Hydride Affinities of Carbonyl Compounds. An *ab Initio* Study

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Abstract: Reaction enthalpies for the addition of hydride ion to carbonyl compounds are calculated at the G2(MP2) level of theory for 34 compounds including carbonyl compounds XYCO (where X, Y = H, CH_3, NH_2, OH, F), α,β-unsaturated aldehydes, cycloalkanones, formaldehyde complexed with Lewis acids, and heterocarbonyl compounds. Hydride affinities are analyzed in terms of two isodesmic reactions. These reactions fit available experimental data extremely well, in most cases within 1 kcal/mol. It is concluded that relative to hydrogen, electron withdrawing substituents stabilize both alkoxides and carbonyls, but stabilize alkoxides more. Interaction with a lone pair on a substituent also stabilizes carbonyls, though alkoxides are unaffected. Hydride affinity is most exothermic when inductive effects are largest and lone pair interactions are minimized. Hydride affinities are strongly correlated to the atomic charges of the carbonyl carbon and oxygen but are independent of geometry. The addition of methide, amide, hydroxide, and fluoride to formyl derivatives is examined. Trends in reaction enthalpies relative to addition to formaldehyde are independent of the identity of the nucleophile.

Introduction

The reduction of a carbonyl compound by the addition of hydride ion is an issue of fundamental importance in chemistry and biochemistry. Consequently, there have been many studies of the reduction of various carbonyl compounds with a wide variety of reagents.[1] Yet certain basic questions still cannot be answered. For instance, is an acid chloride more or less susceptible to reduction than an amide? The answer is dependent on the specific experimental conditions, i.e. the reagents, any additives, the solvent, etc. For most reagents, including $LiAlH_4$, $NaBH_4$, AlH_3, and H_2/catalyst, the acid chloride is more easily reduced, but for B_2H_6 the amide is reduced more readily. To answer the question above, one needs the absolute hydride affinities of these carbonyl compounds. Most introductory organic chemistry texts argue that highly electronegative atoms such as chlorine activate the carbonyl group toward nucleophilic attack and that substituents with basic lone pairs such as NH_2 deactivate the carbonyl group through resonance.[2] This argument will be shown to have two flaws: (1) the effect of groups on the product alkoxide is ignored, and (2) relative to hydrogen, electronegative substituents stabilize carbonyl groups. This paper investigates intrinsic hydride affinities using high level ab initio molecular orbital theory. The results are interpreted by examining the effect of substituents on carbonyl compounds and alkoxides.

In many ways the understanding of hydride affinity is much poorer than that of proton affinity. While both areas are well supported by solution phase results, the study of proton affinities has benefited from a large amount of gas phase and theoretical work.[3] These studies have successfully used gas phase ion chemistry to resolve controversies about solution phase data and

have shown that computational chemistry can reproduce and predict gas phase results with remarkable accuracy.

Gas phase proton affinities have been useful in amending a number of hypotheses about intrinsic basicity and nucleophilicity inferred solely from solution data. For example, though methanol is a stronger acid than *tert*-butyl alcohol in solution, the latter is intrinsically the stronger acid as shown by gas phase studies.[4] The higher solution acidity of methanol is an artifact due to poor solvation of the bulky *tert*-butoxide ion. Another problem clarified by gas phase data is the origin of the unusually high nucleophilicity of anions with adjacent heteroatoms, such as HOO^- Two competing theories which explained the so-called α-effect were either poor solvation of the adjacent heteroatoms[5] or secondary orbital interactions.[6] Gas phase studies show that the former is correct.[7]

Can gas phase ion chemistry by used to determine reaction enthalpies for the addition of hydride to carbonyl compounds? Experimental gas phase hydride affinities of XYCO would require the heats of formation, ΔH_f, of XYCO and $XYCHO^-$.[8] The latter value could be obtained from the proton affinity of $XYCHO^-$ and the ΔH_f of XYCHOH. However, the measurement of proton affinities for $XYCHO^-$ has been limited to species where X,Y are either a hydrogen or an alkyl group.[3g] When X,Y are from {F, OH, NH_2}, data may be very difficult

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to obtain since compounds XYCHO⁻ are reactive intermediates in solution. In the gas phase, Wilbur and Brauman have shown that in the addition of cyanide ion to an acid chloride, the species RC(CN)ClO⁻ is a transition state connecting two ion-dipole complexes.[9] Thus, hydride affinities will be studied by computational methods.

A recent study demonstrated that proton affinities could be calculated within ±0.5 kcal/mol.[3h] The G2 methodology and its time-saving variant, G2(MP2), has been shown to give proton affinities, dissociation energies, ionization energies, and electron affinities with an average absolute deviation from experimental values of 1.21 (G2) and 1.58 kcal/mol (G2(MP2)).[10] The G2-(MP2) methodology, which is used in this study, should give reasonably accurate hydride affinities. Previous computational work on hydride affinities has examined primarily the diastereoselective reduction of ketones, and thus many interesting compounds are omitted.[11]

This paper is composed of a section on computational methods followed by separate sections on the hydride affinities of (a) XYCO, (b) α,β-unsaturated aldehydes, (c) cycloalkanones, (d) formaldehyde complexed by H⁺, Li⁺, and Na⁺, and (e) heterocyclic carbonyl compounds.

Computational Methods

Ab initio calculations were completed using the Gaussian 92 program suite.[12] Structures were optimized using the 3-21G, 6-31G* and 6-31+G* basis sets at the Hartree—Fock level and using 6-31G* at the level of Moeller—Plesset second-order perturbation theory (MP2).[13] The 6-31+G* basis set has been shown to be helpful in describing localized ions.[14] All basis sets were used as implemented in Gaussian.[15] All stationary points were confirmed with analytical second derivatives. Electron correlation was accounted for by using MP perturbation theory and Quadratic Configuration Interaction.[16] Standard notation is employed, i.e. HF/6-31G*//HF/3-21G is equivalent to a HF/6-31G* single-point calculation at the optimized HF/3-21G geometry.

