Allylic Acetoxylation of Δ^5-Steroids at C-4

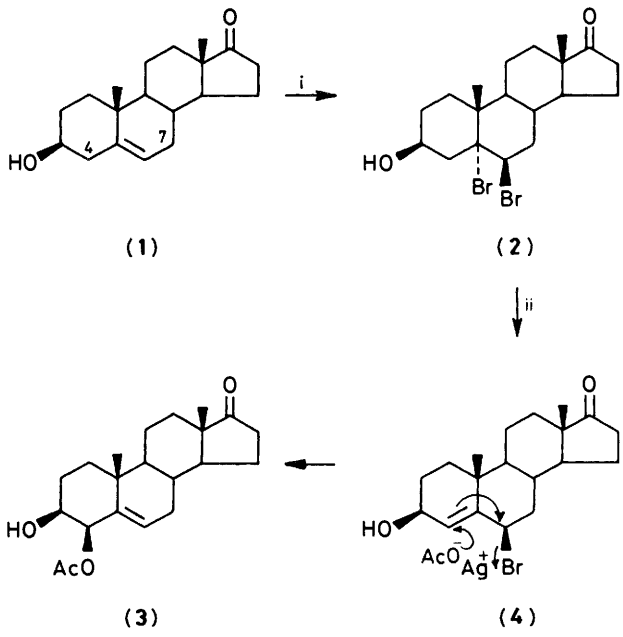
James R. Hanson,* Paul B. Reese, and Harry J. Wadsworth
School of Molecular Sciences, University of Sussex, Brighton, Sussex BN1 9QJ

The allylic acetoxylation of Δ^5-steroids at C-4 by reaction with bromine and silver acetate has been shown to depend upon the nature of the C-3 substituent. ^{2}H Labelling studies have shown that the reaction, which proceeds *via* the 5α,6β-dibromide, involves the *trans* diaxial elimination of a 4β-proton to form a Δ^4-6β-bromide which then undergoes an S_N2' displacement by the incoming acetate assisted by the silver ion.

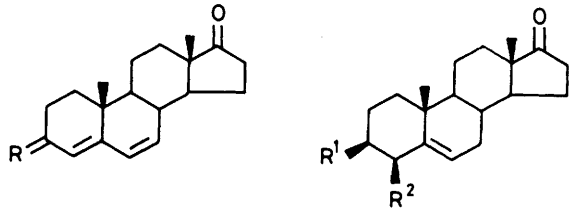
A number of biologically interesting steroids (*e.g.* the withanolides) possess a 4-oxygen function.[1] 4-Acetoxy- and 4-hydroxy-androst-4-ene-3,17-dione are selective inhibitors of oestrogen synthetase (aromatase) in tumour cells.[2] Apart from the partial synthesis of compounds of this type, we have also been interested in the influence of a 4-oxygen function on the course of a number of steroid reactions.[3] Allylic oxidation of Δ^5-steroids occurs at C-4 with some reagents and at C-7 with others.[4] The allylic acetoxylation of dehydroisoandrosterone (**1**) based on the reaction with bromine followed by silver acetate has provided a useful means of introducing substituents at C-4.[5] In this paper we report on some aspects of the scope and limitations of the reaction.

A reasonable reaction path (see Scheme) involves the formation of the 5α,6β-dibromide (**2**), elimination of the elements of hydrogen bromide to form the Δ^4-ene, followed by the *syn* S_N2' allylic substitution of the 6β-bromide possibly facilitated by the silver ion. The 5α,6β-bromide can be detected in the reaction whilst treatment of 5α,6β-dibromo-3β-hydroxyandrostan-17-one (**2**)[6] in chloroform with silver acetate in pyridine gave the 4β-acetate (**3**). When the acetoxylation of dehydroisoandrosterone (**1**) was carried out on a large scale, two minor products were also isolated. The first was the 4,6-diene (**5**) (5%) identified by its u.v. [$\lambda_{max.}$ 240 nm (ε 28 300)] and ^{1}H n.m.r. spectra [δ 5.39 (1 H, d, *J* 2 Hz, 4-H), 5.6 (1 H, dd, *J* 2 and 10 Hz, 6-H), 6.0 (1 H, dd, *J* 1.5 and 10 Hz, 7-H)]. Oxidation of this alcohol with chromium trioxide gave the known androsta-4,6-diene-3,17-dione (**6**).[7] The second product was 3β-acetoxy-4β-hydroxyandrost-5-en-17-one (**8**)[8] which was identified by comparison with an authentic sample prepared by the partial acetylation of the 3β,4β-diol (**9**). It may arise by isomerization of the 4β-acetate (**3**) through a 3β,4β-acetoxylinium ion. This isomerization occurs slowly in pyridine solution.

