288. The Hydrolysis of Acetic Anhydride. Part II.* Catalysis by Pyridine.

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The hydrolysis of acetic anhydride in acetone–water is strongly catalysed by small amounts of pyridine. The dependence of the reaction velocity on the concentrations of pyridine and acetic anhydride appears complex but is satisfactorily explained if the formation of catalytically inactive pyridinium acetate (by interaction of the catalyst and the product of reaction) is allowed for.

It is common knowledge that many preparative acylations are facilitated by the presence of alkali, carboxylate ions, or tertiary amines such as pyridine. The mechanism of the catalysis, superficially suggestive of general base catalysis, has not so far been elucidated and only a few isolated kinetic studies of the phenomena have been reported (*e.g.*, Leman,

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* Part I, *Trans. Faraday Soc.*, 1948, **44**, 506.

Bull. Soc. chim., 1945, **12**, 908; 1947, **14**, 514). The present work deals with the catalysis of the hydrolysis of acetic anhydride by pyridine in 50% acetone–water. The particular choice of solvent is unfortunate in some respects since it necessitates the introduction of an unknown equilibrium constant into the kinetic equations. It was made in order to obtain suitable rates and solubilities in related measurements on the acylation of amines.

EXPERIMENTAL

Solvent Mixtures.—The solvent was made up by weight from distilled water and " AnalaR " acetone, generally without purification of the latter since it was found that this did not significantly affect the relative values of the rate constants of a series of experiments. The rate of the " spontaneous " hydrolysis was redetermined for each separate batch of solvent.

Pyridine (" AnalaR ") was kept over potassium hydroxide for a week and fractionally distilled.

Acetic anhydride (" AnalaR ") was used without purification. Its content of acetic acid was determined by titration of the acid liberated on reaction of a weighed sample of anhydride with aniline.

Rate Measurements.—The hydrolysis was followed by running 10-ml. samples of the reaction mixture, at timed intervals, into aniline. The acid liberated was titrated with carbonate-free alkali (Vles, *Rec. Trav. chim.*, 1933, **52**, 809). First-order rate constants were evaluated from a graph of log ($T_\infty - T_t$) against time, where T_t and T_∞ are the titres corresponding to the times t and ∞ respectively (cf. Emery and Gold, *J.*, 1950, 1447). The catalysed reactions did not accurately follow a first-order course. but first-order rate coefficients at the half-life were evaluated from the same graph by evaluating the slope of the nearly linear curve at that point. Such rate coefficients are described by the symbol k_{HL}. The reason for this procedure will appear later. The results are tabulated.

Influence of stoicheiometric pyridine concentration ($[P]_0$) *on rate for different initial concentrations of acetic anhydride* ($[Ac_2O]_0$) at 25·05°.

$[Ac_2O]_0$ / $[P]_0$	10^4k_{HL} (sec.$^{-1}$)				
	0·038M	0·076M	0·152M	0·303M	0·607M
0	—	—	1·01	—	—
2·43	—	1·39	—	—	—
4·85	2·12	1·79	1·53	—	—
9·71	3·06	2·40	1·89	1·68	—
19·41	—	3·50	2·62	2·11	1·73
38·82	—	—	—	3·24	2·72

Effect of addition of acetic acid on rate of pyridine-catalysed hydrolysis of acetic anhydride at 25·05°.

$[P]_0 = 0{\cdot}00454$M; $[Ac_2O]_0 = 0{\cdot}200$M.

$[AcOH]_0$ (M)	0	0·100	0·200	0·300	0·400	0·600
$[AcOH]_{HL}$ * (M)	0·200	0·300	0·400	0·500	0·600	0·800
10^4k_{HL} (sec.$^{-1}$)	5·39	4·45	3·85	3·51	3·25	2·98

* Concn. of acetic acid in solution after one half-life.

