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THE ACIDOLYSIS OF 2-PYRIDYL BENZOATE

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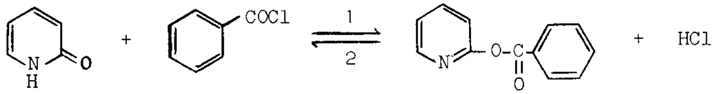
Being interested in the acylation of ambident nucleophiles (cf[1]) we investigated the benzoylation of 2-pyridone. Some controversy exists as to the acetylation of 2-pyridone, which gives partly N-acetylated product either as a transient species which rearranges to the thermodynamically stable O-acetylpyridone (2-pyridyl acetate)[2,3] or together with pyridyl acetate in equilibrium with a product ratio[2] of about 1:10. Benzoylation, however, has been reported to yield only 2-pyridyl benzoate[4] and we could isolate only this compound upon reaction of 2-pyridone with benzoylchloride (yield 90%).

We followed the benzoylation (reaction 1) in acetonitrile at 30°C by UV and IR spectroscopy making use of the absorption of 2-pyridone at 330 nm and the carbonyl stretching bands at 1675 cm^{-1} (pyridone), 1740 cm^{-1} (pyridyl benzoate) and 1770/1740 cm^{-1} (benzoylchloride). Protonated pyridone absorbs below 1640 cm^{-1} near the cut-off wavelength of the solvent (1610 cm^{-1}).



No carbonyl bands other than the three mentioned were found during the reaction so that the presence of transient N-benzoyl-2-pyridone is not detected. Overlapping of the carbonyl bands of N-benzoyl-2-pyridone by the existing bands is not excluded, although improbable, at least one C=O band is expected to absorb between 1700 cm^{-1} and 1720 cm^{-1}.

An interesting feature of reaction (1) is that it does not run to completion. This observation led us to a study of the reverse reaction (2): that between 2-pyridyl benzoate and HCl. Care was taken to exclude all moisture during the experiments and indeed the IR spectra showed a growing carbonyl absorption band at 1770 cm^{-1}. It was checked that other possible causes (such as bwnzoyl anhydride) were not responsible for this absorption.

By UV measurements it is clear that the same equilibrium is reached in reactions (1) and (2). This is illustrated in the figure by curves 1a and 2a. Since pyridone is extensively protonated by HCl curves 1a and 2a do not give direct information on the degree of conversion in the

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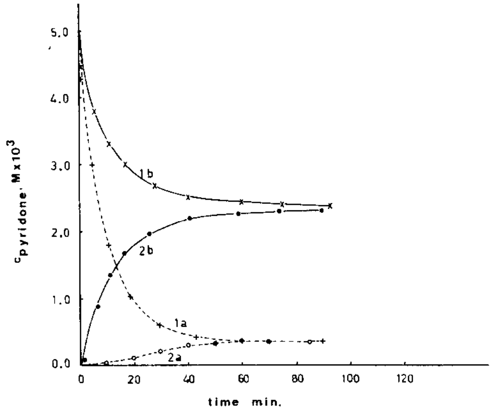
reaction system. Therefore the reaction was quenched at suitable time intervals with an excess of diethylamine which inactivates the acid chloride and liberates pyridone from its hydrochloride (reaction with the ester occurs but is very slow). The results are also given in the figure (curv 1b and 2b), giving the degree of conversion of the reaction system (1,2)*.

It is easily checked that the acidolysis of pyridyl benzoate is not caused by chloride anion (tetraethyl ammonium chloride being inactive either as such or when added to the hydrochloric acid) but also is not an S_N1 reaction of the protonated ester, since HBr gives the same reaction but slower, although HBr in acetonitrile is a stronger acid than HCl.[5]

Since 4-pyridyl benzoate is not acidolysed by HCl it is likely that the transition state is depicted by a structure like 1. Thus a cyclic transition state or intermediat facilitates the reaction whereas the conversion of the "alcohol" 2-hydroxy-pyridine into pyridone stabilizes the left hand products of the reaction (1,2) sufficiently to give a measurable quantit of acidolysis products.



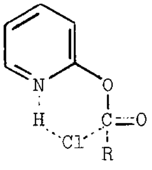


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Figure. The change in pyridone concentration with time measured at 330 nm.

It is interesting that splitting of esters by HCl is found in only a few cases. One example is the reaction of enolesters[6] where also stabilisation of the alcohol part occurs. T dissociation of a thioester[1] (where isothiourea is formally the thiolic part) is another example.

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[*] Unfortunately the reaction is not accessible to quantitative analysis since the protonation of pyridone has not a simple stoichiometry. Equilibria of the type:

$$\text{pyridone-HCl} + \text{Cl}^- \rightleftarrows \text{pyridone-HCl}_2^-$$

have to be invoked[5] in order to describe the degree of protonation of pyridone by HCl in acetonitrile. Some pyridyl benzoate is also protonated under the reaction conditions.