

by the Sullivan method) by heating as a 10% solution in concd. sulfuric acid for 10 minutes at 180°. Only very slight browning of the heated sulfuric acid solution occurred.

Isolation of Lanthionine from Subtilin.—When 6 *N* HCl hydrolyzates of subtilin were fractionated with phosphotungstic acid under the conditions of Van Slyke, *et al.*,⁹ for optimum separation of the basic from the monoamino acids, the sulfur was about equally distributed between the precipitate (basic amino acids) and the filtrate (monoamino acids). Resuspension of the precipitate and chilling of the filtrate yielded phosphotungstic acid with a molar ratio for N:S of 2.3 with essentially all of the nitrogen in the amino form. After removal of the phosphotungstic acid several recrystallizations by solution in ammonium hydroxide and neutralization with acetic acid yielded a small amount of a substance tentatively identified as lanthionine by N analysis of it and its benzoyl derivative (m. p. 192–194°).

Subsequent isolations were made by the method of Horn, Jones and Ringel⁴ (without prior alkali treatment of the subtilin). From 10 g. of active subtilin 345 mg. of recrystallized lanthionine (accounted for 10% of the S) were isolated; another similar isolation from 10 g. of the peptide yielded 300 mg. of the three times crystallized lanthionine. A third isolation from 120 g. of subtilin samples of low bacteriostatic activity gave 2.2 g.

Anal. Calcd. for C₈H₁₂SN₂O₄: N, 13.46; S, 15.47; C, 34.6; H, 5.81. Found: N, 13.4; S, 15.3; C, 34.2; H, 5.85; $[\alpha]^{24}_D = 0 \pm 0.6^\circ$ (*c*, 10 in 2.4 *N* NaOH).

The dibenzoyl derivative was prepared, m. p. 193–195°, with slow decomposition and a preliminary melting and solidification at 100–115°. The m. p. of dibenzoyl-*meso*-lanthionine is variously reported at 205–206°,¹⁰ 210–211°¹¹ and 201°¹² without specification of a preliminary melting point of decomposition. The dibenzoyl derivatives of our *meso*-lanthionine preparations both from subtilin and from Na₂CO₃-treated hair by the method of Horn, Jones and Ringel⁴ (recrystallized several times from NaCN solution according to the method of Brown and du Vigneaud¹³ for elimination of disulfide) are lower than literature values, vary with the rate of heating, and exhibit two melting points as mentioned above. Repeated recrystallizations of either the dibenzoyl derivatives or the untreated lanthionine have not changed this behavior. In baths of constant temperature, melting time varies from 24 min. at 180° to 5 seconds at 210°. Quite reproducible m. p.'s may be obtained by inserting the capillary in a bath with a 6°/min. rise at 185–190° under which conditions the melting points of the dibenzoyl derivatives of lanthionine from subtilin and of *meso*-lanthionine from alkali-treated hair, singly or mixed are 198–200°.

Anal. Calcd. for C₂₀H₂₀O₆N₂S: N, 6.73. Found: N, 6.71.

The dicarbobenzoxy derivative was prepared, m. p. 139–140°; reported¹¹ 138–140°.

Anal. Calcd. for C₂₂H₂₄SN₂O₅: N, 5.88. Found: N, 5.84.

A mixed melting point with dicarbobenzoxy-*meso*-lanthionine (m. p. 140–140.5°) from alkali-treated hair was 140–140.5°.

Hydrogenolysis with Raney Nickel.—A solution of 280 mg. of dibenzoyl-*meso*-lanthionine from alkali-treated hair in 80% alcohol was refluxed with about 10 g. of Raney nickel (prepared by the method of Mozingo¹⁴ with a digestion period of 1 hour at 70°) by the method of Mozingo, *et al.*,⁵ the product (160 mg.) melted at 176–177°. Recrystallization by solution in *N* NaOH, filtration, and acidification with HCl gave 120 mg., m. p. 176–177°.

