J. Am. Chem. Soc. **1996,** *118,* 636−641

Ambident Reactivity of Enolate Anions in the Gas Phase. Experimental Determination of Carbon vs Oxygen Acylation with CF_3COCl

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Received January 23, 1995[⊗]

Abstract: The gas-phase reaction between enolate anions $RCOCH_2^-$ and CF_3COCl has been studied using FT-ICR. Carbon and oxygen acylation with CF_3COCl gives distinct ion products. For the series R = CF_3, *m*-XC_6H_4 (X = CH_3, H, OCH_3, F, CF_3), H, CH_3, $(CH_3)_3C$, $CH_2{=}CH$, and F, carbon attack and oxygen attack are both observed with oxygen attack predominating for most of the enolates. This results from the lower intrinsic activation energy for oxygen attack. The relative reactivity of carbon vs oxygen changes significantly with the substituent R in the enolates. The relationship between the relative overall exothermicity of the two channels and the relative reactivity of carbon vs oxygen of enolates is derived from Marcus theory. The relative overall exothermicity of the two channels is correlated with the energy difference, ΔH_{ke}, between the keto and enol tautomers of the parent ketones.

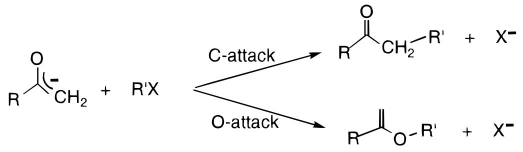
Introduction

Enolate anions are among the most important ambident nucleophiles.[1] The negative charge in an enolate is delocalized between a carbon atom and an oxygen atom, and either site may act as a nucleophile depending on the reaction conditions, providing a powerful method for generating new C−C or C−O bonds. The factors that influence the competition between these two nucleophilic pathways are therefore of great interest. The effects of solvent, counterion, and temperature as well as the structure of the nucleophile and the electrophile on this competition, have been studied systematically and extensively in the condensed phase.[2,3] It is difficult, however, to determine quantitatively the effects of varying the structures of the reactants because the presence of solvent and counterion complicates the system. Calculations show that the oxygen atom has most of the negative charge[4−6] because of its higher electronegativity, and the solvent and counterions are favored to associate with it,[2] thereby enhancing the relative nucleophilic reactivity of the carbon. Therefore, the study of nucleophilic reactions of enolates in the gas phase in which solvent and counterions are absent can provide a better understanding of the intrinsic reactivity of the ambident anions.

In the gas phase, quantitative determination of the relative contribution of the two competing pathways is difficult, because ion−molecule reactions are usually studied with mass spectrometric techniques in which only ionic species are observed. While the two competing reactions produce different neutral products, they generally yield the same product ion and so cannot be distinguished.

Because of this limitation, systematic studies of the ambident enolate anions in the gas phase are scarce, and only recently have some specific systems been approached. Bartmess and co-workers[7] studied the reaction of enolates with esters. Ellison and co-workers[8] have employed neutral product detection to measure the C versus O competition in an S_N2 reaction involving a cyclic enolate, while Trenerry and Bowie[9] have investigated the ambident reactivity of the thioacetate ion. Gross and co-workers[10] used collision-induced dissociation of aldol condensation products to probe bimolecular reactions of enolates with acetaldehyde. Unsaturated polyfluorinated compounds have been used by Squires[11,12] and Nibbering as chemical probes to study a variety of ambident nucleophiles, including enolate anions,[13,14] thioenolate, oximate anions,[15] and imidate anions.[16] The competition between the two nucleophilic centers has been shown to vary widely not only with enolate structure but also with the structure of the neutral substrate. Theoretical studies on a model system have also been conducted.[17]

Scheme 1



[⊗] Abstract published in *Advance ACS Abstracts,* January 1, 1996.

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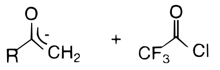
Recently, we have developed a simple method to determine the relative contributions of the competing pathways in the gas-phase reactions of ambident nucleophiles with a carbonyl substrate.[18] To explore the generality of our previous findings, we have studied the system:



R = CF$_3$, C$_6$H$_5$, *m*-CH$_3$C$_6$H$_4$, *m*-CH$_3$OC$_6$H$_4$, *m*-FC$_6$H$_4$,
m-CF$_3$C$_6$H$_4$, H, CH$_3$, (CH$_3$)$_3$C, CH$_2$=CH, F

We report here the effects of enolate anion structure on the selectivity of the carbon and oxygen reaction centers. We find that in all cases both carbon and oxygen attack are observed, and oxygen attack dominates for most of the enolates. The substituent "R" significantly affects the ratio of the two competing channels. The ratio changes consistently with the relative exothermicity of the two pathways, and we employ Marcus theory to help in the interpretation. The relative exothermicity is connected to the energy difference, ΔH_{ke}, between keto and enol forms of the parent carbonyl compound. For the systems presented here, both carbon and oxygen attack pathways are thermodynamically accessible. Therefore, the true kinetic preferences between the two channels are reflected.

