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51. **Haruyuki Ito**: Synthesis of Nitro Compounds by Means of Oxidation of Acylamino Compounds. XIII.[*1] Formation of *cis*-2-Nitrocinnamonitrile by Oxidation of 2-Methylaminoquinoline with Hydrogen Peroxide.

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Recently, 4-nitroquinoline-1-oxide has been known as one of the interesting compounds in its carcinogenic or anticancer actions.[1] It was the first intention of the present study to synthesize 2-nitroquinoline, which seemed to possess the similar chemical properties to 4-nitroquinoline.

For the reaction obtaining nitro group at the low electron density position, the oxidation of amino compounds with Caro's acid has been reported and this was shown in synthesizing 2-nitropyridines from 2-aminopyridines.[2,3] But the oxidation of 2-aminoquinoline to 2-nitroquinoline has not been reported at all.

In the previous paper[4] of this series, a new method of synthesis of aromatic nitro compounds by oxidation of acylamino compounds with hydrogen peroxide has been described, and it would be a promising method for the synthesis of 2-nitroquinoline.

Acylamino compounds, 2-acetamidoquinoline and 2-(N-acetylmethylamino)quinoline were not suitable to the purpose, because they were easily hydrolyzed the corresponding amino compounds in the reaction medium; so that 2-methylaminoquinoline was chosen as the starting material, 2-methylaminoquinoline was oxidized with fifteen moles of hydrogen peroxide in acetic acid for four hours on a boiling water bath. A yellowish product melted at 75~80° was obtained, which gave white silky needles melted at 83~84° by recrystallization from 1:1 petr. ether-benzene. It had the empirical formula of $C_9H_6O_2N_2$ and absorption bands in its infrared spectrum at 2220 (cyano group), 1566 and 1345 cm^{-1} (nitro group), 768 (*ortho*-substituted benzene) and 690 cm^{-1} (*cis* double bond). Judging from these data, it was considered that the substance was not the desired compound but would be *cis*-2-nitrocinnamonitrile. The product was hydrogenated over palladium-carbon catalyst in ethanol absorbing four moles of hydrogen, which were equivalent to reduce one double bond and one nitro group. The reduced product was treated with acetic anhydride and white needles melted at 130~131° were obtained. The substance had empirical formula of $C_{11}H_{12}ON_2$ and infrared absorption bands at 2250 (cyano group), 3360, 1650 and 1585 (amide) 757 cm^{-1} (*ortho*-substituted benzene), and it was identified as 2-(2-cyanoethyl) acetanilide obtained by the analogous reduction and acetylation of *trans*-2-nitrocinnamonitrile, by the mixed melting point determination and comparison of their infrared absorption spectra. Thus, the oxidation product was confirmed to be *cis*-2-nitrocinnamonitrile, since it was not identical with its *trans* isomer.[5] Based on the mechanism of the hydrogen peroxide oxidation discussed in the previous papers, mechanism of this reaction was deduced as shown in Chart 1.

[*1] Part XII: This Bulletin, 12, 345 (1964).

[*2] Oshika, Shizuoka (伊藤晴之).

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3) L.L Bambas: J. Am. Chem. Soc., **67**, 668 (1945).

4) T. Kosuge, *et al.*: Kenkyu Nempo (Faculty of Pharm., Univ. of Kanazawa), **2**, 10 (1952).

5) R. Pschorr: Ber., **31**, 1295 (1898); R.A. Weerman: Ann., **401**, 9 (1913).

