18-Norandrosta-8,11,13-trienes. Part I. 11-Hydroxy-derivatives

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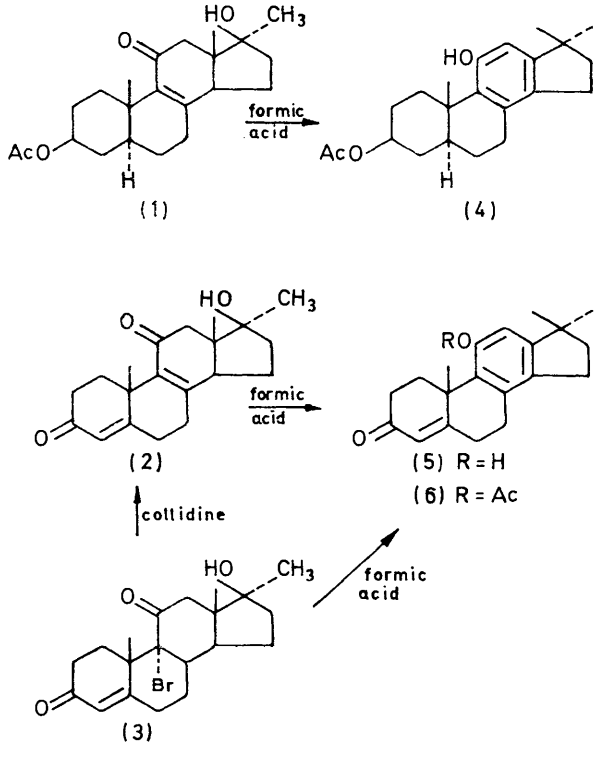
Formic acid rearrangement of 3β-acetoxy-17β-hydroxy-17α-methyl-5α-androst-8-en-11-one (1) and of 9α-bromo-17β-hydroxy-17α-methylandrost-4-ene-3,11-dione (3) gave 3β-acetoxy-11-hydroxy-17,17-dimethyl-18-nor-5α-androsta-8,11,13-triene (4) and 11-hydroxy-17,17-dimethyl-18-norandrosta-4,8,11,13-tetraen-3-one (5) respectively. A similar attempt to form the corresponding 12-phenol from 3β-acetoxy-17β-hydroxy-17α-methyl-5α-androst-9(11)-en-12-one (13) resulted in the formation of 3β-acetoxy-17-methyl-5α-androsta-9(11),16-dien-12-one (14).

As a part of a programme to evaluate the biological activities of ring C aromatic steroids [1-21] we have investigated the possible use of the Wagner–Meerwein shift of the 13β-methyl group to the 17β-position by dehydration of a 17β-alcohol.[22] This paper deals with this migration in a steroid already containing two potential double bonds in ring C, in the form of either an α,β-unsaturated ketone or an α-bromo-ketone, to give 11-hydroxy ring C aromatic steroids. For example, treatment of compounds (1)—(3) with boiling formic acid (*cf.* ref. 23) leads directly to 11-hydroxy ring C aromatic steroids (4) and (5) respectively. The structures of the compounds were confirmed by their n.m.r. spectra which showed the presence of one aromatic proton (δ 6·3) and by the presence of aromatic absorption in the i.r. and u.v. spectra [$\nu_{max.}$ 3020, 1610, and 1590 cm^{-1}, $\lambda_{max.}$ 286 nm (ε *ca.* 4000)].

The intermediate 9α-bromo-11-ketones were obtained by two routes. Firstly, direct bromination of 3β-acetoxy-5α-androstane-11,17-dione with *N*-bromosuccinimide using a modification of the methods of Miescher,[24,25] Djerassi,[26] and Eardley [27] introduced a bromine atom which was shown to have the 9α-configuration from the n.m.r. spectrum, δ 2·35 (12β-H) and 3·39 (12α-H).[28]

Dehydrobromination of 3β-acetoxy-9α-bromo-5α-androstane-11,17-dione with boiling collidine [27,29] gave 3β-acetoxy-5α-androst-8-ene-11,17-dione, $\lambda_{max.}$ 253 nm (ε 9000) (14α-Δ⁸-11-ketone). Treatment of this unsaturated 11,17-diketone with methylmagnesium bromide gave the 17α-methyl-17β-hydroxy derivative (1) in 50% yield.



Because of the unsatisfactory overall yields *via* the direct bromination route an alternative synthesis *via*

