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19. Ryozo Hayashi: Steroid Series. XIX.*1 Rearrangement Reactions of 3β-Acetoxy-6,19-dioxo-5α-steroids.

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3β-Acetoxy-6,19-dioxo-5α-steroid (II) was found to rearrange, under acidic conditions, into 1β,4β-oxido-A-homo-19-nor-$\Delta^{5(10)}$-6-oxo-steroid (III), and, in alkaline medium, into 3β,6α-dihydroxy-5α-steroid-19-oic acid 3,19-lactone (XV). Possible reaction mechanisms involving the same intermedial 3β,19-hemiacetal of initially formed 3β-hydroxy-6,19-dioxo-5α-steroid (IV) were proposed. Anisotropic effects of 19-formyl and 3β,19-lactone carbonyl groups on the chemical shift of 18-methyl protons were also discussed.

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The preceding paper*1 described the conversion of 3α,5α-cyclo-6,19-dioxosteroid (I) under acidic conditions into 1β,4β-oxido-A-homo-19-nor-$\Delta^{5(10)}$-6-oxosteroid (III) through the intermediate, 3β-acetoxy-6,19-dioxo-5α-steroid (II). Under alkaline conditions, on the other hand, 3β-acetoxy-6,19-dioxo-5α-steroid (II) was unexpectedly found to undergo rearrangement into 3β,6α-dihydroxy-5α-steroid-19-oic acid 3,19-lactone (XV). In the present paper will be described these rearrangement reactions catalysed by acid or alkali of 3β-acetoxy-6,19-dioxo-5-steroid (II).

As described in the preceding paper,*1 refluxing 3α,5α-cyclo-6,19-dioxosteroid (I) in a mixture of acetic acid and dilute sulfuric acid gave the rearrangement product (III) together with a small amount of 3β-acetoxy-6,19-dioxo-5α-steroid (II), the latter compound being obtained as a major product on treatment of 3α,5α-cyclo-6,19-dioxosteroid (I) with perchloric or dilute sulfuric acids in acetic acid at room temperature.

Treatment of 3β,17β-dihydroxy-6,19-dioxo-5α-androstane 3,17-diacetate (IIb) with anhydrous hydrogen chloride in absolute ethanol at room temperature and subsequent reacetylation of 17β-hydroxyl function afforeded 3β,,19-oxido-6-oxo-17β-hydroxy-19-ethoxy-5α-androstan 17-acetate (V), whose structure was assigned from its analytical values and NMR spectrum.

The nuclear magnetic resonance (NMR) spectrum of the 19-ethylal (V) had no longer signal due to formyl proton, but newly exhibited a singlet at 5.04τ indicative of 19-proton, a triplet (j=7.5 c.p.s.) centered at 8.84τ and a complex multiplet between 6.0 and 6.5τ ascribable to methyl and methylene protons in ethoxy group, respectively. The formation of the ethylal (V) indicated that the 3β-acetoxy group in the compound (II) possessed β-configuration. The 19-ethylal (V) was in turn smoothly converted to the rearrangement product (IIIb), when refluxed either in benzene containing a catalytic

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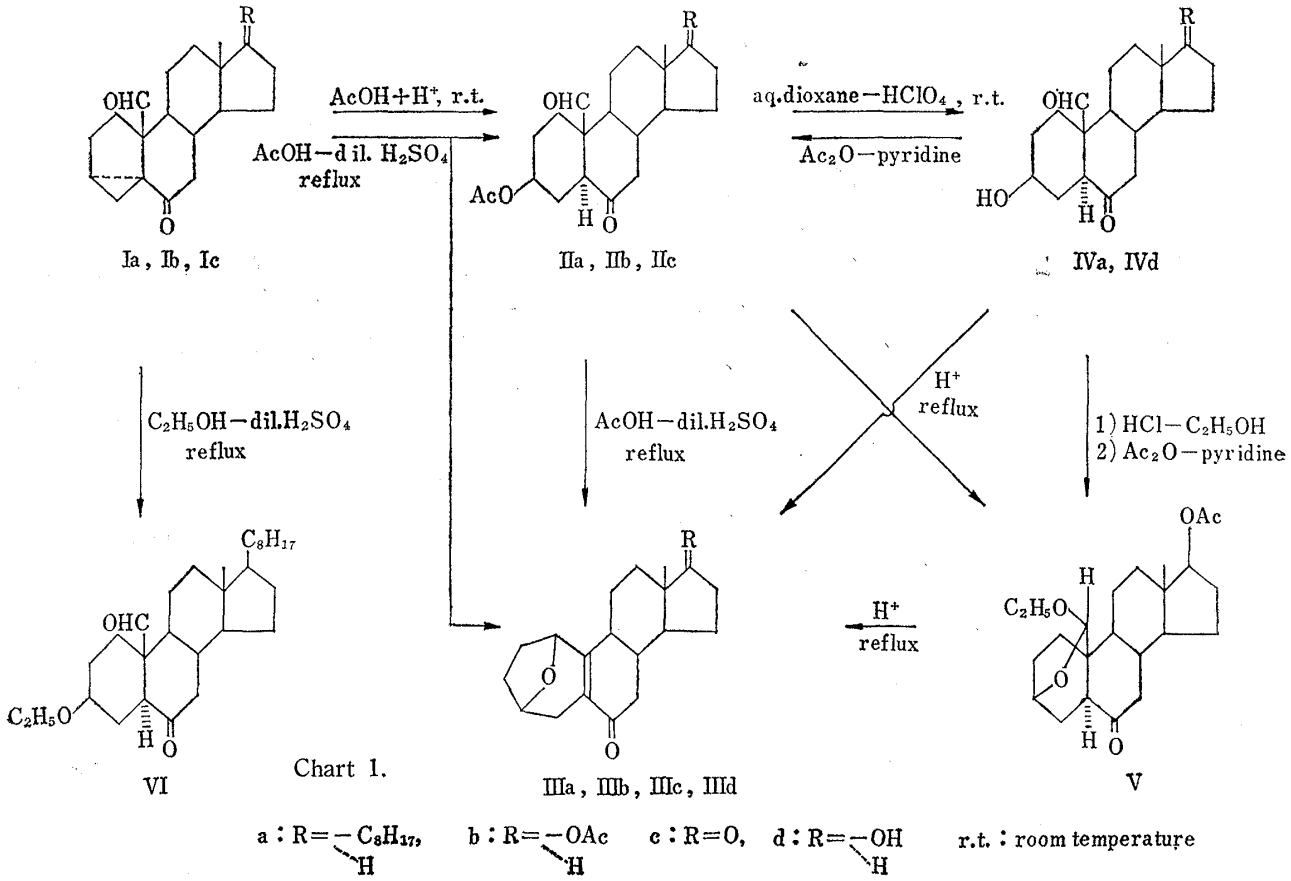


Chart 1.

a : R=—C_8H_{17}, b : R=—OAc c : R=O, d : R=—OH r.t. : room temperature

amount of *p*-toluene sulfonic acid or in absolute ethanol with anhydrous hydrogen chloride. This finding suggested that an oxonium ion resulted by protonation on 19-ethoxy oxygen, participates in the rearrangement reaction as an intermediate. Refluxing 3β,17β-dihydroxy-6,17-dioxo-5α-androstane 3,17-diacetate (IIb) under anhydrous, acidic conditions, such as either in benzene with *p*-toluene sulfonic acid or in ether with boron trifluoride etherate, gave no rearrangement product only to recover the starting material.

Acid-hydrolysis of 3β,17β-dihydroxy-6,19-dioxo-5α-androstane 3,17-diacetate (IIb) in aqueous dioxane containing perchloric acid at room temperature afforded the corresponding 3β,17β-diol (IVd), which was also converted to the rearrangement product (IIId) under the same reaction conditions as those for the 19-ethylal (V). These observations suggested that the acid-catalysed rearrangement reaction of 3β-acetoxy-6,19-dioxo-5α-steroid (II) proceeded through the initially formed 3β-hydroxy compound (IV). In fact, 3β-acetoxy-5α-cholestane-6,19-dione (IIa) was revealed to be partly hydrolyzed into the 3β-ol (IVa) in a mixture of acetic acid and dilute sulfuric acid at 50° for 1.5 hours as disclosed qualitatively by thin-layer chromatography over silica gel. On refluxing this solution for 3 hours, the rearrangement product (IIIa) was detected on thin-layer chromatogram, both the 3β-acetoxy (IIa) and the corresponding 3β-hydroxy compounds (IVa) having disappeared. On the basis of these observations, the acid-catalysed rearrangement of 3α,5α-cyclo-6,19-dioxosteroid (I) might proceed as shown in Chart 2.

