Anhydrotetrahydrotigogenoic Acid.—(a) To a solution of 300 mg. of tigogenoic acid dissolved in 150 cc. of acetic acid was added 300 mg. of Adams catalyst and the mixture was shaken under hydrogen at 45 pounds pressure for ten hours. The solution was filtered and the solvent was removed *in vacuo*. The residue was crystallized from acetone, m. p. 203–205°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.2. Found: C, 75.0; H, 10.1.

(b) To a solution of 12 g. of the monoacetate of dihydrotigogenin in 200 cc. of acetic acid at 30° was added a solution of 4 g. of chromic anhydride in 50 cc. of 90% acetic acid. After standing one hour, the solution was diluted with water and extracted with ether. The ether was removed and the residue was hydrolyzed with alcoholic potassium hydroxide and crystallized from acetone, m. p. 203–305°. When mixed with the above sample it gave no depression in melting point.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.2. Found: C, 74.8; H, 10.0.

Oxidation of Tigogenoic Acid.—A solution of 3 g. of chromic anhydride in 15 cc. of 80% acetic acid was added dropwise with stirring over a period of one hour to a solution of 1.5 g. of tigogenoic acid acetate in 30 cc. of glacial acetic acid at 85°. The stirring and heating was continued for an additional two hours. Methanol was added and the solvent was removed *in vacuo*. The residue was extracted with water and ether. The ethereal extract was washed well with water and a 3% potassium hydroxide solution. Upon evaporation of the ether there was no residue, thus showing the absence of lactonic material.

The alkaline extract was heated on a steam-bath for thirty minutes, cooled, acidified with hydrochloric acid and extracted with ether. The ether was evaporated to 10 cc. and allowed to stand in a refrigerator for several days. Only a small amount of crystalline material was obtained. This melted at 244–247° and gave no depression in melting point when mixed with 3-hydroxy-*etio-allo*-bilianic acid.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.1; H, 9.1.

Summary

Various oxidation products have been obtained from tigogenin and their structures have been discussed. Further support is given to the ketal structure of the steroidal sapogenin side chain.

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

Sterols. CXV. Sapogenins. XLIV. The Relation between Diosgenin and Cholesterol

BY RUSSELL E. MARKER AND D. L. TURNER

The assumption that the carbon skeleton of the side-chain in the steroidal sapogenins is identical with that of cholesterol has been based on the isolation of α-methylglutaric acid from the oxidation products of digitogenic acid[1] and the occurrence of a substance thought to be methyl isohexyl ketone among the products obtained by treating sarsasapogenin with selenium.[2] However, the α-methylglutaric acid might come from the nucleus rather than from the side-chain[3] and the substance of Ruzicka and Van Veen is probably not methyl isohexyl ketone.[4] By converting diosgenin to cholesterol we have now obtained conclusive proof that the steroidal sapogenins have the same carbon skeleton as cholesterol, and that they have 27 carbon atoms. This conversion also provides additional evidence for the 5,6 position of the double bond in diosgenin.

Diosgenin was reduced by the method of Marker and Rohrmann[5] to tetrahydrodiosgenin (I) a substance similar to tetrahydrosarsasapogenin to which the structure of 3,16,27-trihydroxycoprostane was assigned.[5] Catalytic reduction of the double bond in tetrahydrodiosgenin gave tetrahydrotigogenin which is 3,16,27-trihydroxycholestane.

The hydroxyl groups in tetrahydrodiosgenin were replaced by bromine atoms using phosphorus tribromide. The product was treated with less than an equimolar quantity of potassium acetate and then reduced with sodium in propyl alcohol. Two substances were separated from the reduction mixture by distillation at reduced pressure. These were identified as Δ^5-cholestene and cholesterol. The Δ^5-cholestene was reduced catalytically with hydrogen to cholestane.

Tetrahydrodiosgenin forms a triacetate. The oxidation of this with selenious acid followed by hydrolysis gives a substance similar to the Δ^5-3,4-

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[1] Windaus and Willerding, *Z. physiol. Chem.*, **143**, 33 (1925).

[2] Ruzicka and Van Veen, *ibid.*, **184**, 69 (1939).