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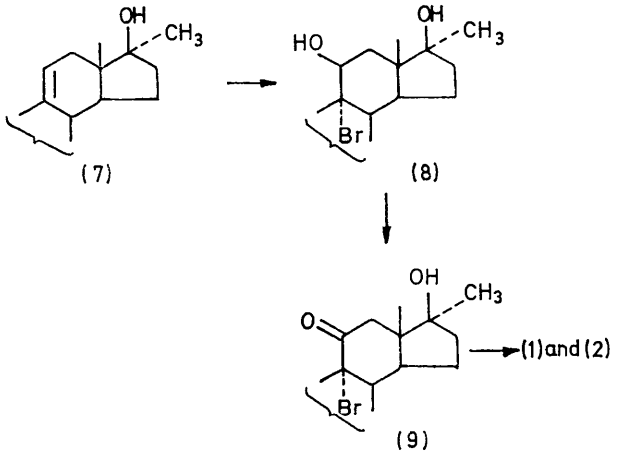
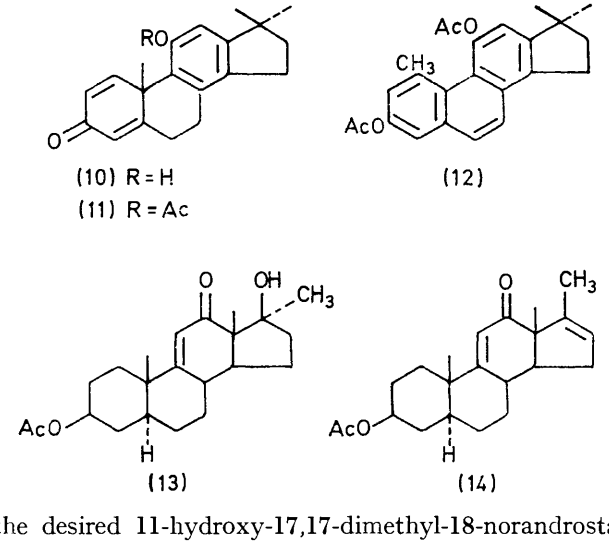
$\Delta^{9(11)}$ unsaturated steroids was investigated. Addition of hypobromous acid [30,31] to the $\Delta^{9(11)}$ unsaturated steroids (7) gave the 9α-bromo-11β-hydroxy-compounds



(8) which on oxidation with chromic acid gave the 9α-bromo-11-ketone (9) [32] in good yield.

Treatment of 3β-acetoxy-17β-hydroxy-17α-methyl 5α-androst-8-en-11-one (1) with boiling formic acid led directly to the ring c aromatic phenol (4). Similarly 17β-hydroxy-17α-methylandrosta-4,8-diene-3,11-dione (2) led to the phenol (5). Dehydrobromination of the 9α-bromide (3) gave a poor yield of the diene-dione (2), but the phenol (5) could be prepared in excellent yield by direct treatment of the 9α-bromide (3) with boiling formic acid.

Treatment of the phenolic acetate (6) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone gave a mixture of



the desired 11-hydroxy-17,17-dimethyl-18-norandrosta-1,4,8,11,13-pentaen-3-one (10), its 11-acetate (11), and 3,11-diacetoxy-1,17,17-trimethyl-15,16-dihydro-17*H*-cyclopenta[*a*]phenanthrene (12). The compounds were separated by chromatography and the identity of the phenanthrene (12) was confirmed by its n.m.r. spectrum, which showed signals for five aromatic protons, three singlets at δ 7·1, 7·2, and 7·6 (corresponding to 2-, 4-, and 12-H) and two doublets at 7·35 and 7·4 (corresponding to 6- and 7-H), two phenolic acetates (δ 2·2 and 2·3), two methyl groups (δ 1·3), and a methyl group on a phenyl ring (δ 2·7).

In contrast to the aromatisation of the Δ^{8}-11-ketone (1) with formic acid, similar treatment of the isomeric 3β-acetoxy-17β-hydroxy-17α-methyl-5α-androst-9(11)-en-12-one (13) resulted simply in dehydration to 3β-acetoxy-17-methyl-5α-androsta-9(11),16-dien-12-one (14). This is not surprising since aromatisation of ring c in this case would involve an unstable tertiary carbonium ion adjacent to the C-12 carbonyl group.

The $\Delta^{9(11)}$ unsaturated ketone (13) was conveniently prepared from 3β,12β-diacetoxy-5α-androstan-17-one. Treatment of this ketone with methylmagnesium bromide, mild acetylation of the crude product, and fractional crystallisation of the resultant mixture of acetates yielded 3β-acetoxy-17α-methyl-5α-androstane-12β,17β-diol which on oxidation with Kiliani's reagent [33] gave the 12-ketone. The $\Delta^{9(11)}$ double bond was introduced by the method of Chia-Chiang Shen and his co-workers [34] using selenium dioxide and pyridine in chlorobenzene.

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 are for solutions in ethanol. Optical rotations were measured for chloroform solutions at room temperature unless otherwise stated. G.l.c. was performed with a Pye-Argon chromatograph. N.m.r. spectra in $CDCl_3$ were determined with a Varian A60 spectrometer. U.v. irradiations were carried out using a Hanovia U.V.S. 500 medium pressure lamp.

3β-*Acetoxy*-9α-*bromoandrostane*-11,17-*dione*.— *N*-Bromosuccinimide (40 g) was suspended in a solution of 3β-acetoxy-5α-androstane-11,17-dione (38 g) in carbon tetrachloride (800 ml) and the mixture was stirred and irradiated with u.v. light for 4 h at 20°. The solution was washed in turn with excess of 10% sodium sulphite solution and water and dried (Na_2SO_4). Evaporation of the solvent and crystallisation from ether gave 3β-*acetoxy*-9α-*bromo*-5α-*androstane*-11,17-*dione* (32 g). Recrystallisation from ether gave a pure sample, m.p. 176—178°, $\nu_{max.}$ (KCl) 1745 (17-ketone), 1725 and 1245 (3-acetate), and 1715 (11-ketone) cm^{-1}, δ 0·84 (3H, s, 13-Me), 1·21 (3H, s, 10-Me), 2·0 (3H, s, 3β-OAc), 2·35 (1H, d, *J* 15 Hz, 12β-H), 3·39 (1H, d, *J* 15 Hz, 12α-H), and 4·68 (1H, m, 3α-H) (Found: C, 59·6; H, 7·0 Br, 19·2. $C_{21}H_{29}BrO_4$ requires C, 59·4; H, 6·8; Br, 18·9%).

