6,7-SECOSTEROIDS WITH POTENTIAL BIOLOGICAL ACTIVITY*

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Preparation of several 6,7-seco derivatives of 3α,5-cyclo-5α-androstane series is reported.

In connection with our studies on structure–antiandrogenic activity relationships, certain 6,7-secosteroids appeared to be of interest. The preparation of several 6,7-seco derivatives of 3α,5-cyclo-5α-androstane series is reported on in the present paper.

As starting material, we used 17β-hydroxy-3α,5-cyclo-5α-androstan-6-one[1] (*I*). The hydroxyl group in this compound was protected by its conversion into a nitrate *II* and the oxidative fission of the B-ring was carried out by treatment with potassium hypobromide in pyridine solution according to an analogous procedure[2]. The 6,7-seco diacid thus formed was methylated with diazomethane to give the dimethyl ester *III* in 69% overall yield, the protecting nitrate group was removed with zinc in acetic acid and the alcohol *IV* oxidized with chromic acid in acetic acid to the ketone *V*. The ketonic group in the compound *V* was protected by converting the latter into the ethylenedioxy derivative *VI* which was submitted to lithium aluminum hydride reduction. The nature of the reaction product is dependent on the solvent used. In ether, only the methoxycarbonyl group attached to the A-ring was reduced to afford the alcohol *VII*; in order to obtain the desired diol *VIII*, use of higher boiling dioxan was necessary. Structure of the alcohol *VII* was established by ^{1}H-NMR-spectroscopy: the signals associated with the CH_2—OH protons appear as doublets at 3·19 and 4·12 p.p.m. while the downfield doublet is split by a long-range coupling with the one of the protons at $C_{(4)}$ ($J_{4,6}$ = 1·5 Hz).

Removal of the protecting ethylenedioxy group in the diol *VIII* afforded the expected ketone *IX*; acetylation of *VIII* in triethylamine gave the 6-monoacetate *XI* along with a small quantity of the diacetate *X*. The major product of acetylation was assigned the structure *XI* on the basis of ^{1}H-NMR data. Similarly to the alcohol *VII*, the signals of the two CH_2—$OCOCH_3$ protons appear as doublets at 3·83 and 4·47 p.p.m., the downfield doublet being further split by long-range coupling with one of the protons at $C_{(4)}$ ($J_{4,6}$ = 1·5 Hz). Tosylation of the monoacetate *XI* with p-toluenesulfonyl chloride in pyridine followed by treatment of the product *XII*

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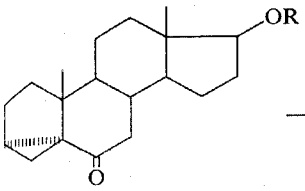

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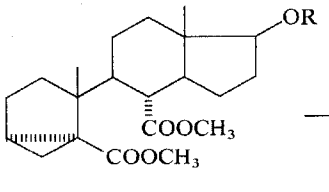

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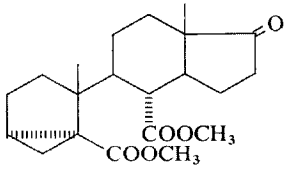
IV, R = H



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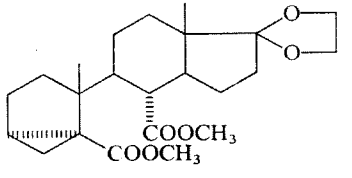
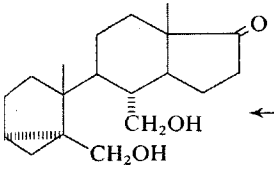
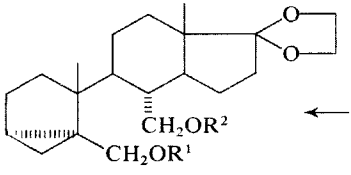


