ON STEROIDS. CXXXIV.*

B-NOR AND B-HOMOSTEROIDS WITH A POTENTIAL ANTIANDROGENIC ACTIVITY

A. KASAL and F. ŠORM

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6

Received July 7th, 1970

The contraction of the ring B in the lactone of 3β-acetoxy-17β-hydroxy-5-androsten-16β-ylacetic acid (*II*) was carried out by oxidation, recyclisation and decarboxylation in two reaction steps. The enlargement of the B-ring in lactone *II* on reaction with diazomethane gave a product resulting from both one and two insertions of the $-CH_2-$ groups, *i.e.* derivatives of B-homo-5-androsten-7a-one (*XIV*) and 7β-acetyl-5-androstene (*XVII*). The transformation of the lactone ring to the tetrahydrofuran ring in substance *X* was carried out on reduction with lithium aluminum hydride and cyclisation of the corresponding 1,4-diol *XII*. Substances *XIII*, *IX* and *XVI* were submitted to biological tests.

Antiandrogenic activity was observed in a number of substances of various types, of steroid and non-steroid character, but up to the present time efforts to correlate this activity with the structure were unsuccessful[1]. The experiences of this Laboratory demonstrated that some steroids with the modified ring B[2,3] also belong to this class, as well as certain steroid derivatives with an oxygen containing ring fused with the ring D[4,5]. In this paper we describe the preparation and the properties of compounds in which both structural features are combined.

To prepare the derivatives of B-nor series we used the lactone of 3β,17-dihydroxy-5-androsten-16β-ylacetic acid[6] (*I*) the ring B of which was contracted by a known procedure[7–10]. Oxidation of lactone *II* gave the seco-acid *III* in a 39·5% yield (average), but the latter would not crystallise. The analyses and the IR spectra corroborating the presence of the acetoxy group (1738, 1250 cm^{-1}), the lactone function (1768, 1178 cm^{-1}), the carboxyl group (2400 – 3500 cm^{-1}), and another carbonyl group (1708 cm^{-1}) are in good agreement with the structure of the expected product. Neutral fraction after oxidation of compound *II* contained 13% of the starting com-

* Part CXXXIV: This Journal *36*, 132 (1971).

I, R = H
II, R = Ac
III
IV
V
VI
VII, R = Ac
VIII, R = H
IX
X
XI
XII
XIII

pound and 28% of a substance containing an additional keto group conjugated with a double bond (1668 and 1635 cm^{-1}). The strongly negative molecular rotation (−413°)[11] and the position of the absorption maximum in the UV spectrum (236 nm, log ε 4·08)[12] show that compound *IV* is a product of allylic oxidation[13] in position 7. From a few other minor products we isolated compound *V* which in addition to an unchanged substitution in positions 3, 16, and 17 also contained a carbonyl group (1705 cm^{-1}) and a tetrasubstituted double bond ($\lambda_{max}^{CH_3OH}$ 203 nm, log ε 3·47; no C=C—H signals in the NMR spectrum). The analysis and the mass spectra show that the molecule of compound *V* contains 2 oxygen atoms more and 2 hydrogen atoms less than the starting substance. In the NMR spectrum signals of $C_{(19)}$-H were observed at 1.065 p.p.m. (singlet), and in the —CH—OR region only the signals for original 3α-H and 17α-H were observed. On the basis of these data we propose for this compound the structure of an unsaturated δ-lactone, *V*, the formation of which we interprete by a Wagner-Meerwein type rearrangement[14] taking place during the oxidation.

Intramolecular condensation of the keto acid of type *III* is usually carried out[8,9] using benzoyl chloride in pyridine and the formed β-lactone is then submitted to pyrolysis giving rise to a Δ^5-double bond in the molecule of the B-norsteroid. When applied to keto acid *III* this procedure led *via* the unisolated intermediate *VI* directly to B-norderivative *VII*, as demonstrated by elemental analysis and the IR spectrum of the product. The total average yield of product *VII* with the contracted ring B was 9%.

The hydrolysis of the acetoxy group in compound *VII* was carried out under the conditions of acid catalysed methanolysis, and Oppenauer oxidation gave the unsaturated ketone *IX*. From it we prepared the ether of B-nortestosterone *XIII* in the following manner: hydride reduction of lactone *IX* afforded 16β-ethyl-4-androstene-3β,16b,17β-triol(*XI*) *via* hydroxy lactone *X*. For the regeneration of the keto group in position 3 we used the method of selective oxidation of the allyl group with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone[15,16]. The cyclisation of diol *XII* was carried out using tosyl chloride in pyridine[4,5,17].

