Amino-steroids. Part 6.[1] Stereospecific Syntheses of Eight, Isomeric, Steroidal Vicinal 2,3-Amino-alcohols

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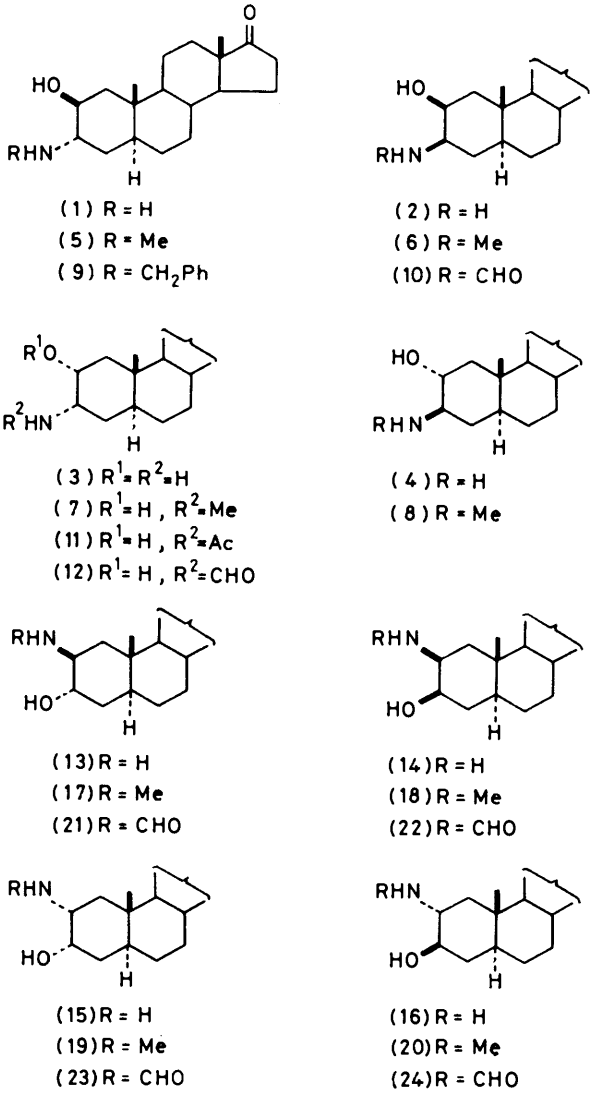
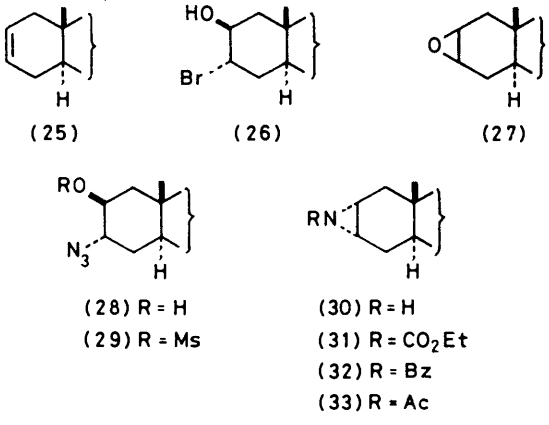
The seven possible 3-amino-2-hydroxy and 2-amino-3-hydroxy isomers of the anti-arrhythmic steroid, 3α-amino-2β-hydroxy-5α-androstan-17-one, were prepared from 5α-androst-2-en-17-one. The intermediate 2α,3α- and 2β,3β-epoxides and aziridines were cleaved to vicinal *trans*-diaxial amino- and azido-alcohols, which in turn yielded the isomers by a series of functional group inversions and transformations.

THE reactions of 2α,3α- and 2β,3β-epoxy-5α-androstanes with amines to give 2β-amino-3α-ols and 3α-amino-2β-ols have been the subject of a previous paper [2] and subsequently the hydrochloride (Org 6001) of 3α-amino-2β-hydroxy-5α-androstan-17-one (1) was prepared [3] and found to be a novel anti-arrhythmic drug.[4] Modifying the amine substituent or altering the 17-function yielded less potent compounds,[5] and it was therefore decided to synthesise and evaluate the seven 3-amino-2-hydroxy and 2-amino-3-hydroxy isomers of Org 6001. Although routes to several vicinal amino-alcohols, in the androstane and cholestane series, were available,[6] it was necessary to develop efficient and stereospecific syntheses of the two groups of diastereoisomers (1)—(4) and (13)—(16), preferably from a readily available common precursor. This paper describes the transformation of the Δ^2-17-ketone (25) [7] into α- and β-epoxides, aziridines, and oxazolines, which were subjected to a series of ring-opening reactions and functional group inversions and transformations, to give the target amino-alcohols. Other routes to the desired products involved vicinal diol and vicinal azido-ketone intermediates derived from starting material (25).



SCHEME 1 Throughout the paper numbers with no suffix refer to compounds having a 17-oxo-group; numbers with the suffix a refer to the 17-ethylene acetal



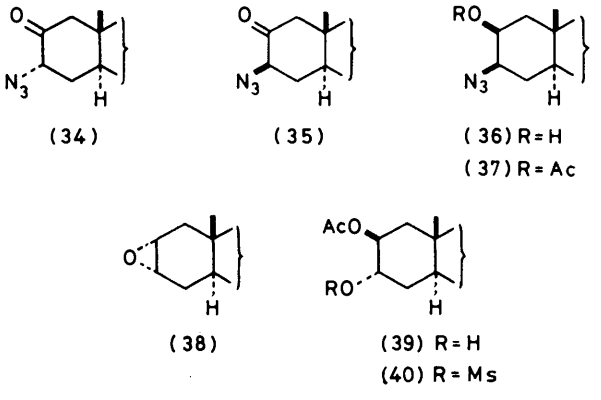
SCHEME 2

The common starting material for isomers (1)—(4), the Δ^2-17-ketone (25), was converted to the 2β,3β-epoxide (27) *via* the bromohydrin (26). *trans*-Diaxial ring-opening [8] of the epoxide (27) by sodium azide gave as the sole product the 2β-hydroxy-3α-azide (28) which was converted to the amine (1) by catalytic hydrogenation. An alternative preparation involved reaction of benzylamine with the oxide (27) at reflux temperature, followed by hydrogenolysis. A further route, based on aziridine

ring opening, utilised the mesylate (29) which was protected as the 17-acetal (29a) and reacted with lithium aluminium hydride [9] to give the α-aziridine (30) * as the 17-acetal (30a).

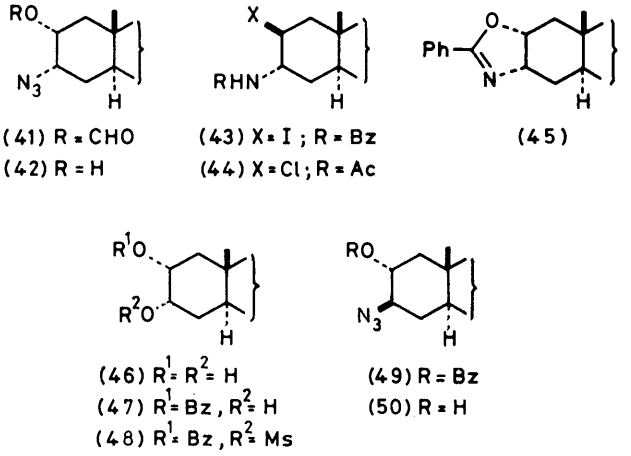
Hydrolysis with aqueous sulphuric acid gave the 2β-hydroxy-3α-amine (1). Thus, the *trans*-diaxial hydroxy-amine (1) was obtained from either the β-epoxide or the α-aziridine. Throughout the series (1)—(4) and (13)—(16) the equatorial protons at C-2 or -3 invariably appeared as ' sharp ' multiplets in the ^{1}H n.m.r. spectrum while the axial protons appeared as broad multiplets, with no indication of unusual conformation of ring A in any of the isomers. Thus, in the 2,3-diaxial compound (1), 2-H was a ' sharp ' multiplet centred on δ 4.90 and 3-H was a ' sharp ' multiplet at δ 4.08.

The 2β-hydroxy-3β-amino steroid (2) was also obtained from the β-epoxide (27) *via* the azido-alcohol (28), which was acetalized and then oxidised with buffered pyridinium chlorochromate [10] to give the 2-oxo-3α-azide 17-acetal (34a). Epimerisation to the thermodynamically more stable 3β-azide (35a) occurred on silica gel, and the reduction to the amino-alcohol (2) was best carried out in two steps, firstly using sodium borohydride in methanol to give the expected axial 2β-alcohol (36a), by steric approach control,[11] followed by lithium aluminium hydride reduction of the azide and deacetalisation. Attempts to convert the 2β-acetoxy-3α-ol (39), obtained from the 2α,3α-epoxide (38), to the 2β-acetoxy-3β-azide (37) *via* the mesylate (40) were unsuccessful, an impure, unidentified rearrangement product being obtained. It is interesting to note that the α-oxide (38) was prepared in 94% yield from unprotected Δ^2-17-ketone (25), with little or no lactone formation, using a two-phase system of chloroform and aqueous peracetic acid.



SCHEME 3

The 2α-hydroxy-3α-amine (3) was also prepared from the azido-alcohol (28). An esterification–inversion sequence [12] using diethyl azodicarboxylate–triphenylphosphine–formic acid gave the 2α-formyloxy-3α-azide (41) which was hydrolysed by hydroxide, the 17-ketone protected, and the azide reduced with lithium aluminium hydride.† Deprotection gave the 2α,3α-product (3). In an alternative route, the *N*-benzoyl-2α,3α-aziridine 17-acetal (32a) was treated with sodium iodide in acetone to



SCHEME 4

give, by *trans*-diaxial ring-opening, the transient 2β-iodo-3α-benzamido-17-acetal (43a), which spontaneously cyclised to the 2α,3α-oxazoline (45a).[13] Hydrolysis using concentrated sulphuric acid gave the amino-alcohol (3), in which 2-H was shown by n.m.r. to be axial and 3-H equatorial. A further route to the *cis*-isomer (3) involved ring opening of the *N*-acetyl-2α,3α-aziridine (33) with hydrogen chloride to give the 2β-chloro-3α-acetamido-steroid (44), followed by acetate displacement of the axial chloro-group (potassium acetate–dimethylformamide–water) to give the 2α-hydroxy-3α-acetamido-5α-androstan-17-one (11), which was hydrolysed to the 2α-hydroxy-3α-amine (3). Alternative routes to (3) based upon the Sharpless vicinal hydroxyamination [14] were not investigated because of the possible formation of both 3β-amino-2β-hydroxy- and 2α-amino-3α-hydroxy-isomers.

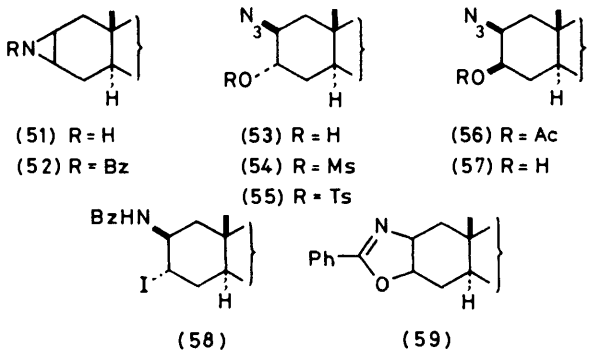
The diequatorial 2α-hydroxy-3β-amine (4) posed a particular problem. Attempts to reduce the 2-oxo-3β-azide (35a) to the equatorial alcohol with sodium–ethanol or aluminium isopropoxide gave a complex mixture of products, while the 3β-azido-2β-ol (36) was unaffected by Bose esterification conditions.[12] However, preferential benzoylation of the equatorial 2α-hydroxy group [15] of the 2α,3α-diol (46), obtained from the Δ^2-compound by oxidation with either osmium tetraoxide [16] or potassium permanganate–tetrabutylammonium bromide in a two-phase system,[17] gave the monobenzoate (47), which was converted to the mesylate (48). Displacement of the mesyloxy group with sodium azide then gave the 3β-azide (49), which was hydrolysed to the azido-alcohol (50) and reduced (hydrogen–

* An alternative route to the aziridine (30) involved reaction of (25) with *p*-nitrophenylsulphonyloxyurethane and triethylamine, leading to the *N*-ethoxycarbonylaziridine (31) which was converted into (30) by potassium hydroxide in ethanol.

† Lithium aluminium hydride reduction of the protected 17-ketone proved to be a generally applicable process, as opposed to catalytic hydrogenation, which was not always effective.

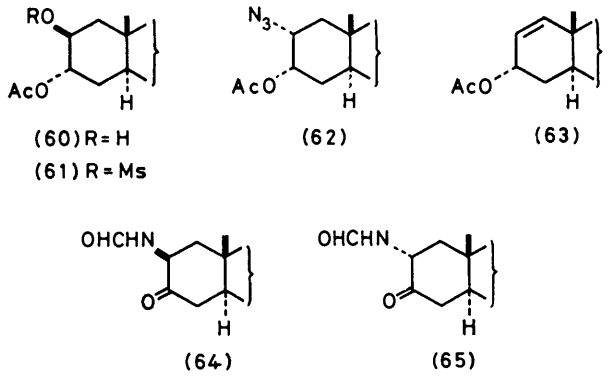
palladium) to the diequatorial amino-alcohol (4). N.m.r. showed the 2- and 3-H signals as broad multiplets.

The 2β-amino-3α-hydroxy steroid (13) was obtained directly from the α-epoxide (38) by *trans*-diaxial ring opening with ammonia.[5] Alternatively, the 17-acetal (51a) of 2β,3β-aziridine (51) [prepared by ring-opening of the 2α,3α-epoxide (38) by azide to give azido-ol (53) followed by mesylation, 17-acetal formation, and reduction of the mesylate (54a) with lithium aluminium hydride [9]] was converted to the amino-alcohol (13) by acid hydrolysis.



