Phosphoryl Transfer promoted by Nitriles in the Presence of Highly Reactive Halides

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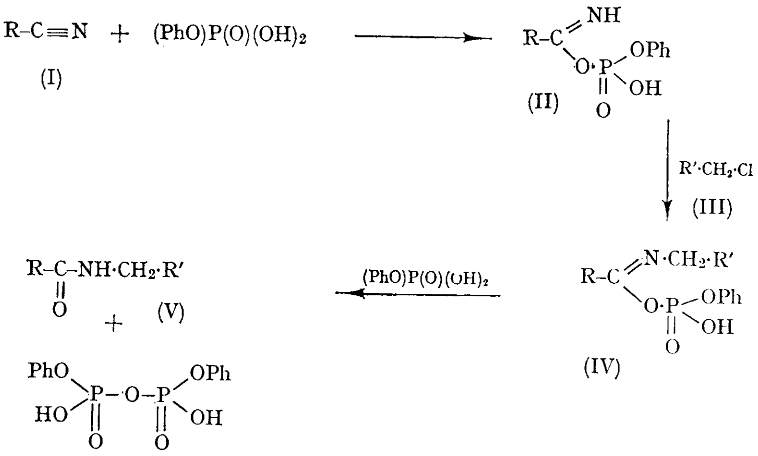
THE activation of phosphate by trichloroacetonitrile (I; R = CCl_3) is well known,[1] protonation of the intermediary imidoyl phosphate (II; R = CCl_3) leading to phosphoryl transfer. We have observed a similar but very much less effective activation with acetonitrile (I; R = Me). For example, when phenyl dihydrogen phosphate is heated under reflux for one hour in dry acetonitrile, P^1P^2-diphenyl pyrophosphate is formed in 4% yield.

However, the reaction is greatly enhanced by the addition of highly reactive alkyl halides (III; R = MeO, MeS, or p-MeO·C_6H_4), equimolar amounts of (III; R = MeO) and phenyl dihydrogen phosphate giving P^1P^2-diphenyl pyrophosphate in 92% yield after one hour under reflux in dry acetonitrile. In the absence of acetonitrile, no pyrophosphate could be detected.

Under analogous conditions benzyl chloride is a poor promoter of phosphoryl transfer. However, the effectiveness of benzyl halides is markedly increased by introduction of a methoxyl group in the *para*-position; a methoxyl group in the *meta*-position has little effect. In addition to the phosphorylated substrate, the other product of reaction is the substituted amide (V; R = Me, R' = MeO).



The reaction most probably proceeds through the *N*-alkylated imidoyl phosphate (IV). An alternative mechanism, involving initial formation of a nitrilium salt (VI), analogous to that postulated as the intermediate in the Ritter reaction[2,3] can be invoked. However, we have been unable to detect any interaction between (I) and (III) in the absence of phosphate, although such salts can be formed in the presence of strong Lewis acid.[4,5]

$$R{\cdot}C{\equiv}N + R'{\cdot}CH_2{\cdot}Cl \rightleftharpoons R{\cdot}C{\equiv}\overset{+}{N}{\cdot}CH_2{\cdot}R'\ \ Cl^- \qquad \text{(VI)}$$

Using phenyl dihydrogen phosphate, alcohols (*e.g.*, methanol, ethanol, and n-butanol) have been acylated in yields of up to 50%. In these cases a significant by-product is the ether arising from (III) and the alcohol.

(*Received, April 5th*, 1966; *Com.* 221.)

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