Energies were calculated using the G2(MP2) procedure.[10a] In short, geometries are optimized at the MP2=full/6-31G* level. Single-point calculations at the QCISD(T)/6-31G**, MP2/6-31G**, and MP2/6-311+G(3df,2p) levels are then performed to correct for correlation beyond the MP4 level and for basis set deficiencies. A zero-point correction is added using 0.893 times the HF/6-31G*//HF/6-31G* determined vibrational frequencies. Finally, a higher level correction of −0.005 hartrees per valence electron pair is added.

The atoms in molecules atomic populations[17] were determined using a modification of the PROAIM program.[18] Full population analyses were preformed at the HF/6-31G**//HF/6-31G* level for neutrals and

Table 1. Isodesmic Reactions and Hydride Affinities of XYCO[a] (kcal/mol)

X	Y	ΔH_RHA	ΔH_CO calc	ΔH_CO exp (0 K)[b]	ΔH_CHO
H	H	0.0	0.0	0.0	0.0
H	CH₃	1.5	11.1	11.4	9.6
H	CF₃	−26.4	−3.0		23.3
H	HN₂	9.7	31.5		21.8
H	OH	2.3	33.3	34.0	31.0
H	OCH₃	3.8	32.8		29.0
H	F	−12.0	26.1		38.2
CH₃	CH₃	1.9	21.5	21.5	19.6
CH₃	NH₂	9.3	40.9	41.2	31.6
CH₃	OH	2.2	44.0	44.7	41.8
CH₃	F	−10.7	37.9	39.5	48.6
NH₂	NH₂	12.7	54.5	56.8[c]	41.7
NH₂	OH	5.2	59.2		54.0
NH₂	F	−9.2	52.9		62.3
OH	OH	−5.5	58.5		64.0
F	OH	−20.3	50.4		70.8
F	F	−35.5	40.6	50.1[c]	76.1
H	CHCH₂	−1.6	12.0	13.4	13.6
H	CCH	−11.1	3.1		14.2
H	CHO	−15.9	3.1	2.2[c]	19.0
H	CN	−28.3	−2.4		25.9

[a] All energiers use the G2(MP2) methodology and are relative to H₂CO; ΔH_RHA, ΔH_CO, and ΔH_CHO are defined in the text. [b] Reference 21. [c] At 298 K, from ref 3g.

at the HF/6-31+G**//HF/6-31+G* level for anions. Population analyses for the carbonyl and alkoxide C and O atoms were performed at the MP2/6-31G*//MP2/6-31G* level for neutrals and the MP2/6-31+G*//MP2/6-31G* level for anions.

Gaussian calculations were performed on a Cray C-90 at the NSF Supercomputer facility at Pittsburgh (CHE940002P) and on a Sparc-Station 10 at SUNY, Geneseo.

Hydride Affinities of XYCO

The section on XYCO is where most of the major ideas in understanding hydride affinities are presented. This section is divided into (A) a Definition of Terms used throughout the rest of the manuscript, (B) General Observations comparing calculated hydride affinities with experimental data, (C) Isodesmic Reactions which explain the observations from B, (D) Geometries, (E) Atomic Charges which are correlated with the isodesmic reactions in C, and (F) a Comparison with Other Nucleophiles, where the observations shown in B are extended to nucleophiles other than H⁻.

A. Definition of Terms. The enthalpy of reaction for [XYCO + H⁻ → XYCHO⁻] can also be called the absolute hydride affinity of XYCO and can be calculated by subtracting the sum of the ΔH_f's of the reactants from the ΔH_f of the product. This work will focus on the hydride affinity of a species relative to the hydride affinity of H₂CO. This term, the relative hydride affinity, ΔH_RHA, is the difference in the absolute hydride affinity between the species of interest and H₂CO. Thus, the ΔH_RHA for XYCO is defined by the equation

$$\Delta H_{RHA}(XYCO) = (\Delta H_f(XYCHO^-) - \Delta H_f(XYCO)) -$$
$$(\Delta H_f(CH_3O^-) - \Delta H_f(H_2CO))$$

B. General Observations. Hydride affinities of XYCO relative to H₂CO (in kcal/mol) are listed under the column heading ΔH_RHA in Table 1. These numbers correspond to differences in reaction enthalpies: [XYCO + H⁻ → XYCHO⁻] − [H₂CO + H⁻ → CH₃O⁻]. The substituents X,Y are taken from the set {H, CH₃, NH₂, OH, F} (second-row species such as H₂CSHO⁻ proved to be unstable relative to dissociation into

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(18) Graciously provided by Professor Curt Breneman.

an ion-dipole complex, $H_2CO\cdots SH^-$, and hence are omitted). Looking at the series HCOY, it is clear that the hydride affinity is most exothermic when $Y = F$ and least exothermic when $Y = NH_2$. This is consistent with solution data where acyl halides react quickly with weak nucleophiles, while amides react slowly even with powerful hydride donors such as $LiAlH_4$. However, when Y is from $\{H, CH_3, OH, OCH_3\}$ the relative hydride affinities are all quite similar. This is surprising since the $NaBH_4$ reduction of aldehydes ($Y = H$) and ketones ($Y = CH_3$) is quite facile, while the reduction of esters ($Y = OCH_3$) is quite slow under normal reaction conditions.[1]

It should be noted that the ab initio data are thermodynamic, while the experimental data are kinetic. However, these two types of data should be strongly correlated since the reactions in question, addition of a hydride to various carbonyls, are quite similar.

