Treatment of 3 α ,5-Cyclo-5 α -androstane-6 β ,17 β ,19-triol (XXI) and its 6 α -Epimer (XXII) with 60% Perchloric Acid in 90% aq. Dioxane—Each solution prepared from 0.04272 g. of 6 β ,17 β ,19-triol (XXI) and 0.04283 g. of 6 α ,17 β ,19-triol (XXII) in 5 ml. of 90% dioxane containing 6 drops of 60% HClO₄ was let stand at 27~28° and the changes of optical rotations were measured separately as shown in Table I.

When the solution of 6 α ,17 β ,19-triol (XXII), after allowing to stand at 27~28° for 66 hr., was heated at 70° for 4 hr., the observed $[\alpha]_D^{25}$ value was finally reached at -40°, the value for 3 β ,17 β ,19-trihydroxyandrost-5-ene (XXIII). The solutions were separately made alkaline with aq. NaHCO₃, concentrated *in vacuo*, and extracted with CHCl₃. Each extract was washed with water, dried, and condensed to dryness to give a crystalline product of the same 3 β ,17 β ,19-trihydroxyandrost-5-ene (XXIII) melting at 222~228°.

3 β ,17 β ,19-Trihydroxyandrost-5-ene (XXIII)—To a solution of 0.10 g. of VIIc in 50 ml. of EtOH was added 0.05 g. of NaBH₄ in water and stirring continued for 2 hr. at room temperature. The reaction mixture was worked up as described for XXI to give a crystalline product, which was recrystallized from EtOH-H₂O to afford needles of XXIII, m.p. 227~232°. An analytical sample was evacuated at 70° for 10 hr. *Anal.* Calcd. for C₁₉H₃₀O₃: C, 74.47; H, 9.87. Found: C, 74.00; H, 9.67. $[\alpha]_D^{25}$ -42.1° (EtOH).

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4. Katsumi Tanabe, Rinji Takasaki, Ryoza Hayashi, Yasuhiro Morisawa, and Teruo Hashimoto: Steroid Series. XVII.*¹ New Synthetic Routes to 19-Norsteroids (1).*²

(Central Research Laboratories, Sankyo Co., Ltd.*³)

19-Nor- Δ^4 -3-oxosteroid (IX) was synthesized starting from 3 α ,5 α -cyclo-6 β ,19-oxidosteroid (I) through 3 β -substituted- Δ^5 -steroid-19-oic acid (VII), whose synthesis was achieved by the three methods: i) Hydrolysis of 3 β -hydroxy- Δ^5 -steroid-19-oic acid 3,19-lactone (VI) which was prepared by oxidizing either 3 β ,19-dihydroxy- Δ^5 -steroid (III) or 3 β -hydroxy-19-oxo- Δ^5 -steroid (V) with Jones reagent or Oppenauer reaction, ii) Oxidation of 3 β ,19-dihydroxy- Δ^5 -steroid 3-acetate (III) with the excess Jones reagent, iii) Reduction of 3 α ,5 α -cyclo-6-oxo-19-oic acid (IV) with sodium borohydride and subsequent acid-catalysed solvolysis of a mixture of resultant 6-epimeric hydroxy acids (XIII and XIV) in a suitable solvent. 3 β -Substituted- Δ^5 -steroid-19-oic acid (VII) was in turn converted to 19-nor- Δ^4 -3-oxosteroid (IX) in two ways: i) Oxidation of 3 β -hydroxy compound and subsequent acid-treatment of the resultant Δ^5 -3-oxosteroid-19-oic acid (VIII), ii) Pyrolysis of the 3 β -acetoxo- Δ^5 -steroid-19-oic acid (VII) to afford 3 β -acetoxo- Δ^5 (10)-steroid (XI), followed by alkaline hydrolysis, Jones oxidation, and acid-treatment, successively.

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In a preceding paper*¹ we described the preparation of 3 α ,5 α -cyclo-6 β ,19-oxido-steroids (I) by the action of lead tetraacetate on 3 α ,5 α -cyclo-6 β -hydroxysteroids and acid-catalysed solvolysis reactions of the products to afford, depending upon the reaction conditions, 19-hydroxylated 3 α ,5 α -cyclo-6 β - (II) or Δ^5 -3 β -substituted steroids (III). Oxidation of the oxido compounds (I) leading directly to 3 α ,5 α -cyclo-6-oxosteroid-19-oic acids (IV) was also described. The present investigation was undertaken in order

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to synthesize biologically important 19-norsteroid derivatives by the use of those 19-functionalized compounds thus obtained.

Oxidation of 3 β ,19-dihydroxyandrost-5-en-17-one (III: R=O; X=OH) with 8N chromic acid solution in acetone¹⁾ yielded a complex mixture, from which 3 β -hydroxyandrost-5-en-17-on-19-oic acid 3,19-lactone (VI)*⁴ was isolated in about 15% yield after chromatography over alumina. The same lactone could also be obtained by Oppenauer or Jones chromic acid¹⁾ oxidations of 3 β -hydroxyandrost-5-ene-17,19-dione (V: R=H),*¹ which was prepared by treating 3 α ,5-cyclo-6 β ,19-oxido-5 α -androstan-17-one (I: R=O) with boron trifluoride etherate in acetic acid, followed by oxidation with one equivalent mole of Jones chromic acid reagent and subsequent alkaline hydrolysis of 3 β -acetoxyl group (I: R=O $\rightarrow$ III: R=O; X=AcO $\rightarrow$ V: R=Ac $\rightarrow$ V: R=H).

The nuclear magnetic resonance (NMR) spectrum of the 3 β ,19-lactone (VI) showed multiplets centered at 4.33 and 5.27 τ ascribable to 6-vinyl and 3 α -protons, respectively. A signal due to 18-methyl protons was observed at 8.93 τ , shifted downfield*⁵ compared with the corresponding one at 9.11 τ in 3 β -hydroxyandrost-5-en-17-one 3-acetate. The ultraviolet spectrum of the lactone exhibited an absorption maximum at 228 m μ with ϵ 2,700. Recently, Bagli, *et al.*²⁾ have observed an analogous lactone, 3 β ,17 β -dihydroxyandrost-5-en-19-oic acid 3,19-lactone 17-acetate to have a maximum at 228 m μ with ϵ 2,410 and attributed the abnormal absorption to $\pi\rightarrow\pi^*$ transition. The lactone (VI) was then subjected to hydrolysis with aqueous alkali to afford 3 β -hydroxyandrost-5-en-17-on-19-oic acid (VII: R=O; R'=H), which was converted to 19-norandrost-4-ene-3,17-dione (X: R=O) by oxidation of the 3-hydroxyl group with 8N chromic acid reagent and a subsequent treatment of the resultant keto acid (VIII: R=O) with acid or alkali.*⁶

