riboflavin from the green fermentation product. The latter compound was then easily isolated by filtration and was washed with methanol and acetone. The compound (600 mg.) thus obtained remained green in the dry state, but upon exposure to air in the presence of water it was readily oxidized to an orange substance which from chromatographic analysis appears to be identical with 6,7-dimethyl-9-(2′-hydroxyethyl) isoalloxazine.

Kuhn and Ströbele[6] reported that one mole of half-reduced flavin could form quinhydrone-like complexes with one mole of flavin (chloroflavin, light green) with one mole of half-reduced flavin (verdoflavin, dark green) or with one mole of dihydroflavin (rhodoflavin, red).

In view of the ready air oxidation to yellow flavin of the green and red substances observed during the fermentation, it appeared possible that these substances are molecular complexes of the kind observed by Kuhn and Ströbele.

Evidence in support of this hypothesis was obtained by showing that when 100 mg. of the green compound (equivalent to 175 μM of presumed complex) was suspended in 2.0 ml. of water and shaken in air for 4 hours in a Warburg respirometer at 26°, 40 μM of oxygen was consumed. No further oxygen uptake occurred even after shaking overnight. The observed oxygen uptake corresponds to 91% of the theoretical uptake expected from a molecular complex composed of one mole of half-reduced and one mole of oxidized flavin. Further evidence in support of the above hypothesis was obtained by showing that when an alkaline solution of the purified bacterial flavin is treated under anaerobic conditions with a solution of sodium hydrosulfite, a dark green precipitate is formed, corresponding to the verdoflavin reported by Kuhn. Addition of concentrated acid caused formation of a bright red solution (rhodoflavin), which, on dilution with water and gradual admission of air became light green (chloroflavin).

It appears very probable, therefore, that the red and green precipitates observed early in the fermentations are in fact quinhydrone-like complexes of partially reduced 6,7-dimethyl-9-(2′-hydroxyethyl)-isoalloxazine.

(6) R. Kuhn and R. Ströbele, *Ber.*, **70**, 753 (1937).

LABORATORY OF CELLULAR PHYSIOLOGY
NATIONAL HEART INSTITUTE
NATIONAL INSTITUTES OF HEALTH
DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
BETHESDA 14, MARYLAND

The Iodination of Tyrosine and its Derivatives

BY L. JURD[1]

RECEIVED JUNE 21, 1955

Early attempts to iodinate tyrosine in various alkaline media were generally unsatisfactory. In recent years, however, tyrosine has been converted into 3,5-diiodotyrosine in good yields by reaction with iodine monochloride[2] and with iodine and ethylamine.[3] Bauer and Strauss[4] reported that iodine did not react with 3-nitrotyrosine in alkaline solutions or in the presence of mercuric oxide. With iodine monochloride, they obtained 3-iodo-5-nitrotyrosine in small yield.

A new method was developed recently for the iodination of phenols and aromatic ethers.[5] This method involved the reaction of the aromatic compound with iodine and hydrogen peroxide in the presence of a strong mineral acid. As part of a research program which has had to be abandoned, this method was used very satisfactorily in the iodination of tyrosine derivatives. Good yields of monoiodo derivatives were obtained from 3-nitrotyrosine and *o*-methyltyrosine and of 3,5-diiodotyrosine from tyrosine.

(1) U. S. Department of Agriculture, Pasadena, California.

(2) (a) P. Block, Jr., and G. Powell, THIS JOURNAL, **65**, 1430 (1943); (b) E. T. Borrows, J. C. Clayton and B. A. Hems, *J. Chem. Soc.*, 5185 (1949).

(3) J. H. Barnes, E. T. Borrows, J. Folks, B. A. Hems and A. G. Long, *ibid.*, 2824 (1950).

(4) (a) H. Bauer and E. Strauss, *Ber.*, **68B**, 1108 (1935); (b) **69**, 245 (1936).

(5) (a) L. Jurd, *Australian J. Sci. Research*, **2A**, 595 (1949); (b) **3A**, 587 (1950).