An analogous reaction has been reported by Jacobs, *et al.*[1] and Fieser, *et al.*[2] describing the rearrangement of dihydrostrophantidine (IX) with concentrated hydrochloric acid into trianhydrostrophantidine (X).

1) W. A. Jacobs, A. M. Collins : J. Biol. Chem., **63**, 123 (1925); W. A. Jacobs, R. C. Elderfield : *Ibid.*, **108**, 693 (1935).
2) L. F. Fieser, T. Goto : J. Am. Chem. Soc., **82**, 1697 (1960).

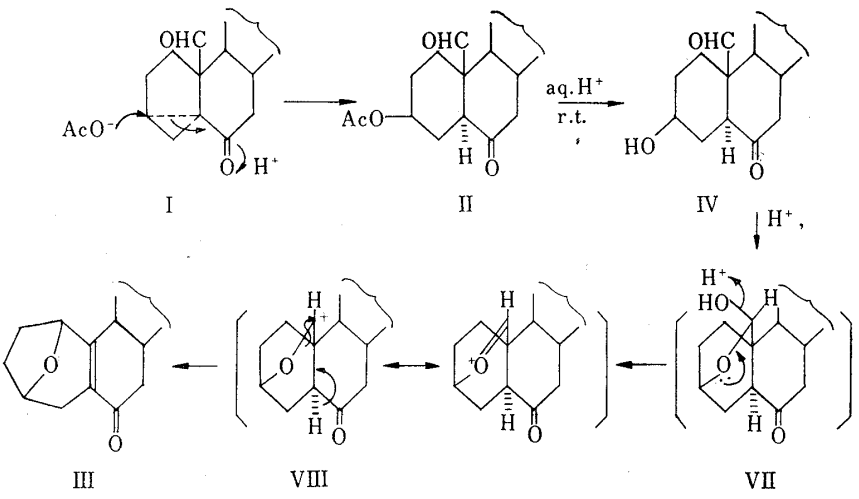


Chart 2.

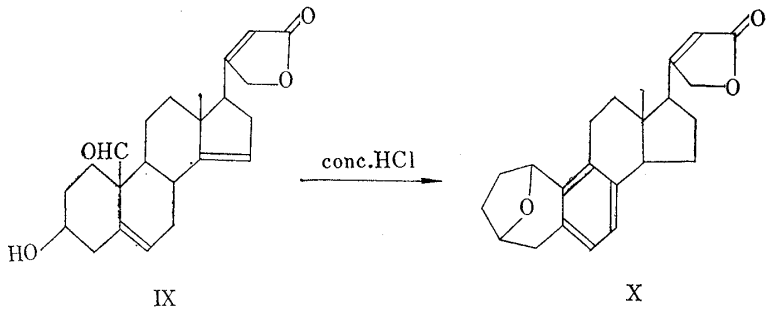


Chart 3.

The NMR spectra of 3β-acetoxy-6,19-dioxo-5α-steroids (II) showed that signals due to 18-methyl protons shifted at appreciably higher field than those for 3α,5α-cyclo-6,19-dioxosteroids (I) : As shown in Chart 4, the 18-methyl signal at 9.40τ in 3β-hydroxy-6,19-dioxo-5α-cholestane 3-acetate (IIa) was shifted upfield by 0.13 p.p.m. compared with the corresponding signal at 9.27τ in 3α,5-cyclo-6,19-dioxo-5α-cholestane (Ia). An analogous upfield shift by 0.14 p.p.m. was observed in 17-oxo-androstane series. On the other hand, diamagnetic shifts of 18-methyl signals of 3β-acetoxy-6-oxo-5α-steroids (XII) relative to the observed values for 3α,5α-cyclo-6-oxosteroids (XI) were 0.06 p.p.m. in both cholestane and 17-oxoandrostane series. Therefore, it is obvious that the 19-formyl function in 3β-acetoxy-6,19-dioxo-5α-steroids (II) has a diamagnetic shielding effect on the 18-methyl protons. The magnitudes of the effect were estimated from the differences of the 18-methyl signals between 3β-acetoxy-6-oxo-5α-steroids (XII) and the corresponding 19-formyl compounds (II) to be 0.06 p.p.m. in cholestane and 0.09 p.p.m. in 17-oxo-androstane series. In contrast to these observations, the 19-formyl function in 3α,5α-cyclo-6,19-dioxosteroids (I) showed essentially no effect on the signal of 18-methyl protons, since the chemical shift under discussion were not significantly moved by the introduction of the 19-formyl group into the 3α,5α-cyclo-6-oxo-steroids (XI).

A possible explanation on these findings might be given in terms of the combined effects of the magnetic anisotropy and restricted rotation of the 19-formyl group. The steric environment of 19-formyl function is less crowded in 3α,5α-cyclo-6,19-dioxo-steroids (I) than in 3β-acetoxy-6,19-dioxo-5α-steroids (II) as depicted in formula XIII and XIV. The 19-formyl group in the former compounds (XIII), therefore, might be expected to rotate more freely and exert no significant shielding effect on the 18-methyl signal

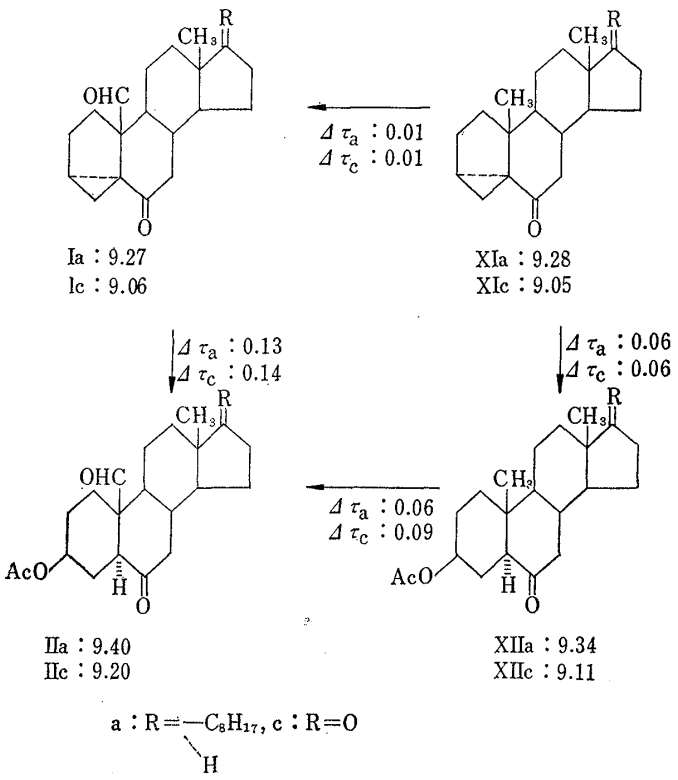
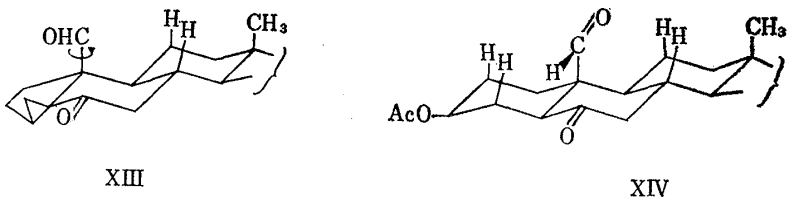


Chart 4. Chemical shifts of 18-methyl protons (τ values) and differences ($\Delta\tau$) between the relative comounds.

as a net result. While, in the latter compounds (XIV), additional 1,3-diaxial interactions between 19-formyl group and 2β- and 4β-hydrogen atoms probably hinder the free rotation of the 19-formyl group to assume its preferred conformation which interposes the formyl oxygen atom between C_2- and C_{11}-axial hydrogens, but not between C_4- and C_8-axial hydrogens owing to the electrostatic repulsion of 19-formyl oxygen against C_6-carbonyl one. Thus, 18-methyl protons in 3β-acetoxy-6,19-dioxo-5α-steroids (XIV) come to lie in the conical region of diamagnetic shielding of the 19-formyl carbonyl.

