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5. **Ryozo Hayashi**: Steroid Series. XVIII.[*1] Acid-Catalysed Rearrangement Product of 3α,5α-Cyclo-6,19-dioxosteroid and its Conversion to 19-Nor-A-homotestosterone.[*2]

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

Treatment of 3α,5α-cyclo-6,19-dioxosteroid (II) in a boiling mixture of diluted sulfuric and acetic acids afforded 1β,4β-oxido-6-oxo-$\Delta^{5(10)}$-A-homo-19-norsteroid (III), together with a small amount of 3β-acetoxy-6,19-dioxosteroid (IV), the latter compound, under the same reaction conditions, being converted to the former. The structure of the rearrangement product (III) was discussed. A-homo-19-nortestosterone (XXV) was synthesized from 1β,4β-oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one acetate (III : R=$\underset{\cdot\cdot H}{\cdots OAc}$).

(Received February 23, 1966)

In the course of studies on the conversion of 3α,5α-cyclo-6β,19-oxidosteroid to 19-norsteroid derivatives,[*1] it was found that 3α,5α-cyclo-6β,19-dioxosteroid (II)1) obtained by oxidation of 3α,5α-cyclo-6β,19-oxide (I) with 8*N* chromic acid solution in acetone afforded a rearrangement product of A-homo-19-norsteroid derivatives (III) under acidic conditions. The present paper deals with the structural elucidation of this rearrangement product and, in connection with this, its conversion to A-homo-19-nortestosterone (XXV).

When 3α,5α-cyclo-6,19-dioxo-5α-cholestane (IIa) was refluxed in a mixture of acetic acid and diluted sulfuric acid, a crystalline product (IIIa) of m.p. 165~167° was

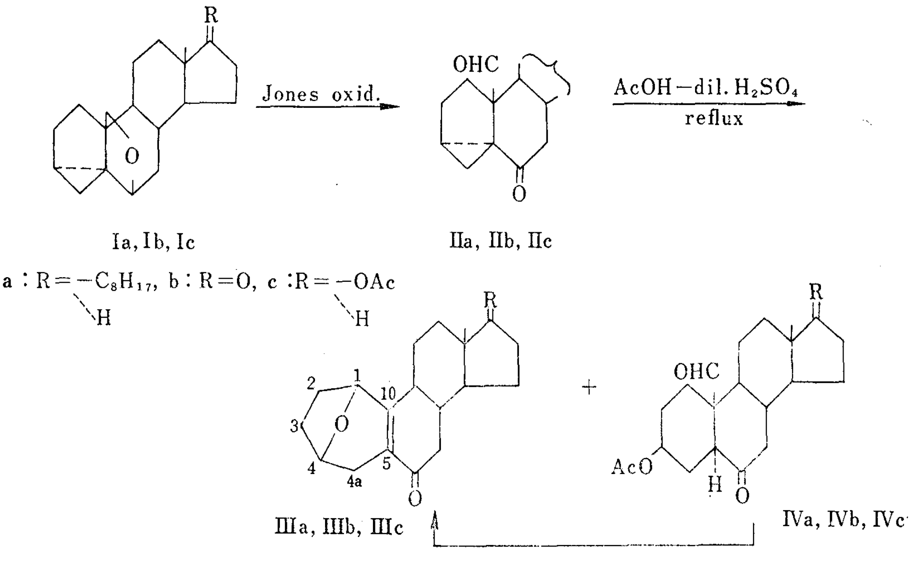

Chart 1.

[*1] Part XVII : This Bulletin, **15**, 27 (1967).

[*2] Presented at the IUPAC Symposium of the Chemistry of Natural Products, Kyoto, April 17, 1964. (This paper comprises a part of the dissertation submitted by the author for Ph. D degree at Tohoku University.)

[*3] 1-2-58, Hiromachi, Shinagawa-ku, Tokyo (林 了三).

1) K. Tanabe, R. Takasaki, K. Sakai, R. Hayashi, Y. Morisawa, T. Hashimoto : Steroid Series. XVI: This Bulletin, **15**, 15 (1967).

obtained in 74% yield, together with a small amount of an expected 3β-hydroxy-6,19-dioxo-5α-cholestane 3-acetate (IVa), which, on further treatment under the same reaction conditions, was found to yield the same compound (IIIa). This was also obtained in good yield on treatment of the 3α,5α-cyclo-6,19-dioxosteroid (IIa) with concentrated sulfuric acid in dioxane.

The infrared spectrum of 3β-acetoxy-6,19-dioxo-5α-cholestane (IVa) exhibited bands at 1739, 1715 and 1706 cm^{-1} assignable to acetate, aldehyde, and a 6-membered ring ketone, respectively. The nuclear magnetic resonance (NMR) spectrum showed no signals characteristic to cyclopropyl protons, but exhibited a singlet at 0.12τ due to formyl proton and an unresolved multiplet centered at 5.23τ ascribable to 3α-proton. These spectral data confirmed the structure assigned for the acetate (IVa).[*4]

The rearrangement product (IIIa), having the same analytical values as those for the starting material, showed infrared absorption bands at 1669 and 1623 cm^{-1} in the carbonyl region and an ultraviolet absorption maximum at 249.5 mμ with $\varepsilon=10,000$, suggesting the presence of a tetrasubstituted α,β-unsaturated carbonyl system in the molecule. The NMR spectrum showed no signals characteristic to formyl and vinyl protons, but unresolved broad one between 5.21 and 5.33τ having two protons area, which may be assignable to protons attached at the carbons adjacent to an ether oxygen atom. The stability of the rearrangement product towards acids, such as hydrogen bromide in acetic acid or zinc chloride in acetic anhydride at room temperature, might exclude the presence of 3- or 4-membered oxide ring moiety. On the basis of these observations the structure of the rearrangement product was proposed as 1β, 4β-oxido-A-homo-19-norcholest-5(10)-en-6-one (IIIa) and this was eventually established by the following chemical evidence.

Treatment of the compound (IIIa) with lithium in ethylamine yielded a mixture of 4β-hydroxy-A-homo-19-norcholest-5(10)-en-6-one (V) and 1β,4β-oxido-A-homo-19-nor-5α-cholestan-6-one (VIa) in 20 and 46% yield, respectively. The former compound (V)

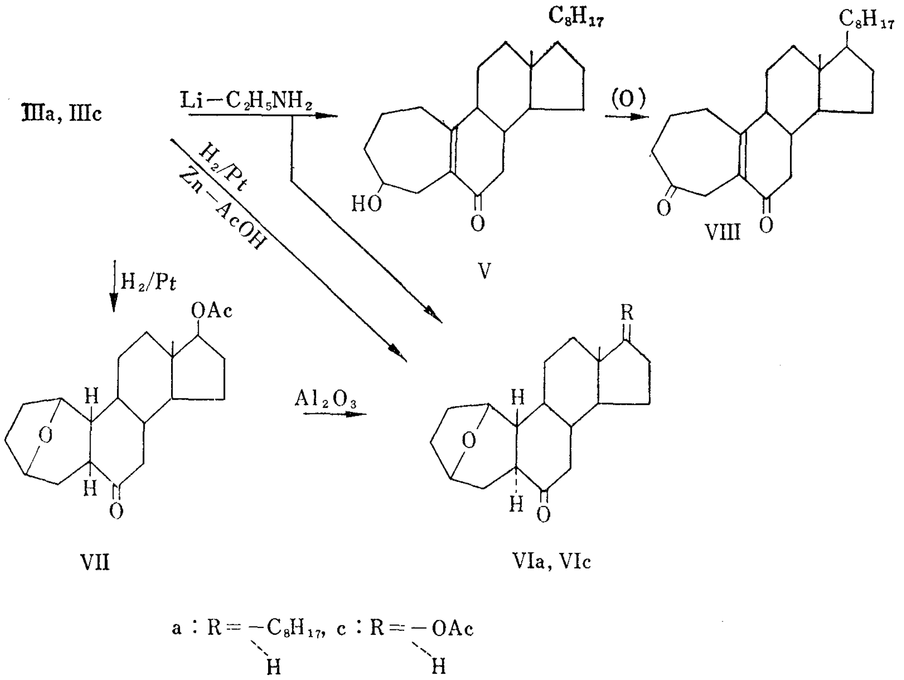

Chart 2.

[*4] Further evidence concerning the structure will be described in a paper of this series, Part XIX, dealing with the reaction path way of the rearrangement.

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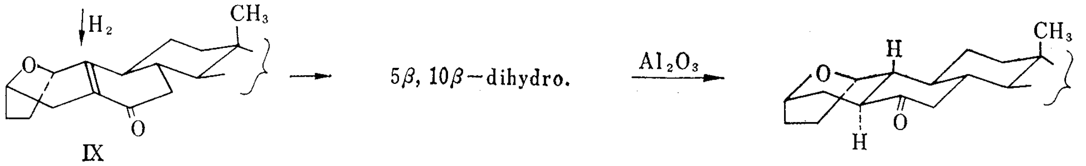
was oxidized with $8N$ chromic acid solution in acetone to afford A-homo-19-norcholest-5(10)-ene-4,6-dione (VIII), which had an ultraviolet absorption maximum at 252 mμ (ε=7,600) and infrared absorption bands at 1709 and 1669 cm^{-1} assignable to an isolated and a conjugated carbonyl groups, respectively. The NMR spectrum exhibited a pair of doublets (J=17.5 c.p.s.) centered at 6.24 and 6.64τ indicating the presence of methylene protons located between a double bond and a carbonyl group. These findings provided evidence that the oxide in III had been bridged over between an allylic and a homoallylic carbon atoms.