Another unusual observation is that the relative hydride affinities of the CH_3COY series are very similar to the HCOY series. Consider the case where $Y = CH_3$, i.e. acetone versus acetaldehyde. A recent calorimetric study showed a difference in the solution phase heats of reduction of acetaldehyde and acetone of 2.45 kcal/mol, while the calculated gas phase value here is 0.41 kcal/mol.[19] This discrepancy could be attributed to a combination of steric and solvation effects caused by the larger methyl group, since other effects would be accounted for in the ab initio calculation. However, in a recent study, both theoretical and experimental methods showed that in the nucleophilic addition of HOH to carbonyl compounds, a successive decrease of about 2 kcal/mol in reaction exothermicity was seen when the electrophile was changed from formaldehyde to acetaldehyde and from acetaldehyde to acetone.[20]

When the substituents X and Y are both from $\{NH_2, OH, F\}$, values of ΔH_{RHA} do not follow any simple pattern. For instance, successive replacement of H in H_2CO by X and Y to form XYCO does not lead to a linear relationship, i.e.:

$$\Delta H_{RHA}(XYCO) \neq \Delta H_{RHA}(HCOX) + \Delta H_{RHA}(HCOY)$$

These ΔH_{RHA} values will be examined more closely in the next section.

C. Isodesmic Reactions. The major focus of this study is to understand the relative enthalpies of reaction of [XYCO + $H^- \rightarrow$ XYCHO$^-$]. Differences in hydride affinities could come from interactions of the substituents, X,Y, with the carbonyl group, the alkoxide, or both. Recently, Wiberg, Hadad, Rablen, and Cioslowski (WHRC)[21] analyzed a series of carbonyl compounds CH_3COX by using the isodesmic reaction

$$CH_3COX + CH_3-CH_3 \rightarrow CH_3COCH_3 + CH_3-X$$
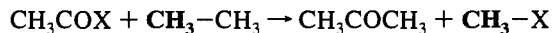
This study will employ a similar methodology at a higher level of theory.[22] In particular, the carbonyl compounds will be studied using the reaction
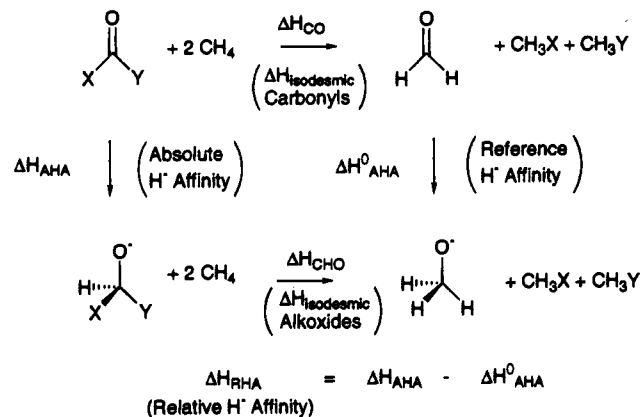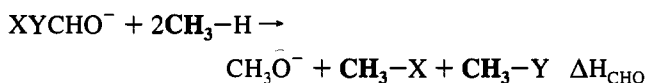
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Figure 1. Relationship between isodesmic reactions and absolute and relative hydride affinities.

$$XYCO + 2CH_3-H \rightarrow$$
$$H_2CO + CH_3-X + CH_3-Y \quad \Delta H_{CO}$$
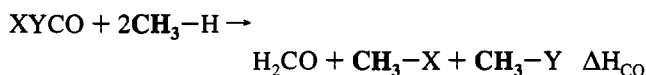
while the alkoxides will be studied using the analogous

$$XYCHO^- + 2CH_3-H \rightarrow$$
$$CH_3O^- + CH_3-X + CH_3-Y \quad \Delta H_{CHO}$$

The relative hydride affinity can be seen from Figure 1 to be the difference between the isodesmic enthalpy for the carbonyl compounds and the alkoxides, i.e.:

$$\Delta H_{RHA} = \Delta H_{CO} - \Delta H_{CHO}$$

Experimental and calculated values of the isodesmic reaction enthalpies for the carbonyl compounds XYCO are shown in the columns labeled ΔH_{CO} in Table 1. Note that increasingly positive values of ΔH_{CO} for XYCO correspond to increasing stabilization of C=O by the groups X,Y. The agreement in ΔH_{CO} between experiment and theory is excellent, usually within 1 kcal/mol. An important exception is the ΔH_{CO} for F_2CO where the difference is nearly 10 kcal/mol. This value is surprisingly large and it is tempting to think that the experimental ΔH_f for the highly reactive F_2CO may be incorrect. WHRC achieved nearly as good agreement for the CH_3COX series using a lower level of theory.

As WHRC have shown for the CH_3COX series, the values of ΔH_{CO} for the HCOX series are due to a competition between two stabilizing factors. The first, inductive electron withdrawal, parallels the electronegativity of the attached group X and follows the order F > OH > NH_2 > CH_3 > H. Stabilization results from Coulombic attraction between the partially negative substituent and the partially positive carbonyl carbon. The second, interaction of the lone pair with the carbonyl, parallels the basicity of the lone pair in the group X and follows the order NH_2 > OH > F. The net effect is that both OH and NH_2 are better at carbonyl stabilization than F.

In comparing the CH_3COX to the HCOX series it is seen that the differences in ΔH_{CO} are a constant factor of about 10 kcal/mol, which is the difference in ΔH_{CO} for CH_3CHO and H_2CO. However, as shown in Figure 2, when both substituents are from the set $\{NH2, OH, F\}$, the isodesmic enthalpies are not additive, i.e.:

