

## Epoxidation of 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -androst-6-en-17-one

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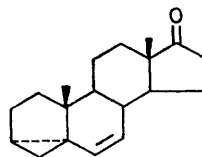
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Treatment of 3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-6-en-17-one with *m*-chloroperbenzoic acid affords 3 $\beta$ ,7 $\alpha$ -dihydroxy-androst-5-en-17-one, 6 $\beta$ ,7 $\alpha$ -dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-17-one, their 3 $\beta$ - and 6 $\beta$ -*m*-chlorobenzoates, and the 6 $\beta$ -methoxy-7 $\alpha$ -hydroxy-cyclo-steroid. The unstable 6 $\alpha$ ,7 $\alpha$ -epoxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-17-one was obtained by epoxidation in ether. A similar range of solvent-dependent products was obtained in the cholestane series.

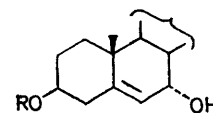
THE participation of a cyclopropane ring in developing carbocation centres has been well documented. The solvolysis of cyclo-steroid toluene-*p*-sulphonates clearly demonstrates such participation.<sup>1</sup> Similar effects would be expected in the reactions of a cyclo-steroid epoxide such as 6 $\alpha$ ,7 $\alpha$ -epoxy-3 $\alpha$ ,5-cycloandrost-17-one (8). We record here some attempts to synthesise this compound by epoxidation of 3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-6-en-17-one (1). The products from these reactions reveal the ready participation of the cyclopropane ring in the epoxidation of the double bond.

3 $\beta$ -*p*-Tolylsulphonyloxyandrost-5-en-17-one<sup>2</sup> was converted into 6 $\beta$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-17-one, which was then dehydrated over alumina in refluxing xylene to afford 3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-6-en-17-one (1)<sup>3</sup> in 28% overall yield from dehydroisoandrosterone. This route gave a better yield than the direct method of preparation.<sup>4</sup> The reaction of 3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-6-en-17-one (1) with *m*-chloroperbenzoic acid in 'solvent grade' dichloromethane afforded a mixture of five products which were separated by column chromatography on alumina followed by preparative layer chromatography on silica. The most polar compound, C<sub>19</sub>H<sub>28</sub>O<sub>3</sub> (17% yield), showed hydroxylic (3400 cm<sup>-1</sup>) and olefinic (750 cm<sup>-1</sup>) i.r. absorption. In the n.m.r. spectrum the cyclopropane proton resonances were absent. The olefinic proton resonances [ $\tau$  4.35

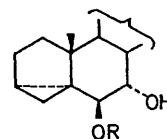
(*J* 5 Hz)] showed coupling to one of the CH·OH resonances [ $\tau$  6.02 (*J* 2 and 5 Hz)], the additional coupling



(1)



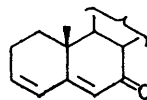
(2) R = H

(4) R = CO·C<sub>6</sub>H<sub>4</sub>Cl - *m*

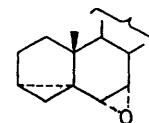
(3) R = H

(5) R = CO·C<sub>6</sub>H<sub>4</sub>Cl - *m*

(7) R = Me



(6)



(8)

in this latter resonance suggesting an axial-equatorial relationship with another proton. This was consistent

<sup>2</sup> A. Romeo and R. Villotti, *Ann. Chim. (Italy)*, 1957, **47**, 684 (*Chem. Abs.*, 1958, **52**, 1194).

<sup>4</sup> T. Nambara and M. Kato, *Chem. and Pharm. Bull. (Japan)*, 1965, **13**, 1435.

<sup>1</sup> For reviews see (a) D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms', Elsevier, London, 1968, p. 236; (b) J. Heywood-Farmer, *Chem. Rev.*, 1974, **74**, 315.