In the course of the studies on acid-catalysed rearrangement described above, 3β-hydroxy-6,19-dioxo-5α-cholestane 3-acetate (IIa), on treatment with aqueous potassium hydroxide in ethanol at room temperature, was found to afford a mixture of the corresponding 3β-ol



XIII XIV

Chart 5.

(IVa) and an alcohol of m.p. 197~199°. The former alcohol (IVa) could be smoothly converted to the latter under refluxing conditions and its structure was firmly established as 3β,6α-dihydroxy-5α-cholestan-19-oic acid 3,19-lactone (XVa) by the spectral data and by chemical reactions shown in Chart 6. The infrared spectrum of XVa in carbon tetrachloride had no carbonyl bands due to both 19-formyl and 6-oxo functions and was also devoid of bending vibration of C_7-methylene, which had appeared at 1420 cm^{-1} in 3β-hydroxy-6,19-dioxo-5α-cholestane 3-acetate (IIa) and at 1422 cm^{-1} in the corresponding 3β-hydroxy compound (IVa). Instead, a strong band at 1750 cm^{-1} due to δ-lactone and a hydroxyl band at 3623 cm^{-1} were exhibited at a concentration of 0.0004 moles. The NMR spectrum showed a broad multiplet centered at 5.30τ assignable to 3α-proton and a quasi sextet at 6.80τ due to 6β-proton, coupled with two axial 5α- and 7α-protons (observed splitting = 10.5 c.p.s.) and one equatorial 7β-proton (observed splitting = 3 c.p.s.), as X portion of A_2BX pattern. Oxidation of the hydroxy-δ-lactone (XVa) with chromic anhydride in pyridine afforded the corresponding keto-δ-lactone (XVIIa), which had infrared absorption bands at 1739 and 1715 cm^{-1}

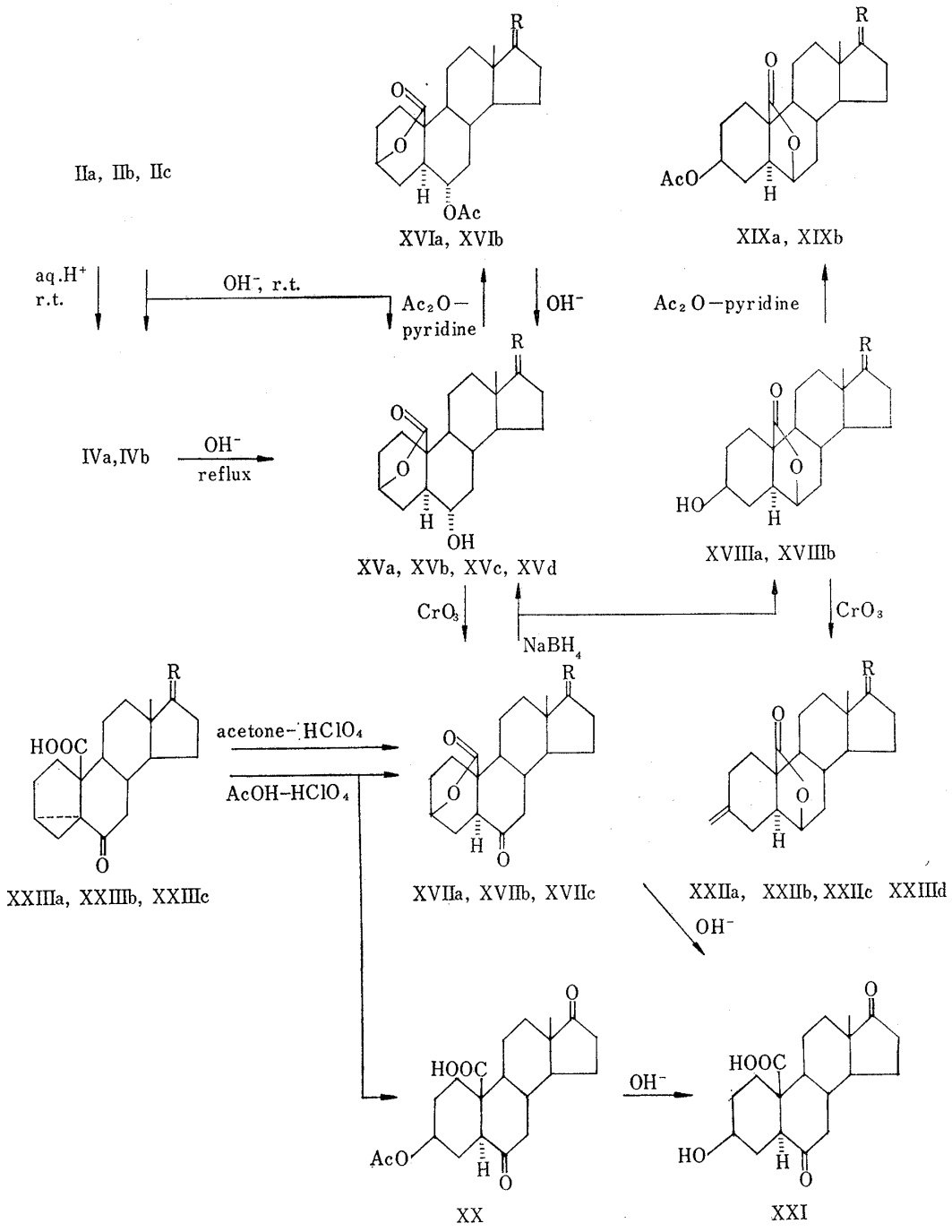


Chart 6.

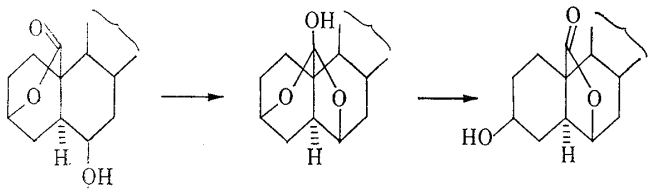
assignable to δ-lactone and a six-membered ring ketone, respectively. The keto-δ-lactone (XVIIa) was found to be identical with 3β-hydroxy-6-oxo-5α-cholestan-19-oic acid 3,19-lactone (XVIIa), which was derived from 3α,5-cyclo-6-oxo-5α-cholestan-19-oic acid (XXIIIa)[3] on treatment with perchloric acid in refluxing acetone. The formation of the δ-lactone (XVIIa) from XXIIIa can well be explained as a nucleophilic attack of 10β-carboxyl function to C_3-cation induced by acid.

3) Part XVI of this series : This Bulletin, **15**, 15 (1967).

3α,5-Cyclo-6,17-dioxo-5α-androstan-19-oic acid (XXIIIc) was similarly treated with perchloric acid in acetic acid at room temperature to yield a mixture of 3β-acetoxy-6,17-dioxo-5α-androstan-19-oic acid (XX) and 3β-hydroxy-6,17-dioxo-5α-androstan-19-oic acid 3,19-lactone (XVIIc), both of which were hydrolysed with aqueous alkali to the same 3β-hydroxy-6,17-dioxo-5α-androstan-19-oic acid (XXI). The 6-oxo-3,19-lactone (XVIIc) thus obtained proved identical with the keto-δ-lactone prepared from 3β-hydroxy-6,19-dioxo-5α-androstan-17-one 3-acetate (IIc) by the same reactions as in the cholestane series.