3β-*Acetoxy*-5α-*androst*-8-*ene*-11,17-*dione*.—A solution of 3β-acetoxy-9α-bromo-5α-androstane-11,17-dione (57 g) in collidine (250 ml) was boiled under reflux for 15 min,

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cooled, poured into 2N-hydrochloric acid (2·5 l), and the precipitated product was extracted with ether. The extracts were washed in turn with 2N-hydrochloric acid, sodium hydrogen carbonate solution, and water and dried. The solution was concentrated, filtered through a column (10 × 1·5 in) of alumina, and eluted with ether. Concentration of the eluate and trituration with ether gave 3β-*acetoxy*-5α-*androst*-8-*ene*-11,17-*dione* (30 g). An analytical sample was prepared by chromatography on a column of alumina (Camag; activity 2; 6 × 1 in) and the combined fractions containing the pure material were crystallised from methanol to give plates, m.p. 158—160°, $\nu_{max.}$ (KCl) 1745 (17-ketone), 1730 and 1235 (3-acetate), 1660 (α,β-unsaturated 11-ketone), and 1589 (Δ^8 double bond) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 1745, 1725, 1663, and 1590 cm^{-1}, $\lambda_{max.}$ 253 nm (ε 8800), δ 0·88 (3H, s, 13-Me), 1·13 (3H, s, 10-Me), 2·0 (3H, s, 3β-OAc), and 4·69 (1H, m, 3α-H) (Found: C, 73·0; H, 8·3. $C_{21}H_{28}O_4$ requires C, 73·2; H, 8·2%).

17α-*Methyl*-5α-*androst*-9(11)-*ene*-3β,17β-*diol*.— Methylmagnesium bromide solution was prepared from dry methyl bromide, magnesium (35 g), and dry ether (500 ml) and the ether was distilled off while replacing with tetrahydrofuran. A solution of 3β-acetoxy-5α-androst-9(11)-en-17-one [35] (136 g) in tetrahydrofuran (750 ml) was added slowly to the stirred Grignard reagent and the resulting solution was boiled under reflux for 2 h. Ether (500 ml) was added and the suspension poured into 2N-hydrochloric acid (5 l) to give 17α-*methyl*-5α-*androst*-9(11)-*ene*-3β,17β-*diol* (77 g) as a crystalline precipitate at the ether–water interface. Concentration of the ether phase gave a second crop (30 g), and extraction of the aqueous layer with methylene chloride gave a further crop (6·5 g). Recrystallisation from acetone furnished an analytical sample, m.p. 205—206°, $[\alpha]_D$ +99·5° (*c* 1·0), $\nu_{max.}$ (KCl) 3600 (free hydroxy), 3310 (bonded hydroxy), and 3030 (double bond) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3615 and 3470 cm^{-1}, δ 0·8 (3H, s, 13-Me), 0·95 (3H, s, 17-Me), 1·20 (3H, s, 10-Me), 3·13 (1H, m, 3α-H), and 5·4 (1H, d, *J* 6 Hz, 11-H) (Found: C, 78·7; H, 10·8. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%).

3β-*Acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-9(11)-*ene*. —17α-Methyl-5α-androst-9(11)-ene-3β,17β-diol (15 g) was acetylated in acetic anhydride (50 ml) and pyridine (100 ml) at room temperature overnight. The solution was poured into water (1 l) and the isolated solid dried and triturated with ether to give 3β-*acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-9(11)-*ene* (14·2 g). Recrystallisation from ether–hexane gave an analytical sample, m.p. 118—119°, $[\alpha]_D$ −24° (*c* 1·0), $\nu_{max.}$ (KCl) 3520 (free hydroxy), 3440 (bonded hydroxy), 3040 (double bond), 1720, 1740, and 1240 (acetate) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3620 (hydroxy) and 1730 (acetate) cm^{-1}, δ 0·8 (3H, s, 13-Me), 1·0 (3H, s, 17-Me), 1·25 (3H, s, 10-Me), 2·0 (3H, s, 3β-OAc), 4·67 (1H, m, 3α-H), and 5·6 (1H, d, *J* 7 Hz, 11-H) (Found: C, 76·6; H, 10·0. $C_{22}H_{34}O_3$ requires C, 76·6; H, 9·9%).

