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Torizo Takahashi and Kan-ichi Ueda : Sulfur-containing Pyridine
Derivatives. XLVII.* Behavior of 3-Nitro-4-thiocyanopyridine
to Aliphatic Alcohols. (2).

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In Part XL¹⁾ of this series, the authors reported of an interesting behavior of the thiocyno group in 3-nitro-4-thiocyanopyridine (1) toward aliphatic alcohols, and it was suggested that the main product in this reaction should be the alkyl thiocarbamate (II) from the fact that it was soluble in alkali, recoverable unchanged on addition of acids, and on hydrolysis it formed the aminopyridine (IV).

In order to define the structure of the above product more clearly, it was submitted to oxidation (Kitamura's reaction²⁾), which led to the urethane. The latter was confirmed by synthesizing it from the aminopyridine and by direct comparison of their infrared spectra, the details of which follow.

Treatment of ethyl 3-nitropyridyl-4-thiocarbamate (II) with hydrogen peroxide in aqueous potassium hydroxide solution provided the sulfurless product of m.p. 63°, which was found to be identical with the product (III) obtained by the condensation of 3-nitro-4-aminopyridine³⁾ (IV) and ethyl chlorocarbonate. The infrared absorption spectrum of (III) (Fig. 1) shows a characteristic absorption for NH type near 3μ in addition to the carbonyl absorption (5.74μ), but that of (II) (Fig. 2) does not show the carbonyl absorption, although absorption by NH type is present. This indicates that

Fig. 1. 3-Nitropyridyl-4-carbamate (in Nujol)

Fig. 2. 3-Nitropyridyl-4-thiocarbamate (in Nujol)

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Experimental⁶⁾

Reaction with Ethanol—a) The preparation was effected by using 1.0 g. of 3-nitro-4-thiocyanopyridine and 30 cc. EtOH, following the same procedure as described in the experimental section of Part XL, and in this case 30 mg. of 3-nitro-4-aminopyridine, which was not described previously, was obtained besides other products. The m.p. of ethyl 3-nitropyridyl-4-thiocarbamate registered 74° after repeated recrystallization from petr. ether-ether. *Anal.* Calcd. for $C_8H_9O_3N_3S$: N, 18.50. Found: N, 18.68.

b) 1.0 g. of the thiocyno compound was heated with 25 cc. of dehyd. EtOH for 14 hrs. In this case, approximately 75% of the starting material was recovered.

Methyl 3-Nitropyridyl-4-carbamate—To a solution of 0.4 g. of methyl 3-nitropyridyl-4-thiocarbamate in aq. KOH solution (0.4 g. of KOH, 8 cc. of water) was added dropwise 4 cc. of 30% H_2O_2 under cooling, and after being allowed to stand at room temperature for 1 hr., the mixture was adjusted to pH 7. The product thus obtained was collected, washed with water, dried, and recrystallized from MeOH to colorless pillars, m.p. 140~142°. Yield, 0.33 g. *Anal.* Calcd. for $C_7H_7O_4N_3$: C, 42.64; H, 3.55. Found: C, 42.61; H, 3.82.

Ethyl 3-Nitropyridyl-4-carbamate—a) In a flask fitted with a mechanical stirrer were placed 0.4 g. of 3-nitro-4-aminopyridine, 0.16 g. of Na_2CO_3 , 20 cc. of ether, and 2 cc. of water. To the two-phase system was added dropwise with stirring 0.60 g. of $ClCOOC_2H_5$ during 30 mins. After the addition had been completed, stirring was continued for a further 30 mins. At the end of this period, the organic layer was separated. The aqueous layer was extracted with ether and these ethereal extracts were combined with the initial organic phase. After washing with water and drying over anhyd. Na_2SO_4 , the ether was distilled off and the residue was recrystallized from petr. ether to colorless needles, m.p. 62°. Yield, 0.16 g. *Anal.* Calcd. for $C_8H_9O_4N_3$: N, 19.91. Found: N, 19.82.

b) To a solution of 0.5 g. of the thiourethane in aq. KOH (0.5 g. of KOH, 8 cc. of water) was added dropwise 3.0 cc. of H_2O_2 under cooling, and the mixture was treated by the same procedure as described for the preparation of the methyl carbamate. Yield, 0.31 g. After recrystallization from petr. ether, this product showed no m.p. depression on admixture with the above-mentioned sample.

Summary

1) The application of Kitamura's reaction to ethyl 3-nitropyridyl-4-thiocarbamate resulted in the formation of ethyl 3-nitropyridyl-4-carbamate, which was identical with the product obtained by the reaction of 3-nitro-4-aminopyridine with $ClCO_2C_2H_5$.

2) The reaction mechanism of the thiocyno compound with alcohols was reconsidered.

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6) All melting points are uncorrected.