The structure of the dihydro ketone (VIa) was deduced from the following observations. Catalytic hydrogenation of 1β,4β-oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one 17-acetate (IIIc) prepared from 3α,5-cyclo-6,19-dioxo-5α-androstan-17β-ol acetate (Ic), over platinum in ethanol yielded, in one experiment,[*5] a dihydroketone (VII) melting at 172~174°, which was converted to an isomeric dihydroketone (VIc) of m.p. 225~227° on chromatography over alumina. The higher melting dihydroketone was also obtained directly from the compound (IIIc) on treatment with zinc powder in acetic acid. This finding can well be understood by considering that the lower melting *cis*-5β,10β-dihydroketone (VII) formed first has isomerized during chromatography at the carbon atom alpha to 6-carbonyl group into a more stable *trans*-5α,10β-isomer (VIc), since adsorption of the double bond to the catalyst would occur predominantly at the sterically less hindered β-side of the rearranged product whose conformation may be depicted as formula (IX). The dihydroketone (VIa) in the cholestane series, the reduction product with lithium in ethylamine, may be expected to have the stable A/B ring juncture from the method of preparation and assigned by analogy with the androstane series to be in *trans*-5α,10β-configuration. The optical rotatory dispersion curve of the compound (VIa) was also in accord with this assignment, showing negative Cotton effect, predictable from the octant rule, similar to that for 5α-cholestan-6-one.2)



IX

VI

Chart 3.

Treatment of the compound (IIIa) with N-bromosuccinimide in a boiling mixture of carbon tetrachloride and benzene containing a small amount of benzoyl peroxide afforded a phenolic compound, 1β,4β-oxido-6-hydroxy-A-homo-19-norcholesta-5,7,9-triene (Xa: R′=H) with simultaneous evolution of hydrogen bromide. Its ultraviolet absorption maxima at 280 (ε=2,740) and 285 mμ (ε=2,830) infrared absorption bands at 3289, 1600 and 1497 cm^{-1} suggested the presence of a phenolic moiety. The NMR spectrum showed a singlet at 3.66τ indicating the presence of an aromatic hydrogen, whose signal was shifted downfield to 3.41τ in its acetate (Xa: R′=Ac). Two unresolved multiplets centered at 4.87 and 5.22τ were assigned to two protons attached to the tertiary carbons adjacent to an ether oxygen. These spectral data indicated that the phenolic moiety is tetrasubstituted and must therefore result from a 6-membered B-ring with an α,β-unsaturated carbonyl system of the rearrangement product. The observation that one proton attached to a carbon atom bearing an ethereal oxygen is strongly affected by an aromatic ring current in the NMR spectrum, appearing at 4.87τ,

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[*5] See experimental.

suggested the location of the etherated carbon atom at the benzylic position. This is in accord with the result described earlier in the reaction of the compound (IIIa) with lithium in ethylamine.

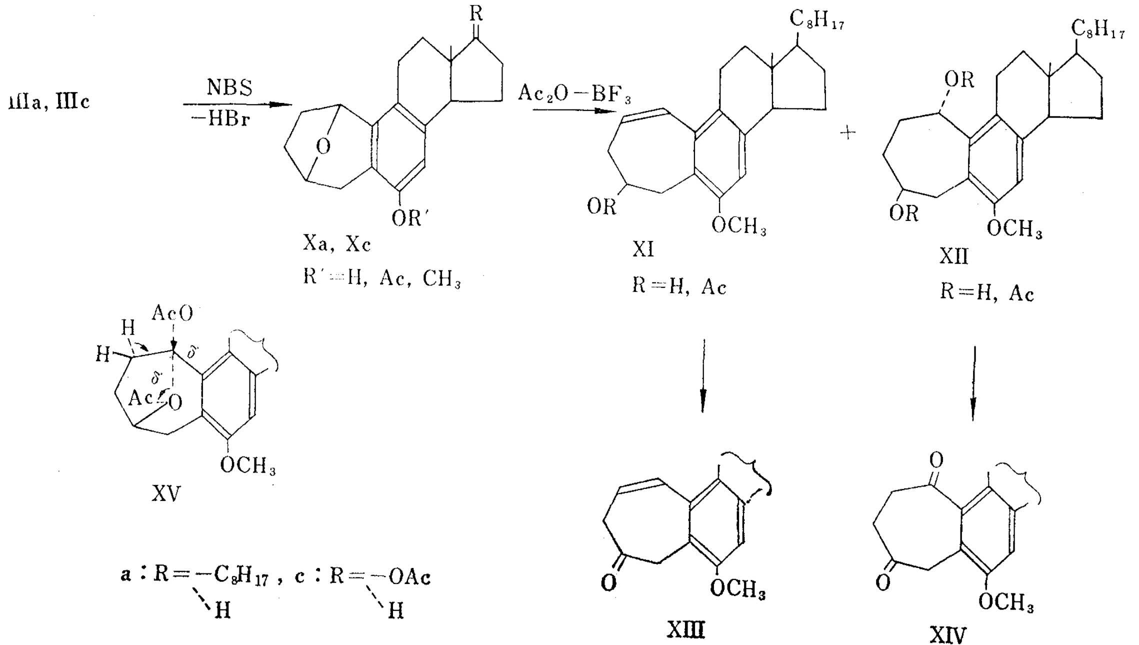

Chart 4.

The phenolic compound (Xa: $R'=H$), after conversion to the corresponding methyl ether (Xa: $R'=CH_3$) with *p*-toluenesulfonic acid methyl ester in Claisen alkali, was treated with boron trifluoride etherate in acetic anhydride to afford a mixture of 4β-hydroxy-6-methoxy-A-homo-19-norcholesta-1,5,7,9-tetraene acetate (XI: $R=Ac$) and 1α,4β-dihydroxy-6-methoxy-A-homo-19-norcholesta-5,7,9-triene 1,4-diacetate (XII: $R=Ac$) in ratio of about 2:3, whose structures were supported by the following spectral data. An ultraviolet spectrum of the monoacetate (XI: $R=Ac$) had absorption maxima at 250 ($\varepsilon=8,400$), 282 ($\varepsilon=2,800$), and 301 mμ ($\varepsilon=3,350$). The NMR spectrum showed, besides a singlet at 3.46τ due to an aromatic proton, a doublet ($J=10.8$ c.p.s.) at 3.31τ and an ill-defined multiplet centered at 3.88τ, both of which were assignable to the olefinic protons at the C_1- and C_2-positions, respectively. In the NMR spectrum of the diacetate (XII: $R=Ac$), resonance signals due to protons at the carbon atoms bearing acetoxyl groups were observed as multiplets at 5.30 and 3.64τ, the latter signal assignable to 1β-proton again appearing at downfield by the effect of aromatic ring current as observed in the phenolic oxide (Xa: $R'=Ac$). This acetolysis reaction might be initiated by the attack of acetyl cation on the ether oxygen atom and proceed as shown in formula (XV) to give either the mono- or diacetates. The monoacetate (XI: $R=Ac$) and the diacetate (XII: $R=Ac$) were separately subjected to alkaline hydrolysis of the acetoxyl functions followed by oxidation with 8*N* chromic acid solution in acetone to yield 6-methoxy-A-homo-19-norcholesta-1,5,7,9-tetraen-4-one (XIII) and 6-methoxy-A-homo-19-norcholesta-5,7,9-triene-1,4-dione (XIV), respectively. The monoketone (XIII) showed an infrared absorption band at 1724 cm^{-1} due to isolated carbonyl, and an ultraviolet absorption maximum at 256 mμ with $\varepsilon=13,000$. The NMR spectrum exhibited a singlet at 3.36τ due to an aromatic proton, a doublet ($J=6.0$ c.p.s.) at 6.99τ and a singlet at 6.25τ, in addition to a doublet ($J=12$ c.p.s.) at 3.08τ and an unresolved multiplet centered at 3.85τ assignable to C_1- and C_2-olefinic protons, respectively. The

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2) C. Djerassi : "Optical Rotatory Dispersion," 43 (1960), McGraw-Hill Book Co., Inc., New York.

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singlet at 6.25τ could be assigned to C_{4a}-methylene protons located between an aromatic ring and a carbonyl group and the doublet at 6.99τ to C_3-methylene protons coupled with an adjacent C_2-olefinic proton. The diketone (XIV) showed infrared absorption bands at 1724 and 1695 cm^{-1} indicating the presence of an isolated and a conjugated carbonyl groups.[*6] An ultraviolet absorption was similar to those for *meta*-methoxy-α-tetralone3) and had maxima at 258 and 318 mμ with $\varepsilon=2,500$ and 2,370, respectively. The abnormally low extinction coefficient may be reasonably explained in terms of steric repulsion between C_1-carbonyl and C_{11}-methylene groups inhibiting coplanarity of the C_1-carbonyl group with the aromatic ring.

