DEOXYGENATION AT THE CARBON $C_{(5)}$ OF 3,6-CYCLO-A-NOR-3,5-SECOANDROSTANES*

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Attempted hydrogenolysis of methanesulfonate *VIII* led to products of elimination and rearrangement only. On treatment with ethanedithiol the hydroxy ketone *VI* yielded dithiolane derivative *XXIV*, besides the product of retroaldol reaction, *XXIII*. Desulfurization of *XXIV* with Raney nickel followed by standard chemical transformations led to the desired analogues of testosterone, androstenedione and androsterone (*XXIX*–*XXXI*).

Recently[1] we published the synthesis of 5-oxygenated 3,6-cyclo-A-nor-3,5-secoandrostane analogues (*I*–*III*) of some androgenic hormones. As oxygen at the carbon $C_{(5)}$ is known[2] to exert a rather adverse effect on pharmacodynamical properties of steroids, we decided to eliminate the oxygen atom of the above mentioned hormone analogues.

The structural system we had to modify was peculiar in two aspects: it was a β-hydroxy ketone with its inherent lability[3] and it was a bicyclo[3.3.1]nonane derivative in a chair-boat conformation. Preliminary experiments[4] revealed that Huang Minlon and Clemmensen reductions[5] of ketone *V* were equally unsuccessful as hydrogenolysis of methanesulfonate *IV*.

The most promising substrate seemed to be (5*R*)-3α-acetoxy-5-methanesulfonate *VIII* in which the 3α-equatorial substituent did not hinder the approach of the hydride reagent to the $C_{(5)}$-carbon atom. The methanesulfonyloxy group in *VIII* occupies the position which is equatorial with respect to the ring A and at the same time axial (or pseudo-axial) with respect to the ring B in the boat conformation. Treatment of compound *VIII* with lithium aluminium hydride yielded as a major product a diol (*X*; 84%): Mass spectrum showed the molecular peak at 278*m*/*e*, ^{1}H-NMR spectrum (Table I) confirmed the presence of two hydroxy groups and revealed the existence in the molecule of a disubstituted double bond. Relative intensities of signals of hydrogen atoms in positions 3, 17, 5 and 6 confirmed the structure of compound *X*.

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The reductive displacement was further attempted by action of sodium iodide and zinc powder[6,7] on methanesulfonate *VIII*. Separation of the resulting mixture of olefins was achieved by chromatography on silica gel with silver nitrate: the pure products, isomers *XI* (10%) and *XIV* (56%) were usefully distinctive in their ^{1}H-NMR and IR spectra (absorption of the exomethylene group at 900 cm^{-1} in the latter case and a signal of methyl group situated at the tetrasubstituted double bond in the former case). To prove the ring contraction in the process of their formation compounds *XI* and *XIV* were deacetylated and oxidized to compounds *XVIII* and *XIX*, respectively, exhibiting spectral properties (IR) of the cyclopentanone moiety.

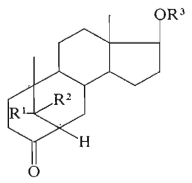
TABLE I

Characteristic Parameters of the ^{1}H-NMR Spectra

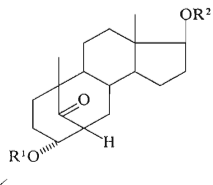
The spectra were measured on a Tesla 60 instrument in deuteriochloroform with tetramethylsilane as internal reference. Chemical shifts are given in δ-scale (ppm).

