The Hydrolysis of Some Steroidal Vicinal Hydroxy-epoxides

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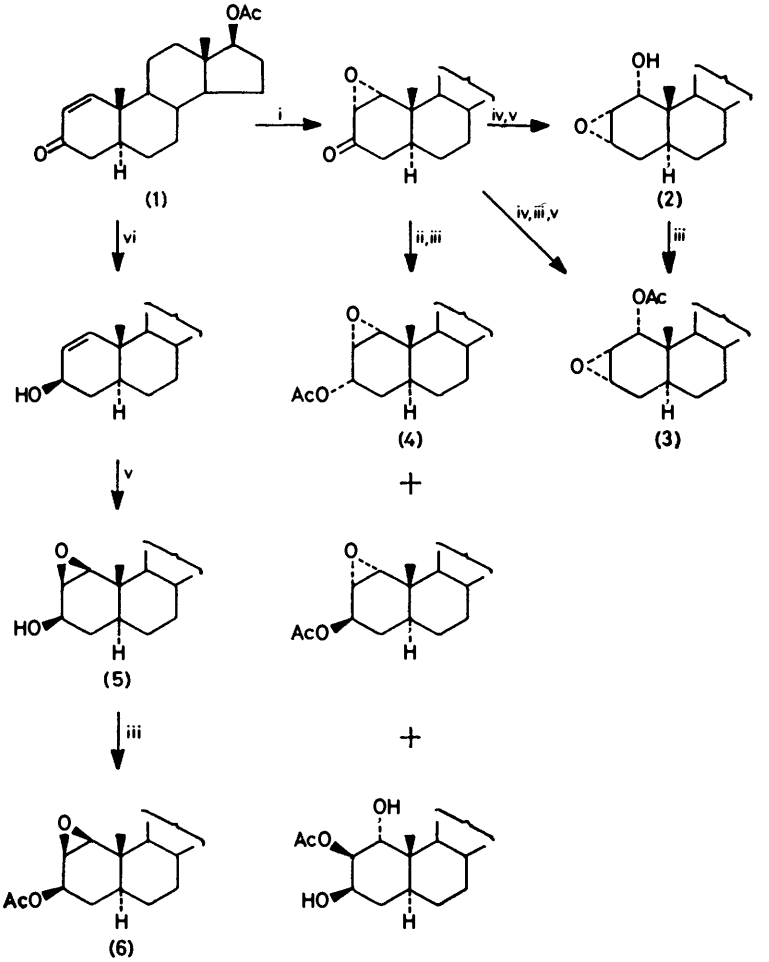
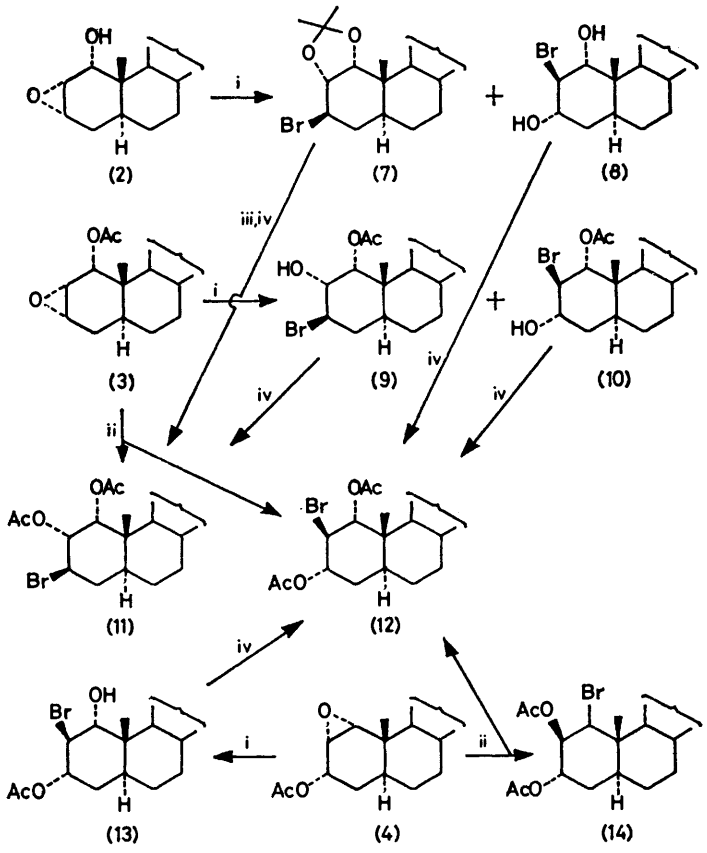
The hydrolysis of 1α-hydroxy-2α,3α-epoxy-, 1α-acetoxy-2α,3α-epoxy-, and 3α-acetoxy-1α,2α-epoxy-androstanes with hydrobromic acid led to the products of both diequatorial and diaxial cleavage of the epoxide. The hydrolysis of 3β-hydroxy- and 3β-acetoxy-1β,2β-epoxides led to diaxial products.

