18-Norandrosta-8,11,13-trienes. Part II.[1] Aromatisation of 18-Norandrost-13-enes by Bromination and Dehydrobromination

By **Colin L. Hewett,* Iain M. Gilbert, James Redpath, David S. Savage, John Strachan, Thomas Sleigh, and Robert Taylor,** Organon Scientific Development Group, Newhouse ML1 5SH, Lanarkshire, Scotland

Bromination of 17,17-disubstituted-18-norandrost-13-enes (1) followed by dehydrobromination gave the corresponding 7,13-dienes (3), which on further bromination and dehydrobromination yielded the 8,11,13-trienes (8). The mechanism of the reaction including the involvement of the 17-substituents is discussed.

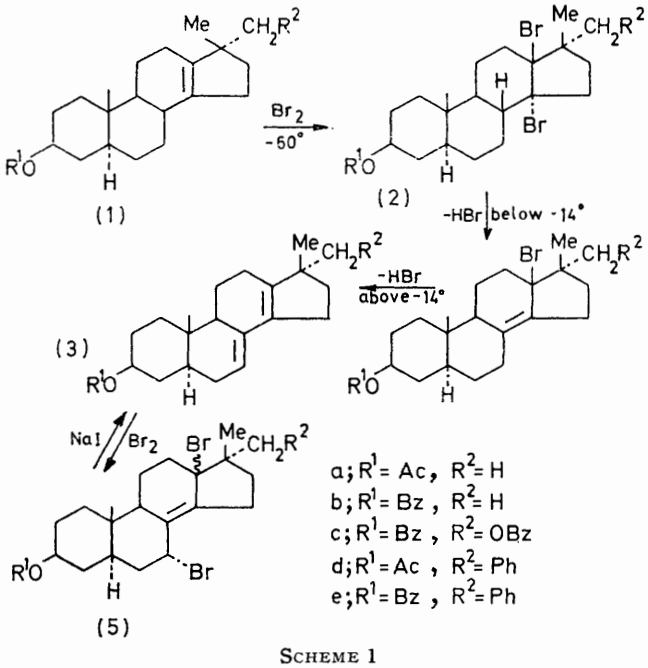
PART I [1] described the synthesis of 11-hydroxy-18-norandrosta-8,11,13-trienes by aromatisation of steroids in which two potential double bonds were present in ring C before introduction of the third by a Wagner–Meerwein shift [2] of the 13-methyl group to the 17-position. As an extension of the programme to evaluate the biological activities of ring-C-aromatic steroids, the present paper describes a useful route in which the Wagner–Meerwein shift precedes introduction of a further two double bonds into ring C to give compounds unsubstituted at position 11.

A number of Δ^{13}-18-norsteroids (1), prepared by treating a 17α-alkyl-17β-alcohol or a 17β-oxiran [3] with formic acid,[4] were subjected to a variety of dehydrogenation reactions.

Direct dehydrogenation by palladium–charcoal in combination with sulphur, which has been shown [5] to be more effective than either reagent alone, resulted in a low yield of the triene (8b) when applied to the Δ^{13}-steroid (1b). Reaction of the Δ^{13}-steroid (1a) did not yield a 8,11,13-triene with dichlorodicyanobenzoquinone (DDQ) [6] as might have been expected.

Bromination followed by dehydrobromination is a well established technique for introducing additional double bonds into steroids [7] and when applied to Δ^{7}-steroids yields 7,9(11)-dienes. It seemed probable therefore that similar treatment of a Δ^{13}-18-norsteroid would proceed *via* a 7,13-diene to a 8,11,13-triene. Bromination of the 13-enes (1), followed by treatment with sodium iodide in acetone, gave the 7,13-dienes (3) as expected. The reaction is presumed to proceed by direct addition of bromine to the 13,14-double bond (Scheme 1) to give the dibromo-compounds (2), which are stable at −70° but which lose hydrogen bromide in two stages as the temperature rises. Slow elimination of hydrogen bromide occurs below −14°, becoming rapid above −14° to give the 7,13-dienes (3), which are partly brominated by the excess of bromine present and have to be regenerated by treatment of the crude product with sodium iodide in acetone.

When the reaction was carried out with exactly 1 mol. equiv. of bromine, 10—20% of starting material (1) remained and further investigation showed that an excess of bromine was required for high yields of the 7,13-dienes (3). Presumably steric hindrance of the 13,14-double bonds of the 18-norandrostenes (1) by the



SCHEME 1

adjacent 17-substituents demands an excess of bromine to drive the reaction to completion. In the 17α-methyl and 17α-benzoyloxymethyl series (1a—c) 1·3—1·5 mol. equiv. of bromine is sufficient whereas the more hindered 17α-benzyl series (1d and e) require 1·8—2·1 mol. equiv.

The structures of the 7,13-dienes (3) were confirmed by their n.m.r. spectra, which show signals for one vinylic proton (δ 5·3—5·4), and by their u.v. spectra ($\lambda_{max.}$ 237, 245, and 255 nm).

[1] Part I, C. L. Hewett, S. G. Gibson, I. M. Gilbert, J. Redpath, and D. S. Savage, *J.C.S. Perkin I*, 1973, 1967.

[2] A. Cohen, J. W. Cook, and C. L. Hewett, *J. Chem. Soc.*, 1935, 445.

[3] (*a*) G. Drefahl, K. Ponsold, and H. Schick, *Chem. Ber.*, 1964, **97**, 3529; (*b*) D. N. Kirk and M. A. Wilson, *J. Chem. Soc.* (*C*), 1971, 414.

[4] (*a*) K. Miescher and H. Kägi, *Helv. Chim. Acta*, 1949, **32**, 761; (*b*) V. Tortorella, G. Lucente, and A. Romeo, *Ann. Chim.* (*Italy*), 1960, **50**, 1198; (*c*) O. S. Madaeva, *J. Gen. Chem.* (*U.S.S.R.*), 1956, **26**, 3267; O. S. Madaeva and Yu. N. Sheinkev, *ibid.*, p. 3569.

[5] H. S. Blair, M. Crawford, J. M. Spence, and V. R. Supanekar, *J. Chem. Soc.*, 1960, 313; M. Crawford and V. R. Supanekar, *ibid.*, 1962, 674, 2380.

