[Chem. Pharm. Bull. 18(10)1974—1980(1970)]

UDC 547.92.04 : 547.473.1.04 : 541.14

Steroid Series. XXIII.[1] Photolysis of Steroidal 6-Oxygenated 5,19-Lactone (β-Lactone)[2]

Koichi Kojima, Ryozo Hayashi and Katsumi Tanabe

Central Research Laboratories, Sankyo Co., Ltd.[3]

(Received February 28, 1970)

Irradiation of 5,6β-dihydroxy-17β-acetoxy-5β-androstan-19-oic acid 5,19-lactone (I) at room temperature using a mercury arc (450W) was found to yield in 30% yield 5,6β-dihydroxy-17β-acetoxy-5α-androstan-19-oic acid 6,19-lactone (II: R=Ac), structure of which was synthetically established. This photoreaction was proved to proceed through the keto-ketene intermediate (XV) generated upon irradiation of β-lactone moiety in I. On the other hand irradiation of 5-hydroxy-6-oxo-17β-acetoxy-5β-androstan-19-oic acid 5,19-lactone (XIX) afforded 17β-acetoxyestra-5(10)-en-6-one (XX) in about 60% yield.

Several reports have appeared on photolysis of β-lactone which seem to involve two types of decomposition: 1) cleavages of the carbon–carbon bond α to the carbonyl and the carbon–oxygen bond β to the carbonyl resulting in the formation of carbon dioxide and an olefin (type a),[4] 2) cleavages of the carbon–carbon and the carbon–oxygen bonds both α to the carbonyl with subsequent isomerization yielding carbon monoxide and an aldehyde (type b).[4a]

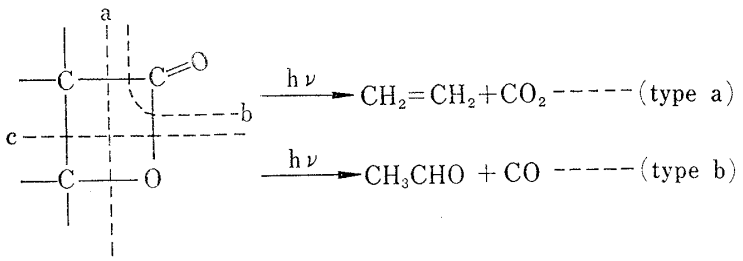

Chart 1

In our previous study[1] on the structure proof of the photoproduct of a 19-oxosteroid, syntheses of steroidal β-lactones, *i.e.* 5,6β-dihydroxy-17β-acetoxy-5β-androstan-19-oic acid 5,19-lactone (I) and 5-hydroxy-6-oxo-17β-acetoxy-5β-androstan-19-oic acid 5,19-lactone (XIX) have been described starting from 6-oxo-17β-acetoxy-5α-androstan-19-oic acid. As part of our interest on the photoreaction of 19-oxygenated steroids photochemical behavior of these β-lactones was investigated and the results provided the third type of photochemical decomposition of β-lactone (type c), including cleavages of the carbon–carbon and the carbon–oxygen bonds β and α to the carbonyl function, respectively, to form such a keto-ketene intermediate as XV.

A solution of the β-lactone (I) in dioxane was irradiated for 2—3 hours in an atmosphere of argon gas using Hanovia high pressure mercury lamp (450 W). Chromatographic separation of the reaction mixture over silica gel column afforded 5,6β-dihydroxy-17β-acetoxy-5α-androstan-19-oic acid 6,19-lactone (II: R=Ac) in 30% yield, together with small amounts of a crystalline substance of mp 224—227°, whose structure could not be determined because of its lack in amount. The photoproduct (II: R=Ac) with the same molecular formula as

1) Part XXII: K. Kojima, R. Hayashi and K. Tanabe, *Chem. Pharm. Bull.* (Tokyo), **18**, 88 (1970).
2) This work was presented at the 88th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, Apr. 1968.
3) Location: *1-2-58 Hiromachi, Shinagawa-ku, Tokyo.*
4) *a*) R.H. Linnell and W.A. Noyes, Jr., *J. Am. Chem. Soc.*, **72**, 3863 (1950); *b*) O.L. Chapman and W.R. Adams, *J. Am. Chem. Soc.*, **90**, 2333 (1968); M. Rosenblum and G.C. Gatsonis, *J. Am. Chem. Soc.*, **89**, 5074 (1967).

the starting material (I) exhibited absorption bands at 3420 and 1767 cm^{-1} in the infrared (IR) spectrum due to a hydroxyl and a five-membered lactone carbonyl groups, respectively. Attempted hydrolysis of the lactone ring in II (R=Ac) with alkali failed[5] merely giving rise to 17-hydroxylactone (II: R=H), which was reverted into the original 17-acetate with acetic anhydride in pyridine.

