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Steroid Series. XXII.[1] Photolysis of 3α,5-Cyclo-6β-methoxy-17β-acetoxy-5α-androstan-19-one[2]

Koichi Kojima, Ryozo Hayashi and Katsumi Tanabe

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

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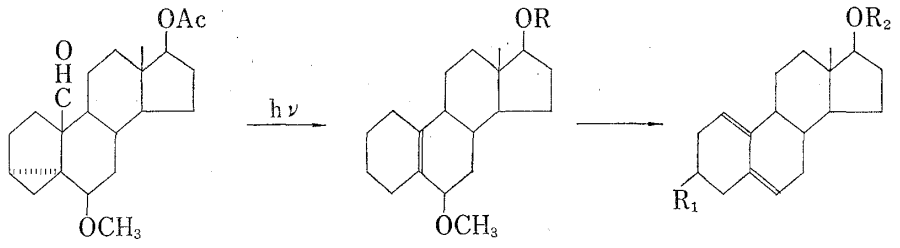
Irradiation of the title compound (I) at room temperature using a high pressure mercury lamp (450W) was found to yield 6β-methoxy-17β-acetoxyestra-5(10)-ene (II: R=Ac) in 35% yield as an oily product. Along with a synthesis of this photoproduct (II:R=Ac) is also described that of its epimeric 6α-methoxy compound (IX: $R_1=CH_3$, $R_2=Ac$).

Photochemical studies of 19-oxosteroid derivatives[4] have been shown to involve mainly decarbonylation reactions, which are facilitated by the presence of a double bond at the β,γ-position to the 19-oxo function. In connection with our synthetic studies[5] of 19-norsteroid derivatives employing a 3α,5α-cyclo-6β,19-oxidosteroid as a key intermediate, photodecarbonylation of 3α,5-cyclo-6β-methoxy-17β-acetoxy-5α-androstan-19-one (I) was undertaken. This intermediate contains a cyclopropane ring instead of a β,γ-double bond. Photolysis of β,γ-cyclopropyl ketones,[6,13a] though limited in number, has been reported to involve a cleavage of the carbon–carbon bond located α to the carbonyl group and β to the cyclopropane moiety with subsequent decarbonylation and isomerization yielding olefinic substances.

A solution of the aldehyde (I) in dry dioxane was irradiated with a quarz immersion apparatus using Hanovia Type A mercury arc (450W) and Corex filter sleeve to yield 6β-methoxy-17β-acetoxyestra-5(10)-ene (II:R=Ac) as an oily substance after chromatography over silica gel in 35% yield. The product (II:R=Ac), after saponification of the 17-acetoxyl function, was characterized as a crystalline phenyl urethane derivative (II:R=CONHPh), mp 188—189°. The nuclear magnetic resonance spectrum of this compound (II:R=Ac) exhibited two singlets at τ 7.98 and τ 6.66 with a shoulder at τ 6.67 due to acetoxyl, 6β-methoxyl, and 6α-proton, respectively. No vinyl proton was observed.

The photoproduct (II:R=Ac) showed end absorption in the ultraviolet spectrum and a light yellow coloration with nitromethane test indicating the presence of a tetrasubstituted olefinic linkage. Mild treatment of this substance (II:R=Ac), after hydrolysis of the acetoxyl function, with perchloric acid in methanol afforded in good yield 17β-hydroxy-estra-1(10),5-diene (III:$R_1=R_2=H$), which had an ultraviolet absorption maximum at 240 mμ (ε=22500), similar to that of an analogous exocyclic diene (III:$R_1=OH, R_2=H$): 242 mμ (ε=26200),[7] and exhibited a broad signal due to two olefinic protons centered at τ 4.50 in the nuclear magnetic resonance spectrum. These spectral and chemical data strongly suggested that

