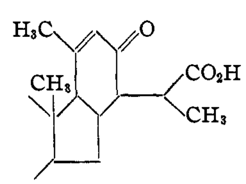
sarsasapogenoic acid it is concluded that the latter substance is an unsaturated γ-keto acid containing the grouping shown. The sapogenin and the sapogenoic acid very probably are correctly represented by the formulas of Tschesche and Hagedorn.



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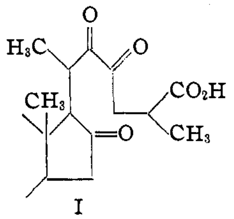
Sarsasapogenin. III. Concerning Desoxysarsasapogenin and the Degradation of the C_{22}-Hydroxy Lactone

BY LOUIS F. FIESER AND ROBERT P. JACOBSEN[1]

Simpson and Jacobs[2] prepared desoxysarsasapogenin by reduction of the sapogenyl chloride with sodium and amyl alcohol, but the over-all yield from the sapogenin was only about 14% and the method was employed only after other possible methods of removing the hydroxyl group had been considered and abandoned as unsatisfactory. Attempted reduction of sarsasapogenone by the Wolff–Kishner method was unsuccessful, and Clemmensen reduction of the ketone was considered unsuitable because of the known sensitivity of the side chain to acids.[3] In our experiments on the acid cleavage of the side chain,[4] we had observed that this sensitivity is manifested particularly when acetic acid is employed as the solvent but that cleavage occurs much less readily in alcoholic solution. It therefore seemed possible that with this solvent reduction of the ketone might be accomplished at an acidity below that at which cleavage occurs. It was also thought that the addition of an immiscible solvent, as in Martin's[5] procedure, might provide added protection for the sensitive steroid. These hopes were realized, for on refluxing sarsasapogenone for five days with amalgamated zinc in a two-phase medium of alcohol, benzene, and 6 *N* hydrochloric acid, pure desoxysarsasapogenin was obtained in an over-all yield of 43.5% from sarsasapogenin.

The comparatively simple new method of preparing the desoxysapogenin may have other applications, and this consideration has prompted us to report the observation at the termination of the fellowship work of the junior author, even though the investigation of the desoxy compound has not yet reached a very advanced stage. In connection with our work on the oxidation of sarsasapogenin acetate,[4,6] we hoped to extend a brief observation of Simpson and Jacobs[2] and gain further information concerning the acidic substances resulting from the oxidation of desoxysarsasapogenin with chromic acid. Simpson and Jacobs were interested chiefly in the lactone $C_{22}H_{34}O_2$, which they obtained in 15–18% yield on conducting the reaction at 75°, but they investigated incidentally the acidic material encountered as a by-product. Neither the acidic product nor the material obtained from it on esterification yielded homogeneous crystals, but the oily ester on reaction with semicarbazide acetate gave in very small yield a pure substance having the composition of the disemicarbazone methyl ester of an acid characterized by the analyses as either $C_{27}H_{40}O_5$ or $C_{27}H_{42}O_5$. Simpson and Jacobs were inclined to accept the first formula and to regard the oxidation product as a triketo acid with one inert carbonyl group, as in I. A similar oxidation product of sarsasapogenin acetate was isolated by Farmer and Kon[7] as the methyl ester acetate, apparently of the acid $C_{27}H_{40}O_6$. We conducted the oxidation at the



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[1] Du Pont Research Fellow.

[2] Simpson and Jacobs, *J. Biol. Chem.*, **110**, 565 (1935).

[3] Jacobs and Simpson, *ibid.*, **105**, 501 (1934).

[4] Fieser and Jacobsen, THIS JOURNAL, **60**, 28 (1938).

[5] Martin, *ibid.*, **58**, 1438 (1936).

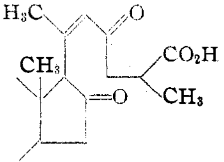
[6] Fieser and Jacobsen, *ibid.*, **60**, 2753 (1938).