The variation of substituents at C-3 revealed some limitations in the reaction sequence. Androst-5-en-17-one (**10**)[9] gave 4β-acetoxyandrost-5-en-17-one (**11**). The presence of a 4-substituent in the product was confirmed by the hydrolysis of the acetate and oxidation of the resultant alcohol with chromium trioxide to give the known androst-5-ene-4,17-dione (**12**).[10] The axial nature of the 4-acetate was revealed by the ^{1}H n.m.r. spectrum in which the 4-H resonance (δ 5.26) appeared as a multiplet ($w_{\frac{1}{2}}$ 6 Hz) and by a downfield shift of the 19-H signal compared to androst-5-en-17-one (δ 1.02—1.10). However, the 3β-chloro- (**13**) and 3β-bromo-androst-5-en-17-ones (**14**)[11,12] gave the 5α,6β-dibromides (**20**) and (**21**) and no substitution products. Molecular rotation differences (see Table)[13] showed that these were the 5α,6β-dibromides rather than their 5β,6α-isomerization products. In the case of the 3β-methoxy compound (**15**)[11] the main product, which was obtained from the dibromide (**22**), was the 4,6-diene (**7**). It was identified by its u.v. spectrum [$\lambda_{max.}$ 234 nm (ε 20 000), 240 (22 000), 249 (15 000)]

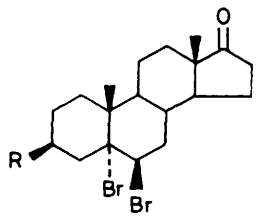


Scheme. *Reagents*: i, Br_2; ii, pyridine

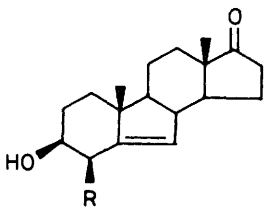


(**5**) R = α-H, β-OH
(**6**) R = O
(**7**) R = α-H, β-OMe

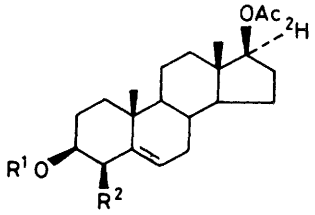
(**8**) R^1 = OAc, R^2 = OH
(**9**) R^1 = R^2 = OH
(**10**) R^1 = R^2 = H
(**11**) R^1 = H, R^2 = OAc
(**12**) R^1 = H, R^2 = O=
(**13**) R^1 = Cl, R^2 = H
(**14**) R^1 = Br, R^2 = H
(**15**) R^1 = OMe, R^2 = H
(**16**) R^1 = α-Cl, R^2 = H
(**17**) R^1 = α-Cl, R^2 = OAc
(**18**) R^1 = α-OH, R^2 = H
(**19**) R^1 = OH, R^2 = OCOEt



(20) R = Cl
(21) R = Br
(22) R = OMe



(23) R = H
(24) R = OH



(25) R^1 = Ac, R^2 = ^2H
(26) R^1 = M, R^2 = ^2H
(27) R^1 = H, R^2 = OAc

and its ^1H n.m.r. spectrum [δ 5.44 (1 H, d, *J* 3 Hz, 4-H), 5.64 (1 H, dd, *J* 1.5 and 10 Hz, 6-H), 5.98 (1 H, dd, *J* 2.5 and 10 Hz, 7-H)]. The 3α-chloro compound (**16**) gave a low yield of the 4β-acetoxy-3α-chloro compound (**17**), the structure of which was confirmed by an *X*-ray analysis.[14] However, an intractable mixture was obtained when 3α-hydroxyandrost-5-en-17-one (**18**)[15] was used as the substrate. The reaction proceeds, albeit in lower yield, with 3β-hydroxy-B-norandrost-5(7)-en-17-one (**23**)[16] which gave, after hydrolysis, the 3β,4β-diol (**24**) [δ 3.5 (m, 3-H), 4.37 (*J* 3 Hz, 4-H)].

