From the ether solution there were isolated 2.55 g. of isopropylbenzene and 2.0 g. of tri-*p*-tolylmethane, b. p. 230–240° (13 mm.). The recovered methane contained an impurity, probably an anthracene derivative, which exhibited an intense blue-violet fluorescence. Not all the unused hydrocarbon was recovered as some of it could not be distilled from the tar remaining in the distilling flask, and some was carried into the aqueous layer by the salt in the extraction process.

Summary

Tri-*o*-tolylmethane undergoes slow exchange with phenylisopropylpotassium to yield a tripotassium derivative which is converted by carbonation into the potassium salt of triphenylmethane-2,2′,2″-triacetic acid. The related compounds, phenyldi-*o*-tolylmethane, diphenyl-*o*-tolylmethane and tri-*p*-tolylmethane, under the same conditions, all form monopotassium derivatives which by carbonation yield triarylacetic acids. Explanations based upon damped resonance and steric hindrance are considered for the relative inertness of the central carbon atom of tri-*o*-tolylmethane.

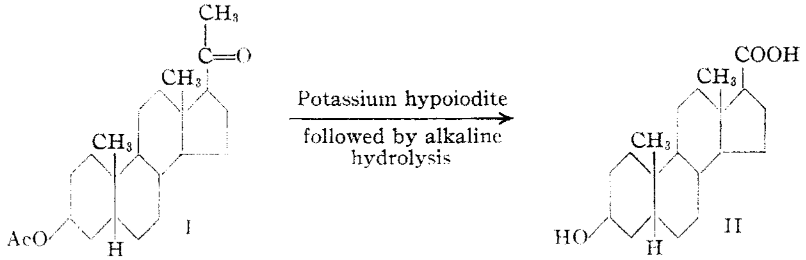
Cambridge, Massachusetts Received May 19, 1942

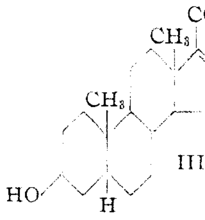
[Contribution from the School of Chemistry and Physics of the Pennsylvania State College]

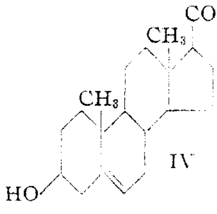
Sterols. CXLIX. The Hypoiodite Oxidation of Pregnanolones and Pregnenolones

By Russell E. Marker and R. B. Wagner

St. Goldschmidt, Middelbeek and Boasson[1] have recently shown that the claims of various patents[2] to the oxidation of 5-pregnen-$3(\beta)$-ol-20-one acetate with hypoiodite to obtain $3(\beta)$-hydroxy-etio-5-cholenic acid are erroneous. We have investigated this type of reaction, treating not only 5-pregnen-$3(\beta)$-acetoxy-20-one but also 16-pregnen-$3(\beta)$-acetoxy-20-one, pregnan-$3(\beta)$-acetoxy-20-one (I) and 5,16-pregnadien-$3(\beta)$-acetoxy-20-one with excess hypoiodite. The reactions used by us gave in every case the corresponding etio-cholanic (II) and etio-cholenic acids (III), (IV), (V).




III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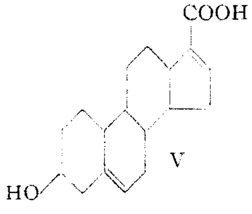
V

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

Experimental

$3(\beta)$-Hydroxy-etio-cholanic Acid.—To a solution of 2 g. of pregnan-$3(\beta)$-ol-20-one acetate in 300 cc. of dioxane was added simultaneously in 5-cc. portions, 80 cc. of an aqueous solution of 20 g. of potassium iodide and 10 g. of iodine, and 80 cc. of an aqueous 10% potassium hydroxide solution. The mixture was stirred at room temperature for one hour and then warmed to 80°. The reaction mixture was cooled and acidified. After the excess iodine was destroyed with sodium bisulfite, the mixture was concentrated *in vacuo* and extracted with ether. The ethereal solution was washed with 10% potassium hydroxide and the combined alkaline washings were warmed for thirty minutes on a steam-bath. After acidification the solid was extracted with ether. The product crystallized from methanol as white needles; m. p. and mixed m. p. with $3(\beta)$-hydroxy-etio-cholanic acid, 224–226°; yield 0.6 g.

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.9; H, 10.1. Found: C, 74.6; H, 10.0.

The methyl ester was prepared by treating an ethereal solution of 50 mg. of the above acid with an ethereal solution of diazomethane. The solvent was evaporated and the residue crystallized from methanol to give white needles; m. p. 128°. This material gave no depression in the melting point of the methyl ester of an authentic sample of $3(\beta)$-hydroxy-etio-cholanic acid methyl ester.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.4; H, 10.3. Found: C, 75.6; H, 10.2.

$3(\beta)$-Hydroxy-etio-16-cholenic Acid.—A solution of 2 g. of 16-pregnen-$3(\beta)$-ol-20-one acetate in 300 cc. of dioxane was treated as described above with hypoiodite. After hydrolysis the product crystallized from methanol; m. p.

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[1] St. Goldschmidt, Middelbeek and Boasson, *Rec. trav. chim.*, **60**, 209 (1941).

[2] British Patent 493,055; French Patent 819,974; Swiss Patent 197,580; U. S. Patent 2,171,959.