Oppenauer oxidation of 4 β -3 β ,19-diol (III: R=O; X=OH), in contrast to the case of the corresponding 10 β -aldehyde (V: R=H), yielded a phenolic compound (X: R=H) and the expected 19-hydroxyandrost-4-ene-3,17-dione was not isolated in this experimental conditions.*⁷ The NMR spectrum of the phenol had a pair of doublets ($j=8.5$ c.p.s.) centered at 2.93 and 3.34 τ , assignable to the protons located at the vicinal positions on an aromatic ring. Besides a singlet at 9.10 τ due to 18-methyl protons, another signal appeared at 7.86 τ , which indicated the presence of methyl group attached to an aromatic ring. The phenolic compound (X: R=H) had a hydroxyl stretching band at 3425 cm⁻¹ and an aromatic skeletal vibrations at 1592 and 1500 cm⁻¹ together with a band at 809 cm⁻¹ indicating the presence of two aromatic hydrogens located at the vicinal positions. The acetate (X: R=Ac) of the phenol showed a band at 1761 cm⁻¹ characteristic to a phenolic acetate. Its ultraviolet spectrum exhibited absorption maxima at 279.5 m μ with ϵ 1,780 and 251.5 m μ with ϵ 300, differing from those observed for 1-hydroxy-4-methylestra-1,3,5(10)-trien-17-one.*^{8,3)} Direct comparison on mixed melting point and infrared spectra proved in fact the unidentity. The structure

*⁴ The formation of the lactone has been suggested, by Bagli, *et al.*,²⁾ to proceed *via* 3 β ,19-hemiacetal of the aldehyde (V: R=H).

*⁵ The effect of 19-carbonyl group on the chemical shift of 18-methyl protons will be discussed in a paper of this series, Part XIX.

*⁶ Since completion of this work a paper has appeared describing the transformation of the analogous lactone to 19-norandrost-4-ene-3,17-dione (X: R=O) by the same sequence of reactions: R. Gardi, C. Pedrali: *Gazz. chim. ital.*, **91**, 1420 (1961).

*⁷ Under specified conditions of Oppenauer oxidation 19-hydroxyandrost-4-ene-3,17-dione could be obtained in high yield: Japan Pat., No. 13067 (1964).

*⁸ Thanks are due to Dr. S. Nozoe, Inst. of Applied Microbiology, the Univ. of Tokyo, for a generous gift of the authentic sample.

1) K. Bowden, I. M. Heilbron, E. R. H. Jones, B. C. C. Weedon: *J. Chem. Soc.*, **1946**, 39.

2) J. F. Bagli, P. F. Morand, R. Gaudry: *J. Org. Chem.*, **28**, 1207 (1963).

3) A. S. Dreiding, A. Voltman: *J. Am. Chem. Soc.*, **76**, 537 (1954).

of the phenol (X: R=H) must therefore be 1-methyl-4-hydroxyestra-1,3,5(10)-trien-17-one. On Oppenauer oxidation of 3 β ,19,20 β -trihydroxy-6-methylpregn-5-ene, Bagli *et al.*²⁾ obtained a similar 'Oppenauer phenol' along with the expected 19-hydroxy-6 α -methylprogesterone and confirmed that the latter compound, on further Oppenauer

Chart 1.

oxidation, was convertible to the former, the exact locations of the hydroxyl and methyl groups on the aromatic ring of the phenol being left unsettled.

The second approach to 19-nor- Δ^4 -3-oxosteroid involves the pyrolysis of 3 β -acetoxy- Δ^5 -steroid-19-oic acids. Oxidation of 3 β ,19-Dihydroxyandrost-5-en-17-one 3-acetate*¹ (III: R=O; X=Ac) with excess 8*N* chromic acid reagent in acetone was found to give the corresponding 10 β -carboxylic acid (VII: R=O; R'=Ac) in only 20% yield. The carboxylic acid, however, was smoothly pyrolysed*⁹ on heating at 250~260° for about 10 minutes with elimination of carbon dioxide and concomitant migration of the double bond to afford 3 β -hydroxyestr-5(10)-en-17-one 3-acetate (XI: R=O; R'=Ac), whose structure was established by the conversion to the known ester-5(10)-ene-3,17-dione (XII: R=O) through the alkaline hydrolysis and subsequent oxidation with 8*N* chromic acid reagent. The $\Delta^{5(10)}$ -3-ketone (XII: R=O) is well known to isomerize into 19-nor-androst-4-ene-3,17-dione (IX: R=O) in the presence of acid or alkali.

Treatment of 3 β -hydroxyestr-5(10)-en-17-one (XI: R=O; R'=H) with lithium aluminum hydride afforded the corresponding $\Delta^{5(10)}$ -3 β ,17 β -diol (XVII: R=H) having m.p. 153~155°, $[\alpha]_D +100.7^\circ$.*¹⁰ The same stereochemical structure had formerly assigned to the reduction product having m.p. 208~209°, $[\alpha]_D +122.5^\circ$, of 17 β -hydroxyestr-5(10)-en-3-one with the same reagent.⁴⁾ In order to settle this problem, the following experiments were undertaken. Reduction of 17 β -hydroxyestr-5(10)-en-3-one (XVIII)⁵⁾ with lithium aluminum hydride in tetrahydrofuran, followed by acetylation and subsequent chromatographic separation of the product, afforded two crystalline diacetates, m.p. 93~95° and m.p. 120~122°, both of which were oxidized, after hydrolysis, to give the same $\Delta^{5(10)}$ -3,17-diketone (XII: R=O), suggesting that the two acetates

Chart 2.

*⁹ Ciba group has also reported the same decarboxylation reaction in their synthetic studies on 19-nor-steroid: J. Kalvoda, K. Heusler, H. Ueberwasser, G. Anner, A. Wettstein: *Helv. Chim. Acta*, **46**, 1361 (1963).

*¹⁰ Reported values⁵⁾: m.p. 130~132°, $[\alpha]_D +112^\circ$.

4) J. Hartman: *J. Am. Chem. Soc.*, **77**, 5151 (1955).

5) A. L. Wilds, N. A. Nelson: *J. Am. Chem. Soc.*, **75**, 5366 (1953).

are epimeric at 3-position each other. The acetate isolated in a minor amount was proved to be identical with the 3 β ,17 β -diacetate (XVII: R=Ac) derived from the Δ^5 (10)-3 β ,17 β -diol (XVII: R=H) having m.p. 153~155°. Consequently, the other diacetate (XX: R=Ac) of m.p. 120~122°, the major product, and also the corresponding diol (XX: R=H) of m.p. 208~209° were established to have 3 α -configuration. Levine, *et al.*⁶⁾ have recently reported investigations on the reduction of 17 β -hydroxyestr-5(10)-en-3-one 17-propionate with lithium aluminum tri-*t*-butoxyhydride and, on the basis of the examination of infrared and NMR spectra, determined the stereochemistry of C₃-hydroxyl group in the major product having m.p. 205~207°, $[\alpha]_D^{25} +186^\circ$ to be α -configuration, this conclusion being coincident with the present result.

