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

Sterols. LXIX. Oxidation Products of Sarsasapogenin. Sarsasapogenoic Acid and Related Substances

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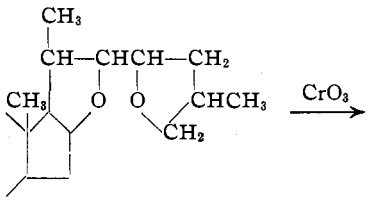
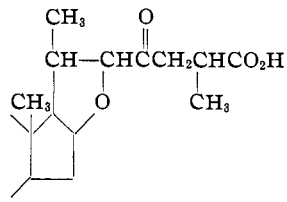
Fieser and Jacobsen[1] in their investigation of the chromic anhydride oxidation products of sarsasapogenin acetate obtained an acid, $C_{27}H_{42}O_5$, which was designated as sarsasapogenoic acid and which is undoubtedly analogous to an acid obtained by Tschesche and Hagedorn[2] by a somewhat similar oxidation of tigogenin acetate. Tschesche and Hagedorn assigned to this the structure of a γ-keto acid, I.



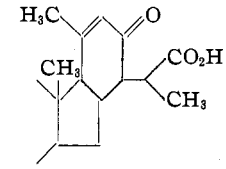
II. Sapogenin Side Chain
(Tschesche and Hagedorn[2])



I. C_{27} Acid

It is evident that this structure is based almost entirely upon the assumption that the sapogenin side chain is correctly represented by II.

While Tschesche and Hagedorn[2] found that the C_{27} acid from tigogenin was inert toward hydrogenation and did not react with carbonyl reagents, Fieser and Jacobsen[1,3] found that sarsasapogenoic acid was somewhat more reactive. Treatment with hydroxylamine at 135° yielded a dioxime. Catalytic hydrogenation gave an acid of the probable composition $C_{27}H_{44}O_4$ designated as anhydrotetra-(or di)-hydrosarsasapogenoic acid. When heated with aqueous alcoholic alkali, sarsasapogenoic acid yielded anhydrosarsasapogenoic acid, $C_{27}H_{40}O_4$, a product which was shown to contain an alpha-beta unsaturated ketone grouping[3,4] and to which structure III was assigned.



III. Anhydrosarsasapogenoic acid
(Fieser and Jacobsen[3])

Fieser and Jacobsen[3] regarded this structure for anhydrosarsasapogenoic acid as secure and offered it as confirmatory evidence in support of the formulations I and II of Tschesche and Hagedorn.[2]

Inasmuch as most of the available evidence now indicates that the sapogenin side chain is not correctly represented by II,[5] it is evident that the structure of the sapogenoic acid is open to serious question. In conformity with our recently proposed structure IV[5] for sarsasapogenin we believe sarsasapogenoic acid to be a diketo acid best represented by V. The two carbonyl groups in such a molecule would be expected to be sterically hindered, which would explain the difficult formation of a dioxime.[3]

The formation of anhydrotetrahydrosarsasapogenoic acid[3] by catalytic hydrogenation of sarsasapogenoic acid is explained by the conversion of the diketone with loss of water to a tetrahydrofuran derivative, VI. This acid appears to be identical with sarsasapogentic acid[5] which we previously prepared by the oxidation of 3-acetoxydihydrosarsasapogenin (VII). This conclusion is based upon a comparison of the free acids, the methyl esters, the methyl ester benzoates and the 3-dehydro acids.

The suggestion of Fieser and Jacobsen[3] that anhydrotetrahydrosarsasapogenoic acid is a saturated γ-keto acid is hardly in accordance with the properties of known γ-keto acids.

Inasmuch as the identity of anhydrotetrahydrosarsasapogenoic acid and sarsasapogentic acid appears to be conclusive, we propose in order to avoid further confusion that the nomenclature of Fieser and Jacobsen[3] be retained and the term sarsasapogentic acid be discontinued.