The observations obtained thus far all strongly suggested that the rearrangement product has the structure (III). In order to establish unambiguously the proposed structure and in view of the biological interest as well, the compound (IIIc) was converted to A-homo-19-nortestosterone. Thus, treatment of 1β,4β-oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one 17-acetate (IIIc) with ethanedithiol in a mixture of acetic acid and borontrifluoride etherate yielded the corresponding thioketal (XVI), which, on refluxing in ethanol with a large excess of Raney Ni catalyst and subsequent chromatography over alumina, gave a mixture of desulfurized products, 1β,4β-oxido-17β-hydroxy-19-norandrost-5(10)-ene 17-acetate (XVII) and 1β,4β-oxido-17β-hydroxy-19-nor-19ξ-*H*-androst-5-ene 17-acetate (XVIII), along with a small amount of the ketone (IIIc) regenerated. The mixture of desulfurized products (XVII and XVIII) had a peak in the NMR spectrum due to a vinyl proton and in the gas chromatography was separated into two components, the minor being estimated to be 16% of the mixture. Repeated recrystallization of this mixture from hexane afforded the pure $\Delta^{5(10)}$-oxide (XVII), the major component in the gas chromatography. The minor component, having a vinyl

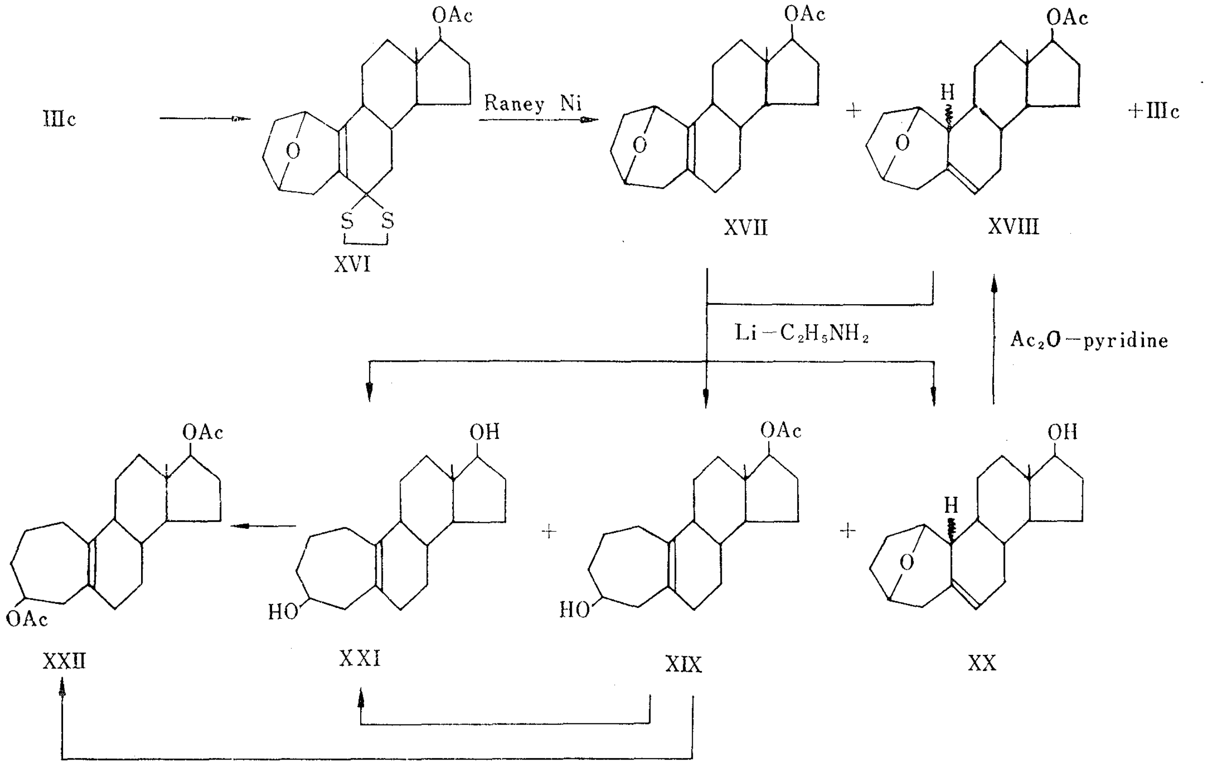

Chart 5.

[*6] Infrared spectrum of 2,3-benzocycloheptanone showed a conjugated carbonyl band at 1672 cm^{-1}, whereas that for the corresponding compound having methoxy groups at the *peri*-positions had the carbonyl band at 1691 cm^{-1}. cf. U.C. Farmer, N.F. Fayes, R.H. Thomson : J. Chem. Soc., **1956**, 3600.

3) S. Ohshiro : Tetrahedron, **10**, 175 (1960).

proton, is obviously the Δ^5-oxide (XVIII) resulted from the migration of double bond during the course of the reaction, but its separation from the mixture in a pure state was unsuccessful. Treatment of the mixture of the isomeric oxide (XVII and XVIII) with lithium in ethylamine, followed by the chromatographic separation, afforded 4β,17β-dihydroxy-A-homo-19-norandrost-5(10)-ene 17-acetate (XIX), 1β,4β-oxido-17β-hydroxy-A-homo-19-nor-19ξ-*H*-androst-5-ene (XX), and 4β,17β-dihydroxy-A-homo-19-norandrost-5(10)-ene (XXI) in the elution order. Acetylation of the 17β-hydroxy-Δ^5-1β, 4β-oxide (XX), separated in about 15% yield, with acetic anhydride and pyridine afforded the corresponding 17β-acetate (XVIII), gas chromatography of which had just the same retension time as that for the minor component contained in the desulfurized mixture. Both hydroxy-acetate (XIX) and the diol (XXI) showed no signal due to a vinyl proton, the former (XIX) was hydrolysed by alkali to afford the latter (XXI), and both were converted to the same diacetate (XXII) on treatment with acetic anhydride in pyridine.

The $\Delta^{5(10)}$-4β,17β-diol (XXI) was then oxidized with 8*N* chromic acid in acetone to afford A-homo-19-norandrost-5(10)-ene-4,17-dione (XXIII), which showed infrared absorption bands at 1745 and 1712 cm^{-1} due to 17- and 4-carbonyl groups, respectively and ultraviolet absorption maximum at 294 mμ with $\varepsilon=218$. The observed intensification*[7] of $n\rightarrow\pi^*$ band is apparently attributed to the presence of homoconjugation[4] between the 4-carbonyl function and the double bond located at the β,γ-position. The NMR spectrum showed a pair of doublets (J=14.5 c.p.s.) at 7.10 and 6.68τ assignable to the non-equivalent C_{4a}-methylene protons located between a carbonyl group and a double bond. These spectral findings seemingly suggest that the β,γ-unsaturated, 7-membered ketone (XXIII) is fixed in some degree to a stable conformation.

Treatment of the $\Delta^{5(10)}$-4,17-diketone (XXIII) with hydrochloric acid in ethanol at room temperature for 3 hours afforded an equilibrium mixture of A-homo-19-norandrost-4*a*-ene-3,17-dione (XXIV) and the unchanged material, as shown by an absorption maximum at 240 mμ having $\varepsilon=4{,}500$. Chromatographic separation of this mixture

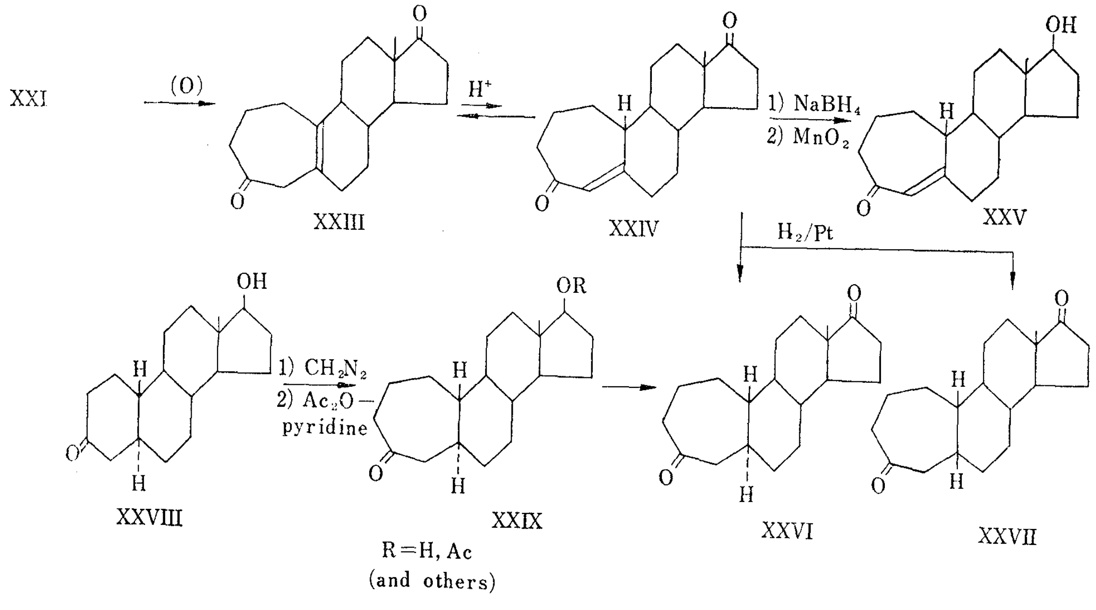

Chart 6.

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*[7] $\varepsilon_{\max}$ of $n\rightarrow\pi^*$ band due to 17-carbonyl function is about 50.

4) H. Labhart, G. Wagniere: Helv. Chim. Acta, **42**, 2219 (1959); R.C. Cookson, J. Hudec: J. Chem. Soc., **1962**, 429; G. Snatzke, B. Zeeh, E. Müller: Tetrahedron Letters, **1963**, 1425.

