

Superacidity and Superselectivity of BF_3 -Carbonyl Complexes

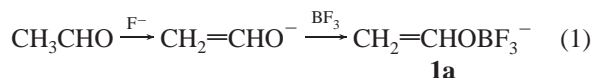
Jianhua Ren,^{*,‡} Christopher J. Cramer,^{*,†} and Robert R. Squires^{‡,§}

The Department of Chemistry, Purdue University
West Lafayette, Indiana 47907
The Department of Chemistry and
Supercomputer Institute, University of Minnesota
Minneapolis, Minnesota 55455

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Lewis acid catalysis constitutes a powerful tool in synthetic organic and organometallic chemistry.¹ Aldol condensations represent a key class of carbon–carbon bond-forming reaction that is subject to Lewis acid catalysis.² Two different activating roles may be played by the Lewis acid in these reactions. Coordination of a ketone or aldehyde reactant by the Lewis acid can promote *enolization* by virtue of the enhanced acidity of the α -hydrogens in the complex. In addition, coordination of the carbonyl group oxygen leads to enhanced electrophilicity at the carbonyl carbon.³ Although the practical utility of these types of Lewis acid activation is well-developed, there is little quantitative information available bearing on their magnitude. Herein we describe gas-phase thermochemical measurements, ab initio calculations, and solvation energy estimates that reveal the spectacular increases in the acidity and electrophilicity of simple aldehydes and ketones when complexed to the common Lewis acid BF_3 in both the gas phase and solution. In fact, this complexation transforms them into *superacids* and *superselectivities*.

Boron trifluoride complexes of simple aldehydes and ketones are not sufficiently stable in the gas phase at room temperature for direct determination of their acid/base and other thermochemical properties through equilibrium measurements.⁴ We have developed an alternative approach based on thermochemical relationships between BF_3 binding energies and other energy properties of the complexes. For example, Scheme 1 illustrates a thermochemical cycle that can be used to derive the gas-phase acidity (ΔH_{acid}) of the $[\text{CH}_3\text{CHO}\cdot\text{BF}_3]$ complex, **1**. The increase in acidity of the α -CH bonds in $[\text{CH}_3\text{CHO}\cdot\text{BF}_3]$ relative to uncomplexed acetaldehyde is equal to the difference in the BF_3 binding energies of the neutral aldehyde and the enolate ion. Thus, from a knowledge of the BF_3 bond strengths and the absolute acidity of CH_3CHO , we can determine the gas-phase acidity of the complex. We use energy-resolved collision-induced dissociation (CID) in a flowing afterglow – triple quadrupole apparatus⁵ to measure the BF_3 binding energy of $[\text{CH}_2\text{CHO}\cdot\text{BF}_3]^-$, **1a**. This ion is easily generated in the flowing afterglow by addition of BF_3 to the preformed enolate ion (eq 1)



[†] University of Minnesota.

[‡] Purdue University.

[§] Deceased September 30, 1998.

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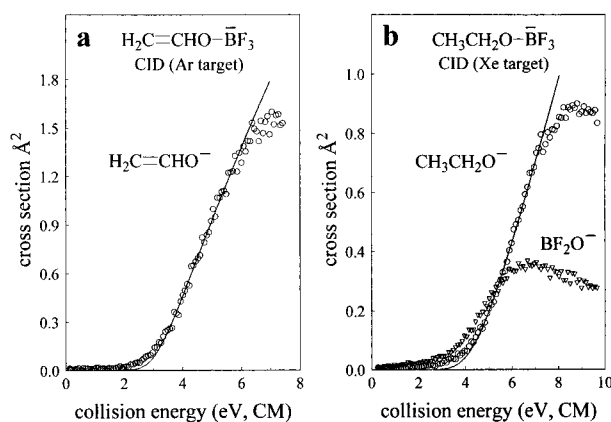
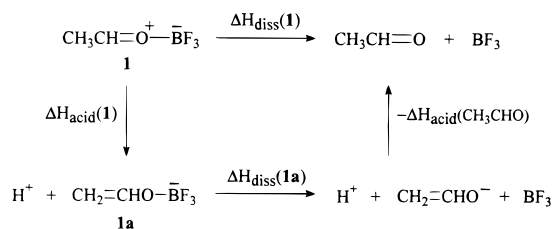


Figure 1. Cross sections for (a) CID of $[\text{CH}_2\text{CHO}\cdot\text{BF}_3]^-$ **1a** with argon target at 0.035 mTorr, and (b) CID of $[\text{CH}_3\text{CH}_2\text{O}\cdot\text{BF}_3]^-$ **1b** with xenon target at 0.035 mTorr. The solid lines are the model appearance curves obtained by the methods described in the refs 6 and 14.

