ON STEROIDS. CXLV.*
SOME ANALOGUES OF B-NORMETHYLTESTOSTERONE

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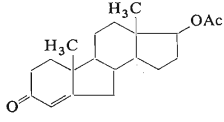
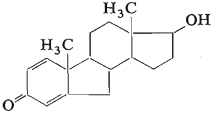
Received February 8th, 1972

Analogues of B-normethyltestosterone with a double bond in position 1,2 or with an oxygen function in position 6 have been prepared.

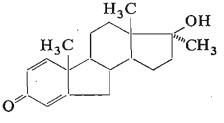
In our previous papers[1] we have described the synthesis of the B-noranalogue of methyltestosterone *V*. This compound has been found by Dorfman and coworkers[2] to be a potent anti-androgen and our attention was therefore turned to some analogues of B-normethyltestosterone. In this paper we describe the syntheses of the Δ^1-unsaturated as well as 6-oxygenated analogues of B-normethyltestosterone. B-Normethyltestosterone[1] (*V*) itself served as the starting compound for the syntheses of the 1,2-unsaturated and 6α-hydroxylated analogues. Dehydrogenation with selenium dioxide gave the dienone *IV*. The reaction has also been studied on B-nortestosterone acetate[1] (*I*) and gave the 1,4-diene *III* in good yield. In order to prepare the 6-hydroxylated analogues the ketone *V* was reduced by lithiumaluminium hydride to the allylic alcohol *VI*. Addition of hypobromous acid[3] to the acetate *VII* afforded next to a small amount of the bromohydrin *VIII* the desired olefin *IX*. It was transformed to the epoxide *X* which on treatment with base yielded the 6α-hydroxylated analogues of B-normethyltestosterone *XI*. The acetate *XII* was also obtained by an alternative route from the 5-hydroxy derivative *XXIII* on reflux with glacial acetic acid in analogy with the reaction observed[4] in the B-norcholestane series. Oxidation of the alco-



I

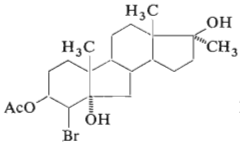


II, R = H
III, R = Ac

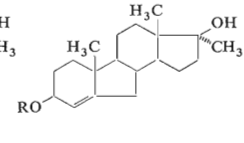


IV

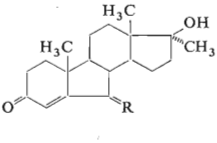
* Part CXLIV: This Journal *37*, 4091 (1972).



VIII

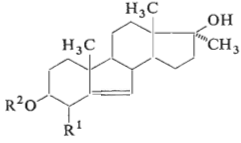


VI, R = H
VII, R = Ac

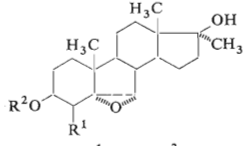


V, R = H_2
XI, R = H, OH
XII, R = H, OAc
XIII, R = O

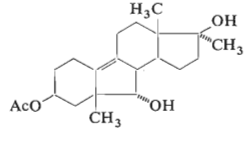
hol *XI* with Jones' reagent gave the 6-oxo-analogue of B-normethyltestosterone *XIII*. The epimeric 6β-hydroxy-B-normethyltestosterone (*XXXIII*) was synthesised from the olefin *XV*: Reaction with peracid afforded the epoxide *XVII* which of treatment with perchloric acid in dioxane yielded the triol *XX* as the main product; small amount of the rearranged[4–6] product *XVIII* was also obtained. Acetylation of the triol *XX* gave the diacetate *XXII*, hydrolysis on the other hand, led to the tetrol *XIX* which was oxidised to the dione *XXIV*. The triol *XX* was oxidised to the ketone *XXV* which on catalytic hydrogenation afforded the 6β-hydroxy derivative *XXVII*, characterised as the tetrol *XXVI*. Benzoylation followed by partial hydrolysis gave the



