benzaldehyde and sodium ethylate gave the corresponding 21-benzal derivatives in excellent yield. Preparation of the acetates of these compounds and oxidation of the acetates with chromic anhydride gave the correspondingly substituted *etio*-cholanic acids in approximately 70% yields. The treatment of pregnanedione with benzaldehyde and sodium ethylate gave a mixture which could not be separated.

STATE COLLEGE, PENNA. RECEIVED MARCH 6, 1939

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

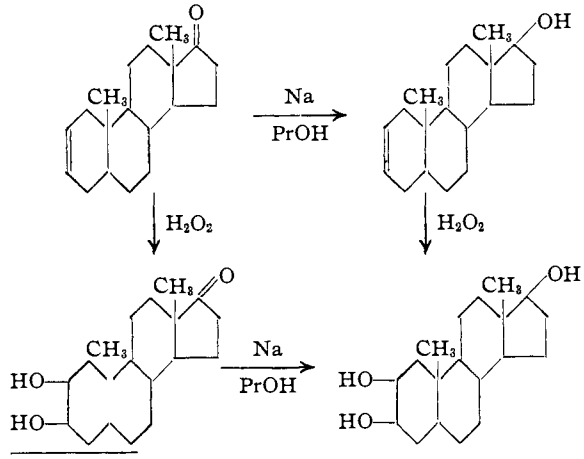
Sterols. LXIII. 2,3-Dihydroxyandrostane Derivatives

BY RUSSELL E. MARKER AND LOUIS PLAMBECK, JR.

In the course of our studies on the preparation of androstane derivatives for androgenic assay we have prepared several derivatives of androsterone which are unreported in the literature.

When Δ^2-cholestene was treated with hydrogen peroxide in acetic acid, cholestanediol-2,3 was obtained in very good yields. This upon oxidation with chromic acid gave the same dicarboxylic acid that was obtained by the vigorous oxidation of cholestanol, showing the position of the hydroxyl groups to be on C-2 and C-3.

In the same manner when Δ^2-androstenone-17[1] was treated with hydrogen peroxide we obtained 2-hydroxyandrosterone. It was very difficult to purify this product from a small amount of other isomeric products formed in the reaction. However, upon reduction with sodium in propyl alcohol it gave 2,3,17-trihydroxyandrostane which was identical with the product obtained by the action of hydrogen peroxide on androstenol-17[1]. None of these products precipitated with digitonin, suggesting that possibly the 3-hydroxyl group may be of the *epi*-configuration.



(1) Marker, Kamm, Jones and Mixon, THIS JOURNAL, **59**, 1363 (1937)

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

Experimental Part

2,3-Dihydroxycholestane.—To a solution of 3.0 g. of Δ^2-cholestene dissolved in 50 cc. of acetic acid on a steam-bath was added 3.0 cc. of 30% hydrogen peroxide over a period of one hour with stirring. Water and ether were added and the acetic acid removed by shaking with sodium carbonate solution. The ether was evaporated and the residue refluxed for forty-five minutes with an excess of alcoholic potassium hydroxide solution. The product was extracted with ether and recrystallized from methanol, m. p. 195–197°.

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.1; H, 12.0. Found: C, 80.2; H, 12.1.

A solution of 5.3 g. of 2,3-dihydroxycholestane in 15 cc. of acetic anhydride was refluxed for one hour. Upon cooling the product crystallized and was separated by filtration. This was recrystallized from methanol to a melting point of 133–135°.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.2; H, 10.7. Found: C, 76.4; H, 10.8.

Upon hydrolysis with alcoholic potassium hydroxide the diacetate gave cholestanediol-2,3, m. p. 201°; mixture with original diol gave no depression.

To a solution of 500 mg. of 2,3-dihydroxycholestane in 25 cc. of acetic acid was added a solution of 2 g. of chromic oxide in 10 cc. of 80% acetic acid. It was heated at 60° for three hours. Water was added and the solid filtered. Crystallization from acetic acid gave a product melting at 193°. This gave no depression in melting point when mixed with the acid obtained by the oxidation of cholestanol.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 75.1; H, 10.7. Found: C, 74.9; H, 10.6.

2-Hydroxyandrosterone.—To a solution of 500 mg. of androstenone-17 in 200 cc. of acetic acid at 100° was added 5 cc. of hydrogen peroxide in 1-cc. portions at ten-minute intervals with stirring. Water was added and the product was extracted with ether. After evaporation of the ether and saponification the product was crystallized from dilute acetone, m. p. 195–198°. This was very difficult to separate from a small amount of other isomeric products present. It did not precipitate with alcoholic digitonin.

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.4; H, 9.9. Found: C, 74.2; H, 9.7.

2,3,17-Trihydroxyandrostane. (a).—The total product including the mother liquors from the above reaction was dissolved in 50 cc. of *n*-propyl alcohol and reduced by adding 5 g. of sodium. When this had dissolved, water was added, the product extracted with ether and the residue crystallized from methanol, m. p. 261–264°. It did not precipitate with alcoholic digitonin.