[3] *Cf.* Fieser, "Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1937, p. 326.

[4] Jacobs and Simpson, *J. Biol. Chem.*, **105**, 501 (1934).

[5] Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).

dihydroxycholestene obtained from cholesterol.[6,7] The tetrahydroxycholestene was converted by treatment with acid to Δ^4-3-keto-16,27-dihydroxycholestene.

The Clemmensen reaction applied to 4-dehydrotigogenone under conditions similar to those used for the preparation of tetrahydrodiosgenin reduced only the ketone group at the 3-position to give 4-dehydrodesoxytigogenin. This follows from the identity of the product with material prepared by the reduction of 4-dehydrotigogenone using unamalgamated zinc which has been shown[5,8] not to attack the side-chain of the sapogenins.

Taking advantage of the similarity in the ring structure of cholesterol and diosgenin we have extended some characteristic reactions of cholesterol to diosgenin. The reactions described do not involve alteration of the sapogenin side-chain.

Thus when 4-dehydrotigogenone[9] was reduced with aluminum isopropylate by the Meerwein–Ponndorff method it gave *epi*-4-dehydrotigogenin (*epi-allo*-diosgenin) analogous to *epi-allo*-cholesterol.[10] The digitonin precipitable material from this reduction gave an unidentified product. *Epi*-4-dehydrotigogenin is dehydrated readily on treatment with acid or acetic anhydride to give a diene which can be assigned the structure of 3,5-dehydrodesoxytigogenin in analogy with the dehydration of *epi-allo*-cholesterol.[11] This was reduced catalytically to desoxytigogenin.

Wettstein[12] has obtained 4,6-dehydro-3-ketosterols by treating Δ^5-3-hydroxy sterols with benzoquinone and aluminum tertiary butylate. When this reaction was applied to diosgenin, 4,6-dehydrotigogenone was obtained.

Cholesterol with phosphorus pentachloride gives cholesteryl chloride. The catalytic reduction of this chloride gives α-cholestyl chloride, while the direct chlorination of β-cholestanol gives β-cholestyl chloride.[13]

3-Chlorodesoxydiosgenin was made following Fujii and Matsukawa.[14] The reduction of this substance gave a 3-chlorodesoxytigogenin differing from that obtained by the direct chlorination of tigogenin. By treating the 3-chlorodesoxytigogenin from the chlorination of tigogenin with quinoline 2-dehydrodesoxytigogenin was obtained.

Finally we have studied the oxidation of diosgenin acetate with chromic acid at 50–55° following the method used by Windaus and his co-workers[15] for the preparation of 7-keto-Δ^5-sterols. The product was separated into neutral and acidic fractions. A considerable amount of diosgenin acetate was recovered unchanged in the neutral fraction. After removal of the unchanged material from the neutral products of the oxidation of diosgenin acetate, a ketone believed to be 7-ketodiosgenin acetate was isolated.

The acid fraction from the oxidation gave an acid, $C_{27}H_{40}O_5$. This acid is possibly analogous in the structure of the side-chain to sarsasapogenoic acid. Treatment of 7-ketodiosgenin acetate with ethanolic potash resulted in dehydration with the formation of a ketodiene. This is analogous to the behavior of 7-ketocholesteryl acetate which gives a cholestadienone-7,[16] assigned the structure $\Delta^{3,5}$-cholestadienenone-7 by Stavely and Bergmann[11] who reduced it by the Wolff–Kishner method to $\Delta^{3,5}$-cholestadiene.

The Wolff–Kishner method applied to the semicarbazone of 7-ketodiosgenin acetate gave a mixture from which a small quantity of 3,5-dehydrodesoxytigogenin was obtained.

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

Experimental Part

Tetrahydrodiosgenin.—To 150 g. of amalgamated zinc was added a solution of 5 g. of diosgenin in 500 cc. of ethanol. This was brought to a reflux and a total of 150 cc. of concentrated hydrochloric acid was added over a period of two and one-half hours. Refluxing was continued for an additional thirty minutes. It was then poured into water and extracted with ether. The ethereal solution was washed well with water and the solvent was removed to about 20 cc. The product crystallized. It was filtered and recrystallized from ethyl acetate in which it is quite insoluble, m. p. 178–179°. When mixed with diosgenin, m. p. 204–206°, it melted at 158–163°, yield 3 g.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.4; H, 11.1. Found: C, 77.3; H, 10.8.

