THE PYRIDINE CATALYSED HYDROLYSIS OF

CARBOXYLIC ANHYDRIDES

C.A. Bunton, N.A. Fuller and S.G. Perry

William Ramsay and Ralph Forster Laboratories,

University College, Gower St., London W.C.1

V.J. Shiner

Department of Chemistry, University of Indiana, Bloomington, Indiana

TERTIARY amines, e.g. pyridine, are effective catalysts of the hydrolysis of carboxylic anhydrides. Pyridine is believed to act by converting the anhydride into an acylpyridinium ion (I). Both the formation of this ion, step 1, and its breakdown to products, step 3, have at times been postulated as the slow step of the reaction.[1a,b]

$$ R.CO.O.CO.R + C_5H_5N \; \underset{2}{\overset{1}{\rightleftharpoons}} \; RCO.\overset{+}{N}C_5H_5 + RCO_2^- $$

$$ I $$

$$ 3 \downarrow H_2O $$

$$ RCO_2H + C_5H_5N + \overset{+}{H} $$

We have attempted to differentiate between these possibilities by studying the concurrent hydrolysis and isotopic exchange of anhydrides with ^{14}C-labelled carboxylate.

In the absence of pyridine, hydrolysis of acetic anhydride in the presence of sodium acetate is accompanied by isotopic exchange between the

[1a] V. Gold and E.G. Jefferson, J.Chem.Soc. 1409 (1953); [b] A.R. Butler and V. Gold, Proc.Chem.Soc. 15 (1960).
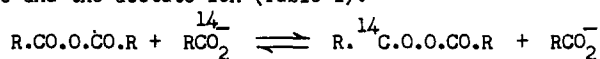
TABLE 1

Rates of Acetate Exchange and Hydrolysis of Acetic Anhydride in Water at 0°

$$[Ac_2O] = 0.3M$$

[Pyridine] mM	[OAc] M	10^3 rate Hydrolysis*	mole l^{-1} sec^{-1} Exchange
0	0.5	0.21	ca. 0.9
0	1.0	0.29	1.3
4	0.5	0.69	13.5
4	1.0	0.74	12.7

*Calculated from experiments with $[Ac_2O]$ $^M/20$

anhydride and the acetate ion (Table 1).

$$R.CO.O.CO.R + \overset{14}{R}CO_2^- \rightleftharpoons R.\overset{14}{C}.O.O.CO.R + RCO_2^-$$

Addition of pyridine accelerates both exchange and hydrolysis (Table 1), and from the extents of these rate increase we can calculate the number of acetylpyridinium ions I which revert to reactants, with isotopic exchange, (step 2) relative to those which go forward to products of hydrolysis (step 3). With both 0.5 M and 1 M sodium acetate the rate of step (2) is ca. 25 times that of step (3), and hence in these conditions we can regard I as being in equilibrium with the reactants. The relative rates of steps (2) and (3) are apparently unaffected by a doubling of the concentration of acetate ion, and because the rate of step (2) should depend upon the concentration of acetate ions we conclude that the rate of step (3), the hydrolysis of I, must also be acetate dependent. Qualitatively similar results are observed for the pyridine catalysed exchange of sodium benzoate with benzoic anhydride in aqueous dioxan; where with 0.4 M sodium benzoate + 0.4 M benzoic acid and 0.05 M pyridine the back reaction was ca. 40 times as fast as the forward.

The large solvent deuterium isotope effect on the pyridine catalysed

hydrolysis of acetic anhydride,[1b] can be explained in terms of hydrogen bonding interactions between the solvent and the reactants and transition state,[2] provided that we assume that the transition state for the overall reaction is that for step (3), the attack of water upon I.

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[2] C.A. Bunton and V.J. Shiner, J.Amer.Chem.Soc. 83, 42 (1961), and forthcoming publications.