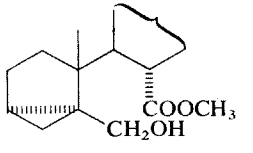
VI



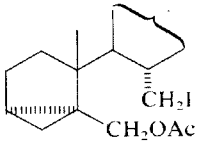
IX



VIII, $R^1 = R^2 = H$
X, $R^1 = R^2 = Ac$
XI, $R^1 = Ac$, $R^2 = H$
XII, $R^1 = Ac$, $R^2 = Ts$

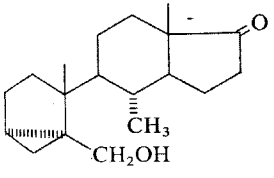


VII

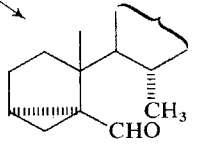


XIII

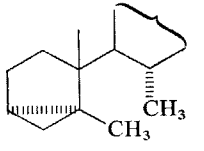
XIV, R = Ac
XV, R = H



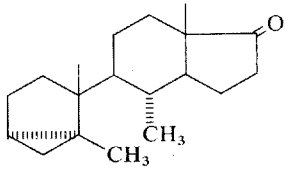
XVI



XVII

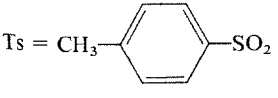


XVIII



XIX

Ac = CH_3CO

Ts = 

with sodium iodide led to the iodo derivative *XIII*. Dehalogenation of the latter compound with Raney nickel in refluxing ethanol afforded the required 17-ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6-ol 6-acetate (*XIV*). Apart from the signals of both angular methyls, the ^{1}H-NMR-spectrum of this substance displays a signal of a further methyl at 0·96 p.p.m. which is split into a doublet by the $C_{(8)}$-proton. The acetate *XIV* was converted to the ketone *XVI*, which was another compound of interest, by lithium aluminum hydride reduction of the acetoxy grouping followed by deketalization with *p*-toluenesulfonic acid in methanol.

In order to prepare the ketone *XIX*, the alcohol *XV* was oxidized with manganese dioxide[3] to the unstable aldehyde *XVII* which, without purification, was submitted to Huang–Minlon reduction to yield the deoxo derivative *XVIII* in 54% yield. Deketalization of the latter substance led to the required ketone *XIX* the structure of which was confirmed by ^{1}H-NMR spectrum. Apart from the signals of angular methyl groups, two additional methyl signals are present; the signal associated with the methyl at $C_{(5)}$ appears as a signlet at 1·02 whereas the signal of the methyl group attached to $C_{(8)}$ is split into a doublet by coupling with the $C_{(8)}$-proton, and is centered at the same position.

Pharmacodynamic properties of the compounds *IX*, *XV* and *XIX* will be reported elsewhere.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Unless stated otherwise, optical rotations were measured in chloroform. The infrared spectra were measured on a Zeiss UR-10 spectrophotometer. Unless stated otherwise, the ^{1}H-NMR spectra were measured in deuteriochloroform on Varian HA-100 apparatus using tetramethylsilane as internal standard; chemical shifts are given in p.p.m. (δ scale) and coupling constants in Hz. The identity of samples prepared by different routes was checked by mixture melting points and by infrared spectra. The statement "worked up as usual" stands for: The solution was washed with 5% hydrochloric acid, 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*.

17β-Hydroxy-3α,5-cyclo-5α-androstan-6-one 17-Nitrate (*II*)

The 17β-hydroxy-3α,5-cyclo-5α-androstan-6-one (*I*) (ref.[1]) (1·5 g) in chloroform (40 ml) was added to a solution prepared at −15°C from acetic anhydride (9 ml) and nitric acid (2·1 ml). The mixture was allowed to stand at −10°C for two hours, poured into cold water and the product was taken up in chloroform. The chloroform extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and evaporated *in vacuo*. The residue (2 g) was repeatedly crystallized from methanol to yield the nitrate *II* (1 g), m.p. 140–141°C, $[\alpha]_D^{22}$ +44·4° (*c* 1·0). Infrared spectrum (tetrachloromethane): 1692, 1635, 1292, 1278 cm^{-1}. For $C_{19}H_{27}NO_4$ (333·4) calculated: 68·44% C, 8·16% H, 4·20% N; found: 68·80% C, 8·24% H, 4·30% N.