Treatment with boiling acetic anhydride for fifteen minutes gave a **triacetate.** It was recrystallized from pentane, m. p. 119.5°.

Anal. Calcd. for $C_{33}H_{52}O_6$: C, 72.8; H, 9.6. Found: C, 73.2; H, 9.6.

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(6) Rosenheim and Starling, *J. Chem. Soc.*, 377 (1937).

(7) Butenandt and Hausmann, *Ber.*, **70**, 1154 (1937).

(8) Marker and Rohrmann, *ibid.*, **61**, 1284 (1939).

(9) Marker, Tsukamoto and Turner, THIS JOURNAL, **62**, 2525 (1940).

(10) Schoenheimer and Evans, *J. Biol. Chem.*, **114**, 567 (1936).

(11) Stavely and Bergmann, *J. Org. Chem.*, **1**, 567 (1937).

(12) Wettstein, *Helv. Chim. Acta*, **23**, 388 (1940).

(13) Marker, Whitmore and Kamm, THIS JOURNAL, **57**, 2358 (1935).

(14) Fujii and Matsukawa, *J. Pharm. Soc., Japan*, **57**, 27, 114 (1937).

(15) Windaus, Lettre and Schenck, *Ann.*, **520**, 98 (1935).

(16) Mauthner and Suida, *Monatsh.*, **17**, 579 (1896).

Tetrahydrodiosgenin triacetate (1.0 g.) was heated with a solution of 1 g. of potassium hydroxide in 100 cc. of ethanol for fifteen minutes on the steam-bath. The solution was poured into water and extracted with ether. The ethereal solution was washed free of ethanol and the ether was removed. The crystalline residue was recrystallized from ethyl acetate, m. p. 178–179°. Mixed with tetrahydrodiosgenin (m. p. 178–179°) the m. p. was 178–179°.

The **tribenzoate** of tetrahydrodiosgenin was made in pyridine with benzoyl chloride in the usual manner. It was recrystallized from ether and from acetone, m. p. 166–167°.

Anal. Calcd. for $C_{48}H_{58}O_6$: C, 78.9; H, 8.0. Found: C, 79.3; H, 7.7.

Tetrahydrotigogenin from Tetrahydrodiosgenin.—A solution of 500 mg. of tetrahydrodiosgenin in 50 cc. of acetic acid was shaken with 200 mg. of platinum oxide catalyst under 3 atm. of hydrogen for two hours. The solution was filtered and the solvent was removed *in vacuo*. The residue was crystallized from ether and from ethyl acetate. It is very soluble in methanol and ethanol, m. p. 195–197°. Mixed with tigogenin, m. p. 204–206°, it melted at 175–187°. Mixed with tetrahydrodiosgenin, m. p. 178–179°, it melted at 162–170°.

Anal. Calcd. for $C_{27}H_{48}O_3$: C, 77.1; H, 11.5. Found: C, 77.0; H, 11.4.

Triacetate of Tetrahydrotigogenin.—(a) The triacetate of tetrahydrodiosgenin (100 mg.) was shaken in acetic acid (20 cc.) with 100 mg. of Adams catalyst under hydrogen at 3 atm. for one hour. The solution was filtered, poured into water and extracted with ether. The ether was evaporated to give an oil which crystallized when treated with pentane and cooled in a carbon dioxide–ether-bath. It was recrystallized from pentane, m. p. 67–78°.

Anal. Calcd. for $C_{33}H_{54}O_6$: C, 72.5; H, 10.0. Found: C, 72.6; H, 10.3.

(b) Tetrahydrotigogenin (100 mg.) was acetylated directly by refluxing for fifteen minutes with an excess of acetic anhydride. The product crystallized from pentane, m. p. 66–67°. When mixed with (a) above there was no depression in melting point.