<sup>3</sup> A. Butenandt and L. A. Suranyi, *Chem. Ber.*, 1942, **75**, 591.

with the presence of a 7 $\alpha$ -hydroxy-5-ene. The second CH·OH resonance was a broad multiplet,  $\tau$  6.45, characteristic of a 3 $\alpha$ -proton. The diol was therefore 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one (2), and was identical with an authentic sample<sup>5</sup> prepared by treating 3 $\beta$ -benzoyloxyandrost-5-en-17-one with *t*-butyl perbenzoate in acetic acid containing a copper catalyst<sup>6</sup> and then hydrolysing the resultant 7 $\alpha$ -acetoxy-3 $\beta$ -benzoyloxyandrost-5-en-17-one.

The second, isomeric product (42% yield) retained the cyclopropane ring [ $\tau$  9.87—9.43 (2H, m);  $\nu_{\max}$  3050 cm<sup>-1</sup>] and possessed hydroxy-absorption ( $\nu_{\max}$  3600 and 3450 cm<sup>-1</sup>) in the i.r. The alcohol formed a diacetate, the n.m.r. spectrum of which contained a doublet,  $\tau$  5.44 (*J* 3 Hz) coupled to a quartet,  $\tau$  5.09 (*J* 2 and 3 Hz). When the diol was acetylated, the change in the 19-H resonance ( $\Delta$  0.02 p.p.m.) was in agreement with the value calculated (0.05 p.p.m.) by utilizing the modified Zurcher's constant<sup>7</sup> for 6 $\beta$ ,7 $\alpha$ -dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-17-one (3). An authentic sample of the diol was prepared by heating a solution of 7 $\alpha$ -hydroxy-3 $\beta$ -*p*-tolylsulphonyloxyandrost-5-en-17-one in aqueous acetone with potassium acetate. The third product, C<sub>26</sub>H<sub>31</sub>ClO<sub>4</sub> (3% yield), had spectral data consistent with its identification as 3 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxyandrost-5-en-17-one (4). On oxidation with 8N-chromium trioxide reagent, it afforded an  $\alpha\beta$ -unsaturated ketone [ $\lambda_{\max}$  237 nm ( $\epsilon$  9430)]; thus the free hydroxy-group was located at C-7.<sup>8</sup> Treatment of the diol (2) with *m*-chlorobenzoyl chloride in pyridine gave an identical mono-*m*-chlorobenzoate. Spectral analysis of the fourth product, C<sub>26</sub>H<sub>31</sub>ClO<sub>4</sub> (11% yield), indicated that it was the mono-*m*-chlorobenzoate (5) of the diol (3), into which it was indeed converted by alkaline hydrolysis. The presence of a doublet [ $\tau$  5.32 (*J* 3 Hz)] in the n.m.r. spectrum suggested that the ester grouping was at C-6. This was substantiated by oxidation with *t*-butyl chromate which led to a *m*-chlorobenzoyloxy-ketone whose n.m.r. spectrum showed a sharp one-proton singlet,  $\tau$  4.31, assigned to the C-6 proton. On alkaline hydrolysis this oxidation product gave a ketol which, on treatment with acid, afforded the known dienedione (6).<sup>9</sup> The authentic sample of the dienedione (6) was prepared by oxidation of androsta-3,5-dien-17-one with *t*-butyl chromate.<sup>10</sup> The fifth product, C<sub>20</sub>H<sub>30</sub>O<sub>3</sub>, isolated as an oil (15% yield), was tentatively identified as the 6 $\beta$ -methoxy-derivative (7). The n.m.r. spectrum showed resonances due to the cyclopropane ring protons [ $\tau$  9.72—9.53 (2H, m)], the methoxy-group ( $\tau$  6.58), and the C-6 and -7 protons [ $\tau$  7.21 (d, *J* 3 Hz) and 6.13 (t, *J* 3 Hz), respectively]. The compound is presumed

<sup>5</sup> R. M. Dodson, R. T. Nicholson, and R. D. Muir, *J. Amer. Chem. Soc.*, 1959, **81**, 6295.

<sup>6</sup> A. L. J. Beckwith and G. W. Evans, *Proc. Chem. Soc.*, 1962, 63.

<sup>7</sup> J. E. Bridgeman, P. C. Cherry, A. S. Clegg, J. M. Evans, Sir Ewart Jones, A. Kasal, V. Kumar, G. D. Meakins, Y. Morisawa, E. E. Richards, and P. D. Woodgate, *J. Chem. Soc. (C)*, 1970, 250.