3β-*Acetoxy*-9α-*bromo*-17β-*hydroxy*-17α-*methyl*-5α-*androstan*-11-*one*.—*N*-Bromoacetamide (36 g) was added in portions over 20 min to a solution of 3β-acetoxy-17β-hydroxy-17α-methyl-5α-androst-9(11)-ene (74 g) in ether (750 ml) and dilute perchloric acid (30 ml; 72% perchloric acid in 150 ml water) at −5° and the two-phase solution was stirred for 90 min before washing with aqueous sodium sulphite solution, aqueous sodium hydrogen carbonate solution, and water. The ether extract was dried (Na_2SO_4) and evaporated to dryness at room temperature under vacuum, the residue was dissolved in acetone (750 ml), cooled to −5°, and Kiliani's [33] reagent (150 ml) was added dropwise over 30 min, keeping the temperature below 10°. After standing a further 30 min at 0°, the solution was diluted with water (750 ml) and 3β-*acetoxy*-9α-*bromo*-17β-*hydroxy*-17α-*methyl*-5α-*androstan*-11-*one* (63 g) was filtered off, washed with water, and air dried. Recrystallisation from ether–methylene chloride gave an analytical sample, decomposing on melting, $[\alpha]_D$ +28° (*c* 0·5), $\nu_{max.}$ (KCl) 3580 (hydroxy), 1740 (acetate), 1700 (11-ketone) and 1250 (acetate) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3610, 1730, and 1710 cm^{-1}, δ 0·8 (3H, s, 13-Me), 1·2 (3H, s, 17-Me), 1·3 (3H, s, 10-Me), 2·0 (3H, s, 3β-OAc), 3·5 (1H, d, *J* 16 Hz, 12α-H), and 4·7 (1H, m, 3α-H) (Found: C, 60·1; H, 7·2; Br, 18·1. $C_{22}H_{34}BrO_4$ requires C, 59·8; H, 7·6; Br, 18·1%).

3β-*Acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-8-*en*-11-*one*.—(*a*) A solution of 3β-acetoxy-5α-androst-8-ene-11,17-dione (25 g) in diethyl ether (200 ml) was added dropwise under nitrogen over 30 min to a solution of methylmagnesium bromide (prepared from 6 g magnesium) in ether (500 ml) and stirring continued under nitrogen for a further 30 min. The solution was poured into 0·2N-hydrochloric acid (1650 ml), extracted with ether, and the combined extracts were washed in turn with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated to dryness. The residue was dissolved in acetic anhydride (25 ml) and pyridine (50 ml), set aside for 16 h, poured into water (500 ml), and extracted with ether. The combined extracts were washed in turn with 2N-hydrochloric acid, sodium hydrogen carbonate solution, and water and dried. The solution was concentrated, the residue dissolved in the minimum amount of benzene, and chromatographed on a column (12 × 1·5 in) of acid-washed alumina. Elution with benzene, containing 10% ethyl acetate gave a brown gum (2·5 g) which could not be crystallised, and was discarded. Elution with benzene containing 30% ethyl acetate gave 3β-*acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-8-*en*-11-*one* (8·1 g). Recrystallisation from ether gave a pure sample, m.p. 180—184°, $[\alpha]_D$ +113° (*c* 1·0), $\nu_{max.}$ (KCl) 3530 (hydroxy), 1713 and 1252 (acetate), and 1663 (αβ unsaturated carbonyl) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3615, 1730, and 1660 cm^{-1}, $\lambda_{max.}$ 255 nm (ε 5000), δ 0·9 (3H, s, 13-Me), 1·1 (3H, s, 17-Me), 1·3 (3H, s, 10-Me), 1·8 (1H, s, 17β-OH), 2·0 (3H, s, 3β-OAc), 2·34 (2H, s, 12α- and 12β-H), 2·88 (1H, d, *J* 15 Hz, 1β-H), and 4·7 (1H, m, 3α-H) (Found: C, 73·1; H, 9·1. $C_{22}H_{32}O_4$ requires C, 73·3; H, 9·0%).

(*b*) 3β-Acetoxy-9α-bromo-17α-hydroxy-17α-methyl-5α-androstan-11-one (1·2 g) was added to boiling collidine (10 ml) and the solution boiled under reflux for 15 min, cooled, poured into 2N-hydrochloric acid (100 ml), and the precipitated product was extracted with ether (2 × 100 ml); the ether extract was washed with aqueous sodium hydrogen carbonate solution and water and dried (Na_2SO_4). Removal of the solvent and trituration with ether gave 3β-acetoxy-17β-hydroxy-17α-methyl-5α-androst-8-en-11-one (0·8 g), identical with the compound described under (*a*).

3β-*Acetoxy*-17,17-*dimethyl*-18-*norandrosta*-8,11,13-*trien*-11-*ol*.— 3β-Acetoxy-17β-hydroxy-17α-methyl-5α-androst-8-en-11-one (400 mg) was added to hot formic acid (2 ml) and the solution boiled under reflux for 15 min, cooled, water (2 ml) was added, and the precipitated solid (370 mg) was filtered off. Recrystallisation from ether gave 3β-*acetoxy*-17,17-*dimethyl*-18-*nor*-5α-*androsta*-8,11,13-*trien*-11-*ol*, m.p.

[35] C. W. Shoppee, *J. Chem. Soc.*, 1946, 1134.

217—220°, $\nu_{max.}$ (KCl) 3400 (hydroxy), 3020, 1610, 1595 and 860 (aromatic H), and 1720 and 1240 (acetate) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3560, 1730, 1610, and 1590 cm^{-1}, $\lambda_{max.}$ 286 nm (ε 3350), δ 1·18 (6H, s, 17,17-Me_2), 1·25 (3H, s, 10-Me), 2·05 (3H, s, 3β-OAc), 2·63 (4H, m, 7- and 15-H_2), 4·75 (1H, m, 3α-H), 5·25 (1H, s, 11-OH), and 6·3 (1H, s, 12-H) (Found: C, 77·6; H, 8·9. $C_{22}H_{30}O_3$ requires C, 77·2; H, 8·8%).