$$\Delta H_{CO}(XYCO) \neq \Delta H_{CO}(HCOX) + \Delta H_{CO}(HCOY)$$

This could be due to a limit in the amount of stabilization achievable by either induction or lone pair interaction. Neither of these factors seems particularly compelling. F_2CO shows
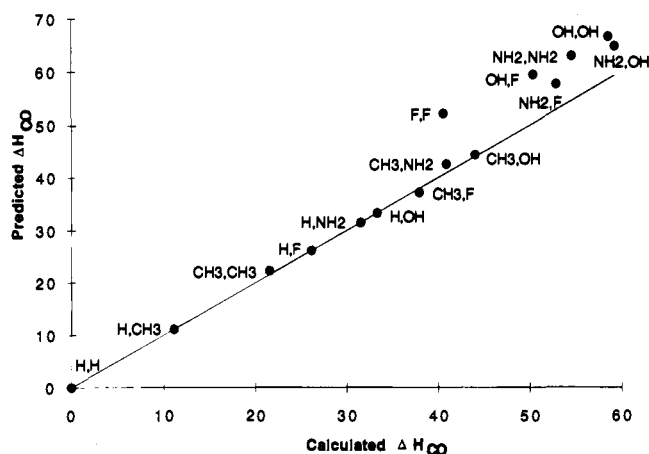
Figure 2. Predicted versus calculated ΔH_{CO} for XYCO. Predicted $\Delta H_{CO}(XYCO) = \Delta H_{CO}(HXCO) + \Delta H_{CO}(HYCO)$.
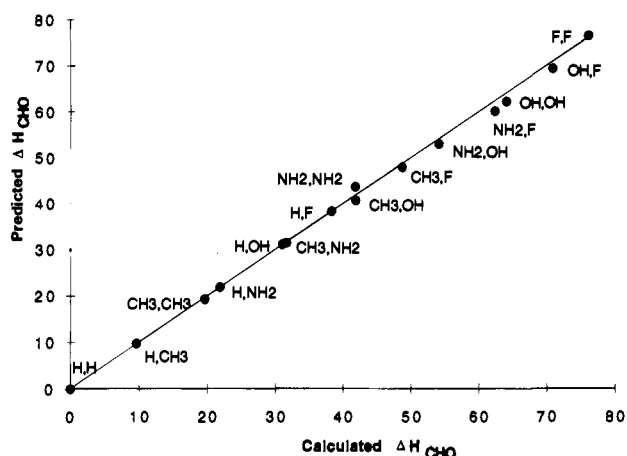

Figure 3. Predicted versus calculated ΔH_{CHO} for XYCHO$^-$. Predicted $\Delta H_{CHO}(XYCHO^-) = \Delta H_{CHO}(H_2CXO^-) + \Delta H_{CHO}(H_2CYO^-)$.

the maximum deviation from linearity, yet lone pair interactions are minimal. While induction might be hindered due to electrostatic repulsion between the partially negative groups X and Y, inductive effects are shown to be additive in the alkoxide series, vide infra.

The isodesmic reaction enthalpies for the alkoxides, XYCHO$^-$, are shown in the column labeled ΔH_{CHO} in Table 1. As is the case for ΔH_{CO}, increasingly positive values of ΔH_{CHO} for XYCHO$^-$ correspond to increasing stabilization of C$-$O$^-$ by the groups X,Y. For the H$_2$CXO$^-$ series, ΔH_{CHO} is maximum when X = F and decreases as such: F > OH > NH$_2$ > CH$_3$ > H. This ordering follows the Pauling electronegativity for the attached atom. Moreover, successive replacement of two hydrogens in H$_2$CHO$^-$ by X and Y to yield XYCHO$^-$ results in a linear relationship, which is plotted in Figure 3, i.e.

$$\Delta H_{CHO}(XYCHO^-) = \Delta H_{CHO}(H_2CXO^-) +$$
$$\Delta H_{CHO}(H_2CYO^-)$$

Thus XYCHO$^-$ is stabilized by induction and this stabilization is additive.

Hydride affinities can now be rationalized. Electron withdrawing substituents stabilize both alkoxides and carbonyls, but they stabilize alkoxides more. Interaction with a lone pair on a substituent also stabilizes carbonyls, though alkoxides are unaffected. The hydride affinity of XYCO is most exothermic when inductive effects are largest and lone pair interactions are minimized, when X = F, and is least exothermic when lone pair interactions are maximized and inductive effects are small,

Table 2. Structures of XYCO and XYCHO$^-$. MP2=full/6-31G* (Å)

X	Y	XYCO $R(C=O)$	XYCHO$^-$ $R(C-O^-)$	X	Y	XYCO $R(C=O)$	XYCHO$^-$ $R(C-O^-)$
H	H	1.220	1.323	NH$_2$	NH$_2$	1.225	1.297
H	CH$_3$	1.222	1.324	NH$_2$	OH	1.219	1.292
H	CF$_3$	1.215	1.318	NH$_2$	F	1.202	1.260
H	NH$_2$	1.224	1.311	OH	OH	1.215	1.292
H	OH	1.212	1.303	OH	F	1.199	1.263
H	OCH$_3$	1.214	1.286	F	F	1.186	1.239
H	F	1.194	1.268	H	CHCH$_2$	1.226	1.321
CH$_3$	CH$_3$	1.227	1.329	H	CCH	1.226	1.340
CH$_3$	NH$_2$	1.228	1.315	H	CHO	1.223	1.351
CH$_3$	OH	1.217	1.306	H	CN	1.220	1.310
CH$_3$	F	1.198	1.269				

Table 3. Atomic Charges for Carbon and Oxygen of XYCO and XYCHO$^-$ [a]

X	Y	XYCO C	XYCO O	XYCO O(MP2)[b]	XYCHO$^-$ C	XYCHO$^-$ C(MP2+)[c]	XYCHO$^-$ O
H	H	1.365	-1.297	-1.257	1.111	0.954	-1.475
H	CH$_3$	1.290	-1.328	-1.290	1.126	1.011	-1.478
H	CF$_3$	1.376	-1.266	-1.218	1.241	1.131	-1.446
H	NH$_2$	1.980	-1.392	-1.357	1.431	1.267	-1.503
H	OH	2.039	-1.388	-1.353	1.549	1.377	-1.503
H	OCH$_3$	2.034	-1.390	-1.355	1.564	1.347	-1.503
H	F	2.049	-1.349	-1.312	1.579	1.438	-1.502
CH$_3$	CH$_3$	1.219	-1.349	-1.311	1.107	1.048	-1.477
CH$_3$	NH$_2$	1.859	-1.406	-1.369	1.414	1.312	-1.501
CH$_3$	OH	1.918	-1.406	-1.371	1.534	1.407	-1.504
CH$_3$	F	1.908	-1.369	-1.333	1.546	1.449	-1.505
NH$_2$	NH$_2$	2.474	-1.430	-1.394	1.766	1.630	-1.510
NH$_2$	OH	2.634	-1.440	-1.404	1.886	1.729	-1.512
NH$_2$	F	2.678	-1.412	-1.375	1.932	1.780	-1.516
OH	OH	2.762	-1.438	-1.401	2.056	1.899	-1.520
OH	F	2.807	-1.404	-1.365	2.111	1.962	-1.519
F	F	2.842	-1.365	-1.322	2.150	2.021	-1.513
H	CHCH$_2$	1.300	-1.321	-1.282	1.146	1.021	-1.472
H	CCH[d]	1.448	-1.285	-1.238	1.267	1.119	-1.468
H	CHO	1.269	-1.282	-1.234	1.096	0.905	-1.467
H	CH	1.496	-1.254	-1.200	1.283	1.164	-1.441