Another substance the pharmacodynamic activity of which had interested us was lactone of 3,7a-dioxo-17-hydroxy-B-homo-4-androsten-16β-ylacetic acid (*XVI*). The keto derivative *IV* described above served as starting material for this substance which on reaction with diazomethane in the presence of aluminum chloride as catalyst[18] gave a mixture in which 2 main components prevailed. On chromatography on silica gel we obtained a polar component (30%) which had the physico-chemical properties expected for product *XIV*: elemental analysis and the mass spectrum showed that one CH_2 group only was inserted into the molecule of the starting ketone. In the IR spectrum the absorption of the cyclohexanone system disappeared and the absorption of a non-conjugated keto group (1712 cm^{-1}) and a double bond (1641 cm^{-1}) appeared. The signals in the NMR spectrum at 3·62 p.p.m. ($C_{(7)}$—H) and

IV
XIV, R = Ac
XV, R = H
XVI
XVII, R = Ac
XVIII, R = H
XIX
XX, R = H
XXI, R = Ac
XXII
XXIII
XXIV

5·45 p.p.m. ($C_{(6)}$—H) have a character identical with those of the corresponding signals of authentic 3β-acetoxy-B-homo-5-cholesten-7a-one[18]. The nonpolar component (25%) contains in addition to a γ-lactone grouping and acetoxyl group (1768, 1178; 1726, 1255, 1032 cm^{-1}) also an acetyl group bound to a carbon atom (1712 cm^{-1}, 2.173 p.p.m., singlet 3 H). The C=C bond in this substance is of secondary-tertiary character (5·175 p.p.m., broad multiplet, 1 H). The mass spectrum of this compound does not contain a molecular peak, but the spectrum of dihydroderivative *XXI* shows that 2 CH_2 groups were inserted into the molecule during the homologisation reaction. These data lead to the formulation of structure *XVII*. In acid and alkaline medium substance *XVII* changes only to the corresponding hydroxy derivative *XVIII* from which on reacetylation the unchanged product *XVII* is obtained. Neither the position of the double bond, nor the configuration of the acetyl group changes, which is in good agreement with the proposed structure *XVII* with a stable[19] β, γ-position of the double bond in relation to the carbonyl group and a thermodynamically more stable configuration of the acetyl group. This stereospecificity cannot be assigned without further experiments directly to the homologisation reaction itself because during the working up and the separation of the reaction mixture isomerisation of the possibly formed 7α-isomer could have taken place. Similarly, neither can the configuration of the intermediates[20,21], *i.e.* of epoxide *XXII* which isomerises under the influence of aluminum chloride to aldehyde *XXIII* which reacts with another molecule of diazomethane and gives methyl ketone *XVII*, be discussed. Both products of homologisation, *XIV* and *XVII*, were submitted after hydrolysis to Oppenauer oxidation to corresponding ketones. Under these conditions the double bond is shifted in both cases to conjugation with the 3-keto group, as shown by UV and IR spectra.

Substances *IX*, *XIII*, and *XVI* were submitted to biological testing and the results of the tests will be published later.

EXPERIMENTAL

Unless stated otherwise IR spectra and specific rotations were measured in chloroform solutions, UV spectra in ethanol, and NMR spectra in deuteriochloroform, using tetramethylsilane as internal standard. Melting points were determined on a Kofler block and they are not corrected.

Lactone of 3β-Acetoxy-17β-hydroxy-5-androsten-16β-ylacetic Acid (*II*)

Hydroxy derivative *I* (ref.[6]) (360 mg) was acetylated with acetic anhydride (3 ml) in pyridine (3 ml) at room temperature for 20 hours. The reaction mixture was worked up in the usual manner to afford 350 mg of crude acetate, m.p. 200—203°C. After crystallisation from acetone the melting point rose to 204—205°C $[\alpha]_D^{20}$ −32° (*c* 2·5). For $C_{23}H_{32}O_4$ (372·5) calculated: 74·16% C, 8·66% H; found: 74·03% C, 8·72% H.