Reduction of 3β-hydroxy-6-oxo-5α-cholestan-19-oic acid 3,19-lactone (XVIIa) with sodium borohydride in ethanol and subsequent chromatography over alumina yielded 3β,6α-dihydroxy-5α-cholestan-19-oic acid 3,19-lactone (XVa) and 3β,6β-dihydroxy-5α-cholestan-19-oic acid 6,19-lactone (XVIIIa) in a ratio of 1:5. The 6α-hydroxy-3β,19-lactone (XVa), a minor reduction product, was found to be identical with the hydroxy-δ-lactone derived from the alkaline treatment of 3β-acetoxy-6,19-dioxo-5α-cholestane (IIa), thus the structure of the alkali-catalysed rearrangement product being unambiguously established.

The structural assignments of the two hydroxy lactones (XVa and XVIIIa) were deduced by the following evidence. The hydroxy lactone (XVIIIa) obtained as a major reduction product had infrared bands at 1776 and 3620 cm^{-1} due to γ-lactone and a secondary hydroxy function, respectively, with no intramolecular hydrogen bonding at a concentration of 0.0004 moles in carbon tetrachloride. Oxidation of the lactone with chromic anhydride in pyridne or with 8*N* chromic acid solution in acetone[4] afforded the corresponding keto-γ-lactone(XXIIa), which apparently differed from the 6-oxo-3β,-19-lactone (XVIIa). The optical rotatory dispersion curve exhibited a positive Cotton effect similar to that for 5α-cholestan-3-one suggesting the presence of 5α-*H*-3-oxo structure. One the basis of these observations the structure was proposed to be 3β,6β-dihydroxy-5α-cholestan-19-oic acid 6,19-lactone (XVIIIa) and this was finally established by the following findings. 3β,6β,17β-Trihydroxy-5α-androstan-19-oic acid 6,19-lactone 17-acetate (XVIIIb) obtained as a major reduction product with sodium borohydride of 3β,17β-dihydroxy-6-oxo-5α-androstan-19-oic acid 3,19-lactone 17-acetate (XVIIb), was treated with acetic anhydride and pyridine to afford the corresponding 3β,17β-diacetoxy-γ-lactone (XIXb), which was identical with authentic 3β,6β,17β-trihydroxy-5α-androstan-19-oic acid 6,19-lactone 3,17-diacetate.*3 The formation of the 3β-hydroxy-6β,19-lactone (XVIII) by sodium borohydride reduction of XVII can be explained to proceed through the intermedial hemiacilal (XXV) of the initially formed 6β-hydroxy-3β,19-lactone (XXIV) into the more stable 6β,19-lactone structure (XVIII).



XXIV XXV XVIII

Chart 7.

From the above-described results the hydroxy-δ-lactone, a minor reduction product of XVII, must have a structure of 6α-hydroxy-3β,19-lactone (XV). These conclusions were also coincident with the well established fact that the metal hydride reduction of a hindered ketone predominantly furnishes an axial hydroxyl group.

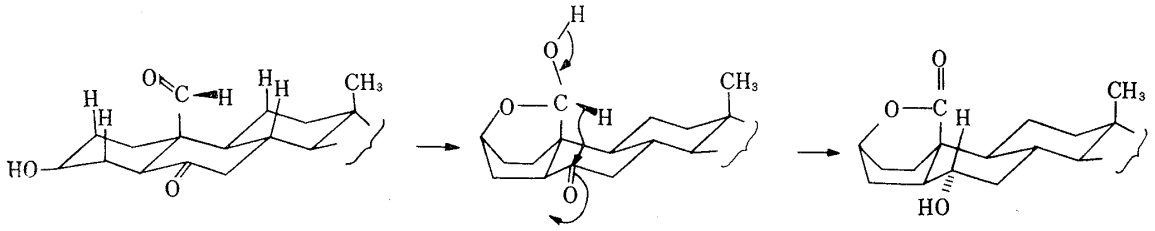
In NMR spectra of the 3β,19-lactones the signals due to 18-methyl protons appeared at a considerably downfield, which is apparently caused by the anisotropic

*3 The author is grateful to Dr. J. Edwards, Syntex Research, Stanford Industrial Park, Palo Alto, California, U. S. A. for giving him the valuable sample.

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

effect of the 3β,19-lactone group : The 6α-hydroxy-3β,19-lactone (XVa) and its 6α-acetate (XVIa) in cholestane series showed the signal at 9.16τ and the 6-oxo-3β,19-lactone (XVIIa) at 9.17τ, whereas 5α-cholestane taken as a reference compound has been reported to have the 18-methyl signal at 9.36τ.[5] This was also the case with 17-oxo-androstane series, where the 18-methyl peaks appeared at 8.93τ in both 6-oxo-(XVIIc) and Δ^5-3β,19-lactone,[6] showing a shift value to downfield by 0.21 p.p.m. compared with the corresponding peak at 9.14τ reported in 17-oxo-5α-androstane.[5] Examination of Dreiding model of the 3β,19-lactone indicates that the 18-methyl protons lie in a plain of trigonal carbon atom of the lactone group and is therefore expected to suffer a paramagnetic shielding effect of the lactone carbonyl. On the other hand, the 6β,19-lactone group showed no significant effect on the chemical shift of the 18-methyl protons; thus the signal of the 3β-hydroxy-6β,19-lactone (XVIIIa) in cholestane series appeared at 9.33τ.

Finally, it will be discussed on the reaction mechanism of the base-catalysed rearrangement of 3β-acetoxy-6,19-dioxo-5α-steroid (II). The fact that the 6α-hydroxy-3β,-19-lactone (XV) was isolated directly from the extract of the alkaline reaction mixture suggested the reaction to proceed through 3β,19-hemiacetal of 3β-hydroxy-6,19-dioxo-5α-steroid (IV) and not through intermedial 19-oic acid derivative. Supporting this, alkaline treatment of 3β-ethoxy-6,19-dioxo-5α-cholestane (VI) and 3α,5-cyclo-6,19-dioxo-5α-cholestane (Ia) in which the formation of 3β,19-hemiacetal bond can not be effected, resulted in isolation of the starting material unchanged. On the basis of these observations coupled which the stereospecific formation of 6α-hydroxyl group in the lactones (XV), a reaction mechanism involving an intramolecular hydride shift from 19- to 6-carbon atoms was proposed as shown in Chart 8. As mentioned earlier the NMR



XXVI XXVII XXVIII

Chart 8.

studies on the chemical shift of the 18-methyl protons suggested a preferred conformation to 3β-acetoxy-6,19-dioxo-5α-steroid as indicated in formula (XIV). The intermedial 3β,19-hemiacetal (XXVII) of 3-hydroxy-6,19-dioxo-5α-steroid*4 (XXVI) might therefore have 19-hydrogen atom extending over the 6-carbonyl carbon atom to facilitate a transfer of the hydrogen with its paired electrons to the 6-carbonyl carbon from the β-side of the molecule affording stereospecifically the 6α-hydroxyl group.

*4 3β-Hydroxy-6,19-dioxo-5α-cholestane (IVa) exhibited two resonance signals of 18-methyl protons at 9.30 and 9.40τ, both having the almost same intensity. The signal at 9.40τ appeared apparently at higher field owing to the presence of diamagnetic shielding of the 19-formyl function as discussed in 3β-acetoxy-6,19-dioxo-5α-steroids (II). The lower signal at 9.30τ at the position normally expected, could be attributed to that for the corresponding 3β,19-hemiacetal structure.

5) R. F. Zürcher : Helv. Chim. Acta, **46**, 2054 (1963).
6) Part XVII of this series; This Bulletin, **15**, 27 (1967).