Scheme 1



B3LYP/6-31+G(d) calculations indicate that the B–O bonded tautomer shown is 11 kcal/mol lower in energy than the B–C bonded form (not shown). Collision-induced dissociation of **1a** in the triple quadrupole analyzer with argon target yields the enolate as the only ionic fragment. The energy-dependent cross sections for CID of **1a** are plotted vs. center-of-mass (CM) collision energy in Figure 1a. Detailed analysis of replicate appearance curves by means of a modeling procedure that takes into account all sources of energy in the CID process, as well as the possibility for a kinetic shift in the onset due to slow dissociation on the instrument time scale,⁶ gives an average value for the 298 K dissociation enthalpy of **1a** of 61 ± 3 kcal/mol.

The complexation energy of $[\text{CH}_3\text{CHO}\cdot\text{BF}_3]$ has not been determined experimentally.⁴ Ab initio calculations carried out at the MP2, B3LYP, CBS, and CCSD(T) levels of theory all point to a value of 11 ± 2 kcal/mol.⁷ Thus, the BF_3 bond strength in enolate **1a** is 50 kcal/mol greater than that in neutral complex **1**. Combining this with the gas-phase acidity of acetaldehyde, $\Delta H_{\text{acid}}(\text{CH}_3\text{CHO}) = 365.8 \pm 2.2$ kcal/mol,⁸ gives a value for the acidity of complex **1** of 316 ± 4 kcal/mol. Theoretical estimates

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(7) Obtained by combining the computed difference in 298 K enthalpy of BF_3 binding of **1** and dimethyl ether with the experimental value for $\Delta H_{\text{diss}}^-[\text{Me}_2\text{O}\cdot\text{BF}_3] = 13.6 \pm 0.2$ kcal/mol; Brown, H. C.; Adams, R. M. *J. Am. Chem. Soc.* **1942**, *64*, 2557.

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Table 1. Dissociation Enthalpies and Gas-Phase Acidities for BF₃-Carbonyl Complexes, kcal/mol

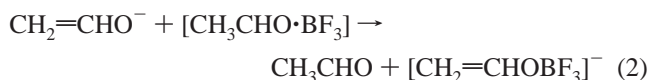
CH ₃ CRO	ΔH_{diss}^- [CH ₃ CRO· BF ₃] ^a	ΔH_{diss}^- [CH ₂ CRO· BF ₃] ^b	ΔH_{acid}^- (CH ₃ CRO) ^c	ΔH_{acid}^- [CH ₃ CRO· BF ₃] ^d
CH ₃ CHO	11 ± 2	61 ± 3	365.8 ± 2.2	316 ± 4
CH ₃ COCH ₃	13 ± 2	58 ± 3	369.1 ± 2.1	324 ± 4
CH ₃ COCF ₃	6 ± 2	50 ± 3	349.2 ± 2.1	306 ± 4

^a Calculated enthalpy of dissociation of BF₃-carbonyl complex obtained from isodesmic reaction analysis relative to $\Delta H_{\text{diss}}[\text{Me}_2\text{O} \cdot \text{BF}_3] = 13.6 \pm 0.2$ kcal/mol⁷ at the MP2/6-31+G(d), B3LYP/6-31+G(d), CCSD(T)/6-31+G(d), and CBS-4 levels of theory. ^b Measured dissociation enthalpy for BF₃-enolate. ^c Ref 8. ^d Cf. Scheme 1.

for $\Delta H_{\text{acid}}(\mathbf{1})$ obtained from B3LYP/6-31+G(d) (315.7 kcal/mol) and CBS-4 (314.7 kcal/mol) calculations are in excellent agreement with the value given above. Similar results are obtained for the BF₃ complexes of acetone ($\Delta H_{\text{acid}} = 324$ kcal/mol) and 1,1,1-trifluoroacetone ($\Delta H_{\text{acid}} = 306$ kcal/mol) (Table 1). The extremely low values for ΔH_{acid} rank these BF₃-carbonyl complexes among the strongest gas-phase acids known,⁸ including HI (314 kcal/mol) and HBr (323 kcal/mol). BF₃ coordination has essentially transformed the carbonyl compounds into gas-phase *superacids*, molecules with Brønsted acidities comparable to or greater than that of sulfuric acid ($\Delta H_{\text{acid}} = 309$ kcal/mol) and the hydrogen atom ($\Delta H_{\text{acid}} = 314$ kcal/mol).⁹

α -Deprotonation of a BF₃-carbonyl complex results in the conversion of a weak, dative B-O bond to a strong covalent bond in the BF₃-enolate. Natural population analysis (NPA)¹⁰ shows that the negative charge in **1a** resides almost entirely on the fluorine atoms, accounting for significant charge stabilization.

The pK_a of acetaldehyde is ~25 in DMSO and 17 in water.¹¹ An acidity increase of 50 kcal/mol for the BF₃ complex corresponds to a drop of 36 pK_a units. However, the actual difference in pK_a between CH₃CHO and **1** in solution is likely to be much smaller, since the solvation energy of the free enolate ion will be larger than that of the BF₃ complex **1a**. That is, the change in solvation free energy for eq 2, $\Delta\Delta G_{\text{sol}}$, will be large and positive, offsetting the favorable $\Delta\Delta G_{\text{acid}}$ term.



