ON STEROIDS. CLVI.*

6-METHYLANALOGUES OF B-NORSTEROIDS

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Dedicated to Professor E. Lederer on the occasion of his 65th birthday.

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Reaction of the 6-oxo-B-norcholestane derivatives with methylmagnesium iodide has been studied and the structures of the products established by chemical and spectral means. Synthesis of 6β-methyl-B-normethyltestosterone is described.

In one of our previous papers[1] we have described the synthesis of B-normethyltestosterone which was shown by Dorfman and co-workers[2] to possess a pronounced antihormonal activity. Encouraged by this finding we decided to synthesise some analogues of this compound. In this paper we describe the synthesis of the 6β-methyl analogue of B-normethyltestosterone together with the model experiments carried out in the B-norcholestane series.

In these model experiments the reaction of the ketone[3] *I* with methylmagnesium iodide has been studied. Both expected epimers *II* and *VI* were obtained in a relation of about 1 : 3. To prove the structure of these compounds the alcohol *VI* was oxidised to the ketone *X* which on metal hydride reduction afforded mixture of the alcohols *VI* and *VII*, epimeric at $C_{(3)}$. The 6α-hydroxy compound *VII* showed a strong intramolecular hydrogen bonding in IR which is possible only in the 3α,6α-diol of the 5β-series. This problem had been studied in detail previously[4,5]. The minor product of the Grignard reaction must be therefore the diol *II*, the main product is the 6α-hydroxy-6β-methyl derivative *VI*. These structures are also in agreement with the elimination reactions of these diols: Thus the 6β-hydroxy derivative *III* afforded on dehydration the 6,8-olefin *V*, whereas the epimer *VIII* yielded the isomeric 5,6-unsaturated compound *XV*. This is in close analogy to the dehydration of the analogous epimeric cyanohydrins we have described some time ago[6]: There also 6β-ol gave the dextrorotatory 6,8-olefin and the 6α-ol the levorotatory 5,6-isomer. The 5,6-olefin *XV* was also obtained by an alternative route: The ketone of the 5α-series[7] *XI* was trans-

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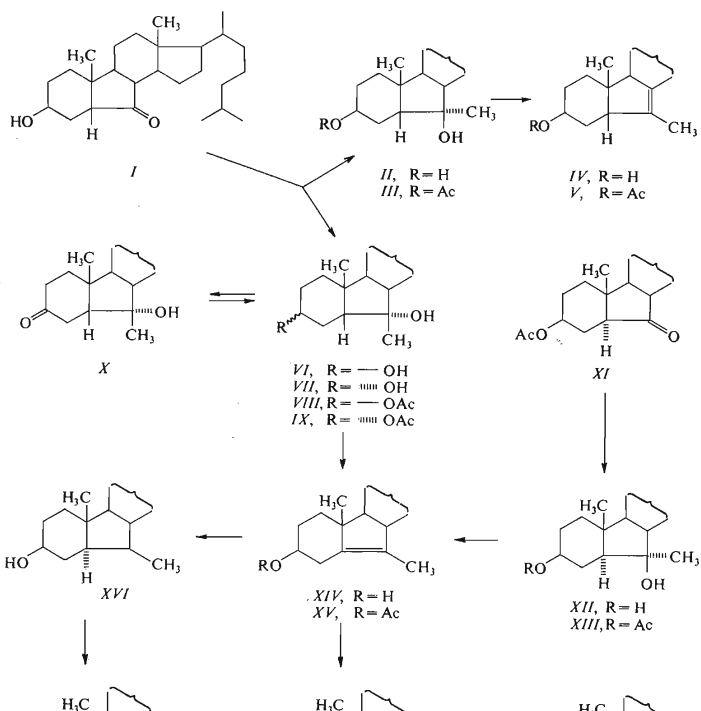
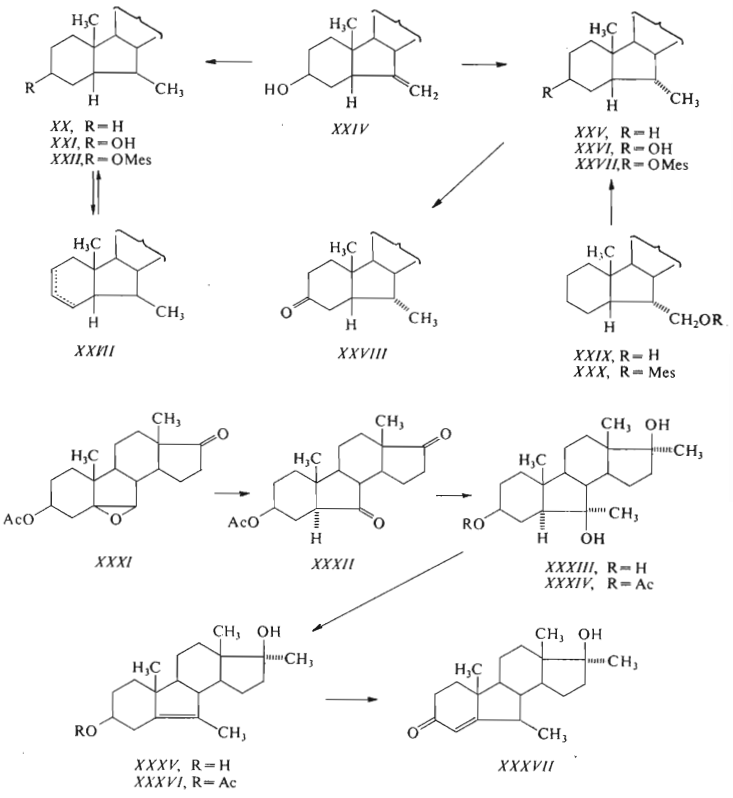