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furnished a conjugated ketone (XXIV) in 21% yield together with the unconjugated starting material (XXIII).

A-Homo-19-norandrost-4a-ene-4,17-dione (XXIV) exhibited an ultraviolet absorption maximum at 242 mμ with ε=15,200, infrared absorption bands at 1742 and 1642 cm^{-1} assigned to 17-carbonyl and conjugated 4-carbonyl groups, respectively, and NMR peak at 4.02τ due to 4a-vinyl proton. The extinction coefficient at 241 mμ of the conjugated Δ^{4a}-4,17-diketone (XXIV) decreased to 5,500, when treated with hydrochloric acid in ethanol. Gas chromatogaphic determination of the resultant mixture indicated the conjugated diketone (XXIV) to be contained in 27%. These observations showed that the conjugated and unconjugated diketones (XXIV and XXIII) exist as an equilibrium mixture in a ratio of 1 to 2～3 in acidic medium.*8

Stereochemical assignment of 10β-hydrogen in the conjugated diketone (XXIV) was made from the following experiments. Catalytic hydrogenation of the conjugated diketone (XXIV) in the presence of platinum catalyst in ethanol afforded, after chromatography over alumina, A-homo-19-nor-5α-androstane-4,17-dione (XXVI) and A-homo-19-nor-5β-androstane-4,17-dione (XXVII) in a ratio of 1 to 4. The 5α-diketone, a minor product eluted first from alumina, was shown to be identical with the compound which was prepared from 17β-hydroxy-5α-estran-3-one (XXVIII)5) by A-ring enlargement with diazomethane in a mixture of methanol and ether and subsequent conversion of the 17-acetoxy function to the corresponding 17-oxo-group. The structure of the minor reduction product (XXVI) was accordingly established to have 5α- and 10β-configurations and consequently, the conjugated diketone (XXIV) must have the 10β-hydrogen.

Treatment of the Δ^{4a}-4,17-diketone (XXIV) with sodium borohydride in ethanol, followed by oxidation of the product with active manganese dioxide in refluxing chloroform furnished A-homo-19-nortestosterone (XXV), whose optical rotatory dispersion curve had a negative Cotton effect similar to that for 19-nortestosterone,2) but showed no fine structure in dioxane.

Thus, the rearrangement product (III) of the 3α,5α-cyclo-6,19-dioxosteroid was conclusively established to have the structure of 1β,4β-oxido-A-homo-19-nor-$\Delta^{5(10)}$-6-ketone.*9

Experimental*10

Treatment of 3α,5-Cyclo-6,19-dioxo-5α-cholestane (IIa) with Diluted Sulfuric Acid in Acetic Acid—— A mixture of 8.1 g. of IIa in 1.0 L. of AcOH and 200 ml. of 14% H_2SO_4 was refluxed for 3 hr. The reaction mixture was diluted with 2 L. of H_2O and extracted with ether. The ether extract was washed consecutively with H_2O, aq. $NaHCO_3$, and H_2O and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave 8.5 g. of a crystalline residue, which was recrystallized from hexane to yield 4.5 g. of crystals melting at 161～164°. Further 0.58 g. of crystals melting at 157～163° was obtained from mother liquor. The filtrate of recrystallization was chromatographed over 90 g. of Al_2O_3 (neutral, Woelm Grade III). The eulate with benzene-hexane (2:3), after evaporation, afforded 0.8 g. of needles of m.p. 161～164°. The combined crystals (5.88 g., 74% yield) was further recrystallized from MeOH to afford 1β,4β-oxido-A-homo-19-norcholest-5(10)-en-6-one (IIIa) as needles, m.p. 165～167°. $[\alpha]_D$ −30.5° (c=0.49). *Anal.* Calcd. for $C_{27}H_{42}O_2$: C, 81.35; H, 10.62. Found : C, 81.12; H, 10.47. IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1669 and 1623 ($\Delta^{5(10)}$-6-CO). UV λ_{max} mμ (ε) : 249.5 (10,000). NMR τ : 9.30 (18-CH_3), 5.21 (1α-H), 5.33 (4α-H).

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*8 A specimen of the unconjugated $\Delta^{5(10)}$-4,17-diketone (XXIII) in a solution of aq. alkaline ethanol at room temperature for 20 hr. showed an ultraviolet absorption maximum at 240 mμ having ε=2,800.

*9 Evidence for the β-configuration of 1,4-oxide bridge will be described in the next paper.

*10 All melting points were uncorrected. The infrared spectra were recorded on Perkin Elmer Model 21. The nuclear magnetic resonance spectra were measured with Varian A-60 spectrometer using tetramethylsilane as internal standard in deuteriochloroform. The optical rotatory dispersion curves were taken with JASCO Model ORD/UV-5, Japan Spectroscopic Co., Ltd. $[\alpha]_D$s refer to chloroform, ultraviolet spectra to 99% ethanol and infrared spectra to nujol, unless otherwise stated.

5) F. L. Weisenborn, H. E. Applegate : J. Am. Chem. Soc., **81**, 1960 (1959).

The second fraction eluted with benzene–hexane (2:3) on chromatography gave 0.46 g. of crystals melting at 153~162°, which was recrystallized from hexane to afford 3β-hydroxy-6,19-dioxo-5α-cholestane 3-acetate (IVa) as leaflets, m.p. 166~170°, $[\alpha]_D$ −23.5°(c=0.76). *Anal.* Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.74; H, 10.16. IR ν_{max} cm^{-1}: 1739 (OAc), 1715 (shoulder, CHO), 1706 (6-CO). NMR τ: 9.40 (18-CH_3), 7.97 (OAc), 5.23 (3α-H), 0.12 (CHO).

Treatment of 3α,5-Cyclo-6,19-dioxo-17β-hydroxy-5α-androstane 17-Acetate (IIc) with Diluted Sulfuric Acid in Acetic Acid——A solution of 5.2 g. of IIc in 650 ml. of AcOH and 150 ml. of 14% H_2SO_4 was refluxed for 2 hr. The reaction mixture was concentrated *in vacuo* to about one half, diluted with 1.5 L. of H_2O and extracted with ether. The ether extract worked up as above to yield 5.1 g. of a crystalline residue, which was chromatographed over 150 g. of Al_2O_3. The eluate of benzene gave 2.81 g. of crystals melting at 201~204°, which was recrystallized from benzene–hexane to afford needles of 1β,4β-oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one 17-acetate (IIIc), m.p. 202~204°, $[\alpha]_D$ −48°(c=0.75). *Anal.* Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.03; H, 8.27. IR ν_{max} cm^{-1}: 1733 (OAc), 1664 and 1621 ($\Delta^{5(10)}$-6-CO). UV λ_{max} mμ (ε): 249 (9,100). NMR τ: 9.16 (18-CH_3), 7.92 (OAc), 5.16~5.41 (1α- and 4α-H). 2,4-dinitrophenylhydrazone: needles (from EtOH–hexane), m.p. 279° (decomp.). *Anal.* Calcd. for $C_{27}H_{32}O_7N_4$: C, 61.82; H, 6.15; N, 10.68. Found: C, 61.43; H, 6.24; N, 10.67.

The eluate with benzene–ether (20:3), after evaporation of the solvent, afforded 0.30 g. of crystals, which was recrystallized from acetone–hexane to give needles of 3β,17β-dihydroxy-6,19-dioxo-5α-androstane 3,17-diacetate (IVc), m.p. 181~188°. *Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.26; H, 7.92. IR ν_{max} cm^{-1}: 1736 (OAc), 1727 (CHO), 1709 (shoulder, 6-CO). NMR τ: 9.28 (18-CH_3), 7.98 and 7.96 (2-OAc), 5.33 (3α- and 17α-H), 0.33 (CHO).

Treatment of 3α,5-Cyclo-6,17,19-trioxo-5α-androstane (IIb) with Diluted Sulfuric Acid in Acetic Acid——A mixture of 0.32 g. of IIb in 65 ml. of AcOH and 15 ml. of 14% H_2SO_4 was treated as described above to yield 0.42 g. of a reaction product, which was chromatographed over 15 g. of Al_2O_3. The combined eluates with benzene–hexane (1:1) and benzene gave 0.25 g. of crystals, which was recrystallized from benzene–hexane to afford needles of 1β,4β-oxido-6,17-dioxo-A-homo-19-norandrost-5(10)-ene (IIIb), m.p. 180~181°, $[\alpha]_D$ +31.2°(c=0.86). *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.74; H, 7.89. IR ν_{max} cm^{-1}: 1664 and 1621 ($\Delta^{5(10)}$-6-CO). UV λ_{max} mμ (ε): 249 (9,200). NMR τ: 9.07 (18-CH_3), 5.18 (1α-H), 5.30 (4α-H). Di-2,4-dinitrophenylhydrazone: m.p. 285~290°(decomp.). *Anal.* Calcd. for $C_{31}H_{32}O_9N_8$: C, 56.36; H, 4.88; N, 16.95. Found: C, 56.42; H, 4.98; N, 16.51. UV λ_{max} mμ (ε): 380 (40,000).

The eluate with ether on the above chromatography gave 0.03 g. of crystals, which was recrystallized from benzene–hexane to afford 3β-hydroxy-6,17,19-trioxo-5α-androstane 3-acetate (IVb) as needles, m.p. 206~212°, $[\alpha]_D$ +14°(c=6.67). *Anal.* Calcd. for $C_{21}H_{28}O_5$: C, 69.97; H, 7.83. Found: C, 69.57; H, 7.77. IR ν_{max} cm^{-1}: 1733 (OAc and 17-CO), 1712 (6-CO, CHO). NMR τ: 9.20 (18-CH_3), 8.00 (OAc), 5.33 (3α-H), 0.03 (CHO).