SCHEME 5

The 2β-amino-3β-alcohol (14) was prepared from the α-epoxide (38) by an azide–tosylation–acetolysis sequence to give the azido-acetate (56) in poor yield, the product being contaminated with elimination products. Acetalisation, reduction with lithium aluminium hydride, and deprotection afforded the *cis*-isomer. A complementary synthesis from the *N*-benzoyl-2β,3β-aziridine (52) involved ring-expansion * to the β-oxazoline (59) [*via* the unisolable 2β-benzamido-3α-iodide (58)] and hydrolysis by sulphuric acid. The equatorial proton 2-H and the axial proton 3-H appeared in the n.m.r. spectrum as sharp and broad multiplets respectively.



SCHEME 6

In contrast to the earlier unsuccessful attempt to obtain the 2β-acetoxy-3β-azide (37) from the 2β-acetoxy-3α-mesylate [18] (40), 2α-amino-3α-hydroxy-5α-androstan-17-one (15) was obtained from the β-epoxide (27) by ring opening to the 3α-acetoxy-2β-ol (60) with acetic acid, mesylation to give (61), and then azide displacement of the axial mesyloxy group giving the 2α-azido-3α-acetate (62), together with the by-product (63). Protection of the 2α-azido-3α-acetoxy-17-ketone as the acetal (62a), followed by reduction and deprotection gave the 2α-amino-3α-ol (15).

The final isomer (16) was obtained in poor yield, by equilibrating the 17-acetal of the 2β-formamido-3-ketone (64a) on alumina, to a mixture of the 2β-formamido-3-ketone (64a) and the 2α-formamido-3-ketone (65a), which was reduced with sodium borohydride to a mixture of the 2β-formamido-3β-ol (22a) and the 2α-formamido-3β-ol (24a). The required *trans*-diequatorial isomer (24a) was isolated by chromatography and hydrolysed to give 2α-amino-3β-hydroxy-5α-androstan-17-one (16).

Five of the corresponding methylamino-alcohols (5)—(8) and (17)—(20) were obtained from the primary amines by a four-stage sequence, involving *N*-formylation, acetalisation, lithium aluminium hydride reduction, and deprotection. The 2β-hydroxy-3α-methylamino isomer (5) was obtained by direct opening of the β-oxide with methylamine. [Inadequate supplies of the diequatorial compounds (4) and (16) were available.] All the amino-alcohols were converted to their hydrochlorides for pharmacological testing.

In conclusion, the single precursor (25) has been converted into 2α,3α- and 2β,3β-epoxides, aziridines, and oxazolines which have been stereospecificially converted by an inter-related sequence of transformations into the eight isomeric amino-alcohols. The anti-arrhythmic activity of 3α-amino-2β-hydroxy-5α-androstan-17-one hydrochloride (Org 6001), which is at present undergoing clinical trials, has already been reported [4] and the pharmacology of the other isomers and derivatives will be the subject of a further communication.

EXPERIMENTAL

M.p.s were taken with a Kofler micro-hot-stage apparatus and are uncorrected. I.r. spectra were determined with a Perkin-Elmer 457 spectrometer. Optical rotations were measured for solutions in chloroform at room temperature unless otherwise stated. N.m.r. spectra were determined at 60 MHz with a Perkin-Elmer R12B spectrometer (tetramethylsilane as internal standard). Light petroleum refers to the fraction of b.p. 40—60° and ether refers to diethyl ether.

Hydrochloride salts were prepared by treating a solution of free base in dichloromethane with a saturated solution of hydrogen chloride in ether. If the product precipitated, it was removed by filtration; otherwise the solution was evaporated to dryness and the residue slaked with ether.

3α-Bromo-2β-hydroxy-5α-androstan-17-one (26.)—A solution of perchloric acid (70%, 60 ml) in water (280 ml) was added to a stirred solution of 5α-androst-2-en-17-one (25) (200 g) in ether (1.15 l) at 15—20 °C, followed by addition of 1,3-dibromo-5,5-dimethylhydantoin (116 g) in portions over 10 min. After stirring for 1 h, the precipitated crystalline solid was filtered off and washed with ether and water to pH

* Photochemical ring-expansions were unsuccessful, and it is of interest that thermolysis led only to the oxazoline (59), none of the alternative 2β,3β-isomer being isolated.

7 giving a first crop of 3α-bromo-2β-hydroxy-5α-androstan-17-one (26) (148 g), m.p. 154—157°. The liquors were transferred to a separating funnel and the ether layer was washed neutral, dried (Na_2SO_4), and evaporated under reduced pressure to give a second crop (43 g), m.p. 152—156°.

2β,3β-*Epoxy*-5α-*androstan*-17-*one* (27).—3α-Bromo-2β-hydroxy-5α-androstan-17-one (26) (191 g) was added to a stirred solution of potassium hydroxide (10N, 96 ml) in methanol (910 ml) at 60 °C and the mixture was slowly distilled over 30 min. Water (320 ml) was added, the distillation was continued for a further 30 min, and the resulting crop of 2β,3β-epoxy-5α-androstan-17-one (27) (129 g) was filtered off. An excess of water was added to the filtrate giving a small quantity of a yellow gum, which was discarded. The solid was recrystallised from ether–methanol to give a first crop (83 g), m.p. 117—122°, and a second crop (12 g), m.p. 116—119°.

3α-*Azido*-2β-*hydroxy*-5α-*androstan*-17-*one* (28).—2β,3β-Epoxy-5α-androstan-17-one (27) (100 g) was dissolved in dimethylacetamide (860 ml) and sodium azide (27.0 g, 1.2 mol) in water (81 ml) added. The solution was refluxed for 4.5 h, cooled to room temperature, and poured into water (10 vol). The precipitated product was filtered off, washed with water, dried, and crystallised from ether–light petroleum to give pure 3α-*azido*-2β-*hydroxy*-5α-*androstan*-17-*one* (28) (93.76 g, 81.5%) as prisms, m.p. 164—166°, $[\alpha]_D$ +147° (*c* 0.84), $\nu_{max.}$(KCl) 3 430 (OH), 2 080 (N_3), and 1 725 (C=O) cm^{-1}, δ($CDCl_3$) 0.82 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 3.75sh (1 H, m, 3β-H), and 3.95sh (1 H, m, 2α-H) (Found: C, 68.7; H, 8.9; N, 12.6. $C_{19}H_{29}N_3O_2$ requires C, 68.85; H, 8.8; N, 12.7%).

3α-*Benzylamino*-2β-*hydroxy*-5α-*androstan*-17-*one* (9).—A solution of 2β,3β-epoxy-5α-androstan-17-one (27) (95 g) in benzylamine (380 ml) and water (108 ml) was heated at reflux temperature for 24 h. Water (3.8 l) was added and the precipitated product was filtered, washed with water, and dissolved in acetic acid (1.71 l) and water (190 ml). The solution was heated on the water-bath for 1 h, then cooled. A small amount of insoluble material was filtered off and the filtrate was basified by the addition of sodium hydroxide solution (4N, 9.16 l). The product was filtered off, washed with water, and dissolved in dichloromethane. The solution was washed well with water, dried (Na_2SO_4), and concentrated. Crystallisation from dichloromethane–ether gave 3α-*benzylamino*-2β-*hydroxy*-5α-*androstan*-17-*one* (9) as needles (84 g), m.p. 173—180°. An analytical sample had m.p. 189—190°, $[\alpha]_D$ +102° (*c* 1.1), $\nu_{max.}$(KCl) 3 570, 3 440, and 3 325 (OH, NH), 1 735 (C=O), and 755, 742, 720, and 705 (Ph) cm^{-1}, δ($CDCl_3$) 0.80 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 2.77sh (1 H, m, 3β-H), 3.77 (2 H, s, CH_2Ph), 3.85sh (1 H, m, 2α-H), and 7.28 (5 H, s, Ph) (Found: C, 79.0; H, 9.6; N, 3.6. $C_{26}H_{37}NO_2$ requires C, 78.9; H, 9.4; N, 3.5%).

3α-*Azido*-17-*oxo*-5α-*androstan*-2β-*yl Mesylate* (29).—To a solution of 3α-azido-2β-hydroxy-5α-androstan-17-one (28) (4.0 g, 12.2 mmol) in pyridine (80 ml), methanesulphonyl chloride (4 ml) was added dropwise and the resulting mixture was left at 0 °C for 18 h. Water was added and the product was extracted with dichloromethane and the extracts were washed with water and sodium hydrogencarbonate solution, concentrated, and hydrochloric acid and water were added until neutral. The resultant extracts were dried ($MgSO_4$) and concentrated *in vacuo*, yielding a solid. Recrystallisation from ether–light petroleum afforded the *mesylate* (29) (3.43 g, 70%) as needles, m.p. 190—193°, $[\alpha]_D$ +118° (*c* 1.47), $\nu_{max.}$(CH_2Cl_2) 2 100, 1 735, and 1 180 cm^{-1}, δ($CDCl_3$) 0.84 and 0.97 (each 3 H, s, 13- and 10-Me), 3.00 (3 H, s, 2β-OSO_2Me), 3.95sh (1 H, m, 3β-H), and 4.74sh (1 H, m, 2α-H) (Found: C, 58.4; H, 7.7; N, 10.2. $C_{20}H_{31}N_3O_4S$ requires C, 58.65; H, 7.65; N, 10.3%).

3α-*Azido*-17-*oxo*-5α-*androstan*-2β-*yl Mesylate Ethylene Acetal* (29a).—Steroid (29) (3.0 g, 6.62 mmol), ethylene glycol (3.0 ml), triethyl orthoformate (6.0 ml), and toluene-*p*-sulphonic acid (0.19 g) were heated to reflux for 1 h. The solution was allowed to cool to room temperature, poured into sodium carbonate solution, and the product was extracted with ether. The combined ethereal extracts were washed with water, dried ($MgSO_4$), and concentrated *in vacuo* giving a pale yellow oil. Crystallisation from ether yielded the *ethylene acetal* (29a) (2.89 g, 87%), m.p. 172—174°, $[\alpha]_D$ +43° (*c* 0.93), $\nu_{max.}$(CH_2Cl_2) 2 100 and 1 180 cm^{-1}, δ($CDCl_3$) 0.81 and 0.94 (each 3 H, s, 13- and 10-Me), 3.00 (3 H, s, 2β-OSO_2Me), 3.84 (4 H, s, 17-acetal), 3.95sh (1 H, m, 3β-H), and 4.74sh (1 H, m, 2α-H) (Found: C, 58.4; H, 7.8; N, 9.2. $C_{22}H_{35}N_3O_5S$ requires C, 58.25; H, 7.8; N, 9.3%).

2α,3α-*Imino*-5α-*androstan*-17-*one Ethylene Acetal* (30a).—To a solution of acetal (29a) (2.54 g, 5.6 mmol) in ether (120 ml) at 0 °C, lithium aluminium hydride (2.5 g) was added and the resultant mixture was stirred at room temperature for 1.5 h. The excess of lithium aluminium hydride was reacted with 'wet' ether and the aluminium salts were filtered off through Dicalite. The ethereal extracts were washed with water, dried ($MgSO_4$), and concentrated *in vacuo* to give a pale yellow oil. Crystallisation from methanol afforded the *ethylene acetal* (30a) (1.62 g, 85%), m.p. 107—109°, $[\alpha]_D$ −3.8° (*c* 0.98), $\nu_{max.}$(CH_2Cl_2) 1 170 and 795 cm^{-1}, δ($CDCl_3$) 0.76 and 0.82 (each 3 H, s, 13- and 10-Me), 2.10 (2 H, m, 2β- and 3β-H), and 3.84 (4 H, s, 17-acetal) (Found: C, 76.1; H, 10.05; N, 4.2. $C_{21}H_{33}NO_2$ requires C, 76.1; H, 10.0; N, 4.2%).

3α-*Amino*-2β-*hydroxy*-5α-*androstan*-17-*one* (1).—(a) Charcoal (30 g) was added to a solution of 3α-azido-2β-hydroxy-5α-androstan-17-one (28) (300 g) in propan-2-ol (4 l) and the mixture was heated under reflux for 15 min. The charcoal was filtered off, washed with propan-2-ol (1 l), and the combined solution and washings were hydrogenated for 8 h over 5% palladium–charcoal (30 g), which was added as a paste with water (45 ml), purging the reaction vessel with fresh hydrogen at 30 min intervals. The catalyst was filtered off and the solution was concentrated to give the crude product in two crops (205 g). The combined crops were crushed and stirred with water (6 l) and hydrochloric acid solution (2N, 303 ml) for 1 h. The insoluble, neutral steroid was filtered off and the filtrate was basified with an excess of potassium hydroxide solution (10N) to give 3α-*amino*-2β-*hydroxy*-5α-*androstan*-17-*one* (1) as a solid (171 g). Recrystallisation of a sample from dichloromethane–ether gave prisms, m.p. 190—192°, $[\alpha]_D$ +110° (*c* 0.81), $\nu_{max.}$(KCl) 3 240br (OH,NH_2) and 1 740 (C=O) cm^{-1}, δ(C_5D_5N) 0.80 (3 H, s, 13-Me), 1.28 (3 H, s, 10-Me), 3.36sh (1 H, m, 3β-H), and 4.04sh (1 H, m, 2α-H) (Found: C, 74.5; H, 10.4; N, 4.9. $C_{19}H_{31}NO_2$ requires C, 74.7; H, 10.2; N, 4.6%).

The *hydrochloride* was obtained as prisms, m.p. >300° (decomp.), $[\alpha]_D$ +103° (*c* 0.88), $\nu_{max.}$(KCl) 3 340, 3 240, and 3 180 (OH,NH_2), and 1 730 (C=O) cm^{-1}, δ(C_5D_5N) 0.77 (3 H, s, 13-Me), 1.23 (3 H, s, 10-Me), 4.08sh (1 H, m, 3β-H), and 4.90sh (1 H, m, 2α-H) (Found: C, 66.9; H, 9.7; Cl, 10.5; N, 4.3. $C_{19}H_{32}ClNO_2$ requires C, 66.7; H, 9.4; Cl, 10.4; N, 4.1%).

