864. 4 : 4-*Dimethylsteroids. Part II.*[1] *Some Androstane and Pregnane Derivatives.*

By (Mrs.) W. J. Adams, D. K. Patel, V. Petrow, (Mrs.) I. A. Stuart-Webb, and B. Sturgeon.

The conversion of some 3-oxo-Δ^4-derivatives of androstane and pregnane into the corresponding 4 : 4-dimethyl-3-oxo-Δ^5-derivatives and thence into the 3β-hydroxy-4 : 4-dimethyl-Δ^5-steroids is described.

4 : 4-Dimethyl-17β-propionyloxy- and 17β-hydroxy-4 : 4 : 17α-trimethyl-androsta-1 : 5-dien-3-one have been prepared from the corresponding 5-enes by procedures involving bromination at $C_{(2)}$ and dehydrobromination with lithium chloride–dimethylformamide.

Work on 4 : 4-dimethyl-steroids is now extended to some derivatives of androstane and pregnane, which were required for biological study.

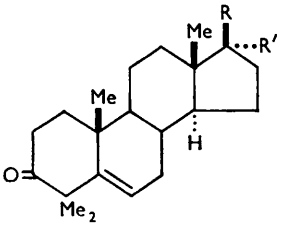
Dimethylation of testosterone propionate by the method described in Part I,[1,2]

[1] Part I, Cooley, Ellis, and Petrow, *J.*, 1955, 2998.
[2] Woodward, Patchett, Barton, Ives, and Kelly, *J. Amer. Chem. Soc.*, 1954, **76**, 2852.

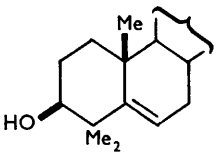
followed by propionylation gave 4 : 4-dimethyl-17β-propionyloxyandrost-5-en-3-one (I; R = O·COEt, R′ = H), reduced by lithium aluminium hydride to 4 : 4-dimethylandrost-5-ene-3β : 17β-diol (II; R = OH, R′ = H). 17β-Acetoxy-17α-methylandrost-4-en-3-one [3] gave 17β-acetoxy-4 : 4 : 17α-trimethylandrost-5-en-3-one (I; R = OAc, R′ = Me) on dimethylation, converted into 4 : 4 : 17α-trimethylandrost-5-ene-3β : 17β-diol (II; R = OH, R′ = Me) by lithium aluminium hydride. 17β-Acetoxy-17α-ethynylandrost-4-en-3-one [4] similarly furnished 17β-acetoxy-17α-ethynyl-4 : 4-dimethylandrost-5-en-3-one (I; R = OAc, R′ = C:CH) and 17α-ethynyl-4 : 4-dimethylandrost-5-ene-3β : 17β-diol (II; R = OH, R′ = C:CH). 17β-Acetoxy-17α-vinylandrost-4-en-3-one [5] gave 17β-acetoxy-4 : 4-dimethyl-17α-vinylandrost-5-en-3-one (I; R = OAc, R′ = $CH{:}CH_2$).

Extension of the dimethylation procedure to 17-oxoandrostane and 20-oxopregnane derivatives in general required protection of these oxo-groups, for which purpose the ethylenedioxy-derivatives proved suitable.

3β-Hydroxyandrost-5-en-17-one was converted into 17 : 17-ethylenedioxyandrost-5-en-3β-ol,[6] which passed into 17 : 17-ethylenedioxyandrost-4-en-3-one on Oppenauer oxidation. This method of preparation of the last compound is preferred to the direct monoketalisation of androstenedione.[7] Dimethylation of 17 : 17-ethylenedioxyandrost-4-en-3-one furnished 17 : 17-ethylenedioxy-4 : 4-dimethylandrost-5-en-3-one, reduced to 17 : 17-ethylenedioxy-4 : 4-dimethylandrost-5-en-3β-ol, which was converted into 3β-hydroxy-4 : 4-dimethylandrost-5-en-17-one on treatment with acid. Pregnenolone was



(I)



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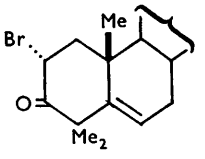

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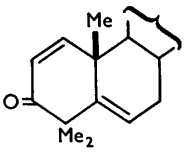

