SYNTHESIS OF 19-HYDROXYLATED ANALOGUES OF ANDROSTENEDIONE AND TESTOSTERONE WITH THE CYCLOPROPANE RING IN 4,5-POSITION*

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Synthesis of 19-hydroxylated analogues of androstenedione and testosterone carrying the cyclopropane ring in position 4β,5β is described. The starting allylic alcohol *XIII* was prepared by standard reactions from the epoxide *I* and transformed by Simmons–Smith methylenation to the cyclopropano derivative *XXI*. Hydrolyses and oxidations afforded the desired analogues *XXIII* and *XXV*.

In one of our earlier papers[1] we described synthesis of 19-hydroxylated analogues of methyltestosterone and methylandrostenediol with the cyclopropane ring in 4β,5β position. In continuation of these studies of the relationship between the structural changes in the steroid molecule and biological activity we describe in this paper the synthesis of this type of analogues of testosterone and androstenedione.

The analogue of androstenedione – the cyclopropano derivative *XXIII* – was prepared from the known[2] diol *II*. Jones' oxidation afforded the dione[3] *VI* which on steam distillation with pyridine and sodium bicarbonate gave the unsaturated ketone[4] *VII*. The epoxide ring was cleaved with zinc dust in acetic acid and the 19-hydroxy derivative[5,6] *VIII* was transformed to the acetate *IX*. Sodium borohydride reduction afforded the triol monoacetate *XIX* which was submitted to the Simmons–Smith methylenation to yield the cyclopropano derivative *XXII*. Jones' oxidation and subsequent hydrolysis of the acetate *XXIV* gave the analogue *XXIII*.

The analogue of testosterone *XXV* was synthesised from the ketone *I* which was reduced with lithium tri-tert-butoxyaluminium hydride to the alcohol *III*. Benzoylation gave the benzoate *V* which was partially hydrolysed to the mono ester *IV*. Oxidation and steam distillation of the ketone *X* with pyridine and sodium bicarbonate afforded the unsaturated ketone *XII*. Reductive fission of the epoxide ring with zinc dust in acetic acid yielded the diol monobenzoate *XIV* which was hydrolysed to the diol[7] *XIII* with potassium hydroxide in methanol. This diol was transformed to the diacetate *XV* which on borohydride reduction yielded the allylic alcohol *XVIII*.

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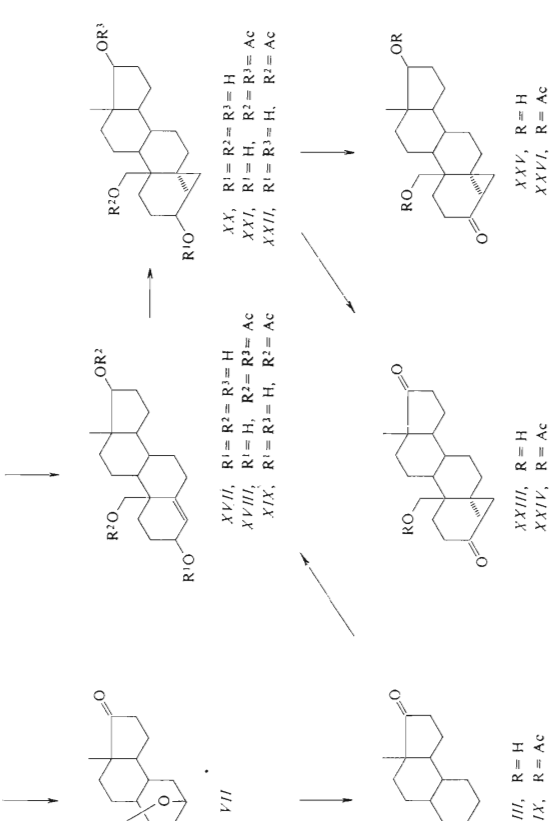
OCOC6H5
Br
O
X
OR
XI, R = H
XII, R = C6H5CO
OR2
R1O
Br
O
II, R1 = R2 = H
III, R1 = Ac, R2 = H
IV, R1 = H, R2 = C6H5CO
V, R1 = Ac, R2 = C6H5CO
XIII, R1 = R2 = H
XIV, R1 = H, R2 = C6H5CO
XV, R1 = R2 = Ac
XVI, R1 = Ac, R2 = C6H5CO
AcO
Br
O
I
O
Br
O
VI

Simmons–Smith methylenation led to the cyclopropano derivative *XXI* which on Jones' oxidation and hydrolysis of the acetate *XXVI* afforded the analogue *XXV*.



