INVESTIGATION OF THE CHEMISTRY OF PHENYLPYRIDINES

I. AMINATION OF 2-PHENYLPYRIDINE

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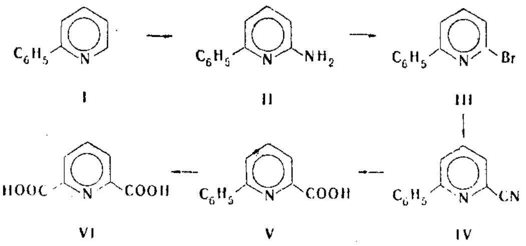
Amination of 2-phenylpyridine under the conditions of the Chichibabin reaction gave 6-amino-2-phenylpyridine.

In connection with the study of the effect of a phenyl group in isomeric phenylpyridines on the direction of their amination under the conditions of the Chichibabin reaction, we accomplished the amination of 2-phenylpyridine (I). The yield of amination product was 87% when the reaction was carried out in dimethylaniline at 130-140°C for 8 h. Aminophenylpyridine is formed in only 32% yield under the conditions of the amination of pyridine (about 110° for 10 h); in this case, about half of the starting phenylpyridine is recovered. The amination product has the 6-amino-2-phenylpyridine structure (II). Its structure was proved by conversion to dipicolinic acid (VI) via the scheme



EXPERIMENTAL

6-Amino-2-phenylpyridine (II). A solution of 15.5 g (0.1 mole) of I in 20 ml of dimethylaniline was added with stirring to 4 g (0.1 mole) of freshly prepared $NaNH_2$ in 20 ml of dimethylaniline, and the mixture was heated to 130-140° and held at this temperature for 8 h. It was then cooled to 0°, 20 ml of 5% KOH solution was added dropwise until the vigorous reaction ceased, and the mixture was diluted with 100 ml of water. The dimethylaniline was extracted with petroleum ether, and the mixture was saturated with solid KOH and extracted with benzene. The benzene extract was dried with KOH and distilled to give 14.5 g (87%) of II with bp 205-210° (20-22 mm) and mp 72-74° (from hexane). Found,%: N 16.5. $C_{11}H_{10}N_2$. Calculated,%: N 16.5. The picrate had mp 217-219° (from methanol). Found,%: N 17.5. $C_{11}H_{10}N_2 \cdot C_6H_3N_3O_7$. Calculated,%: N 17.5. Analysis of the residue after distillation of II by thin-layer chromatography (activity II Al_2O_3 with elution by ether and development by iodine) demonstrated the presence of a substance with R_f 0.18, which is probably 4-amino-2-phenylpyridine.

6-Bromo-2-phenylpyridine (III). A 4.3-g (25 mmole) sample of II was added in the course of 10 min with cooling to 10° to 15 ml of 48% hydrobromic acid, after which the temperature was lowered to −5 to −10°, and 5 ml of bromine was added dropwise. A solution of 4.5 g (0.06 mole) of $NaNO_2$ in 7 ml of water was then added dropwise in the course of 1 h. The mixture was then stirred for 0.5 h, and a solution of 10 g of NaOH in 10 ml of water was added. The mixture was extracted with ether, and the ether extract was

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dried with potassium carbonate. The ether was removed, and the residue was treated with hot hexane. Cooling of the hexane solution precipitated 5.5 g (91%) of colorless crystals of III with mp 50-51°. Found,%: N 6.0. $C_{11}H_8BrN$. Calculated,%: N 6.0.

6-Cyano-2-phenylpyridine (IV). A mixture of 1.2 g (5 mmole) of III, 1.4 g (5.6 mmole) of $K_3Fe(CN)_6$, and 0.6 g (0.096 g-atom) of copper powder was heated in a sealed tube at 180° for 8 h. Sublimation of the reaction product gave 0.7 g (81%) of IV with mp 64-65° (from hexane). Found,%: N 15.5. $C_{12}H_8N_2$. Calculated,%: N 15.6.

6-Carboxy-2-phenylpyridine (V). A solution of 0.85 g (4 mmole) of IV in 10 ml of concentrated hydrochloric acid was refluxed for 10 h. The mixture was evaporated, and the residue was treated several times with hot hexane, from which 0.7 g (70%) of colorless crystals of V with mp 95-97° precipitated. Found,%: N 7.0. $C_{12}H_9NO_2$. Calculated,%: N 7.0.

Dipicolinic Acid (VI). A solution of 10 g of $KMnO_4$ in 500 ml of water was added in portions to a solution of 1 g (5 mmole) of V in 10 ml of 5% hydrochloric acid. After 12 h, the excess oxidizing agent was removed by the addition of methanol, and the resulting precipitate was removed by filtration. The filtrate was evaporated to a volume of 20 ml and neutralized with 20 ml of concentrated hydrochloric acid. The solution was then heated to the boiling point and allowed to stand for 12 h. The precipitated acid (VI) was removed by filtration and washed several times with water to give 0.36 g (42%) of a product with mp 230-232° (dec.) (mp 233-234° [1]).

LITERATURE CITED

1. G. Black, E. Depp, and B. B. Corson, J. Org. Chem., 14, 14 (1949).