9α-*Bromo*-11β,17β-*dihydroxy*-17α-*methylandrost*-4-*en*-3-*one*.—A solution of perchloric acid (66 ml) in water (264 ml) was added to a stirred solution of 17β-hydroxy-17α-methylandrosta-4,9(11)-dien-3-one (200 g) in tetrahydrofuran (1 l), followed by *N*-bromoacetamide (100 g) in portions over 15 min and stirring was continued for a further 45 min at 20—25°. Evaporation under reduced pressure to half volume followed by addition of water (5 l) precipitated 9α-bromo-11β,17β-dihydroxy-17α-methylandrost-4-en-3-one as a white solid (265 g). Crystallisation from methylene dichloride–methanol furnished an analytical sample, m.p. 147—150° (lit.,[30] 153—155°), $[\alpha]_D$ +101° (*c* 0·5), $\lambda_{max.}$ 244 nm (ε 15,200) (Found: C, 58·6; H, 7·4; Br, 18·8. Calc. for $C_{20}H_{29}BrO_3,CH_3OH$: C, 58·7; H, 7·7; Br, 18·6%).

9α-*Bromo*-17β-*hydroxy*-17α-*methylandrost*-4-*ene*-3,11-*dione*.—Kiliani's [33] reagent (590 ml) was added over 20 min to a stirred suspension of 9α-bromo-11β,17β-dihydroxy-17α-methylandrost-4-ene-3-one (264 g) in acetone (800 ml) at 20—25° and after 45 min water (4 l) added to precipitate a yellow crystalline solid which was filtered off, washed with water, and dissolved in methylene dichloride (750 ml). The solution was washed with water till neutral, dried (Na_2SO_4), concentrated under reduced pressure, and triturated with ether to give 9α-*bromo*-17β-*hydroxy*-17α-*methylandrost*-4-*ene*-3,11-*dione* (142 g). Crystallisation from methylene dichloride–ether gave an analytical sample, m.p. 162—163° (decomp.), $[\alpha]_D$ +24° (*c* 0·6), $\nu_{max.}$ (KCl) 3400 (17-hydroxy), 1750 (11-ketone), 1670 (Δ^4-3-ketone), and 1625 (Δ^4) cm^{-1}, $\lambda_{max.}$ 237 nm (ε 16,150), δ 0·9 (3H, s, 13-Me), 1·3 (3H, s, 17-Me), 1·6 (3H, s, 10-Me), 1·8 (1H, s, 17-OH), and 5·8 (1H, s, 4-H) (Found: C, 60·4; H, 6·9; Br, 20·4. $C_{20}H_{27}BrO_3$ requires C, 60·8; H, 6·9; Br, 20·2%).

11-*Hydroxy*-17,17-*dimethyl*-18-*norandrosta*-4,8,11,13-*tetraen*-3-*one*.—(*a*) A solution of 9α-bromo-17β-hydroxy-17α-methylandrost-4-ene-3,11-dione (141 g) in formic acid (250 ml) was boiled under reflux for 5 min, cooled, water (1 l) was added, and the precipitated product was filtered off, washed with water, dried, and slaked with ether to give 11-*hydroxy*-17,17-*dimethyl*-18-*norandrosta*-4,8,11,13-*tetraen*-3-*one* (100 g). Crystallisation from methylene dichloride–methanol gave an analytical sample, m.p. 269—273° (decomp.), $[\alpha]_D$ +309° (*c* 0·8), $\nu_{max.}$ (KCl) 3300—3260 (hydroxy), 3020, 1590, and 855 (aromatic), 1650 (Δ^4-3-ketone), and 1620 and 769 (Δ^4) cm^{-1}, $\lambda_{max.}$ 236 (ε 22,040) and 290 nm (4375), δ 1·2 (6H, s, 17,17-Me_2), 1·9 (3H, s, 10-Me), 6·0 (1H, s, 4-H), and 6·9 (1H, s, 12-H) (Found: C, 80·6; H, 8·1. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%).

(*b*) 9α-Bromo-17β-hydroxy-17α-methylandrost-4-ene-3,11-dione (700 mg) and added to boiling collidine (10 ml) and the solution was boiled under reflux for 25 min, cooled, and poured into 5N-hydrochloric acid (10 ml) and ice. The product was extracted with ether and the ether extract was washed with aqueous sodium hydrogen carbonate solution, water, and dried (Na_2SO_4). Removal of the solvent and trituration with ether gave 17β-*hydroxy*-17α-*methylandrosta*-4,8-*diene*-3,11-*dione* as prisms (600 mg), $\lambda_{max.}$ 238 nm (ε 15,840). This compound (500 mg) was boiled in formic acid (2 ml) under reflux for 5 min, cooled, water (10 ml) was added, and the precipitate was filtered off, washed, dried, and slaked with ether to give 11-hydroxy-17,17-dimethyl-18-norandrosta-4,8,11,13-tetraen-3-one (180 mg), m.p. 268—272° (decomp.), shown to be identical with the material prepared under (*a*) by i.r. and t.l.c.