1) Part XXI: Y. Morisawa and K. Tanabe, *Chem. Pharm. Bull.* (Tokyo), **17**, 1212 (1969).
2) This work was presented at the Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April 1968.
3) Location: *1-2-58, Hiromachi, Shinagawa-ku, Tokyo.*
4) J. Hills, J. Iriarte, K. Schaffner and O. Jeger, *Helv. Chim. Acta.*, **49**, 292 (1966); K. Schaffner, *Chimia*, **19**, 575 (1965); D.E. Poel, H. Wehrli, K. Schaffner and O. Jegar, *Chimia*, **20**, 110 (1966).
5) K. Tanabe, R. Takasaki, R. Hayashi, Y. Morisawa and T. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), **15**, 27 (1967).
6) L. D. Hess, J. L. Jackson, K. Schaffner and J. N. Pitts, Jr., *J. Am. Chem. Soc.*, **89**, 3684 (1967).
7) R. Ginsig and A. D. Cross, *J. Org. Chem.*, **31**, 1761 (1966).



I II III

Chart 1

the photoproduct (II:R=Ac) contains an allylic methoxyl system as formulated in II (R=Ac). This structure was synthetically established as described below.

3α,5-Cyclo-17β-acetoxy-5α-androstan-6-on-19-oic acid (V), obtained directly by Jones oxidation[8] of 3α,5-cyclo-17β-acetoxy-5α-androstan-6β,19-oxide (IV), was hydrogenated with palladium on charcoal catalyst in the presence of a small amount of 70% perchloric acid yielding 17β-acetoxy-5α-androstan-6-on-19-oic acid (VI:R_1=H, R_2=Ac). This acid was also obtained by treatment of compound (V) with 47% hydrobromic acid in acetone and subsequent treatment of the resultant 3β-bromo-17β-hydroxy-5α-androstan-6-on-19-oic acid (VI:R_1=Br, R_2=H) with powdered zinc in acetic acid. A solution of this acid (VI:R_1=H, R_2=Ac) in acetic acid and ether mixture (2:1) was treated with molecular bromine at room temperature to give unexpectedly in high yield 5-hydroxy-17β-acetoxy-5β-androstan-6-on-19-oic acid, 5,19-lactone (VII), which was identified by the characteristic infrared absorption band at 1836 cm^{-1} of a β-lactone moiety. This reaction might proceed *via* an intermedial 5-bromo-17β-acetoxy-5α-androstan-6-on-19-oic acid,[9] which is considered unstable due to 1—3 diaxial interactions between 5α bromine and C_1,C_3,C_7 and C_9 hydrogens. An intramolecular displacement of the 5α-bromine with 10β-carboxyl function leads to the β-lactone (VII).

The stability of the β-lactone function[10] in VII towards such nucleophiles as Br^- and AcO^- is possibly due to stereo-chemical features, which prevent a nucleophile from attacking at C_5 position from the α side of the molecule. Pyrolysis of the β-lactone (VII) with a loss of carbon dioxide furnished an α,β-unsaturated ketone (VIII:R=Ac), which showed a characteristic ultraviolet absorption maximum at 249 mμ (ε=11200) and infrared absorption bands at 1666 and 1624 cm^{-1}. The same α,β-unsaturated ketone (VIII:R=Ac) was obtained by alkaline treatment of the β-lactone (VII), followed by reacetylation of the 17-hydroxyl function with acetic anhydride–pyridine mixture. Reduction of the α,β-unsaturated ketone (VIII:R=Ac) with sodium borohydride afforded almost exclusively 6α-hydroxy-17β-acetoxyestra-5(10)-ene (IX:R_1=H, R_2=Ac)[11]. The 6β-hydroxy epimer could be observed only on thin-layer chromatogram of the reaction mixture. The stereospecificity of this reaction is analogous to that of lithium aluminium hydride reduction of 3β,17β-dihydroxyestra-5(10)-en-6-one.[7] The allylic alcohol (IX:R_1=H, R_2=Ac) with an excess of methyl iodide and silver oxide was in turn converted to the corresponding methyl ether (IX:R_1=CH_3, R_2=Ac), which differed from the photoproduct (II:R=Ac) in both the infrared absorption spectrum