In the synthesis of 19-norandrost-4-ene-3,17-dione (K: R=O) described thus far, the intermediates of 3 β -substituted- Δ^5 -steroid-19-oic acids (VII: R=O, R'=H, Ac) could be obtained only in poor yields. In connection with this problem a route to these important intermediates has been developed by conveniently utilizing 3 α ,5 α -cyclo-6-oxosteroid-19-oic acids (IV), which could be prepared directly by Jones oxidation of 3 α ,5 α -cyclo-6 β ,19-oxides (I) in good yields.*¹

Reduction of 3 α ,5-cyclo-6,17-dioxo-5 α -androstan-19-oic acid (V: R=O) with sodium borohydride in aqueous ethanol yielded, after chromatography over silica gel, 3 α ,5-cyclo-6 α ,17 β -dihydroxy-5 α -androstan-19-oic acid (XIV: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$) and its 6 β -epimer (XIII: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$) in a ratio of 5:4. The configurational assignments at C₆-hydroxyl groups were

deduced from the following observations. 3 α ,5-Cyclo-6 α ,17 β -dihydroxy-5 α -androstan-19-oic acid (XIV: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$), after conversion to its methyl ester with diazomethane,

was reduced with lithium aluminum hydride to afford the corresponding triol which was identical with the known 3 α ,5-cyclo-6 α ,17 β ,19-trihydroxy-5 α -androstan-19-oic acid (XV) described in the preceding paper*¹ and therefore the stereochemistry at C₆-hydroxyl group in the compound (XIV: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$) was established to be α -configuration.

The reaction of 3 α ,5-cyclo-5 α -cholestan-6-one in ether solution of lithium aluminum hydride has been reported⁷⁾ to be almost completely stereospecific and yielded the corresponding 6 α -alcohol in 85% yield. Sodium borohydride reduction of 3 α ,5-cyclo-5 α -androstan-6,17,19-trione was shown, in our preceding paper,*¹ to yield a mixture of the corresponding 6 α ,17 β ,19-triol and its 6 β -epimer in a ratio of 11:1. In contrast to these results, reduction of 3 α ,5-cyclo-6,17-dioxosteroid-19-oic acid (V: R=O) resulted in a markedly increasing formation of 6 β -hydroxylated compound (XIII: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$) and this might come from prevention of the approach of the reagent from the β -side to the C₆-carbonyl carbon atom owing to the bulkier 19-carboxyl group.

The reaction mixture of the epimeric 3 α ,5 α -cyclo-6,17 β -dihydroxy-19-carboxylic acids (XIII and XIV: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$) was treated, without further purification, with boron trifluoride etherate in acetic acid to afford a single product, 3 β ,17 β -dihydroxyandrost-5-en-19-oic acid 3-acetate (VII: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$; R'=Ac) in high yield. The mixture of 6,17 β -diacetates of the carboxylic acids (XIII and XIV: R= $\begin{smallmatrix} \text{OH} \\ \vdots \\ \text{H} \end{smallmatrix}$) afforded 3 β ,17 β -dihydroxyandrost-5-en-19-oic acid 3,17-diacetate (VII: R= $\begin{smallmatrix} \text{OAc} \\ \vdots \\ \text{H} \end{smallmatrix}$; R'=Ac) by the same solvolysis reaction. When the mixture of 6-epimeric alcohols was subjected to the solvolysis in

6) S. G. Levine, N. H. Eudy, E. C. Farthing: Tetrahedron Letters, No. 23, 1517 (1963).

7) A. F. Wagner, N. E. Wolff, E. S. Wallis: J. Org. Chem., 17, 529 (1952).

aqueous dioxane with a small amount of 60% perchloric acid, a mixture of 3 β ,17 β -dihydroxyandrost-5-en-19-oic acid (VII: R= $\begin{smallmatrix} \text{OH} \\ | \\ \text{H} \end{smallmatrix}$; R'=H) and its 3 β ,19-lactone (XVI) was obtained, the latter lactone being hydrolysed with aqueous alkali to the former acid.

By utilizing the reactions described above involving pyrolysis of 3 β -acetoxycholest-5-en-19-oic acid (VII: R= $\begin{smallmatrix} \text{C}_8\text{H}_{17} \\ | \\ \text{H} \end{smallmatrix}$; R'=Ac), 19-norcholest-4-en-3-one (IX: R= $\begin{smallmatrix} \text{C}_8\text{H}_{17} \\ | \\ \text{H} \end{smallmatrix}$) was synthesized through 3 α ,5-cyclo-6-oxo-5 α -cholestan-19-oic acid (V: R= $\begin{smallmatrix} \text{C}_8\text{H}_{17} \\ | \\ \text{H} \end{smallmatrix}$) as shown in detail in the experimental part.

19-Nortestosterone benzoate (X: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$) could also be prepared by a sequence of reactions described below. Reduction of 3 α ,5-cyclo-6 β ,19-oxido-5 α -androstan-17-one (I: R=O) with lithium aluminum hydride in ether and subsequent benzylation with benzoyl chloride in pyridine gave the corresponding 17 β -benzoate, which was then oxidized with 8*N* chromic acid reagent in acetone to yield 3 α ,5-cyclo-6-oxo-17 β -hydroxy-5 α -androstan-19-oic acid 17-benzoate (IV: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$). Treatment of the keto acid with sodium borohydride, followed by solvolysis of the resultant mixture of 6-hydroxy acid (XIII and XIV: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$) in formic acid in the presence of borontrifluoride etherate, afforded 3 β ,17 β -dihydroxyandrost-5-en-19-oic acid 3-formate 17-benzoate (VII: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$; R'=HCO). Partial hydrolysis of the formate at 3-position with sodium carbonate in methanol to the corresponding 3 β -hydroxy acid (VII: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$; R'=H) and subsequent oxidation with 8*N* chromic acid solution afforded 3-oxo-17 β -hydroxyandrost-5-en-19-oic acid 17-benzoate (VIII: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$), which was finally converted into 19-nortestosterone benzoate (X: R= $\begin{smallmatrix} \text{OBz} \\ | \\ \text{H} \end{smallmatrix}$) by treating with hydrochloric acid in ethanol.

