Treatment of 3α,5-Cyclo-5α-androstane-6β,17β,19-triol (XXI) and its 6α-Epimer (XXII) with 60% Perchloric Acid in 90% aq. Dioxane——Each solution prepared from 0.04272 g. of 6β,17β,19-triol (XXI) and 0.04283 g. of 6α,17β,19-triol (XXII) in 5 ml. of 90% dioxane containing 6 drops of 60% $HClO_4$ was let stand at 27~28° and the changes of optical rotations were measured separately as shown in Table I.

When the solution of 6α,17β,19-triol (XXII), after allowing to stand at 27~28° for 66 hr., was heated at 70° for 4 hr., the observed $[\alpha]_D$ value was finally reached at −40°, the value for 3β,17β,19-trihydroxyandrost-5-ene (XXIII). The solutions were separately made alkaline with aq. $NaHCO_3$, concentrated *in vacuo*, and extracted with $CHCl_3$. Each extract was washed with water, dried, and condensed to dryness to give a crystalline product of the same 3β,17β,19-trihydroxyandrost-5-ene (XXIII) melting at 222~228°.

3β,17β,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 $NaBH_4$ 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-H_2O to afford needles of XXIII, m.p. 227~232°. An analytical sample was evacuated at 70° for 10 hr. *Anal.* Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.00; H, 9.67. $[\alpha]_D^{29}$ −42.1° (EtOH).

The authors are grateful to Prof. K. Tsuda, Director of Institute of Applied Microbiology, the Univ. of Tokyo and Dr. G. Sunagawa, Director of this Laboratories for their continuing encouragement. Thanks are also due to Mr. Nakazawa for skilled technical help and to the members of Section of Physical Chemistry in this Laboratories for measurements of physical and elemental analytical data.

[Chem. Pharm. Bull. 15(1) 27 ~ 37 (1967)] UDC 547.92.07

4. Katsumi Tanabe, Rinji Takasaki, Ryozo 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 3α,5α-cyclo-6β,19-oxidosteroid (I) through 3β-substituted-Δ^5-steroid-19-oic acid (VII), whose synthesis was achieved by the three methods: i) Hydrolysis of 3β-hydroxy-Δ^5-steroid-19-oic acid 3,19-lactone (VI) which was prepared by oxidizing either 3β,19-dihydroxy-Δ^5-steroid (III) or 3β-hydroxy-19-oxo-Δ^5-steroid (V) with Jones reagent or Oppenauer reaction, ii) Oxidation of 3β,19-dihydroxy-Δ^5-steroid 3-acetate (III) with the excess Jones reagent, iii) Reduction of 3α,5α-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. 3β-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 3β-hydroxy compound and subsequent acid-treatment of the resultant Δ^5-3-oxosteroid-19-oic acid (VIII), ii) Pyrolysis of the 3β-acetoxy-Δ^5-steroid-19-oic acid (VII) to afford 3β-acetoxy-$\Delta^{5(10)}$-steroid (XI), followed by alkaline hydrolysis, Jones oxidation, and acid-treatment, successively.

(Received February 23, 1966)

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

*1 Part XVI: This Bulletin, **15**, 15 (1967).

*2 A part of this work was presented at the 82th Annual Meeting of the Pharmaceutical Society of Japan at Shizuoka, Oct. 1962.

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

Oxidation of 3β,19-dihydroxyandrost-5-en-17-one (Ⅲ: R=O; X=OH) with 8N chromic acid solution in acetone[1] yielded a complex mixture, from which 3β-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 acid[1] oxidations of 3β-hydroxyandrost-5-ene-17,19-dione (Ⅴ : R=H),*1 which was prepared by treating 3α,5-cyclo-6β,19-oxido-5α-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 3β-acetoxyl group (Ⅰ : R=O→Ⅲ : R=O; X=AcO→Ⅴ : R=Ac→Ⅴ : R=H).