8) K. Bowden, I. M. Heilbron, E. H. R. Jones and B. C. C. Weedon, *J. Chem. Soc.* **1946**, 39.
9) Bromination of the 6-oxo-5α-steroid was reported to give 5α-bromo-6-oxosteroid. I. M. Heilbron, H. Jackson, E. H. R. Jones and F. S. Spring, *J. Chem. Soc.* **1937** 801.
10) G. Machell, *The Industrial Chemist*, January, 13, (1960).
11) This assignment can also be supported by comparing $[M]_D$ value of the epimeric compound XII (R_1=R_2=H) and IX (R_1=R_2=H). $[M]_D$ of XII (R_1=R_2=H)= +422° $[M]_D$ of IX (R_1=R_2=H)= +301°. This result is compatible with the Mills Rule: L. F. Fieser and M. Fieser, "Steroid," Reinhold Pub. Corp., New York,1959, p. 331.

and thin-layer chromatogram. The same exocyclic diene (III:R_1=R_2=H) described for the photoproduct (II:R=Ac) was obtained by treatment of the compound (IX:R_1=CH_3, R_2=Ac), after saponification of 17β-acetoxy function, with 70% perchloric acid in methanol. These data show that the photoproduct (II: R=Ac) and the synthetic allylic ether (IX: R_1=CH_3, R_2=Ac) are epimeric at the C_6 position. The exact stereochemical assignment at C_6 position was verified in full by synthesizing the 6β-methoxyl epimer.

