248. *Studies in the Steroid Series. Part LXXIV.* Some Tricyclic Analogues of Steroid Sex Hormones: The Bromination of Enol Acetates.*

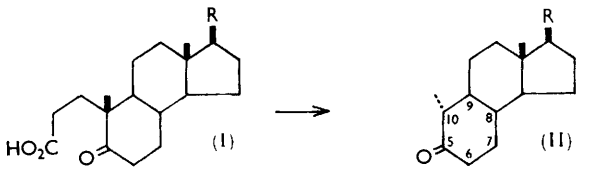
By M. P. Hartshorn and E. R. H. Jones.

From the tricyclic ketone (II) with the cholesteryl side chain, two enol acetates were prepared and from these, by kinetically controlled bromination and then dehydrobromination, the isomeric αβ-unsaturated ketones (V and IX; R = C_8H_{17}).

Ozonolysis of testosterone acetate followed by pyrolysis of the sodium salt of the keto-acid (I; R = OAc) gave the ketone (II; R = OH). Similar enol acetylation, bromination and dehydrobromination led to the tricyclic testosterone analogues (V and IX; R = OAc and OBz). However, hydrolysis of the ketones (IX; R = OAc and OBz) gives an inseparable mixture of the αβ- and βγ-unsaturated isomers.

Whereas bromination of the enol acetates (III) invariably gave only the bromo-compounds (IV), the conditions for bromination of the isomeric enol acetates had a marked effect on the product composition, either the 6β(axial)-compounds or a mixture of 6α- and 6β-isomers being obtained.

Modifications of the structures of the natural steroid hormones have produced notable and usually unpredictable variations in their biological activities.[1] In connection with the structure of lumisterol it was found [2] that tricyclic ketones, *e.g.*, (II; R = C_9H_{17}), the so-called des-A-ketones, devoid of ring A, could be obtained fairly readily by pyrolysis of the sodium salts of the keto-acids, *e.g.*, (I; R = C_9H_{17}), in molten sodium phenylacetate. It therefore seemed worthwhile to attempt to prepare tricyclic analogues of the sex hormones [2a] containing 17-oxygen groups and an αβ-unsaturated ketone system in ring B,



e.g., (V and IX; R = OH). It was also expected that whilst investigating methods of introducing ethylenic linkages into the 9,10- and 6,7-positions useful information would be obtained regarding the enolisation and other properties of the 5-ketones, which could be compared with the data for steroid 3-ketones, in which the rôle of the 10β-methyl group is probably of prime importance. [During the course of our work Villotti, Ringold, and Djerassi,[3] by studies on the enol acetylation and bromination of 3-keto-19-nor-steroids, demonstrated the predominant rôle of the angular methyl group.]

Des-A-cholestane Series (R = C_8H_{17}).—Pilot experiments were carried out in this series. Yields of the des-A-ketone (II; R = C_8H_{17}) increased with temperature from 43% at 265° and 60% at 280° to 66% at 295°. Above this temperature the amount of dibenzyl ketone formed is considerable and impedes the isolation of the ketone (II).

Direct bromination of des-A-cholestanone (II) gave a mixture of monobromo-ketones eventually estimated to comprise *ca.* 47% of 10β-, 38% of 6β-, and 8% of 6α-monobromo-compounds † (IV, VIII, and VII). Chromatography on alumina caused decomposition

* Part LXXIII, Jones and Wluka, *J.*, 1959, 911.

† Throughout this paper the compounds are named, and therefore also numbered, as steroid derivatives. This simplifies the steric designations (see " Handbook for Chemical Society Authors," *Chem. Soc. Special Publ.*, 1960, No. 14, p. 195).

[1] Cf. Fieser and Fieser, " Steroids," Reinhold Publ. Corp., 1959.

[2] Castells, Jones, Meakins, and Williams, *J.*, 1959, 1159.

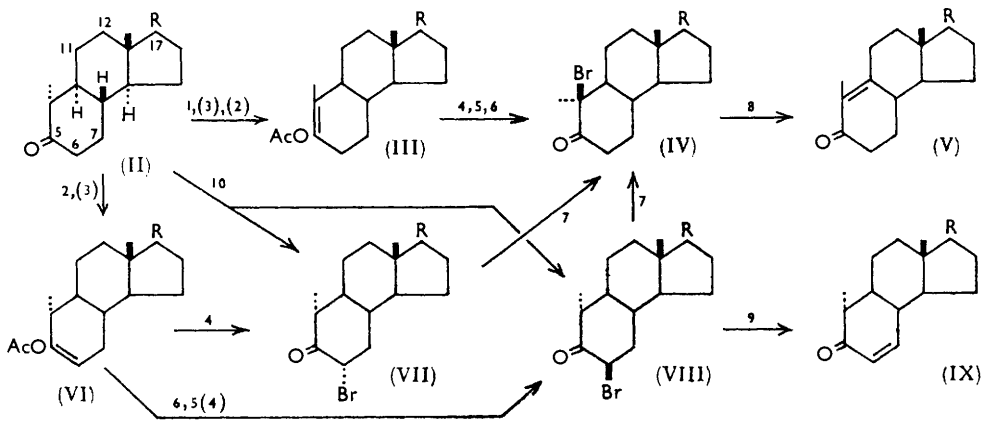
[2a] Cf. Chinn, Dryden, and Burtner, *J. Org. Chem.*, 1961, **26**, 3910.

[3] Villotti, Ringold, and Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 5693.

and, although separation of the axial(10β and 6β) from the equatorial(6α) isomers was achieved by use of silica gel, the mixture of axial isomers could not be resolved. Under mild dehydrobrominating conditions (lithium carbonate in dimethylformamide at 80°) the tertiary 10β-bromo-compound (IV) loses hydrogen bromide, so that when the crude bromination product was so treated, although considerable conversion of 6β- into 6α-bromo-isomer occurs (as shown in a control experiment), the resulting mixture of 6β(*ax*)- and 6α(*eq*)-bromo-ketones and the αβ-unsaturated ketone (V) could be resolved chromatographically, making it possible to determine the above-mentioned composition of the crude bromination product.

