Anal. Calcd. for $C_{23}H_{36}O$: C, 79.7; H, 11.1. Found: C, 80.0; H, 11.1.

Uranedione-11,20.—Uranetrione (600 mg.) was reduced by the Clemmensen method as described for uranedione-3,11. After sublimation in high vacuum, the product was crystallized from ether–pentane as white needles, m. p. 199–201°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 80.0; H, 10.2.

Summary

The following reactions of urane derivatives have been observed:

1. Uranedione on partial oxidation with chromic anhydride yielded uraneol-3(β)-one-11. Uranediol on oxidation with aluminum isopropylate gave uraneol-11-one-3.

2. Mild catalytic hydrogenation of uranedione-3,11 gave uraneol-3(β)-one-11. Similar results were obtained on mild reduction with aluminum isopropylate.

3. Mild Clemmensen reduction of uranedione-3,11 gave uranone-11. Vigorous reduction gave urane. Mild Clemmensen reduction of uranetrione gave uranedione-11,20.

4. Urenedione has been prepared from bromouranedione.

STATE COLLEGE, PENNA. RECEIVED JULY 5, 1939

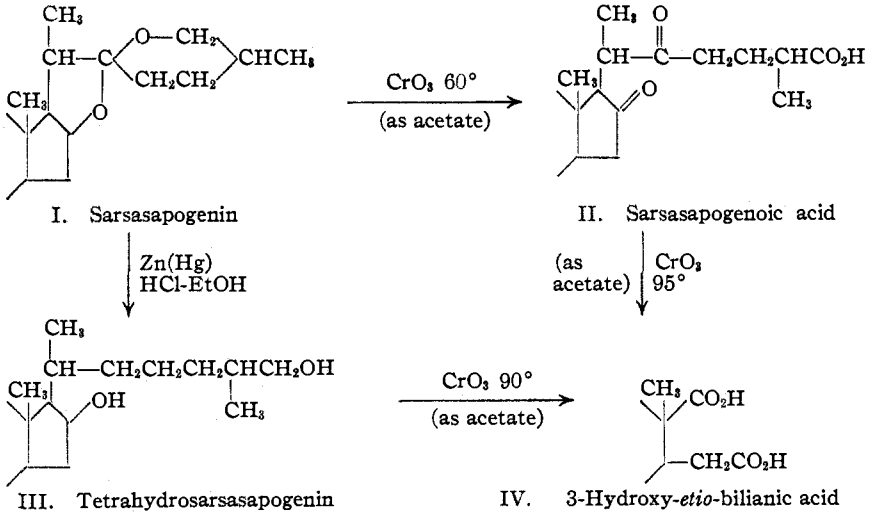
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXII. Oxidation Products of Sarsasapogenin. C_{19} Dibasic Acid

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The fact that sarsasapogenin contains a substituent at C-16 and has by indirect methods been degraded to *etio*-bilianic acid[1] suggests that 3-hydroxy-*etio*-bilianic acid might be expected among the acidic products obtained by the direct oxidation of sarsasapogenin acetate with chromic anhydride.

In extending our investigation of the acidic products from the chromic anhydride oxidation of sarsasapogenin acetate (conducted at 85°), we have isolated from the hydrolyzed acidic fraction in addition to the C_{22} keto acid previously reported[2] a dibasic hydroxy acid of the composition $C_{19}H_{30}O_5$. The acid gives a dimethyl ester with diazomethane. The resulting dimethyl ester was characterized further by the formation of an acetate. Treatment of the acid with acetic anhydride either by refluxing or by the pyridine method resulted in the formation of an acetate anhydride of the composition $C_{21}H_{30}O_5$ which upon alkaline hydrolysis yielded the original acid.



I. Sarsasapogenin

II. Sarsasapogenoic acid

III. Tetrahydrosarsasapogenin

IV. 3-Hydroxy-*etio*-bilianic acid

Mild oxidation of the acid followed by Clemmensen reduction yielded a desoxy acid of the composition $C_{19}H_{30}O_4$, m. p. 232°. With acetic anhydride the desoxy acid yielded an anhydride, m. p. 207°. Although no direct comparison was made, the desoxy acid is very probably identical with *etio*-bilianic acid first reported by Wieland[3] and co-workers, who reported a melting point of 228° for the acid and 206° for the anhydride.

The same hydroxy dibasic acid was obtained in almost 12% yield by the oxidation of sarsasapogenoic acid acetate at 90–95° with chromic anhydride. A similar oxidation of the product ob-

(1) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).

(2) Marker and Rohrmann, THIS JOURNAL, 61, 1285 (1939).