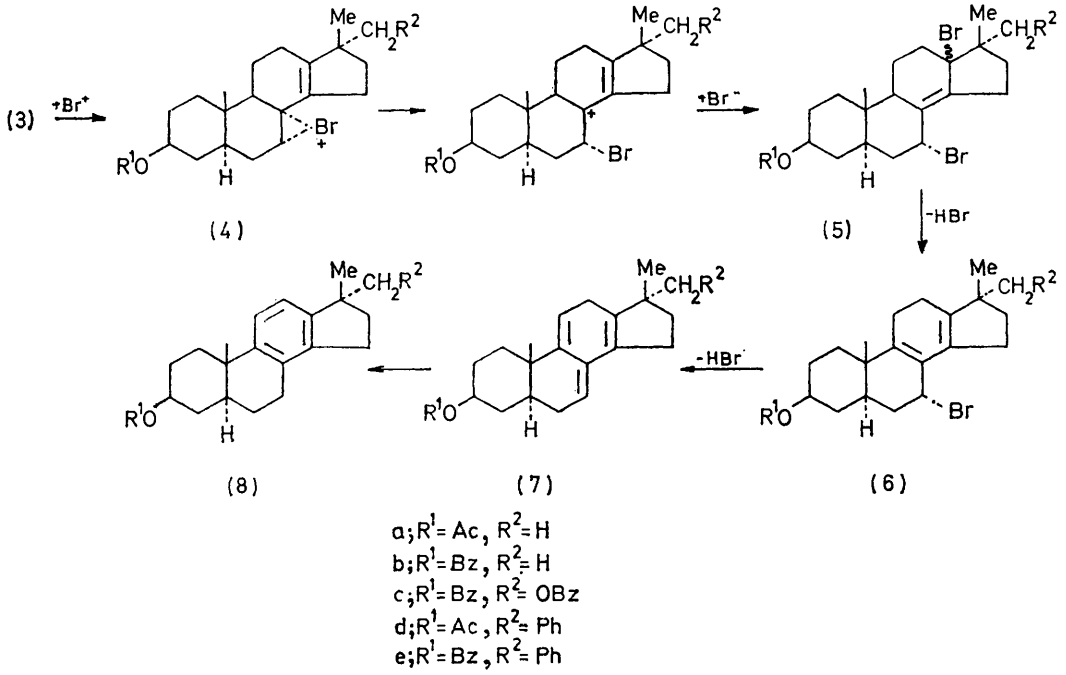
[6] S. G. Boots and W. S. Johnson, *J. Org. Chem.*, 1966, **31**, 1285; E. W. Cantrall, R. B. Conrow, and S. Bernstein, *ibid.*, 1967, **32**, 4081; W. Brown and A. B. Turner, *Chem. Comm.*, 1968, 561.

[7] A. L. Morrison and J. C. E. Simpson, *J. Chem. Soc.*, 1932, 1710; J. C. Eck and E. W. Hollingsworth, *J. Amer. Chem. Soc.*, 1942, **64**, 140; R. C. Anderson, R. Stevenson, and F. S. Spring, *J. Chem. Soc.*, 1952, 2901; C. F. Hammer, D. S. Savage, J. B. Thomson, and R. Stevenson, *Tetrahedron*, 1964, **20**, 929.

Further bromination of the 7,13-dienes (3) under similar conditions gave predominantly the dibromides (5), two of which (5b and c) were sufficiently stable to be isolated and characterised. The structures of these dibromides (5b and c) were confirmed by the n.m.r. spectra, which show the presence of an equatorial 7β-proton (δ 5·03 and 4·98, respectively, $W_{\frac{1}{2}}$ 6·6 Hz), indicating a 7α-bromo-substituent. The placing of the other bromine atom at the 13-position follows from a comparison of the 17-methyl signals. The spectrum of the benzoyloxymethyl dibromide (5c) shows the 17α-methylene signal at δ 3·97, which allows the peak at δ 1·36 to be attributed to the 17β-methyl group. The 17,17-dimethyl dibromide (5b) shows signals for the 17-methyl groups at δ 0·84 (17α-Me) and 1·26 (17β-Me). By analogy with the bromination of a 7,9(11)-diene system, which gives the *trans*-diaxial 7α,11β-dibromide,[8] the configuration of compounds (5) at position C-13 is assumed to be 13β, but the n.m.r. evidence is insufficient to prove this point.

Dehydrobromination by stirring a solution of the total crude dibromides (5) in benzene with silica gave the 8,11,13-trienes (8) in good yields with the exception of the 17α-benzyl derivative (5d), which gave a poor yield by this method owing to the formation of a by-product. This has been assigned the structure (9a) on the basis of its mass spectrum (M^+ 400·24048), its n.m.r. spectrum, which showed the presence of 5 aromatic protons (δ 7·19, 7·24, and 7·50), and its u.v. absorption at 272, 280, and 309 nm (ε 18,800, 18,200, and 6700), similar to that of 9,10-dihydrophenanthrene[9] but in marked contrast to the low-intensity aromatic absorption (ε 1340 at 266—277 nm) of the 17α-benzyl-8,11,13-triene (8d). To obtain the 8,11,13-triene (8d) in good yield, the dibromide (5d) was heated in benzene at reflux temperature.

The suggested mechanism for this bromination and subsequent aromatisation is shown in Scheme 2. Attack of the less hindered 7,8-double bond of the 7,13-diene (3) gives an α-bromonium ion (4), which yields the dibromo-ene (5) *via* an intermediate carbonium ion. The dibromide (5) loses 1 mole of hydrogen bromide to give the intermediate bromo-diene (6), which on loss of a further mole of hydrogen bromide gives the 7,9(11),13-triene (7); this isomerises to the 8,11,13-triene (8) in acidic medium. In an attempt to achieve aromatisation in one step the Δ^{13}-compound (1b) was treated with 2·3 mol. equiv. of bromine and although the main product (92% by g.l.c.) was the aromatic compound (8b), an unidentified impurity was present which made isolation difficult.



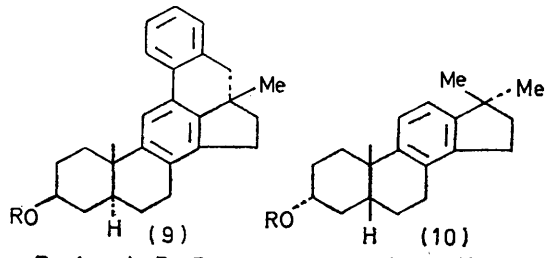
SCHEME 2

The structures of the ring-C-aromatic compounds (8) were confirmed by their n.m.r. spectra, which show the presence of two coupled aromatic protons as an AB quartet (δ 6·94 and 7·14, J_{AB} 8 Hz), and also by the aromatic absorption in the i.r. spectra ($\nu_{max.}$ 3058, 3010, and 830 cm^{-1}).

To demonstrate that the reaction is of general application and not affected by changes of configuration at the AB ring junction, the bromination–dehydrobromination procedure was carried out on the 5β-steroid, 3α-benzoyloxy-17,17-dimethyl-18-nor-5β-androst-13-ene, in the same

[8] D. S. Savage, Ph.D. Thesis, University of Glasgow, 1960.
[9] R. N. Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 1658.

manner, and the corresponding 5β-ring-C-aromatic compounds (10) were isolated in good yield.



a;R = Ac b;R = Bz a;R = Bz b;R = H

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were determined with a Perkin-Elmer 457 spectrometer. U.v. spectra were determined with a Perkin-Elmer 402 spectrometer and refer to ethanolic solutions. Optical rotations were measured for solutions in chloroform at room temperature unless otherwise stated. G.l.c. was performed with a Pye Argon chromatograph. Quoted retention times are relative to cholestane (t_R = 1·0). N.m.r. spectra (solvent $CDCl_3$) were determined at 60 MHz with a Perkin-Elmer R12 B spectrometer (tetramethylsilane as internal standard). Light petroleum refers to the fraction b.p. 40—60°.