Complete kinetic control of the direct bromination of ketones is difficult to achieve and at first it seemed possible that the 6-bromo-ketones might have arisen by isomerisation (catalysed by hydrogen bromide) of the 10-bromo-isomer. [It was subsequently discovered that both 6α- and 6β-bromo-ketones (VII and VIII) are converted into the more stable 10β-bromo-isomer (IV) by hydrogen bromide in acetic acid–chloroform.] Kinetic control is effected in the bromination of enol acetates, however, by operating in the presence of bases.[4]

In acetic anhydride–carbon tetrachloride–perchloric acid [5] the ketone (II; R = C_8H_{17}) was partially (70%) converted into the 5(10)-enol acetate (III). Isopropenyl acetate–toluene-*p*-sulphonic acid gave a mixture containing 70% of the 5-enol acetate (VI), separated from the 5(10)-isomer by careful chromatography. The method employing



(1) Ac_2O–CCl_4-$HClO_4$. (2) CH_2=CMe·OAc-*p*-C_6H_4Me·SO_3H. (3) Ac_2O–*p*-C_6H_4Me·SO_3H. (4) Br_2–Pyridine–AcOH. (5) Br_2–K_2CO_3–CCl_4. (6) Br_2–epichlorohydrin–CCl_4. (7) HBr–AcOH-$CHCl_3$. (8) Li_2CO_3–NMe_2·CHO at 80°. (9) Li_2CO_3-NMe_2·CHO at the b. p. (10) Br_2–AcOH–Et_2O.

acetic anhydride–toluene-*p*-sulphonic acid was of no preparative value since it yielded a 55 : 45 mixture of the 5(10)- and 5-isomers; separation would have been very tedious. These variations in the proportions of the two enol acetates with the experimental conditions parallel those observed by Berkoz, Chavez, and Djerassi [6] with dihydro-4α-methyl-19-nortestosterone and confirm, as suggested by Professor Djerassi, that the factors controlling the direction of enol acetylation under different conditions reside largely in the bicyclic ketonic environment. The two enol acetates differed in m. p. and rotation, and the infrared spectrum of the 5-isomer (VI) contained strong bands at *ca.* 1150 and 910 cm.$^{-1}$ which were absent from the spectrum of the 5(10)-isomer (III).[7] In contrast to the behaviour of 17(20)- and 20-enol acetates [8] and 6- and 7-enol acetates [7] of the steroid

[4] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041.
[5] Barton, Evans, Hamlet, Jones, and Walker, *J.*, 1954, 747.
[6] Berkoz, Chavez, and Djerassi, *J.*, 1962, **1323**.
[7] Cf. Jones and Wluka, *J.*, 1959, 911.
[8] Vanderhaeghe, Katzenellenbogen, Dobriner, and Gallagher, *J. Amer. Chem. Soc.*, 1952, **74**, 2810.

series, the 5-enol acetate (VI) was stable in the presence of acetic anhydride–carbon tetrachloride–perchloric acid, and the 5(10)-enol acetate (III) was unaffected by acetic anhydride–toluene-*p*-sulphonic acid.

Bromination of the 5(10)-enol acetate (III) in pyridine–acetic acid, collidine–acetic acid, or potassium carbonate–carbon tetrachloride gave the 10β-bromo-ketone (IV) in 72—80% yield. Its structure follows from its smooth conversion into the αβ-unsaturated ketone (V) ($\lambda_{max.}$ 2485 Å); the axial(10β) conformation of the bromine atom is indicated by the absence of shift in infrared carbonyl frequency and a displacement of 200 Å in the ultraviolet maximum compared with the parent ketone and the strong positive Cotton effect in the optical rotatory dispersion curve, whereas (II) exhibits a negative Cotton effect.[9] Bromination of the 5-enol acetate (VI) in carbon tetrachloride in the presence of epichlorohydrin (cf. Kirk, Patel, and Petrow [10] who used ethylene and propylene oxide) as proton acceptor gave the 6β-bromo-ketone (VIII) in 85% yield. The configurations of these two isomers follow from their conformations, as indicated by light absorption and optical rotatory dispersion measurements, and from the production of the (non-crystalline) αβ-unsaturated ketone (IX) ($\lambda_{max.}$ 2300 Å) by lithium carbonate in boiling dimethylformamide. Less efficient acid-binding resulted in the formation of amounts (up to 50%) of the 6α-isomer (VII) that increase in the order epichlorohydrin $<K_2CO_3$–CCl_4 <pyridine–acetic acid. Treatment of the bromo-compounds (VII and VIII) with hydrogen bromide in chloroform–acetic acid, the changes being followed by optical rotation measurements, suggested that the axial isomer (VIII) is rapidly (*ca.* 25 min.) converted into the equatorial isomer (VII) which is much more slowly transformed into the 10β-isomer (IV); the latter was isolated from preparative experiments in each case.

Previous examples of hydrogen bromide-catalysed isomerisation in the steroid series have involved either the migration of a bromine atom to a less substituted carbon atom, *i.e.*, 5α ⟶ 7α,[11] 9α ⟶ 12α,[12] 8β ⟶ 6α,[7] 2,2 ⟶ 2α,4α,[13] or inversion to the more stable configuration, *i.e.*, 6β ⟶ 6α,[14] the configuration of the bromine atom being determined by the result of competition between the opposed steric and C=O and C–Br dipole interactions.[15] These factors are probably of considerable importance in deciding also the location of the bromine atom in the hydrogen bromide-isomerisation product. In the present instance steric interactions are very small (only 1,3-Br–H), comparable to those in bromocyclohexanone; hence the preferred 10β(*ax*)-configuration in which the dipole interactions are minimised. Bromine substitution on the more substituted carbon atoms seems to be in line with the direct-bromination behaviour of aliphatic ketones,[16] although whether true thermodynamic control is achieved in these simple cases does not appear to have been established.

The slowness (~16 hr.) of the 6α ⟶ 10β-isomerisation with high hydrogen bromide concentrations, compared with the speed (10 min.) of the formation of the 10β-isomer in the direct bromination, indicates clearly that in the latter the 10β-bromo-compound is formed directly. On the other hand it is possible that the small quantity of 6α-bromo-compound produced by direct bromination arises by hydrogen bromide-catalysed isomerisation of the 6β-isomer; the high yield of the latter in the epichlorohydrin experiment with the 5-enol acetate supports this suggestion.