The nuclear magnetic resonance (NMR) spectrum of the 3β,19-lactone (Ⅵ) showed multiplets centered at 4.33 and 5.27τ ascribable to 6-vinyl and 3α-protons, respectively. A signal due to 18-methyl protons was observed at 8.93τ, shifted downfield*5 compared with the corresponding one at 9.11τ in 3β-hydroxyandrost-5-en-17-one 3-acetate. The ultraviolet spectrum of the lactone exhibited an absorption maximum at 228 mμ with ε 2,700. Recently, Bagli, *et al.*[2] have observed an analogous lactone, 3β,17β-dihydroxyandrost-5-en-19-oic acid 3,19-lactone 17-acetate to have a maximum at 228 mμ 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 3β-hydroxyandrost-5-en-17-on-19-oic acid (Ⅶ : R=O; R'=H), which was converted to 19-norandrost-4-ene-3,17-dione (Ⅸ : 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

Oppenaner oxidation of Δ^5-3β,19-diol (Ⅲ : R=O; X=OH), in contrast to the case of the corresponding 10β-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 3.34τ, assignable to the protons located at the vicinal positions on an aromatic ring. Besides a singlet at 9.10τ due to 18-methyl protons, another signal appeared at 7.86τ, 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 mμ with ε 1,780 and 251.5 mμ 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 unidenty. The structure

*4 The formation of the lactone has been suggested, by Bagli, *et al.*,[2] to proceed *via* 3β,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 (Ⅸ : 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 3β,19,20β-trihydroxy-6-methylpregn-5-ene, Bagli *et al.*[2] obtained a similar 'Oppenauer phenol' along with the expected 19-hydroxy-6α-methylprogesterone and confirmed that the latter compound, on further Oppenauer