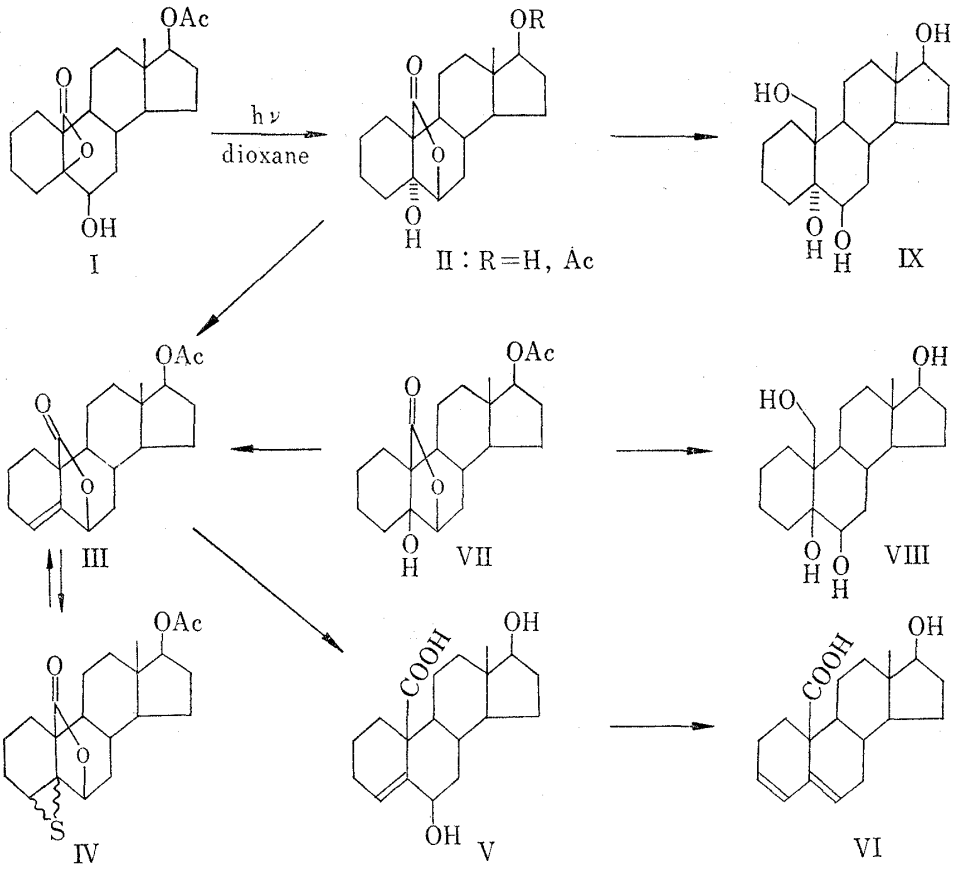

Chart 2

Treatment of II (R=Ac) with thionyl chloride in pyridine at room temperature resulted in a recovery of the starting material even after standing for two days, while dehydration reaction has taken place at 50° yielding an unsaturated lactone (III) which showed an olefinic proton signal centered at τ 4.38 in the nuclear magnetic resonance (NMR) spectrum. The same reaction at such an elevated temperature as 90° furnished the olefinic lactone (III) and an episulfide (IV), which showed a signal centered at τ 6.73 assignable to an episulfide proton[6] in the NMR spectrum. The episulfide was converted with triphenyl phosphin[7] into the olefin (III), which was reconverted to the former with thionyl chloride in pyridine and seems therefore to be an intermediate in the episulfide formation.

The lactone ring of the olefin (III) was now smoothly opened with alkali to yield 6β,17β-dihydroxyandrost-4-en-19-oic acid (V), which was transformed with hydrochloric acid into the known 17β-hydroxyandrosta-3,5-dien-19-oic acid (VI), identified with the authentic specimen[8] by comparison of the infrared spectrum. It is therefore evident that the photo-

5) 6β,19-Lactone ring of 3β,6β,17β-trihydroxy-5α-androstan-19-oic Acid 6,19-lactone also resisted to be opened by alkaline treatment.
6) N.S. Bhacca and D.H. Williams, "Applications of NMR Spectroscopy in organic chemistry," Holden-Day, Inc. 1964, p. 99.
7) D.B. Denney and N.J. Boskin, *J. Am. Chem. Soc.*, **82**, 4736 (1960).
8) K. Tanabe, R. Takasaki, R. Hayashi, Y. Morisawa, T. Hashimoto and T. Nakazawa, *Chem. Pharm. Bull.* (Tokyo), in press.