We have shown that the rearrangement of various androstane hydroxy-epoxides with hydrobromic acid in glacial acetic acid affords 4-methyloestra-1,3,5(10)-trienes by a spiro-diene pathway.[1] The substrates which we have examined in this context have all possessed a potential carbonium ion source which would initiate rearrangement either at C-5 or sufficiently close to generate this by elimination and reprotonation. However when ring B hydroxy-epoxides are subjected[2] to these conditions, it is ring A which undergoes aromatization suggesting that under these conditions there is considerable double-bond mobility. In an effort to delineate the scope of the rearrangement, we have examined the reaction of some isomeric 1-hydroxy-2,3-epoxy- and 3-hydroxy-1,2-epoxy-androstanes and their acetates with hydrobromic acid. By analogy with the isolation[3] of 1-methyloestradiol diacetate from the reaction of 17β-acetoxy-1α,2α-epoxyandrostan-3-one with toluene-*p*-sulphonic acid in acetic anhydride, these compounds present a possible alternative route to aromatization. The formation of a C-1 carbonium ion might, in turn, induce a C(10)–C(1) methyl group rearrangement and thence the formation of a 1-methyloestra-1,3,5(10)-triene. This C(10)–C(1) methyl group migration also occurs in the reaction of hydroxy-epoxides which possess a C-6 ketone which destabilizes a C-5 carbonium ion.[1] In the event the reactions took a different course affording the products of hydrolysis. During this work the hydrolysis of some similar cholestane hydroxy-epoxides with hydrobromic acid, was reported.[4] Where the systems overlap, our results are in substantial agreement.



SCHEME 1 *Reagents* i, H_2O_2–NaOH; ii, $NaBH_4$, MeOH; iii, Ac_2O–pyr; iv, $N_2H_4 \cdot H_2O$; v, *m*-$ClC_6H_4CO_3H$; vi, $LiAl(O^tBu^t)_3H$

The substrates (2)—(6) were prepared from 17β-acetoxyandrost-1-en-3-one (1) [5] by standard methods which are summarized in Scheme 1.[6]



SCHEME 2 *Reagents* i, HBr–HOAc–Me_2CO; ii, HBr–HOAc, reflux; iii, $CH_3C_6H_4{\cdot}SO_3H$; iv, Ac_2O–pyr

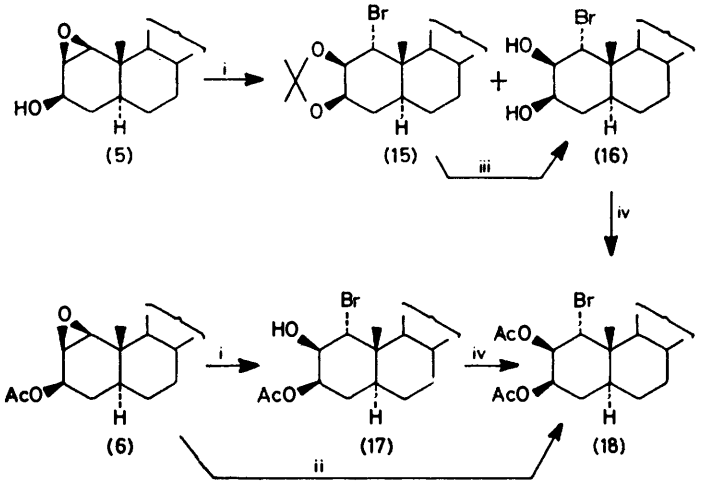
The hydrolysis of steroidal 2α,3α-epoxides to afford the diaxial 2β,3α-bromohydrins is well-documented.[7] However treatment of 17β-acetoxy-2α,3α-epoxyandrostan-1α-ol (2) in acetone with hydrobromic acid in glacial acetic acid gave the bromo-acetonide (7) arising from a diequatorial opening of the 2,3-epoxide and the diaxial bromohydrin (8) in approximately equal amounts. The corresponding 1α-acetate (3) gave predominantly the diequatorial bromohydrin (9) together with a smaller amount of the diaxial isomer (10). With hydrobromic acid in refluxing glacial acetic acid, it afforded mainly the diequatorial bromo-acetate (11) together with a small amount of 2β-bromo-1α,3α-diacetate (12). No aromatic products were detected. These compounds were inter-related (see Scheme 2) by hydrolysis of the acetonide and acetylation.

