# ANTIANDROGENIC A-HOMO-B,19-DINOR-ANALOGUES OF ANDROGENS FROM 6β-CHLORO-5-METHYL-19-NOR--5β-ANDROST-9-ENES*

Alexander KASAL

*Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6*

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6β-Chloro derivatives of 5-methyl-19-nor-5β-androst-9-enes (Westphalen diol type) with oxygen functionalities in positions 3 and 17 were converted into diene *VI* by treatment with lithium aluminium hydride. The lipophilic product of hydrogenation of *VI* was shown to be 4aα-methyl--A-homo-B,19-dinor-5β,10α-androstane-3β,17β-diol (*IX*). Various paths leading to dihydrotestosteron analogues, e.g. selective acylation or oxidation of diol *IX* and partial hydrolysis of diacetate *X*, have been realized. 17β-Hydroxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstan--3-one (*XVI*) has been found to exhibit antiandrogenic activity.

Although most of the hitherto known steroid antiandrogens are suitably substituted modified gestagens, some belong to modified analogues of androgens[1]. Structural modifications, successfully employed in this direction, involve cleavage of the C—C bond (seco-steroids), expansion or reduction of a ring in the steroid nucleus (homo- and norsteroids), bridging of some positions in the steroid nucleus (cyclosteroids), replacement of carbon atom with a hetero atom (heterosteroids), and combination of these operations[1]. A recent paper reports that the azulenone derivative *I* inhibits the effect of 5α-reductase in skin and thus has an antiandrogenic activity in this organ. We therefore decided to prepare a dihydrotestosterone analogue in which the rings A and B would be similar to those in compound *I*.

The synthesis started from chloro derivative *II* (ref.[3]) which on Westphalen rearrangement[4] afforded chloro derivative *III*. This compound, or its derivatives *IV* and *V* prepared by the standard procedures, was treated with lithium aluminium hydride. As we have found recently[5], this reaction leads to the desired A-homo-B-nor--derivatives of the type *VI*, along with 3,4-seco-derivative *VII* as the fragmentation product[6,7]. The best results were obtained with the diacetate *III*; the reduction of the tetrahydropyranyl derivative *V* required subsequent acid hydrolysis at the stage of sensitive intermediates and reduction of the free diol *IV* was incomplete because

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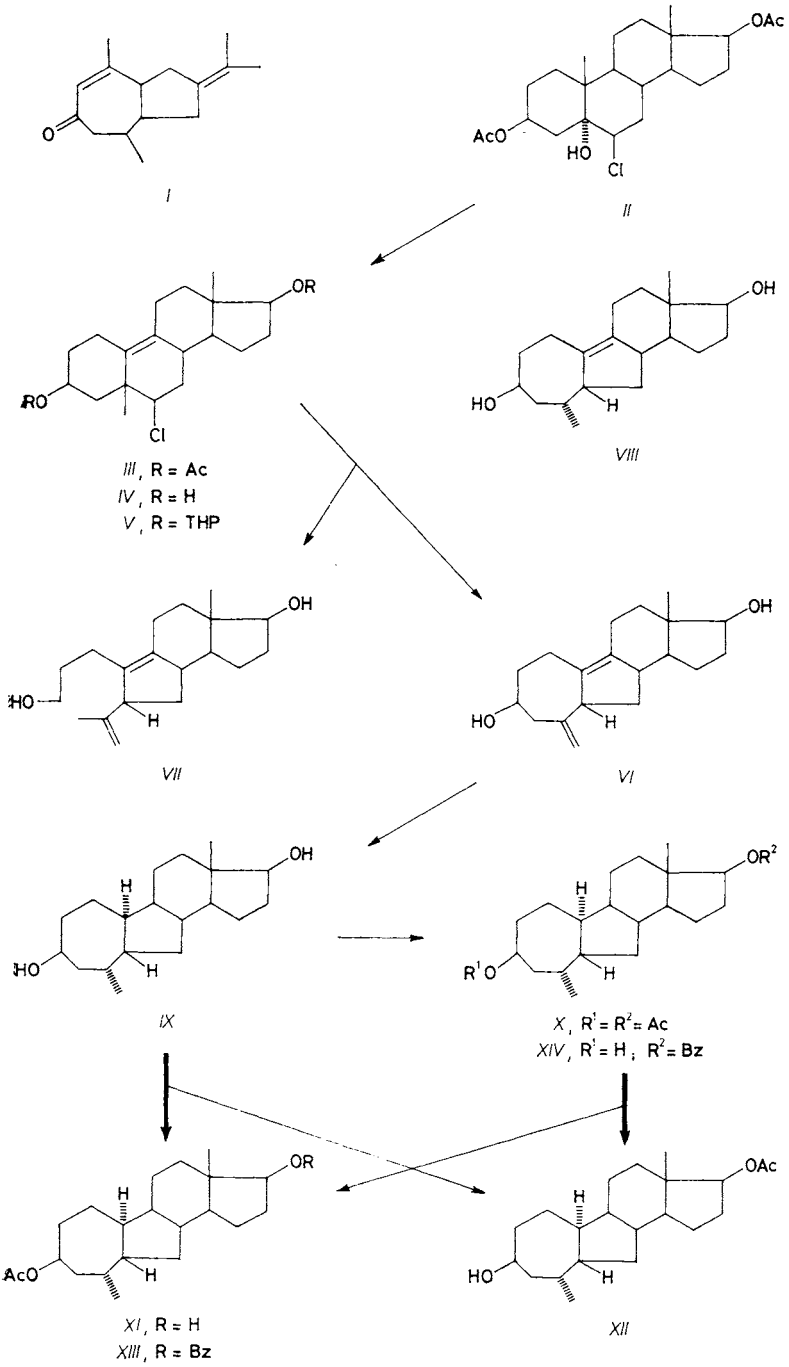