Anal. Calcd. for $C_{19}H_{32}O_3$: C, 74.0; H, 10.5. Found: C, 74.0; H, 10.4.

(b).—To a solution of 500 mg. of androstenol-17 in 50 cc. of acetic acid at 100° was added 5 cc. of hydrogen peroxide. The product was worked up as described for 2,3-dihydroxyandrostanone. It was crystallized from methanol to give a melting point of 264°. It gave no depression in melting point when mixed with the product obtained in the former case.

2,3,17-Trihydroxyandrostane Triacetate.—A solution of 100 mg. of the triol was refluxed with 3 cc. of acetic anhydride for thirty minutes. After cooling the crystalline product was filtered and recrystallized from methanol, m. p. 188°. Upon hydrolysis of this product the original triol, m. p. 264°, was obtained.

Anal. Calcd. for $C_{25}H_{38}O_6$: C, 69.1; H, 8.8. Found: C, 69.0; H, 8.7.

Summary

Upon treatment of Δ^2-cholestene with hydrogen peroxide, 2,3-cholestanediol is obtained. In a similar manner Δ^2-androstenone-17 gave androstanone-17-diol-2,3, which upon reduction with sodium gave 2,3,17-androstanetriol identical to the product obtained by treatment of Δ^2-androstenol-17 with hydrogen peroxide.

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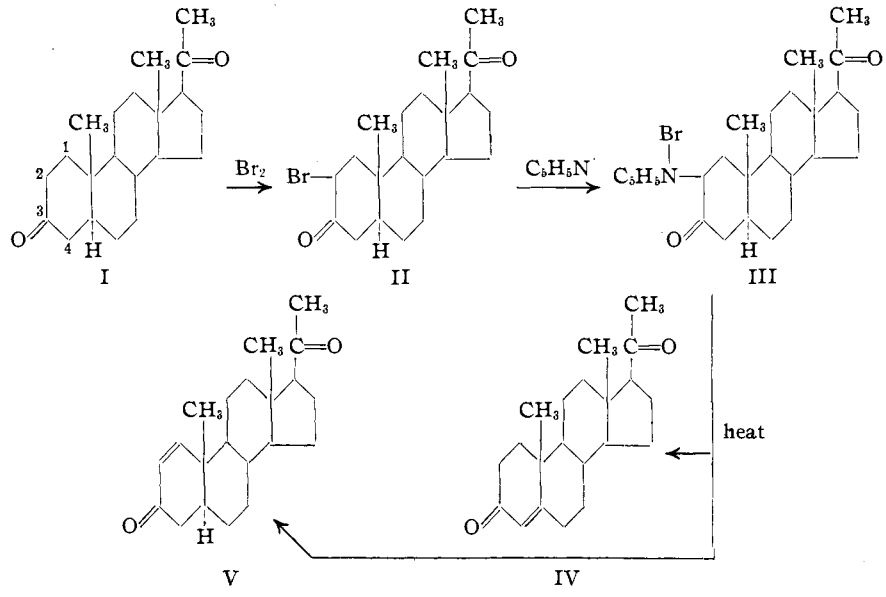
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXV. Progesterone from *allo*-Pregnanedione

BY RUSSELL E. MARKER, EUGENE L. WITTLE AND LOUIS PLAMBECK, JR.

One of the properties of steroids of the *allo*-series (H at C-5 *trans* to methyl at C-10) possessing a carbonyl group at C-3 is that bromination takes place almost exclusively at position C-2 (II) of the sterol molecule, while those of the coprostane series (H at C-5 *cis* to methyl at C-10) brominate almost exclusively at C-4.[1] When these latter C-4 bromides are refluxed with pyridine they suffer a splitting of hydrogen bromide from the molecule to form α,β-unsaturated ketones of the type (IV). In contrast to this, C-2 bromides under the same conditions form stable pyridine salts (III).



Recently Ruzicka[2] has shown that when the pyridine salt of 2-bromocholestanone is decomposed by dry distillation, a mixture of products is formed in which the most readily isolated compound is cholestenone and not the expected $\Delta^{1,2}$-*allo*-cholestenone. In this reaction a shift of the double bond from $\Delta^{1,2}$ to $\Delta^{4,5}$ has taken place. In the present work this reaction has been studied with *allo*-pregnanedione and a similar shift has been found to take place.

Treatment of 2-bromo-*allo*-pregnanedione (II) with pyridine forms the stable pyridine salt (III). Dry distillation of this salt at reduced pressure gave a mixture from which two substances, pro-

(1) Butenandt and Mamoli, *Ber.*, **68**, 1854 (1935); Butenandt and Wolff, *ibid.*, **68**, 2091 (1935).

(2) Ruzicka, Plattner, and Aeschbacher, *Helv. Chim. Acta*, **21**, 870 (1938).