formed by Grignard reagent to the diol *XII* and its monoacetate *XIII* gave on reaction with thionyl chloride again the olefin *XV* as the sole product. The structure of the diol *XII* was assigned on the basis of the course of this elimination reaction.

Oppenauer oxidation of the alcohol *XIV* afforded the unsaturated ketone *XVIII* which was hydrogenated to the saturated derivative *XIX*. Its structure was proved as folows: The methylene derivative *XXIV* with secured[6] 5β-configuration afforded on hydrogenation a mixture of epimers *XXI* and *XXVI* which were transformed



through the mesylates to the corresponding hydrocarbons *XX* and *XXV*. The authentic hydrocarbon *XXV* with 6α-configuration of the methyl group was synthesised from the known[6] 6α-hydroxymethyl derivative *XXIX via* the mesylate *XXX*. The 6-methyl group in compounds *XX* and *XXI* is therefore β-oriented and as the oxidation of the alcohol *XXI* led to the ketone *XIX* this must have 5β,6β-configuration.

Hydrogenation of the olefin *XIV* afforded one single saturated product which was oxidised to a ketone not identical with the 6α-methyl derivative of the 5β-series

XXVIII. It must have therefore structure *XVII* and the hydrogenation product is the 6β-methyl derivative *XVI*.

6β-Methyl-B-normethyltestosterone (*XXXVII*) was synthesised by following reaction sequence: The epoxide[8] *XXXI* was transformed with borontrifluoride etherate to the dione *XXXII* which on reaction with methylmagnesium iodide gave the triol *XXXIII*. Its monoacetate *XXXIV* on reflux with acetic acid gave the olefin *XXXVI* which after hydrolysis to the alcohol *XXXV* and Oppenauer oxidation afforded the desired 6β-analogue of B-normethyltestosterone (*XXXVII*).

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 with an error of ±1. The infrared spectra were recorded on the Zeiss UR 10 spectrometer. UV spectra were recorded on the CF 4 spectrometer in ethanol. The mass spectra were recorded on the mass spectrometer AEI MS 902. The NMR spectra were recorded on the Varian HA-100 instrument in deuteriochloroform unless otherwise stated with tetramethylsilane as internal reference. The chemical shift is given in p.p.m. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin-layer chromatography, and by infrared spectra. Ligroin of b.p. 40—60°C was used as solvent. Working up of an ethereal solution means extraction with 5% hydrochloric acid, water, 5% sodium hydrogen carbonate, water, drying with magnesium sulphate, and evaporation of the solvent.