17β-Hydroxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-dioic Acid Dimethyl Ester 17-Nitrate (*III*)

The nitrate *II* (9·5 g) was added with occasional shaking to a solution prepared from 10% potassium hydroxide (380 ml) and bromine (9·5 ml); the temperature was raised to about 50°C. After cooling to room temperature pyridine (950 ml) was added and the mixture was shaken for 20 h. After cooling to 0°C 35% hydrochloric acid was added in small portions till the acid reaction. The precipitate was taken up in ether, the ethereal extract was washed with 5% potassium hydroxide and the acidic product was precipitated with 35% hydrochloric acid. The product was extracted with ether, the ethereal extract was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residual oil (10 g) was dissolved in ether (200 ml) and excess of ethereal diazomethane (130 ml) was added. After 15 minutes the excess diazomethane was destroyed with acetic acid and the solvent was evaporated *in vacuo*. The residual oil (10 g) was repeatedly crystallized from ligroin to yield 8 g of the dimethyl ester *III*, m.p. 107–109°C, $[\alpha]_D^{22}$ −10·9° (*c* 1·0). Infrared spectrum (tetrachloromethane): 3050, 3090, 1730, 1636, 1438, 1150 cm^{-1}. For $C_{21}H_{31}NO_7$ (409·5) calculated: 61·60% C, 7·63% H, 3·42% N; found: 61·77% C, 7·51% H, 3·50% N.

17β-Hydroxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-dioic Acid Dimethyl Ester (*IV*)

To a solution of the nitrate *III* (3·3 g) in acetic acid (260 ml) zinc powder (15 g) was added in small portions at 0°C. The mixture was allowed to stand for 15 minutes at 0°C and another 15 minutes at room temperature. The zinc powder was filtered off, the filtrate evaporated *in vacuo* to one third of the volume and poured into water. The product was extracted with ether, the ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After chromatography on silica gel (300 g) in benzene–ether (75 : 25) the residual oil (3·2 g) afforded 3 g of the alcohol *IV* which was crystallized from ligroin, m.p. 109–111°C, $[\alpha]_D^{22}$ −16·5° (*c* 1·0). Infrared spectrum (tetrachloromethane): 3630, 3090, 1730, 1436, 1149 cm^{-1}. For $C_{21}H_{32}O_5$ (364·5) calculated: 69·20% C, 8·85% H; found: 68·90% C, 8·51% H.

17-Oxo-3α,5-cyclo-6,7-seco-5α-androstan-6,7-dioic Acid Dimethyl Ester (*V*)

Chromium trioxide (2·2 g) in water–acetic acid (42 ml, 1 : 1) was added to a stirred solution of the alcohol *IV* (3·2 g) in acetic acid (220 ml) and the mixture was allowed to stand at room temperature overnight. The excess reagent was destroyed with methanol, the mixture was concentrated under reduced pressure and the product extracted with ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After crystallization from ligroin the residual oil (3 g) afforded 2·1 g of the ketone *V*, m.p. 122–124·5°C, $[\alpha]_D^{22}$ +52·2° (*c* 1·0). Infrared spectrum (tetrachloromethane): 1744, 1436, 1148, 1730, 3090. 3050 cm^{-1}. For $C_{21}H_{30}O_5$ (362·5) calculated: 69·58% C, 8·34% H; found: 69·93% C, 8·38% H.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-dioic Acid Dimethyl Ester (*VI*)

A mixture of the ketone *V* (2·2 g), *p*-toluenesulfonic acid (260 mg), ethylene glycol (15·2 ml) and benzene was refluxed in a flask provided with a water separator for 24 h. The mixture was poured into water, the benzene layer was separated and extracted with 5% potassium hydrogen carbonate, water then dried over sodium sulfate and the solvent evaporated *in vacuo*. After crystallization from ligroin the residue (2·6 g) afforded 1·7 g of the ethylenedioxy derivative *VI*,

m.p. 94–96°C, $[\alpha]_D^{22}$ −30·7° (*c* 1·0). Infrared spectrum (tetrachloromethane): 1729, 1436, 1152, 1195, 1129, 1055, 951, 3090, 3050 cm^{-1}. ^{1}H-NMR: 0·71 (1 H, $C_{(4)}$—H, $J_{4,4} = J_{4,3} = 4·5$); 0·82 (s, 3 H, 18-CH_3); 1·08 (s, 3 H, 19-CH_3); 2·26 (t, 1 H, $C_{(8)}$—H, $J_{8,9} = J_{8,14} = 10·5$); 3·61 (s, 3 H, —$COOCH_3$); 3·64 (s, 3 H, —$COOCH_3$); 3·85 (mt, 4 H, —O—$CH_2$—$CH_2$—O—). For $C_{23}H_{34}O_6$ (406·5) calculated: 67·95% C, 8·43% H; found: 68·35% C, 8·41% H.