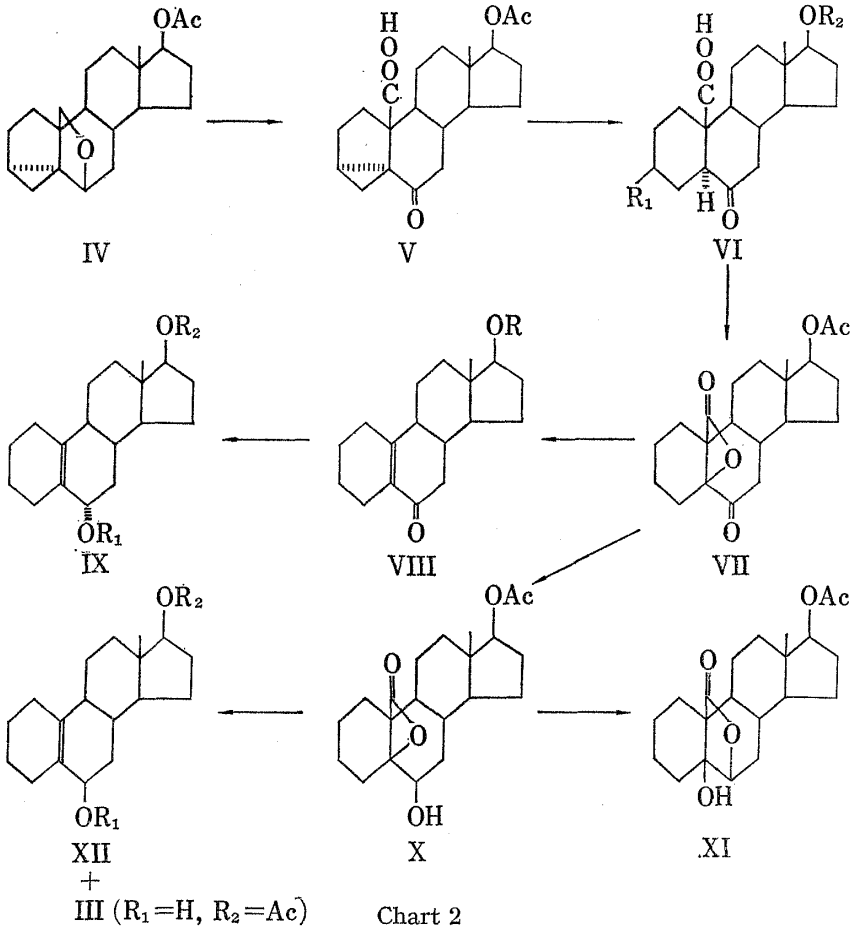


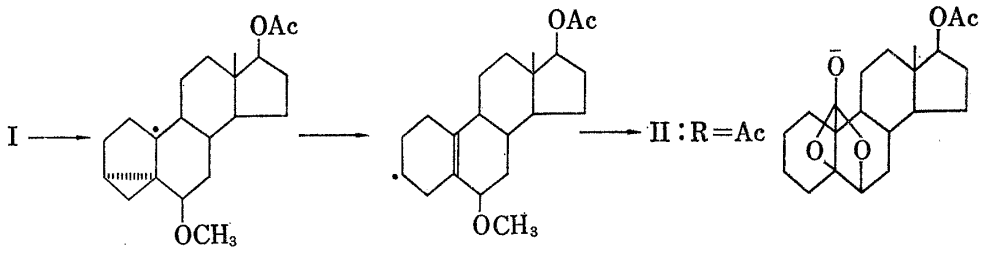
Chart 2

Reduction of the keto-lactone (VII) with sodium borohydride at 0° yielded the corresponding 5,6β-dihydroxy-17β-acetoxy-5β-androstan-19-oic acid 5,19-lactone (X). That the β-lactone moiety of the compound (VII) was remained intact in this reduction was shown by its characteristic infrared absorption band at 1815 cm^{-1} in the reduction product (X). The 6β-configuration of X was confirmed by its isomerisation with sodium carbonate in aqueous ethanol into 5,6β-dihydroxy-17β-acetoxy-5β-androstan-19-oic acid 6,19-lactone (XI),[12] which had an infrared absorption band at 1776 cm^{-1} due to a γ-lactone ring. The formation of the γ-lactone (XI) by an alkaline treatment of the reduction product (X) can be explained as proceeding through an intermedial hemiacylal (XIII) into the more stable 5β-hydroxy-6,19-lactone (XI). Pyrolysis of X yielded smoothly 6β-hydroxy-17β-acetoxyestra-5(10)-ene (XII) with an evolution of carbon dioxide, along with a small amount of an exocyclic diene (III:R_1=H, R_2=Ac).

The allylic 6β-alcohol was converted with silver oxide in methyl iodide into the corresponding methyl ether, which proved to be identical with the photoproduct (II:R=Ac) in both the infrared absorption spectrum and thin-layer chromatogram. Its crystalline phenyl

12) The 5β-configuration was further established in the following paper: K. Kojima, R. Hayashi and K. Tanabe, *Chem. Pharm. Bull.* (Tokyo), in press.

urethane derivatives was further identified with that of the photoproduct (II:R=Ac) in all respects.



XIV XV XIII

Chart 3

The formation of the photoproduct (II: R=Ac) can be rationalised by the intermediation of the radical (XIV) *via* decarbonylation of the 19-formyl function, which could rapidly rearrange into a more stable homoallylic radical (XV).[13] This radical (XV) must give rise to the photoproduct (II: R=Ac) by abstracting a hydrogen from the solvent or steroid molecule.

Experimental[14]

Photolysis of 3α,5-Cyclo-6β-methoxy-17β-acetoxy-5α-androstan-19-one (I)——A solution of the methoxy aldehyde (I: 1.5 g) in dry dioxane (120 ml) was irradiated[15] using Corex filter sleeve. After 5 hours' irradiation, the solvent was evaporated *in vacuo* to give a syrupy residue which was chromatographed over silica gel. Elution with hexane–benzene (2:1) yielded 372 mg of 6β-methoxy-17β-acetoxyestra-5(10)-ene (II: R=Ac) as an oily substance, which failed to crystallize in all attempts. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1722 (OAc). NMR τ: 9.19 (18-CH_3), 7.98 (OAc), 6.66 (OCH_3), 6.67 (6α-H), 5.32 (17α-H). A mixture of the compound (II: R=Ac; 120 mg) and 10% KOH–MeOH (5 ml) was heated under reflux for 1 hr. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave 102 mg of 6β-methoxy-17β-hydroxyestra-5(10)-ene (II: R=H) as an oily substance, which was reconverted to the acetate (II: R=Ac) by acetylation with Ac_2O–pyridine mixture. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: no C=O. NMR τ: 9.22 (18–CH_3), 6.34 (OCH_3), 6.26 (6α-H).

