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Studies on the Coal Tar Bases. VI. Synthesis of
3,4,5-Collidine.

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In the previous paper, it was reported by the authors that all the monomethyl and polymethyl derivatives of pyridine except 3,4,5-collidine were synthesized¹⁻³⁾ that the three picolines, six lutidines, and five collidines were accurately isolated⁴⁾ from coal tar bases of low-temperature coke, and the infrared absorption spectra of eighteen polymethylpyridines, except 3,4,5-collidine, were taken⁵⁾.

For the purpose of obtaining a sample that may be compared with that isolated from coal tar bases, 3,4,5-collidine (III), only one of the methyl derivatives of pyridine that has not been synthesized or isolated from any natural source, was synthesized. It was derived from 2,6-dihydroxy-3,4,5-trimethylpyridine⁶⁾ (I) as a starting material. Concerning this dihydroxyl compound, Rogerson and Thorpe published a report titled "Some Alkyl Derivatives of Glutaconic Acid and of 2,6-Dihydroxypyridine."

To confirm the structure of 3,4,5-collidine synthesized by us, though no one could object to its structure, it was oxidized to a tricarboxylic acid (IV) and esterified to trimethyl ester (V). It was found that these derivatives were identical with those derived from pentacarboxylic acid⁷⁾ (VI) of pyridine by the mixed fusion showing no depression.

3,4,5-Collidine is a colorless liquid at room temperature, melts at 10~13°, boils at 205~207°, and has a characteristic odor.

This synthetic process is illustrated by the following schema:

The infrared absorption curve and specific absorption band of this collidine are shown in Figs. 1 and 2, respectively.

The infrared absorption curve is subject principally to the general rule that: "In accordance with the increasing of the number of methyl groups, the situation of specific absorption band shifts to shorter wave and decreases its intensity." This rule was found by

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1) This Bulletin, 1, 142(1953). 2) *Ibid.*, 1, 126(1953). 3) *Ibid.*, 1, 122(1953). 4) *Ibid.*, 1, 149(1953). 5) *Ibid.*, 1, 146(1953). 6) H. Rogerson, J. F. Thorpe: J. Chem. Soc., 87, 1685 (1905). 7) J. Weber: Ann., 241, 16(1887).

Fig. 1. Infrared Absorption Spectra of 3,4,5-Collidine

Fig. 2. Specific Absorption of 3,4,5-Collidine

the comparison of specific absorption bands of a series of methyl homologs of pyridine⁵). This fact gives further basis for the infrared absorption spectra of the pyridines.

Experimental

2,6-Dichloro-3,4,5-trimethylpyridine (II)—A mixture of 4 g. of dihydroxy compound (I) and 12 g. of phosphoryl chloride is heated, the reaction mixture is poured into ice-water, and an oil deposited is extracted with ether. The ethereal solution is dried and the ether is evaporated. The crude product melts at 92°. By recrystallisation from a mixture of methanol and water, the colorless needles melt at 96~96.3°. Yield, 3 g. (62%). *Anal.* Calcd. for $C_8H_9Cl_2N$ (2,6-Dichloro-3,4,5-trimethylpyridine): N, 7.36. Found: N, 7.37.

2,6-Dichlorocollidine is soluble in methanol, ethanol, ether, benzene, and petroleum, insoluble in water and it has almost no basicity.

3,4,5-Trimethylpyridine (III)—2.5 g. of 2,6-dichloro compound (II) dissolved in 25 cc. of methanol, containing 1 g. of potassium acetate, is mixed with 1 g. of palladium-charcoal (50%) as a catalyst. In an atmosphere of hydrogen gas, dichloro compound is reduced, and absorbs 580 cc. (95% of the theoretical) of hydrogen. On evaporating the methanol, the product from residual oil boils at 205~207°. Yield, 1.2 g. (80%).

3,4,5-Collidine melts at 10~13°. The picrate, m.p. 174°; picrolonate, m.p. 188°; chloroplatinate, m.p. 197~198°. *Anal.* Calcd. for $C_8H_{11}N \cdot C_6H_3O_7N_3$ (3,4,5-Trimethylpyridine picrate): C, 48.0; H, 4.0; N, 16.00. Found: C, 47.80; H, 4.2; N, 15.74. Calcd. for $C_8H_{11}N \cdot C_{10}H_8O_5N_4$ (3,4,5-Trimethylpyridine picrolonate): N, 18.2. Found: N, 17.54.

Pyridine-3,4,5-tricarboxylic acid (IV)—0.5 g. of 3,4,5-collidine suspended in 20 cc. of water is oxidized with 2% solution of $KMnO_4$ on a water bath. After taking off the MnO_2 , potassium salt of the tricarboxylic acid is derived to silver salt as usual and to the free acid by H_2S . Pyridine-3,4,5-tricarboxylic acid, white needles from water, m.p. 261°(decomp.).

3,4,5-Tricarbomethoxypyridine (V)—The above carboxylic acid mixed with a small quantity of ether is treated with diazomethane. 3,4,5-tricarbomethoxypyridine, m.p. 90~91°. *Anal.* Calcd. for $C_{11}H_{11}O_5N$ (3,4,5-Tricarbomethoxypyridine): N, 5.5. Found: N, 5.8.

This ester was also obtained from pyridine-tricarboxylic acid derived by means of decarboxylation of pyridine-pentacarboxylic acid (VI) and the mixed melting point of these esters showed no depression.

Summary

3,4,5-Collidine was synthesized in order to compare with the polymethylpyridine obtained from coal tar bases.

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