product (II: R=Ac) was formed without any skeletal rearrangement during the irradiation of the β-lactone (I). Furthermore the unsaturated lactone (III) was also obtainable by a smooth dehydration of the known 5,6β-dihydroxy-17β-acetoxy-5β-androstan-19-oic acid 6,19-lactone (VII)[1] with thionyl chloride in pyridine at 0°. This finding indicates that the photoproduct (II: R=Ac) and the lactone (VII) are epimeric at the C_5-position, and thus the lactone (II: R=Ac) must possess a 5α-hydroxyl function. This assignment was further verified by periodate oxidation reaction of the C_5-epimeric tetraols (VIII and IX), each of which was derived from the 5β- and 5α-hydroxy lactones (VII and II: R=H), respectively, by lithium aluminum hydride reduction: The tetraol (VIII) rapidly consumed one molar equivalent of periodate, while the tetraol (IX) did not consume any detectable amount of periodate even after three days' operation at room temperature.

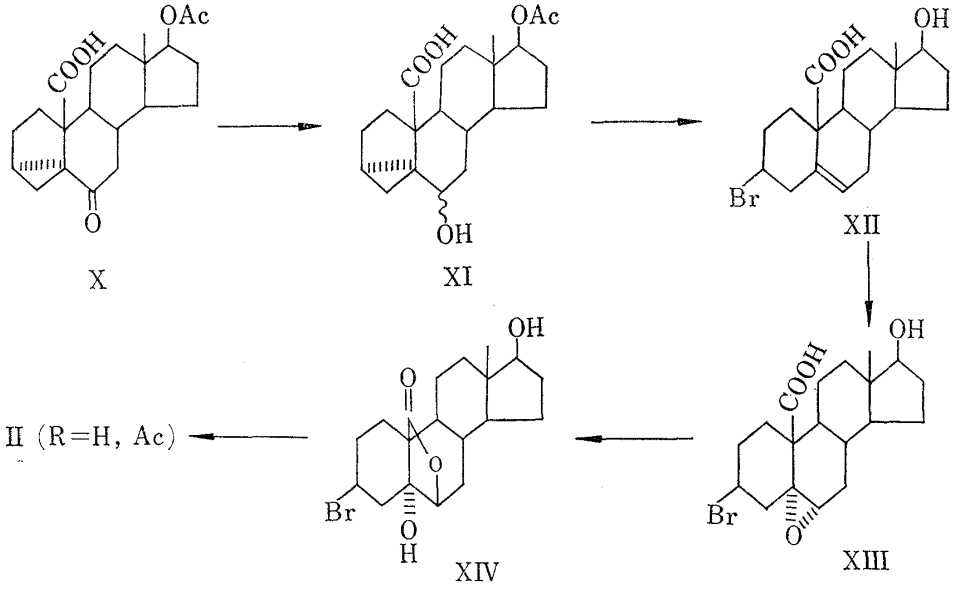

Chart 3

This assigned structure (II: R=Ac) was finally established by synthesis. Reduction of 3α,5-cyclo-6-oxo-17β-acetoxy-5α-androstan-19-oic acid (X)[9] with sodium borohydride yielded a mixture of the corresponding 6α- and 6β-hydroxy epimers (XI), which was treated, without further purification, with 10% hydrobromic acid in acetone to afford a homoallylically rearranged 3β-bromo-17β-hydroxyandrost-5-en-19-oic acid (XII).[9] Epoxidation of XII with monoperphthalic acid gave rise to 3β-bromo-5,6α-epoxy-17β-hydroxy-5α-androstan-19-oic acid (XIII), which was characterized by a typical 6β-proton signal as a doublet (J=3.5 cps) centered at τ 6.88.[6] Treatment of the epoxide (XIII) with 10% sulfuric acid in dioxane formed 3β-bromo-5,6β,17β-trihydroxy-5α-androstan-19-oic acid 6,19-lactone (XIV), which showed a characteristic infrared absorption band for a γ-lactone at 1768 cm^{-1}. The γ-lactone (XIV) must be formed by an acid catalysed ring opening of the epoxide with a simultaneous internal β-attack by the carboxyl function. Reductive debromination of the lactone (XIV) using palladium on charcoal catalyst yielded 5,6β,17β-trihydroxy-5α-androstan-19-oic acid 6,19-lactone (II: R=H), whose 17-acetate was confirmed to be identical with the photoproduct (II: R=Ac).

9) K. Tanabe, R. Takasaki, K. Sakai, R. Hayashi, Y. Morisawa and T. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), 15, 15 (1967).