Des-A-androstane Series (R = OH).—Ozonolysis of testosterone acetate, followed by hydrolysis gave the crystalline hydroxy-keto-acid (I; R = OH). Pyrolysis was best

[9] Djerassi, " Optical Rotatory Dispersion," McGraw-Hill, 1960, p. 115.
[10] Kirk, Patel, and Petrow, *J.*, 1956, 627.
[11] Heilbron, Jones, and Spring, *J.*, 1937, 801.
[12] Jones and Wluka, *J.*, 1959, 907; Henbest, Jones, Wagland, and Wrigley, *J.*, 1955, 2477; Wrigley, Ph.D. Thesis, Manchester, 1956.
[13] Crowne, Evans, Green, and Long, *J.*, 1956, 4351.
[14] Barr, Heilbron, Jones, and Spring, *J.*, 1938, 334.
[15] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301.
[16] Favorski, *J. Russ. Phys. Chem. Soc.*, 1913, **44**, 1358; *J. prakt. Chem.*, 1913, **88**, 658.

effected with the sodium salt of the acetoxy-keto-acid (I; R = OAc); with the salt of the hydroxy-keto-acid an oxidation–reduction system involving the 17-hydroxyl group seemed to be set up since, in addition to the required tricyclic hydroxy-ketone (II), some diketone and a mixture of epimeric dihydroxy-compounds was obtained.

For solubility and melting-point reasons the enol acetylation and bromination were carried out on the 17-benzoate (II; R = OBz). As in the des-A-cholestane series treatment with acetic anhydride–perchloric acid gave the 5(10)-enol acetate (III; R = OBz) that was brominated in 80% yield to the 10β-bromo-compound (IV; R = OBz); lithium carbonate in dimethylformamide then produced the αβ-unsaturated keto-benzoate (V; R = OBz) that was hydrolysed to the hydroxy-ketone (V; R = OH). On the other hand, enol acetylation with isopropenyl acetate–toluene-*p*-sulphonic acid gave the 5-enol acetate (VI; R = OBz), and bromination in the presence of epichlorohydrin produced the 6β-bromo-compound (VIII; R = OBz) in 85% yield. (With collidine–acetic acid a 1 : 1 mixture of the 6α- and 6β-bromo-compounds, separated by chromatography, was obtained.) Dehydrobromination under more vigorous conditions with lithium carbonate in boiling dimethylformamide gave the αβ-unsaturated keto-benzoate (IX; R = OBz).

In spite of the expected difficulties the enol-acetylation–bromination experiments were repeated in the 17-acetoxy-series. The two enol-acetylation procedures again produced specific compounds (III and VI; R = OAc), although they were waxy solids which did not crystallise. Bromination of the 5(10)-enol acetate (III; R = OAc) gave the 10β-bromo-compound (IV; R = OAc), and dehydrobromination afforded the αβ-unsaturated ketone (V; R = OAc), identical with that obtained directly by the " benzoate " route. When the 5-enol acetate (VI; R = OAc) was brominated in the presence of epichlorohydrin the 6β-bromo-ketone (VIII; R = OAc) was again the sole product, and dehydrobromination yielded the αβ-unsaturated keto-acetate (IX; R = OAc).

Efforts to obtain the true testosterone analogue (IX; R = OH) have not yet been successful. Hydrolysis of the esters (IX; R = OAc and OBz) yields unresolvable mixtures of the required hydroxy-ketone (50—80%) and material, presumably the βγ-isomer, containing an unconjugated carbonyl group. A similar result was obtained when the ketone (IX; R = C_8H_{17}) was treated with methanolic potassium hydroxide.

A route which offered promise of obviating this difficulty has been explored. The saturated keto-alcohol (II; R = OH) was brominated directly, the mixture of bromo-ketones was treated with lithium carbonate in boiling dimethylformamide, and the product, which should have contained only the isomeric αβ-unsaturated keto-alcohols (V and IX; R = OH), was chromatographed on alumina. The isomer (V) was separated but the light-absorption properties of the other crystalline product [$\lambda_{max.}$ 2280 Å, ε 9600; $\nu_{max.}$ 3546 (OH), 1730 ms(!), 1678 cm.$^{-1}$ (C=C–C=O)] were not exactly as expected for the pure isomer (IX; R = OH).

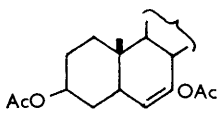
Bromination of Enol Acetates.—In their recent publication Villotti, Ringold, and Djerassi [3] carefully examined the bromination of certain 3-keto-steroids and their enol acetates. They concluded, *inter alia*, that, on bromination, enol acetates and ketones react very similarly. Such a conclusion may well be valid as far as 3-ketones of the steroid and 19-nor-steroid series are concerned but in other types marked differences occur.

Thus in the experiments described in this paper it is clear that the products of bromination of enol acetates depend very markedly upon the experimental conditions. All three 5-enol acetates (VI) examined produced 6β(*ax*)-bromo-compounds (VIII) in yields of 80—85%, with no sign of the 6α(*eq*)-isomer, when the epichlorohydrin–carbon tetrachloride conditions were employed. In the presence of pyridine in acetic acid, the 5-enol acetates (VI; R = C_8H_{17} and OBz) gave practically equal amounts of 6β- and 6α-bromo-ketones. On the other hand, variation in the experimental conditions was without effect on the bromination of the three 5(10)-enol acetates, (III), 10β(*ax*)-bromo-ketones (IV) being formed (usually in 80% yield). Direct bromination of the ketone produced all three isomers (10β : 6β : 6α = ~47 : 38 : 8) and from this, and the results of hydrogen

bromide-isomerisations, it seems improbable that the sole difference between, *e.g.*, the epichlorohydrin and the pyridine experiments, might be the complete suppression of hydrogen bromide-isomerisation in the former case. There must be substantial variations in the bromination mechanisms under these different conditions.

Villotti, Ringold, and Djerassi [3] referred to the bromination of 7-keto-steroids, partly on the basis of which Corey [17] made his generalisation regarding the preferred axial orientation of the bromine atom in the products of kinetically controlled brominations. In previous studies on the bromination of enol acetates [7] attention was drawn to the fact that the major product in the bromination of 3β,7-diacetoxycholest-6-ene (X) in the presence of pyridine in acetic acid is the more stable 6α(*eq*)-isomer, the ratio 6α : 6β being at least 2·5 : 1, but more probably 5 : 1. We now find that when this bromination is effected in the presence of epichlorohydrin, conditions which are known to favour the formation of the axial isomers, the ratio is *ca.* 55 : 45, *i.e.*, a considerable proportion of the equatorial bromo-compound is still formed.

Much more remains to be done before the bromination of cyclic ketones and their enol acetates can be said to be fully understood. Not only must careful analysis of the immediate products be made, as most usefully carried out by optical rotatory dispersion measurements in the work of Villotti, Ringold, and Djerassi,[3] but also the formation and



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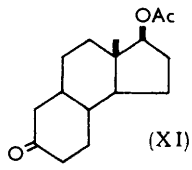

(XI)

purification of enol esters and their bromination under various experimental conditions will have to be studied. Appreciable progress along these lines is reported in a paper by Berkoz, Chavez, and Djerassi.[6] It is our intention to repeat some of the work described in the present paper using the des-A-19-norandrostane derivative (XI) in the expectation that the factors influencing the direction of enolisation and the production and stabilities of the bromo-compounds might be more clearly perceived in the absence of the 10-methyl group.