3β-Acetoxy-5-oxo-17β-hydroxy-16β-ethyl-5,6-secoandrostane-6,16b-dioic Acid, 16b→17 Lactone (*III*)

A solution of chromium trioxide (2·3 g) in 50% aqueous acetic acid (7 ml) was added dropwise over one hour to a stirred solution of lactone *II* (2·8 g) in acetic acid (30 ml) and after another hour of stirring at 55°C the excess oxidant was eliminated by the addition of methanol (3 ml). The reaction mixture was concentrated *in vacuo* to one third of its volume from a bath the temperature of which did not exceed 40°C. The product was extracted with ether and the extract was reextracted four times with 3% sodium hydrogen carbonate solution. The alkaline extract was washed with ether and then acidified with hydrochloric acid. The separated acidic material was extracted with ether and the dried extract was evaporated to give a non-crystalline residue (0·98 g). IR spectrum: 1178, 1250, 1708, 1738, 1768, 2400–3500 cm^{-1}. For $C_{23}H_{32}O_7$ (420·5) calculated: 65·69% C, 7·67% H; found: 65·41% C, 7·92% H.

Lactone of 3β-Acetoxy-7-oxo-17β-hydroxy-5-androsten-16β-ylacetic Acid (*IV*)

The ethereal neutral fraction from the preceding experiment, from which acidic material was extracted with sodium hydrogen carbonate, was separated chromatographically to 2 components: the less polar one (250 mg) was identical with the starting lactone *II* and the more polar (610 mg) had m. p. 215–217 °C (from acetone). $[\alpha]_D^{20} -107°$ (*c* 0·9). UV spectrum: λ_{max} 236 nm (log ε 4·09). IR spectrum: 1175, 1250, 1635, 1668, 1728, and 1765 cm^{-1}. For $C_{23}H_{30}O_5$ (386·5) calculated: 71·48% C, 7·82% H; found: 71·45% C, 7·98% H. When reproduced at a larger scale the oxidation of 50 g of lactone gave 22·2 g acid *III*, 14·8 g of 7-ketone *IV*, and 6·5 of the regenerated starting compound *II*.

3β-Acetoxy-5α-17β-dihydroxy-5β-methyl-16β-ethyl-19-nor-5,6-seco-androst-9-ene-6,16b-dioic Acid Dilactone (*V*)

During the above described chromatography of the neutral fraction after oxidation of compound *II* (50 g) we isolated a compound having the probable proposed structure (450 mg); m.p. 237–238°C (acetone–heptane), $[\alpha]_D^{20} +57°$ (*c* 2·3). IR spectrum: 1176, 1250, 1705, 1730, and 1767 cm^{-1} UV spectrum: $\lambda_{max}^{CH_3OH}$ 203 nm (log ε 3·47); mas spectrum: $(M\text{-}60)^+/_e = 342$. NMR spectrum: 0·72 p.p.m. (s, 3 H,), 1·065 p.p.m. (s, 3 H), 2·02 p.p.m. (s, 3 H), 4·36 p.p.m. (d, I = 9 Hz, 1 H), 4·91 p.p.m. (m, 1 H). For $C_{23}H_{30}O_6$ (402·5) calculated: 68·63% C, 7·51% H; found: 68·60% C, 7·52% H.

Lactone of 3β-Acetoxy-17β-hydroxy-B-nor-5-androsten-16β-ylacetic Acid (*VII*)

A solution of keto acid *III* (860 mg) in pyridine (3 ml) was mixed with benzoyl chloride (1 ml) and allowed to stand at room temperature for 50 hours. The reaction mixture was decomposed by pouring it onto ice. The mixture was extracted with ether and the extract washed with dilute hydrochloric acid, water, sodium hydrogen carbonate solution, and water and dried over sodium sulfate. After filtration ether was evaporated under reduced pressure to dryness. The residue was chromatographed on silica gel (5% ether in benzene) to give 190 mg of product. After crystallisation from acetone m.p. was 209–210°C (166 mg), $[\alpha]_D^{20} -102°$ (*c* 1·6). For $C_{22}H_{30}O_4$ (385·5) calculated: 73·71% C, 8·44% H; found: 73·51% C, 8·31% H.

