and ethylamine hydrochloride decomposed on distillation at 1 mm. pressure.

5-Dimethylaminomethylfurfuryl Alcohol.—The amine was prepared in 12% yield from furfuryl alcohol, formaldehyde and dimethylamine hydrochloride by the method described previously[1]; b. p. 110–111° (3 mm.), $n^{25}D$ 1.4968, d_{25} 1.07. Calcd. for $C_8H_{13}NO_2$: N, 9.0. Found: N, 9.1.

The compound was completely soluble in water. The hydrochloride crystallized as prisms from alcohol melting at 120–121°, and is hygroscopic. Calcd. for $C_8H_{14}NO_2Cl$: N, 7.3; Cl, 18.6. Found: N, 7.5; Cl, 18.6.

5-N-Morpholinomethylfurfuryl Alcohol.—This compound is a very viscous, light yellow oil that was prepared in 42% yield: b. p. 128–130° (1 mm.), $n^{30}D$ 1.5195; 134–135° (2 mm.), d_{30} 1.12. Calcd. for $C_{10}H_{15}NO_3$: N, 7.1. Found: N, 6.9.

This amine was also completely soluble in water. The hydrochloride crystallized as plates from alcohol that melted at 136–136.5°. Calcd. for $C_{10}H_{16}NO_3Cl$: N, 6.0; Cl, 15.2. Found: N, 5.9; Cl, 15.4. The salt is very deliquescent.

The author wishes to thank the Quaker Oats Co. for a generous supply of furfuryl alcohol and furoic acid.

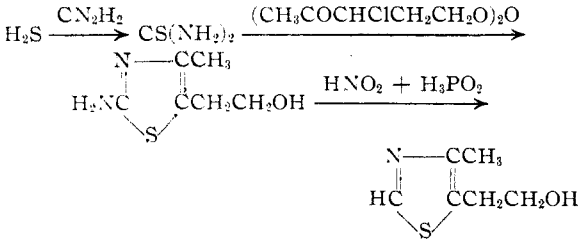
RICHARDSON CHEMISTRY LABORATORY
TULANE UNIVERSITY
NEW ORLEANS 15, LOUISIANA

RECEIVED NOVEMBER 18, 1946

The Reduction of 2-Amino-4-methyl-5-β-hydroxyethylthiazole in the Synthesis of Thiamin

BY J. B. HATCHER[1]

In the course of studies involving the use of thiamin labelled with radioactive sulfur[2] the low yields, as based on sulfur, of the usual synthesis resulted in samples of the vitamin very weak in radioactivity. It is felt desirable to record the preliminary work, discontinued at the beginning of the war, which indicated the feasibility of an alternative synthesis for the thiazole portion of the vitamin. The steps are



Experimental

The first step was not studied, but should offer no particular difficulties in obtaining high yields since there are no significant side reactions. The second step was found to give yields of 80% when an excess of the acetopropyl ether was slowly run into an aqueous solution of thiourea at 100°. The third step is essentially new, since the literature records an impressive list of failures with this type reaction with various amino thiazoles. However, the first trials of the reaction step above gave good yields, *e. g.*, 31%, as follows: 2 g. of the aminothiazole dihydrochloride was dissolved in about 15 ml. of 12 *N* hydrochloric acid in a 50-ml. Erlenmeyer flask and cooled to 0° by swirling in an ice-bath. An equivalent amount (4.1 ml.) of 2 *M* sodium nitrate solution was run in slowly drop by drop with vigorous shaking and swirling of the flask. Fifteen ml. of 30–32% H_3PO_2 was then added slowly, with the flask still in the ice-bath, and finally the mixture was allowed to warm to room temperature. It was then made alkaline with 6 *N* sodium hydroxide and diluted to about 1 liter, and extracted with five 10-ml. portions of ethyl ether. The ether extracts were combined, evaporated on a hot-plate to about 10 ml. and transferred to a distilling flask. The remainder of the ether was removed under vacuum at room temperature, and the residue vacuum distilled at 120–130° giving 0.38 g. of a colorless liquid. This liquid gave a picrate melting at 162° (uncor.) and the picrate gave no depression of the melting point when mixed with a sample of the picrate prepared from the pure thiamin thiazole prepared by the usual methods.

On the basis of these results it was concluded that the proposed synthesis would offer considerable advantages in the preparation of vitamin B_1 for the purposes, and that the removal of amino groups from thiazoles by diazotization and reduction is by no means as difficult as the literature indicates.