Substance	19-H[a]	18-H[a]	3-H[b]	17-H[c]	Other signals
VI	0·95	0·88	3·83	4·83	7·42[d], 8·05[e]
VII	1·00	0·84	4·75	4·56	1·18[f], 2·03[g], 3·19[i]
VIII	1·04	0·83	4·72	4·58	1·19[f], 2·02[g], 3·02[h], 4·19[i]
X	0·90	0·75	3·65	3·65	5·52[j], 5·28[j]
XI	4·67[k]	0·81	5·01	4·59	1·19[f], 2·02[g]
XIV	1·61[l]	0·88	5·10	4·55	1·18[f], 2·03[g]
XV	1·60[l]	0·89	4·47	4·58	1·20[f]
XVII	1·62[l]	0·87	5·10	4·58	2·03[g]
XVIII	4·83[k]	0·81	—	4·62	1·19[f]
XIX	1·69[l]	0·89	—	4·50	1·18[f]
XXII	*o*	0·86	5·28	4·49	1·18[f], 2·01[g], 3·16[m]
XXIII	1·06	0·90	4·40	4·83	3·17[n], 3·21[n], 7·47[d], 8·05[e]
XXIV	1·14	0·99	4·20	4·83	3·17[m], 7·50[d], 8·05[e]
XXV	0·84	0·82	4·61	4·61	1·18[f], 2·01[g]
XXVII	0·86	0·95	3·60	4·83	7·48[d], 8·08[e]
XXVIII	0·96	0·96	—	4·83	7·48[d], 8·05[e]
XXIX	0·95	0·74	—	3·62	
XXX	0·84	0·86	3·65	—	
XXXI	0·97	0·88	—	—	

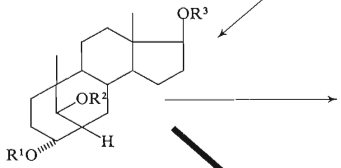
[a] Singlet unless stated otherwise; [b] broad multiplet, $W_{1/2}$ = 21 Hz; [c] triplet, J = 8 Hz; [d] mt aromatic protons; [e] mt aromatic protons; [f] singlet (9 H) of 3 methyl groups of the pivaloyloxy group; [g] singlet (3 H) of the methyl group in the acetoxy group; [h] singlet (3 H) of the methanesulfonyloxy group; [i] doublet (1 H) of the $C_{(5)}$-proton, J = 2·5 Hz; [j] multiplet of vinylic protons in the positions 5 and 6; [k] doublet (2 H), J = 6 Hz (*XI*) or 8 Hz (*XVIII*); [l] broad singlet; [m] narrow multiplet of protons in the dithiolane ring; [n] singlet (4 H) of protons of the dithiolane ring; [o] obscured by other signals.



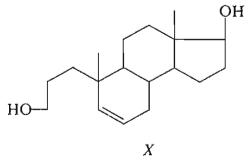
I, R^1 = HO, R^2 = H, R^3 = H
II, R^1 = H, R^2 = OH, R^3 = H
III, $R^1 + R^2$ = O, R^3 = Ac
IV, R^1 = MsO, R^2 = H, R^3 = Ac



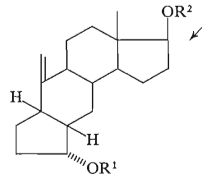
V, R^1 = Ac, R^2 = Piv
VI, R^1 = H, R^2 = Bz



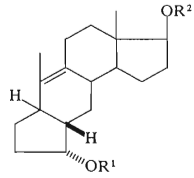
VII, R^1 = Ac, R^2 = H, R^3 = Piv
VIII, R^1 = Ac, R^2 = Ms, R^3 = Piv
IX, R^1 = H, R^2 = H, R^3 = H



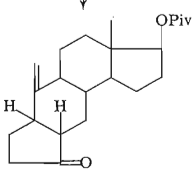
X



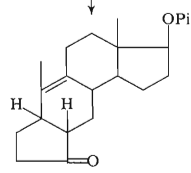
XI, R^1 = Ac, R^2 = Piv
XII, R^1 = H, R^2 = Piv
XIII, R^1 = H, R^2 = H



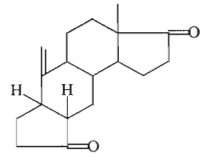
XIV, R^1 = Ac, R^2 = Piv
XV, R^1 = H, R^2 = Piv
XVI, R^1 = H, R^2 = H
XVII, R^1 = Ac, R^2 = Ac