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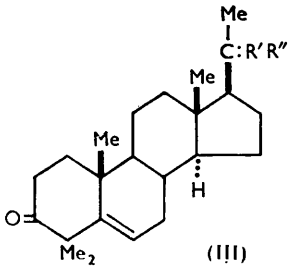

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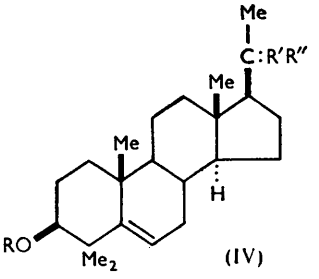

(IV)

The partial formula omitted from (II), (V), and (VI) is as in (I).

converted into 20 : 20-ethylenedioxypregn-5-en-3β-ol and thence into 20 : 20-ethylenedioxypregn-4-en-3-one. Dimethylation gave 20 : 20-ethylenedioxy-4 : 4-dimethylpregn-5-en-3-one (III; R′R″ = O·CH_2·CH_2·O) which passed into 3β-hydroxy-4 : 4-dimethylpregn-5-en-20-one (IV; R = H, R′R″ = O) on reduction and hydrolysis. Surprisingly, direct dimethylation of progesterone gave the dimethyl derivative (III; R′R″ = O) in *ca.*

[3] Miescher and Klarer, *Helv. Chim. Acta*, 1939, **22**, 962.
[4] Ruzicka and Meldahl, *ibid.*, 1938, **21**, 1760.
[5] Ruzicka, U.S.P. 2,272,131/1942.
[6] Fieser, *J. Amer. Chem. Soc.*, 1954, **76**, 1945.
[7] Herzog, Jevnik, Tully, and Hershberg, *ibid.*, 1953, **75**, 4425.

45% yield. This result contrasts with the oxalylation of progesterone which yields only the 21-oxalyl derivative.[8,9]

Monobromination of 4 : 4-dimethylcholest-5-en-3-one furnished 2α-bromo-4 : 4-dimethylcholest-5-en-3-one (V; R = C_8H_{17}, R′ = H),[10] no evidence for 5 : 6-addition being obtained. The compound failed to form a dinitrophenylhydrazone and was not dehydrobrominated in this reaction. Treatment with collidine gave 4 : 4-dimethylcholest-5-en-3-one and a small quantity of the required 4 : 4-dimethylcholesta-1 : 5-dien-3-one (VI; R = C_8H_{17}, R′ = H), which was readily obtained, however, by the use of lithium chloride in dimethylformamide for the dehydrobromination.[11] The dienone (VI; R = C_8H_{17}, R′ = H) was additionally obtained, albeit in very low yield, by direct dimethylation of cholesta-1 : 4-dien-3-one. An attempt to enforce the molecular rearrangement of the dienone (VI; R = C_8H_{17}, R′ = H) with sulphuric acid–acetic anhydride proved unsuccessful. Dibromination of 4 : 4-dimethylcholest-5-en-3-one gave the dibromo-derivative (see Experimental section). Bromination of 17β-acetoxy-4 : 4 : 17α-trimethylandrost-5-en-3-one (I; R = OAc, R′ = Me) followed by dehydrobromination of the product, gave 17β-acetoxy-4 : 4 : 17α-trimethylandrosta-1 : 5-dien-3-one (VI; R = OAc, R′ = Me), which was converted into 17β-hydroxy-4 : 4 : 17α-trimethylandrosta-1 : 5-dien-3-one (VI; R = OH, R′ = Me) by lithium aluminium hydride reduction followed by oxidation with chromic acid–pyridine. 4 : 4-Dimethyl-17β-propionyloxyandrosta-1 : 5-dien-3-one (VI; R = O·COEt, R′ = H) was prepared similarly from 4 : 4-dimethyl-17β-propionyloxyandrost-5-en-3-one (I; R = O·COEt, R′ = H).

Experimental

Optical rotations were measured in chloroform in a 1-dm. tube. Spectroscopic transparency in ethanol of the methylated steroid in the 240-mμ region and other spectroscopic data were kindly determined by Mr. M. T. Davies, B.Sc.