Treatment of 3α,5-Cyclo-6,19-dioxo-5α-cholestane (IIb) with Concentrated Sulfuric Acid in Dioxane——To a solution of 0.05 g. of IIb in 10 ml. of anhyd. dioxane cooled in ice-water, 2 ml. of conc. H_2SO_4 was added dropwise with stirring and the mixture was allowed to stand at room temperature for 21 hr. The reaction mixture was poured into H_2O and extracted with ether. The extract was treated as above to yield a crystalline residue, showing only one spot on thin-layer chromatography corresponding to IIIa. Recrystallization from MeOH afforded leaflets, m.p. 165~167° of IIIa.

Treatment of 3β-Hydroxy-6,19-dioxo-5α-cholestane 3-Acetate (IVa) with Diluted Sulfuric Acid in Acetic Acid——A mixture of 0.40 g. of IVa, 50 ml. of AcOH and 10 ml. of 14% H_2SO_4 was heated under reflux for 3 hr. The reaction mixture was poured into water and extracted with ether. The extract was washed with 5% $NaHCO_3$, H_2O, and dried. Evaporation of the solvent yielded 0.38 g. of a crystalline residue, which was recrystallized from MeOH to give IIIa as needles, m.p. 160~163°.

Treatment of 3β-Hydroxy-6,17,19-trioxo-5α-androstane 3-Acetate (IVb) with Diluted Sulfuric Acid and Acetic Acid——A solution of 0.10 g. of IVb in 20 ml. of AcOH and 4 ml. of 14% H_2SO_4 was refluxed for 2 hr. The reaction mixture was worked up as above to yield, after recrystallization from benzene–hexane, needles of IIIb, m.p. 180~181°.

Reaction of 1β,4β-Oxido-A-homo-19-norcholest-5(10)-en-6-one (IIIa) with Lithium in Ethylamine——To a cooled solution at 5° of 0.20 g. of Li in 30 ml. of freshly distilled $C_2H_5NH_2$, a solution of 0.50 g. of IIIa in 40 ml. of freshly distilled $C_2H_5NH_2$ was added dropwise with stirring for about 7 min. After stirring for additional 10 min., 7 g. of NH_4Cl was added to the reaction mixture in small portions. The reaction mixture was diluted with H_2O and extracted with ether. The ether extract was washed consecutively with H_2O, dil. HCl, 5% $NaHCO_3$, and H_2O and dried over Na_2SO_4. Evaporation of ether gave 0.40 g. of an oily residue, which was chromatographed over 20 g. of Al_2O_3. Elution with benzene–hexane (1:2) yielded 0.23 g. of crystals. Recrystallization from MeOH afforded needles of 1β,4β-oxido-A-homo-19-nor-5α-cholestan-6-one (VIa), m.p. 142~144°. ORD (c=1.02, dioxane): $[\alpha]_{400}$ −47°; $[\alpha]_{312}$ −436°; $[\alpha]_{275}$ +313°. $[\alpha]_D$ ±0°. *Anal.* Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.87; H, 11.20. IR ν_{max} cm^{-1}: 1709 (6-CO). NMR τ: 9.325 (18-CH_3), 5.43 (1α- and 4α-H).

Further elution with ether afforded 0.16 g. of an amorphous substance, which was rechromatographed over Al_2O_3. The eluate with benzene-ether (5:1) was evaporated to afford 0.108 g. of 4β-hydroxy-A-homo-19-norcholest-5(10)-en-6-one (V) as an amorphous substance. IR ν_{max} cm^{-1}: 3472 (OH), 1661 and 1610 ($\Delta^{5(10)}$-6-CO). NMR τ: 9.3 (18-CH_3), 6.45 (4α-H). The acetate obtained by acetylation with Ac_2O in pyridine also failed to crystallize.

A-Homo-19-norcholest-5(10)-ene-4,6-dione (VIII)——To a stirred solution of 0.108 g. of V in 15 ml. of acetone cooled at 7~8°, 0.15 ml. of 8*N* chromic acid solution (26.72 g. of CrO_3 and 23 ml. of conc. H_2SO_4 were dissolved to total 100 ml. of solution by adding H_2O) was added dropwise and stirring continued for further 6 min. The excess reagent was decomposed by adding MeOH. The reaction mixture was diluted with H_2O and extracted with ether. The ether extract was washed with 5% $NaHCO_3$, water and dried over anhyd. Na_2SO_4. Evaporation of the solvent yielded a crystalline residue, which was recrystallized from MeOH to afford Ⅷ as needles, m.p. 111~112°, $[\alpha]_D^{27}$ +104°. *Anal.* Calcd. for $C_{27}H_{42}O_2$: C, 81.35; H, 10.62. Found: C, 81.05; H, 10.55. IR ν_{max} cm^{-1}: 1709 (4-CO), 1667 and 1603 ($\Delta^{5(10)}$-6-CO). UV λ_{max} mμ (ε): 252 (7,600). NMR τ: 9.275 (18-CH_3), 6.24 (doublet) and 6.64 (doublet) (j=17.5 c.p.s., 4*a*-CH_2-).

Catalytic Hydrogenation of 1β,4β-Oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one 17-Acetate (IIIc) with Platinum Catalyst in Ethanol——A solution of 0.138 g. of Ⅲc in 20 ml. of EtOH was hydrogenated over Pt catalyst prepared from 0.060 g. of PtO_2 in 20 ml. of EtOH, and 10 ml. of H_2 was absorbed for 38 min. at 26°. Inorganic material was removed by filtration and the filtrate was evaporated to give a crystalline residue, which was recrystallized from EtOH to afford 0.10 g. of 1β,4β-oxido-17β-hydroxy-A-homo-19-nor-5β-androstan-6-one 17-acetate (Ⅶ) as sticks, m.p. 172~174°. *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.49; H, 8.61. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1742 (17-OAc), 1715 (6-CO).

The mother liquor of recrystallization was chromatographed over Al_2O_3 and the eluate with benzene, after recrystallization from EtOH, gave prisms of 1β,4β-oxido-17β-hydroxy-A-homo-19-nor-5α-androstan-6-one 17-acetate (Ⅵc) melting at 225.5~227°. *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.45; H, 8.63. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1742 (17-OAc), 1724 (6-CO).

Chromatography of Ⅶ (0.015 g.) of m.p. 172~174° over 3.0 g. of Al_2O_3 gave, from the benzene eluate, 0.014 g. of crystals, which was recrystallized from EtOH to afford prisms of Ⅵc melting at 221~226°.

Treatment of 1β,4β-Oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one 17-Acetate (IIIc) with Zinc Powder in Acetic Acid——A mixture of 0.050 g. of Ⅲc, 5 ml. of AcOH and 0.3 g. of Zn powder was refluxed for 2 hr. Additional 0.3 g. of Zn powder was added and refluxing further continued for 6 hr. Inorganic material was removed by filtration and the filtrate, after dilution with H_2O, was extracted with ether. The ether extract was washed with H_2O, aq. $NaHCO_3$, and H_2O, successively and dried over anhyd. Na_2SO_4. Evaporation of ether afforded a crystalline residue, which was chromatographed over 5 g. of Al_2O_3. The eluate with benzene, after recrystallization from ether, gave prisms of Ⅵc, m.p. 221~226°.

1β,4β-Oxido-6,17β-dihydroxy-A-homo-19-norandrosta-5,7,9-triene 17-Acetate (Xc: R′=H)——A solution of 0.172 g. of Ⅲc in 10 ml. of benzene and 10 ml. of CCl_4 was heated to boiling and 10 ml. of distillate removed. To the solution was added 0.126 g. of NBS and 0.02 g. of benzoyl peroxide in one portion and the mixture was refluxed by heating with IR-lamp for 18 min., during which time HBr gas evolved. After cooling, the reaction mixture was diluted with H_2O, extracted with ether. The ether extract was washed with 5% $NaHCO_3$, H_2O, dried over Na_2SO_4. Evaporation of the solvent yielded 0.203 g. of a crystalline residue, which was recrystallized from acetone-hexane to give 0.056 g. of crystals melting at 204~209°. The mother liquor, after evaporation of the solvent, was chromatographed over 5 g. of Al_2O_3. Elution with benzene gave 0.078 g. of crystals. The combined crystals were recrystallized from acetone-hexane to afford Xc (R′=H) as sticks, m.p. 205~210°. *Anal.* Calcd. for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66. Found: C, 73.43; H, 7.63. IR ν_{max} cm^{-1}: 3390 (OH), 1709*[11] (17-OAc), 1608 and 1600 (aromatic ring). UV λ_{max} mμ (ε): 279.5 (3,100), 286.5 (2,970).

The phenol (Xc: R′=H) was acetylated with Ac_2O and pyridine at room temperature for 15 hr. The reaction mixture was evaporated *in vacuo* to leave a crystalline residue, which was chromatographed over 3.0 g. of Al_2O_3. Elution with benzene gave, after recrystallization from hexane, 1β,4β-oxido-6,17β-dihydroxy-A-homo-19-norandrosta-5,7,9-triene 6,17-diacetate (Xc: R′=Ac) as leaflets, m.p. 156~158°. *Anal.* Calcd. for $C_{23}H_{28}O_5$: C, 71.85; H, 7.38. Found: C, 71.48; H, 7.31. IR ν_{max} cm^{-1}: 1767 (phenolic acetate), 1739 (17β-OAc).