The difficulty encountered in purification of the hydrogenation product of sarsasapogenoic acid is

(1) Fieser and Jacobsen, THIS JOURNAL, **60**, 28 (1938).
(2) Tschesche and Hagedorn, *Ber.*, **68**, 1412, 2247 (1935).
(3) Fieser and Jacobsen, THIS JOURNAL, **60**, 2753 (1938).
(4) Fieser and Jones, *ibid.*, **61**, 532 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).

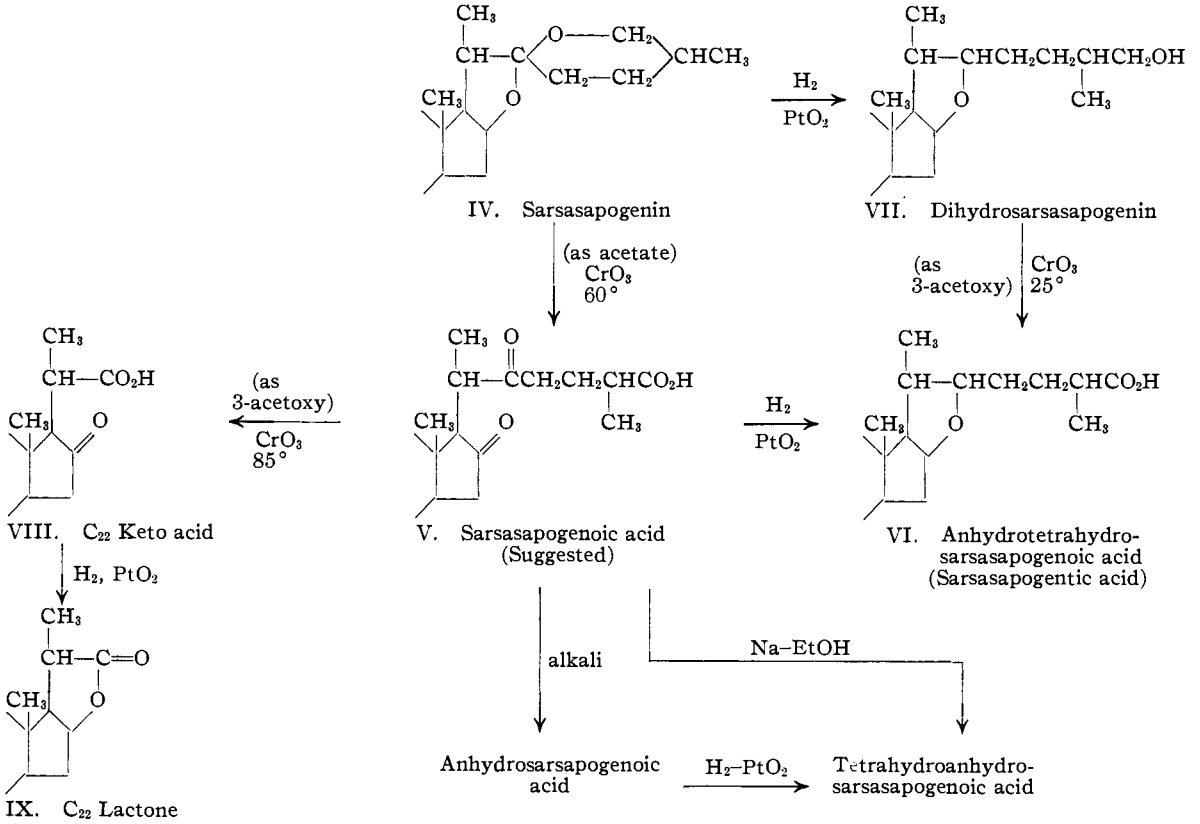
possibly due to the formation of an isomeric mixture which would not be unexpected.

Reduction of sarsasapogenoic acid with sodium and ethanol readily yielded tetrahydroanhydrosarsasapogenoic acid which Fieser and Jacobsen[3] first prepared from anhydrosarsasapogenoic acid by catalytic hydrogenation and by reduction with sodium and *n*-propyl alcohol. Reduction of sarsasapogenoic acid with aluminum isopropylate gave a poor yield of an acidic substance of the probable composition $C_{27}H_{46}O_5$. This reduction product was not studied further.

