Anal: Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 74.0; H, 9.9.

(c) **With Sodium in Isopropyl Alcohol.**—To a solution of 2 g. of 5-pregnenol-3(β)-dione-16,20 in 200 cc. of dry isopropyl alcohol was added 10 g. of sodium in small strips at the reflux temperature. Water was added and the product was extracted with ether. It was crystallized from dilute methanol, m. p. 180–183°. This is 5-pregnenediol-3(β),20(α). Yield was 1.6 g.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.0; H, 10.7.

To prove the identity of the above product it was reduced catalytically using platinum oxide catalyst, acetic acid and hydrogen. The product was crystallized from acetone, m. p. 214–216°. It gave no depression when mixed with allo-pregnanediol-3(β),20(α).

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.7; H, 11.3. Found: C, 78.8; H, 11.3.

To a solution of 3.2 g. of 5-pregnenediol-3(β),20(α) in 100 cc. of acetic acid was added a solution of 1.65 g. of bromine in 20 cc. of acetic acid. To this was added a solution of 1.6 g. of chromic anhydride in 5 cc. of water and 20 cc. of acetic acid, keeping the temperature at 20°. It was allowed to stand for thirty minutes and then 5 g. of zinc dust was added and the product heated on a steam-bath for fifteen minutes. It was allowed to stand for three hours at room temperature. The zinc was filtered and the solvent was removed under reduced pressure. The product was extracted with ether, washed well with water and sodium bicarbonate solution and finally crystallized from methanol, m. p. and mixed m. p. with progesterone 128.5°; yield 2.1 g. The same product was obtained when 5-pregnenediol-3(β),20(α) was oxidized with aluminum *t*-butylate in acetone and benzene.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.4; H, 9.6.

(d) **By Mild Clemmensen.**—To a solution of 10 g. of 5-pregnenol-3(β)-dione-16,20 in 500 cc. of alcohol was added 100 g. of zinc strips; 100 cc. of concentrated hydrochloric acid was slowly dropped in over a period of one and one-half hours at the reflux temperature. It was heated for an additional two hours, filtered and the solvent removed under reduced pressure. The product was extracted with ether, the solvent was removed and the residue was crystallized from alcohol, m. p. and mixed m. p. with 5-pregnenol-3(β)-one-20, 196°; yield, 8.13 g. The same product was obtained when the original oxidation product of nologenin diacetate was treated with zinc, alcohol and hydrochloric acid.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.0; H, 11.0.

Acetylization and crystallization from methanol and from ethyl acetate gave pregnenol-3(β)-one-20 acetate, m. p. and mixed m. p. 146–148°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.6; H, 10.1. Found: C, 76.7; H, 10.2.

(e) **With Aluminum Isopropylate.**—A mixture of 2 g. of 5-pregnenol-3(β)-dione-16,20, 10 g. of aluminum isopropylate and 200 cc. of dry isopropyl alcohol was refluxed for seven hours. The solvent was then slowly distilled over a period of three hours. The residue was refluxed with alcoholic potassium hydroxide for fifteen minutes, extracted with ether and the solvent was removed and the residue was crystallized from ether, m. p. 170–172°. This is 5,16-pregnadienediol-3(β),20(β); yield 0.8 g.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.7; H, 10.0.

Acetylation gave a diacetate which was crystallized from dilute methanol, m. p. 121°.

Anal. Calcd. for $C_{25}H_{36}O_4$: C, 74.9; H, 9.1. Found: C, 75.0; H, 9.0.

A mixture of 1 g. of the above dienediol, 100 cc. of methanol and 500 mg. of platinum oxide catalyst was shaken with hydrogen at 30 pounds pressure for thirty minutes. The solution was filtered and the solvent removed. The residue was crystallized from acetone, m. p. and mixed m. p. with allo-pregnanediol-3(β),20(β), 194°.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.7; H, 11.3. Found: C, 78.9; H, 11.0.

Summary

Experiments on the conversion of nologenin into pregnane derivatives have been described.

TEXCOCO, MEXICO

RECEIVED MAY 24, 1946

[CONTRIBUTION FROM THE LABORATORY OF BOTANICA-MEX., S. A.]

