Then, with continuous stirring, the solution was heated at 150° for two hours. The solution became dark red; and on cooling, a tan solid was formed and no liquid remained. This solid is soluble in water and insoluble in ether or benzene. Recrystallization from ethylene dichloride gave a white solid, m.p. 88°, yield 96%.

Anal. Calcd. for $C_{16}H_{32}N_2O_4$: C, 60.7; H, 10.1; N, 8.8; mol wt., 316. Found: C, 60.2; H, 9.8; N, 9.2; mol. wt. (by Rast method), 323.

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Phenyl-N-(1-carboxyethyl)-nitrone[1]

Hantzsch and Wild's synthesis[2] of phenyl-N-(carboxymethyl)-nitrone involved the condensation of β-benzaldoxime and chloroacetic acid. In the present work 2-bromopropionic acid was substituted for chloroacetic acid to form phenyl-N-(1-carboxyethyl)-nitrone,

$$C_6H_5CH{=}N(O){-}CH(CH_3){-}COOH$$

To an aqueous solution of 5.6 g. of potassium hydroxide was added dropwise 2-bromopropionic acid to the discharge of phenolphthalein pink (8.8 ml. of acid). This solution was added to a mixture of 12.1 g. of β-benzaldoxime and 500 ml. of water in which was dissolved 5.6 g. of potassium hydroxide. The mixture was stirred at 100° until homogeneous, then was left on the steam-bath for 13 hours. When cool, it was acidified with hydrochloric acid. The white precipitate which formed was collected and washed with ether, in which it was insoluble. The aqueous filtrate was stored overnight at −10° and a further precipitation occurred. The combined precipitates weighed 3.3 g. After two recrystallizations from methanol, the product decomposed at temperatures varying with the rate of heating: rapid heating gave a decomposition temperature of 167–170°, while an attempt to dry the nitrone in an oven at 115° resulted in decomposition, accompanied by the odor of benzaldehyde.

Anal. (by V. Hobbs and J. Sorenson). Calcd. for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.75; N, 7.25. Found: C, 62.36; H, 5.63; N, 7.37.

The product was acidic. It did not reduce Fehling solution in the cold but did reduce it on brief heating. After heating the product with mineral acid, the cold reaction mixture reduced Fehling solution.

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RECEIVED DECEMBER 4, 1950

(1) Investigation supported by a research grant from Swift and Company.

(2) A. Hantzsch and W. Wild, *Ann.*, **289**, 290, 305 (1896).

Derivatives of β-Hydroxypropyl Sulfides

N,N′-Bis-(2-hydroxy-3-methylthiopropyl)-1,2-diaminoethane.—A mixture of 14.5 g. of 69% 1,2-ethanediamine hydrate and 27.2 g. of 1-methylthio-2,3-epoxypropane was heated on a steam-bath to initiate reaction. After the reaction subsided, the mixture was refluxed for one hour. Liquid impurities were removed from the cooled, solidified reaction product by pressing between clay plates. The resulting material was recrystallized from ethyl acetate to give a white crystalline solid melting at 122–123°; yield 21% based upon the starting diamine.

Anal. Calcd. for $C_{10}H_{24}N_2O_2S_2$: N, 10.43. Found: N, 10.23.

N,N′-Bis-(2-hydroxy-3-ethylthiopropyl)-1,2-diaminoethane.—This white crystalline compound, prepared by the above method, melts at 118–119°; yield 22% based upon the starting diamine.

Anal. Calcd. for $C_{12}H_{28}N_2O_2S_2$: N, 9.44. Found: N, 9.29.

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COMMUNICATIONS TO THE EDITOR

THE REARRANGEMENT OF EPINOCHROME[1]

Sir:

We have reported the synthesis and isolation of crystalline epinochrome,[2] a dark-red crystalline compound of m.p. 78° by oxidative cyclization of epinine hydrochloride. This reaction is analogous to the oxidation of 3,4-dihydroxyphenylalanine to the "red pigment" in Raper's scheme of melanin formation. We now wish to report the spontaneous and the catalytic rearrangement of this crystalline compound into the colorless 5,6-dihydroxy-N-methylindole, an intramolecular oxidation–reduction which parallels the step in melanin formation where the "red pigment" is decolorized.

