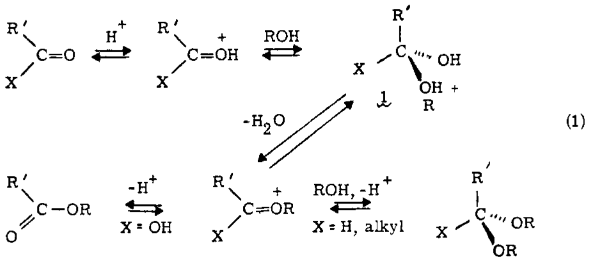
Mechanisms of Ionic Reactions in the Gas Phase. Displacement Reactions at Carbonyl Carbon

James K. Pau, Jhong K. Kim, and Marjorie C. Caserio*

Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received September 12, 1977*

Abstract: Ion cyclotron resonance methods have been used to study the ion-molecule reactions of carbonyl compounds with alcohols. The selectivity and site of C-O bond cleavage in gas-phase esterification and related reactions have been determined in several cases. Thus, protonated acetic acid reacted with ^{18}O-labeled methanol and 2-propanol to give protonated esters and neutral water by *O*-acyl cleavage. Protonated esters and hydroxycarbocations, $CH_3CH{=}OH^+$ and $(CH_3)_2C{=}OH^+$, condensed only with secondary and tertiary alcohols by *O*-alkyl cleavage. The mechanisms indicated by these and related results are discussed, and we conclude that formation of tetrahedral intermediates is *not* required in the particular gas-phase reactions studied.

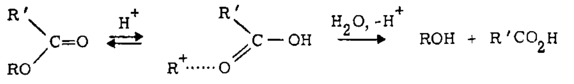
Solution reactions of carbonyl compounds with nucleophiles generally are acid or base catalyzed and lead to products of substitution at (or addition to) the carbonyl carbon. Important examples of acid-catalyzed reactions include the formation and hydrolysis of carboxylic esters, acetals, ketals, and ortho esters. A multiplicity of mechanisms exist for such reactions depending on the reactants and conditions used, but key steps in many cases involve preequilibrium proton transfer to the carbonyl oxygen followed by addition of the nucleophile to the carbonyl carbon. The tetrahedral intermediate **1** so formed can dissociate to re-form a trigonal carbon, which leads to products of substitution or addition depending on whether the carbonyl reactant is an acid, ester, aldehyde, or ketone.[1,2]



(1)

Compelling evidence exists in support of the carbonyl-addition mechanism of reaction 1 derived from kinetic, stereochemical, and isotope exchange data for acid-catalyzed ester, acetal, and ketal hydrolysis.[1,2] The mechanism, which requires that the carbonyl (acyl)-oxygen bond ruptures rather than the alkyl-oxygen bond, is commonly designated as $A_{AC}2$ for ester hydrolysis and A-1 for acetal hydrolysis.

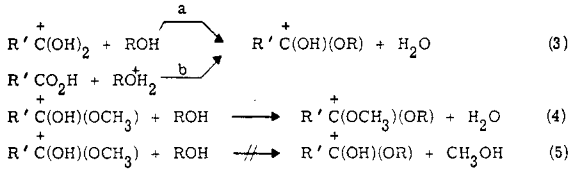
An alternate pathway for acid-catalyzed ester hydrolysis involving alkyl-oxygen cleavage ($A_{AL}1$) has been demonstrated and, as might be expected, this pathway dominates for tertiary alkyl esters.[3]



(2)

Positive ions equivalent to the conjugate acids of carbonyl compounds that are the reactants in reactions 1 and 2 can be produced in the gas phase by chemical ionization[4] and ion cyclotron resonance (ICR) techniques.[5] In many instances it is possible to observe condensation reactions of these ions with neutral alcohols in processes that formally are analogous to the solution-phase reactions 1 and 2. A study of such reactions is of special interest because it provides an opportunity to compare the behavior of gaseous ions (free of solvent and counterion effects) with that of the corresponding solvated ions. Because it is incorrect to assume that the gaseous ions will necessarily react by the same pathways as the solvated ions, a direct study of the gaseous reactions is clearly warranted.

A definitive gas-phase study of the ion-molecule reactions of carboxylic acids and esters with alcohols has been reported by Tiedemann and Riveros.[6] They showed by ICR techniques that esterification of the conjugate acid of a carboxylic acid (reaction 3a) is sensitive to the structure of both the acid and the alcohol. They report, as have we,[7] that protonated methyl esters react with alcohols by elimination of water (reaction 4) rather than methanol (reaction 5)—that is to say, alcoholysis (trans esterification) is not observed.



$$R'\overset{+}{C}(OH)_2 + ROH \xrightarrow{a} R'\overset{+}{C}(OH)(OR) + H_2O \qquad (3)$$

$$R'CO_2H + RO\overset{+}{H}_2 \xrightarrow{b} R'\overset{+}{C}(OH)(OR) + H_2O$$

$$R'\overset{+}{C}(OH)(OCH_3) + ROH \longrightarrow R'\overset{+}{C}(OCH_3)(OR) + H_2O \qquad (4)$$

$$R'\overset{+}{C}(OH)(OCH_3) + ROH \not\longrightarrow R'\overset{+}{C}(OH)(OR) + CH_3OH \qquad (5)$$

The structural effects noted for reactions 3 and 4 have been attributed to the relative gas-phase basicities (proton affinities) of the acid and alcohol or ester and alcohol.[6,8] Thus, a transition in mechanism from *O*-acyl to *O*-alkyl cleavage was suggested to occur in esterification as the reactant ion changes from the protonated acid (reaction 3a) to the protonated alcohol (reaction 3b). However, the site of C-O bond cleavage was not determined.

In the present paper we describe the results of related studies of the gas-phase ion molecule reactions of carbonyl compounds with alcohols and thiols. Our main objectives in this work were to elaborate on the scope of the reactions of alcohols with acids, esters, thioesters, and protonated aldehydes and ketones, and to determine the site of C-O bond cleavage using ^{18}O-labeling techniques.[7] We hoped thereby to delineate the mechanistic details of the gas-phase reactions and to compare them with their solution-phase counterparts.

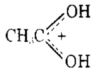
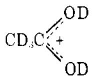
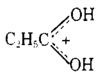
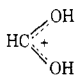
Experimental Section

Instrumentation. The gaseous ion-molecule chemistry of mixtures of an alcohol and a carbonyl compound was investigated by pulsed ICR techniques using a trapped-ion analyzer cell.[9] Sample pressures were on the order of 5×10^{-6} Torr and the ratio of the alcohol to the carbonyl compound was maintained within the range of 1:1 to 1.5:1. Reaction times were varied from 10 to 200 ms. The ion chemistry of each neutral reactant is well known,[10] which assisted greatly in the identification of product ions arising from mixtures of reactants. The precursor ion for each observed reaction was identified by double resonance techniques and by measuring the change in ion intensities with time.