The magnitude (2 Hz) of the 1-H,2-H coupling constant in (9) and the formation of the acetonide (7) served to establish the C-1 and C-2 stereochemistry in the series of products arising by diequatorial opening of the epoxide. The C*H*(Br) resonance in (11) appeared as a triplet (*J* 11.5 Hz) of doublets (*J* 5.5 Hz) with one of the 11.5 Hz couplings to the 2-H. In the other series, arising by diaxial opening of the epoxide, the C*H*(Br) resonance [in, for example, (12)] appeared as a quartet, 1.5 and 3 Hz, coupled (1.5 Hz) to the 1-H and (3 Hz) to the 3-H. The latter, typical of a 3β-H, had a relatively narrow half-width (6 Hz). Furthermore, the 1 : 3-diaxial interaction between the electronegative substituent and the C-10 methyl group was reflected in the downfield shift of this resonance.

Treatment of the isomeric 3α-acetoxy-1α,2α-epoxide (4) in acetone with hydrobromic acid in acetic acid at room temperature gave a 1α-hydroxy-2β-bromo-steroid (13) associated with the normal opening of the epoxide. Under more vigorous conditions the 2β-bromo-1α,3α-diacetate (12) was formed together with a smaller amount of a compound formulated as (14) on the basis of its n.m.r. spectrum.

Reaction of 17β-acetoxy-1β,2β-epoxyandrostan-3β-ol (5) in acetone with hydrobromic acid in glacial acetic acid afforded the bromo-acetonide (15) and the corresponding diol (16) (see Scheme 3). Under these conditions the 3β-acetoxy-1β,2β-epoxide (6) afforded the diaxial bromohydrin (17) and the 1α-bromo-2β,3β-diacetate (18) under more vigorous conditions. The magnitude of the 1-H : 2-H coupling constant (2 Hz) in (18) and the inter-relationship (see Scheme 3) with the 2 : 3-acetonide provided the evidence for the formulation of these hydrolysis products. No aromatic products were detected.

The absence of aromatic products from the hydrobromic acid–glacial acetic acid reactions contrasts with the reactivity of other ring A and ring B hydroxy-epoxides.[1,2] The formation of diequatorial products



SCHEME 3 *Reagents* i, HBr–HOAc–Me_2CO; ii, HBr–HOAc, reflux; iii, $CH_3C_6H_4SO_3H$; iv, Ac_2O–pyr

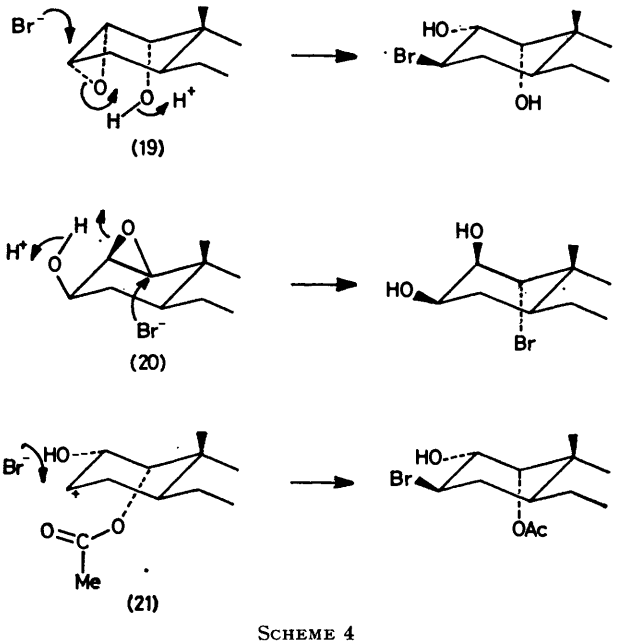
from the hydroxy-epoxide (2) may be rationalized in terms of hydrogen bonding between the alcohol and the epoxide (19) (see Scheme 4). Protonation on the alcohol would then direct the opening of the epoxide as in Scheme 4. In the case of the 1α-hydroxy-2α,3α-epoxide this would afford diequatorial products whereas in the case of the 3β-hydroxy-1β,2β-epoxide (20), it would favour the diaxial opening. The formation of the diequatorial products in the case of the 1α- and 3α-acetates may arise through the axially oriented acetate stabilizing the carbonium ion through a 1 : 3-diaxial acetoxonium ion (21). The participation by a vicinal *trans*-axial acetoxy-group in the boron trifluoride-catalysed opening of steroidal epoxides, has been described recently.[8]

EXPERIMENTAL

General experimental details have been described previously.[9]

