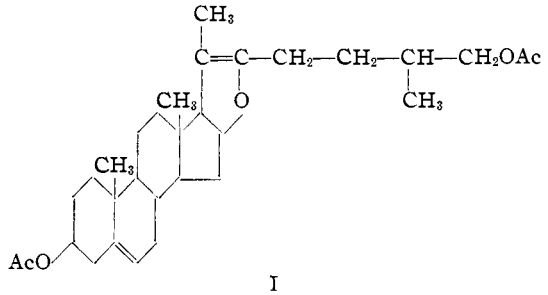
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. CXXXIII. Sapogenins. LV. 20-Methylpregnanetriol and Related Compounds

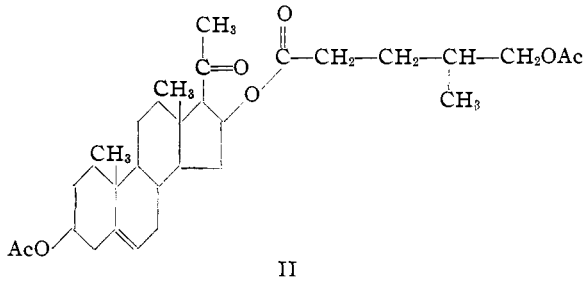
BY RUSSELL E. MARKER AND D. L. TURNER

Recently, we reported[1,2] the isolation of intermediate oxidation products which arise in the conversion of the pseudosapogenins to 16-pregnen-20-one compounds by the method of Marker and Rohrmann. Thus, pseudodiosgenin diacetate (I) gave an oxidation product[3] to which the formula II was assigned. The oxidation products from the diacetates of the other pseudosapogenins have an identical side-chain structure. The reduction of the oxidation products gave pregnanetriols. Pseudodiosgenin diacetate was converted to 5-pregnene-3(β),16,20-triol by this method. The other oxidation products gave triols differing in their nuclear structure.

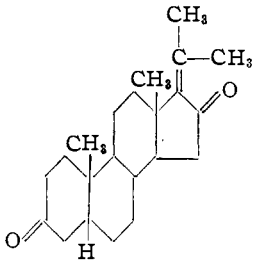
We have now obtained the expected 20-methyl-5-pregnene-3(β),16,20-triol (IV) by the reaction of methylmagnesium iodide with diosone diacetate. Similarly, tigone diacetate gave 20-methyl-*allo*-pregnane-3(β),16,20-triol, and the oxidation product from pseudosarsasapogenin diacetate gave 20-methylpregnane-3(β),16,20-triol. The last compound was oxidized by the method of Oppenauer. The product may be assigned the structure of 20-methyl-17,20-pregnene-3,16-dione



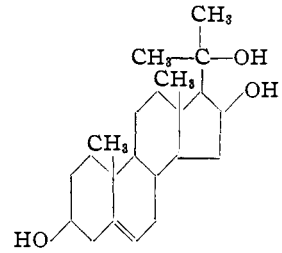
I



II



III



IV

(III). While the 20-methylpregnanetriols are characterized by extreme insolubility the diketone was very soluble in most organic solvents.

We wish to thank Parke, Davis and Company for their assistance.

Experimental Part

20-Methyl-*allo*-pregnane-3(β),16,20-triol.—A solution of 3.0 g. of tigone diacetate, prepared by the oxidation of pseudotigogenin diacetate[1] in 100 cc. of ether, was added to a Grignard reagent prepared from 75 g. of methyl iodide, 12 g. of magnesium and 150 cc. of ether. The mixture was stirred for six hours, the ether was distilled and 300 cc. of benzene was added. The mixture was refluxed for thirty-six hours. The Grignard complex was decomposed with ice and dilute hydrochloric acid. The product (1.6 g.) was filtered and recrystallized from methanol. It melted at 262–264°.

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.4; H, 10.9. Found: C, 75.1; H, 10.7.

20-Methyl-pregnane-3(β),16,20-triol.—Pseudosarsasapogenin (74 g.) was acetylated and oxidized as described previously.[2] The dried oxidation product was dissolved in 500 cc. of absolute ether and added to a Grignard reagent from 900 g. of methyl iodide, 150 g. of magnesium and 1500 cc. of ether. The subsequent procedure followed that given above. The product was crystallized from methanol several times; yield 36 g.; m. p. 234–236°.

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.4; H, 10.9. Found: C, 75.0; H, 11.1.

20-Methyl-5-pregnane-3(β),16,20-triol.—This was prepared as described above from the oxidation product of pseudodiosgenin diacetate (from 50 g. of pseudodiosgenin) and methylmagnesium iodide. The product which appeared to be a mixture of isomers was recrystallized from methanol until material of m. p. 275–276° was obtained.

Anal. Calcd. for $C_{22}H_{36}O_3$: C, 75.8; H, 10.4. Found: C, 75.9; H, 10.6.

