steam-bath for five days with thiourea (76 g.). After removal of the excess of alcohol under diminished pressure the residue was then dissolved in 800 cc. of water and chlorination applied below 10° as described for ethyl sulfonyl chloride. The yield was 117–130 g.

Benzyl Sulfonyl Chloride.[2]—Thiourea (76 g.), benzyl chloride (126 g.) and alcohol (150 cc.) were heated under reflux on a steam-bath for thirty minutes. The vigorous reaction was controlled by cooling in water. Water (1 liter) was added and the solution chlorinated as described for ethyl sulfonyl chloride. The solid product was filtered off in several portions during the chlorination. The yield was 155 g., m. p. 90–92°. This was recrystallized from benzene, m. p. 91–92°.

Summary

1. The utilization of thiourea as a key reagent for the preparation of sulfonyl chloride has been extended.

2. The preparation of three sulfonyl chlorides on a laboratory scale is described.

3. The branching of the alkyl group in the alkyl isothiourea salts favors the elimination of sulfur as sulfate, thereby limiting the yield of sulfonyl chloride obtainable.

4. No sulfonyl chloride was obtained on chlorination of *t*-butyl isothiourea hydrochloride, the sulfur being oxidized to sulfate.

5. S-Cyclohexyl and S-*t*-butyl isothiourea hydrohalide were prepared by a modified procedure.

NEW HAVEN, CONN. RECEIVED JULY 1, 1937

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE AND THE PARKE, DAVIS & CO. RESEARCH LABORATORIES]

Sterols. XIX. *epi*-Ergosterol and *epi*-α-Ergostenol

BY RUSSELL E. MARKER, OLIVER KAMM, JOSEPH F. LAUCIUS AND THOMAS S. OAKWOOD

Due to the fact that lumisterol, an irradiation product of ergosterol, failed to precipitate digitonin, it was considered that lumisterol might be *epi*-ergosterol and that the primary action of irradiation on ergosterol was therefore an inversion of the configuration of carbon atom 3. Dimroth[1] on the contrary has suggested that irradiation resulted in the inversion of the methyl group on carbon atom 10, which change would prevent digitonin precipitation. From dehydration studies of lumisterol and ergosterol, Heilbron, Spring and Stewart[2] considered that Dimroth's postulation was correct, but recent studies on the dehydration of *epi*-cholesterol and cholesterol,[3] in which different hydrocarbons were obtained, seem to cast doubt upon the validity of Heilbron's inference.

We have prepared *epi*-ergosterol by the reduction of ergostatrienone[4] with aluminum isopropylate and separation of the resulting ergosterol from *epi*-ergosterol by means of digitonin. That there is no shift in the double bonds in the preparation of ergostatrienone by the aluminum *t*-butylate oxidation of ergosterol is shown by the fact that upon reduction with aluminum isopropylate, ergosterol is recovered from the insoluble digitonide.

epi-α-Ergostenol was prepared in the same manner by the aluminum isopropylate reduction of α-ergostenone, giving α-ergostenol and *epi*-α-ergostenol which were separated by means of their digitonides.

A comparison of the properties of *epi*-ergosterol, as prepared by us, with those reported for lumisterol shows conclusively that the two compounds are dissimilar. Appended is a list of compounds derived from ergosterol with their properties.

TABLE I

	Melting point, °C.	$(\alpha)_D$	Acetates melting point, °C.	$(\alpha)_D$
Ergosterol	163	−133	172	−87.4
epi-Ergosterol	152	+ 50	126	
α-Ergostenol	131	+ 17.8	111	+ 5.1
epi-α-Ergostenol	188.5	+ 5.3	119.5	
α-Ergostanol	184	− 20	166	− 7.5
epi-α-Ergostanol	207	+ 13.5		
Lumisterol	118	+191.5	100	+130.5

Experimental

***epi*-Ergosterol.**—Ergostatrienone was prepared by the aluminum *t*-butylate oxidation of ergosterol according to the method of Oppenauer.[4]

A mixture of 10 g. of ergostatrienone (m. p. 132°) and 4.5 g. of aluminum isopropylate in 60 cc. of dry isopropyl alcohol was heated for four hours at reflux and then 45 cc. of solvent was distilled slowly during an additional four hours. To the residue, a hot solution of 5 g. of potassium hydroxide in 75 cc. of methyl alcohol was added and the mixture allowed to stand for thirty minutes. The solution was poured into 250 cc. of water and the precipitate filtered

(1) Dimroth, *Ber.*, **69**, 1123 (1936).

(2) Heilbron, Spring and Stewart, *J. Chem. Soc.*, 1221 (1935).

(3) H. E. Staveley and Werner Bergmann, *J. Org. Chem.*, **1**, 575 (1937).