Other silver carboxylates such as the propionate gave the corresponding 4β-esters [*e.g.*(**19**)] whilst silver trifluoroacetate gave the corresponding 3β,4β-diol (**9**). The use of silver toluene-*p*-sulphonate was not successful. A series of metal salts were examined but only lead acetate gave any indication of reaction in this context lending support to the suggestion that the silver ion facilitates the solvolysis of the halide. Variation in the base led to an improvement in the yield with 1,5-diazabicyclo-[5.4.0]undec-5-ene (DBU).

The stereochemistry of the reaction at C-4 was established by examining the fate of a 4β-deuterium label. [4β,17α-$^2H_2$]-3β,17β-Diacetoxyandrost-5-ene (**25**) was prepared by reduction of 3β-acetoxy-6β-chloroandrost-4-en-17-one[17] with lithium aluminium deuteride and subsequent acetylation. The ^2H n.m.r. spectrum, determined in chloroform at 55.28 MHz, showed signals at δ 2.29 (4β-^2H) and 4.59 (17α-^2H). Partial hydrolysis with methanolic potassium carbonate gave [4β,17α-$^2H_2$]-17β-acetoxy-3β-hydroxyandrost-5-ene (**26**). When this compound was treated with bromine and then silver acetate in pyridine, the resultant 4β,17β-diacetoxy-3β-hydroxyandrost-5-ene (**27**) only showed a ^2H n.m.r. signal at δ 4.58 and no signal at δ 5.37 which could be associated with a 4α-^2H. This signal remained in the ^1H n.m.r. spectrum. Hence the reaction has proceeded with an overall retention of configuration at C-4.

In conclusion we have established that the basic reaction pathway proceeds through the 5α,6β-dibromide, *trans* diaxial elimination of HBr and S_N2' substitution probably facilitated by silver. However the utility of the reaction may be limited by the nature of the C-3 substituent.

Table. Molecular rotation differences of dibromo-17-oxo steroids

3-Substituent	Molecular rotation (M) (°) Dibromide	Δ^5-ene	Difference (ΔM) (°)*
OAc	−99	−13	−86
OMc	−126	−6	−120
Cl	−114	38	−152
Br	−127	65	−192

* For 5α,6β-dibromides ΔM is negative (−80 to −160°); for 5β-6α-dibromides ΔM is positive (400—600°).

Experimental

Acetoxylation of Dehydroisoandrosterone (**1**).—3β-Hydroxyandrost-5-en-17-one (**1**) (10 g) in chloroform (75 ml) was cooled to −60 °C and bromine (1.8 ml) was added with swirling. Freshly prepared silver acetate (10 g) in pyridine (15 ml) was then added and the mixture was stirred at −60 °C for a further 30 min. The mixture was allowed to attain room temperature in the dark during 24 h and then filtered. The filtrate was washed with dil. hydrochloric acid, water, and aqueous sodium hydrogen carbonate. The solvent was evaporated and the white solid residue was chromatographed on silica. Elution with 15% ethyl acetate–light petroleum gave 3β-*hydroxyandrosta*-4,6-*dien*-17-*one* (**5**) (500 mg) which crystallized from acetone as prisms, m.p. 166—167 °C, $[\alpha]_D$ +38° (*c* 0.3) (Found: C, 79.65; H, 9.1. $C_{19}H_{26}O_2$ requires C, 79.68; H, 9.15%); $\nu_{max.}$ 3 490, 1 745, 1 665, and 1 615 cm^{-1}; $\lambda_{max.}$ 234 (ε 26 400), 2 400 (28 300), and 248 nm (20 500); δ 0.94 (3 H, s, 18-H), 1.04 (3 H, s, 19-H), 4.18 (1 H, m, $w_{\frac{1}{2}}$ 15 Hz, 3-H), 5.39 (2 H, d, *J* 2 Hz, 4-H), 5.6 (1 H, dd, *J* 2 and 10 Hz, 6-H), and 6.0 (1 H, dd, *J* 1.5 and 10 Hz, 7-H). Elution with 20% ethyl acetate–light petroleum gave 3β-acetoxy-4β-hydroxyandrost-5-en-17-one (**8**) (200 mg), identified by comparison (i.r. and n.m.r.) with an authentic sample. Elution with 25% ethyl acetate–light petroleum gave 4β-acetoxy-3β-hydroxyandrost-5-en-17-one (**3**) (8.5 g) which crystallized from acetone as needles, m.p. 198.5—200 °C, $[\alpha]_D$ −62° (*c* 0.3) (lit.,[8] m.p. 192—193 °C, $[\alpha]_D$ −60.7°), identified by its i.r. and n.m.r. spectrum.