6α-Methyl-5β-B-norcholestan-3β, 6β-diol (*II*)

A refluxing solution of the ketone[3] *I* (700 mg) in ether (100 ml) was treated dropwise with a solution of methylmagnesium iodide prepared from 550 mg of magnesium (18 ml) and the reflux continued for 1 h. Ether was then replaced with benzene (60 ml) and refluxed for additional 5 h. The reaction mixture was cooled to 0°C with ice, decomposed with a ammonium chloride solution, and the product was isolated with ether. Usual working up afforded a residue 740 mg which was chromatographed on a silica gel column (100 g) in benzene–ether (9 : 1). Fractions containing the polar component were combined, evaporated, and the residue was crystallised from ligroin to yield 146 mg of the diol *II*, m.p. 154—155°C, $[\alpha]_D^{20}$ +6° (*c* 1·25). For $C_{27}H_{48}O_2$ (404·7) calculated: 80·14% C, 11·96% H; found: 79·93% C, 11·78% H.

3β-Acetoxy-6α-methyl-5β-B-norcholestan-6β-ol (*III*)

The diol *II* (70 mg) was acetylated with acetic anhydride (0·2 ml) in pyridine (0·4 ml) at room temperature for 20 h. The reaction mixture was decomposed with ice, the product was taken into ether, and the ethereal solution was worked up to yield 85 mg of a product which on crystallisation from methanol gave 48 mg of the acetate *III*, m.p. 151—152°C, $[\alpha]_D^{20}$ −4° (*c* 2·02). For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 78·03% C, 11·23% H.

6-Methyl-5β-B-norcholest-6-en-3β-ol (*IV*)

The acetate *V* (50 mg) in methanol (3 ml) was refluxed with a solution of potassium carbonate (50 mg) in water (0·5 ml) for 2 h. Methanol was removed under reduced pressure, the product taken into ether, and the ethereal solution was washed with water, dried, and ether distilled off. The residue was chromatographed preparatively on one plate of silica gel (20 × 20 cm) in benzene–ether (9 : 1). The corresponding zone was collected, the product eluted with ether, and the solvent distilled off. Crystallisation from dilute acetone yielded 20 mg of the alcohol *IV*, m.p. 108—110°C, $[\alpha]_D^{20}$ +35° (*c* 1·13). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·63% C, 12·14% H.

3β-Acetoxy-6-methyl-5β-B-nor-6-cholestene (*V*)

The alcohol *III* (90 mg) in pyridine (1 ml) was treated at 0°C with thionyl chloride (0·1 ml) and allowed to stand at room temperature for 30 min. The reaction mixture was decomposed with ice and water, the product extracted into ether, and worked up. The residue was chromatographed over silica gel (4 g) in ligroin–benzene (9 : 1). The corresponding fractions were combined and evaporated to yield 22 mg of the olefin *V* $[\alpha]_D^{20}$ +42° (*c* 1·12) resisting all attempts at crystallisation. For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·02% C, 11·16% H.

6β-Methyl-5β-B-norcholestan-3β,6α-diol (*VI*)

a) *From* 3β-*hydroxy*-5β-B-*norcholestan*-6-*one* (I): Fractions from the chromatography of the epimeric compound *II* containing the lipophilic component were combined, evaporated, and the residue was crystallised from methanol–water to yield 465 mg of the diol *VI*, m.p. 67—69°C, $[\alpha]_D^{20}$ +9·8° (*c* 1·44). For $C_{27}H_{48}O_2$ (404·7) calculated: 80·14% C, 11·96% H; found: 79·85% C, 11·70% H.

b) *From* 6α-*hydroxy*-6β-*methyl*-5β-B-*norcholestan*-3-*one* (X): A solution of the ketone *X* (430 mg) in tetrahydrofuran (9 ml) was colled to 0°C and treated with solid lithium tri-tert-butoxyaluminium hydride (900 mg). After 45 min at room temperature the excess hydride was decomposed with 2% acetic acid (50 ml) the product taken into ether, and the ethereal solution was worked up. The residue was chromatographed on a silica gel column (40 g) in benzene–ether (2 : 1). Franctions containing the polar minor component were combined, evaporated, and the residue was crystallised from methanol–water to yield 21 mg of the diol *VI*, m.p. 66—68°C, $[\alpha]_D^{20}$ +8° (*c* 1·10).