4 : 4-*Dimethyl*-17β-*propionyloxyandrost*-5-*en*-3-*one* (I; R = O·COEt, R′ = H).—Testosterone propionate (4·96 g.) was added with stirring at room temperature to potassium (1·7 g.) and dry *tert.*-butyl alcohol (50 ml.) under nitrogen. Methyl iodide (5·5 ml.) was added dropwise and the stirred mixture refluxed for 1½ hr. The mixture was taken to dryness under reduced pressure, the product isolated with ether and propionylated (20 ml. of propionic anhydride and 20 ml. of pyridine for 16 hr. at room temperature), and the propionate passed through a short column of alumina in benzene solution and crystallised from aqueous methanol, giving 4 : 4-*dimethyl*-17β-*propionyloxyandrost*-5-*en*-3-*one*, m. p. 120°, $[\alpha]_D^{27}$ −29° (*c*, 0·376) (Found: C, 77·5; H, 9·5. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·7%).

4 : 4-*Dimethylandrost*-5-*ene*-3β : 17β-*diol* (II; R = OH, R′ = H).—The propionate (300 mg.) in ether (30 ml.) was added dropwise during 15 min. to a stirred solution of lithium aluminium hydride (300 mg.) in ether (30 ml.). After being refluxed for 30 min. the mixture was cooled to 0°, decomposed with water, and acidified with dilute sulphuric acid, and the product isolated with chloroform. 4 : 4-*Dimethylandrost*-5-*ene*-3β : 17β-*diol* formed needles, m. p. 210—211°, $[\alpha]_D^{23}$ −79° (*c*, 0·207) (Found: C, 75·8; H, 11·0. $C_{21}H_{34}O_2,H_2O$ requires C, 75·0; H, 10·7%), after crystallisation from aqueous methanol. The *diacetate*, after crystallisation from methanol, formed needles, m. p. 170°, $[\alpha]_D^{25}$ −83° (*c*, 0·210) (Found: C, 73·3; H, 9·1. $C_{25}H_{38}O_4,\frac{1}{2}H_2O$ requires C, 73·0; H, 9·5%).

17β-*Acetoxy*-4 : 4 : 17α-*trimethylandrost*-5-*en*-3-*one* (I; R = OAc, R′ = Me) formed plates, m. p. 162—163°, $[\alpha]_D^{23}$ −21° (*c*, 0·297) (Found: C, 77·3; H, 9·8. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·7%).

4 : 4 : 17α-*Trimethylandrost*-5-*ene*-3β : 17β-*diol* (II; R = OH, R′ = Me) crystallised from aqueous methanol, yielding needles, m. p. 218°, $[\alpha]_D^{25}$ −118° (*c*, 0·243) (Found: C, 79·3; H, 11·0. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·8%). The 3-monoacetate had m. p. 149°, $[\alpha]_D^{25}$ −89° (*c*, 0·248). The *diacetate*, prepared by refluxing the diol for 6 hr. with acetic anhydride–pyridine, separated from aqueous methanol in fine needles, m. p. 164°, $[\alpha]_D^{26}$ −71° (*c*, 0·284) (Found: C, 75·1; H, 9·8. $C_{26}H_{40}O_4$ requires C, 75·0; H, 9·6%).

[8] Upjohn Company, B.P. 738,445/1955.

[9] Cf. Hogg, Beal, Nathan, Lincoln, Schneider, Magerlein, Hanze, and Jackson, *J. Amer. Chem. Soc.*, 1955, **77**, 4436.

[10] See Corey, *ibid.*, 1953, **75**, 4832; 1954, **76**, 175, for configuration of 2-bromo-compounds.

[11] Cf. Holysz, *ibid.*, 1953, **75**, 4432.

17β-*Acetoxy*-17α-*ethynyl*-4 : 4-*dimethylandrost*-5-*en*-3-*one* (I; R = OAc, R′ = C:CH) formed plates, m. p. 199—200°, $[\alpha]_D^{24}$ −67° (*c*, 0·410) (Found: C, 78·3; H, 8·6. $C_{25}H_{34}O_3$ requires C, 78·5; H, 8·9%), after crystallisation from acetone–hexane. The infrared absorption spectrum, kindly determined by Dr. A. E. Kellie, showed the presence of an acetylenic hydrogen atom, showing that methylation at the acetylenic centre had not occurred.