Oxidation of 3β-*Hydroxyandrosta*-4,6-*dien*-17-*one* (**5**).—The steroid (**5**) (100 mg) in acetone (15 ml) was treated with the 8N-chromium trioxide reagent (0.4 ml) dropwise and with stirring at 0 °C. After 10 min, methanol was added and the solvents were evaporated. Water was added and the product recovered in ethyl acetate and chromatographed on silica. Elution with 50% ethyl acetate in light petroleum gave androsta-4,6-diene-3,17-dione (**6**) (30 mg), m.p. 172—173 °C, $[\alpha]_D$ +141.2° (*c* 0.3) (lit.,[7] 171—173 °C, $[\alpha]_D$ +136°), identified by its i.r., u.v. and n.m.r. spectra.

Acetoxylation of Androst-5-*en*-17-*one* (**10**).—Androst-5-en-17-one (**10**) (400 mg) in methylene dichloride (10 ml) at −60 °C was treated with bromine (0.1 ml) followed by silver acetate (1 g) in pyridine (2 ml). The mixture was allowed to warm to room temperature after 1 h at −60 °C. After 24 h, the mixture was filtered, diluted with ethyl acetate, and the organic solution was washed with dil. hydrochloric acid, water, and aqueous sodium hydrogen carbonate. The solvent was evaporated and the residue chromatographed on silica. Elution with 10% ethyl acetate–light petroleum gave 4β-acetoxyandrost-5-en-17-one (**11**) (245 mg) as a gum which did not crystalllize, $\nu_{max.}$ 1 740, 1 660 cm^{-1}; δ 0.82 (3 H, s, 18-H), 1.10 (3 H, s, 19-H), 2.00 (3 H,

s, 4-OAc), 5.30 (1 H, m, $w_{\frac{1}{2}}$ 6 Hz, 4-H), and 5.68 (1 H, d, *J* 4 Hz, 6-H); *m/z* 270 ($M^+ - 60$), 255, 237, 227, 213, 199, 145, and 121.

Androst-5-ene-4,17-dione (**12**).—A solution of 4β-acetoxyandrost-5-en-17-one (**11**) (175 mg) in methanol (15 ml) was stirred with sodium hydroxide (200 mg) in water (1 ml) overnight. The solution was neutralized and concentrated under reduced pressure. The product was recovered in ethyl acetate to give a gum (150 mg) which was taken up in acetone (15 ml) and cooled to −12 °C. The 8N-chromium trioxide reagent (0.3 ml) was added during 5 min and the mixture was stirred at −12 °C for 30 min. Methanol was added and the solution was allowed to warm to room temperature. The solvents were evaporated and the product was recovered in ethyl acetate and chromatographed on silica. Elution with 20% ethyl acetate–light petroleum gave androst-5-ene-4,17-dione (**12**) (60 mg) m.p. 141—143 °C,$[\alpha]_D$ +2°(lit.,[10] 122—123 °C,$[\alpha]_D$ +6°);$\nu_{max.}$ 1 735, 1 685, 1 670, and 1 630 cm^{-1}; $\lambda_{max.}$ 243 nm (ε 7 000) (Calc. 242 nm); δ 0.9 (3 H, s, 18-H), 0.98 (3 H, s, 19-H), and 6.42 (1 H, d, *J* 8 Hz, 6-H).