Reduction and Acetylation of 17β-*Acetoxy*-1α,2α-*epoxy-androstan*-3-*one*.—A slurry of the steroid (2 g) [5] in methanol (50 ml) was treated with sodium borohydride (350 mg) at room temperature for 2 h. Water (500 ml) was added and the precipitate was collected and dried *in vacuo*. It was treated with acetic anhydride (4 ml) in pyridine (25 ml) at room temperature for 24 h. The mixture was poured into dilute hydrochloric acid and the product recovered in ethyl acetate and chromatographed on silica. Elution with 15% ethyl acetate–light petroleum gave 3β,17β-*diacetoxy*-1α,2α-*epoxyandrostane* (400 mg) which crystallized from light petroleum as needles, m.p. 135—137 °C, $[\alpha]_D$ −6° (*c* 0.2) (Found: C, 70.8; H, 8.8. $C_{23}H_{34}O_5$ requires C, 70.7; H, 8.8%), $\nu_{max.}$ 1 735 cm^{-1}; δ 0.80 (3 H, s, 18-H), 0.96 (3 H, s, 19-H), 1.90 and 2.03 (each 3 H, s, OAc), 3.02 (2 H, m, 1- and 2-H), 4.56 (1 H, dd, *J* 8 and 10 Hz, 17-H), 4.95br (1 H, m, 3-H). Elution with 20% ethyl acetate–light petroleum gave 3α,17β-*diacetoxy*-1α,2α-*epoxyandrostane* (4) (900 mg) which crystallized from aqueous methanol as needles, m.p. 140—141 °C, $[\alpha]_D$ −49.3° (*c* 0.2) (Found: C, 70.7; H, 8.7. $C_{23}H_{34}O_5$ requires C, 70.7; H, 8.8%), $\nu_{max.}$ 1 725 cm^{-1}; δ 0.80 (3 H, s, 18-H), 0.85 (3 H, s, 19-H), 2.00 and 2.10 (each 3 H, s, OAc), 3.15 (1 H, d, *J* 5 Hz, 1-H), 3.35 (1 H, t, *J* 5 Hz, 2-H), 4.60 (1 H, dd, *J* 8 and 10 Hz, 17-H), and 5.10 (1 H, t, *J* 5 Hz, 3-H). Further elution with 80% ethyl acetate–light petroleum gave 2β,17β-*diacetoxy*-1α,3β-*dihydroxyandrostane* (485 mg) which crystallized from methanol as needles, m.p. 200—202 °C, $[\alpha]_D$ +11° (*c* 0.22) (Found: C, 67.7; H, 8.9. $C_{23}H_{36}O_6$ requires C, 67.7; H, 8.9%), $\nu_{max.}$ 3 480, 3 370, and 1 720 cm^{-1}; δ 0.76 (3 H, s, 18-H), 0.88 (3 H, s, 19-H), 1.98 and 2.04 (each 3 H, s, OAc), 3.91 (1 H, d, *J* 2.5 Hz, 1-H), 4.04 (1 H, m, 3-H), 4.54 (1 H, t, *J* 9 Hz, 17-H), and 5.00 (1 H, t, *J* 2.5 Hz, 2-H). The 1α,2β,3β,17β-*tetra-acetate*, prepared with acetic anhydride in pyridine, crystallized from light petroleum as needles, m.p. 155—157 °C, $[\alpha]_D$ +2.5° (*c* 0.19) (Found: C, 65.7; H, 8.1. $C_{27}H_{40}O_8$ requires C, 65.8; H, 8.2%), $\nu_{max.}$ 1 735 cm^{-1}; δ 0.76 (3 H, s, 18-H), 1.06 (3 H, s, 19-H), 1.95 (3 H, s), 2.02 (3 H, s), 2.10 (6 H, s, each OAc), 4.60 (1 H, t, *J* 9 Hz, 17-H), 5.00br (3 H, m, 1-, 2-, and 3-H).

17β-*Acetoxy*-2α,3α-*epoxyandrostan*-1α-*ol*.— 17β-Acetoxy-androst-2-en-1α-ol [6] (500 mg) in chloroform (50 ml) was treated with *m*-chloroperbenzoic acid (500 mg) at room temperature for 3 h. The solution was washed with aqueous iron(II) sulphate, dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water and was then dried. Evaporation of the solvent gave 17β-*acetoxy*-2α,3α-*epoxy-androstan*-1α-*ol* (2) (480 mg) which crystallized from light petroleum as needles, m.p. 145—147 °C, $[\alpha]_D$ +67° (*c* 0.2) (Found: C, 72.5; H, 9.3. $C_{21}H_{32}O_4$ requires C, 72.4; H, 9.3%), $\nu_{max.}$ 3 495 and 1 735 cm^{-1}; δ 0.73 (3 H, s, 18-H), 0.80 (3 H, s, 19-H), 2.05 (3 H, s, OAc), 3.37 (2 H, m, 2- and 3-H), 3.65 (1 H, s, 1-H), and 4.50 (1 H, dd, *J* 8 and 10 Hz, 17-H). The 1α,17β-*diacetate*, prepared with acetic anhydride in pyridine, crystallized from acetone–light petroleum as needles, m.p. 130—131 °C, $[\alpha]_D$ +85° (*c* 0.2) (Found: C, 70.4; H, 8.8. $C_{23}H_{34}O_5$ requires C, 70.7; H, 8.8%), $\nu_{max.}$ 1 735 cm^{-1}; δ 0.75 (3 H, s, 18-H), 0.78 (3 H, s,



