sulfuric acid produces a deep orange color. This solution is poured with stirring onto crushed ice. A light yellow solid separates out which soon becomes sticky. It cannot be crystallized from alcohol. Its alcoholic solution gives a deep greenish-blue color with ferric chloride, which color fades rapidly; it bleaches iodine and indophenol solutions instantly. On exposure to atmospheric oxygen, it changes to a yellow solid which is identified as diphenyltriketone, melting and mix-melting with an authentic sample at 70°.

Diphenylacetyleneglycol Diacetate (X).—Separate solutions of 10.0 g. each of desyl bromide, acetylbenzoin and benzoin in 50 cc. of acetic anhydride are refluxed gently with equal weights of freshly fused potassium acetate for thirty minutes. Each solution turns yellow to light brown. After cooling, they are poured into large volumes of cold water and stirred vigorously until the acetic anhydride is decomposed. A cream-colored granular solid separates out. The solid is filtered, washed with water, and dried over solid potassium hydroxide. It is then crystallized from methyl alcohol, yielding 3.0 g. of a crystalline solid, melting at 153° and 6.0 g. of material melting at 70°. The material melting at 70° mix-melts with acetylbenzoin at 70°, and is hydrolyzed quantitatively by alkali to benzoin. Repeated recrystallizations do not change the melting point of 70°. When refluxed with acetic anhydride and potassium acetate, it yields the 153° substance. It is a mixture of acetylbenzoin and diphenylacetyleneglycol diacetate. The diacetate, melting at 153°, is hydrolyzed quantitatively by both alkali and cold concd. sulfuric acid to benzoin, identified by its melting point and mixed-melting point. Hot glacial acetic acid converts the diacetate to acetylbenzoin.

Acetylbenzoin (IV).—A solution of 10.0 g. of desyl bromide in 50 cc. of glacial acetic acid is refluxed with 10.0 g. of freshly fused potassium acetate for thirty minutes, cooled and poured into a large volume of water. An oily solid separates, which is crystallized from methyl alcohol, melting and mix-melting with acetylbenzoin at 84°.

Summary

Herein is reported the use of an acetylating combination which seems to be more powerful than acetic anhydride in the presence of concd. sulfuric acid, converting certain compounds which have the group —CH(Br)— or —CH(OCOCH$_3$)— or —CH(OH)— adjacent to a >C=O group, into diacetates of acetyleneglycol.

The properties of the ene-diol, phenylbenzoylacetyleneglycol, resulting from the hydrolysis of its diacetate are given.

Further possibilities of this acetylating combination are now under investigation.

WASHINGTON, D. C. RECEIVED JANUARY 22, 1940

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

Sterols. XCV. Acid Isomerization of Pseudosapogenins to Sapogenins

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The reaction of the sapogenins with acetic anhydride to yield the isomeric pseudosapogenins is now a well-established reaction which has been applied to sarsasapogenin,[1] *epi*-sarsasapogenin,[2] sarsasapogenone,[2] isosarsasapogenin,[2] tigogenin[3] and chlorogenin.[2] Although there may be some question concerning the structure of the pseudosapogenins all of the available evidence indicates the presence of an ethylenic linkage at C-16, C-17 and a reactive grouping at C-22 possibly as in I.[4]

In studying the reduction of pseudosarsasapogenone[2] by the Clemmensen method, it was observed that the essential reaction product was desoxysarsasapogenin and not desoxypseudosarsasapogenin. That this isomerization of the pseudosapogenin side chain to the sapogenin side chain is due to the presence of hydrochloric acid is clearly shown in succeeding experiments.