(1) Present address: The Argonne National Laboratory, Chicago, Illinois.

(2) Buchman, Hatcher, Yost, and McMillan, *Proc. Natl. Acad. Sci.*, **26**, 412 (1940).

PASADENA, CALIFORNIA RECEIVED AUGUST 7, 1946

2-Octyl Nitrite

BY NATHAN KORNBLUM AND EUGENE P. OLIVETO

In the course of another investigation it became necessary to know the refractive index, density, and boiling point of 2-octyl nitrite. Since the literature does not contain definitive values for these constants (*cf.* Table I) this compound was prepared by two different procedures, one involving the action of nitrosyl chloride on a pyridine solution of 2-octanol and the other the interaction of 2-octanol with sodium nitrite and sulfuric acid. The samples of 2-octyl nitrite thus obtained had $n^{20}D$ 1.4082 and 1.4083; d^{20}_4 0.8644 and 0.862, respectively, which values are distinctly different from those in the literature.[1–5] Upon analysis of these preparations the correct carbon, hydrogen and nitrogen values were found.

TABLE I

Compound, nitrite	B. p., °C. (mm.)	$n^{20}D$	Density		Ref.
dl-2-Octyl	165–166°	....	d^0	0.881	1
dl-2-Octyl	65 (15)	....	d_4^0	.879	2
l-2-Octyl	63–65 (15)	1.4202[a]	d^{18}_4	.861	3
l-2-Octyl	85–90 (18)	1.4218	d^{20}_{20}	.857	4
l-2-Octyl	70–75 (18)	1.4270	d^{20}_{20}	.852	5
d-2-Octyl	70–75 (18)	1.4270	d^{20}_{20}	.852	5
dl-2-Octyl	72–74 (18)	1.4272	d^{20}_{20}	.852	5
d-2-Octyl	86–90 (18)	1.4279	d^{20}_{20}	.852	4

[a] Taken at 18.5°.

The nitrite ester of 2-octanol decomposes on standing at room temperature, especially in the presence of light, and this may account for the discrepancies noted.[6]

(1) Bertoni, *Gazz. chim. ital.*, **16**, 521 (1886).

(2) Bouveault and Wahl, *Bull. soc. chim.*, (3) **29**, 959 (1903).

(3) Kenyon and Young, *J. Chem. Soc.*, 965 (1938).

(4) Shriner and Young, THIS JOURNAL, **53**, 3332 (1930).

(5) Pezold and Shriner, *ibid.*, **54**, 4707 (1932).

(6) The instability of nitrite esters has been noted previously; *cf.* Horswell and Silverman, *Ind. Eng. Chem., Anal. Ed.*, **13**, 555 (1941).

Experimental

(A) Preparation of 2-Octyl Nitrite by the Action of Nitrosyl Chloride on 2-Octanol.—In a 500-cc., 3-necked flask fitted with a Hershberg-type tantalum stirrer, thermometer, and a calcium chloride drying tube was placed 78.0 g. (0.60 mole) of 2-octanol $n^{20}D$ 1.4264 (prepared by the action of methylmagnesium iodide on *n*-heptanal) and 240 cc. of dry pyridine (freshly distilled from barium oxide). Over a period of two and one-half to three hours 60 g. (0.95 mole) of liquid nitrosyl chloride[7] was allowed to evaporate into the stirred alcohol–pyridine solution; during this time the temperature of the mixture was kept between 0 and 10°. As soon as all the nitrosyl chloride had been introduced 100 cc. of water and 100 cc. of petroleum ether (35–37°) were run in at such a rate that the temperature of the mixture did not rise above 20°. The petroleum ether phase was separated, washed once with dilute hydrochloric acid, once with water and then dried over potassium carbonate. The solvent was removed and the residue rectified under reduced pressure through an 18″ modified Widmer column[8] fitted with a total reflux head. There was obtained 76.1 g. (80%) of a pale yellow-green liquid: b. p. 60–61° (15 mm.); d^{20}_4 0.8644; $n^{20}D$ 1.4082; M_d (calcd.) 45.48[9], M_d (found) 45.44.

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.24; H, 10.70; N, 8.80. Found: C, 60.44, 60.42; H, 10.67, 10.67; N, 8.74.