[a] Calculated at the HF/6-31G**//HF/6-31G* level for neutrals and the HF/6-31+G**//HF/6-31+G* level for anions. In units of electrons. [b] Calculated at the MP2/6-31G*//MP2/6-31G* level. [c] Calculated at the MP2/6-31+G*//MP2/6-31G* level. [d] This anion was unstable at the 6-31+G* geometry, the charges are calculated at the HF/6-31+G**//HF/6-31G* level.

when X = NH$_2$. This reasoning is significantly different from the view presented in elementary texts, where electronegative groups are said to destabilize C=O groups and the effect of these groups on alkoxides is ignored.[2]

D. Geometries. A substituent X has a pronounced effect on the isodesmic reactions shown above. Perhaps X will also have a similar effect on other molecular properties such as the C$-$O bond length, R_{CO}, or the carbon or oxygen atomic populations.

The bond lengths R_{CO} for XYCO are listed in Table 2. Using H$_2$CO as a reference, substitution by F or OH leads to relatively short values of R_{CO}, and by NH$_2$ to long R_{CO}'s. These bond lengths have been explained by using a combination of electrostatic and lone pair effects.[21] These effects are arguably quite small, as the range of R_{CO} is only 0.042 Å. Importantly, the correlation between R_{CO} and ΔH_{CO} shows no relationship ($r^2 = 0.029$) between the variables.

The bond lengths R_{CO} for XYCHO$^-$ are listed in Table 2. R_{CO}'s for XYCHO$^-$ are maximum when X,Y are from {CH$_3$, H} and decrease in the order CH$_3$, H > OH, NH$_2$ > F, which is inversely proportional to the electronegativity of the attached atom. An increasing electronegativity difference between
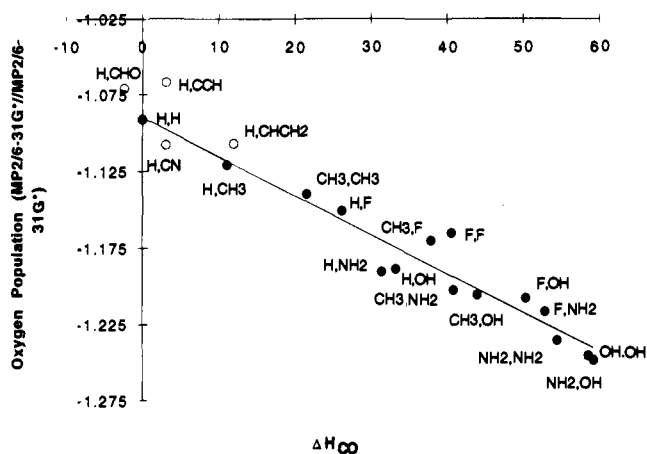
Figure 4. Relationship between carbonyl O atomic charges and ΔH_{CO} for compounds XYCO. The dark circles for XYCO define the line (slope $= -0.00255$, $r^2 = 0.93$). The open circles are data for α,β-unsaturated aldehydes.

Figure 5. Relationship between carbonyl C atomic charges and ΔH_{CHO} for compounds XYCHO$^-$. The dark circles for XYCHO$^-$ define the line (slope $= 0.0138$, $r^2 = 0.97$). The open circles are data for the hydride reduction products of α,β-unsaturated aldehydes.

carbon and X leads to greater charge separation. Consequently, the $C^{\delta+}-O^-$ bond length shortens to minimize electrostatic energy. The range of R_{CO} is twice as large as that for carbonyls. The correlation between R_{CO} and ΔH_{CHO} shows an improved, but poor, relationship ($r^2 = 0.724$) between the variables.

Perhaps it is not surprising that the geometric parameter, R_{CO}, correlates poorly with ΔH_{CO} and ΔH_{CHO}. Yet, as will be seen in the next section, atomic populations correlate reasonably well with both ΔH_{CO} and ΔH_{CHO}.

E. Atomic Changes. With no loss of generality, atomic charges rather than atomic populations will be used in this discussion. Charge on an atom is obtained by subtracting the integrated populations of each atom from the atomic number.

Atomic charges for XYCO are listed in Table 3. The charge on oxygen, which spans a narrow range of only 0.16 e, will be shown to correlate with ΔH_{CO}. Oxygen charge is most negative when substituents are from {OH, NH$_2$} and increases in the order OH, NH$_2$ < F < H, CH$_3$. It may seem counterintuitive that the purely inductive substituent, F, leads to higher charge on oxygen than {H, CH$_3$}. However, as seen in the previous section, substitution by F also leads to a short C=O bond length, which allows the oxygen to better attract electron density from carbon. Another factor which increases charge on oxygen is lone pair interactions, which helps to explain the high oxygen charges for {OH, NH$_2$}. Recall that both inductive withdrawal and lone pair interaction also lead to greater endothermicity in ΔH_{CO}. Indeed, in Figure 4, a plot of charge on oxygen versus ΔH_{CO} shows a good correlation between these variables.