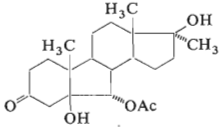
IX, R^1 = Br, R^2 = Ac
XIV, $R^1 = R^2$ = H
XV, R^1 = H, R^2 = Ac



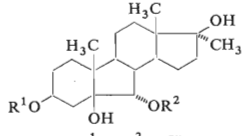
X, R^1 = Br, R^2 = Ac
XVI, $R^1 = R^2$ = H
XVII, R^1 = H, R^2 = Ac



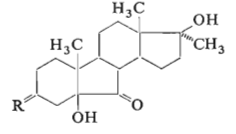
XVIII



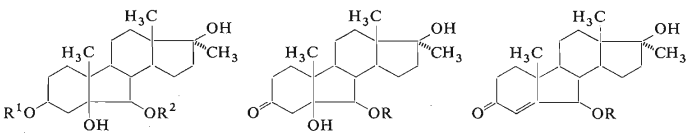
XXIII



XIX, $R^1 = R^2$ = H
XX, R^1 = Ac; R^2 = H
XXI, R^1 = H; R^2 = Ac
XXII, $R^1 = R^2$ = Ac



XXIV, R = O
XXV, R = H, OAc



XXVI, $R^1 = R^2 = H$
XXVII, $R^1 = Ac$; $R^2 = H$
XXVIII, $R^1 = H$; $R^2 = C_6H_5CO$
XXIX, $R^1 = Ac$; $R^2 = C_6H_5CO$

XXX, R = H
XXXI, R = Ac
XXXII, $R = C_6H_5CO$

XXXIII, R = H
XXXIV, R = Ac

alcohol *XXVIII* which was oxidised to the ketone *XXXII*, hydrolysed to the alcohol *XXX* and acetylated to the acetate *XXXI*. Dehydration with glacial acetic acid led smoothly to the unsaturated ketone *XXXIV* which was hydrolysed to the desired 6β-hydroxy-B-normethyltestosterone (*XXXIII*). This compound has recently been prepared[7] in our Laboratory by a different route. The biological evaluation of the compounds prepared is in progress and will be reported elsewhere.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 80°C/0·2 Torr. Optical measurements were carried out in chloroform solution unless otherwise stated. The IR measurements were carried out in tetrachloromethane. The identity of samples prepared by different routes was checked by mixture-melting points determinations, thin-layer, chromatography and by IR spectra. Ligroin of a b.p. 40—50°C was used unless otherwise stated.

17β-Hydroxy-B-norandrosta-1,4-dien-3-one (*II*)

The acetate[1] *III* (100 mg) in methanol (10 ml) was heated to 50°C for 1 h with a solution of potassium hydroxide (100 mg) in the same solvent. The excess alkali was removed with acetic acid, the organic solvents were distilled off under reduced pressure, and the product taken into ether. The ethereal solution was washed with water, dried, and the residue after evaporation of the solvent was chromatographed on a silica gel column (10 g) in benzene–ether (1 : 1). The corresponding fractions were combined, evaporated, and the residue was crystallised from ethyl acetate to yield 65 mg of the alcohol *II*, m.p. 157—159°C, $[\alpha]_D^{20}$ −62·5° (*c* 1·28). For $C_{18}H_{24}O_2$ (272·4) calculated: 79·37% C, 8·88% H; found: 79·18% C, 8·69% H.

17β-Acetoxy-B-norandrosta-1,4-dien-3-one (*III*)

A solution of the acetate[1] *I* (400 mg) in tert-butanol (30 ml) was treated with pyridine (0·1 ml) and selenium dioxide (250 mg) and the reaction mixture was heated to 100°C in a nitrogen atmosphere for 3 days. Water was then added, the product extracted into ether, and the ethereal solution was washed with dilute HCl, a $NaHCO_3$ solution, water, dried, and evaporated. The crude product was chromatographed over silica gel (50 g) in benzene–ether (9 : 1). Working up and crystallisation from ether–ligroin afforded 65 mg of the diene *III*, m.p. 146—147°C. $[\alpha]_D^{20}$ −53·5° (*c* 1·72); IR 1 740, 1 695, 1 664, 1 640, 1 605, 1 245, 1 036 cm^{-1}; UV: λ_{max} 242 nm (log ε 4·05). For $C_{20}H_{26}O_3$ (314·4) calculated: 76·40% C, 8·34% H; found: 76·51% V, 8·36% H.