(B) By the Action of Sodium Nitrite and Sulfuric Acid on 2-Octanol.—Sixty-five grams (0.50 mole) of 2-octanol, $n^{20}D$ 1.4260 (Eastman Kodak Co. White Label material purified through the acid phthalate ester[10]) was converted to the nitrite ester according to the procedure of Pezold and Shriner[6] with but slight modifications. These were: (a) the temperature of the reaction mixture was kept between 0–5° during the addition of sulfuric acid, (b) the crude ester was dried over potassium carbonate, and (c) the crude ester was vacuum fractionated through a modified Widmer column fitted with a total reflux head. There was obtained 47 g. (59%) of pale yellow-green liquid having b. p. 50–51° (9 mm.); d^{20}_4 0.862; $n^{20}D$ 1.4083; M_d (calcd.) 45.48,[9] M_d (found) 45.48. Calcd. for $C_8H_{17}NO_2$: N, 8.80. Found: N, 8.60.

(7) Nitrosyl chloride may be obtained in small tanks from the Solvay Process Co., Hopewell, Va.

(8) Smith and Adkins, THIS JOURNAL, **60**, 657 (1938).

(9) Values for the calculation of the molecular refractivity were taken from Leermakers and Weissberger in Gilman's "Organic Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751, and Cohen, "Organic Chemistry," Vol. II, p. 27, Edward Arnold and Co., London, 1928.

(10) Ingersoll, "Organic Reactions" (edited by Roger Adams), Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 400.

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA

RECEIVED SEPTEMBER 18, 1946

Measurement of the Cresolase Activity of Tyrosinase

BY M. FRANK MALLETTE[1] AND CHARLES R. DAWSON

As the result of experience with highly purified preparations of mushroom tyrosinase it has been found necessary to develop a new method for determining the enzyme's catecholase activity[2] and now to modify the manometric method of Nelson and co-workers[3,4] for measuring the monophenolase (cresolase) activity of the enzyme. The changes have been made necessary by the observation that the highly purified enzyme rapidly loses activity when allowed to stand in a highly diluted condition such as is necessary for the usual activity measurement. The enzyme is much more stable, however, in relatively concentrated solutions or solutions containing other protein matter.

It has been the practice of earlier workers in this and other laboratories to equilibrate the manometer flasks and contents in the 25° thermostat for about fifteen to twenty minutes prior to mixing the enzyme and *p*-cresol to initiate the enzymatic oxidation of the latter. Recently it has been observed, however, that the sooner the reaction is started after the enzyme has been diluted, the higher is the measured rate of oxygen uptake. In other words, inactivation of the highly diluted enzyme occurs during the temperature equilibration period.

The data of Table I show how the measured cresolase activity of a purified tyrosinase preparation depends on the length of time that the enzyme stands in the highly diluted condition prior to measurement. In practice it was found difficult to start the activity measurements in much less than three minutes after making the final enzyme dilution. The data shown in Table I were obtained using the highly purified high catecholase enzyme C175BI prepared from the common mushroom, *Psalliota campestris*, by procedures described elsewhere.[5] The stock solution contained 34 cresolase units per ml. as measured by the modified procedure given below.

TABLE I

THE EFFECT OF STANDING IN COLD DILUTE SOLUTION (0 TO 2°) ON THE MEASUREMENT OF THE CRESOLASE ACTIVITY OF THE HIGHLY PURIFIED TYROSINASE PREPARATION C175BI (DILUTION FACTOR = 21)

Time between dilution and addition to reaction mixture, min.	3	28	60	95
Oxygen uptake, cu. mm./min.	16.3 ± 0.2	12.2 ± 0.2	5.6 ± 0.3	1.4 ± 0.1
Measured cresolase units in flask	1.63	1.22	0.56	0.14
Activity of stock solution, units per ml.	34.2	25.6	11.8	2.9

To obtain the rate data shown in the table, the stock solution of enzyme was diluted with 20 volumes of ice-cold water and 1.00 ± 0.01 ml. aliquots were used. The time intervals recorded represent the minutes elapsed between the dilution of the stock enzyme solution and its addition to the reaction mixture. As can be seen from the table, a marked inactivation of highly purified enzyme may occur when it is allowed to stand in the highly diluted state for long periods of time

(1) Present address: Department of Chemistry, Cornell University, Ithaca, N. Y.

(2) W. H. Miller, M. F. Mallette, L. J. Roth and C. R. Dawson, THIS JOURNAL, **66**, 514 (1944).

(3) M. H. Adams and J. M. Nelson, *ibid.*, **60**, 2472 (1938).

(4) D. C. Gregg and J. M. Nelson, *ibid.*, **62**, 2500 (1940).

(5) M. F. Mallette, Stanley Lewis, Stanley R. Ames, Charles R. Dawson and J. M. Nelson, to be published.