Anal. Calcd. for C₁₀H₁₇O₃N: C, 60.3; H, 8.54; N, 7.04. Found: C, 60.1; H, 8.54; N, 6.99.

This compound was identified as cyclohexanecarbonyl-*dl*-alanine (reported m. p. 171–171.5°¹⁵) by synthesis from cyclohexane carbonyl chloride and *dl*-alanine.

(9) Van Slyke, Hiller and Dillon, *J. Biol. Chem.*, **146**, 137 (1942).

(10) Horn, Jones and Ringel, *ibid.*, **138**, 141 (1941).

(11) du Vigneaud and Brown, *ibid.*, **138**, 151 (1941).

(12) Sakai, Tsurumi and Inukai, *Bull. inst. phys. chem. res.*, **22**, 694 (1943).

(13) Brown and du Vigneaud, *J. Biol. Chem.*, **140**, 767 (1941).

(14) *Org. Syntheses*, **21**, 15 (1941).

(15) Bernhard, *Z. physiol. Chem.*, **248**, 256 (1937).

The ethyl ester was prepared by refluxing in absolute ethanol containing 1% by volume of 11 *N* aq. HCl, m. p. 77–78°; reported 77–78°.¹⁶

Anal. Calcd. for C₁₂H₂₁O₃N: N, 6.17. Found: N, 6.08.

The same treatment of lanthionine from subtilin gave the same product in 60% yield, m. p. 176–177°.

Anal. Calcd. for C₁₀H₁₇O₃N: C, 60.3; H, 8.54; N, 7.04. Found: C, 60.4; H, 8.59; N, 7.00.

Refluxing benzoyl-*dl*-alanine with Raney nickel under similar conditions gave the same product in 71% yield.

X-Ray Powder Diagrams.—X-Ray powder diagrams of *meso*-lanthionine isolated from alkali-treated hair by the method of Horn, Jones and Ringel,⁴ *meso*-lanthionine from active subtilin, and *meso*-lanthionine from low-potency subtilin were all identical and differed from a powder diagram of *dl*-lanthionine from alkali-treated hair.

Acknowledgment.—We are indebted to K. J. Palmer for the X-ray photographs, and to L. M. White and co-workers for the elementary analyses.

(16) Freudenberg and Rhino, *Ber.*, **57**, 1554 (1924).

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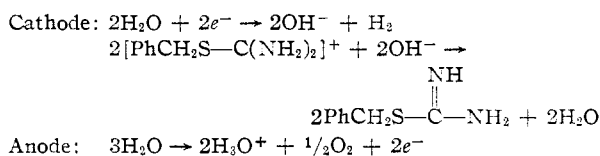
The Action of Direct Current on Aqueous Solutions of S-Benzyl- and S-1-Naphthylmethylthiuronium Chlorides

BY WILLIAM A. BONNER

While widely studied in other connections, the S-alkylthiuronium salts have never been electrolyzed. To gain information on this point, we have studied the effect of direct current on aqueous solutions of S-benzyl- and S-1-naphthylmethylthiuronium chlorides.

When a dilute aqueous solution of S-benzylthiuronium chloride is electrolyzed using platinum electrodes, hydrogen is evolved at the cathode and oxygen at the anode in a volume ratio 2:1. Further, the cathode becomes rapidly coated with a white solid characterized as S-benzylthiourea. The acidity which builds up during electrolysis prevents further deposition of S-benzylthiourea after a short period. An aqueous solution of S-1-naphthylmethylthiuronium chloride behaved similarly, S-1-naphthylmethylthiourea precipitating over the cathode.