[7] Farmer and Kon, *J. Chem. Soc.*, 414 (1937).

lower temperature of 60–65° and from the neutral fraction isolated the desoxy lactone $C_{22}H_{34}O_2$[8] in 13% yield. The acidic fraction afforded two crystalline products. One of these was obtained in amounts too small for thorough purification but corresponded approximately in composition to a desoxysarsasapogenoic acid ($C_{27}H_{42}O_4$).

The other substance, isolated in 20% yield as flat needles, m. p. 111°, is a monobasic acid of the formula $C_{27}H_{42}O_5$. The composition is that of a hydroxydiketo acid, and this formula was recognized by Simpson and Jacobs as an alternative possibility for the substance which they characterized as the methyl ester disemicarbazone. It is doubtful, however, that our acid is the substance which they characterized, for the behavior toward carbonyl reagents is quite different. Our acid with diazomethane gave a crystalline anhydro ester, a molecule of water being eliminated in the process, and the pure ester gave no crystalline product on prolonged refluxing with semicarbazide acetate in methanol, in contrast to the behavior of the crude ester investigated by Simpson and Jacobs. The anhydro ester liberates approximately one mole of methane in the Zerewitinoff test. Our acid was found to react with hydroxylamine at 100°, but the product proved to be an anhydro-monoxime.

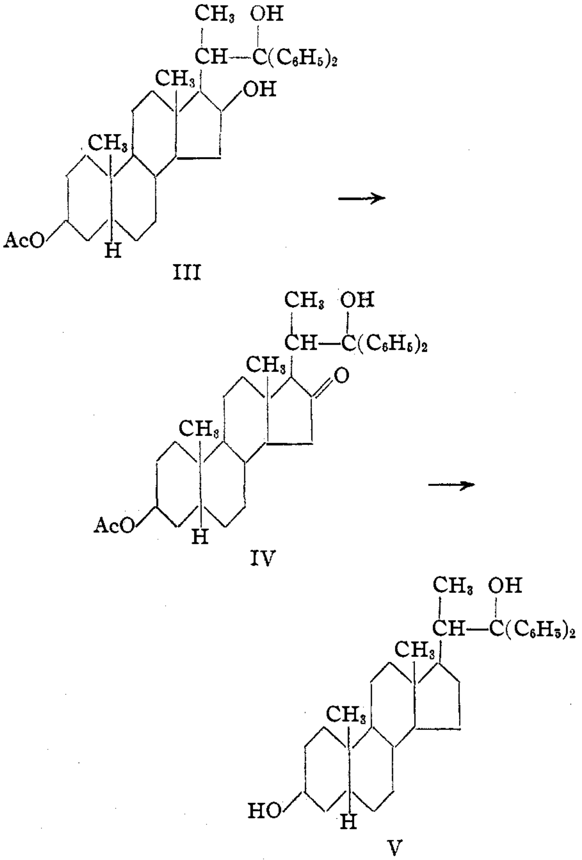
The interesting oxidation product gave no crystalline material on attempted acetylation, and was recovered unchanged after being heated with acetic–hydrochloric acid or with *o*-phenylenediamine. It decolorizes permanganate on warming, but not in the cold. The formation of an anhydro ester and an anhydro oxime may mean that the substance contains an easily eliminated hydroxyl group, but it seems unlikely that dehydration of an alcoholic group should occur on treatment with diazomethane in ether but not on refluxing with an acetic–hydrochloric acid mixture. The low-melting acid more probably is a hydrate, possibly of the unsaturated diketo acid II.



II

The behavior of the anhydro ester in the Zerewitinoff test would then be attributable to enolization, and some analogy for the failure of a carbonyl group at C_{16} to exhibit normal response to typical reagents is furnished by the results of the following series of experiments.

A Grignard degradation of the hydroxy lactone $C_{22}H_{34}O_3$ was carried in Part I[4] to the stage of a diphenylcarbinol monoacetate of the probable structure III (position of the substituent in Ring A still uncertain), only the less hindered secondary hydroxyl group at C_3 being acetylated in pyridine solution. Under controlled conditions (20–25°) it has been possible to oxidize this compound to a monoketone (IV) in good yield.