SCHEME 4

19-H), 2.01 and 2.10 (each 3 H, s, OAc), 3.23 (1 H, m, 3-H), 3.46 (1 H, q, *J* 4 and 6 Hz, 2-H), 4.63 (2 H, m, 1- and 17-H). This epoxide was also obtained by epoxidation of 1α,17β-diacetoxyandrost-2-ene [10] with *m*-chloroperbenzoic acid in chloroform.

Epoxidation of 17β-*Acetoxyandrost*-1-*en*-3β-*ol*.—The steroid [5] (7.5 g) in chloroform (200 ml) was cooled to 0 °C and treated with *m*-chloroperbenzoic acid (7.5 g). After 15 h at room temperature, the solution was washed with iron(II) sulphate, dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, and was then dried and the solvent evaporated. The residue was chromatographed on silica. Elution with 15% ethyl acetate–light petroleum gave 17β-acetoxy-1β,2β-epoxyandrostan-3β-ol (5.37 g) which crystallized from acetone–light petroleum as needles, m.p. 198—200 °C, $[\alpha]_D$ +42° (*c* 0.2) (lit.,[6] m.p. 189—191.5 °C, $[\alpha]_D$ +40°), $\nu_{max.}$ 3 420 and 1 735 cm^{-1}; δ 0.82 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 2.00 (3 H, s, OAc), 3.20br (2 H, s, 1- and 2-H), 3.94 (1 H, m, 3-H), and 4.56 (1 H, dd, *J* 8 and 10 Hz, 17-H). The 3β-17β-*diacetate*, prepared with acetic anhydride in pyridine, crystallized from acetone–light petroleum as needles, m.p. 128—130 °C, $[\alpha]_D$ +45° (*c* 0.24) (Found: C, 70.6; H, 8.7. $C_{23}H_{34}O_5$ requires C, 70.7; H, 8.8%), $\nu_{max.}$ 1 740 cm^{-1}; δ 0.82 (3 H, s, 18-H), 0.95 (3 H, s, 19-H), 2.02 and 2.08 (each 3 H, s, OAc), 3.22 (2 H, s, 1- and 2-H), 4.61 (1 H, dd, *J* 8 and 10 Hz, 17-H), and 5.15 (1 H, t, *J* 7.5 Hz, 3-H). Further elution of the column with 18% ethyl acetate–light petroleum afforded 17β-*acetoxy*-1α,2α-*epoxyandrostan*-3β-*ol* (820 mg) which crystallized from acetone–light petroleum as prisms, m.p. 144—146 °C, $[\alpha]_D$ +3° (*c* 0.2) (Found: C, 72.2; H, 9.4. $C_{21}H_{34}O_4$ requires C, 72.4; H, 9.3%), $\nu_{max.}$ 3 420 and 1 725 cm^{-1}; δ 0.80 (3 H, s, 18-H), 0.95 (3 H, s, 19-H), 2.00 (3 H, s, OAc), 3.20 (2 H, s, 1- and 2-H), 4.00 (1 H, m, 3-H), and 4.55 (1 H, dd, *J* 8 and 10 Hz, 17-H).