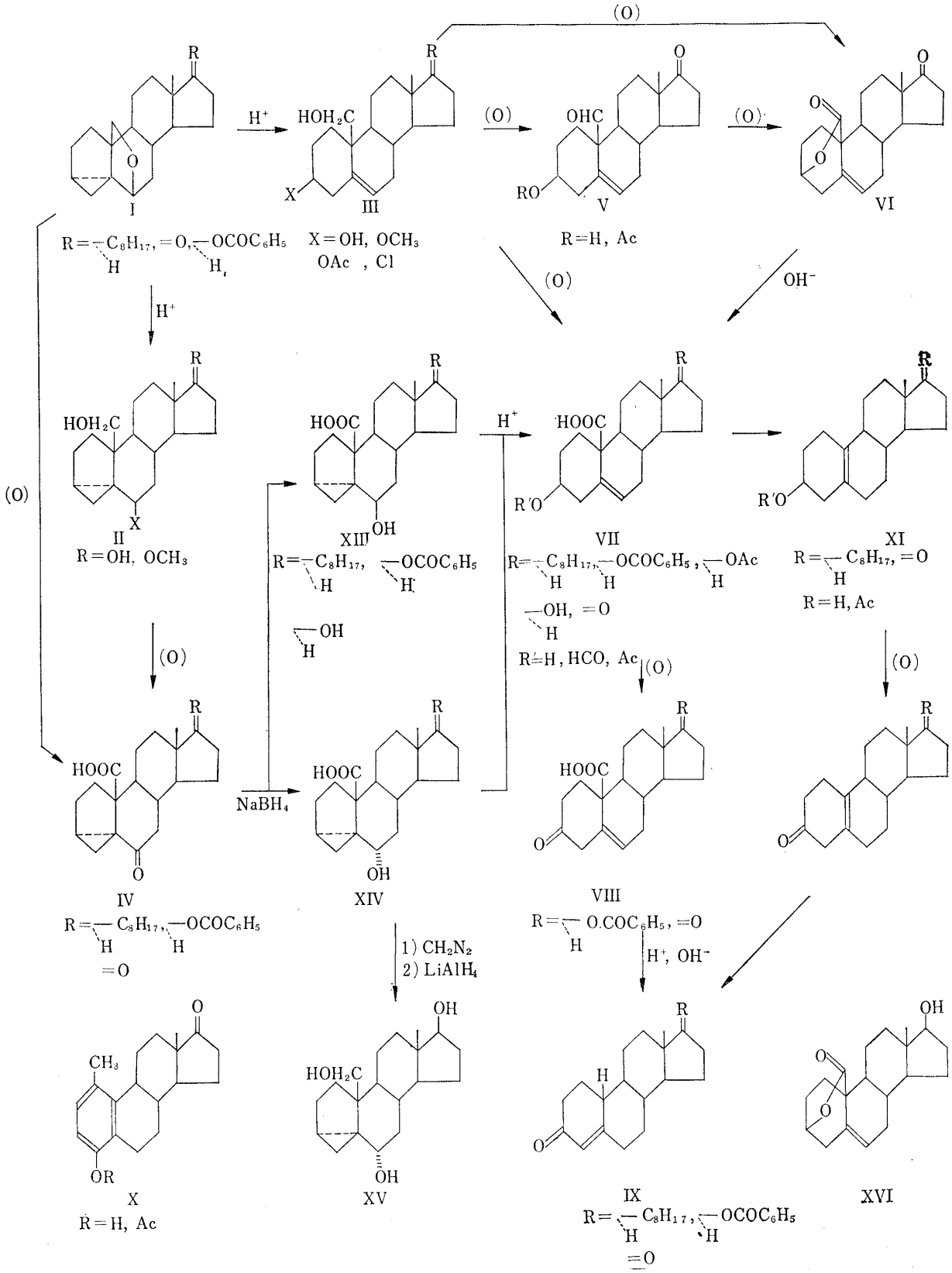

Chart 1.

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 3β-acetoxy-Δ^5-steroid-19-oic acids. Oxidation of 3β,19-Dihydroxyandrost-5-en-17-one 3-acetate*[1] (Ⅲ: R=O; X=Ac) with excess 8N chromic acid reagent in acetone was found to give the corresponding 10β-carboxylic acid (Ⅵ: 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 3β-hydroxyester-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 8N 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 3β-hydroxyestr-5(10)-en-17-one (Ⅺ: R=O; R′=H) with lithium aluminum hydride afforded the corresponding $\Delta^{5(10)}$-3β,17β-diol (XVⅡ: R=H) having m.p. 153~155°, $[\alpha]_D$ +100.7°.*[10] The same stereochemical structure had formerly assigned to the reduction product having m.p. 208~209°, $[\alpha]_D$ +122.5°, of 17β-hydroxy-estr-5(10)-en-3-one with the same reagent.[4] In order to settle this problem, the following experiments were undertaken. Reduction of 17β-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

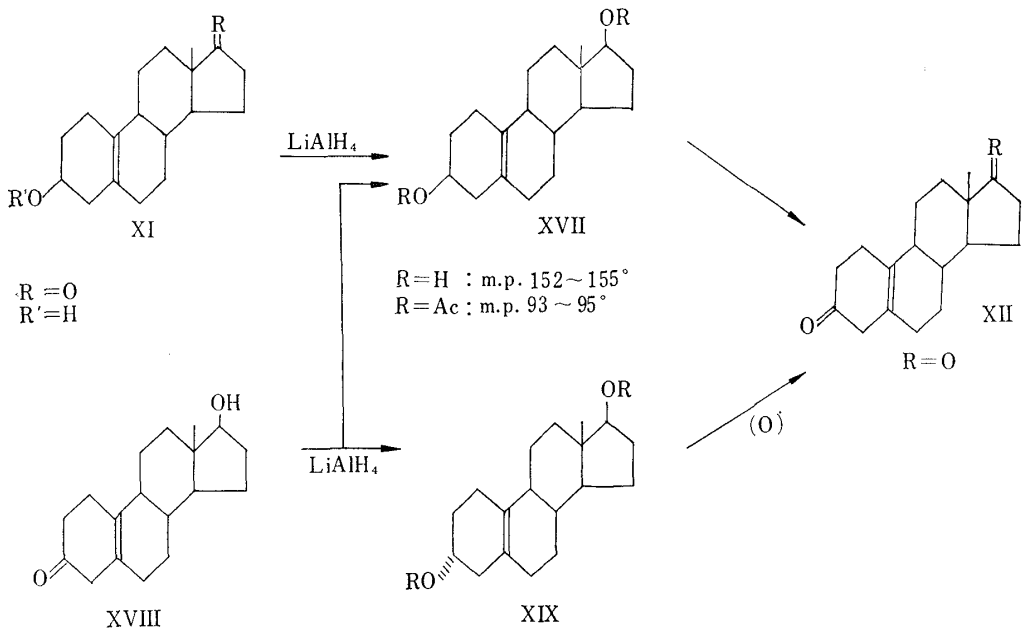

Chart 2.