Acetoxylation of 3β-*Chloroandrost-5-en-17-one* (**13**).—Bromine (0.2 ml) was added to a solution of 3β-chloroandrost-5-en-17-one (**13**) (1 g) in methylene dichloride (15 ml) at −60 °C. Silver acetate (2 g) in pyridine (4 ml) was then added slowly and the mixture was allowed to attain room temperature in the dark during 24 h. The mixture was diluted with methylene dichloride and the organic solvents were washed with dil. hydrochloric acid, water, and sodium hydrogen carbonate. The solvent was evaporated and the residue was chromatographed on silica. Elution with 10% ethyl acetate–light petroleum gave 3β-*chloro*-5α,6β-*dibromoandrostan*-17-*one* (**20**) (550 mg) which crystallized from acetone as prisms, m.p. 169—170.5 °C, $[\alpha]_D$ −24° (*c* 0.3) (Found: C, 49.1; H, 6.0. $C_{19}H_{27}Br_2ClO$ requires C, 48.9; H, 5.8%); $\nu_{max.}$ 1 740 cm^{-1}; δ 0.84 (3 H, s, 18-H), 1.44 (3 H, s, 19-H), 4.56 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, 3-H), and 4.75 (1 H, m, $w_{\frac{1}{2}}$ 6 Hz, 6-H).

Similar treatment of 3β-bromoandrost-5-en-17-one (**14**) (2 g) gave 3β,5α,6β-*tribromoandrostan*-17-*one* (**21**) (1.25 g) which crystallized from ethyl acetate as prisms, m.p. 174.5 °C, $[\alpha]_D$ −25° (*c* 0.4) (Found: C, 44.9; H, 5.3. $C_{19}H_{27}Br_3O$ requires C, 44.6; H, 5.3%); $\nu_{max.}$ 1 745 cm^{-1}; δ 0.9 (3 H, s, 18-H), 1.5 (3 H, s, 19-H), 4.68 (1 H, m, $w_{\frac{1}{2}}$ 18 Hz, 3-H), and 4.78 (1 H, m, $w_{\frac{1}{2}}$ 6 Hz, 6-H).

5α,6β-*Dibromo*-3β-*methoxyandrostan*-17-*one* (**22**).—3β-Methoxyandrost-5-en-17-one (**15**) (1 g) was dissolved in chloroform (10 ml) and the solution was cooled to −60 °C. Bromine (0.2 ml) was added with swirling. The solution was diluted with chloroform, washed with cold aqueous sodium hydrogen carbonate, and dried. The solvent was evaporated to afford 5α,6β-*dibromo*-3β-*methoxyandrostan*-17-*one* (**22**) (1.1 g) which crystallized from ethyl acetate as prisms, m.p. 124—126 °C, $[\alpha]_D$ −27° (*c* 0.4) (Found: C, 52.1; H, 6.3. $C_{20}H_{30}Br_2O_2$ requires C, 52.0; H, 6.5%); $\nu_{max.}$ 1 745 cm^{-1}; δ 0.95 (3 H, s, 18-H), 1.4 (3 H, s, 19-H), 3.34 (3 H, s, OMe), 3.88 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, 3-H), and 4.82 (1 H, m, $w_{\frac{1}{2}}$ 6 Hz, 6-H).

Reaction of 5α,6β-*Dibromo*-3β-*methoxyandrostan*-17-*one* (**22**) *with Silver Acetate in Pyridine*.—Silver acetate (1 g) in pyridine (2 ml) was added to a solution of the bromo steroid (**22**) (1 g) in chloroform (10 ml) at −60 °C. The mixture was stirred and allowed to attain room temperature during 24 h. The solution was filtered and diluted with chloroform. It was washed with dilute hydrochloric acid, water, and aqueous sodium hydrogen carbonate. The solvent was evaporated to give a gum which was chromatographed on silica. Elution with 5% ethyl acetate in light petroleum gave 3β-*methoxyandrosta*-4,6-*dien*-17-*one* (**7**) (400 mg) which crystallized from acetone–ethyl acetate as plates, m.p. 154—158 °C, $[\alpha]_D$ +16° (*c* 0.3) (Found: C, 78.9; H, 9.35. $C_{20}H_{28}O_2$ requires C, 79.9; H, 9.4%); $\nu_{max.}$ 1 735, 1 645, and 1 610 cm^{-1}; $\lambda_{max.}$ 234 (20 000), 240 (22 000), and 249 nm (15 000) (Calc. 234 nm); δ 0.98 (3 H, s, 18-H), 1.02 (3 H, s, 19-H), 3.36 (3 H, s, OMe), 3.86 (1 H, m, 3-H), 5.44 (1 H, d, *J* 3 Hz, 4-H), 5.64 (1 H, d, *J* 1.5 and 10 Hz, 6-H), and 5.98 (1 H, dd, *J* 2.5 and 10 Hz, 7-H).