Experimental*11

3 β -Hydroxy-17-oxoandrost-5-en-19-oic acid 3,19-Lactone (VI)—i) To a stirred solution of 0.30 g. of III (R=O, X=OH) in 100 ml. of purified acetone cooled at 14°, 0.8 ml. of Jones reagent was added dropwise with nitrogen bubbling and stirring further continued for 14 min. The excess reagent was decomposed by adding MeOH. The reaction mixture was diluted with H₂O, concentrated *in vacuo*, and extracted with CHCl₃. The extract was washed with 5% NaHCO₃, H₂O, dried over anhyd. Na₂SO₄ and evaporated to leave 0.31 g. of a residue. Recrystallization of the residue from benzene-hexane afforded 0.072 g. of crystals melting at 220~250° (decomp.). Analytical sample was further recrystallized from benzene-hexane to give leaflets of 3 β -hydroxy-17-oxoandrost-5-en-19-oic acid 3,19-lactone (VI), m.p. 261~263° (decomp.). [α]_D -108.4° (c=1.19). *Anal.* Calcd. for C₁₉H₂₄O₃: C, 75.97; H, 8.05. Found: C, 75.93; H, 8.03. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 1753 (δ -lactone), 1743 (17-CO). UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (ϵ): 228 (2,700). NMR τ : 8.93 (18-CH₃), 5.27 (3 α -H), 4.33 (6-H).

ii) To a stirred solution of 0.352 g. of 3 β -hydroxyandrost-5-ene-17,19-dione (V: R=H) in 40 ml. of acetone cooled at 15°, 0.4 ml. of 8*N* CrO₃-H₂SO₄ solution was added dropwise. After stirring for additional 4 min., the reaction mixture was treated with EtOH to decompose the excess reagent and diluted with H₂O to separate crystals, which was collected by filtration and dried to afford 0.13 g. of VI as needles melting at 245~253°.

iii) A solution of 0.91 g. of V (R=H) in 100 ml. of toluene and 6 g. of cyclohexane was heated to boiling and 20 ml. of distillate removed. To the boiling mixture was added dropwise with stirring, 1.5 g. of aluminum isopropoxide in 12 ml. of toluene for 10 min., during which time 20 ml. of distillate was removed.

*11 Melting points were uncorrected. The nuclear magnetic resonance spectra were taken with Varian A-60 in CDCl₃ solutions containing tetramethylsilane as an internal standard. Unless otherwise stated, optical rotations were measured in CHCl₃ solutions.

After stirring under reflux for 2 hr., the reaction mixture was cooled, treated with 5% H_2SO_4 to decompose the excess reagent and extracted with ether. The extract was washed with 5% NaHCO_3 , H_2O , and dried over anhyd. Na_2SO_4 . Evaporation of the solvent gave 2.0 g. of an oily residue and the residue was then taken up into hexane and stored in an ice box to separate crystals, which was collected by filtration to afford 0.164 g. of crude lactone (VI) melting at $235\sim 245^\circ$. Recrystallization from acetone-hexane gave VI as needles of m.p. $258\sim 262^\circ$ (decomp.).

3 β -Hydroxy-17-oxoandrost-5-en-19-oic Acid 3-Acetate (VII : R=O, R'=Ac)—To a stirred solution of 1.18 g. of III (R=O, X=OAc) in 120 ml. of purified acetone cooled at 18° , 3.0 ml. of Jones' reagent was added dropwise under a stream of nitrogen and stirring continued for 5 min. Additional 1.5 ml. of Jones' reagent was added and stirring further continued for 7 min. The reaction mixture was treated with MeOH to decompose the excess reagent, diluted with H_2O , concentrated *in vacuo* and extracted with AcOEt. The extract was shaken with 5% NaHCO_3 for several times, the combined aq. layers were acidified with dil. HCl and extracted with AcOEt. The extract was washed with water, dried, and evaporated to yield 0.255 g. of a crystalline residue, which was recrystallized from acetone-ether to afford 3 β -hydroxy-17-oxoandrost-5-en-19-oic acid 3-acetate (VII : R=O, R'=Ac) as plates, m.p. 253° (decomp.). *Anal.* Calcd. for $\text{C}_{21}\text{H}_{28}\text{O}_5$: C, 69.97; H, 7.83. Found: C, 69.60; H, 7.73. IR ν_{max} cm^{-1} : 1730, 1706.

1-Methyl-4-hydroxyestra-1,3,5(10)-triene-17-one (X : R=H)—From a boiling solution of 0.60 g. of 3 β ,19-dihydroxyandrost-5-en-17-one (III : R=O, X=OH) in 100 ml. of toluene and 6 ml. of cyclohexanone, 20 ml. of distillate was removed. To the mixture was added dropwise 1.5 g. of aluminum iso-propoxide in 10 ml. of toluene in about 5 min., during which time further 20 ml. of distillate was removed. After stirring under reflux for 3.5 hr., the reaction mixture was treated as described for V (R=H) to yield an oily product, which was chromatographed over 30 g. of Al_2O_3 . The eluate with benzene-ether (5:1) gave 0.06 g. of crystals melting at $215\sim 223^\circ$, which was recrystallized from benzene-hexane to afford needles of X (R=H), m.p. $234\sim 236^\circ$, $[\alpha]_D^{30} + 140.2^\circ$ ($c=0.77$). *Anal.* Calcd. for $\text{C}_{19}\text{H}_{24}\text{O}_2$: C, 80.24; H, 8.51. Found: C, 79.95; H, 8.11. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3425 (OH), 1730 (17-CO), 1592 and 1500 (aromatic ring), 809 (aromatic 2- and 3-H). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 279.5 (1,780), 251.5 (300).

The phenol (X : R=H) was acetylated with Ac_2O and pyridine at room temperature for 5 hr. The reaction mixture was condensed *in vacuo* to leave a crystalline residue, which was chromatographed over Al_2O_3 . The eluate with benzene-hexane (3:7), after evaporation and recrystallization of the residue from MeOH, gave prisms of 1-methyl-4-hydroxy-17-oxoestra-1,3,5(10)-triene 4-acetate (X : R=Ac), m.p. $124\sim 126^\circ$, $[\alpha]_D^{25} + 104.4^\circ$ ($c=1.08$). *Anal.* Calcd. for $\text{C}_{21}\text{H}_{26}\text{O}_3$: C, 77.27; H, 8.03. Found: C, 76.88; H, 7.68. IR ν_{max} cm^{-1} : 1761 (phenolic acetate), 1736 (17-CO), 814 (2- and 3-H). NMR τ : 9.09 (18-CH₃), 7.96 (4-OAc), 7.66 (1-CH₃), 2.76 (doublet) and 3.16 (doublet) ($j=8.2$ c.p.s.).

3 β -Hydroxyandrost-5-en-17-on-19-oic Acid (VII : R=O, R'=H)—A solution of 0.50 g. of Δ^5 -3 β ,19-lactone (VI) in 100 ml. of EtOH and 50 ml. of 10% KOH was refluxed for 2 hr. The reaction mixture was condensed *in vacuo*, acidified with AcOH and extracted with ether. The extract was washed with H_2O , dried and condensed to dryness to yield 0.50 g. of a crystalline residue melting at $254\sim 257^\circ$. Recrystallization from benzene afforded leaflets of VII (R=O, R'=H), m.p. $256\sim 258^\circ$. $[\alpha]_D - 113^\circ$ ($c=2.85$, pyridine). *Anal.* Calcd. for $\text{C}_{19}\text{H}_{26}\text{O}_4$: C, 71.67; H, 8.23. Found: C, 71.39; H, 8.20. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3448 (OH), 1742 (17-CO), 1712 (δ -lactone).