Experimental*5

3β-Ethoxy-6,19-dioxo-5α-cholestane (VI)——A solution of 0.20 g. of Ia in 20 ml. of 99% EtOH and 4 ml. of 14% H_2SO_4 was heated under reflux for 2 hr. on a water bath. The reaction mixture was concentrated *in vacuo*, diluted with water, and extracted with ether. The ether extract was washed with 5% $NaHCO_3$, water and dried over anhyd. Na_2SO_4. Removal of the solvent afforded 0.20 g. of a crystalline residue, which was chromatographed over 8 g. of Al_2O_3 (neutral, Woelm grade III). The first fraction eluted with hexane–benzene (1:1) gave 0.08 g. of the starting material melting at 117~122°. The second fraction eluted with the same mixture of the solvents yielded 0.048 g. of a crystalline product, which was recrystallized from MeOH to afford silky needles of VI, m.p. 141~144°. $[\alpha]_D$ −33° (c=1.00). *Anal.* Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 77.95; H, 11.09. IR ν_{max}^{Nujol} cm^{-1}: 1715 (shoulder), 1709. NMRτ: 9.41 (18-CH_3), 8.83 (triplet, J=7.0 c.p.s.) and 6.35~6.70 (13 to 14 peaks, 3β-OC_2H_5), 0.30 (10-CHO).

3β-Hydroxy-6,19-dioxo-5α-cholestane 3-Acetate (IIa)——i) A mixture of 0.20 g. of Ia in 20 ml. of AcOH and 4 ml. of 5*N* H_2SO_4 was set aside at room temperature for 40 hr. The reaction mixture was poured into water and extracted with ether. The ether extract was washed with water, 5% $NaHCO_3$, water and dried over anhyd. Na_2SO_4. Evaporation of the solvent afforded an amorphous residue, which was chromatographed over 8 g. of Al_2O_3. The eluate with benzene–hexane (2:3) gave a crystalline material of Ia recovered. The second eluate with the same mixture of solvents yielded 0.10 g. of a crystalline product, which was recrystallized from MeOH to afford leaflets of IIa, m.p. 164~169°.

ii) To a solution of 0.90 g. of Ia in 20 ml. of AcOH, 1.0 ml. of 60% $HClO_4$ was added dropwise with stirring. After standing at room temperature for 16 hr., the reaction mixture was poured into water and extracted with ether. The ether extract was washed with water, aq. $NaHCO_3$, water and dried over anhyd. Na_2SO_4. Removal of the solvent afforded a crystalline residue, which was recrystallized from MeOH to give 0.46 g. of IIa as needles melting at 158~168°. The filtrate of recrystallization, after evaporation of the solvent, was chromatographed over 20 g. of Al_2O_3. The eluate with benzene–hexane (1:1) gave further 0.16 g. of IIa as needles of m.p. 162~169° (combined yield, 0.62 g.). For analytical and spectral data, see experimental in Part XVIII of this series.

3β,17β-Dihydroxy-6,19-dioxo-5α-androstane 3,17-Diacetate (IIb)——A mixture of 0.932 g. of Ib, 25 ml. of AcOH and 1.0 ml. of 60% $HClO_4$ was set aside at room temperature for 15 hr. The reaction mixture was treated as described above to yield 1.0 g. of a crystalline product, which was recrystallized from benzene–hexane to afford 0.44 g. of IIb, m.p. 181~184°. The mother liquor of recrystallization was chromatographed over 20 g. of Al_2O_3 and elution with benzene–ether (4:1) yielded further 0.287 g. of IIb. For analytical and spectral data see experimental in Part XVIII of this series.

3β-Hydroxy-6,17,19-trioxo-5α-androstane 3-Acetate (IIc)——To a solution of 0.45 g. of Ic in 18 ml. of AcOH was added dropwise 0.4 ml. of 60% $HClO_4$ with stirring and the mixture was set aside at room temperature for 15 hr. The solution was poured into water and extracted with ether. The extract was washed with aq. $NaHCO_3$, water and dried over Na_2SO_4. Evaporation of the solvent gave 0.373 g. of a crystalline residue, which was recrystallized from benzene–hexane to afford needles of IIc melting at 204~217°.

3β-Hydroxy-6,19-dioxo-5α-cholestane (IVa)——A mixture of 0.117 g. of IIa, 30 ml. of 80% aq. dioxane and 1.7 ml. of 60% $HClO_4$ was set aside at room temp. for 2 days and the solution was diluted with water and extracted with ether. The extract was washed with 5% $NaHCO_3$, water and dried. Evaporation of the solvent gave an amorphous product of IVa, showing a single spot on TLC, which resisted attempts for crystallization from several solvents. $[\alpha]_D$ +10.2° (c=2.35). IR ν_{max}^{Nujol} cm^{-1}: 3390 (OH), 1718 (shoulder, 10-CHO), 1706 (6-CO). NMRτ: 9.30 and 9.40 (18-CH_3), 0.37 (CHO).

The 3β-ol (IVa) was treated with Ac_2O in pyridine at room temperature for 15 hr. The acetylated product was recrystallized from MeOH to give leaflets of IIa melting at 163~169°.

3β,19-Oxido-6-oxo-17β-hydroxy-19-ethoxy-5α-androstan (V)——i) A solution of 0.20 g. of IIb in 60 ml. of abs. EtOH containing 4.0 g. of dry HCl was allowed to stand at room temp. for 40 hr. The reaction mixture was concentrated *in vacuo*, diluted with water and extracted with ether. The extract was washed with 5% $NaHCO_3$, water and dried over Na_2SO_4. Removal of the solvent yielded 0.157 g. of an amorphous residue, which was chromatographed over 10 g. of Al_2O_3. The combined eluates with benzene and benzene–ether (4:1) gave 0.11 g. of an amorphous product, which resisted attempts to crystallize. The amorphous product (0.11 g.) was acetylated with 1.5 ml. of Ac_2O in 5 ml. of pyridine. After allowing to stand at room temperature for 16 hr., the reaction mixture was condensed to dryness *in vacuo* to afford an oily residue, which was chromatographed over 8 g. of Al_2O_3. The eluate with hexane–benzene (1:1) gave, after recrystallization from hexane, 0.052 g. of V as needles, m.p. 146~148°. $[\alpha]_D$ −2.5° (c=2.08). *Anal.*

*5 All melting points were uncorrected. The nuclear magnetic resonance spectra were determined with Varian A-60 spectrometer in deuteriochloroform solution containing tetramethylsilane as internal standard. The optical rotatory dispersion curves were taken with JASCO Model ORD/UV-5, Japan Spectroscopic Co., Ltd. $[\alpha]_D$ values were measured in $CHCl_3$ solution.

Calcd. for $C_{23}H_{34}O_5$: C, 70.70; H, 8.77. Found : C, 70.26; H, 8.73. IR ν_{max}^{Nujol} cm^{-1} : 1733 (OAc), 1709 (6-CO). NMRτ : 9.18 (18-CH_3), 7.90 (OAc), 8.84 (triplet, j=7.4 c.p.s.) and 6.0~6.6 (13 to 14 peaks, 19-OC_2H_5), 5.92 (3α-H), 5.04 (19-H), 5.22 (17α-H).

ii) A solution of 0.14 g. of Ⅳd in 50 ml. of 10% HCl-abs. EtOH was set aside at room temperature for 40 hr. Removal of the solvent *in vacuo* gave an amorphous residue, which was treated with Ac_2O in pyridine at room temperature overnight. The reaction mixture was condensed to dryness *in vacuo* to afford an amorphous product, which was chromatographed over 8 g. of Al_2O_3. Elution with benzene gave 0.075 g. of Ⅴ as needles.