1β,4β-Oxido-6-hydroxy-A-homo-19-norcholesta-5,7,9-triene (Xa: R′=H)——A solution of 0.40 g. of Ⅲa in 15 ml. of benzene and 15 ml. of CCl_4 was heated to boiling and 10 ml. of distillate was removed. To the solution was added 0.25 g. of NBS and 0.04 g. of benzoyl peroxide in one portion and the mixture was

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*[11] Appearance at abnormally low frequency of 17-acetoxyl band is probably due to the intermolecular hydrogen bonding between 17β-acetoxyl and phenolic hydroxyl groups, since the corresponding one in its 6,17-diacetate (X: $R=\underset{\cdot\cdot H}{-}OAc$, R′=Ac) was observed at 1739 cm^{-1}.

refluxed over IR-lamp for 12 min. After cooling, the reaction mixture was treated as described above to yield 0.40 g. of a crystalline product, which was chromatographed over 15 g. of Al_2O_3. Elution with hexane-benzene (1:1) and benzene gave 0.30 g. of crystls. Recrystallization from hexane-benzene afforded needles of Xa (R'=H), m.p. 201~204°, $[\alpha]_D$ +64.2° (c=1.45). *Anal.* Calcd. for $C_{27}H_{40}O_2$: C, 81.70; H, 10.17. Found : C, 81.42; H, 10.15. IR ν_{max} cm^{-1} : 3289 (phenolic OH), 1600 and 1497 (aromatic ring). NMR τ : 9.42 (18-CH_3), 5.22 (4α-H), 4.87 (1α-H), 3.66 (7-H). UV λ_{max} mμ (ε) : 280 (2,740), 285 (2,830).

The phenol (Xa : R'=H) was acetylated with Ac_2O and pyridine at room temperature and the reaction mixture was condensed *in vacuo* to leave an oily residue, which was chromatographed over alumina. Elution with benzene-hexane (1:4) and (1:2) gave Xa (R'=Ac) as a syrupy substance. IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1767 (phenolic OAc). NMR τ : 9.40 (18-CH_3), 7.73 (OAc), 4.85 (1α-H), 5.25 (4α-H), 3.41 (7-H).

1β,4β-Oxido-6-methoxy-A-homo-19-norcholesta-5,7,9-triene (Xa : R'=CH_3)——A mixture of 1.25 g. of Xa (R'=H), 21 ml. of EtOH, 5.4 ml. of 10% aq. KOH, and 1.8 g. of methyl *p*-toluenesulfonate was refluxed on a water bath for 3 hr. Additional 5.4 ml. of 10% aq. KOH and 1.8 g. of methyl *p*-toluenesulfonate was added and refluxing further continued for 1.5 hr. The reaction mixture was finally refluxed with 3.0 ml. of 10% aq. KOH for 20 min. and was poured into water, extracted with ether. The ether extract was washed with H_2O, dried and the solvent was evaporated to leave 1.4 g. of a gummy residue, which was chromatographed over 43 g. of Al_2O_3. The eluate with benzene-hexane (1:5) gave 1.228 g. of 1β,4β-oxido-6-methoxy-A-homo-19-norcholesta-5,7,9-triene (Xa : R'=CH_3) as a syrupy substance. NMR τ : 9.4 (18-CH_3), 6.24 (6-OCH_3), 4.86 (1α-H), 5.27 (4α-H), 3.57 (7-H).

Reaction of 1β,4β-Oxido-6-methoxy-A-homo-19-norcholesta-5,7,9-triene (Xa : R'=CH_3) with Boron Trifluoride Etherate in Acetic Anhydride——To a solution of 1.02 g. of Xa (R'=CH_3) in 58 ml. of Ac_2O cooled in ice-water bath, 0.3 ml. of BF_3-etherate was added dropwise with stirring and the mixture was allowed to stand in refrigerator for 14 hr. The reaction mixture was poured onto ice-water, neutralized with aq. $NaHCO_3$, and extracted with ether. The ether extract was washed with H_2O, dried, and the solvent was evaporated to afford 1.20 g. of a dark brown oily residue, which was chromatographed over 40 g. of Al_2O_3. First fraction eluted with hexane-benzene (5:1) gave 0.30 g. of crystals, which was recrystallized from MeOH to afford leaflets of 4β-hydroxy-6-methoxy-A-homo-19-norcholesta-1,5,7,9-tetraene 4-acetate (XI : R=Ac), m.p. 115~117°, $[\alpha]_D$ +49.1° (c=1.3). *Anal.* Calcd. for $C_{30}H_{44}O_3$: C, 79.60; H, 9.80. Found : C, 79.80; H, 9.80. IR ν_{max} cm^{-1} : 1736 (OAc), 1580 (aromatic ring). UV λ_{max} mμ (ε) : 250 (8,400), 282 (2,800), 301 (3,350). NMR τ : 9.39 (18-CH_3), 7.93 (OAc), 6.20 (OCH_3), 4.4~4.8 (4α-H), 3.65~4.1 (2-H), 3.46 (7-H), 3.31 (doublet, j=10.8 c.p.s., 1-H).

Second fraction with hexane-benzene (5:1) yielded 0.48 g. of crystals, which was recrystallized from MeOH to give prisms of 1α,4β-dihydroxy-6-methoxy-A-homo-19-norcholesta-5,7,9-triene 1,4-diacetate (XII : R=Ac), m.p. 117~119°, $[\alpha]_D$ +59.5° (c=1.2). *Anal.* Calcd. for $C_{32}H_{48}O_5$: C, 74.96; H, 9.44. Found : C, 74.94; H, 9.47. IR ν_{max} cm^{-1} : 1736 (OAc), 1608 and 1582 (aromatic ring). NMR τ : 9.42 (18-CH_3), 7.92 (OAc), 6.23 (OCH_3), 5.15~5.45 (4α-H), 3.64 (1β-H), 3.42 (7-H).

4-Oxo-6-methoxy-A-homo-19-norcholesta-1,5,7,9-tetraene (XIII)——A suspension of 0.16 g. of XI (R=Ac) in 50 ml. of 0.5% KOH-MeOH was stirred for 7 hr. at room temperature to give a clear solution, which was neutralized with AcOH, concentrated *in vacuo*, and extracted with ether. The ether extract was washed with 5% $NaHCO_3$, H_2O and dried over anhyd. Na_2SO_4. Evaporation of the solvent yielded 0.14 g. of a syrupy residue, which was chromatographed over 6 g. of Al_2O_3. The eluate with benzene, after recrystallization from MeOH, gave 4β-hydroxy-6-methoxy-A-homo-19-norcholesta-1,5,7,9-tetraene (XI : R=H) as prisms, m.p. 107~109°. IR ν_{max} cm^{-1} : 3623 and 3472 (4β-OH). UV λ_{max} mμ (ε) : 250 (9,100), 285 (3,040), 299 (3,400).

To a stirred solution of 0.134 g. of XI (R=H) in 20 ml. of acetone cooled at 6°, 0.15 ml. of 8*N* chromic acid-H_2SO_4 solution was added dropwise and stirring continued for 6 min. The excess reagent was decomposed by adding EtOH. The reaction mixture was diluted with H_2O, concentrated *in vacuo*, and extracted with ether. The extract was washed with 5% $NaHCO_3$, H_2O, dried, and the solvent was evaporated to leave 0.14 g. of a gummy residue, which was crystallized by trituration with MeOH. Recrystallization from MeOH afforded needles of 4-oxo-6-methoxy-A-homo-19-norcholesta-1,5,7,9-tetraene (XIII), m.p. 102~103°, $[\alpha]_D^{29}$ +56.0° (c=1.00). *Anal.* Calcd. for $C_{28}H_{40}O_2$: C, 81.77; H, 9.75. Found : C, 82.30; H, 9.87. IR ν_{max} cm^{-1} : 1724 (4-CO), 1585 (aromatic ring). UV λ_{max} mμ (ε) : 256 (13,000). NMR τ : 9.38 (18-CH_3), 6.99 (doublet, j=6 c.p.s., 3-CH_2-), 6.25 (4a-CH_2-), 6.17 (6-OCH_3), 3.7~4.0 (2-H), 3.36 (7-H), 3.08 (doublet, j=12 c.p.s., 1-H).

1,4-Dioxo-6-methoxy-A-homo-19-norcholesta-5,7,9-triene (XIV)——A solution of 0.50 g. of XII (R=Ac) in 60 ml. of 0.5% KOH-MeOH was set aside at room temperature for 15 hr. The reaction mixture was acidified with AcOH, condensed *in vacuo*, and extracted with ether. The ether extract, after washing with H_2O and drying, was concentrated to leave 0.45 g. of a crystalline residue melting at 185~195°. Recrystallization from benzene-hexane gave 1α,4β-dihydroxy-6-methoxy-A-homo-19-norcholesta-5,7,9-triene (XII : R=H) as silky needles, m.p. 194~196°, $[\alpha]_D$ +50.3° (c=1.3). *Anal.* Calcd. for $C_{28}H_{44}O_3$: C, 78.45; H, 10.35. Found : C, 78.01; H, 10.47. IR ν_{max} cm^{-1} : 3356 and 3247 (1α- and 4β-OH), 1600 and 1577 (aromatic ring).