Since it is well known¹ that alkali liberates the free base when acting on solutions of S-benzylthiuronium salts, it is reasonable to formulate our electrode processes as



In an analytically inadequate paper Bernthsen and Klinger² claim the preparation of S-benzylthiourea, m. p. 70–71°, by action of alkali on the hydrochloride. Werner¹ repeated this, reporting the base, unpurified but analyzing correctly, to melt at 88°. On recrystallization of the 88° product from ethanol-water mixtures, the 70–71°

(1) E. A. Werner, *J. Chem. Soc.*, **57**, 285 (1890).

(2) A. Bernthsen and H. Klinger, *Ber.*, **12**, 575 (1879).

product was obtained, but Werner failed to identify the latter. We have duplicated this work, finding the melting point of S-benzylthiourea as 94° on recrystallization from a mixture of benzene and petroleum ether. Several recrystallizations from dilute ethanol produced the 70–71° product, which we have characterized as benzyl disulfide.

Experimental Part

Electrolysis of Aqueous S-Aralkylthiuronium Chloride Solutions.—A 5–10% aqueous solution (25 ml.) of S-benzylthiuronium chloride was electrolyzed in a cell containing platinum electrodes (1 × 4 cm.) one centimeter apart. The initial current was 0.2–0.6 amp. at ca. 10 volts. At the outset, the cathode became covered with the fluffy product, trapping bubbles of hydrogen. The product could be removed by scraping the electrode or, better, by momentarily reversing the polarity. The maximum yield of product was 0.06–0.08 g. before its formation was stopped by the acidity produced simultaneously. The crude product had m. p. 92.5–93°. This was recrystallized from benzene and petroleum ether, decolorizing with Norit and keeping the temperature below 60°. The pure product had m. p. 94° dec., and showed no mixed m. p. depression and an identical absorption spectrum with the S-benzylthiourea below.

When the electrolyte solution was acidified prior to electrolysis, no cathode product was formed.

S-1-Naphthylmethylthiuronium chloride³ in 1% aqueous solution gave crude S-1-naphthylmethylthiourea, m. p. 100° dec., when treated as above. On Norit treatment and recrystallization from a mixture of benzene and petroleum ether the m. p. was raised to 107° dec., unchanged when admixed with the free base described below.

S-Aralkylthioureas.—Werner¹ recommends the addition of one equivalent of dilute alkali to an aqueous solution of S-benzylthiuronium chloride for preparing S-benzylthiourea. We have had better results by adding dropwise just sufficient 30% sodium hydroxide solution to a 5–10% solution of the salt to form a thick slurry. This is filtered, and the filtrate similarly treated, until no more solid is formed. The water-rinsed, air-dried product had m. p. 92.5° dec., and showed a mixed m. p. of 93° dec. with the corresponding electrolytically deposited product above.

One gram of S-1-naphthylmethylthiuronium chloride in water (75 ml.) was treated with 30% sodium hydroxide solution as before. The total yield of crude, dried product, m. p. 104–105° dec., was 0.72 g. (84%). On recrystallization as before the m. p. was 108° dec.

Anal. Calcd. for C₁₂H₁₂N₂S: N, 12.98; S, 14.80. Found: N, 13.27; S, 14.97.

On melting, S-benzylthiourea rapidly resolidifies and remelts at ca. 190°. When S-benzylthiourea was heated at 115° for 15 minutes, it partially melted and small amounts of ammonia were evolved. The residue, smelling strongly of benzyl mercaptan, was recrystallized twice, with Norit treatment, from a mixture of benzene and methanol. The sulfur-free product had m. p. 207.5–208° and showed no mixed m. p. depression with an authentic sample of dicyandiamide of m. p. 209°. These results accord with those of Bernthsen and Klinger,² reported with no supporting experimental data.

