

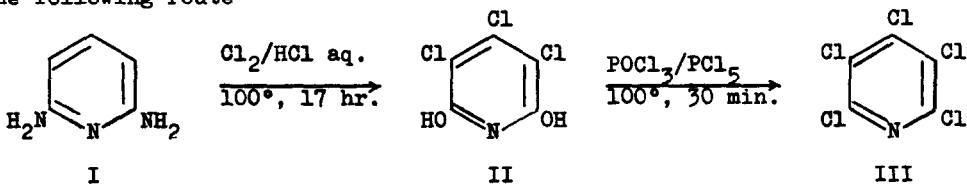
SYNTHESIS AND REACTIONS OF PENTACHLOROPYRIDINE

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Current interest in pentafluoropyridine, now readily prepared¹ from pentachloropyridine, makes it necessary for new routes to the latter to be developed which avoid the use of autoclaves, with accompanying corrosion problems, or of precursors which are not readily available.² The following route



satisfies these requirements.

Chlorination of commercially-available 2,6-diaminopyridine (I) in hydrochloric acid solution gives 3,4,5-trichlorodihydroxypyridine (II) (m.p. $108-9^\circ$) in 57% yield, and this is converted almost quantitatively into pentachloropyridine (III) by treatment with a mixture of phosphorus oxychloride and phosphorus pentachloride. Chlorination of the starting material for a shorter time (5 hr.) gives 2,3,4,5-tetrachlorohydroxypyridine which, as previously reported,² is difficult to convert into pentachloropyridine.

It is well-established that nucleophiles react with

pentafluoropyridine to give initially and exclusively the 4-substituted derivative; it has been claimed recently^{2,3} that pentachloropyridine behaves similarly. However, our investigations have shown that a mixture of products results because (a) displacement takes place initially at both the 2- and 4- positions, larger nucleophiles favouring the 2-position presumably since it is less sterically hindered, and (b) the remaining chlorines in the monosubstituted product are nearly as reactive as those in pentachloropyridine, so that a mixture of mono-, di- and tri-substituted products is usually obtained. By careful control of the reactant ratio and the temperature it is possible to make the mixture of the 2- and 4-isomers (Table I) or the mixtures of 2,6- and 2,4-isomers (Table II) predominate.

The tables show the ratio of analytically-pure isomers, as determined by g.l.c., obtained from reactions carried out under comparable conditions of temperature, concentration etc.; the orientation has been definitely established by n.m.r. and mass spectroscopic studies.

TABLE I

<u>Monosubstituted Products</u>		
<u>Substituent</u>	<u>Reactant/Solvent</u>	<u>Ratio of 4- : 2-substitution</u>
NH ₂	NH ₃ , EtOH	70 : 30
ⁿ BuNH	ⁿ BuNH ₂ , EtOH	25 : 75
Me ₂ N	Me ₂ NH, EtOH	20 : 80
Et ₂ N	Et ₂ NH, EtOH	1 : 99
OMe	MeOK, MeOH	85 : 15
OEt	EtOK, EtOH	65 : 35
O ⁿ Bu	ⁿ BuOK, ⁿ BuOH	57 : 43

TABLE II

<u>Disubstituted Products</u>	
<u>Substituent</u>	<u>Ratio of 2,6- : 2,4-disubstituted product</u>
NH ₂	0 : 100
Me ₂ N	70 : 30
OMe	0 : 100
OEt	1 : 99

Use of an excess of these reagents and increased temperature leads to breakdown in the case of amine reactants, but gives the stable 2,4,6-trisubstituted derivatives derived from alcohols or phenols (MeOH, EtOH, PhOH, p-MeO·C₆H₄OH, o-NO₂·C₆H₄OH) in high yield. Displacement of chlorine from position 3 has been detected only in the reaction of pentachloropyridine with lithium aluminium hydride, when 2,5,6-trichloropyridine is a major product.

References

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- 2 A. Roedig and K. Grohe, Ber., 98, 923, (1965).
- 3 Dow Chem.Co., Neth.Pat. 6,402,443, (1964); Chem.Abst. 64, 8152, (1966).