III

IV

V

This substance failed to form an oxime or semicarbazone under the usual conditions. Clemmensen reduction gave a desoxy diphenyl carbinol of the probable formula V, but the yield was so low that the degradation could not be carried further with the amount of material available.

Experimental Part[9]

Desoxysarsasapogenin.—The crude sarsasapogenone prepared from 15 g. of sarsasapogenin by the method of

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[8] The formula was incorrectly written as $C_{22}H_{36}O_2$ in Part I,[4] p. 31.

[9] All melting points are corrected. Analyses by Mrs. G. M. Wellwood, Mrs. Verna R. Keevil, the Arlington Laboratories, and Lyon Southworth.

Simpson and Jacobs[10] was dissolved in 150 cc. of benzene and refluxed for seventy hours with 75 g. of zinc (amalgamated with 7.5 g. of mercuric chloride), 50 cc. of 6 *N* hydrochloric acid, and 50 cc. of alcohol, with the addition at five- to ten-hour intervals of 5-cc. portions of concentrated hydrochloric acid. The benzene layer was separated and combined with benzene extracts of the aqueous layer. After washing the benzene solution with water and concentrating it to a volume of about 150 cc., the reduction was continued, using 25 g. of amalgamated zinc to supplement the unused metal from the first treatment and adding fresh concentrated acid. After refluxing for fifty hours more, the benzene layer was washed and concentrated. On adding alcohol to the concentrated benzene solution, there was obtained 7.4 g. of crude desoxysarsasapogenin in the form of diamond-shaped plates, m. p. 209–216°. The mother liquors yielded only a sticky gum readily soluble in alcohol. One further crystallization of the solid product from benzene–alcohol gave 6.3 g. of material, m. p. 214–217°; yield from sarsasapogenin, 43.5%. Simpson and Jacobs[2] report the melting point 216–217°.

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.64; H, 10.76.

Oxidation of Desoxysarsasapogenin.—A suspension of 5.1 g. of the desoxysapogenin in 400 cc. of glacial acetic acid was stirred mechanically and treated with a solution of 4.3 g. of chromic anhydride in 75 cc. of 80% acetic acid, keeping the temperature at 60–65°. The addition was completed in one-half hour, and stirring was continued for one and one-quarter hours longer. The mixture was poured into water, and after standing overnight the gummy solid which separated was taken into ether. The ethereal solution was washed thoroughly with water and extracted with dilute sodium hydroxide solution. The alkaline extract was washed once with ether and acidified, and the precipitated solid was dried over sulfuric acid in vacuum. Crystallized from dilute acetone, this yielded 1.2 g. of small leaves of acidic material, m. p. 103–106°. When treated with cold methanol, a very small amount of amorphous solid remained undissolved. (When purified partially by crystallization from dilute acetone, this material, m. p. 218–220°, corresponded most nearly in composition to desoxysarsasapogenoic acid, calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.87; H, 9.02.) The solution was concentrated and a few drops of water added, and on cooling, the pure **desoxy acid** separated in the form of flat needles (1.15 g.), m. p. (well dried) 108–111°. There was no change in melting point after two further crystallizations from aqueous methanol. The sample for analysis was dried at 80° (18 mm.) over phosphorus pentoxide.

Anal. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48; neut. equiv., 447. Found: C, 72.49, 72.23; H, 9.80, 9.56; neut. equiv., 447.

The acid is saturated to alkaline permanganate in the cold but rapidly decolorizes the reagent on warming. Attempted acetylation gave a gummy product. The substance was recovered unchanged after heating with *o*-phenylenediamine in alcoholic solution and also after being refluxed with acetic acid (10 cc.) and concentrated hydrochloric acid (2 cc.). It does not reduce Tollens' reagent.