EXPERIMENTAL

Melting points were determined on a Kofler block. Optical measurements were carried out in chloroform with an error of ±2°. The infrared spectra were recorded on the Zeiss UR 20 spectrometer in tetrachloromethane. Mass spectra were recorded on the mass spectrometer AEI MS 902. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin-layer chromatography (TLC) and by spectral evidence. Usual working up of a solution implies washing the solution with 5% aqueous hydrochloric acid, water, drying over sodium sulphate, and evaporation of the solvent under reduced pressure. Ligroin refers to the fraction of b.p. 40–60°C.

5-Bromo-6β,19-epoxy-5α-androstane-3β,17β-diol (*II*)

The diester *V* (22 g) in tetrahydrofuran (220 ml) was treated with a solution of potassium hydroxide (150 mg) in methanol (40 ml) and allowed to stand at 16°C for 90 min. The mixture was acidified with acetic acid. Solvents were removed under reduced pressure and the residue was diluted with water. The product was collected by succion and crystallized from methanol water to yield 16·5 g of the monoester *IV*. The mother liquors were chromatographed over silica gel (100 g) in chloroform and the fractions with the polar component were crystallized from methanol–ethyl acetate to yield 2·1 g of the diol *II*, m.p. 236–237°C, $[\alpha]_D^{20}$ −13° (*c* 1·2) in accordance with the literature[2].

5-Bromo-6β-19-epoxy-5α-androstane-3β,17β-diol 3-Acetate (*III*)

The ketone *I* (2 g) in tetrahydrofuran (35 ml) was treated with solid lithium tri-tert-butoxyaluminium hydride (4 g) and allowed to stand at room temperature for 40 min. The mixture was diluted with water, the excess hydride was decomposed with 5% hydrochloric acid, and the product was isolated with ether. The ethereal solution was worked up, ether removed, and the residue was crystallized from methanol to yield, 1·8 g of the alcohol *III*, m.p. 152–154°C, $[\alpha]_D^{20}$ −20° (*c* 1·1). For $C_{21}H_{31}BrO_4$ (427·4) calculated: 59·01% C, 7·31% H, 18·69% Br; found: 58·79% C, 7·20% H; 18·12% Br.

5-Bromo-6β,19-epoxy-5α-androstane-3β,17β-diol 17-Benzoate (*IV*)

As described under preparation of the diol *II*, crystallization of the crude product gave 16·5 g of *IV*. Chromatography of the mother liquors afforded additional 1·6 g of the monoester *IV* as the lipophilic component. Yield 18·1 g of the benzoate *IV*, m.p. 231–233°C, $[\alpha]_D^{20}$ +34° (*c* 1·2). For $C_{26}H_{33}BrO_4$ (489·4) calculated: 63·80% C, 6·79% H, 16·33% Br; found: 63·70% C, 6·61% H, 15·90% Br.

5-Bromo-6β,19-epoxy-5α-androstane-3β,17β-diol 3-Acetate 17-Benzoate (*V*)

The alcohol *III* (2 g) in pyridine (30 ml) was treated with benzoyl chloride and set aside at room temperature for 24 h. The mixture was decomposed with water, diluted by water, and the product was collected by succion and washed well with water. The dry product was crystallized from chloroform–methanol to yield 1·8 g of the diester *V*, m.p. 253–255°C, $[\alpha]_D^{20}$ +30° (*c* 1·2). For $C_{28}H_{35}BrO_5$ (531·5) calculated: 63·27% C, 6·64% H, 15·04% Br; found: 63·10% C, 6·49% H, 14·70% Br.