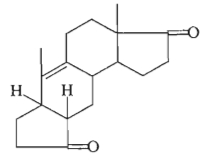
XVIII



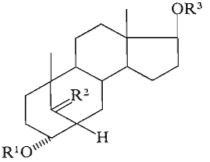
XIX



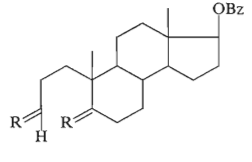
XX



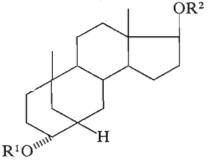
XXI



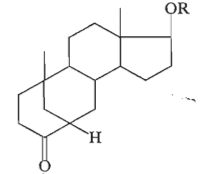
XXII, R^1 = Ac, R^2 = $C_2H_4S_2$, R^3 = Piv
XXIV, R^1 = H, R^2 = $C_2H_4S_2$, R^3 = Bz



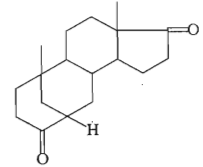
XXIII, R = $C_2H_4S_2$



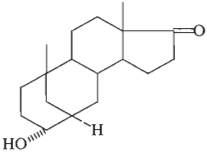
XXV, R^1 = Ac, R^2 = Piv
XXVI, R^1 = H, R^2 = H
XXVII, R^1 = H, R^2 = Bz



