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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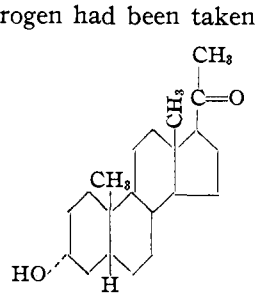
Sterols. XX. The Pregnanolones

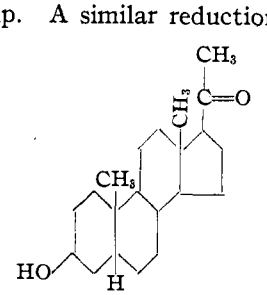
BY RUSSELL E. MARKER, OLIVER KAMM AND EUGENE L. WITTLE

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).

carried out in acid solution gave mainly pregnanol-3-one-20, which precipitated digitonin and which differed from the epimeric form only in the configuration of the hydroxyl group at C_3.

The partial hydrogenation of androstandione in acid solution gave androsterone as the main product.

It has been shown previously that under controlled conditions the 3-acetoxy group of pregnandiol diacetate may be hydrolyzed to the exclusion of the 20-acetoxy group.[4] Conversely, we have acetylated pregnandiol, using a limited amount of acetic anhydride. Oxidation of the partially acetylated product gave an excellent yield of *epi*-pregnanol-3-one-20. The same procedure gave good yields of *epi-allo*-pregnanolone when applied to *allo*-pregnandiol.[5] The purification of all the hydroxy ketones was accomplished by treatment of the crude reaction product with Girard's reagent to separate ketonic constituents, followed by the preparation of the half succinic ester of the ketonic material. The half ester was extracted with sodium carbonate solution and the alkaline extract was hydrolyzed to give a fraction which consisted of hydroxy ketones. Digitonin was used to separate small amounts of isomeric compounds or to isolate the main reaction product. In this connection, neither natural pregnandiol nor *allo*-pregnandiol precipitates with digitonin, showing that both compounds have *epi*-OH groups.

When the pregnanolones were prepared from pregnandiol and *allo*-pregnandiol, we obtained slightly higher melting points than those reported previously for the naturally occurring products. We have repurified larger amounts of the natural compounds than were previously available and find them in agreement with the compounds artificially made from the pregnandiols, namely, *epi-allo*-pregnanolone, m. p. 176°, and *epi*-pregnanolone, 149°.

Experimental

***epi*-Pregnanol-3-one-20 from Pregnandione.**—To a solution of 5 g. of pregnandione (m. p. 120°) in 200 cc. of alcohol was added 500 mg. of platinum oxide catalyst. The product was shaken with hydrogen under a pressure of 45 pounds (3 atm.) for ten minutes. The catalyst was filtered and the alcohol was evaporated to 100 cc. To this was added 5 g. of Girard's reagent. The solution was warmed for fifteen minutes, cooled and diluted with water. The solution was extracted with ether. The aqueous layer was acidified and warmed on a steam-bath. The total ketones were extracted with ether and the ether was evaporated. The residue was warmed for thirty minutes with 10 cc. of pyridine and 5 g. of succinic anhydride. This was diluted with ether and the ether solution was freed of pyridine by shaking with dilute hydrochloric acid. The ether solution was then shaken with sodium carbonate solution. The alkaline aqueous layer was heated on a steam-bath with potassium hydroxide solution. The keto sterol derivatives were extracted with ether and a small amount of regular pregnanolone separated from the *epi*-form by means of digitonin precipitation. The filtrate from the digitonide was evaporated to dryness and extracted with ether. The residue after evaporation of the ether was crystallized from alcohol-water to a constant melting point of 149°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.4; H, 10.8.

***epi*-Pregnanol-3-one-20 from Pregnandiol (Natural).**—A solution of 5 g. of pregnandiol of m. p. 242° in 50 cc. of acetic acid containing 4 cc. of acetic anhydride was refluxed for three hours. The solution was cooled to room temperature and 1 g. of chromic oxide in 10 cc. of 90% acetic acid was added. The solution was let stand overnight, water was added and the solution was extracted with ether. The ether solution was washed free of acetic acid and the *epi*-pregnanolone was purified and isolated as described in the preceding experiment, m. p. 149°. Mixed melting points with natural *epi*-pregnanol-3-one-20 gave no depression.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.7; H, 11.0.

Acetate of *epi*-Pregnanol-3-one-20.—A solution of 100 mg. of *epi*-pregnanol-3-one-20 in 5 cc. of acetic anhydride was refluxed for thirty minutes. The product was crystallized from alcohol–water, m. p. 112°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.8; H, 10.1. Found: C, 77.1; H, 10.3.

Semicarbazone of *epi*-Pregnanol-3-one-20.—The semicarbazone was prepared by the usual method and crystallized from alcohol, m. p. 245°.

Anal. Calcd. for $C_{22}H_{37}N_3O_2$: C, 70.3; H, 9.9. Found: C, 69.9; H, 9.9.