On mild oxidation with chromic anhydride sarsasapogenoic acid yields 3-dehydrosarsasapogenoic acid, m. p. 163–164°. This acid is very probably identical with an acid of the composition $C_{27}H_{40}O_5$, m. p. 162°, obtained by Jacobs and Simpson[6] by the oxidation of sarsasapogenin with chromic anhydride at 25–30°. The 3-dehydro acid reacts with one mole of bromine to yield a monobromo derivative $C_{27}H_{39}O_5Br$. Sarsasapogenoic acid showed no tendency to react with bromine under similar conditions.

If sarsasapogenoic acid is a γ-keto acid, I, it is obvious that the acid would have to be considered as an intermediate product formed in the oxidation of the sapogenin to the C_{22} lactone (IX). Further oxidation should yield the C_{22} lactone. Fieser and Jacobsen[3] failed to obtain an appreciable neutral fraction when sarsasapogenoic acid acetate was oxidized with chromic anhydride at 95°. By carrying out the oxidation at 85° we were likewise unable to obtain an appreciable neutral fraction. However, a 5% yield of a C_{22} keto acid was obtained. This was identical with the C_{22} keto acid (VIII) previously reported[7] from the chromic anhydride oxidation products of sarsasapogenin acetate. The acid was further identified by its conversion to the C_{22} lactone by catalytic hydrogenation.

Anhydrosarsasapogenoic acid was prepared in 20% yield by allowing sarsasapogenoic acid to stand at 25° for nine hours with aqueous alcoholic potassium hydroxide solution. In preparing anhydrosarsasapogenoic acid by the method of Fieser and Jacobsen,[1] we encountered a more soluble acid (m. p. 184°) having the same composition as the anhydro acid, C_{27}-



(6) Jacobs and Simpson, *J. Biol. Chem.*, **109**, 565 (1935).

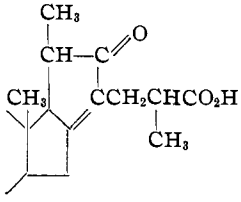
(7) Marker and Rohrmann, THIS JOURNAL, **61**, 1285 (1939).

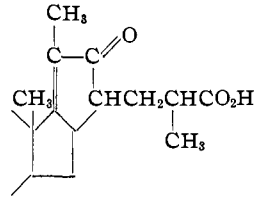
$H_{40}O_4$, m. p. 243°. This isomeric acid on heating with aqueous alcoholic alkali is converted into anhydrosarsasapogenoic acid. This lower melting isomeric acid could not be isolated when the preparation was carried out at 25°, probably due to the presence of unreacted sarsasapogenoic acid which appears to have about the same solubility.

The facile elimination of a molecule of water from sarsasapogenoic acid under the influence of alkali to yield an acid containing an α,β-unsaturated ketone grouping suggests that the reaction involves an intramolecular aldol condensation followed by elimination of a molecule of water.

The fact that anhydrosarsasapogenoic acid gives no semicarbazone under the usual conditions indicates that the carbonyl group is hindered. More difficult to understand is the fact that the acid is not reduced by aluminum isopropylate but this likewise may be attributed to the hindered nature of the group.

At present anhydrosarsasapogenoic acid has not been characterized sufficiently to be assigned a definite structure. However, it seems that the following formulations are the most likely possibilities