(b) Charcoal (5 g) was added to a solution of 3α-benzyl-

amino-2β-hydroxy-5α-androstan-17-one (9) (100 g) in ethanol (1.5 l) and the mixture was heated under reflux for 15 min. The charcoal was filtered off, washed with hot ethanol (300 ml), and the combined solution and washings were shaken in the presence of hydrogen for 2.5 h at 50 °C over 5% Pd–charcoal (20 g). The catalyst was filtered off and the filtrate was evaporated to dryness to give the crude product (73 g), which was crushed and treated with water (2.2 l) and hydrochloric acid (2N, 108 ml). The mixture was allowed to stand at room temperature for 1 h, and the insoluble neutral steroid (1.2 g) was removed by filtration. The filtrate was basified with potassium hydroxide solution (10N, 35 ml) to give pure 3α-amino-2β-hydroxy-5α-androstan-17-one (1) (65 g), identical (t.l.c. and i.r. spectrum) with material obtained as described above.

(c) A suspension of 2α,3α-imino-5α-androstan-17-one ethylene acetal (30a) (0.2 g, 0.61 mmol) in sulphuric acid (2M, 10 ml) was refluxed for 2 h. The acid was neutralised with aqueous sodium hydrogencarbonate solution and the free base product was extracted with dichloromethane. The organic solution was washed with water and dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a solid. Crystallisation from ether yielded 3α-amino-2β-hydroxy-5α-androstan-17-one (1) (141 mg, 71%), identical in all respects with material obtained as described above.

2α,3α-(N-*Ethoxycarbonyl*)*imino*-5α-*androstan*-17-*one* (31). —To a solution of 5α-androst-2-en-17-one (25) (2.72 g, 10 mmol) and *p*-nitrophenylsulphonyloxyurethane (5.8 g, 10 mmol) in dichloromethane (30 ml) was added a solution of triethylamine (4 ml) in dichloromethane (20 ml) over 30 min. The mixture was allowed to stir at room temperature for 18 h after which it was washed with water (3 × 200 ml), dried ($MgSO_4$), and the solvent removed *in vacuo* yielding a deep red oil. High pressure chromatography on silica gel afforded the starting material (0.6 g) and the *ethoxycarbonylaziridine* (31) (1.53 g, 56%), recrystallised from ether–light petroleum, m.p. 155—156°, $[\alpha]_D$ +89° (*c* 1.52), $\nu_{max.}$(KBr) 1 740, 1 720, 1 298, and 795 cm^{-1}, δ($CDCl_3$) 0.77 (3 H, s, 13-Me), 0.83 (3 H, s, 10-Me), 1.24 (3 H, t, *J* 8 Hz, CH_2CH_3), 2.62 (2 H, m, 2β- and 3β-H), and 4.11 (2 H, q, *J* 8 Hz, CH_2CH_3) (Found: C, 73.6; H, 9.4; N, 3.8. $C_{22}H_{33}NO_3$ requires C, 73.5; H, 9.3; N, 3.9%).

2α,3α-*Imino*-5α-*androstan*-17-*one* (30).—(a) A suspension of α-aziridine acetal (30a) (2.0 g) in a mixture of acetic acid (8 ml) and water (36 ml) was heated on the water bath for 15 min. The solution was cooled, basified (dilute Na_2CO_3), and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and evaporated to give a yellow oil. Crystallisation of the residue from ether–light petroleum afforded 2α,3α-*imino*-5α-*androstan*-17-*one* (30) (1.29 g), m.p. 147—149°, $[\alpha]_D$ +111° (*c* 0.69), $\nu_{max.}$(CH_2Cl_2) 3 300, 1 740, and 810 cm^{-1}, δ($CDCl_3$) 0.81 (3 H, s, 13-Me) and 0.87 (3 H, s, 10-Me) (Found: C, 79.5; H, 10.3; N, 4.6. $C_{19}H_{29}NO$ requires C, 79.4; H, 10.2; N, 4.9%).

(b) The ethoxycarbonylaziridine (31) (358 mg, 1 mmol) in a 5% solution of potassium hydroxide in ethanol (30 ml) was stirred at room temperature for 2 h. The mixture was watered out and the product was extracted into dichloromethane. The organic layer was washed with water, dried ($MgSO_4$), and the solvent was evaporated *in vacuo* to yield a pale yellow oil. Repeated chromatography on alumina afforded 2α,3α-imino-5α-androstan-17-one (30) (100 mg, 35%), m.p. 145—147°, $[\alpha]_D$ +109° (*c* 0.7), i.r. spectrum identical with that of material prepared above.

3α-*Azido*-2β-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (28a).—To 3α-azido-2β-hydroxy-5α-androstan-17-one (28) (93.5 g) was added ethylene glycol (93.5 ml), triethyl orthoformate (187 ml), and toluene-*p*-sulphonic acid (5.8 g) and the solution was refluxed under nitrogen for 1 h. The mixture was cooled to room temperature and poured into sodium carbonate solution. The precipitated product was filtered off, washed with water, and dried ($MgSO_4$). Crystallisation from ether afforded 3α-*azido*-2β-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (28a) (95.76 g, 90.4%) as needles, m.p. 159—160°, $[\alpha]_D$ +47° (*c* 0.88), $\nu_{max.}$(KCl) 3 470 (OH) and 2 100 (N_3) cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 3.75sh (1 H, m, 2α-H), 3.82sh (1 H, m, 3β-H), and 3.87 (4 H, s, acetal) (Found: C, 66.9; H, 9.1; N, 11.4. $C_{21}H_{33}N_3O_3$ requires C, 67.2; H, 8.9; N, 11.2%).

3α-*Azido*-5α-*androstane*-2,17-*dione* 17-*Ethylene Acetal* (34a).—3α-Azido-2β-hydroxy-5α-androstan-17-one ethylene acetal (28a) (95.5 g) was dissolved in dichloromethane (700 ml) and added in one portion to a stirred mixture of pyridinium chlorochromate (109.7 g) and anhydrous sodium acetate (62.0 g) in dichloromethane (700 ml). The mixture was stirred for 2 h at room temperature and sodium-dried ether (700 ml) was added. The resulting mixture was filtered through Dicalite, to remove inorganic material, and the liquors were concentrated under reduced pressure. Ether (700 ml) was added and again the insoluble material was filtered off through Dicalite. The solution was then filtered through a short silica column to remove colour and the liquors were evaporated under reduced pressure to give an off-white solid. Crystallisation from ether afforded 3α-*azido*-5α-*androstane*-2,17-*dione* 17-*ethylene acetal* (34a) (55.6 g), as prisms, m.p. 132—135°, $[\alpha]_D$ +8.4° (*c* 1.07), $\nu_{max.}$(KCl) 2 120, 2 090 (N_3), and 1 715 (C=O) cm^{-1}, δ($CDCl_3$) 0.72 (3 H, s, 13-Me), 0.79 (3 H, s, 10-Me), 2.30 (2 H, s, 1-H_2), 3.80 (4 H, s, acetal), and 3.85sh (1 H, m, 3β-H) (Found: C, 67.8; H, 8.5; N, 10.9. $C_{21}H_{31}N_3O_3$ requires C, 67.5; H, 8.4; N, 11.25%).

3β-*Azido*-5α-*androstane*-2,17-*dione* 17-*Ethylene Acetal* (35a).—3α-Azido-5α-androstane-2,17-dione 17-ethylene acetal (34a) (20.0 g) was dissolved in toluene (400 ml) and silica gel (Kieselgel, 0.05—0.2 mm, 200 g) was added. The resulting mixture was stirred at room temperature for 24 h. Ether (200 ml) was added and the solution was filtered, washed with ether, and evaporated under reduced pressure to give a yellow oil. Crystallisation from methanol afforded 3β-*azido*-5α-*androstane*-2,17-*dione* 17-*ethylene acetal* (35a) (14.6 g, 73%) as prisms, m.p. 139—141°, $[\alpha]_D$ +51° (*c* 1.06), $\nu_{max.}$(KCl) 2 110 (N_3) and 1 725 (C=O) cm^{-1}, δ($CDCl_3$) 0.75 (3 H, s, 13-Me), 0.82 (3 H, s, 10-Me), 2.53 (1 H, ½ ABq, *J* 13 Hz, 1β-H), 3.82 (4 H, s, acetal), and 3.85br (1 H, m, 3α-H) (Found: C, 67.7; H, 8.4; N, 11.1. $C_{21}H_{31}N_3O_3$ requires C, 67.5; H, 8.4; N, 11.25%).

3β-*Azido*-2β-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (36a).—3β-Azido-5α-androstane-2,17-dione 17-ethylene acetal (35a) (12.0 g) was suspended in methanol (240 ml) and cooled to 10° in an ice–water bath. Sodium borohydride (3.0 g) was added in portions to the stirred suspension over 10 min and the resulting solution stirred at room temperature for 1 h. The solution was concentrated under reduced pressure and water (200 ml) was added. The resultant mixture was extracted with ether and the ether extracts were washed with water, dried (Na_2SO_4), and concentrated to give an off-white solid. Crystallisation from ether–light petroleum afforded 3β-*azido*-2β-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (36a) (10.0 g, 82.9%) as needles, m.p. 123—125°, $[\alpha]_D$ +0.7° (*c* 0.82), $\nu_{max.}$(KCl) 3 440 (OH) and 2 100

(N_3) cm^{-1}, δ($CDCl_3$) 0.82 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 3.40br (1 H, m, 3α-H), 3.83 (4 H, s, acetal), and 3.95sh (1 H, m, 2α-H) (Found: C, 67.3; H, 8.7; N, 10.8. $C_{21}H_{33}N_3O_3$ requires C, 67.2; H, 8.9; N, 11.2%).

3β-*Amino*-2β-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (2a).—3β-Azido-2β-hydroxy-5α-androstan-17-one ethylene acetal (36a) (10.0 g) was dissolved in sodium-dried ether and added to a stirred suspension of $LiAlH_4$ (2.5 g) in sodium-dried ether (50 ml) at 10°. After the addition the mixture was refluxed 1 h, cooled in an ice-bath, and the excess of lithium aluminium hydride was destroyed by cautious addition of water. The salts formed were filtered off through Dicalite and the filtrate was washed with water, dried (Na_2SO_4), and concentrated to give a solid. The crude product was crystallised from dichloromethane–ether to give 3β-*amino*-2β-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (2a) (8.50 g, 91.3%) as prisms, m.p. 200—202°, $[\alpha]_D$ +7.3° (*c* 1.8), $\nu_{max.}$(KCl) 3 370, 3 140 (OH,NH_2), and 1 175 (COC) cm^{-1}, δ(C_5D_5N) 0.89 (3 H, s, 13-Me), 1.19 (3 H, s, 10-Me), 2.70br (1 H, m, 3α-H), 3.35 (3 H, m, OH,NH_2), 3.78 (4 H, s, acetal), and 4.00sh (1 H, m, 2α-H) (Found: C, 72.1; H, 10.2; N, 4.0. $C_{21}H_{35}NO_3$ requires C, 72.2; H, 10.1; N, 4.0%).

3β-*Amino*-2β-*hydroxy*-5α-*androstan*-17-*one* (2).—3β-Amino-2β-hydroxy-5α-androstan-17-one ethylene acetal (2a) (8.42 g) was dissolved in a mixture of glacial acetic acid (168.4 ml) and water (16.8 ml) and heated on a steam-bath for 30 min. Water was added and the reaction basified. The precipitated product was filtered, washed free of base, and dried. Crystallisation from dichloromethane–ether afforded 3β-*amino*-2β-*hydroxy*-5α-*androstan*-17-*one* (2) (6.42 g, 87.2%) as an amorphous solid, m.p. >300° (decomp.), $[\alpha]_D$ +106° (*c* 1.06), $\nu_{max.}$(KCl) 3 340 (OH,NH_2) and 1 738 (C=O) cm^{-1}, δ($CDCl_3$) 0.84 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 2.15 (3 H, m, OH,NH_2), 2.70br (1 H, m, 3α-H), and 3.78sh (1 H, m, 2α-H) (Found: C, 74.3; H, 9.95; N, 4.55. $C_{19}H_{31}NO_2$ requires C, 74.7; H, 10.2; N, 4.6%).

A sample of 3β-amino-2β-hydroxy-5α-androstan-17-one (2) was converted into the hydrochloride, which was recrystallised from ethanol–ether to give pure 3β-*amino*-2β-*hydroxy*-5α-*androstan*-17-*one hydrochloride* as an amorphous solid, m.p. >300° (decomp.), $[\alpha]_D$ +102° (*c* 0.63 in MeOH), $\nu_{max.}$ 3 300, 3 200 (OH,NH_2), and 1 735 (C=O) cm^{-1} (Found: C, 65.1; H, 9.4; Cl, 9.8; N, 3.7. $C_{19}H_{32}ClNO_2,0.5H_2O$ requires C, 65.0; H, 9.5; Cl, 10.1; N, 4.0%).

2α,3α-*Epoxy*-5α-*androstan*-17-*one* (38).—Peracetic acid (46% w/v in acetic acid, 196 ml, 1.7 mol. equiv.) was diluted with water (800 ml) to give 996 ml of 9% peracetic in acetic acid–water. Sodium acetate (48.0 g) was added to the stirred solution at 10 °C, followed by 5α-androst-2-en-17-one (25) (200 g) in chloroform (1 500 ml) over 30 min, keeping the temperature below 10 °C. The cooling bath was then removed and the mixture was stirred vigorously at room temperature overnight (17 h). (A t.l.c. sample taken after this time showed no starting material.) The mixture was poured into water, the organic layer was separated, washed with water, then with saturated potassium hydrogencarbonate solution, and finally with water until neutral, and dried ($MgSO_4$). Evaporation to dryness gave a crystalline solid (228.1 g), which was recrystallised from ether–dichloromethane–light petroleum to give needles (199.1 g, 94%), m.p. 125—127°.