XXVIII, R = Bz
XXIX, R = H

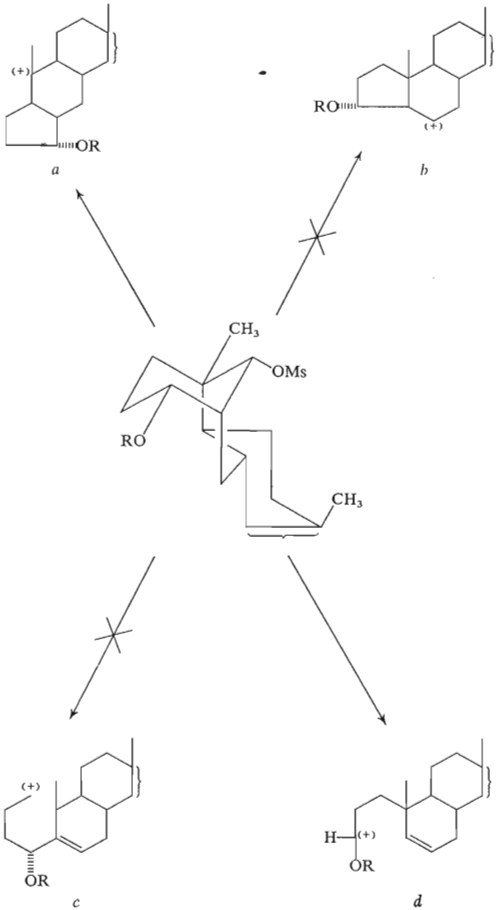


XXXI



XXX

Ac = CH_3CO, Piv = $(CH_3)_3CCO$, Bz = C_6H_5CO, Ms = CH_3SO_2



SCHEME 1

Regiospecificity of the reactions of compound *VIII* with both reagents was very high: the hydride treatment yielded only 3% of the mixture of diols *XIII* and *XVI* while no seco diol *X* could be detected (TLC) as the product of the alternative pathway (*i.e.* sodium iodide-zinc treatment followed by hydrolysis). The treatment of compound *VIII* with sodium iodide in the absence of zinc powder gave the same mixture of compounds *XI* and *XIV*. In all cases the reagents bring about an elimination which is followed by rearrangements. Dreiding models reveal conformational identity of both $C_{(1)}$—$C_{(10)}$- and $C_{(3)}$—$C_{(6)}$-bonds. However, one bridgehead atom ($C_{(10)}$) is a quaternary while the other one ($C_{(6)}$) is a tertiary carbon atom. Furthermore, one β-carbon to the $C_{(5)}$-carbon atom bears an oxygen function while the other one is unsubstituted. Taking into account the stability of intermediary carbocations (Scheme *1*) the Wagner–Meerwein rearrangement is likely to proceed with migration of the $C_{(1)}$-carbon atom and ring opening with the cleavage of the $C_{(3)}$—$C_{(6)}$-bond. The latter process is utilized when lithium aluminium hydride is the reagent, as excess of the reagent immediately reduced the intermediate (*d*) to an alcohol. In the absence of lithium aluminium hydride the $C_{(3)}$—$C_{(6)}$-cleavage is not significant and the Wagner–Meerwein rearrangement takes place.

Deoxygenation of the system without any rearrangement was eventually carried out *via* dithiolanes. Under carefully controlled conditions the hydroxy ketone[1] *VI* afforded the desired dithiolane *XXIV* accompanied by a small amount of the starting material and a less polar compound *XXIII*. On prolonged treatment the less polar compound becomes the major product. Its elemental analysis and ^{1}H-NMR spectra (relative intensities of singlets at 3·2 ppm, downfield shift of the 3-proton signal) are in agreement with the structure of bis-dithiolane *XXIII*. Using the more stable 3-acetoxy derivative *V* as the starting material the reaction becomes slower (*XXII*) and the retroaldol reaction leading eventually to a bis-dithiolane product is suppressed.

Desulfurization of dithiolanes *XXII* and *XXIV* with Raney nickel affords derivatives of 3,6-cyclo-A-nor-3,5-secoandrostan-3α,17β-diol (*XXVI*), *i.e.* compounds *XXV* and *XXVII* resp. Oxidation and hydrolysis of compound *XXVII* gave the corresponding testosterone analogue (*XXIX*). Most convenient synthesis of the androsterone analogue (*XXX*) was based on selective reduction of the dione *XXXI* by means of lithium tri-tert-butoxy aluminum hydride which gives the desired product (*XXX*) accompanied by a negligible amount of the diol *XXVI*.

Pharmacodynamic activity of compounds *XXIX*, *XXX* and *XXXI* will be reported later.

EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. Analytical samples were dried over phosphorus pentoxide at 50°C/0·2 Torr. Optical rotation and infrared spectra were measured in chloroform unless stated otherwise. ^{1}H-NMR spectra were measured in deuteriochloroform, the chemical shifts are given in δ-scale (ppm).

(5*R*)-3α-Acetoxy-5-methanesulfonyloxy-17β-pivaloyloxy-3,6-cyclo-A-nor-3,5-seco-6β-androstane (*VIII*)

A solution of hydroxy derivative[1] *VII* (1·4 g) in pyridine (4 ml) and methanesulfonyl chloride (1·4 ml) was set aside for 18 h at 0°C. The mixture was poured into ice and the product taken up in ether, the ethereal layer was washed with dilute hydrochloric acid (5%), brine, aqueous potassium hydrogen carbonate, water and dried over anhydrous sodium sulfate. The product was crystallized from ether and heptane, m.p. 122—124°C (1·1 g), $[\alpha]_D^{20}$ +5° (*c* 2·0). For $C_{26}H_{42}O_7S$ (498·7) calculated: 62·62% C, 8·49% H; found: 62·43% C, 8·38% H.

3,5-Seco-4-nor-5-androsten-3,17β-diol (*X*)

Compound *VIII* (1·0 g) was added to a solution of lithium aluminum hydride (c. 0·5 g) in dioxane (30 ml) and the solution was refluxed for 5 h. The reagent was carefully decomposed with a few drops of water and the product extracted with chloroform. Chromatography on silica gel (30 g, 50% ether in toluene) yielded the major product *X* (470 mg), m.p. 142—144°C (acetone), $[\alpha]_D^{20}$ −36° (*c* 1·5); mass spectrum: 278*m/e* (M^+); IR spectrum: 3620, 1053 (OH), 1659 (C=C) cm^{-1}. For $C_{18}H_{30}O_2$ (278·4) calculated: 77·65% C, 10·86% H; found: 77·29% C, 10·39% H.

