but contraction begins at a pressure of about 15 dynes per centimeter and at higher pressures the film collapses. However, it remains mobile as shown by dusting with talc, even at 32 dynes per centimeter.

The data for gitogenin (curve II) were obtained using a sample kindly supplied to us several years ago by Dr. W. A. Jacobs of the Rockefeller Institute for Medical Research. The value of 39.5 Å. for the area per molecule at zero pressure is identical with that obtained previously[2] and served to check our technique and procedure. Evidently under pressure the molecules of chlorogenin can be made to stand on end and occupy an area very close to that occupied by gitogenin, thus furnishing additional evidence for the close relationship in the structure of these two compounds.

Chlorogenin diacetate gives a curve, III, which is very similar to that for chlorogenin except that the lower attraction of the acetate groups for water is manifest in the greater tendency to remain in the gaseous state and the greater instability of the close packed film. The diketone obtained by the oxidation of chlorogenin (curve IV) shows no tendency to form a close packed film but collapses at pressures of about 6 dynes per centimeter.

Experimental

The surface pressures were measured on a Cenco Hydrophil Balance by the general procedure developed by Adam and his co-workers.[3] The solvent used was a mixture of eight parts by volume of purified cyclohexane and two parts of purified dioxane. From 0.01 to 0.02 g. of compound was weighed accurately into a tared glass-stoppered 25-cc. Erlenmeyer flask and dissolved in 10–20 cc. of solvent with warming if necessary. After cooling to room temperature the flask was stoppered and the weight of solvent determined.

For placing the solution on the surface a 1-cc. ground-glass syringe was used, whose tip was drawn out and ground so that small drops would form and leave the pipet without wetting the outer surface of the tip. The tip was fitted with a small cap by means of a ground joint to prevent evaporation during the weighing of the syringe. The space between plunger and barrel of the syringe was sealed by a narrow band of glycerol.

All films were spread on 0.02 *N* hydrochloric acid. The films were not examined for collapse with a dark ground illuminator[3] but the phenomenon of contraction was observed shortly before collapse was obvious.

Summary

Measurements on surface films of chlorogenin, chlorogenin diacetate and the diketo derivative are in agreement with the view that the two hydroxyl groups are in different rings in the molecule. They also confirm the close relationship in structure previously assumed to exist between chlorogenin and gitogenin.

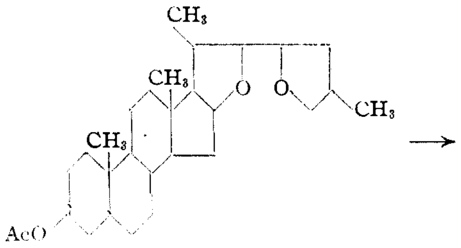
Stanford University, Calif. Received May 4, 1938

[Contribution from the Department of Chemistry of Stanford University]

Saponins and Sapogenins. VII. The Structure of the Side Chain of Chlorogenin

By F. M. McMillan and C. R. Noller

In previous chemical investigations on the structure of chlorogenin,[1] it has been assumed that the two unreactive oxygen atoms of chlorogenin are in a side chain whose structure is similar to that of the isomeric compound gitogenin and of other steroid sapogenins. This side chain is generally believed to consist of two tetrahydrofuran rings, the chief chemical evidence being the oxidation of tigogenin acetate[2] to an acid and a lactone as formulated in the equation



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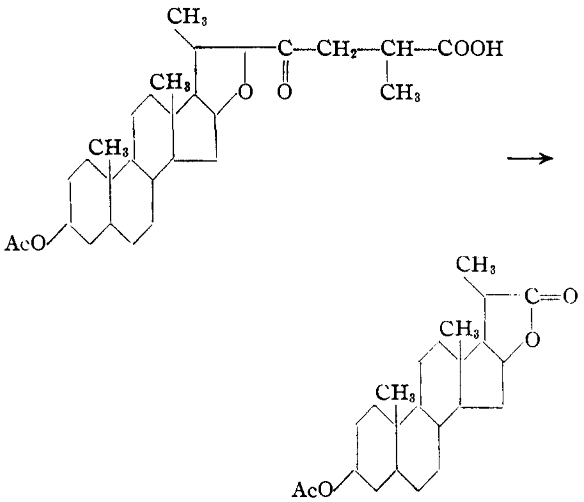
(1) Noller, This Journal, **59**, 1092 (1937); **60**, 1629 (1938).