Atomic charges for XYCHO$^-$ are listed in Table 3. The charge on carbon will be shown to correlate with ΔH_{CHO}. As the inductive abilities of the groups X,Y are increased, the charge on carbon is increasingly positive. Moreover, successive replacement of two hydrogens in H$_2$CHO$^-$ by X and Y to yield XYCHO$^-$ results in a linear relationship in the charge on carbon, Charge$_C$, i.e.:

$$\text{Charge}_C(\text{XYCHO}^-) =$$

$$\text{Charge}_C(\text{H}_2\text{CXO}^-) + \text{Charge}_C(\text{H}_2\text{CYO}^-)$$

In Figure 5, a plot of Charge$_C$ versus ΔH_{CHO} for XYCHO$^-$ shows a strong correlation between these variables. This correlation lends further support to the arguments that the value of ΔH_{CHO} is due to purely inductive effects and that these effects are additive.
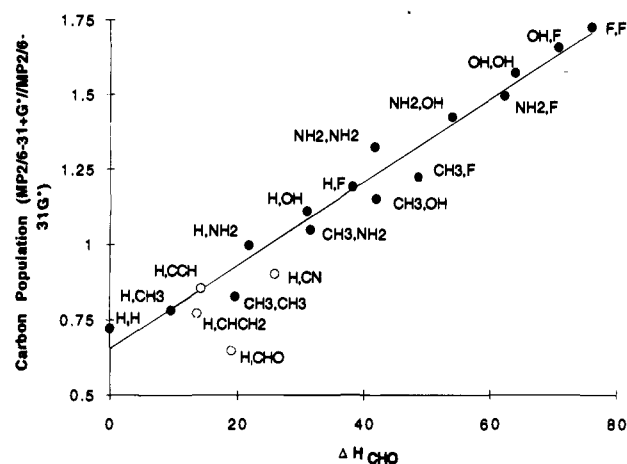
Table 4. Comparison of H$^-$ to Other Nucleophiles Y$^-$: Affinity for H$_2$CO, Proton Affinity, Absolute Hardness, and Reaction Enthalpies with HCOX (kcal/mol)

Properties of Nucleophiles Y$^-$

property	nucleophiles Y$^-$				
	hydride	fluoride	hydroxide	amide	methide
affinity for H$_2$CO[a]	-55.7	-20.9	-30.8	-38.2	-48.1
affinity for H$^+$ [a]	-418.9	-371.1	-389.1	-402.1	-416.8
absolute hardness[b]	157	161	129	122	92

Relative Enthalpies of Addition of Y$^-$ to HCOX (H$_2$CO $= 0.0$ kcal/mol)

X	nucleophiles Y$^-$				
	hydride	fluoride	hydroxide	amide	methide
H	0.0	0.0	0.0	0.0	0.0
F	-12.0	-11.8	-13.7	-14.4	-12.9
OH	2.3	0.7	0.2	1.1	1.0
NH$_2$	9.7	7.4	8.5	11.6	9.4
CH$_3$	1.5	0.6	0.2	1.2	1.0

[a] Calculated at the G2(MP2) level. [b] Reference 24.

F. Comparison with Other Nucleophiles. Compiled in Table 4 are reaction enthalpies for the reaction [HCOX + Y$^-$ → XYCHO$^-$]. In this discussion, X,Y will be taken from the set {H, CH$_3$, NH$_2$, OH, F}. When X $=$ H, it is seen that the absolute affinity of the anion Y$^-$ for H$_2$CO parallels its basicity. It is also interesting to look at the relative affinities of a given ion Y$^-$ for the series HCOX using the affinity for H$_2$CO as a reference point. Qualitatively, it is seen that for each nucleophile Y$^-$, reaction with HCOX is most exothermic when X $=$ F and is decreasingly exothermic in the order F $\gg$ H > CH$_3$ $\approx$ OH $\gg$ NH$_2$. Quantitatively, it is seen that relative affinities for each HCOX are independent of the identity of Y$^-$, with ranges in Y$^-$ of 1.3 to 4.2 kcal/mol depending on the identity of X.[23] Given absolute hardness values of Y$^-$ which vary by over 70 kcal/mol, it is surprising that the relative affinities of the series Y$^-$ for a given HCOX are (1) so similar to each other and (2) completely unrelated to the values of absolute hardness.[24] Finally, since trends in the addition of Y$^-$ to HCOX are so similar for different Y$^-$'s, it may be possible to generalize the conclusions from this work to the addition of an arbitrary nucleophile to a carbonyl.

(23) A reviewer has questioned this conclusion "since the major difference from the identity of Y$^-$ has been deducted by using the affinity of H$_2$CO as a reference point."

(24) Parr, R. G.; Pearson, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 7512.

Hydride Affinities of α,β-Unsaturated Aldehydes

Values of ΔH_{RHA} for compounds with an unsaturated center bonded to a carbonyl group are listed in Table 1. Two trends are evident in the data. In the series {acetaldehyde, acrolein, propynal}, ΔH_{RHA} becomes increasingly negative as the s character on the α carbon increases from sp^3 to sp^2 to sp. ΔH_{RHA} also becomes significantly more exothermic when the β atom is changed from carbon to a heteroatom, i.e. acrolein to glyoxal, and propynal to propanenitrile. Both trends show that increasing electron demand by the α carbon, through hybridization and/or induction, leads to more negative ΔH_{RHA}'s.

As in the previous section, hydride affinity can be broken down into a difference in the enthalpies of isodesmic reactions between carbonyls and alkoxides, $\Delta H_{RHA} = \Delta H_{CO} - \Delta H_{CHO}$, listed in Table 1. The ΔH_{CO}'s for HCOX are similar for acetaldehyde (X = CH_3) and acrolein (X = $CHCH_2$) but are significantly lower when X is from {CCH, CN, CO}. As noted earlier, low values of ΔH_{CO} indicate decreased stability of the carbonyl compound relative to H_2CO. This relative instability is due to electrostatic repulsion between the partial positive charges on the carbonyl carbon and the α carbon. Note that the electrostatic repulsion more than offsets any stabilizing resonance contribution by the conjugated double bond.[25] Another compound with similar behavior is $HCOCF_3$, which has a ΔH_{CO} 14 kcal/mol lower than that of $HCOCH_3$. When the carbonyl group is reduced to an alkoxide, the ΔH_{CHO} of H_2CXO^- increases from a minimum when X = CH_3 and follows the order $CH_3 < CHCH_2 < CCH < CHO < CN$. As shown previously, increasing inductive ability of a substituent leads to higher values of ΔH_{CHO}. The combination of low ΔH_{CO}'s and high ΔH_{CHO}'s gives rise to the large negative ΔH_{RHA}'s for this class of compounds.