6β-Methoxy-17β-hydroxyestra-5(10)-ene 17-Phenylurethane (II:R=CONHPh)——A mixture of the compound (II:R=H; 110 mg) and phenylisocyanate (20 drops) was heated on a water bath for 8 hr. This reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with aq. $NaHCO_3$, then water and dried over anhyd. Na_2SO_4. After evaporation of the solvent the residue obtained was dissolved in $CHCl_3$–CCl_4 mixture. Insoluble material was removed by filtration and the filtrate was evaporated to dryness to give a crude gummy residue which was chromatographed over silical gel. Elution with benzene gave a crystalline residue which was recrystallized from iso-Pr_2O to give 52 mg of the compound (II:R=CONHPh) of mp 188—189°. *Anal.* Calcd. $C_{25}H_{35}O_3N$: C, 75.53; H, 8.87. Found: C, 75.74; H, 8.66. IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O), 1609 (C=C). NMR τ: 9.17 (18–CH_3), 6.63 (OCH_3), 5.28 (17α–H), 2.6 (aromatic protons).

17β-Hydroxyestra-1(10), 5(6)-diene (III:R_1=R_2=H)——A solution of the compound (II:R=H; 203 mg) in MeOH (5 ml) containing a few drops of 70% $HClO_4$ was set aside at room temperature for 2 hr. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with water, dried over anhyd. Na_2SO_4 and condensed to dryness to give 150 mg of a gummy residue which was recrystallized from ether, yielding the compound (III: R_1=R_2=H) of mp 90—91°. *Anal.* Calcd. for $C_{18}H_{26}O \cdot 1/3$ ether: C, 81.95; H, 10.35. Found: C, 81.71; H, 10.32. IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 1632 (C=C). NMR τ: 9.24 (18-CH_3), 6.33 (17α-H), 4.50 (olefinic protons). UV λ_{max}^{EtOH} mμ (ε): 240 (22500). $[\alpha]_D$ dioxane: −123°.

13) *a*) R. H. Eastman, J. E. Starr, R. S. Martin and M. K. Sakata, *J. Org. Chem.*, **28**, 2161 (1963); J. E. Starr and R. H. Eastman, *J. Org. Chem.*, **31**, 1393 (1966); *b*) C. K. Montgomery and J. W. Matt, *J. Am. Chem. Soc.*, **89**, 934 (1967); S. J. Cristol and R. Barbour, *J. Am. Chem. Soc.*, **90**, 2832 (1968).

14) All meltings were uncorrected. The NMR spectra were recorded on Varian A-60 in deuteriochloroform containing tetramethylsilane as an internal standard. The IR spectra were taken with Hitachi Model EPI S-2.

15) Irradiation was conducted using Hanovia high pressure mercury lamp (450 W) and a quarz water cooled immersion wells and mixing of the solution was attained by introduction of a stream of argon gas through a jet opening at the bottom of the apparatus.