11-*Acetoxy*-17,17-*dimethyl*-18-*norandrosta*-4,8,11,13-*tetraen*-3-*one*.— 11-Hydroxy-17,17-dimethyl-18-norandrosta-4,8,11,13-tetraen-3-one (85 g) was acetylated in pyridine (180 ml) and acetic anhydride (180 ml) at 95° for 25 min, the solution was cooled, and water (1·5 l) was added. The precipitated product was dried, dissolved in ether, and filtered down a column (6 × 1·5 in) of acid-washed alumina. Concentration of the ether eluate yielded 11-*acetoxy*-17,17-*dimethyl*-18-*norandrosta*-4,8,11,13-*tetraen*-3-*one* as a crystalline solid (85 g). Further crystallisation from ether yielded an analytical sample, m.p. 148—150°, $[\alpha]_D$ +287° (*c* 1·5), $\nu_{max.}$ (KCl) 1750 and 1225—1210 (11-acetate), 1675 (Δ^4-3-ketone), 1630 (Δ^4), 1607, and 913 and 867 (aromatic) cm^{-1}, $\lambda_{max.}$ 233 (ε 22,470), 272 (2305), and 281 nm (1824), δ 1·2 (6H, s, 17,17-Me_2), 1·6 (3H, s, 10-Me), 2·3 (3H, s, 11-OAc), 5·8 (1H, s, 4-H), and 6·7 (1H, s, 12-H) (Found: C, 77·7; H, 7·5. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%).

11-*Hydroxy*-17,17-*dimethyl*-18-*norandrosta*-1,4,8,11,13-*pentaen*-3-*one and its* 11-*Acetate*.—A solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (10·0 g), maleic acid (1·0 g), and 11-acetoxy-17,17-dimethyl-18-norandrosta-4,8,11,13-tetraen-3-one (10·0 g) in benzene (50 ml) was boiled under reflux for 16 h, cooled, and filtered. The residue obtained after a removal of solvent was dissolved in benzene and filtered through a column (5 × 1·5 in) of acid-washed alumina. Elution with light petroleum–benzene (2 : 1) (250 ml) yielded a fraction (4·3 g) which crystallised from ether to give 11-*acetoxy*-17,17-*dimethyl*-18-*norandrosta*-1,4,8,11,13-*pentaen*-3-*one* in small prisms, m.p. 170—173°, $[\alpha]_D$ +336°, $\nu_{max.}$ (KCl) 1753 and 1220 (phenolic acetate), 1675 (conjugated ketone), 1633 and 1608 (double bonds), and 911, 890, 870, and 816 (double bonds and aromatic) cm^{-1}, $\lambda_{max.}$ 207 (ε 34,600) and 226—236 nm (23,000), δ 1·21 and 1·23 (6H, 2s, 17,17-Me_2), 1·63 (3H, s, 10-Me), 2·41 (3H, s, 11-OAc), 6·18 (1H, s, 4-H), 6·23 (1H, q, *J* 9·3 and 2·14 Hz, 2-H), 6·75 (1H, s, 12-H), and 7·84 (1H, d, *J* 11·5 Hz, 1-H) (Found: C, 78·6; H, 7·3. $C_{22}H_{24}O_3$ requires C, 78·5; H, 7·2%).

Further elution with ether yielded a fraction (2·5 g) which crystallised from ether to give 11-*hydroxy*-17,17-*dimethyl*-18-*norandrosta*-1,4,8,11,13-*pentaen*-3-*one* as yellow needles, m.p. 207—216°, $\nu_{max.}$ (KCl) 1658 and 1648 (unsaturated ketone), 1620 and 1610 (double bonds), and 1595, 889, 878, 858, and 810 (double bonds and aromatic) cm^{-1}, $\lambda_{max.}$ 229—235 (ε 24,400), 282 (5900), and 291 nm (4900), δ 1·2 (6H, s, 17,17-Me_2), 1·8 (3H, s, 10-Me), 3·64 (1H, s, 11-OH), 6·25 (1H, d, *J* 3 Hz, 4-H), 6·26 (1H, q, *J* 12 and 2·9 Hz, 2-H), 6·56 (1H, s, 12-H), and 8·6 (1H, d, *J* 12 Hz, 1-H) (Found: C, 81·3; H, 7·6. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%).

3,11-*Diacetoxy*-1,17,17-*trimethyl*-15,16-*dihydro*-17H-*cyclopenta*[a]*phenanthrene* was isolated from the ether–ethyl acetate eluates and crystallised from ether as yellow blades, m.p. 153—158°, $[\alpha]_D$ +1°, $\nu_{max.}$ (KCl) 1760 and 1200 (phenolic acetates) and 1605 and 910 (aromatic) cm^{-1}, $\lambda_{max.}$ 262 (ε 54,000), 293 (11,000), 307 (11,900), and 318 nm (12,800), δ 1·2 (6H, s, 17,17-Me_2), 2·18 and 2·32 (6H, 2s, 3- and 11-OAc), 2·7 (3H, s, 1-Me), 3·2 (1H, d, *J* 7 Hz) and 3·33 (1H, d, *J* 7·5 Hz) (15-H_2), 7·4 (1H, d, *J* 12·5 Hz) and 7·35 (1H, d, *J* 12·5 Hz) (6- and 7-H), and 7·1, 7·2, and 7·6 (3H, 3s,

2-, 4-, and 12-H) (Found: C, 75·6; H, 6·9. $C_{23}H_{24}O_4$ requires C, 75·8; H, 6·6%).