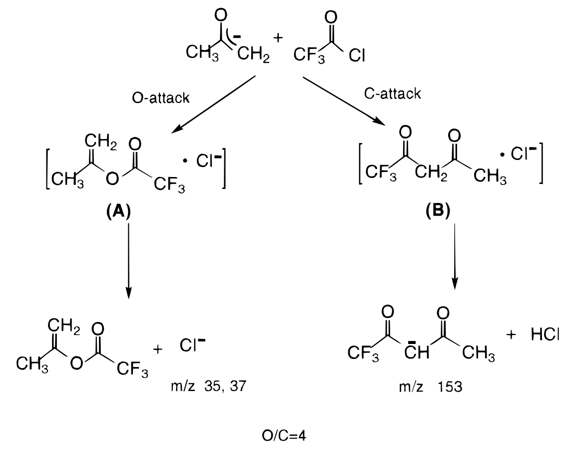
Experimental Section

Materials. NF$_3$ was obtained from Ozark Mahoning and CF$_3$COCl from PCR, Inc. 3,5-Bis(trifluoromethyl)toluene was synthesized by quenching the Grignard reagent, 3,5-bis(trifluoromethyl)benzyl magnesium chloride, with water. 3,5-(CF$_3$)$_2$C$_6$H$_3$CH$_2$COCF$_3$ was synthesized using Greif's method.[19] All other chemicals were purchased from Aldrich. The samples were used without further purification and were subjected to multiple freeze−pump−thaw cycles before introduction into the ICR cell.

Instrumentation. All the experiments were performed with two Fourier transform IonSpec OMEGA ion cyclotron resonance (FT-ICR) spectrometers equipped with impulse excitation. Details of the experimental apparatus can be found elsewhere.[20,21] Briefly, one ICR consists of a 1 × 1 × 1.5 in. rectangular cell, constructed of polished 0.020 in. oxygen-free hard copper plates; the other, in which all the kinetic experiments were performed, consists of a 2 × 2 × 2 in. cubic cell, constructed from six stainless steel plates mounted on Vespel rods.[22] All ions were trapped with magnetic fields in the range 0.6−0.8 T. Neutral samples were admitted to the high-vacuum can by means of Varian leak valves. During the kinetic experiments, pressures of neutral species within the ICR cell were monitored with an ion gauge (Varian 844) which was calibrated against a capacitance manometer (MKS 170 baratron with a 315 BH-1 head). Typical operating pressures were between 10^{-7} and 10^{-6} Torr. Primary ions were generated by electron impact on neutral precursors. The kinetic energy of the incident electrons was controlled by varying the potential applied to the filament and the bias on the trapping plates. Typical operating current and voltage for the filament were 2−3 A and 1−3 V, respectively. Standard notched ejection techniques were used to remove unwanted ions from the detection region of the ICR cell and thereby isolate the ions of interest. All experiments were carried out at a temperature estimated to be 350 K.[20]

Data Collection. (a) Determination of the Relative Contributions from the Two Competing Channels. The enolate anions were produced through deprotonation of ketone precursors by fluoride ion which was generated by electron impact on nitrogen trifluoride (NF$_3$). The duty cycle involved fluoride ion formation for 20−40 ms followed by ejection of free electrons for 20 ms. After a short time delay (ca. 30−50 ms), fluoride ion and chloride ion were ejected from the detection region. Products were analyzed at 300−400 ms after ejection. The ratio of the product ions changes slightly with the delay time. At very early delay times few products are produced, and therefore signal to noise is poor. At long delay times, differential ion loss becomes a problem. Taking data at the intermediate time range minimizes the error. The ratios in this range are relatively constant. For each data point, multiple scans (500−1000) were averaged to obtain reproducible ion abundances, and multiple data points were averaged at each pressure. The data collections were repeated on different days and at a variety of pressures of CF$_3$COCl. The ratio of the product ions varied on different days within 5%.

Scheme 2



(b) Kinetic Data Collection. The enolates were isolated after ejecting all the other ions including fluoride and chloride ions. The ion signals were measured using signal averaging (50−100 times) at 10 different increments of time. The kinetic runs were repeated on different days. We believe the major error in the kinetic measurement is determined by the pressure measurements which are accurate to within 20−30%.

Results

Method. We recently studied the gas-phase reaction between acetone enolate and trifluoroacetyl chloride.[18] The relative contribution of the two competing pathways, i.e. reaction at the carbon nucleophilic center and the oxygen center, could be determined because these two channels yield distinct ionic products, with *m*/*z* 153 and 35, 37, respectively (Scheme 2).