Hydrolysis of 17β-*Acetoxy*-2α,3α-*epoxyandrostan*-1α-*ol*.—The steroid (2) (200 mg) in acetone (100 ml) was treated with a solution of 48% hydrobromic acid (3 ml) in glacial acetic acid (6 ml) at room temperature for 1 h. The solution was neutralized with sodium carbonate, concentrated, diluted with water, and the product recovered in chloroform. The mixture was separated by preparative layer chromatography on silica in 20% ethyl acetate–light petroleum. Elution of the faster running component gave 17β-*acetoxy*-3β-*bromo*-1α,2α-*isopropylidenedioxyandrostane* (7) (55 mg) which crystallized from acetone–light petroleum as needles, m.p. 209—210 °C, $[\alpha]_D$ −32° (*c* 0.2) (Found: C, 61.6; H, 8.1. $C_{24}H_{37}BrO_4$ requires C, 61.4; H, 7.9%), $\nu_{max.}$ 1 745 cm^{-1}; δ 0.78 (3 H, s, 18-H), 0.90 (3 H, s, 19-H), 1.32 and 1.50 (each 3 H, s, isopropylidene CH_3), 2.00 (3 H, s, OAc), 4.05 (3 H, m, 1-, 2-, and 3-H), and 4.56 (1 H, dd, *J* 8 and 10 Hz, 17-H). The slower running component, 17β-*acetoxy*-2β-*bromo*-1α,3α-*dihydroxyandrostane* (8) (50 mg) crystallized from methanol as plates, m.p. 153—155 °C, $[\alpha]_D$ +6° (*c* 0.25) (Found: C, 58.8; H, 7.8. $C_{21}H_{33}BrO_4$ requires C, 58.7; H, 7.8%), $\nu_{max.}$ 3 450 and 1 725 cm^{-1}; δ 0.80 (3 H, s, 18-H), 1.14 (3 H, s, 19-H), 2.00 (3 H, s, OAc), 3.90 (1 H, *J* 2, 1-H), 4.18 (1 H, m, 3-H), 4.28 (1 H, dd, *J* 2 and 4 Hz, 2-H), and 4.55 (1 H, t, *J* 9 Hz, 17-H). The 1α,3α,17β-*triacetate*, prepared with acetic anhydride in pyridine, crystallized from light petroleum as plates, m.p. 228—230 °C, $[\alpha]_D$ +20° (*c* 0.2) (Found: C, 58.4; H, 7.3. $C_{25}H_{37}O_6Br$ requires C, 58.5; H, 7.3%), $\nu_{max.}$ 1 740 cm^{-1}; δ 0.78 (3 H, s, 18-H), 1.22 (3 H, s, 19-H), 1.97 (3 H, s) and 2.00 (6 H, s, OAc), 4.13 (1 H, q, *J* 1.5 and 3 Hz, 2-H), 4.56 (1 H, dd, *J* 8 and 10 Hz, 17-H), 4.99 (1 H, d, *J* 1.5 Hz, 1-H), 5.17 (1 H, m, $w_{1/2}$ 6 Hz, 3-H).

Hydrolysis of 1α,17β-*Diacetoxy*-2α,3α-*epoxyandrostane* (3).—(i) The steroid (3) (1 g) in acetone (100 ml) was treated with a solution of 48% hydrobromic acid (3 ml) in glacial acetic acid (6 ml) at room temperature for 30 min (t.l.c. control). The solution was neutralized with sodium carbonate, concentrated, and diluted with water (200 ml). The product was recovered in chloroform and purified by dry-column chromatography on silica. Elution with 25% ethyl acetate–light petroleum afforded 1α,17β-*diacetoxy*-3β-*bromoandrostan*-2α-*ol* (9) (700 mg) which crystallized from light petroleum as plates, m.p. 88—89 °C, $[\alpha]_D$ −2° (*c* 0.2) (Found: C, 58.5; H, 7.4. $C_{23}H_{35}BrO_5$ requires C, 58.6; H, 7.5%), $\nu_{max.}$ 3 450 and 1 745 cm^{-1}; δ 0.77 (3 H, s, 18-H), 0.94 (3 H, s, 19-H), 1.98 (3 H, s) and 2.06 (3 H, s, OAc), 4.05 (2 H, m, 2- and 3-H), 4.57 (1 H, dd, *J* 8 and 10 Hz, 17-H), and 5.19 (1 H, d, *J* 2 Hz, 1-H). Acetylation with acetic anhydride in pyridine afforded 1α,2α,17β-triacetoxy-3β-bromoandrostane (11) identical (m.p., i.r., and n.m.r.) to the material described below.

(ii) The steroid (3) (500 mg) in 48% hydrobromic acid (1.5 ml) and glacial acetic acid (6 ml) was heated under reflux for 15 min. The solution was poured into aqueous sodium hydrogen carbonate and the product recovered in ethyl acetate and chromatographed on alumina. Elution with 5% ethyl acetate–light petroleum gave 1α,2α,17β-*triacetoxy*-3β-*bromoandrostane* (11) (110 mg) which crystallized from light petroleum as needles, m.p. 185—186 °C, $[\alpha]_D$ −54.5° (*c* 0.2) (Found: C, 58.3; H, 7.1. $C_{25}H_{37}BrO_6$ requires C, 58.5; H, 7.3%), $\nu_{max.}$ 1 745, 1 740, and 1 730 cm^{-1}; δ 0.76 (3 H, s, 18-H), 1.00 (3 H, s, 19-H), 1.97 (6 H, s) and 2.05 (3 H, s, OAc), 4.10 (1 H, t of d, *J* 11.5 and 5.5 Hz, 3-H), 4.54 (1 H, dd, *J* 8 and 10 Hz, 17-H), 5.12 (1 H, q, *J* 11.5 and 2 Hz, 2-H), and 5.20br (1 H, s, 1-H). Further elution with 7.5 and 10% ethyl acetate–light petroleum afforded 1α,3α,17β-triacetoxy-2β-bromoandrostane (12) (32 mg) identical (m.p., i.r., and n.m.r.) to the material described above.