17α-*Methyl*-5α-*androstane*-3β,12β,17β-*triol*.—A solution of 3β,12β-diacetoxy-5α-androstan-17-one (30·0 g) in dry diethyl ether (500 ml) was added to a solution of methylmagnesium bromide [prepared from magnesium (10·0 g) in dry diethyl ether (500 ml)] while stirring under nitrogen. When addition was complete the solution was heated under reflux for 2 h, cooled, and poured into dilute hydrochloric acid (550 ml; 0·5N) to precipitate the *triol*, which was crystallised from methanol–diethyl ether. A further crystallisation from methanol–ether furnished the pure material (25·2 g), m.p. 225—227°, $[\alpha]_D$ −10° (*c* 0·4, EtOH), R_t 0·812 (OV 1; 240°), $\nu_{max.}$ (KCl) 3380 (OH) cm^{-1}, δ 0·86 (6H, s, 13- and 17-Me), 1·34 (3H, s, 10-Me), 3·6 (1H, m 3α-H), and 3·68 (1H, q, *J* 11 and 5·5 Hz, 12α-H) (Found: C, 74·2; H, 10·7. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·6%).

Acetylation of 17α-*Methyl*-5α-*androstan*-3β,12β,17β-*triol*.—Acetic anhydride (22 ml) was added to a solution of 17α-methyl-5α-androstane-3β,12β,17β-triol (22·0 g) in pyridine (220 ml) and the solution was allowed to stand at room temperature for 48 h with occasional stirring, the course of the reaction being followed on t.l.c. The mixture was poured into water (2 l), allowed to stand for 2 h, and the aqueous layer was decanted off. The residue was dissolved in benzene (100 ml) and the solution was washed in turn with 2N-hydrochloric acid, sodium hydrogen carbonate solution, and water and dried (Na_2SO_4). The solution was chromatographed on a column (1·5 × 10 in) of silica (Merck; 0·2—0·5 mm), eluting with benzene, ether, and finally with ethyl acetate. The fractions were examined by t.l.c. and similar fractions were combined. The initial fractions from the column were crystallised from hexane–ether to give 3β-*acetoxy*-17α-*methyl*-5α-*androstane*-12β,17β-*diol* (13·0 g), m.p. 184—186°, $[\alpha]_D$ −19° (*c* 0·6), R_t 1·12 (SE 30; 225°), $\nu_{max.}$ (KCl) 3430 (OH), and 1732 and 1248 (acetate) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3610 (OH) cm^{-1}, δ 0·85 (3H, s, 13-Me), 0·95 (3H, s, 17-Me), 1·34 (3H, s, 10-Me), 2·02 (3H, s, 3β-OAc), 2·14 (1H, s, OH), 3·74 (1H, q, *J* 11 and 5 Hz, 12α-H), and 4·77 (1H, m, 3α-H) (Found: C, 73·0; H, 10·4. $C_{22}H_{36}O_4$ requires C, 72·5; H, 10·0%). The later fractions from the column were crystallised from hexane to give 3β,12β-*diacetoxy*-17α-*methyl*-5α-*androstan*-17β-*ol* (5·0 g), m.p. 115—117°, $[\alpha]_D$ −28·5° (*c* 1·39), R_t 1·30 (SE 30; 227°) and 2·64 (OV 17; 240°), $\nu_{max.}$ (KCl) 3530 (OH) and 1740 and 1240 (acetate) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3610 (OH) cm^{-1}, δ 0·84 (3H, s, 13-Me), 0·98 (3H, s, 17-Me), 1·26 (3H, s, 10-Me), 1·99 and 2·02 (6H, 2s, 3β- and 12β-OAc), and 4·75 (2H, m, 3α- and 12α-H) (Found: C, 70·90; H, 9·6. $C_{24}H_{38}O_5$ requires C, 70·9; H, 9·4%).

3β-*Acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androstan*-12-*one*.—Kiliani's [33] reagent (15 ml) was added dropwise to a stirred suspension of 3β-acetoxy-17α-methyl-5α-androstane-12β,17β-diol (7·5 g) in acetone (150 ml) at 20° and after stirring for 30 min an excess of water was added and the product was extracted into ether (200 ml). The solution was washed with water, dried (Na_2SO_4), concentrated, and hexane was added to give the 12-*ketone* (4·5 g), m.p. 131—136°, $[\alpha]_D$ +15° (*c* 1·0), $\nu_{max.}$ (KCl) 3440 (OH), 1720 and 1250 (acetate), and 1705 (carbonyl) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3580 (OH), 1725 (acetate), and 1700 (carbonyl) cm^{-1}, δ 0·93 (3H, s, 13-Me), 1·18 (3H, s, 17-Me), 1·44 (3H, s, 10-Me), 2·02 (3H, s, 3β-OAc), 2·2 (1H, s, 11-H), and 4·7 (1H, m, 3α-H) (Found: C, 73·1; H, 9·6. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·5%).

