Nucleophilic Reactions of Pentachloropyridine 1-Oxide and Pentachloropyrine

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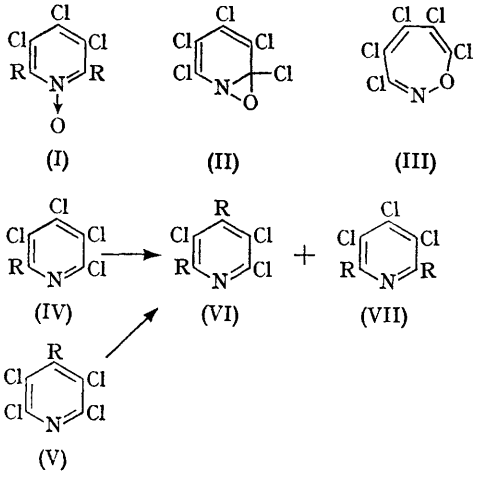
IN view of the current interest in the chemistry of pentachloropyridine[1] and our own in halogen-substituted *N*-oxides[2] we prepared the title compound (I; R = Cl) m.p. 178°, from pentachloropyridine and trifluoroperacetic acid in 20% yield by heating to 50° for 5 hr. Prolonged heating in this medium caused deoxygenation of the *N*-oxide until its concentration was *ca.* 10%. Structural assignment followed from its analysis, infrared spectrum (a band at 1180 cm.$^{-1}$; N → O), and its ready conversion into pentachloropyridine by PCl_3 or heating. The mass spectrum (inlet temperature 50°) also confirmed the structure because of a parent ion at *m/e* 267 and a base peak $(P-16)^+$ ion due to loss of an oxygen atom as expected for an amine oxide.[3] At higher temperatures expulsion of oxygen was not observed but a new base-peak ion (*m/e* 204) appeared which is explained by fragmentation of the *N*-oxide to give C_4Cl_4N with loss of COCl. This is probably caused by thermal rearrangement of the *N*-oxide to the oxaziridine (II) or the oxazepine (III) by analogy with photolytic changes recently observed in certain quinoline 1-oxides.[4]

The *N*-oxide (I; R = Cl) was found to be more susceptible to nucleophilic attack than pentachloropyridine as it reacted with an excess of various secondary amines (*e.g.*, pyrrolidine and piperidine) at room temperature to give the 2,6-disubstituted products (I; R = C_4H_8N or $C_5H_{10}N$) in practically quantitative yield. Pentachloropyridine under similar conditions gave only the 2-substituted product (IV; R = C_4H_8N or $C_5H_{10}N$). When the *N*-oxide was heated with an excess of these amines, again 2,6-disubstitution occurred and no 2,4- or 2,4,6-substituted pyridines were found to be present. Monosubstitution, in the 2-position only, took place in high yield (79%) when the *N*-oxide (1 mol.) was made to react with a benzene, dioxan, or ethanol solution of the above amines (2 mol.) on the water-bath. The nature of these *N*-oxide derivatives was established by their deoxygenation to give the corresponding chloropyridines of known orientation.

In contrast to its *N*-oxide the outcome of substitution in pentachloropyridine was affected by the nature of the solvent. For instance a benzene solution of pentachloropyridine (1 mol.) gave on boiling with various *N*-heteroparaffins (2 mol.) almost exclusively the 2-substituted derivatives while an ethanolic solution furnished a mixture of the 2- and the 4-isomer with the former prevailing (*cf.* Table). The predominance of 2-substitution in ethanol is in accord with Haszeldine's observation on the behaviour of other bulky reagents[1d] with this substrate (IV; R = Cl). A similar solvent dependence has also been reported for the related polyfluoroaryl compounds.[5]

The position of the substituents was determined by chemical means as physical methods (n.m.r. and

mass spectra) proved unreliable in our case. In a typical orientation experiment the two monopiperidinopyridines obtained in ethanol which were obviously the 2-(IV; R = $C_5H_{10}N$) and the 4-(V; R = $C_5H_{10}N$) isomers, were each treated with more piperidine to obtain disubstituted products. The fact that one gave two disubstituted isomers and the other only one which was identical with one of the former, is rationally accounted for by the reaction schemes (IV → VI + VII) and (V → VI; R = $C_5H_{10}N$) and thus enabled orientation of all derivatives. Morpholine gave only one monosubstituted product with pentachloropyridine whatever the solvent. Since the 4-piperidinocompound (V; R = $C_5H_{10}N$) furnished the same disubstituted isomer with morpholine as the morpholino-derivative gave with piperidine, the latter is clearly the 2-derivative (IV; R = morpholino). It was found to be identical with the morpholine prepared by Roedig's method[1a] which was claimed to give the 4-isomer. The solvent independence of the reaction with morpholine is probably due to its lower nucleophilicity—as compared to the other *N*-heteroparaffins—which enables a successful attack on the most active position only.



TABLE

Products from pentachloropyridine and various nucleophiles (reactant ratio 1 : 2) after 30 hr. reflux in benzene (A) *and ethanol* (B) *with relative yields in brackets.*

Nucleophile	Position of substituent A	B
C_4H_8N	2—(100)	2—(80); 4—(20)
$C_5H_{10}N$	2—(96); 4—(4)	2—(63); 4—(37)
$C_6H_{12}N$	2—(100)	2—(80); 4—(20)
Morpholine	2—(100)	2—(100) —
Me_2NH	2—(100)	2—(66); 4—(34)

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