SCHEME 1

Ac = $CH_3CO$; Bz = $C_6H_5CO$; THP = tetrahydropyranyl

of low solubility in the reaction medium. The principal reaction product (*VI*) was 4a-methyleno-A-homo-B,19-dinor-5β-androst-9-ene-3β,17β-diol (arising by elimination and rearrangement). Its structure was confirmed by IR and $^1$H NMR spectra which exhibit characteristics of all the groups present (analogously to the cholestane analogue prepared previously[5]; see Experimental and Table I). The diene *VI* was accompanied with small amount of chromatographically identical dihydro derivative (see the mass spectrum) which, on the basis of our previous work[5], was assigned the olefin structure *VIII*. No separation of these compounds was attempted because they were considerably unstable; moreover, this separation was not necessary for the further reaction steps.

We isolated a more polar side-product which has been shown ($^1$H NMR, IR and MS spectra; oxidation to the acid with the same number of carbon atoms) to be

TABLE I

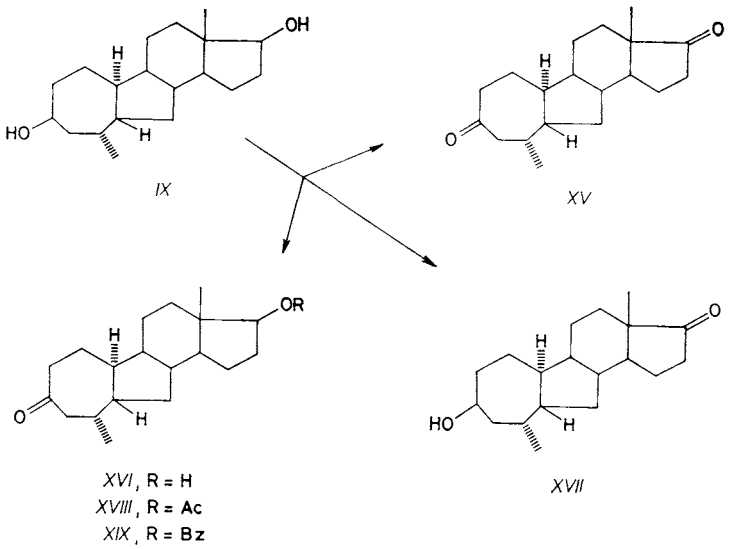
Characteristic parameters of $^1$H NMR spectra. The spectra were taken on Tesla BS-467 (60 MHz, CW mode) instrument in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) and half-height widths (*W*) in Hz. All values were obtained by first-order analysis