The product complex (**A**) from oxygen attack dissociates to yield exclusively Cl$^-$ (*m*/*z* 35, 37) because the addition and elimination neutral product CH$_3$C(CH$_2$)OCOCF$_3$ has no hydrogen acidic enough to allow proton transfer to Cl$^-$ even at the high internal energies at which the product complex is formed.[18] The other channel, carbon attack, gives proton transfer, leading to the ionic product with *m*/*z* 153 instead of directly dissociating to give Cl$^-$. This channel is quite exothermic (about 6 kcal/mol more than the direct dissociation[23]) and we assume that essentially all the product is proton transfer. In order to evaluate the validity of this assumption, we studied the addition−elimination reaction between 3,5-bis(trifluoromethyl)benzyl anion and CF$_3$COCl (Scheme 3).

This reaction has two possible pathways after the addition−elimination product complex (**C**) is produced: one is proton transfer and the other is direct dissociation of the complex to give chloride. Of the ionic products detected, 93% come from proton transfer. The reaction of 3,5-bis(trifluoromethyl)benzyl anion and CF$_3$COCl forms the complex **C** with approximately the same amount of excess internal energy as the complex **B**

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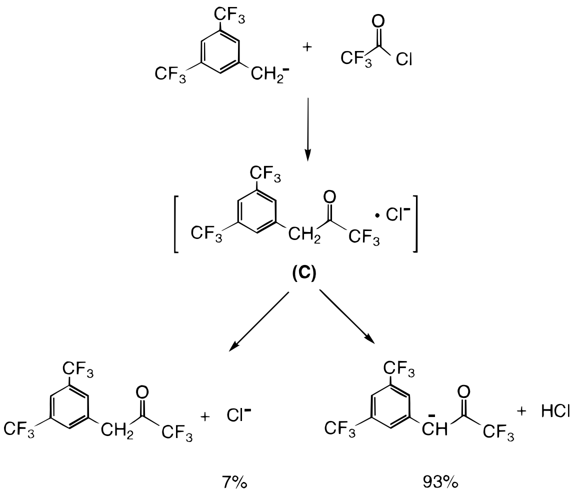
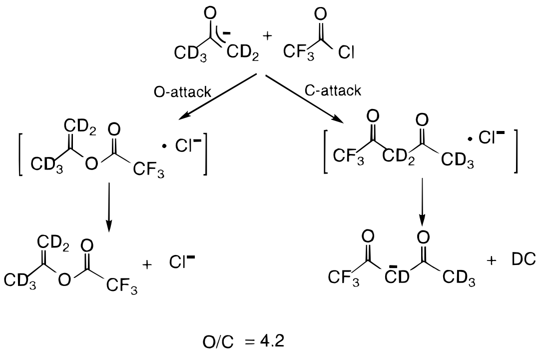
Scheme 3



Scheme 4

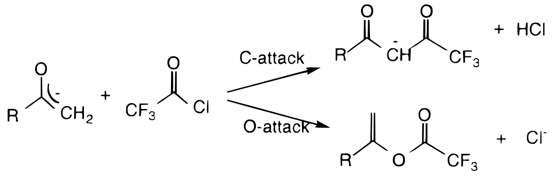


for the reaction in Scheme 2. To compare the acidities of the addition−elimination product, 3,5-$(CF_3)_2C_6H_3CH_2COCF_3$ (**1**) and $CF_3COCH_2COCH_3$ (**2**), we measured the equilibrium constant between **1** and **2** and their respective conjugated bases. **1** is more acidic than **2** by 2.9 kcal/mol ($\Delta\Delta G_{acid}$). However, since $CF_3COCH_2COCH_3$ is mainly in the enol form, and the keto form is less stable than the enol by more than 3.3 kcal/mol,[24] the keto form should be 3.3 kcal/mol more acidic than the enol form. Therefore, the keto form of $CF_3COCH_2COCH_3$ produced from the addition−elimination of the “C” attack of $CH_3COCH_2^-$ with CF_3COCl should have an acidity slightly higher than that of **1**. The proton transfer reaction rate for Cl^- with $CF_3COCH_2COCH_3$ was measured at 350 K and was observed to proceed at the collision rate and faster than that for Cl^- with **1**.[25] Moreover, the O/C ratio of the reaction of deuterated acetone $CD_3COCD_2^-$ and CF_3COCl, 4.2, is observed to be almost the same as that of the undeuterated acetone enolate reaction, 4.0 (see Scheme 4 and Scheme 2).

As shown in Scheme 3, the reaction between 3,5-bis(trifluoromethyl)benzyl anion and CF_3COCl gives 7% Cl^-. Considering the higher acidity of the keto form of $CF_3COCH_2COCH_3$ than that of **1** and all other results described above, we believe the error resulting from Cl^- loss in the carbon attack channel, if there is any, will be less than 7%.