17α-*Ethynyl*-4 : 4-*dimethylandrost*-5-*ene*-3β : 17β-*diol* (II; R = OH, R′ = C:CH) separated from acetone–hexane in micro-crystals, m. p. 222—224°, $[\alpha]_D^{23}$ −133° (*c*, 0·29) (Found: C, 80·5; H, 9·4. $C_{23}H_{34}O_2$ requires C, 80·7; H, 9·9%).

17β-*Acetoxy*-4 : 4-*dimethyl*-17α-*vinylandrost*-5-*en*-3-*one* (I; R = OAc, R′ = CH:CH_2) formed prisms, m. p. 191—192°, $[\alpha]_D^{22}$ +19° (*c*, 0·313) (Found: C, 78·6; H, 9·4. $C_{25}H_{36}O_3$ requires C, 78·1; H, 9·4%), after crystallisation from acetone–hexane.

17 : 17-Ethylenedioxyandrost-4-en-3-one was prepared by Oppenauer oxidation of 17 : 17-ethylenedioxyandrost-5-en-3β-ol with aluminium *tert.*-butoxide in toluene–*cyclo*hexanone.

17 : 17-*Ethylenedioxy*-4 : 4-*dimethylandrost*-5-*en*-3-*one* formed prisms, m. p. 128—129°, $[\alpha]_D^{27}$ −40° (*c*, 0·741) (Found: C, 77·0; H, 9·7. $C_{23}H_{34}O_3$ requires C, 77·1; H, 9·5%), after crystallisation from acetone–hexane.

17 : 17-*Ethylenedioxy*-4 : 4-*dimethylandrost*-5-*en*-3β-*ol* was purified from methanol, yielding needles, m. p. 214°, $[\alpha]_D^{25}$ −109° (*c*, 0·355) (Found: C, 76·7; H, 9·7. $C_{23}H_{36}O_2$ requires C, 76·7; H, 10·0%).

3β-*Hydroxy*-4 : 4-*dimethylandrost*-5-*en*-17-*one* was prepared by refluxing the ethylenedioxy-compound (2·08 g.) in ethanol (110 ml.) with dilute sulphuric acid (15 ml. of 8·5% v/v) for 1 hr.; it formed needles, m. p. 190—191°, $[\alpha]_D^{27}$ +35° (*c*, 0·29) (Found: C, 79·2; H, 10·1. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·1%), after crystallisation from aqueous methanol.

20 : 20-*Ethylenedioxypregn*-5-*en*-3β-*ol* was obtained as needles, m. p. 160—161°, $[\alpha]_D^{25}$ −45° (*c*, 0·396) (Found: C, 73·0; H, 10·1. $C_{23}H_{36}O_3,H_2O$ requires C, 73·0; H, 10·1%) after crystallisation from ethanol, by heating pregnenolone (5 g.) dissolved in ethylene glycol (50 ml.) and anhydrous benzene (150 ml.) containing toluene-*p*-sulphonic acid (150 mg.) in a Dean and Stark apparatus for 16 hr. The acetate formed shimmering plates, m. p. 159—160°, $[\alpha]_D^{25}$ −54° (*c*, 0·4) (Found: C, 74·6; H, 9·5. $C_{25}H_{38}O_4$ requires C, 74·6; H, 9·5%).

The foregoing compound (2·8 g.) was dissolved in *cyclo*hexanone (18 ml.) and toluene (20 ml.), and all traces of water were removed by distillation. Aluminium *tert.*-butoxide (4 g.) in toluene (10 ml.) was added and the stirred mixture refluxed for 3 hr. The product was isolated in the usual way and purified from methanol. 20 : 20-*Ethylenedioxypregn*-4-*en*-3-*one* formed shimmering plates, m. p. 188—190°, $[\alpha]_D^{26}$ +101° (*c*, 0·458) (Found: C, 76·8; H, 9·5. $C_{23}H_{34}O_3$ requires C, 77·1; H, 9·5%).

20 : 20-*Ethylenedioxy*-4 : 4-*dimethylpregn*-5-*en*-3-*one* (III; R′R″ = O·CH_2CH_2·O) separated from acetone in prismatic needles, m. p. 189—191°, $[\alpha]_D^{25}$ −8° (*c*, 0·404) (Found: C, 77·7; H, 10·0. $C_{25}H_{38}O_3$ requires C, 77·3; H, 9·9%).

