oxidation product of pseudotigogenin diacetate, m. p. 161–163°, the m. p. was unchanged.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.1; H, 9.2. Found: C, 69.9; H, 9.1.

Catalytic Reduction of the Oxidation Product of Pseudodiosgenin Diacetate.—A mixture of 2 g. of the oxidation product of the diacetate of pseudodiosgenin, 2 g. of platinum oxide catalyst and 100 cc. of glacial acetic acid were shaken for two hours at room temperature under 45 pounds of hydrogen. The temperature was then raised to 70° for one hour. The solution was filtered and the acetic acid was removed *in vacuo*. The residue was refluxed for fifteen minutes with a 2% alcoholic potassium hydroxide solution. Water was added and the product was filtered and recrystallized from methanol, m. p. 287–289°. When mixed with the triol from the catalytic reduction of the oxidation product of the diacetate of pseudotigogenin, m. p. 286–288°, there was no depression in melting point.

Reduction of the Oxidation Product of Pseudodiosgenin Diacetate with Aluminum Isopropylate.—A mixture of 10 g. of aluminum isopropylate, 5 g. of the oxidation product of pseudodiosgenin diacetate and 400 cc. of dry isopropyl alcohol was refluxed for seven hours. The solvent was removed over a five-hour period and the residue was refluxed with 500 cc. of 2% methanolic potassium hydroxide for thirty minutes. Water was added and the precipitated product was filtered and crystallized from methanol, m. p. 281–285°. When mixed with the saturated triol there was a depression in melting point.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.4; H, 10.3. Found: C, 75.2; H, 10.1

When refluxed with acetic anhydride it gave a triacetate which was crystallized from ether–pentane, m. p. 143°.

Anal. Calcd. for $C_{27}H_{40}O_6$: C, 70.4; H, 8.8. Found: C, 70.3; H, 8.8.

Catalytic Hydrogenation of Δ^5-Pregnenetriol-3,16,20 to *allo*-Pregnanetriol-3,16,20.—A mixture of 500 mg. of the triacetate of Δ^5-pregnenetriol-3,16,20, 1 g. of platinum oxide catalyst and 200 cc. of glacial acetic acid was shaken under hydrogen at 45 pounds pressure for one hour. The solution was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in alcohol and refluxed for fifteen minutes with a 2% alcoholic potassium hydroxide solution. Water was added and the precipitated product was filtered, and recrystallized from ethanol, m. p. 285–287°. When mixed with the triol obtained by the catalytic reduction of the oxidation product of pseudotigogenin diacetate, m. p. 286–288°, there was no depression in m. p.

Summary

1. Dihydro-pseudotigogenin diacetate and pseudotigogenin diacetate give an identical oxidation product, $C_{31}H_{48}O_7$ (A).

2. Similarly pseudodiosgenin diacetate gives an oxidation product, $C_{31}H_{46}O_7$ (B). Catalytic reduction of this gives the product A. Further oxidation of A gives 3-hydroxy-*etio-allo*-bilianic acid.

3. Hydrolysis of A gives Δ^{16}-*allo*-pregnenol-3(β)-one-20. Hydrolysis of B gives $\Delta^{5,16}$-pregnadienol-3(β)-one-20.

4. Reduction of A with aluminum isopropylate or catalytically gives an *allo*-pregnanetriol-3,16,20 (C), while reduction of B with aluminum isopropylate gives a Δ^5-pregnenetriol-3,16,20, which can be catalytically reduced to C. Direct catalytic reduction of B followed by hydrolysis gives C.

5. Reduction of A with sodium in alcohol gives *allo*-pregnanediol-3(β),20(α). B gives Δ^5-pregnenediol-3(β),20(α).

STATE COLLEGE, PENNA. RECEIVED OCTOBER 25, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. CXVIII. The Action of Selenious Acid on Δ^5-Pregnenediol and on Δ^5-Androstenediol

BY RUSSELL E. MARKER, HARRY M. CROOKS, JR., AND EMERSON L. WITTBECKER

Two previous papers of this series have dealt with the conversion of sitosterol[1] and stigmasterol[2] to the corresponding Δ^5-3,4 and Δ^4-3,6-diols by oxidation with selenious acid in the manner of Rosenheim and Starling[3] with cholesterol. Refluxing of these unsaturated diols with alcoholic hydrogen chloride led in each case to the formation of the corresponding Δ^4-3-ketone.

