246. *Modified Steroid Hormones. Part II.** (i) *Monohalogenation of* 5α : 6β-*Dibromocholestan-3-one.* (ii) *Some* 2α-*Halogenated Androgens.*

By Bernard Ellis and Vladimir Petrow.

A method has been developed for the preparation of 2α-halogenated cholest-4-en-3-ones (VIII*a*) from 5α : 6β-dibromocholestan-3-one (IV*a*), and extended to the preparation of some 2α-halogenated androgens.

Some 2-halogenated derivatives (VIII*b* and VIII*c*) of testosterone and methyltestosterone were required for biological study. Their preparation by the method used for 2-bromotestosterone hexahydrobenzoate [1] was unattractive as both 3-hydroxyandrostanone and 3-hydroxymethylandrostanone are relatively inaccessible. Halogenation at position 2 of the corresponding 5α : 6β-dibromo-17β-hydroxyandrostan-3-ones, followed by 5 : 6-debromination, seemed a more attractive route. Barton and Miller,[2] it is true, had stated that such halogenation at this position was improbable on mechanistic grounds. The work of Djerassi *et al.*,[3] however, appeared to indicate the feasibility of this approach and we therefore re-examined the bromination of 5α : 6β-dibromocholestan-3-one (IV*a*). The results obtained with this compound confirmed our expectations regarding the halogenation (section i) so we also studied the preparation of the required 2-halogenated androgens (section ii).

(i) By monobrominating 5α : 6β-dibromocholestan-3-one [4] (IV*a*) in ether–acetic acid, Inhoffen [5] obtained a tribromo-ketone, m. p. 138°. A second tribromo-ketone, m. p. 106°, was obtained almost simultaneously by Butenandt and Schramm,[6] who carried out the monobromination in acetic acid alone. The two compounds were regarded by their discoverers as epimeric 4 : 5 : 6-tribromocholestan-3-ones [6] (see also Corey [7]), not only on account of their chemical reactions, but also because of their conversion into the same tetrabromo-ketone, formulated as a 4 : 4 : 5 : 6-tetrabromocholestan-3-one. The higher-melting isomer, on treatment with potassium acetate, was shown to lose the elements of hydrogen bromide to give an unsaturated ketone, regarded as a 4 : 6-dibromocholest-4-en-3-one [5*b*] and additionally obtained [5*c*] from cholestenone and 6-bromocholestenone by di- and mono-bromination, respectively.

The foregoing structural assignments remained unchallenged till 1950 when Djerassi *et al.*[3] showed the need for their revision by proving that dibromination of cholest-4-en-3-one in acetic acid leads, in fact, to the formation of a 2 : 6- and not a 4 : 6-dibromocholest-4-en-3-one (cf. Inhoffen [5*c*]). The American authors, however, failed to indicate the incompatibility of this conclusion with the 4 : 5 : 6-tribromo-structures then generally accepted for the Inhoffen–Butenandt tribromo-ketones, with the result that in 1954 Corey [7] still retained the original formulations in his discussion on the stereochemistry of α-brominated keto-steroids. Corey isomerised the lower-melting tribromo-ketone (Butenandt) to the isomer, m. p. 138° (Inhoffen). He concluded that Inhoffen's substance was the stable 4α(equatorial)-epimer and the product of thermodynamic control, while Butenandt's tribromo-ketone, m. p. 106°, was the unstable 4β(axial)-epimer and the product of kinetic control. We confirm Corey's conversion of the lower-melting into the higher-melting bromo-ketone, but are unable to accept his formulations. In our view [8] Inhoffen's and Butenandt's compounds should be reformulated as 2α : 5α : 6β- (VI*a*; R = Br) and 2β : 5α : 6β-tribromocholestan-3-one (V*a*; R = Br), respectively, on the basis of the following transformations.

* Part I, *J.*, 1956, 627.

[1] Inhoffen and Zuhlsdorff, *Ber.*, 1943, **76**, 233; Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1947, **69**, 2404.

[2] Barton and Miller, *ibid.*, 1950, **72**, 1066.

