The Reaction of n-Butyl-lithium with Pentachloropyridine: a Solvent Effect

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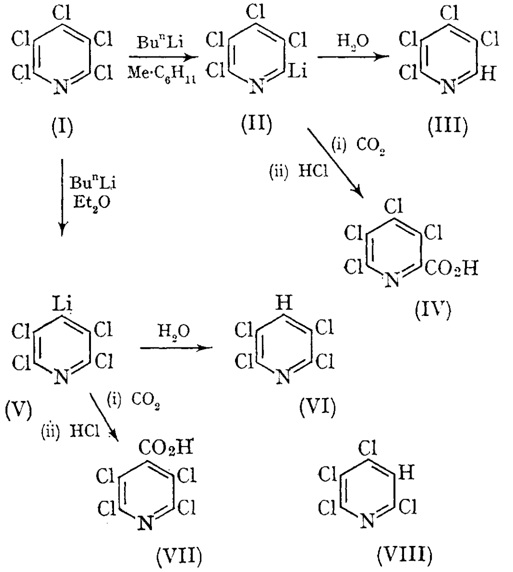
THE reaction of organolithium compounds with pentafluoropyridine leads mainly to 4-alkyl- or 4-aryl-tetrafluoropyridines.[1,2] In contrast, we have found that n-butyl-lithium reacts with pentachloropyridine (I) mainly by metal–halogen exchange, to give solutions of tetrachloropyridyl-lithium compounds. Similar behaviour has recently been reported in the benzene series, hexafluorobenzene being alkylated by organolithium compounds,[3] whereas hexachlorobenzene gives pentachlorophenyl-lithium.[4] In the reaction of pentachloropyridine with n-butyl-lithium we have also observed that the orientation of the products depends on the solvent used. Thus, reaction of n-butyl-lithium with pentachloropyridine (I) in methylcyclohexane at room temperature gave, after hydrolysis, an inseparable liquid mixture of tetrachloropyridines (43%); the ^{1}H n.m.r. spectrum of the mixture indicated that it contained 2,3,4,5-tetrachloropyridine (III), 2,3,5,6-tetrachloropyridine (VI) and 2,3,4,6-tetrachloropyridine (VIII), in the proportions 68 : 16 : 16. Other minor products from the reactions were (a) a mixture of pentachloropyridine and what is believed to be a n-butyltetrachloropyridine and (b) a mixture of high-boiling products, possibly derived from trichloropyridyne. Carboxylation of the product from the reaction of n-butyl-lithium with pentachloropyridine in methylcyclohexane gave a mixture of acids (approx. 40%), from which 3,4,5,6-tetrachloropyridine-2-carboxylic acid (IV) was isolated.



We conclude that the main product from the reaction in methylcyclohexane is 3,4,5,6-tetrachloro-2-pyridyl-lithium (II).

When similar experiments were carried out using diethyl ether as solvent, the hydrolysis product was a solid mixture (approx. 45%) of 2,3,5,6-tetrachloropyridine (VI) and 2,3,4,6-tetrachloropyridine (VIII), in a ratio of 78 : 22, together with some pentachloropyridine and higher-boiling material. A reaction carried out at between −60° and −40° gave a similar ratio of isomers but the yield was raised to approximately 70%.

Carboxylation of the product from the reaction in diethyl ether gave a mixture of acids (36%), from which 2,3,5,6-tetrachloropyridine-4-carboxylic acid was obtained.

We conclude that the main product from the reaction in diethyl ether is 2,3,5,6-tetrachloro-4-pyridyl-lithium.

An attractive explanation for the solvent effect is that, in methylcyclohexane, pentachloropyridine is co-ordinated with the electron-deficient organolithium compound[5] which is thus held close to the α-chlorine atoms; in diethyl ether, the organolithium compound is solvated,[6] and if the very weakly basic pentachloropyridine is unable to displace solvent molecules from the complex, reaction takes place at the site most susceptible to nucleophilic attack, *viz.*, the 4-position.

A second explanation involves the fact that attack of the 4-position in pentachloropyridine is subject to greater steric hindrance than attack of the 2-position.[7] n-Butyl-lithium is hexameric in hydrocarbon solvents,[8] whereas in diethyl ether it is probably present as a smaller solvated dimer.[9]

Solutions of the tetrachloropyridyl-lithium compounds appear to be fairly stable (*cf.*, ref. 10).

However, the formation of high-boiling byproducts which could have arisen *via* trichloropyridyne intermediates has been noted above, and experiments designed to trap such intermediates are in progress.*

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* We have now obtained an adduct of 2,5,6-trichloro-3,4-pyridyne and mesitylene.

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