Since the pregnane derivatives are readily available[4] this series of reactions has now been extended to the preparation of 20-dihydroprogesterone and testosterone, using as starting materials Δ^5-pregnenediol and Δ^5-androstenediol, respectively. In both cases the selenious acid oxidation gives apparently a great preponderance of a single isomer, presumably the Δ^5-3,4-diol, in contrast to the almost equal yields of the two isomeric diols in the case of the sterols previously reported.

(1) Marker, Kamm and Wittle, THIS JOURNAL, **60**, 1071 (1938).
(2) Marker and Rohrmann, *ibid.*, **60**, 1073 (1938).
(3) Rosenheim and Starling, *J. Chem. Soc.*, 377 (1937).
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 3592 (1939), *et seq.*

The 20-dihydro-progesterone was isolated by means of its relative insolubility and converted to progesterone by direct oxidation with chromic acid in acetic acid. The testosterone was isolated by means of its semicarbazone. The free testosterone was obtained by oxalic acid hydrolysis of the semicarbazone.

We wish to thank Parke, Davis and Company for their assistance.

Experimental Part

Reduction of $\Delta^{5,16}$-Pregnadienol-3(β)-one-20 with Sodium and Ethanol.—To a boiling solution of 10 g. of $\Delta^{5,16}$-pregnadienol-3(β)-one-20 in 1 liter of absolute ethanol was added 50 g. of sodium in small pieces. When the sodium had all reacted, water was added and the solution was extracted with ether. The ethereal extract was washed with water, evaporated and the residue taken up in acetone and water. The Δ^5-pregnenediol-3(β),20(α) was filtered and recrystallized three times from ether. It melted at 174–176°.

With boiling acetic anhydride an acetate was formed. It crystallized from methanol and melted at 144–146°.

Anal. Calcd. for $C_{25}H_{38}O_4$: C, 74.5; H, 9.5. Found: C, 74.4; H, 9.5.

Δ^5-Pregnenetriol-3,4,20.—To a solution of 6 g. of Δ^5-pregnenediol-3(β),20(α) diacetate in 30 cc. of benzene was added a hot solution of 4 g. of selenious acid in 70 cc. of 98% acetic acid. The solution was refluxed for one hour, then 7 g. of sodium acetate was added and refluxing continued for ten minutes to coagulate the selenium. The mixture was filtered, and the filtrate poured into water. The solution was extracted with ether. The ethereal extract was washed with water, then evaporated and the residue was hydrolyzed with a solution of 5 g. of potassium hydroxide in 100 cc. of ethanol. Water was added to the solution and it was extracted with ether. The ether layer was washed with water, evaporated and the residue taken up in acetone. The crystals were filtered off and recrystallized twice from acetone to give Δ^5-pregnenetriol-3,4,20, melting at 207–210°.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.4; H, 10.2. Found: C, 75.2; H, 10.3.

Refluxing with acetic anhydride for one-half hour gave a triacetate which crystallized from dilute methanol, m. p. 153–154°.

Anal. Calcd. for $C_{27}H_{40}O_6$: C, 70.4; H, 8.7. Found: C, 70.4; H, 8.8.

Δ^4-Pregnenol-20(α)-one-3.—A solution of 1.5 g. of Δ^5-pregnenetriol-3,4,20 in 50 cc. of ethanol was boiled with 10 cc. of concentrated hydrochloric acid for one hour. The solution was diluted and then extracted with ether. The ether layer was washed with alkali and water and then evaporated to approximately 15 cc. The crystals that separated were filtered, washed with ether and recrystallized from ether; yield 900 mg., m. p. 158–160°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.3; H, 10.4.