[3] Djerassi, Rosenkranz, Romo, Kaufmann, and Pataki, *ibid.*, p. 4534.

[4] See ref. 2 for the stereochemistry of the compound.

[5] Inhoffen, *Ber.*, 1936, **69**, (*a*) 1134, (*b*) 1702, (*c*) 2141.

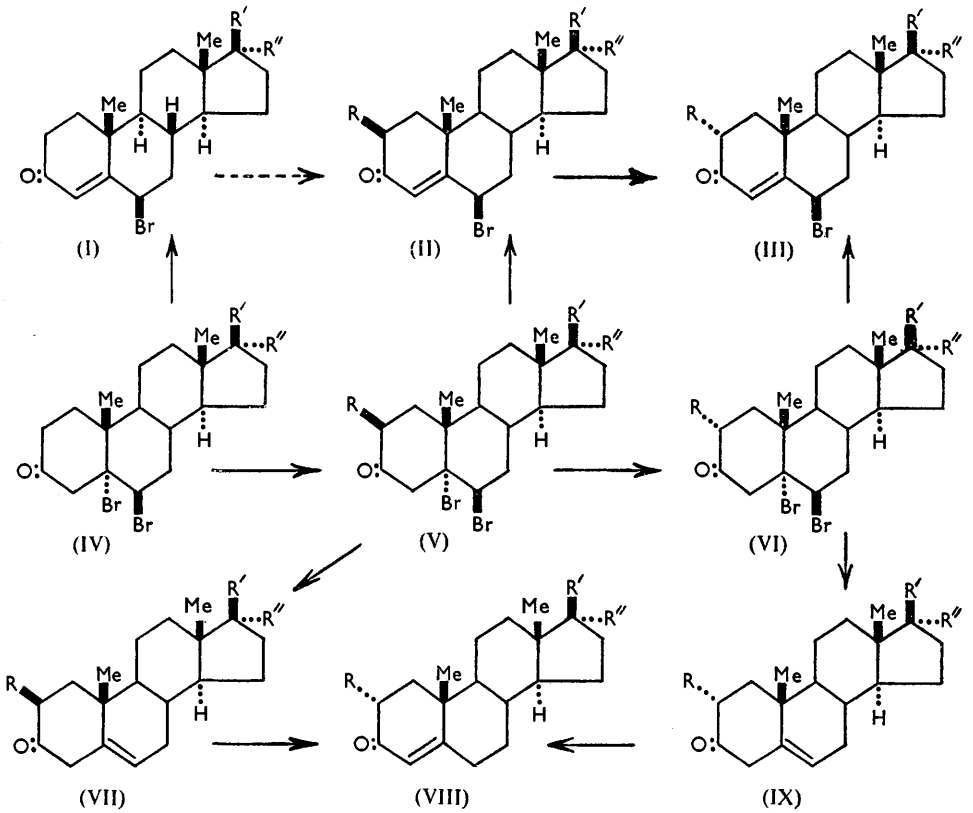
[6] Butenandt and Schramm, *ibid.*, p. 2289.

[7] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.

[8] Cf. Fieser, Romero, and Fieser, *ibid.*, 1955, **77**, 3305, which appeared while our work was in manuscript.

Partial dehydrobromination of the Butenandt tribromo-ketone (V*a*; R = Br) by brief warming with pyridine gave 2β : 6β-dibromocholest-4-en-3-one (II*a*; R = Br), which passed smoothly in the presence of mineral acid into the more stable 2α-epimer (III*a*; R = Br), also obtained directly from the Inhoffen tribromo-ketone (VI*a*; R = Br) by similar treatment with pyridine. The β-configuration is assigned to the 6-bromine atom in both (II*a*; R = Br) and (III*a*; R = Br) as (*a*) partial dehydrobromination of the dibromo-compound (IV*a*) under similar conditions leads to the formation of 6β- (I*a*; R = Br) and not 6α-bromocholest-4-en-3-one [2] and (*b*) treatment of the monobromo-compound (I*a*) with mineral acids under conditions effecting the change of the 2β- (II*a*) into the 2α-compound (III*a*) leads only to recovery of starting material.