Materials. All reagents whether obtained commercially or by synthesis were purified by preparative GLC. **Methanol-^{18}O** was prepared by the procedure of Sawyer[11] in which tri-*n*-butyl ortho-

0002-7863/78/1500-3831$01.00/0

Table I. Gas-Phase Esterification Reactions of Carboxylic Acids with Alcohols

Reactant Ion[a] (PA),[b] kcal mol^{-1}	Alcohol (PA),[b] kcal mol^{-1}	Product ion	Product neutral	$-\Delta H_{3a}$,[c] kcal mol^{-1}	$-\Delta H_{3b}$,[c] kcal mol^{-1}
 $CH_3C(OH)_2^+$ (187.4)[d]	$H_2{}^{18}O$ (170.3)	$CH_3C(OH)({}^{18}OH)^+$	H_2O	0	0
	$CH_3{}^{18}OH$ (182.2)	$CH_3C(OH)({}^{18}OCH_3)^+$	H_2O	13	18
	CH_3CH_2OH (186.7)	$CH_3C(OH)(OC_2H_5)^+$	H_2O	16	17
	$CD_3CH_2CH_2OH$ (188.8)	$CH_3C(OH)(OC_3H_4D_3)^+$	H_2O	16	16
	$CH_2{=}CHCH_2OH$ (—)	$CH_3C(OH)(OC_3H_5)^+$	H_2O		
 $CD_3C(OD)_2^+$	$(CH_3)_2CH^{18}OH$ (189)[e]	$CD_3C(OD)({}^{18}OC_3H_7)^+$	HDO	16	15
	$(CH_3)_3COH$ (192)[e]	*f*	—	11	7.3
 $C_2H_5C(OH)_2^+$ (190)[d]	CH_3OH (182.2)	$C_2H_5C(OH)(OCH_3)^+$	H_2O[g]	16	24
	CH_3CH_2OH (186.7)	$C_2H_5C(OH)(OC_2H_5)^+$	H_2O[g]	16	19
 $HC(OH)_2^+$ (180.1)	CH_3OH (182.2)	$CH_3OH_2^+$	HCO_2H[g]	11	8.3
	CH_3CH_2OH (186.7)	$C_2H_5OH_2^+$	HCO_2H[g]	11	4.7
	$(CH_3)_2CHOH$ (189)[e]	$HC(OH)(OC_3H_7)^+$	H_2O[g]	11	2.4
	$(CH_3)_3COH$ (192)[e]	$HC(OH)(OC_4H_9)^+$	H_2O[g]	9.0	−3.0

[a] Formed by proton transfer to the neutral from acidic fragment ions. [b] The gas-phase proton affinity (PA) of the neutral base is given in parentheses and corresponds to the enthalpy change in the reaction B: + $H^+ \rightarrow BH^+$. The PA values are taken mostly from the data of ref 14 and are based on the absolute value PA(NH_3) = 202.3 kcal mol^{-1}, or PA(H_2O) = 170.3 kcal mol^{-1}. [c] Enthalpies calculated from proton affinities[14,15] and heats of formation of neutrals listed by B. J. Zwolinski and R. C. Wilhoit in American Petroleum Institute Research Project 44, Thermodynamics Research Center, Texas A & M University, 1968; and by J. L. Franklin, J. G. Dillard, and F. H. Field in "Ionization Potentials, Appearance Potentials, and Heats of Formation of Gaseous Positive Ions", Vol. 26, National Bureau of Standards, Washington, D.C., 1969. [d] References 15 and 32. [e] PA values are estimated values based on the assumption that increasing methyl substitution at the α carbon will increase the PA to the same degree in ethanol as in ethylamine. The increment is 2.5 kcal for the first methyl and 2.3 for the second. The validity of this assumption is described in ref. 14. [f] Ion intensity was too low to obtain valid double resonance data. [g] Reference 6.

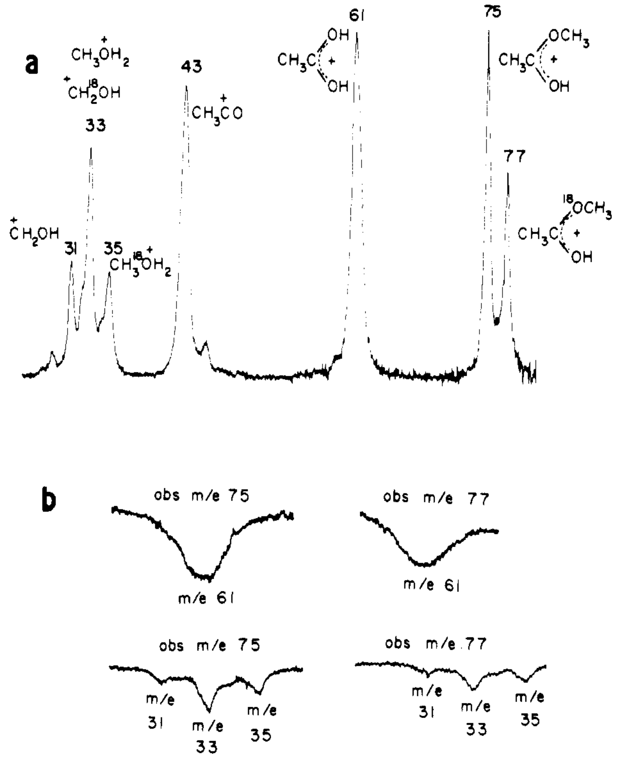
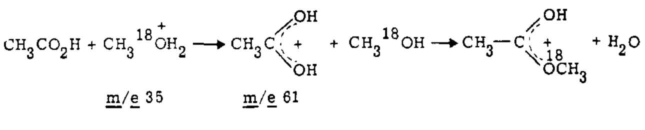


Figure 1. (a) Single resonance mass spectrum of a mixture of methanol, 36.8% enriched in ^{18}O, at 1.4 × 10^{-5} Torr and acetic acid at 0.6 × 10^{-5} Torr; (b) double resonance spectrum on observing *m/e* 75 and 77 indicating that both ions are derived from the same precursor ions.

formate was hydrolyzed by $H_2{}^{18}O$ (42% enriched) under acid conditions to give butyl formate-*carbonyl*-^{18}O. Reduction of the formate ester with lithium aluminum hydride gave methanol-^{18}O in 60.5% overall yield. Mass spectral analysis showed an isotopic enrichment of 36.8%. **2-Propanol-^{18}O** was obtained from acetone by acid-catalyzed ^{18}O exchange with $H_2{}^{18}O$ followed by reduction of the acetone-^{18}O with lithium aluminum hydride. The recovered alcohol was 25% enriched in ^{18}O. **2-Methyl-2-propanol-^{18}O** was prepared by the hydrolysis of *tert*-butyl chloride in $H_2{}^{18}O$-pyridine and had an isotopic enrichment of 42%.[10h] **1-Propanol-*3,3,3*-d_3** was prepared from ethylene oxide and methyllithium-d_3, **2-methyl-2-propanol-d_9** from hexadeuterioacetone and methylmagnesium-d_3 iodide, and **2-butanol-*1,1,1*-d_3** from propionaldehyde and methylmagnesium-d_3 iodide.[10g]