We have observed that this rearrangement takes place (A) spontaneously on standing of pure epinochrome at room temperature *in vacuo* in a sealed tube for several months when it has turned into a grayish white powder which essentially consists of 5,6-dihydro-N-methylindole; (B) on shaking the solution of epinochrome in water or in absolute methanol with palladium on charcoal in the presence of hydrogen or even in an atmosphere of pure nitrogen, when the solution becomes decolorized within a few minutes without the uptake of hydrogen. From the colorless solution more than 80% of the theoretical amount of 5,6-dihydroxy-N-methylindole m.p. 133° (reported 136°)[3] is isolated. *Anal.* Calcd. for $C_9H_9O_2N$: C, 66.12; H, 5.55; N, 8.57. Found: C, 66.41; H, 5.68; N, 8.85. Under the same conditions 2-carbethoxyepinochrome was decolorized without the uptake of hydrogen and with development of carbon dioxide.

The rearrangement of adrenochrome to 3,5,6-trihydroxy-*N*-methylindole ("adrenolutine")[4] bears a formal relationship to the rearrangement of

(1) This work was supported by the Life Insurance Medical Research Fund.

(2) Sobotka and Austin, THIS JOURNAL, **73**, in press (1951).

(3) Harley-Mason, *J. Chem. Soc.*, 1276 (1950).

(4) Lund, *Acta Pharm. et Tox.*, **5**, suppl. 1, 75, 121 (1949).

epinochrome; however, adrenochrome under non-reductive conditions as described above remains unchanged.

5,6-Dihydroxy-N-methylindole was first obtained by Duliere and Raper[5] by intramolecular oxidation-reduction in the presence of sulfur dioxide of the red solution of enzymatically oxidized N-methyltyrosine (or from a red solution resulting from oxidation of epinine with silver oxide). They isolated it as the dimethyl ether which was subsequently identified by Burton[6] who had observed the same rearrangement in the presence of alkali and who also prepared the diacetate. 5,6-Dihydroxy-N-methylindole itself was first isolated by partial reduction of adrenochrome,[3] after Bergel and Morrison[7] had demonstrated its formation by reduction of iodoadrenochrome, but isolated its diacetate only.

In a communication that has just come to our attention, Harley-Mason and Bu'Lock[8] report that zinc ion catalyses the decolorization of the red solution from the oxidation of epinine or of its carboxy derivative. Our observations on the spontaneous rearrangement of pure epinochrome in the solid state and on the catalytic rearrangement of its solutions over palladium emphasize the facility with which this oxidation–reduction occurs under a variety of conditions.

(5) Duliere and Raper, *Biochem. J.*, **24**, 239 (1930).
(6) Burton, *J. Chem. Soc.*, 546 (1932).
(7) Bergel and Morrison, *ibid.*, 48 (1943).
(8) Harley-Mason and Bu'Lock, *Nature*, **166**, 1036 (1950).

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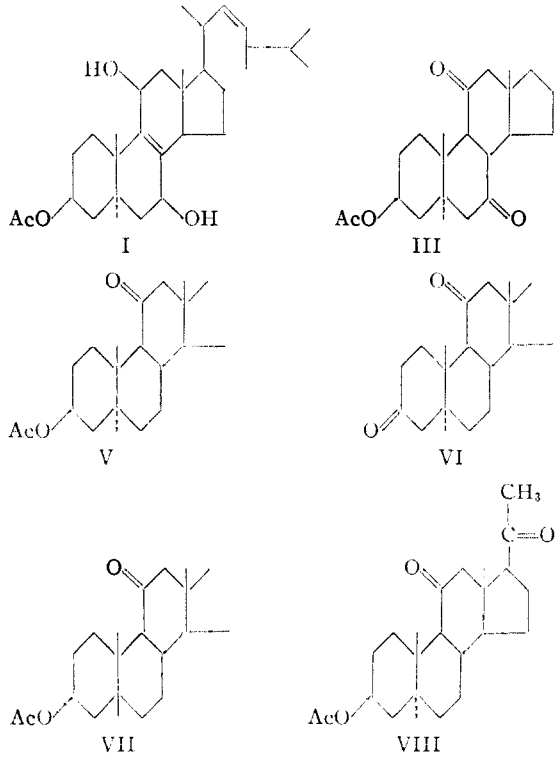
RECEIVED JANUARY 16, 1951

SYNTHESIS OF 11-KETO STEROIDS

Sir:

We wish to report a practical and general scheme for the synthesis of 11-keto steroids from $\Delta^{5,6}$ steroids, devoid of functional groups in ring C, which has been successfully applied to ergosterol, stigmasterol, diosgenin and to certain of their degradation products.