17β-Hydroxy-17α-methyl-B-norandrosta-1,4-dien-3-one (*IV*)

The ketone *V* (3 g) in tert-butanol (240 ml) was heated to 100°C with pyridine (1 ml) and selenium dioxide (1·8 g) for 3 days. Similar working up as given in the foregoing experiment and chromatography over silica gel (300 g) in the same solvent mixture gave after crystallisation from ether–ligroin 552 mg of the ketone *IV*, m.p. 121—123°V, $[\alpha]_D^{20}$ −87° (*c* 1·37). For $C_{19}H_{26}O_2$ (286·4) calculated: 79·68% C, 9·15% H; found: 79·50% C, 9·09% H.

17α-Methyl-B-norandrost-4-ene-3β,17β-diol (*VI*)

A solution of the ketone *V* (4 g) in tetrahydrofuran (40 ml) and ether (100 ml) was treated with a solution of lithiumaluminum hydride (1·7 g) in ether (130 ml). The reaction mixture was stirred at room temperature for 30 min, the excess hydride was decomposed with ethyl acetate and wet ether, the ethereal solution was washed with dilute HCl, a $NaHCO_3$ solution, water, dried, and evaporated. The crude product was chromatographed on a silica gel column (200 g) in benzene–ether (2 : 1) to yield after working up and crystallisation from methanol–ethyl acetate 3·1 g of the alcohol *VI*, m.p. 110—111°C, $[\alpha]_D^{20}$ −71° (*c* 1·33). For $C_{19}H_{30}O_2$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·37% C, 10·19% H.

3β-Acetoxy-17α-methyl-B-norandrost-4-en-17β-ol (*VII*)

The diol *VI* (600 mg) was acetylated at room temperature with acetic anhydride (2 ml) in pyridine (7 ml) for 20 h. The reaction mixture was decomposed with ice, the product isolated with ether and the ethereal solution was worked up. Evaporation and crystallisation from methanol–water yielded 420 mg of the acetate *VII*, m.p. 55—57°C, $[\alpha]_D^{20}$ −115° (*c* 1·26). For $C_{21}H_{32}O_3$ (332·5) calculated: 75·86% C, 9·70% H; found: 75·91% C, 9·50% H.

3β-Acetoxy-4β-bromo-17α-methyl-5α-B-norandrostane-5,17β-diol (*VIII*)

A solution of the acetate *VII* (720 mg) in dioxane (45 ml) was treated succesively with water (8·2 ml), 9% perchloric acid (1·8 ml) and N-bromoacetamide (310 mg) and allowed to stand at room temperature for 1 h. The reaction mixture was diluted with water, the product taken into ether, and the ethereal solution was worked up, and evaporated. The residue was chromatographed over silica gel (100 g) in benzene–ether (4 : 1) to give after working up of the fractions containing the lipophilic component and crystallisation from methanol–water 160 mg of the diol *VIII*, m.p. 156—158°C, $[\alpha]_D^{20}$ −37° (*c* 1·44). For $C_{21}H_{33}BrO_4$ (429·4) calculated: 58·73% C, 7·74% H, 18·61% Br; found: 58·60% C, 7·52% H, 18·59% Br. Fractions containing the polar component (foregoing experiment) were combined, evaporated, and the product was crystallised from methanol to yield 510 mg of 3β-acetoxy-4β-bromo-17α-methyl-B-norandrost-5-en-17β-ol (*IX*), m.p. 142—144°C, $[\alpha]_D^{20}$ −170° (*c* 1·24). For $C_{21}H_{31}BrO_3$ (411·4) calculated: 61·30% C, 7·59% H, 19·42% Br; found: 61·14% C, 7·42% H, 19·30% Br.