6β-Methyl-5β-B-norcholestan-3α,6α-diol (*VII*)

Fractions containing the lipophilic component (previous experiment *b*) were combined, evaporated, and the residue was crystallised from ether to yield 190 mg of the diol *VII*, m.p. 131—132°C, $[\alpha]_D^{20}$ +6·5° (*c* 1·27). For $C_{27}H_{48}O_2$ (404·7) calculated: 80·14% C, 11·96% H; found: 80·05% C, 11·80% H.

3β-Acetoxy-6β-methyl-5β-B-norcholestan-6α-ol (*VIII*)

The diol *VI* (150 mg) in pyridine (0·8 ml) was acetylated with acetic anhydride (0·4 ml) for 20 h at room temperature. The reaction mixture was decomposed with ice, the product extracted with ether, and worked up. The residue was crystallised from methanol to yield 120 mg of the acetate *VIII*, m.p. 74—75°C, $[\alpha]_D^{20}$ +3·7° (*c* 1·60). For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 77·78% C, 10·89% H.

3α-Acetoxy-6β-methyl-5β-B-norcholestan-6α-ol (*IX*)

The diol *VII* (100 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (0·5 ml) for 20 h at room temperature. Usual working up and crystallisation from methanol gave 65 mg of the acetate *IX*, m.p. 109—110°C, $[\alpha]_D^{20}$ +12° (*c* 1·51). For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 77·83% C, 11·12% H.

6α-Hydroxy-6β-methyl-5β-B-norcholestan-3-one (*X*)

The diol *VI* (200 mg) in acetone (20 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 15 min. Methanol was then added to remove the excess oxidising agent, the reaction mixture was diluted with water, and the product isolated with ether. The ethereal solution was washed with water, $NaHCO_3$, water, dried, and evaporated. The residue was crystallised from methanol to yield 120 mg of the ketone *X*, m.p. 126–127°C, $[\alpha]_D^{20}$ +67° (*c* 1·53). For $C_{27}H_{46}O_2$ (402·6) calculated: 80·54% C, 11·52% H; found: 80·57% C, 11·34% H.

6α-Methyl-5α-B-norcholestan-3β,6β-diol (*XII*)

The ketone *XI* (2 g) in ether (300 ml) was treated with a solution of methylmagnesium iodide prepared from 2 g of magnesium in ether (68 ml) and refluxed for 1 h. Ether was then replaced by benzene (150 ml) and refluxed for 2 hours. The reaction mixture was cooled to 0°C, decomposed with saturated solution of ammonium chloride (150 ml) and the product isolated with ether. The ethereal solution was washed with water, sodium thiosulphate, water, dried, and evaporated. The residue was chromatographed on a silica gel column (200 g) in benzene–ether (9 : 1). Working up of the corresponding fractions and crystallisation from ether–ligroin gave 1·03 g of the diol *XII*, m.p. 134–135°C, $[\alpha]_D^{20}$ +26° (*c* 1·23). For $C_{27}H_{48}O_2$ (404·7) calculated: 80·14% C, 11·96% H; found: 79·99% C, 11·73% H.

3β-Acetoxy-6α-methyl-5α-B-norcholestan-6β-ol (*XIII*)

The diol *XII* (600 mg) was acetylated with acetic anhydride (1·5 ml) in pyridine (2 ml) for 20 h at room temperature. Usual working up and crystallisation from methanol gave 470 mg of the acetate *XIII*, m.p. 116–117°C, $[\alpha]_D^{20}$ +13° (*c* 1·48). For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 77·98% C, 11·25% H.

6-Methyl-B-nor-5-cholesten-3β-ol (*XIV*)

The acetate *XV* (260 mg) in methanol (20 ml) was refluxed with a solution of potassium hydroxide (200 mg) in methanol (10 ml) for 30 minutes. Water was added, the product isolated with ether, the ethereal solution was washed with water, dried, and evaporated. The residue on crystallisation from ligroin afforded 210 mg of the alcohol *XIV*, m.p. 138–139°C, $[\alpha]_D^{20}$ −83° (*c* 1·28). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·96% C, 12·04% H.