19-Norandrost-4-ene-3,17-dione (IX : R=O)—To a stirred solution of 0.077 g. of VII (R=O, R'=H) in 70 ml. of acetone cooled at $14\sim 15^\circ$ with N_2 bubbling, 0.09 ml. of 8N CrO_3 - H_2SO_4 reagent was added dropwise. After stirring for 6 min., the reaction mixture was treated with a small amount of EtOH to decompose the excess reagent, diluted with H_2O , concentrated *in vacuo* and extracted with CHCl_3 . The CHCl_3 solution was shaken with 5% NaHCO_3 and the aqueous layer was separated, made acidic with dil. HCl and again extracted with CHCl_3 . The extract was washed with H_2O and dried over Na_2SO_4 . Evaporation of the solvent gave 0.057 g. of androst-5-ene-3,17-dion-19-oic acid (VIII : R=O) as a crystalline residue melting at $138\sim 143^\circ$. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1725.

Fifty milligrams of the Δ^5 -keto acid (VIII : R=O) in 8.0 ml. of MeOH containing 4 drops of 10% KOH was gently warmed on a water-bath for about 7 min. The reaction mixture was concentrated *in vacuo*, diluted with H_2O and extracted with ether. The ether extract was washed with H_2O , dried and the solvent was evaporated to leave 0.021 g. of a crystalline residue. Recrystallization from iso-propyl ether afforded leaflets of IX (R=O), m.p. $163\sim 167^\circ$. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1743 (17-CO), 1672 and 1623 (Δ^4 -3-CO). This was confirmed to be identical with the specimen obtained by Jones oxidation of 19-nortestosterone by the mixed m.p. determination and infrared spectral comparison.

3 β -Hydroxyestr-5(10)-en-17-one 3-Acetate (XI : R=O, R'=Ac)—A round-bottomed flask containing 0.12 g. of VII (R=O, R'=Ac) was immersed into an oil-bath preheated at $260\sim 270^\circ$. The content in the flask melted with a simultaneous evolution of CO_2 . After 10 min. heating, the oil-bath was removed and an oily product taken up in ether. The ether solution, after washing with H_2O and drying, was condensed to leave an oily residue, which was chromatographed over 5 g. of Al_2O_3 . Elution with benzene-hexane (1:1) gave 0.073 g. of oil, which crystallized on addition of acetone and was recrystallized from aq. acetone to afford XI (R=O, R'=Ac), m.p. $76.5\sim 77.5^\circ$. *Anal.* Calcd. for $\text{C}_{20}\text{H}_{28}\text{O}_3$: C, 75.91; H, 8.92. Found: C, 75.85; H, 8.71. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1742.

3 β -Hydroxyestr-5(10)-en-17-one (XI : R=O, R'=H)—A solution of 0.07 g. of XI (R=O, R'=Ac) in 10 ml. of 2% KOH-MeOH was refluxed for 1.5 hr. The reaction mixture was poured into water and extracted with ether. The ether extract was washed with H₂O, dried and condensed to yield 0.045 g. of an oily residue, which crystallized on adding hexane. Recrystallization from hexane afforded XI (R=O, R'=H), m.p. 131~132°. *Anal.* Calcd. for C₁₈H₂₆O₂: C, 78.29; H, 9.55. Found: C, 78.13; H, 9.41. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3491 (OH), 1733 (17-CO).

Estr-5(10)-ene-3,17-dione (XII : R=O)—i) To a solution of 0.04 g. of XI (R=O, R'=H) in 5 ml. of acetone under ice-cooling, 0.05 ml. of 8N CrO₃-H₂SO₄ reagent was added dropwise with N₂ bubbling and stirring. After stirring for 3 min., the reaction mixture was worked up as the manner described for Δ^5 -3 β ,19-dialcohol (III : R=O, X=OH) to yield an oily product, which was crystallized on addition of ether. Recrystallization from ether afforded (XII : R=O), m.p. 148°. *Anal.* Calcd. for C₁₈H₂₄O₂: C, 79.39; H, 8.88. Found: C, 79.52; H, 8.72. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1748 (17-CO), 1727 (3-CO).

ii) To a stirred solution of 0.10 g. of XVII (R=H) was added 0.6 ml. of Jones' reagent at 5° and the mixture was stirred for 5 min. The reaction mixture was treated with MeOH to decompose the excess oxidant, diluted with water, concentrated *in vacuo* and extracted with ether. The extract was washed with water, dried and removal of the solvent yielded 0.075 g. of a crystalline residue, which was recrystallized from ether to afford XII (R=O) as prisms, m.p. 147~148°.

Reduction of 3 β -Hydroxyestr-5(10)-en-17-one (XI : R=O, R'=H) with Lithium Aluminum Hydride in Ether—To a stirred suspension of 0.20 g. of LiAlH₄ in 10 ml. of anhyd. ether under ice-cooling, 0.372 g. of XI (R=O, R'=H) in 20 ml. of anhyd. ether was added dropwise and stirring continued for 2.5 hr. The reaction mixture was treated with AcOEt to decompose the excess reagent, diluted with water and extracted with ether. The extract was washed with 5% NaHCO₃, H₂O, dried and the solvent was evaporated to afford 0.314 g. of a crystalline residue, which was chromatographed on 9 g. of Al₂O₃. Elutions with benzene, benzene-ether (4:1 and 3:2), after evaporation of the solvent, gave 0.249 g. of crystals, which was recrystallized from benzene-hexane to afford 3 β ,17 β -dihydroxyestr-5(10)-ene (XVII : R=H), m.p. 153~155°. [α]_D + 100.7° (c=1.85). *Anal.* Calcd. for C₁₈H₂₈O₂: C, 78.21; H, 10.21. Found: C, 78.29; H, 10.03. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3378 (OH).

The $\Delta^5(10)$ -3 β ,17 β -diol (XVII : R=H) was treated with Ac₂O and pyridine and worked up as usual to afford an oily product, which was chromatographed over 9 g. of Al₂O₃. The eluates with benzene and benzene-ether (4:1 and 3:2) gave 0.249 g. of crystals, which was recrystallized from hexane to yield 3 β ,17 β -dihydroxyestr-5(10)-ene 3,17-diacetate (XVII : R=Ac), m.p. 93~95°.

Reduction of 17 β -Hydroxyestr-5(10)-en-3-one (XVIII) with Lithium Aluminum Hydride in Tetrahydrofuran—To a stirred suspension of 0.30 g. of LiAlH₄ in 30 ml. of anhyd. tetrahydrofuran under ice-cooling, 0.5 g. of XVIII in 60 ml. of anhyd. tetrahydrofuran was added dropwise in about 7 min. and stirring continued for 2 hr. The reaction mixture was treated as described above to give 0.46 g. of a crystalline residue, which was acetylated with Ac₂O and pyridine at room temperature overnight. The mixture was condensed *in vacuo* to leave 0.671 g. of an oily residue, which was chromatographed over 67 g. of Al₂O₃. The eluates with hexane and hexane-benzene (10:1) afforded 0.139 g. of a syrupy substance, which crystallized on addition of hexane. Recrystallization from hexane afforded 3 β ,17 β -dihydroxyestr-5(10)-ene 3 β ,17-diacetate (XVII : R=Ac), m.p. 93~95°.