<sup>8</sup> A. I. Scott, 'Interpretation of the Ultraviolet Spectra of Natural Products,' Pergamon, Oxford, 1964, p. 400.

to arise from methanol present as an impurity in the solvent.

A similar range of products was obtained on epoxidation of 3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholest-6-ene<sup>11</sup> in dichloromethane. The ratio of the products depended on the purity of the dichloromethane. In the presence of methanol, the major product was 7 $\alpha$ -hydroxy-6 $\beta$ -methoxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestane whereas with a purified solvent the major product was 6 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestane. 3 $\beta$ -(*m*-Chlorobenzoyloxy)-7 $\alpha$ -hydroxycholest-5-ene and 6 $\beta$ ,7 $\alpha$ -dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestane were minor products.

When the epoxidation of 3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-6-en-17-one was carried out at -78° in the presence of anhydrous sodium carbonate, 6 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androst-17-one (5) was the major product. When the epoxidation was carried out in diethyl ether with *m*-chloroperbenzoic acid the desired epoxide (8) was obtained. Its n.m.r. spectrum showed resonances at  $\tau$  7.11 and 6.66 (d, *J* 4.5 Hz) which were assigned to the C-6 and 7 protons. The epoxide was assigned the ' $\alpha$ ' configuration on the basis of the known<sup>12</sup> mode of attack on C-6 olefins from the ' $\alpha$ ' face. The epoxide decomposed on attempted purification. Thus on sublimation it gave a triene which was tentatively identified as androsta-3,5,7-trien-17-one [ $\lambda_{\max}$  297 ( $\epsilon$  6155), 308 (6830), and 322 nm (4530)]. Although not all the products are necessarily derived *via* the epoxide, nevertheless the range of products obtained during this epoxidation suggests that the epoxide is readily cleaved and that the adjacent cyclopropane ring participates in stabilizing the incipient carbocation. The individual products are then determined by the nucleophilic components of the medium with a preference for attack at C-6 as is found in the *i*-steroid system.

#### EXPERIMENTAL

General experimental details have been described previously.<sup>13</sup>

3 $\alpha$ ,5-Cycloandrost-6-en-17-one (1) had m.p. 136—137°, [ $\alpha$ ]<sub>D</sub><sup>20</sup> +47° (*c* 3.4) {lit.,<sup>3</sup> 137—138°, [ $\alpha$ ]<sub>D</sub> +13° (in MeOH)} (Found: C, 84.9; H, 10.0. Calc. for C<sub>19</sub>H<sub>26</sub>O: C, 84.4; H, 9.7%),  $\nu_{\max}$  1750, 1642, and 742 cm<sup>-1</sup>,  $\tau$  9.70—9.40 (1H, m), 9.06 (6H, s, 18- and 19-H), 4.76 (1H, dd, *J* 2 and 10 Hz), and 4.47 (1H, dd, *J* 1 and 10 Hz).

*Epoxidation of 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -androst-6-en-17-one (1).*—(a) *m*-Chloroperbenzoic acid (2.5 g) in dichloromethane (30 ml) was added slowly with stirring to a solution of 3 $\alpha$ ,5-cycloandrost-6-en-17-one (3.6 g) in dichloromethane (50 ml). T.l.c. indicated that the reaction was essentially complete after 5 min. The solution was treated with aqueous 10% sodium sulphite (5 ml) and then washed with

<sup>9</sup> J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, 1948, **31**, 629.

<sup>10</sup> K. Yasuda and H. Mori, *Chem. and Pharm. Bull. (Japan)*, 1967, **15**, 179.

<sup>11</sup> B. Riegel, G. P. Hager, and B. L. Zenitz, *J. Amer. Chem. Soc.*, 1946, **68**, 2562.

<sup>12</sup> D. R. James, R. W. Rees, and C. W. Shoppee, *J. Chem. Soc.*, 1955, 1370; S. J. Angyal and R. J. Young, *J. Amer. Chem. Soc.*, 1959, **81**, 5251.

