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HALIDE-DIRECTED NITRILE HYDROLYSIS

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Abstract: Sodium bromide is an effective catalyst for promoting the hydrolysis of aroyl cyanides such that loss of the cyano group is greatly minimized.

Synthetic routes to benzoylformic acid esters and amides are of interest owing to the ability of these compounds to initiate polymerization of acrylates under UV irradiation.[1] Benzoylformates can be obtained by acid-promoted hydrolysis-alcoholysis of aroyl cyanides[2] which in turn are conveniently synthesized by a phase transfer catalyzed reaction of aromatic acid chlorides with aqueous sodium cyanide.[3] Initial attempts to prepare methyl benzoylformate from benzoyl cyanide, methanol and HCl according to published procedures[2,4] gave methyl benzoate. In fact, merely mixing benzoyl cyanide with methanol or ethanol without an acid catalyst at room temperature resulted in an exothermic reaction giving exclusively methyl or ethyl benzoate. Clearly a new method was required that would retard cleavage of the cyano functionality from acyl cyanides during hydrolysis. A study was undertaken to determine the effect on the reaction of hydrogen halide introduced in the form of the sodium salt. *ortho*-Toluyl cyanide was selected for the study. The results are summarized below.

HYDROLYSIS-METHANOLYSIS OF *o*-$CH_3C_6H_4COCN$

Equivalents of NaX Added	Relative % *o*-Toluate	Relative % *o*-Toluylformate	Isolated % Yield
None	100	0	100
0.18 NaCl	90	10	95
1.00 NaCl	70	30	95
0.10 NaBr	5	95	82
0.07 NaI	90	10	95

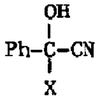
The acyl cyanide was added dropwise at room temperature to a slurry of 85% sulfuric acid and the appropriate sodium halide. The reaction mixture was heated at 70° and then refluxed with methyl alcohol. A yield of 82% of *o*-toluylformate was obtained in the presence of a catalytic amount of sodium bromide.

In the case of benzoyl cyanide it was found that in addition to the halide catalyst, the presence of acetic anhydride served to further minimize the amount of benzoate and to reduce the exothermicity of the hydrolysis reaction. Addition of an equivalent amount of acetic anhydride resulted in complete miscibility of benzoyl cyanide and 85% sulfuric acid. No reaction occurred up to temperatures of 40°. Addition of a few crystals of sodium bromide initiated an exothermic reaction. When the temperature was kept below 40° and the reaction mixture was then poured onto crushed ice, a quantitative yield of benzoylformamide, m.p. 89-90° (lit. m.p. 90-91°)[5] was obtained (eq. 1). A reaction temperature of 70° and addition of methyl alcohol led to an 85% isolated yield of methyl benzoylformate (eq. 2).

$$\mathrm{PhCOCN} \xrightarrow[\text{2) } H_2O]{\text{1) 85\% } H_2SO_4\text{, 20-40}^\circ \text{ (NaBr)}} \mathrm{PhCOCONH_2} \qquad (1)$$

$$\mathrm{PhCOCN} \xrightarrow[\text{2) } CH_3OH]{\text{1) 85\% } H_2SO_4\text{, 70}^\circ \text{ (NaBr)}} \mathrm{PhCOCO_2CH_3} \qquad (2)$$

The role of halide can be rationalized in at least two ways. A kinetic study[6] has reveale that the rate of decomposition of benzoyl cyanide to benzoic acid in water decreases at lower p This was explained by the occurrence of a two-step mechanism involving initial slow hydration o the carbonyl (ia). Hydrogen bromide might function similarly to give an intermediate such as i in which the process of hydrolysis of the cyano group would be enhanced by the inductive effect of the α-halogen atom. Alternatively hydrogen bromide might add to the cyano group with form tion of the imidoyl bromide intermediate, ii. Acylation of ii by benzoyl chloride, benzoyl cya or acetic anhydride giving iii could occur, and this would account for a decrease in the amount benzoate when acetic anhydride was also present during hydrolysis.



$$\mathrm{Ph{-}\overset{OH}{\underset{X}{C}}{-}CN}$$

ia, X = OH
ib, X = Br

$$\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}\overset{NH}{\overset{\|}{C}}{-}Br} \longrightarrow \mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}\overset{NCOR}{\overset{\|}{C}}{-}Br}$$

ii

iii, R = CH_3, ∅

In an attempt to observe a reaction intermediate, m-toluyl cyanide was reacted with 98% su furic acid in the presence of excess sodium bromide at 70° for three hours. The resulting brig red-orange colored solution was examined by ^{13}C nmr. No cyano-carbon signal was present. In a tion to the expected methyl and aromatic carbon resonances, a signal was observed at 170.1 ppm. This is assigned to the imidoyl group carbon atom of ii by analogy with data published for similar imine type structures.[7] Workup of the nmr solution afforded a pale yellow solid identified as m-toluylformamide.

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References and Footnotes

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