Lactone of 3β,17β-Dihydroxy-B-nor-androsten-16β-ylacetic Acid (*VIII*)

A solution of acetate *VII* (4·4 g) in chloroform (24 ml) and methanol (240 ml) was acidified with conc. hydrochloric acid (5 ml) and allowed to stand at 30°C for 20 hours. After evaporation

of the reaction mixture *in vacuo* the product was dissolved in chloroform and washed with potassium hydrogen carbonate and water. The organic extract was dried over sodium sulfate and evaporated to dryness. The residue was crystallised from acetone; m.p. 217–218°C (3·7 g). $[\alpha]_D^{20}$ −100° (*c* 1·6). For $C_{20}H_{28}O_3$ (316·4) calculated: 75·91% C, 8·29% H; found: 75·70% C, 8·88% H.

Lactone of 17β-Hydroxy-3-oxo-B-nor-4-androsten-16β-ylacetic Acid (*IX*)

Hydroxy derivative *VIII* (3·1 g) was oxidised according to Oppenauer using cyclohexanone (40 ml), toluene (150 ml), and aluminum isopropylate (2·6 g). After 15 minutes refluxing the mixture was decomposed by pouring it onto ice and acidifying with hydrochloric acid. The product was extracted with benzene, washed with water until neutral, and the volatile components were eliminated by steam distillation. Crystallisation from acetone afforded ketone *IX* (2·1 g), m.p. 253–254°C, $[\alpha]_D^{20}$ −21° (*c* 1·5). IR spectrum: 1 030, 1175, 1659, 1765 cm^{-1}. For $C_{20}H_{26}O_3$ (314·4) calculated: 76·40% C, 8·34% H; found: 76·68% C, 8·49% H.

Lactone of 3β, 17β-Dihydroxy-B-nor-4-androsten-16β-ylacetic Acid (*X*)

Keto lactone *IX* (1·5 g) was reduced using 300 mg of lithium aluminum hydride in tetrahydrofuran (20 ml). After 2 hours refluxing of the mixture the excess of the hydride was decomposed with a saturated sodium sulfate solution and the reaction mixture was saturated with anhydrous sodium sulfate. The inorganic material was filtered off with suction and washed with chloroform. The filtrate was concentrated and the residue crystallised 3 times from ethanol; m.p. 251–253°C (250 mg), $[\alpha]_D^{20}$ −51° (methanol, *c* 0·6). For $C_{20}H_{28}O_3$ (316·5) calculated: 75·91% C, 8·92% H; found: 75·73% C, 8·92% H.

16β-Ethyl-B-nor-4-androstene-3β,16b,17β-triol (*XI*)

A) *From keto lactone* IX: The mother liquors from the preceding experiment were crystallised from a mixture of methanol and chloroform and we obtained thus a triol, m.p. 203–206°C (930 mg). The sample for analysis was obtained on crystallisation from methanol, chloroform, and heptane, m.p. 206–208°C; $[\alpha]_D^{20}$ −52° (methanol, *c* 0·5). IR (KBr): 1034, 1054, 1082, and 3020 cm^{-1}). For $C_{20}H_{32}O_3$ (320·5) calculated: 74·95% C, 10·07% H; found: 74·95% C, 9·93% H.

B) *From hydroxy lactone* X: A solution of compound *X* (200 mg) in tetrahydrofuran (15) was refluxed with lithium aluminum hydride (approx. 150 mg) for 5 hours. The excess reagent was decomposed by addition of ethyl acetate and then with aqueous sodium sulfate solution. The mixture was saturated with anhydrous sodium sulfate, filtered, and the inorganic material on the filter was washed with chloroform. The filtrate was concentrated to 2 ml and after short standing the precipitated crystals were filtered off under suction (150 mg). The melting point and the mixture melting point with the substance prepared under *A* were identical.

16b,17β-Dihydroxy-16β-ethyl-B-nor-4-androsten-3-one (*XII*)

To a suspension of triol *XI* (300 mg) in boiling tetrahydrofuran (20 ml) 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (360 mg) were added after cooling and the mixture was allowed to stand at room temperature for 4 hours. Methanol (20 ml) was added to the mixture which was then evaporated under reduced pressure to a quarter of its volume. Benzene (20 ml) was added and the mixture was evaporated once more to one quarter of its volume. The product was partitioned between

benzene and an aqueous potassium hydrogen carbonate solution. The organic phase was washed with a sodium chloride solution, dried over sodium sulfate and evaporated to dryness. The residue was crystallised from acetone. M.p. 201—203°C (150 mg). It increased after repeated crystallisation from dichloromethane and heptane to 204—206°C; $[\alpha]_D^{20}$ −28° (*c* 0·7). IR spectrum: 3600, 3400, and 1657 cm^{-1}. For $C_{20}H_{30}O_3$ (318·4) calculated: 75·43% C, 9·50% H; found: 75·52% C, 9·57% H.