5-Bromo-6β,19-epoxy-5α-androstane-3,17-dione (*VI*)

The diol *II* (7 g) in acetone (400 ml) was treated with excess Jones' reagent and set aside for 15 min. The excess oxidising agent was removed with methanol, the mixture was diluted with water, and the product was collected by succion. The filtrate was extracted with ethyl acetate and the organic layer was worked up. The residue after evaporation of the solvent and the collected product were crystallized from chloroform–methanol to yield 5·8 g of the dione *VI*, m.p. 163 to 165°C (decomp.), $[\alpha]_D^{20}$ −30° (*c* 1·7). For $C_{19}H_{25}BrO_3$ (381·3) calculated: 59·84% C, 6·60% H; 20·95% Br; found: 59·70% C, 6·49% H, 20·50% Br.

6α,19-Epoxyandrost-4-ene-3,17-dione (*VII*)

The bromo ketone *VI* (5·7 g) in pyridine (250 ml) was treated with a solution of sodium hydrogen carbonate (20 g) in water (120 ml) and pyridine was removed by steam distillation (about 2·5 h). The product was taken into ethyl acetate, the extract was worked up and the residue (4·6 g) was chromatographed on a silica gel column (250 g) in benzene–ether (3 : 1). Fractions with the desired product were combined, solvents removed, and the residue was crystallized from methanol–ether to yield 4·02 g of the dione *VII*, m.p. 187—188°C, $[\alpha]_D^{20}$ −40° (*c* 1·5) in accordance with the literature[4]. IR spectrum: 1 678, 1 633 (=C—C—CO), 1 740 (carbonyl), 1 027, 1 012, 878 cm^{-1} (ether).

19-Hydroxyandrost-4-ene-3,17-dione (*VIII*)

Zinc dust (40 g) was activated by washing it with three portions of 50% acetic acid and then with three portions of glacial acetic acid (50 ml each) and added to a solution of the oxide *VII* (4·8 g) in glacial acetic acid (250 ml) heated to 90°C. The mixture was stirred at 90°C for 45 min. The metal was removed by succion, washed with acetic acid and the filtrate was diluted with water (100 ml). The volume of the filtrate was reduced under reduced pressure and the product was extracted with ethyl acetate. The extract was washed with a sodium hydrogen carbonate solution, water, dried , and the residue (4·4 g) was chromatographed over silica gel (350 g) in benzene–ether (1 : 1). The corresponding fractions were worked up and the crude product was crystallized from ethyl acetate to yield 3·3 g of the alcohol *VIII*, m.p. 170—172°C, $[\alpha]_D^{20}$ +189° (*c* 1·4), in accordance with the literature[5]. IR spectrum: 3 630, 1 058 (hydroxyl), 1 738 (carbonyl), 1 666, 1 624 cm^{-1} (=C—C—CO).

19-Acetoxyandrost-4-ene-3,17-dione (*IX*)

The alcohol *VIII* (3 g) in pyridine (20 ml) was acetylated with acetic anhydride (8 ml) at room temperature for 18 h. The mixture was decomposed with ice and water and the product taken into ethyl acetate. The organic layer was worked up, solvent was distilled off to yield 1·5 g of the acetate *IX* which resisted all attempts at crystallization; $[\alpha]_D^{20}$ +188° (*c* 1·5). For $C_{21}H_{28}O_4$ (344·4) calculated: 73·23% C, 8·19% H; found: 73·12% C, 8·10% H.

5-Bromo-6β,19-epoxy-17β-hydroxy-5α-androstan-3-one 17-Benzoate (*X*)

The alcohol *IV* (16·4 g) in acetone (1 200 ml) was treated under moderate cooling with excess Jones' reagent and allowed to stand at room temperature for 20 min. The excess reagent was removed with methanol, the mixture was diluted with water and the product was collected by succion. It was dissolved in chloroform, dried with sodium sulphate, the volume of the solu-

tion was reduced to about 50 ml and diluted with methanol. Yield 15·8 g of the ketone *X*, m.p. 189–191°C, $[\alpha]_D^{20}$ +81° (*c* 1·6). For $C_{26}H_{31}BrO_4$ (487·4) calculated: 64·06% C, 6·41% H, 16·39% Br; found: 65·81% C, 6·28% H, 15·87% Br.