The $\Delta^5(10)$ -3 β ,17 β -diacetate (XVII : R=Ac) was hydrolysed with 2% KOH-MeOH at room temperature and worked up as usual to afford XVII (R=H) melting at 153~155°. [α]_D + 100.7°.

The second eluate with hexane-benzene (10:1) gave 0.346 g. of 3 α ,17 β -dihydroxyestr-5(10)-ene 3,17-diacetate (XIX : R=Ac), which showed m.p. 120~122° after recrystallization from hexane.

The $\Delta^5(10)$ -3 α ,17 β -diacetate (XIX : R=Ac) was hydrolysed with 2% KOH-MeOH and worked up as usual to afford, after recrystallization from MeOH, 3 α ,17 β -dihydroxyestr-5(10)-ene (XIX : R=H), m.p. 208~209°. [α]_D + 159° (c=0.79).

The $\Delta^5(10)$ -3 α ,17 β -diol (XIX : R=H) was oxidized with 8N CrO₃-H₂SO₄ reagent under ice-cooling and worked up as described for XI (R=O, R'=H) to give XII (R=O) of m.p. 148°.

Reduction of 3 α ,5-Cyclo-6,17-dioxo-5 α -androstan-19-oic Acid (IV : R=O) with Sodium Borohydride in Ethanol—To a stirred solution of 20 g. of IV (R=O)*¹ in 1500 ml. of EtOH and 200 ml. of H₂O under ice-cooling, an aq. solution of 20 g. of NaBH₄ was added dropwise and stirring continued at room temperature for 4 hr. The reaction mixture was treated with AcOH to decompose the excess reagent, then condensed *in vacuo* and extracted with AcOEt. The extract was washed with water, dried over Na₂SO₄. Removal of the solvent afforded a crystalline residue, which was recrystallized from AcOEt to yield 5.92 g. of 3 α ,5-cyclo-6 α ,17 β -dihydroxy-5 α -androstan-19-oic acid (XIV : R= $\overline{\text{H}}$ -OH). Repeated recrystallization from AcOEt

afforded needles of pure sample, m.p. 248~249° (decomp.). *Anal.* Calcd. for C₁₉H₂₈O₄: C, 71.22; H, 8.81. Found: C, 71.39; H, 8.80. The filtrate of the recrystallization was condensed to dryness and chromatographed over 700 g. of silica gel. The first fraction eluted with benzene-AcOEt (4:6) afforded 0.717 g. of an oily mixture of unknown substances, which was not examined further.

The second eluate with the same mixture of solvents gave additional 3.381 g. of XIV ($R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$) (combined crystals : 9.30 g.).

The third one yielded 5.12 g. of about 1:1 mixture of 6 α - and 6 β -epimers as disclosed by TLC on silica gel.

The last fractions eluted with benzene-AcOEt (4:6) and AcOEt gave 7.32 g. of 3 α ,5-cyclo-6 β ,17 β -dihydroxy-5 α -androstane-19-oic acid (XIII : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$). An analytical sample was obtained by recrystallization from ether as needles of m.p. 204~206° (decomp.). *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found : C, 71.12; H, 8.95.

3 α ,5-Cyclo-6 α ,17 β ,19-trihydroxy-5 α -androstane (XV)—A solution of 0.10 g. of 3 α ,5-cyclo-6 α ,17 β -dihydroxy-5 α -androstane-19-oic acid (XIV : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$) in 15 ml. of ether containing a small amount of MeOH

was treated with an ethereal solution of CH_2N_2 and the yellow colored solution was set aside at room temperature for 15 min. The excess reagent was decomposed by adding AcOH and the ether solution was washed with aq. $NaHCO_3$, water and dried over Na_2SO_4 . Evaporation of the solvent and recrystallization of the product from AcOEt afforded sticks of methyl 3 α ,5-cyclo-6 α ,17 β -dihydroxy-5 α -androstane-19-oate melting at 147~149°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3500, 3420, 3280 and 3170 (OH), 1710.

A mixture of 0.20 g. of the methyl ester, 0.20 g. of $LiAlH_4$ and 20 ml. of anhd. dioxane was refluxed for 4 hr. The reaction mixture was treated with aq. AcOH to decompose the excess reagent and shaken with ether. The ether extract was washed with aq. $NaHCO_3$, water and dried over anhyd. Na_2SO_4 . The solvent was evaporated to give 0.187 g. of an amorphous product, which crystallized by adding aq. MeOH. Recrystallization from aq. MeOH afforded 0.131 g. of XV as needles melting at 166°. The identity with an authentic sample*¹ was confirmed by mixed melting point determination and comparison of R_f values of thin-layer chromatography (TLC) on silica gel.

Treatment of the Mixture of Dihydroxyacids (XIII and XIV : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$) with Perchloric Acid in

aq. Dioxane—A solution of 0.55 g. of the mixture of XIII and XIV ($R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$) which was obtained by reduction of the keto acid (IV : $R = O$) with $NaBH_4$ as described above, in 65 ml. of 70% aq. dioxane and 1 ml. of 60% $HClO_4$ was refluxed for 3 hr. and allowed to stand at room temperature overnight. The solution was diluted with H_2O , condensed *in vacuo* to a small volume and extracted with AcOEt. The extract was shaken well with 5% $NaHCO_3$. The alkaline layer was acidified with AcOH to separate needles, which was collected by filtration and dried to give 0.1 g. of 3 β ,17 β -dihydroxyandrost-5-en-19-oic acid (VII : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$, $R' = H$), m.p. 276~277° (decomp.). *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found :

C, 70.82; H, 8.63. The mother liquor of filtration was extracted with AcOEt and the extract was washed with H_2O , dried and condensed to afford additional 0.2 g. of crude VII.

The organic layer was washed with H_2O , dried and the solvent was removed to give 0.3 g. of a crystalline residue. Recrystallization from benzene-hexane afforded sticks of the 3 β ,19-lactone (XVI), m.p. 206~207°. *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found : C, 75.08; H, 8.43.

The 3 β ,19-lactone (XVI; 0.20 g.) was hydrolysed in a solution of 20 ml. of EtOH and 0.20 g. of NaOH by refluxing for 30 min. The reaction mixture was diluted with H_2O and shaken with AcOEt. The alkaline layer was acidified with AcOH to separate needles, which was filtered on a glass-filter and dried to give 0.181 g. of VII ($R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$, $R' = H$), m.p. 275~276° (decomp.).

3 β ,17 β -Dihydroxyandrost-5-en-19-oic Acid 3,17-Diacetate (VII : $R = \begin{smallmatrix} \text{OAc} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$, $R' = Ac$)—A solution of 0.94 g. of the mixture of dihydroxyacids (XIII and XIV : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$), obtained by reduction of IV ($R = O$)

with $NaBH_4$ as described above, in 30 ml. of pyridine and 10 ml. of Ac_2O was set aside at room temperature overnight. The reaction mixture was poured onto ice-water and extracted with AcOEt. The extract was washed with water, dried over anhyd. Na_2SO_4 . Evaporation of the solvent gave a crude mixture of 6 α ,17 β - and 6 β ,17 β -diacetates. The mixture of the diacetates (0.40 g.) was dissolved in 30 ml. of AcOH containing 1 ml. of BF_3 -etherate and the mixture was left standed at room temperature for 26 hr. The solution was poured onto ice-water and extracted with AcOEt. The extract was washed with H_2O , dried and the solvent evaporated to give a crystalline residue, which, after recrystallization from ether-hexane, afforded needles of VII ($R = \begin{smallmatrix} \text{OAc} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$, $R' = Ac$), m.p. 202~203°. *Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found : C, 68.25; H, 8.00.