17-Ethylenedioxy-6-hydroxy-3α,5-cyclo-6,7-seco-5α-androstan-7-oic Acid Methyl Ester (*VII*)

Lithium aluminum hydride (60 mg) was added to a solution of the dimethyl ester *VI* (60 mg) in ether (5 ml) and the mixture was refluxed for one hour. The excess hydride was destroyed with saturated aqueous solution of sodium sulfate and the mixture was passed through a small column of sodium sulfate. After concentration *in vacuo* the filtrate afforded 50 mg of the crude product, which was preparatively chromatographed on one plate of silica gel (20 × 20 cm) in benzene–ether (7 : 3). The corresponding zone was collected, eluted with ether and the solvent evaporated *in vacuo*. After crystallization from ligroin at 0°C the residue (35 mg) afforded the alcohol *VII* (18 mg), m.p. 110–112°C, $[\alpha]_D^{22}$ +11·2° (*c* 1·0). Infrared spectrum (chloroform): 3620, 3615 inflex, 3065, 1725, 1437, 1158 cm^{-1}. ^{1}H-NMR: 0·27 (t, 1 H, $C_{(4)}$—H); 0·52 (dd, 1 H, $C_{(4)}$—H); 0·87 (s, 3 H, 18-CH_3); 1·02 (s, 3 H, 19-CH_3); 3·19 (d, 1 H, $C_{(6)}$—H, $J_{6,6} = 12$); 4·12 (d, 1 H, $C_{(6)}$—H, $J_{6,6} = 12$, $J_{6,4} = 1·0$ to 1·5); 3·88 (center of multiplet, 4 H, —O—CH_2—CH_2—O—); 3·62 (s, 3 H, —$COOCH_3$). For $C_{22}H_{34}O_5$ (378·5) calculated: 69·81% C, 9·05% H; found: 70·11% C, 9·17% H.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-diol (*VIII*)

a) A solution of the methyl ester *VII* (1·7 g) in dioxane (40 ml) was added to a stirred solution of lithium aluminum hydride (0·8 g) in dioxane (40 ml) and the mixture was refluxed for 5 h. The excess hydride was destroyed with saturated aqueous solution of sodium sulfate, the mixture was passed through a small column of sodium sulfate and the filtrate was concentrated *in vacuo*. After crystallization from heptane the residue (1·7 g) afforded the diol *VIII* (1 g), m.p. 161 to 163°C, $[\alpha]_D^{22}$ −30·3° (*c* 1·0). Infrared spectrum (chloroform): 3625, 1180, 1149, 1095, 1058, 1035, 1030, 965, 3065 cm^{-1}. ^{1}H-NMR: 0·33 (t, 1 H, $C_{(4)}$—H, $J_{4,4} = J_{4,3} = 4·5$); 0·50 (dd, 1 H, $C_{(4)}$—H, $J_{4,4} = 4·5$, $J_{4,3} = 8$); 0·89 (s, 3 H, 18-CH_3), 1·41 (s, 3 H, 19-CH_3); 1·99 (s, 2 H, 2 × OH); 3·12 (d, 1 H, $C_{(6)}$—H, $J_{6,6} = 11.5$); 4·19 (dd, 1 H, $C_{(6)}$—H, $J_{6,6} = 11·5$, $J_{6,4} = 1·2$); 3·59 (dd, 1 H, $C_{(7)}$—H, $J_{7,7} = 12$, $J_{7,8} = 1·9$); 4·02 (dd, 1 H, $C_{(7)}$—H, $J_{7,7} = 12$, $J_{7,8} = 2·1$); 3·87 (mt, 4 H, —O—CH_2—CH_2—O—). For $C_{21}H_{34}O_4$ (350·5) calculated: 71·96% C, 9·78% H; found: 71·94% C, 9·65% H.