The triacetate of tetrahydrotigogenin (500 mg.) was dissolved in a solution of 2 g. of potassium hydroxide in 100 cc. of ethanol and heated on the steam-bath for thirty minutes. The mixture was poured into water and extracted with ether. The material from the ether melted at 195–197°. Mixed with tetrahydro-tigogenin (m. p. 195–197°) there was no depression in melting point.

The **tribenzoate of tetrahydrotigogenin** was prepared in the usual manner with benzoyl chloride in pyridine. The product crystallized from ether, m. p. 162°.

Anal. Calcd. for $C_{48}H_{60}O_6$: C, 78.7; H, 8.25. Found: C, 79.0; H, 8.0.

Oxidation of Tetrahydrodiosgenin Triacetate with Selenious Acid.—To a solution of 4.0 g. of the triacetate of tetrahydrodiosgenin in 25 cc. of benzene was added a hot solution of 2.0 g. of selenious acid in 75 cc. of 97% acetic acid. The mixture was refluxed vigorously for one hour. Then 5 g. of potassium acetate was added and the mixture was refluxed for an additional ten minutes. The mixture was poured into water and the product was taken up in ether. The ethereal solution was washed free of acetic acid, the ether was removed and the residue was hydrolyzed with ethanolic potash. The solution was poured into water and extracted with ether. The ether was washed with water and evaporated. The residue was crystallized from acetone, m. p. 196°, yield 0.5 g.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Found: C, 73.9; H, 10.5.

This material (1.0 g.) was dissolved in 100 cc. of ethanol containing 5 cc. of concentrated hydrochloric acid. The solution was refluxed for ten minutes, then poured into water and extracted with ether. The ether was washed and evaporated. The residue was recrystallized from ethyl acetate, m. p. 163–164°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.7; H, 10.6.

Δ^5-Cholestene and Cholesterol from Tetrahydrodiosgenin.—A mixture of 4 g. of tetrahydrodiosgenin, 300 cc. of dry benzene and 12 cc. of phosphorus tribromide was refluxed for two hours. The benzene was removed under vacuum and the residue was dissolved in ether. The ethereal solution was washed well with water and sodium carbonate solution. The solvent was removed and the residue, 4.7 g., was dissolved in 150 cc. of acetic acid to which was added 600 mg. of potassium acetate (fused). The mixture was refluxed for three hours, the acetic acid was vacuum distilled and to the residue was added 300 cc. of propyl alcohol. This was heated to boiling and a total of 25 g. of sodium was added over a period of one hour. When all the sodium was dissolved, water was added and the product was extracted with ether. The solvent was removed and the residue was sublimed in a high vacuum to give fractions at 80–100° and at 120–140°. There was very little material between these two fractions. The fraction subliming at 80–100° was crystallized from acetone, m. p. 89–91°. When mixed with an authentic sample of Δ^5-cholestene, m. p. 89–90°, it gave no depression in melting point.

Anal. Calcd. for $C_{27}H_{46}$: C, 87.5; H, 12.6. Found: C, 87.6; H, 12.7.

Reduction with platinum oxide and hydrogen in acetic acid gave a product melting at 78–79° which gave no depression in melting point when mixed with cholestane, m. p. 78–80°.

The fraction distilling at 120–140°, 1.4 g., was dissolved in a small amount of ethanol and a solution of 5 g. of digitonin in 250 cc. of ethanol was added. The precipitate was filtered, dried and decomposed in the usual manner by heating with pyridine. The sterol thus obtained was crystallized from acetone, m. p. 147–148°. When mixed with cholesterol, m. p. 147–148°, it gave no depression in melting point.

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.8; H, 12.0. Found: C, 83.8; H, 11.9.

When refluxed with acetic anhydride it gave an acetate which was crystallized from methanol–acetone, m. p. 114°. When mixed with cholesteryl acetate, m. p. 114°, there was no depression in melting point.