3 β ,17 β -Dihydroxyandrost-5-en-19-oic Acid 3-Acetate (VII : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$, $R' = Ac$)—A solution of 0.50 g. of the mixture of dihydroxy acids (XIII and XIV : $R = \begin{smallmatrix} \text{OH} \\ | \\ \text{---} \\ | \\ \text{H} \end{smallmatrix}$) in 40 ml. of AcOH and 10 drops of BF_3 -

etherate was allowed to stand at room temperature for 15 hr. The reaction mixture was diluted with H₂O and concentrated *in vacuo* to dryness to leave a crystalline product, which was recrystallized from EtOH to afford VII (R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac) as needles, m.p. 255~256° (decomp.). *Anal.* Calcd. for C₂₁H₃₀O₅: C, 69.58; H, 8.34. Found: C, 69.24; H, 8.47.

3 β -Hydroxycholest-5-en-19-oic Acid 3-Acetate (VII : R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac)—To a stirred solution of 4.33 g. of 3 α ,5-cyclo-6-oxo-5 α -cholestan-19-oic acid (IV : R= $\text{---}\text{C}_8\text{H}_{17}$) in 400 ml. of 99% EtOH and 300 ml. of H₂O was added dropwise 4.40 g. of NaBH₄ in 30 ml. of H₂O at 10~15° and stirring continued for 7.5 hr. at room temperature. The reaction mixture was treated with AcOH to decompose the excess reagent and condensed *in vacuo* to a small volume. The concentrate was extracted with AcOEt. The extract was washed with H₂O, dried and the solvent was removed to yield 4.3 g. of a mixture of XIII and XIV (R= $\text{---}\text{C}_8\text{H}_{17}$).

The mixture (3.9 g.) was dissolved in 400 ml. of AcOH and 1.0 ml. of BF₃-etherate and the solution set aside at room temperature for 15 hr. The reaction mixture was poured onto ice-water and concentrated *in vacuo* to separate a crystalline product, which was collected by filtration and dried to give 4.0 g. of crystals melting at 194~198°. Recrystallization from hexane afforded VII (R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac), m.p. 200~202°, [α]_D -71.1° (c=2.24). *Anal.* Calcd. for C₂₉H₄₆O₄: C, 75.94; H, 10.11. Found: C, 75.64; H, 10.17. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1734, 1695.

3 β -Hydroxy-19-norcholest-5(10)-ene 3-Acetate (XI : R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac)—A round-bottomed flask containing 3.11 g. of VII (R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac) was immersed into an oil-bath preheated at 260~270°. The content melted with evolution of CO₂. After heating for 15 min. an oil-bath was removed and the oily product was taken into hexane. The hexane solution was cooled in a refrigerator to separate crystals, which was collected by filtration and dried to give 0.35 g. of VII (R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac) recovered. The filtrate

was chromatographed over Al₂O₃ and the eluate with hexane afforded 1.41 g. of an oily material. This crystallized by adding MeOH and recrystallized from MeOH to afford XII (R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac), m.p. 70~71°. [α]_D +83.3°. *Anal.* Calcd. for C₂₈H₄₆O₂: C, 81.10; H, 11.18. Found: C, 80.50; H, 11.22. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1739, 1247 and 1037 (OAc).

19-Norcholest-4-en-3-one (IX : R= $\text{---}\text{C}_8\text{H}_{17}$)—A solution of 1.233 g. of XII (R= $\text{---}\text{C}_8\text{H}_{17}$, R'=Ac) in 60 ml. of 1% KOH-MeOH was allowed to stand at room temperature overnight. The reaction mixture was concentrated *in vacuo* to a small volume, diluted with H₂O to separate crystals, which was collected by filtration and dried to weigh 1.068 g. of needles melting at 99~103°. Recrystallization from MeOH-ether to afford 3 β -Hydroxy-19-norcholest-5(10)-ene (X : R= $\text{---}\text{C}_8\text{H}_{17}$, R'=H) as needles, m.p. 108~109°.

[α]_D +10.1°. *Anal.* Calcd. for C₂₆H₄₄O: C, 83.80; H, 11.90. Found: C, 83.43; H, 11.83. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3330 (OH). To a stirred solution of 0.071 g. of the 3 β -alcohol (X : R= $\text{---}\text{C}_8\text{H}_{17}$, R'=H) in 20 ml. of purified acetone was added dropwise 0.10 ml. of 8N CrO₃-H₂SO₄ reagent at 10~15° and stirring continued for 5 min.

The reaction mixture was treated with MeOH to decompose the excess reagent, diluted with H₂O and extracted with ether. The ether extract was washed with H₂O, dried and removal of the solvent gave 0.042 g. of an oily residue of 19-norcholest-5(10)-en-3-one (XII).

The oily residue (0.248 g.) of XII in 30 ml. of MeOH containing 0.3 ml. of conc. HCl was heated on a water bath for 15 min. The solution was diluted with H₂O and extracted with ether. The extract was washed with 5% NaHCO₃, H₂O, dried and condensed to yield 0.238 g. of an oily residue, which was chromatographed over Al₂O₃. Elution with benzene gave IX (R= $\text{---}\text{C}_8\text{H}_{17}$) as an oily substance. IR

$\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1681 and 1623 (Δ^4 -3-CO). UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (ϵ): 239 (9,300).

3 α ,5-Cyclo-6-oxo-17 β -hydroxy-5 α -androstan-19-oic Acid 17-Benzoate (IV : R= $\text{---}\text{OBz}$)—To a stirred suspension of 2.0 g. of LiAlH₄ in 150 ml. of dry ether a solution of 3.05 g. of I (R=O) in 150 ml. of dry ether was added dropwise for 1 hr. under ice-cooling and stirring continued for additional 1.5 hr.

The excess reagent was decomposed by careful addition of H₂O. The resulting mixture was made acidic with dil. H₂SO₄ and extracted with ether. The ether extract was washed with H₂O, aq. NaHCO₃, H₂O and dried over anhyd. Na₂SO₄. Removal of the solvent gave 2.9 g. of a crystalline residue, which was recrystallized from benzene-hexane to afford plates of the corresponding 17 β -ol, m.p. 181~183°.