(5*R*)-3,6-Cyclo-A-nor-3,5-seco-6β-androstan-3α,5,17β-triol (*IX*)

The more polar compound isolated by means of chromatography of the preceeding diol *X* (compound *IX*, 14 mg) was crystallized, m.p. 262—265°C (acetone). For $C_{18}H_{30}O_3$ (294·4) calculated: 74·43% C, 10·27% H; found: 71·17% C, 10·28% H.

1α-Acetoxy-17β-pivaloyloxy-1(10→6β*H*)abeo-A-nor-5β-androst-8-ene (*XIV*)

Methanesulfonate *VIII* (0·9 g) was added to a boiling mixture of zinc powder (c. 5 g), sodium iodide (c. 1 g) in dimethoxyethane (50 ml), and the mixture was refluxed for 5 h. Inorganic compounds were filtered off and the mother liquors were diluted with toluene (c. 200 ml), washed with aqueous solution of sodium thiosulfate and water and evaporated *in vacuo*. The residue was applied on silica gel containing 5% of silver nitrate. Benzene eluted 450 mg of the major product (*XIV*), $[\alpha]_D^{20}$ +51° (*c* 0·9); IR spectrum: 1716, 1292, 1286, 1174 (OPiv), 1725, 1255 (OAc) cm^{-1}. For $C_{25}H_{38}O_4$ (402·6) calculated: 74·59% C, 9·51% H; found: 74·30% C, 9·63% H.

1α-Acetoxy-17β-pivaloyloxy-1(10→6β*H*)abeo-A-nor-5β-androst-10(19)-ene (*XI*)

More polar fractions of the preceeding chromatography yielded 70 mg of the isomeric olefin (*XI*), $[\alpha]_D^{20}$ +21° (*c* 0·8), IR spectrum: 1714, 1293, 1285, 1173 (OPiv), 1722, 1257 (OAc), 3090, 1640, 899 (C=CH$_2$) cm^{-1}. For $C_{25}H_{38}O_4$ (402·6) calculated: 74·59% C, 9·51% H; found: 74·10% C, 9·49% H.

17β-Pivaloyloxy-1(10→6β*H*)abeo-A-nor-5β-androst-9-en-1α-ol (*XV*)

A solution of acetate *XIV* (400 mg) in methanol (8 ml) was made alkaline by means of 0·7 ml of aqueous potassium hydroxide (1·5M). The mixture was concentrated to a quarter of its volume *in vacuo*, diluted with brine and extracted with chloroform. The washed extract was evaporated and the residue was crystallized from acetone, m.p. 169—170°C, (300 mg), $[\alpha]_D^{20}$ +3° (*c* 0·9). For $C_{23}H_{36}O_3$ (360·5) calculated: 76·62% C, 10·07% H; found: 76·48% C, 10·21% H.

17β-Pivaloyloxy-1(10→6 β*H*)abeo-A-nor-5β-androst-10(19)-en-1α-ol (*XII*)

Analogously acetate *XI* (50 mg) was hydrolyzed with potassium hydroxide, the product was purified by thin layer chromatography (silica gel, 10% ether in benzene). M.p. 139—140°C (heptane), $[\alpha]_D^{20}$ −14° (*c* 0·9).

