

GENERAL BASE-CATALYSIS IN A CARBOXYLIC ESTER EXCHANGE REACTION

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EVIDENCE that a tetrahedral intermediate must lie on the reaction path for carboxylic ester solvolysis has been obtained. Tetrahedral intermediates have been strongly implicated in imido ester ammonolysis (1) and thiol ester hydrolysis (2) on the basis of kinetic evidence. In the case of carboxylic esters ($\text{RCO}_2\text{R}'$) tetrahedral intermediates are generally assumed to occur on the reaction path for solvolysis (3). Such intermediates have never been observed as transients. The observation of O^{18} exchange between an ester and H_2O^{18} during hydrolysis (4) does not prove that a tetrahedral intermediate must lie on the reaction path; it could just be a blind alley.

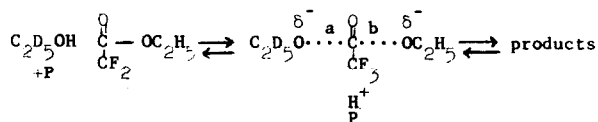
Because general base-catalysis of ester hydrolysis is an unsymmetrical reaction sequence, and can be interpreted by seven kinetically indistinguishable mechanistic schemes, we have studied a symmetrical reaction: the pyridine-catalyzed ethanolysis of ethyl trifluoroacetate for which there are only three kinetically indistinguishable mechanisms.

The ethanolysis was followed in pyridine-pyridinium nitrate buffers of various concentrations in deuterated ethanol ($\text{C}_2\text{D}_5\text{OH}$) by following the disappearance of the ethyl ester N.M.R. signal and the appearance of the ethanol ($\text{C}_2\text{H}_5\text{OH}$) signal at 38° . Strong general base-catalysis was found, but no general acid-catalysis was found. Also, no simultaneous general

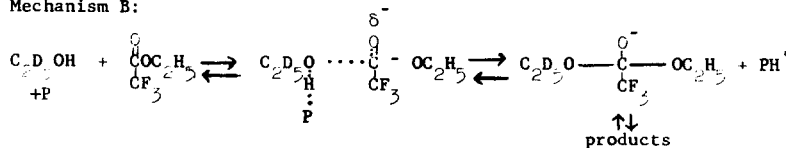
acid-, general base-catalysis was found. The catalytic coefficient for this reaction is, $7.4 \times 10^{-4} \text{ M}^{-1} \text{ sec.}^{-1}$.

The symmetrical paths consistent with this symmetrical general base-catalyzed process are: A, the symmetrical analogue of the concerted S_N2 process, in which the carbonyl bond is largely undisturbed in the transition state; B, the general base-catalyzed formation of the anionic tetrahedral intermediate; and C, the specific base-, general acid-catalyzed formation of the neutral tetrahedral intermediate. The pyridine base in the following schemes is denoted by P.

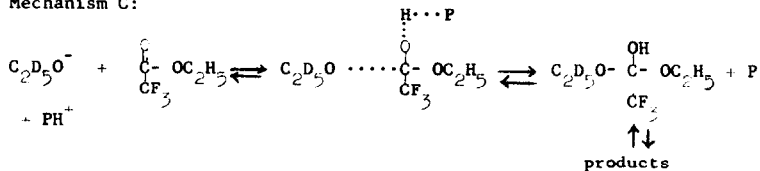
Mechanism A:



Mechanism B:



Mechanism C:



In the concerted mechanism A, the general base P and the proton must be symmetrically situated with respect to the two equal C-OEt bonds a and b.¹ This requires complete proton transfer to P in the transition state, which is inconsistent with the observation of

general base-catalysis (5). In the case of bifunctional catalysts partial proton transfer and therefore general base-catalysis by mechanism A is not inconceivable. For catalysis by the monofunctional pyridine, mechanism A may be discarded.

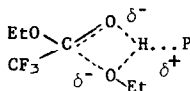
Mechanism C which involves the neutral intermediate formation may be ruled out by a consideration of the rate constant k^* for the rate-determining step needed according to this scheme. Since a termolecular process is unlikely, the reaction must proceed via the reaction of ethoxide with an ester $\dots\text{HP}^+$ complex. The catalytic coefficient is equal the $\frac{k}{2} \frac{K_{\text{EtOH}}}{K_{\text{PH}^+}} \times K_{\text{complex}}$ where K_{EtOH} is the autoprotolysis constant of ethanol, $10^{-19.1}$ (6), K_{PH^+} is the acid dissociation constant of pyridinium ion in ethanol, $10^{-6.4}$, and K_{complex} is the hydrogen bonding constant of $\text{C}_5\text{H}_5\text{NH}^+$ with $\text{CF}_3\text{CO}_2\text{C}_2\text{H}_5$, which is given a very generous value of 0.5 M^{-1} for the present purposes.³ From these values the lower limit of k^* is calculated to be $7.4 \times 10^9 \text{ M}^{-1} \text{ sec.}^{-1}$. This lower limit to k^* is much too high to be a reasonable value for a carbon to oxygen bond making rate-determining process. (6) Therefore mechanism C may be discarded. An alternative process, the interaction

¹ If an unsymmetrical transition state is considered, the reaction path would necessarily be unsymmetrical with respect to the two C-O bonds being formed and broken. There would be two ways to achieve such a transition state (1) by the interaction of EtOH, P, and ester, (2) by the interaction of EtO⁻, HP⁺, and ester. Both of these modes of forming the transition state would be included on the same (unsymmetrical) path. A mirror image to this unsymmetrical path must also exist. The superpositioning of these two unsymmetrical paths on a potential energy surface shows that these two paths cross when the two C-O bonds are of equal length and the HP⁺ moiety is symmetrically situated with respect to the two C-O bonds. This crossover allows a lower energy symmetrical path to be taken.

² Weak acids of the type PH⁺ have pKa values in ethanol which are 1.2 units higher than in water (7).

³ The K_{complex} value is expected to be very small because in ethanol both the donor and the acceptor are hydrogen bonded to the solvent. Carbonyl compounds are very poor H bond acceptors in carbon tetrachloride (8) where their H bonding properties should be maximized. Therefore in ethanol the complex formation will be even less favored.

of EtO^- with the ester followed by a rate-controlling protonation of the complex, leads again to a value of k^* which is too high since, in this case $k_{\text{cat}} = \frac{k^*}{2} \frac{K_{\text{EtOH}}}{K_{\text{PH}^+}} K'_{\text{complex}}$, where K'_{complex} is the complexing constant of EtO^- with the ester. The value of K'_{complex} in methanol is very low in the case of the interaction of LiOMe with MeO_2CCF_3 in MeOH (10) and should be equally low in the present case. An alternative mechanism C is the formation of a complex from EtOH and ester followed by a rate-determining proton transfer from the HOEt group to the carbonyl oxygen in a transition state resembling I. Such a transition state would not be expected unless the catalyst were bifunctional. Pathway B, therefore, is most likely.



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