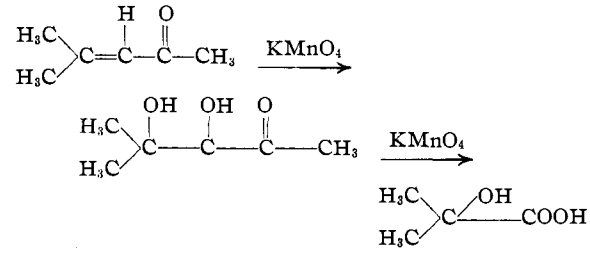




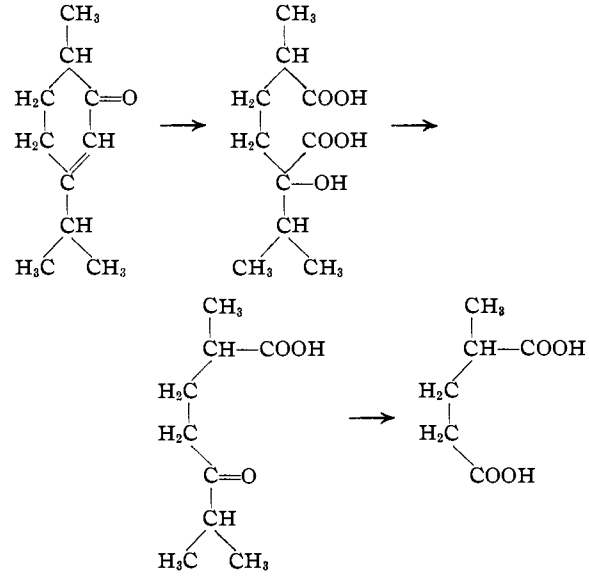
In regard to the composition of the dibasic acid obtained by the permanganate oxidation of anhydrosarsasapogenoic acid,[3] our results indicate quite definitely that the composition of the acid is $C_{27}H_{42}O_7$ and not $C_{27}H_{40}O_7$ as concluded by Fieser and Jacobsen.[3] This conclusion is based on check analyses of the free acid, the dimethyl ester and the dimethyl ester acetate. In addition a number of the analyses reported by Fieser and Jacobsen[3] for the acid and its derivatives are also in accordance with the composition $C_{27}H_{42}O_7$.

There are numerous examples in the literature which indicate that the initial reaction in the oxidation of an α,β-unsaturated ketone with permanganate is the formation of a keto glycol as represented in the oxidation of mesityl oxide.[8] Scission of the carbon–carbon linkage then occurs[9] as indicated, while further oxidation of the hydroxy acid gives further scission.

(8) Harries and Pappos, *Ber.*, **34**, 2979 (1901).
(9) Pinner, *ibid.*, **15**, 591 (1882).



Perhaps a more striking and more pertinent example of the mechanism of permanganate oxidations is afforded by the work of Tiemann and Semmler[10] on the oxidation of carvenone, the reaction going through the stages



A similar case is given by the permanganate oxidation of piperitone.[11]

If structure III proposed for anhydrosarsasapogenoic acid by Fieser and Jacobsen is correct then it appears that permanganate oxidation should yield either a C_{27} tribasic acid or a C_{26} dibasic acid. The fact that a C_{27} dibasic acid is obtained suggests that the double bond links completely substituted carbons.

The amount of data concerning the dibasic acid is far too limited to make possible the assignment of any definite structure for the substance.

We have also investigated incidentally the C_{29} neutral product which Fieser and Jacobsen[1] first reported to be unreacted sarsasapogenin acetate but later[3] recognized as the acetate of a neutral oxidation product of an unknown nature. They

(10) Tiemann and Semmler, *ibid.*, **31**, 2889 (1898).
(11) Simonsen, "The Terpenes," Vol. I, Cambridge University Press, London, 1931, p. 323.

reservedly suggested the substance to be a hydroxysarsasapogenin.

Our analyses of the neutral acetate (m. p. 164°) do not distinguish between $C_{29}H_{44}O_5$ and $C_{29}H_{46}O_5$. In agreement with Fieser and Jacobsen[3] we find that the carbon analyses for the hydrolyzed product (m. p. 217°) are about 0.7% high for the composition $C_{27}H_{44}O_4$.

The neutral acetate readily forms a semicarbazone indicating the presence of a free carbonyl group or possibly of a potential aldehyde group. Reduction of the neutral acetate by the Clemmensen method gave a good yield of tetrahydrosarsasapogenin previously obtained by an analogous reduction of sarsasapogenin.[5] Oxidation of the neutral acetate with chromic anhydride at 80° yielded some of the C_{22} keto acid.[7]

The neutral acetate appeared to be unaffected by catalytic hydrogenation with Adams catalyst in neutral medium while in acidic medium it yielded after hydrolysis a product of the probable composition $C_{27}H_{46}O_4$ or $C_{27}H_{48}O_4$.