Experimental[6]

3,5-Diiodotyrosine.—Powdered iodine (2.8 g.) was suspended in a solution of tyrosine (2.0 g.) in glacial acetic acid (14.0 cc.) and 36 *N* hydrochloric acid (8.0 cc.). Thirty per cent. hydrogen peroxide solution was then added in small portions with shaking during five minutes until the iodine color had disappeared, the temperature of the reaction being maintained at 60–65°. Approximately 1.3 cc. of the hydrogen peroxide solution was required. The yellow solution was cooled and diluted successively with water (10 cc.), 0.880 *M* ammonia solution (9.0 cc.), and 10% sodium hydrogen sulfite solution (5 cc.). 0.880 *M* ammonia solution was then added dropwise until crystallization began. 3,5-Diiodotyrosine separated in flat, almost colorless needles. It was collected, washed with water and alcohol and air-dried, m.p. 198° (lit. 201° (cor.)[2a]) (3.4 g., 71%).

3-Iodo-5-nitrotyrosine.—Concentrated nitric acid (3.0 cc.) was added to a suspension of 3-nitrotyrosine (6.0 g.) and powdered iodine (3.4 g.) in 95% alcohol (45 cc.). Thirty per cent. hydrogen peroxide solution was then added in 0.5-cc. portions until the color of iodine had disappeared. 4.0 cc. of hydrogen peroxide solution was required and the heat of the reaction maintained the temperature at 45–50° throughout the addition. The reaction mixture was heated to 70° for five minutes, diluted with water (30 cc.) and treated with concentrated ammonia, added dropwise, until a heavy yellow solid separated. After standing at 0° for two hours, the solid was collected, washed with a small quantity of water and alcohol and heated under reflux with alcohol (30 cc.) for ten minutes. On cooling, the crystalline solid was collected. It was dissolved in hot dilute hydrochloric acid and precipitated with ammonia (5.6 g., 60%, m.p. 220°). For analysis the 3-iodo-5-nitrotyrosine was recrystallized from water and separated in golden-yellow needles, m.p. 224–226° dec. (lit. 225–226°).

Monoiodo-*o*-methyltyrosine.—Concentrated sulfuric acid (1.0 cc.) and finely powdered iodine (1.48 g.) were added to a suspension of *o*-methyltyrosine hydrogen sulfate[7] (3.40 g.) in alcohol (15 cc.). The reaction mixture was maintained at 50° and treated slowly with 30% hydrogen peroxide solution (1.4 cc.) during ten minutes. The temperature was raised to 65° for five minutes, the solution then was diluted with water (10 cc.) and adjusted to *p*H 7.5 with concentrated ammonia when crystallization of the product began. Ten per cent. aqueous sodium hydrogen sulfite (3.0 cc.) was added and the mixture was cooled. The white crystalline mass was collected, washed with alcohol, and air-dried (3.12 g., 84%, m.p. 220–221°). Recrystallized from water, the monoiodo-*o*-methyltyrosine separated in colorless needles, m.p. 222°.

Anal. Calcd. for $C_{10}H_{12}INO_3 \cdot {}^1/_2H_2O$: C, 36.3; H, 4.0; I, 38.5; N, 4.2. Found: C, 36.3; H, 4.0; I, 39.2; N, 4.4.

(6) All melting points are uncorrected.

(7) L. D. Behr and H. T. Clarke, THIS JOURNAL, **54**, 1630 (1932).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

The Chemistry of Nitroacetic Acid and its Esters. III. The Synthesis of Tryptamine from Ethyl-α-nitro-β-(3-indole)-propionate[1]

BY DOUGLAS A. LYTTLE AND DAVID I. WEISBLAT

RECEIVED JUNE 27, 1955

Ethyl α-nitro-β-(3-indole)-propionate (I) is a key intermediate in our synthesis of *dl*-tryptophan from ethyl nitroacetate[2a] or ethyl nitromalonate[2b] and

(1) D. I. Weisblat and D. A. Lyttle, U. S. Patent 2,616,896.

(2) (a) D. A. Lyttle and D. I. Weisblat, THIS JOURNAL, **69**, 2118 (1947); (b) **71**, 3079 (1949).