b) A solution of the dimethyl ester *VI* (8·3 g) in dioxane (250 ml) was added to a stirred solution of lithium aluminum hydride (8·3 g) in dioxane (200 ml) and the mixture was refluxed for 2 h. After the same working up as in *a*) the reaction mixture afforded 8·2 g of the crude product which was crystallized from heptane to yield 5 g of the diol *VIII*, m.p. 161–163°C, $[\alpha]_D^{22}$ −30° (*c* 1·0).

6,7-Dihydroxy-3α,5-cyclo-6,7-seco-5α-androstan-17-one (*IX*)

p-Toluenesulfonic acid (100 mg) was added to a solution of the ethylenedioxy derivative *VIII* (100 mg) in methanol and the mixture was allowed to stand at room temperature for 1 h. The mixture was then concentrated *in vacuo* to one third of the volume, poured into water and the product taken up in ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After crystallization

from methanol–ligroin the residue (99 mg) afforded 60 mg of the ketone *IX*, m.p. 155–157°C. Infrared spectrum (chloroform): 1735, 3625, 3065 cm^{-1}. For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·39% C, 10·25% H.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-diol 6-Acetate (*XI*)

The diol *VIII* (3·3 g) was acetylated with acetic anhydride (10·5 ml) in triethylamine (70 ml) overnight. The usual workup gave 3·5 g of the crude product which was chromatographed on silica gel (360 g) in light petroleum–acetone–ether (9 : 0·5 : 0·5). The fractions containing the less polar product were combined and evaporated. The residue (600 mg) was crystallized from ligroin at 0°C to yield diacetate of 17-ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-diol (*X*), m.p. 68–70°C, $[\alpha]_D^{22} \pm 0°$ (*c* 1·0). Infrared spectrum (tetrachloromethane): 1740, 1030, 1245, 1059, 965, 3075 cm^{-1}. For $C_{25}H_{38}O_6$ (434·55) calculated: 69·09% C, 8·81% H; found: 69·19% C, 9·05% H.

After the same working up the fractions containing the more polar product afforded 2·7 g of the oily acetate *XI*, $[\alpha]_D^{22}$ −16·9° (*c* 1·0). Infrared spectrum (tetrachloromethane): 3640, 1741, 1245, 1030, 3070 cm^{-1}. ^{1}H-NMR: 0·33–0·62 (mt, 2 H, $C_{(4)}$—H); 0·895 (s, 3 H, 18-CH_3); 1·37 (s, 3 H, 19-CH_3); 2·05 (s, 3 H, —$OCOCH_3$); 3·61 (broad d, 1 H, $C_{(7)}$—H); 3·98 (broad d, 1 H, $C_{(7)}$—H); 3·89 (mt, 4 H, —O—CH_2—CH_2—O—); 3·83 (d, 1 H, $C_{(6)}$—H, $J_{6,6} = 12$); 4·47 (dd, 1 H, $C_{(6)}$—H, $J_{6,6} = 12$, $J_{6,4} = 1·0–1·5$). For $C_{23}H_{36}O_5$ (392·5) calculated: 70·37% C, 9·25% H; found: 70·01% C, 7·26% H.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6,7-diol 6-Acetate 7-Tosylate (*XII*)

The alcohol *XI* (1·5 g) was tosylated with *p*-toluenesulfonyl chloride (1·5 g) in pyridine (30 ml) overnight. The usual workup gave a crude product (1·8 g) which, after chromatography on silica gel (100 g) in light petroleum–acetone–ether (9 : 0·5 : 0·5), afforded 1·62 g of the oily tosyloxy derivative *XII*. All attempts at crystallization of the derivative *XII* were unsuccessful. Infrared spectrum (tetrachloromethane): 3070, 1742, 1246, 1600, 1370, 1189, 1179, 1098, 1060, 1032, 961, 925 cm^{-1}. For $C_{30}H_{42}O_7S$ (546·6) calculated: 65·91% C, 7·74% H; found: 65·92% C, 7·76% H.