3β-Acetoxy-4β-bromo-5,6α-epoxy-17α-methyl-5α-B-norandrostan-17β-ol (*X*)

A solution of perphthalic acid (960 mg) in chloroform (8 ml) was added to a solution of the olefin *IX* (1 g) in the same solvent (15 ml) and allowed to stand at room temperature for 24 h. The reaction mixture was diluted with ether, the excess peracid was extracted with 5% Na_2CO_3, and the ethereal solution was evaporated. The residue on crystallisation from methanol gave 660 mg of the epoxide *X*, m.p. 148—150°C, $[\alpha]_D^{20}$ −78° (*c* 1·48). For $C_{21}H_{31}BrO_4$ (427·4) calculated: 59·01% C, 7·31% H, 18·70% Br; found: 58·79% C, 7·18% H, 19·00% Br.

6α,17β-Dihydroxy-17α-methyl-B-norandrost-4-en-3-one (*XI*)

The epoxide *X* (660 mg) in methanol (30 ml) was treated with a solution of KOH (900 mg) in the same solvent (60 ml) and the reaction mixture was kept at 50°C for 1 h. Water was added, the product extracted with ethyl acetate, the extract was washed with water, dried, and evaporated. The residue was chromatographed over silica gel (100 g) in ether to yield after working up and crystallisation from ethyl acetate–ether 370 mg of the diol *XI*, m.p. 204—205°C, $[\alpha]_D^{20}$ −32° (*c* 1·19); IR (nujol): 3470, 3370, 1642 cm^{-1}. For $C_{19}H_{28}O_3$ (304·4) calculated: 74·96% C, 9·27% H; found: 75·26% C, 9·35% H.

17β-Hydroxy-6α-acetoxy-17α-methyl-B-norandrost-4-en-3-one (*XII*)

a) The diol *XXIII* (420 mg) in glacial acetic acid (15 ml) was refluxed for 5 hours. The reaction mixture was diluted with water, the product taken into ether, and the ethereal solution was washed with a $NaHCO_3$ solution, water, dried, and evaporated. The residue on crystallisation from ethyl acetate–ligroin yielded 295 mg of the ketone *XII*, m.p. 148—149°C, $[\alpha]_D^{20}$ −136° (*c* 1·29). For $C_{21}H_{30}O_4$ (346·5) calculated: 72·80% C, 8·73% H; found: 72·81% C, 8·56% H. *b*) The diol *XI* (100 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (0·4 ml) at room temperature for 20 h. Usual working up and crystallisation from ethyl acetate–ligroin gave 58 mg of the acetate *XII*, m.p. 147—149°C, $[\alpha]_D^{20}$ −133° (*c* 1·18).

17β-Hydroxy-17α-methyl-B-norandrost-4-ene-3,6-dione (*XIII*)

A mixture of the diol *XI* (500 mg) in pyridine (15 ml) was treated with chromic acid (220 mg) in pyridine (6 ml) and allowed to stand at room temperature for 20 h, poured into 5% $NaHCO_3$, and the product extracted with ethyl acetate. The extract was washed with dilute HCl, a $NaHCO_3$ solution, water, dried, and evaporated. The residue was chromatographed on a silica gel column (60 g) in ligroin–acetone (4 : 1). Working up and crystallisation from ethyl acetate gave 310 mg of the dione *XIII*, m.p. 168—170°V, $[\alpha]_D^{20}$ +168° (*c* 1·65); IR (nujol): 3440, 1720, 1670, 1635 cm^{-1}. For $C_{19}H_{26}O_3$ (302·4) calculated: 75·46% C, 8·67% H; found: 75·18% C, 8·60% H.