3α-*Azido*-17-*oxo*-5α-*androstan*-2α-*yl Formate* (41).—To a stirred solution of 3α-azido-2β-hydroxy-5α-androstan-17-one (28) (39.8 g), triphenylphosphine (125.8 g, 4 mol. equiv.), formic acid (18.35 ml), (4 mol. equiv.), and tetrahydrofuran (2.1 l) at room temperature, a solution of diethyl azodicarboxylate (83.2 g, 4 mol. equiv.) in tetrahydrofuran (440 ml) was added. The resulting solution was stirred at room temperature for 2 days, then the solvent was removed, and the residue was taken to dryness with toluene. The residue was then triturated with toluene and the insoluble material was removed by filtration. The filtrate was passed down a silica column and the eluate taken to dryness to give a gum which crystallised from ether to give the *formate* (41) (12.0 g, 27%) as needles, m.p. 165—170°, $[\alpha]_D$ +81° (*c* 0.82), $\nu_{max.}$(KCl) 2 130 and 2 090 (N_3), 1 740 (17-C=O), and 1 705 (formate, C=O) cm^{-1}, δ($CDCl_3$) 0.82 (3 H, s, 13-Me), 0.85 (3 H, s, 10-Me), 4.00sh (1 H, m, 3β-H), and 8.03 (1 H, s, formate) (Found: C, 66.8; H, 8.3; N, 11.8. $C_{20}H_{29}N_3O_3$ requires C, 66.8; H, 8.1; N, 11.7%).

3α-*Azido*-2α-*hydroxy*-5α-*androstan*-17-*one* (42).—3α-Azido-17-oxo-5α-androstan-2α-yl formate (41) (11.9 g) was dissolved in ethanol (59.5 ml) and potassium hydroxide (10N, 11.9 ml) was added. The mixture was refluxed for 30 min, poured into water, and the precipitated product was filtered, washed neutral, and dried. Crystallisation from dichloromethane–ether afforded 3α-*azido*-2α-*hydroxy*-5α-*androstan*-17-*one* (42) (9.53 g, 87%) as prisms, m.p. 184—186°, $[\alpha]_D$ +161° (*c* 0.27), $\nu_{max.}$(KCl) 3 380 (OH), 2 130 and 2 090 (N_3), 1 740, and 1 730 (C=O) cm^{-1}, δ($CDCl_3$), 0.85 (6 H, s, 13- and 10-Me), 3.70br (1 H, m, 2β-H), and 3.95sh (1 H, m, 3β-H) (Found: C, 68.35; H, 8.8; N, 12.6. $C_{19}H_{29}N_3O_2$ requires C, 68.85; H, 8.8; N, 12.7%).

3α-*Azido*-2α-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (42a).—3α-Azido-2α-hydroxy-5α-androstan-17-one (42) (9.44 g) was added to ethylene glycol (9.44 ml), triethyl orthoformate (18.9 ml), and toluene-*p*-sulphonic acid (0.58 g) and the mixture was refluxed under nitrogen for 1 h. The solution was then allowed to cool to room temperature and poured into sodium carbonate solution. The precipitated product was filtered, washed with water, and dried. Crystallisation from ether afforded 3α-*azido*-2α-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (42a) (9.28 g, 86.8%) as prisms, m.p. 154—156°, $[\alpha]_D$ +62° (*c* 0.98), $\nu_{max.}$(KCl) 3 460 (OH) and 2 130 and 2 090 (N_3) cm^{-1}, δ($CDCl_3$) 0.82 (6 H, s, 13- and 10-Me), 3.70br (1 H, m, 2β-H), 3.85 (4 H, s, acetal), and 3.95sh (1 H, m, 3β-H) (Found: C, 66 95; H, 9.1; N, 11.3. $C_{21}H_{33}N_3O_3$ requires C, 67.2; H, 8.9; N, 11.2%).

3α-*Amino*-2α-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (3a).—3α-Azido-2α-hydroxy-5α-androstan-17-one ethylene acetal (42a) (9.0 g) was dissolved in ether (Na-dried; 90 ml) and lithium aluminium hydride (2.25 g) was added at <10°. After the addition the mixture was refluxed for 1 h, cooled in an ice-bath, and the excess of lithium aluminium hydride was destroyed by careful addition of water. The mixture was filtered through Dicalite and the filtrate was washed with water, dried ($MgSO_4$), and concentrated to give an off-white solid. The crude product was crystallised from dichloromethane–ether to give 3α-*amino*-2α-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (3a) (7.42 g, 88.5%) as prisms, m.p. 210—211°, $[\alpha]_D$ +5.4° (*c* 0.90), $\nu_{max.}$(KCl) 3 180 (OH, NH_2) cm^{-1}, δ($CDCl_3$) 0.82 (6 H, s, 13- and 10-Me), 3.10sh (1 H, m, 3β-H), 3.70br (1 H, m, 2β-H), and 3.85 (4 H, s, acetal) (Found: C, 71.7; H, 10.3; N, 3.9. $C_{21}H_{35}NO_3$ requires C, 72.2; H, 10.1; N, 4.0%).

2α,3α-(N-*Benzoylimino*)-5α-*androstan*-17-*one Ethylene Acetal* (32a).—To a solution of α-aziridine acetal (30a) (0.6 g, 1.37 mmol) in pyridine (12 ml) at 5 °C, benzoyl chloride (3 ml) was added dropwise. The resulting solution was stirred

at room temperature for 4 h. Ice was added and the solution was stirred for a further 30 min. The solid which precipitated was filtered and crystallised from ether to yield 2α,3α-(N-*benzoylimino*)-5α-*androstan*-17-*one ethylene acetal* (32a) (0.63 g, 79%), m.p. 188—191°, $[\alpha]_D$ +6.7° (*c* 1.14), $\nu_{max.}$(KBr) 1 662, 1 305, and 720 cm^{-1}, δ($CDCl_3$) 0.8 and 0.83 (each 3 H, s, 13- and 10-Me), 2.74 and 2.77 (2 H, m, 2β- and 3β-H), 3.85 (4 H, s, 17-acetal), and 7.50 and 8.0 (3 H and 2H respectively, m, phenyl) (Found: C, 77.2; H, 8.6; N, 3.3. $C_{28}H_{37}NO_3$ requires C, 77.2; H, 8.6; N, 3.2%).

4′β,5′β-*Dihydro*-2′-*phenyl*-17-*oxo*-5α-*androstano*[3,2-d]-*oxazole Ethylene Acetal* (45a).—To a solution of steroid (32a) (100 mg, 0.23 mmol) in acetone (8 ml), sodium iodide (400 mg, 2.66 mmol) was added and the resulting solution was refluxed for 20 h. Water was added and the precipitate formed was filtered, and extracted with dichloromethane. The organic solution was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo* yielding a solid. Crystallisation from methanol afforded 4′β,5′β-*dihydro*-2′-*phenyl*-17-*oxo*-5α-*androstano*[3,2-d]*oxazole ethylene acetal* (45a) (860 mg, 86%), m.p. 173—174°, $[\alpha]_D$ +20° (*c* 1.3), $\nu_{max.}$(KBr) 1 640, 1 100, and 955 cm^{-1}, δ($CDCl_3$) 0.79 and 0.82 (each 3 H, s, 13- and 10-Me), 3.85 (4 H, s, acetal), 4.15 and 4.80 (each 1 H, m, 2β- and 3β-H), and 7.42 and 7.98 (3 H and 2 H respectively, m, 2′-phenyl) (Found: C, 77.1; H, 8.6; N, 3.3. $C_{28}H_{37}NO_3$ requires C, 77.2; H, 8.6; N, 3.2%).

2α,3α-(N-*Acetylimino*)-5α-*androstan*-17-*one Ethylene Acetal* (33a).—To a solution of the α-aziridine acetal (30a) (330 mg, 1 mmol) in pyridine (6.6 ml), acetic anhydride (1.3 ml) was added and the resultant mixture was stirred for 2 h at room temperature. The mixture was poured into ice–water and the solid precipitate was filtered off and dissolved in dichloromethane. The organic solution was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo* yielding a solid. Crystallisation from ether afforded 2α,3α-(N-*acetylimino*)-5α-*androstan*-17-*one ethylene acetal* (33a) (320 mg, 86%), m.p. 157—159°, $[\alpha]_D$ +4.5° (*c* 1.0), $\nu_{max.}$(KBr) 1 685, 1 215, and 1 170 cm^{-1}, δ($CDCl_3$) 0.75 (3 H, s, 13-Me), 0.81 (3 H, s, 10-Me), 2.08 (3 H, s, MeCO), 2.60sh (2 H, m, 2β- and 3β-H), and 3.86 (4 H, s, acetal) (Found: C, 74.1; H, 9.5; N, 3.5. $C_{23}H_{35}NO_3$ requires C, 73.95; H, 9.45; N, 3.75%).

3α-*Acetamido*-2β-*chloro*-5α-*androstan*-17-*one* (44).—2α,3α-Imino-5α-androstan-17-one ethylene acetal (30a) (2.8 g) was dissolved in dry pyridine (5.6 ml) and acetic anhydride (11.2 ml) was added dropwise to the cooled solution. The resulting mixture was stirred at room temperature for 1 h, and water (500 ml) was added. The product was extracted into ether and the ether extract was washed with hydrochloric acid (5N) and water, dried (Na_2SO_4), and evaporated to give a solid. Crystallisation from ether afforded pure 3α-*acetamido*-2β-*chloro*-5α-*androstan*-17-*one* (44) (1.08 g) as prisms, m.p. 190—198°, $[\alpha]_D$ +114° (*c* 0.88), $\nu_{max.}$(KCl) 3 370br (NH), 1 720 (C=O), and 1 680 (acetamido) cm^{-1}, δ($CDCl_3$) 0.80 (3 H, s, 13-Me), 1.13 (3 H, s, 10-Me), 2.00 (3 H, s, MeCO), 4.28sh (2 H, m, 2α- and 3β-H), and 6.55br (1 H, m, NH) (Found: C, 68.8; H, 9.0; Cl, 10.3; N, 3.6. $C_{21}H_{32}ClNO_2$ requires C, 68.9; H, 8.8; Cl, 9.7; N, 3.8%).

3α-*Acetamido*-2α-*hydroxy*-5α-*androstan*-17-*one* (11).—3α-Acetamido-2β-chloro-5α-androstan-17-one (44) (1.09 g) was dissolved in dimethylformamide (5.45 ml) and potassium acetate (1.09 g) in water (0.55 ml) was added. The resultant mixture was heated at 100° for 1 h. Water (55 ml) was added and the crystalline solid obtained was filtered, washed with water, and dissolved in dichloromethane. The solution was washed with water, dried (Na_2SO_4), and evaporated to low volume while ether was added to give 3α-*acetamido*-2α-*hydroxy*-5α-*androstan*-17-*one* (11) (0.6 g) as needles, m.p. 260—295° (decomp.), $\nu_{max.}$(KCl) 3 430, 3 310br (OH, NH), 1 725 (C=O), and 1 640 (acetamide) cm^{-1}, δ($CDCl_3$ + 2—3 drops MeOD) 0.83 (6 H, s, 10- and 13-Me), 1.98 (3 H, s, MeCO), 3.70br (1 H, m, 2β-H), 4.10sh (1 H, m, 3β-H), and 6.70br (1 H, m, NH) (Found: C, 72.0; H, 9.3; N, 4.0. $C_{21}H_{33}NO_3$ requires C, 72.6; H, 9.6; N, 4.0%).

3α-*Amino*-2α-*hydroxy*-5α-*androstan*-17-*one* (3).—(a) 3α-Amino-2α-hydroxy-5α-androstan-17-one ethylene acetal (3a) (7.4 g) was dissolved in a mixture of glacial acetic acid (148 ml) and water (14.8 ml) and heated on a steam-bath for 30 min. Water was added and the reaction was basified. The precipitated product was filtered, washed free of base, and dried. Crystallisation from ether afforded 3α-*amino*-2α-*hydroxy*-5α-*androstan*-17-*one* (3) (5.40 g, 83.5%) as prisms, m.p. 150—152°, $[\alpha]_D$ +102° (*c* 1.1), $\nu_{max.}$(KCl) 3 360 (OH,NH_2) and 1 740 (C=O) cm^{-1}, δ($CDCl_3$) 0.85 (6 H, s, 13- and 10-Me), 3.10sh (1 H, m, 3β-H), and 3.60br (1 H, m, 2β-H) (Found: C, 73.95; H, 10.1; N, 4.4. $C_{19}H_{31}NO_2$ requires C, 74.7; H, 10.2; N, 4.6%).

A sample of 3α-amino-2α-hydroxy-5α-androstan-17-one (3) was converted into the hydrochloride, which was recrystallised from ethanol–ether to give pure 3α-*amino*-2α-*hydroxy*-5α-*androstan*-17-*one hydrochloride* as prisms, m.p. 284° (decomp.), $[\alpha]_D$ +94° (*c* 0.48 in EtOH), $\nu_{max.}$(KCl) 3 380 (OH,NH_2) and 1 735 (C=O) cm^{-1} (Found: C, 65.8; H, 9.4; Cl, 10.3; N, 3.9. $C_{19}H_{32}ClNO_2$,0.125H_2O requires C, 66.3; H, 9.5; Cl, 10.3; N, 4.1%).

(b) A suspension of the acetal (45a) (100 mg, 0.23 mmol) in sulphuric acid (5N, 20 ml) was refluxed for 3 h. The solution was basified with potassium carbonate solution and the product was extracted into dichloromethane. The organic layer was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo* yielding a solid. Crystallisation from dichloromethane–ether afforded the amine (3) (46 mg, 66%) characterised by t.l.c., i.r., n.m.r., and mass spectroscopy.

(c) 3α-Acetamido-2α-hydroxy-5α-androstan-17-one (11) (0.51 g) was dissolved in ethoxyethanol (5.1 ml) and potassium hydroxide (10N, 1 ml) and the solution was refluxed for 4 h. Water (50 ml) was added and the precipitated product was filtered and dried. The i.r. and n.m.r. spectra compared favourably with those of 3α-amino-2α-hydroxy-5α-androstan-17-one (3) prepared as described in (a).

2α,3α-*Dihydroxy*-5α-*androstan*-17-*one* (46).—(a) A solution of 5α-androst-2-en-17-one (25) (1.07 g, 3.94 mmol) and osmium tetraoxide (1.0 g, 3.94 mmol) in pyridine (15 ml) was stirred overnight at room temperature. A solution of sodium metabisulphite (1.8 g) in water (30 ml) and pyridine (20 ml) was added with constant stirring and the black osmate complex cleared to give a dark red solution. The product was extracted with dichloromethane and the organic solution was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo*. Crystallisation from ethyl acetate afforded 2α,3α-*dihydroxy*-5α-*androstan*-17-*one* (46) (810 mg, 69%), m.p. 168—170°, $[\alpha]_D$ +87° (*c* 1.0), $\nu_{max.}$ 3 440 and 1 730 cm^{-1}, δ($CDCl_3$) 0.83 and 0.86 (each 3 H, s, 13- and 10-Me), 2.93sh (2 H, m, 2α- and 3α-OH), 3.70br (1 H, m, 2β-H), and 3.95sh (1 H, m, 3β-H) (Found: C, 74.7; H, 10.0. $C_{19}H_{30}O_3$ requires C, 74.5; H, 9.8%).