1β,4β-Oxido-6-oxo-17β-hydroxy-A-homo-19-norandrost-5(10)-ene 17-Acetate (IIIb)——i) A solution of 0.042 g. of Ⅴ in 40 ml. of benzene containing 0.05 g. of *p*-toluene sulfonic acid monohydrate was boiled to remove about 10 ml. of distillate and refluxed for 2 hr. on a water bath. The benzene solution was washed with 5% $NaHCO_3$, water, dried over anhyd. Na_2SO_4 and condensed to dryness to afford a crystalline product, which was recrystallized from ether to give 0.035 g. of Ⅲb melting at 204~205°.

ii) A solution of 0.05 g. of Ⅳd in 30 ml. of benzene containing 0.05 g. of *p*-toluene sulfonic acid monohydrate was heated under reflux for 2 hr. The reaction mixture was diluted with water and extracted with ether. The extract was washed with 5% $NaHCO_3$, water, dried over anhyd. Na_2SO_4 and condensed to yield 0.04 g. of an amorphous product, which was acetylated with Ac_2O in pyridine at room temperature. The reaction mixture was condensed to dryness *in vacuo* to give a crystalline residue. Recrystallization from ether afforded Ⅲb as scales melting at 202~205°.

iii) A solution of 0.050 g. of Ⅳd in 5 ml. of AcOH and 1.0 ml. of 14% H_2SO_4 was refluxed for 2 hr., cooled to room temperature, poured into water and extracted with ether. The extract was washed with 5% $NaHCO_3$, water, dried over anhyd. Na_2SO_4 and condensed to dryness to give 0.050 g. of a crystalline residue, which was dissolved in 5 ml. of pyridine and 1.5 ml. of Ac_2O and set aside at room temperature for 12 hr. The reaction mixture was condensed to dryness *in vacuo* to yield a crystalline product, showing a single spot in thin-layer chromatography (TLC). Recrystallization from ether afforded scales of Ⅲb, m.p. 201~204°.

iv) A solution of 0.05 g. of Ⅴ in 14 ml. of 7% dry HCl-EtOH was heated under reflux for 2 hr. and condensed to dryness *in vacuo* to yield an amorphous product, which was dissolved in 5 ml. of pyridine and 1 ml. of Ac_2O and allowed to stand at room temperature for 15 hr. The solution was condensed to dryness *in vacuo* to give an oily residue, which was chromatographed over 12 g. of Al_2O_3. The eluate with benzene ether (8:1) afforded Ⅲb melting at 187~195° (crude crystals).

Treatment of 3β-Hydroxy-6,19-dioxo-5α-cholestane 3-Acetate (IIa) with KOH in EtOH at Room Temperature——A mixture of 0.46 g. of Ⅱa and 50 ml. of 2% KOH-EtOH was warmed on a water bath for a few minutes to obtain a clear sotution and then allowed to stand at room temperature for 18 hr. The reaction mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried over anhyd. Na_2SO_4 and the solvent was evaporated to give 0.50 g. of an amorphous residue, which was chromatographed over 20 g. of Al_2O_3. The first fraction eluted with benzene-ether (5:1) yielded 0.14 g. of a crystalline product, which was recrystallized from hexane-benzene-EtOH to afford needles of XVa, m.p. 197~199°. $[\alpha]_D$ +47° (c=1.22). *Anal.* Calcd. for $C_{27}H_{44}O_3$: C, 77.83: H, 10.65. Found : C, 77.56: H, 10.51. IR $\nu_{max}^{CCl_4}$ cm^{-1} : 3623 (OH), 1750 (3β,19-lactone). NMRτ : 9.13 (18-CH_3), 6.80 (6β-H), 5.30 (3α-H). The second fraction eluated with the same mixture of solvents gave 0.14 g. of Ⅳa as an amorphous substance.

Treatment of 3β,17β-Dihydroxy-6,19-dioxo-5α-androstane 3,17-Diacetate (IIb) with KOH-EtOH at Room Temperature——i) A solution of 0.24 g. of Ⅱb in 30 ml. of 2% KOH-EtOH was set aside at room temperature for 14 hr. The reaction mixture was acidified with AcOH, condensed *in vacuo* to a small volume and diluted with water to separate a crystalline substance, which was collected by filtration and dried to give 0.075 g. of crystals. Recrystallization from benzene-EtOH afforded prisms of XVd, m.p. 230~232°. *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found : C, 70.87; H, 8.68. IR ν_{max}^{Nujol} cm^{-1} : 3390 and 3356 (6α- and 17β-OH), 1709 (3β,19-lactone).

The aq. filtrate obtained above was extracted with $CHCl_3$–AcOEt for several times. The combined extracts were washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvents afforded 0.12 g. of a crystalline residue, which was recrystallized from benzene-EtOH to afford Ⅳd as scales of m.p. 193~194°. An analytical sample was evacuated at 100° for 10 hr. *Anal.* Calcd. $C_{19}H_{28}O_4 \cdot 1/2H_2O$: C, 69.32; H, 8.87. Found : C, 69.34; H, 8.67. IR ν_{max}^{Nujol} cm^{-1} : 3378, 3165 and 3106 (3β-and 17β-OH), 1718 (CHO), 1706 (6-CO).

ii) A solution of 0.50 g. of Ⅱb in 30 ml. of 2% KOH-aq. 95% EtOH was refluxed on a water bath for 20 min. The reaction mixture was cooled, neutralized with AcOH, condensed *in vacuo* at room temperature, diluted with water and extracted with AcOEt. The AcOEt extract was washed with aq. Na_2CO_3, water, dried and condensed to dryness to yield 0.379 g. of a crystalline residue of XVd, showing a single spot in TLC.

3β,6α-Dihydroxy-5α-cholestan-19-oic Acid 3,19-Lactone (XVa)——i) A solution of 0.40 g. of Ⅱa in 50 ml. of 2% KOH-EtOH was heated under reflux for 70 min. on a water bath. The reaction mixture was diluted with water and extracted with ether. The combined extracts were washed with water, dried

and condensed to dryness *in vacuo* to yield 0.287 g. of a crystalline residue, showing a single spot in TLC, which was recrystallized from MeOH gave needles of XVa, m.p. 194~196°.

ii) A solution of 0.10 g. of IVa in 30 ml. of 2% KOH-EtOH was refluxed on a water bath for 1.5 hr., cooled to room temperature, poured into water and extracted with ether. The extract was washed with water, dried over anhyd. Na_2SO_4 and condensed to dryness to yield 0.08 g. of a crystalline residue, showing a single spot in TLC. Recrystallization from MeOH afforded XVa as needles of m.p. 194~196°.

3β,6α-Dihydroxy-17-oxo-5α-androstan-19-oic Acid 3,19-Lactone (XVc)——A solution of 0.163 g. of IIc in 20 ml. of 2% KOH-aq. 95% EtOH was refluxed on a water bath for 40 min. The reaction mixture was poured into water and extracted with $CHCl_3$. The extract was washed with water, dried and condensed to dryness to leave 0.099 g. of a crystalline residue, which was recrystallized from benzene-MeOH to afford granules of XVc, m.p. 283~286°. $[\alpha]_D$ +207.5° (c=1.02). *Anal.* Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.59; H, 8.39. IR ν_{max}^{Nujol} cm^{-1}: 3510 (OH), 1740 (17-CO), 1725 (3β,19-lactone). NMRτ: 8.95 (18-CH_3), 6.70 (quasi sextet as X part of A_2BX system, observed splittings=11.0 and 4.0 c.p.s., 6β-H), 5.25 (multiplet, 3α-H).

3β,6α-Dihydroxy-5α-cholestan-19-oic Acid 3,19-Lactone 6-Acetate (XVIa)——XVa was treated with Ac_2O in pyridine at room temperature for 18 hr. The mixture was condensed to dryness *in vacuo* to yield a crystalline product, which was recrystallized from MeOH to afford XVIa as silky needles, m.p. 155~156°. $[\alpha]_D^{30}$ +76° (c=1.59). *Anal.* Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.89; H, 9.95. IR ν_{max}^{Nujol} cm^{-1}: 1739 and 1730 (shoulder) (OAc and 3β,19-lactone). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750 (OAc and 3β,19-lactone). NMRτ: 9.17 (18-CH_3), 7.93 (OAc), 5.25~5.38 (3α- and 6β-H).

3β,6α,17β-Trihydroxy-5α-androstan-19-oic Acid 3,19-lactone 6,17-Diacetate (XVIb)——XVd was acetylated with Ac_2O in pyridine at room temperature for 15 hr. The acetylated product was chromatographed over Al_2O_3 and the eluate with benzene gave, after recrystallization from hexane-acetone, needles of XVIb, m.p. 168~170°. $[\alpha]_D$ +55.5° (c=2.0). *Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.96. Found: C, 68.29; H, 7.89. IR ν_{max}^{Nujol} cm^{-1}: 1742 (6α- and 17β-OAc), 1725 (3β,19-lactone). NMRτ: 9.02 (18-CH_3), 5.22~5.37 (3α,6β- and 17α-H).