(4) Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937).

and dissolved in ether. After distilling the ether, the residue was crystallized twice from acetone, dissolved in 200 cc. of alcohol and treated with 25 g. of digitonin in 800 cc. of boiling alcohol. After standing overnight at room temperature, the precipitated digitonide was filtered and washed with alcohol. The filtrate was evaporated and the residue was extracted well with ether and filtered. The ether was distilled and the residue of *epi*-ergosterol was crystallized from acetone: m. p. 152°; $[\alpha]^{25}D$ +50°, in chloroform.

Anal. Calcd. for $C_{28}H_{44}O$: C, 84.8; H, 11.2. Found: C, 84.4; H, 11.3.

A mixture of 15 g. of the digitonide and 150 cc. of dry pyridine was heated for five minutes over a steam-bath and then poured into 400 cc. of ether. The precipitate was filtered and the ergosterol was crystallized from alcohol, m. p. 160°. A mixture with an authentic sample of ergosterol gave no depression in melting point. A mixture of ergosterol acetate with the acetate of the above reduction product also showed no depression in melting point.

***epi*-Ergosterol Acetate.**—This was prepared by refluxing a mixture of *epi*-ergosterol and acetic anhydride for fifteen minutes. The excess acetic anhydride was removed by distillation and the residue was crystallized from alcohol, m. p. 126°.

Anal. Calcd. for $C_{30}H_{46}O_2$: C, 82.1; H, 10.6. Found: C, 82.0; H, 10.6.

***epi*-α-Ergostenol.**—A mixture of 5 g. of α-ergostenol of m. p. 131° and 7.5 g. of copper powder was heated at 250° under 4 mm. pressure. The product was then distilled at a slightly higher temperature. The distillate was crystallized from ether–methyl alcohol mixture to give a product melting at 127°, yield 4 g. This was α-ergostenone.

A mixture of 8.6 g. of α-ergostenone, 3.9 g. of aluminum isopropylate and 70 cc. of dry isopropyl alcohol was refluxed for four hours, then 45 cc. of solvent was distilled slowly over a period of four hours. The residue was hydrolyzed with potassium hydroxide, and the solid was filtered. The residue was dissolved in 250 cc. of alcohol and heated to boiling with 25 g. of digitonin in one liter of alcohol. It was allowed to stand at room temperature overnight, then the insoluble digitonide was filtered. The filtrate was distilled and the residue was extracted with ether. After evaporation of the ether, the residue was crystalized from ethyl alcohol, m. p. 188.5°, $[\alpha]^{25}D$ +5.3° in chloroform.

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.9; H, 12.1. Found: C, 84.2; H, 11.9.

The insoluble digitonide was decomposed as described previously, giving α-ergostenol, m. p. 129°. This gave no depression in melting point when mixed with authentic α-ergostenol of m. p. 131°.

***epi*-α-Ergostenol Acetate.**—This was prepared by refluxing *epi*-α-ergostenol with an excess of acetic anhydride. After evaporation of the excess of acetic anhydride, the residue was crystallized from ethyl alcohol, m. p. 119.5°.

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.4; H, 11.3. Found: C, 81.7; H, 11.3.

Summary

epi-Ergosterol and *epi*-α-ergostenol were prepared by the aluminum isopropylate reduction of the corresponding ketones. The physical properties of *epi*-ergosterol differ greatly from those of lumisterol.

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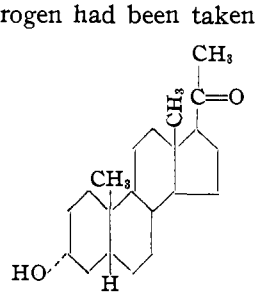
Sterols. XX. The Pregnanolones

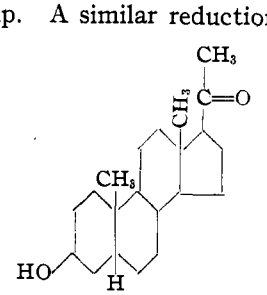
BY RUSSELL E. MARKER, OLIVER KAMM AND EUGENE L. WITTLE

Previously the isolation of *epi-allo*-pregnanol-3-one-20[1] and *epi*-pregnanol-3-one-20[2] from human pregnancy urine was reported from these Laboratories. The present work describes satisfactory methods of preparing *epi*-pregnanol-3-one-20 (I) and its isomer pregnanol-3-one-20 from pregnandiol and pregnandione.

Kawai[3] has shown that the rate of reduction of the ketonic groups in 3,7,12-triketocholanic acid is in the order $C_3 > C_7 > C_{12}$. An investigation of the partial hydrogenation of pregnandione showed that the 3-keto group may be reduced exclusively. The catalytic reduction of pregnandione in alcoholic solution produced good yields of *epi*-pregnanol-3-one-20, if the hydrogenation was interrupted when the calculated amount of hydrogen had been taken up. A similar reduction



epi-Pregnanol-3-one-20



Pregnanol-3-one-20

(1) Marker, Kamm and McGrew, THIS JOURNAL, **59**, 616 (1937).
(2) Marker and Kamm, *ibid.*, **59**, 1373 (1937).
(3) Kawai, *Z. physiol. Chem.*, **214**, 71 (1933).