(b) To a solution of 5α-androst-2-en-17-one (25) (30.1 g, 0.11 mol) in dichloromethane (110 ml), sodium hydroxide solution (110 ml, 4N) and tetrabutylammonium bromide (1.1

g) were added. The mixture was cooled to 0° (ice–salt-bath) and small portions of potassium permanganate (17.4 g, 0.11 mol) were added over 1 h maintaining the temperature at 0 °C. The mixture was stirred vigorously for 20 h. Sulphur dioxide was bubbled through the mixture, the resulting two-phase system was separated, and the organic phase was washed several times with water, dried ($MgSO_4$), and the solvent removed *in vacuo* to yield an oil (35 g). Column chromatography on silica yielded 5α-androst-2-en-17-one (22 g) and 2α,3α-dihydroxy-5α-androstan-17-one (46) (4.0 g, 44.5%) (corrected).

3α-*Hydroxy*-17-*oxo*-5α-*androstan*-2α-*yl Benzoate* (47).—To a solution of 2α,3α-dihydroxy-5α-androstan-17-one (46) (500 mg, 1.63 mmol) in pyridine (10 ml), benzoyl chloride (252 mg, 1.1 mol. equiv.) was added and the mixture was allowed to stand at room temperature for 14 h. Water was added and the product was extracted into dichloromethane. The organic solution was then washed with hydrochloric acid (5N), water, dilute potassium hydrogencarbonate solution, and water until neutral, dried ($MgSO_4$), and the solvent was removed *in vacuo*. Crystallisation from ether yielded the 2-benzoate (47) (410 mg, 61%), m.p. 180—184°, $[\alpha]_D$ +62° (*c* 0.46), $\nu_{max.}$ 3 578, 3 420, 1 742, 1 718, 1 280, and 718 cm^{-1}, δ($CDCl_3$) 0.88 and 0.96 (each 3 H, s, 13- and 10-Me), 2.13 (1 H, m, 3α-OH), 4.25sh (1 H, m, 3β-H), 5.21br (1 H, m, 2β-H), and 7.50 and 8.10 (3 H and 2 H respectively, m, phenyl).

17-*Oxo*-5α-*androstane*-2α,3α-*diyl* 2-*Benzoate* 3-*Mesylate* (48).—To a solution of the 2-benzoate (47) (190 mg, 0.46 mmol) in pyridine (5 ml) at 0 °C, methanesulphonyl chloride (0.2 ml) was added and the resulting solution left for 18 h. Water was added and the precipitated product was filtered off and dissolved in dichloromethane. The organic solution was washed with water, dried ($MgSO_4$), and the solvent removed *in vacuo*. Crystallisation from ether afforded the 2-*benzoate* 3-*mesylate* (48) (189 mg, 90%), m.p. 212—214°, $[\alpha]_D$ +72° (*c* 0.52), $\nu_{max.}$(KBr) 1 745, 1 730, 1 280, 1 180, 915, and 720 cm^{-1}, δ($CDCl_3$) 0.86 and 0.96 (each 3 H, s, 13- and 10-Me), 2.94 (3 H, s, $MeSO_2$), 5.18sh (1 H, m, 3β-H), 5.22br (1 H, m, 2β-H), and 8.12 and 7.54 (3 H and 2 H respectively, m, phenyl) (Found: C, 66.6; H, 7.7; S, 6.7. $C_{27}H_{36}O_6S$ requires C, 66.4; H, 7.4; S, 6.55%).

3β-*Azido*-17-*oxo*-5α-*androstan*-2α-*yl Benzoate* (49).—To a solution of the 2-benzoate 3-mesylate (48) (2.5 g, 5.11 mmol) in dimethylformamide (100 ml), sodium azide (1.0 g, 15.38 mmol) was added, and the resultant mixture was refluxed for 3.5 h. The mixture was watered out and the product was extracted with ethyl acetate. The organic solution was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo*. Crystallisation from methanol afforded the *benzoate* (49) (1.8 g, 82%), m.p. 172—175°, $[\alpha]_D$ −25° (*c* 0.70), $\nu_{max.}$(KBr) 2 105, 1 750, 1 720, 1 280, and 720 cm^{-1}, δ($CDCl_3$) 0.85 and 0.98 (each 3 H, s, 13- and 10-Me), 3.58br (1 H, m, 3α-H), 5.14br (1 H, m, 2β-H), and 7.50 and 8.03 (3 H and 2 H respectively, m, phenyl).

3β-*Azido*-2α-*hydroxy*-5α-*androstan*-17-*one* (50).—To a solution of the 2-benzoate (49) (1.51 g, 3.47 mmol) in methanol (100 ml), a solution of sodium hydroxide in methanol (100 ml, 4%) was added and the suspension was stirred at room temperature for 2 h. The resulting solution was reduced in volume and dichloromethane was added. The organic solution was then washed with water until neutral, dried ($MgSO_4$), and the solvent was removed *in vacuo* to yield a solid. Crystallisation from ether afforded 3β-*azido*-2α-*hydroxy*-5α-*androstan*-17-*one* (50) (1.11 g, 96%), m.p. 184—186°, $[\alpha]_D$ +54° (*c* 0.95), $\nu_{max.}$(KBr) 3 440, 2 100, and 1 740 cm^{-1}, δ($CDCl_3$) 0.88 (6 H, s, 13- and 10-Me), 2.58 (1 H, m, 2α-OH), and 3.45br (2 H, m, 2β- and 3α-H) (Found: C, 69.1; H, 8.5; N, 12.6. $C_{19}H_{29}N_3O_2$ requires C, 68.8; H, 8.8; N, 12.7%).

3β-*Amino*-2α-*hydroxy*-5α-*androstan*-17-*one* (4).—To a solution of 3β-azido-2α-hydroxy-5α-androstan-17-one (50) (1.11 g, 2.98 mmol) in ethanol (200 ml), 5% palladium–charcoal (0.51 g) was added and the resultant mixture was degassed and stirred at room temperature for 1 h under an atmosphere of hydrogen. The palladium–charcoal was filtered off on a Celite pad and the solvent was removed *in vacuo* yielding crude 3β-amino-2α-hydroxy-5α-androstan-17-one (4) (0.81 g, 80%), which was converted to the hydrochloride in the usual way. Crystallisation from ethanol–ether afforded 3β-*amino*-2α-*hydroxy*-5α-*androstan*-17-*one hydrochloride* (0.85 g, 75%), m.p. *ca.* 340° (decomp.), $[\alpha]_D$ +56° (*c* 1.06), $\nu_{max.}$(KBr) 3 400, 3 220, and 1 740 cm^{-1}, δ(DMSO) 0.79 and 0.81 (each 3 H, s, 13- and 10-Me), 2.60br (1 H, m, 3α-H), 3.70br (1 H, m, 2β-H), 4.91 (1 H, s, 2α-OH), and 8.18 (3 H, m, 3β-NH_3) (Found: C, 65.1; H, 9.5; Cl, 10.0; N, 3.9. $C_{19}H_{32}ClNO_2,0.5H_2O$ requires C, 65.0; H, 9.5; Cl, 10.1; N, 4.0%).

2β-*Amino*-3α-*hydroxy*-5α-*androstan*-17-*one* (13).—2α,3α-Epoxy-5α-androstan-17-one (38) (10.0 g) in ethanol (85 ml) and water (5 ml) was heated with liquid ammonia (20 ml) in an autoclave at 170° for 6 h. The mixture was evaporated to dryness and the residue was dissolved in acetic acid (15 ml) and water (15 ml) and warmed on a steam-bath for 1 h. Addition of water (400 ml) containing potassium hydroxide (50 ml, 10N) to the cooled mixture gave a solid which was filtered, washed with water, and dissolved in dichloromethane. This solution was dried ($MgSO_4$) and evaporated to dryness. Crystallisation of the residue from ether afforded 2β-*amino*-3α-*hydroxy*-5α-*androstan*-17-*one* (13) (5.0 g), m.p. 121—127°, $[\alpha]_D$ +94° (*c* 1.0), $\nu_{max.}$(KCl) 3 390br (OH, NH_2) and 1 745 (C=O) cm^{-1}, δ($CDCl_3$) 0.88 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 1.70 (s, exchangeable protons), 3.03sh (1 H, m, 2α-H), and 3.60sh (1 H, m, 3β-H) (Found: C, 74.6; H, 10.05; N, 4.2. $C_{19}H_{31}NO_2$ requires C, 74.7; H, 10.2; N, 4.6%). The *hydrochloride* was obtained as a crystalline solid (from EtOH), m.p. >280°, $[\alpha]_D$ +112° (*c* 1.33 in EtOH), $\nu_{max.}$(KCl) 3 415br (OH), 3 110br ($\overset{+}{N}H_3$), 2 700—2 500 (salt), 1 740 (C=O), and 1 600 (NH_3) cm^{-1} (Found: C, 65.7; H, 9.2; Cl, 11.7; N, 3.8. $C_{19}H_{32}ClNO_2$, $0.25H_2O$ requires C, 65.9; H, 9.5; Cl, 10.2; N, 4.0%).

2β-*Azido*-3α-*hydroxy*-5α-*androstan*-17-*one* (53).—2α,3α-Epoxy-5α-androstan-17-one (38) (25 g) in dimethylacetamide (215 ml) was treated with sodium azide (8.5 g) in water (20.5 ml) and the mixture was stirred under reflux for 11 h. The mixture was cooled, poured into water (1.2 l), and the resultant gum was extracted into ether. The combined extracts were washed with water, dried ($MgSO_4$), and evaporated to dryness to afford a crystalline mass (28 g). Recrystallisation from acetone–ether gave 2β-azido-3α-hydroxy-5α-androstan-17-one (53), m.p. 162—165°, $[\alpha]_D$ +102° (*c* 1.25), $\nu_{max.}$(KCl) 3 410 (OH), 2 100 (N_3), and 1 720 (C=O) cm^{-1}, δ($CDCl_3$) 0.88 (3 H, s, 13-Me), 1.02 (3 H, s, 10-Me), 1.92 (1 H, m, exchangeable OH), and 3.80sh (2 H, m, 2α- and 3β-H) (Found: C, 68.6; H, 8.6; N, 12.6. $C_{19}H_{29}N_3O_2$ requires C, 68.85; H, 8.8; N, 12.7%) (lit.,[19] m.p. 164—165.5°, $[\alpha]_D$ +103°).

2β-*Azido*-17-*oxo*-5α-*androstan*-3α-*yl Mesylate* (54).—To a solution of azido-alcohol (53) (4.0 g, 12.2 mmol) in pyridine

(80 ml), methanesulphonyl chloride (4 ml) was added dropwide and the resulting mixture was left at 0 °C for 18 h. The product was isolated as described above and obtained as a solid. Crystallisation from ether gave the mesylate (54) (3.5 g), m.p. 149—154°, $[\alpha]_D$ +77° (*c* 1.08), $\nu_{max.}$(KBr) 2 100 (N_3), 1 732 (C=O), and 1 175 cm^{-1}, δ($CDCl_3$) 0.87 and 1.03 (each 3 H, s 13- and 10-Me), 3.05 (3 H, s, 3α-OSO_2Me), 4.06 (1 H, m, 2α-H), and 4.59 (1 H, m, 3β-H) (Found: C, 58.6; H, 7.7; N, 10.2. $C_{20}H_{31}N_3O_4S$ requires C, 58.65; H, 7.6; N, 10.3%) (lit.,[19] m.p. 151—153°, $[\alpha]_D$ +92.5°).

2β-*Azido*-17-*oxo*-5α-*androstan*-3α-*yl Tosylate* (55).—The azido-alcohol (53) (5 g) in pyridine (50 ml), was treated with toluene-*p*-sulphonyl chloride (7.5 g) and the solution was stored at 40 °C. After 24 h, fresh tosyl chloride (7.5 g) was added to the mixture. After a further 48 h, the reaction mixture was poured onto crushed ice (500 ml), allowed to attain room temperature, and the solid was filtered and dissolved in ether. The solution was washed with hydrochloric acid (2N) and water, dried ($MgSO_4$), and evaporated to a crystalline mass (7 g). Recrystallisation from acetone–ether afforded the tosylate (55) as needles, m.p. 167—168°, $[\alpha]_D$ +66° (*c* 0.98), $\nu_{max.}$(KCl) 2 100 (N_3), 1 740 (C=O), and 1 600 and 1 500 (phenyl) cm^{-1}, δ($CDCl_3$) 0.80 (3 H, s, 13-Me), 0.92 (3 H, s, 10-Me), 2.42 (3 H, s, ArMe), 3.75sh (1 H, s, 2α-H), 4.38sh (1 H, m, 3β-H), and 7.22—7.84 (4 H, m, ArH) (Found: C, 64.4; H, 7.3; N, 8.7. $C_{26}H_{35}N_3O_4S$ requires C, 64.3; H, 7.3; N, 8.65%) (lit.,[6a] m.p. 166—168°, $[\alpha]_D$ +66°).

2β-*Azido*-17-*oxo*-5α-*androstan*-3α-*yl Mesylate Ethylene Acetal* (54a).—The 17-oxo-steroid (54) (3.3 g, 8.06 mmol), ethylene glycol (3.3 ml), triethyl orthoformate (6.6 ml), and toluene-*p*-sulphonic acid (210 mg) were heated to reflux for 2 h. The solution was allowed to cool to room temperature, ice was added, followed by aqueous sodium hydrogencarbonate solution, and the resulting precipitate was filtered off. The solid was dissolved in ether and the etheral solution was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo* yielding a solid. Crystallisation from ether yielded the *mesylate ethylene acetal* (54a) (3.48 g, 95%), m.p. 129—130°, $[\alpha]_D$ −13° (*c* 1.2), $\nu_{max.}$(KBr) 2 100, 1 180, and 1 170 cm^{-1}, δ($CDCl_3$) 0.93 and 1.09 (each 3 H, s, 13- and 10-Me), 3.09 (3 H, s, 3α-OSO_2CH_3), 3.91 (4 H, s, acetal), 4.10 (1 H, m, 2α-H), and 4.72 (1 H, m, 2β-H) (Found: C, 58.3; H, 7.8; N, 9.2. $C_{22}H_{35}N_3O_5S$ requires C, 58.25; H, 7.8; N, 9.2%).