3β-Acetoxy-6-methyl-B-nor-5-cholestene (*XV*)

a) *From* 3β-*acetoxy*-6β-*methyl*-5β-B-*norcholestan*-6α-*ol* (VIII): A solution of the acetate *VIII* (150 mg) in pyridine (2 ml) was cooled to 0°C and treated dropwise with thionyl chloride (0·15 ml). After 30 min at 0°C the reaction mixture was diluted with ether, washed with water, and worked up. The residue was filtered through a silica gel bed in benzene–ligroin (3 : 1), the filtrate was evaporated, and the residue crystallised from methanol to yield 65 mg of the olefin *XV*, m.p. 108–109°C, $[\alpha]_D^{20}$ −79° (*c* 1·30). For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·18% C, 11·27% H.

b) *From* 3β-*acetoxy*-6α-*methyl*-5α-B-*norcholestan*-6β-*ol* (XIII): The acetate *XIII* (410 mg) in pyridine (4 ml) was treated with thionyl chloride (0·3 ml) and worked up as given in the foregoing experiment. Similar working up and crystallisation from methanol gave 310 mg of the olefin *XV*, m.p. 108–109°C, $[\alpha]_D^{20}$ −76° (*c* 1·25).

6β-Methyl-5α-B-norcholestan-3β-ol (*XVI*)

The olefin *XIV* (300 mg) was hydrogenated over Adams' catalyst (25 mg) in acetic acid (4 ml) for 4 h. The catalyst was filtered off, washed with ether (100 ml), and the filtrate was washed with water, sodium hydrogen carbonate, water, dried, and evaporated. The residue was crystallised from methanol to yield 256 mg of the alcohol *XVI*, m.p. 112—114°C, $[\alpha]_D^{20}$ +16° (*c* 1·67). For $C_{27}H_{48}O$ (388·7) calculated: 83·43% C, 12·45% H; found: 83·41% C, 12·65% H.

6β-Methyl-5α-B-norcholestan-3-one (*XVII*)

The alcohol *XVI* (100 mg) in acetone (6 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 15 min. The excess agent was removed with methanol, the reaction mixture was diluted with water, and the product isolated with ether. Working up and crystallisation from methanol afforded 65 mg of the ketone *XVII*, m.p. 109—110°C, $[\alpha]_D^{20}$ +64° (*c* 1·35). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 84·10% C, 11·93% H.

6β-Methyl-B-nor-4-cholesten-3-one (*XVIII*)

The alcohol *XIV* (200 mg) was dissolved in toluene (12 ml) and cyclohexanone (3 ml) and 2 ml of the solvent were distilled off. The reaction mixture was then treated with aluminium isopropoxide (100 mg) in toluene (1 ml) and within 1 h 5 ml of the distillate were collected. The reaction mixture was decomposed with 5% hydrochloric acid (15 ml), the product was extracted into ether, and the ethereal solution was worked up. The residue was chromatographed on a silica gel column (20 g) in benzene–ligroin (1 : 1). Fractions containing the ketone were combined, evaporated, and the residue was crystallised from acetone–water to yield 105 mg of the ketone *XVIII*, m.p. 61—62°C, $[\alpha]_D^{20}$ (*c* 1·37). For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·53% H; found: 84·51% C, 11·38% H.

6β-Methyl-5β-B-norcholestan-3-one (*XIX*)

a) *From* 6β-*methyl*-B-*nor*-4-*cholesten*-3-*one* (XVIII): The olefin *XVIII* (1·1 g) in dioxan (60 ml) and ethanol (120 ml) was hydrogenated over 5% $Pd/CaCO_3$ catalyst (4 g) for 4 h. Catalyst was filtered off, washed with ether, and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in ether, and the ethereal solution was worked up to yield 910 mg of a product which was chromatographed over silica gel (30 g) in ligroin–benzene (6 : 4). The corresponding fractions were combined, evaporated, and the residue was crystallised from methanol to yield 640 mg of the ketone *XIX*, m.p. 52—54°C, $[\alpha]_D^{20}$ +42·5° (*c* 1·51). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·81% C, 11·96% H.

b) *From* 6β-*methyl*-5β-B-*norcholestan*-3β-*ol* (XXI): The alcohol *XXI* (80 mg) in acetone (4 ml) was treated with excess Jones' reagent and allowed to stand for 15 min. Methanol was added to destroy the agent, the reaction mixture was diluted with water, the product taken into ether, and the ethereal solution was worked up. The residue on crystallisation from methanol afforded 40 mg of the ketone *XIX*, m.p. 51—53°C, $[\alpha]_D^{20}$ +44° (*c* 0·70).

