

REACTION OF CHLOROPICOLINE 1-OXIDES IN LIQUID AMMONIA IN THE
PRESENCE OF POTASSIUM AMIDE ¹⁾

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Amination of chloropicoline 1-oxides with
potassium amide in liquid ammonia is described.

Although there is considerable literature dealing with the pyridyne intermediate in the reaction of halopyridines with potassium amide in liquid ammonia, few references are available concerning the pyridyne 1-oxide intermediate.^{2,3,4)}

The present communication reports the reaction of chloro-2 (and 4)-picoline 1-oxides with potassium amide in liquid ammonia to give amino derivatives, presumably via methylpyridyne 1-oxide intermediates.

Reactions were carried out by adding 5 millimoles of chloropicoline 1-oxide to a solution of potassium amide, prepared from 20 mg-atom of potassium and 150 ml of liquid ammonia, in the presence of some ferric chloride, and stirring for 1.5 hours at -33°. The reactions were quenched by adding ammonium chloride. After evaporation of ammonia, the residue was extracted with 200 ml of 99% ethanol. The ethanol was refluxed with 0.5 g of Norit for a few minutes and filtered. The filtrate was concentrated to small volume (ca. 30 ml) and placed in a reduction vessel, Raney Nickel, prepared from 1 g

of Nickel Alloy was added, and the mixture was shaken in H_2 until absorption was complete. The catalyst was filtered off and the filtrate was concentrated. The resulting residue was subjected to analysis by gas chromatography and thin layer chromatography along with the corresponding authentic aminopicolines.

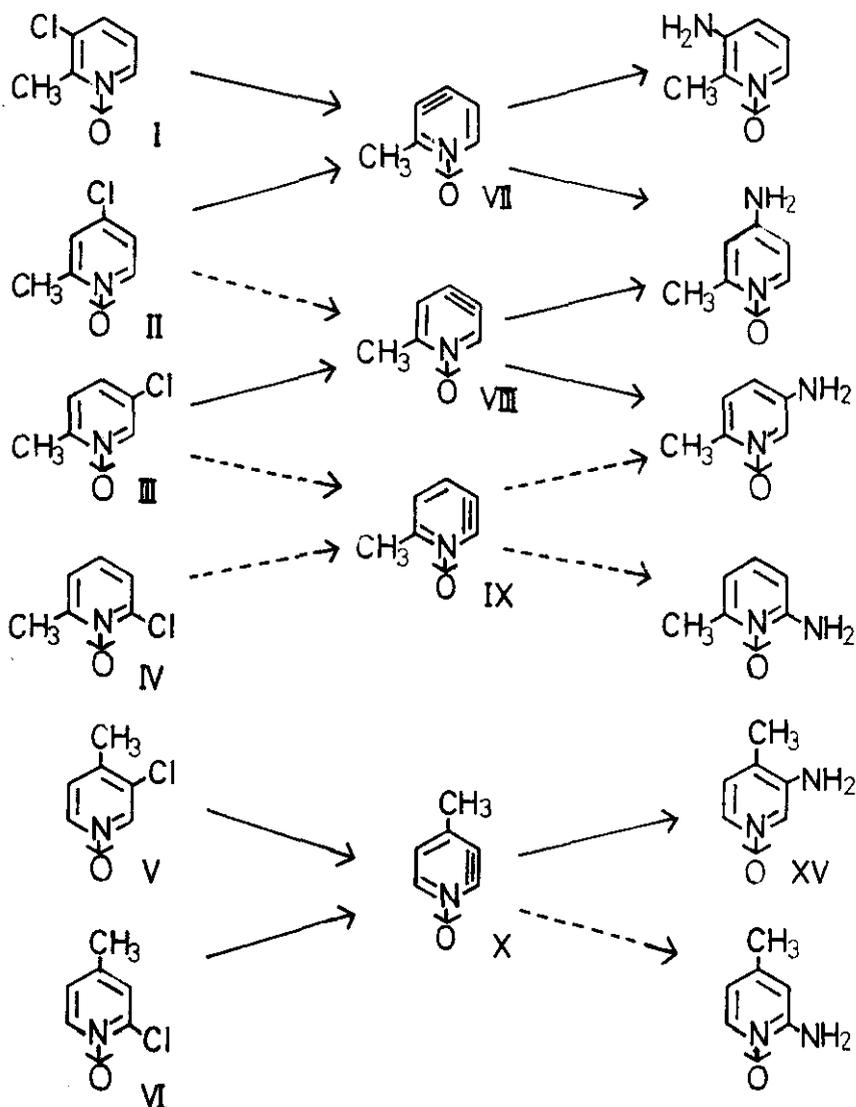
Analysis by gas-liquid chromatography was carried out in a Hitachi gas chromatograph KGL-2 provided with a 2 m. copper column (filled with 20% PEG 6000, 30-60 mesh celite) which was kept at 180° , helium being used as a carrier gas (flow rate 150/min.). The relative retention times (min.) were as follows: 3-amino-2-picoline (21.9); 4-amino-2-picoline (53.5); 5-amino-2-picoline (26); 6-amino-2-picoline (24.7); 2-amino-4-picoline (11.1); and 3-amino-4-picoline (23.5).

Analysis by thin layer chromatography was carried out using alumina plates, and solvent systems and R_f values were as follows: 3-amino-2-picoline, acetone-benzene (2:1), R_f (0.80); 4-amino-2-picoline, acetone-chloroform (2:1), R_f (0.56); 5-amino-2-picoline, acetone-benzene (2:1), R_f (0.74); 6-amino-2-picoline, acetone-benzene (2:1) R_f (0.77); 2-amino-4-picoline, ethyl acetate, R_f (0.89); and 3-amino-4-picoline, acetone-chloroform (2:1), R_f (0.78).

In the amination of 3-chloro-2-picoline 1-oxide (I, mp $73-74^\circ$, colorless needles from cyclohexane) followed by catalytic reduction with Raney Nickel, 4-amino-2-picoline was detected by thin layer chromatography.

The same reaction with 4-chloro-2-picoline 1-oxide (II)⁵⁾ gave rise to 3-amino-2-picoline and 4-amino-2-picoline in 4% and 7% yields respectively, but none of 5-amino-2-picoline was detected. Amination of 5-chloro-2-picoline 1-oxide (III, picrate mp $110-111^\circ$, yellow

needles from EtOH) afforded 4-amino-2-picoline and 5-amino-2-picoline, but 6-amino-2-picoline could not be detected. In the amination of 6-chloro-2-picoline 1-oxide (IV, bp₁ 106-108°), none of products corresponding to amino-2-picolines could be identified.



In the same reaction of 3-chloro-4-picoline 1-oxide (V, hygroscopic crystals) and 2-chloro-4-picoline 1-oxide (VI, mp 130-131° colorless needles from benzene), 3-amino-4-picoline was detected as the sole reaction product.

It may be concluded from these results that though 3-amino-2-picoline could not be detected, the reaction of 3-chloro-2-picoline 1-oxide (I) proceeded via 3,4-pyridyne 1-oxide (VII), which was also formed in the reaction of 4-chloro-2-picoline 1-oxide (II).

The 4,5-pyridyne 1-oxide intermediate (VIII) was involved in the amination of 5-chloro-2-picoline 1-oxide (III).

Concerning to 2,3-pyridyne 1-oxide intermediates (IX and X), no evidences could be observed in 2-picoline series; however, the formation of 3-amino-4-picoline from 3- and 2-chloro-4-picoline 1-oxides (V and VI) might support the formation of such an intermediate.

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Received, 25th September, 1973