17β-Pivaloyloxy-1(10→6β*H*)abeo-A-nor-5β-androst-10(19)-en-1-one (*XVIII*)

Hydroxy derivative *XII* (40 mg) was oxidized according to Jones at room temperature, the mixture was poured into aqueous potassium hydrogen carbonate, the precipitate was taken up in ether and washed. M.p. 124—126°C (heptane, 25 mg); $[\alpha]_D^{20}$ −3° (*c* 1·0); IR spectrum (CCl_4): 1734 (cyclopentanone moiety), 1730, 1290, 1284, 1164 (OPiv), 3095, 1641, 899 (C=CH_2) cm^{-1}. For $C_{23}H_{34}O_3$ (358·5) calculated: 77·05% C, 9·70% H; found: 76·81% C, 9·70% H.

17β-Pivaloyloxy-1(10→6β*H*)abeo-A-nor-5β-androst-9-en-1-one (*XIX*)

Hydroxy derivative *XV* (130 mg) was oxidized according to the preceeding experiment, m.p. 97—98°C (ether, 54 mg), $[\alpha]_D^{20}$ +37° (*c* 1·9); IR spectrum: 1725, 1292, 1288, 1171 (OPiv), 1730 (cyclopentanone moiety) cm^{-1}. For $C_{23}H_{34}O_3$ (358·5) calculated: 77·05% C, 9·56% H; found: 77·14% C, 9·76% H.

1(10→6β*H*)Abeo-A-nor-5β-androst-9-ene-1α,17β-diol (*XVI*)

The least polar (column of silica gel) component of the mixture obtained from compound *VIII* on reaction with lithium aluminum hydride (see the preparation of compound *X*) was crystallized from chloroform and ether, m.p. 173—176°C. For $C_{18}H_{28}O_2$ (276·4) calculated: 78·21% C, 10·21% H; found: 77·91% C, 10·18% H.

1α,17β-Diacetoxy-1(10→6β*H*)abeo-A-nor-5β-androst-9-ene (*XVII*)

Acetylation of compound *XVI* under standard conditions yielded diacetate *XVII*, m.p. 121—124°C (methanol), $[\alpha]_D^{20}$ +56° (*c* 1·3); IR spectrum (CCl_4): 1740, 1248, 1046 (OAc), 1675 (C=C) cm^{-1}. For $C_{22}H_{32}O_4$ (360·5) calculated: 73·30% C, 8·95% H; found: 73·02% C, 9·07% H.

1(10→6β*H*)Abeo-A-nor-5β-androstane-1,17-diones (*XX* and *XXI*)

Mother liquors obtained on crystallization of compound *XVI* were oxidized according to Jones. The product was separated by thin layer chromatography on silica gel with silver nitrate. The less polar compound (*XXI*, 19 mg) was assigned the structure of 1(10→6β*H*)abeo-A-nor-5β--androst-9-ene-1,17-dione on the basis of its IR spectrum (CCl_4): 1744 (cyclopentanone moiety), 3020 and 1660 (C=C) cm^{-1}. The more polar component (7 mg) was assigned analogously the

structure of 1(10→6β*H*)abeo-A-nor-5β-androst-10(19)-ene-1,17-dione (*XX*); IR spectrum: 1735 (C=O), 3095, 1642, 902 (C=C) cm^{-1}.

17β-Benzoyloxy-3α-hydroxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-5-one (*VI*)

Tri-tert-butyloxylithium aluminum hydride (40 g) was added to a solution of 17β-benzoyloxy--4-oxa-5-androsten-3-one[8] (20 g) in tetrahydrofuran (180 ml) at −70°C. Stirring was continued for another hour while the temperature was allowed to rise to 15°C. The mixture was acidified with dilute hydrochloric acid (5%, 200 ml) and the product was taken up in chloroform. The extract was washed with water and dried and the solvent was evaporated *in vacuo*. The residue (20 g) crystallized from ether and heptane, m.p. 200–203°C (*VI*, 7 g), $[\alpha]_D^{20}$ +25° (*c* 1·1). For $C_{25}H_{32}O_4$ (396·5) calculated: 75·72% C, 8·14% H; found: 75·63% C, 8·19% H.