The results concerning this neutral substance are difficult to interpret, especially in view of the uncertainty of the analytical data. We feel that the formation of the neutral substance probably represents an important stage of the oxidation of the sapogenin to the various oxidation products. The neutral product was not encountered when the oxidation of sarsasapogenin acetate was carried out at 80–85°.

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

Experimental Part[12]

Reduction of Sarsasapogenoic Acid. (a) By Catalytic Hydrogenation.—Catalytic hydrogenation of sarsasapogenoic acid in acetic acid at 3 atmospheres pressure at 25° with Adams catalyst gave a product which after crystallization from acetone formed white needles, m. p. 180–184°, which agrees with **anhydrotetrahydrosarsasapogenoic acid.**[12] No lactonic material was obtained in the reduction.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 75.0; H, 10.25.

In another preparation the reduction product was crystallized first from acetone and then from aqueous methanol to give flat white needles, m. p. 183–187°. Mixed with a sample of sarsasapogentic acid (m. p. 185–187°) the melting point range was 182–187°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 74.7; H, 10.2.

(12) Compounds previously reported by Fieser and Jacobsen.

With diazomethane anhydrotetrahydrosarsasapogenoic acid yielded a **methyl ester** which was crystallized from ether–pentane as small white plates, m. p. 125–127°. This gave no depression with a sample of the methyl ester of sarsasapogentic acid (m. p. 123.5–126°).

Anal. Calcd. for $C_{28}H_{46}O_4$: C, 75.3; H, 10.4. Found: C, 75.3; H, 10.3.

Anhydrotetrahydrosarsasapogenoic acid when treated with chromic anhydride in acetic acid at room temperature for one hour gave **3-dehydroanhydrotetrahydrosarsasapogenoic acid** which after treatment with Norite was crystallized from acetone as white needles, m. p. 196–199°. This gave no depression with a sample of 3-dehydrosarsasapogentic acid.[5]

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.3; H, 9.8. Found: C, 75.1; H, 9.9.

Anhydrotetrahydrosarsasapogenoic acid with benzoyl chloride in pyridine gave the **methyl ester, benzoate,**[12] m. p. 140–141.5°.

Anal. Calcd. for $C_{35}H_{50}O_5$: C, 76.3; H, 9.15. Found: C, 76.0; H, 9.1.

The methyl ester of sarsasapogentic acid with benzoyl chloride in pyridine yielded a **methyl ester benzoate** which after sublimation in high vacuum at 140–180° was crystallized from methanol as small white plates, m. p. 139–141°. This gave no depression with the methyl ester benzoate of the anhydrotetrahydro acid described above.

Anal. Calcd. for $C_{35}H_{50}O_5$: C, 76.3; H, 9.15. Found: C, 76.2; H, 9.2.

(b) **With Sodium and Ethanol.**—To a boiling solution of 500 mg. of sarsasapogenoic acid in 150 cc. of absolute ethanol was added 12 g. of sodium over a period of two hours. The solution was cooled, diluted with water, acidified with hydrochloric acid and the precipitated solid extracted with ether. The residue remaining upon evaporation of the ether was crystallized from ether–acetone–pentane as small white needles, m. p. 179–181° dec. This gave no depression with a sample of tetrahydroanhydrosarsasapogenoic acid[12] (m. p. 179–181°) obtained by the catalytic hydrogenation of anhydrosarsasapogenoic acid.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 74.9; H, 10.2.

(c) **With Aluminum Isopropylate.**—A solution of 600 mg. of sarsasapogenoic acid and 1 g. of aluminum isopropylate in 30 cc. of isopropyl alcohol was refluxed for fifteen hours. The solvent was then distilled off over a period of one hour. The residual material yielded a product which crystallized from ether–pentane as compact white crystals, m. p. 206–208° dec.

Anal. Calcd. for $C_{27}H_{44}O_5$: C, 72.3; H, 9.9. Calcd. for $C_{27}H_{46}O_5$: C, 71.95; H, 10.3. Found: C, 71.9, 71.9; H, 10.2, 10.3.