3β-Hydroxy-6-oxo-5α-cholestan-19-oic Acid 3,19-Lactone (XVIIa)——i) To a solution of 0.185 g. of XVa in 10 ml. of pyridine was added 0.30 g. of CrO_3 under ice-cooling and the mixture was allowed to stand at room temperature for 38 hr. The reaction mixture was poured into water and extracted with ether. The extract was washed successively with dil. HCl, water, 5% $NaHCO_3$, and water and dried over anhyd. Na_2SO_4. Evaporation of the solvent afforded a crystalline residue, which was recrystallized from EtOH to give needles of XVIIa, m.p. 217~220°. $[\alpha]_D^{24}$ −11.1° (c=2.99). *Anal.* Calcd for $C_{27}H_{42}O_3$: C, 78.21; H, 10.21. Found: C, 78.09; H, 10.21. IR ν_{max}^{Nujol} cm^{-1}: 1739 (3β,19-lactone), 1715 (6-CO). NMRτ: 9.17 (18-CH_3), 5.20 (3α-H).

ii) To a stirred solution of 0.174 g. of XVa in 30 ml. of purified acetone was added dropwise 0.2 ml. of 8*N* CrO_3-H_2SO_4 solution under ice-cooling. After stirring for 7 min., a small amount of *iso*-PrOH was added to decompose the excess reagent. The reaction mixture was diluted with water and extracted with ether. The extract was washed with aq. $NaHCO_3$ and water, dried over anhyd. Nr_2SO_4 and condensed to dryness to afford a crystalline residue, which was recrystallized from EtOH-benzene to give XVIIa as needles of m.p. 218~221°.

iii) A solution of 1.0 g. of XXIIIa in 100 ml. of acetone and 5.0 ml. of 70% $HClO_4$ was refluxed on a water bath for 40 min. The dark-brown colored solution was poured into water, extracted with ether. The ether extract was washed with aq. $NaHCO_3$ and water, dried over anhyd. Na_2SO_4 and condensed to give a crystalline residue, which was digested with MeOH to yield 0.78 g. of XVIIa (crude material, m.p. 210~220°).

3β-Hydroxy-6,17-dioxo-5α-androstan-19-oic Acid 3,19-Lactone (XVIIc)——i) A mixture of 0.22 g. of XVd, 14 ml. of pyridine and 0.45 g. of CrO_3 was allowed to stand at room temperature for 20 hr. The reaction mixture was worked up as described for XVIIa to give a crystalline product. Recrystallization from EtOH-benzene afforded pillars of XVIIc, m.p. 325~330°, $[\alpha]_D$ +51° (c=0.41). *Anal.* Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found: C, 71.86; H, 7.53. IR ν_{max}^{Nujol} cm^{-1}: 1736 (3β,19-lactone and 17-CO), 1721 (6-CO). NMRτ: 8.93 (18-CH_3), 5.22 (3α-H).

ii) To a stirred solution of 0.020 g. of XVc in 18 ml. of purified acetone was added 2 drops of Jones reagent under ice-cooling and stirring was continued for 7 min. at room temperature. The reaction mixture was treated with *iso*-PrOH to decompose the excess oxidant, diluted with water and extracted with AcOEt. The extract was washed with water, dried and removal of the solvent gave a crystalline residue, which was recrystallized from ether to afford prisms of XVIIc melting at 325°.

Treatment of 3α,5-Cyclo-6,17-dioxo-5α-androstan-19-oic Acid (XXIIIc) with 70% Perchloric Acid in Acetic acid——A solution of 0.64 g. of XXIIIc in 17 ml. of glac. AcOH containing 0.67 ml. of 70% $HClO_4$ was heated at 50° for 4 hr. The reaction mixture was poured onto ice-water and extracted several times with $CHCl_3$. The combined extracts were shaken with aq. $NaHCO_3$ and the $CHCl_3$ layer was separated, washed with water, dried and condensed to dryness *in vacuo* to give 0.251 g. of a crystalline residue. Recrystallization from $CHCl_3$-EtOH afforded XVIIc melting at 325~330° (decomp.).

The alkaline layer was acidified with 14% H_2SO_4 and extracted with $CHCl_3$. The extract was washed with water, dried and condensed to give 0.378 g. of a crystalline product, which was recrystallized from AcOEt-hexane afforded XX as needles of m.p. 300° (decomp.). *Anal.* Calcd. for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.96; H, 7.56. NMRτ: 9.16 (18-CH_3), 7.96 (OAc), 5.30 (3α-H).

3β-Hydroxy-6,17-dioxo-5α-androstan-19-oic Acid (XXI)——i) A mixture of 0.02 g. of XVIIc, 20 ml. of 99% EtOH and 10 ml. of 10% KOH was warmed on a water bath for a few min. to obtain a clear solution and allowed to stand at room temperature for 19 hr. The solution was diluted with water, shaken well with $CHCl_3$-AcOEt. The alkaline layer was separated, acidified with 5% HCl and extracted with AcOEt. The extract was washed with saturated NaCl solution, dried and condensed to dryness to give a crystalline residue, showing a single spot in TLC. Recrystallization from AcOEt afford prisms of XXI, which turned brown at about 240° and black at about 300°. IR ν_{max}^{Nujol} cm^{-1}: 3623, 3484 and 3311 (OH and COOH), 1730, 1706 and 1695 (COOH, 6-CO and 17-CO).

ii) A sample of XX was hydrolysed with 2% KOH-EtOH at room temperature as described for XVIIc to give XXI.

3β,17β-Dihydroxy-6-oxo-5α-androstan-19-oic Acid 3,19-Lactone 17-Acetate (XVIIb)——A solution of 8.3 g. of XXIIIb in 700 ml. of acetone and 18 ml. of BF_3-etherate was heated under reflux for 4 hr. The dark brown solution was concentrated *in vacuo* to about 200 ml., then poured onto ice-water and extracted with AcOEt. The extract was washed with water, aq. $NaHCO_3$ and water, dried over anhyd. Na_2SO_4 and the solvent was evaporated to dryness *in vaouo* to yield 7.5 g. of an yellow solid, which was chromatographed over 250 g. of Al_2O_3. The benzene eluate gave, after recrystallization from EtOH, 3.2 g. of XVIIb, m.p. 236~237°. $[\alpha]_D$ −35.7°. *Anal.* Calcd. for $C_{21}H_{28}O_5$: C, 69.97; H, 7.83. Found: C, 70.24; H, 8.08.

Reduction of 3β-Hydroxy-6-oxo-5α-cholestan-19-oic Acid 3,19-Lactone (XVIIa) with Sodium Borohydride in Ethanol——To a stirred solution of 0.85 g. of XVIIa in 300 ml. of 99% EtOH was added dropwise 0.160 g of $NaBH_4$ in 30 ml. of 90% EtOH at room temperature and stirring continued for 2 hr. The excess reagent was decomposed by adding 2 ml. of AcOH and the resulted mixture was condensed *in vacuo*, diluted with water and extracted with ether. The extract was washed with water, dried and condensed to yield a crystalline residue (IR ν_{max}^{Nujol} cm^{-1}: 1761 (6β,19-lactone), 1741 (3β,19-lactone)) which was chromatographed over 50 g. of Al_2O_3. The first fraction eluted with benzene-ether (12:1) afforded 0.179 g. of a crystalline product, which was recrystallized from hexane-benzene to give XVa as silky needles of m.p. 195~197°.

Further elution with benzene-ether (10:1) gave 0.20 g. of a mixture of the two components. The last fraction with benzene-ether (10:1 and 5:1) yielded 0.636 g. of a crystalline product, which was recrystallized from hexane-benzene to afford needles of XVIIIa, m.p. 186~188°, $[\alpha]_D^{27.5}$ +9.8° (c=7.1). *Anal.* Calcd. for $C_{27}H_{44}O_3$: C, 77.83; H, 10.65. Found: C, 77.37; H, 10.64. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1776 (6β,19-lactone), 3620 (OH). NMRτ: 9.33 (18-CH_3), 6.22~6.57 (3α-H), 5.63 (quasi doublet, j=4.6 c.p.s.).