254–256°; yield 0.3 g. This substance gave a 10° elevation when mixed with 3(β)-hydroxy-17,20-pregnenoic acid-21; m. p. 254–256°.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.4; H, 9.5. Found: C, 75.6; H, 9.5.

The methyl ester was prepared as described above. It crystallized from methanol as white plates; m. p. 150–152°. It depressed the melting point of the methyl ester of 3(β)-hydroxy-17,20-pregnenoic acid-21 (m. p. 153–155°) twenty-five degrees.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.9; H, 9.8. Found: C, 75.8; H, 9.8.

Catalytic Reduction of 3(β)-Hydroxy-etio-16-cholenic Acid.—A solution of 100 mg. of the above 3(β)-hydroxy-etio-16-cholenic acid in 100 cc. of acetic acid was shaken with hydrogen and Adams catalyst for two hours at 3 atm. pressure and room temperature. The reaction mixture was filtered and the filtrate was evaporated to dryness *in vacuo*. The residue was crystallized from methanol as white needles; m. p. and mixed m. p. with 3(β)-hydroxy-etio-cholanic acid, 224–227°. A mixed melting point with 3(β)-hydroxy-pregnanoic acid (m. p. 219–221°) was at 195°.

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.9; H, 10.1. Found: C, 75.0; H, 10.0.

3(β)-Hydroxy-etio-5-cholenic Acid.—From the reaction of 2 g. of 5-pregnen-3(β)-ol-20-one acetate with potassium hypoiodite as described above was isolated a product which crystallized from dioxane; m. p. and mixed m. p. with an authentic sample of 3(β)-hydroxy-etio-5-cholenic acid, 273–274°; yield 0.2 g. pure product.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.4; H, 9.5. Found: C, 75.2; H, 9.3.

3(β)-Hydroxy-etio-5,16-choladienic Acid.—From the reaction of 2 g. of 5,16-pregnadien-3(β)-ol-20-one acetate as described above was isolated a product which crystallized from methanol as white plates; m. p. 255–257°; yield 250 mg.

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.9; H, 8.9. Found: C, 76.0; H, 8.8.

Summary

Conditions are described for the hypoiodite oxidation of 20-keto-pregnane derivatives to the corresponding 20-carboxylic acids. 3(β)-Hydroxy-etio-cholanic (II), 3(β)-hydroxy-etio-16-cholenic (III), 3(β)-hydroxy-etio-5-cholenic (IV), and 3(β)-hydroxy-etio-5,16-choladienic (V) acids have been produced by this method.

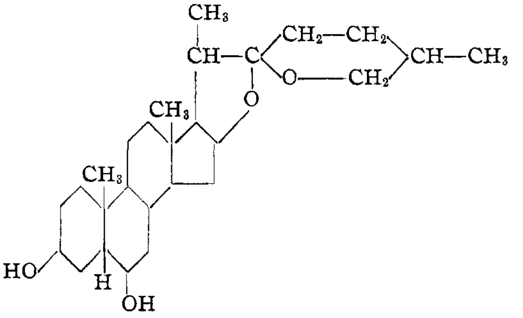
STATE COLLEGE, PENNA. RECEIVED APRIL 15, 1942

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

Sterols. CL. Sapogenins. LXIII. The Position of the Hydroxyl Groups in Digitogenin*

BY RUSSELL E. MARKER, D. L. TURNER AND PAUL R. ULSHAFER

The position of the hydroxyl groups in chlorogenin has been established with certainty by a large number of interconversions reported from this Laboratory[1,2,3] and chlorogenin is undoubtedly 6-hydroxy-tigogenin (I). However, Noller[4] is unable to reconcile this structure of chlorogenin with the fact that the oxidation of chlorogenin gives a keto-dibasic acid which is neither identical to digitoic acid nor to digitogenic acid. A revision of Noller's interpretation of the non-identity of the two acids is now necessary since the structure of chlorogenin is certain.



We find that oxidation of 6-keto-tigogenone[2,3] (tigogen-3,6-dione) prepared from diosgenin gives a keto-dibasic acid identical to that from natural chlorogenin and this acid differs from digitoic and digitogenic acid. The keto-dibasic acid melts with decomposition and gas evolution. Cholestane-3,6-dione was oxidized by Windaus[5] to a ketodibasic acid which melts with decomposition and gas evolution. This acid can be converted by Wolff–Kishner reduction[6] to cholestane–2,3–diacid the structure of which is certain.[6,7] We have also effected this reduction by the Clemmensen method. It, therefore, seems reasonable to suppose that the oxidation of 6-keto-tigogenone

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* Original manuscript received July 2, 1941.

(1) Marker, *et al.*, THIS JOURNAL, **61**, 946 (1939); **61**, 1516 (1939); **62**, 2525 (1940); **63**, 767 (1941); **64**, 221 (1942).

(2) Marker, Jones and Turner, *ibid.*, **62**, 2537 (1940).

(3) Marker, Jones, Turner and Rohrmann, *ibid.*, **62**, 3006 (1940).

(4) Noller, *ibid.*, **59**, 1092 (1937).

(5) Windaus, *Ber.*, **36**, 3752 (1903).

(6) Windaus, Staden and Seng, *Z. physiol. Chem.*, **117**, 146 (1921).

(7) Windaus, *ibid.*, **213**, 147 (1932).