The ethereal solution containing the neutral fraction was evaporated and the residue crystallized from benzene–alcohol. The first material separating was crude desoxysarsasapogenin, amounting to 0.75 g., and after this had been removed the residue from the mother liquor was dissolved in hot aqueous methyl alcoholic sodium hydroxide and heated for twenty minutes on the steam-bath. The alkaline solution was diluted with water, filtered hot through a thin layer of Norite, cooled, and acidified. The precipitated solid on crystallization from aqueous methanol gave 0.55 g. (13%) of flat needles, m. p. 125.5–127.5°, and a further crystallization raised the melting point to 127–129°. This gave no depression when mixed with the sample of the desoxy lactone $C_{22}H_{34}O_2$, m. p. 129.3–130.5°, prepared in our earlier work.[4]

Anhydro-methyl Ester of the Desoxy Acid.—The acid (200 mg.) was treated with excess diazomethane in ether and the crude product left on evaporation of the solvent melted at 74–76°. Crystallized from dilute methanol, this was obtained in the form of thin, glistening leaves, m. p. 78.5–79.5°.

Anal. Calcd. for $C_{28}H_{42}O_4$: C, 75.97; H, 9.57. Found: C, 75.97, 75.79; H, 9.96, 9.91.

The ester was recovered unchanged after short heating with acetic anhydride and potassium acetate. In a Zerewitinoff determination it liberated 0.63 mole of methane. In an attempt to prepare a semicarbazone the ester was heated on the steam-bath for seventeen hours with semicarbazide acetate in methanol, but no crystalline product was obtained.

Anhydro-oxime from the Desoxy Acid.—This was obtained by heating 200 mg. of the acid with hydroxylamine acetate in absolute methanol in a sealed tube at 100° for two hours. The gummy solid separating on dilution with water was dried and taken up in ether; on standing there separated 60 mg. of crystalline solid, m. p. 177–178°, dec. This material, which is very sparingly soluble in ether, was crystallized repeatedly from acetone and gave in poor yield small leaves melting with decomposition at 193–195° in a bath preheated to 188°. On rapid heating, starting with a cold bath, the substance began to turn brown at about 178° and melted at 189–191°, dec.

Anal. Calcd. for $C_{27}H_{41}O_4N$: C, 73.10; H, 9.32; N, 3.16. Found: C, 72.58; H, 9.72; N, 3.76.

Oxidation of the Monoacetate of the Diphenyl Carbinol $C_{34}H_{46}O_3$: Ketone Acetate IV.—A solution of 650 mg. of the previously described[4] monoacetate (III, m. p. 189–190°) in 50 cc. of glacial acetic acid was stirred at 20–25° and treated with 100 mg. of chromic anhydride in 10 cc. of 90% acetic acid, added in ten minutes. After ten minutes more the mixture was poured into cold water and the collected solid was washed, dried, and crystallized from ether–petroleum ether, giving 500 mg. of silky needles, m. p. 156–159°. After a further crystallization from ether–hexane the **ketone acetate** melted at 157–159° (well dried).

Anal. Calcd. for $C_{36}H_{46}O_4$: C, 79.67; H, 8.54. Found: C, 79.56; H, 8.90.

Attempts to prepare an oxime or semicarbazone were

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(10) Simpson and Jacobs, *J. Biol. Chem.*, **109**, 573 (1935).

unsuccessful. Reduction with hydrazine according to Staudinger[11] was tried without success.

Clemmensen Reduction of the Ketone Acetate: Desoxy Diphenyl Carbinol V.—The above ketone acetate (390 mg.) was refluxed for seven hours with 1.2 g. of amalgamated zinc in 25 cc. of alcohol and 7 cc. of 8 *N* hydrochloric acid. The solid material obtained on diluting the filtered solution with water yielded no crystals and was refluxed for one-half hour with alcoholic alkali for saponification. The solid which precipitated on dilution was dried and crystallized from ether–hexane, the solution depositing glistening prisms mixed with slightly gummy, fine, felt-like needles. The prisms were separated mechanically (m. p. 224–226°) and recrystallized repeatedly from ether–hexane, giving 20 mg. of satisfactory material, m. p. 226–228° (well dried). The composition is approximately that of the desired **desoxy diphenyl carbinol.**

Anal. Calcd. for $C_{34}H_{46}O_2$: C, 83.90; H, 9.53. Found: C, 84.26; H, 9.04.