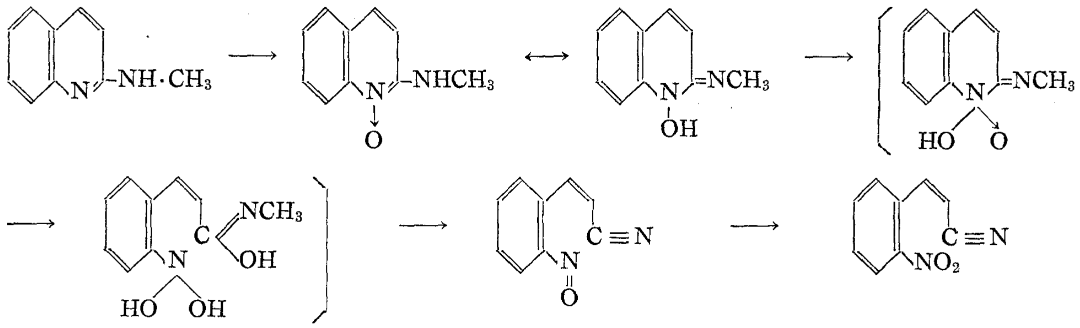

Chart 1.

A small amount of carbostyril was obtained as a by-product, separated by chromatography. 2-Nitroquinoline was not obtained after all, but the product *cis*-2-nitrocinnamonitrile gave the evidence of N-C cleavage of quinoline during the oxidation.

Experimental*3

2-Methylaminoquinoline——A mixture of 16.3 g. of 2-chloroquinoline, 160 ml. of 30% $MeNH_2$ and 1 g. of Cu_2Cl_2 was heated in autoclave at 150~160° for 6 hr. The mixture was extracted with benzene and the benzene solution was evaporated to dryness after drying over Na_2SO_4. The residue was distilled *in vacuo* and 12.6 g. of distillate, b.p$_3$ 134~143°, m.p. 63~68°, was obtained. Recrystallization from a mixture of petr. ether-benzene gave colorless prisms, m.p. 70.5~71.5°. Yield, 10.2 g. *Anal.* Calcd. for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found : C, 76.14; H, 5.28; N, 17.68. Picrate, yellow needles, m.p. 230~231° (from EtOH-H_2O). *Anal.* Calcd. for $C_{16}H_{13}O_7N_5$: C, 49.62; H, 3.38. Found : C, 49.41; H, 3.91.

2-(N-Acetylmethylamino)quinoline——Six g. of 2-methylaminoquinoline was added to 10 ml. of Ac_2O and heated on oil bath at 140° for 2 hr. The mixture was evaporated to dryness under reduced pressure. The residue was recrystallized from a mixture of benzene-ligroin to colorless prisms, m.p. 75.5~76.5°. Yield, 5.2 g. *Anal.* Calcd, for $C_{12}H_{12}ON_2$: C, 71.98; H, 6.04; N, 13.99. Found : C, 71.78; H, 6.93; N, 14.02.

Oxidation of 2-(N-Acetylmethylamino)quinoline——a) One ml. of 30% H_2O_2 and 2 ml. of AcOH were added to 0.2g. of 2-(N-acetylmethylamino) quinoline, and it was warmed on a water bath at 55~60° for 20 hr. The mixture was poured into cracked ice and neutralized with conc. NH_4OH and extracted with benzene, and the benzene solution was submitted to Al_2O_3 column chromatography after drying over Na_2SO_4, and 0.1 g. of yellowish prisms (m.p. 66~69°) was obtained from a part of benzene eluate. Recrystallization from a mixture of hexane-benzene gave white prisms (m.p. 70.5~71.5°), which was undepressed on admixture with 2-methylaminoquinoline. Picrate, yellow needles, m.p. 230~231° and when admixed with picrate 2-methylaminoquinoline, no depression of melting point was observed.

b) The same quantity of materials was mixed and heated at 80° for 10 hr., and the mixture was treated by the same manner and 80 mg. of 2-methylaminoquinoline was obtained from a part of benzene eluate of Al_2O_3 chromatography, and 25 mg. of light brown needles (m.p. 179~188°) was obtained from a part of $CHCl_3$ eluate. Recrystallization from benzene gave colorless needles, m.p. 195~196°, which were identified as carbostyril by admixture and comparison of their IR spectra.