6β-Methyl-5β-B-norcholestane (*XX*)

The olefin *XXIII* (100 mg) in ethyl acetate (8 ml) was hydrogenated over Adams' catalyst (20 mg) for 2 h. The catalyst was filtered off, washed with ether, the filtrate was washed with dilute hydrochloric acid, water, sodium hydrogen carbonate, water, dried, and evaporated. Yield 95 mg of the

hydrocarbon *XX*, $[\alpha]_D^{20}$ +35° (*c* 1·33), oil. For $C_{27}H_{48}$ (372·6) calculated: 87·03% C, 12·97% H; found: 86·98% C, 12·91% H.

6β-Methyl-5β-B-norcholestan-3β-ol (*XXI*)

The olefin *XXIV* (650 mg) in acetic acid (6 ml) was hydrogenated over Adams' catalyst (60 mg) for 2 h. The catalyst was filtered off, washed with ether, the filtrate was diluted with ether, washed with sodium hydrogen carbonate, water, dried, and evaporated. The oily residue contained according to the thin-layer chromatography two components in about equal quantities. It was chromatographed on a silica gel column (200 g) in benzene–ether (9 : 1). Fractions containing the lipophilic component were combined and evaporated to yield 148 mg of the oily alcohol *XXI*, $[\alpha]_D^{20}$ +39° (*c* 1·07). For $C_{27}H_{48}O$ (388·7) calculated: 83·43% C, 12·45% H; found: 83·29% C, 12·34% H.

3β-Methanesulphonyloxy-6β-methyl-5β-B-norcholestane (*XXII*)

The alcohol *XXI* (120 mg) in pyridine (2 ml) was treated at 0°C with methanesulphonyl chloride (0·2 ml) and allowed to stand at room temperature for 20 h. The reaction mixture was decomposed with ice, diluted with water, the product extracted with ether, and the ethereal solution was worked up. The residue was crystallised from ligroin to yield 42 mg of the mesylate *XXII* (the mother liquors were converted directly to the olefin *XXIII*), m.p. 81—83°C, $[\alpha]_D^{20}$ +36° (*c* 1·57). For $C_{28}H_{50}O_3S$ (466·7) calculated: 72·05% C, 10·80% H, 6·87% S; found: 71·83% C, 10·71% H, 7·13% S.

6β-Methyl-5β-B-nor-2(or 3)-cholestene (*XXIII*)

The mother liquors after crystallisation of the mesylate *XXII* (previous experiment) were dissolved in ligroin–benzene (3 : 1) and chromatographed over silica gel (6 g) in the same solvent mixture. Fractions containing the lipophilic component were evaporated to yield 55 mg of the oily olefin mixture *XXIII*. For $C_{27}H_{46}$ (370·6) calculated: 87·49% C, 12·51% H; found: 87·26% C, 12·43% H.

6α-Methyl-5β-B-norcholestane (*XXV*)

a) *From* 6α-*methanesulphonylmethyl*-5β-B-*norcholestane* (XXX): The mesylate *XXX* (490 mg) in ether (15 ml) was treated with a solution of lithiumaluminium hydride (750 mg) in the same solvent (30 ml) and refluxed for 6 h. The reaction mixture was diluted with ether, decomposed with ethyl acetate, and worked up. The residue after evaporation of the solvent was dissolved in ligroin and chromatographed on a silica gel colum (30 g) in the same solvent. Fractions containing the lipophilic component were combined, evaporated, and the residue was crystallised from methanol to yield 210 mg of the hydrocarbon *XXV*, m.p. 89—90°C, $[\alpha]_D^{20}$ −24° (*c* 1·23). For $C_{27}H_{48}$ (372·6) calculated: 87·03% C, 12·97% H; found: 86·84% C, 13·06% H.