(2) Tschesche and Hagedorn, *Ber.*, **68**, 1412, 2247 (1935).



Since the present work was completed, Fieser and Jacobsen[3] have reported the isolation of an acid from sarsasapogenin which they have named sarsasapogenoic acid and which is analogous to the acid obtained by Tschesche and Hagedorn from tigogenin. The acetate of the C_{22}-lactone from sarsasapogenin was first reported by Farmer and Kon.[4]

Oxidation of chlorogenin diacetate gives the diacetate of a C_{27}-acid which, in conformity with the nomenclature of Fieser and Jacobsen, we shall call chlorogenoic acid. Conditions have been worked out for obtaining directly the diacetate of the acid in good yields and little difficulty was encountered in its purification. In the case of sarsasapogenin Fieser and Jacobsen found it necessary to saponify the crude acetate and purify the dihydroxy acid. The tigogenoic acid of Tschesche and Hagedorn was likewise isolated after saponification. In both cases removal of the acetyl groups apparently takes place on extracting the acid with aqueous alkali. It is of interest to note the narrow range of temperature in which it is possible to get good yields of chlorogenoic acid diacetate. At 25° chlorogenin diacetate is not attacked whereas at 40° only difficultly crystallizable gums are formed.

Chlorogenoic acid diacetate crystallizes with a molecule of water of crystallization which at first led us to believe that a hydroxy acid was formed in the oxidation. This has been shown definitely to be not the case. Like tigogenoic acid and sarsasapogenoic acid, chlorogenoic acid diacetate does not form a semicarbazone under the usual conditions. We have not tried as yet the more drastic treatment with hydroxylamine by which Fieser and Jacobsen converted sarsasapogenoic acid into the compound $C_{27}H_{44}O_5N_2$.

Under the optimum conditions for preparing chlorogenoic acid diacetate, no neutral oxidation products could be detected. Under more drastic conditions very poor yields were obtained of a compound which has the characteristic properties of a lactone. If this is analogous to the lactones from tigogenin and sarsasapogenin, it should have the empirical formula $C_{26}H_{38}O_6$. Our analyses indicate the formula $C_{27}H_{44}O_7$. Similarly the saponified lactone should have the formula $C_{22}H_{34}O_4$, whereas our analyses indicate $C_{23}H_{40}O_5$. The best explanation seems to be that both of these compounds contain methyl alcohol of crystallization which would lead to the formulas $C_{27}H_{42}O_7$ and $C_{23}H_{38}O_5$, respectively.

Numerous attempts were made to obtain oxidation products intermediate between chlorogenoic acid diacetate and the lactone diacetate, most of which were unsuccessful. In several of the oxidations starting with chlorogenoic acid diacetate, minute amounts of an acid were obtained having the empirical formula $C_{27}H_{42}O_6$. This is the same as that for chlorogenoic acid but the compound is definitely different and we have no evidence concerning its structure.

By heating sarsasapogenin or gitogenin with a mixture of glacial acetic acid and concentrated hydrochloric acid, Jacobs and Simpson[5] obtained a liquid ketone which gave a semicarbazone melting at 119.5–120°. Chlorogenin behaves similarly except that the semicarbazone was extremely difficult to purify and the melting point could not be raised above 114–118°. The amount of this material was vanishingly small in spite of the fact that as much as 10 g. of chlorogenin was used in the decomposition.

It is planned to continue these investigations as soon as we can replenish our stock of raw materials.