5,6α-Epoxy-17α-methyl-5α-B-norandrostane-3β,17β-diol (*XVI*)

A solution of the diol[1] *XIV* (1 g) in chloroform (75 ml) was treated with a solution of perbenzoic acid (400 mg) in the same solvent (8 ml) and allowed to stand at room temperature for 2 days. The reaction mixture was diluted with ether, the excess peracid removed with 5% Na_2CO_3 and the ethereal solution was worked up. Evaporation and crystallisation from ethyl acetate afforded 850 mg of the epoxide *XVI*, m.p. 193—195°C, $[\alpha]_D^{20}$ −63° (*c* 1·27 in ethanol). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·68% C, 9·78% H.

3β-Acetoxy-5,6α-epoxy-17α-methyl-5α-B-norandrostan-17β-ol (*XVII*)

A solution of perphthalic acid (6 g) in ether (60 ml) was added to a solution of the acetate *XV* (7·2 g) in the same solvent (150 ml) and allowed to stand at room temperature for 20 h. The reaction mixture was worked up similarly as described in the foregoing experiment, and the product was crystallised from methanol–water to yield 7 g of the epoxide *XVII*, m.p. 73—75°C, $[\alpha]_D^{20}$ −66·5° (*c* 1·29). For $C_{21}H_{32}O_4.CH_3OH$ (380·5) calculated: 69·44% C, 9·54% H; found: 69·21% C, 9·34% H.

3β-Acetoxy-5β,17α-dimethyl-B,19-bisnorandrost-9-ene-6α,17β-diol (*XVIII*)

The epoxide *XVII* (3 g) in acetone (120 ml) was treated with perchloric acid (70%; 2·5 ml) in water (6 ml) and allowed to stand at room temperature for 80 min. The reaction mixture was neutralised with $NaHCO_3$, diluted with water, the product extracted with ethyl acetate, and the extract worked up. The residue was chromatographed over silica gel (400 g) in benzene–ether (1 : 1). The corresponding fraction containing the lipophilic component were combined, evaporated, and the residue was crystallised from ligroin–ethyl acetate to yield 270 mg of the diol *XVIII*, m.p. 131–133°C, $[\alpha]_D^{20}$ +33° (*c* 1·50). For $C_{21}H_{32}O_4$ (348·5) calculated: 72·38% C, 9·26% H; found: 72·63% C, 9·49% H.

17α-Methyl-5β-B-norandrostane-3β,5β,6α,17β-tetrol (*XIX*)

The acetate *XX* (1·68 g) in methanol (75 ml) was refluxed for 2 h with a solution of K_2CO_3 (1·4 g) in water (15 ml). Methanol was removed under reduced pressure, the residue treated with water, and the product extracted into ethyl acetate. Working up and crystallisation from ligroin afforded 1·2 g of the tetrol *XIX*, m.p. 99–101°C, $[\alpha]_D^{20}$ −15° (*c* 1·92 in ethanol). For $C_{19}H_{32}O_4$ (324·5) calculated: 70·33% C, 9·94% H; found: 70·60% C, 9·73% H. Elution of the chromatography after isolation of the diol *XVIII* with the same solvent mixture, working up of the fractions containing the polar component, and crystallisation from ligroin–ethyl acetate gave 1·6 g of the 3β-acetoxy-17α-methyl-5β-B-norandrostane-5β,6α,17β-triol (*XX*), m.p. 78–81°C, $[\alpha]_D^{20}$ −14·2° (*c* 2·68 in ethanol). For $C_{21}H_{34}O_5$ (366·5) calculated: 68·82% C, 9·35% H; found: 68·70% C, 9·13% H.