Interestingly, as seen in Table 2, R_{CO} in the four α,β-unsaturated compounds (1.220−1.226 Å) varies very little from acetaldehyde (1.222 Å) despite the variety of substituents attached. It has previously been noted that, in contrast with resonance interaction theories, conjugation with an unsaturated center has little effect on the length of the CO bond.[25] As listed in Table 2, R_{CO} changes unpredictably for the corresponding alkoxides. Importantly, there is no correlation between the isodesmic reaction enthalpies and R_{CO}.

In the series XYCO, it was noted that oxygen charge correlated with the isodesmic enthalpy, ΔH_{CO}. This general trend is not clearly evident for atomic charge data of unsaturated aldehydes from Table 3, as shown by the open circles in Figure 4. In the compounds $XYCHO^-$, it was seen that charge on carbon was a good indication of the isodesmic enthalpy, ΔH_{CHO}. As revealed by the open circles in Figure 5, this trend is no longer present for the corresponding compounds in this section.

As with the series XYCO, the relative hydride affinities of α,β aldehydes can be understood by looking at the relation $\Delta H_{RHA} = \Delta H_{CO} - \Delta H_{CHO}$. Typically, ΔH_{CO} decreases and ΔH_{CHO} increases as the α carbon becomes more positive. Unlike the series XYCO, charge on oxygen in the aldehyde series and charge on carbon in the alkoxide series are unreliable indicators of ΔH_{CO} and ΔH_{CHO}, respectively. The geometric variable, R_{CO}, is a poor indicator in both cases.

Hydride Affinities of Cycloalkanones

The ΔH_{RHA}'s of selected cycloalkanones are shown in Table 5. In all cases the hydride affinities of the cyclic compounds are more exothermic than acetone, an acyclic, dialkyl ketone.

Table 5. Relative Hydride Affinities (ΔH_{RHA}) of Cycloalkanones (kcal/mol)

basis set	ring size (Eq or Ax[a])				
	C3	C4 Eq	C4 Ax	C6 Eq	C6 Ax
G2(MP2)	−17.2	−2.2	1.1		
MP2$[b]	−18.2	−2.8	0.9	−0.6	−1.6

[a] The O^- group can be oriented in either the equatorial (Eq) or axial (Ax) position in the case of C4 and C6 rings. [b] MP2$ equals the MP2/6-311++G(3df,2p)//MP2=full/6-31G* level.

Table 6. Hydride Affinities, Structures, and Atomic Charges of $H_2CO\cdots M^+$ and CH_3OM

		$H_2CO\cdots M^+$			CH_3OM		
M^+	$\Delta H_{RHA}[a]$	R(CO)[b]	C[c]	O[c]	R(CO)[b]	C[c]	O[c]
H^+	−212.6	1.256	1.141	−1.284	1.423	0.848	−1.259
Li^+	−143.7	1.231	1.289	−1.416	1.384	0.992	−1.554
Na^+	−122.7	1.229	1.307	−1.387	1.378	1.038	−1.511

[a] In kcal/mol using G2(MP2). [b] In Å, at MP2=full/6-31G* geometry. [c] Atomic charges in electrons at the HF/6-31G**//HF/6-31G* level.

In particular, cyclopropanone has a hydride affinity which is more exothermic than HCOF. Experimentally, cyclopropanones are very reactive electrophiles in nucleophilic addition reactions.[26]

Since hydride reduction converts an sp^2 carbon to an sp^3 carbon and solvolysis reactions typically proceed from an sp^3 starting material through an sp^2 intermediate, one might expect an inverse correlation between ΔH_{RHA} and *rates* of solvolysis. Indeed, cyclopropyl chlorides and tosylates solvolyze much slower than their cyclohexyl counterparts, which in turn solvolyze slower than the analogous cyclobutyl compounds.[27] Not surprisingly then, the ΔH_{RHA}'s of cycloalkanones can be qualitatively understood in terms of torsional and ring strain.

Isodesmic reactions and geometric and charge data have not proved useful in understanding the ΔH_{RHA}'s of these compounds.

Hydride Affinities of Formaldehyde Complexed by Lewis Acids

Experimentally, hydride reductions have been shown to be sensitive to the nature of the counterion present in the reducing agent, possibly due to Lewis acid catalysis.[1a] This phenomenon is investigated by looking at the energies of the complexes of both H_2CO and CH_3O^- with the Lewis acids H^+, Li^+, and Na^+.

The ΔH_{RHA}'s of these compounds are listed in Table 6. Not surprisingly, these values are extremely high relative to H_2CO. A large increase is also seen in gas phase acidities when comparing a charged to an uncharged species. For instance, in the gas phase $PhNH_3^+$ is known to have an acidity 150 kcal/mol higher than that of $PhNH_2$, though the solution phase difference is only 37 kcal/mol.[28]

As the Lewis acid is changed from H^+ to Li^+ to Na^+, the $M^+\cdots O$ bond becomes less covalent and more ionic, with the greater change occurring between H^+ and Li^+. This feature compactly accounts for much of the ΔH_{RHA}, geometry, and charge data listed for these compounds in Table 6. The exothermicity of ΔH_{RHA} for $H_2CO\cdots M^+$ follows the expected order in M^+, [$H^+ \gg Li^+ > Na^+$]. The geometric parameter, R_{CO}, shows similar trends in both the $H_2CO\cdots M^+$ and $CH_3O^-\cdots M^+$ species. In both cases CO bond lengths increase

(25) (a) Wiberg, K. B.; Rablen, P. R.; Marquez, M. *J. Am. Chem. Soc.* **1992**, *114*, 8654. (b) Wiberg, K. B.; Rosenberg, R. E.; Rablen, P. R. *J. Am. Chem. Soc.* **1991**, *113*, 2890.