Tetrahydrofurano[3′,2′ : 16β,17β]-B-nor-4-androsten-3-one (*XIII*)

To a solution of dihydroxyketone *XII* (530 mg) in pyridine (10 ml) 1 g of *p*-toluenesulfonyl chloride was added and the mixture allowed to stand at 35°C for 48 hours. The reaction mixture was decomposed by pouring it on ice. The product was extracted with heptane which was then washed with a solution of sodium chloride, dried over sodium sulfate, filtered and evaporated *in vacuo*. The residue, m.p. 100—110°C (550 mg), was crystallised from ether at −64°C. The product had m.p. 126—127°C (160 mg), $[\alpha]_D^{20}$ 0° (*c* 1·0). IR spectrum: 1660, 1091, 1080, and 1070 cm^{-1}. For $C_{20}H_{28}O_2$ (300·4) calculated: 79·95% C, 9·38% H; found: 79·85% C, 9·44% H.

Lactone of 3β-Acetoxy-17β-hydroxy-7β-acetyl-5-androsten-16β-ylacetic Acid (*XVII*)

To a solution of lactone *II* (2·6 g) in benzene (250 ml) a dried diazomethane solution in ether (approx. 1·5 g in 120 ml) was added followed by anhydrous aluminum chloride (approx. 100 mg) and the reaction mixture was allowed to stand under occasional shaking at room temperature for 1 hour. Excess diazomethane was decomposed by acetic acid and the solution was filtered through a layer of aluminum oxide (neutral, act. III—IV). The filtrate was evaporated *in vacuo* and chromatographed on silica gel with benzene containing 10% of ether. Crystalline fraction of *XVII* was obtained (1·15 g), m.p. 200°C which was recrystallised from acetone (790 mg, 245—248°C) and then from acetone–heptane; m.p. of the analytical sample was 249—251°C; $[\alpha]_D^{20}$ +26° (*c* 1·6). IR spectrum: 1032, 1178, 1255, 1712, 1726, 1768 cm^{-1}. NMR spectrum: 0·78 p.p.m. (s, 3 H), 1·070 p.p.m. (s, 3 H), 2·020 p.p.m. (s, 3 H), 2.173 p.p.m. (S, 3 H), 4·345 p.p.m. (d, $J = 9$ Hz), 4·590 p.p.m. (mt, 1 H), 5·175 p.p.m. (broad multiplet). For $C_{25}H_{34}O_5$ (414·6) calculated: 72·43% C 8·27% H; found: 72·38% C, 8·12% H.

Lactone of 3β-Acetoxy-7a-oxo-17β-hydroxy-B-homo-5-androsten-16β-ylacetic Acid (*XIV*)

The more polar fractions from the chromatography described in the preceding experiment gave 1·1 g of compound *XIV* which after crystallisation from acetone–heptane had m.p. 212—213°C; $[\alpha]_D^{20}$ +72° (*c* 1·6). IR spectrum: 1046, 1474, 1641, 1712, 1770 cm^{-1}. NMR spectrum: 0·805 p.p.m. (s, 3 H), 1·018 p.p.m. (s, 3 H), 2·020 p.p.m. (s, 3 H), 3·625 p.p.m. (d, $J = 13$ Hz, 1 H), 4·415 p.p.m. (d mt, $J = 9$ Hz), 4·560 p.p.m. (mt, 1 H), and 5·445 p.p.m. (d mt, $J = 9$ Hz, 1 H). For $C_{24}H_{32}O_5$ (400·5) calculated: 71·97% C, 0·05% H; found: 72·12% C, 8·09% H.

Lactone of 7-Oxo-17β-hydroxy-3,5-androstadiene-16β-ylacetic Acid (*XXIV*)

A) Non-polar fractions from the above described chromatography gave substance *XXIV* (75 mg), m.p. 267—270°C (acetone, heptane); $[\alpha]_D^{20}$ −322° (*c* 1·0); IR spectrum: 1595, 1625, 1656, 1769 cm^{-1}. UV spectrum: log $\varepsilon_{280\,nm}^{EtOH}$ 4·33. For $C_{21}H_{26}O_3$ (326·4) calculated: 77·27% C, 8·03% H; found: 77·26% C, 7·96% H.