When refluxed with acetic anhydride for one-half an hour it gave an acetate which crystallized from dilute methanol, m. p. 138–140°.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.1; H, 9.6. Found: C, 76.9; H, 9.6.

Progesterone.—A solution of 0.7 g. of Δ^4-pregnenol-20-one-3 in 25 cc. of acetic acid was oxidized at room temperature with 300 mg. of chromium trioxide for one-half an hour. Water was added to the solution and it was extracted with ether. The ether layer was washed with alkali, water and then evaporated. The residue crystallized from ether, m. p. 119–122°. It was recrystallized from acetone and melted at 124–126°. A mixed melting point with progesterone gave no depression.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.1; H, 9.8.

Δ^5-Androstenetriol-3,4,17.—To a solution of 4.6 g. of Δ^5-androstenediol-3,17 diacetate in 25 cc. of benzene was added 3.5 g. of selenious acid in 60 cc. of 98% acetic acid. This mixture was refluxed for one hour, 6 g. of sodium acetate added and the refluxing continued for ten minutes. The coagulated selenium was filtered off. Water was added to the filtrate, and the solution extracted with ether. The ether layer was washed with water and then evaporated. The residue was dissolved in acetone and methanol. The crystals were filtered and recrystallized from acetone–methanol, m. p. 258–261°.

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.5; H, 9.9. Found: C, 74.2; H, 9.9.

Refluxing 0.1 g. of the Δ^5-androstenetriol-3,4,17 with acetic anhydride for one-half an hour gave an acetate which crystallized from methanol and melted at 155–156°.

Anal. Calcd. for $C_{25}H_{36}O_6$: C, 69.4; H, 8.4. Found: C, 69.2; H, 8.5.

Testosterone.—To a solution of 0.5 g. of Δ^5-androstenetriol-3,4,17 in 50 cc. of methanol was added 10 cc. of concentrated hydrochloric acid. This mixture was refluxed for forty-five minutes. The crystals obtained when the methanol was evaporated melted at 137–143°. These were dissolved in 25 cc. of methanol and to this was added a methanol solution of 1 g. of semicarbazide acetate. The mixture was boiled for two hours, and then the semicarbazone was isolated by adding water and ether and filtering. The solid was washed well with ether. It melted at 225° dec.

Anal. Calcd. for $C_{20}H_{31}O_2N_3$: C, 69.55; H, 9.05 Found: C, 69.2; H, 9.0.

The semicarbazone was refluxed two hours with a solution of 1 g. of oxalic acid in 30 cc. of 75% ethanol. The product was taken up in ether, washed with water and the ether evaporated. The residue was crystallized from ether, and then methanol; m. p. 147–149°. The product was distilled and crystallized from aqueous acetone, m. p. 150–152°. A mixed melting point with testosterone gave no depression.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.05; H, 9.8. Found: C, 78.9; H, 9.7.

Summary

1. Oxidation of Δ^5-pregnenediol with selenious acid, followed by dehydration with hydrochloric

acid and oxidation of the resulting product, gave progesterone.

2. Oxidation of Δ^5-androstenediol with selenious acid, followed by dehydration with hydrochloric acid gave testosterone.

STATE COLLEGE, PENNA. RECEIVED DECEMBER 21, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. CXIX. Sapogenins. XLVII. Pregnanetriols from Pseudosapogenins

BY RUSSELL E. MARKER, D. L. TURNER, R. B. WAGNER, PAUL R. ULSHAFER, HARRY M. CROOKS, JR., AND EUGENE L. WITTLE

Recently we described the oxidation of the diacetates of pseudosapogenins and the conversion of the oxidation products to pregnanetriols.[1] The present work was undertaken in the hope of obtaining from *epi*-tigogenin the *allo*-pregnanetriol-3(α),16,20 which occurs in the urine of pregnant mares[2,3]; instead an isomeric triol was formed.