The ultraviolet absorption spectrum of 2β : 6β-dibromocholest-4-en-3-one (II*a*; R = Br) shows a maximum at 257 mμ in contrast to that at 248—250 mμ reported [5c,3] for the 2-epimeric dibromo-ketone (III*a*; R = Br). There is, consequently, a bathochromic shift in passing from the 2α(equatorial)- to the 2β(axial)-bromo-substituent. A bathochromic shift of similar order has also been observed with certain epimeric 6-bromo-3-oxo-Δ^4-steroids.[2,3]



(*a*) R′ = C_8H_{17}, R″ = H. (*b*) R′ = OAc, R″ = H. (*c*) R′ = OH, R″ = Me.

Partial debromination of the tribromo-ketones (V*a* and VI*a*; R = Br) by brief treatment with sodium iodide in acetone furnished two epimeric unsaturated bromo-ketones which lacked significant ultraviolet absorption, and to which the constitutions 2β- (VII*a*; R = Br) and 2α-bromocholest-5-en-3-one (IX*a*; R = Br), respectively, have been assigned. Both compounds were readily isomerised to 2α-bromocholest-4-en-3-one (VIII*a*; R = Br), a known ketone of proved structure.[9]

[9] Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003.

Monochlorination of the dibromo-ketone (IV*a*) in acetic acid gave 5α : 6β-dibromo-2β-chlorocholestan-3-one (V*a*; R = Cl), which could be isolated only when the mixture was worked up immediately absorption of chlorine was complete; otherwise epimerisation occurred, to give the 2α-isomer (VI*a*; R = Cl). Partial dehydrobromination of these chlorinated derivatives with warm pyridine furnished the epimeric unsaturated chloro-bromo-ketones (II*a* and III*a*; R = Cl), respectively. The latter compound was also obtained by epimerisation of the former with mineral acid, and by monochlorination of 6β-bromocholest-4-en-3-one (I). The ultraviolet absorption spectrum of the 2α-compound (III*a*; R = Cl) showed a maximum at 249 mμ which corresponds closely to that of its 2α-bromo-analogue (III*a*; R = Br). The isomeric chloro-bromo-ketone gave a maximum at 254 mμ, a value consistent with the proposed formulation (II*a*; R = Cl).

2β- (VII*a*; R = Cl) and 2α-Chlorocholest-5-en-3-one (IX*a*; R = Cl), obtained from the chlorodibromo-compounds (V*a* and VI*a*; R = Cl), respectively, by debromination with sodium iodide, were severally isomerised by mineral acid to 2α-chlorocholest-4-en-3-one (VIII*a*; R = Cl), identical with a specimen prepared by an alternative route.[10]

(ii) Dibromination of 17α-methylandrost-5-ene-3β : 17β-diol, followed by oxidation with chromium trioxide, furnished 5α : 6β-dibromo-17β-hydroxy-17α-methylandrostan-3-one (IV*c*). Monochlorination of the latter in acetic acid gave the corresponding 2β- (V*c*; R = Cl) and 2α-chloro-derivative (VI*c*; R = Cl), depending upon the conditions employed. Debromination of the 2β-isomer with sodium iodide followed by isomerisation of the product by mineral acid afforded the required 2α-chloro-17α-methyltestosterone (VIII*c*; R = Cl).

2α-Chlorotestosterone acetate (VIII*b*; R = Cl) was prepared by the reaction sequence : 17β-acetoxyandrost-5-en-3β-ol ⟶ 5α : 6β-dibromide ⟶ 3-ketone ⟶ 2β-chloro-derivative followed by debromination and isomerisation. 2α-Bromomethyltestosterone (VIII*c*; R = Br) was similarly obtained.

Experimental

Optical rotations were measured for $CHCl_3$ solutions in a 1 dm tube. Ultraviolet absorption spectra (in propan-2-ol) were kindly determined by Mr. M. Davies, B.Sc. (values in parentheses are log ε).