b) *From* 3β-*methanesulphonyloxy*-6α-*methyl*-5β-B-*norcholestane* (XXVII): The mesylate *XXVII* (50 mg) was dissolved in ligroin and chromatographed over silica gel (5 g). The eluate was evaporated (39 mg) dissolved in ethyl acetate (6 ml) and hydrogenated over Adams' catalyst (10 mg) for 2 h. The catalyst was filtered off, washed with ether, and the filtrate was worked up. The residue was chromatographed over silica gel (2 g) in ligroin. Working up of the corresponding fractions and crystallisation from methanol gave 25 mg of the hydrocarbon *XXV*, m.p. 89—90°C, $[\alpha]_D^{20}$ −22° (*c* 1·35).

6α-Methyl-5β-B-norcholestan-3β-ol (*XXVI*)

Elution of the chromatography after isolation of the 6β-epimer *XXI* with the same solvent mixture afforded fractions with the polar component. Working up and crystallisation from ligroin afforded 210 mg of the alcohol *XXVI*, m.p. 104–105°C, $[\alpha]_D^{20}$ −14° (*c* 1·02). For $C_{27}H_{48}O$ (388·7) calculated: 83·43% C, 12·45% H; found: 83·29% C, 12·37% H.

3β-Methanesulphonyloxy-6α-methyl-5β-B-norcholestane (*XXVII*)

A solution of the alcohol *XXVI* (100 mg) in pyridine (1·5 ml) was treated at 0°C with methanesulphonyloxy chloride (0·15 ml) and allowed to stand at the same temperature for 6 h. The reaction mixture was decomposed with ice, the product isolated with ether, and the ethereal solution was worked up. The residue was crystallised from ligroin to yield 65 mg of the mesylate *XXVII*, m.p. 96–97°C, $[\alpha]_D^{20}$ −10° (*c* 1·22). For $C_{28}H_{50}O_3S$ (466·7) calculated: 72·05% C, 10·80% H, 6·87% S; found: 71·89% C, 10·70% H, 7·12% S.

6α-Methyl-5β-B-norcholestan-3-one (*XXVIII*)

The alcohol *XXVI* (40 mg) in acetone (2 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. The excess agent was removed with methanol, the reaction mixture was diluted with water, and the product was taken into ether. The ethereal solution was worked up and the residue was crystallised from methanol to afford 22 mg of the ketone *XXVIII*, m.p. 99–100°C, $[\alpha]_D^{20}$ −44° (*c* 0·95). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·76% C, 12·04% H.

6α-Methanesulphonyloxymethyl-5β-B-norcholestane (*XXX*)

The alcohol[6] *XXIX* (800 mg) in pyridine (10 ml) was treated at 0°C with methanesulphonyl chloride (1·25 ml) and allowed to stand at the same temperature for 2 h. The reaction mixture was decomposed with ice, diluted with water, the product taken into ether, and worked up. The oily residue was chromatographed on a silica gel column (30 g) in benzene. The corresponding fractions afforded after working up 685 mg of the oily mesylate *XXX*, $[\alpha]_D^{20}$ −23° (*c* 1·29). For $C_{28}H_{50}O_3S$ (466·7) calculated: 72·05% C, 10·80% H, 6·87% S; found: 71·89% C, 10·61% H, 6·83% S.

3β-Acetoxy-5α-B-norandrostan-6,17-dione (*XXXII*)

The epoxide[8] *XXXI* (2 g) in ether (80 ml) was treated with borontrifluoride etherate (0·2 ml) and allowed to stand at room temperature for 2 h. The reaction mixture was poured into 5% sodium hydrogen carbonate (200 ml), the ethereal solution was separated, washed with water, and evaporated. The residue was crystallised from methanol to yield 1·85 g of the dione *XXXII*, m.p. 184–185°C, $[\alpha]_D^{20}$ +160° (*c* 1·61). For $C_{20}H_{28}O_4$ (332·4) calculated: 72·26% C, 8·49% H; found: 72·03% C, 8·45% H.