| Compound | 18-H[a] | 5β-$CH_3$[a] | 4b-H | 3-H | 17-H | Other signals |
|---|---|---|---|---|---|---|
| *III* | 0·92 | 1·25 | — | 5·07[b] | 4·59[c] | 2·06[d], 2·03[d], 3·92[e] |
| *IV* | 0·82 | 1·28 | — | 4·07[f] | 4·07[f] | 3·92[e] |
| *V* | 0·89 | 1·29[g] | — | [f] | [f] | |
| *VI* | 0·83 | — | 4·88[h] | 3·63[f] | 3·63[f] | 3·3[i] |
| *VII* | 0·83 | — | 1·59[k] | 3·85[j] | 3·63[j] | 3·23[i], 4·65[h] |
| *IX* | 0·73 | — | 0·89[l] | 3·75[f] | 3·75[f] | |
| *X* | 0·80 | — | 0·89[l] | 4·98[m] | 4·26[c] | 2·01[d], 2·03[d] |
| *XI* | 0·76 | — | 0·90[l] | 4·96[m] | 3·65[c] | 2·00[d] |
| *XII* | 0·78 | — | 0·90[l] | 3·93[m] | 4·63[c] | 2·03[d] |
| *XIII* | 0·78 | — | 0·89[l] | 4·17[f] | 4·17[f] | 2·02[d], 7·49[n], 8·05[n] |
| *XIV* | 0·92 | — | 0·88[l] | 3·92[m] | 4·87[c] | 7·50[n], 8·05[n] |
| *XV* | 0·87 | — | 0·96[l] | — | — | |
| *XVI* | 0·72 | — | 0·93[l] | — | 3·68[c] | |
| *XVII* | 0·86 | — | 0·91[l] | 3·92[m] | — | |
| *XVIII* | 0·78 | — | 0·95[l] | — | 4·48[c] | 2·01[d] |
| *XIX* | 0·91 | — | 0·93[l] | — | 4·90[c] | 7·47[n], 8·04 |

[a] Singlet, 3 H; [b] m, $W = 10$, 1 H; [c] dd, $J = 7·5$ and 9, 1 H; [d] 3 H, $CH_3COO$; [e] dd, $J = 11$ and 5, 6α-H; [f] overlapping signals; [g] the other diastereomer exhibits 5β-$CH_3$ at δ 1·23; [h] broad singlet, 2 H; [i] m, 1 H, $\sum J = 16$, 5β-H; [j] t, 1 H, $J = 8$; [k] s, 3 H; [l] d, $J = 6·5$; [m] m, $W = 21$; [n] m, aromatic protons.

4a-methyl-A-homo-B,19-dinor-3,4-seco-5β-androsta-4,9-diene-3,17β-diol (*VII*), in analogy with the results of a similar reaction with a cholestane model[5].

Catalytic hydrogenation of the crude mixture of compounds *VI* and *VIII* afforded a mixture of perhydro derivatives from which the main product was obtained in 44% yield by repeated crystallization. According to analogy with the cholestane model[8], we have assigned this product the desired structure, 4aα-methyl-A-homo-B,19--dinor-5β,10α-androstane-3β,17β-diol (*IX*). This assignment was confirmed by the method of molecular rotation differences (in the cholestane series, the diene of the type *VI* was hydrogenated to give the perhydro derivative with proven 5β,10α-configuration, the transformation being accompanied by a molecular rotation shift $\Delta M_D$ −344°; hydrogenation of the androstane dienes of the type *VI* resulted in a mean shift $\Delta M_D$ −370°).




SCHEME 2

For the preparation of the analogue of compound *I* it was necessary to differentiate the reactivities of the hydroxyl groups on the seven-membered (3β) and the five-membered (17β) rings in the dihydroxy derivative *IX*. We have found that the 3β-hydroxyl is only slightly more reactive than the 17β-hydroxyl: in an attempted partial acetylation we isolated (along with the starting diol *IX* and diacetate *X*) the 3-monoacetate *XI* and 17-monoacetate *XII* in the ratio 6 : 4 (structures of the compounds could be easily determined from the shape of the CHOH and CHOAc proton signals in the $^1$H NMR spectra). A larger difference in reactivities was found in the

partial hydrolysis of diacetate *X* which gave compounds *XII* and *XI* in the ratio 9 : 4. Partial oxidation of diol *IX* gave (along with the starting *IX* (38%) and dione *XV* (32%)) the 3-keto alcohol *XVI* and 17-keto alcohol *XVII* in the ratio 3 : 2 (the products *XVI* and *XVII* were very easily distinguished by their IR spectra; see Experimental).