<sup>13</sup> J. R. Hanson and T. D. Organ, *J. Chem. Soc. (C)*, 1970, 513.

saturated aqueous sodium hydrogen carbonate, water, and saturated aqueous sodium chloride. The solution was dried and evaporated to give a gum which was purified first by chromatography on an alumina column and then by preparative layer chromatography on silica with *n*-hexane-ethyl acetate (1 : 1) as the mobile phase to afford the following fractions in decreasing order of polarity: (i) 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one (2) (690 mg) which crystallized from chloroform-ether as needles, m.p. 177—179.5°,  $[\alpha]_D^{19}$  -73° (*c* 1.4) (lit.,<sup>5</sup> 180—182.5°;  $[\alpha]_D$  -70.7°) (Found: C, 70.8; H, 9.4%; *m/e*, 304. Calc. for C<sub>19</sub>H<sub>28</sub>O<sub>3</sub>.H<sub>2</sub>O: C, 70.8; H, 9.4%. Calc. for C<sub>19</sub>H<sub>28</sub>O<sub>3</sub>: *M*, 304),  $\nu_{\max}$  3400, 1720, 1025, and 1050 cm<sup>-1</sup>,  $\tau$  9.10 (3H, s, 18-H), 8.98 (3H, s, 19-H), 6.45 (1H, m, *W*<sub>3</sub> 22 Hz, 3-H), 6.02 (1H, dd, *J* 2 and 5 Hz, 7-H), and 4.35 (1H, d, *J* 5 Hz, 6-H); (ii) 6 $\beta$ ,7 $\alpha$ -dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one (3) (1.7 g) which sublimed at *ca.* 130° (0.5 mmHg); m.p. 172—174°,  $[\alpha]_D^{20}$  +95° (*c* 3.0) (Found: C, 74.7; H, 9.3%; *m/e*, 304. C<sub>19</sub>H<sub>28</sub>O<sub>3</sub> requires C, 75.0; H, 9.3%; *M*, 304),  $\nu_{\max}$  3600, 3450, 3050, and 1720 cm<sup>-1</sup>,  $\tau$  9.87—9.43 (2H, m, cyclopropyl H), 9.07 (3H, s, 18-H), 8.93 (3H, s, 19-H), 6.80 (1H, d, *J* 3 Hz, 6-H), and 6.15br (1H, t, 7-H) [the diacetate, prepared with acetic anhydride in pyridine, crystallized from ether as needles, m.p. 152.5—153°,  $[\alpha]_D^{18.5}$  +130° (*c* 2.76) (Found: C, 71.0; H, 8.5%; *m/e*, 388. C<sub>23</sub>H<sub>32</sub>O<sub>5</sub> requires C, 71.1; H, 8.3%; *M*, 388),  $\nu_{\max}$  3040, 1750, 1740, 1250, 1225, 1140, 1110, and 1030 cm<sup>-1</sup>,  $\tau$  9.66—9.46 (2H, cyclopropyl H), 9.05 (3H, s, 18-H), 8.95 (3H, s, 19-H), 7.94 and 7.91 (3H, s, each OAc), 5.44 (1H, d, *J* 3 Hz, 6-H), and 5.09 (1H, dd, *J* 2 and 3 Hz, 7-H)]; (iii) 7 $\alpha$ -hydroxy-6 $\beta$ -methoxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one (7) (50 mg), obtained as a gum, *m/e* 318 (C<sub>20</sub>H<sub>30</sub>O<sub>3</sub>),  $\nu_{\max}$  3600, 3420, 3040, 1730, and 1080 cm<sup>-1</sup>,  $\tau$  9.72—9.53 (2H, m, cyclopropyl H), 9.07 (3H, s, 18-H), 8.97 (3H, s, 19-H), 7.21 (1H, d, *J* 3 Hz, 6-H), and 6.58 (3H, s, OCH<sub>3</sub>); (iv) 3 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxyandrost-5-en-17-one (4) (650 mg) which crystallized from ether as needles, m.p. 190—194°,  $[\alpha]_D^{20}$  -21° (*c* 1.3) (Found: *M*<sup>+</sup>, 442.1914. C<sub>26</sub>H<sub>31</sub><sup>35</sup>ClO<sub>4</sub> requires *M*, 442.1911),  $\nu_{\max}$  3520, 3400, 1730, 750, and 735 cm<sup>-1</sup>,  $\tau$  9.10 (3H, s, 18-H), 8.92 (3H, s, 19-H), 6.00 (1H, dd, *J* 1 and 5 Hz, 7-H), 5.10 (1H, m, *W*<sub>3</sub> 18 Hz, 3-H), 4.27 (1H, d, *J* 5 Hz, 6-H), and 2.3 (4H, m, ArH) [treatment of 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one (200 mg) with *m*-chlorobenzoyl chloride (115 mg) in pyridine (4.5 ml) overnight afforded the same 3 $\beta$ -monochlorobenzoate (*i.r.* and *n.m.r.* spectrum)]; (v) 6 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one (5) (884 mg), which crystallized from *n*-hexane as plates, m.p. 137—139.5°,  $[\alpha]_D^{21}$  +59° (*c* 1.2) (Found: C, 70.7; H, 7.2; Cl, 8.0%; *m/e*, 442. C<sub>26</sub>H<sub>31</sub>ClO<sub>4</sub> requires C, 70.5; H, 7.05; Cl, 8.0%; *M*, 442),  $\nu_{\max}$  3620, 3420, 3080, 3060, 1725, 1700, 1575, 1080, 750, and 730 cm<sup>-1</sup>,  $\tau$  9.82—9.32 (3H, cyclopropyl H), 9.06 (3H, s, 18-H), 8.83 (3H, s, 19-H), 6.10 (1H, d, *J* 3 Hz, 7-H), 5.52 (1H, d, *J* 3 Hz, 6-H), and 2.40 (4H, m, ArH).