17β-Acetoxyandrostan-6-on-19-oic Acid (VI: R_1=H, R_2=Ac)——i) A solution of 3α,5-cyclo-17β-acetoxy-5α-androstan-6-on-19-oic acid (V: 1.2 g) in AcOH (80 ml) containing a small amount of 70% $HClO_4$ was hydrogenated in the presence of Pd–C catalyst for 4 hr. The catalyst was filtered off and the filtrate was condensed to a small volume, diluted with water and extracted with benzene. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a crystalline residue which was recrystallized from acetone–iso-Pr_2O to afford 823 mg of the compound (VI: R_1=H, R_2=Ac). mp 237—238°. *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.94, H, 8.32. IR ν_{max}^{KBr} cm^{-1}: 1735 (C=O), 1700 (COOH). NMR τ: 9.26 (18-CH_3), 7.95 (OAc), 5.33 (17α-H), 2.05 (COOH). $[\alpha]_D$ −37.2° (dioxane). ii) A mixture of the compound (V; 300 mg) in acetone (20 ml), 30% HBr (5 ml) and water (3 ml) was heated under reflux for 5 hr. The reaction mixture was concentrated *in vacuo*, diluted with water and extracted with $CHCl_3$. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave 167 mg of a crystalline residue (VI: R_1=Br, R_2=H) which was recrystallized from AcOEt. mp 240—241°. *Anal.* Calcd. for $C_{19}H_{27}O_4Br$: C, 57.15; H, 6.76. Found: C, 56.95; H, 6.78. IR ν_{max}^{KBr} cm^{-1}: 1713 (COOH).

To a solution of the compound (VI: R_1=Br, R_2=H; 163 mg) in AcOH (10 ml), zinc powder (2 g) was added and the reaction mixture was heated under reflux for 5 hr. Inorganic material was filtered off and the filtrate was concentrated *in vacuo* to a small volume, diluted with water and extracted with $CHCl_3$. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a syrupy residue which was chromatographed over silica gel. Elution with MeOH–$CHCl_3$ (1:99) afforded 75 mg of the compound (VI: R_1=H, R_2=Ac) which was recrystallized from AcOEt–*iso*-Pr_2O. mp 236—238°.

5-Hydroxy-17β-acetoxy-5β-androstan-6-on-19-oic Acid 5,19-Lactone (VII)——To a solution of the compound (VI: R_1=H, R_2=Ac; 432 mg) in AcOH–ether (2:1; 33 ml) was added Br_2 (231 mg) and 30% HBr–AcOH (3 drops) at 0° and the mixture was allowed to stand at room temperature until the yellow–brown color of bromine disappeared. Sodium bicarbonate (250 mg) in small amount of water was added to the reaction mixture which was evaporated to dryness to give a crystalline residue. Recrystallization from MeOH–water afforded 273 mg of the compound (VII). mp 170—172°. *Anal.* Calcd. for $C_{21}H_{28}O_5$: C, 69.97; H, 7.83. Found: C, 69.95; H, 7.67. IR ν_{max}^{KBr} cm^{-1}: 1836 (β-lactone), 1737 (OAc). NMR τ: 9.15 (18-CH_3), 7.93 (OAc). $[\alpha]_D$ −51.6° (dioxane). The compound (VII) was also formed without adding sodium bicarbonate.

17β-Acetoxyestra-5(10)-en-6-one (VIII: R=Ac)——i) Pyrolysis of the compound (VII: 58 mg) at 160—190° under reduced pressure gave a crystalline residue, which was recrystallized from *iso*-Pr_2O to afford 14 mg of the compound (VIII: R=Ac). mp 129—130°. *Anal.* Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.86; H, 8.81. IR ν_{max}^{KBr} cm^{-1}: 1749 (OAc), 1666 (C=O), 1624 (C=C). NMR τ: 9.17 (18-CH_3), 7.96 (OAc), 5.28 (17α-H). UV λ_{max}^{EtOH} mμ (ε): 249 (11200). $[\alpha]_D$ dioxane: +73.6°.

ii) A solution of the compound (VII: 73 mg) in 10% KOH–MeOH (5 ml) was heated at reflux for 2 hr. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a crystalline residue which was recrystallized from iso-Pr_2O to afford 23 mg of the compound (VIII: R=H). mp 156—157°. *Anal.* Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.67; H, 9.45. IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1645 (C=O), 1609 (C=C). UV λ_{max}^{EtOH} mμ (ε): 249 (11200). Acetylation of the compound (VIII: R=H) with Ac_2O–pyridine gave the compound (VIII: R=Ac).