Oxidation of 2-Methylaminoquinoline——Two g. of 2-methylaminoquinoline was added to a mixture of 19.5 ml. of 30% H_2O_2 and 40 ml. of AcOH and the mixture was heated on a boiling water bath for 4 hr. It was evaporated under reduced pressure, 10 ml. of H_2O was added to the residue and evaporated again and 20 ml. of H_2O and 20 ml. of $CHCl_3$ were added. The H_2O layer was extracted twice with 10 ml. of $CHCl_3$, the combined $CHCl_3$ solution was washed twice with 10 ml. of H_2O. The starting material, 2-methylaminoquinoline was recovered from the combined H_2O layer as its picrate (1.17 g.). The $CHCl_3$ solution was evaporated after drying over Na_2SO_4 and the residue was dissolved in benzene and chromatographed on a silica gel column, and 0.18 g. of yellowish silky needles, m.p. 75~80°, were obtained from a part of benzene eluate. Recrystallization from petr. ether-benzene (1:1) gave colorless silky needles, m.p. 83~84°. *Anal.* Calcd. for $C_9H_6O_2N_2$: C, 62.07; H, 3.47; N, 16.09. Found : C, 62.03; H, 3.42; N, 16.35. IR ν_{max}^{Nujol} cm^{-1} : 2220 (C≡N), 1566, 1345 (NO_2), 768 (*o*-substituted benzene); 690 (*cis* double bond). It depressed with *trans*-2-nitrocinnamonitrile, m.p. 91~92° on admixture.

Eighty mg. of this substance was dissolved in EtOH and hydrogenated over Pd-C catalyst (1 ml. of 1% $PdCl_2$, 0.2 g. of C). Forty five ml. of H_2 gas was absorbed. Pd-C was filtered off and the filtrate

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*3 All melting points are uncorrected.

was evaporated to dryness. One ml. of Ac_2O was added and heated on a boiling water bath for 2 hr. The mixture was evaporated under reduced pressure to dryness and the residue was dissolved in benzene. It was purified by chromatography on Al_2O_3 column using benzene as the eluent. White prisms, 30 mg., m.p. 130~131°, were obtained from benzene eluate. *Anal.* Calcd. for $C_{11}H_{12}ON_2$: C, 70.18; H, 6.43; N, 14.88. Found: C, 70.10; H, 6.50; N, 14.76. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2250 (C≡N), 3360, 1650 and 1586 (-CONH-), 757 (*o*-substituted benzene). It was confirmed to be cyanoethyl-*o*-acetanilide by admixture and comparison of their IR spectra.

Fifty mg. of light brown needles, m.p. 180~190°, was obtained from apart of $CHCl_3$ eluate of the silica-gel chromatography. Recrystallization from benzene gave colorless needles, m.p. 195~196°. *Anal.* Calcd. for C_9H_7ON: N, 9.65. Found: N, 9.69. Mixed melting point determination and comparison of IR spectra established that this substance was identical with carbostyril.

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Summary

In oxidation of 2-methylaminoquinoline with hydrogen peroxide, *cis*-2-nitrocinnamonitrile and a small amount of carbostyril were obtained. And a reaction mechanism was proposed.

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52. **Takuzo Nishimura and Issei Iwai**: Studies on Synthetic Nucleosides. I. Trimethylsilyl Derivatives of Pyrimidines and Purines.

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Recently, a great attention has been drawn to the studies of organosilicon compounds containing the reactive Si-N linkage. Birkofer, *et al.*[1] reported that N-acylated heterocyclic compound were easily obtained by the reaction of their N-trialkylsilyl derivatives with acylchlorides.

Authors developed a new synthetic method for nucleosides using trimethylsilyl derivatives of pyrimidines and purines, namely fusion of acylhalogeno sugars with these silyl compounds gave acylated nucleosides in good yields. These results will be reported in the following papers.

This paper describes the preparation and properties of trimethylsilyl derivatives of pyrimidines and purines.

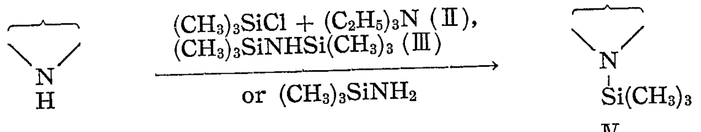

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Chart 1.

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