Hydrolysis of 17β-*Acetoxy*-3β-*bromo*-1α,2α-*isopropylidenedioxyandrostane* (7).—The steroid (7) (45 mg) in methanol (10 ml) was treated with toluene-*p*-sulphonic acid (100 mg) at room temperature for 3 days. The solution was treated with sodium hydrogen carbonate, concentrated, and diluted with water. The organic product was recovered in ethyl acetate. The solvent was dried and evaporated to afford a gum which was treated with acetic anhydride (1 ml) in pyridine (5 ml) overnight. The solution was poured in dilute hydrochloric acid and the steroid recovered in ethyl acetate. The solvent was dried and evaporated to afford 1α,2α,17β-triacetoxy-3β-bromoandrostane (11) (30 mg) identical (m.p., i.r., and n.m.r.) to the sample described above.

Hydrolysis of 3α,17β-*Diacetoxy*-1α,2α-*epoxyandrostane* (4).—(i) The steroid (4) (200 mg) in acetone (50 ml) was treated with 48% aqueous hydrobromic acid (2 ml) in glacial acetic acid (4 ml) at room temperature for 30 min (t.l.c. control). The solution was neutralized with sodium carbonate and concentrated *in vacuo*. Water was added and the products were recovered in ethyl acetate. Evaporation of the solvent gave a gum which was crystallized from light petroleum–acetone to afford 3α,17β-*diacetoxy*-2β-*bromo*-1α-*hydroxyandrostane* (13) (129 mg) as needles, m.p. 200—202 °C, $[\alpha]_D$ 57° (*c* 0.19) (Found: C, 58.4; H, 7.5. $C_{23}H_{35}BrO_5$ requires C, 58.6; H, 7.5%), $\nu_{max.}$ 3 505, 1 725, and

1 705 cm^{-1}; δ 0.82 (3 H, s, 18-H), 1.20 (3 H, s, 19-H), 2.07 and 2.12 (each 3 H, s, OAc), 3.90br (1 H, s, 1-H), 4.28br (1 H, s, 2-H), 4.60 (1 H, t, *J* 9 Hz, 17-H), and 5.25br (1 H, s, 3-H). Acetylation with acetic anhydride in pyridine afforded 1α,3α,17β-triacetoxy-2β-bromoandrostane (12) identical to the material described above.

(ii) The steroid (4) (500 mg) in 48% hydrobromic acid (1.5 ml) and glacial acetic acid (5 ml) was heated under reflux for 15 min. The solution was poured into aqueous sodium carbonate and the organic products recovered in ethyl acetate. The solvent was dried and evaporated to afford a gum which was separated by preparative layer chromatography on silica in 20% ethyl acetate–light petroleum. Elution of the faster-running component gave 2α,3α,17β-*triacetoxy*-1β-*bromoandrostane* (14) (180 mg) which crystallized from acetone–light petroleum as needles, m.p. 201—203 °C, $[\alpha]_D$ +16° (*c* 0.24) (Found: C, 58.6; H, 7.3. $C_{25}H_{37}BrO_6$ requires C, 58.5; H, 7.3%), $\nu_{max.}$ 1 730 cm^{-1}; δ 0.80 (3 H, s, 18-H), 1.19 (3 H, s, 19-H), 2.06 (6 H, s) and 2.11 (3 H, s, OAc), 4.20 (1 H, m, 1-H), 4.60 (1 H, t, *J* 9 Hz, 17-H), 5.02 (1 H, 2-H), 5.23br (1 H, s, 3-H). The slower-running component 1α,3α,17β-triacetoxy-2β-bromo-androstane (12) (300 mg) was identical (m.p., i.r., and n.m.r.) to the material described above.