6β,19-Epoxy-17β-hydroxy-androst-4-en-3-one (*XI*)

The benzoate *XII* (1 g) in tetrahydrofuran (25 ml) was treated with a solution of potassium hydroxide (80 mg) in methanol (7 ml) and allowed to stand at 45°C for 5 h. The mixture was acidified with acetic acid, the solvents were removed under reduced pressure, and the residue was treated with water. The precipitate was taken into ethyl acetate and the solution was washed with a sodium hydrogen carbonate solution, water, dried, and solvent was distilled off. The residue was crystallized from ethyl acetate to yield 600 mg of the alcohol *XI*, m.p. 76–79°C, $[\alpha]_D^{20}$ −96° (*c* 1·4) in accordance with the literature[4]. IR spectrum: 3 270 (hydroxyl) 1 730, 1 675, 1 605 (carbonyl), 1 064, 1 030, 1 020 cm^{-1} (ether).

6β,19-Epoxy-17β-hydroxy-androst-4-en-3-one 17-Benzoate (*XII*)

a) *From the alcohol* IV: Chromium oxide–pyridine complex was prepared by addition of chromium oxide (45 g) into pyridine (520 ml) under cooling and stirring. This complex was treated with a solution of the alcohol *IV* (17 g) in pyridine (90 ml) and stirred at room temperature for 6 h. The mixture was allowed to stand for 18 h, treated with solid sodium hydrogen carbonate, stirred for 30 min and steam distilled for about 3 h to remove pyridine. The crystalline product was taken into ethyl acetate–chloroform, the solution was worked up in the usual way and the product after evaporation of the solvents was chromatographed on a silica gel column (700 g) in benzene–ether (7 : 1). Working up of the corresponding fractions gave 13·1 g of a product which on crystallization from ethyl acetate afforded 12 g of the unsaturated ketone *XII*, m.p. 213–215°C $[\alpha]_D^{20}$ −11° (*c* 1·2). For $C_{26}H_{30}O_4$ (410·5) calculated: 76·06% C, 8·35% H; found: 76·20% C, 8·05% H.

b) *From the ketone* X: The bromo ketone *X* (15·8 g) in pyridine (500 ml) was treated with a solution of sodium hydrogen carbonate (60 g) in water (200 ml) and the mixture was steam distilled for 3 h. The crystalline product was collected by succion, dried and crystallized from ethyl acetate to yield 12·5 g of the unsaturated ketone *XII*, m.p. 212–214°C, $[\alpha]_D^{20}$ −13° (*c* 1·1).

17β-19-Dihydroxandrost-4-en-3-one (*XIII*)

a) *From the diester* XVI: The diester *XVI* (2·5 g) in methanol (300 ml) was treated with a solution of potassium hydroxide (2 g) in methanol (20 ml) and heated to 50°C under nitrogen for 8 h. The excess alkali was removed with acetic acid, solvents were removed under reduced pressure and the product was taken into ethyl acetate. The extract was washed with a sodium hydrogen carbonate solution, water, dried, and the solvent was distilled off. The residue was crystallized from ethyl acetate to afford 1·7 g of the diol *XIII*, m.p. 203–204°C, $[\alpha]_D^{20}$ +112° (*c* 1·1, ethanol) in accordance with the literature[7].

b) *From the benzoate* XIV: The benzoate *XIV* (3 g) in methanol (300 ml) was hydrolysed with potassium hydroxide (2 g) in methanol (25 ml) under analogous conditions as described under *a*). Similar working up and crystallization from ethyl acetate gave 1·8 g of the diol *XIII*, m.p. 202–204°C, $[\alpha]_D^{20}$ +110° (*c* 1·2 in ethanol).

17β,19-Dihydroxandrost-4-en-3-one 17-Benzoate (*XIV*)

The epoxide *XII* (12 g) in glacial acetic acid (700 ml) was treated with zinc dust (100 g) which was previously activated with acetic acid as described for the preparation of the ketone *VIII*. The mixture was stirred in a boiling water bath for 40 min. Zinc was filtered off, washed with acetic acid, and the filtrate was diluted with water (200 ml) and the volume was reduced to about 250 ml *in vacuo*. The residue was diluted with water and the product was extracted into ethyl acetate. The extract was worked up in the usual way and solvent was distilled off. The residue was chromatographed on a silica gel column (600 g) in chloroform. Fractions with the polar component were combined, solvents were removed, and the residue was crystallized from chloroform–ethyl acetate to afford 6·7 g of the benzoate *XIV*, m.p. 244–246°C, $[\alpha]_D^{20}$ +142° (*c* 1·3). For $C_{26}H_{32}O_4$ (408·5) calculated: 76·44% C, 7·90% H; found: 76·30% C, 7·81% H.

