

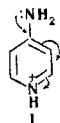
ALKYLATION OF 4-AMINOPYRIDINE

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4-Alkylaminopyridines are formed by the alkylation of 4-aminopyridine with cyclohexanol, cyclopentanol, and 2-propanol in sulfuric acid.

In developing our studies of the alkylation of nitrogen-containing compounds by alcohols and alkenes in sulfuric acid solutions, we accomplished the alkylation of 4-aminopyridine. The latter exists as cation I in acidic solutions.



Starting from the assumption that the unshared pair of electrons of the nitrogen of the amino group is capable of reacting with strong electrophilic agents, we alkylated 4-aminopyridine with cyclohexanol, cyclopentanol, and isopropyl alcohols. 4-Alkylaminopyridines were obtained in yields up to 73%.

A method for the synthesis of 4-alkyl- and 4-dialkylaminopyridines by the reaction of 4-phenoxy-pyridine with salts of the appropriate amines at 200–210° is described in [1].

Our method is distinguished by its simplicity, the availability of the starting materials, and by the fact that no dialkylation products are obtained.

EXPERIMENTAL

4-Cyclohexylaminopyridine. A solution of 4.7 g (0.05 mole) of 4-aminopyridine in 70 ml of 80% sulfuric acid was heated to 60°C, 7.5 g (0.075 mole) of cyclohexanol was added dropwise with continuous stirring, and the mixture was stirred at 60° for another 6 h. The reaction mixture was cooled to room temperature, poured over 100 g of ice, and neutralized with concentrated ammonium hydroxide. The amine was filtered, washed with water, and dried to give 6 g (68%) of colorless crystals with mp 147–148° (from heptane [1]).

4-Cyclopentylaminopyridine. This compound was similarly obtained. The neutralized solution was allowed to stand overnight in a cold room to give 50% of a product with mp 99–100° (from heptane). Found %: N 17.3. $C_{10}H_{14}N_2$. Calculated %: N 17.3.

4-Isopropylaminopyridine. This compound was similarly obtained from 4.7 g (0.05 mole) of 4-aminopyridine and 6 g (0.1 mole) of isopropyl alcohol in 70 ml of 80% sulfuric acid by heating at 80° for 6 h. After neutralization, the base was extracted with benzene (3 × 50 ml), the extract was dried with anhydrous sodium sulfate, the benzene was removed, and the residue was vacuum distilled to give 5 g (74%) of a colorless oil which crystallized on cooling to give a product with bp 115–120° (3 mm) and mp 76–77° (from heptane). Found %: N 20.5. $C_8H_{12}N_2$. Calculated %: N 20.6.

LITERATURE CITED

1. A. F. Vompe, N. V. Monich, N. F. Turitsina, and L. V. Ivanova, Dokl. Akad. Nauk SSSR, **114**, 1235 (1957).

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