Experimental

Chlorogenin Diacetate.—To 7 g. of chlorogenin, m. p. 272–276°, were added 38 cc. of 99% acetic anhydride, 4 cc. of glacial acetic acid and 6.5 g. of fused sodium acetate. The mixture was refluxed over a free flame until all of the sodium acetate dissolved and then heated on a steam-bath for two hours. The solution was poured into 400 cc. of water with rapid stirring. The product separated as an oil which soon crystallized. It was filtered, washed with water, dried and crystallized from 40 cc. of methyl alcohol

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(3) Fieser and Jacobsen, THIS JOURNAL, **60**, 28 (1938).

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

(5) Jacobs and Simpson, *J. Biol. Chem.*, **105**, 501 (1934).

giving 6.1 g., m. p. 152.5–155°. On recrystallization it melted at 154–155° and a third crystallization did not change the melting point.

Anal.[6] Calcd. for $C_{31}H_{48}O_6$: C, 72.05; H, 9.37; sap. equiv., 258.3. Found: C, 72.14; H, 9.53; sap. equiv., 257.9, 259.3.

Chlorogenoic Acid Diacetate.—A solution of 4 g. of chlorogenin diacetate in 175 cc. of glacial acetic acid was kept at 32–33° in a water-bath while a solution of 5 g. of chromium trioxide in 75 cc. of 90% aqueous acetic acid was added slowly through a motor-driven hollow stirrer in order to ensure rapid mixing. The addition of the reagent required twenty-five minutes and stirring was continued for ten minutes after all the reagent had been added. The solution was poured into water, giving a light-colored gummy precipitate. After standing for several hours the precipitate hardened and was filtered, washed with water and dried. The product, weighing 3.5 g., was dissolved in ether and extracted with three portions of 5% aqueous sodium carbonate and washed with water. The aqueous extracts were counter extracted with ether which was added to the previous ether solution.

Evaporation of the ether solution gave about 0.3 g. of a light-colored glass which after three crystallizations from methyl alcohol gave crystals which were shown by melting point and mixed melting point to be unchanged chlorogenin diacetate.

Acidification of the combined sodium carbonate extracts gave a cream-colored precipitate which was filtered, washed and dried *in vacuo* over potassium hydroxide. It weighed 2.4 g. and melted at 102–106°. It was extremely soluble in all the common organic solvents with the exception of the paraffin hydrocarbons, in which it was only slightly soluble. It crystallized from 70% aqueous acetic acid, 70% aqueous acetone, and from ligroin (100–120°) containing a small amount of absolute ethyl alcohol. After the acid had been purified fairly well from 70% acetone, it could be crystallized readily from 80% aqueous methyl alcohol. It then melted at 114–116° to a viscous glass which gradually gave off bubbles and crystallized on the walls of the melting point tube, after which it melted again at 211–213.5°. This behavior was observed from all aqueous solvents. If, however, the compound was boiled in ligroin (100–120°) and then just sufficient absolute alcohol added to take it into solution, the crystals obtained on cooling melted at 210–211° without first melting at the lower temperature. The same result was obtained by heating at 140° at 20 mm. for five hours. As the analyses show, the acid melting at 114–116° is a monohydrate which goes over above its melting point to the anhydrous acid.

Anal. of hydrate. Calcd. for $C_{31}H_{46}O_8 \cdot H_2O$: C, 65.93; H, 8.57; acetyl, 15.25; OH, 6.00, neut. equiv., 564.7. Found: C, 65.43; H, 8.32; acetyl, 15.30, 14.72; OH (Zerewitinow), 7.03; neut. equiv., 566.3, 563.5, 563.5, 566.9.

Anal. (Anhydrous acid). Calcd. for $C_{31}H_{46}O_8$: C, 68.10; H, 8.49; OH, 3.10; neut. equiv., 546.7. Found: C, 67.87; H, 8.55; OH (Zerewitinow), 3.35; neut. equiv., 548.2.

In order to obtain satisfactory yields of chlorogenoic acid diacetate, the above conditions for the oxidation must be followed closely. If the reaction was carried out at 25° only a trace of acidic material was formed and a large amount of the diacetate was recovered unchanged. When carried out at 40° over a period of one and one-half hours, the acid fraction was a gum which could be recrystallized only with difficulty.

