tions from ethyl and methyl alcohols melted at 92.5–93°, and showed no depression with the same derivative of 2,2-dimethylpentanol-3. A mixed melting point with the 3,5-dinitrobenzoate of 4,4-dimethylpentanol-2 (m. p. 95–96°) was 87–90°. The α-naphthylurethan of both our heptanol and 2,2-dimethylpentanol-3 melted at 107–108°. *Anal.* Calcd. for $C_{18}H_{23}NO_2$: C, 75.8; H, 8.1. Found: C, 75.4; H, 8.3. The distillation residue was treated with phthalic anhydride and pyridine in an attempt to extract therefrom any primary alcohol formed by reverse addition, however without success.

While we admit that the boiling point of fraction 3 was quite close to that of 4,4-dimethylpentanol-2,[5] yet from this we were able to isolate and identify only a derivative of 2,2-dimethylpentanol-3 (b. p. 133°). The only reaction we can prove then is another example of the well-known rearrangement of these oxides, or their halohydrins to (in this case) propionaldehyde, and thus by normal addition to 2,2-dimethylpentanol-3. A rearrangement to acetone instead would give 1,1,2,2-tetramethylpropanol-1, b. p. 130°. Inasmuch as this tertiary alcohol forms a readily recognized hydrate during ether extractions, and since we observed no such hydrate formation, we believe this isomeric heptanol was not formed in this reaction to any extent.

No reverse addition[6] resulting in the formation of 2,3,3-trimethylbutanol-1 was observed. This carbinol, hitherto unreported, was prepared by first adding hydrogen bromide in the presence of ascaridole at −78° to 2,3,3-trimethylbutene-1,[7] and then converting the primary bromide to the Grignard reagent, and treating this with oxygen.[8] It boiled at 159.5–162° (761 mm), $n^{25}D$ 1.4288.

(5) Whitmore and Homeyer, THIS JOURNAL, **55**, 4194 (1933), reported 137–137.5° at 736 mm.

(6) Kharasch and Clapp, *J. Org. Chem.*, **3**, 355 (1938).

(7) The primary bromide was formed exclusively; compare Michael and Weiner, *ibid.*, **4**, 531 (1939).

(8) Thanks are due Mr. J. Calder, Honor Student of McGill University, 1940, for the preparation of this carbinol.

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The Preparation and Bioassay of Thiamine Hydriodide

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We have observed that certain pyrimidine-thiazole combinations, linked together by a methylene group as in thiamine, are split when dissolved in glacial acetic acid and treated with sodium. Thiamine hydrochloride, however, resists this cleavage; instead, both chlorine atoms are removed by the sodium, and the vitamin base itself can be extracted from the reaction mixture with ether or chloroform. On addition of hydriodic acid to the extract, thiamine iodide hydriodide is obtained. Inasmuch as this compound is not described in the literature, its antineuritic potency has been studied.

Experimental[1]

Thiamine Iodide Hydriodide.—To a solution of 0.125 g. of thiamine hydrochloride in 9 cc. of glacial acetic acid and 2–3 drops of water, kept under a reflux condenser, was gradually added 0.126 g. of sodium under stirring or shaking. The mixture, which still showed an acid reaction, was then evaporated under reduced pressure and the residue extracted with 15 cc. of dry chloroform (or ether) for one to two hours. To the extract a 57% aqueous solution of hydriodic acid was added dropwise with stirring. (Addition of hydrogen iodide in absolute alcohol solution delays somewhat the precipitation of the crystals, but a purer product is produced thereby.) The crystalline precipitate was purified by solution in boiling methanol and precipitation with dry ether. Light yellow crystals, m. p. 230–231° (decomp.), were obtained in 49% yield.

Anal. Calcd. for $C_{12}H_{18}ON_4I_2S$: C, 27.69; H, 3.46; N, 10.77; I, 48.85; S, 6.15. Found: C, 27.81; H, 3.54; N, 10.83; I, 48.60; S, 6.07.

Similar treatment of an ether extract of the reaction product with a 40% solution of hydrogen bromide yielded thiamine bromide hydrobromide, m. p. 218–221°. Andersag and Westphal[2] give 220°.

Anal. Calcd. for $C_{12}H_{18}ON_4Br_2S$: N, 13.37. Found: N, 13.11.

Bioassay.—The antineuritic activity of thiamine hydroiodide was tested on rats according to the method of Chase and Sherman.[3] The material was injected in aqueous solution in doses of 7.7 μg. and 5 μg. daily (double doses on Saturdays). The results obtained are summarized in Table I. For comparison the data obtained with corresponding doses (on a molar basis) of thiamine hydrochloride have been included.

TABLE I

BIOASSAY OF THIAMINE HYDRIODIDE AND THIAMINE HYDROCHLORIDE

Substance	Dose, μg.	No. of rats	Mean increase in weight in 25 days, g.
Thiamine hydriodide	5	5	34
Thiamine hydrochloride	3.2	2	38
Thiamine hydriodide	7.7	5	45
Thiamine hydrochloride	5	5	39

The data show that on a molar basis the antineuritic potency of thiamine hydriodide is at least as high as that of thiamine hydrochloride.

(1) Microanalyses by Mr. Joseph Alicino of this Laboratory.

(2) Andersag and Westphal, *Ber.*, **70**, 2035 (1937).

(3) Chase and Sherman, THIS JOURNAL, **53**, 3506 (1931).

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