3-Dehydrosarsasapogenoic Acid.—To a solution of 500 mg. of sarsasapogenoic acid in 30 cc. of glacial acetic acid was added a solution of 300 mg. of chromic anhydride in 10 cc. of 80% acetic acid. The mixture was allowed to stand at room temperature for thirty minutes. Dilution with water gave a solid which was taken up in ether, treated with Norite and crystallized from ether–pentane as small white plates, m. p. 162–164°.

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

With an ethereal solution of diazomethane the acid yielded a **methyl ester** which crystallized from ether–pentane as white needles, m. p. 125°.

Anal. Calcd. for $C_{28}H_{44}O_5$: C, 73.0; H, 9.6. Found: C, 73.0; H, 9.3.

3-Dehydro-4-bromosarsasapogenoic Acid.—To a solution of 1.2 g. of 3-dehydrosarsasapogenoic acid in 30 cc. of acetic acid acidified with a few drops of 48% hydrobromic acid was added 2.7 cc. of 1.05 *M* bromine in acetic acid. The solution was diluted with water and the precipitated solid collected, washed with water and dried. After treatment with Norite the substance was crystallized from acetone to give white crystals, m. p. 188.5–191°.

Anal. Calcd. for $C_{27}H_{39}O_5Br$: C, 61.9; H, 7.5. Found: C, 61.4; H, 7.3.

3-Dehydro-$\Delta^{4,5}$-sarsasapogenoic Acid.—A solution of 800 mg. of the 3-dehydro-4-bromo acid in 20 cc. of dry pyridine was refluxed for six hours. The solution was poured into an excess of dilute sulfuric acid and the precipitated solid taken up in ether. The material was crystallized from acetone–ether as white plates, m. p. 199–201°.

Anal. Calcd. for $C_{27}H_{38}O_5$: C, 73.25; H, 8.7. Found: C, 73.4; H, 8.5.

Oxidation of Sarsasapogenoic Acid Acetate.—A solution of 5 g. of chromic anhydride in 30 cc. of 80% acetic acid was added dropwise with stirring over a period of ninety minutes to a solution of 2.5 g. of sarsasapogenoic acid acetate in 60 cc. of glacial acetic acid at 80–85°. The stirring and heating were continued for an additional two hours after which the mixture was evaporated *in vacuo* to 40 cc. The residue was diluted with water and extracted with ether. The ethereal extract, after thorough washing with water, was washed with 3% sodium hydroxide solution. Evaporation of the remaining ethereal extract gave an insignificant amount of neutral material which was not investigated further.

The sodium hydroxide extract was warmed on the steam-bath for fifteen minutes to hydrolyze any remaining acetates. The solution was then cooled, acidified with hydrochloric acid and the precipitated gum extracted with ether. The ethereal extract was washed with water and the ether allowed to evaporate to a volume of 20 cc. at room temperature over a period of three days. At the end of this time compact white crystals separated. These were collected, washed with ether and crystallized from methanol–ether to give a product, m. p. 287° dec. This gave no depression with an authentic sample of the C_{22} keto acid previously described.[7]

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.5; H, 9.5.

When shaken with hydrogen (3 atm.) and Adams catalyst in ethanol solution the keto acid yielded a neutral product, m. p. 199–201°. This gave no depression with an authentic sample of the hydroxy lactone of sarsasapogenin.

Anhydrosarsasapogenoic Acid.[12]—A solution of 500 mg. of sarsasapogenoic acid in 5 cc. of ethanol and 10 cc. of 30% aqueous potassium hydroxide solution was allowed to stand at room temperature for nine hours. The solution was then diluted with water, acidified with hydrochloric acid and the precipitated solid taken up in ether. Evaporation of the ether yielded a product which was crystallized from ether–chloroform to give compact white crystals (150 mg.), m. p. 242–244° dec.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.4, 75.3; H, 9.2, 9.4.

Catalytic hydrogenation of the anhydro acid in ethanol with Adams catalyst yielded **tetrahydroanhydrosarsasapogenoic acid,**[12] m. p. 179–181°. In another preparation the acid was obtained as white needles, m. p. 194–196°. This gave no depression with the lower melting product.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 74.8; H, 10.1.