7-Ketodiosgenin Acetate.—Diosgenin acetate (25 g.) was dissolved in 1 liter of acetic acid. The solution was kept at 50–53° and vigorously stirred. A solution of 17 g. of chromium trioxide in 25 cc. of 50% acetic acid was dropped into the diosgenin acetate solution during seventy-five minutes. After three additional hours at the same temperature 20 g. of zinc dust was added. After shaking vigorously the solution was filtered. The solvent was removed *in vacuo* until only 100 cc. remained. The residue was extracted with ether. Acetic acid was removed from the ethereal solution by washing with water. An acid fraction was removed by washing with dilute sodium hydroxide solution. The acid was precipitated from this with cold dilute hydrochloric acid. The acid was taken up in ether. Evaporation of the ether gave an oil which was dissolved in acetone. It gave 50 mg. of crystals after standing at 0°. The crystals melted at 184–187°. After recrystallization from acetone the substance decomposed at 226° when heated rapidly to 200° and slowly from this point.

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.9; H, 9.1. Found: C, 72.7; H, 9.2.

The original ethereal solution remaining after removal of the acid gave a neutral product on evaporation of the ether. This was washed with methanol and melted at 165–174°, yield 6 g. It contained no lactone. A 10-g. portion of this material was purified in the following manner. It was dissolved in 3 liters of methanol and on cooling 4.4 g. of a substance of m. p. 183–190° crystallized. This was recrystallized from acetone and melted at 187–190°. When mixed with diosgenin acetate there was no depression in melting point.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.0; H, 9.3.

The methanol mother liquors were concentrated to 200 cc. and gave 2.8 g. of material of m. p. 174–179° on cooling. Further concentration of the mother liquor gave a third crop of m. p. 191–194° (2 g.). This was extracted with pentane, the insoluble part being rejected. The material which crystallized from pentane was repeatedly crystallized from pentane. It melted sharply at 197°. Mixed with diosgenin acetate it melted at 177–190° and with free diosgenin at 167–172°.

Anal. Calcd. for $C_{29}H_{42}O_5$: C, 74.0; H, 9.0. Found: C, 74.2; H, 9.3.

On refluxing with an aqueous alcoholic solution of semicarbazide hydrochloride in the presence of potassium acetate it gave a semicarbazone which was recrystallized from ethanol. It decomposed at 282°.

Anal. Calcd. for $C_{30}H_{45}O_5N_3$: C, 68.3; H, 8.6. Found: C, 68.5; H, 8.5.

Treatment of the Semicarbazone of 7-Ketodiosgenin Acetate with Sodium Ethylate.—The semicarbazone of 7-ketodiosgenin acetate (0.9 g.) was heated with a solution of 500 mg. of sodium in 10 cc. of dry ethanol in a sealed tube for four hours at 180°. The product was poured into water. The dark brown mixture was extracted with ether. The ethereal solution was washed, dried and filtered through a column of aluminum oxide. The material remaining after evaporation of the ether was crystallized several times from acetone, m. p. 163–165°.

Anal. Calcd. for $C_{27}H_{40}O_2$: C, 81.8; H, 10.2. Found: C, 81.5; H, 10.3.

When mixed with 3,5-dehydrodesoxytigogenin (m. p. 168–169°) there was no depression in m. p.

Treatment of 7-Ketodiosgenin Acetate with Ethanolic Potash.—A solution of 50 mg. of 7-ketodiosgenin (m. p. 197°) was heated on the steam-bath for fifteen minutes with 15 cc. of a 15% ethanolic potash solution. The mixture turned dark green and it was poured into water. The product was taken up in ether, the ethereal solution washed and the ether removed. The residue was recrystallized from pentane, m. p. 197–198°. When mixed with the starting material the m. p. was 165–187°; it is possibly 3,5-dihydro-7-ketotigogenin.

Anal. Calcd. for $C_{27}H_{38}O_3$: C, 79.0; H, 9.3. Found: C, 78.6; H, 8.9.

4-Dehydrodesoxytigogenin.—(a) A mixture of amalgamated zinc (100 g.) with a solution of 3 g. of 4-dehydrotigogenone in 500 cc. of ethanol was heated to boiling. Hydrochloric acid (170 cc.) was added over a period of two and one-half hours. The mixture was refluxed for an additional thirty minutes. The solution was decanted from the zinc, poured into water and extracted with ether. The ethereal solution was washed free of ethanol and evaporated. The product was recrystallized from acetone using Norit; long needles, m. p. 145.5–146°, yield 500 mg.