There is a difference between the preliminary result of the C/O ratio for acetone enolate we reported previously[18] and the result shown below. In the preliminary work, we observed a significant amount of *m/z* 113, $CF_3CO_2^-$. This ion results from the reaction of Cl^- with CF_3COOH which itself results from hydrolysis of CF_3COCl, and suggests that the amount of Cl^- observed was too low. Thus the amount of oxygen attack was underestimated and the C/O ratio reported was too high. The data for the series we report here were taken at a more reasonable delay time (see Experimental Section) and with very little impurity (CF_3COO^-). They were verified in repeated experiments on different days, and they were all taken at the same delay time, so that they can be compared.

The Reaction of $RCOCH_2^-$ and CF_3COCl. The method described above can be generalized and used to study the ambident reactivity of a series of enolate anions $RCOCH_2^-$ (R = CF_3, C_6H_5, *m*-$CH_3C_6H_4$, *m*-$CH_3OC_6H_4$, *m*-FC_6H_4, *m*-$CF_3C_6H_4$, H, $(CH_3)_3C$, CH_3, $CH_2{=}CH$, F). All of the enolate anions have been generated by proton abstraction from the carbonyl precursors by F^- (see Experimental Section). Because each compound has only one kind of hydrogen acidic enough for proton abstraction by F^-, no mixture of enolate anions is produced initially. All of the compounds used here are equal to or more acidic than acetone, so that the carbon addition−elimination product, $RCOCH_2COCF_3$, is more acidic than $CH_3COCH_2COCF_3$. Therefore the product complexes from carbon attack undergo exclusively proton transfer and give only the ionic product $RCOCHCOCF_3^-$ (the error, if there is any, should be less than 7% based on the previous analysis). The ratio of $RCOCHCOCF_3^-$ to Cl^- represents the relative rate of carbon attack to oxygen attack.



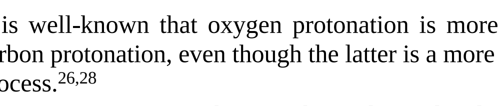
(1)

The ionic product abundances obtained from the reaction of CF_3COCl with eleven different enolate ions are listed in Table 1. These reactions are all fast, with measured rate constants in the range 5−8 × 10^{-10} cm^3 $molecule^{-1}$ s^{-1} corresponding to an efficiency of about 50−70%.

For most enolates, only the usual ionic products from carbon attack ($RCOCHCOCF_3^-$) and from oxygen attack (Cl^-) are observed. In the case of $FCOCH_2^-$, however, ions of *m/z* 137 (major) and 55, 57 (minor) are also observed. We believe that these products are the result of carbon attack, as shown in Scheme 5.

Discussion

The ambident reactivity of enolate ions has long been a topic of significant interest. The protonation of enolate ions[26−29] is the key to understanding much of the ambident reactivity (eq 2).



(2)

It is well-known that oxygen protonation is more rapid than carbon protonation, even though the latter is a more exothermic process.[26,28]

For protonation on the α-carbon, charge localization leads proton transfer,[30] and two of the electrons in the π-system become localized in the developing C−H bond as the proton-

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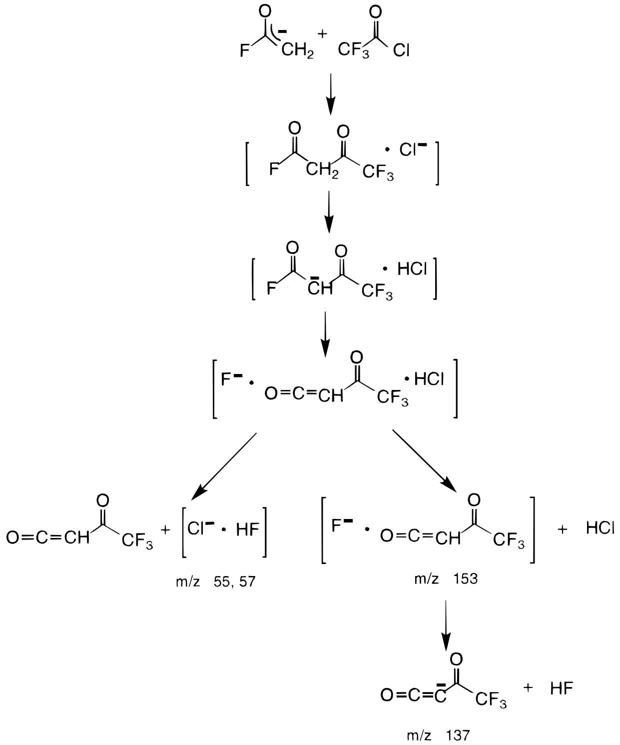
Table 1. Carbon vs Oxygen Attack in the Reaction between $RCOCH_2^-$ and CF_3COCl