4 : 4-*Dimethylpregn*-5-*ene*-3 : 20-*dione* (III; R′R″ = O) was prepared by treating the foregoing compound (100 mg.) in acetone (10 ml.) with toluene-*p*-sulphonic acid (100 mg.) for 16 hr. at room temperature. It formed prisms, m. p. 128° and 140—141°, $[\alpha]_D^{24}$ +64° (*c*, 0·466) (Found: C, 80·6; H, 10·2. $C_{23}H_{34}O_2$ requires C, 80·7; H, 9·9%), after crystallisation from ether–pentane.

Alternatively, progesterone (10 g.) was added at room temperature to potassium (3·73 g.) and *tert.*-butyl alcohol (100 ml.) under nitrogen. The stirred mixture was treated dropwise with methyl iodide (14 ml.), heated under reflux for 1 hr., and evaporated to dryness under reduced pressure, and the product isolated with ether, dissolved in benzene, and chromatographed on alumina (200 g.). The benzene–light petroleum (b. p. 60—80°) eluates yielded 4 : 4-*dimethylpregn*-5-*ene*-3 : 20-*dione*, m. p. 141—142°, $[\alpha]_D^{26}$ +58° (*c*, 0·422) (Found: C, 80·7; H, 10·1%); the m. p. was not depressed on admixture with a sample prepared by the indirect route.

When the foregoing compound (4·6 g.) was heated with toluene-*p*-sulphonic acid (150 mg.) in benzene (700 ml.) and ethylene glycol (75 ml.) under reflux in a Dean and Stark apparatus for 16 hr., 20 : 20-ethylenedioxy-4 : 4-dimethylpregn-5-en-3-one was obtained; it formed prismatic needles, m. p. 190—193°, $[\alpha]_D^{25}$ −6° (*c*, 1·035) (Found: C, 77·9; H, 9·5. Calc. for $C_{25}H_{38}O_3$: C, 77·3; H, 9·9%), the m. p. not being depressed on admixture with a sample prepared as above.

Reduction of the ketal (640 mg.) in tetrahydrofuran (20 ml.) with lithium aluminium hydride (400 mg.) in tetrahydrofuran (50 ml.), followed by acetylation of the product, yielded 3β-acetoxy-20 : 20-ethylenedioxy-4 : 4-dimethylpregn-5-ene (IV; R = Ac, R′R″ = O·CH_2·CH_2·O), m. p. 171—173°, $[\alpha]_D^{24}$ −50° (*c*, 0·39).

3β-*Acetoxy*-4 : 4-*dimethylpregn*-5-*en*-20-*one* (IV; R = Ac, R′R″ = O) was prepared by treating the ethylenedioxy-compound (180 mg.) in acetone (20 ml.) with toluene-*p*-sulphonic

acid (150 mg.) for 16 hr. at room temperature, and formed plates, m. p. 178—180°, $[\alpha]_D^{25}$ +4° (*c*, 0·356) (Found : C, 77·8; H, 9·9. $C_{25}H_{38}O_3$ requires C, 77·7; H, 9·8%), from methanol.

3β-*Hydroxy*-4 : 4-*dimethylpregn*-5-*en*-20-*one*, leaflets, m. p. 199—202° (Found : C, 79·9; H, 10·5. $C_{23}H_{36}O_2$ requires C, 80·2; H, 10·3%), from acetone, was prepared by heating under reflux the acetate (570 mg.) in methanol (45 ml.) with potassium carbonate (500 mg.) in water (5 ml.) for 1 hr.

2α-*Bromo*-4 : 4-*dimethylcholest*-5-*en*-3-*one* (V; R = C_8H_{17}, R′ = H).—To a stirred solution of 4 : 4-dimethylcholest-5-en-3-one (10·2 g.) in dry ether (750 ml.), bromine (4·2 g.) in acetic acid (29 ml.) was added during 5 min. After 30 min. the mixture was poured into water, and the product isolated with ether and purified from ethanol. 2α-*Bromo*-4 : 4-*dimethylcholest*-5-*en*-3-*one* formed plates, m. p. 136—137°, $[\alpha]_D^{27}$ −35° (*c*, 1·1) (Found : C, 70·9; H, 9·4; Br, 16·4. $C_{29}H_{47}OBr$ requires C, 70·9; H, 9·6; Br, 16·3%). The starting material was regenerated on reduction of the bromo-compound with zinc dust and acetic acid–ether at room temperature.