Experimental

M. p.s were determined on a Kofler block and are corrected. Rotations were measured for chloroform solutions at room temperature. Unless otherwise specified, infrared and ultraviolet spectra were recorded for carbon disulphide and ethanol solutions, respectively. Alumina used for chromatography was Peter Spence's grade H; deactivated alumina refers to grade H material to which 5% of 10% acetic acid had been added. Silica gel was Crosfield Sorbsil Grade 60—120. Light petroleum refers to the fraction of b. p. 60—80°.

10α-*Des*-A-*cholestan*-5-*one* (II; R = C_8H_{17}).—The sodium salt of 5-oxo-A-nor-3,5-seco-cholestan-3-oic acid (12·25 g.; dried at 100°/15 mm.) and sodium phenylacetate (45 g.) were heated at 295°/0·04 for 3 hr. The distillate (8·5 g.) which collected in the wide-bore U-shaped side arm was purified by chromatography and crystallisation, giving 10α-des-A-cholestan-5-one (7·5 g.), m. p. 62—63°, $[\alpha]_D$ +15° (*c* 1·0). Julia, Eschenmoser, Heusser, and Tarköy [18] give m. p. 60°, $[\alpha]_D$ +18°, Pinder and Robinson [19] m. p. 52°.

Enol-acetylation of 10α-*Des*-A-*cholestan*-5-*one*.—(*a*) A solution of the ketone (3 g.) in carbon tetrachloride (28 c.c.) was treated with acetic anhydride (1·5 c.c.) and 66% aqueous perchloric acid (0·06 c.c.) and kept at 20° for 24 hr. The mixture was diluted with ether (600 c.c.) and washed successively with sodium hydrogen carbonate solution, water, and brine, and dried. Evaporation afforded an oil (3·62 g.) which was adsorbed on deactivated alumina (330 g.).

[17] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301; 1954, **76**, 175.
[18] Julia, Eschenmoser, Heusser, and Tarköy, *Helv. Chim. Acta*, 1953, **36**, 1885.
[19] Pinder and Robinson, *J.*, 1952, 1224.

Elution with light petroleum and crystallisation from acetone–methanol gave 5-*acetoxy-des*-A-*cholest*-5(10)-*ene* (III; R = C_8H_{17}) (2·39 g.) as needles, m. p. 73—74°, $[\alpha]_D$ +75° (*c* 0·99) (Found: C, 80·05; H, 11·3. $C_{25}H_{42}O_2$ requires C, 80·15; H, 11·3%), $\nu_{max.}$ 1754 and 1212 (OAc), 1692 cm.$^{-1}$ (C=C). R.D. in MeOH: [*M*] (5890 Å), +200°; (5000), +350°; (4000), +700° (3000), +1600°.

(*b*) The solvent was fractionally distilled at 96° from a solution of 10α-des-A-cholestan-5-one (6·68 g.) and toluene-*p*-sulphonic acid (0·9 g.) in isopropenyl acetate (125 c.c.). After 5 hr., during which 40 c.c. of solvent had distilled, the remaining solvent was removed at 20 mm. The residue was worked up *via* ether and adsorbed on deactivated alumina (500 g.). Elution with light petroleum and crystallisation from acetone–methanol gave an enol acetate mixture, m. p. 62—63°, $[\alpha]_D$ +45° (*c* 1·01). The nuclear magnetic resonance spectra of this material and of the $\Delta^{5(10)}$-enol acetate indicated that the mixture, $[\alpha]_D$ +45°, contained *ca.* 30% of the $\Delta^{5(10)}$-isomer.

The mixture (500 mg.) was adsorbed on deactivated alumina (120 g.) and elution with light petroleum (b. p. 30—40°) afforded 5-*acetoxy*-10α-*des*-A-*cholest*-5-*ene* (VI; R = C_8H_{17}) (152 mg.) that crystallised from acetone–methanol as needles, m. p. 42—44°, $[\alpha]_D$ +26° (*c* 0·97) (Found: C, 79·95; H, 11·1%), $\nu_{max.}$ 1754 and 1212 (OAc), 1689 cm.$^{-1}$ (C=C). R.D. in methanol: [*M*] (5890 Å), +200°; (5000), +250°; (4000), +500°; (3000), +1200°.

(*c*) The solvent was fractionally distilled through a short column packed with glass helices from a solution of the ketone (500 mg.) and toluene-*p*-sulphonic acid (170 mg.) in acetic anhydride (20 c.c.). After 6 hr., during which 5 c.c. of solvent had distilled, the remaining solvent was evaporated at 20 mm. and the residue worked up *via* ether. The product (640 mg.) was adsorbed on deactivated alumina (60 g.) and light petroleum (10 × 15 c.c.) eluted solid fractions with rotations increasing stepwise from fraction 1, $[\alpha]_D$ +42° (*c* 1·06), to fraction 10, $[\alpha]_D$ +75° (*c* 0·99) (pure 5-acetoxydes-A-cholest-5(10)-ene. On the basis of rotations the estimated yields of the isomers were: 5-enol acetate, 46%; 5(10)-enol acetate, 54%.

10β-*Bromo*-10α-*des*-A-*cholestan*-5-*one* (IV; R = C_8H_{17}).—(*a*) Bromine (342 mg., 1·5 mol.) in acetic acid (1 c.c.) was added to a solution of 5-acetoxy-10α-des-A-cholest-5(10)-ene (500 mg.) in 1 : 10 v/v pyridine–acetic acid (6 c.c.) under nitrogen. The flask was stoppered, and kept in the dark at 20° for 24 hr. An aqueous solution of sodium sulphite was added, and the product was isolated *via* ether and adsorbed on silica gel (50 g.). Elution with light petroleum–benzene (10 : 1) and crystallisation from ethyl acetate–methanol gave 10β-*bromo*-10α-*des*-A-*cholestan*-5-*one* (400 mg.) as needles, m. p. 72—73°, $[\alpha]_D$ +137° (*c* 1·01) (Found: C, 66·8; H, 9·5; Br, 19·5. $C_{23}H_{39}BrO$ requires C, 67·1; H, 9·55; Br, 19·4%), $\nu_{max.}$ 1710 cm.$^{-1}$ (*ax*-bromo-ketone), $\lambda_{max.}$ 3070 Å (ε 110). R.D. in methanol: [*M*] (5890 Å), +700°; (3300), +14,400°; (2900), −5600°.