The diacetate of *epi*-pseudotigogenin was oxidized as described previously[1] and the crude product was reduced catalyticaly to *allo*-pregnanetriol-3(α),16,20. It differs from the *allo*-pregnanetriol-3(α),16,20 obtained from the oxidation of *epi*-tigogenin with Caro's acid[4] and neither is identical with the naturally occurring triol. Extending the same procedure to dihydro-pseudosarsasapogenin diacetate and pseudosarsasapogenin diacetate, an identical pregnanetriol-3(β),16,20 was obtained from both by catalytic reduction of the crude intermediate oxidation product. Unacetylated pseudosarsasapogenin gave the same triol. *epi*-Pseudosarsasapogenin diacetate gave a pregnanetriol-3(α),16,20(β). The preganetriols prepared by this method all differ from the corresponding triols prepared by the oxidation of sapogenins with Caro's acid.[3,4,5] On the basis of the formulas assigned to the sapogenins[6] and pseudosapogenins[6] the difference must be in configuration at C-20. The reduction of the carbonyl group at C-20 under analogous conditions has been shown in the case of the various pregnanone-20 and *allo*-pregnanone-20 compounds to give one of the isomers to which the configuration "β" has been assigned.[7,8] By analogy to these results the new triols described in this paper and in the preceding one[1] may all be assigned the β-configuration at C-20 and the triols produced by oxidation with Caro's acid would be 20(α) triols. Since the new triols can also be prepared by Meerwein reduction of the pseudosapogenin oxidation products,[1] it seemed of interest to determine the configuration of the principal product of the Meerwein reduction of the carbonyl group at C-20 in Δ^{16}-*allo*-pregnenol-3(β)-one-20 and $\Delta^{5,16}$-pregnadienol-3-(β)-one-20. The products obtained were Δ^{16}-*allo*-pregnenediol,3(β),20(β) and $\Delta^{5,16}$-pregnadienediol-3(β),20(β), respectively. This follows from the conversion of both diols to *allo*-pregnanediol-3(β),20(β). The $\Delta^{5,16}$-pregnadienediol-3(β),-20(β) has been obtained by Butenandt[9] using a considerably different method. The melting points for the substance and its acetate reported in this paper are in agreement with those recorded by Butenandt.

The hydrolysis of the oxidation product from unacetylated pseudotigogenin gave Δ^{16}-*allo*-pregnenedione while that from free pseudosarsasapogenin gave Δ^{16}-pregnenedione. The acid fraction from both of these hydrolyses gave a good yield of α-methylglutaric acid, presumably identical with the acid of Windaus and Willerding.[10] Their acid was obtained from the energetic oxidation of digitogenic acid and there is some doubt of its origin from the side-chain.[11] By analogy with the formula previously given for the oxidation products of the acetylated pseudosapogenins,[1] the unacetylated pseudosapogenins would be expected to give oxidation products with the structure II. This readily accounts for the products obtained by hydrolysis.

Finally we have oxidized the acetate of pseudodesoxysarsasapogenin. Hydrolysis of the prod-

(1) Marker, Turner, Wagner, Ulshafer, Crooks and Wittle, THIS JOURNAL, **63**, 774 (1941).
(2) Marker and Wittle, *ibid.*, **61**, 855 (1939).
(3) Marker and Turner, *ibid.*, **62**, 2540 (1940).
(4) Marker, Turner, Wagner and Ulshafer, *ibid.*, **63**, 772 (1941).
(5) Marker, *et al.*, *ibid.*, **62**, 525 (1940).
(6) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(7) Marker, *et al.*, *ibid.*, **59**, 2291 (1937).
(8) Marker and Lawson, *ibid.*, **61**, 588 (1939).
(9) Butenandt and Schmidt-Thomé, *Ber.*, **72**, 1960 (1939).
(10) Windaus and Willerding, *Z. physiol. Chem.*, **143**, 33 (1925).
(11) Fieser, "Chemistry of Natural Products Related to Phenanthrene," 2d ed., Reinhold Publ. Corp., New York, N. Y., 1937, p. 326.