

however, by extracting the crude crystals once with absolute ether in a Soxhlet apparatus. A mixed melting point with authentic vanillic acid² with the recorded m. p. 208–210°³ was undepressed.

Veratric Acid and 4-Aminoveratrole.—The condensation of veratraldehyde 27.6 g., sodium azide 12.5 g. and concentrated sulfuric acid 118 ml. was essentially as described above but the time of hydrolysis was somewhat longer. Slightly discolored veratric acid, 25.4 g. or 84%, separated from the reaction mixture. One recrystallization from water and ethanol gave a pure product with the recorded⁴ m. p. 179–181°. Extraction of the acid mother liquor with benzene gave less than 1 g. of oily crystals. The acidic solution was made strongly alkaline and extracted again with benzene. Evaporation of this extract and distillation of the residue under reduced pressure yielded 1.6 g. of colorless crystals that darkened in air. Their melting point of 87–88° agreed with that reported for 4-aminoveratrole.¹⁰

(8) Misani and Bogert, *J. Org. Chem.*, **10**, 355 (1945).

(9) Goldschmidt, *Monatsh.*, **6**, 379 (1885).

(10) Buck and Ide in "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1943, p. 44.

DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY
MCGILL UNIVERSITY
MONTREAL, CANADA

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8-Amino-2,4-Dimethylquinoline¹

BY WYMAN R. VAUGHAN²

As a consequence of the tremendous recent interest in the derivatives of 8-aminoquinoline as antimalarial drugs it was found desirable to develop a satisfactory synthesis for 8-amino-2,4-dimethylquinoline. The present procedure was found to be a rapid and efficient method for the preparation of this substance, one of its advantages being that it obviates any extensive purification of the intermediate 8-nitro-2,4-dimethylquinoline.

Experimental

8-Nitro-2,4-dimethylquinoline.—One mole (157 g., 150 ml.) of 2,4-dimethylquinoline³ was cooled to 0° and treated with 250 ml. of concentrated sulfuric acid which was added as rapidly as possible with good mechanical stirring. The resulting solution was then cooled to 0° and treated with a solution of 115 g. of potassium nitrate in 300 ml. of concentrated sulfuric acid with vigorous mechanical stirring, the temperature being maintained between 0 and 5° by means of an ice-salt-bath. When all of the nitrating solution had been added, the mixture was stirred for an additional fifteen minutes without cooling and then was poured onto 2500 g. of cracked ice. The resulting mixture was treated with 1500 ml. of concentrated ammonia and diluted to 6 l. with cold water, cooled to room temperature and filtered. The filter cake was placed in a 2-l. beaker with 1 l. of cold water and stirred vigorously until a uniformly fine suspension was obtained. It was then filtered with good suction, and the moist

filter cake was recrystallized from 1 l. of 95% ethanol using norit and a heated funnel: yield 113–115 g. (51–67%), m. p. 115–125°. This impure product is a mixture of 8-nitro-2,4-dimethylquinoline with one or more isomers. A second isomer, m. p. 109.6–110.1° cor., was isolated from the mother liquors from the recrystallization of the major product, but the structure of this substance has not as yet been determined.

Anal. Calcd. for $C_{11}H_{10}O_2N_2$: N, 13.86. Found: N, 14.0.

In view of the work of Price, Velzen and Guthrie⁴ who isolated 6-nitro-2,4-dimethylquinoline, it would appear that this substance is either 5- or 7-nitro-2,4-dimethylquinoline, probably the former in view of the well-known resistance of the 7-position in quinoline toward nitration.⁶

8-Amino-2,4-dimethylquinoline.—A solution of 101 g. (0.5 mole) of 8-nitro-2,4-dimethylquinoline (m. p. 115–125°) in 375 ml. of concentrated hydrochloric acid was added from a dropping funnel to a well-stirred solution of 375 g. of stannous chloride dihydrate in 136 ml. of concentrated hydrochloric acid, the temperature being maintained at 40–50° by means of an ice-bath. Near the end of the reduction a yellow precipitate appeared. After complete addition of the nitro compound to the reducing solution there was added 2000 g. of cracked ice and a cooled solution of 850 g. of potassium hydroxide in 1 l. of water. The resulting mixture was vigorously stirred for 30 minutes and then filtered, and the residue was washed in the funnel with three portions of cold water totaling 1 l. The filter cake was pressed dry and then was dissolved in 1 l. of water containing 50 ml. of concentrated hydrochloric acid. In order to effect solution the mixture was boiled and then was treated at the boiling temperature with a liberal quantity of norit and filtered through a steam-heated funnel. Upon cooling there separated from the filtrate a mass of golden yellow needles, 71–87 g.⁷ This product was dissolved in 500 ml. of boiling water, and the resulting solution was treated with 30 ml. of concentrated ammonia. The 8-amino-2,4-dimethylquinoline separated as an oil which solidified upon rapid cooling with continuous agitation. The mixture was allowed to stand for 30 minutes at room temperature, and then it was filtered: yield 51–61 g. (59–71%), m. p. 86–90°. If a very pure product is desired, the initial product may be recrystallized directly from 70–90° ligroin (10 ml. per g.) or converted to the hydrochloride, which is readily recrystallized from water. Highly purified 8-amino-2,4-dimethylquinoline is a colorless crystalline substance, m. p. 93.7–94.2° cor.⁸

Anal. Calcd. for $C_{11}H_{12}N_2$: N, 16.27. Found: N, 16.3, 16.23.

(4) Repeated recrystallization of a portion of this product from ethanol-water and finally from 95% ethanol yielded a very pure 8-nitro-2,4-dimethylquinoline, m. p. 147–147.5°. Price, Velzen and Guthrie give 149.5–150° cor., cf. ref. 5.

(5) Price, Velzen and Guthrie, *J. Org. Chem.*, **12**, 203 (1947).

(6) Bacharach, Haut and Caroline, *Rec. trav. chim.*, **52**, 413 (1933); cf. ref. 8.

(7) The hydrochloride thus obtained appears to be a dihydrate which loses some of its water of hydration upon standing in a dry atmosphere.

(8) Roberts and Turner, *J. Chem. Soc.*, 1856 (1927), give 89–92°.

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Some 2,3-Dialkylpyridines and their Derivatives¹

BY HENRY M. WOODBURN AND MAX HELLMANN

Our extension of Elderfield's work² on 2,3-dimethylpyridine to the synthesis of other 2,3-dialkylpyridines was interrupted by the war, and

(1) From the M.A. thesis of Max Hellmann, University of Buffalo, June, 1947.

(2) Elderfield and Tracy, *J. Org. Chem.*, **6**, 54 (1941).

(1) Part of the work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Dartmouth College.

(2) Present address: Department of Chemistry, University of Michigan, Ann Arbor, Michigan.

(3) Vaughan, "Organic Syntheses," Vol. 28, in preparation; cf. Craig, *This Journal*, **60**, 1458 (1938).