2β : 6β-*Dibromocholest*-4-*en*-3-*one* (II; R = Br).—2β : 5α : 6β-Tribromocholestan-3-one (m. p. 106°, $[\alpha]_D^{21}$ +9°) (1 g.) in dry pyridine (5 ml.) was warmed for 3 min. on the steam-bath. 2β : 6β-*Dibromocholest*-4-*en*-3-*one* crystallised from acetone–methanol as prisms (0·6 g.), m. p. 124° (decomp.), $[\alpha]_D^{20}$ −41° (*c*, 0·54), $\lambda_{max.}$ 257 mμ (4·08) (Found : C, 59·5; H, 7·5. $C_{27}H_{42}OBr_2$ requires C, 59·8; H, 7·8%).

2α : 6β-*Dibromocholest*-4-*en*-3-*one* (III; R = Br).—(*a*) The foregoing compound (200 mg.) in ether (10 ml.) and acetic acid (10 ml.) was treated with 10 drops of hydrogen bromide in acetic acid (50% w/w) and kept for 18 hr. at room temperature. Crystallisation of the product from acetone–methanol gave 2α : 6β-dibromocholest-4-en-3-one (150 mg.), needles, m. p. 162—163°, not depressed on admixture with a specimen prepared by dibrominating cholest-4-en-3-one.

(*b*) Treatment of 2α : 5α : 6β-tribromocholestan-3-one (m. p. 138°, $[\alpha]_D^{21}$ −44·5°) (1·5 g.) with pyridine (8 ml.) for 3 min. at 100° gave a product (1 g.) which crystallised from acetone–methanol in needles, m. p. 162—163°, not depressed on admixture with a specimen prepared by method (*a*).

6β-*Bromocholest*-4-*en*-3-*one* (I).—5α : 6β-Dibromocholestan-3-one (5 g.) in pyridine (20 ml.) was warmed for 2 min. on the steam-bath, and the solids obtained on dilution with water were purified from aqueous ethanol, to give needles (3·3 g.) of 6β-bromocholest-4-en-3-one, m. p. and mixed m. p. 130—132°. The compound was recovered unchanged after treatment with hydrogen bromide in ether–acetic acid.

2β-*Bromocholest*-5-*en*-3-*one* (VII; R = Br).—Sodium iodide (4 g.) was added to 2β : 5α : 6β-tribromocholestan-3-one (3·6 g.) in acetone (60 ml.). The mixture was stirred for 5 min., then diluted with 5% aqueous sodium thiosulphate, precipitating an oil which soon solidified. Purified from aqueous acetone, 2β-*bromocholest*-5-*en*-3-*one* formed needles (1·7 g.), m. p. 109—110° (decomp.), $[\alpha]_D^{22}$ +115° (*c*, 1·12) (Found : C, 70·1; H, 9·3. $C_{27}H_{43}OBr$ requires C, 69·95; H, 9·35%).

[10] Ellis and Petrow, *J.*, 1953, 3869; Beereboom, Djerassi, Ginsberg, and Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 3500.

2α-*Bromocholest*-5-*en*-3-*one* (IX; R = Br), prepared from 2α : 5α : 6β-tribromocholestan-3-one (1·4 g.) by the foregoing procedure, separated (0·75 g.) from aqueous acetone in needles, m. p. 109—110°, $[\alpha]_D^{19}$ +0·5° (*c*, 1·02) (Found : C, 70·0; H, 9·4. $C_{27}H_{43}OBr$ requires C, 69·95; H, 9·35%).

2α-*Bromocholest*-4-*en*-3-*one* (VIII; R = Br).—The foregoing compound (500 mg.) in ether (25 ml.) and acetic acid (12·5 ml.) was treated with concentrated hydrochloric acid (0·5 ml.). Next morning, the mixture was poured into water and the product isolated with ether. 2α-Bromocholest-4-en-3-one (350 mg.) formed needles (from methanol), m. p. 132—134°, $[\alpha]_D^{19}$ +94° (*c*, 0·8), $\lambda_{max.}$ 245 mμ (4·13) (Found : C, 69·8; H, 9·25%) {Djerassi [3] gives m. p. 117—119°, $[\alpha]_D^{22}$ +81°, $\lambda_{max.}$ 243 mμ (4·15).} Reaction with 2 : 4-dinitrophenylhydrazine in hot acetic acid gave the deep red cholesta-4 : 6-dien-3-one 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 227—228°.