R	O/C[a]	ΔH_{ke}[b]
CF_3	7.5	5
H	5.9	9.8
m-$CF_3C_6H_4$	6.9	9.8[c]
m-FC_6H_4	5.9	10[c]
m-$CH_3OC_6H_4$	5.8	10.1[c]
C_6H_5	6.0	10.3[c]
m-$CH_3C_6H_4$	6.4	10.3[c]
$(CH_3)_3C$	4.1	12.3
CH_3	4.0	13.9
$CH_2{=}CH$	3.3	15
F	0.9	28

[a] The ratio of Cl^-/R^- was reproducible within ±5%. The error in O/C resulting from the ionic product scrambling of the carbon attack, if there is any, will be less than 7% (see text for detail). [b] kcal/mol. Values are taken from ref 12. [c] From MOPAC 6.00 AM1 calculation.

Scheme 5



ation transition state is reached. The loss of delocalization is responsible in part for the higher barrier. This effect is not observed when protonation occurs at oxygen, because the lone-pair electrons on oxygen allow protonation to occur orthogonal to the π-system, obviating loss of delocalization.

Alkylation of enolates has also been studied theoretically and experimentally. Ab initio calculations by Houk et al.[17] on the reaction of acetaldehyde enolate with methyl fluoride indicate that the activation energy for O-alkylation is lower than that for C-alkylation even though C-alkylation is favored thermodynamically. The inherent preference for O-alkylation was attributed to the same factors that result in a lower intrinsic barrier for the reaction $HO^- + CH_3OH \rightarrow HOCH_3 + OH^-$ compared with $CH_3^- + CH_3{-}CH_3 \rightarrow CH_3{-}CH_3 + CH_3^-$.

Brickhouse and Squires studied a number of enolate anions reacting with hexafluoropropene in a flowing afterglow mass spectrometer[12] and observed that most aldehyde and ketone enolates react mainly through oxygen, while enolates with electronegative central substituents react mainly through carbon. The carbon vs oxygen reactivity was related to the keto and enol energy difference, ΔH_{ke}, of the parent carbonyl compound. An empirical relationship between ΔH_{ke} and the relative contribution from the two pathways was proposed. Compounds with low ΔH_{ke} values (10−15 kcal mol^{-1}) react mainly through oxygen, while compounds with higher values (30−40 kcal mol^{-1}) react mainly through carbon, but notable exceptions are evident.

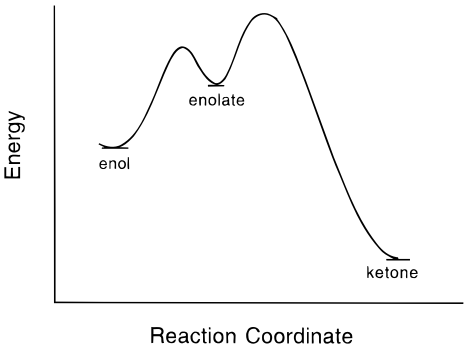
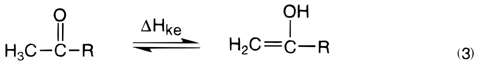


Figure 1. Protonation of enolate ions. The keto form is more stable than the enol form, but the activation energy for oxygen protonation is lower than that for carbon protonation.



$$\mathrm{H_3C{-}\overset{O}{\overset{\|}{C}}{-}R} \quad \xrightleftharpoons{\Delta H_{ke}} \quad \mathrm{H_2C{=}\overset{OH}{\overset{|}{C}}{-}R} \qquad (3)$$

Using FT-ICR, Nibbering et al.[13] studied gas-phase reactions of hexafluorobenzene with a series of acyclic enolate anions. The ambident chemical behavior of these enolates was rationalized with a molecular orbital model in which interactions between specific frontier orbitals of the reactants determine the competition between the two nucleophilic centers. The enolate ions with low-energy HOMOs (<-1.9 eV) react preferentially via the carbon center, while the ions with high-energy HOMOs (>-1.7 eV) react through the oxygen center. There are, however, exceptions of some enolate anions that have reversed selectivities despite having the same HOMO energies.

In this paper we report experiments that address the ambident reactivities of enolate ions with trifluoroacetyl chloride. The acylation of enolate ions with trifluoroacetyl chloride occurs through addition of either oxygen or carbon to a carbonyl group followed by the elimination of Cl^-. The oxygen additions give Cl^-, while for the carbon addition, proton transfer products are produced from the product complexes.

As seen in Table 1, carbon attack and oxygen attack compete with each other; oxygen attack dominates in all of the enolates except $FCOCH_2^-$. Assuming that the system dynamics behave statistically, the product distributions depend on the sum of states for each channel. Since the frequencies and moments of inertia are similar for the two channels, the relative distributions of the products should depend on the relative activation energies. We can understand the activation energies in terms of an intrinsic activation energy (the barrier without thermodynamic driving force) and the thermodynamic driving force or the exothermicity of the reaction. Since carbon attack is thermodynamically more favorable than oxygen attack,[31] observation of oxygen attack suggests that the oxygen attack must have a lower intrinsic activation energy.