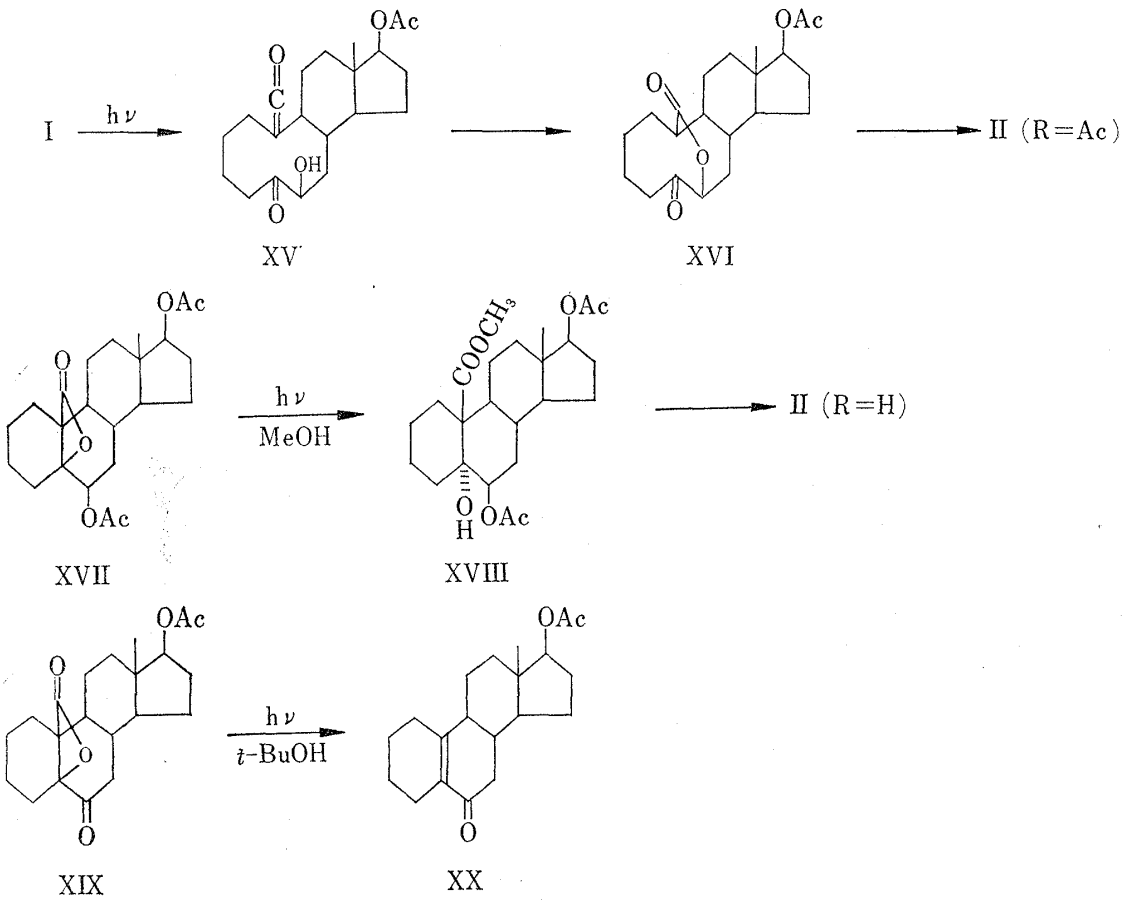

Chart 4

This photochemical reaction is rationalyzed by an initial activation of the carbonyl function of the β-lactone moiety to yield a keto-ketene intermediate (XV)[10] *via* a type c cleavage in Chart 1. The ketene function was then trapped intramolecularly by the 6β-hydroxy group affording a keto-6,19-lactone (XVI), which cyclized to form the final photoproduct (II: R=Ac) presumably through a photochemical process.[11]

Evidence for the intermediacy of the keto-ketene (XV) in the above photolysis comes from the following experiment. Irradiation of 5-hydroxy-6β,17β-diacetoxy-5β-androstan-19-oic acid 5,19-lactone (XVII) in methanol under the same photolytic conditions as for the β-lactone (I) furnished, in about 25% yield, methyl 5-hydroxy-6β,17β-diacetoxy-5α-androstan-19-oate (XVIII),[12] which showed a characteristic NMR signal of a carbomethoxy function at τ 6.29. Confirmation of the structure (XVIII) was obtained by its transformation with potassium hydroxide into the 5α-hydroxy-6,19-lactone (II: R=H).

Irradiation of 5-hydroxy-6-oxo-17β-acetoxy-5β-androstan-19-oic acid 5,19-lactone (XIX) under the same photolytic conditions as for the β-lactone (I) gave a complex mixture of products, while irradiation in *t*-butanol equipped with a Corex filter sleeve cutting off the wave length shorter than 260 mμ afforded 17β-acetoxyestra-5(10)-en-6-one (XX) with evolution of

10) Irradiation of 2-pyrone was reported to proceed *via* a keto-ketene intermediate (O=C=CH–CH=CH–CHO) to yield *trans* 4-formyl-3-butenoate; W.H. Pirkle and L.H. Mckendry, *J. Am. Chem. Soc.*, **91**, 1179 (1969) and references therein.