Except the 3-keto alcohol *XVI*, which already was the desired compound, all these differently substituted derivatives were utilized for preparation of the desired "azulenone" analogue of dihydrotestosterone in the following manner: the 17-acetoxy alcohol *XII* was directly oxidized to give acetate of the desired compound (*XVIII*), the 3-acetoxy alcohol *XI* was benzoylated to afford 3β-acetoxy-17β-benzoyloxy derivative *XIII* whose acetoxy group was selectively hydrolyzed and the obtained hydroxy derivative on oxidation furnished another ester of the desired compound (*XIX*). Hydrolysis of the esters *XVIII* and *XIX* also led to the desired analogue *XVI* which according to preliminary results exhibited antiandrogenic activity. A more detailed report on the biological tests will be published later.

## EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. Optical rotations and IR spectra (wavenumbers in $cm^{-1}$) were measured in chloroform, unless stated otherwise. Mass spectra were taken on an AEI 901 spectrometer. Column chromatography was carried out on silica gel according to Pitra (60—120 μm), preparative thin-layer chromatography (TLC) on 200 × 200 × 0·3 mm plates, prepared from silica gel ICN. Identity of substances prepared by different procedures was checked by comparison of their IR and $^1H$ NMR spectra, chromatographic behaviour (TLC) and mixture melting points.

3β,17β-Diacetoxy-6β-chloro-5-methyl-19-nor-5β-androst-9-ene (*III*)

A solution of chloro derivative *II* (ref.[3]; 35 g) in acetic anhydride (390 ml) was distilled at atmospheric pressure. After 65 ml of distillate had been collected, the mixture was allowed to cool and sulfuric acid (19 drops) was added with stirring at 30°C. After standing for 2 h at room temperature, the mixture was poured under stirring and cooling with ice into saturated aqueous solution of sodium chloride (1 350 ml). After 18 h the separated product was filtered, dissolved in ether, the solution was washed with aqueous potassium hydrogen carbonate and water and dried over sodium sulfate. Evaporation of the solvent and crystallization of the residue from heptane afforded 11·6 g (35%) of compound *III*, 138—145°C. Recrystallization from acetone gave material, melting at 144—145°C; $[\alpha]_D$ +150° (*c* 1·0). For $C_{23}H_{33}ClO_4$ (409·0) calculated: 67·55% C, 8·13% H, 8·67% Cl; found: 67·29% C, 8·18% H, 8·31% Cl.

6β-Chloro-5-methyl-19-nor-5β-androst-9-ene-3β,17β-diol (*IV*)

Diacetate *III* (250 mg) was dried by distillation with benzene, dissolved in tetrahydrofuran (10 ml) and reduced with lithium aluminium hydride (about 200 mg) at 0°C. After 18 h the mixture was diluted with ether, the excess hydride was decomposed with a drop of water, the mixture was filtered through a layer of sodium sulfate and the solvent was evaporated. Crystallization of the residue from chloroform, methanol and heptane gave 150 mg (76%) of diol *IV*, m.p.

185—187°C. IR spectrum (KBr): 3 300, 1 057, 1 018 (OH). For $C_{19}H_{29}ClO_2$ (324·9) calculated: 70·24% C, 9·00% H; found: 70·14% C, 9·29% H.

6β-Chloro-5-methyl-3β,17β-di(tetrahydropyranyloxy)-19-nor-5β-androst-9-ene (*V*)

Dihydropyran (2 ml) and *p*-toluenesulfonic acid monohydrate (100 mg) were added to a solution of dihydroxy derivative *IV* (1 g) in dichloromethane (10 ml) and ethyl acetate (50 ml). After standing at room temperature for 2 h, the solution was diluted with ethyl acetate, washed with aqueous potassium hydrogen carbonate and water, dried over sodium sulfate and filtered through a short column of alumina (activity III). The eluate was concentrated in vacuo and the product was crystallized from methanol (10 ml) and acetone (3 ml). Yield 0·78 g (51%), m.p. 125—128°C; $[\alpha]_D$ +143° (*c* 0·9). IR spectrum ($CCl_4$): 1 135, 1 118, 1 036, 1 024, 984. For $C_{29}H_{45}ClO_4$ (493·1) calculated: 70·63% C, 9·20% H, 7·19% Cl; found: 70·73% C, 9·30% H, 6·95% Cl.