2β,3β-*Imino*-5α-*androstan*-17-*one Ethylene Acetal* (51a).—To a solution of the above acetal (54a) (3.45 g, 7.6 mmol) in ether (175 ml) at 0 °C, lithium aluminium hydride (3.5 g) was added and the mixture was stirred for 2 h. The excess of lithium aluminium hydride was destroyed with 'wet' ether and the aluminium salts were filtered off on Celite. The ethereal extracts were washed with water, dried ($MgSO_4$), and the solvent was removed to give a solid. Crystallisation from methanol afforded 2β,3β-*imino*-5α-*androstan*-17-*one ethylene acetal* (51a) (2.20 g, 87%), m.p. 140—141°, $[\alpha]_D$ +7.7° (*c* 1.2), $\nu_{max.}$ 3 290, 1 170, and 800 cm^{-1}, δ($CDCl_3$) 0.83 and 0.85 (each 3 H, s, 13- and 10-Me), 2.19 (2 H, m, 2α- and 3α-H), and 3.85 (4 H, s, acetal) (Found: C, 76.1; H, 9.95; N, 4.3. $C_{21}H_{33}NO_2$ requires C, 76.1; H, 10.0; N, 4.2%).

2β,3β-*Imino*-5α-*androstan*-17-*one* (51).—A solution of aziridine acetal (51a) (1.0 g, 3.02 mmol) in 15% aqueous acetic acid was stirred for 3 h and then neutralised by the addition of sodium hydrogencarbonate solution. The product was extracted into dichloromethane and the organic layer was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo* to yield a solid. Column chromatography on alumina afforded the *ketone* (51) (400 mg, 46%), m.p. 186—188°, $[\alpha]_D$ +8° (*c* 1.0), $\nu_{max.}$(KBr) 3 300, 1 735, and 810 cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me) and 0.88 (3 H, s, 10-Me) (Found: C, 79.2; H, 10.4; N, 4.8. $C_{19}H_{29}NO$ requires C, 79.4; H, 10.2; N, 4.9%).

Opening of 2β,3β-*Aziridine with Dilute Acid*.—A suspension of the β-aziridine acetal (51a) (220 mg, 0.66 mmol) in sulphuric acid (15 ml, 4N) was refluxed for 2 h. The acid was neutralised (dilute sodium hydrogencarbonate solution) and the free base was extracted with dichloromethane. The organic solvent was removed *in vacuo* yielding a solid and any water present was removed by azeotroping with toluene. The product was then converted to the hydrochloride, which was crystallised from dichloromethane–ether to give 2β-amino-3α-hydroxy-5α-androstan-17-one (13) hydrochloride (182 mg), m.p. *ca.* 300° (decomp.), i.r. spectrum identical with that of material prepared *via* the epoxide.

2β,3β-(N-*Benzoylimino*)-5α-*androstan*-17-*one Ethylene Acetal* (52a).—Benzoyl chloride (2.5 ml) was added dropwise to a stirred solution of 2β,3β-imino-5α-androstan-17-one ethylene acetal (51a) (0.5 g, 1.5 mmol) in pyridine (10 ml) at *ca.* 10 °C. The resulting solution was stirred at room temperature for 2 h. Addition of water gave a yellow gum which was extracted into dichloromethane. The organic solution was washed with dilute sodium hydrogencarbonate solution and water until neutral, dried ($MgSO_4$), and the solvent was removed *in vacuo* yielding a pale yellow oil. Crystallisation from methanol afforded 2β,3β-(N-*benzoylimino*)-5α-*androstan*-17-*one ethylene acetal* (52a) (0.55 g, 83%), m.p. 204—206°, $[\alpha]_D$ −21° (*c* 0.73), $\nu_{max.}$(KCl) 1 680 and 1 290 cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 0.98 (3 H, s, 10-Me), 2.73 (2 H, m, 2α- and 3α-H), 3.84 (4 H, s, acetal), and 7.0—8.5 (5 H, m, Ph) (Found: C, 77.1; H, 8.8; N, 3.0. $C_{28}H_{37}NO_3$ requires C, 77.2; H, 8.6; N, 3.2%).

4′α,5′α-*Dihydro*-2′-*phenyl*-17-*oxo*-5α-*androstano*[2,3-d]-*oxazole Ethylene Acetal* (59a).—(a) To a solution of the aziridine (52a) (200 mg, 0.46 mmol) in acetone (16 ml), sodium iodide (0.8 g) was added and the resulting mixture was refluxed for 4 h. The precipitate formed on addition of water was filtered off and dissolved in dichloromethane. The organic solution was washed with water, dried ($MgSO_4$), and the solvent was removed *in vacuo* yielding a solid. Crystallisation from methanol afforded 4′α,5′α-*dihydro*-2′-*phenyl*-17-*oxo*-5α-*androstano*[2,3-d]*oxazole ethylene acetal* (59a) (155 mg, 77%), m.p. 165—168°, $[\alpha]_D$ −19° (*c* 0.91), $\nu_{max.}$(KCl) 1 637, 1 600, 1 580, 1 172, and 700 cm^{-1}, δ($CDCl_3$) 0.82 (3 H, s, 13-Me), 0.87 (3 H, s, 10-Me), 3.83 (4 H, s, acetal), 4.20 (1 H, m, 3α-H), 4.68 (1 H, m, 2α-H), and 7.2—8.0 (5 H, m, Ph) (Found: C, 76.6; H, 8.7; N, 2.9. $C_{28}H_{37}NO_3$ requires C, 77.2; H, 8.6; N, 3.2%).

(b) The aziridine (52a) (250 mg, 0.57 mmol) was heated to 200 °C for 2 h in an open vessel. The dark brown solid formed was chromatographed on silica and afforded the oxazole 17-acetal (59a) (130 mg, 52%), m.p. 162—165° (from methanol), characterised by t.l.c. and i.r. and n.m.r. spectroscopy.

2β-*Azido*-17-*oxo*-5α-*androstan*-3β-*yl Acetate* (56).—2β-Azido-3α-hydroxy-5α-androstan-17-one tosylate (55) (7 g) was dissolved in dimethylformamide (70 ml), potassium acetate (3.5 g) was added, and the mixture was stirred at 100° for 48 h. The mixture was cooled, poured into water (350 ml), and the resultant gum was extracted into ether, and the extracts were washed with water, dried ($MgSO_4$),

and evaporated to dryness. The crude product was purified by chromatography on silica gel, eluting with acetone–n-hexane (1 : 9) to yield 2β-*azido*-17-*oxo*-5α-*androstan*-3β-*yl acetate* (56) as a crystalline solid (1.75 g). Recrystallisation from acetone–n-hexane yielded needles, m.p. 132—133°, $[\alpha]_D$ +78° (*c* 0.97), $\nu_{max.}$(KCl) 2 110 (N_3) and 1 740 (C=O and acetate) cm^{-1}, δ($CDCl_3$) 0.84 (3 H, s, 13-Me), 1.01 (3 H, s, 10-Me), 2.07 (3 H, s, OAc), 4.03sh (1 H, m, 2α-H), and 4.82br (1 H, m, 3α-H) (Found: C, 67.5; H, 8.5; N, 11.3. $C_{21}H_{31}N_3O_3$ requires C, 67.5; H, 8.4; N, 11.25%).

2β-*Amino*-3β-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (14a).—2β-Azido-17-oxo-5α-androstan-3β-yl acetate (56) (6 g) was suspended in a mixture of ethylene glycol (6 ml) and triethyl orthoformate (12 ml). Toluene-*p*-sulphonic acid (360 mg) was added and the mixture was heated at 110° for 1.5 h then cooled, treated with potassium carbonate (0.5 g), and diluted with water (90 ml). The resulting solid was extracted into ether, and the extracts were washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to yield a mixture of ethylene acetals (56a) and (57a).

The crude acetal mixture was suspended in dry ether (100 ml) and treated with lithium aluminium hydride (2.5 g) in portions. The mixture was heated under reflux for 1 h then cooled in an ice-bath and the excess of metal hydride was destroyed with 'wet' ethyl acetate. The mixture was filtered through Dicalite and the filtrate was evaporated *in vacuo* to give a crystalline solid (6.7 g). Recrystallisation from ethyl acetate gave 2β-*amino*-3β-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (14a), m.p. 157—159°, $[\alpha]_D$ +5.7° (*c* 0.77), $\nu_{max.}$(KCl) 3 350br (OH, NH_2) cm^{-1}, δ($CDCl_3$) 0.80, (3 H, s, 13-Me), 0.96 (3 H, s, 10-Me), 1.83 (3 H, m, exchangeable OH,NH_2), 3.12sh (1 H, m, 2α-H), 3.68br (1 H, m, 3α-H), and 3.83 (4 H, s, acetal) (Found: C, 71.2; H, 9.7; N, 3.7%; M^+, 349.2630. $C_{21}H_{35}NO_3$ requires C, 72.2; H, 10.1; N, 4.0%; *M*, 349.2617).

2β-*Amino*-3β-*hydroxy*-5α-*androstan*-17-*one* (14).—(a) 2β-Amino-3β-hydroxy-5α-androstan-17-one ethylene acetal (14a) (6.5 g) was dissolved in glacial acetic acid (35 ml), water (12 ml) was added, and the solution was warmed on a steam-bath for 1 h. The mixture was cooled, then made basic with aqueous sodium hydroxide (4N). The resulting solid was filtered, washed with water, and dried ($CaCl_2$) at 60° under vacuum. Recrystallisation from dichloromethane–ether afforded 2β-*amino*-3β-*hydroxy*-5α-*androstan*-17-*one* (14), m.p. 165—170°, $[\alpha]_D$ +110° (*c* 0.93), $\nu_{max.}$(KCl) 3 335br (OH, NH_2), 1 735 (C=O), and 1 575 (NH_2) cm^{-1}, δ($CDCl_3$) 0.88 (3 H, s, 13-Me), 1.03 (3 H, s, 10-Me), 3.40br (2 H, m, 2α- and 3α-H) (Found: C, 74.5; H, 10.4; N, 4.6. $C_{19}H_{31}NO_2$ requires C, 74.7; H, 10.2; N, 4.6%).

The *hydrochloride*, recrystallised from ethanol–ether, had m.p. 283° (decomp.), $[\alpha]_D$ +88° (*c* 0.86 in DMSO), $\nu_{max.}$(KCl) 3 400br (OH), 3 200br (NH_2), 2 520 (amine salt), 1 742 (C=O), and 1 600 ($\overset{+}{N}H_3$) cm^{-1}, δ([$^2H_6$]DMSO) 0.78 (3 H, s, 13-Me), 0.92 (3 H, s, 10-Me), 3.30sh (2 H, m, exchangeable NH_2), 3.40sh (1 H, m, 2α-H), 3.70br (1 H, m, 3α-H), and 5.39sh (1 H, m, exchangeable OH) (Found: C, 66.5; H, 9.1; Cl, 10.7; N, 4.1. $C_{19}H_{32}ClNO_2$ requires C, 66.7; H, 9.4; Cl, 10.4; N, 4.1%).

(b) A suspension of the phenyloxazoline (59a) (100 mg, 0.23 mmol) in 5N-sulphuric acid (20 ml) was refluxed for 3.5 h. The solution was then basified with potassium carbonate solution and the product was extracted into dichloromethane, dried ($MgSO_4$), and the solvent was removed *in vacuo* to yield a solid. Crystallisation from dichloromethane–ether afforded the amine (14) (40 mg, 57%), characterised by t.l.c., i.r., n.m.r., and mass spectroscopy.

2β-*Hydroxy*-17-*oxo*-5α-*androstan*-3α-*yl Acetate* (60).—2β,3β-Epoxy-5α-androstan-17-one (27) (20 g) was dissolved in glacial acetic acid (280 ml) and the solution was warmed on a steam-bath for 1.5 h. The mixture was then evaporated under vacuum and the residue was azeotroped with toluene and recrystallised from acetone–ether to afford the acetate (60) as needles (13.8 g), m.p. 183—185°, $[\alpha]_D$ +101° (*c* 1.22), $\nu_{max.}$(KCl) 3 500 (OH), 1 740 (C=O), and 1 710 and 1 260 (OAc) cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 1.02 (3 H, s, 10-Me), 2.02 (3 H, s, OAc), 2.16 (1 H, s, exchangeable OH), 3.87sh (1 H, m, 2α-H), and 4.83sh (1 H, m, 3β-H) (Found: C, 72.4; H, 9.2. $C_{21}H_{32}O_4$ requires C, 72.4; H, 9.3%) (lit.,[20] m.p. 190—192°, $[\alpha]_D$ +107.5°).

17-*Oxo*-5α-*androstane*-2β,3α-*diyl* 2-*Mesylate* 3-*Acetate* (61).—The acetate (60) (53.1 g) in pyridine (530 ml) was cooled in an ice-bath and treated with methanesulphonyl chloride (26.5 g). The mixture was stored at room temperature for 16 h and then poured onto crushed ice (3 l), allowed to attain room temperature, and the resulting solid was filtered off and dissolved in dichloromethane–ether. The organic extracts were washed with hydrochloric acid (2N) and water, dried ($MgSO_4$), and evaporated to dryness under vacuum to afford the 2-*mesylate* 3-*acetate* (61) as a crystalline mass (63 g). Recrystallisation from acetone–ether yielded needles, m.p. 163—164°, $[\alpha]_D$ +87° (*c* 1.2), $\nu_{max.}$(KCl) 1 735 (C=O and OAc), 1 360br (mesylate), and 1 243 and 1 180 (OAc) cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 0.98 (3 H, s, 10-Me), 2.05 (3 H, s, OAc), 3.02 (3 H, s, OSO_2Me), 4.70sh (1 H, m, 2α-H), and 4.93sh (1 H, m, 3β-H) (Found: C, 62.0; H, 8.2. $C_{22}H_{34}O_6S$ requires C, 61.9; H, 8.0%).