11) M. Barnard and N.C. Yang, *Proc. Chem. Soc.*, **1958**, 302.

12) Irradiation of the 6β-acetoxy-β-lactone (XVII) in MeOH using Corex filter sleeve to cut off the wave length shorter than 260 mμ gave the starting material (XVII) unchanged. Formation of ester was demonstrated to occur through reaction of alcohol with a ketene. G. Quinkert, E. Blanke and F. Hamburg, *Chem. Ber.*, **97**, 1799 (1964).

carbon dioxide in about 60% yield. In this case a cleavage of the carbon–oxygen bond situated at β to the 6-carbonyl group has predominantly occurred by a selective activation of the 6-oxo function. The same decarboxylation reaction was also observed on pyrolysis[1] or alkaline[1] treatment of the β-lactone (XIX).

Experimental

Irradiations were conducted using Hanovia high pressure mercury arc (450W) inserted into a water-cooled, quarz immersion probe. The filter employed was Corex (9700) which was a glass sleeve insertable between the lamp and the probe. The solution was stirred by introduction of argon gas through a jet opening at the bottom of the apparatus and argon was continuously bubbled through the solution during irradiation.

Photolysis of 5,6β-Dihydroxy-17β-acetoxy-5β-androstan-19-oic Acid 5,19-Lactone (I)——A solution of the compound (I; 630 mg) in dry dioxane (130 ml) was irradiated for 2—3 hr. Evaporation of the solvent under reduced pressure gave a pale yellow syrupy residue which was chromatographed over silica gel. Elution with benzene afforded a crystalline substance which was recrystallized from i-Pr_2O to afford 2 mg of an unidentified material, mp 224—227°. IR ν_{max}^{KBr} cm^{-1}: 3410, 1748. NMR ($CDCl_3$) τ: 9.25, 5.78, 4.17.

Elution with 2% ether–benzene gave a crystalline material which was recrystallized from i-Pr_2O to give 223 mg of 5,6β-dihydroxy-17β-acetoxy-5α-androstan-19-oic acid 6,19-lactone (II: R=Ac) mp 234—235°, α_D −254° (dioxane). *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34, mol. wt., 362.5. Found: C, 69.31; H, 8.37, mol. wt. (osmometric), 436.8. IR ν_{max}^{KBr} cm^{-1}: 1725 (Ac), 1767 (γ-lactone), 3420 (OH). NMR (D-DMSO): 9.30 (3H, s, 18-CH_3), 8.01 (3H, s, OAc), 5.88 (1H, br, 6 α-H), 5.40 (1H, 17 α-H), 4.73 (OH).

5,6β,17β-Trihydroxy-5α-androstan-19-oic Acid 6,19-Lactone (II: R=H)——A solution of the compound (II: R=Ac, 42 mg) in 10% KOH–MeOH (3.5 ml) was heated at reflux for 8 hr and was allowed to stand at room temperature overnight. The reaction mixture was diluted with water and extracted with $CHCl_3$.

The combined extracts were washed with H_2O dried over anhyd. Na_2SO_4, and stripped off the solvent, yielding a crystalline residue which was recrystallized from acetone i-Pr_2O to afford compound (II: R=H, 24 mg), mp 267—268°. *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 70.93; H, 8.63. IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1750 (γ-lactone). NMR (D-DMSO) τ: 9.41 (3H, s, 18-CH_3), 6.76 (17α-H), 5.91 (1H, br, 6 α-H). Acetylation of the compound (II: R=H; 33 mg) with Ac_2O (0.3 ml) and pyridine (1 ml) at room temperature overnight regenerated 24 mg of the starting substance (II: R=Ac) by working up as usual.

6β-Hydroxy-17β-acetoxyandrost-4-en-19-oic Acid 6,19-Lactone (III)——Thionyl chloride (0.7 ml) was added to a solution of the compound (II: R=Ac, 160 mg) in pyridine (3 ml) at 0° (ice cooled) and the reaction mixture was allowed to stand at 50° for 4.5 hr. Chloroform was added to the reaction mixture and the organic layer separated was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a crystalline residue which was purified by alumina (neutral; G III) column chromatography. Elution with hexane gave light yellow atomic sulfur. Elution with benzene afforded a crystalline product which upon recrystallization from i-Pr_2O gave 85 mg of the 6,19-lactone (III), mp 172—173°. *Anal.* Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.38; H, 8.20. IR ν_{max}^{KBr} cm^{-1}: 1769 (γ-lactone), 1733 (Ac). NMR ($CDCl_3$) τ: 9.15 (3H, s, 18-CH_3), 7.93 (3H, s, OAc), 5.36 (1H, 17α-H), 5.02 (1H, d, J=4.5 cps, 6α-H), 4.38 (1H, t, J=3.5 cps 4-H).