4a-Methyleno-A-homo-B,19-dinor-5β-androst-9-ene-3β,17β-diol (*VI*)

A solution of chloro derivative *III* (1·0 g) in dioxane (25 ml) was added dropwise to a boiling solution of lithium aluminium hydride (about 300 mg) in dioxane (50 ml). The mixture was refluxed under nitrogen for 4 h, cooled and the excess hydride was decomposed with several drops of saturated aqueous sodium sulfate. The mixture was saturated with anhydrous sodium sulfate, the inorganic material was filtered and washed with dioxane. The solvent was evaporated in vacuo and the dry residue was immediately subjected to flash chromatography on a column of silica gel. Ethyl acetate–toluene (3 : 7) eluted compound *VI* (310 mg; 44%), which contained the chromatographically unseparable compound *VIII*, mass spectrum (*m/z*): 288 ($M_1^+$, 100%), 290 ($M_2^+$, 47%). Repeated crystallization of a sample from acetone under argon at −18°C afforded the pure diene *VI*, m.p. 141—143°C; $[\alpha]_D$ +60° (*c* 1·1, methanol). IR spectrum: 3 420, 1 035 (OH), 3 070, 1 664, 1 632 906 (C=$CH_2$). For $C_{19}H_{28}O_2$ (288·4) calculated: 79·12% C 9·78% H; found: 78·83% C, 9·66% H.

4a-Methyl-A-homo-B,19-dinor-3,4-seco-5β-androsta-4,9-diene-3,17β-diol (*VII*)

The title compound was obtained as further fraction in the chromatography of reaction mixture after hydrogenolysis of chloride *III*, described in the preceding experiment. Yield 280 mg (39%) of *VII*, m.p. 93—96°C (acetone–heptane); $[\alpha]_D$ +130° (*c* 0·9). IR spectrum: 3 625 (OH), 3 080, 1 651, 1 643, 897 (C=C). For $C_{19}H_{30}O_2$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·70% C, 10·33% H.

4aα-Methyl-A-homo-B,19-dinor-5β,10α-androstane-3β,17β-diol (*IX*)

A mixture of diene *VI* and olefin *VIII* (see preparation of *VI*; 500 mg) was dissolved in ethanol (2 ml) and acetic acid (5 ml) and shaken with Adams platinum oxide catalyst (80 mg) in an atmosphere of hydrogen at room temperature. After 6 h the catalyst was filtered off and washed with ethanol. The filtrate was concentrated in vacuo and the residue was chromatographed on silica gel (50 g) in ether–toluene (1 : 3), affording 225 mg (44%) of *IX*, m.p. 185—186°C (acetone); $[\alpha]_D$ −47° (*c* 0·7). IR spectrum: 3 620, 1 065, 1 035. For $C_{19}H_{32}O_2$ (92·4) calculated: 78·03% C, 11·03% H; found: 78·06% C, 11·14% H.

Partial Acetylation of 4a-Methyl-A-homo-B,19-dinor-5β,10α-androstane-3β,17β-diol (*IX*)

Diol *IX* (400 mg) was suspended in toluene (40 ml) and 20 ml of azeotropic mixture was distilled off. After cooling, the mixture was dissolved in pyridine (20 ml) and acetic anhydride (20 ml)

and the solution was set aside at room temperature for 100 min. The mixture was diluted with methanol (50 ml) and taken down in vacuo. The dry residue was again coevaporated with methanol and subjected to TLC on silica gel (10 plates) in toluene–ether (7 : 3) which afforded the following fractions (in the order of increasing polarity):

3β,17β-*Diacetoxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstane* (X), yield 191 mg (37%), m.p. 124–125°C (ethanol), $[\alpha]_D$ −56° (*c* 1·1). IR spectrum ($CCl_4$): 1 735, 1 242, 1 022 (OAc). For $C_{23}H_{36}O_4$ (376·5) calculated: 73·26% C, 9·64% H; found: 73·41% C, 9·59% H.

17β-*Acetoxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstan*-3β-*ol* (XII), yield 66 mg (14·4%), m.p. 88–90°C (acetone–heptane); $[\alpha]_D$ −56° (*c* 1·3). IR spectrum ($CCl_4$): 3 620 (OH); 1 740, 1 245 (OAc). For $C_{21}H_{34}O_3$ (334·5) calculated: 75·40% C, 10·25% H; found: 75·13% C, 10·27% H.