(b) *In the presence of sodium carbonate.* 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -androst-6-en-17-one (27 mg) in dichloromethane (2 ml) over an excess of anhydrous sodium carbonate, was treated with *m*-chloroperbenzoic acid (18 mg) in dichloromethane (1 ml) for 20 min at -78°. T.l.c. indicated that the major product was 6 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one, which was recovered as before and identified by its *i.r.* spectrum.

(c) *In diethyl ether.* 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -androst-6-en-17-one (600 mg) in dry ether (50 ml) was treated with *m*-chloroperbenzoic acid (750 mg) at 0° for 30 min. The solution

was diluted with ether and rapidly washed with cold aqueous iron(II) sulphate, water, aqueous sodium hydrogen carbonate, and water, then dried and evaporated *in vacuo*. The resulting 6 $\alpha$ ,7 $\alpha$ -epoxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one (8) (210 mg) crystallized from dry ether-light petroleum as needles, m.p. 160—163° (Found: C, 79.6; H, 9.1%; *m/e*, 286.1938. C<sub>19</sub>H<sub>26</sub>O<sub>2</sub> requires C, 79.7; H, 9.15%; *M*, 286.1933),  $\nu_{\max}$  3060, 1730, 1020, and 860 cm<sup>-1</sup>,  $\tau$  9.60 (3H, m, cyclopropyl H), 9.09 (3H, s, 18-H), 9.05 (3H, s, 19-H), 7.11 (1H, d, *J* 4.5 Hz, 6-H), and 6.77 (1H, d, *J* 4.5 Hz, 7-H). The product did not give a reproducible rotation value in chloroform or methanol and t.l.c. indicated that it decomposed in these solvents. Sublimation at 140° (0.5 mmHg) gave a mixture containing a triene, m.p. 100—120°,  $\nu_{\max}$  1730, 1660, and 1600 cm<sup>-1</sup>,  $\tau$  9.06 (3H, s, 18-H), 9.02 (3H, s, 19-H), and 4.34—3.92 (4H, m, 3-, 4-, 6-, and 7-H),  $\lambda_{\max}$  277 ( $\epsilon$  6160), 308 (6830), and 322 nm (4550).