*[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 values[6] : m.p. 130~132°, $[\alpha]_D$ +112°.

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 3β,17β-diacetate (XVII: R=Ac) derived from the $\Delta^{5(10)}$-3β,17β-diol (XVII: R=H) having m.p. 153~155°. Consequently, the other diacetate (XIX: R=Ac) of m.p. 120~122°, the major product, and also the corresponding diol (XIX: R=H) of m.p. 208~209° were established to have 3α-configuration. Levine, *et al.*[6] have recently reported investigations on the reduction of 17β-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 C_3-hydroxyl group in the major product having m.p. 205~207°, $[\alpha]_D$ +186° to be α-configuration, this conclusion being coincident with the present result.

In the synthesis of 19-norandrost-4-ene-3,17-dione (IX: R=O) described thus far, the intermediates of 3β-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 3α,5α-cyclo-6-oxosteroid-19-oic acids (IV), which could be prepared directly by Jones oxidation of 3α,5α-cyclo-6β,19-oxides (I) in good yields.*1

Reduction of 3α,5-cyclo-6,17-dioxo-5α-androstan-19-oic acid (IV: R=O) with sodium borohydride in aqueous ethanol yielded, after chromatography over silica gel, 3α,5-cyclo-6α,17β-dihydroxy-5α-androstan-19-oic acid (XIV: R=$\underset{H}{\cdots OH}$) and its 6β-epimer (XIII: R=$\underset{H}{\cdots OH}$) in a ratio of 5:4. The configurational assignments at C_6-hydroxyl groups were deduced from the following observations. 3α,5-Cyclo-6α,17β-dihydroxy-5α-androstan-19-oic acid (XIV: R=$\underset{H}{\cdots OH}$), after convertion to its methyl ester with diazomethane, was reduced with lithium aluminum hydride to afford the corresponding triol which was identical with the known 3α,5-cyclo-6α,17β,19-trihydroxy-5α-androstane (XV) described in the preceding paper*1 and therefore the stereochemistry at C_6-hydroxyl group in the compound (XIV: R=$\underset{H}{\cdots OH}$) was established to be α-configuration.

The reaction of 3α,5-cyclo-5α-cholestan-6-one in ether solution of lithium aluminum hydride has been reported[7] to be almost completely stereospecific and yielded the corresponding 6α-alcohol in 85% yield. Sodium borohydride reduction of 3α,5-cyclo-5α-androstane-6,17,19-trione was shown, in our preceding paper,*1 to yield a mixture of the corresponding 6α,17β,19-triol and its 6β-epimer in a ratio of 11:1. In contrast to these results, reduction of 3α,5-cyclo-6,17-dioxosteroid-19-oic acid (IV: R=O) resulted in a markedly increasing formation of 6β-hydroxylated compound (XIII: R=$\underset{H}{\cdots OH}$) and this might come from prevention of the approach of the reagent from the β-side to the C_6-carbonyl carbon atom owing to the bulkier 19-carboxyl group.