3β-*Acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-9(11)-*en*-12-*one*.—A solution of 3β-acetoxy-17β-hydroxy-17α-methyl-5α-androstan-12-one (4·0 g) in chlorobenzene (20 ml) and pyridine (0·4 ml) was stirred and heated to reflux [34] with selenium dioxide (2·0 g) and Dicalite (2·0 g) for 18 h. The suspension was cooled, filtered over Dicalite, and the solvent was removed under vacuum. The residue was dissolved in benzene and the solution was filtered through a column of alumina (5 × 1·5 in). The eluate and column washings were concentrated and the residue was crystallised from ether–hexane to give 3β-*acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-9(11)-*en*-12-*one* (3·0 g), m.p. 124—125°, $[\alpha]_D$ +2° (*c* 1·0), $\nu_{max.}$ (KCl) 3480 (OH), 1730 and 1240 (acetate), 1670 (carbonyl), and 1592 (C=C) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3575 (OH), 1730 (acetate), 1665 (carbonyl), and 1590 (C=C) cm^{-1}, $\lambda_{max.}$ 239 nm (ε 13,900), δ 1·01 (3H, s, 13-Me), 1·08 (3H, s, 17-Me), 1·38 (3H, s, 10-Me), 2·02 (3H, s, 3β-OAc), 2·07 (1H, s, 17β-OH), 4·65 (1H, m, 3α-H), and 5·72 (1H, d, *J* 2 Hz, 11-H) (Found: C, 73·7; H, 9·0. $C_{22}H_{32}O$ requires C, 73·3; H, 9·0%).

Attempted Rearrangement of 3β-*Acetoxy*-17β-*hydroxy*-17α-*methyl*-5α-*androst*-9(11)-*en*-12-*one*.— 3β-Acetoxy-17β-hydroxy-17α-methyl-5α-androst-9(11)-en-12-one (4·0 g) was added to hot formic acid (10 ml) and the mixture was heated under reflux for 15 min, cooled, and an excess of water was added. The aqueous layer was decanted off and the residue was dissolved in diethyl ether (100 ml). The solution was washed with sodium hydrogen carbonate solution and water and dried (Na_2SO_4). Removal of solvent and crystallisation of the residue from ether gave 3β-*acetoxy*-17-*methyl*-5α-*androsta*-9(11),16-*dien*-12-*one* (3·0 g), m.p. 186—192°, $[\alpha]_D$ +149° (*c* 1·1), R_t 0·66 (SE 30; 225°), $\nu_{max.}$ 3040 (CH=C), 1725 and 1240 (acetate), 1680 (carbonyl), and 1597 (C=C) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 1730 (acetate), 1679 (carbonyl), and 1593 (C=C) cm^{-1}, $\lambda_{max.}$ 238 nm (ε 12,000), δ 0·97 (3H, s, 13-Me), 1·10 (3H, s, 10-Me), 2·01 (6H, s, 3β-OAc and 17-Me), 4·67 (1H, m, 3α-H), 5·34 (1H, s, 16-H), and 5·64 (1H, d, *J* 2 Hz, 11-H) (Found: C, 77·2; H, 8·9. $C_{20}H_{30}O_3$ requires C, 77·2; H, 8·8%).

17β-*Hydroxy*-17α-*methyl*-5α-*androstane*-3,12-*dione*.—Kiliani's [33] reagent (20 ml) was added to a stirred suspension of 17α-methyl-5α-androstane-3β,12β,17β-triol (5·0 g) in acetone (100 ml) over 15 min, keeping the temperature below 30°. The suspension was stirred for a further 1·5 h, filtered, poured into an excess of water, and extracted with ether. The extract was washed neutral with water, dried (Na_2SO_4), concentrated, and filtered through a column (3 × 1·5 in) of alumina. The eluate was concentrated and hexane added to give 17β-*hydroxy*-17α-*methyl*-5α-*androstane*-3,12-*dione* (3·5 g), m.p. 122—125°, $[\alpha]_D$ +44° (*c* 1·0), $\nu_{max.}$ (KCl) 3480 (OH) and 1710 (carbonyls) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 3582 (OH) and 1707 (carbonyls) cm^{-1}, δ 1·08 (3H, s, 13-Me), 1·17 (3H, s, 17-Me), 1·45 (3H, s, 10-Me), and 2·03 (1H, s, 17β-OH) (Found: C, 75·7; H, 9·6. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%).

Attempted Rearrangement of 17β-*Hydroxy*-17α-*methyl*-5α-*androstane*-3,12-*dione*.— 17β-Hydroxy-17α-methyl-5α-androstane-3,12-dione (0·5 g) was added to hot formic acid (2 ml) and the solution was heated to reflux for 30 min, cooled, poured into water, and the product was isolated by filtration. The solid was dissolved in benzene, filtered through a column (3 × 0·5 in) of alumina and the eluate was evaporated to dryness. Recrystallisation from methylene chloride–ether gave 17-*methyl*-5α-*androst*-16-*ene*-3,12-*dione* (0·4 g), m.p. 204—205°, $[\alpha]_D$ +173° (*c* 0·7), $\nu_{max.}$ (KCl)

3060 (CH=C) and 1710 (carbonyls) cm^{-1}, δ 1·09 (6H, s, 10- and 13-Me), 1·94 (3H, s, 17-Me), and 5·33 (1H, s, 16-H) (Found: C, 80·2; H, 9·4. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·4%).

We thank Dr. L. A. van Dijck for n.m.r. measurements and Dr. W. McMeekin for t.l.c., g.l.c., and elemental analyses and for i.r. and u.v. spectra.

[3/883 *Received*, 26*th April*, 1973]