Furthermore, for this series, the ratio of carbon vs oxygen attack varies with the substituent of the enolate. As shown in Table 1, the fraction of carbon increases as ΔH_{ke} increases in accord with the suggestion of Squires,[12] i.e., when the relative stability of keto form to enol form is greater, carbon attack

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[31] The stability difference of the products from the two channels is correlated with the energy difference between the keto and enol forms of the parent carbonyl compounds (see later discussion). The keto form is more stable than the enol form by at least 5 kcal/mol in this series (see Table 1).

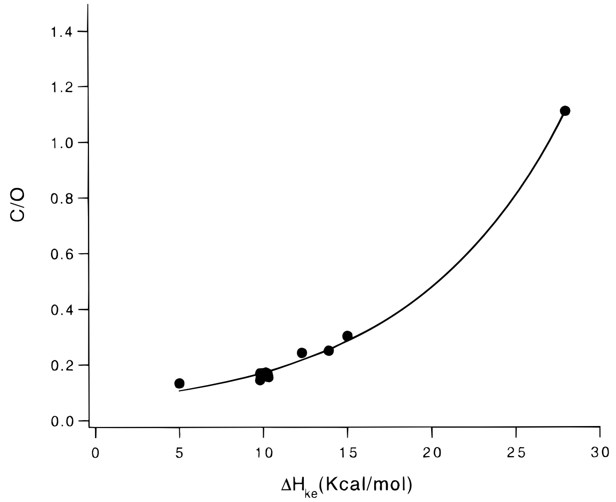

Figure 2. Relative ratio of carbon to oxygen attack vs ΔH_{ke} for the reactions between enolates and CF_3COCl.

becomes more important (Figure 2). The more exothermic carbon attack is relative to oxygen attack, the higher the ratio of carbon attack to oxygen attack. This can be understood in the context of Marcus theory,[32]

$$\Delta E^* = \Delta E_0^* + \frac{(\Delta E^\circ)}{16\Delta E_0^*} \tag{4}$$

where ΔE^* is the activation energy, ΔE_0^* is the intrinsic activation energy, and ΔE° is the reaction energy.

The reformulated Marcus equation appropriate for gas-phase ion−molecule reactions is[33,34]

$$E_{\text{diff}} = E_{\text{diff}}^\circ + \frac{\Delta E_{\text{rxn}}^\circ}{2} + \frac{(\Delta E_{\text{rxn}}^\circ)^2}{16(E_{\text{diff}}^\circ\, E_{\text{w}})} \tag{5}$$

E_{diff} is the activation energy (energy difference between loose and tight transition states); E_{diff}° is E_{diff} at $\Delta E_{\text{rxn}}^\circ = 0$, i.e. the intrinsic activation energy; $\Delta E_{\text{rxn}}^\circ$ is the overall reaction energy; and E_{w} is the complexation energy.

After applying this to our system, the relative activation energy for the two channels is

$$\Delta E_{\text{diff}} = E_{\text{diff}}(\text{C}) - E_{\text{diff}}(\text{O}) = E_{\text{diff}}^\circ(\text{C}) - E_{\text{diff}}^\circ(\text{O}) + \frac{\Delta E_{\text{rxn}}^\circ(\text{C}) - \Delta E_{\text{rxn}}^\circ(\text{O})}{2} + \frac{(\Delta E_{\text{rxn}}^\circ(\text{C}))^2}{16(E_{\text{diff}}^\circ(\text{C}) - E_{\text{w}}(\text{C}))} - \frac{(\Delta E_{\text{rxn}}^\circ(\text{O}))^2}{16(E_{\text{diff}}^\circ(\text{O}) - E_{\text{w}}(\text{O}))} \tag{6}$$

The second-order terms in eq 6 have opposite signs, and they are also estimated to have comparable values, so we ignore them. Therefore:

$$\Delta E_{\text{diff}} = E_{\text{diff}}(\text{C}) - E_{\text{diff}}(\text{O}) = E_{\text{diff}}^\circ(\text{C}) - E_{\text{diff}}^\circ(\text{O}) + \frac{\Delta E_{\text{rxn}}^\circ(\text{C}) - \Delta E_{\text{rxn}}^\circ(\text{O})}{2} \tag{7}$$

The relative activation energy is directly related to the relative total exothermicities of the two channels. The intrinsic activation energies (when $\Delta E_{\text{rxn}}^\circ = 0$) for both channels should remain constant through the series, the usual assumption expected for a group of similar reactions.

