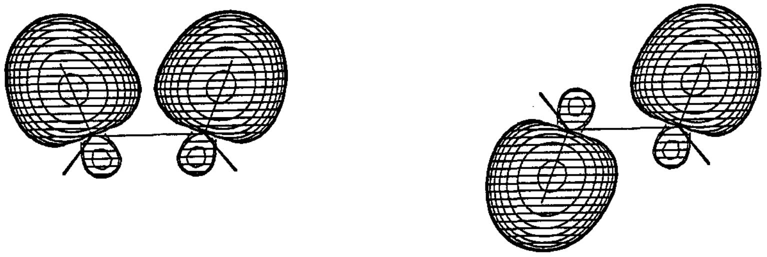


Figure 1. Electron density plots for the CH bond orbitals of eclipsed (right) and staggered (left) ethane. The contour level is 0.001 e/au^3.

It is more difficult to explain the 6 kcal/mol decrease in hydrogenation energies on going from formaldehyde to acetaldehyde. Electron withdrawing groups normally lead to stabilization, and a methyl group must provide another type of interaction.

In order to gain information on the stabilization, we have examined the changes in electron density that occur on going from formaldehyde to acetaldehyde and acetone. The C=O bond length was kept at the average value, but all other geometrical parameters were allowed to relax at the MP2/6-31G* level. The deformation density is defined as the change in electron density on going from spherically symmetrical "proatoms" to the compounds in question. A plot of this type for acetone is shown in Figure 2. Here, one may see the lone-pairs at oxygen and the general trend towards placing extra electron density into the bonds, and taking it away from the atoms.

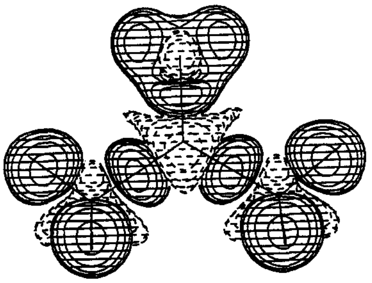


Figure 2. Deformation density plot for the molecular plane of acetone. The contour level is 0.001 e/au^3.

The changes in electron density on going from formaldehyde to acetaldehyde and acetone were examined by subtracting the deformation density for formaldehyde from that of the other compounds. The regions corresponding to the methyl groups were eliminated, and the difference densities at the carbonyl groups were visualized as 3-D contour plots (Figure 3).

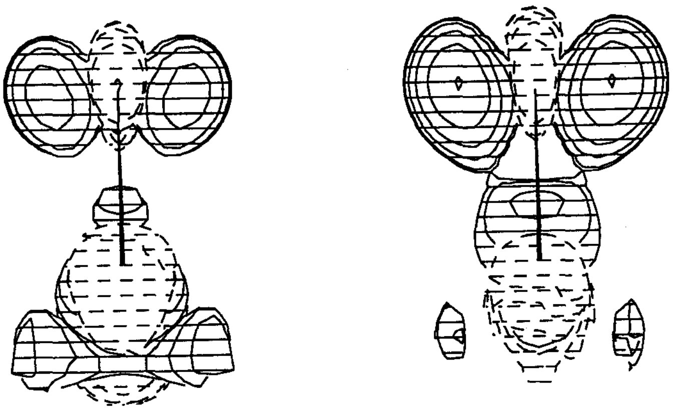


Figure 3. Differences in electron density distributions between acetaldehyde and formaldehyde (right) and between acetone and formaldehyde (left). The carbonyl oxygen is at the top. The contour level is 0.001 e/au^3.

The molecules are viewed looking down the symmetry planes that include all of the non-hydrogen atoms. It can be seen that there is a region about the carbonyl oxygen where π-type electron density is accumulated, and that it is larger for acetone-formaldehyde than for acetaldehyde-formaldehyde. Thus, there is a π-type interaction, which must involve the out-of-plane hydrogens. The interaction may then be properly described as a hyperconjugative interaction between the methyl groups and the carbonyl groups leading to some electron transfer to the carbonyl oxygen. The hyperconjugative interaction could also contribute to the conformational preference. However, it is likely that with a methyl group the interaction will have little conformational preference, and the bond orbital repulsion model does account for the bond lengthening on rotation.

Population analyses lead to the same conclusion. Using the NPA analysis,[19] the charge on oxygen becomes more negative by 0.032 e on going from formaldehyde to acetaldehyde, and by 0.061 on going from formaldehyde to acetone. The corresponding changes derived from the AIM analysis[20] are 0.031 and 0.052 e respectively. Both analyses find the charge at the carbonyl carbon to become more positive with increasing methyl substitution.

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