4ξ,5ξ-Epithio-6β-hydroxy-17β-acetoxyandrostan-19-oic Acid 6,19-Lactone (IV)——To the compound (II: R=Ac, 290 mg), dissolved in pyridine (5 ml) and cooled in an ice bath, was added 1.5 ml of $SOCl_2$. The reaction mixture was heated on a water bath for 1.5 hr, and then diluted with $CHCl_3$. The organic layer was separated, washed with water and dried with anhyd. Na_2SO_4. Removal of the solvent *in vacuo* left a gummy residue which was chromatographed through a silica gel column with hexane to yield an atomic sulfur and with benzene to afford a crystalline product which was recrystallized from i-Pr_2O yielding 90 mg of the episulfide (IV), mp 191—193°. *Anal.* Calcd. for $C_{21}H_{28}O_4S$: C, 67.01; H, 7.43; S, 8.52. Found: C, 66.30; H, 7.53; S, 8.28. IR ν_{max}^{KBr} cm^{-1}: 1778 (γ-lactone), 1728 (Ac). NMR ($CDCl_3$) τ: 9.19 (3H, s, 18-CH_3), 7.97 (3H, s, OAc), 6.73 (1H, q, J=7.5, 3 cps, 4-H), 5.84 (1H, d, J=4 cps, 6 α-H), 5.32 (1H, 17 α-H). Mass Spectrum *m/e*: 376 (M^+). Further elution with benzene gave a crystalline substance which on recrystallization from i-Pr_2O afforded 39 mg of the olefin (III), mp 172—173°.

Desulfurization of 4ξ,5ξ-Epithio-6β-hydroxy-17β-acetoxyandrostan-19-oic Acid 6,19-Lactone (IV)——To a solution of the episulfide (IV, 74 mg) in purified $CHCl_3$ (6 ml), triphenylphosphine (55 mg) was added and the reaction mixture was then heated under reflux for 10 hr. Evaporation of the solvent *in vacuo* gave a brown colored residue which was chromatographed through silica gel column. Elution with hexane afforded triphenylphosphine sulfide mp 158°. Further elution with 1—2% ether–benzene gave a crystalline residue which was recrystallized from i-Pr_2O–hexane affording 29 mg of the olefin (III) described above, mp 172—173°.

6β,17β-Dihydroxyandrost-4-en-19-oic Acid (V)——A mixture of the compound (III; 360 mg) and 10% KOH–MeOH (5 ml) was heated at reflux for 1 hr. The reaction mixture was diluted with water and then acidified with 10% HCl solution and extracted with chloroform.

The extract was washed with water. The concentrate from the dry extract (anhyd. Na_2SO_4) gave a crystalline product which was recrystallized from AcOEt to afford 175 mg of the compound (V), mp 185—187°. *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.43; H, 8.82. IR ν_{max}^{KBr} cm^{-1}: 3340, 3150, 2600 (OH), 1705 (COOH). NMR (D-DMSO) τ: 9.36 (3H, s, 18-CH_3), 4.12 (1H, br, 4-H).

17β-Hydroxyandrosta-3,5-dien-19-oic Acid (VI)——A mixture of the compound (V, 55 mg) in dioxane (3 ml) and 10% HCl (3 ml) was heated on a water bath for 10 min. The reaction mixture after dilution with water was extracted with $CHCl_3$. The extract was washed with water and dried over anhyd. Na_2SO_4. Upon removal of the chloroform a gummy product was obtained. This product was crystallized from AcOEt to give 6 mg of the compound (VI), mp 198—200°. *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 74.70; H, 8.72. IR ν_{max}^{KBr} cm^{-1}: 1687 (COOH). UV λ_{max}^{EtOH} mμ (ε): 229 (17500), 235 (17500), 244.5 (shoulder). NMR (D-pyridine) τ: 9.02 (3H, s, 18-CH_3), 4.26 (2H, br, olefin), 3.70 (1H, br, olefin).

Dehydration of 5,6β-Dihydroxy-17β-acetoxy-5β-androstan-19-oic Acid 6,19-Lactone (VII)——Thionyl chloride (0.5 ml) was added to a solution of the compound (VII; 228 mg) in pyridine (2 ml) at 0° (cooled in ice–water) and the reaction mixture was maintained at 0° for 40 min. Excess $SOCl_2$ was decomposed with ice–water and the reaction mixture was then extracted with CH_2Cl_2. The combined extracts were washed with water and dried with anhyd. Na_2SO_4. Condensation of the extract *in vacuo* followed by recrystallization from *i*-Pr_2O yielded 103 mg of the compound (III), mp 172—173°.