Results and Discussion

Carboxylic Acids. The most prominent reaction besides proton transfer in the ion chemistry of acetic acid and methanol is esterification of protonated acetic acid $CH_3C(OH)_2^+$ (*m/e* 61) to give protonated methyl acetate $CH_3C(OH)(OCH_3)^+$ (*m/e* 75). Using methanol that was 36.8% enriched in ^{18}O, product ions of *m/e* 77 were observed in addition to *m/e* 75 (see Figure 1a). The product ion *m/e* 77 corresponds to protonated methyl acetate-^{18}O and its appearance confirms that the oxygen of the neutral alcohol is retained in the product ion. The abundance ratio *m/e* 75 to *m/e* 77 was measured from the spectrum to be (63 ± 3)/(37 ± 3), which corresponds to 37% enrichment of ^{18}O in the ester ion. Therefore, virtually all the oxygen from the methanol is retained in the product ion. The oxygen of the neutral water molecule must then come from the acetic acid, and we may conclude that reaction occurs by cleavage of the *O*-acyl bond.[12] Protonated acetic acid *m/e* 61 was established as the reactant ion responsible for both *m/e* 75 and 77 from double resonance experiments (see Figure 1b). Other ions, *m/e* 31, 33, and 35 also lead to *m/e* 75 and 77, but they do so indirectly by way of *m/e* 61.



$$\underset{\underline{m/e}\ 35}{CH_3CO_2H + CH_3{}^{18}\overset{+}{O}H_2} \longrightarrow \underset{\underline{m/e}\ 61}{CH_3C(OH)_2^+} + CH_3{}^{18}OH \longrightarrow CH_3{-}C(OH)({}^{18}OCH_3)^+ + H_2O$$

The conjugate acid of acetic acid also reacted with $H_2{}^{18}O$ to produce the ^{18}O-labeled ion $CH_3C(OH)({}^{18}OH)^+$ in a thermoneutral exchange reaction that must involve acyl-oxygen cleavage. These and related results are summarized in Table I.

Condensation of $CH_3C(OH)_2^+$ (*m/e* 61) with 2-propanol was observed, but the reaction presented difficulties in interpretation because the product ion of interest $CH_3C(OH)(OC_3H_7)^+$ (*m/e* 103) has the same mass as the product ion derived from 2-propanol by reaction 6. However by using

$$(CH_3)_2CHOH + (CH_3)_2CH\overset{+}{O}H_2 \longrightarrow [(CH_3)_2CH]_2\overset{+}{O}H + H_2O \qquad (6)$$

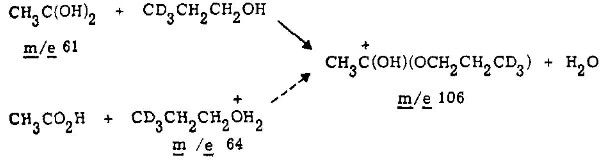
$$\underline{m}/\underline{e}\ 103$$

CD_3CO_2D it was possible to distinguish between the product ions of the two reactions because the ester ions now had *m/e* 106 and 107 corresponding to $CD_3C(OH)(OC_3H_7)^+$ and $CD_3C(OD)(OC_3H_7)^+$. 2-Propanol that was 25% enriched in ^{18}O reacted with CD_3CO_2D to give product ions *m/e* 106, 107, 108, and 109, clearly showing the incorporation of ^{18}O of the alcohol into the ester ion. By making the reasonable assumption that the ions *m/e* 107 and 109 correspond respectively to $CD_3C(OD)(OC_3H_7)^+$ and $CD_3C(OD)(^{18}OC_3H_7)^+$, the extent of ^{18}O incorporation estimated from the abundance ratio *m/e* 107:*m/e* 109 was 22% at 25-ms reaction time and 20% at 50-ms reaction time.[13] Therefore, reaction occurs extensively but perhaps not exclusively by *O*-acyl cleavage.

The esterification reaction 3 showed a pronounced structural dependence, as noted previously.[6] Thus, the qualitative order of reactivity of alcohols toward acetic acid in the ICR experiment is methanol > propanol > *tert*-butyl alcohol. The ion intensity of *m/e* 117 ascribable to the condensation of $CH_3C(OH)_2^+$ (*m/e* 61) with *tert*-butyl alcohol was so small that reliable double resonance data could not be obtained. Therefore, no ^{18}O studies were attempted with the acetic acid-*tert*-butyl alcohol system.

An initially puzzling observation of Tiedmann and Riveros[6] was that formic acid behaved quite differently from acetic acid toward simple alcohols, the opposite order of reactivity being observed, *tert*-ROH, *sec*-ROH ≫ *prim*-ROH. In the case of primary alcohols, only proton transfer occurred. These results have been explained as the consequence of the lower proton affinity of formic acid relative to acetic acid, and to the simple alcohols. The data of Table I certainly suggests that condensation with alcohols occurs only if the basicity (proton affinity) of the acid is greater than the alcohol. Under these circumstances the reactant ion is $R'CO_2H_2^+$, as in reaction 3a, and forms products with primary and secondary alcohols by *O*-acyl cleavage. However, if the acid has the lower proton affinity (as in formic acid) proton transfer to give ROH_2^+ dominates. Under these circumstances the reactants conform to reaction 3b, and it is of interest to know if this reaction channel is important and, if so, which C-O bond breaks.

The 1-propanol-acetic acid system represents an interesting test of the relative importance of reactions 3a and 3b for primary alcohols because the proton affinities of the two neutrals are comparable (Table I) and the intensities of their respective conjugate acids are almost equal. However, the $(M + 1)^+$ ions both have the same mass, *m/e* 61, and to differentiate between them we used deuterium-labeled 1-propanol, $CD_3CH_2CH_2OH$, which gave an $(M + 1)^+$ of *m/e* 64. The product ion of interest had *m/e* 106, and by double resonance it was determined that *m/e* 106 was formed mainly from *m/e* 61, $CH_3CO_2H_2^+$, with a very minor contribution from *m/e* 64. Reaction 3b is not then important for 1-propanol and acetic acid.



Regarding the behavior of secondary alcohols in reaction 3b, we attempted to determine the label distribution in the product derived from protonated 2-propanol-^{18}O (25% enriched) and formic acid. Regrettably, the abundance of *m/e* 89, which is presumed to be $HC(OH)(OC_3H_7)^+$, was low and reaction 3b must therefore be relatively unimportant. The intensity of *m/e* 91, which would correspond to the ^{18}O-containing product, was therefore negligible. In the case of *tert*-butyl alcohol, no significant reaction was observed with either acetic or formic acids. Therefore, we are led to the conclusion that carboxylic acids do not react readily with protonated alcohols in the gas phase, even when the structure of the alcohol favors ionic dissociation by *O*-alkyl cleavage.

In the hope that some understanding of the selectivity observed in the esterification reactions could be obtained from enthalpy data, the enthalpies of reactions 3a and 3b were estimated from heats of formation and proton affinity data of the neutral reactants and products. The values obtained are included in Table I. Both eq 3a and 3b are exothermic reactions with the single exception of reaction between formic acid protonated *tert*-butyl alcohol ($\Delta H \sim +3$ kcal). In themselves, the ΔH values for reaction 3a for the cases studied are not widely different ($-\Delta H = 9-16$ kcal) and are consistently more exothermic than proton transfer from the acid to the alcohol. Also, there is no striking difference between the ΔH values of reactions 3a and 3b for any one alcohol except in the case of formic acid esterification—here at least the ΔH_{3a} values are consistently more exothermic than ΔH_{3b}. Overall, the data offer little explanation of the observed reactivity differences.