Combined mother liquors were chromatographed on a column of silica gel (toluene with 15% ether). Besides additional crop of compound *VI* isomeric 17β-benzoyloxy-3β-hydroxy-3,6-cyclo--A-nor-3,5-seco-6β-androstan-5-one (4·4 g) was obtained, m.p. 200–204°C (chloroform, ether), $[\alpha]_D^{20}$ +8° (1·2); ^{1}H-NMR spectrum: 0·87 (s, 3 H), 0·98 (s, 3 H), 4·21 (mt, $W_{1/2}$ = 9 Hz, 1 H), 4·82 (t, J = 8 Hz, 1 H) ppm. For $C_{25}H_{32}O_4$ (396·5) calculated: 75·72% C, 8·14% H; found: 75·59% C, 8·04% H.

3α-Acetoxy-17β-pivaloyloxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-5-one, Cyclic Ethylene Mercaptal (*XXII*)

Boron trifluoride etherate (0·3 ml) was added to a solution of ketone *V* (108 mg) in benzene (0·3 ml) and ethanedithiol (0·13 ml). The mixture was diluted with benzene (25 ml) after 6 hours, washed with 6% aqueous potassium hydroxide and water and evaporated *in vacuo*. The major product was crystallized from heptane, m.p. 130–132°C (70 mg), $[\alpha]_D^{20}$ +38° (*c* 0·9). For $C_{27}H_{42}O_4S_2$ (497·8) calculated: 65·54% C, 8·65% H; found: 65·71% C, 8·69% H.

17β-Benzoyloxy-3α-hydroxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-5-one, Cyclic Ethylene Mercaptal (*XXIV*)

Boron trifluoride etherate (2 ml) was added to a solution of ketone *VI* (1·2 g) in chloroform (8 ml) and ethanedithiol (3 ml). After 35 min standing at 20°C the mixture was diluted with benzene (c. 150 ml) and washed with 10% solution of potassium hydroxide in water and with water. The solvent was evaporated *in vacuo* and the residue was applied on a column of silica gel. Benzene eluates were collected (500 ml) and then 30% ether in benzene eluted the dithiolane derivative *XXIV* (1·1 g), $[\alpha]_D^{20}$ +27° (*c* 2·1). For $C_{27}H_{36}O_3S_2$ (472·7) calculated: 68·60% C, 7·68% H; found: 68·41% C, 7·54% H.

17β-Benzoyloxy-5-oxo-3,5-seco-A-norandrostan-3-al,3,5-bis-ethylene Cyclic Mercaptal (*XXIII*)

Benzene eluates from the preceeding experiment were purified on a thin layer of silica gel. Crystallization afforded dithiolane derivative *XXIII* (70 mg), 173–175°C, $[\alpha]_D^{20}$ +46° (*c* 1·2). For $C_{29}H_{40}O_2S_4$ (548·9) calculated: 63·46% C, 7·34% H, 23·37% S; found: 63·57% C, 7·49% H, 22·95% S.

3α-Acetoxy-17β-pivaloyloxy-3,6-cyclo-A-nor-3,5-seco-6β-androstane (*XXV*)

Dithiolane derivative *XXIV* (21 mg) was refluxed in ethanol (2 ml) containing 0·5 ml of Raney nickel. After 5 h the mixture was diluted with ethanol (10 ml) and inorganic material was filtered off. The product was purified on a thin layer of silica gel (5% ether in benzene) and crystallized from methanol. M.p. 117–120°C. For $C_{25}H_{40}O_4$ (404·6) calculated: 74·21% C, 9·97% H; found: 73·95% C, 10·16% H.

17β-Benzoyloxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-3α-ol (*XXVII*)

Dithiolane derivative *XXIV* (150 mg) was analogously treated with Raney nickel to yield 120 mg of compound *XXVII* which after crystallization from acetone and heptane melted at 172–173°C, $[\alpha]_D^{20}$ +62° (*c* 1·1). For $C_{25}H_{34}O_3$ (382·5) calculated: 78·49% C, 8·96% H; found: 78·16% C, 9·09% H.

