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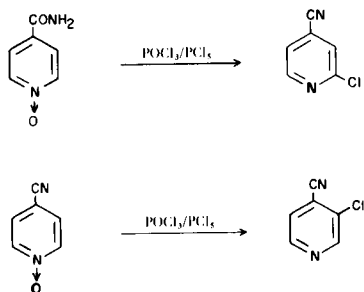
Reaction of 4-cyanopyridine *N*-oxide with phosphorus oxychloride/phosphorus pentachloride gave 3-chloro-4-cyanopyridine in good yield in sharp contrast to the expected chlorination in the 2-position. A mechanistic interpretation of the results is proposed involving a chloride attack at the 4-position as the main feature.

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Pyridine *N*-oxides react with chlorinating agents such as sulfonyl chloride, phosphorus oxychloride and phosphorus pentachloride to yield essentially 2- and 4-chloro-substituted pyridines (1). 3-Chloro or halo-substituted pyridines are much more difficult to obtain by direct substitution (2).

French and Japanese workers have reported that 4-carboxamidopyridine *N*-oxide, when heated for an hour at 120° in a mixture of phosphorus oxychloride and phosphorus pentachloride, produced 2-chloro-4-cyanopyridine in 50-60% yield (3). We have repeated and confirmed this finding. In sharp contrast to this result and to known chlorination of pyridine *N*-oxides, we have found that 4-cyanopyridine *N*-oxide when treated under the same conditions yielded 3-chloro-4-cyanopyridine in good yield (73%).

Scheme 1

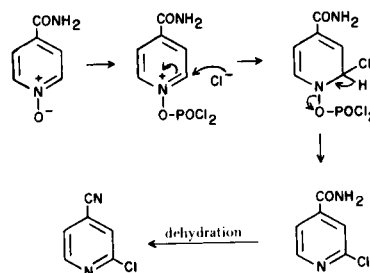


The ir and nmr spectra of 3-chloro-4-cyanopyridine, as well as a comparison with the physical and spectral properties of the 2-chloro isomer, are in accordance with the assigned structure. In fact the nmr of the two isomers clearly and unambiguously establish their structure (see Experimental).

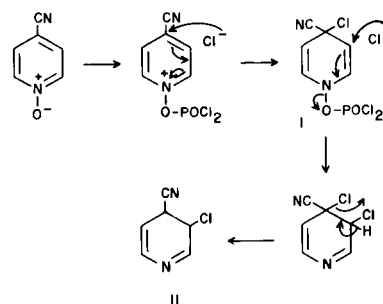
3-Chloro-4-cyanopyridine has been reported once in the literature (4) and involves an elaborate and very low yield process. The easy one-step high-yield synthesis from a commercial precursor of 3-chloro-4-cyanopyridine reported here will allow easier access to more elaborate syntheses of substituted pyridines.

The totally different behaviour in the chlorination of the two compounds resides most probably in the strong inductive effect of the cyano group.

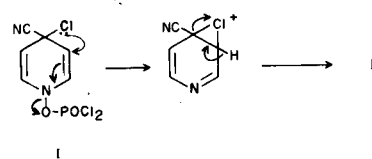
In the case of 4-carboxamidopyridine *N*-oxide, the usually accepted mechanism (1) applies.



In the case of the 4-cyanopyridine *N*-oxide, the strong electron withdrawing effect of the cyano group renders the 4-position more susceptible to nucleophilic attack.



It is also possible that intermediate I rearranges as follows to yield II.



## EXPERIMENTAL

4-Cyanopyridine *N*-oxide was purchased from Aldrich Chemical Company and also prepared by oxidation of 4-cyanopyridine with *m*-chloroperbenzoic acid in chloroform. 4-Carboxamidopyridine *N*-oxide was prepared from 4-carboxamidopyridine as described above, m.p. 305-307° dec., reported 306° dec. (3a). The melting points are uncorrected.

## 2-Chloro-4-cyanopyridine.

The title compound was prepared in 70% yield from 4-carboxamidopyridine *N*-oxide according to Suzuki, *et al.*, (3b), m.p. 69.5-71.5° (petroleum ether), reported 67-68°; nmr (deuteriochloroform):  $\delta$  7.45 (dd,  $J_{5,3} = 1$  Hz and  $J_{5,6} = 5$  Hz, C<sub>5</sub>H), 7.60 (d,  $J_{3,5} = 1$  Hz, C<sub>3</sub>H), 8.55 (d,  $J_{6,5} = 5$  Hz, C<sub>6</sub>H); ir  $\nu$  max (potassium bromide): 2220 cm<sup>-1</sup> (CN); M<sup>+</sup> 138 (Cl<sup>35</sup>).

*Anal.* Calcd. for  $C_6H_3ClN_2$ : C, 51.98; H, 2.16; Cl, 25.63; N, 20.21. Found: C, 52.01; H, 2.15; Cl, 25.57; N, 20.18.

#### 3-Chloro-4-cyanopyridine.

4-Cyanopyridine *N*-oxide (10 g.), phosphorus oxychloride (32 ml.) and phosphorus pentachloride (24 g.) were heated at 120-130° for 1.5 hours. The mixture was cooled down and poured carefully on ice. The aqueous mixture was neutralized carefully with sodium bicarbonate and extracted several times with ether. The extracts were dried over sodium sulfate, and evaporated to dryness to yield a solid residue which was triturated in petroleum ether and filtered to yield 8.4 g. solid (73%), m.p. 71-72° (petroleum ether), reported 71° (4), mixed m.p. with 2-chloro-4-cyanopyridine 40-42°; nmr (deuteriochloroform):  $\delta$  7.55 (d,  $J_{5,6} = 5$  Hz,  $C_5H$ ), 8.65 (d,  $J_{5,6} = 5$  Hz,  $C_6H$ ), 8.80 (s,  $C_2H$ ); ir  $\nu$  max (potassium bromide): 2220  $cm^{-1}$  (CN);  $M^+$  138 ( $Cl^{35}$ ).

*Anal.* Calcd. for  $C_6H_3ClN_2$ : C, 51.98; H, 2.16; Cl, 25.63; N, 20.21. Found: C, 52.14; H, 2.15; Cl, 25.46; N, 20.06.

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