17,17-*Dimethyl*-18-*nor*-5α-*androst*-13-*en*-3β-*yl Formate*.—A suspension of 17α-methyl-5α-androstane-3β,17β-diol [4,10] (175·6 g) in formic acid (90%; 500 ml) was boiled under reflux for 20 min then cooled, and water was added to precipitate a pale yellow solid which was filtered off, washed neutral with water, and dried (174·7 g). Crystallisation from ether–methanol gave the *ester* as prisms, m.p. 76—79°, $[\alpha]_D$ −41° (*c* 1·0), $\nu_{max.}$ (CH_2Cl_2) 1724 and 1190 (3-formate) cm^{-1}, δ 0·9 (3H, s, 10-Me), 1·0 (6H, s, 17,17-Me_2), 4·9 (1H, m, 3α-H), and 8·1 (1H, s, 3β-O·CHO) (Found: C, 79·7; H, 10·2. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·2%).

17,17-*Dimethyl*-18-*nor*-5α-*androst*-13-*en*-3β-*ol*.—Hydrolysis of the foregoing ester (170 g) in aqueous methanolic potassium hydroxide yielded a white solid (153·5 g) which was crystallised from acetone to give the 3β-ol as prisms, m.p. 130—135°, $[\alpha]_D$ −40° (*c* 1·0) (lit.,[4b] m.p. 130—132°, $[\alpha]_D^{20}$ in EtOH −35·9°), $\nu_{max.}$ (CH_2Cl_2) 3600 (3-OH) cm^{-1}, δ 0·8 (3H, s, 10-Me), 0·9 (6H, s, 17,17-Me_2) and 3·6 (1H, m, 3α-H) (Found: C, 83·3; H, 10·8. Calc. for $C_{20}H_{32}O$: C, 83·3; H, 11·2%).

17,17-*Dimethyl*-18-*nor*-5α-*androst*-13-*en*-3β-*yl Acetate* (1a).—Acetylation of 17,17-dimethyl-18-nor-5α-androst-13-en-3β-ol (153 g) with pyridine (150 ml) and acetic anhydride (150 ml) on a water-bath for 1·25 h gave the 3β-*acetate* (1a) (157 g), which formed prisms (from ether–methanol), m.p. 106—110°, $[\alpha]_D$ −42° (*c* 1·3), $\nu_{max.}$ (KCl) 1733 and 1248 (3-OAc) cm^{-1}, δ 0·8 (3H, s, 10-Me), 0·9 (6H, s, 17,17-Me_2), 2·0 (3H, s, 3β-OAc), and 4·7 (1H, s, 3α-H) (Found: C, 80·0; H, 10·5. $C_{22}H_{34}O_2$ requires C, 80·0; H, 10·4%).

17,17-*Dimethyl*-18-*nor*-5α-*androsta*-7,13-*dien*-3β-*yl Acetate* (3a).—Bromine (14·3 ml, 1·3 mol. equiv.) was added to a stirred solution of the acetate (1a) (71 g) in ether (710 ml) and methylene chloride (71 ml) at −70°, and the temperature was allowed to rise to −20°. A solution of sodium iodide (100 g) in acetone (500 ml) was added, and the solution was concentrated and washed with water, aqueous sodium sulphite solution, water, and saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. Crystallisation of the residue from ether–methanol gave the 7,13-*diene* (3a) (70·3 g), m.p. 85—88°, $[\alpha]_D$ −150° (*c* 0·4), $\nu_{max.}$ (KCl) 1735 and 1260 (3-OAc) cm^{-1}, $\lambda_{max.}$ 237 (ε 21,600), 245 (22,600), and 255 nm (5200), δ 0·75 (3H, s, 10-Me), 0·99 (6H, s, 17,17-Me_2), 2·03 (3H, s, 3β-OAc), 4·7 (1H, m, 3α-H), and 5·4 (1H, m, 7-H) (Found: C, 80·1; H, 10·1. $C_{22}H_{32}O_2$ requires C, 80·4; H, 9·8%).

17,17-*Dimethyl*-18-*nor*-5α-*androsta*-8,11,13-*trien*-3β-*yl Acetate* (8a).—Bromine (16·5 ml, 1·6 mol. equiv.) was added to a stirred solution of the 7,13-diene (3a) (65 g) in ether (600 ml) and methylene chloride (65 ml) at −65°, and the temperature of the mixture was allowed to rise to 25°, hydrobromic acid gas being evolved above −5°. The solution was washed with aqueous sodium sulphite solution and sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. A solution of the residue in benzene (250 ml) was boiled under reflux to remove hydrogen bromide, cooled, and filtered down a column (4 × 3 in) of alumina. Elution with benzene (700 ml) gave a fraction from which the product (39·0 g) was obtained as a gum on evaporation. Crystallisation from ether–methanol yielded the 8,11,13-*triene* (8a) as prisms (20·0 g), m.p. 102—104·5°, $[\alpha]_D$ +39° (*c* 1·2), $\nu_{max.}$ (KCl) 3058, 3010, and 831 (aromatic), and 1732 and 1245 (3-OAc) cm^{-1}, $\lambda_{max.}$ 266 (ε 750) and 275 nm (660), δ 1·12 (3H, s, 10-Me), 1·32 (6H, s, 17,17-Me_2), 2·03 (3H, s, 3β-OAc), 2·7 (4H, m, 7- and 15-H_2), 4·8 (1H, m, 3α-H), and 6·94 and 7·24 (2H, q, J_{AB} 8 Hz, 11- and 12-H) (Found: C, 81·1; H, 9·3. $C_{22}H_{30}O_2$ requires C, 81·0; H, 9·3%).

Attempted Dehydrogenation of 17,17-*Dimethyl*-18-*nor*-5α-*androst*-13-*en*-3β-*yl Acetate* (1a) *by DDQ*.—A solution of compound (1a) (1 g) and dichlorodicyanobenzoquinone (1·54 g) in toluene (15 ml) was heated to reflux for 45 min, cooled, and filtered, and the filtrate was washed with water and 0·5N-sodium hydroxide solution and dried (Na_2SO_4). Evaporation gave starting material (0·93 g) (t.l.c. and i.r.).

17,17-*Dimethyl*-18-*nor*-5α-*androst*-13-*en*-3β-*yl Benzoate* (1b).—A stirred solution of 17,17-dimethyl-18-nor-5α-androst-13-en-3β-ol (286 g) in pyridine (700 ml) was cooled to 12° and benzoyl chloride (174 ml, 1·5 mol. equiv.) was added over 25 min with cooling to keep the reaction temperature below 35°. A white solid precipitated and was filtered off, washed with 2N-hydrochloric acid, and water, and dried *in vacuo* (384 g). Crystallisation from ether–methanol yielded prisms (380 g) of the 3β-*benzoate* (1b), m.p. 133—137°, $[\alpha]_D$ −24° (*c* 1·1), t_R 2·31 (SE 30; 230°) and 4·6 (OV17; 245°), $\nu_{max.}$ (KCl) 1715 and 1280 (3β-OBz) cm^{-1}, δ 0·86 (3H, s, 10-Me), 0·95 (6H, s, 17,17-Me_2), 4·9 (1H, m, 3α-H), and 7·4 and 8·1 (5H, m, 3β-OBz) (Found: C, 83·2; H, 9·0. $C_{27}H_{36}O_2$ requires C, 83·4; H, 9·3%).