When anhydrosarsasapogenoic acid was refluxed with semicarbazide hydrochloride and sodium acetate in 85% ethanol solution for one hour the acid was recovered unchanged. Anhydrosarsasapogenoic acid was also recovered unchanged after refluxing for fourteen hours with aluminum isopropylate and dry isopropyl alcohol.

Anhydrosarsasapogenoic acid was also prepared as described by Fieser and Jacobsen.[1] The filtrate remaining after removal of the anhydro acid yielded a relatively soluble isomeric acid, which crystallized from ethyl acetate–ether as compact white crystals, m. p. 181–184° dec. (gas). The yield was less than that of the anhydro acid.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.4; H, 9.4.

A mixture of 500 mg. of this isomeric acid, 60 cc. of 95% ethanol, 2 cc. of water, and 200 mg. of sodium hydroxide was refluxed for two hours. The product was worked up as described for anhydrosarsasapogenoic acid to yield 200 mg. of compact white crystals, m. p. 241–243°. This gave no depression with anhydrosarsasapogenoic acid.

Attempts to prepare a crystalline acetate, methyl ester, or methyl ester acetate of the isomeric acid were unsucessful. The acid readily reacted with alkaline potassium permanganate at 0°, but no crystalline products were obtained. Catalytic hydrogenation in ether–ethanol at three atmospheres pressure gave a non-crystalline product.

Dibasic Acid.[12]—The dibasic acid was prepared as described by Fieser and Jacobsen.[3]

Anal. Calcd. for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Calcd. for $C_{27}H_{42}O_7$: C, 67.74; H, 8.84. Found: C, 67.40, 67.68; H, 8.94, 8.80.

An attempt to prepare a crystalline acetate by heating with acetic anhydride was unsuccessful.

The acid appears to be altered by treatment with periodic acid in methanol solution at room temperature for eighteen hours but no crystalline products were isolated even after sublimation in high vacuum. Treatment of the dibasic acid with chromic anhydride at 20° for fifteen hours in acetic acid gave a gum which did not crystallize even after sublimation in high vacuum.

The acid was recovered unchanged after treatment with semicarbazide acetate under the usual conditions.

When subjected to catalytic hydrogenation in ethanol–ether with Adams catalyst at 3 atmospheres pressure for fourteen hours the acid was recovered unchanged. Hydrogenation in ethanol acidified with hydrochloric acid with Adams catalyst at 3 atmospheres pressure for twenty-four hours gave a sirup which could not be crystallized.

The acid gave a **dimethyl ester,**[12] m. p. 161–162°.

Anal. Calcd. for $C_{29}H_{44}O_7$: C, 69.0; H, 8.79. Calcd. for $C_{29}H_{46}O_7$: C, 68.73; H, 9.15. Found: C, 68.63, 68.58; H, 9.20, 9.21.

Treatment of the dimethyl ester with boiling acetic anhydride for twenty minutes gave a product which was crystallized from ether–pentane to give long white needles of the **dimethyl ester acetate,** m. p. 158–160°.

Anal. Calcd. for $C_{31}H_{46}O_8$: C, 68.10; H, 8.47. Calcd. for $C_{31}H_{48}O_8$: C, 67.85; H, 9.01. Found: C, 67.74, 67.93; H, 8.93, 8.91.

C_{27} Neutral Oxidation Product from Sarsasapogenin.—The neutral fraction obtained in the chromic anhydride oxidation of sarsasapogenin acetate was crystallized from acetone to give white needles, m. p. 162–164°, of a **neutral acetate.**[12]

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.65; H, 9.4. Calcd. for $C_{29}H_{46}O_5$: C, 73.4; H, 9.8. Found: C, 73.2; H, 9.7.

Hydrolysis of this product with an excess of ethanolic potassium hydroxide gave the **3-hydroxy compound**[12] which crystallized from acetone as small white plates, m. p. 215–217°.

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.3; H, 9.85. Calcd. for $C_{27}H_{44}O_4$: C, 74.9; H, 10.2. Found: C, 75.6, 75.7; H, 10.0, 10.1.