To a stirred solution of 0.616 g. of XII (R=H) in 150 ml. of purified acetone cooled at 8°, 1.4 ml. of 8*N* chromic acid-H_2SO_4 solution was added dropwise and stirring continued for 13 min. Work up of the reaction mixture as described above yielded 0.60 g. of crystals. Recrystallization from MeOH afforded 0.30 g. of scales melting at 121～129°. The mother liquor, after evaporation of the solvent, was chromatographed over 12 g. of Al_2O_3. Elution with hexane-benzene (2:1) gave further 0.10 g. of crystals. The combined crystals were recrystallized from MeOH to afford XIV as scales, m.p. 127～129°, $[\alpha]_D$ +75.8°(c=1.05). *Anal.* Calcd. for $C_{28}H_{40}O_3$: C, 79.20; H, 9.50. Found: C, 78.85; H, 9.33. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1724 (4-CO), 1695 (1-CO), 1594 (aromatic ring). UV λ_{max} mμ (ε): 258 (2,500), 318 (2,370).

1β,4β-Oxido-17β-acetoxy-A-homo-19-norandrost-5(10)-en-6-one Ethylenethioketal (XVI)——To a solution of 11.0 g. of IIIc in 150 ml. of AcOH was added 35 ml. of ethanedithiol and 40 ml. of BF_3-etherate and the mixture set aside at room temperature for 3 hr. The reaction mixture was poured onto ice-water and extracted with ether. The ether extract was washed with aq. $NaHCO_3$, H_2O and dried. Removal of the solvent afforded a crystalline residue, which was recrystallized from MeOH to give 11.0 g. of prisms of 1β,4β-oxido-17β-acetoxy-A-homo-19-norandrost-5(10)-en-6-one ethylenethioketal (XVI), m.p. 162～164°. The filtrate of recrystallization, after evaporation of the solvent and chromatography over Al_2O_3 with hexane-benzene (2:1 and 1:1), gave further 1.5 g. of crystals of the ethylene thioketal (XVI). $[\alpha]_D$ +22°(c=2.57). *Anal.* Calcd. for $C_{23}H_{32}O_3S_2$: C, 65.67; H, 7.67; S, 15.21. Found: C, 65.48; H, 7.56; S, 15.48. NMR τ: 9.14 (18-CH_3), 7.93 (OAc), 6.6～6.7 (S-$(CH_2)_2$-S), 5.33 (1α-, 4α- and 17α-H).

Desulfurization of XVI with Raney Ni Catalyst in Ethanol——A mixture of 5.0 g. of XVI, 500 ml. of abs. EtOH, and about 50 g. of freshly prepared Raney Ni*12 (W-2) was stirred under reflux for 4.5 hr. After cooling, inorganic material was removed by filtration. The filtrate was evaporated *in vacuo* to leave 4.2 g. of a crystalline residue, which was chromatographed over 120 g. of Al_2O_3. First fraction eluted with benzene gave 2.90 g. of crystals melting at 142～153°, gas chromatography*13 of which showed two peaks indicating the presence of 83.7% of XVII and 16.3% of XVIII. Recrystallization of the mixture from MeOH or hexane failed to separate into two components. Repeated chromatography of the mixture over Al_2O_3 and recrystallizations of each fraction afforded again a mixture of prisms and sticks, but combined mother liquors of recrystallization of each fraction, after evaporation of the solvent, was recrystallized from hexane to afford plates of 1β,4β-oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-ene 17-acetate (XVII), m.p. 158～160°, showing a single peak on gas chromatography. $[\alpha]_D$ −15°(c=2.21). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.28; H, 9.14. Found: C, 75.77; H, 8.96. IR ν_{max} cm^{-1}: 1736 (OAc). NMR τ: 9.17 (18-CH_3), 7.90 (OAc), 5.1～5.5 (1α- and 4α-H).

Second fraction obtained from the eluate with benzene, after recrystallization from MeOH, gave 0.5 g. of 1β,4β-oxido-17β-hydroxy-A-homo-19-norandrost-5(10)-en-6-one 17-acetate (IIIc) as needles, m.p. 200～204°.

Treatment of the Desulfurized Mixture (XVII and XVIII) with Lithium in Ethylamine——To a stirred solution of 0.5 g. of Li in 60 ml. of freshly distilled $C_2H_5NH_2$ cooled in an ice-bath, 1.0 g. of desulfurized mixture (XVII and XVIII) dissolved in 120 ml. of $C_2H_5NH_2$ was added dropwise for 13 min. and stirring further continued for 15 min. To the reaction mixture was added 18 g. of NH_4Cl in small portions and then water. The mixture was extracted with ether, the ether extract was washed with water, dried over Na_2SO_4. Evaporation of the solvent gave 1.0 g. of a gummy residue, which was chromatographed over 36 g. of Al_2O_3. First fraction eluted with C_6H_6 afforded 0.14 g. of crystals, which, after recrystallization from hexane, gave 4β,17β-dihydroxy-A-homo-19-norandrost-5(10)-ene 17-acetate (XIX) as prisms, m.p. 123～126°. *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.85; H, 9.76. Found: C, 75.56; H, 9.61. IR ν_{max} cm^{-1}: 3470 (OH), 1742 (OAc), 1661 ($\Delta^{5(10)}$). NMR τ: 9.17 (18-CH_3), 7.93 (OAc), 6.33 (4α-H), 5.33 (17α-H).

Acetylation of XIX with Ac_2O and pyridine at room temperature, after usual work-up and recrystallization from MeOH, afforded 4β,17β-dihydroxy-A-homo-19-norandrost-5(10)-ene 3,17-diacetate (XXII) as leaflets, m.p. 137～139°. *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.85; H, 9.76. Found: C, 75.56; H, 9.61. IR ν_{max} cm^{-1}: 1730 (OAc). NMR τ: 9.18 (18-CH_3), 7.93 and 7.97 (4β- and 17β-OAc).

A solution of 1.1 g. of XIX in 50 ml. of 2% KOH-95% EtOH was refluxed on a water bath for 1 hr. The reaction mixture was diluted with H_2O, extracted with ether-$CHCl_3$ and AcOEt. The combined extracts were washed with H_2O, dried, and evaporated to leave a crystalline residue. Recrystallization from benzene-hexane afforded 0.626 g. of XXI as prisms melting at 151～157°. From the mother liquor additional 0.28 g. of XXI was obtained.

Second fraction obtained from further elution with benzene gave 0.135 g. of crystals, which was recrystallized from MeOH to afford 1β,4β-oxido-17β-hydroxy-A-homo-19-nor-19ξ-*H*-androst-5-ene (XX) as needles, m.p. 113～116°. $[\alpha]_D$ −4.0°(c=2.68). *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 78.92; H, 9.75. NMR τ: 9.23 (18-CH_3), 7.75 (OH), 6.2～6.55 (17α-H), 5.6 (1α- and 4α-H), 4.4～4.53 (6-H).

Acetylation of XX with Ac_2O and pyridine, after usual work-up and recrystallization from MeOH, afforded needles of XVIII, m.p. 170～171°. $[\alpha]_D$ −15° (c=1.01). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.28; H, 9.14.

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*12 R. Mozingo: Org. Syntheses, Coll. Vol. III, 181 (1955).

*13 Barber-Coleman Model-10. 1% FS-1265 on Chromosorb W, 80～100 mesh. 2 m. × 6 mm. i. d. column. Column temp. 175°. Flash temp. 265°. Cell temp. 175°. Carrier gas, Ar. Tritium detector.

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Found : C, 75.98; H, 9.25. IR ν_{max} cm^{-1} : 1733 (OAc). NMR τ : 9.17 (18-CH_3), 7.93 (OAc), 5.32∼5.58 (1α-, 4α- and 17α-H), 4.37∼4.52 (6-H).

Third fraction obtained from the eluate with benzene-ether (7:1) gave 0.509 g. of crystals, which was recrystallized from MeOH to yield 0.435 g. of 4β,17β-dihydroxy-A-homo-19-norandrost-5(10)-ene (XXI) as prisms, having double melting point at 124° and 160∼164°. Analytical sample was evacuated at 100° for 10 hr., having m.p. 156∼162°. *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found : C, 78.42; H, 10.40. IR ν_{max} cm^{-1} : 3280 (broad, 4β- and 17β-OH), 1660 ($\Delta^{5(10)}$). NMR τ : 9.24 (18-CH_3), 6.2∼6.4 (4α- and 17α-H).

Treatment of XXI with Ac_2O and pyridine at room temperature for 18 hr., followed by usual work-up and recrystallization from MeOH, afforded leaflets of XXⅡ, m.p. 136∼138°.

A-Homo-19-norandrost-5(10)-ene-4,17-dione (**XXIII**)——To a stirred solution of 0.354 g. of XXI in 40 ml. of acetone cooled at 4°, 0.7 ml. of 8*N* CrO_3-H_2SO_4 was added dropwise and stirring further continued for 6 min. The excess reagent was decomposed by addition of EtOH. The reaction mixture was diluted with H_2O and extracted with ether. The ether extract was washed with 5% $NaHCO_3$, H_2O, and dried. The solvent was evaporated to afford 0.34 g. of a crystalline residue, which was chromatographed over 15 g. of Al_2O_3. Elution with hexane-benzene (2:1 and 1:1) afforded 0.21 g. of crystals, which was recrystallized from MeOH to give prisms of A-homo-19-norandrost-5(10)-ene-4,17-dione (XXⅢ), m.p. 117∼119°, $[\alpha]_D^{26}$ +229° (c=1.3). *Anal.* Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found : C, 79.22; H, 9.10. IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1745 (17-CO), 1712 (4-CO). UV λ_{max} mμ (ε) : 294 (218). NMR τ : 9.08 (18-CH_3), 7.1 (doublet) and 6.68 (doublet) (j=14.5 c.p.s., 4*a*-CH_2-).