3 $\beta$ ,7 $\alpha$ -Dihydroxyandrost-5-en-17-one.—*t*-Butyl perbenzoate (4.5 ml) in glacial acetic acid (5 ml) was added dropwise over 15 min with stirring to a solution of 3 $\beta$ -benzoyloxyandrost-5-en-17-one<sup>14</sup> (3.9 g) in glacial acetic acid (15 ml) containing copper(I) bromide (0.3 g) at 120° under nitrogen. The solution was heated for a further 10 min, cooled, and diluted with benzene. This solution was washed with water, saturated aqueous sodium hydrogen carbonate, water, and saturated sodium chloride. The solvent was evaporated off to leave a waxy solid which was chromatographed on alumina to afford the starting material (1.3 g) and a mixture of the 7 $\alpha$ - and 7 $\beta$ -acetoxo-3 $\beta$ -benzoyloxyandrost-5-en-17-one. The latter was heated under reflux with methanolic 2*N*-potassium hydroxide (10 ml) for 5 h. The solution was concentrated and diluted with water, and the product (750 mg) was recovered in ether. Preparative layer chromatography (five developments in *n*-hexane-ethyl acetate, 1 : 1) afforded a band which was split into three fractions to afford (i) 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one (80 mg), identical (*i.r.* and *n.m.r.*) with the product described above, (ii) (320 mg) 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one contaminated with a trace of 3 $\beta$ ,7 $\beta$ -dihydroxyandrost-5-en-17-one, and (iii) 3 $\beta$ ,7 $\beta$ -dihydroxyandrost-5-en-17-one contaminated with a trace of 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one (*t.l.c.*).

6 $\beta$ ,7 $\alpha$ -Dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one.— 3 $\beta$ ,7 $\alpha$ -Dihydroxyandrost-5-en-17-one (150 mg) in dry pyridine (0.6 ml) was treated with toluene-*p*-sulphonyl chloride (105 mg) in dry pyridine (0.6 ml) for 6 days at 20°. The solution was poured into ice-water and the product was recovered in ether to afford the 3-monotoluene-*p*-sulphonate,  $\tau$  9.18 (3H, s, 18-H), 9.06 (3H, s, 19-H), 7.59 (3H, s, ArMe), 6.13 (1H, d,d, *J* 2 and 5 Hz, 7-H), 5.76 (1H, m, 3-H), 4.68 (1H, d, *J* 5 Hz, 6-H), and 2.50 (4H, m, ArH), which was not further purified. The crude toluene-*p*-sulphonate was heated under reflux for 6 h with potassium acetate (37 mg) in 50% aqueous acetone (8 ml). The solution was poured into water and the organic product recovered in dichloromethane. The product was purified by preparative layer chromatography on silica to afford 6 $\beta$ ,7 $\alpha$ -dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstan-17-one (30 mg), identical (*t.l.c.* and *n.m.r.*) with the material described above, and 3 $\beta$ ,7 $\alpha$ -dihydroxyandrost-5-en-17-one (50 mg), identified by *t.l.c.* and *n.m.r.*

3 $\beta$ -(*m*-Chlorobenzoyloxy)androst-5-ene-7,17-dione.— 3 $\beta$ -(*m*-Chlorobenzoyloxy)-7 $\alpha$ -hydroxyandrost-5-en-17-one (44 mg) in acetone (3.5 ml) was treated with 8*N*-chromium trioxide

<sup>14</sup> N. H. Callow and R. K. Callow, *Biochem. J.*, 1940, **34**, 276.

reagent (0.1 ml) for 30 min. The solution was poured into water and the product recovered in ether to afford the 7,17-dione, which crystallized from acetone as prisms, m.p. 237—240°,  $[\alpha]_D^{20} - 172^\circ$  ( $c$  0.3) (Found:  $m/e$ , 440.1745).  $C_{26}H_{29}^{35}ClO_4$  requires  $M$ , 440.1755,  $\nu_{max}$ , 1740, 1720, 1675, 750, and 740  $cm^{-1}$ ,  $\lambda_{max}$ , 237 nm ( $\epsilon$  9430),  $\tau$  9.08 (3H, s, 18-H), 8.69 (3H, s, 19-H), 5.02 (1H, m, 3-H), 4.18 (1H, s, 6-H), and 2.20 (4H, m, ArH).