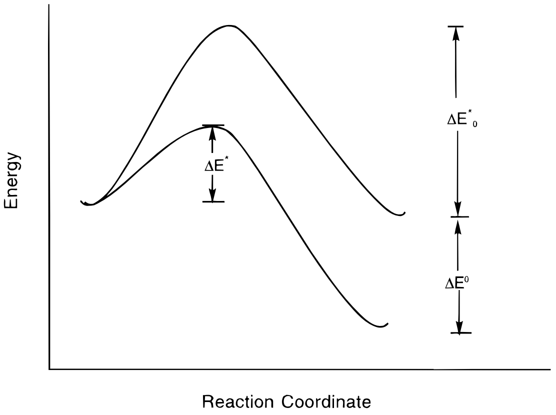

Figure 3. Marcus theory. ΔE^* is the activation energy, ΔE_0^* is the intrinsic activation energy, and ΔE° is the reaction energy.

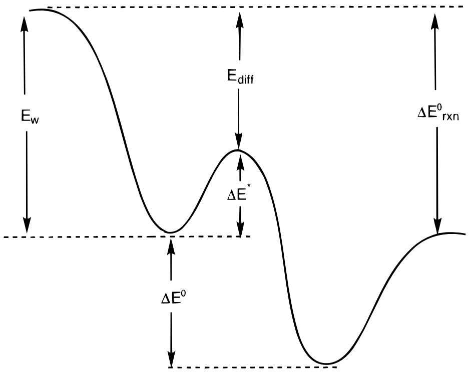

Figure 4. Potential energy surface.

$$\Delta E_{\text{diff}} = E_{\text{diff}}(\text{C}) - E_{\text{diff}}(\text{O}) = \frac{\Delta E_{\text{rxn}}^\circ(\text{C}) - \Delta E_{\text{rxn}}^\circ(\text{O})}{2} + \text{constant} \tag{8}$$

Although the heats of formation of many of the products, and therefore the total exothermicities of some reactions, are not known, we can correlate the relative stabilities of the addition−elimination product for the two channels with the energy differences between the keto and enol forms of the parent carbonyl compounds, ΔH_{ke}. As shown in Scheme 6, the relative stability of the addition−elimination products lies in the $COCF_3$ binding energy to the enolate, while for the tautomers of the ketone, the energy difference is the proton binding energy. It is reasonable to assume that the $COCF_3$ and proton binding energies are proportional, based on previous work that showed that proton affinity is roughly proportional to methyl cation affinity.[35]

From eq 8, we have

$$\Delta E_{\text{diff}} = E_{\text{diff}}(\text{C}) - E_{\text{diff}}(\text{O}) = \alpha\Delta H_{ke} + \text{constant} \tag{9}$$

Thus the relative activation energies for carbon and oxygen attack are proportional to ΔH_{ke}. As can be seen in Figure 2, the ratio of carbon vs oxygen attack increases exponentially with ΔH_{ke}. At high enough values of ΔH_{ke} (for example, with $FCOCH_3$), carbon attack can dominate. The origin of the exponential dependence in Figure 2 is currently being examined.[36]

HOMO−LUMO Interaction vs ΔH_{ke} Effect. The condensed-phase ambident reactivity of enolates has been explained in terms of frontier orbital interactions and electrostatic inter-

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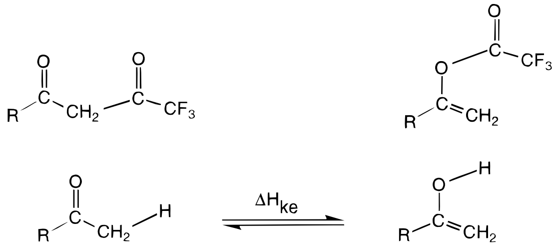
Scheme 6



actions.[4] Recently, Nibbering[13] studied the reactions of enolates with hexafluorobenzene and proposed that the HOMO−LUMO interaction also plays a leading role in determining the relative activation energies of the two competing pathways in the gas phase. In both the present system and the earlier study of the reactions of hexafluoropropene with enolates by Squires et al.,[12] however, the thermodynamic effect (correlation with ΔH_{ke}) was the determining factor for the relative selectivity. It is of interest to understand the importance of these two effects on the relative activation energy of the two competing pathways in different systems. We approach this by studying the effects of the two factors in our system and comparing this system with the other two systems: $RCOCH_2^-$ with $CF_3CF{=}CF_2$, C_6F_6. The effects of ΔH_{ke} and HOMO−LUMO interaction are shown in Figures 5 and 6, respectively. The HOMO energies and ΔH_{ke} are not correlated with each other, so the effect we see from the two figures should be additive. In Figure 5, the logarithm of the ratios of "O" to "C" attack plotted against ΔH_{ke} gives a straight line. If we also plot the data of the other two systems, there are some deviations although they have a similar trend to our system: C attack becomes more important when ΔH_{ke} becomes higher. A straight line is expected if ΔH_{ke} is the dominant factor.[36] Thus, the thermodynamic effect plays an important role in all three systems, but it is not the exclusive determining factor for the $CF_3CF{=}CF_2$ and C_6F_6 systems. The HOMO−LUMO interaction effect for our system is shown in Figure 6. The ratio of "O" vs "C" attack does not change much with the HOMO energy (the $FCOCH_2^-$ point is off line because of the much higher ΔH_{ke}); therefore, the HOMO−LUMO interaction plays a minor role in determining the relative contribution. If we look at the data of the two other systems, we see that the HOMO−LUMO interaction affects the ratio similarly for the hexafluoropropene and hexafluorobenzene systems: the low HOMO energy favors "C" attack, and HOMO−LUMO interaction plays an important role in the two systems. Therefore, both ΔH_{ke} and HOMO−LUMO interaction factors are important, and neither one of them is sufficient for a good fit. Multiple regression analysis shows that HOMO−LUMO interaction is more important in the hexafluoropropene and hexafluorobenzene systems while ΔH_{ke} is essentially all that is required in our system.