(*b*) Bromine (342 mg., 1·5 mol.) in acetic acid (1 c.c.) was added to a solution of the 5(10)-enol acetate (500 mg.) in 1 : 10 v/v collidine–acetic acid (6 c.c.) under nitrogen. After 24 hr. at 20° the product was isolated *via* ether and adsorbed on silica gel (60 g.). Elution with light petroleum–benzene (10 : 1), and crystallisation from ethyl acetate–methanol gave 10β-bromo-10α-des-A-cholestan-5-one (450 mg.), m. p. 72—73°, $[\alpha]_D$ +135° (*c* 0·98).

(*c*) Bromine (250 mg., 1·1 mol.) in carbon tetrachloride (0·7 c.c.) was added to a stirred ice-cold suspension of anhydrous potassium carbonate (350 mg.) in a solution of the 5(10)-enol acetate (500 mg.) in carbon tetrachloride (20 c.c.). The mixture was stirred for a further 10 min., and then worked up *via* chloroform. The product was adsorbed on silica gel (60 g.); elution with light petroleum–benzene (10 : 1) and crystallisation from ethyl acetate–methanol gave 10β-bromo-compound (420 mg.), m. p. 72—73°, $[\alpha]_D$ +135° (*c* 0·99).

Des-A-*cholest*-9-*en*-5-*one* (V; R = C_8H_{17}) (with R. W. J. Williams).—A solution of the 10β-bromo-10α-des-A-cholestan-5-one (1·0 g.) in dimethylformamide (50 c.c.) was heated at 100° for 2 hr. with lithium carbonate (1·5 g.). The suspension was cooled, diluted with ether (500 c.c.), and washed successively with 10% hydrochloric acid (100 c.c.), sodium hydrogen carbonate solution, and brine, dried, and evaporated, finally at 20 mm. The residual oil (835 mg.) was adsorbed on deactivated alumina (70 g.). Light petroleum eluted *des*-A-*cholest*-9-*en*-5-*one* (760 mg.) as an oil that was purified for analysis by distillation at 175—180° (bath temp.)/3 × 10^{-3} mm. and then had $[\alpha]_D$ −8° (*c* 3·3) (Found: C, 83·45; H, 11·5. $C_{23}H_{38}O$ requires C, 83·55; H, 11·6%), $\nu_{max.}$ 1661 cm.$^{-1}$ (C=C–C=O), $\lambda_{max.}$ 2485 Å (ε 16,300). R.D. in methanol: [*M*] (5890 Å), +50°; (3800), +200°; (3580), 0°; (3300), +1150°; (2850), −5000°.

The conjugated ketone was converted into its 2,4-*dinitrophenylhydrazone* which crystallised

from chloroform–ethanol as crimson needles, m. p. 179—181° (Found: C, 67·85; H, 8·15; N, 10·5. $C_{29}H_{42}N_4O_4$ requires C, 68·2; H, 8·3; N, 10·95%), $\lambda_{max.}$ (in $CHCl_3$) 3940 (ε 27,300), 2950 (ε 10,600), 2600 Å (ε 16,700).

6β-*Bromo*-10α-*des*-A-*cholestan*-5-*one* (VIII; R = C_8H_{17}).—Bromine (50 mg., 1·1 mol.) in carbon tetrachloride (0·15 c.c.) was added to a stirred ice-cold solution of the 5-enol acetate (100 mg.; $[\alpha]_D$ +26°) and epichlorohydrin (0·05 c.c.) in carbon tetrachloride (10 c.c.). The solution was stirred for a further 10 min., and then worked up *via* chloroform. The residual oil (110 mg.) was adsorbed on silica gel (15 g.). Light petroleum–benzene (20 : 1) eluted 6β-*bromo*-10α-*des*-A-*cholestan*-5-*one* (90 mg.), which crystallised from ethyl acetate–methanol as needles, m. p. 68—69°, $[\alpha]_D$ −134° (*c* 0·99) (Found: C, 67·3; H, 9·6; Br, 19·35. $C_{28}H_{39}BrO$ requires C, 67·1; H, 9·55; Br, 19·4%), $\nu_{max.}$ 1709 cm.$^{-1}$ (*ax*-bromo-ketone), $\lambda_{max.}$ 3050 Å (ε 130). R.D. in methanol: [*M*] (5890 Å), −800°; (3280), −14,700; (2800), +18,500°; (2750), +17,800°.

Bromination of 10α-*Des*-A-*cholestan*-5-*one:* 6α-*Bromo*-10α-*des*-A-*cholestan*-5-*one* (VII; R = C_8H_{17}).—Bromine (495 mg., 1·02 mol.) in acetic acid (2·24 c.c.) was added dropwise to an ice-cold stirred solution of the ketone (1 g.) in dry ether (100 c.c.) during 10 min. The excess of bromine was removed with sodium sulphite solution and the product isolated *via* ether as an oil (1·34 g.), which was adsorbed on silica gel (150 g.). Light petroleum–benzene (10 : 1) eluted an intractable oil (1·06 g.), $[\alpha]_D$ +18° (*c* 1·03), $\nu_{max.}$ 1710 cm.$^{-1}$ (*ax*-bromo-ketone).

Light petroleum–benzene (10 : 3) eluted 6α-*bromo*-10α-*des*-A-*cholestan*-5-*one* (100 mg.) which crystallised from ethyl acetate–methanol as plates, m. p. 98—99°, $[\alpha]_D$ −18° (*c* 0·97) (Found: C, 67·3; H, 9·5; Br, 19·4. $C_{28}H_{39}BrO$ requires C, 67·1; H, 9·55; Br, 19·4%), $\nu_{max.}$ 1730 (*eq*-bromo-ketone), 745 cm.$^{-1}$ (*eq*-bromo-ketone), $\lambda_{max.}$ 2850 Å (ε 30). R.D. in methanol: [*M*] (5890 Å), −200°; (3250), −3900°; (2700), +4800°; (2650), +4500°.

The above intractable oil was partially dehydrobrominated with lithium carbonate (2·5 g.) in dimethylformamide (20 c.c.) at 100° for 2 hr. After being worked up *via* ether the oily residue (934 mg.) was adsorbed on silica gel (110 g.). Elution with light petroleum–benzene (10 : 1) and crystallisation from ethyl acetate–methanol afforded 6β-bromo-10α-des-A-cholestan-5-one (149 mg.), m. p. 68·5—69°, $[\alpha]_D$ −133° (*c* 0·98), $\nu_{max.}$ 1710 cm.$^{-1}$.

