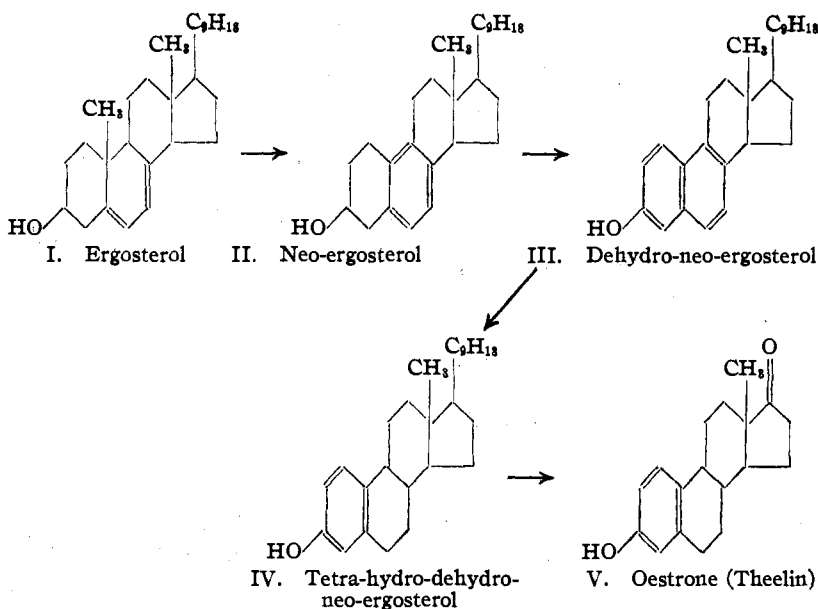


and Chakravarty, *Ber.*, **67**, 2021 (1934)] which is also obtainable from dihydro-cholesterol. This acid can give rise to isoandrosterone which differs from androsterone only in configuration of the hydroxyl group in the 3-position. Therefore, with the preparation of oestrone from ergosterol, a complete connection between the hormones, male and female, has been established.



In the present work, dehydro-neo-ergosterol, III, was prepared from ergosterol by the method of Windaus [Windaus and Borgeaud, *Ann.*, **520**, 235, 460 (1928)], Inhoffen [Inhoffen, *ibid.*, **497**, 130 (1932)], and Honigmann [Honigmann, *ibid.*, **511**, 292 (1934)]. Taking advantage of the fact that naphthalene derivatives may be reduced to tetrahydro derivatives with sodium and amyl alcohol, dehydro-neo-ergosterol, III, m. p. 147–150°, was reduced to give tetrahydro-dehydro-neo-ergosterol, IV, m. p. 170.5–171.5°. This substance is phenolic and forms sodium salts.

Anal. Calcd. for $C_{27}H_{41}O$: C, 85.1; H, 10.8. Found: C, 85.7; H, 10.8.

The tetrahydro-dehydro-neo-ergosterol was then acetylated and this product oxidized with chromic acid. The total neutral oxidation product was hydrolyzed with alcoholic sodium hydroxide and then treated with semicarbazide acetate. The crude semicarbazone was hydrolyzed with alcoholic sulfuric acid to the free ketone, which was then distilled at 200° under high vacuum. The sublimate was crystallized from

95% alcohol to give a white crystalline compound m. p. 259–261.5° (uncorr.). This gave no depression in melting point with a sample of natural oestrone of m. p. 255°. It is soluble in alkali. It gave a rotation of $[\alpha]^{25}_D +159^\circ$ in alcohol, $c = 514$ mg. per 100 cc.

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.9; H, 8.3. Found: C, 79.4; H, 8.4.

The product gave a benzoate by the Schotten-Baumann reaction, m. p. 205–207° (uncorr.), which gave no depression to a sample of natural oestrone benzoate m. p. 205° (uncorr.).

Anal. Calcd. for $C_{25}H_{26}O_3$: C, 80.2; H, 7.0. Found: C, 80.6; H, 7.2.

It gave a semicarbazone of m. p. 252–253° (uncorr.). From the analysis this semicarbazone calculates to have one-half molecule of water of crystallization. Butenandt [*Z. physiol. Chem.*, **208**, 129 (1932); **208**, 149 (1932)] observed the same thing on the preparation of the semi-

carbazone from natural oestrone.

