Gas-phase Ionic Reactions Related to Acid-catalysed Carbonyl Reactions in Solution

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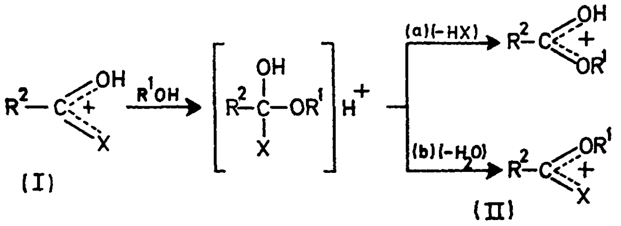
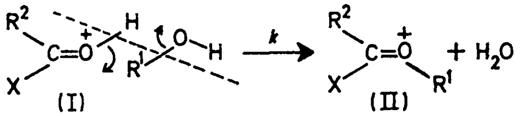
Summary Protonated esters, aldehydes, and ketones react with secondary and tertiary alcohols in the gas phase by way of nucleophilic displacement to eliminate water by alkyl–oxygen cleavage of the attacking alcohol, whereas alkoxycarbonium ions react with alcohols by an addition–elimination sequence.

Acid-catalysed solvolysis reactions of carboxylic acid derivatives commonly proceed by addition–elimination mechanisms involving tetrahedral intermediates. These are formed by initial proton transfer to the carbonyl oxygen, then nucleophilic attack of the solvent R^1OH at the carbonyl carbon with the result that the acyl group is transferred to the oxygen of the attacking nucleophile [equation (1) path (a)].[1] Related reactions of the protonated carbonyl compounds (I) can be studied in the gas phase by ion cyclotron resonance techniques.[2] Thus neutral esters on electron impact generate acidic fragment ions which transfer a labile proton to the parent neutral to give ions of type (I); these ions may react with neutral alcohols to give the products (II) by elimination of water in what may be described as a type of esterification. However, we report that in the case of the acetate esters (I; R^2 = Me, X = OMe, OEt) the reaction is not an addition-elimination [equation

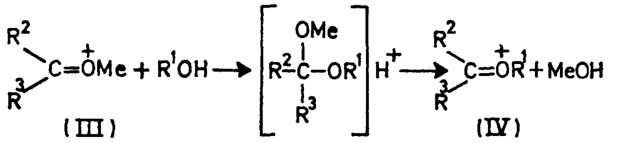
(1) path (b)] but a displacement reaction at carbon of the alcohol. By using ^{18}O-labelled alcohols (R^1 = Bu^t, Pr^i)



(1)



(2)



(3)

and unlabelled methyl and ethyl acetates we observe that the oxygen of the alcohol is not incorporated into the product ion (II). This result suggests that reaction involves proton transfer from the ion to the alcohol oxygen accompanied by displacement of water with alkyl-oxygen cleavage [equation (2)].† Reaction is sensitive to the structure of the alcohol since the reactivity sequence observed was Bu^{t}OH > Bu^{s}OH, Pr^{i}OH >> Bu^{n}OH. Rate constants k for the reaction of protonated methyl acetate with Bu^{t}OH, Bu^{s}OH, and Pr^{i}OH were determined as 6·6, 2·6, and $0{\cdot}9 \times 10^{10}$ cm^3 mol^{-1} s^{-1}, respectively. We were unable to detect any significant reaction of the primary alcohols R^1OH where R^1 = Et, Pr, Bu, allyl with either methyl or ethyl acetate. With the more electrophilic ester, methyl trifluoroacetate, labelled Bu^{t}OH and Pr^{i}OH reacted similarly by loss of the alcohol oxygen [equation (2)] although the ionic reactant was $\overset{+}{\mathrm{ROH}_2}$ rather than (I; R^2 = CF_3, X = OMe). Elimination of HX corresponding to equation (1) path (a) was not observed for any of the ester–alcohol mixtures studied, meaning that reaction involves the hydroxy function of (I) in preference to the alkoxy function.

Acetal formation is closely related to esterification under acidic conditions and generally proceeds in solution by way of carbonyl addition (*i.e.*, *A*-1 mechanism).[3] In the gas phase, acetal formation can be realized in part by generating protonated aldehydes or ketones from simple alcohols by electron impact (I; X = H, Me). The ions so formed may condense with the alcohols R^1OH to give the product ions (II).[4] We find that tertiary alcohols condense readily, secondary alcohols less so, the primary alcohols react only as proton acceptors. Using ^{18}O-labelled reactants, either in the ion or the neutral, the oxygen of the reactant ion is retained in the product while that of the neutral alcohol is lost, implying that reaction proceeds by displacement at carbon of the alcohol rather than by carbonyl addition [equation (2)].

Clearly the reactant ions (I) play the role of protic acids rather than electrophiles while the alcohols function as bases rather than as nucleophiles. With strongly acidic ions ($\overset{+}{\mathrm{CH_2{=}OH}}$)[5] only proton transfer to R^1OH is observed, regardless of the alkyl group R^1. With less acidic reactants such as the alkoxycarbonium ions (III), proton transfer to alcohols is unimportant but condensation can be observed to give the product ions (IV) [equation (3)].[6] Using ^{18}O-labelled methyl ethyl ether to generate m/e 47 $\mathrm{Me^{18}\overset{+}{O}{=}CH_2}$ and m/e 61 $\mathrm{Me^{18}\overset{+}{O}{=}CHMe}$ we find that both ions condense with 2-methoxyethanol with no retention of the label in the product ion. Nucleophilic addition of the alcohol evidently does occur at the electrophilic carbon of the reactant ions in these examples. It remains, however, difficult to account for the lack of reactivity of protonated esters towards primary alcohols; even when proton transfer to R^1OH does not occur, nucleophilic attack of R^1OH at the trigonal carbon is not observed.[7]

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† The acidic proton of (I) and the R^1 group of (II) are shown to be on the acyl oxygen although they could be associated with the group X.

[1] S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237.

[2] J. D. Baldeschwieler and S. S. Woodgate, *Accounts Chem. Res.*, 1971, **4**, 114.

[3] E. H. Cordes, *Progr. Phys. Org. Chem.*, 1967, **4**, 1.

[4] J. L. Beauchamp and M. C. Caserio, *J. Amer. Chem. Soc.*, 1972, **94**, 2638; J. L. Beauchamp, *ibid.*, 1969, **91**, 5925; J. L. Beauchamp and R. C. Dunbar, *ibid.*, 1970, **92**, 1477.

[5] Proton affinity of $CH_2{=}O$ is 166 kcal/mol; J. L. Beauchamp *Ann. Rev. Phys. Chem.*, 1971, **22**, 527.

[6] J. K. Kim, M. C. Findlay, W. G. Henderson, and M. C. Caserio, *J. Amer. Chem. Soc.*, 1973, **95**, 2184.

[7] Gas-phase esterification of protonated carboxylic acids with primary, secondary, and tertiary alcohols by way of tetrahedral intermediates has been observed: J. L. Beauchamp and J. H. Cook, personal communication.