Chlorogenoic acid diacetate does not form a semicarbazone on refluxing for two hours with semicarbazine in 90% ethyl alcohol, nor does it form a triacetate or an unsaturated compound on heating with acetic anhydride.

On heating the hydrate at 140° and 20 mm. for two hours it lost weight equivalent to 3.37% of the original sample as compared with the calculated amount of 3.18% for loss of one molecule of water. The gas evolved on heating at its melting point contained no carbon dioxide and the decrease in volume on washing with ammoniacal cuprous chloride solution corresponded to only 3.5% of the amount calculated for the evolution of one mole of carbon monoxide. No other combustible gases could be detected. The residue after heating was recrystallized and proved to be unchanged chlorogenoic acid diacetate.

On heating the acid with concentrated sulfuric acid, the amount of gas evolved which could be absorbed by ammoniacal cuprous chloride solution corresponded to about 11% of that calculated for the evolution of one mole of carbon monoxide per mole of compound.

Chlorogenoic Acid.—The brown gummy residue remaining after the acetyl determinations on chlorogenoic acid diacetate, partially crystallized on standing. Crystallization from methyl alcohol gave white crystals which shrank from the tube at 161° and melted at 169–170°.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.09; H, 9.16. Found: C, 70.01; H, 9.00.

Methyl Ester of Chlorogenoic Acid Diacetate.—To a solution of 0.50 g. of chlorogenoic acid diacetate in methyl alcohol was added an ether solution of diazomethane until a slight excess was present. The solution was evaporated to a volume of about 4 cc. and filtered hot. On cooling 0.34 g. of methyl ester, m. p. 162.5–163°, crystallized and evaporation of the filtrate from this crop gave 0.15 g., m. p. 159–162°. Recrystallization from methyl alcohol did not raise the melting point above 163°. The same ester was obtained from the acid showing a double melting point as from the dehydrated material.

Anal. Calcd. for $C_{32}H_{48}O_8$: C, 68.54; H, 8.63; OH, none; sap. equiv., 186.9. Found: C, 68.39; H, 8.76; OH (Zerewitinow), 0.71, 0.79; sap. equiv., 187.7, 187.8.

Lactone Diacetate.—When the oxidation of chlorogenin diacetate was carried out under more vigorous conditions than described above, for example, at 40° for one and one-half hours, or 45° for six hours, crystalline chlorogenoic acid diacetate could not be isolated readily but a small amount of a neutral product was obtained from the ether solution after extraction with sodium carbonate. The crude product, m. p. 190–208°, after two crystallizations from methyl alcohol melted at 249–252°, after which there was no further change. The compound did not form an oxime on refluxing with hydroxylamine in methyl alcohol for three and one-half hours.

The compound was insoluble in cold aqueous alkali and

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(6) All carbon and hydrogen analyses are by Dr. A. Schoeller, Berlin.

a solution in 50% aqueous alcohol absorbed no alkali on titration. A few milligrams of the compound was refluxed for forty-five minutes with 1 *N* ethyl alcoholic potassium hydroxide solution after which the solution was poured into water. No precipitation occurred but acidification with hydrochloric acid precipitated a compound which after solution in 50% alcohol absorbed no alkali on titration. These properties indicate that the neutral product is a lactone diacetate which is saponified by alcoholic alkali to a dihydroxy lactone.

Anal. Calcd. for $C_{26}H_{38}O_6$: C, 69.93; H, 6.58. Calcd. for $C_{26}H_{38}O_6 \cdot CH_3OH$: C, 67.76; H, 8.84. Calcd. for $C_{27}H_{44}O_7$: C, 67.46; H, 9.26. Found: C, 67.85; H, 9.36.