Treatment of A-Homo-19-norandrost-5(10)-ene-4,17-dione (**XXIII**) **with Concentrated Hydrochloric Acid in Ethanol**——A solution of 1.075 g. of XXⅢ in 40 ml. of EtOH containing 0.3 ml. of conc. HCl was set aside at room temperature for 17 hr. The reaction mixture was diluted with H_2O, extracted with ether. The ether extract was washed with H_2O, 5% $NaHCO_3$, again with H_2O, and dried. The solvent was evaporated to give 1.1 g. of a residue, which was chromatographed over 40 g. of Al_2O_3. Elution with hexane-benzene (2:1 and 1:1) afforded 0.75 g. of crystals, which was recrystallized from MeOH to give starting material (XXⅢ) melting at 115∼119°.

Second fraction eluted with benzene, after evaporation of the solvent, afforded 0.23 g. of crystals, which was recrystallized from hexane to afford A-homo-19-norandrost-4*a*-ene-4,17-dione (XXIV) as scales, m.p. 152∼154°, $[\alpha]_D^{26}$ +96.7° (c=1.2). *Anal.* Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found : C, 79.44; H, 9.14. IR ν_{max} cm^{-1} : 1742 (17-CO), 1642 and 1616 (Δ^{4a}-4-CO). UV λ_{max} mμ (ε) : 242 (15,200). NMR τ : 9.07 (18-CH_3), 4.02 (4*a*-H).

A-Homo-19-nortestosterone (**XXV**)——To a stirred solution of 0.16 g. of XXIV in 30 ml. of MeOH cooled in ice-water, 0.060 g. of $NaBH_4$ dissolved in 5 ml. of MeOH was added and stirring further continued for 2 hr. at room temperature. The excess reagent was decomposed by adding AcOH, the reaction mixture diluted with H_2O and extracted with ether. The extract was washed with 5% $NaHCO_3$, H_2O and dried over anhyd. Na_2SO_4. The solvent was evaporated to leave 0.15 g. of an amorphous residue. This was taken up in 30 ml. of $CHCl_3$, and the solution was shaken with 2 g. of active MnO_2 at room temperature for 5 hr. The suspension was filtered from inorganic material, which was washed well with hot $CHCl_3$. The combined filtrates were evaporated to give 0.16 g. of an oily residue, which was chromatographed over 8 g. of Al_2O_3. The eluate with benzene afforded, after recrystallization from hexane-benzene, 0.090 g. of XXV as leaflets, m.p. 158∼160°. ORD (c=2.07, dioxane) : $[\alpha]_{272}$ +3180°; $[\alpha]_{294}$ +3043°; $[\alpha]_{355}$ −1256°. *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.72. Found : C, 79.50; H, 9.76. IR ν_{max} cm^{-1} : 1655 and 1622 (Δ^{4a}-4-CO), 3450 (OH). UV λ_{max} mμ (ε) : 243 (16,000).

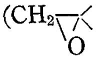
Catalytic Hydrogenation of A-Homo-19-norandrost-4*a*-ene-4,17-dione (**XXIV**) **with Platinum in Ethanol**——A solution of 0.143 g. of XXIV in 20 ml. of EtOH was shaken with H_2 over Pt-catalyst prepared from 0.05 g. of $PtO_2 \cdot 2H_2O$ and 17.3 ml. of H_2 was absorbed at room temperature for 16 min. Inorganic material was removed by filtration, the filtrate was evaporated *in vacuo* to leave a residue, which was chromatographed over 12 g. of Al_2O_3. First eluate with benzene-hexane (1:2) gave 0.025 g. of crystals, which was recrystallized from hexane to afford needles of A-homo-19-nor-5α-androstane-4,17-dione (XXVI), m.p. 139∼140°, $[\alpha]_D$ +198.4° (c=2.48). *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found : C, 78.86; H, 9.56. IR ν_{max} cm^{-1} : 1745 (17-CO), 1698 (4-CO).

Second fraction with hexane-benzene (1:2 and 1:1), after recrystallization from hexane, afforded 0.065 g. of A-homo-19-nor-5β-androstane-4,17-dione (XXVⅡ) as needles, m.p. 133∼135°. ORD (c=2.10, dioxane) : $[\alpha]_{283}$ −1667°; $[\alpha]_{319}$ +2286°. *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found : C, 79.12; H, 9.80. IR ν_{max} cm^{-1} : 1742 (17-CO), 1698 (4-CO). Rechromatography of the combined mother liquors of recrystallization furnished further 0.034 g. of XXVⅡ.

Treatment of 17β-Hydroxy-19-nor-5α-androstan-3-one (**XXVIII**) **with Diazomethane in Methanol-Ether**——To a solution of 6.0 g. of XXVⅢ in 120 ml. of MeOH was added. 140 ml. of diazomethane-ether solution[*14] and the mixture was allowed to stand at room temperature for 17 hr. The reaction mixture was condensed to give 6.40 g. of an oily residue, which was acetylated with 60 ml. of Ac_2O and 120

[*14] Th. J. de Boer, H. J. Backer : Org. Synthesis, Coll. Vol. Ⅳ, 96 (1954).

ml. of pyridine at 50° for 3 hr. The acetylated mixture was poured onto ice-water, extracted with ether. The ether extract was washed with dil. HCl, H_2O, 5% $NaHCO_3$, and H_2O, successively and dried. Evaporation of the solvent yielded 7.15 g. of a crystalline residue, which was recrystallized from hexane to afford 1.35 g. of needles, m.p. 136.5～137.5°. Further 0.58 g. of needles melting at 137～138° was obtained from the mother liquor of recrystallization. A specimen (0.50 g.) of the combined crystals was hydrolyzed by dissolving in a mixture of 7 ml. of benzene, 20 ml. of MeOH containing 0.30 g. of KOH. After allowing to stand at room temperature for 3 hr., the reaction mixture was worked up as usual to yield 0.422 g. of crystals melting at 135～136°. Recrystallization from benzene-hexane afforded a crystalline substance of unknown structure,*[15] m.p. 136～137°. *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found : C, 78.84; H, 10.45. IR ν_{max} cm^{-1} : 1697. This 17β-alcohol having m.p. 136～137° was oxidized with $8N$ CrO_3-H_2SO_4 solution in acetone under ice-cooling and the reaction product obtained was chromatographed over Al_2O_3 to yield, after recrystallization from hexane, needles of m.p. 122～123°. *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found : C, 79.07; H, 9.63. IR ν_{max} cm^{-1} : 1736 (17-CO), 1712.

The mother liquor of recrystallization was chromatographed over 510 g. of Al_2O_3. First eluate with hexane-benzene (82:18) yielded 0.704 g. of crystalline substance, which was recrystallized from hexane to give prisms of unknown compound,*[16] m.p. 142～143°. IR ν_{max} cm^{-1} : 1736 (17-OAc). NMR τ : 9.18 (18-CH_3), 7.95 (OAc), 7.35 ($\underset{O}{CH_2{-}}\!<$?), 5.36 (17α-H).

Second fraction with hexane-benzene (82:18) afforded 0.603 g. of crystals, which was recrystallized from hexane to afford 17β-hydroxy-A-homo-19-nor-5α-androstan-4-one 17-acetate (XXIX : R=Ac), m.p. 111～112°. ORD (c=2.07, dioxane) : $[\alpha]_{273}$ $-1164°$; $[\alpha]_{314}$ $+1436°$; $[\alpha]_{589}$ $+84°$. *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found : C, 78.65; H, 10.38. IR ν_{max} cm^{-1} : 1730 (17-OAc), 1705 (4-CO).

A solution of 0.162 g. of XXIX (R=Ac) in 20 ml. of EtOH containing 0.2 g. of KOH was heated at 70° for 2 hr. The reaction mixture was poured into water and extracted with ether. The ether extract, after washing and drying, was condensed to afford 0.137 g. of crystals. Recrystallization from benzene-hexane gave 17β-hydroxy-A-homo-19-nor-5α-androstan-4-one (XXIX : R=H), m.p. 162～164°. $[\alpha]_D$ +111° (c=3.35). *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found : C, 78.65; H, 10.38. IR ν_{max} cm^{-1} : 3378 (OH), 1692 (4-CO).

To a stirred solution of 0.050 g. of XXIX (R=H) in 15 ml. of purified acetone cooled with ice, 0.08 ml. of $8N$ CrO_3-H_2SO_4 solution was added dropwise and stirring continued for 5 min. The reaction mixture was treated as usual to afford 0.050 g. of a crystalline product, which was recrystallized from hexane to give needles of A-homo-19-nor-5α-androstane-4,17-dione (XXVI), m.p. 139.5～140°. The identity of the compound with the specimen having 139～140° obtained by catalytic hydrogenation of XXIV was proved by mixed m.p. determination and infrared spectral comparison.

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*[15] A structure of 7- or 8-membered ring ketone may be suggested.

*[16] It is probably an epoxide, which could be formed by addition of diazomethane to the double bond of carbonyl function.