DISCUSSION

Although the kinetics of the catalysed reaction appear superficially complicated, the observations can be explained by elaborating the plausible assumption that the conjugate acid of pyridine is without catalytic activity and that there is a linear catalysis law for the unchanged pyridine. The velocity of the hydrolysis is then given by

$$v = -\frac{d[Ac_2O]}{dt} = [Ac_2O]\left\{k_0 + k_P([P]_0 - [PH^+])\right\} \quad . \quad . \quad . \quad . \quad . \qquad (1)$$

where k_0 is the velocity coefficient of the " spontaneous " reaction and k_P the catalytic coefficient of pyridine (P). The subscript zero is used to indicate that the concentration term refers to an initial stoicheiometric concentration. It is not necessary for our purposes to introduce the catalytic coefficients for hydrogen, hydroxide, and acetate ions which do not occur in catalytically significant concentrations.

Application of the law of mass action to the equilibrium

$$\mathrm{P} + \mathrm{AcOH} \rightleftharpoons \mathrm{PH}^+ + \mathrm{OAc}^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (A)$$

leads to

$$K = \frac{K_{\mathrm{AcOH}} \cdot K_{\mathrm{p}}}{K_{\mathrm{w}}} = \frac{[\mathrm{PH}^+][\mathrm{OAc}^-]f_{\mathrm{PH}^+}f_{\mathrm{OAc}^-}}{\{[\mathrm{P}]_0 - [\mathrm{PH}^+]\}[\mathrm{AcOH}}$$

and hence

$$[\mathrm{PH}^+] = \frac{\dfrac{K}{f_{\mathrm{I}}^2} \cdot [\mathrm{P}]_0}{\dfrac{[\mathrm{OAc}^-]}{[\mathrm{AcOH}]} + \dfrac{K}{f_{\mathrm{I}}^2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where K_{AcOH} and K_{p} are thermodynamic dissociation constants for acetic acid and pyridine, K_{w} is the ionic product for water, and $f_{\mathrm{I}}^2 = f_{\mathrm{PH}^+} f_{\mathrm{OAc}^-}$. Activity coefficients for uncharged species have been assumed to be unity. Combining equations (1) and (2), we get

$$v = [\mathrm{Ac_2O}]\left\{k_0 + k_{\mathrm{p}}[\mathrm{P}]_0\left(1 + \frac{K}{f_{\mathrm{I}}^2} \cdot \frac{[\mathrm{AcOH}]}{[\mathrm{OAc}^-]}\right)^{-1}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

We may assume that reaction (*A*) does not seriously reduce the concentration of acetic acid molecules in solution after an appreciable amount of hydrolysis has taken place (such as after one half-life) since then $[\mathrm{AcOH}] \gg [\mathrm{P}]_0$. If it is valid to assume that

$$\frac{K}{f_{\mathrm{I}}^2} \cdot \frac{[\mathrm{AcOH}]}{[\mathrm{OAc}^-]} \gg 1 \ (\textit{i.e.},\ [\mathrm{PH}^+]/[\mathrm{P}] \gg 1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

we obtain

$$v = [\mathrm{Ac_2O}]\left\{k_0 + k_{\mathrm{p}}[\mathrm{P}]_0 \frac{f_{\mathrm{I}}^2}{K} \cdot \frac{[\mathrm{OAc}^-]}{[\mathrm{AcOH}]}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The correctness of assumption (4) cannot be shown rigorously in the absence of measurements of the relevant dissociation constants in aqueous acetone. By analogy with the dependence of dissociation constants on the dielectric constant in dioxan–water (Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," New York, 1950, p. 581; James and Knox, *Trans. Faraday Soc.*, 1950, **46**, 254) we conclude that $K_{\mathrm{AcOH}} \sim 10^{-6}$ mole l.$^{-1}$, that $K \sim 1$, and that assumption (4) is probably valid after one half-life of reaction for the experiments with the lowest initial concentration of acetic acid (and, therefore, the lowest concentration of acetic acid at the half-life) and even more so at the higher concentrations.