6α,17α-Dimethyl-5α-B-norandrostane-3β,6β,17β-triol (*XXXIII*)

The dione *XXXII* (3·4 g) in ether (500 ml) and benzene (500 ml) was added dropwise to a solution of methylmagnesium iodide prepared from 7 g of magnesium in ether (180 ml). Ether was then replaced by benzene and the reaction mixture was refluxed 4 h. The mixture was then de-

composed with a saturated solution of ammonium chloride (500 ml) at 0°C, the organic layer was separated, washed with water, dried, and evaporated. The residue was chromatographed on a silica gel column (300 g) in benzene–ether (1 : 1). Working up of the corresponding fractions and crystallisation from ether–ligroin afforded 2·3 g of the triol *XXXIII*, m.p. 115—117°C, $[\alpha]_D^{20}$ +3° (*c* 1·14 in ethanol). For $C_{20}H_{34}O_3$ (322·5) calculated: 74·49% C, 10·63% H; found: 74·30% C, 10·51% H.

3β-Acetoxy-6α,17α-dimethyl-5α-B-norandrostane-6β,17β-diol (*XXXIV*)

The triol *XXXIII* (2·2 g) was acetylated with acetic anhydride (6 ml) in pyridine (8 ml) for 20 h at room temperature. The reaction mixture was decomposed with ice, diluted with ether, and the product was isolated with ether. Working up and crystallisation from ether–ligroin afforded 2 g of the acetate *XXXIV*, m.p. 145—146°C (recrystallisation at 92—95°C), $[\alpha]_D^{20}$ −18° (*c* 1·39). For $C_{22}H_{36}O_4$ (364·5) calculated: 72·49% C, 9·96% H; found: 72·21% C, 10·26% H.

6,17α-Dimethyl-B-nor-5-androstene-3β,17β-diol (*XXXV*)

A solution of the acetate *XXXVI* (1 g) in methanol (70 ml) was refluxed with a solution of potassium carbonate (1 g) in water (12 ml) for 2 h. After cooling off the reaction mixture was diluted with water, the product extracted into ethyl acetate, the solution was washed with water, dried, and the solvent distilled off. The residue was crystallised from ethyl acetate to yield 890 mg of the diol *XXXV*, m.p. 182—184°C, $[\alpha]_D^{20}$ −100° (*c* 0·98 in ethanol). For $C_{20}H_{32}O_2$ (304·5) calculated: 78·89% C, 10·60% H; found: 78·67% C, 10·49% H.

3β-Acetoxy-6,17α-dimethyl-B-nor-5-androsten-17β-ol (*XXXVI*)

The diol *XXXIV* (2 g) in acetic (30 ml) was refluxed for 2 h. The reaction mixture was diluted with water, the product taken into ether, the ethereal solution was washed with water, sodium hydrogen carbonate, water, dried, and evaporated. The residue was chromatographed over silica gel (100 g) in benzene to yield after working up of the corresponding fractions and crystallisation from methanol 1·2 of the olefin *XXXVI*, 164—165°C, $[\alpha]_D^{20}$ −109° (*c* 1·52). For $C_{22}H_{34}O_3 . CH_3OH$ (378·5) calculated: 72·97% C, 10·12% H; found: 72·95% C, 10·09% H.

17β-Hydroxy-6β,17α-dimethyl-B-nor-4-androsten-3-one (*XXXVII*)*

The alcohol *XXXV* (870 mg) in toluene (80 ml) and cyclohexanone (15 ml) was oxidised with aluminium isopropoxide (500 mg) in toluene (5 ml) as described for the ketone *XVIII*. Similar working up afforded a product which was chromatographed over silica gel (80 g) in benzene–ether (2 : 1). Working up of the corresponding fractions and crystallisation from ethyl acetate–ligroin gave 618 mg of the ketone *XXXVII*, m.p. 146—148°C, $[\alpha]_D^{20}$ −11° (*c* 1·25); IR: 1633, 1671, 3610 cm^{-1}. For $C_{20}H_{30}O_2$ (302·4) calculated: 79·42% C, 10·00% H; found: 79·63% C, 10·04% H.

The analyses were carried out in the Analytical Laboratories of this Institute by Mr V. Štěrba, Mrs V. Rusová and Mrs E. Sýkorová under the direction of Dr J. Horáček. The IR spectra were recorded by Mrs K. Matoušková and by Mr P. Formánek under the direction of Dr J. Smolíková.

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