Light petroleum–benzene (10 : 3) eluted 6α-bromo-10α-des-A-cholestan-5-one (322 mg.), m. p. 98—99°, $[\alpha]_D$ −18° (*c* 1·01), $\nu_{max.}$ 1724, 745 cm.$^{-1}$.

Elution with benzene afforded des-A-cholest-9-en-5-one (457 mg.), $\nu_{max.}$ 1661 cm.$^{-1}$, $\lambda_{max.}$ 2485 Å (ε 15,900).

Epimerisation of 6β-*Bromo-ketone* (VIII; R = C_8H_{17}) *with Lithium Carbonate and Dimethylformamide.*—The bromo-ketone (100 mg.) was heated at 80° for 2 hr. with lithium carbonate (0·4 g.) in dimethylformamide (20 c.c.). The mixture was cooled, then worked up *via* ether, and the residual oil was adsorbed on silica gel (25 g.). Elution with light petroleum and crystallisation from ethyl acetate–methanol gave unchanged 6β-bromo-10α-des-A-cholestan-5-one (27 mg.), m. p. (and mixed m. p.) 68—69°, $[\alpha]_D$ −130° (*c* 1·01). Further elution with light petroleum–benzene (10 : 3), and crystallisation from ethyl acetate–methanol, afforded 6α-bromo-10α-des-A-cholestan-5-one (69 mg.), m. p. and mixed m. p. 98—99°, $[\alpha]_D$ −19° (*c* 0·99).

Treatment of 10β-*Bromo*-10α-*des*-A-*cholestan*-5-*one* (IV; R = C_8H_{17}) *with Hydrogen Bromide.*—The specific rotation of a solution of the 10β-bromo-ketone (100 mg.) in 1 : 1 chloroform–acetic acid (10 c.c.) containing hydrogen bromide (0·3 c.c.; 50% in acetic acid) only changed from +133° to +111° in 7 hr.; the solution was then too dark for further observation. After 24 hr. the product was isolated *via* ether and adsorbed on silica gel (7 g.). Light petroleum–benzene (10 : 1) eluted starting material (85 mg.), m. p. 72—73°, $[\alpha]_D$ +135° (*c* 0·99), $\nu_{max.}$ 1710 cm.$^{-1}$.

Isomerisation of 6α-*Bromo*-10α-*des*-A-*cholestan*-5-*one* (VII; R = C_8H_{17}) *with Hydrogen Bromide.*—The specific rotation of a solution of the 6α-bromo-ketone (100 mg.) in 1 : 1 chloroform–acetic acid (10 c.c.) containing hydrogen bromide (0·3 c.c.; 50% in acetic acid) changed from −44° to +80° in 7 hr.; the solution was then too dark for further observation. After 24 hr. the product was isolated *via* ether and adsorbed on silica gel (7 g.). Light petroleum–benzene (10 : 1) eluted 10β-bromo-10α-des-A-cholestan-5-one (87 mg.), m. p. 71—72°, $[\alpha]_D$ +136° (*c* 0·98), $\nu_{max.}$ 1710 cm.$^{-1}$. Further elution with light petroleum–benzene (10 : 3) afforded starting material (8 mg.), m. p. 98—99°, $[\alpha]_D$ −18° (*c* 0·71).

Isomerisation of 6β-*Bromo*-10α-*des*-A-*cholestan*-5-*one* (VIII; R = C_8H_{17}) *with Hydrogen Bromide.*—The specific rotation of a solution of the 6β-bromo-ketone (100 mg.) in 1 : 1 chloroform–acetic acid (10 c.c.) containing hydrogen bromide (0·3 c.c.; 50% in acetic acid) changed

from −130° to +96° in 8 hr.; the solution was then too dark for further observation. After 24 hr. the product was isolated *via* ether and adsorbed on silica gel (7 g.). Light petroleum–benzene (10 : 1) eluted 10β-bromo-10α-des-A-cholestan-5-one (90 mg.), m. p. 71—72°, $[\alpha]_D$ +134° (*c* 0·99), $\nu_{max.}$ 1710 cm.$^{-1}$.

10α-*Des*-A-*cholest*-6-*en*-5-*one* (IX; R = C_8H_{17}).—6α-Bromo-10α-des-A-cholestan-5-one (200 mg.) was heated with lithium carbonate (300 mg.) in boiling dimethylformamide (20 c.c.) for 5 hr., then cooled. The product (175 mg.) was isolated *via* ether and adsorbed on deactivated alumina (20 g.). Light petroleum–benzene (10 : 1) eluted 10α-des-A-cholest-6-en-5-one (151 mg.) as an oil, for which no satisfactory analytical values could be obtained; it had $\nu_{max.}$ 1675 (C=C–C=O), 810 cm.$^{-1}$ (*cis*-disubstituted C=C), $\lambda_{max.}$ 2290 Å (ε 8900) [cf. Sondheimer and Mazur [20] who for 4α-methylcholest-1-en-3-one give $\lambda_{max.}$ 2300 Å (ε 9500)]. R.D. in methanol: [*M*] (5890 Å), +1050°; (4070), −100°; (3700), +750°; (3200), −4100°; (2950), −3100°; (2800), −4000°.

10α-Des-A-cholest-6-en-5-one was converted into its 2,4-*dinitrophenylhydrazone*, orange-red plates (from chloroform–ethanol), m. p. 183° (Found: C, 68·1; H, 8·2; N, 10·9. $C_{29}H_{42}N_4O_4$ requires C, 68·2; H, 8·3; N, 10·95%), $\lambda_{max.}$ 3820 (ε 31,100), 2580 Å (ε 15,800) [cf. Djerassi, Cais, and Mitscher,[21] who for 4α-ethylcholest-1-en-3-one 2,4-dinitrophenylhydrazone give $\lambda_{max.}$ 3810 Å (ε 24,500)].