(3) Wieland, Schlichting and Jacobi, *Z. physiol. Chem.*, 161, 80 (1926).

tained by the acetylation of tetrahydrosarsasapogenin in pyridine in the cold gave only a poor yield of the dibasic acid. This is in accordance with our recently suggested structure for the tetrahydro compound[4] (III). Such a substance would not be expected to yield readily an easily oxidizable intermediate β-diketone or β-keto acid such as would be formed from our suggested formulation of sarsasapogenoic acid[5] (II).

The fact that sarsasapogenoic acid is oxidized easily to the dibasic acid suggests that it is an intermediate in the oxidation of sarsasapogenin to the bilianic acid.

The recent work of Litvan and Robinson[6] on the conversion of estric acid the dibasic acid from estrone analogous to *etio*-bilianic acid, to estrone suggests a very interesting possible method of converting 3-hydroxy-*etio*-bilianic acid to testosterone.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

C_{19} Dibasic Acid. (a) **From Sarsasapogenin Acetate.**—The hydrolyzed acidic fraction obtained from the oxidation of sarsasapogenin acetate with twice its weight of chromic anhydride at 85° was taken up in ether and allowed to stand for several days. The C_{22} keto acid which separated was collected and the filtrate evaporated to a sirup. Upon dilution of the sirup with chloroform, white crystals separated. These were collected, washed with chloroform and crystallized from acetone–chloroform to give a product, m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9; neut. equiv., 169. Found: C, 67.2; H, 9.0; neut. equiv., 175.

(b) **From Sarsasapogenoic Acid Acetate.**—The acidic fraction obtained by the chromic anhydride oxidation of sarsasapogenoic acid acetate (3.3 g.) at 90–95° after being freed from most of the C_{22} keto acid was crystallized from chloroform to give 300 mg. of compact white crystals, m. p. 219–222°. This gave no depression with the above sample.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.4; H, 9.1.

(c) **From Tetrahydrosarsasapogenin.**—Tetrahydrosarsasapogenin (3 g.) was acetylated with acetic anhydride in pyridine for twenty hours at room temperature. The sirupy product was dissolved in 100 cc. of acetic acid and to this solution heated at 90–95° was added 8 g. of chromic anhydride in 60 cc. of 80% acetic acid over a period of one hour. The mixture was heated for an additional two hours at 95° and the products separated into neutral and acidic fractions in the usual manner. Only a very small amount of neutral material was obtained and this was not investigated further.

The alkaline extract was heated and hydrolyzed by heating for twenty minutes on the steam-bath. The acids obtained would not crystallize. The acid fraction was acetylated with hot acetic anhydride and sublimed in high vacuum, the fraction distilling at 160–180° being collected, hydrolyzed with ethanolic potassium hydroxide and the acid crystallized from chloroform to give 40 mg. of white crystals, m. p. 219–222°. This gave no depression with samples obtained previously.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.0; H, 8.9.

Acetate Anhydride of C_{19} Dibasic Acid.—A mixture of 200 mg. of the dibasic acid and 4 cc. of acetic anhydride was refluxed for thirty minutes. The excess acetic anhydride was destroyed with water and the white solid collected and crystallized from aqueous acetone to give small flat white needles, m. p. 203–204°.

Anal. Calcd. for $C_{21}H_{30}O_6$: C, 69.6; H, 8.3. Found: C, 69.6; H, 8.4.

The same product was obtained by allowing the acid (50 mg.) to stand at room temperature for twenty hours with 10 cc. of pyridine and 0.3 cc. of acetic anhydride.

Hydrolysis of the acetate anhydride with ethanolic potassium hydroxide yielded the original dibasic acid.

Dimethyl Ester of Dibasic Acid.—A solution of 200 mg. of the acid in 15 cc. of ether and 2 cc. of methanol was treated with an excess of diazomethane in ether. The solvent was evaporated and the residual sirup crystallized from ether–pentane to give white needles, m. p. 121–122°.

Anal. Calcd. for $C_{21}H_{34}O_5$: C, 68.8; H, 9.3. Found: C, 68.9; H, 9.3.

A mixture of 50 mg. of the dimethyl ester and 3 cc. of acetic anhydride was refluxed for twenty minutes. The excess acetic anhydride was destroyed with water and the oily product crystallized from ether–pentane to give compact white crystals of a **dimethyl ester acetate**, m. p. 103–104°.

Anal. Calcd. for $C_{23}H_{36}O_6$: C, 67.6; H, 8.9. Found: C, 67.6; H, 8.8.

Desoxy Dibasic Acid.—To a solution of 500 mg. of the C_{19} dibasic acid in 20 cc. of acetic acid was added a solution of 300 mg. of chromic anhydride in 8 cc. of 80% acetic acid. After standing at room temperature for one hour the mixture was diluted with water and the precipitated solid taken up in ether. Evaporation of the ether gave a non-crystalline residue. This product was dissolved in 40 cc. of acetic acid and to this solution was added 6 g. of amalgamated zinc (20-mesh) and 20 cc. of concentrated hydrochloric acid. The resulting mixture was refluxed for six hours, diluted with water and extracted with ether. The residue remaining upon evaporation of the ether was refluxed with an excess of ethanolic potassium hydroxide for thirty minutes. Acidification with hydrochloric acid yielded a product which was crystallized from ether–pentane as small white crystals, m. p. 230–232°.