**Hydrolysis of 6 $\beta$ -(*m*-Chlorobenzoyloxy)-7 $\alpha$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-17-one.**—The monochlorobenzoate (180 mg) in methanolic 2*N*-potassium hydroxide (25 ml) was heated under reflux for 4.5 h. The solution was concentrated, then diluted with water, and the product was recovered in ether and purified by preparative layer chromatography to afford 6 $\beta$ ,7 $\alpha$ -dihydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-17-one (40 mg), m.p. 172—174°, identified by its i.r., n.m.r., and mass spectra.

**6 $\beta$ -(*m*-Chlorobenzoyloxy)-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-7,17-dione.**—A solution of 6 $\beta$ -(*m*-chlorobenzoyloxy)-7 $\alpha$ -hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-17-one (3.2 g) in benzene (20 ml), acetic acid (1 ml), and acetic anhydride (1 ml) was treated with *t*-butyl chromate [from chromium trioxide (2.76 g)] in benzene (50 ml) at 20° for 2 days. The solution was poured into water and the organic product recovered in benzene and chromatographed on alumina. Elution with benzene gave the 7,17-dione (300 mg), m.p. 167—169°,  $[\alpha]_D^{20} + 104^\circ$  ( $c$  1.03) (Found: C, 71.0; H, 6.8%;  $m/e$ , 440).  $C_{26}H_{29}ClO_4$  requires C, 70.8; H, 6.6%;  $M$ , 440,  $\nu_{max}$ , 1730 and 1250  $cm^{-1}$ ,  $\tau$  9.50 (3H, m, cyclopropyl H), 9.06 (3H, s, 18-H), 8.69 (3H, s, 19-H), 4.51 (1H, s, 6-H), and 2.20 (4H, m, ArH).

**6 $\beta$ -Hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-7,17-dione.**—6 $\beta$ -(*m*-Chlorobenzoyloxy)-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-7,17-dione (180 mg) was heated under reflux in methanol (10 ml) containing potassium hydroxide (100 mg) for 2 h. The solution was concentrated, water was added, and the product was recovered in ether to give the hydroxy-dione (100 mg) as a gum,  $[\alpha]_D^{20} + 4^\circ$  ( $c$  1.27) (Found: C, 75.5; H, 8.85).  $C_{19}H_{26}O_3$  requires C, 75.5; H, 8.7%,  $\nu_{max}$ , 3475, 1740, 1695, and 1090  $cm^{-1}$ ,  $\tau$  9.50 (3H, m, cyclopropyl H), 9.08 (3H, s, 18-H), 8.86 (3H, s, 19-H), 7.83 (1H, s, OH, exchanged with D<sub>2</sub>O), and 6.10 (1H, s, 6-H).

**Action of Sulphuric Acid on 6 $\beta$ -Hydroxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -androstane-7,17-dione.**—A solution of the steroid (80 mg) in acetone (4 ml) was heated under reflux with sulphuric acid (1 ml) for 4 h. Water was added and the product was recovered in ether. Androsta-3,5-diene-7,17-dione (26 mg) crystallized from aqueous acetone as needles, m.p. 167—169°, identical with the sample described below.

**Androsta-3,5-diene-7,17-dione.**—A solution of androsta-3,5-diene-17-one<sup>15</sup> (1.25 g) in carbon tetrachloride (50 ml) was heated under reflux with *t*-butyl chromate [from chromium trioxide (1.53 g)] in carbon tetrachloride (20 ml)

and acetic anhydride (1.5 ml) for 8 h. Oxalic acid (2 g) and hot water were added and the solution was then stirred for 1 h. The solution was extracted with ether and the extract was washed with water, aqueous sodium hydroxide, and water, dried, and evaporated to give androsta-3,5-diene-7,17-dione (330 mg), which crystallized from aqueous acetone as needles, m.p. 168—170°,  $[\alpha]_D^{20} - 301^\circ$  ( $c$  1.75) (lit.,<sup>9</sup> 164°;  $[\alpha]_D - 327^\circ$ ),  $\nu_{max}$ , 1742, 1654, 1622, 1592, and 809  $cm^{-1}$ ,  $\tau$  9.06 (3H, s, 18-H), 8.84 (3H, s, 19-H), 4.36 (1H, s, 6-H), and 3.85 (2H, s, 3- and 4-H).