17,17-*Dimethyl*-18-*nor*-5α-*androsta*-7,13-*dien*-3β-*yl Benzoate* (3b).—A solution of bromine (34 ml, 1·3 mol. equiv.) in methylene chloride (30 ml) was added to a stirred solution of the benzoate (1b) (200 g) in methylene chloride (200 ml) and ether (1 l) at −65° over 3 min. The temperature was allowed to rise to −5° over 45 min, sodium iodide (160 g) in acetone (1 l) was added, and the mixture was boiled under reflux for 20 min. The solution was cooled and an excess of aqueous sodium sulphite was added. The organic layer was washed with water, dried (Na_2SO_4), and evaporated to dryness to give a white solid which on trituration with

[10] L. Ruzicka, M. W. Goldberg, and H. R. Rosenberg, *Helv. Chim. Acta*, 1935, **18**, 1487.

methanol yielded prisms of the 7,13-*diene* 3β-*benzoate* (3b) (186·0 g), m.p. 127—131°, $[\alpha]_D$ −99° (*c* 0·74), t_R 2·76 (SE 30; 230°) and 5·3 (OV17; 245°), $\nu_{max.}$ (KCl) 1715 and 1277 (3β-OBz) cm^{-1}, $\lambda_{max.}$ 237 (ε 25,000), 245sh (22,500), and 254 nm (13,700), δ 0·79 (3H, s, 10-Me), 0·98 (6H, s, 17,17-Me_2), 4·9 (1H, m, 3α-H), 5·4 (1H, m, 7-H), and 7·5 and 8·1 (5H, m, 3β-OBz) (Found: C, 82·9; H, 8·9. $C_{27}H_{34}O_2$ requires C, 83·0; H, 8·8%).

17,17-*Dimethyl*-18-*nor*-5α-*androsta*-8,11,13-*trien*-3β-*yl Benzoate* (8b).—(*a*) Bromine (28·4 ml, 1·2 mol. equiv.) was added to a stirred suspension of the 7,13-diene (3b) (174 g) in methylene chloride (174 ml) and ether (1·7 l) at −60° over 3 min, and the solution was kept at this temperature for a further 10 min. The reaction temperature was allowed to rise to −20° and the solid which had precipitated was filtered off, washed with cold ether, and dried (133 g). A sample (10 g) was washed again with cold ether to give 7α,13ξ-*dibromo*-17,17-*dimethyl*-18-*nor*-5α-*androst*-8(14)-*en*-3β-*yl benzoate* (5b) (6·0 g), decomposing on heating, $\nu_{max.}$ (KCl) 1710, 1600, and 1270 (benzoate) and 710 (CBr) cm^{-1}, $\nu_{max.}$ (CCl_4) 1725, 1604, 1277, and 710 cm^{-1}, δ 0·84 (6H, s, 17α-Me and 10-Me), 1·26 (3H, s, 17β-Me), 5·0 (1H, m, 3α-H), 5·03 (1H, m, $W_{\frac{1}{2}}$ 6·5 Hz, 7β-H), and 7·45 and 8·0 (5H, m, 3β-OBz) (Found: C, 58·5; H, 6·2; Br, 30·0. $C_{27}H_{34}Br_2O_2$ requires C, 58·9; H, 6·2; Br, 29·0%). The filtrate was washed with aqueous sodium hydrogen sulphite and water, dried, and evaporated to dryness under reduced pressure to give a solid residue (192 g). Silica gel (352 g) was added to a solution of the combined solids (315 g) in benzene (1·2 l) and the mixture was stirred for 12 h. The silica gel was filtered off and washed with benzene, and the filtrate was evaporated to dryness to yield a pale yellow solid, which crystallised from ether–methanol to give the 8,11,13-*triene* (8b) (151 g) as prisms, m.p. 139—145°, $[\alpha]_D$ +38° (*c* 1·1), t_R 6·2 (OV17; 245°), $\nu_{max.}$ (KCl) 1716 and 1272 (3β-OBz) and 1600 and 825 (aromatic) cm^{-1}, $\lambda_{max.}$ 281 nm (ε 1800), δ 1·16 (3H, s, 10-Me), 1·23 (6H, s, 17,17-Me_2), 2·17 (4H, m, 7- and 15-H_2), 5·0 (1H, m, 3α-H), 6·96 and 7·14 (2H, q, J_{AB} 8 Hz, 11- and 12-H), and 7·5 and 8·1 (5H, m, 3β-OBz) (Found: C, 83·2; H, 8·3. $C_{27}H_{32}O_2$ requires C, 83·4; H, 8·3%).

(*b*) A solution of bromine (0·595 ml, 2·27 mol. equiv.) in methylene chloride (0·6 ml) was added to a stirred solution of the 13-ene 3β-benzoate (1b) in methylene chloride (2 ml) and ether (10 ml) at −57° and the temperature was allowed to rise to −5° over 0·5 h. After a further 1 h at −5° a small sample was treated with a solution of sodium iodide in acetone to effect dehydrobromination, and the product was shown to be 3β-benzoyloxy-17,17-dimethyl-18-nor-androsta-7,13-diene (3b), over 90% pure by g.l.c., t_R 5·3 (OV17; 245°), containing a trace of starting material, t_R 4·6 (OV17; 245°) and 5% of aromatic product, t_R 6·2 (OV17; 245°).

The main portion of the reaction mixture was treated with aqueous sodium hydrogen sulphite and the crude product in benzene (12 ml) was stirred with silica (4·0 g) for 16 h. Removal of solvent and crystallisation from ether–methanol gave the 8,11,13-triene (8b) (1·2 g), t_R 6·2 (OV17; 245°) containing an impurity (*ca.* 8%), t_R 5·8 (OV17; 245°) which was not identified.

(*c*) Carbon dioxide was passed through a suspension of 5% palladium–charcoal (2·0 g) and sulphur (0·5 g) in dimethylacetamide (30 ml) to remove adsorbed gases. 3β-Benzoyloxy-17,17-dimethyl-18-nor-5α-androst-13-ene (1b) (5·0 g) was added and the resulting mixture was heated under reflux for 18 h. The catalyst was filtered off, water was added to the filtrate, and the product was extracted into ether. The extract was concentrated and methanol added to give an oily deposit. Crystallisation of material from the supernatant liquors (ether–methanol) gave the triene (8b) (0·7 g), identical (i.r. and u.v. spectra) with the product obtained by bromination and dehydrobromination of the 7,13-diene (3b).

17,17-*Dimethyl*-18-*nor*-5α-*androsta*-8,11,13-*trien*-3β-*ol*.—(*a*) Hydrolysis of the 3β-acetate (8a) (71 g) in aqueous methanolic potassium hydroxide yielded the 3β-*alcohol* (63·3 g), which was recrystallised from ether–hexane to give prisms (56·5 g), m.p. 107—110°, $[\alpha]_D$ +56·6° (*c* 1·3), $\nu_{max.}$ (KCl) 3280 (3-OH) and 3032 and 820 (aromatic) cm^{-1}, $\lambda_{max.}$ 266 (ε 1010) and 275 nm (930), δ 1·1 (3H, s, 10-Me), 1·23 (6H, s, 17,17-Me_2), 2·7 (4H, m, 7- and 15-H_2), 3·7 (1H, m, 3α-H), and 6·94 and 7·14 (2H, q, J_{AB} 8 Hz, 11- and 12-H) (Found: C, 84·3; H, 10·0. $C_{20}H_{28}O$ requires C, 84·4; H, 9·9%).