The 17 β -ol (0.50 g.) was dissolved in 10 ml. of dry pyridine and 0.25 g. of BzCl and the mixture allowed to stand at 22° for 15 hr. The solution was diluted with H₂O to separate a crystalline product,

which was collected by filtration, washed with H_2O and dried to afford 0.65 g. of crystals melting at $195\sim 198^\circ$. Recrystallization from benzene-hexane gave prisms of $3\alpha,5\text{-cyclo-}6\beta,19\text{-oxido-}17\beta\text{-hydroxy-}5\alpha\text{-androstan-}17\text{-benzoate}$ (I: $\text{R}=\text{---OBz}$), m.p. $197\sim 198^\circ$, $[\alpha]_{\text{D}}^{25} +91.5^\circ$ ($c=3.43$). *Anal.* Calcd. for $\text{C}_{26}\text{H}_{32}\text{O}_3$: C, 79.55; H, 8.22. Found: C, 79.41; H, 8.11. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1718, 1603, 1587, 1276, and 720.

To a stirred solution of 2.9 g. of the $17\beta\text{-benzoate}$ in 350 ml. of acetone, 15 ml. of $8N \text{CrO}_3\text{-H}_2\text{SO}_4$ reagent was added dropwise for 7 min. at 15° and stirring continued for 25 min. at 21° . The reaction mixture was cooled in ice-bath, then treated with EtOH to decompose the excess reagent and condensed *in vacuo* to a small volume, which was extracted with AcOEt. The extract was shaken with three portions of 10% Na_2CO_3 . The combined alkaline extracts were made acidic with $2N \text{HCl}$ under ice-cooling to a separate crystalline product, which, after storing in refrigerator overnight, was filtered on a glass-filter, washed with H_2O and dried to yield 1.8 g. of crystals melting at $193\sim 197^\circ$. The water filtrate was extracted with AcOEt and the extract was washed with water, dried and condensed to give additional 0.41 g. of a crystalline residue. Recrystallization from AcOEt-benzene afforded prisms of IV ($\text{R}=\text{---OBz}$), m.p.

$195\sim 197^\circ$, $[\alpha]_{\text{D}}^{25} +61.9^\circ$ ($c=1.94$). *Anal.* Calcd. for $\text{C}_{26}\text{H}_{30}\text{O}_5$: C, 73.91; H, 7.16. Found: C, 73.43; H, 7.20. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1724, 1656, 714.

$3\beta,17\beta\text{-Dihydroxyandrost-5-en-19-oic Acid 3-Formate 17-Benzoate}$ (VII: $\text{R}=\text{---OBz}$, $\text{R}'=\text{HCO}$)—

To a stirred solution of 0.95 g. of IV ($\text{R}=\text{---OBz}$) in 120 ml. of 99% EtOH was added dropwise 1.0 g. of NaBH_4 in 20 ml. of H_2O and stirring continued for 6.5 hr. at about 20° . The reaction mixture was treated as described for IV ($\text{R}=\text{O}$) to yield 0.88 g. of a mixture of reduction products (XIII and XIV: $\text{R}=\text{---OBz}$).

The reduction mixture (1.07 g.) was dissolved in 100 ml. of 98% HCOOH containing 0.9 ml. of $\text{BF}_3\text{-etherate}$ and the solution was set aside at room temp. for 2 hr. The reaction mixture was poured into ice-water to separate crystals, which were filtered on a glass-filter, washed with H_2O and dried to weigh 1.05 g. Recrystallization from benzene-hexane afforded 0.365 g. of needles melting at $210\sim 214^\circ$. From the mother liquor additional 0.73 g. of crystals of m.p. $205\sim 214^\circ$ was obtained. An analytical sample was obtained on further recrystallization from benzene-hexane as needles of VII ($\text{R}=\text{---OBz}$, $\text{R}'=\text{HCO}$), m.p. $214\sim 217^\circ$. *Anal.*

Calcd. for $\text{C}_{27}\text{H}_{32}\text{O}_6$: C, 71.60; H, 7.13. Found: C, 71.41; H, 7.06. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1733, 1724, 1692, 1678.

$3\beta,17\beta\text{-Dihydroxyandrost-5-en-19-oic Acid 17-Benzoate}$ (VII: $\text{R}=\text{---OBz}$, $\text{R}'=\text{H}$)—A mixture of

0.365 g. of VII ($\text{R}=\text{---OBz}$, $\text{R}'=\text{HCO}$) in 40 ml. of MeOH and 0.18 g. of anhyd. Na_2CO_3 in 3.0 ml. of H_2O

was shaken at room temperature for 12 hr. The reaction mixture was neutralized with AcOH, concentrated *in vacuo* and diluted with H_2O to separate crystals, which was collected by filtration and dried to afford 0.32 g. of needles melting at $217\sim 219^\circ$. Recrystallization from benzene-EtOH gave needles of VII ($\text{R}=\text{---OBz}$, $\text{R}'=\text{H}$), m.p. $218\sim 219^\circ$. An analytical sample was obtained by evacuation at 75° for 15 hr. *Anal.*

Calcd. for $\text{C}_{26}\text{H}_{36}\text{O}_5$: C, 73.56; H, 7.60. Found: C, 73.33; H, 7.57. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3484 (OH), 1712 (OBz).

$19\text{-Nortestosterone Benzoate}$ (IX: $\text{R}=\text{---OBz}$)—To a stirred solution of 0.20 g. of VII ($\text{R}=\text{---OBz}$, $\text{R}'=\text{H}$)

in 30 ml. of purified acetone was added dropwise 0.40 ml. of $8N \text{CrO}_3\text{-H}_2\text{SO}_4$ reagent at $12\sim 13^\circ$ and stirring continued for 5 min. The reaction mixture was treated as described for $\Delta^5\text{-}3\beta,19\text{-dialcohol}$ (III: $\text{R}=\text{O}$, $\text{X}=\text{OH}$) to afford 0.195 g. of an amorphous product, which was taken into 10 ml. of EtOH containing 0.5 ml. of conc. HCl and heated on a water-bath for 6 min. The solution was condensed *in vacuo*, diluted with H_2O and extracted with ether. The extract was washed with H_2O , dried and removal of the solvent gave 0.165 g. of an amorphous residue, which was chromatographed over 5 g. of Al_2O_3 . Elution with benzene-hexane (1:1), after evaporation and recrystallization from acetone-hexane, afforded 0.06 g. of X ($\text{R}=\text{---OBz}$) as sticks, m.p. $176\sim 178^\circ$. $[\alpha]_{\text{D}}^{25} +110^\circ$ ($c=0.95$).^{*12} *Anal.* Calcd. for $\text{C}_{25}\text{H}_{30}\text{O}_3$: C,

79.33; H, 7.99. Found: C, 79.20; H, 7.94. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1714, 1276 and 1114 ($17\beta\text{-OBz}$), 1646 and 1618 ($\Delta^4\text{-}3\text{-CO}$). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 233 (31,000).

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^{*12} Lit.: m.p. $178.4\sim 180.6^\circ$; $[\alpha]_{\text{D}}^{25} +97.3^\circ$. cf. J. A. Hartman, A. J. Tomaszewski, A. S. Dreiding: J. Am. Chem. Soc., **78**, 5662 (1956).