Steroidal Sapogenins. No. 168. The Structural Relationship of Botogenin. A New Steroidal Sapogenin, to all Other Known Sapogenins

BY RUSSELL E. MARKER[1] AND JOSEFINA LOPEZ

A new steroidal sapogenin, botogenin, has been isolated from the acid hydrolysis mixture of sapogenins of *Dioscorea mexicana*. Removal of its ketonic group by the Wolff–Kishner reaction gave diosgenin. Hydrogenation under mild conditions reduced its double bond to give hecogenin, whereas hydrogenation under more drastic conditions reduced both its double bond and the ketone group to give rockogenin. This shows a structure of 12-keto-diosgenin for botogenin.

The correlation of the structures of the various steroidal sapogenins having the smilagenin or normal side-chain is now established as shown in the accompanying chart. This is self-explanatory from the results given in the experimental part of this paper. The relationship between the structures of mexogenin, samogenin and smilagenin had previously been established.[2]

Experimental

Botogenin.—An alcoholic extract of the saponides of freshly dried *Dioscorea mexicana* was hydrolyzed with hydrochloric acid. The crude sapogenins were extracted with ether and the ethereal solution was washed with sodium hydroxide solution to free of acids. The ether was distilled to a small volume and the crystalline sapogenins were separated by filtration. The mother liquors were concentrated and the residue was hydrolyzed with alcoholic sodium hydroxide. The product was again extracted with ether and a second crop of sapogenins was obtained which were combined with the first. Two kilograms of these crude sapogenins was refluxed for thirty minutes with five liters of acetic anhydride and the mixture was allowed to crystallize overnight at room tem-

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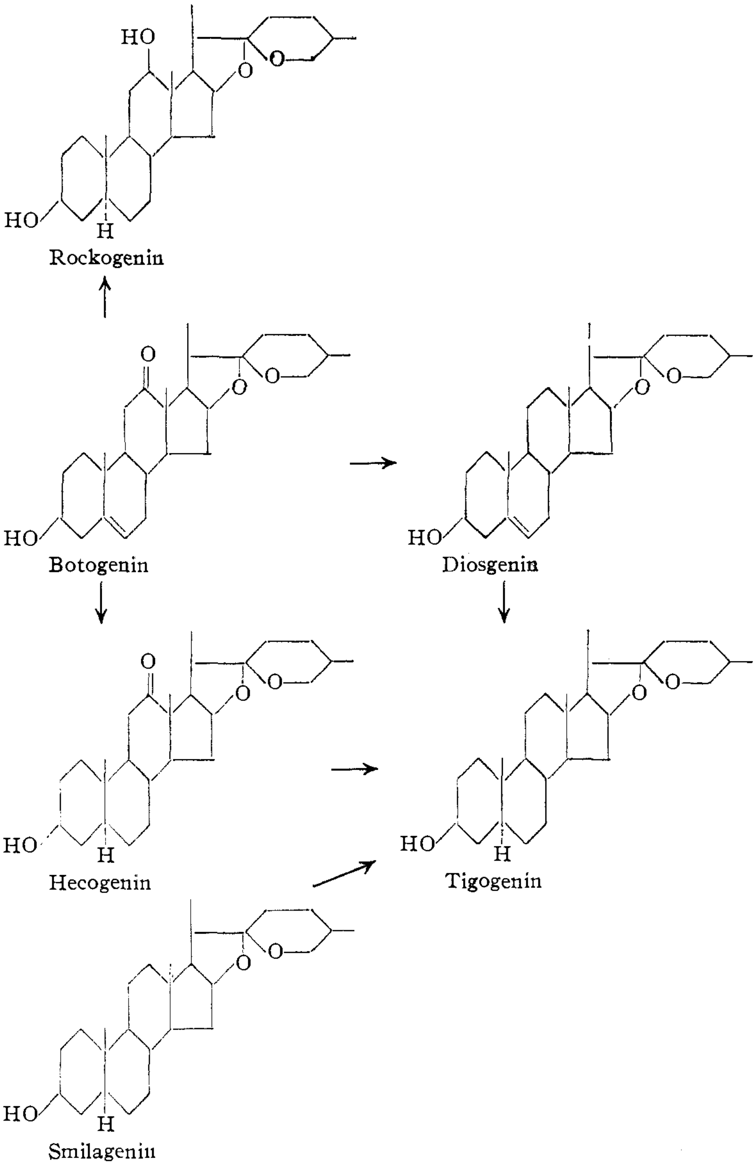
[1] Present address: Hotel Geneve, Mexico City, Mexico.