Since the stoicheiometric concentration of pyridine was always negligible compared with the half-life concentration of acetic acid we may assume that the concentration of acetate ions is entirely governed by the reaction

$$\mathrm{AcOH} + \mathrm{H_2O} \rightleftharpoons \mathrm{H_3O}^+ + \mathrm{OAc}^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (B)$$

i.e.,

$$[\mathrm{OAc}^-] = [\mathrm{H_3O}^+] = \frac{\sqrt{K_{\mathrm{AcOH}}}[\mathrm{AcOH}]}{f_{\mathrm{II}}}$$

where

$$f_{\mathrm{II}}^2 = f_{\mathrm{OAc}^-} \cdot f_{\mathrm{H_3O}^+}$$

Since the degree of ionisation is small we may assume that the concentration of acetic acid molecules in the above equation is equal to the stoicheiometric concentration of acetic acid in the system. Substituting for [OAc$^-$] in equation (5) we obtain

$$v = [\mathrm{Ac_2O}]\{k_0 + R[\mathrm{P}]_0[\mathrm{AcOH}]^{-\frac{1}{2}}\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where

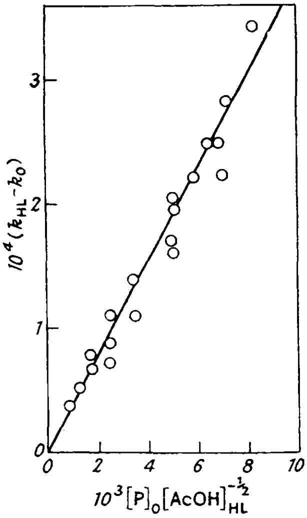
$$R = k_{\mathrm{p}} \cdot \frac{\sqrt{K_{\mathrm{AcOH}}}}{K} \cdot \frac{f_{\mathrm{I}}^2}{f_{\mathrm{II}}} = k_{\mathrm{p}} \cdot \frac{K_{\mathrm{w}}}{K_{\mathrm{p}}\sqrt{K_{\mathrm{AcOH}}}} \cdot \frac{f_{\mathrm{I}}^2}{f_{\mathrm{II}}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

In the absence of additional acetic acid, the concentration of acetic acid at the half-life is equal to the initial concentration of anhydride, and therefore the first-order rate coefficient at the half-life (k_{HL}) is given by

$$k_{HL} = k_0 + R[P]_0[Ac_2O]_0^{-\frac{1}{2}} \quad . \quad . \quad . \quad . \quad (8)$$

Equations (6) and (7) only apply at low values of the ratio $[P]_0 : [Ac_2O]_0^{\frac{1}{2}}$ where the assumptions made are least objectionable.

An experimental test of equations (6) and (8) is given in the Figure in which ($k_{HL} - k_0$) is plotted against $[P]_0[AcOH]_{HL}^{-\frac{1}{2}}$, where $[AcOH]_{HL}$ is the concentration of acetic acid in the system after one half-life. The experimental points represent data for systematic variation of $[Ac_2O]_0$, $[P]_0$, and added acetic acid (see Tables). From the slope, R is found to have the value 0·038 sec.$^{-1}$ (mole l.$^{-1}$)$^{-\frac{1}{2}}$.



Test of equation (6).

By using this value of R in equation (6) it is possible to account quantitatively for the decrease of the first-order rate coefficient during the reaction.

From the rough estimates for K_{AcOH} (1×10^{-6} mole l.$^{-1}$) and K ($\sim$1) given, we obtain an approximate value for the catalytic coefficient of pyridine in 50% acetone–water as $k_P \sim 40$ sec.$^{-1}$ mole^{-1} l. Without discussing this result further at this stage we may note that this is an uncommonly large catalytic effect for an uncharged species in any heterolytic reaction in solution. The catalytic constant is approximately 30,000 times greater than that for acetate ions in this solvent, which is remarkable since the acetate ion and pyridine are bases of similar strengths.

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