Anal. Calcd. for $C_{27}H_{42}O_2$: C, 81.4; H, 10.6. Found: C, 81.6; H, 10.7.

(b) To a refluxing solution of 15 g. of 4-dehydrotigogenone in 2500 cc. of ethanol containing 400 g. of 20-mesh unamalgamated zinc was added 450 cc. of concentrated hydrochloric acid gradually over eight hours. The mixture was heated an additional half-hour. It was concentrated *in vacuo* to one-half volume and cooled. Twelve grams of crude product separated. This was recrystallized from acetone using Norit, m. p. 145–146°. When mixed with (a) above there was no depression in melting point.

Anal. Calcd. for $C_{27}H_{42}O_2$: C, 81.4; H, 10.6. Found: C, 81.4; H, 10.5.

3,5-Dehydrodesoxytigogenin.—A mixture of 5 g. of 4-dehydrotigogenone, 8 g. of aluminum isopropylate and 200 cc. of dry isopropyl alcohol was refluxed for six hours. It was then slowly distilled for six hours to half of the original volume. The residue was poured into dilute hydrochloric acid and the product was taken up in ether. The ether was removed. The residue did not form a digitonide on treatment with digitonin in alcohol. It did not react with boiling acetic anhydride. It was recrystallized from acetone as flat plates, m. p. 168–169°. When mixed with 4-dehydrotigogenone the melting point was 142–160°, yield 2.5 g.

Anal. Calcd. for $C_{27}H_{40}O_2$: C, 81.8; H, 10.2. Found: C, 81.8; H, 10.1.

Desoxytigogenin.—A mixture of 3,5-dehydrodesoxytigogenin (390 mg.), palladium-barium sulfate catalyst (2 g.) and 100 cc. of ether was shaken with hydrogen at room temperature for six hours. The solution was filtered and the solvent was removed. The product was recrystallized from acetone, m. p. 173°. When mixed with the starting material it melted at 162–167°. A mixture with an authentic sample of desoxytigogenin, m. p. 173°, melted at 173°.

Anal. Calcd. for $C_{27}H_{42}O_2$: C, 80.9; H, 11.1. Found: C, 81.2; H, 11.4.

4,6-Dehydrotigogenone.—Diosgenin (3 g.) was mixed with benzoquinone (17 g.) and dry toluene (200 cc.). Then 50 cc. of toluene was distilled from the mixture *in vacuo*. Aluminum isopropylate (5 g.) was added to the residue and the mixture was refluxed for one hour. It was poured into 200 cc. of 2 *N* hydrochloric acid. The product was taken up in ether. The ethereal solution was washed with sodium carbonate solution, then with alkaline bisulfite solution and water. The ether was dried and evaporated to 50 cc. This was filtered through a column of 40 g. of aluminum oxide. The solvent was removed and the residue was treated with succinic anhydride in pyridine to remove carbinols. The product was taken up in ether. The solution was freed of pyridine with 2 *N* hydrochloric acid and of the half succinates with sodium carbonate solution. The material obtained on evaporation of the ether was recrystallized from acetone and melted at 205–207°, yield 0.9 g. When mixed with diosgenin it melted at 180–186°.

Anal. Calcd. for $C_{27}H_{36}O_3$: C, 79.0; H, 9.3. Found: C, 79.2; H, 9.4.

Chlorination of Diosgenin.—Chlorodesoxydiosgenin was obtained following the method of Fujii and Matsukawa.[14] Recrystallized from acetone it melted at 211–213°.

Anal. Calcd. for $C_{27}H_{41}O_2Cl$: C, 74.9; H, 9.5. Found: C, 74.9; H, 9.3.

This substance decolorized an acetic acid solution of pyridine dibromide hydrobromide instantaneously.

3 - Chlorodesoxytigogenin.—3 - Chlorodesoxydiosgenin (1.8 g.) was reduced in acetic acid with Adams catalyst. The product was recrystallized from acetone, m. p. 204–207°.