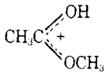
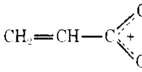
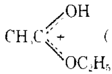
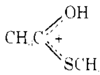
Carboxylic Esters. We and others have reported that protonated carboxylic esters react with certain alcohols in the gas phase to give dialkoxy carbocations and water (reaction 4).[6,7] This reaction more nearly resembles ortho ester formation than trans esterification (reaction 5). Although trans esterification was not observed in the ICR experiment, it is a major reaction in the ion-molecule chemistry of esters in chemical ionization studies[4a,18,19] where the reactant ion is a carbocation R^+.

Reaction 4 is strongly dependent on the structure of the starting alcohol as may be seen from the summary of our data in Table II. *No condensation of primary alcohols with esters was observed* even though, in almost every case, the basicity of the ester was greater than that of the alcohol. The evidence for this comes from the reactions of methyl acetate, ethyl acetate, and methyl thioacetate with primary alcohols from methanol to butanol, none of which gave dialkoxy carbocations, as expected of reaction 4. However, reaction 4 was observed between protonated esters (methyl acetate, ethyl acetate, methyl propenoate, methyl trifluoroacetate, and methyl thioacetate) and secondary alcohols (2-propanol and 2-butanol) and is a dominant process with tertiary butyl alcohol. These results contrast sharply with the behavior of acetic acid with alcohols where the primary alcohols condensed with $CH_3C^+(OH)_2$ (*m/e* 61) more easily than secondary alcohols, and where little or no reaction was evident with tertiary alcohols (Table I).

A more quantitative measurement of the relative reactivity of various alcohols toward methyl acetate was determined from the kinetics of reaction. By measuring ion intensity as a function of time at known sample pressures, the specific rates of reaction can be calculated.[9] The kinetic results are given in Table III and confirm that the tertiary alcohol reacts most rapidly.

To determine the site of C-O bond cleavage in the ester-alcohol reactions, we investigated their reactions using ^{18}O-labeled alcohols. The results are shown in Table II, and in every case studied the product ions of condensation of 2-propanol-^{18}O and of *tert*-butyl alcohol-^{18}O with the esters showed *no* incorporation of the isotopic label. The label was presumably

Table II. Condensation Reactions of Esters with Alcohols, Thiols, and Amines

Reactant ion[a] (PA),[b] kcal mol^{-1}	Reactant neutral (PA),[b] kcal mol^{-1}	Product ion	Product neutral
 $CH_3C(OH)(OCH_3)^+$ (195.4)	CH_3OH (182.2)		
	CH_3CH_2OH (186.7)		
	$CH_3CH_2CH_2OH$ (188.8)		
	$CH_3CH_2CH_2CH_2OH$ (189.3)		
	$CH_2{=}CHCH_2OH$ (—)		
	$(CH_3)_2CH^{18}OH$ (189)[c]	$CH_3C(OCH_3)(OC_3H_7)^+$	$H_2{}^{18}O$
	$(CH_3)_3C^{18}OH$ (192)[c]	$CH_3C(OCH_3)(OC_4H_9)^+$	$H_2{}^{18}O$
	$CH_3CH_2CH(CD_3)OH$ (193)	$CH_3C(OCH_3)(C_4H_6D_3)^+$	H_2O
	$C_2H_5NH_2$ (213.9)[d]	$C_2H_5NH_3{}^+$	$CH_3CO_2CH_3$
	$(C_2H_5)_2NH$ (222.7)[d]	$(C_2H_5)_2NH_2{}^+$	$CH_3CO_2CH_3$
	C_2H_5SH (189.3)[c]		
	$(CH_3)_2CHSH$ (192)[c]		
	$CH_3CH(C_2H_5)SH$ (192.5)		
	$(CH_3)_3CSH$ (194.6)	$CH_3C(OCH_3)(OC_4H_9)^+$	H_2S
$(CH_3)_3CSH_2{}^+$ (194)	$CH_3CO_2CH_3$ (195.4)	$CH_3C(OCH_3)(OC_4H_9)^+$	H_2S
 $CH_2{=}CH{-}C(OH)(OCH_3)^+$	$(CH_3)_2CH^{18}OH$ (189)[c]	$CH_2{=}CHC(OCH_3)(OC_3H_9)^+$	$H_2{}^{18}O$
	$(CH_3)_3C^{18}OH$ (192)[c]	$CH_2{=}CHC(OCH_3)(OC_4H_9)^+$	$H_2{}^{18}O$
 $CH_3C(OH)(OC_2H_5)^+$ (198.1)	$CH_3CH_2CH_2CH_2OH$ (189.3)		
	$(CH_3)_2CH^{18}OH$ (189)[c]	$CH_3C(OC_2H_5)(OC_3H_7)^+$	$H_2{}^{18}O$
	$C_2H_5CH(CD_3)OH$ (193)	$CH_3C(OC_2H_5)(OC_4H_6D_3)^+$	H_2O
	$(CH_3)_3C^{18}OH$ (192)	$CH_3C(OC_2H_5)(OC_4H_9)^+$	$H_2{}^{18}O$
	$(CD_3)_3COH$ (192)[c]	$CH_3C(OC_2H_5)(OC_4D_9)^+$	H_2O
$(CH_3)_2CH^{18+}OH_2$ (189.8)	$CF_3CO_2CH_3$ (177.3)	$CF_3C(OCH_3)(OC_3H_7)^+$	$H_2{}^{18}O$
$(CH_3)_3C^{+18}OH_2$ (192.3)	$CF_3CO_2CH_3$ (177.3)	$CF_3C(OCH_3)(OC_4H_9)^+$	$H_2{}^{18}O$
 $CH_3C(OH)(SCH_3)^+$ (~197)	C_2H_5OH (186.7)		
	$(CH_3)_2CHOH$ (189)		
	$CH_3CH(C_2H_5)OH$ (193)	$CH_3C(SCH_3)(OC_4H_9)^+$	H_2O
	$(CH_3)_3COH$ (192)	$CH_3C(SCH_3)(OC_4H_9)^+$	H_2O

[a] Formed by proton transfer to the neutral from acidic fragment ions. [b] See footnote *b*, Table I. [c] See footnote *e*, Table I. [d] References 16 and 17. Because of the revised value of PA(NH_3) = 202.3 kcal, the PA values in ref 17 are too high by 7 kcal.

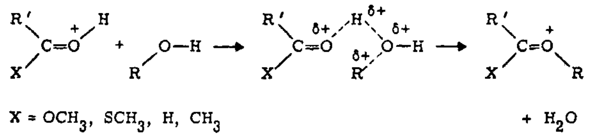
Table III. Kinetics of Reaction of Protonated Methyl Acetate with Alcohols

ROH[a]	*k*,[b] cm^3 mol^{-1} s^{-1}	Relative rate
$(CH_3)_2CHOH$	9.02×10^{-11}	1
$CH_3(C_2H_5)CHOH$	2.63×10^{-10}	2.9
$(CH)_3COH$	6.86×10^{-10}	7.6

[a] Pressure of alcohol was 2.3×10^{-6} Torr; pressure of ester was 1.7×10^{-6} Torr. [b] The absolute rate constants are estimated to have error limits of ±20%, the large uncertainty arising from the error in measuring the absolute pressure. The relative rates are more reliable because of cancellation of errors.

eliminated as neutral water. *This result requires that the esters react with alcohols by cleavage of the alcohol C–O bond.* A reasonable mechanism consistent with the evidence is one in which the ion–molecule complex initially formed undergoes a complete or partial proton transfer from the carbonyl oxygen to the alcohol oxygen, and this step is accompanied or succeeded by displacement of water from the alcohol (Scheme I).