The compound (VIII; R = Br) was also obtained by similar isomerisation of (VII; R = Br).

Monochlorination of 5α : 6β-*Dibromocholestan*-3-*one*.—Chlorine (287 mg., 1 mol.) was added to 5α : 6β-dibromocholestan-3-one (2·2 g.) in acetic acid (200 ml.). When absorption of chlorine was complete (*ca.* 30 min.), the mixture was poured into water (200 ml.) and the solids were collected, washed, and air-dried. Purified from acetone–methanol, 5α : 6β-*dibromo*-2β-*chlorocholestan*-3-*one* (1·6 g.) formed prisms, m. p. 114—116° (decomp.), $[\alpha]_D^{20}$ +2° (*c*, 1·1) (Found : C, 55·9; H, 7·4. $C_{27}H_{43}OClBr_2$ requires C, 56·0; H, 7·5%). The epimeric 5α : 6β-*dibromo*-2α-*chlorocholestan*-3-*one* (1·5 g.), needles (from acetone–methanol), m. p. 150—151° (decomp.), $[\alpha]_D^{21}$ −41° (*c*, 1·29) (Found : C, 55·5; H, 7·3%), was obtained when the mixture was set aside overnight.

6β-*Bromo*-2β-*chlorocholest*-4-*en*-3-*one* (II; R = Cl).—5α : 6β-Dibromo-2β-chlorocholestan-3-one (5 g.) in pyridine (20 ml.) was warmed for 3 min. on the steam-bath. The solids obtained by the addition of water crystallised from acetone–methanol, giving the bromochloro-ketone (3·4 g.), m. p. 110—112°, $[\alpha]_D^{21}$ −39° (*c*, 0·96), $\lambda_{max.}$ 254 mμ (4·09) (Found : C, 64·5; H, 8·4. $C_{27}H_{42}OClBr$ requires C, 65·1; H, 8·5%).

6β-*Bromo*-2α-*chlorocholest*-4-*en*-3-*one* (III; R = Cl).—(*a*) The foregoing compound (500 mg.) in ether (25 ml.) and acetic acid (15 ml.) was treated with concentrated hydrochloric acid (0·5 ml.). After 18 hr. at 0°, the mixture was poured into water, and the product isolated with ether. The *bromochloro-ketone* (400 mg.) crystallised from acetone–methanol in needles, m. p. 144—145° (decomp.), $[\alpha]_D^{22}$ +39° (*c*, 1·09), $\lambda_{max.}$ 249 mμ (4·09) (Found : C, 65·3; H, 8·5%).

(*b*) Partial dehydrobromination of 5α : 6β-dibromo-2α-chlorocholestan-3-one (1 g.) with warm pyridine (5 ml.) gave 6β-bromo-2α-chlorocholest-4-en-3-one (600 mg.), needles (from acetone–methanol), m. p. 145° (decomp.), identical with the compound prepared by method (*a*).

(*c*) A stirred solution of 6β-bromocholest-4-en-3-one (4·1 g.) in ether (100 ml.) at 0° was treated with chlorine (0·63 g., 1 mol.) in acetic acid (20 ml.) dropwise during 15 min. After 24 hr. at 0°, the product was isolated and purified from acetone–methanol, to give the bromochloro-ketone (2·5 g.), m. p. and mixed m. p. 144—145°.