Anal. Calcd. for $C_{27}H_{43}O_2Cl$: C, 74.5; H, 10.0. Found: C, 74.8; H, 9.7.

It did not absorb bromine from pyridine dibromide hydrobromide solution in acetic acid.

Chlorination of Tigogenin.—Tigogenin (5 g.) was dissolved in 100 cc. of chloroform and 5 g. of calcium carbonate was added to the solution. Phosphorus pentachloride (5 g.) was added in small portions to the stirred mixture at 20° during thirty minutes. The mixture was allowed to stand for an additional hour. It was poured into cold sodium bicarbonate solution. After one hour hydrochloric acid (2 *N*) was added to neutralize the excess bicarbonate and the product was taken up in ether. Evaporation of the ether gave colorless crystals which were washed with acetone, yield 2.8 g. The substance was recrystallized from ethyl acetate and melted at 210–212°. When mixed with 3-chlorodesoxytigogenin prepared by the reduction of 3-chlorodesoxydiosgenin the melting point was 189–204°.

Anal. Calcd. for $C_{27}H_{43}O_2Cl$: C, 74.5; H, 10.0. Found: C, 74.9; H, 9.6.

2 - Dehydrodesoxytigogenin.—3 - Chlorodesoxytigogenin (1.3 g.) prepared by the chlorination of tigogenin was dissolved in 30 cc. of quinoline. The solution was refluxed for one hour. It was then poured into water and the product was taken up in ether. The ethereal solution was washed with dilute hydrochloric acid, dilute sodium hydroxide solution and water. Evaporation of the ether and crystallization of the residue from acetone using Norit gave 350 mg. of material which was recrystallized from acetone and melted at 163–166°.

Anal. Calcd. for $C_{27}H_{42}O_2$: C, 81.4; H, 10.6. Found: C, 81.6; H, 10.6.

***epi*-4-Dehydrotigogenin.**—A solution of 5 g. of 4-dehydrotigogenone and 15 g. of aluminum isopropylate in 500 cc. of dry isopropyl alcohol was refluxed for six hours. It was distilled slowly for twenty-four hours and then rapidly to half volume. The mixture was cooled and 300 cc. of cold 8% methanolic potassium hydroxide was added. It stood one hour, was poured into water and the product taken up in ether. The ethereal solution was washed with water and dilute potassium hydroxide solution. Evaporation of the ether gave solid material which was dissolved in 500 cc. of ethanol. After standing overnight the insoluble digitonide was removed by filtration. The filtrate was concentrated to one-third volume, poured into water, and the product taken up in ether. The ether was washed with water and filtered. Evaporation of the ether gave a product which when recrystallized from acetone gave 1.1 g. of 4-dehydro-*epi*-tigogenin; recrystallized from acetone, m. p. 208–210°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.4; H, 10.4.

When refluxed for thirty minutes in acetic anhydride this gave material which was recrystallized from acetone and melted at 167–169°. When mixed with $\Delta^{3,5}$-desoxytigogenin it melted at 168–169°.

Anal. Calcd. for $C_{27}H_{40}O_2$: C, 81.8; H, 10.2. Found: C, 81.8; H, 10.1.

The digitonide from the above product was decomposed with pyridine. Ether was added and the solution was filtered. The ethereal solution was washed with dilute hydrochloric acid and with water and the ether was evaporated. The product was dissolved in acetone and when the solution was cooled a first crop of amorphous material separated of m. p. 178–185°. A crystalline product was obtained from the mother liquor. This was recrystallized from methanol. It melted at 167–169°. When mixed with $\Delta^{3,5}$-dehydro-desoxytigogenin (m. p. 168–169°) it melted at 145–150°. It was dried in a high vacuum at 100° for analysis.

Anal. Found: C, 76.95, 76.83; H, 9.98, 10.0.

Another sample was dried for several hours in high vacuum at 100°. As a result of this treatment the melting point became 125–137° and the analysis indicated that dehydration had occurred.

Anal. Found: C, 80.0; H, 10.2.

Summary

1. Diosgenin has been converted to cholesterol.

2. Various reactions of cholesterol have been extended to diosgenin.

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