The reaction mixture of the epimeric 3α,5α-cyclo-6,17β-dihydroxy-19-carboxylic acids (XIII and XIV: R=$\underset{H}{\cdots OH}$) was treated, without further purification, with boron trifluoride etherate in acetic acid to afford a single product, 3β,17β-dihydroxyandrost-5-en-19-oic acid 3-acetate (VII: R=$\underset{H}{\cdots OH}$; R'=Ac) in high yield. The mixture of 6,17β-diacetates of the carboxylic acids (XIII and XIV: R=$\underset{H}{\cdots OH}$) afforded 3β,17β-dihydroxy-androst-5-en-19-oic acid 3,17-diacetate (VII: R=$\underset{H}{\cdots OAc}$; 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 3β,17β-dihydroxyandrost-5-en-19-oic acid (Ⅶ: R=⋱OH; R′=H) and its 3β,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 3β-acetoxycholest-5-en-19-oic acid (Ⅶ: R=⋱C_8H_{17}; R′=Ac), 19-norcholest-4-en-3-one (Ⅸ: R=⋱C_8H_{17}) was synthesized through 3α,5-cyclo-6-oxo-5α-cholestan-19-oic acid (Ⅳ: R=⋱C_8H_{17}) as shown in detail in the experimental part.

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

Experimental*11

3β-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 H_2O, concentrated *in vacuo*, and extracted with $CHCl_3$. The extract was washed with 5% $NaHCO_3$, H_2O, dried over anhyd. Na_2SO_4 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 3β-hydroxy-17-oxoandrost-5-en-19-oic acid 3,19-lactone (Ⅵ), m.p. 261~263° (decomp.). $[\alpha]_D$ −108.4° (c=1.19). *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.93; H, 8.03. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1753 (δ-lactone), 1743 (17-CO). UV λ_{max}^{EtOH} mμ (ε): 228 (2,700). NMRτ: 8.93 (18-CH_3), 5.27 (3α-H), 4.33 (6-H).

ii) To a stirred solution of 0.352 g. of 3β-hydroxyandrost-5-ene-17,19-dione (Ⅴ: R=H) in 40 ml. of acetone cooled at 15°, 0.4 ml. of 8*N* CrO_3-H_2SO_4 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 H_2O 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 $CDCl_3$ solutions containing tetramethylsilane as an internal standard. Unless otherwise stated, optical rotations were measured in $CHCl_3$ 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 235~245°. Recrystallization from acetone-hexane gave VI as needles of m.p. 258~262° (decomp.).

3β-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 3β-hydroxy-17-oxoandrost-5-en-19-oic acid 3-acetate (VII : R=O, R′=Ac) as plates, m.p. 253° (decomp.). *Anal.* Calcd. for $C_{21}H_{28}O_5$: 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)-trien-17-one (X : R=H)——From a boiling solution of 0.60 g. of 3β,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 215~223°, which was recrystallized from benzene-hexane to afford needles of X (R=H), m.p. 234~236°, $[\alpha]_D^{30}$ +140.2° (c=0.77). *Anal.* Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found : C, 79.95; H, 8.11. IR ν_{max}^{Nujol} cm^{-1} : 3425 (OH), 1730 (17-CO), 1592 and 1500 (aromatic ring), 809 (aromatic 2- and 3-H). UV λ_{max}^{EtOH} mμ (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. 124~126°, $[\alpha]_D^{28}$ +104.4° (c=1.08). *Anal.* Calcd. for $C_{21}H_{26}O_3$: 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-CH_3), 7.96 (4-OAc), 7.66 (1-CH_3), 2.76 (doublet) and 3.16 (doublet) (j=8.2 c.p.s.).

3β-Hydroxyandrost-5-en-17-on-19-oic Acid (VII : R=O, R′=H)——A solution of 0.50 g. of Δ^5-3β, 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 254~257°. Recrystallization from benzene afforded leaflets of VII (R=O, R′=H), m.p. 256~258°. $[\alpha]_D$ −113° (c=2.85, pyridine). *Anal.* Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found : C, 71.39; H, 8.20. IR ν_{max}^{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 14~15° with N_2 bubbling, 0.09 ml. of 8*N* 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 138~143°. IR ν_{max}^{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 affoded leaflets of IX (R=O), m.p. 163~167°. IR ν_{max}^{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.

3β-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 260~270°. 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. 76.5~77.5°. *Anal.* Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found : C, 75.85; H, 8.71. IR ν_{max}^{Nujol} cm^{-1} : 1742.