Scheme I



The energetics of Scheme I are almost certainly favorable provided that the ion–molecule complex is strongly hydrogen bonded, as indicated. Enthalpies of formation of hydrogen-bonded cluster ions of the type $CH_3OH_2{}^+$-CH_3OH ($\Delta H = -33.1$ kcal[20a]) and $C_2H_5OH_2{}^+$-H_2O ($\Delta H = -24$ kcal[20b]) are substantial. Therefore, cluster formation in the present case is probably exothermic by 10–40 kcal, which is the range of energies expected for strongly hydrogen-bonded cluster ions.[8a]

In the case of methyl trifluoroacetate, the proton affinity of the ester is less than that of the alcohol such that the reactant ion is the protonated alcohol rather than the protonated ester. Alkyl–oxygen cleavage was observed for this ester with both 2-propanol-^{18}O and *tert*-butyl alcohol-^{18}O. The reaction is best described as a nucleophilic displacement of water from the protonated alcohol by the ester molecule.

$$CF_3CO_2CH_3 + R^{18}OH_2{}^+ \longrightarrow CF_3\overset{+}{C}(OCH_3)(OR) + H_2{}^{18}O$$

According to the mechanistic description in Scheme I, the alkyl group of the alcohol acquires the character of a carbocation in the intermediate complex of reaction. This picture is supported by the reactivity sequence *tert*-ROH > *sec*-ROH > *prim*-ROH. Among primary alcohols, 2-propenol appears suited to react by Scheme I because of its potential to form a stabilized carbocation; yet no reaction was observed between 2-propenol and methyl acetate other than proton transfer.

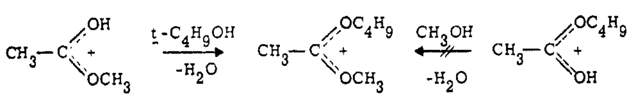
As shown in Table II, protonated methyl acetate reacts with *tert*-butyl alcohol to produce an ion of composition and presumed structure **2**. An alternate route to the same product ion

Table IV. Reactions of Hydroxycarbocations with Alcohols

Reactant ion[a] (PA),[b] kcal mol^{-1}	Alcohol (PA),[b] kcal mol^{-1}	Product ion	Product neutral
$CH_2{=}OH^+$ (174.6)	$H_2{}^{18}O$ (170.3)	$H_3{}^{18}O^+$	HCHO
	CH_3OH (182.2)	$CH_3OH_2{}^+$	HCHO
	CH_3CH_2OH (186.7)	$C_2H_5OH_2{}^+$	HCHO
	$CH_3CH_2CH_2CH_2OH$ (189.3)	$C_4H_9OH_2{}^+$	HCHO
	$CH_2{=}CHCH_2OH$ (—)	$C_3H_5OH_2{}^+$	HCHO
	$(CH_3)_2CHOH$ (189)[c]	$C_3H_7OH_2{}^+$	HCHO
	$(CH_3)_3COH$ (192)[c]	$C_4H_9OH_2{}^+$	HCHO
$CH_3CH{=}OH^+$ (185)	$H_2{}^{18}O$ (170.3)		
	CH_3CH_2OH (186.7)	$C_2H_5OH_2{}^+$	CH_3CHO
	$CH_3CH_2CH_2CH_2OH$ (189.3)	$C_4H_9OH_2{}^+$	CH_3CHO
	$(CH_3)_2CH^{18}OH$ (189)[c]	$CH_3CH{=}OCH(CH_3)_2{}^+$	$H_2{}^{18}O$
$CH_3CH{=}{}^{18}OH^+$	$(CH_3)_2CHOH$	$CH_3CH{=}{}^{18}OCH(CH_3)_2{}^+$	H_2O
$CD_3CH{=}OH^+$	$(CD_3)_2CHOH$	$CD_3CH{=}OCH(CD_3)_2{}^+$	H_2O
$CH_3CH{=}OH^+$	$(CH_3)_3COH$ (192)[c]	$C_4H_9OH_2{}^+$	CH_3CHO
$(CD_3)_2C{=}OH^+$ [d] (193.9)	$CH_3CH_2CH_2OH$ (188.8)		
$(CH_3)_2C{=}OH^+$ (193.9)	$CH_3CH_2CH_2CH_2OH$ (189.3)	$C_4H_9OH_2{}^+$	$(CH_3)_2C{=}O$
	$(CH_3)_2CH^{18}OH$ (189)[c]	$(CH_3)_2C{=}OCH(CH_3)_2{}^+$	$H_2{}^{18}O$
	$(CD_3)_2CHOH$	$(CH_3)_2C{=}OCH(CD_3)_2{}^+$	H_2O
$(CH_3)_2C{=}{}^{18}OH^+$	$(CH_3)_2CHOH$	$(CH_3)_2C{=}{}^{18}OCH(CH_3)_2{}^+$	H_2O
	$(CD_3)_2CHOH$	$(CH_3)_2C{=}{}^{18}OCH(CD_3)_2{}^+$	H_2O
$(CD_3)_2C{=}OH^+$	$(CH_3)_2CH^{18}OH$	$(CD_3)_2C{=}OCH(CH_3)_2{}^+$	$H_2{}^{18}O$
$(CH_3)_2C{=}OH^+$ (193.9)	$(CH_3)_3C^{18}OH$ (192)[c]	$(CH_3)_2C{=}OC(CH_3)_3{}^+$	$H_2{}^{18}O$
$(CH_3)_2C{=}{}^{18}OH^+$	$(CH_3)_3COH$	$(CH_3)_2C{=}{}^{18}OC(CH_3)_3{}^+$	H_2O
	$(CD_3)_3COH$	$(CH_3)_2C{=}{}^{18}OC(CD_3)_3{}^+$	H_2O
$(CD_3)_2C{=}OH^+$	$(CH)_3C^{18}OH$	$(CD_3)_2C{=}OC(CH_3)_3{}^+$	$H_2{}^{18}O$

[a] Reactant ions are fragment ions of α cleavage of alcohols on electron impact. [b] See footnote *b*, Table I. [c] See footnote *e*, Table I. [d] Formed from hexadeuterioacetone-propanol mixtures.

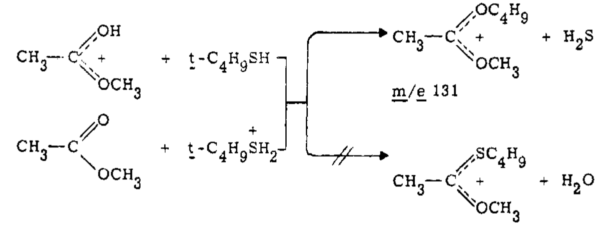
by way of protonated *tert*-butyl acetate and methanol is conceivable. If the driving force of ion-molecule reactions in an ICR experiment is solely the exothermicity of reaction, then the product ion **2** should be obtainable from both methyl and *tert*-butyl acetates because the enthalpies of the two reactions differ by only 1-2 kcal. In fact, no reaction was observed between methanol and protonated *tert*-butyl acetate. Therefore, the transition state or intermediate complex that produces **2** from methyl acetate and *t*-C_4H_9OH cannot be attained readily from the direction of *tert*-butyl acetate and methanol.