Hydrolysis of 17β-*Acetoxy*-1β,2β-*epoxy*-3β-*hydroxyandrostane* (5).—The steroid (5) (500 mg) in acetone (100 ml) was treated with 48% hydrobromic acid (3 ml) in glacial acetic acid (6 ml) at room temperature for 1 h. The solution was neutralized with sodium carbonate, concentrated *in vacuo*, and diluted with water. The product was recovered in chloroform and purified by preparative layer chromatography on silica in 20% ethyl acetate–light petroleum. Elution of the faster-running component gave 17β-*acetoxy*-1α-*bromo*-2β,3β-*isopropylidenedioxyandrostane* (15) (270 mg) which crystallized from light petroleum as needles, m.p. 145—146 °C, $[\alpha]_D$ +55° (*c* 0.2) (Found: C, 61.4; H, 7.9. $C_{24}H_{37}BrO_4$ requires C, 61.4; H, 7.9%), $\nu_{max.}$ 1 728 cm^{-1}; δ 0.78 (3 H, s, 18-H), 1.15 (3 H, s, 19-H), 1.30 and 1.48 (each 3 H, s, isopropylidenedioxy CH_3), 1.98 (3 H, s, OAc), and 4.45 (4 H, 1-, 2-, 3-, and 17-H). The slower-running component gave 17β-*acetoxy*-1α-*bromo*-2β.3β-*dihydroxyandrostane* (16) (240 mg) which crystallized from acetone–light petroleum as needles, m.p. 197—199 °C, $[\alpha]_D$ +37.5° (*c* 0.20) (Found: C, 58.8; H, 7.7. $C_{21}H_{33}BrO_4$ requires C, 58.7; H, 7.7%), $\nu_{max.}$ 3 460, 3 300, and 1 710 cm^{-1}; δ 0.78 (3 H, s, 18-H), 1.16 (3 H, s, 19-H), 4.20 (3 H, m, 1-, 2-, and 3-H), and 4.55 (1 H, dd, *J* 8 and 9 Hz, 17-H). Acetylation with acetic anhydride in pyridine, gave 2β,3β,17β-*triacetoxy*-1α-*bromoandrostane* (17) which crystallized from light petroleum as needles, m.p. 202—204 °C, $[\alpha]_D$ +14° (*c* 0.2) (Found: C, 58.6; H, 7.2. $C_{25}H_{37}BrO_6$ requires C, 58.5; H, 7.3%), $\nu_{max.}$ 1 730 cm^{-1}; δ 0.78 (3 H, s, 18-H), 1.12 (3 H, s, 19-H), 1.96, 2.00, and 2.06 (each 3 H, s, OAc), 4.16 (1 H, d, *J* 3 Hz, 1-H), 4.56 (1 H, t, *J* 8 Hz, 17-H), and 5.46 (2 H, m, 2- and 3-H).

Hydrolysis of 17β-*Acetoxy*-1α-*bromo*-2β,3β-*isopropylidenedioxyandrostane*.—The steroid (16) (240 mg) in methanol (20 ml) was treated with toluene-*p*-sulphonic acid (100 mg) at room temperature for 3 days. The solution was neutralized with sodium hydrogen carbonate and concentrated. Water was added and the product was recovered in ethyl acetate. The solvent was dried and evaporated to afford 17β-acetoxy-1α-bromo-2β,3β-dihydroxyandrostane (16) which was identified by its m.p. and i.r. and n.m.r. spectra.

Hydrolysis of 3β,17β-*Diacetoxy*-1β,2β-*epoxyandrostane* (6).—(i) The steroid (6) (250 mg) in acetone (50 ml) was treated with 48% hydrobromic acid (2 ml) in glacial acetic acid (4 ml) at room temperature for 1 h. The solution was neutralized with sodium carbonate and concentrated *in vacuo*. Water was added and the products were recovered in ethyl acetate. The residue (203 mg) was crystallized from light petroleum to afford 3β,17β-*diacetoxy*-1α-*bromo*-2β-*hydroxyandrostane* (17) as plates, m.p. 87—90 °C, $[\alpha]_D$ +42° (*c* 0.24) (Found: C, 58.6; H, 7.6. $C_{23}H_{35}BrO_5$ requires C, 58.6; H, 7.5%), $\nu_{max.}$ 3 450, 1 740, and 1 715 cm^{-1}; δ 0.80 (3 H, s, 18-H), 1.13 (3 H, s, 19-H), 2.02 and 2.06 (3 H, s, OAc), 4.40 (3 H, m, 1-, 2-, and 17-H), and 5.32 (1 H, m, 3-H). Acetylation with acetic anhydride in pyridine, gave 2β,3β,17β-triacetoxy-1α-bromoandrostane (17) identical (m.p., i.r., and n.m.r.) to the material described above.

(ii) The steroid (6) (250 mg) in 48% hydrobromic acid (1 ml) and glacial acetic acid (4 ml) was heated under reflux for 15 min. The solution was poured into aqueous sodium carbonate and the product recovered in ethyl acetate. The solvent was dried and evaporated to afford an oil (176 mg). This was crystallized from light petroleum to afford 2β,3β,17β-triacetoxy-1α-bromoandrostane (17) identical (m.p., i.r., and n.m.r.) to the material described above.

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