(*b*) Hydrolysis of the 3β-benzoate (8b) (50 g) in a similar manner yielded the 3β-alcohol (42·8 g), m.p. 108—110°, identical with the product prepared in (*a*).

17β,20-*Epoxy*-21-*nor*-5α,17α-*pregnan*-3β-*ol*.—This was prepared in almost quantitative yield by treatment of 3β-hydroxy-5α-androstan-17-one with dimethylsulphonium methylide according to the procedure described by Kirk and Wilson.[3b] The product, crystallised from acetone–light petroleum had m.p. 152—167°, $[\alpha]_D$ +40° (*c* 1·7) (lit.,[3a] m.p. 171—173°, $[\alpha]_D$ +11°).

17β-*Methyl*-18,21-*bisnor*-5α,17α-*pregn*-13-*ene*-3β,20-*diol*.—17β,20-Epoxy-21-nor-5α,17α-pregnan-3β-ol (100 g) was added with stirring, over 10 min, to formic acid (98—100%; 450 ml), with the temperature kept between 5 and 10°. Stirring was continued for 1 h, the temperature was allowed to rise to 20° over a further 1 h, and water was added. The product was extracted into ether and the extract was washed with water, 2N-sodium hydroxide solution, and water, dried (Na_2SO_4), and evaporated. A solution of the residual gum in methanol (600 ml) was heated at reflux temperature for 40 min with 10N-potassium hydroxide (65 ml); the mixture was then cooled and water was added. The product was dried and crystallised from methylene chloride–light petroleum to give the *diol* (83 g). Recrystallisation from ether gave a sample of m.p. 172—175°, $[\alpha]_D$ −41° (*c* 1·5), $\nu_{max.}$ (CH_2Cl_2) 3610 (free OH) cm^{-1}, δ 0·79 (3H, s, 10-Me), 0·98 (3H, s, 17-Me), 3·36 (2H, s, 20-H_2), and 3·55 (1H, m, 3α-H) (Found: C, 78·7; H, 10·3. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%).

17β-*Methyl*-18,21-*bisnor*-5α,17α-*pregn*-13-*ene*-3β,20-*diyl Dibenzoate* (1c).—17β-Methyl-18,21-bisnor-5α,17α-pregnane-3β,20-diol (82·5 g) was benzoylated with benzoyl chloride (97·5 ml) in pyridine (450 ml) at room temperature. Crystallisation of the product from ether–methanol gave the *dibenzoate* (1c) (115·8 g). Recrystallisation from ether–methanol gave prisms, m.p. 135—137°, $[\alpha]_D$ −24° (*c* 2·3), $\nu_{max.}$ (KCl) 1708 and 1280 (benzoate) cm^{-1}, δ 0·83 (3H, s, 10-Me), 1·12 (3H, s, 17-Me), 4·07 and 4·25 (2H, q, J_{AB} 10 Hz, 20-H_2), 5·0 (1H, m, 3α-H), and 7·5 and 8·1 (10H, m, 3β- and 20-OBz) (Found: C, 79·4; H, 7·7. $C_{34}H_{40}O_4$ requires C, 79·7; H, 7·9%).

17β-*Methyl*-18,21-*bisnor*-17α-*pregna*-7,13-*diene*-3β,20-*diyl Dibenzoate* (3c).—Bromine (5·7 ml, 1·5 mol. equiv.) was added to a stirred solution of the dibenzoate (1c) (38 g) in methylene chloride (38 ml) and ether (190 ml) at −65°. The temperature was allowed to rise to −5°, and a solution

of sodium iodide (25 g) in acetone (100 ml) was added. The mixture was washed with aqueous sodium hydrogen sulphite, potassium hydrogen carbonate solution, and water. The methylene chloride layer was dried (Na_2SO_4) and evaporated to give a gum (37·2 g), which was crystallised from ether–methanol to give the 7,13-*diene* (3c) (30·0 g). Recrystallisation from ether–methanol gave a sample of m.p. 108—112°, $[\alpha]_D$ −78° (*c* 1·7), $\nu_{max.}$ (KCl) 1717 and 1272 (benzoate) cm^{-1}, $\lambda_{max.}$ 231 (ε 38,900), 236 (38,350), 243 (27,800), and 253 nm (16,650), δ 0·82 (3H, s, 10-Me), 1·18 (3H, s, 17-Me), 4·18 (2H, s, 20-H_2), 5·0 (1H, m, 3α-H), 5·45 (1H, m, 7-H), and 7·5 and 8·1 (10H, m, 3β- and 20-OBz) (Found: C, 79·8; H, 7·7. $C_{34}H_{38}O_4$ requires C, 80·0; H, 7·5%).

17β-*Methyl*-18,21-*bisnor*-5α,17α-*pregna*-7,13-*diene*-3β,20-*diol*.—Hydrolysis of the dibenzoate (3c) (1·0 g) with 4N-sodium hydroxide in methanol at 90° for 1 h gave the *diol* (420 mg) as prisms (from ether), m.p. 151—163°, $[\alpha]_D$ −169° (*c* 1·1), $\nu_{max.}$ (CH_2Cl_2) 3610 (free OH) cm^{-1}, $\lambda_{max.}$ 238·5 (ε 17,500), 246 (19,800), and 255 nm (13,200), δ 0·75 (3H, s, 10-Me), 1·00 (3H, s, 17-Me), 3·41 (2H, s, 20-H_2), 3·6 (1H, m, 3α-H), and 5·45 (1H, m, 7-H) (Found: C, 79·6; H, 10·2. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%).

7α,13ξ-*Dibromo*-17β-*methyl*-18,21-*bisnor*-5α,17α-*pregn*-8(14)-*ene*-3β,20-*diyl Dibenzoate* (5c).—A stirred solution of the 7,13-diene (3c) (100 g) in ether (1 l) was cooled to −60° giving a fine suspension. A solution of bromine (13·1 ml, 1·3 mol. equiv.) in methylene chloride (15 ml) was added, causing the solid to dissolve and the temperature to rise to −44°. The solution was cooled to −55° for 15 min and the temperature was then allowed to rise to −12° over 30 min to precipitate the *dibromo-derivative* (5c) as an almost colourless crystalline solid (111·4 g), which decomposed on heating. A sample dried at room temperature and in darkness had $[\alpha]_D$ ±0 (*c* 2·3 in CCl_4), $\nu_{max.}$ (KCl) 1726 and 1275 (benzoate) cm^{-1}, δ 0·83 (3H, s, 10-Me), 1·36 (3H, s, 17-Me), 3·87 (2H, s, 20-H_2), 4·9 (1H, m, 3α-H), 5·0 (1H, m, $W_{\frac{1}{2}}$ 6·7 Hz, 7β-H), and 7·4 and 7·9 (10H, 2m, 3β- and 20β-OBz) (Found: C, 60·4; H, 5·9; Br, 23·8. $C_{34}H_{38}Br_2O_4$ requires C, 60·9; H, 5·7; Br, 23·8%).