The slightly gummy needles (180 mg.) could not be freed completely from the above material by repeated crystallization from ether–hexane. Acetylation gave a resin and this on saponification gave an intractable mixture separating from methanol in clusters of small needles and soft wax-like nodules.

Summary

Conditions have been found for the reduction of sarsasapogenone to desoxysarsasapogenin in good yield by the Clemmensen method without alteration of the side chain. A preliminary account is given of a new C_{27}-acid obtained by the oxidation of desoxysarsasapogenin with chromic acid, and further observations are reported on the degradation of the hydroxy lactone $C_{22}H_{34}O_3$.

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[11] Staudinger, *Ber.*, **44**, 2204 (1911).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

Heats of Organic Reactions. VII. Addition of Halogens to Olefins

BY JOHN B. CONN, G. B. KISTIAKOWSKY AND ELGENE A. SMITH

It has been shown in the earlier papers of this series[1] that the heats of addition of hydrogen to the olefinic bond vary in a regular manner with the constitutional make-up of the rest of the molecule. It seemed highly desirable to investigate whether these variations are specific for hydrogenations or are characteristic generally of addition reactions opening the ethylenic bond. The reaction with halogens was selected to test the question because of its convenience and the lack of accurate combustion data on dihalides. Another reaction considered, the addition of hydrogen halides, had to be discarded because we were unsuccessful in creating catalytic conditions under which this reaction occurs rapidly in the gas phase at temperatures below *ca.* 150°, the upper limit of usefulness of the present calorimeter. The results to be presented here unfortunately are neither as reliable nor as extensive as those on the heats of hydrogenation; nevertheless, even allowing for all possible errors, they are many times more accurate than the available combustion data.

Method and Compounds

The calorimeter itself and the general procedure were the same as described in the first paper of this series and only changes need to be recorded.

To avoid premature reaction, bromine or chlorine was carried to the calorimeter through a separate conduit in a stream of inert gas and mixed with excess hydrocarbon in the catalyst chamber within the calorimeter. Upon reaction and heat exchange the gases passed through a valve which directed the stream either to a cold trap for collection of a sample and tests for completeness and cleanliness of the reaction (in the fore- and after-periods), or, during the calorimetric run, to a jet where the gases were burned in excess oxygen and the halogens determined as such and as hydrogen halides.

The halogens were contained in an efficient spiral bubbler, kept at constant temperature (ice for bromine, Dry-Ice and alcohol for chlorine), through which passed a metered stream of inert gas (carbon dioxide with bromine, argon with chlorine).[2] Frequently additional inert gas was by-passed around the bubbler and added to the main gas stream to dilute the reaction mixture and so avoid the condensation of the product in the calorimeter. The hydrocarbon vapor also was metered, so that a condition of constant gas flow prevailed in the calorimeter during a run.

Several substances have been tried for their catalytic effect on the halogenation reaction, the choice being finally calcium bromide and calcium chloride for the bromination and the chlorination, respectively. Glass wool, asbestos, platinized asbestos, ferric halides, bismuth halides and activated charcoal were also experimented with but discarded either because of insufficient activity at the temperatures in question (around 100°) or because substitution reactions took place with the hydrocarbons used. The catalysts were made by evaporating a solution of cal-

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[1] THIS JOURNAL, **57**, 65 (1935); **57**, 876 (1935); **58**, 137 (1936); **58**, 146 (1936); **59**, 831 (1937); **60**, 440 (1938).

[2] Nitrogen had to be avoided since nitrogen oxides are formed in the free flame used in the analytical system, and disturb the analysis.