In the three systems, the relative importance of the ΔH_{ke} effect (the relative stability of the products from two channels) and the HOMO−LUMO interaction in the determination of the selectivity of the ambident enolates depends on the nature of the substrate. While the HOMO−LUMO interaction plays an important role in the reactions between $RCOCH_2^-$ and $CF_3CF{=}CF_2$ and C_6F_6, it contributes little to the reaction between $RCOCH_2^-$ and CF_3COCl. Among other reasons, CF_3COCl has a much higher LUMO energy than the other two neutral substrates. Therefore, the HOMO−LUMO interaction in our system is much weaker. The system we present in this paper is a thermodynamically controlled one.

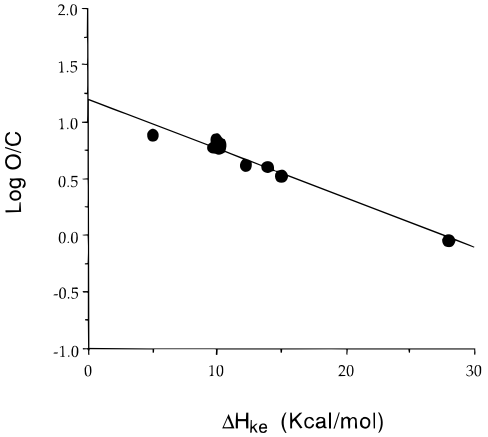


Figure 5. Logarithm of the ratio of "O" to "C" (log O/C) vs ΔH_{ke}.

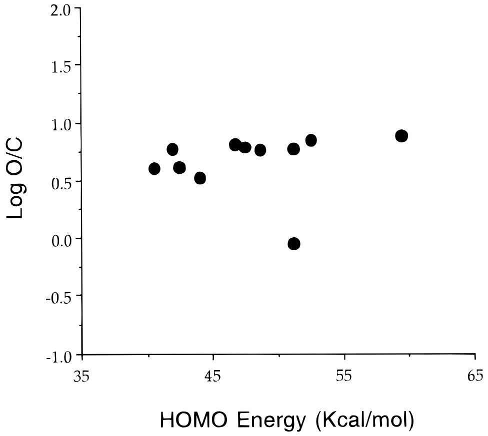


Figure 6. Logarithm of the ratio of "O" to "C" (log O/C) vs HOMO energies of enolate reactants.

Summary

The ambident chemical behavior of enolate anions $RCOCH_2^-$ in the reaction with CF_3COCl has been studied. For R = CF_3, C_6H_5, m-$CH_3C_6H_4$, m-$CH_3OC_6H_4$, m-FC_6H_4, m-$CF_3C_6H_4$, H, CH_3, $(CH_3)_3C$, $CH_2{=}CH$, and F, carbon attack and oxygen attack compete with each other while oxygen attack dominates for most of the enolates. This is due to the lower intrinsic activation energy for oxygen attack, since oxygen attack is less thermodynamically favorable than carbon attack. Furthermore, the ratio of carbon attack vs oxygen attack changes significantly with the substituent "R" in the enolates. The relative overall exothermicity of the two channels is found to affect the ratio and this has been rationalized by using Marcus theory. The relative overall exothermicity is correlated to the energy difference of the keto−enol form of parent ketones, ΔH_{ke}. With a higher ΔH_{ke}, the carbon attack product is more stable relative to oxygen attack product, and more carbon attack is observed. The system we present here is mainly controlled by this thermodynamic effect, not the HOMO−LUMO interaction effect which plays an important role in the two previously studied systems.

Acknowledgment. We are grateful to the National Science Foundation for support of this work. We thank Dr. J. L. Wilbur, Dr. B. D. Wladkowski, Stephen L. Craig, Professor R. R. Squires, Professor W. L. Jorgensen, and Professor K. N. Houk for helpful discussions.

JA9502233