Ozonolysis of Testosterone Acetate.—Ozonised oxygen (12·12 mmoles/hr.) was passed into a solution of testosterone acetate (20 g.) in ethyl acetate (500 c.c.) at −80° for 5 hr. The excess of ozone was removed by a stream of nitrogen, and 5% potassium hydrogen carbonate (200 c.c.) and 30% hydrogen peroxide (100 c.c.) were added.[22]. The two-phase system was stirred vigorously for 24 hr. at −6° and for a further 24 hr. at 25°. The acid fraction was separated in the usual way and isolated *via* chloroform, after which it was hydrolysed by boiling with potassium hydroxide (10 g.) in 90% methanol (100 c.c.) in nitrogen for 1 hr. The usual isolation and then crystallisation from chloroform–ether yielded 17β-*hydroxy*-5-*oxo*-A-*nor*-3,5-*secoandrostan*-3-*oic acid* (I; R = OH) (14·2 g.) as needles, m. p. 195—197°, $[\alpha]_D$ +27° (*c* 0·96) (Found: C, 69·8; H, 9·1. $C_{18}H_{28}O_4$ requires C, 70·1; H, 9·15%), $\nu_{max.}$ (in Nujol) 3390 (OH), 1704 (C=O and CO_2H), and 1057 cm.$^{-1}$ (OH).

5,17-*Dioxo*-A-*nor*-3,5-*secoandrostan*-3-*oic Acid* (I; R = O).—8N-Chromic acid [23] (2·0 c.c., 1·05 mol.) was added to a stirred solution of the above hydroxy-acid (2 g.) in acetone (100 c.c.) at 0°. After 10 min. methanol (2 c.c.) was added, the solvent was removed at 12 mm., and the product isolated *via* ether and adsorbed on silica gel (200 g.). Benzene–ether (9 : 1) eluted the acid (1·9 g.) which crystallised only slowly and then had m. p. 108—109°, $[\alpha]_D$ +95° (Found: C, 70·4; H, 8·4. Calc. for $C_{18}H_{26}O_4$: C, 70·6; H, 8·35%), $\nu_{max.}$ (in $CHCl_3$) 1739 (C=O in 5-membered ring), 1704 cm.$^{-1}$ (C=O in 6-membered ring and CO_2H) (Robinson [24] gives m. p. 107—109°).

10α-*Des*-A-*androstane*-5,17-*dione* (II; R = O).—The sodium salt of the keto-acid was prepared by titration of its methanolic solution with sodium methoxide in methanol to phenolphthalein. The sodium salt (1·49 g.), isolated by evaporation of solvent, was pyrolysed with sodium phenylacetate (4·5 g.) at 295°/0·1 mm. for 3 hr. The solid distillate (537 mg.) was adsorbed on alumina (50 g.). Elution with benzene and crystallisation from light petroleum afforded 10α-des-A-androstane-5,17-dione (430 mg.) as plates, m. p. 122·5—123°, $[\alpha]_D$ +92° (*c* 1·07) (Found: C, 77·2; H, 9·6. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·5%), $\nu_{max.}$ 1739 (5-membered ring C=O), 1709 cm.$^{-1}$ (6-membered ring C=O). R.D. in methanol: [*M*] (5890 Å) +500°; (3150), +4450°; (2900), −2550° (Robinson [24] gives m. p. 119—120°, $[\alpha]_D$ +89°).

Pyrolysis of Sodium 17β-*Hydroxy*-5-*oxo*-A-*nor*-3,5-*secoandrostan*-3-*oate* (cf. I; R = OH).—The sodium salt (1·44 g.) was prepared in the usual manner and pyrolysed with sodium phenylacetate (4·5 g.) at 295°/0·04 for 3 hr. The oily distillate (920 mg.) was adsorbed on alumina (80 g.) from which benzene eluted 10α-des-A-androstane-5,17-dione (170 mg.), m. p. 122—123°, $[\alpha]_D$ +92° (*c* 1·02), $\nu_{max.}$ 1739 and 1709 cm.$^{-1}$.

Elution with ether–methanol (10 : 1) afforded an oil (520 mg.) which was re-adsorbed on deactivated alumina (40 g.). Benzene eluted 17β-*hydroxy*-10α-*des*-A-*androstan*-5-*one* (200 mg.)

[20] Sondheimer and Mazur, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.
[21] Djerassi, Cais, and Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 2386.
[22] Cf. Fujimoto and Prager, *J. Amer. Chem. Soc.*, 1953, **75**, 3259.
[23] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2556.
[24] Robinson, *J.*, 1958, 2311.

which crystallised as needles (from ether–light petroleum), m. p. 94—95°, $[\alpha]_D$ +2° (*c* 0·96) (Found: C, 76·4; H, 10·2. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%), $\nu_{max.}$ 3571 (OH), 1709 (C=O), and 1059 cm.$^{-1}$ (OH). R.D. in methanol: [*M*] (5890 Å), 0°; (3050), −2650°; (2800), +2350°. Oxidation in acetone solution with 8N-chromic acid gave 10α-des-A-androstane-5,17-dione, m. p. 122—123°, in good yield.

Further elution with benzene–ether (10 : 1) afforded an oil (123 mg.), $\nu_{max.}$ 3575 cm.$^{-1}$ (OH), (no C=O band), possibly 10α-des-A-androstane-5,17-diol, which was not examined further.

Pyrolysis of Sodium 17β-*Acetoxy*-5-*oxo*-A-*nor*-3,5-*secoandrostan*-3-*oate* (cf. I; R = OAc).—(*a*) The hydroxy-acid (2 g.) was acetylated with pyridine–acetic anhydride (20 c.c.; 3 : 1 v/v) at 20° for 24 hr. The product was isolated *via* ether and heated under reflux with 95% acetone (100 c.c.) for 3 hr. to decompose the mixed anhydride which had been formed. The acetone was removed at 12 mm. and the acetoxy-keto-acid (1·9 g.) isolated *via* ether. The sodium salt of the acid (1·25 g.), prepared in the usual manner, was pyrolysed with sodium phenylacetate (4·8 g.) at 295°/0·04 mm. for 3½ hr. The oily distillate (520 mg.) was reacetylated at 20° for 16 hr. with pyridine–acetic anhydride (15 c.c.; 2 : 1 v/v). Isolation *via* ether afforded an oil, which was adsorbed on deactivated alumina (30 g.). Light petroleum–benzene (100 : 35) eluted 17β-*acetoxy*-10α-*des*-A-*androstan*-5-*one* (300 mg.), which sublimed as a waxy solid, m. p. 53—56°, $[\alpha]_D$ +16° (*c* 0·95) (Found: C, 73·6; H, 9·3. $C_{17}H_{26}O_3$ requires C, 73·3; H, 9·4%), $\nu_{max.}$ 1742 and 1239 (OAc), 1709 cm.$^{-1}$ (C=O). R.D. in methanol: [*M*] (5890 Å), +50°; (3020), −2400°; (2800), +1300°.