17β-*Methyl*-18,21-*bisnor*-5α,17α-*pregna*-8,11,13-*triene*-3β,20-*diyl Dibenzoate* (8c).—A solution of the dibromide (5c) (110 g) in benzene (1 l) was heated under reflux for 4·5 h and cooled. The solution was washed in turn with water, saturated potassium hydrogen carbonate solution, and water, dried (Na_2SO_4) and evaporated. The residue was crystallised from ether–hexane to give the *triene* (8c) (64 g). Recrystallisation from ether–hexane gave a sample of m.p. 136—139°, $[\alpha]_D$ +65° (*c* 2·9), $\nu_{max.}$ (CH_2Cl_2) 1716 and 1287 (benzoate) and 822 (aromatic) cm^{-1}, δ 1·18 (3H, s, 10-Me), 1·42 (3H, s, 17-Me), 2·72 (4H, m, 7- and 15-H_2), 4·25 (2H, s, 20-H_2), 5·0 (1H, m, 3α-H), and 7·1, 7·5, and 8·1 (12H, m, aromatic) (Found: C, 80·3; H, 7·4. $C_{34}H_{38}O_4$ requires C, 80·0; H, 7·5%).

17β-*Methyl*-18,21-*bisnor*-5α,17α-*pregna*-8,11,13-*triene*-3β,20-*diol*.—Hydrolysis of the dibenzoate (8c) (25 g) in methanol (250 ml) with 10N-potassium hydroxide (25 ml) gave the *diol* (11·6 g). Recrystallisation from methanol–di-isopropyl ether gave prisms, m.p. 201—203°, $[\alpha]_D$ +61° (*c* 2·2), $\nu_{max.}$ (KCl) 3470 (OH) and 822 (aromatic) cm^{-1}, $\lambda_{max.}$ 266 (ε 590) and 275 nm (530), δ 1·10 (3H, s, 10-Me), 1·25 (3H, s, 17-Me), 2·7 (4H, m, 7- and 15-H_2), 3·47 (2H, s, 20-H_2), 3·6 (1H, m, 3α-H), and 6·96 and 7·14 (2H, q, J_{AB} 8 Hz, 11- and 12-H) (Found: C, 79·6; H, 9·3. $C_{20}H_{28}O_2$ requires C, 79·95; H, 9·4%).

17α-*Benzyl*-5α-*androstane*-3β,17β-*diol*.—Benzyl chloride (135 ml) in dry ether (500 ml) was added with stirring to a suspension of magnesium turnings (27·5 g) in dry ether (500 ml) at such a rate that constant refluxing was maintained. When the magnesium had reacted completely, a solution of epiandrosterone (50 g) in dry benzene (1 l) was added quickly, precipitating a white solid. The mixture was refluxed with stirring for 3 h, cooled, and poured into an excess of 5N-hydrochloric acid and ice to give 17α-*benzyl*-5α-*androstane*-3β,17β-*diol* as a white crystalline solid (52·8 g), m.p. 218—220°. The organic layer of the filtrate was washed neutral with water, dried (Na_2SO_4), and evaporated to give a semi-crystalline mass, which on trituration with ether gave more product as a white, crystalline solid (14·2 g), m.p. 219—221°. Recrystallisation from acetone gave a sample of m.p. 219—221°, $[\alpha]_D$ −15° (*c* 0·7), $\nu_{max.}$ (KCl) 3560 and 3520 (OH), and 1603, 757, 719, and 708 (aromatic) cm^{-1} (Found: C, 81·7; H, 9·9. $C_{26}H_{38}O_2$ requires C, 81·6; H, 10·0%).

17α-*Benzyl*-17β-*methyl*-18-*nor*-5α-*androst*-13-*en*-3β-*yl Acetate* (1d).—A solution of 17α-benzyl-5α-androstane-3β,17β-diol (57 g) in formic acid (450 ml) was refluxed for 15 min, then cooled, and water was added to give a brown gum, which was extracted into ether. The extract was washed with saturated potassium hydrogen carbonate solution and with water to neutrality, dried (Na_2SO_4), and evaporated to give the 3-formate as a light brown gum. The product was dissolved in methanol (570 ml) and heated under reflux with 10N-potassium hydroxide (30 ml) for 1 h to give the 3β-alcohol as a gum (*ca.* 50 g). Acetylation with acetic anhydride and pyridine at 90° for 1 h gave the *acetate* (1d) as a buff solid (56 g), m.p. 107—112°. Crystallisation from di-isopropyl ether gave plates, m.p. 114—115°, $[\alpha]_D$ −86° (*c* 1·0), $\nu_{max.}$ (KCl) 1730, 1240, and 1029 (3-OAc) and 717 and 702 (aromatic) cm^{-1} (Found: C, 82·5; H, 9·55. $C_{28}H_{38}O_2$ requires C, 82·7; H, 9·4%).

17α-*Benzyl*-17β-*methyl*-18-*nor*-5α-*androst*-13-*en*-3β-*yl Benzoate* (1e).—A sample of crude 3β-alcohol (4·0 g) in pyridine (20 ml) was treated with benzoyl chloride (10 ml) for 1 h at room temperature, then water was added to give the 3-*benzoate* as a white crystalline solid (4·1 g), m.p. 158—162° (from methylene chloride–methanol). A second recrystallisation gave colourless crystals, m.p. 163—164°, $[\alpha]_D$ −73° (*c* 0·83), $\nu_{max.}$ (KCl) 1713 and 1280 (3-OBz) and 713 (aromatic) cm^{-1} (Found: C, 84·4; H, 8·7. $C_{33}H_{40}O_2$ requires C, 84·6; H, 8·6%).

17α-*Benzyl*-17β-*methyl*-18-*nor*-5α-*androsta*-7,13-*dien*-3β-*yl Acetate* (3d).—Bromine (14·6 ml, 2·1 mol. equiv.) was added to a stirred solution of the acetate (1d) (55 g) in ether (2·2 l) at −70°. The temperature of the resultant suspension was allowed to rise to −15°, a solution of sodium iodide (126·5 g) in acetone (1·1 l) was added, and the mixture was refluxed for 30 min, cooled, and poured into sodium hydrogen sulphite solution. The product was extracted into ether and the extract was washed with water, saturated potassium hydrogen carbonate solution, and finally water, dried (Na_2SO_4), and evaporated to a colourless solid. Trituration with ether–methanol gave the *diene* (3d) as crystals (38·2 g), m.p. 95—97°. The mother liquor gave a second crop (1·75 g), m.p. 92—94°. A recrystallised sample (ether–methanol) had m.p. 96—97°, $[\alpha]_D$ −206° (*c* 0·8), $\nu_{max.}$ (KCl) 1725, 1248, and 1025 (OBz) and 758 and 705 (aromatic) cm^{-1}, $\lambda_{max.}$ 240 (ε 21,200), 248 (23,800), and 257 nm (15,800) (Found: C, 83·25; H, 9·1. $C_{28}H_{36}O_2$ requires C, 83·1; H, 9·0%).