2

Another illustration that the reactants do not necessarily give the most stable products comes from the reaction of methyl acetate with thiols. Only 2-methyl-2-propanethiol reacted, and the neutral product was H_2S rather than H_2O even though the loss of water is almost certainly the most exothermic channel.[21] The thiol reaction very clearly must proceed by rupture of the C-S bond. Also significant is the fact that both the ester and thiol have comparable basicities and form major $(M + 1)^+$ ions. Double resonance showed that the product ion *m/e* 131 was formed from both $(M + 1)^+$ ions, protonated methyl acetate and protonated 2-methyl-2-propanethiol. The conclusion seems inescapable that the thiol, like the alcohols, reacts with esters by a gas-phase ionic displacement reaction, as described by Scheme I.

Scheme I



Conceivably, protonated esters could react with amines in the gas phase to produce protonated or O-alkylated amides of structure $RC(OH)NH_2{}^+$ or $RC(OR)NH_2{}^+$. However, attempts to identify product ions of either type were unsuccessful. The proton affinities of the amines employed (ethylamine and diethylamine) were substantially higher than methyl acetate. Hence only proton transfer to the neutral amine was observed.

Hydroxy Carbocations with Alcohols. Ionization of alcohols on electron impact leads to fragmentation of the molecular ion by α cleavage. The fragment ions, which are the gaseous analogues of protonated aldehydes or ketones, react further with the parent alcohol in a variety of ways.[10] A reaction of interest in the context of the present study is a condensation whereby neutral water is eliminated (reaction 7). This reaction is formally related to acid-catalyzed formation or hydrolysis of acetals and ketals in solution where ions of type **3** are key intermediates.[2] The most commonly observed pathway for the solution-phase reaction is consistent with the steps in eq 1 where the acyl-oxygen bond is broken by way of tetrahedral addition intermediates **1**. We were curious to see if the corresponding gaseous reaction (7) took a similar pathway. We therefore investigated the scope of the reaction and the site of C-O bond cleavage.[10h] The results are summarized in Table IV.

$$R'_2C{=}\overset{+}{O}H + ROH \longrightarrow R'_2C{=}\overset{+}{O}R + H_2O \qquad (7)$$

3

It has been noted previously[10] that protonated formaldehyde does not condense with alcohols by reaction 7. Table IV shows that, regardless of whether the alcohol is primary, secondary, or tertiary, the only reaction involving $CH_2{=}OH^+$ is proton transfer to the alcohol. The reason is almost certainly that formaldehyde is much less basic than any of the alcohols, which makes proton transfer substantially exothermic (8-23 kcal) and more rapid than any other reaction channel available to these reagents. Nonetheless, water has a *lower* proton affinity than $CH_2{=}O$, yet does not undergo ^{18}O exchange with $CH_2{=}OH^+$. With $CH_3CH{=}OH^+$ and $(CH_3)_2C{=}OH^+$ as reactant ions, the situation is more interesting. Neither ion condensed with primary alcohols to any detectable extent. This was so regardless of whether the reactant ion was formed from α cleavage of an alcohol or from protonation of the parent carbonyl compound. Both ions condensed with 2-propanol to give product ions that presumably are alkoxy carbocations **3**. With 2-propanol-^{18}O as the neutral reactant and with either $CH_3CH{=}OH^+$ or $(CH_3)_2C{=}OH^+$ as the reactant ion, the product ions contained *no* ^{18}O label; with either $CH_3CH{=}^{18}OH^+$ or $(CH_3)_2C{=}^{18}OH^+$ and unlabeled 2-propanol, the product ions corresponded respectively to $CH_3CH{=}^{18}OC_3H_7^+$ and $(CH_3)_2C{=}^{18}OC_3H_7^+$. These results leave no doubt that reaction occurs with cleavage of the C—O bond of 2-propanol.

With *tert*-butyl alcohol and $CH_3CH{=}^+OH$, proton transfer is exothermic by 13 kcal and is the only reaction observed. With *tert*-butyl alcohol and $(CH_3)_2C{=}^+OH$ condensation was observed, and reaction between unlabeled reactant ion and ^{18}O-labeled alcohol produced *unlabeled* product ion; reaction between $(CH_3)_2C{=}^{18}OH^+$ and unlabeled alcohol produced $(CH_3)_2C{=}^{18}OC_4H_9$, confirming that reaction occurs by alkyl-oxygen cleavage.[10h]

These results are quite similar to the condensation reactions of esters with alcohols and are best formulated by the sequence in Scheme I (X = H or CH_3).

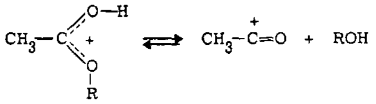
Conclusions

Overall, the ICR results are complementary to the solution behavior of carbonyl compounds toward alcohols in that either *O*-acyl or *O*-alkyl cleavage occurs depending on the structures of the neutral reactants. The structural dependence may seem unremarkable, *O*-acyl cleavage dominating in esterification of acids with primary alcohols, and *O*-alkyl cleavage dominating in the reactions of the conjugate acids of esters and ketones with tertiary alcohols. However, a closer look at the selectivity in the gas-phase reactions reveals some apparent inconsistencies.

The observed selectivity in the gas-phase esterification of carboxylic acids with alcohols (Table I) can certainly be attributed to the basicity of the acid relative to the alcohol. Provided that the acid is the stronger base, the reactants are the protonated acid and the neutral alcohol, which react to form protonated ester by *O*-acyl cleavage in the order of reactivity *prim*-ROH > *sec*-ROH ≫ *tert*-ROH. By analogy, we would expect a similar mode of behavior in the gas-phase ionic reactions of other carbonyl compounds with alcohols, but, in fact, surprising differences exist. The most notable difference is the absence of observable condensation between protonated esters, thioesters, aldehydes, or ketones with primary alcohols, even when the carbonyl reactant is the stronger base. The facts are that condensation is restricted to secondary and tertiary alcohols by way of *O*-alkyl cleavage.