[2] Marker and Lopez, THIS JOURNAL, **69**, 2373 (1947).



perature and then filtered. The mother liquors were concentrated to about half volume and chilled in ice–salt and filtered. The filtrate from this was distilled *in vacuo* and the residue was hydrolyzed with alcoholic sodium hydroxide. The hydrolyzed product was extracted with ether and combined with the filtrate from the original crude sterols. The solvent was removed and the residue was dissolved in alcohol and treated with Girard reagent to remove the ketonic fraction. The ketonic portion was dissolved in 1 liter of alcohol containing 100 cc. of hydrochloric acid and refluxed for sixty hours to convert any neosapogenins present into those of the diosgenin side-chain configuration. The solution was extracted with ether and the solvent was removed. Upon standing in a refrigerator overnight with a small amount of ether the product crystallized. The solution was filtered and the product was recrystallized again from ether. A mixture of 5 g. of this product and 15 cc. of acetic anhydride was refluxed for twenty minutes and cooled overnight in a refrigerator. The solution was filtered and the product was recrystallized from acetone and from methanol, m. p. 248°.

Anal. Calcd. for $C_{29}H_{42}O_5$: C, 74.0; H, 9.0. Found: C, 74.3; H, 9.2.

Hydrolysis with alcoholic potassium hydroxide and crystallization from ether gave botogenin, m. p. 262°.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 76.0; H, 9.4.

Diosgenin from Botogenin.—To a solution of 4 g. of sodium in 80 cc. of absolute ethanol was added 5 cc. of 85 per cent. hydrazine hydrate and 0.5 g. of botogenin. The product was heated in a bomb tube for twelve hours at 200°. The reaction mixture was poured into water, extracted with ether and the solvent was removed to a small volume. Upon cooling the product crystallized and was filtered. It was recrystallized from acetone and from methanol to give diosgenin, m. p. and mixed m. p. 212–214°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.0; H, 10.0.

Acetylation and crystallization from acetic anhydride and from methanol gave diosgenin acetate, m. p. and mixed m. p. 202–204°.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.2; H, 9.9.

Hecogenin from Botogenin.—A solution of 0.3 g. of botogenin acetate in 200 cc. of ether containing a few drops of acetic acid was shaken with 0.3 g. of platinum oxide catalyst and hydrogen at room temperature and 45 pounds pressure for fifteen minutes. The solution was filtered and the product was crystallized from methanol to give hecogenin acetate, m. p. and mixed m. p. 242°.

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.7; H, 9.4. Found: C, 73.6; H, 9.2.

Hydrolysis with alcoholic potassium hydroxide and crystallization from ether gave hecogenin, m. p. and mixed m. p. 257°.

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.3; H, 9.8. Found: C, 75.3; H, 9.9.

Rockogenin from Botogenin.—An ethereal solution of 0.5 g. of botogenin containing several drops of acetic acid was shaken with hydrogen and 0.5 g. of platinum oxide catalyst for three hours at room temperature and 45 pounds pressure. The solution was filtered and the solvent was removed. The residue was refluxed with acetic anhydride for thirty minutes and the solvent was removed *in vacuo*. The residue was crystallized from methanol, m. p. and mixed m. p with rockogenin diacetate, 206°.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.1; H, 9.4. Found: C, 72.4; H, 9.2.

Hydrolysis with alcoholic potassium hydroxide and crystallization from ether gave rockogenin, m. p. and mixed m. p. 218–220°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.3. Found: C, 75.2; H, 10.4.

Summary

A new steroidal sapogenin, botogenin, has been isolated and its structure and correlation with the other known steroidal sapogenins is established.

TEXCOCO, MEXICO RECEIVED AUGUST 22, 1946