5,6β,17β,19-Tetrahydroxy-5α-androstane (IX)——To a solution of the compound (II: R=H; 188 mg) in anhyd. tetrahydrofuran (20 ml), $LiAlH_4$ (200 mg) was added and after 30 hrs' heating at reflux excess hydride was quenched with aqueous tetrahydrofuran. The reaction mixture was filtered to remove undissolved material (LiOH) and washed several times with tetrahydrofuran.

The filtrate and washing were evaporated to dryness to yield a gummy residue which was chromatographed over a column of silica gel with 4% MeOH–CH_2Cl_2 as eluent. A total of 127 mg of a crystalline solid eluted after recrystallization from AcOEt–*i*-Pr_2O, gave 77 mg of the compound (IX) melting at 214—215°. *Anal.* Calcd. for $C_{19}H_{32}O_4$: C, 70.33; H, 9.94. Found: C, 70.28; H, 9.77. IR ν_{max}^{KBr} cm^{-1}: 3300 (OH). NMR (D-DMSO): 9.34 (3H, s, 18-CH_3).

5,6β,17β,19-Tetrahydroxy-5β-androstane (VIII)——To a stirred solution of the compound (VII, 240 mg) in anhyd. tetrahydrofuran was added $LiAlH_4$ (150 mg) and stirring was continued for 4.5 hr at room temperature. The reaction mixture was treated with aq. tetrahydrofuran to decompose the excess reagent and filtered to remove undissolved inoganic material (LiOH). The filtrate was diluted with CH_2Cl_2 and CH_2Cl_2 layer was successively washed with dil AcOH, then water and dried over anhyd. Na_2SO_4. The methylene chloride was removed on a rotary evaporator to afford a crystalline substance which was recrystallized from acetone to give 123 mg of the compound (VIII), mp 178—180°. *Anal.* Calcd. for $C_{19}H_{32}O_4$: C, 70.33; H, 9.94. Found: C, 69.82; H, 9.85. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH).

3β-Bromo-17β-hydroxyandrost-5-en-19-oic Acid (XII)——To a stirred solution of the compound (X, 5.0 g) in EtOH (140 ml) and water (60 ml), $NaBH_4$ (3 g) was added and the resulting reaction mixture was stirred for 3 hr at room temperature. The excess reagent was decomposed with AcOH under cooling and the reaction mixture was acidified with AcOH, diluted with water and extracted with $CHCl_3$. The extract was washed with water and dried with anhyd. Na_2SO_4. The solvent was condensed to dryness under reduced pressure to give a gummy monool (XI) which, without further purification, was treated with 10% aq. HBr (80 ml) in acetone (200 ml). The reaction mixture was heated to refiux for 5 hr. After removal of excess acetone the reaction mixture was stored in refrigerator affording a crystalline precipitate which was collected by filtration to give 4.320 g of the compound (XII). This was recrystallized from acetone to give an analytical sample, mp 250—251°. *Anal.* Calcd. for $C_{19}H_{27}O_3Br$: C, 59.53; H, 7.05; Br, 20.99. Found: C, 59.35; H, 7.12; Br, 20.79. IR ν_{max}^{KBr} cm^{-1}: 3540 (OH), 1700 (COOH). NMR (D-DMSO) τ: 9.40 (3H, s, 18-CH_3), 4.33 (1H, br, olefin). Mass Spectrum *m/e*: 382 (M^+, Br^{79}), 384 (M^+, Br^{81}).

3β-Bromo-5,6α-epoxy-17β-hydroxy-5α-androstan-19-oic Acid (XIII)——A mixture of the compound (XII, 1 g) in tetrahydrofuran (40 ml) and monoperphthalic acid (1.5 g) in ether (50 ml) was allowed to stand at room temperature overnight and then heated at reflux for 4 hr. After cooling the reaction mixture was treated with aq. KI and extracted with $CHCl_3$. The extract was washed with aq. $Na_2S_2O_3$ solution, then water and dried over anhyd. Na_2SO_4. The chloroform was concentrated *in vacuo*. The residual product was recrystallized from *i*-Pr_2O to yield 612 mg of the compound (XIII), mp 168—170°. *Anal.* Calcd. for $C_{19}H_{27}O_4Br$: C, 57.11: H, 6.76. Found: C, 56.78; H, 6.65. IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1698 (COOH). NMR (D-DMSO) τ: 9.45 (3H, s, 18-CH_3), 6.88 (1H, d, J=3.5 cps, 6β-H). Mass Spectrum *m/e*: 398 (M^+, Br^{79}), 400 (M^+, Br^{81}).