We have carried out solvation free energy calculations using the SM5.4 model¹² to estimate the magnitude of $\Delta\Delta G_{\text{sol}}(2)$ for water, dichloromethane, and tetrahydrofuran to be in the range from 16 to 18 kcal/mol. Therefore, the acidity enhancement for **1** in these solvents is reduced to about 33 kcal/mol, corresponding to a change in pK_a of 24 units. On this basis we predict a solution pK_a for **1** of about -7 in water, ranking it in its solution acidity with compounds such as hydrobromic acid.¹¹

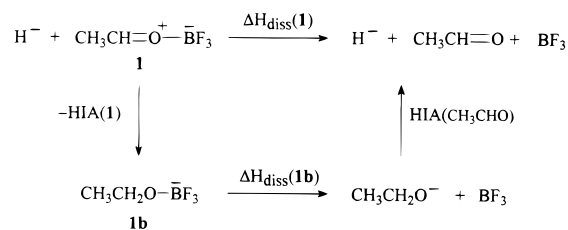
Coordination of a carbonyl compound by a Lewis acid increases its electrophilicity, i.e., its (kinetic) reactivity toward nucleophilic addition to the carbonyl carbon. A useful thermochemical correlate

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Scheme 2

for electrophilicity of a carbonyl group is its *hydride ion affinity*, HIA, which is defined as the enthalpy change for the reaction: $\text{RH}^- \rightarrow \text{R} + \text{H}^-$.¹³ Gas-phase hydride affinities of simple aldehydes and ketones are in the 38–45 kcal/mol range; for acetaldehyde HIA = 39.5 ± 2.2 kcal/mol.⁸ Scheme 2 illustrates a thermochemical cycle that can be used to derive the increase in hydride affinity of the [CH₃CHO·BF₃] complex relative to CH₃-CHO from the difference in BF₃ binding energies of CH₃CHO and ethoxide ion, CH₃CH₂O⁻. Energy-resolved CID can be used to determine the B-O bond strength in CH₃CH₂OBF₃⁻ **1b**. Energy-dependent CID cross sections for **1b** are illustrated in Figure 1b. The BF₂O⁻ fragment is believed to arise from a dissociative rearrangement that leads to HF and CH₂=CH₂ as neutral cofragments. Direct cleavage yielding CH₃CH₂O⁻ has a comparable threshold and dominates at collision energies above 5 eV. Analysis of replicate CH₃CH₂O⁻ appearance curves with the CID threshold model^{6,14} gives an average value for the B-O bond strength in CH₃CH₂OBF₃⁻ of 78 ± 4 kcal/mol. Combining this with the B-O bond energy of **1** and the hydride affinity of CH₃CHO according to Scheme 2 gives a hydride affinity for [CH₃-CHO·BF₃] of 106 ± 4 kcal/mol. Predictions for HIA(**1**) obtained from B3LYP/6-31+G(d) (106.0 kcal/mol) and CBS-4 (105.3 kcal/mol) calculations are in excellent agreement. Complex **1** ranks at the very top of the hydride affinity scale,¹³ along with BH₃CN (HIA = 96 kcal/mol) and free, gaseous atoms such as S (HIA = 121 kcal/mol).⁸ Coordination of CH₃CHO by BF₃ has made it a gas-phase *superelectrophile*.¹⁵ The origin of the hydride affinity increase is fundamentally the same as that of the acidity enhancement. Addition of H⁻ to the carbonyl carbon in **1** converts the weak dative B-O bond to a strong covalent B-O bond in the BF₃-alkoxide **1b** which, in turn, enables substantial negative charge stabilization by the fluorine atoms.

The experimental approach described here has general utility for evaluating Brønsted acidities and other thermochemical properties of Lewis acid-base complexes. Using this method, we demonstrate that coordination of BF₃ transforms simple carbonyl compounds into gas-phase *superacids* and *superelectrophiles* with enhancements in acidity of up to 50 kcal/mol and hydride affinity of up to 66 kcal/mol. In the condensed phase, changes in acidity of up to 24 pK_a units are obtained by combining the measured gas-phase acidities with the computed solvation energies for these species.

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(14) Average 298 K vibrational energy for **1b** computed to be 4 kcal/mol. A kinetic shift of ca. 23 kcal/mol was estimated from fitting the EtO⁻ appearance curve with a loose transition state model ($\Delta S^\ddagger_{1000} = 9$ eu). A small competitive shift in the EtO⁻ onset due to the BF₃O⁻ dissociation channel (calculated to proceed through a tight, cyclic transition structure) is evident from simultaneous fitting of the two cross sections, cf. Rodgers, M. T.; Armentrout, P. B. *J. Chem. Phys.* **1998**, *109*, 1787.

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