Possibly the difference in the reactions of acids and esters with alcohols is in the site of protonation of the reactant ion. The evidence as to which oxygen is more basic is not entirely clear. There seems little doubt that both acids and esters protonate on the carbonyl oxygen in strongly acidic media,[22,23] but it does not follow that the neutrals will protonate the same way in the gas phase. Ab initio calculations favor carbonyl protonation for formic acid,[22d] but, in the case of esters, experimental gas-phase data has been advanced for both carbonyl protonation[24] and *O*-alkyl protonation.[25]

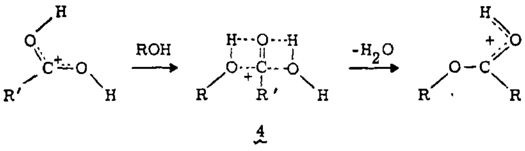
Actually the site of protonation in the acid or ester may be irrelevant to the outcome of reaction with alcohols because of the rapidity of proton transfers between basic sites of a molecule. For instance, in acidic media at −70 °C, methyl acetate protonates at the carbonyl oxygen yet dissociates on warming by $A_{AC}1$ cleavage.[23] Likewise, in the gas phase, association of an acetyl ion with water reportedly gives protonated acetic acid (ΔH = 19 kcal).[26]



Related proton transfers can be formulated for the gas-phase esterification of protonated acids with alcohols (Scheme II). The reactant ion is visualized as initially protonated at the carbonyl oxygen but, on collision with the neutral alcohol, forms a complex **4** which is a type of "solvated" acyl cation where the carbonyl group is associated with both the entering and leaving hydroxyl groups. Dissociation of water can easily occur in this configuration, and the net reaction more nearly resembles a concerted displacement than a stepwise addition–elimination reaction.[27]

Scheme II is attractive because it avoids postulating a tetrahedral addition intermediate such as **1** which is estimated to be formed in a step that is energetically unfavorable by ~20 kcal.[28] The low pressure conditions of an ICR experiment do not normally allow ion–molecule reactions to proceed at observable rates if they are endothermic or require thermal activation. Most ion–molecule reactions produce reaction complexes of *lower* enthalpy than the reactants, and for this reason the complexes are usually forced to dissociate to disperse their excess internal energy.[8] Hence, a reaction by way of **1** may well be less likely than by way of **4**. However, addition intermediates in the reactions of carbonyl compounds have been detected in gas phase ICR experiments, but only with negative ion nucleophiles and when the endothermicity of forming the addition intermediate is minimal.[9,30] In the present case, the plausibility of the displacement route for esterification (Scheme II) depends on the energetics of formation of the ion–molecule complex **4**. Unfortunately, the enthalpy of formation of a cluster ion of the type $H_2O{\cdots}R^+{\cdots}OH_2$ in which the association is between a vacant carbon orbital and two neutral n-donor molecules is not known. In fact, a cluster ion of this configuration is normally regarded as a transition state, but, regardless of whether **4** is a cluster ion or a transition state, it is possible to estimate that its enthalpy of formation should be less than that of **1** from the following considerations. Dissociation of protonated acetic acid, to give CH_3CO^+ and water is endothermic by 19 kcal[26] (reaction 8). The gain in energy resulting from cluster formation between methanol, water, and CH_3CO^+ to give **4** (reaction 9) will make the overall process of complex formation between protonated acetic acid and methanol (reactions 8 and 9) less endothermic (more favorable) than 19 kcal. By this reasoning, formation of **1** is less favorable than formation of **4** from the same reactants.

Scheme II



$$\begin{array}{lll} CH_3CO_2H_2^+ \longrightarrow & CH_3\overset{+}{C}O + H_2O & (8) \\ & \Big\downarrow CH_3OH & \\ & CH_3\overset{+}{C}O(H_2O)(CH_3OH) & (9) \end{array}$$

A reliable estimate of the association energy in reaction 9 is not available by direct measurement, but a reasonable estimate can be made by comparing reaction 9 with the hydration of alkali metal ions in the gas phase:[20b]

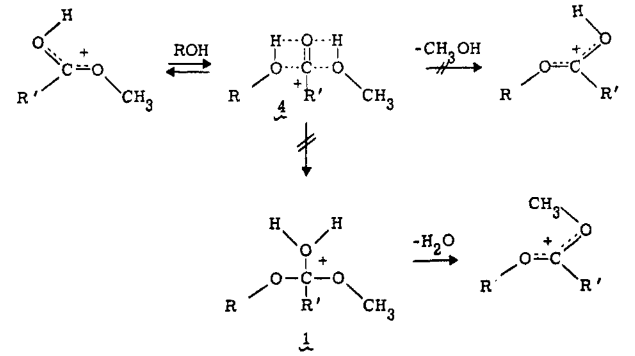
$$M^+ + H_2O \rightarrow M^+(H_2O) \quad -\Delta H = 14\text{-}34 \text{ kcal}$$

$$M^+(H_2O) + H_2O \rightarrow M^+(H_2O)_2 \quad \Delta H = 12\text{-}26 \text{ kcal}$$

In both **4** and the metal hydrates, interaction between the ion and the neutrals is probably one of ion-dipole association rather than covalent bond formation. Assuming that the association energies of an acyl cation with water and methanol are comparable to the hydration energies of M^+, then reaction 9 should be exothermic by at least 26 kcal. Formation of **4** by Scheme II is therefore energetically favorable by at least 26 − 19 = 7 kcal. By this reasoning, we conclude that esterification by a displacement route (Scheme II) is a more likely pathway than by way of a tetrahedral covalent intermediate.

Why then do esters not react with alcohols by a route similar to Scheme II? An explanation of this anomaly is that such a pathway for esters could lead only to alcoholysis or ester interchange, which is *not* observed (Scheme III).

Scheme III



There is no reasonable way of describing a reaction of protonated esters with alcohols that would lead to loss of neutral water by *O*-acyl cleavage without postulating the formation of a tetrahedral intermediate or something very like it. Put another way, there is no simple way to describe the loss of water from protonated ester and alcohol such that the entering and departing oxygens utilize opposing lobes of the *same* orbital at the carbonyl carbon. An alternate but apparently unfavorable pathway is by way of an intermediate **1**.

Similar arguments can be made to explain why it is that ions of the type $CH_3CH{=}OH^+$ and $(CH_3)_2C{=}OH^+$ do not react with alcohols by addition-elimination, either by way of a tetrahedral covalent intermediate or a cluster ion similar to **4**. The observed pathway for reaction of protonated esters, aldehydes, and ketones with alcohols corresponds to the energetically preferred route of ion-molecule association through strong hydrogen-bond formation (Scheme I) which leads to *O*-alkyl cleavage.

In summary, we conclude that the conjugate acids of carbonyl compounds investigated here do not react readily with alcohols in the gas phase at low pressures unless they can do so by a displacement reaction which, in the case of carboxylic acids, is best described in Scheme II and, in the case of esters, aldehydes and ketones, by Scheme I.

Acknowledgment. We are grateful to the National Science Foundation (CHE 74-08023 A02) for support of this work and to the Guggenheim Foundation for a fellowship (M.C.C.).