Acetoxylation of 3α-*Chloroandrost-5-en-17-one* (**16**).—The chloro steroid (**16**) (180 mg) in chloroform (5 ml) was treated with bromine (0.04 ml) at −60 °C. Silver acetate (400 mg) in pyridine (1 ml) was added slowly and the solution was allowed to attain room temperature during 24 h in the dark. The mixture was filtered and poured into dil. hydrochloric acid and the product was recovered in chloroform and chromatographed on silica. Elution with 10% ethyl acetate–light petroleum gave 4β-*acetoxy*-3α-*chloroandrost*-5-*en*-17-*one* (**17**) (72 mg) which crystallized from acetone as prisms, m.p. 154—156 °C, $[\alpha]_D$ −99° (*c* 0.2) (Found: C, 69.1; H, 8.1. $C_{21}H_{29}ClO_3$ requires C, 69.12; H, 8.0%); $\nu_{max.}$ 1 750, 1 665 cm^{-1}; δ 0.89 (3 H, s, 18-H), 1.15 (3 H, s, 19-H), 2.05 (3 H, s, OAc), 4.23 (1 H, q, *J* 2.6 and 5.5 Hz, 3-H), 5.27 (1 H, s, 4-H), and 5.88 (1 H, dd, *J* 2.2 and 5.2 Hz, 6-H).

3β,4β-*Dihydroxy*-B-*norandrost*-5-*en*-17-*one* (**24**).—3β-Hydroxy-B-norandrost-5-en-17-one (**23**) (2 g) in chloroform (20 ml) was treated with bromine (1.16 g) at −60 °C. Dry silver acetate (2.44 g) in pyridine (10 ml) was added and the reaction mixture was allowed to warm to room temperature during 4 h, then filtered, and the product recovered in chloroform. The solvent was evaporated off and the residue taken up in methanol and treated with aqueous saturated sodium hydroxide (2 ml) at room temperature for 2 h. Acetic acid (2 ml) was added and the solvent was removed under reduced pressure. The steroid was recovered in ethyl acetate and chromatographed on silica to afford 3β,4β-*dihydroxy*-B-*norandrost*-5-*en*-17-*one* (**24**) (600 mg) which crystallized from diethyl ether as needles, m.p. 180—185 °C, $[\alpha]_D$ −66° (*c* 0.6) (Found: C, 74.5; H, 8.9. $C_{18}H_{26}O_3$ requires C, 74.4; H, 9.0%); $\nu_{max.}$ 3 475, 1 735, and 1 620 cm^{-1}; δ 0.77 (3 H, s, 18-H), 1.07 (3 H, s, 19-H), 3.5 (1 H, m, 3-H), 4.37 (1 H, d, *J* 3 Hz, 4-H), and 5.83 (1 H, s, 6-H). The *diacetate*, prepared with acetic anhydride in pyridine, crystallized from light petroleum as needles, m.p. 159—160 °C; $[\alpha]_D$ 102.5° (*c* 0.6) (Found: C, 70.7; H, 8.1. $C_{22}H_{30}O_5$ requires C, 70.6; H, 8.1%), $\nu_{max.}$ 1 730 cm^{-1}; δ 0.9 (3 H, s, 18-H), 1.03 (3 H, s, 19-H), 2.03 (6 H, s, OAc), 4.77 (1 H, d of t, *J* 4 and 12 Hz, 3-H), 5.7 (1 H, d, *J* 4 Hz, 4-H), and 5.9 (1 H, s, 6-H).