Anal. Calcd. for $(C_{19}H_{25}O_2N_3)_2 \cdot H_2O$: C, 67.9; H, 7.9. Found: C, 68.1; H, 8.2.

This synthesis was repeated independently by two of us. We wish to thank Dr. George H. Fleming of this Laboratory for the micro-analyses reported in this paper.

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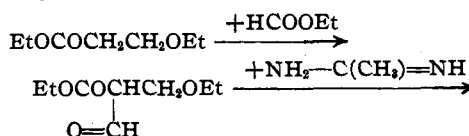
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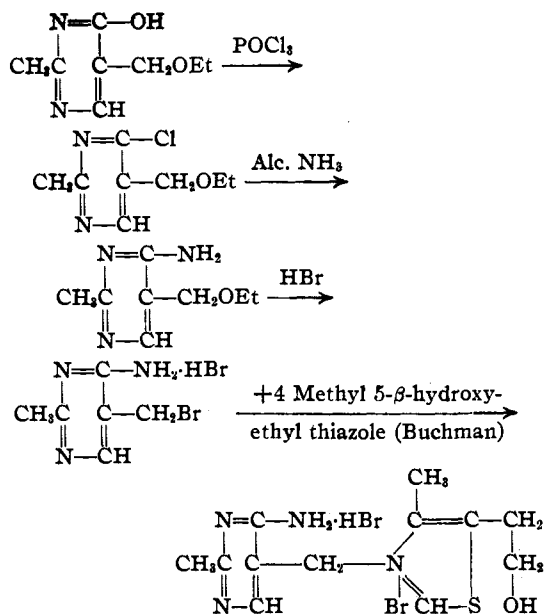
RECEIVED JULY 20, 1936

SYNTHESIS OF VITAMIN B₁

Sir:

As foreshadowed in a recent communication [THIS JOURNAL, **58**, 1063 (1936)] we have effected a synthesis of the vitamin by the following route.





The resulting bromide agreed in molecular absorption with the natural vitamin and when air dried analyzed for the composition $\text{C}_{12}\text{H}_{17}\text{N}_4\text{SOBr} \cdot \text{HBr} \cdot \frac{1}{2}\text{H}_2\text{O}$. The curative dose for polyneuritic rats is $6 \gamma \approx 1 \gamma$.

Converted into the chloride, it was found identical with the natural in composition (5 elements) ultraviolet absorption and antineuritic potency (5γ). Comparing melting points led us to observe two crystal forms in varying proportions in the natural chloride and especially in the picrolonate; the synthetic chloride and picrolonate respectively correspond in appearance to one of these forms. The synthetic chloride melts at $232-234^\circ$; our present specimen of natural at 246° ; mixed melting point is $242-244^\circ$. Kinnersley, O'Brien and Peters have called attention to a variably low

melting antineuritic chloride [*Biochem. J.*, **27**, 232 (1933)] and it seems probable that the natural as isolated is often a mixture of two stereoisomers [*cis-trans* on 5 C of pyrimidine? Nishikawa, *T. Mem. Ryojun Coll. Eng.*, **3**, 277 (1931)] of equal potency and that in our synthetic material the low form predominates in higher degree.

The details of structural evidence and of the method of synthesis will appear in forthcoming papers.

In making this announcement the writers wish to express their indebtedness to all those who have participated in the work and whose names have appeared in the authorship of the current series of papers "Studies of Crystalline Vitamin B₁." Mention should also be made of Mr. Jacob Finkelstein, who has performed many syntheses of both known and new compounds.

The senior author is grateful to Dr. E. R. Buchman, who continued to participate in the work when financial support was lacking during the greater part of 1935 and to Mr. R. E. Waterman who joined the writer in meeting this emergency. Through the kindness of Dr. Walter H. Eddy, laboratory space was provided at Teachers College during this as well as earlier phases of the undertaking. More recently funds and facilities have been provided by Merck & Co., Inc., under the auspices of the Research Corporation of New York. Grateful acknowledgment is made to Dr. Eddy and to both of these corporations.

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