17-Ethylenedioxy-7-iodo-3α,5-cyclo-6,7-seco-5α-androstan-6-ol 6-Acetate (*XIII*)

The tosylate *XII* (1·8 g) in acetone (25 ml) was treated with sodium iodide (5·4 g), the mixture refluxed for 2 h, then poured into water and the product was taken up in ether. The ethereal extract was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After chromatography on silica gel (180 g) in light petroleum–acetone–ether the residue (1·8 g) afforded the iodo derivative *XIII* (1·6 g) which was crystallized from methanol, m.p. 114·5 to 116·5°C, $[\alpha]_D^{22}$ +19·8° (*c* 1·0). Infrared spectrum (tetrachloromethane): 3070, 1742, 1243, 1060, 1032 cm^{-1}. For $C_{23}H_{35}IO_4$ (502·4) calculated: 54·98% C, 7·02% H, 25·26% I; found: 55·59% C, 7·11% H, 25·83% I.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6-ol 6-Acetate (*XIV*)

The iodo derivative *XIII* (1·0 g) in ethanol (60 ml) was treated with excess of Ranney nickel (c 2 g). The mixture was refluxed for 2 h, passed through a small column of silica gel and the filtrate was concentrated *in vacuo*. After chromatography on silica gel (80 g) in light petroleum–acetone–ether (8 : 1 : 1) the residue (800 mg) afforded an oily acetate *XIV* (550 mg). Infrared spectrum

(tetrachloromethane): 3070, 1740, 1245, 1232, 1170, 1114, 1060, 963 cm^{-1}. ^{1}H-NMR: 0·885 (s, 3 H, 18-CH_3); 0·96 (d, with virtual coupling, 3 H, $C_{(7)}$—CH_3); 1·235 (s, 3 H, 19-CH_3); 2·03 (s, 3 H, —$OCOCH_3$); 3·76 (d, 1 H, $C_{(6)}$—H, $J_{6,6} = 11·5$); 4·39 (broad d, 1 H, $C_{(6)}$—H, $J_{6,6} = 11·5$, $J_{6,4} = 1·5$); 3·84 (mt, 4 H, —O—CH_2—CH_2—O—). For $C_{23}H_{36}O_4$ (376·5) calculated: 73·36% C, 9·64% H; found: 73·81% C, 9·58% H.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6-ol (*XV*)

Lithium aluminum hydride (600 mg) was added to a solution of the acetate *XIV* (600 mg) in ether (35 ml) and the mixture was allowed to stand at room temperature for one hour. The excess hydride was decomposed with saturated aqueous solution of sodium sulfate and the mixture was then passed through a small column of sodium sulfate. The filtrate was concentrated *in vacuo* to yield 500 mg of the crude product which was chromatographed on silica gel (50 g) in light petroleum–acetone–ether (8 : 1 : 1). The fractions containing the pure product were combined, evaporated *in vacuo* and the residue (480 mg) was crystallized from heptane to yield the alcohol *XV* (300 mg), m.p. 88—90°C, $[\alpha]_D^{22}$ −16·3° (*c* 1·0). Infrared spectrum (tetrachloromethane): 3645, 3630, 3615, 3510, 3065, 1170, 1114, 1059, 1039, 1023, 1008 cm^{-1}. For $C_{21}H_{34}O_3$ (334·5) calculated: 75·40% C, 10·25% H; found: 75·09% C, 10·27% H.

6-Hydroxy-3α,5-cyclo-6,7-seco-5α-androstan-17-one (*XVI*)

p-Toluenesulfonic acid (200 mg) was added to a solution of the ethylenedioxy derivative *XV* (200 mg) in methanol (20 ml). The mixture was allowed to stand at room temperature for 2 h, concentrated *in vacuo* to one third of the volume, poured into water and the product was taken up in ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After crystallization from ligroin the residue (170 mg) afforded the ketone *XVI* (100 mg), m.p. 136—137·5°C, $[\alpha]_D^{22}$ +75·4° (*c* 0·5). Infrared spectrum (tetrachloromethane): 3635, 3620, 1060, 1024, 1003, 1742, 3065 cm^{-1}. For $C_{19}H_{30}O_2$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·04% C, 10·34% H.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstan-6-al (*XVII*)