(26) Turro, N. J. *Acc. Chem. Res.* **1969**, *2*, 25.

(27) Streitwieser, A., Jr. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962; pp 94−97.

(28) Taft, R. W.; Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 463.

Table 7. Hydride Affinities and Atomic Charges of Heterocarbonyl Compounds

species	$\Delta H_{RHA}{}^a$	heterocarbonyls		reduced species	
		C^b	S or N^b	C^b	S or N^b
H_2CS	−35.9	−0.569	0.523	0.110	−0.750
CH_3CSCH_3	−18.4	−0.637	0.373	0.073	−0.740
H_2CNH	15.5	1.098	−1.392	0.649	−1.273
$CH_3C(NH)CH_3$	15.2	0.977	−1.434	0.671	−1.275
$H_2CNH_2{}^+$	−180.1	1.034	−1.487	0.672	−1.166
$CH_3C(NH_2{}^+)CH_3$	−157.1	0.779	−1.502	0.606	−1.200
CH_3CN	19.4	1.170	−1.533	1.086	−1.654

^{a} In kcal/mol using G2(MP2). ^{b} Atomic charges in electrons at the HF/6-31G**//HF/6-31G* level for neutrals and cations and the HF/6-31+G**//HF/6-31+G* level for anions.

compared to H_2CO and CH_3O^-, following the expected order in M^+, $[H^+ \gg Li^+ > Na^+]$.

Like the values of R_{CO}, trends in atomic charges are similar for both the $H_2CO\cdots M^+$ and $CH_3O^-\cdots M^+$ series. As M^+ changes from H^+ to Li^+ to Na^+, the charge on carbon becomes more positive and the charge on oxygen becomes more negative. As the $M^+\cdots O$ bond becomes more covalent, the charge on oxygen is neutralized by M^+, which leads to less Coulombic attraction between oxygen and carbon, and thus a lower charge on carbon.

Hydride Affinities of Heterocarbonyl Compounds

The ΔH_{RHA}'s, bond lengths, and atomic charges of compounds with multiple carbon to heteroatom bonds are listed in Table 7.

Experimentally, thioketones are quite susceptible to nucleophilic attack and thioaldehydes are even more reactive.[1b] The large negative ΔH_{RHA}'s of CH_3CSCH_3 (−18.4 kcal/mol) and H_2CS (−35.9 kcal/mol) are consistent with these data. Unlike the C=O species, the carbonyl carbons in thiocarbonyl species are negatively charged, reflecting the higher electronegativity of carbon over sulfur.

The ΔH_{RHA}'s of the imines of formaldehyde and acetone are 15.5 and 13.3 kcal/mol less exothermic than their carbonyl precursors, respectively. Presumably this is due to the higher electronegativity of oxygen over nitrogen. This view is consistent with the lower atomic charges on carbon in the simple imines of formaldehyde (1.098 e) and acetone (0.977 e) compared to their carbonyl counterparts (1.365 and 1.219 e, respectively).

Experimentally, nitriles are seen to be less reactive to reduction by $LiAlH_4$ than amides.[1c] Indeed, CH_3CN has an ΔH_{RHA} which is 10.2 kcal/mol more endothermic than CH_3CONH_2. Protonation of H_2CNH leads to a large increase in the exothermicity of ΔH_{RHA}, similar to the increase in ΔH_{RHA} found when H_2CO is protonated.

Conclusions

In this work, a scale of intrinsic hydride affinities is produced at the G2(MP2) level of theory for 34 compounds. Hydride

affinities for carbonyl compounds XYCO (X,Y = {H, CH_3, NH_2, OH, F}), α,β-unsaturated aldehydes, cycloalkanones, formaldehyde complexed with Lewis acids, and heterocarbonyl compounds have been calculated. Isodesmic reactions of the reactant carbonyl and product alkoxide are shown to be useful in explaining hydride affinities. Carbon to oxygen bond lengths correlate poorly with hydride affinities. However, the atomic charges of carbon and oxygen are found to be related to hydride affinities. The affinity of the nucleophiles Y^- for compounds HCOX (X,Y = {H, CH_3, NH_2, OH, F}) is also examined.

For the compounds XYCO, a number of conclusions about hydride affinities can be drawn. Relative to hydrogen, electron withdrawing substituents stabilize both alkoxides and carbonyls, but they stabilize alkoxides more. Interaction with a lone pair on a substituent also stabilizes carbonyls, though alkoxides are unaffected. This reasoning is significantly different from the view presented in elementary texts, where electronegative groups are said to destabilize C=O groups and the effect of these groups on alkoxides is ignored.

The hydride affinities of α,β-unsaturated aldehydes are increasingly exothermic as the partial positive charge on the α carbon increases due to either an increase in s character or attachment to electronegative atoms. Positive charge on the α carbon destabilizes the carbonyl form through electrostatic repulsion but stabilizes the alkoxide form through induction.

In cycloalkanones, formaldehyde complexed to Lewis acids, and heterocarbonyl compounds, the calculated data are consistent with experimental results.

The reaction $[Y^- + HCOX \rightarrow XYCHO^-]$ was also studied. The absolute affinities of the anions Y^- for H_2CO parallel their basicity. Using the affinity for H_2CO as a reference point, the relative affinities of a given ion Y^- for the series HCOX were found to be both qualitatively and quantitatively independent of the identity of Y^-. Thus, it may be possible to generalize the conclusions from this work to the addition of an arbitrary nucleophile to a carbonyl.

Supporting Information Available: Tables of energies and tables of atomic charges and Z-matrices with MP2=full/6-31G* optimized geometries (34 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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