3β-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 H_2O, dried and condensed to yield 0.045 g. of an oily residue, which crystallizied on adding hexane. Recrystallization from hexane afforded XI (R=O, R′=H), m.p. 131~132°. *Anal.* Calcd. for $C_{18}H_{26}O_2$: C, 78.29; H, 9.55. Found : C, 78.13; H, 9.41. IR ν_{max}^{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 8*N* CrO_3-H_2SO_4 reagent was added dropwise with N_2 bubbling and stirring. After stirring for 3 min., the reaction mixture was worked up as the manner described for Δ^5-3β,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 $C_{18}H_{24}O_2$: C, 79.39; H, 8.88. Found : C, 79.52; H, 8.72. IR ν_{max}^{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 Jone's 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 3β-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 $LiAlH_4$ 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% $NaHCO_3$, H_2O, dried and the solvent was evaporated to afford 0.314 g. of a crystalline residue, which was chromatographed on 9 g. of Al_2O_3. 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 3β,17β-dihydroxyestr-5(10)-ene (XVII : R=H), m.p. 153~155°. $[\alpha]_D$ + 100.7° (c=1.85). *Anal.* Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found : C, 78.29; H, 10.03. IR ν_{max}^{Nujol} cm^{-1}: 3378 (OH).

The $\Delta^{5(10)}$-3β,17β-diol (XVII : R=H) was treated with Ac_2O and pyridine and worked up as usual to afford an oily product, which was chromatographed over 9 g. of Al_2O_3. 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 3β,17β-dihydroxyestr-5(10)-ene 3,17-diacetate (XVII : R=Ac), m.p. 93~95°.

Reduction of 17β-Hydroxyestr-5(10)-en-3-one (XVIII) with Lithium Aluminum Hydride in Tetrahydrofuran——To a stirred suspension of 0.30 g. of $LiAlH_4$ 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 Ac_2O 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 Al_2O_3. 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 3β,17β-dihydroxyestr-5(10)-ene 3β,17-diacetate (XVII : R=Ac), m.p. 93~95°.

The $\Delta^{5(10)}$-3β,17β-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°. $[\alpha]_D$ + 100.7°.

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

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

The $\Delta^{5(10)}$-3α,17β-diol (XIX : R=H) was oxidized with 8*N* CrO_3-H_2SO_4 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 3α,5-Cyclo-6,17-dioxo-5α-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 H_2O under ice-cooling, an aq. solution of 20 g. of $NaBH_4$ 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 Na_2SO_4. Removal of the solvent afforded a crystalline residue, which was recrystallized from AcOEt to yield 5.92 g. of 3α,5-cyclo-6α,17β-dihydroxy-5α-androstan-19-oic acid (XIV : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$OH). Repeated recrystallization from AcOEt afforded needles of pure sample, m.p. 248~249° (decomp.). *Anal.* Calcd. for $C_{19}H_{28}O_4$: 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=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH) (combined crystals : 9.30 g.).

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

The last fractions eluted with benzene–AcOEt (4:6) and AcOEt gave 7.32 g. of 3α,5-cyclo-6β,17β-dihydroxy-5α-androstan-19-oic acid (XIII : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH). 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.

3α,5-Cyclo-6α,17β,19-trihydroxy-5α-androstane (XV)——A solution of 0.10 g. of 3α,5-cylo-6α,17β-dihydroxy-5α-androstan-19-oic acid (XIV : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH) 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 3α,5-cyclo-6α,17β-dihydroxy-5α-androstan-19-oate melting at 147~149°. IR ν_{max}^{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 Rf values of thin-layer chromatography (TLC) on silica gel.

Treatment of the Mixture of Dihydroxyacids (XIII and XIV : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH) with Perchloric Acid in aq. Dioxane——A solution of 0.55 g. of the mixture of XIII and XIV (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH) 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 3β,17β-dihydroxyandrost-5-en-19-oic acid (VII : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH, 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 3β,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 3β,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=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH, R′=H), m.p. 275~276° (decomp.).