6α-Acetoxy-17α-methyl-5β-B-norandrostane-3β,5β,17β-triol (*XXI*)

A solution of the diacetate *XXII* (1·27 g) in methanol (75 ml) was heated to 50°C for 10 min with a solution of K_2CO_3 (960 mg) in water (14 ml). The alkali was neutralised with acetic acid, methanol distilled of *in vacuo*, and the product isolated with ethyl acetate. Working up and evaporation left 1·05 g of a crude product which after chromatography over silica gel (100 g) in ether and crystallisation from ligroin–ethyl acetate afforded 720 mg of the acetate *XXI*, m.p. 166–168°C, $[\alpha]_D^{20}$ −57° (*c* 1·33). For $C_{21}H_{34}O_5$ (366·5) calculated: 68·82% C, 9·35% H; found: 68·83% C, 9·13% H.

3β,6α-Diacetoxy-17α-methyl-5β-B-norandrostane-5β,17β-diol (*XXII*)

The monoacetate *XX* (1·5 g) was acetylated with acetic anhydride (4·5 ml) in pyridine (6 ml) at room temperature for 24 h. Usual working up gave 1·8 g of the crude product which was chromatographed on a silica gel column (300 g) in benzene–ether (1 : 1). Crystallisation from ether–ligroin afforded 1·35 g of the diacetate *XXII*, m.p. 150–151°C, $[\alpha]_D^{20}$ −16° (*c* 1·54). For $C_{23}H_{36}O_6$ (408·5) calculated: 67·62% C, 8·88% H; found: 67·88% C, 8·80% H.

6α-Acetoxy-5,17β-dihydroxy-17α-methyl-5β-B-norandrostan-3-one (*XXIII*)

The acetate *XXI* (600 mg) in acetone (25 ml) was treated with excess Jones' reagent (1 ml) and stirred at room temperature for 6 min. Methanol was then added to destroy the excess chromic acid, the reaction mixture was diluted with water, and the product extracted into ethyl acetate. Working up and crystallisation from ethyl acetate–ligroin yielded 430 mg of the ketone *XXIII*, m.p. 188–189°C, $[\alpha]_D^{20}$ +8° (*c* 1·27). For $C_{21}H_{32}O_5$ (364·5) calculated: 69·20% C, 8·85% H; found: 69·25% C, 8·99% H.

5,17β-Dihydroxy-17α-methyl-5β-B-norandrostane-3,6-dione (*XXIV*)

The tetrol *XIX* (100 mg) in acetone (6 ml) was oxidised with excess Jones' reagent (0·5 ml) as given in the foregoing experiment. Similar working up and crystallisation from ethyl acetate gave 40 mg of the dione *XXIV*, m.p. 223—225°C, $[\alpha]_D^{20}$ —133° (*c* 1·86 in ethanol). For $C_{19}H_{28}O_4$ (320·4) calculated: 71·22% C, 8·81% H; found: 71·44% C, 8·90% H.

3β-Acetoxy-5,17β-dihydroxy-17α-methyl-5β-B-norandrostan-6-one (*XXV*)

The triol *XX* (10 g) in acetone (300 ml) was treated with excess Jones' reagent (30 ml) at +8°C and stirred at the same temperature for 10 min under nitrogen. Similar working up as given in the foregoing experiments and crystallisation from acetone–ligroin gave 6·2 g of the ketone *XXV*. The mother liquors were chromatographed over silica gel (300 g) in ligroin–aceton (4 : 1) to yield after working up and crystallisation 1·15 g of the ketone *XXV*, m.p. 110—112°C, $[\alpha]_D^{20}$ +25° (*c* 1·36). For $C_{21}H_{32}O_5$ (364·5) calculated: 69·20% C, 8·85% H; found: 69·09% C, 8·70% H.