This monobromo-derivative (4·1 g.) in warm acetic acid (150 ml.) was treated with bromine (1·6 g.) in acetic acid (10 ml.). After being set aside overnight the mixture was evaporated to turbidity, which was cleared with ether; it slowly gave a product (1·6 g.) which was cautiously recrystallised from ethanol with the minimum of heating to yield a *dibromo-derivative*, m. p. 94—96° (Found : C, 61·7; H, 8·3; Br, 25·5. $C_{29}H_{46}OBr_2$ requires C, 61·1; H, 8:1; Br, 28·1%). Debromination of a portion with collidine, followed by chromatography, gave a fraction having $\lambda_{max.}$ 254 mμ, a value consistent with a 2-bromo-3-oxo-Δ¹-steroid.

4 : 4-*Dimethylcholesta*-1 : 5-*dien*-3-*one* (VI; R = C_8H_{17}, R′ = H).—(*a*) The monobromo-ketone (10 g.), lithium chloride (10 g.; anhydrous), and dimethylformamide (150 ml.) were heated under reflux for 5 hr. The product was isolated with ether and purified from ethanol. 4 : 4-*Dimethylcholesta*-1 : 5-*dien*-3-*one* formed needles, m. p. 77—78°, $[\alpha]_D^{23}$ +53° (*c*, 1·00), $\lambda_{max.}$ 227 mμ (log ε 3·98) (Found : C, 84·7; H, 11·2. $C_{29}H_{46}O$ requires C, 84·9; H, 11·2%). (*b*) The monobromo-compound (5 g.) and collidine (50 ml.) were heated under reflux in nitrogen for 5 hr. After removal of collidine hydrobromide, the product was isolated with ether and purified from methanol to give 4 : 4-dimethylcholest-5-en-3-one, m. p. 169—170° not depressed on admixture with an authentic specimen. The mother liquors were taken to dryness and chromatographed in light petroleum (b. p. 60—80°) on alumina (40 g.). Elution with light petroleum (b. p. 60—80°) gave 4 : 4-dimethylcholesta-1 : 5-dien-3-one (500 mg.), m. p. 75—76°, $[\alpha]_D^{24}$ +48° (*c*, 1·14), $\lambda_{max.}$ 227 mμ (log ε 3·97). The m. p. was not depressed on admixture with an authentic sample. (*c*) A cold solution from potassium (2·4 g.) and *tert.*-butyl alcohol (125 ml.) was treated with cholesta-1 : 4-dien-3-one (7·5 g.). Methyl iodide (7·5 ml.) was added dropwise during 30 min. and the mixture then heated under reflux for 2 hr. The product, in light petroleum (b. p. 60—80°), was chromatographed on alumina (150 g.). The materials eluted by light petroleum (1000 ml.; b. p. 60—80°) and benzene–light petroleum (250 ml. of 1 : 9 v/v) were combined and similarly chromatographed on alumina (15 g.). Elution with light petroleum (2000 ml.; b. p. 60—80°) followed by crystallisation from ethanol, gave 4 : 4-dimethylcholesta-1 : 5-dien-3-one (150 mg.), m. p. and mixed m. p. 76—77°, $[\alpha]_D^{25}$ +48° (*c*, 1·1), $\lambda_{max.}$ 227 mμ (log ε 3·98).

17β-*Acetoxy*-4 : 4 : 17α-*trimethylandrosta*-1 : 5-*dien*-3-*one* (VI; R = OAc, R′ = Me).—17β-Acetoxy-4 : 4 : 17α-trimethylandrost-5-en-3-one (2·55 g.) in ether (150 ml.) was treated with bromine in acetic acid (0·155 g./ml.; 7·5 ml.) to give a crude 2-bromo-derivative (2·7 g.) (V; R = OAc, R′ = Me), m. p. 136—138° after crystallisation from methanol. Dehydrobromination with lithium chloride (6·0 g.) in dimethylformamide (100 ml.) gave 17β-*acetoxy*-4 : 4 : 17α-*trimethylandrosta*-1 : 5-*dien*-3-*one*, as prisms, m. p. 168—170°, $[\alpha]_D^{24}$ +35° (*c*, 1·36), $\lambda_{max.}$ 227 mμ (log ε 3·99) (Found : C, 78·0; H, 9·3. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·2%).