2α-*Azido*-17-*oxo*-5α-*androstan*-3α-*yl Acetate* (62).—The 2-mesylate 3-acetate (61) (56.8 g) in dimethylformamide (560 ml) was treated with sodium azide (50 g) and the mixture was stirred at 100° for 16 h under nitrogen. The mixture was cooled, poured into water (2.5 l), and the resulting brown solid was filtered off and dried. The crude product was purified by chromatography on silica gel eluting with 9 : 1 n-hexane–acetone to give a 1 : 1 mixture of acetates (62) and (63) (16.7 g). A portion, rechromatographed on silica gel, afforded 2α-azido-17-oxo-5α-androstan-3α-yl acetate (62) m.p. 165—169° (decomp.), $\nu_{max.}$(KCl) 2 097 (N_3), 1 735 (C=O and OAc), and 1 240 (OAc) cm^{-1}, δ($CDCl_3$) 0.82 (6 H, s, 13- and 10-Me), 2.03 (3 H, s, OAc), 3.23br (1 H, m, 2β-H), and 5.13sh (1 H, m, 3β-H). Earlier fractions contained 17-oxo-5α-androst-1-en-3α-yl acetate (63), isolated as a crude gum, δ($CDCl_3$) 0.80 and 0.82 (each 3 H, s, 13- and 10-Me), 1.98 (3 H, s, OAc), and 5.08, 5.56, and 6.09 (3 H, ABC system, $J_{1.2}$ *ca.* 10, $J_{2.3}$ *ca.* 4.5 Hz, 3-, 2-, and 1-H).

2α-*Amino*-3α-*hydroxy*-5α-*androstan*-17-*one* (15).—A 1 : 1 mixture of acetates (62) and (63) (15.7 g) was suspended in ethylene glycol (16 ml) and triethyl orthoformate (32 ml); toluene-*p*-sulphonic acid (900 mg) was added and the solution was heated at 110° for 1.5 h. The mixture was cooled and potassium carbonate (1.6 g) was added followed by water (200 ml). The resulting suspension was extracted into ether and the organic extract was washed with water, dried ($MgSO_4$), and evaporated under vacuum to afford a mixture of ethylene acetals (62a) and (63a). The crude acetal mixture was dissolved in dry ether (130 ml), stirred at room temperature, and lithium aluminium hydride (3 g) was added in portions. The resulting mixture was refluxed for 1 h then cooled in an ice-bath and the excess of lithium

aluminium hydride was destroyed by addition of 'wet' ethyl acetate. The mixture was filtered through Dicalite and the filtrate was evaporated to dryness under vacuum. The crude reduction product was dissolved in glacial acetic acid (70 ml), water (24 ml) was added, and the solution was warmed on a steam-bath for 1 h. After cooling and filtration of insoluble material, the filtrate was basified with potassium hydroxide (10N) and extracted into ethyl acetate. The organic extract was washed with hydrochloric acid (5N) and water and the acid washings were basified with potassium hydroxide (10N). The resulting solid was filtered, washed with water and dried at 50° ($CaCl_2$) under vacuum (3.83 g). Recrystallisation from methanol afforded 2α-*amino*-3α-*hydroxy*-5α-*androstan*-17-*one* (15) as needles, m.p. 205—206°, $[\alpha]_D$ +92° (*c* 1.2), $\nu_{max.}$(KCl) 3 600 (OH), 3 330 and 3 130 (NH_2), 1 745 (C=O), and 1 575 (NH_2) cm^{-1}, δ($CDCl_3$) 0.83 (6 H, s, 13- and 10-Me), 1.90 (m, exchangeable protons), 2.93br (1 H, m, 2β-H), and 3.7sh (1 H, m, 3β-H) (Found: M^+, 305.2356. $C_{19}H_{31}NO_2$ requires M^+, 305.2355). The *hydrochloride* was recrystallised from ethanol to give needles, m.p. >280° (decomp.), $[\alpha]_D$ +93° (*c* 0.98 in DMSO), $\nu_{max.}$ 3 380 (OH), 3 040 ($\overset{+}{N}H_3$), 1 735 (C=O), and 1 600 ($\overset{+}{N}H_3$) cm^{-1}, δ([$^2H_6$]DMSO), 0.78 (6 H, s, 13- and 10-Me), 3.10br (1 H, m, 2β-H), and 3.92sh (1 H, m, 3β-H) (Found: C, 64.6; H, 9.6; Cl, 9.5; N, 3.8. $C_{19}H_{32}ClNO_2$,0.75H_2O requires C, 64.2; H, 9.5; Cl, 10.0; N, 3.9%).

2α-*Formamido*-3β-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (24a).—A stirred solution of 2β-formamido-3α-hydroxy-5α-androstan-17-one ethylene acetal (21a) (3 g) in dichloromethane (180 ml) was treated with potassium acetate (1.8 g) and pyridinium chlorochromate (7.2 g) for 16 h at room temperature. The mixture was diluted with ether (900 ml) and the insoluble material was filtered off. The filtrate was concentrated under reduced pressure and passed through a short column of alumina. The ether eluate was evaporated to dryness and the residue was dissolved in ethyl acetate and washed with aqueous sodium carbonate (5%) and water. The organic layer was dried ($MgSO_4$) and evaporated to dryness to afford a 2 : 1 mixture of ethylene acetals (65a) and (64a) (1.6 g). The crude mixture was dissolved in ethanol (30 ml), sodium borohydride (0.89 g) was added, and the mixture was stirred for 1.5 h. The mixture was concentrated, poured into water, and extracted into ethyl acetate. The organic extracts were washed with water, dried ($MgSO_4$), and evaporated to dryness. The crude product was purified by chromatography on alumina, eluting with dichloromethane–ether–methanol (90 : 7 : 3) to yield 2α-formamido-3β-hydroxy-5α-androstan-17-one ethylene acetal (24a) as a solid (0.5 g), $\nu_{max.}$(CH_2Cl_2) 3 600 (OH), 3 420, 1 685, and 1 503 (amide) cm^{-1}, δ($CDCl_3$) 0.82 (3 H, s, 13-Me), 0.88 (3 H, s, 10-Me), 1.40 (m, exchangeable proton), 3.40br (1 H, m, 2β-H), 3.80br (1 H, m, 3α-H), 3.85 (4 H, s, acetal), 6.20 (1 H, m, N*H*CHO), and 8.15 (1 H, m, NHCHO).

2α-*Amino*-3β-*hydroxy*-5α-*androstan*-17-*one* (16) *Hydrochloride*.— 2α-Formamido-3β-hydroxy-5α-androstan-17-one ethylene acetal (24a) (0.5 g) in methanol (5 ml) was treated with 2N-hydrochloric acid (5 ml). The mixture was heated on a steam-bath for 1 h, cooled, and poured into water (30 ml) containing potassium hydroxide (2 ml, 10N). The resulting solid was filtered off, dissolved in ethyl acetate, and the solution was washed with water, dried ($MgSO_4$), and evaporated to dryness to afford 2α-amino-3β-hydroxy-5α-androstan-17-one (8) (0.4 g). The crude product was converted to the hydrochloride, which was recrystallised from ethanol–ether to give 2α-*amino*-3β-*hydroxy*-5α-*androstan*-17-*one* (16) *hydrochloride* (200 mg), m.p. >280°, $[\alpha]_D$ +55° (*c* 0.86 in MeOH), $\nu_{max.}$(KCl) 3 400br (OH, NH_2), 2 540 (amine salt), 1 738 (C=O), and 1 610 (NH_3^+) cm^{-1}, δ([$^2H_6$]DMSO) 0.79 (6 H, s, 13- and 10-Me), 2.90br (1 H, m, 2β-H), 3.50br (1 H, m, 3α-H), 4.25 (s, exchangeable protons), and 8.1 (1 H, m, HCl salt) (Found: C, 65.2; H, 9.55; Cl, 9.9; N, 3.8. $C_{19}H_{32}ClNO_2$,0.5H_2O requires C, 65.1; H, 9.4; Cl, 10.1; N, 4.0%).

3α-*Formamido*-2α-*hydroxy*-5α-*androstan*-17-*one* (12).—3α-Amino-2α-hydroxy-5α-androstan-17-one (3) (3.31 g) was dissolved in formic acid (33.1 ml) and heated at 100° for 6 h. Water was added, the mixture was basified by the addition of potassium hydroxide solution (10N), and the product was extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a solid. Crystallisation from dichloromethane–ether afforded 3α-*formamido*-2α-*hydroxy*-5α-*androstan*-17-*one* (3.05 g) as needles, m.p. 266—268°, $[\alpha]_D$ +103° (*c* 0.48), $\nu_{max.}$(KCl) 3 360, 3 320 (OH,NH), 1 725 (C=O), and 1 655 and 1 525 (formamide) cm^{-1}, δ([$^2H_6$]DMSO) 0.80 (6 H, s, 10- and 13-Me), 3.65br (1 H, m, 2β-H), 4.00sh (1 H, m, 3β-H), 4.45 (1 H, m, OH), 7.80 (1 H, m, NH), and 8.05 (1 H, m, CHO) (Found: C, 70.6; H, 9.5; N, 3.9. $C_{20}H_{31}NO_3$,0.5H_2O requires C, 70.1; H, 9.4; N, 4.1%).

In a similar manner 3β-amino-2β-hydroxy-5α-androstan-17-one (2) (5.5 g) gave 3β-*formamido*-2β-*hydroxy*-5α-*androstan*-17-*one* (10) (5.22 g) as prisms, m.p. 283—286°, $[\alpha]_D$ +101° (*c* 1.2), $\nu_{max.}$(KCl) 3 310 (OH, NH), 1 740 (C=O), and 1 665 and 1 525 (formamide) cm^{-1}, δ($CDCl_3$–trace MeOD) 0.86 (3 H, s, 13-Me), 1.04 (3 H, s, 10-Me), 3.85br (1 H, m, 3α-H), 3.95sh (1 H, m, 2α-H), 6.70 (1 H, m, NH), and 8.09 (1 H, m, CHO) (Found: C, 70.4; H, 9.6; N, 4.25. $C_{20}H_{31}NO_3$,0.5H_2O requires C, 70.1; H, 9.4; N, 4.1%).

2β-Amino-3α-hydroxy-5α-androstan-17-one (13) (5.7 g) was converted into 2β-formamido-3α-hydroxy-5α-androstan-17-one (21) (4.9 g), m.p. 239—244°, $\nu_{max.}$(KCl) 3 320br (OH, NH), 1 735 (C=O), and 1 650 and 1 520 (amide) cm^{-1}.

2β-Amino-3β-hydroxy-5α-androstan-17-one (14) afforded 2β-formamido-3β-hydroxy-5α-androstan-17-one (22), m.p. 240—245°, $\nu_{max.}$(CH_2Cl_2) 3 600 (OH), 3 420 (NH), 1 738 (C=O), 1 690 (amide I), and 1 500 (amide II) cm^{-1}, δ($CDCl_3$–CD_3OD) 0.82 (3 H, s, 13-Me), 0.91 (3 H, s, 10-Me), 3.75br (1 H, m, 3α-H), 4.23sh (1 H, m, 2α-H), and 8.17 (1 H, s, CHO).

2α-Amino-3α-hydroxy-5α-androstan-17-one (15) afforded 2α-formamido-3α-hydroxy-5α-androstan-17-one (23), m.p. 250—253° (decomp.), $\nu_{max.}$(KCl) 3 360br (OH, NH), 1 740 (C=O), and 1 640 and 1 525 (amide) cm^{-1}.

3α-*Formamido*-2α-*hydroxy*-5α-*androstan*-17-*one Ethylene Acetal* (12a).—3α-Formamido-2α-hydroxy-5α-androstan-17-one (12) (2.93 g) was suspended in ethylene glycol (10.8 ml), triethyl orthoformate (17.6 ml), and toluene-*p*-sulphonic acid (0.18 g). The solution obtained on heating was refluxed under nitrogen for 2 h, poured into sodium carbonate solution, and the precipitated solid was filtered, washed with water and dried. The above reaction sequence was repeated to achive complete conversion to the acetal. Crystallisation of the crude product from dichloromethane–ether afforded 3α-*formamido*-2α-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (12a) (1.29 g) as prisms, m.p. 245—246°, $[\alpha]_D$ +7.0° (*c* 0.68), $\nu_{max.}$(KCl) 3 280 (OH, NH) and 1 665 and 1 540 (formamide) cm^{-1}, δ($CDCl_3$) 0.80 (6 H, s, 10- and 13-Me), 3.66br (1 H, m, 2β-H), 4.25sh (1 H, m, 3β-H), 6.25 (1 H, m, NH), and 8.20

(1 H, m, CHO) (Found: C, 69.7; H, 9.05; N, 3.5. $C_{22}H_{35}NO_4$ requires C, 70.0; H, 9.35; N, 3.7%).

In a similar manner 3β-formamido-2β-hydroxy-5α-androstan-17-one (10) (5.00 g) gave 3β-*formamido*-2β-*hydroxy*-5α-*androstan*-17-*one ethylene acetal* (10a) (2.13 g) as prisms, m.p. 252—255°, $\nu_{max.}$(KCl) 3 370 (OH,NH), 1 680 and 1 650 (formamide) cm^{-1}, δ($CDCl_3$–trace MeOD) 0.83 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 3.85br (1 H, m, 3α-H), 3.88 (4 H, s, acetal), 3.95sh (1 H, m, 2α-H), and 8.05 (1 H, m, CHO) (Found: C, 68.9; H, 9.3; N, 3.6. $C_{22}H_{35}NO_4$·0.25H_2O requires C, 69.2; H, 9.4; N, 3.7%).

2β-Formamido-3α-hydroxy-5α-androstan-17-one (13) gave 2β-formamido-3α-hydroxy-5α-androstan-17-one ethylene acetal (13a) as a crystalline solid, m.p. 214—217°, $\nu_{max.}$(KCl) 3 310br (OH, NH) and 1 660 (amide) cm^{-1}, δ($CDCl_3$) 0.82 (3 H, s, 13-Me), 0.92 (3 H, s, 10-Me), 2.85 (1 H, m, exchangeable OH), 3.84 (4 H, s, acetal), 3.9 (2 H, m, 2α- and 3β-H), 5.90 (1 H, m, exchangeable NH), and 8.12 (1 H, s, CHO).