2β-*Chlorocholest*-5-*en*-3-*one* (VII; R = Cl).—5α : 6β-Dibromo-2β-chlorocholestan-3-one (5·4 g.) in acetone (60 ml.) at 35° was treated with sodium iodide (7 g.). The mixture was stirred for 5 min., then poured into water, and the product extracted with ether. The extract was washed with aqueous sodium thiosulphate and water, then dried, and the solvent removed *in vacuo*. The insoluble fraction obtained on trituration of the residue with a small volume of cold ethanol was purified from aqueous ethanol, to give the chloro-ketone (2·6 g.), needles, m. p. 114—116°, $[\alpha]_D^{21}$ +98° (*c*, 0·59) (Found : C, 76·8; H, 10·3. $C_{27}H_{43}OCl$ requires C, 77·4; H, 10·35%).

2α-*Chlorocholest*-5-*en*-3-*one* (IX; R = Cl), prepared from the 2α-compound (VI; R = Cl) (3 g.) by the foregoing procedure, separated (1·7 g.) from aqueous acetone in needles or plates, m. p. 141—142°, $[\alpha]_D^{22}$ −5° (*c*, 1·09) (Found : C, 76·9; H, 10·1%).

2α-*Chlorocholest*-4-*en*-3-*one* (VIII; R = Cl).—The foregoing compound (1 g.) in ether (50 ml.) and acetic acid (30 ml.) was treated with concentrated hydrochloric acid (1 ml.), then kept overnight at room temperature. The product crystallised from methanol, 2α-chlorocholest-4-en-3-one (0·9 g.) separating in needles, $[\alpha]_D^{21}$ +86°, m. p. 98°, alone or mixed with an authentic specimen.[10]

5α : 6β-*Dibromo*-17β-*hydroxy*-17α-*methylandrostan*-3-*one* (IV*c*).—17α-Methylandrost-5-ene-3β : 17β-diol (12 g.) in acetic acid (320 ml.) was treated with bromine (6·4 g.) in acetic acid (40 ml.). After the addition of chromium trioxide (4 g.) in acetic acid (40 ml. of 80%), the mixture was kept for 2 hr., then poured into water. The washed and air-dried solids were crystallised from aqueous methanol and then from chloroform–methanol, to give the *dibromo-ketone*

(6·1 g.), tablets, m. p. 110—113° (decomp.), $[\alpha]_D^{20}$ −89·5° (*c*, 1·1) (Found : C, 51·4; H, 6·9. $C_{20}H_{30}O_2Br_2$ requires C, 51·9; H, 6·5%).

5α : 6β-*Dibromo*-2β-*chloro*-17β-*hydroxy*-17α-*methylandrostan*-3-*one* (V*c*; R = Cl) *and its* 2α-*Chloro-epimer* (VI*c*; R = Cl).—The foregoing compound (6·5 g.) in acetic acid (140 ml.) was treated with chlorine (1 g.) in acetic acid (28 ml.), absorption of halogen being complete in 12 min. The mixture was poured into water and the product isolated with ether. The insoluble fraction (4·9 g., m. p. 120—121°) obtained by trituration of the material with a small volume of cold acetone was purified from aqueous acetone, to give the *dibromo*-2β-*chloro-ketone*, prisms, m. p. 130° (decomp.), $[\alpha]_D^{22}$ −34° (*c*, 1·04) (Found : C, 48·4; H, 5·9. $C_{20}H_{29}O_2ClBr_2$ requires C, 48·4; H, 5·9%). The 2α-*chloro-epimer*, plates (from aqueous ethanol), m. p. 135—136° (decomp.), $[\alpha]_D^{21}$ −72·5° (*c*, 1·2) (Found : C, 48·0; H, 5·6%), was obtained if the mixture was kept overnight.

2α-*Chloro*-17α-*methyltestosterone* (VIII*c*; R = Cl).—Sodium iodide (7 g.) was added to a suspension of the foregoing dibromo-2β-chloro-ketone (5 g.) in acetone (70 ml.). The mixture was stirred for 5 min., then poured into water, and the product extracted with ether. The extract was washed with aqueous sodium thiosulphate and water, dried, and concentrated to 150 ml. After addition of acetic acid (75 ml.) and concentrated hydrochloric acid (3 ml.), the mixture was stored at 0° for 18 hr. The product, isolated with ether, was purified from aqueous methanol, to give 2α-*chloro*-17α-*methyltestosterone* (2·1 g.), plates, m. p. 154—155° (sinters 100—110°), $[\alpha]_D^{23}$ +79° (*c*, 1·08), $\lambda_{max.}$ 243 mμ (4·10) (Found : C, 67·4; H, 8·8. $C_{20}H_{29}O_2Cl,H_2O$ requires C, 67·7; H, 8·8%). The crystals became opaque and then yellow on brief drying at 100°.

