supply of the samples of the alcohol and its acetate from *Kopsia longiflora* and to Professor F.N. Lahey of Chemistry Department, University of Queensland, Brisbane, Australia, for carrying out the determation of a mixed melting point and for his keen discussions.

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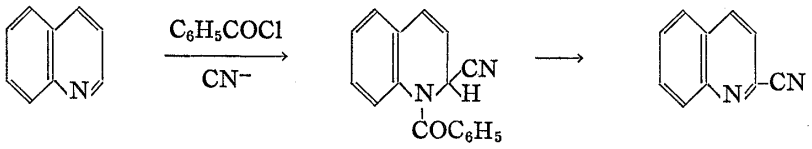
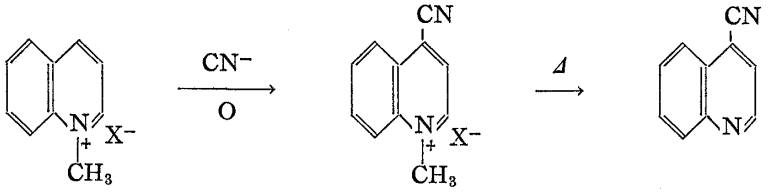
Synthesis of 2- and 4-Cyanopyridines

A method for direct introduction of cyano group at 2- or 4- position in pyridine ring includes the reactions reported by Reissert[1] and by Kaufmann.[2] These reactions gave good results with quinolines but generally did not proceed with pyridines.

Reissert :



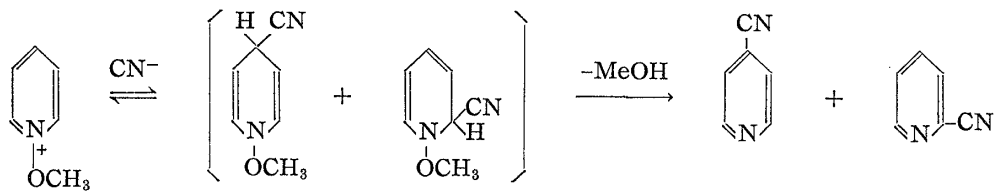
Kaufmann :



Pyridine and quinoline N-oxides easily form their quaternary salts. On considering the nucleophilic reactivity at 2- and 4-positions in the quaternary salts, a new method of directly introducing cyano group into pyridine rings was developed.

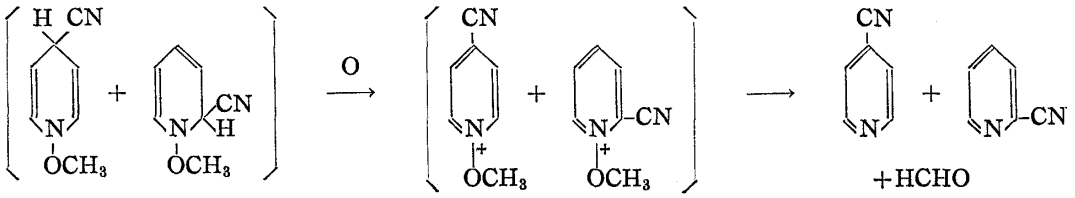
Pyridine or quinoline N-oxides were reacted with methyl iodide or dimethyl sulfate and to the solution of the resulting quaternary salts, potassium cyanide was added and stirred for about one hour at room temperature, by which the reaction was completed. The products, 2- and 4-cyanopyridines were extracted with chloroform and the isomers were separated by vacuum distillation or alumina chromatography. As the solvent for this reaction, water or water-dioxane mixture, and also other solvents are used. The reaction was completed at room temperature but higher temperature could also be used to advantage.

The possible mechanism of this reaction can be written as follows : The first step should be the attack by cyanide ion at 2- or 4-position of the pyridine ring and in the



1) A. Reissert : Ber., **38**, 1603, 3415(1905).
2) A. Kaufmann, *et al.* : Ber., **42**, 3776(1909); **44**, 2058(1911); **45**, 1805(1912); **51**, 116(1918).

next step, these dihydropyridine-type intermediates would lose methanol to form the products. However, another mechanism similar to Kaufmann reaction also should not be rejected. In this case, the dihydro compounds would be oxidized to cyanopyridinium derivatives with air. The cyano derivative should easily decompose into the final product, liberating formaldehyde.[3]



The ratio of isomers formed in the product greatly depends on reaction conditions. Table I summarizes the results of several experiments on this reaction and physical properties of the products. These products were identified by admixture with samples synthesized by different routes.

The details of these experiments will be presented in the near future.

Table I.

N-Oxide of	Product	Yield[g] (%)	m.p. (°C) b.p. (°C/mm. Hg)	Picrate, m.p. (°C)
Pyridine	4-Cyanopyridine	25	78~80 (79)[a]	197~199 (198~199)[a]
	2-Cyanopyridine	50	110~117/20[e] (114~116/24)[b]	—
2-Picoline	4-Cyano-2-picoline	18	— (44~46)[a]	164~165 (165~167)[a]
	6-Cyano-2-picoline	45	70~72 (69~71)[b]	—
3-Picoline	4-Cyano-3-picoline	15	— (50~52)[c]	154~156 (154~156)[c]
	2-Cyano-3-picoline	30	85~86 (87~88)[b]	—
4-Picoline	2-Cyano-4-picoline	28	88~91 (88~89)[b]	—
2,6-Lutidine	4-Cyano-2,6-lutidine	13	80~83 (81~82)[a]	175~178 (175~177)[a]
	6-Cyanomethyl-2-picoline	33	125~133/22 (125~130/19)[f]	176~179 (176~179)[f]
Quinoline	4-Cyanoquinoline	trace	— (100~101.5)[a]	175~177 (175~177)[a]
	2-Cyanoquinoline	70	91~95 (93)[a]	—

Solvent: Water-dioxane mixture. Room temperature.

a) E. Ochiai, Y. Suzuki: This Bulletin, **2**, 247(1954).
b) Y. Suzuki: *Ibid.*, **5**, 13(1957). *c*) Y. Suzuki: *Ibid.*, **5**, 78(1957).
d) M. Henze: Ber., **69**, 1566(1936).
e) Identified as picolinic acid, m.p. 136~139°.
f) This compound was synthesized by reacting sodium cyanide with ω-chloro compound. (picrate, m.p. 160~162°)(cf. G. Kobayashi, *et al.*: Yakugaku Zasshi, **74**, 790(1954))
g) Calculated from the N-oxide.

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3) cf. E. Ochiai, *et al.*: Yakugaku Zasshi, **64**, 210(1944).