17β,19-Dihydroxandrost-4-en-3-one 17,19-Diacetate (*XV*)

A solution of the diol *XIII* (2·8 g) in pyridine (20 ml) was treated with acetic anhydride (10 ml) and allowed to stand at room temperature for 18 h. The excess anhydride was decomposed with ice and water, and the product was isolated with ether. Usual working up gave a crude product which was chromatographed over silica gel (300 g) in benzene–ether (19 : 1). The corresponding fractions were worked up and the product was crystallized from methanol–water to yield 2·4 g of the diacetate *XV*, m.p. 125–127°C, $[\alpha]_D^{20}$ +132° (*c* 1·4), in accordance with the literature[7]. IR spectrum: 1 743, 1 240, 1 044 (acetate), 1 688, 1 624 cm^{-1} (=C=CO).

17β,19-Dihydroxyandrost-4-en-3-one 17-Benzoate 19-Acetate (*XVI*)

Fractions with the lipophilic component after isolation of the alcohol *XIV* were worked up and the product was crystallized from methanol to yield 2·5 g of the diester *XVI*, m.p. 127–129°C, $[\alpha]_D^{20}$ +165° (*c* 1·3). For $C_{28}H_{34}O_5$ (450·5) calculated: 74·64% C, 7·61% H; found: 74·39% C, 7·48% H.

4-Androstene-3β,17β,19-triol (*XVII*)

a) *From the diacetate* XVIII: The diacetate *XVIII* (800 mg) in methanol (100 ml) was treated with a solution of potassium hydroxide (400 mg) in methanol (5 ml) and heated to 50°C under nitrogen for 1 h. The mixture was acidified with acetic acid and solvents were distilled off *in vacuo* The residue was diluted with water and the product was taken into ethyl acetate. The extract was washed with a sodium hydrogen carbonate solution, water, dried, and the residue after evaporation of the solvent was crystallized from acetone–hexane to yield 450 mg of the triol *XVII*, m.p. 199–202°C, $[\alpha]_D^{20}$ +42° (*c* 1·1 in ethanol), in accordance with the literature[7].

b) *From the acetate* XIX: The acetate *XIX* (100 mg) in methanol (10 ml) was hydrolyzed with potassium hydroxide (50 mg) as described above. Similar working up and crystallization from acetone–hexane gave 65 mg of the triol *XVII*, m.p. 198–200°C, $[\alpha]_D^{20}$ +44° (*c* 1·4 in ethanol).

4-Androstene-3β,17β,19-triol 17,19-Diacetate (*XVIII*)

A solution of the ketone *XV* (2·4 g) in methanol (70 ml) and ethyl acetate (25 ml) was treated with sodium borohydride (1·2 g) in the course of 45 min at room temperature. The mixture was stirred for 2 h, neutralized with acetic acid, diluted with water and the volume was reduced

in vacuo. The product was isolated with ethyl acetate, the extract was worked up in the usual way to yield after evaporation of the solvent 2·5 g of a solid. It was chromatographed on a silica gel column (150 g) in benzene–ether (2 : 1). Working up of the corresponding fractions gave 2 g of a product which was crystallized from methanol–water to afford 1·7 g of the alcohol *XVIII*, m.p. 97–99°C, $[\alpha]_D^{20}$ +57° (*c* 1·6). IR spectrum: 3 610, 3 265 (hydroxyl) 3 095, 1 660 (double bond), 1 244, 1 241 cm^{-1} (acetate). For $C_{23}H_{34}O_5$ (390·5) calculated: 70·74% C, 8·78% H; found: 70·60% C, 8·52% H.