Starting with ergosterol acetate, the derived known $\Delta^{7,9(11),22}$ ergostatrien-3β-ol acetate (ergosteryl-D-acetate)[1] is treated with one equivalent of perbenzoic acid to give a crystalline epoxide; m.p. 202–205°; α_D −35° ($CHCl_3$); found: C, 79.01; H, 10.50. Hydrolytic rearrangement of the epoxide yielded $\Delta^{8,22}$-ergostadien-3β,7,11-triol 3-acetate (I) m.p. 248–252°; α_D +85° ($CHCl_3$); found: C, 76.04; H, 10.24; active hydrogens (Zerewitinoff determination) 2.1. Chromic acid oxidation of the triol monoacetate afforded $\Delta^{8,22}$-ergostadien-3β-ol-7,11-dione acetate, II; m.p. 135–136°; α_D +18.5° ($CHCl_3$); $\lambda_{max.}$ 266 mμ, E_m 9360 (isoöctane); $\lambda_{max.}$ 270 mμ, E_m 8700 (alcohol); found: C, 76.91; H, 9.58. The dienedione on reduction with zinc and acetic acid was converted into Δ^{22}-ergostene-3β-ol-7,11-dione (III); m.p. 197–200°; α_D −30° ($CHCl_3$); found: C, 76.68; H, 7.59. Modified Wolff–Kishner reduction[2] of the latter provided a monoketone, Δ^{22}-ergostene-3β-ol-11-one (IV); m.p. 173–174°; α_D +26.6° ($CHCl_3$); found: C, 81.72; H, 11.29. Ozonolysis of the acetylated ketoergostene, and esterification of the acidic side chain degradation product yielded an ester which proved to be methyl 3β-hydroxy-11-keto-bisnor*allo*cholanate acetate (V); m.p. 191–194°; α_D +24° ($CHCl_3$); found: 71.89; H, 9.15. The structure of the degradation product was unequivocally established by relating it to methyl 3,11-diketo-bisnor*allo*cholanate (VI) (m.p. 201–204°; α_D +63°; found: C, 74.18; H, 9.20) prepared by an independent synthesis from the known methyl 3-acetoxy-11-keto-bisnorcholanate (VII).[3]



Methyl Δ^5-3-hydroxy-bisnorcholenate acetate, obtained from either stigmasterol or cholesterol, was converted into methyl $\Delta^{5,7}$-3-hydroxybisnorcholadienate acetate[4] which was transformed into methyl 3-hydroxy-7,11-diketo-bisnor*allo*cholanate acetate (m.p. 228,–230°; α_D − 16° ($CHCl_3$); found: C, 69.30; H, 8.46) in the manner described for the ergosterol series. Wolff–Kishner reduction of the latter and subsequent esterification of the reduction product afforded V identical with that prepared from ergosterol.

Diosgenin acetate was converted to the Δ^7-dehydrodiosgenin acetate[5] which by the same sequence

(1) Windaus and Brunken, *Ann.*, **460**, 225 (1928); Heilbron and Sexton, *J. Chem. Soc.*, 921 (1929); Windaus and Luttringhaus, *Ann.*, **481**, 119 (1930); Heilbron, Johnstone and Spring, *J. Chem. Soc.*, 2248 (1929).

(2) Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).
(3) Sarett, *J. Biol. Chem.*, **162**, 601 (1946).
(4) Prepared previously by Bergmann and Stevens, *J. Org. Chem.*, **13**, 10 (1948).
(5) Since completion of this work, the preparation of this compound was reported by Rosenkranz, Romo and Berlin, *J. Org. Chem.*, **16**, 290 (1951). The physical constants of the two products are essentially the same.