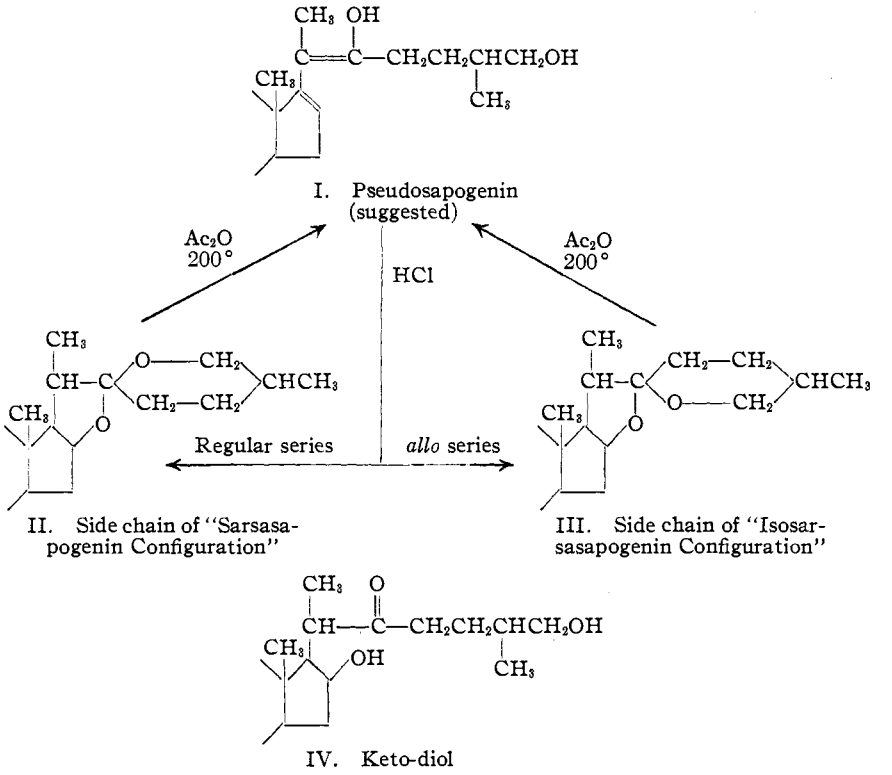
Pseudosarsasapogenin upon standing with aqueous ethanolic hydrochloric acid at 25° for one day is almost quantitatively converted into sarsasapogenin. Pseudotigogenin and pseudochlorogenin readily were converted into the corresponding sapogenins by short refluxing with aqueous ethanolic hydrochloric acid. It seems probable that this reaction involves the addition of hydrogen chloride to ethylenic linkages followed by elimination of hydrogen chloride and subsequent ring closure to yield the spiro ketal system. It is significant that dihydropseudosarsasapogenin[4] is unaffected by similar treatment.

In previous work we have shown that the side chains of tigogenin, chlorogenin and diosgenin and probably of gitogenin and digitogen differ in

(1) Marker and Rohrmann, THIS JOURNAL, **62**, 518 (1940).
(2) Marker, Rohrmann and Jones, *ibid.*, **62**, 648 (1940).
(3) Marker and Rohrmann, *ibid.*, **62**, 898 (1940).
(4) Marker and Rohrmann, *ibid.*, **62**, 521 (1940).

configuration from the side chain of sarsasapogenin. This was shown by the conversion of sarsasapogenin to neotigogenin,[5,6] a substance differing from tigogenin only in the configuration of the side chain. That the configuration of the side chain of the sapogenins derived from the acid isomerization of the pseudosapogenins is determined largely by the configuration at C-5 is indicated by the fact that pseudosarsasapogenin (pseudoisosarsasapogenin[2]) yields largely sarsasapogenin rather than isosarsasapogenin, while pseudotigogenin yields largely tigogenin rather than neotigogenin. Thus it may be generalized that pseudosapogenins having the regular configuration at C-5 give rise to a spiro ketal side chain of the "sarsasapogenin configuration" (II), while those having the *allo*-configuration give rise to one having the "isosarsasapogenin configuration" (III). It seems most probable that these reactions are of an equilibrium nature and that the isomerization of pseudosarsasapogenin probably gives rise to small amounts of isosarsapogenin besides the sarsasapogenin. Likewise the isomerization of pseudotigogenin probably gives small amounts of neotigogenin in addition to the tigogenin.

The behavior of the pseudosapogenins on acid isomerization raises the interesting question concerning the structure of the side chains of unhydrolyzed saponins. It would appear that some of these substances such as tigonin[7] and amolonin,[8] the parent saponins of tigogenin, give rise to more sugar groups on acid hydrolysis than one would reasonably expect to be attached to a single hydroxyl group such as exists in tigogenin. This suggests that the nucleus of the saponins may be that of the pseudosapogenins (I) or more probably that of the keto-diol IV, which is the equivalent of a spiro ketal (II and III). Such substances, during the course of the acid hydrolysis necessary for the cleavage of the glycoside linkages, would be converted to spiro ketals (II and III). The existence of a nucleus such as I or IV, on the basis of the previously mentioned equilibrium, satisfactorily explains the existence of smilagenin[9,10,11] (isosarsasapogenin) and neotigogenin[6] among the hydrolysis products of the saponins.



I. Pseudosapogenin (suggested)

II. Side chain of "Sarsasapogenin Configuration"

III. Side chain of "Isosarsasapogenin Configuration"

IV. Keto-diol

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

Experimental Part[12]

Clemmensen Reduction of Pseudosarsasapogenone.—To a boiling solution of 200 mg. of pseudosarsasapogenone in 50 cc. of ethanol in the presence of 5 g. of 20-mesh zinc was added 8 cc. of concentrated hydrochloric acid over a period of two hours. Water was added and the precipitated solid taken up in ether and crystallized from acetone to give white plates, m. p. 214–216°. This gave no depression with a sample of desoxysarsasapogenin of m. p. 214–216°.

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.9; H, 11.1. Found: C, 81.2; H, 11.1.