Pregnanol-3-one-20.—A solution of 2 g. of pregnandione in 200 cc. of acetic acid containing 1 cc. of constant boiling hydrobromic acid was added to 50 cc. of acetic acid containing 200 mg. of previously reduced platinum oxide catalyst. The product was shaken with hydrogen at 45 pounds (3 atm.) pressure for twenty minutes. The material was isolated by means of Girard's reagent, and its half succinic ester. It was then heated to boiling with 6 g. of digitonin in 300 cc. of alcohol. This was let stand overnight. The precipitate was filtered and washed well with alcohol. After drying it weighed 5.5 g. The digitonide was heated on a steam-bath for five minutes with 20 cc. of pyridine. Ether was added and the digitonin filtered. The ether solution was evaporated to dryness and the residue was crystallized from alcohol–water, m. p. 149°; mixing with *epi*-pregnanol-3-one gave a depression in melting point to 125°.

(4) Marker, Kamm, Jones and Oakwood, THIS JOURNAL, **59**, 614 (1937).

(5) Marker and Kamm, *ibid.*, **59**, 1373 (1937).

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.5; H, 11.1.

Acetate of Pregnanol-3-one-20.—A solution of 100 mg. of pregnanolone in 5 cc. of acetic anhydride was refluxed for thirty minutes. The product was crystallized from alcohol–water, m. p. 121°. A mixture of this compound with the acetate of *epi*-pregnanolone, m. p. 112°, gave a 20° depression in melting point.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.8; H, 10.1. Found: C, 76.4; H, 10.1.

Semicarbazone of Pregnanol-3-one-20.—Pregnanolone gave a semicarbazone of m. p. 245°.

Anal. Calcd. for $C_{22}H_{37}N_3O_2$: C, 70.3; H, 9.9. Found: C, 69.8; H, 9.8.

Androsterone from Androstanedione.—A solution of 100 mg. of androstanedione in 50 cc. of glacial acetic acid containing 1 cc. of constant boiling hydrobromic acid was added to 50 cc. of glacial acetic acid containing 25 mg. of previously reduced platinum oxide catalyst. The solution was shaken with hydrogen at 45 pounds (3 atm.) pressure for fifteen minutes. The product was isolated and purified by means of Girard's reagent and the half succinic ester. A small amount of isoandrosterone was removed by means of digitonin precipitation. The androsterone was crystallized from dilute alcohol, m. p. 184°; mixing with an authentic sample of androsterone gave no depression in melting point.

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.6; H, 10.4. Found: C, 79.0; H, 10.3.

Summary

epi-Pregnanol-3-one-20, a natural product of human pregnancy urine, was prepared from pregnandione by partial catalytic reduction in alcohol and from pregnandiol by partial acetylation, followed by oxidation. Pregnanol-3-one-20 was prepared by catalytic reduction of pregnandione in acid solution. Androsterone was prepared by partial catalytic reduction of androstanedione in acid solution.

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The Photolysis of the Aliphatic Aldehydes. IV. *n*- and Isobutyraldehydes

BY PHILIP A. LEIGHTON, LEO D. LEVANAS, FRANCIS E. BLACET AND ROBERT D. ROWE

Since the appearance of the first paper in this series,[1] new experimental data have been accumulated which are of importance in determining the nature of the processes involved in the photolysis of the aliphatic aldehydes. This work, which has dealt chiefly with acetaldehyde, includes a study of the effects of wave length and pressure on quantum yields[2] and of the effect of wave length on the yield of hydrogen,[3] a demonstration of the production of free raidcals during the reaction,[4] and the discovery of a high temperature chain reaction apparently propagated by radicals.[5] As a result, the originally divergent hypotheses of Norrish and Kirkbride[6] and the authors' have become modified[3,7] until they are in agreement that the decomposition may involve two possibilities: (A) an effective splitting of the aldehyde molecule into a hydrocarbon and carbon monoxide, and (B) a dissociation into independent free radicals. While process A predominates at longer wave lengths, the importance of B would appear to increase at shorter wave lengths.[3,8] From this point of view the low yield of free radicals observed by Pearson and Purcell[4] is not surprising since, in the source they used, the greater part of the effective radiation was at wave lengths above 3000 Å.

The photochemical behavior of *n*- and isobutyraldehydes, here reported, is in the main analogous to that of the lighter aldehydes. In all cases both decomposition and apparent polymerization occur at room temperature, and in common with acetaldehyde the butyraldehydes show chain decompositions at higher temperatures. There are also marked differences in behavior, which we will attempt to bring out.

Experimental

1. Purification of Materials.—The middle fraction of a sample of Eastman *n*-butyraldehyde was distilled onto anhydrous copper sulfate in the first of a series of bulbs sealed to the reaction system. After evacuation, several additional first fractions and residues were removed by low temperature distillation. Isobutyraldehyde was treated in a similar manner in some cases and in others it was prepared by the acid catalyzed rearrangement of methallyl alcohol.

(1) Leighton and Blacet, THIS JOURNAL, **54**, 3165 (1932).
(2) Leighton and Blacet, *ibid.*, **55**, 1766 (1933).
(3) Blacet and Roof, *ibid.*, **58**, 278 (1936).
(4) Pearson and Purcell, *J. Chem. Soc.*, 1151 (1935).
(5) Leermakers, THIS JOURNAL, **56**, 1537 (1934); Akeroyd and Norrish, *J. Chem. Soc.*, 890 (1936).
(6) Kirkbride and Norrish, *Trans. Faraday Soc.*, **27**, 404 (1931).
(7) Norrish, *Cold Spring Harbor Symposia on Quantitative Biology*, **3**, 51 (1935); *Acta Physicochim. U. S. S. R.*, **3**, 171 (1935).
(8) Rollefson, *J. Phys. Chem.*, **41**, 259 (1937).