Attempts to determine the equivalent weight of the lactone diacetate by saponifying with an excess of standard alkali and back titrating did not give consistent results due to the hydrolysis of the sodium salt and reformation of the lactone. The **dihydroxy lactone** recovered from these saponifications consisted of needles, m. p. 255–256°.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.88; H, 9.46. Calcd. for $C_{22}H_{34}O_4 \cdot CH_3OH$: C, 70.01; H, 9.71. Calcd. for $C_{23}H_{40}O_5$: C, 69.66; H, 10.17. Found: C, 69.62; H, 10.01.

Oxidation of Chlorogenoic Acid Diacetate.—Of the many attempts made to obtain intermediate oxidation products between the acid and the lactone, the most successful was the oxidation with potassium permanganate. A neutral solution of the sodium salt from 0.1 g. of chlorogenoic acid diacetate was refluxed for thirty minutes with an aqueous solution of 0.038 g. of potassium permanganate. Precipitation of manganese dioxide began almost immediately and the purple color disappeared in a few minutes. After thirty minutes, the solution was filtered and the precipitate washed well with water. Acidification of the filtrate gave a flocculent white precipitate, m. p. 175–190°. After two crystallizations from 70% aqueous acetone and one from acetone it melted at 221–222°. The compound is much more soluble in 70% aqueous acetone than in acetone alone but is precipitated from the 70% acetone on further dilution with water.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.09; H, 9.16; neut. equiv., 462.6. Found: C, 69.81, 70.05; H, 9.23, 8.85; neut. equiv., 484.

The same acid was isolated in small amounts after oxidation of the sodium salt with hydrated manganese dioxide at 65–70° and in one of the chromic oxide oxidations at 40°. In none of the oxidations yielding this acid could the results be duplicated consistently since the acid appears to undergo further oxidation with the formation of oils and gums that could not be crystallized. Chlorogenoic acid diacetate was recovered unchanged after treatment in acetic acid solution with lead tetraacetate.

Cleavage of the Side Chain of Chlorogenin.—A fragrant oil was obtained on treating 10 g. of chlorogenin with acetic acid–hydrochloric acid according to the procedure of Jacobs and Simpson.[5] This was converted into a semicarbazone but extreme difficulty was encountered in attempting to isolate a pure product. Recrystallization from ether–petroleum ether mixtures failed to give a product melting above 100°. A large number of other solvents and solvent mixtures were tried without success. By passing an ether solution of the semicarbazone through a column packed with a mixture of magnesium oxide and Celite, evaporating successive portions of the filtrate separately and rubbing up the solid residues with small amounts of ether, a product was obtained from the middle fractions that melted at 114–118°. This material consisted of tiny microcrystals but was still somewhat gummy and could not be purified further by crystallization. The melting point given by Jacobs and Simpson for the semicarbazone of the ketone from sarsasapogenin and gitogenin is 119.5–120°.

Summary

Oxidative and acid degradation of chlorogenin indicates that the structure of the side chain is very similar to, if not identical with, that of the other steroid sapogenins.

STANFORD UNIVERSITY, CALIF.

RECEIVED MAY 10, 1938

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

Dielectric Constants of Some Fluorine Compounds

BY RAYMOND M. FUOSS

I. Introduction.—In contrast to the other halogens, the properties of fluorine compounds have been studied comparatively little. Recent technical interest in new refrigerants has, however, made a large number of fluorinated methanes and ethanes available. Below are presented the results of an investigation of the dielectric constants of fifteen fluorine compounds.

II. Materials, Apparatus and Method.—The fluorine compounds were presented to us by the Jackson Laboratory of E. I. du Pont de Nemours and Company, to whom grateful acknowledgment is made.

The bench apparatus consisted of a manifold to which were connected an oil pump, three distilling bulbs with an ascarite tube between the first two, a manometer and a guarded condenser. The ascarite served to remove traces of water or of hydrogen halides which might have been present. The stopcocks were lubricated with a sirup of phosphoric acid and anhydride for the higher boiling compounds; ordinary heavy grease was used for the others. The samples were distilled from the supply cartridges into the first bulb, and then distilled back and forth through the ascarite. After each of the first few condensations, the samples were pumped to remove small amounts of dissolved air. Then the sample was distilled from the first bulb in small portions, and a dielectric constant determina-