When S-benzylthiourea was recrystallized four times from dilute ethanol after the method of Werner,¹ the product consisted of splendid needles, m. p. 70–71°. These showed no mixed m. p. depression and an identical absorption spectrum with an authentic sample of benzyl disulfide, m. p. 70–71°, prepared by the convenient method of Märker.⁴

Electrode Gases.—A solution of S-benzylthiuronium chloride was electrolyzed as before while inverting a water-filled tube over the cathode; 5.0 ml. of gas resulted after 5 minutes. Exactly the same procedure was employed at the anode, 2.6 ml. of gas resulting in the same length of time. When these gases were mixed and an electric spark passed through them, explosion resulted. These quantities and results are in accord with the liberation of hydrogen and oxygen at the electrodes.

(3) W. A. Bonner, *THIS JOURNAL*, **70**, 3508 (1948).

(4) C. Märker, *Ann.*, **140**, 86 (1866).

Absorption Spectra.—The spectra in Fig. 1 were obtained with a Beckman model DU spectrophotometer, using 95% ethanol as solvent and making observations every 5 m μ .

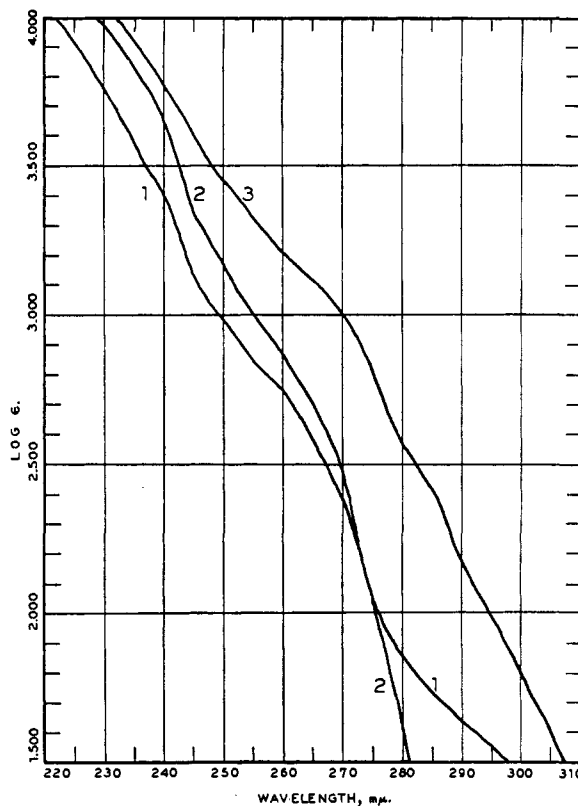


Fig. 1.—Absorption spectra: 1, S-benzylthiourea; 2, S-benzylthiuronium chloride; 3, benzyl disulfide.

STANFORD, CALIFORNIA

RECEIVED OCTOBER 2, 1950

The Exchange Reaction between Sulfur and Dibenzothiophene-5-dioxide

BY RAYMOND R. BROWN, SAM KIRKWOOD, LÉO MARION, STANLEY NALDRETT, ROBERT K. BROWN AND REUBEN B. SANDIN

Cullinane and Davies¹ have reported the conversion of dibenzothiophene-5-dioxide (I) to dibenzothiophene (II) by means of sulfur. The same reaction was carried out independently by Gilman and Jacoby² who obtained a 54% yield of recrystallized II from 5 g. (0.023 mole) of the sulfone and 0.9 g. (0.028 g. atom) of sulfur. This reaction is of considerable theoretical and preparative interest, and in view of this we have investigated the reaction between dibenzothiophene-5-dioxide and radiosulfur.

There are two possible reaction mechanisms: (1) sulfur removes oxygen atoms from the sulfone group, (2) sulfur displaces the sulfone group as sulfur dioxide. The relative stability of sulfones toward reducing agents makes the first reaction mechanism highly improbable. Moreover, it has been shown that when dibenzothiophene-5-dioxide is heated with tellurium the products are sulfur

(1) N. M. Cullinane and C. G. Davies, *Rec. trav. chim.*, **55**, 881 (1936).

(2) H. Gilman and A. L. Jacoby, *J. Org. Chem.*, **3**, 108 (1939).