**Reaction of 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -cholest-6-ene with *m*-Chloroperbenzoic Acid.**—*m*-Chloroperbenzoic acid (1.8 g) in dichloromethane (25 ml) was added with stirring to a solution of the steroid (3.6 g)<sup>11</sup> in dichloromethane (25 ml). After 10 min, the solution was worked up as described above to afford 6 $\beta$ -(*m*-chlorobenzoyloxy)-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-7 $\alpha$ -ol (2.5 g), which crystallized from acetone as plates, m.p. 78—84°,  $[\alpha]_D^{20} + 34^\circ$  ( $c$  2.5) (Found: C, 74.9; H, 8.8).  $C_{28}H_{40}ClO_3$  requires C, 75.4; H, 9.1%,  $\nu_{max}$ , 3485, 1725, 1570, 1260, 1130, and 750  $cm^{-1}$ ,  $\tau$  9.5 (3H, m, cyclopropyl H), 9.22 (6H, d,  $J$  5 Hz, 26- and 27-H), 9.10 (3H, d,  $J$  5 Hz, 21-H), 9.08 (3H, s, 18-H), 8.86 (3H, s, 19-H), 6.21br (1H, s,  $W_{\frac{1}{2}}$  6 Hz, 7-H), 5.36 (1H, d,  $J$  3 Hz, 6-H), and 2.20 (4H, m, Ar-H). The following minor products were obtained by preparative layer chromatography: (i) 3 $\beta$ -(*m*-chlorobenzoyloxy)cholest-5-en-7 $\alpha$ -ol, which crystallized from ether-hexane as plates, m.p. 149—154°,  $\nu_{max}$ , 3540, 1720, 1120, and 740  $cm^{-1}$ ,  $\tau$  9.21 (6H, d,  $J$  5 Hz, 26- and 27-H), 9.06 (3H, d,  $J$  5 Hz, 21-H), 9.05 (3H, s, 18-H), 8.92 (3H, s, 19-H), 6.22br (1H, d,  $J$  5 Hz, 7-H), 5.06 (1H, m, 3-H), 4.30 (1H, d,  $J$  5 Hz, 5-H), and 2.20 (4H, m, ArH); (ii) 6 $\beta$ -methoxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-7 $\alpha$ -ol, which crystallized from acetone as needles, m.p. 79—80°,  $[\alpha]_D^{20} - 62^\circ$  ( $c$  0.90) (Found: C, 80.6; H, 11.6%;  $m/e$ , 416).  $C_{28}H_{48}O_2$  requires C, 80.7; H, 11.6%;  $M$ , 416,  $\nu_{max}$ , 3600, 3040, and 1080  $cm^{-1}$ ,  $\tau$  9.50 (3H, m, cyclopropyl H), 9.20 (6H, d,  $J$  5 Hz, 26- and 27-H), 9.07 (3H, d,  $J$  5 Hz, 21-H; 3H, s, 18-H), 8.94 (3H, s, 19-H), 7.12 (1H, d,  $J$  3 Hz, 6-H), and 6.75 (4H, s and m, OCH<sub>3</sub> and 7-H); (iii) 3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-6 $\beta$ ,7 $\alpha$ -diol, obtained as a gum,  $\nu_{max}$ , 3615, 3440, 3060, and 1020  $cm^{-1}$ ,  $\tau$  9.55 (3H, m, cyclopropyl H), 9.20 (6H, d,  $J$  5 Hz, 26- and 27-H), 9.07 (3H, d,  $J$  5 Hz, 21-H; 3H, s, 18-H), 8.94 (3H, s, 19-H), 6.80 (1H, d,  $J$  3 Hz, 6-H), and 6.25 (1H, q,  $J$  3 and 4 Hz, 7-H). When the reaction was conducted in dichloromethane containing methanol, 6 $\beta$ -methoxy-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-7 $\alpha$ -ol was the major product. In benzene solution, 6 $\beta$ -(*m*-chlorobenzoyloxy)-3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-7 $\alpha$ -ol was the major product.

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<sup>15</sup> W. C. J. Ross, *J. Chem. Soc.*, 1945, 25.