References and Notes

(1) The mechanisms of esterification and hydrolysis are summarized in (a) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 2nd ed, 1969, Chapter 15; (b) J. Hine, "Physical Organic Chemistry", 2nd ed, McGraw-Hill, N.Y., 1962, Chapter 12; (c) M. L. Bender, *Chem. Rev.*, **60,** 53 (1960); (d) A. G. Davies and J. Kenyon, *Quart. Rev.* (London), **9,** 203 (1955); (e) E. K. Euranto in "The Chemistry of Carboxylic Acids and Esters", S. Patai, Ed., Interscience, New York, N.Y., 1969, Chapter 11.
(2) Mechanism and catalysis in acetal, ketal, and ortho ester hydrolysis have been reviewed by (a) E. H. Cordes, *Prog. Org. Chem.*, **4,** 1 (1967); (b) T. H. Fife, *Acc. Chem. Res.*, **5,** 264 (1972); (c) E. H. Cordes in "The Chemistry of Carboxylic Acids and Esters", S. Patai, Ed., Interscience, New York, N.Y., 1969, Chapter 13: (d) E. H. Cordes and H. G. Bull, *Chem. Rev.*, **74,** 581 (1974).
(3) S. G. Cohen and A. Schneider, *J. Am. Chem. Soc.*, **63,** 3382 (1941).
(4) (a) M. S. B. Munson and F. H. Field, *J. Am. Chem. Soc.*, **88,** 4337 (1966); (b) F. H. Field, *Acc. Chem. Res.*, **1,** 42 (1968); (c) M. S. B. Munson, *Anal. Chem.*, **43,** 28A, No. 13 (1971).
(5) (a) J. D. Baldeschwieler, *Science*, 159, 263 (1968); (b) C. J. Drewery, G. C. Goode, and K. R. Jennings, *MTP Int. Rev. Sci.: Phys. Chem., Ser. One*, **5,** 259 (1972); (c) J. L. Beauchamp, *Ann. Rev. Phys. Chem.*, **22,** 527 (1971).
(6) P. W. Tiedemann and J. M. Riveros, *J. Am. Chem. Soc.*, **96,** 185 (1974).
(7) For a preliminary account of the work reported in this paper, see J. K. Pau, J. K. Kim, and M. C. Caserio, *J. Chem. Soc., Chem. Commun.*, 120 (1974).
(8) J. L. Beauchamp in "Interactions Between Ions and Molecules", P. Ausloos, Ed., Plenum Press, New York, N.Y., 1975, pp 418–436.
(9) R. T. McIver, Jr., *Rev. Sci. Instrum.*, **49,** 111 (1977); **41,** 555 (1970). R. T. McIver, Jr., and A. D. Baranyi, *Int. J. Mass Spectrom. Ion Phys.*, **14,** 449 (1974).
(10) (a) M. S. B. Munson, *J. Am. Chem. Soc.*, **87,** 5313 (1965); (b) J. M. S. Henis, *ibid.*, **90,** 844 (1968); (c) L. W. Sieck, F. P. Abramson, and J. H. Futrell, *J. Chem. Phys.*, **45,** 2859 (1966); (d) K. R. Ryan, L. W. Sieck, and J. H. Futrell, *J. Chem. Phys.*, **41,** 111 (1964); (e) J. L. Beauchamp and R. C. Dunbar, *J. Am. Chem. Soc.*, **92,** 1477 (1970); (f) T. A. Lehman, T. A. Elwood, J. T. Bursey, M. M. Bursey, and J. L. Beauchamp, *ibid.*, **93,** 2108 (1971); (g) J. L. Beauchamp and M. C. Caserio, *ibid.*, **94,** 2638 (1972); (h) J. L. Beauchamp, M. C. Caserio, and T. B. McMahon, *ibid.*, **96,** 6243 (1974).
(11) C. B. Sawyer, *J. Org. Chem.*, **37,** 4225 (1972).
(12) In unpublished work, J. Cook and J. L. Beauchamp have investigated the gaseous ionic reactions of ^{18}O-labeled acetic acid with unlabeled alcohols. Their results are entirely consistent with those reported here. See ref 8.
(13) The ratios (106 + 107):(108 + 109) and 106:108 should give the same result as 107:109 but unfortunately the measured intensity of *m/e* 106 is too high because of contributions from $(C_3H_7)_2{}^{18}OD^+$.
(14) J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver, Jr., J. L. Beauchamp, and R. W. Taft, *J. Am. Chem. Soc.*, **99,** 5417 (1977).
(15) J. Long and B. Munson, *J. Am. Chem. Soc.*, **95,** 2427 (1973).
(16) R. H. Staley, M. Taagepera, W. G. Henderson, I. Koppel, J. L. Beauchamp, and R. W. Taft, *J. Am. Chem. Soc.*, **99,** 326 (1977).
(17) D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Am. Chem. Soc.*, **98,** 311 (1976).
(18) W. A. Laurie and F. H. Field, *J. Am. Chem. Soc.*, **94,** 2913 (1972).
(19) R. J. Weinkam and J. Gal, *Org. Mass. Spectrom.*, **11,** 188, 197 (1976).
(20) (a) E. P. Grimsrud, P. Kebarle, *J. Am. Chem. Soc.*, **95,** 7939 (1973); K. Hiraoka, P. Kebarle, *J. Chem. Phys.*, **62,** 2267 (1975); (b) P, Kebarle, *Ann. Rev. Phys. Chem.*, **28,** 445 (1977).
(21) The enthalpy difference between the two reactions is estimated to be at least 7 kcal in favor of water elimination based on $\Delta H_f(H_2O) = -57.8$ kcal, $\Delta H_f(H_2S) = -4.5$ kcal and an estimated difference of 46 kcal between the heats of formation of the product ions. In making this estimate it was assumed that $\Delta\Delta H_f$ of the product ions is equal to the $\Delta\Delta H_f$ of protonated methyl acetate and thioacetate. Using $\Delta H_f(CH_3C^+(OH)(OCH_3)) = 70.6$ kcal and $\Delta H_f(CH_3C(O)SCH_3) = -51$ kcal[31] and the observation that the proton affinity of methyl thioacetate is ~2 kcal higher than methyl acetate (private communication of results of R. W. Taft and J. L. Abboud), then $\Delta H_f(CH_3C(OH)(SCH_3)^+)$ was estimated as 117 kcal and $\Delta H_f(CH_3C(OH)(OCH_3)^+) - \Delta H_f(CH_3C(OH)(SCH_3)^+)$ as 46 kcal.
(22) (a) G. Fraenkel, *J. Chem. Phys.*, **34,** 1466 (1961); (b) H. Hogeveen, A. F. Bickel, C. W. Hilbers, E. L. Mackor, and C. MacLean, *Recl. Trav. Chim. Pays-Bas*, **86,** 687 (1967); (c) G. A. Olah, and A. M. White, *J. Am. Chem. Soc.*, **89,** 3591 (1967); (d) A. C. Hopkinson, K. Yates, and I. G. Csizmadia, *J. Chem. Phys.*, **52,** 1784 (1970).
(23) (a) G. A. Olah, D. H. O'Brien, and M. White, *J. Am. Chem. Soc.*, **89,** 5694 (1967).
(24) T. X. Carroll, S. R. Smith, and T. D. Thomas, *J. Am. Chem. Soc.*, **97,** 659 (1975).
(25) C. V. Pescheck and S. E. Buttrill, Jr., *J. Am. Chem. Soc.*, **96,** 6027 (1974).
(26) K. Hiraoka and P. Kebarle, *J. Am. Chem. Soc.*, **99,** 366 (1977).
(27) Concerted displacement vs. addition–elimination has been argued for and against in solution-phase acyl transfer reactions.[1]
(28) Estimated from the proton affinity of acetic acid (187 kcal), the proton affinity of $CH_3C(OH)_3$ taken as 190 kcal, and the enthalpy of hydration of acetic acid calculated from bond energies assuming a resonance energy of 14 kcal for the carboxyl group.
(29) O. I. Asubiojo, L. K. Blair, and J. I. Brauman, *J. Am. Chem. Soc.*, **97,** 6685 (1975).
(30) J. H. Bowie and B. D. Williams, *Aust. J. Chem.*, **27,** 1923 (1974).
(31) H. Mackle, *Tetrahedron*, **19,** 1159 (1963).
(32) R. Yamdagni and P. Kebarle, *J. Am. Chem. Soc.*, **98,** 1320 (1976).