17α-*Benzyl*-17β-*methyl*-18-*nor*-5α-*androsta*-7,13-*dien*-3β-*yl Benzoate* (3e).—The 3β-benzoate (1e) (3·0 g) was treated with bromine (0·6 ml, 1·8 mol. equiv.) exactly as for the 3-acetate (1d). The crude solid product was triturated with ether to give the *diene* (3e) as crystals (2·47 g), m.p. 173—175°. A recrystallised sample (methylene chloride–methanol) had m.p. 174—176°, $[\alpha]_D$ −116° (*c* 1·02), $\nu_{max.}$ (KCl) 1712 and 1278 (OBz) and 718 and 711 (aromatic) cm^{-1}, $\lambda_{max.}$ 232·5 (ε 28,000), 238·5 (28,300), 248·5 (24,200), and 257 nm (15,800), δ 0·80 (3H, s, 10-Me), 1·05 (3H, s, 17-Me), 2·60 (2H, s, 17-CH_2), 5·0 (1H, m, 3α-H), 5·33 (1H, m, 7-H) and 7·2, 7·5, and 8·0 (10H, m, aromatic) (Found; C, 84·6; H, 8·2. $C_{33}H_{38}O_2$ requires C, 84·9; H, 8·2%).

17α-*Benzyl*-17β-*methyl*-18-*nor*-5α-*androsta*-8,11,13-*trien*-3β-*yl Benzoate* (8e).—Bromine (24·0 ml, 1·4 mol. equiv.) was added with stirring to a solution of the 7,13-diene 3β-acetate (3d) (133·5 g) in methylene chloride (130 ml) and dry ether (1·33 l) at −65°. The temperature was allowed to rise to −35° and the intermediate bromo-compound (180 g) was filtered off. A solution of the bromo-compound (180 g) in benzene (540 ml) was refluxed for 1 h and evaporated to dryness to give 17α-benzyl-17β-methyl-18-nor-5α-androsta-8,11,13-trien-3β-yl acetate (8d) as a light brown gum (132 g), t_R 2·17 (SE 30; 226°), $\nu_{max.}$ (CH_2Cl_2) 1725 and 1035 (acetate) and 820 (aromatic) cm^{-1}, $\lambda_{max.}$ 266—277 nm (ε 1340), which could not be crystallised. Hydrolysis of the 3-acetate (132 g) with ethanolic sodium hydroxide gave 17α-benzyl-17β-methyl-18-nor-5α-androsta-8,11,13-trien-3β-ol (116 g), which was also non-crystalline.

The crude 3β-ol (4·29 g) was benzoylated with benzoyl chloride (3 ml) and pyridine (10 ml) overnight at room temperature to give the *benzoate* (8e) as a crystalline solid (3·31 g). Three crystallisations from methylene chloride–acetone gave plates, m.p. 154—161°, $[\alpha]_D$ +21° (*c* 1·07), $\nu_{max.}$ (KCl) 1709 and 1273 (OBz) and 820, 768, and 710 (aromatic) cm^{-1}, $\lambda_{max.}$ 267—274 nm (ε 1550), δ 1·17 (3H, s, 10-Me), 1·26 (3H, s, 17-Me), 2·5 (4H, m, 7- and 15-H_2), 2·75 (2H, s, 17-CH_2), 5·0 (1H, m, 3α-H), and 7·1, 7·5, and 8·0 (12H, m, aromatic) (Found: C, 85·3; H, 7·8. $C_{33}H_{36}O_2$ requires C, 85·3; H, 7·8%).

The 3-hydroxy-compound and the 3-acetate (8d) still could not be induced to crystallise after preparation from a pure sample of crystalline 3-benzoate (8e).

Treatment of the Intermediate Dibromo-compound from the 7,13-*Diene* 3β-*Acetate* (3d) *with Silica Gel–Benzene.*—The acetate (3d) (20 g) was brominated exactly as described above to give an almost colourless solid (20·2 g) and a mother liquor which was evaporated to dryness to give a yellow gum (10·8 g). The solid was dissolved in sodium-dried benzene (250 ml) and stirred with silica gel (50 g) for 4 h in a nitrogen atmosphere. The silica gel was filtered off and washed well with benzene. The combined filtrate and washings were evaporated to give a yellow gum (11 g), from which a small crop of colourless needles (340 mg), m.p. 234—239°, was obtained on trituration with ether. The mother liquor material (10·8 g) from the dibromo-intermediate was treated in the same way with silica gel (25 g) in sodium-dried benzene (125 ml) to give a yellow gum (3·1 g), which was triturated with ether to give colourless needles (341 mg), m.p. 232—237°. The mother liquors from the crops of crystalline material were combined and evaporated to give a brown gum, which was dissolved in light petroleum and chromatographed on acid-washed alumina [11] (250 g).

Elution with light petroleum (1 l) gave the triene (8d) as a yellow gum (4·7 g), t_R 2·05 (SE 30; 228°), $\nu_{max.}$ (CH_2Cl_2) 1728 and 1031 (OAc), and 820 (aromatic) cm^{-1}. The i.r. spectrum was identical with that of material (8d) obtained by heating the dibromo-compound in benzene at reflux temperature. Elution with light petroleum–benzene (1 : 1; 500 ml) gave a pale yellow gum (3·6 g), which gave colourless needles (237 mg), m.p. 232—238° (ether). This was combined with the two crops of crystalline material obtained before chromatography and recrystallised twice from methylene chloride–di-isopropyl ether to give 3′,4′-*dihydro*-17β-*methylnaphtho*[1′,2′,3′:12,13,17]-18-*nor*-5α-*androsta*-8,11,13-*trien*-3β-*yl acetate* (9a) as needles (488 mg), m.p. 233—238°, $[\alpha]_D$ +202° (*c* 1·0), $\nu_{max.}$ (CH_2Cl_2) 1729 and 1032 (OAc) cm^{-1}, $\lambda_{max.}$ 272 (ε 18,800), 282 (18,200), and 309 nm (6700), δ 1·00 (3H, s, 10-Me), 1·18 (3H, s, 17-Me), 2·02 (3H, s, 3β-OAc), 2·7 (4H, m, 7- and 15-H_2), 2·87 (2H, s, 17-CH_2), 4·8 (1H, m, 3α-H) and 7·17, 7·19, 7·45, and 7·75 (5H, m, aromatic) (Found: C, 83·8; H, 8·2%; M^+, 400·24048. $C_{28}H_{32}O_2$ requires C, 84·0; H, 8·05%; *M*, 400·24021).

Hydrolysis of the 3-acetate (9a) (200 mg) with methanolic potassium hydroxide gave the hydroxy-compound as a white solid, which was treated with benzoyl chloride–pyridine to give the 3-*benzoate* (9b). Two recrystallisations from methylene chloride–methanol gave white blades (170 mg), m.p. 209—212°, $[\alpha]_D$ +145° (*c* 0·76), $\nu_{max.}$ (KCl) 1725 and 1275 (OBz), and 778 and 720 (aromatic) cm^{-1}, $\lambda_{max.}$ 234 (ε 29,100), 272 (20,600), 281 (19,800), and 305 nm (7100), δ 1·04 (3H, s, 10-Me), 1·27 (3H, s, 17-Me), 2·75 (4H, m, 7- and 15-H_2), 2·95 (2H, s, 17-CH_2), 5·0 (1H, m, 3α-H), and 7·3, 7·6, and 8·1 (10H, m, aromatic) (Found: C, 85·5; H, 7·45. $C_{33}H_{34}O_2$ requires C, 85·7; H, 7·4%).