17α-Methyl-5β-B-norandrostane-3β,5,6β,17β-tetrol (*XXVI*)

The acetate *XXVII* (80 g) in methanol (6 ml) was heated to 60°C with a solution of K_2CO_3 (80 mg) in water (1 ml) for 2 h. The reaction mixture was diluted with water, the product isolated with ethyl acetate, and the extract worked up. The residue on crystallisation from ethyl acetate–ligroin gave 42 mg of the tetrol *XXVI*, m.p. 216—218°C, $[\alpha]_D^{20}$ +26° (*c* 1·10) in ethanol. For $C_{19}H_{32}O_4$ (324·5) calculated: 70·33% C, 9·94% H; found: 70·39% C, 9·99% H.

3β-Acetoxy-17α-methyl-5β-B-norandrostane-5,6β,17β-triol (*XXVII*)

The ketone *XXV* (2·5 g) was dissolved in acetic acid (50 ml) and hydrogenated over prehydrogenated Adams' catalyst (2 g) until the theoretical amount of hydrogen has been absorbed (18 h). The catalyst was filtered off, washed with ether, and the solvents removed under reduced pressure. The residue was treated with water, the product dissolved in ether, the ethereal solution was washed with a $NaHCO_3$ solution, water, dried, and evaporated. The crude product was chromatographed over silica gel (400 g) in ligroin–acetone (3 : 1) to yield after working up and crystallisation from ethyl acetate–ligroin 2·2 g of the triol *XXVII*, m.p. 70—72°C, $[\alpha]_D^{20}$ +25° (*c* 1·27). For $C_{21}H_{34}O_5$ (366·5) calculated: 68·82% C, 9·35% H; found: 68·81% C, 9·42% H.

6β-Benzoyloxy-17α-methyl-5β-B-norandrostane-3β,5,17β-triol (*XXVIII*)

A solution of the diester *XXIX* (2 g) in chloroform (35 ml) and methanol (100 ml) was treated with conc. HCl and allowed to stand at 20°C for 60 h. The reaction mixture was diluted with ether, washed with water and a $NaHCO_3$ solution, dried, and evaporated. The residue on crystallisation from ethyl acetate–ligroin gave 1·8 g of the benzoate *XXVIII*, m.p. 108—110°C, $[\alpha]_D^{20}$ +37° (*c* 0·90 in ethanol). For $C_{26}H_{36}O_5$ (428·6) calculated: 72·86% C, 8·47% H; found: 72·70% C, 8·31% H.

3β-Acetoxy-6β-benzoyloxy-17α-methyl-5β-B-norandrostan-5,17β-diol (*XXIX*)

The alcohol *XXVII* (2·1 g) in pyridine (10 ml) was treated at 0°C with benzoyl chloride (2 ml) and allowed to stand at room temperature for 5 h. The reaction mixture was decomposed with ice, the product extracted into ether, and the ethereal solution was washed with dilute HCl, a $NaHCO_3$ solution, water, and evaporated. The residue on crystallisation from acetone–water gave 2·1 g

of the benzoate *XXIX*, m.p. 126—128°C, $[\alpha]_D^{20}$ +37° (*c* 1·59); IR: 3590, 1735, 1275, 1250 cm^{-1}. For $C_{28}H_{38}O_6$ (470·6) calculated: 71·46% C, 8·14% H; found: 71·29% C, 8·17% H.

5,6β,17β-Trihydroxy-17α-methyl-5β-B-norandrostan-3-one (*XXX*)

A solution of the benzoate *XXXII* (1·5 g) in methanol (200 ml) was treated with a solution of KOH (1·6 g) in the same solvent (50 ml) and allowed to stand at room temperature for 5 min under nitrogen. After neutralisation with acetic acid methanol was distilled off under reduced pressure, the residue was treated with a saturated solution of sodium chloride, and the product taken into ethyl acetate. Working up and crystallisation from methanol-ethyl acetate gave 904 mg of the triol *XXX*. Chromatography of the mother liquors over silica gel (60 g) in benzene–ethyl acetate (1 : 1) afforded additional 153 mg of the triol *XXX*, m.p. 227—229°C, $[\alpha]_D^{20}$ −45° (*c* 1·15 in ethanol); IR: (nujol) 3490, 3440, 3350, 1708 cm^{-1}. For $C_{19}H_{30}O_4$ (322·4) calculated: 70·77% C, 9·38% H; found: 70·81% C, 9·21% H.