2β-Formamido-3β-hydroxy-5α-androstan-17-one (22) afforded 2β-formamido-3β-hydroxy-5α-androstan-17-one ethylene acetal (22a), m.p. 237—239°, $\nu_{max.}$(KCl) 3 300br (OH, NH), 1 650, and 1 535 (amide) cm^{-1}.

2α-Formamido-3α-hydroxy-5α-androstan-17-one (23) afforded 2α-formamido-3α-hydroxy-5α-androstan-17-one ethylene acetal (23a), m.p. 274—280°, $\nu_{max.}$(KCl) 3 300 (OH, NH), 1 660, and 1 520 (amide) cm^{-1}.

2α-*Hydroxy*-3α-*methylamino*-5α-*androstan*-17-*one Ethylene Acetal* (7a).—3α-Formamido-2α-hydroxy-5α-androstan-17-one ethylene acetal (12a) (1.22 g) was dissolved in tetrahydrofuran (25 ml; sodium-dried) and added dropwise to a suspension of lithium aluminium hydride (0.61 g) in tetrahydrofuran (25 ml) at <10°. After the addition was complete the mixture was refluxed 15 min, cooled to <10°, and the excess of metal hydride destroyed by the cautious addition of water. The salts formed were filtered off on a Dicalite pad and the filtrate was washed with water, dried (Na_2SO_4), and concentrated to give a clear oil. The crude product was crystallised from dichloromethane–ether to give 2α-*hydroxy*-3α-*methylamino*-5α-*androstan*-17-*one ethylene acetal* (7a) (0.86 g) as prisms, m.p. 170—172°, $[\alpha]_D$ +36° (*c* 0.72), $\nu_{max.}$(KCl) 3 400 and 3 290 (OH,NH) cm^{-1}, δ($CDCl_3$) 0.81 (6 H, s, 10- and 13-Me), 2.38 (2 H, m, OH, NH), 2.41 (3 H, s, NMe), 2.70sh (1 H, m, 3β-H), 3.70br (1 H, m, 2β-H), and 3.85 (4 H, s, acetal) (Found: C, 72.4; H, 10.4; N, 3.6. $C_{22}H_{37}NO_3$ requires C, 72.7; H, 10.3; N, 3.85%).

In a similar manner 3β-formamido-2β-hydroxy-5α-androstan-17-one ethylene acetal (10a) (2.03 g) gave 2β-*hydroxy*-3β-*methylamino*-5α-*androstan*-17-*one ethylene acetal* (6a) (1.72 g) as prisms, m.p. 211—215°, $[\alpha]_D$ 0° (*c* 1.00), $\nu_{max.}$(KCl) 3 400 and 3 280 (OH, NH) cm^{-1}, δ($CDCl_3$) 0.81 (3 H, s, 13-Me), 0.98 (3 H, s, 10-Me), 2.20br (1 H, m, 3α-H), 2.38 (3 H, s, N-Me), 2.48 (2 H, m, OH, NH), 3.82 (4 H, s, acetal), and 3.90sh (1 H, m, 2α-H) (Found: C, 71.7; H, 10.1; N, 3.7. $C_{22}H_{37}NO_3$,0.25H_2O requires C, 71.8; H, 10.3; N, 3.8%).

2α-*Hydroxy*-3α-*methylamino*-5α-*androstan*-17-*one* (7).—2α-Hydroxy-3α-methylamino-5α-androstan-17-one ethylene acetal (7a) (0.74 g) was dissolved in a mixture of glacial acetic acid (14.8 ml) and water (1.48 ml) and heated on a steam-bath for 30 min. Water was added and the reaction was basified. The mixture was extracted with dichloromethane and the extracts were washed with water, dried (Na_2SO_4), and evaporated to give a solid. Crystallisation from dichloromethane–ether afforded 2α-*hydroxy*-3α-*methylamino*-5α-*androstan*-17-*one* (7) (0.63 g) as prisms, m.p. 182—184°, $[\alpha]_D$ +119° (*c* 0.81), $\nu_{max.}$(KCl) 3 430 (OH,NH) and 1 730 (C=O) cm^{-1}, δ($CDCl_3$) 0.84 (6 H, s, 10- and 13-Me), 2.41 (3 H, s, N-Me), 2.50 (2 H, m, OH, NH), 2.70sh (1 H, m, 3β-H), and 3.60br (1 H, m, 2β-H) (Found: C, 73.0; H, 10.4; N, 4.1. $C_{20}H_{33}NO_2$,0.5H_2O requires C, 73.1; H, 10.4; N, 4.3%).

A sample of 2α-hydroxy-3α-methylamino-5α-androstan-17-one (7) was converted into the hydrochloride, which was recrystallised from ethanol–ether to give 2α-*hydroxy*-3α-*methylamino*-5α-*androstan*-17-*one hydrochloride* as prisms, m.p. 268—278° (decomp.), $[\alpha]_D$ +95° (*c* 0.65 in MeOH), $\nu_{max.}$(KCl) 3 280 (OH,NH) and 1 740 (C=O) cm^{-1} (Found: C, 67.4; H, 9.5; Cl, 10.0; N, 3.65. $C_{20}H_{34}ClNO_2$ requires C, 67.5; H, 9.6; Cl, 10.0; N, 3.9%).

2β-*Hydroxy*-3β-*methylamino*-5α-*androstan*-17-*one* (6).—In a similar manner 2β-hydroxy-3β-methylamino-5α-androstan-17-one ethylene acetal (6a) (1.6 g) was converted into crude 2β-hydroxy-3β-methylamino-5α-androstan-17-one (6) (1.11 g), $\nu_{max.}$(KCl) 3 350 (OH, NH) and 1 740 (C=O) cm^{-1}, δ($CDCl_3$–trace MeOD) 0.85 (3 H, s, 13-Me), 1.02 (3 H, s, 10-Me), 2.58 (3 H, s, N-Me), and 2.80sh (1 H, m, 2α-H).

The free base was converted into the hydrochloride, which was recrystallised from ethanol–ether to give pure 2β-*hydroxy*-3β-*methylamino*-5α-*androstan*-17-*one hydrochloride* as prisms, m.p. >300° (decomp.), $[\alpha]_D$ +103° (*c* 0.54 in MeOH), $\nu_{max.}$(KCl) 3 370 (OH, NH) and 1 740 (C=O) cm^{-1}, δ([$^2H_6$]DMSO) 0.78 (3 H, s, 13-Me), 0.98 (3 H, s, 10-Me), 2.46 (3 H, s, N-Me), 2.95br (1 H, m, 3α-H), 3.30 (1 H, m, OH), 4.13sh (1 H, m, 2α-H), 5.45 (1 H, m, NH), and 8.70 (1 H, m, HCl) (Found: C, 65.65; H, 9.5; Cl, 9.5; N, 3.4. $C_{20}H_{34}ClNO_2$,0.5H_2O requires C, 65.8; H, 9.7; Cl, 9.7; N, 3.8%).

2β-*Methylamino*-3α-*hydroxy*-5α-*androstan*-17-*one* (17).—A solution of 2β-formamido-3α-hydroxy-5α-androstan-17-one ethylene acetal (21a) (8.0 g) in dry tetrahydrofuran (100 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (4.0 g) in dry tetrahydrofuran (100 ml). The mixture was heated under reflux for 45 min, cooled in an ice-bath, and the excess of lithium aluminium hydride was destroyed by careful addition of water. The mixture was filtered through Dicalite and the filtrate was concentrated under vacuum. The residual oil was dissolved in glacial acetic acid (20 ml) and water (6 ml) and the solution was warmed on a steam-bath for 1 h, cooled and basified with potassium hydroxide (10N). The resulting precipitate was extracted into dichloromethane and the extracts were filtered through Dicalite, washed with water, dried ($MgSO_4$), and evaporated to dryness. Recrystallisation from dichloromethane–ether afforded 2β-*methylamino*-3α-*hydroxy*-5α-*androstan*-17-*one* (17), m.p. 142—143°, $[\alpha]_D$ +102° (*c* 0.87), $\nu_{max.}$(KCl) 3 400br (OH, NH_2) and 1 740 (C=O) cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 0.95 (3 H, s, 10-Me), 1.58 (m, exchangeable protons), 2.39 (3 H, s, N-Me), 2.60sh (1 H, m, 2α-H), and 3.80sh (1 H, m, 3β-H) (Found: C, 75.0; H, 10.45; N, 4.6. $C_{20}H_{33}NO_2$ requires C, 75.2; H, 10.4; N, 4.4%). The *hydrochloride* had m.p. >280°, $[\alpha]_D$ +138° (*c* 0.41 in MeOH), $\nu_{max.}$(KCl) 3 400 (OH), 3 000—2 000 (amine salt), 1 738 (C=O), and 1 601 (amine salt) cm^{-1} (Found: C, 67.7; H, 9.8; Cl, 10.1; N, 4.0. $C_{20}H_{34}ClNO_2$ requires C, 67.5; H, 9.6; Cl, 10.0; N, 3.9%).

In a similar manner 2β-formamido-3β-hydroxy-5α-androstan-17-one ethylene acetal (22a) afforded 2β-*methylamino*-3β-*hydroxy*-5α-*androstan*-17-*one* (18), m.p. 152—154°, $[\alpha]_D$ +113° (*c* 0.73), $\nu_{max.}$(KCl) 3 420 (OH, NH) and 1 735 (C=O) cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 0.95 (3 H, s, 10-

Me), 2.42 (3 H, s, NMe), 2.75sh (1 H, m, 2α-H), and 3.55br (1 H, m, 3α-H) (Found: M^+, 319.2493. $C_{20}H_{33}NO_2$ requires M, 319.2511). The *hydrochloride* had m.p. 285—289° (decomp.), $[\alpha]_D$ +83° (*c* 0.84 in MeOH), $\nu_{max.}$(KCl) 3 280 (NH, OH), 2 460 and 2 420 (salt), 1 738 (C=O), and 1 588 ($\overset{+}{N}H$) cm^{-1}, δ([$^2H_6$]DMSO) 0.78 (3 H, s, 13-Me), 0.97 (3 H, s, 10-Me), 2.63 (3 H, s, NMe), 3.30sh (1 H, s, 2α-H), 3.31 (1 H, s, exchangeable OH), 3.80br (1 H, m, 3α-H), 5.6 (1 H, m, exchangeable NH), and 8.54br (1 H, m, exchangeable HCl salt) (Found: C, 67.5; H, 9.7; Cl, 9.5; N, 4.2. $C_{20}H_{34}ClNO_2$ requires C, 67.5; H, 9.6; Cl, 10.0; N, 3.9%).

2α-Formamido-3α-hydroxy-5α-androstan-17-one ethylene acetal (23a) afforded *2α-methylamino-3α-hydroxy-5α-androstan-17-one* (19), m.p. 176—180°, $\nu_{max.}$(KCl) 3 400—3 140 (OH, NH) and 1 743 (C=O) cm^{-1}, δ($CDCl_3$) 0.86 (6 H, s, 10- and 13-Me), 2.38 (3 H, s, NMe), and 3.90sh (1 H, m, 3β-H) (Found: C, 74.9; H, 10.25; N, 4.15. $C_{20}H_{33}NO_2$ requires C, 75.2; H, 10.4; N, 4.4%). The *hydrochloride* had m.p. >280° (decomp.), $[\alpha]_D$ +88° (*c* 0.74 in DMSO), $\nu_{max.}$(KCl) 3 290 and 3 080 (OH, NH), 2 700—2 400 (amine salt), 1 725 (C=O), and 1 590 ($\overset{+}{N}H_3$) cm^{-1}, δ([$^2H_6$]DMSO and MeOD) 0.80 (6 H, s, 10- and 13-Me), 2.53 (3 H, s, NMe), 3.13br (1 H, m, 2β-H), and 3.58sh (1 H, m, 3β-H) (Found: C, 67.4; H, 9.75; Cl, 10.0; N, 3.8. $C_{20}H_{34}ClNO_2$ requires C, 67.5; H, 9.6; Cl, 10.0; N, 3.9%).

2β-Hydroxy-3α-methylamino-5α-androstan-17-one (5).—A suspension of 2β,3β-epoxy-5α-androstan-17-one (27) (15 g) in methylamine (132 ml; 33% solution in ethanol) and water (18 ml) was heated in an autoclave at 170° for 4 h and the product was isolated as described for the 2β-amino-3α-hydroxy compound (13). The crude product was crystallised from dichloromethane–ether to give *2β-hydroxy-3α-methylamino-5α-androstan-17-one* (5) as a solid (10.0 g). Recrystallisation from ether gave an analytical sample, m.p. 181—183°, $[\alpha]_D$ +101° (*c* 0.6), $\nu_{max.}$(KCl) 3 545 (OH), 3 210 (NH), and 1 740 (C=O) cm^{-1}, δ($CDCl_3$) 0.83 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 2.42 (3 H, s, NMe), 2.64sh (1 H, m, 3β-H), and 3.92sh (1 H, m, 2α-H) (Found: C,73.3; H, 10.1; N, 4.1. $C_{20}H_{33}NO_2,0.5H_2O$ requires C, 73.3; H, 10.4; N, 4.3%). The *hydrochloride* had m.p. 270—281°, $[\alpha]_D$ +119° (*c* 1.07 in MeOH), $\nu_{max.}$(KCl) 3 440 (OH, NH), 2 480 (salt), 1 740 (C=O), and 1 590 (NH^+) cm^{-1}, δ([$^2H_6$]-DMSO) 0.77 (3 H, s, 13-Me), 0.93 (3 H, s, 10-Me), 2.50 (3 H, s, NMe), 3.00sh (1 H, m, 3β-H), and 4.00sh (1 H, m, 2α-H) (Found: C, 66.1; H, 9.9; Cl, 9.8; N, 3.8. $C_{20}H_{34}ClNO_2,0.5H_2O$ requires C, 65.8; H, 9.7; Cl, 9.7; N, 3.8%).

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