The alcohol *XV* (300 mg) in dichloromethane (30 ml) was treated with manganese dioxide (4 g). The mixture was stirred for 6 days at room temperature, passed through a small column of silica gel and the filtrate was concentrated *in vacuo*. After chromatography on silica gel (30 g) in light petroleum–acetone–ether (8 : 1 : 1) the residue (300 mg) afforded the unstable oily aldehyde *XVII* (210 mg). Infrared spectrum (tetrachloromethane): 2705, 2740, 2830 inflex, 1706, 3080, 3010 cm^{-1}. Even after short standing of *XVII* in the air, bands at 2400 and 3400 cm^{-1} (carboxylic acid) could be detected in the spectrum. Because of rapid air oxidation of the aldehyde *XVII* to corresponding acid, the crude aldehyde was used for the next step without purification.

17-Ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstane (*XVIII*)

The solution of the crude aldehyde *XVII* (350 mg) in triethylene glycol (24 ml) was treated with hydrazine hydrate (2·4 ml, 100%) and solid potassium hydroxide (640 mg) and heated in an open flask. The temperature was allowed to rise to 140°C and the mixture was refluxed at this temperature for 30 minutes whereupon the condenser was removed until the temperature reached 200°C and refluxing was continued for 3 h. The mixture was then cooled, poured into water and the product extracted with ether. The ethereal extract was washed with water, dried over

sodium sulfate and the solvent evaporated in vacuo. After chromatography on silica gel (30 g) in light petroleum–acetone–ether (9 : 0·5 : 0·5) the residue (300 mg) afforded 180 mg of the oily ethylenedioxy derivative *XVIII* which resisted all attempts at crystallization, $[\alpha]_D^{22}$ −7·2° (*c* 1·0). Infrared spectrum (tetrachloromethane): 3065, 1170, 1115, 1061, 1040 cm^{-1}. For $C_{21}H_{34}O_2$ (318·5) calculated: 79·19% C, 10·76% H; found: 79·15% C, 10·70% H.

3α,5-Cyclo-6,7-seco-5α-androstan-17-one (*XIX*)

p-Toluenesulfonic acid (130 mg) was added to a solution of the ethylenedioxy derivative *XVIII* (130 mg) in methanol (10 ml) and the mixture was allowed to stand at room temperature for 2 h. The same workup as in the preparation of the ketone *XV* gave 130 mg of the crude product which was preparatively chromatographed on two plates of silica gel (20 × 20 cm) in light petroleum–acetone–ether (9 : 0·5 : 0·5). The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. After crystallization from methanol at 0°C the residue (120 mg) afforded the ketone *XIX* (68 mg), m.p. 59–61°C, $[\alpha]_D^{22}$ +91·7° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1744, 1408, 3065 cm^{-1}. ^{1}H-NMR: −0·03 to +0·23 (mt, 2 H, $C_{(4)}$—H); 0·885 (s, 1 H, 18-CH_3); 1·02 (s, 3 H, 6-CH_3); 1·02 (d, 3 H, 7-CH_3, $J_{7,8} = 6$); 1·165 (s, 3 H, 19-CH_3). For $C_{19}H_{30}O$ (274·4) calculated: 83·15% C, 11·02% H; found: 83·57% C, 11·06% H.

The analyses were carried out in the Analytical laboratories of our Institute under the direction of Dr J. Horáček. The IR *spectra were recorded by Mr P. Formánek (direction Dr J. Smolíková), the* ^{1}H-NMR *spectra by Dr M. Buděšínský.*

REFERENCES

1. Burn D., Butcher F. K., Cole A., Coombs R. A., Davies M. T., Green M. J., Petrow V.: Tetrahedron *24*, 4033 (1968).
2. Gates S., Wallis E. S.: J. Org. Chem. *20*, 610 (1955).
3. Ohloff G., Farnow H., Philipp W., Schade G.: Justus Liebigs Ann. Chem. *625*, 206 (1959).

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