17β-*Hydroxy*-4 : 4 : 17α-*trimethylandrosta*-1 : 5-*dien*-3-*one*.—The acetate (700 mg.) in ether (20 ml.) was reduced with lithium aluminium hydride (1 g.) in ether. The crude dry product was oxidised for 16 hr. at room temperature with chromic acid (1 g.) in pyridine (20 ml.). The product was extracted with hot benzene, the extract filtered through " Hyflo," and the benzene filtrate then washed with dilute hydrochloric acid and water, and dried. The product in 50% benzene–light petroleum was trickled through a short column of alumina and then purified from acetone–hexane. 17β-*Hydroxy*-4 : 4 : 17α-*trimethylandrosta*-1 : 5-*dien*-3-*one* formed silky needles, m. p. 168—169°, $[\alpha]_D^{26}$ +24° (*c*, 1·04), $\lambda_{max.}$ 226—227 mμ (log ε 3·97) (Found : C, 80·3; H, 9·7. $C_{22}H_{32}O_2$ requires C, 80·5; H, 9·8%).

4 : 4-*Dimethyl*-17β-*propionyloxyandrosta*-1 : 5-*dien*-3-*one* (VI; R = O·COEt, R′ = H) formed prisms, m. p. 125°, $[\alpha]_D^{22}$ +50° (*c*, 0·11), $\lambda_{max.}$ 227 mμ (log ε 4·0) (Found : C, 77·3; H, 9·0. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·2%).

7ξ-*Methoxy*-4 : 4-*dimethylcholest*-5-*en*-3-*one*.[12]—A suspension of 4 : 4-dimethylcholest-5-en-3-one (4·1 g.) and *N*-bromosuccinimide (2 g.) in dry carbon tetrachloride (50 ml.) was treated with benzoyl peroxide (*ca.* 20 mg.) in carbon tetrachloride. The mixture was heated under reflux for 1 hr., the succinimide removed, the filtrate evaporated to small bulk, and methanol added with warming until crystallisation commenced. 7ξ-*Methoxy*-4 : 4-*dimethylcholest*-5-*en*-3-*one* formed long silky needles, m. p. 155—156°, $[\alpha]_D^{26}$ +80° (*c*, 1·06) (Found : C, 81·4; H, 11·7. $C_{30}H_{50}O_2$ requires C, 81·5; H, 11·3%), after purification from ethanol. 7ξ-*Ethoxy*-4 : 4-*dimethylcholest*-5-*en*-3-*one* was obtained by boiling the crude bromination product with ethanol and formed prismatic needles, m. p. 129—130°, $[\alpha]_D^{26}$ +77° (*c*, 0·83) (Found : C, 81·1; H, 11·3. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·4%), from light petroleum (b. p. 40—60°).

4 : 4-*Dimethylcholesta*-5 : 7-*dien*-3-*one*.—4 : 4-Dimethylcholest-5-en-3-one (6·2 g.) was brominated with *N*-bromosuccinimide (3 g.) in carbon tetrachloride. Succinimide was filtered off, collidine (40 ml.) added to the filtrate, and the carbon tetrachloride evaporated off. The solution was heated in nitrogen under reflux for ½ hr. The product was isolated with ether and purified by chromatography to give 4 : 4-*dimethylcholesta*-5 : 7-*dien*-3-*one* as plates, m. p. 160°, $[\alpha]_D^{24}$ −20° (*c*, 1·27), $\lambda_{max.}$ 274 (log ε 4·00), 283 mμ (log ε 4·02), $\lambda_{infl.}$ 295 mμ (Found : C, 85·1; H, 11·4. $C_{29}H_{46}O$ requires C, 84·9; H, 11·2%), after crystallisation from propan-2-ol.

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[12] Cf. Greenhalgh, Henbest, and Jones, *J.*, 1952, 2380, for $C_{(7)}$-bromination of a 5-ene followed by replacement of the bromine atom by an alkoxyl group.