3β-*Acetoxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstan*-17β-*ol* (XI), yield 100 mg (22%), m.p. 169–170°C (acetone–heptane); $[\alpha]_D$ −43° (*c* 1·1). IR spectrum ($CCl_4$): 3 625 (OH); 1 732, 1 242 (OAc). For $C_{21}H_{34}O_3$ (33·45) calculated: 75·40% C, 10·25% H; found: 75·33% C, 10·27% H.

4aα-*Methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstane*-3β,17β-*diol* (IX), yield 92 mg (23%), m.p. 184–185°C (acetone).

Partial Oxidation of 4aα-Methyl-A-homo-B,19-dinor-5β,10α--androstane-3β,17β-diol (*IX*)

Water (1 ml) and N-bromoacetamide (200 mg) were added in one portion at 0°C to a stirred solution of diol *IX* (130 mg) in acetone (10 ml). After 5 min the excess oxidation reagent was destroyed with a solution of potassium hydrogen sulfite, the mixture was concentrated in vacuo to one tenth of the original volume and mixed with saturated salt solution. The product was extracted continuously with ether. The concentrated extract was chromatographed on a thin layer of silica gel (4 plates) in ether–benzene (1 : 3). The following compounds were isolated (in the order of increasing polarity):

4aα-*Methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstane*-3,17-*dione* (XV), yield 42 mg (33%), m.p. 115–117°C and 160–162°C (acetone–heptane); $[\alpha]_D$ +138° (*c* 1·1). IR spectrum ($CCl_4$): 1 747 (17-C=O); 1 712 (3-C=O). For $C_{19}H_{28}O_2$ (288·4) calculated: 79·12% C, 9·78% H; found: 78·90% C, 9·66% H.

17β-*Hydroxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstan*-3-*one* (XVI), yield 13·4 mg (10%).

3β-*Hydroxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstan*-17-*one* (XVII), yield 9·3 mg (7%).

4aα-*Methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstane*-3β,17β-*diol* (IX), yield 50 mg (38%).

Partial Hydrolysis of 3β,17β-Diacetoxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstane (*X*)

A solution of potassium carbonate (33 mg) in water (0·9 ml) and methanol (1·9 ml) was added to a solution of diacetate *X* (168 mg) in methanol (14 ml). After standing at room temperature for 12 h, the mixture was acidified with acetic acid (4 drops) and the solvent was evaporated in vacuo. A solution of the residue in chloroform was washed with potassium hydrogen carbonate solution and water, dried and concentrated. The product was chromatographed on thin layer of silica gel (5 plates) in benzene–ether (5 : 1). The following substances were isolated:

3β,17β-*Diacetoxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstane* (X), yield 46·8 mg (28%);

17β-*Acetoxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstan*-3β-*ol* (XII), yield 57 mg (38%), m.p. 88–90°C (acetone–heptane);

3β-*Acetoxy*-4aα-*methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstan*-17β-*ol* (XI), yield 24·5 mg (16·4%), m.p. 169–170°C (acetone–heptane);

4aα-*Methyl*-A-*homo*-B,19-*dinor*-5β,10α-*androstane*-3β,17β-*diol* (IX), yield 23·7 mg (18%).

3β-Acetoxy-17β-benzoyloxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstane (*XIII*)

Pyridine (2 ml) and benzoyl chloride (0·5 ml) were added to a solution of acetate *XI* (250 mg; dried by distillation with toluene). After standing for 18 h at room temperature the mixture was poured into warm water (about 20 ml), cooled and the separated product was taken up in ether. The solution was washed successively with 5% hydrochloric acid, water and aqueous potassium hydrogen carbonate and dried by filtration through a short column of sodium sulfate. The product was purified by TLC, yield 280 mg (85%) of *XIII*, $[\alpha]_D$ −21° (*c* 1·0). IR spectrum ($CCl_4$): 1 730, 1 250, 1 028 (OAc), 1 724, 1 276 ($C_6H_5COO$). For $C_{28}H_{38}O_4$ (438·6) calculated: 76·67% C, 8·73% H; found: 76·2% C, 9·05% H.

