standing one hour, an iodimetric titration of the reaction mixture in methanol indicated that about 80% of the mercaptan had undergone reaction. The mixture was allowed to stand at room temperature for one week prior to being distilled. Distillation of the product resulted in the recovery of unused mercaptoethanol and vinyl acetate and a residue yield of crude thiodiglycol monoacetate weighing 54.4 g. This material on distillation boiled at 137–138° at 8 mm.; yield of distilled product, 51%. *Anal.* Calcd. for $C_6H_{12}O_3S$: S, 19.5. Found: S, 19.2.

Photosynthesis in Presence of Diphenyl Disulfide.—Vinyl acetate, 90 g., (practical grade, stabilized) obtained from the Eastman Kodak Company was mixed with 78 g. of mercaptoethanol obtained from the Carbide and Carbon Chemicals Corporation. No reaction ensued. These reagents together with 0.8 g. of diphenyl disulfide (1% of the mercaptan used) were placed in a 300-ml. Pyrex test-tube and suspended in a water-bath at 20–25°. An S-4, 100-watt mercury vapor lamp was also suspended under water and placed 11 cm. from the center of the test-tube. On turning on the light the temperature of the reaction mixture rose from 22 to 34° receding slowly after about one hour of irradiation. Irradiation was continued for an additional two hours and subsequently, the reaction product was distilled. After two distillations 72 g. of a product was obtained boiling at 147.7 to 148° at 13–14 mm.

Anal. Calcd. for $C_6H_{12}O_3S$: C, 43.9; H, 7.4; S, 19.5. Found: C, 43.7; H, 7.4; S, 19.9.

Acknowledgment.—The authors are indebted to Messrs. N. Beitsch, S. Sass, E. A. Green and B. Zeffert for having performed the analytical and physical work presented in this paper.

CHEMICAL CORPS TECHNICAL COMMAND
ARMY CHEMICAL CENTER, MARYLAND

RECEIVED JANUARY 14, 1948

Preparation of Vanillonitrile and Vanillic Acid from Vanillin

BY CONRAD SCHUERCH, JR.

The acid catalyzed condensation of hydrazoic acid with aldehydes is included in the more general Schmidt reaction,[1] and in the case of acetaldehyde, benzaldehyde and *m*-nitrobenzaldehyde, results in the corresponding nitriles and N-substituted formyl derivatives.

$$\text{I.}\quad RCHO + HN_3 \xrightarrow{H^+} RC{\equiv}N + H_2O + N_2$$

$$\text{II.}\quad RCHO + HN_3 \xrightarrow{H^+} RNH{-}CHO + N_2$$

Vanillin has now been found to react readily in the presence of sulfuric acid according to equation I, and crystalline vanillonitrile has been easily isolated in a yield of about 70%. The formanilide, which was presumably formed at the same time according to equation II, did not interfere appreciably in the purification of the nitrile. When the original reaction mixture was diluted with water and boiled, hydrolysis of the nitrile occurred and almost pure vanillic acid crystallized in more than 70% yield from the liquors. This observation is of interest because vanillic acid is not readily available by the direct oxidation of vanillin, and because Pearl's catalytic oxidation with silver oxide[2] was found to be somewhat sensitive to obscure differences in the experimental conditions. Substitution of veratraldehyde for the vanillin used in the condensation with hydrazoic acid resulted in more than an 80% yield of crystalline veratric acid, and a small amount of 4-aminoveratrole (equation II) was also isolated from the hydrolysate.

As would be expected from the known reactions of ketones and the mechanism recently proposed for the Schmidt reaction[3,4,5,6] vanillin reacted with hydrazoic acid in the presence of reagents such as a dioxane solution of hydrogen chloride, that are milder than sulfuric acid. Although it is probable that a proper choice of solvent would give a homogeneous system and a smooth condensation with much smaller quantities of acid than those now used, the decrease might well alter the relative amounts of the products formed.[1]

Acknowledgment.—The author wishes to express his gratitude to Professor C. B. Purves for his kind interest and assistance in this and related work.

Vanillonitrile and Vanillic Acid.—One hundred grams (0.658 mole) of pure vanillin was dissolved completely in 375 ml. of concentrated reagent grade sulfuric acid kept at 0–10° in a 2-liter 3-necked flask, with mercury-sealed stirrer, condenser, thermometer and gas exit tube attached. Powdered sodium azide (45 g., 0.69 mole), contained in a small flask attached to the reaction vessel by means of a rubber connector, was added to the red solution at 0–11° over a period of one and one-half hours. The cooling bath was removed and the mixture was stirred for another half hour. The flask was again chilled and about 900 ml. of distilled water was added cautiously from a separatory funnel without allowing the temperature to rise above 18°. This addition caused the nitrile to separate as a yellow solid which completely filled the aqueous layer. When desired, the nitrile could be extracted with ether, and isolated after washing the extract with small amounts of sodium bisulfite and sodium bicarbonate solutions. The yield from smaller quantities of reactants was about 70% and most of the product melted at 87.5–88.3°; m. p. 89–90° is the recorded value for vanillonitrile.[7]

When vanillic acid was required, the original reaction mixture was diluted with 900 ml. of water as already described. The stirrer and thermometer were then removed and washed with 100 ml. of water which was added to the reaction flask, and the mixture boiled gently under reflux. Crystals of vanillic acid appeared after two and one-half hours, and after three hours of boiling the mixture was allowed to cool overnight. The crystals were filtered with suction under an efficient hood, washed five times with a total volume of 1700 ml. of distilled water and dried: yield of vanillic acid 81.5 g. or 73.8%; m. p., 201–203°; and neutralization equivalent (by electrometric titration to *p*H 7), 171. Calcd. for vanillic acid, neut. equiv., 168. Decolorization and recrystallization from water gave beautiful needles but raised the m. p. only slowly. A melting point of 208–210° was obtained,

---

[1] R. Adams, "Organic Reactions," Vol. 3, John Wiley and Sons, New York, N. Y., 1947, article by H. Wolfe, The Schmidt Reaction, p. 307.

[2] Pearl, THIS JOURNAL, **68**, 429 (1946).

[3] Sanford, Blair, Arroya and Sherk, *ibid.*, **67**, 1941 (1945).

[4] Smith, *ibid.*, **70**, 320 (1948).

[5] (a) Newman, Organic Chemistry Symposium, Boston, Mass., 1947; (b) Newman and Gildenhorn, THIS JOURNAL, **70**, 317 (1948).

[6] Schuerch and Huntress, presented at the 112th Meeting of the American Chemical Society in New York, N. Y., September, 1947.

[7] Rupe, *Ber.*, **30**, 2449 (1898).

however, by extracting the crude crystals once with absolute ether in a Soxhlet apparatus. A mixed melting point with authentic vanillic acid[8] with the recorded m. p. 208–210°[8] 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 recorded[9] 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) Goldschmiedt, *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

RECEIVED MARCH 9, 1948

[CONTRIBUTION FROM THE STEELE CHEMICAL LABORATORY OF DARTMOUTH COLLEGE, AND THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MICHIGAN]

8-Amino-2,4-Dimethylquinoline[1]

BY WYMAN R. VAUGHAN[2]

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-dimethylquinoline[3] 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°.[4] 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 Guthrie[5] 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.

---

(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).

(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°.

ANN ARBOR, MICHIGAN

RECEIVED DECEMBER 23, 1947

Some 2,3-Dialkylpyridines and their Derivatives[1]

BY HENRY M. WOODBURN AND MAX HELLMANN

Our extension of Elderfield's work[2] 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).