The neutral acetate when treated with semicarbazide hydrochloride under the usual conditions gave a **semicarbazone** which crystallized from acetone as small white needles, m. p. 249–251° dec.

Anal. Calcd. for $C_{30}H_{47}O_5N_3$: C, 68.0; H, 9.0; N, 7.9. Calcd. for $C_{30}H_{49}O_5N_3$: C, 67.75; H, 9.3; N, 7.9. Found: C, 67.5, 67.5; H, 8.9, 8.7; N, 7.6.

Reduction of C_{27} Neutral Oxidation Product. (a) **By Catalytic Hydrogenation.**—A mixture of 1.5 g. of the neutral acetate, 1 g. of Adams catalyst, 100 cc. of glacial acetic acid and 30 cc. of 99% ethanol was shaken with hydrogen at 3 atmospheres pressure at 25° for fourteen hours. The mixture was filtered and the filtrate diluted with water, the precipitated solid was extracted with ether and the ethereal extract washed with sodium carbonate solution. The ether was evaporated and the residue refluxed for twenty minutes with an excess of ethanolic potassium hydroxide. The product was crystallized from methanol–ethanol as white plates, m. p. 215–217°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.9; H, 10.3. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Calcd. for $C_{27}H_{48}O_4$: C, 74.26; H, 11.1. Found: C, 74.6, 74.4; H, 10.7, 10.9.

The neutral acetate was recovered unchanged after shaking with Adams catalyst and hydrogen at 3 atmospheres pressure for six hours at 28° in ethanol solution.

(b) **By Clemmensen Reduction.**—To a boiling solution of 300 mg. of the neutral acetate in 100 cc. of 95% ethanol with 20 g. of amalgamated 20-mesh zinc was added 16 cc. of concentrated hydrochloric acid over a period of nine hours. The solution was decanted into water and the precipitated solid extracted with ether. The ether was evaporated and the residue crystallized from acetone–ethyl acetate to give 200 mg. of compact white crystals, m. p. 191–193°. This gave no depression with a sample of tetrahydrosarsasapogenin.

Anal. Calcd. for $C_{27}H_{48}O_3$: C, 77.1; H, 11.5. Found: C, 76.8; H, 11.5.

Summary

The structure of sarsasapogenoic acid and its transformation products is discussed in terms of the ketone spiro acetal structure for the sapogenin side chain.

STATE COLLEGE, PENNA. RECEIVED MAY 3, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Gossypol. XXII. Gossypol Ethers and their Reduction Products[1]

BY ROGER ADAMS AND W. R. DIAL[2]

Gossypol hexamethyl ether[3] was one of the most important gossypol derivatives since it served as the compound from which many significant degradation products were obtained.[4] It was assigned the structure I on the basis of its reactions with a drop of sulfuric acid in acetic acid to give gossypol dimethyl ether (II), with phenylhydrazine in glacial acetic acid to give a phenylhydrazone of a gossypol tetramethyl ether (III), which on treatment with methanolic or ethanolic hydrogen chloride reverted to gossypol hexamethyl ether (I) or gossypol tetramethyl diethyl ether (IV).[5]

The study of gossypol ethers has now been extended to a variety of others. Gossypol tetramethyl ether (V)[3] has been ethylated to gossypol diethyl tetramethyl ether (VI), isomeric with IV. This same ether (VI) was also prepared by methylation of gossypol diethyl ether (VII).[5]

The new ether (VI) formed a phenylhydrazone of gossypol dimethyl diethyl ether which with methanolic hydrogen chloride gave back VI or

(1) For previous paper see Adams and Baker, THIS JOURNAL, **61**, 1138 (1939).

(2) Dow Chemical Company Fellow, 1936–1939.

(3) Adams, Geissman and Morris, THIS JOURNAL, **60**, 2967 (1938).

(4) Adams, Morris, Geissman, Butterbaugh and Kirkpatrick, *ibid.*, **60**, 2193 (1938).

(5) Adams and Geissman, *ibid.*, **60**, 2166 (1938).