17β-Benzoyloxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-3-one (*XXVIII*)

Hydroxy derivative *XXVII* (440 mg) was oxidized according to Jones at 5°C. After 10 min the mixture was decomposed with a solution of potassium hydrogen carbonate, the product was taken up in ether and washed with brine. The solution was dried over sodium sulfate and evaporated. Ketone *XXVIII* (410 mg) crystallized from acetone and heptane, m.p. 121–123°C, $[\alpha]_D^{20}$ +83° (*c* 1·3); IR spectrum (CCl_4): 1721, 1277 (BzO), 1713 (inflex, cyclohexanone moiety) cm^{-1}. For $C_{25}H_{32}O_3$ (380·5) calculated: 78·91% C, 8·48% H; found: 78·72% C, 8·40% H.

17β-Hydroxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-3-one (*XXIX*)

Benzoate *XXVIII* (105 mg) was refluxed with 5% solution of potassium hydroxide in methanol in nitrogen atmosphere. After 1 h the mixture was diluted with benzene (c. 70 ml) and washed with water. The dried solution was evaporated and the residue was crystallized from ether. M.p. 137–139°C (63 mg), $[\alpha]_D^{20}$ +38° (*c* 1·1). For $C_{18}H_{28}O_2$ (288·4) calculated: 78·31% C, 10·16% H; found: 78·21% C, 10·21% H.

3,6-Cyclo-A-nor-3,5-seco-6β-androstane-3,17-dione (*XXXI*)

The hydroxy ketone *XXIX* (1·5 g) was oxidized according to Jones. The usual work-up and crystallization afforded 1·2 g of dione *XXXI*, m.p. 114–117°C (ether and heptane), $[\alpha]_D^{20}$ +114° (*c* 1·5); IR spectrum (CCl_4): 1744, 1408 (cyclopentanone moiety), 1711, 1421 (cyclohexanone moiety) cm^{-1}. For $C_{18}H_{26}O_2$ (274·4) calculated: 78·79% C, 9·55% H; found: 78·82% C, 9·76% H.

3α-Hydroxy-3,6-cyclo-A-nor-3,5-seco-6β-androstan-17-one (*XXX*)

Diketone *XXXI* (100 mg) was dissolved in tetrahydrofuran (4 ml) and treated with tri-tert-butoxylithiumaluminum hydride (130 mg) at 20°C. After 5 min the mixture was poured in dilute hydrochloric acid (5%, 5 ml) and the precipitate was taken up in chloroform. The product was separated on a thin layer of silica gel (35% ether in benzene). The major product (*XXXI*, 67 mg) was crystallized from acetone and heptane, m.p. 144–147°C, $[\alpha]_D^{20}$ +88° (*c* 1·5). For $C_{18}H_{28}O_2$ (276·4) calculated: 78·21% C, 10·21% H; found: 78·43% C, 10·36% H. The less polar admixture (10 mg) was found identical with isomeric compound *XXIX*.

3,6-Cyclo-A-nor-3,5-seco-6β-androstane-3α,17β-diol (*XXVI*)

The more polar admixture isolated in the preceeding experiment (*XXVI*, 18 mg) crystallized from acetone and heptane, m.p. 208–210°C, $[\alpha]_D^{20}$ +13° (50% methanol in chloroform, *c* 1·3). For $C_{18}H_{30}O_2$ (278·4) calculated: 77·65% C, 11·50% H; found: 77·41% C, 11·39% H. Diol *XXVI* was sought in the products of both the lithium aluminum hydride reduction and the sodium iodide treatment of methanesulfonate *VIII* followed by hydrolysis. Thin layer chromatography on silica gel (50% ether in benzene, threefold development) did not reveal the presence of diol *XXVI* in the mixtures.

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