B) Acetoxy derivative *II* (20 mg) was dissolved in chloroform (0·2 ml) and methanol (2 ml) and 1 drop of hydrochloric acid was added. After 22 hours standing at 35°C 5 ml of chloroform

were added and the mixture was evaporated in vacuo to 1/4 of its volume. The product was then partitioned between chloroform and an aqueous solution of potassium hydrogen carbonate. The organic layer was washed with water, then dried and evaporated. The residue (15 mg) melted at 260—265°C. After crystallisation from acetone and heptane the melting point was undepressed on admixture of the preparation from the preceding experiment (*A*). IR spectra of both samples are also identical.

Lactone of 3β,17β-Dihydroxy-7a-oxo-B-homo-5-androsten-16β-ylacetic Acid (*XV*)

A solution of the acetoxy derivative *XIV* (350 mg) in a mixture of chloroform (2·5 ml), methanol (25 ml), and conc. hydrochloric acid (0·5 ml) was allowed to stand at 35°C for 24 hours. The solution was concentrated under reduced pressure to one fourth of its volume and the product was partitioned between chloroform and aqueous potassium hydrogen carbonate. The dried extract was evaporated to dryness and crystallised from benzene; m.p. 226—228°C (215 mg) $[\alpha]_D^{20}$ +111° (*c* 1·2). IR spectrum: 1030, 1047, 1175, 1420, 1639, 1709, 3600 cm^{-1}. UV spectrum: 285 nm (log ε 2·10). For $C_{22}H_{30}O_4$ (358·5) calculated: 73·71% C, 8·44% H; found: 73·97% C, 8·38% H.

Lactone of 3,7a-Dioxo-17β-hydroxy-B-homo-4-androsten-16β-ylacetic Acid (*XVI*)

Hydroxy derivative *XV* (350 mg) was oxidised according to Oppenauer using cyclohexanone (8 ml), toluene (30 ml), and aluminum isopropylate (0·5 g). The reaction mixture was worked up as in the case of substance *IX* and the product was crystallised from benzene and heptane; m.p. 201—203°C (240 mg); $[\alpha]_D^{20}$ −93° (*c* 1·0). For $C_{22}H_{28}O_4$ (356·4) calculated: 74·13% C, 7·92% H; found: 74·19% C, 7·86% H.

Lactone of 3β,17β-Dihydroxy-7β-acetyl-5-androsten-16β-ylacetic Acid (*XVIII*)

Acetoxy derivative *XVII* (1·3 g) was hydrolysed in a solution of hydrochloric acid (2 ml) in methanol (100 mg) and chloroform (10 ml) at 34°C for 24 hours. The reaction mixture was worked up exactly as in the case of substance *XV*. The melting point of the product before crystallisation was 260—263°C (1·1 g), after crystallisation from chloroform and heptane it rose to 266—268°C; $[\alpha]_D^{20}$ +77° (*c* 1·4). IR spectrum: 1712, 1768, 3600 cm^{-1}. For $C_{23}H_{32}O_4$ (372·5) calculated: 74·16% C, 8·66% H; found: 74·12% C, 8·71% H. Acetylation of a sample of this compound with acetic anhydride in pyridine gave acetate *XVII*, mixture m.p. with compound *XVII* undepressed.

Lactone of 3-Oxo-17β-hydroxy-7β-acetyl-4-androsten-16β-ylacetic Acid (*XIX*)

Hydroxy derivative *XVIII* (50 mg) was oxidised according to Oppenauer using cyclohexanone (3 ml), toluene (10 ml), and aluminum isopropylate (0·1 g). The reaction product was worked up as in the case of substance *IX*, and the product was crystallised from a mixture of acetone and heptane; m.p. 215—218°C; $[\alpha]_D^{20}$ −7° (*c* 0·7). IR spectrum: 1178, 1359, 1622, 1663, 1714, 1770 cm^{-1}. For $C_{23}H_{30}O_4$ (370·5) calculated: 74·56% C, 8·16% H; found: 74·68% C, 8·18% H.