Anal. Calcd. for $C_{19}H_{30}O_4$: C, 70.8; H, 9.4. Found: C, 70.7; H, 9.6.

(4) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 2072 (1939).
(6) Litvan and Robinson, *J. Chem. Soc.*, 1997 (1938).

This gave no depression with a sample, m. p. 228–231°, prepared by oxidizing desoxysarsasapogenin with chromic anhydride at 90–95°.

The desoxy acid (75 mg.), m. p. 230–232°, was refluxed for thirty minutes with acetic anhydride and the reaction product was sublimed in high vacuum at 120–140°. The sublimate was crystallized from ether–pentane to give white needles of the **desoxy anhydride,** m. p. 205.5–207°.

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 75.0; H, 9.3. Found: C, 75.0; H, 9.4.

Treatment of the desoxy anhydride with hot ethanolic potassium hydroxide gave the desoxy acid, m. p. 230–232°.

Summary

The acetates of sarsasapogenin, tetrahydrosarsasapogenin, and sarsasapogenoic acid upon oxidation with chromic anhydride yield a C_{19} dibasic acid, probably 3-hydroxy-*etio*-bilianic acid.

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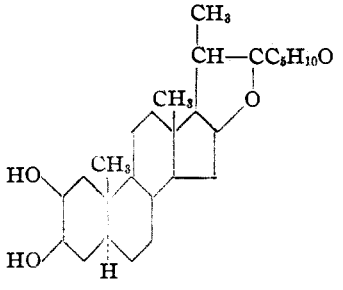
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXIII. Reactions of Digitogenin and Gitogenin

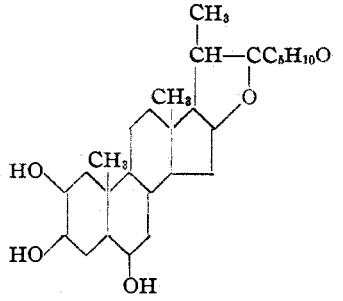
BY RUSSELL E. MARKER AND EWALD ROHRMANN

Although digitogenin (II) and gitogenin (I) were the first steroidal sapogenins to be studied,[1] the chemistry of the substances appears to be still in a somewhat confused state, particularly in regard to the nature of various oxidative degradation products. Unfortunately in all of the oxidation studies which have been reported on these substances no attempt was made to protect the reactive hydroxyl groups and therefore conclusions derived from such studies concerning the nature of the two less reactive oxygens must be regarded as of doubtful value.

The fact that tigogenin has been oxidized to gitogenic acid,[2,3] identical with that obtained by the chromic anhydride oxidation of gitogenin, shows conclusively that gitogenin is of the *allo*-configuration at C-5 and also offers strong support to the work of Tschesche and Hagedorn,[4] concerning the position of the nuclear hydroxyl groups. The evidence concerning the configuration of digitogenin at C-5 is not certain in spite of the fact that it has been degraded to gitogenic acid by the Wolff–Kishner reduction of digitogenic acid, inasmuch as inversion at C-5 may have occurred under the influence of alkali.



I. Gitogenin



II. Digitogenin

The fact that both α-methylglutaric acid and methylsuccinic acids have been reported from the chromic anhydride oxidation of digitogenic acid[2,4] is in accordance with our recently proposed structure of the sapogenin side chain III.[5] It is no longer necessary to regard the formation of α-methylglutaric acid as arising from the oxidation of the nucleus of the sapogenin as was necessitated by structure IV of Tschesche and Hagedorn.[4,6]

Contrary to Tschesche and Hagedorn,[7] we have found that both digitogenin and gitogenin yield insoluble digitonides, a characteristic which evidently is shown by all of the known steroidal sapogenins.

Digitogenin and gitogenin both readily yield dihydro compounds[5] upon catalytic hydrogenation in acidic medium. These dihydro compounds have not been investigated further. The acetates of digitogenin and gitogenin yield with

(1) Fieser, "Chemistry of Natural Products Related to Phenanthrene." Reinhold Publishing Corp., New York, N. Y., 1936.

(2) Tschesche and Hagedorn, *Ber.*, **68**, 1090 (1935).
(3) Jacobs and Simpson, *J. Biol. Chem.*, **110**, 429 (1935).
(4) Tschesche and Hagedorn, *Ber.*, **69**, 797 (1936).
(5) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).
(6) Tschesche and Hagedorn, *Ber.*, **68**, 1412 (1935).
(7) Tschesche and Hagedorn, *ibid.*, **68**, 2247 (1935).