6α,17β-Dihydroxyestra-5(10)-ene (IX: R_1=R_2=H)——A solution of the compound (VIII: R=H, 1.510 g) in EtOH–H_2O (5:2; 300 ml) and $NaBH_4$ (600 mg) was stirred at room temperature for 3 hr. The reacion mixture was diluted with water and extracted with chloroform. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a crystalline residue which was recrystallized from benzene to give 1.114 g of the compound (IX: R_1=R_2=H). mp 175—177°. *Anal.* Calcd. for $C_{18}H_{28}O_2$·1/2 benzene: C, 79.79; H, 10.19. Found: C, 79.68; H, 9.82. IR ν_{max}^{KBr}: 3340 cm^{-1}. NMR τ; 9.22 (18-CH_3), 6.30 (17α-H), 5.82 (6β-H). $[M]_D$ =+301° (corrected for benzene).

6α-Hydroxy-17β-acetoxyestra-5(10)-ene (IX: R_1=H, R_2=Ac)——To a stirred solution of the compound (VIII: R=Ac; 271 mg) in iso-PrOH (15 ml) and water (7 ml), $NaBH_4$ (100 mg) was added. After 3.5 hours' stirring at room temperature excess $NaBH_4$ was decomposed with AcOH and the reaction mixture was diluted with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a syrupy residue which was chromatographed over silica gel. Elution with 4% ether–benzene gave 203 mg of the compound (IX: R_1=H, R_2=Ac) as an oily substance. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3680 (OH), 1741 (OAc). NMR τ: 9.20 (18-CH_3), 7.96 (OAc), 5.82 (6β-H), 5.32 (17α-H).

6α-Methoxy-17β-acetoxyestra-5(10)-ene (IX: R_1=CH_3, R_2=Ac)——A solution of the compound (IX: R=H; 410 mg) in CH_3I (7 ml) was stirred with Ag_2O (3 g) at room temperature for 80 hr. Undissolved material was removed by filtration and the filtrate obtained was evaporated *in vacuo* to give a syrupy residue which was chromatographed over silica gel. Elution with hexane–benzene (1:1) afforded 241 mg of the compound (IX: R_1=CH_3, R_2=Ac) as an oily substance. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728 (OAc), 1088 (C–O–C). NMR τ: 9.19 (18-CH_3), 7.97 (OAc), 6.68 (OCH_3), 6.22 (6β-H), 5.32 (17α-H).

Acid Treatment of the Compound (IX: R_1=CH_3, R_2=Ac)——The compound (IX: R_1=CH_3, R_2=Ac; 269 mg) was hydrolysed with 10% KOH–MeOH as usual to give 6α-methoxy-17β-hydroxyestra-5(10)-ene.

IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1089 (C–O–C). This compound (105 mg) in MeOH (3 ml) containing 70% $HClO_4$ (3 drops) was maintained at room temperature for 50 min. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a gummy residue, which was chromatographed over silica gel. Elution with 3% ether–benzene gave a crystalline residue which was recrystallized from ether to afford 12 mg of the compound (III: $R_1=R_2=H$), mp 90—91°.

5,6β-Dihydroxy-17β-acetoxy-5β-androstan-19-oic Acid 5,19-Lactone (X)——A mixture of the compound (VII: 800 mg) in tetrahydrofuran (40 ml) and $NaBH_4$ (300 mg) in water (6 ml) was stirred at −10°—0° for 30 min. The reaction mixture was diluted with excess water. A resulting crystalline precipitate was collected by filtration and recrystallized from AcOEt–iso-Pr_2O to afford 474 mg of the compound (X). mp 139—141°. *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.53; H, 8.40. IR ν_{max}^{KBr} cm^{-1}: 3460 (OH), 1815 (β-lactone), 1741 (OAc). NMR τ: 9.20 (18-CH_3), 7.94 (OAc), 6.25 (6α-H), 5.25 (17α-H).