Lactone of 3β,17β-Dihydroxy-7β-acetyl-5α-androstan-16β-ylacetic Acid (*XX*)

Substance *XVIII* (170 mg) was hydrogenated in acetic acid (4 ml) on platinum oxide (70 mg) to completion. After 2 hours the catalyst was filtered off and the filtrate concentrated under

reduced pressure to dryness. The residue was crystallised from acetone, m.p. 302—305°C (90 mg). NMR spectrum: 0·755 p.p.m. (s, 3 H), 0·830 p.p.m. (c, 3 H), 2·6 p.p.m. (s, 3 H), 3·55 p.p.m. (mt, 1 H), 4·27 p.p.m. (d, $J = 9·5$ Hz). For $C_{23}H_{34}O_4$ 0·5 H_2O (383·5) calculated: 72·03% C, 9·19% H; found: 71·72% C, 9·02% H.

Lactone of 3β-Acetoxy-17β-hydroxy-7β-acetyl-5α-androstan-16β-ylacetic Acid (*XXI*)

A) *From compound* XX: Hydroxy derivative *XX* (60 mg) was acetylated with acetic anhydride in pyridine at room temperature for 20 hours. The reaction mixture was worked up in the conventional manner and the product recrystallised from acetone–heptane, m.p. 223—225°C, $[\alpha]_D^{20}$ −25° (*c* 0·7). IR spectrum: 1177, 1260, 1715, 1769 cm^{-1}. Mol. weight (mass spectrometry): 416. For $C_{25}H_{36}O_5$ (416·5) calculated: 72·08% C, 8·71% H; found: 71·89% C, 8·77% H.

B) *From compound* XVII: Lactone *XVII* (250 mg) was hydrogenated in acetic acid (5 ml) on platinum catalyst (60 mg). After filtration and evaporation of the solvent *in vacuo* the product was crystallised from acetone and heptane, m.p. 221—223°C (150 mg), undepressed on admixture of a sample prepared as under *A*; $[\alpha]_D^{20}$ −28° (*c* 1·1). IR spectrum is identical with that of the sample prepared under *A*.

For the measurement and the interpretation of the spectra our thanks are due to Mrs J. Smolíková, Mr P. Sedmera and Dr L. Dolejš. For the determination of elemental analyses we thank the group headed by Dr J. Horáček and for technical assistance Mrs J. Neumannová.

REFERENCES

1. Dorfman R. I.: *Methods of Hormone Research*, IV., p. 77. Academic Press, New York 1965.
2. Dorfman R. I., Fajkoš J., Joska J.: Steroids *3*, 675 (1964).
3. Saunders H. L., Holden K., Kerwin J. F.: Steroids *3*, 687 (1964).
4. Kasal A., Černý V.: This Journal *31*, 2759 (1966).
5. Kasal A., Linet O.: This Journal *34*, 3479 (1969).
6. Kurath P., Cole W.: J. Org. Chem. *26*, 1939 (1961).
7. Šorm F.: This Journal *12*, 437 (1947).
8. Šorm F., Dyková H.: This Journal *13*, 407 (1948).
9. Joska J., Fajkoš J., Šorm F.: This Journal *25*, 2341 (1960).
10. Boswell G. A , Dauben W. G., Ourisson G., Rull T.: Bull. Soc. Chim. France *1958*, 1598.
11. Barton D. H. R., Klyne W.: Chem. Ind. (London) *1948*, 755.
12. Dorfman L.: Chem. Rev. *53*, 47 (1953).
13. Vindaus A., Lettré H., Schenck F.: Ann. *520*, 98 (1935).
14. Lettré H., Müller M.: Ber. *70*, 1947 (1937).
15. Barton D. H. R., Hesse R. H., O'Brien R. E., Pechet M. M. J. Org. Chem. *33*, 1562 (1968).
16. Burn D., Petrow V., Weston G. O.: Tetrahedron Letters *9*, 14 (1960).
17. Kurath P., Oslapas R.: J. Med. Chem. *12*, 5 (1969).
18. Kohout L., Fajkoš J., Šorm F.: This Journal *34*, 601 (1969).
19. Hubert A. J., Reimlinger H.: Synthesis *1969*, 97.
20. Dittus G. in: Houben-Weyl: *Methoden in der Organischen Chemie* Vol. 6/3, p. 414. Georg Tieme-Verlag, Stuttgart 1965.
21. Jones B., Price P.: Chem. Commun. *1969*, 1478.

Translated by Ž. Procházka.