Reduction of 20-Methyl-5-pregnene-3(β),16,20-triol.—A mixture of 200 mg. of the above triol, 0.5 g. of Adams catalyst and 1 liter methanol was shaken under hydrogen

(1) Marker, *et al.*, THIS JOURNAL, **63**, 774 (1941).
(2) Marker, *et al.*, *ibid.*, **63**, 779 (1941).
(3) We propose the name "diosone diacetate" for this product and "tigone diacetate" for the oxidation product from pseudotigogenin diacetate.

at 3 atm. for eight hours. The solution was filtered and concentrated. The product crystallized from the methanol and was recrystallized from the same solvent. It melted at 262–264°. Admixture with the 20-methyl-*allo*-pregnanetriol described above gave no depression of the melting point. The product, unlike the unsaturated triol, did not absorb bromine in acetic acid.

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.4; H, 10.9. Found: C, 75.4; H, 11.1

Oppenauer Oxidation of 20-Methyl-pregnane-3(β),16,-20-triol.—A mixture of 4.0 g. of triol, 20 g. of aluminum *t*-butylate, 400 cc. of dry acetone and 2 liters of dry benzene was refluxed for thirty hours. The mixture was distilled to dryness *in vacuo* and the product decomposed with dilute hydrochloric acid and extracted with ether. The product remaining after the evaporation of the ether was treated with acetone in which a little starting material remained undissolved. The acetone soluble material was recrystallized from ether–pentane. It melted at 193–195°.

Anal. Calcd. for $C_{22}H_{32}O_2$: C, 80.4; H, 9.8. Found: C, 80.2; H, 10.2.

Summary

The oxidation products obtained from the pseudosapogenin diacetates have been treated with methylmagnesium iodide to give the related triols.

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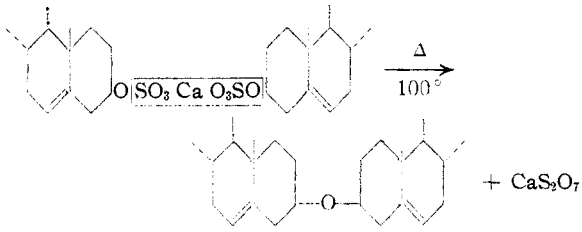
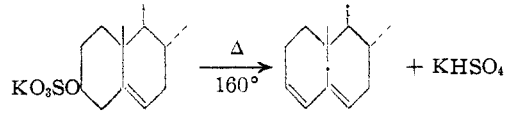
Steryl Sulfates. IV. Thermal Decomposition of Calcium Cholesteryl Sulfate

BY ALBERT E. SOBEL[1] AND PAUL E. SPOERRI

Since a great variety of cholesteryl sulfates are available at present,[2] an interesting question arises: Does the cation in the cholesteryl sulfates influence the thermal decomposition of these compounds? This may be answered in the affirmative as a result of present investigations in which the thermal decomposition of calcium cholesteryl sulfate was studied as a typical representative of the divalent alkali earth cations. This decomposition takes place readily at 100° (in the dry state) with the formation of dicholesteryl ether.



In contrast to this, the monovalent potassium salt decomposes (in the dry state) to form 3,5-cholestadiene[3]



The presence of water inhibits the thermal decomposition of calcium cholesteryl sulfate in some manner as shown by the fact that on heating calcium cholesteryl sulfate for one hour in refluxing water, only 6 to 7% decomposition takes place with the formation of cholesterol. This may be compared to the complete decomposition of the dry solid in forty minutes. It was also observed on further investigation that complete decomposition takes place in refluxing benzene (b. p. 80.1°) in thirty minutes with the formation of calcium sulfate, sulfuric acid and some unidentified reaction product in which cholesterol and sulfur are absent. This decomposition in benzene takes place also in the presence of barium oxide, used to remove the sulfuric acid formed in the decomposition. Here again the main reaction products were not identified, but free cholesterol and sulfur were absent. Thus the presence of inert solvents which boil even lower than water does not inhibit thermal decomposition. Water, therefore, must have some specific inhibitory effect which may be due to the dissociation of the calcium cholesteryl sulfate as shown

$$Ca(Chol.SO_4)_2 \rightleftharpoons Ca^{++} + 2Chol.SO_4^-$$

Or possibly the hydrated form of the compound is more resistant to thermal decomposition.

Experimental

Thermal Decomposition of Calcium Cholesteryl Sulfate in a Sealed Tube.—Four grams of calcium cholesteryl sulfate was sealed in an evacuated Pyrex tube which was

(1) From the dissertation submitted to the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1940.

(2) A. E. Sobel and P. E. Spoerri, THIS JOURNAL, **63**, 1259 (1941).

(3) S. Natelson and S. P. Gottfried, *ibid.*, **61**, 971 (1939); A. E. Sobel and M. J. Rosen, *ibid.*, **63**, 3536 (1941).