3β,17β-Dihydroxyandrost-5-en-19-oic Acid 3,17-Diacetate (VII : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OAc, R′=Ac)——A solution of 0.94 g. of the mixture of dihydroxyacids (XIII and XIV : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH), 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 6α,17β- and 6β,17β-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=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OAc, 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.

3β,17β-Dihydroxyandrost-5-en-19-oic Acid 3-Acetate (VII : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH, R′=Ac)——A solution of 0.50 g. of the mixture of dihydroxy acids (XIII and XIV : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH) 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 H_2O and concentrated *in vacuo* to dryness to leave a crystalline product, which was recrystallized from EtOH to afford VII (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OH, R′=Ac) as needles, m.p. 255～256° (decomp.). *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.24; H, 8.47.

3β-Hydroxycholest-5-en-19-oic Acid 3-Acetate (VII: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=Ac)——To a stirred solution of 4.33 g. of 3α,5-cyclo-6-oxo-5α-cholestan-19-oic acid (IV: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$) in 400 ml. of 99% EtOH and 300 ml. of H_2O was added dropwise 4.40 g. of $NaBH_4$ in 30 ml. of H_2O 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 H_2O, dried and the solvent was removed to yield 4.3 g. of a mixture of XIII and XIV (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$).

The mixture (3.9 g.) was dissolved in 400 ml. of AcOH and 1.0 ml. of BF_3-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=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=Ac), m.p. 200～202°, $[\alpha]_D$ −71.1° (c=2.24). *Anal.* Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.64; H, 10.17. IR ν_{max}^{Nujol} cm^{-1}: 1734, 1695.

3β-Hydroxy-19-norcholest-5(10)-ene 3-Acetate (XI: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=Ac)——A round-bottomed flask containing 3.11 g. of VII (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=Ac) was immersed into an oil-bath preheated at 260～270°. The content melted with evolution of CO_2. 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=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=Ac) recovered. The filtrate was chromatographed over Al_2O_3 and the eluate with hexane afforded 1.41 g. of an oily material. This crystallized by adding MeOH and recrystallized from MeOH to afford XI (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=Ac), m.p. 70～71°. $[\alpha]_D$ +83.3°. *Anal.* Calcd. for $C_{28}H_{46}O_2$: C, 81.10; H, 11.18. Found: C, 80.50; H, 11.22. IR ν_{max}^{Nujol} cm^{-1}: 1739, 1247 and 1037 (OAc).

19-Norcholest-4-en-3-one (IX: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$)——A solution of 1.233 g. of XI (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, 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 H_2O 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 3β-Hydroxy-19-norcholest-5(10)-ene (XI: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=H) as needles, m.p. 108～109°, $[\alpha]_D$ +10.1°. *Anal.* Calcd. for $C_{26}H_{44}O$: C, 83.80; H, 11.90. Found: C, 83.43; H, 11.83. IR ν_{mxx}^{Nujol} cm^{-1}: 3330 (OH). To a stirred solution of 0.071 g. of the 3β-alcohol (XI: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$, R′=H) in 20 ml. of purified acetone was added dropwise 0.10 ml. of 8*N* CrO_3-H_2SO_4 reagent at 10～15° and stirring continued for 5 min. The reaction mixture was treated with MeOH to decompose the excess reagent, diluted with H_2O and extracted with ether. The ether extract was washed with H_2O, 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 H_2O and extracted with ether. The extract was washed with 5% $NaHCO_3$, H_2O, dried and condensed to yield 0.238 g. of an oily residue, which was chromatographed over Al_2O_3. Elution with benzene gave IX (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—$C_8H_{17}$) as an oily substance. IR ν_{max}^{Nujol} cm^{-1}: 1681 and 1623 (Δ^4-3-CO). UV λ_{max}^{EtOH} mμ (ε): 239 (9.300).

3α,5-Cyclo-6-oxo-17β-hydroxy-5α-androstan-19-oic Acid 17-Benzoate (IV: R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$—OBz)——To a stirred suspension of 2.0 g. of $LiAlH_4$ 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 H_2O. The resulting mixture was made acidic with dil. H_2SO_4 and extracted with ether. The ether extract was washed with H_2O, aq. $NaHCO_3$, H_2O and dried over anhyd. Na_2SO_4. Removal of the solvent gave 2.9 g. of a crystalline residue, which was recrystallized from benzene-hexane to afford plates of the corresponding 17β-ol, m.p. 181～183°.