17α-*Methyl*-5β-*androstane*-3α,17β-*diol*.—Sodium borohydride (10 g) was added in portions to a stirred solution of 17β-hydroxy-17α-methyl-5β-androstan-3-one (39·6 g) in methanol (80 ml) with the temperature kept below 20°; the mixture was stirred for 20 min, diluted with water, and extracted with methylene chloride. The extract was washed with water until neutral, dried (Na_2SO_4), and evaporated. Fractional crystallisation of the residue from ether gave the 3α,17β-*diol* (17·3 g) as needles, m.p. 166—168°, $[\alpha]_D$ −2° (*c* 1·4), δ 0·84 (3H, s, 13-Me), 0·96 (3H, s, 10-Me), 1·24 (3H, s, 17-Me), and 1·76 (2H, s, 3α- and 17β-OH) (Found: C, 78·6; H, 11·4. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2%).

3α-*Benzoyloxy*-17α-*methyl*-5β-*androstan*-17β-*ol*.— Benzoyl chloride (10 ml, 1·5 mol. equiv.) was added dropwise to a stirred solution of 17α-methyl-5β-androstane-3α,17β-diol (17·3 g) in pyridine (83 ml) with cooling so that the reaction temperature did not exceed 5°. Stirring was continued for 1 h at 5°, and water was added to precipitate the product, which was filtered off, washed with water, and dried (21·5 g). Crystallisation from ether–methanol yielded needles of the 3α-*benzoate*, m.p. 199—204°, $[\alpha]_D$ +22·5° (*c* 2·5), δ 0·85 (3H, s, 13-Me), 0·97 (3H, s, 10-Me), 1·23 (3H, s, 17-Me), 4·9 (1H, m, 3β-H), and 7·5 (5H, m, 3α-OBz) (Found: C, 79·0; H, 9·4. $C_{27}H_{38}O_3$ requires C, 79·0; H, 9·3%).

17,17-*Dimethyl*-18-*nor*-5β-*androst*-13-*en*-3α-*yl Benzoate*.—3α-Benzoyloxy-17α-methyl-5β-androstan-17β-ol (21·5 g) was added to hot formic acid (98—100%; 100 ml) and the solution was boiled under reflux for 1 h. The mixture was allowed to cool and the steroidal and formic acid layers

[11] K. R. Farrar, J. C. Hamlet, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 1952, 2657.

were separated. The steroidal layer was diluted with ether and washed with water, saturated potassium hydrogen carbonate solution, and finally water to neutrality. The solution was dried (Na_2SO_4) and concentrated, yielding the product as a pale yellow gum (19·6 g), t_R 2·88 (OV 17; 245°) and 1·67 (SE 30; 245°).

Hydrolysis of the product (1·0 g) in ethanolic potassium hydroxide (10% w/v) yielded 17,17-*dimethyl*-18-*nor*-5β-*androst*-13-*en*-3α-*ol* in quantitative yield. Crystallisation from aqueous acetone gave needles, m.p. 103—105°, $[\alpha]_D$ −10·4° (*c* 0·8), δ 0·93 (3H, s, 10-Me), 1·0 (6H, s, 17,17-Me_2), 1·72 (1H, s, 3α-H), and 3·7 (1H, m, 3β-H) (Found: C, 83·2; H, 11·5. $C_{20}H_{36}O$ requires C, 83·3; H, 11·2%).

17,17-*Dimethyl*-18-*nor*-5β-*androsta*-7,13-*dien*-3α-*yl Benzoate*.—A stirred solution of 17,17-dimethyl-18-nor-5β-androst-13-en-3α-yl benzoate (18·6 g) in methylene chloride (20 ml) and ether (100 ml) was cooled to −55° and bromine (3·8 ml, 1·4 mol. equiv.) in methylene chloride (3·8 ml) was added over 15 min. The temperature was allowed to rise to −10° over 30 min, sodium iodide (16 g) in acetone (100 ml) was added, and the mixture was boiled under reflux for 20 min. It was then cooled and the iodine produced was discharged by addition of aqueous sodium hydrogen sulphite. The organic layer was washed with water, N-sodium hydroxide solution, and water until neutral, dried (Na_2SO_4), and concentrated to a yellow gum which on crystallisation from ether–ethanol yielded the *diene* (14·1 g) as prisms, m.p. 99—102°, $[\alpha]_D$ +40·4° (*c* 1·7), δ 0·88 (3H, s, 10-Me), 1·05 (6H, s, 17,17-Me_2), 5·05 (1H, m, 3β-H), 5·35 (1H, m, 7-H), and 7·5 (5H, m, 3α-OBz) (Found: C, 82·8; H, 8·6. $C_{27}H_{34}O_2$ requires C, 83·0; H, 8·8%).

17,17-*Dimethyl*-18-*nor*-5β-*androsta*-8,11,13-*trien*-3α-*yl Benzoate* (10a).—A stirred solution of the foregoing diene (13 g) in methylene chloride (13 ml) and ether (130 ml) was cooled to −65° and bromine (2·2 ml, 1·3 mol. equiv.) was added over 3 min with the reaction temperature kept below −50°. The solution was then cooled to −60° and maintained at this temperature for 10 min before allowing the temperature to rise to −15°. The excess of bromine was discharged by addition of aqueous sodium hydrogen sulphite. The organic layer was washed with water, dried (Na_2SO_4), and concentrated. Silica gel (13 g) was added to a solution of the residue in benzene (39 ml) and the mixture was stirred for 4 h. The silica gel was filtered off and washed with benzene and the filtrate was concentrated and filtered down a column (9 × 0·75 in) of alumina. Elution with benzene (500 ml) gave a fraction from which the triene (10a) was obtained as a gum (10 g), which, although pure, resisted crystallisation; t_R 3·80 (OV 17; 245°) and 1·52 (SE 30; 245°).

17,17-*Dimethyl*-18-*nor*-5β-*androsta*-8,11,13-*trien*-3α-*ol* (10b).—A solution of the benzoate (10a) (10 g) in ethanolic potassium hydroxide (5% w/v; 100 ml) was boiled under reflux for 75 min, cooled, diluted with water, and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to dryness. A solution of the residue (7·0 g) in light petroleum was filtered down a column (9 × 1·25 in) of alumina. Elution with light petroleum (750 ml) and light petroleum–benzene (9 : 1; 375 ml) yielded a fraction (0·56 g) which was discarded. Further elution with benzene (500 ml) and benzene–ether (9 : 1; 250 ml) yielded fractions which on evaporation and crystallisation from ether–light petroleum gave the *trienol* (10b) (4 g) as prisms, m.p. 152—154°, $[\alpha]_D$ +56° (*c* 2·0), $\lambda_{max.}$ 267 (ε 830), 271 (725), and 271 nm (780), δ 1·19 (3H, s, 10-Me), 1·25 (6H, s, 17,17-Me_2), 1·49 (1H, s, 3α-OH), 3·65 (1H, m, 3β-H), and 6·9 and 7·1 (2H, q, J_{AB} 8·5 Hz, 11- and 12-H) (Found: C, 84·5; H, 9·9. $C_{20}H_{28}O$ requires C, 84·5; H, 9·9%).

We thank Drs. L. A. van Dijck and W. McMeekin for analytical and spectral services and Dr. P. Bladon (Strathclyde University) for the mass spectrum.

[3/2156 *Received*, 22*nd October*, 1973]