4-Androstene-3β,17β,19-triol 19-Acetate (*XIX*)

The dione *IX* (3 g) in methanol (120 ml) and ethyl acetate (45 ml) was reduced with sodium borohydride (2·5 g) as described in the foregoing experiment. Similar working up gave 2·8 g of a crude product which was chromatographed over silica gel (300 g) in ether. The corresponding fractions gave after combination and removal of the solvent 2·4 g of a product which was crystallized from ethyl acetate to yield 2·1 g of the acetate *XIX*, m.p. 154–156°C, $[\alpha]_D^{20}$ +90° (*c* 1·1). For $C_{21}H_{32}O_4$ (348·5) calculated: 72·38% C, 9·26% H; found: 72·12% C, 9·17% H.

4β,5-Cyclopropano-5β-androstane-3β,17β,19-triol (*XX*)

A solution of the acetate *XXII* (80 mg) in methanol (10 ml) was hydrolysed with potassium hydroxide (40 mg) in methanol (5 ml) at 50°C under nitrogen for 1 h. After cooling off the alkali was neutralised with acetic acid, volume was reduced *in vacuo* and the residue was diluted with water. The product was taken into ethyl acetate and the solution was worked up. The residue after evaporation of the solvent was crystallized from ethyl acetate to yield 35 mg of the triol *XX*, m.p. 164–166°C, $[\alpha]_D^{20}$ −12° (*c* 1·1). For $C_{20}H_{32}O_3$ (320·5) calculated: 74·95% C, 10·07% H, found: 74·71% C, 9·95% H.

4β,5-Cyclopropano-5β-androstane-3β,17β,19-triol 17,19-Diacetate (*XXI*)

The Zn–Cu couple (0·5%) was prepared by adding zinc dust (19·5 g; Baker 60–200 mesh) into a solution of cupric acetate monohydrate (450 mg) in acetic acid (150 ml) at 50–60°C and shaking until the solution decolorized. The solvent was poured off, the metal was washed first with acetic acid (80 ml) and then with eight portions of absolute ether (80 ml each). The metal was covered with absolute ether (40 ml), iodine (80 mg) and diiodomethane (18 ml) were added and the mixture was refluxed under argon for 3 h. After cooling off to room temperature the olefin *XVIII* (4 g) in ether (40 ml) and tetrahydrofuran (40 ml) was added and the mixture was stirred at room temperature for 6 h in an argon atmosphere. The mixture was diluted with ether, poured into 5% sodium hydrogen carbonate solution, the ethereal layer was washed with 5% sodium thiosulphate, water, dried, and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel column (350 g) in benzene–ether (3 : 1). Fractions containing the desired adduct and the starting material as well were combined, solvents removed, and the residue (3·45 g) was dissolved in ether and treated with a solution perphthalic acid (1·3 g) in ether (20 ml). After 18 h at room temperature the peracid was extracted into 5% sodium carbonate solution, the ethereal solution was washed with water, dried, and ether removed. The residue (3·3 g) was chromatographed on a silica gel column (350 g) in benzene–ether (3 : 1). Fractions with the lipophilic component were combined, solvents distilled off and the product (2·84 g) was crystallized from acetone–ligroin to yield 2 g of the cyclopropano derivative *XXI*, m.p. 99–100°C, $[\alpha]_D^{20}$ −10° (*c* 1·3). IR spectrum: 3 620 (hydroxyl), 3 075 (cyclopropane), 1 742, 1 246 cm^{-1} (acetate). For $C_{24}H_{36}O_5$ (404·5) calculated: 71·25% C, 8·97% H; found: 71·05% C, 8·79% H.

4β,5-Cyclopropano-5β-androstane-3β,17β,19-triol 19-Acetate (*XXII*)

The acetate *XIX* (4 g) was submitted to the Simmons–Smith methylenation as described in the foregoing experiment. Similar working up gave 4 g of a crude product which was chromatographed on a silica gel column (400 g) in ether to yield after working up of the corresponding fractions 2·4 g of a mixture of the starting material and the desired cyclopropano derivative. The mixture was dissolved in chloroform (100 ml) and treated with a solution of perphthalic acid (1·5 g) in ether (20 ml). Working up as described above and chromatography over silica gel (600 g) in ether afforded fractions with the lipophilic component. Combination and evaporation gave 1·9 g of a product which was crystallized from ethyl acetate to afford 1·32 g of the cyclopropano derivative *XXII*, m.p. 152–155°C, $[\alpha]_D^{20}$ +2° (*c* 1·2). Mass spectrum: M^+ • 362. IR spectrum: 3 605, 3 550 (hydroxyl), 3 070 (cyclopropane), 1 730, 1 240 cm^{-1} (acetate). For $C_{22}H_{34}O_4$ (362·5) calculated: 72·89% C, 9·45% H; found: 72·67% C, 9·30% H.