3β-*Hydroxy*-4β-*propionyloxyandrost*-5-*en*-17-*one* (**19**).—3β-Hydroxyandrost-5-en-17-one (1 g) was treated with bromine (0.2 ml) and silver acetate (2 g) in pyridine (4 ml) as above to afford 3β-*hydroxy*-4β-*propionyloxyandrost*-5-*en*-17-*one* (**19**) (500 mg) which crystallized from ethyl acetate–light petroleum as prisms, m.p. 155—158 °C, $[\alpha]_D$ −65° (*c* 0.3) (Found: C, 73.2; H, 8.8. $C_{22}H_{32}O_4$ requires C, 73.3; H, 8.9%); $\nu_{max.}$ 3 480, 1 745, 1 730, and 1 660 cm^{-1}; δ 0.88 (3 H, s, 18-H), 0.92 (3 H, t, *J* 7 Hz), 1.14 (3 H, s, 19-H), 3.6 (1 H, m, $w_{\frac{1}{2}}$ 14 Hz, 3-H), 5.4 (1 H, d, *J* 4 Hz, 4-H), and 5.84 (1 H, m, $w_{\frac{1}{2}}$ 6 Hz, 6-H).

Reaction of Dehydroisoandrosterone with Silver Trifluoroacetate.—3β-Hydroxyandrost-5-en-17-one (**1**) (1 g) in chloroform (10 ml) was cooled to −60 °C and bromine (0.2 ml) was added. Dry silver trifluoroacetate (2 g) in pyridine (5 ml) was then added with stirring. The mixture was allowed to warm to room temperature in the dark during 24 h. The mixture was filtered and poured into dil. hydrochloric acid. The steroids

were recovered in chloroform and chromatographed on silica. Elution with 25% ethyl acetate–light petroleum gave 3β,4β-dihydroxyandrost-5-en-17-one (**9**) (300 mg) which was identified by its i.r. and n.m.r. spectra.

Variation of the Metal Ions.—A series of flasks each containing 3β-hydroxyandrost-5-en-17-one (250 mg) in chloroform (5 ml) were cooled to −60 °C. Bromine (0.05 ml) was added to each followed by a suspension of the metal acetate in pyridine (2 ml). The reaction mixtures were examined by t.l.c. for the presence of 4β-acetoxy-3β-hydroxyandrost-5-en-17-one during 2 days. Silver acetate (300 mg) was used as a control. The acetates investigated were cadmium acetate (500 mg), copper acetate (400 mg), manganese acetate (500 mg), chromium(III) acetate (500 mg), lead acetate (750 mg), nickel acetate (500 mg), iron acetate (500 mg), cobalt acetate (500 mg). Only the lead acetate showed a trace of the 4β-acetate.

Variation in Base.—The reaction was repeated with the addition of triethylamine (1 ml), DBU (1.5 g), and *N,N*-dimethylaminopyridine (1.2 g) to the silver acetate–pyridine mixture (4 ml). There was an increase in yield, from 62% in the control to 73% in the case of DBU.

Acetoxylation of [4β,17α-$^2H_2$]-17β-*Acetoxy*-3β-*hydroxyandrost*-5-*ene* (**26**).—The alcohol (125 mg) in chloroform (5 ml) was treated with bromine (0.1 ml) at −60 °C. Silver acetate (400 mg) in pyridine (1 ml) was added in two portions and the mixture was stirred in the dark at room temperature for 24 h. An excess of dil. hydrochloric acid was added and the steroids were extracted with chloroform. The solvent was evaporated and the residue was chromatographed on silica. Elution with 25% ethyl acetate–light petroleum gave [17α-^{2}H]-4β,17β-*diacetoxy*-3β-*hydroxyandrost*-5-*ene* (**27**) (90 mg) which crystallized from acetone–light petroleum as plates, m.p. 125—128 °C, $[\alpha]_D$ −119° (*c* 0.3) (Found: C, 70.8; H, 8.8. $C_{23}H_{34}O_5$ requires C, 70.7; H, 8.8%); $\nu_{max.}$ 3 530, 3 490, 3 380, 1 740, and 1 700 cm^{-1}; δ 0.79 (3 H, s, 18-H), 1.09 (3 H, s, 19-H), 2.03 (3 H, s, OAc), 2.07 (3 H, s, OAc), 3.64 (1 H, m, 3-H), 4.56 (1 H, t, *J* 8 Hz, 17-H), 5.37 (1 H, q, *J* 3.4 and 1 Hz, 4-H), and 5.82 (1 H, q, *J* 5 and 2 Hz, 6-H). The deuteriated sample showed a ^{2}H n.m.r. signal at δ 4.58.

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