6β-Acetoxy-5,17β-dihydroxy-17α-methyl-5β-B-norandrostan-3-one (*XXXI*)

The triol *XXX* (1 g) was acetylated with acetic anhydride (3 ml) in pyridine (4 ml) for 6 h at room temperature. The reaction mixture was decomposed with ice, diluted with water, and the product isolated with ethyl acetate. Usual working up and crystallisation from methanol–ethyl acetate yielded 810 mg of the acetate *XXXI*, m.p. 233—235°C, $[\alpha]_D^{20}$ −34° (*c* 1·53 in ethanol). For $C_{21}H_{32}O_5$ (364·5) calculated: 69·20% C, 8·85% H; found: 69·03% C, 8·69% H.

6β-Benzoyloxy-5,17β-dihydroxy-17α-methyl-5β-B-norandrostan-3-one (*XXXII*)

The alcohol *XXVIII* (2·1 g) in acetone (100 ml) was oxidised with excess Jones' reagent (3 ml) for 10 min at room temperature. The excess chromic acid was destroyed with methanol, the reaction mixture diluted with water, and the product taken into ether–chloroform. After working up and evaporation the residue was crystallised from methanol to yield 813 mg of the diol *XXXII*. The mother liquors were chromatographed over silica gel (100 g) in benzene–ethyl acetate (4 : 1) to yield after working up and crystallisation from methanol additional 700 mg of the diol *XXXII*, m.p. 227—229°C, $[\alpha]_D^{20}$ +9° (*c* 1·28 in ethanol). For $C_{26}H_{34}O_5$ (426·5) calculated: 73·21% C, 8·03% H; found: 73·49% C, 8·05% H.

6β,17β-Dihydroxy-17α-methyl-B-norandrost-4-en-3-one (*XXXIII*)

The acetate *XXXIV* (170 mg) in methanol (40 ml) was treated under nitrogen with a solution of $KHCO_3$ (200 mg) in water (8 ml) and allowed to stand at 35°C for 48 h. The reaction mixture was diluted with water, the product extracted with ethyl acetate, and after working up was chromatographed over silica gel (50 g) in benzene–ethyl acetate (2 : 1), combination of the corresponding fractions, evaporation, and crystallisation from ethyl acetate–ligroin gave 80 mg of the diol *XXXIII*, m.p. 115—117°C and 175—177°C, $[\alpha]_D^{20}$ −46° (*c* 1·15 in ethanol). For $C_{19}H_{28}O_3$ (304·4) calculated: 74·96% C, 9·27% H; found: 74·75% C, 9·16% H.

6β-Acetoxy-17β-hydroxy-17α-methyl-B-norandrost-4-en-3-one (*XXXIV*)

A solution of the acetate *XXXI* (350 mg) in acetic acid (15 ml) was heated to 100°C for 6 h. The reaction mixture was diluted with water, and the product isolated with chloroform–ethyl acetate. The residue after working up and evaporation was chromatographed over silica gel

(60 g) in benzene–ethyl acetate (2 : 1). Combination and evaporation of the corresponding fractions and crystallisation from ethyl acetate–ligroin yielded 290 mg of the acetate *XXXIV*, m.p. 191–193°C, $[\alpha]_D^{20}$ +39° (*c* 0·88 in ethanol). For $C_{21}H_{30}O_4$ (346·5) calculated: 72·80% C, 8·73% H; found: 72·90% C, 8·54% H.

The analyses were carried out in the Analytical Laboratory of this Institute by Mr V. Štěrba, Mrs E. Šípová, and Mrs E. Sýkorová (head Dr J. Horáček). The IR spectra were recorded under the direction of Dr J. Smolíková.

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Translated by the author (J. F.).