5,6β-Dihydroxy-17β-acetoxy-5β-androstan-19-oic Acid 6,19-Lactone (XI)——To a stirred solution of the compound (X; 100 mg) in EtOH (5 ml) and water (3 ml), Na_2CO_3 (200 mg) was added. After 2 hours' stirring the reaction mixture was neutralized with AcOH and extracted with CH_2Cl_2. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a gummy residue which was recrystallized from AcOEt–iso-Pr_2O to afford 22 mg of the compound (XI), mp 228—229°. *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.48; H, 8.44. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1776 (γ-lactone), 1740 (OAc). NMR τ: 9.22 (18-CH_3), 7.96 (OAc), 5.42 (6α-H), 5.34 (17α-H).

6β-Hydroxy-17β-acetoxyestra-5(10)-ene (XII: R_1=H, R_2=Ac) and 17β-Acetoxyestra-1(10), 5(6)-diene (III: R_1=H, R_2=Ac)——Pyrolysis of the compound (X: 213 mg) *in vacuo* at 140° gave rise to a residue which was chromatographed over silica gel. Elution with benzene gave a crystalline residue which was recrystallized from ether to afford 5 mg of the compound (III: $R_1=H$, $R_2=Ac$), mp 72—74°. *Anal.* Calcd. for $C_{20}H_{28}O_2 \cdot 1/3$ ether: C, 78.76; H, 9.75. Found: C, 78.84; H, 9.45. IR ν_{max}^{KBr} cm^{-1}: 1732 (OAc). $[\alpha]_D$ −145° (dioxane). Elution with 3.6% ether–benzene afforded a crystalline residue which was recrystallized from AcOEt–iso-Pr_2O to afford 67 mg of the compound (XII: $R_1=H$, $R_2=Ac$), mp 135—137° *Anal.* Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.24, H, 9.45. IR ν_{max}^{KBr} cm^{-1}: 3510 (OH), 1721 (OAc). NMR ($CDCl_3$) τ: 9.17 (18-CH_3), 7.96 (OAc), 6.13 (6α-H), 5.35 (17α-H). $[\alpha]_D$ +113° (dioxane).

6β- 17β-Dihydroxyestra-5(10)-ene (XII: $R_1=R_2=H$)——A solution of the compound (XII: $R_1=H$, $R_2=Ac$; 110 mg) in 5% KOH–MeOH solution (10 ml) was heated under reflux for 30 min. The reaction mixture was diluted with water and extracted with chloroform. The extract was washed with water and dried over anhyd. Na_2SO_4. Evaporation of the solvent gave a crystalline residue which was recrystallized from chloroform and AcOEt mixture to afford 52 mg of the compound XII ($R_1=R_2=H$), mp 198—200°. *Anal.* Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.16; H, 10.37. IR ν_{max}^{KBr}: 3350, 3300 (OH), 1660 (C=C) NMR τ: 9.21 (18-CH_3) 6.28 (17α-H), 6.13 (6α-H). $[M]_D=+422°$.

Methylation of the Compound (XII: R_1=H, R_2=Ac)——A mixture of the compound (XX: $R_1=H$, $R_2=Ac$; 552 mg) in CH_3I (5 ml) and Ag_2O (5 g) was stirred at room temperature for 8 hr. An additional amount of the reagents, Ag_2O (3 g) in CH_3I (3 ml) was charged and stirred for further 24 hr. After a final addition of Ag_2O (1.8 g) and CH_3I (3 ml) stirring was continued for total seven days. Acetone was added to the reaction mixture and Ag_2O was filtered off. The filtrate was condensed to dryness. The residue obtained was chromatographed over silica gel. Elution with hexane–benzene (1:1) gave 269 mg of the photoproduct (II: R=Ac) as an oily substance. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1722 (OAc). The compound (II: R=Ac) was further converted into the crystalline phenylurethane (II: R=CONHPh) as described, which was identical in all respects with that of the photoproduct (II: R=Ac). Elution with 5% ether–benzene gave 220 mg of the starting material (XII: $R_1=H$, $R_2=Ac$) unchanged.

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