19-Hydroxy-4β,5-cyclopropano-5β-androstane-3,17-dione (*XXIII*)

A solution of the acetate *XXIV* (100 mg) in methanol (6 ml) was treated with a solution of potassium hydroxide (80 mg) in methanol (3 ml; 50%) and heated to 50°C for 2 h. The alkali was removed with acetic acid and the solvents were partly distilled off *in vacuo*. The residue was diluted with water and the product was taken into ethyl acetate. The extract was washed with a sodium hydrogen carbonate solution, water, dried, and the product after removal of the solvent was crystallized from ethyl acetate to afford 65 mg of the alcohol *XXIII*, m.p. 221–223°C, $[\alpha]_D^{20}$ +154° (*c* 1·2). IR spectrum: 3 630, 1 053 (hydroxyl), 1 738, 1 407 (17-oxo group), 1 677 cm^{-1} (3-oxo group). Fro $C_{20}H_{28}O_3$ (316·4) calculated: 75·91% C, 8·92% H; found: 75·70% C, 8·79% H.

19-Acetoxy-4β,5-cyclopropano-5β-androstane-3,17-dione (*XXIV*)

A solution of the acetate *XXII* (500 mg) in acetone (50 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. The excess oxidising agent was removed with methanol, the mixture was diluted with water and the product was extracted with ethyl acetate. The extract was worked up in the usual way and the product after evaporation of the solvent was chromatographed on a silica gel column (60 g) in benzene–ether (15 : 1). Fractions with the desired compound were combined, solvents distilled off, and the residue was crystallized from ether to yield 340 mg of the dione *XXIV*, m.p. 148–150°C, $[\alpha]_D^{20}$ +158° (*c* 1·4). IR spectrum: 1 740, 1 248 (acetate), 1 732 (17-oxo group), 1 681 $c.^{-1}$ (3-oxo group). For $C_{22}H_{30}O_4$ (358·5) calculated: 73·71% C, 8·44% H; found: 73·78% C, 8·40% H.

17β,19-Dihydroxy-4β,5-cyclopropano-5β-androstan-3-one (*XXV*)

The diacetate *XXVI* (100 mg) in methanol (5 ml) was hydrolysed with potassium hydroxide (100 mg) in 50% methanol (3 ml) at 50°C for 2 h. Usual working up (as described for *XXIII*) and crystallization from ethyl acetate gave 55 mg of the diol *XXV*, m.p. 184–186°C, $[\alpha]_D^{20}$ +74° (*c* 1·3). For $C_{20}H_{30}O_3$ (318·4) calculated: 75·43% C, 9·50% H; found: 75·10% C, 9·20% H.

17β,19-Diacetoxy-4β,5-cyclopropano-5β-androstan-3-one (*XXVI*)

The diacetate *XXI* (1·7 g) in acetone (100 ml) was oxidized with Jones' reagent as described for preparation of the dione *XXIV*. Similar working up gave 1·6 g of a product which was chromatographed on a silica gel column (150 g) in benzene–ether (19 : 1). The corresponding frac-

tions afforded after working up and crystallization from ether–ligroin 1·25 g of the diacetate *XXVI*, m.p. 118–120°C, $[\alpha]_D^{20}$ +77° (*c* 1·3). IR spectrum: 3 090, 3 020 (cyclopropane), 1 744, 1 248, 1 048, 1 039, 1 030 (acetate), 1 690 cm^{-1} (3-oxo group). For $C_{24}H_{34}O_5$ (402·5) calculated: 71·61% C, 8·51% H; found: 71·87% C, 8·70% H.

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