17β-*Acetoxy*-5α : 6β-*dibromoandrostan*-3-*one* (IV*b*).—17β-Acetoxyandrost-5-en-3β-ol (3·3 g.) in acetic acid (100 ml.) was treated with bromine (1·6 g.) in acetic acid (10 ml.). Several minutes later, chromium trioxide (1 g.) in 80% acetic acid (10 ml.) was added, and the mixture kept for 18 hr. The solids obtained on precipitation with water were crystallised from aqueous ethanol. The *dibromo-ketone* (2·9 g.) formed plates, m. p. 98—100° (decomp.), $[\alpha]_D^{21}$ −72° (*c*, 1·25) (Found : C, 51·7; H, 5·8. $C_{21}H_{30}O_3Br_2$ requires C, 51·4; H, 6·2%).

17β-*Acetoxy*-5α : 6β-*dibromo*-2β-*chloroandrostan*-3-*one* (V*b*; R = Cl).—The foregoing compound (9·1 g.) in acetic acid (150 ml.) was treated with chlorine (1·44 g., 1·1 mol.) in acetic acid (25 ml.), absorption of halogen being accompanied by the separation of crystals. After 10 min., the mixture was diluted with water and the solids were washed and air-dried. Crystallised from chloroform–methanol, the *dibromochloro-ketone* (7·3 g.) formed needles, m. p. 118° to 130° (decomp.), depending on the rate of heating, $[\alpha]_D^{22}$ −24° (*c*, 1·02) (Found : C, 47·5; H, 5·1. $C_{21}H_{29}O_3ClBr_2$ requires C, 48·1; H, 5·6%).

2α-*Chlorotestosterone Acetate* (VIII*b*; R = Cl).—Prepared from the foregoing compound (5 g.) by the method employed for the preparation of 2α-chloro-17α-methyltestosterone (above), 2α-*chlorotestosterone acetate* (2·7 g.) formed needles (from methanol), m. p. 199—200°, $[\alpha]_D^{23}$ +90° (*c*, 1·22), $\lambda_{max.}$ 242 mμ (4·14) (Found : C, 69·0; H, 7·9. $C_{21}H_{29}O_3Cl$ requires C, 69·1; H, 8·0%).

2α-*Bromo*-17α-*methyltestosterone* (VIII*c*; R = Br).—Bromine (4 g.) in acetic acid (40 ml.) was added to the dibromo-compound (IV*c*) (11·4 g.) in acetic acid (300 ml.), absorption being complete in 5 min., then the mixture was poured into water. The product, isolated with ether, was purified from methylene chloride–hexane, giving prisms (7·5 g.), m. p. 126—128° (decomp.). This material was partially debrominated with sodium iodide (10 g.) in acetone (80 ml.), and the product crystallised from aqueous ethanol, to give prisms (2·7 g.), m. p. 108—110°. Treatment of the latter compound with hydrochloric acid in ether–acetic acid gave a product which was triturated with cold methanol. The insoluble fraction (2·2 g.) on purification from aqueous ethanol gave 2α-*bromo*-17α-*methyltestosterone*, needles, m. p. 155° (decomp.), $[\alpha]_D^{23}$ +90·5° (*c*, 0·86), $\lambda_{max.}$ 244 mμ (4·15) (Found : C, 62·9; H, 7·6. $C_{20}H_{29}O_2Br$ requires C, 63·0; H, 7·7%).

The authors thank the Directors of The British Drug Houses, Ltd. for permission to publish this work.

CHEMICAL RESEARCH LABORATORIES,
THE BRITISH DRUG HOUSES, LTD., LONDON, N.1.

[*Received, October 6th,* 1955.]