17β-Benzoyloxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstan-3β-ol (*XIV*)

Hydrochloric acid (0·2 ml) was added to a solution of diester *XIII* (103 mg) in chloroform (1 ml) and methanol (10 ml) and the solution was set aside for 48 h at room temperature. The mixture was concentrated in vacuo to one quarter of the original volume, diluted with ether and washed successively with water, dilute solution of potassium hydrogen carbonate and water. The solvents were evaporated and the product was purified by TLC in benzene–ether (9 : 1) mixture. Yield of *XIV* was 75 mg (80%), m.p. 153–155°C (ethanol–ether). IR spectrum ($CCl_4$): 3 620 (OH), 1 719, 1 274 ($C_6H_5COO$). For $C_{26}H_{36}O_3$ (396·6) calculated: 78·74% C, 9·15% H; found: 78·50% C, 9·04% H.

17β-Benzoyloxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstan-3-one (*XIX*)

Hydroxy benzoate *XIV* (130 mg) was oxidized in acetone (4 ml) with Jones reagent, the product was extracted with ether, washed with water, dried over sodium sulfate, concentrated and crystallized; yield 110 mg (85%), m.p. 159–161°C (acetone); $[\alpha]_D$ +59° (*c* 1·3). For $C_{26}H_{43}O_3$ (394·5) calculated: 79·15% C, 8·69% H; found: 78·94% C, 8·65% H.

17β-Acetoxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstan-3-one (*XVIII*)

Hydroxy acetate *XII* (300 mg) was oxidized with Jones reagent (see the preceding experiment) to give 290 mg of *XVIII*, m.p. 109–111°C (acetone–heptane); yield after crystallization 225 mg (75%), $[\alpha]_D$ +45° (*c* 1·1). IR spectrum ($CCl_4$): 1 741, 1 249, 1 048, 1 032 (OAc), 1 706 (C=O). For $C_{21}H_{32}O_3$ (332·5) calculated: 75·86% C, 9·70% H; found: 75·70% C, 9·81% H.

17β-Hydroxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstan-3-one (*XVI*)

*A*) By hydrolysis of acetoxy ketone *XVIII*. Acetate *XVIII* (505 mg) was added to a solution of potassium hydroxide (300 mg) in ethanol (20 ml). The mixture was heated under nitrogen until the starting compound dissolved and then set aside at room temperature for 18 h. After acidification with acetic acid (0·5 ml), the mixture was concentrated to a quarter of the original volume, diluted with saturated sodium chloride solution in water and the product was extracted with chloroform. The extract was washed with water, dried over sodium sulfate and the solvent

was evaporated to give 420 mg of crude *XVI* which was crystallized from acetone–heptane (yield 310 mg; 70%) m.p. 111–112°C; $[\alpha]_D$ +58° (*c* 1·0). IR spectrum ($CCl_4$): 3 630, 1 060 (OH), 1 706 (C=O). For $C_{19}H_{30}O_2$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·40% C, 10·18% H.

*B*) By hydrolysis of benzoyloxy ketone *XIX*. Compound *XIX* (525 mg) was hydrolyzed in the same manner as described in the preceding experiment except that the reaction temperature was 80°C and the extract was washed, in addition, with aqueous potassium hydrogen carbonate. Yield 350 mg (90%).

3β-Hydroxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-androstan-17-one (*XVII*)

Acetoxy alcohol *XI* (80 mg) was oxidized in acetone (3 ml) with Jones reagent at room temperature, the mixture was decomposed by pouring into a solution of potassium hydrogen carbonate and the product was extracted with ether. The extract was washed with water, dried over sodium sulfate, concentrated in vacuo and the residue was hydrolyzed by standing with a solution of hydrochloric acid (0·5 ml) in chloroform (1 ml) and methanol (10 ml) at room temperature. After 18 h the mixture was concentrated in vacuo to a fifth of the original volume, diluted with a solution of potassium hydrogen carbonate and the separated product was taken up in ether. The extract was washed, concentrated and chromatographed on thin layer of silica gel (2 plates) in ether–benzene (1 : 9). Crystallization from acetone–heptane gave 46 mg (66%) of *XVII*, m.p. 98–99°C, $[\alpha]_D$ +14° (*c* 1·1). IR spectrum ($CCl_4$): 1 742 (C=O), 3 625, 1 041 (OH). For $C_{19}H_{30}O_2$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·29% C, 10·56% H.

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