(5) Marker and Rohrmann, THIS JOURNAL, **62**, 647 (1940).
(6) Goodson and Noller, *ibid.*, **61**, 2420 (1939).
(7) Tschesche, *Ber.*, **69**, 1665 (1936).
(8) Jurs and Noller, THIS JOURNAL, **58**, 1251 (1936).
(9) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).
(10) Askew, Farmer and Kon, *ibid.*, 1399 (1936).
(11) Kon, Soper and Woolman, *ibid.*, 1201 (1939).
(12) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

Isomerization of Pseudosapogenins. (a) Pseudosarsasapogenin.—To a solution of 500 mg. of pseudosarsasapogenin, m. p. 170–173°, in 100 cc. of 95% ethanol was added a mixture of 85 cc. of ethanol and 15 cc. of concentrated hydrochloric acid. After standing at 25° for twenty hours, water was added and the precipitated solid taken up in ether and crystallized from acetone to give 400 mg. of white needles, m. p. 199–201°. This gave no depression with a sample of sarsasapogenin, m. p. 199–201°.

With chromic anhydride at room temperature, this gave a neutral product which crystallized from acetone as white plates, m. p. 223–226°. This gave no depression with a sample of sarsasapogenone, m. p. 223–226°.

With hot acetic anhydride an acetate was formed which was crystallized repeatedly from acetone–methanol to give white plates, m. p. 125–127°. When mixed with a sample of sarsasapogenin acetate, m. p. 143–145°, the mixture melted from 126–144°. When seeded with a crystal of sarsasapogenin acetate, m. p. 143–145°, a product of m. p. 142–144° was obtained. This gave no depression with sarsasapogenin acetate.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.8; H, 10.2.

Similar results were obtained when pseudosarsasapogenin was refluxed in ethanol solution with aqueous hydrochloric acid for ninety minutes.

Dihydropseudosarsasapogenin, m. p. 169°, was recovered unchanged after refluxing for two hours in aqueous ethanolic hydrochloric acid solution.

(b) Pseudotigogenin.—Pseudotigogenin when refluxed for one hour with aqueous ethanolic hydrochloric acid gave a good yield of a product which crystallized from acetone as white needles, m. p. 203–205°. This gave no depression with a sample of tigogenin, m. p. 204–206°.

With boiling acetic anhydride this yielded an acetate, m. p. 202–204°, which gave no depression with an authentic sample of tigogenin acetate, m. p. 202–204°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.7; H, 10.0.

(c) Pseudochlorogenin.—Pseudochlorogenin when treated as described for pseudotigogenin gave a good yield of a product which crystallized from acetone as white needles, m. p. 269–272°. This gave no depression with a sample of chlorogenin, m. p. 270–273°.

With boiling acetic anhydride this yielded a diacetate, m. p. 149–151°, which gave no depression with a sample of chlorogenin diacetate, m. p. 149–151°.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.05; H, 9.4. Found: C, 72.1; H, 9.3.

Summary

Pseudosarsasapogenin, pseudotigogenin and pseudochlorogenin are isomerized by hydrochloric acid to the original sapogenins.

STATE COLLEGE, PENNA. RECEIVED JANUARY 29, 1940

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

Sterols. XCVI. *allo*-Pregnanediols from Tigogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In a recent publication[1] the conversion of sarsasapogenin to $\Delta^{16,17}$-pregnenedione-3,20 and the subsequent reduction of this to various pregnane derivatives was described. In the present work we have extended some of these reactions to tigogenin (I), a substance having the *allo*-configuration at C-5.

Tigogenin upon treatment with acetic anhydride at 200° is converted to pseudotigogenin which upon mild oxidation with chromic anhydride is converted to an unsaturated diketone of the composition $C_{21}H_{30}O_2$. This substance is undoubtedly $\Delta^{16,17}$-*allo*-pregnenedione-3,20 (II) a substance first reported by Butenandt, Mamoli and Heusner.[2] Their product was prepared from androsterone by conversion to the nitrile, reaction with methyl Grignard reagent and subsequent oxidation. The product was reported to melt at 205–208°, while our product from tigogenin melts at 210–212°.

Reduction of the unsaturated diketone with sodium and ethanol yields *allo*-pregnanediol-3(β),20(α) while reduction with Adams catalyst yields *allo*-pregnanediol-3(β),20(β). The ease of reduction with sodium and ethanol indicates the presence of an α,β-unsaturated ketone grouping.

Although data have been presented indicating that the configuration of the C-3 hydroxyl group in tigogenin is *beta*, none of this evidence can be considered conclusive inasmuch as it has been derived from digitonin precipitation data[3] and from reduction experiments on $\Delta^{4,5}$ unsaturated ketones,[4] reactions which might conceivably be influenced by the presence of the complex side chain.

(1) Marker and Rohrmann, THIS JOURNAL, **62**, 518 (1940).
(2) Butenandt, Mamoli and Heusner, *Ber.*, **72**, 1614 (1939).
(3) Tschesche and Hagedorn, *ibid.*, **68**, 2247 (1935).
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 1291 (1939).