3β-Bromo-5,6β,17β-trihydroxy-5α-androstane-19-oic Acid 6,19-Lactone (XIV)——A mixture of the compound (XIII, 309 mg) in dioxane (10 ml) and dil. H_2SO_4 (10 ml) was warmed on a water bath for 2 hr and then cooled to room temperature. The reaction mixture was diluted with water and extracted with $CHCl_3$. The combined extracts were washed with 10% $NaHCO_3$, then water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a gummy substance which gave 178 mg of the compound (XIV) crystallized from chloroform, mp 249—250°. *Anal.* Calcd. for $C_{19}H_{27}O_4Br$: C, 57.14; H, 6.77. Found: C, 57.12; H, 6.80. IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1768 (γ-lactone). NMR (D-DMSO) τ: 9.42 (3H, s, 18-CH_3), 5.75 (6α-H).

Debromination of 3β-Bromo-5,6β,17β-trihydroxy-5α-androstan-19-oic Acid 6,19-Lactone (XIV)——The compound (XIV, 108 mg) in EtOH (20 ml) containing KOH (90 mg) in small amount of water was catalytically debrominated in the presence of Pd-C catalyst (prepared from 50 mg of 5% Pd-C and 250 mg of $PdCl_2$ in 25 ml of 5% HCl). After hydrogen up take had ceased, Pd/C catalyst was removed by filtration and the filtrate and washings were diluted with water and then extracted with $CHCl_3$.

The extract was washed with sat. salt solution and dried with anhyd. Na_2SO_4. After evaporation of the solvent there remained a crystalline solid which was recrystallized from acetone–*i*-Pr_2O affording 54 mg of the compound (II: R=H), mp 267—268°.

5-Hydroxy-6β,17β-diacetoxy-5β-androstan-19-oic Acid 5,19-Lactone (XVII)——A mixture of the compound (I, 280 mg) in Ac_2O (1 ml) and pyridine (3 ml) was allowed to stand at room temperature for 6.5 hr. The reaction mixture was evaporated *in vacuo* to give a gummy residue which was dissolved in $CHCl_3$.

The $CHCl_3$ solution was washed with water and dried over anhyd. $NaSO_4$.

Removal of chloroform gave a acetylated product which was subjected to recrystallization from ether to yield 84 mg of the compound (XVII), mp 127—127.5°. *Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.35; H, 8.03. IR ν_{max}^{KBr} cm^{-1}: 1830 (β-lactone), 1751, 1741 (Ac).

Photolysis of 5-Hydroxy-6β,17β-diacetoxy-5β-androstan-19-oic Acid 5,19-Lactone (XVII)——A solution of the compound (XVII; 1.460 g) in abs. MeOH (170 ml) was irradiated for 4.5 hr. The solvent was removed under reduced pressure yielding a syrupy residue which was chromatographed over silica gel. Elution with 4% ether–benzene gave 390 mg of methyl 5-hydroxy-6β,17β-diacetoxy-5α-androstan-19-oate (XVIII) as an oily substance. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3470 (OH), 1730 (C=O). NMR ($CDCl_3$) τ: 9.12 (3H, s, 18-CH_3), 8.01 (3H, s, OAc), 7.98 (3H, s, OAc), 6.29 (3H, s, $COOCH_3$), 5.38 (1H, 17α-H), 5.28 (1H, 6α-H).

Alkaline Treatment of Methyl 5-Hydroxy-6β,17β-diacetoxy-5α-androstan-19-oate (XVIII)——A mixture of the compound (XVIII; 128 mg) and 10% KOH–MeOH (7 ml) was heated under reflux for 3 hr. The reaction mixture was diluted with water and thoroughly extracted with $CHCl_3$. The extract was washed with water and dried with anhyd. Na_2SO_4. Evaporation of chloroform under vacuum left a crystalline product which was recrystallized from AcOEt–*i*-Pr_2O to yield 31 mg of the compound (II: R=H), mp 267—268°.

Photolysis of 5-Hydroxy-6-oxo-17β-acetoxy-5β-androstan-19-oic Acid 5,19-Lactone (XIX)——A suspension of the compound (XIX: 300 mg) in dry *t*-BuOH (180 ml) was irradiated using corex filter sleeve for 2.5 hr.

Evaporation of the solvent gave a gummy residue which was chromatographed through silica gel column. Elution with benzene ~3% ether–benzene gave 278 mg of a crystalline substance which afforded 17β-acetoxyestra-5(10)-en-6-one (XX)[1] recrystallized from *i*-Pr_2O melted at 128—129°.

Acknowledgement The authors are grateful to Dr. G. Sunagawa, Director of this Laboratories for his continuing encouragement. Thanks are also due to the members of Section of Physical chemistry in this Laboratories for measurements of physical and elemental analytical data.