The 17β-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 H_2O 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 195～198°. Recrystallization from benzene-hexane gave prisms of 3α,5-cyclo-6β,19-oxido-17β-hydroxy-5α-androstane 17-benzoate (I : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz), m.p. 197～198°, $[\alpha]_D$ +91.5° (c=3.43). *Anal.* Calcd. for $C_{26}H_{32}O_3$: C, 79.55; H, 8.22. Found : C, 79.41; H, 8.11. IR ν_{max}^{Nujol} cm^{-1} : 1718, 1603, 1587, 1276, and 720.

To a stirred solution of 2.9 g. of the 17β-benzoate in 350 ml. of acetone, 15 ml. of 8*N* CrO_3-H_2SO_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 2*N* 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 193～197°. 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 (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz), m.p. 195～197°, $[\alpha]_D$ +61.9° (c=1.94). *Anal.* Calcd. for $C_{26}H_{30}O_5$: C, 73.91; H, 7.16. Found : C, 73.43; H, 7.20. IR ν_{max}^{Nujol} cm^{-1} : 1724, 1656, 714.

3β,17β-Dihydroxyandrost-5-en-19-oic Acid 3-Formate 17-Benzoate (VII : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz, R′=HCO)——To a stirred solution of 0.95 g. of Ⅳ (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$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 (R=O) to yield 0.88 g. of a mixture of reduction products (XIII and XIV : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz). The reduction mixture (1.07 g.) was dissolved in 100 ml. of 98% HCOOH containing 0.9 ml. of BF_3-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 210～214°. From the mother liquor additional 0.73 g. of crystals of m.p. 205～214° was obtained. An analytical sample was obtained on further recrystallization from benzene-hexane as needles of Ⅶ (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz, R′=HCO), m.p. 214～217°. *Anal.* Calcd. for $C_{27}H_{32}O_6$: C, 71.60; H, 7.13. Found : C, 71.41; H, 7.06. IR ν_{max}^{Nujol} cm^{-1} : 1733, 1724, 1692, 1678.

3β,17β-Dihydroxyandrost-5-en-19-oic Acid 17-Benzoate (VII : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz, R′=H)——A mixture of 0.365 g. of Ⅶ (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz, R′=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 217～219°. Recrystallization from benzene-EtOH gave needles of Ⅶ (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz, R′=H), m.p. 218～219°. An analytical sample was obtained by evacuation at 75° for 15 hr. *Anal.* Calcd. for $C_{26}H_{36}O_5$: C, 73.56; H, 7.60. Found : C, 73.33; H, 7.57. IR ν_{max}^{Nujol} cm^{-1} : 3484 (OH), 1712 (OBz).

19-Nortestosterone Benzoate (IX : R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz)——To a stirred solution of 0.20 g. of Ⅶ (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz, R′=H) in 30 ml. of purified acetone was added dropwise 0.40 ml. of 8*N* CrO_3-H_2SO_4 reagent at 12～13° and stirring continued for 5 min. The reaction mixture was treated as described for Δ^5-3β,19-dialcohol (Ⅲ : R=O, X=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 Ⅸ (R=$\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{—}}}$OBz) as sticks, m.p. 176～178°. $[\alpha]_D$ +110° (c=0.95). [*12] *Anal.* Calcd. for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found : C, 79.20; H, 7.94. IR ν_{max}^{Nujol} cm^{-1} : 1714, 1276 and 1114 (17β-OBz), 1646 and 1618 (Δ^4-3-CO). UV λ_{max}^{EtOH} mμ (ε) : 233 (31,000).

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[*12] Lit. : m.p. 178.4～180.6°; $[\alpha]_D^{27}$ +97.3°. cf. J. A. Hartman, A. J. Tomasewski, A. S. Dreiding : J. Am. Chem. Soc., **78**, 5662 (1956).