Reduction of 3β,17β-Dihydroxy-6-oxo-5α-androstan-19-oic Acid 3,19-Lactone 17-Acetate (XVIIb) with Sodium Borohydride in Ethanol——To a stirred solution of 1.20 g. of XVIIb in 300 ml. of 99% EtOH was added dropwise 0.30 g. of $NaBH_4$ in 50 ml. of 80% EtOH at room temperature and stirring continued for 2.0 hr. The excess reagent was decomposed by adding 2.0 ml. of AcOH and the reaction mixture was condensed *in vacuo*, diluted with water and extracted with ether. The extract was washed with aq. $NaHCO_3$ and water, dried and evaporated to give 1.1 g. of a crystalline residue (IR ν_{max}^{Nujol} cm^{-1}: 3490 (OH), 1768 (6β,19-lactone), 1735 (3β,19-lactone), 1710*[6] (17-OAc)), which was chromatographed over 60 g. of Al_2O_3 and eluted with benzene-ether (5:1). The first fraction yielded 0.20 g. of XVb as an amorphous substance. The amorphous sample (0.20 g.) of XVb was acetylated with 1.5 ml. of Ac_2O in 5.0 ml. of pyridine on standing at room temperature for 20 hr. The mixture was condensed to dryness *in vacuo* to give a crystalline product, repeated recrystallizations of which from hexane-acetone afforded needles of XVIb melting at 168~170°.

Further elution gave 0.235 g. of a mixture of XVb and XVIIIb.

The last fraction yielded 0.798 g. of an amorphous product, which turned crystalline on adding ether. Recrystallization from hexane-benzene gave prisms of XVIIIb, m.p. 197~198° (not clear). $[\alpha]_D^{27}$ −17.1° (c=6.9). *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.48; H, 8.29. IR ν_{max}^{Nujol} cm^{-1}: 3520 (OH), 1767 (6β,19-lactone), 1712*[6] (17β-OAc). NMRτ: 9.20 (18-CH_3), 7.95 (OAc), 5.58 (quasi doublet, j=4.6 c.p.s.), 4.5 (broad, 3α-H).

3β,6β-Dihydroxy-5α-cholestan-19-oic Acid 6,19-Lactone 3-Acetate (XIXa)——A sample (0.26 g.) of XVIIIa was acetylated with 2.0 ml. of Ac_2O in 6.0 ml. of pyridine on allowing to stand at room temperature for 2 days. Condensation of the reaction mixture *in vacuo* gave a crystalline product, which was recrystallized from MeOH to afford XIXa as needles of m.p. 180~183°, $[\alpha]_D$ ±0.0° (c=5.2). *Anal.* Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.38; H, 9.77. IR ν_{max}^{Nujol} cm^{-1}: 1763 (6β,19-lactone), 1747 (3β-OAc). NMR: 9.33 (18-CH_3), 5.57 (quasi doublet, j=4.6 c.p.s.), 5.33 (broad, 3α-H).

*[6] Shifted to longer wave-length owing to the presence of an intermolecular hydrogen bonding.

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3β,6β,17β-Trihydroxy-5α-androstan-19-oic Acid 6,19-Lactone 3,17-Diacetate (XIXb)——A solution of 0.080 g. of XVIIIb in 5.0 ml. of pyridine and 1.2 ml. of Ac_2O was set aside at room temperature for 39 hr. and condensed to dryness *in vacuo* to leave a crystallne residue, which was recrystallized from hexane acetone afforded XIXb as needles of m.p. 214~216°, $[\alpha]_D^{27.5}$ −27.6° (c=.15). *Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 67.90; H, 7.86. IR ν_{max}^{Nujol} cm^{-1}: 1767 (6β,19-lactone), 1735 (OAc). The identity with an authentic sample was confirmed by mixed melting point determination, the infrared spectral comparison and Rf values on TLC (lit.[7]: m.p. 212~214°, $[\alpha]_D$ +8°).

6β-Hydroxy-5α-cholestan-6-on-19-oic Acid 6,19-Lactone (XXIIa)——To a solution of 0.20 g. of XVIIIa in 10 ml. of pyridine was added 0.3 g. of CrO_3 under ice-cooling and swirling and the mixture was set aside at room temperature for 18 hr. After adding water, the resultant mixture was extracted with ether. The extract was washed with 2*N*-H_2SO_4 and water, dried over anhyd. Na_2SO_4, and the solvent was removed to give 0.18 g. of a crystalline residue, which was chromatographed over 12 g. of Al_2O_3. Elution with benzene and recrystallization from MeOH gave needles of XXIIa, m.p. 209~211°. *Anal.* Calcd. for $C_{27}H_{42}O_3$: C, 78.21; H, 10.21. Found: C, 78.07; H, 9.93. ORD (c=0.24, dioxane): $[\alpha]_{274}$ −810°; $[\alpha]_{317}$ +1230°. $[\alpha]_D^{25}$ +39.6 (c=6.7.).

3-Oxo-6β,17β-dihydroxy-5α-androstan-19-oic Acid 6,19-Lactone 17-Acetate (XXIIb)——A mixture of 0.25 g. of XVIIIb, 10 ml. of pyridine and 0.3 g. of CrO_3 was set aside at room temperature for 39 hr. The dark brown mixture was worked up as described for XXIIa to afford 0.24 g. of a crystalline residue, which was chromatographed over 15 g. of Al_2O_3. Elution with benzene and recrystallization from hexane-acetone furnished needles of XXIIb melting at 212~214°, $[\alpha]_D^{20}$ +24.6° (c=2.6). IR ν_{max}^{Nujol} cm^{-1}: 1767 (6β,19-lactone), 1737 (OAc), 1717 (shoulder, 3-CO). NMR τ: 9.18 (18-CH_3), 7.94 (OAc), 5.53 (quasi doublet, j=4.6 c.p.s.).

3-Oxo-6β,17β-dihydroxy-5α-androstan-19-oic Acid 6,19-Lactone (XXIId)——A solution of 0.114 g. of XXIIb in 14 ml. of EtOH and 10 ml. of 10% KOH was heated under reflux on a water bath for 2 hr. The mixture was diluted with water and shaken with AcOEt-ether. The alkaline layer was acidified with 2*N*-HCl and extracted with AcOEt. The extract was washed with aq. NaCl dried, and removal of the solvent afforded 0.11 g. of an amorphous residue, which was dissolved in 8 ml. of EtOH containing 0.50 ml. of conc. HCl. The solution was refluxed on a water bath for 40 min., condensed *in vacuo*, diluted with water, and extracted with ether. The extract was washed with aq. $NaHCO_3$ and water, dried, and evaporated to yield 0.055 g. of a crystalline residue. Recrystallization from hexane-acetone afforded XXIId as prisms of m.p. 263~266°. *Anal.* Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.57; H, 8.34. IR ν_{max}^{Nujol} cm^{-1}: 3420 (OH), 1770 (6β,19-lactone), 1710 (3-CO).

3,17-Dioxo-6β-hydroxy-5α-androstan-19-oic Acid 6,19-Lactone (XXIIc)——To a stirred solution of 0.040 g. of XXIId in 20 ml. of purified acetone was added dropwise 0.1 ml. of 8*N* CrO_3-H_2SO_4 reagent at room temperature. After stirring for 6 min., the excess reagent was decomposed by adding *iso*-PrOH and the resultant mixture was diluted with water, extracted with AcOEt-$CHCl_3$. The extract was washed with aq. $NaHCO_3$ and water, dried, and condensed to dryness *in vacuo* to yield an amorphous residue, which was recrystallized from hexane-acetone to give needles of XXIIc melting at 206~209°, $[\alpha]_D^{23}$ +89° (c=1.02). *Anal.* Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found: C, 71.88; H, 7.47. IR ν_{max}^{Nujol} cm^{-1}: 1766 (6β,19-lactone), 1742 (17-CO), 1733 (shoulder) (lit.[7]: m.p. 194~196°. $[\alpha]_D$ +71°).

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