(*b*) The sodium salt of the acetoxy-acid (5·85 g.), prepared as above, was pyrolysed at 295°/0·3 mm. for 3½ hr. with sodium phenylacetate (35 g.). The oily distillate was hydrolysed with potassium hydroxide (1 g.) in 95% methanol (20 c.c.) under reflux for 1 hr. under nitrogen. The product was isolated *via* ether and adsorbed on deactivated alumina (250 g.). Benzene eluted 17β-hydroxy-10α-des-A-androstan-5-one (1·02 g.), m. p. 94—95°, $[\alpha]_D$ +1° (*c* 1·01).

17β-*Benzoyloxy*-10α-*des*-A-*androstan*-5-*one* (II; R = OBz).—A solution of the above hydroxy-ketone (5·96 g.) in pyridine (120 c.c.) was treated with benzoyl chloride (3·2 c.c., 1·05 mol.) and kept at 20° for 24 hr. Isolation *via* ether and crystallisation from ether–light petroleum gave the *benzoate* (4·42 g.) as prisms, m. p. 125—126°, $[\alpha]_D$ +62° (*c* 1·04) (Found: C, 77·2; H, 8·1. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%), $\nu_{max.}$ 1724 (OBz and C=O), 1274 cm.$^{-1}$ (OBz). R.D. in methanol: [*M*] (5890 Å), 0°; (3050), −2060°; (2820), +2750°. The residues from the mother liquor were adsorbed on deactivated alumina (250 g.). Light petroleum–benzene (5 : 1) eluted more benzoate (2·71 g.), m. p. and mixed m. p. 125—126°.

5-*Acetoxy*-17β-*benzoyloxy*-10α-*des*-A-*androst*-5-*ene* (VI; R = OBz).—The solvent was fractionally distilled from a solution of 17β-benzoyloxy-10α-des-A-androstan-5-one (3·01 g.) and toluene-*p*-sulphonic acid (0·42 g.) in isopropenyl acetate (70 c.c.). After 7 hr. (20 c.c. of distillate) the residual solvent was removed at 20 mm. and the product isolated *via* ether and adsorbed on deactivated alumina (300 g.). Elution with light petroleum–benzene (100 : 15) and crystallisation from ether afforded needles of the *enol acetate* (1·36 g.), m. p. 147—148°, $[\alpha]_D$ +45° (*c* 0·94) (Found: C, 75·5; H, 7·8. $C_{24}H_{30}O_4$ requires C, 75·4; H, 7·9%), $\nu_{max.}$ 1761 (OAc), 1724 (OBz and C=O), 1274 (OBz), and 1212 cm.$^{-1}$ (OAc). R.D. in methanol: [*M*] (5890 Å), +200°; (5000), +300°; (4000), +550°; (3000), +1700°. Elution with light petroleum–benzene (2 : 1) afforded unchanged starting material (0·95 g.).

5-*Acetoxy*-17β-*benzoyloxydes*-A-*androst*-5(10)-*ene* (III; R = OBz).—A solution of 17β-benzoyloxy-10α-des-A-androstan-5-one (4·1 g.) in carbon tetrachloride (38 c.c.) was treated with acetic anhydride (2·5 c.c.) and 60% perchloric acid (0·08 c.c.) and kept at 20° for 24 hr. The product was isolated *via* ether and adsorbed on deactivated alumina (400 g.). Light petroleum–benzene (5 : 1) eluted the *enol acetate* (3·26 g.), which after sublimation at 100°/0·01 mm. was a waxy solid, m. p. 74—76°, $[\alpha]_D$ +69° (*c* 0·99) (Found: C, 75·0; H, 8·0. $C_{24}H_{30}O_4$ requires C, 75·4; H, 7·9%), $\nu_{max.}$ 1754 cm.$^{-1}$ (OAc), 1724 (OBz), 1274 (OBz), and 1212 cm.$^{-1}$ (OAc). R.D. in methanol: [*M*] (5890 Å) +250°; (5000), +350°; (4000), +650°; (3000), +1500°.

17β-*Benzoyloxy*-10β-*bromo*-10α-*des*-A-*androstan*-5-*one* (IV; R = OBz).—Bromine (330 mg., 1·5 mol.) in acetic acid (1 c.c.) was added to a solution of 5-acetoxy-17β-benzoyloxydes-A-androst-5(10)-ene (500 mg.) in collidine–acetic acid (6 c.c; 1 : 10, v/v) under nitrogen. The mixture was then kept in the dark at 20° for 24 hr. Aqueous sodium sulphite was added and the product isolated *via* chloroform and adsorbed on silica gel (60 g.). Benzene eluted the *bromo-ketone* (429 mg.), needles (from ether), m. p. 163—164° (decomp.), $[\alpha]_D$ +129° (*c* 0·97)

(Found: C, 62·9; H, 6·5; Br, 19·05. $C_{22}H_{27}O_3Br$ requires C, 63·0; H, 6·5; Br, 19·1%), $\nu_{max.}$ 1721 (OBz and *ax*-bromo-ketone), 1272 cm.$^{-1}$ (OBz). R.D. in methanol: [*M*] (5890 Å), +125°; (3270), +9780°; (2820), −10,900°

17β-*Benzoyloxydes*-A-*androst*-9-*en*-5-*one* (V; R = OBz).—A solution of 17β-benzoyloxy-10β-bromo-10α-des-A-androstan-5-one (260 mg.) in dimethylformamide (50 c.c.) was heated under reflux for 2 hr. with lithium carbonate (600 mg.) and lithium bromide (600 mg.). The suspension was cooled, diluted with ether (500 c.c.), and washed successively with 10% hydrochloric acid (100 c.c.), sodium hydrogen carbonate solution, and brine, dried, and evaporated at 20 mm. The residual oil (204 mg.) was adsorbed on deactivated alumina (15 g.). Light petroleum–benzene (10 : 3) eluted the conjugated *ketone* (180 mg.), which crystallised from acetone–methanol as needles, m. p. 107—108°, $[\alpha]_D$ +48° (*c* 0·94) (Found: C, 78·3; H, 7·6. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%), $\nu_{max.}$ 1721 (OBz), 1667 (C=C–C=O), 1271 cm.$^{-1}$ (OBz), $\lambda_{max.}$ 2365 Å, (ε 22,300). R.D. in methanol: [*M*] (5890 Å), +400°; (5000), +400°; (4000), +350°; (3200), +2800°; (3000), +2300°.

17β-*Hydroxydes*-A-*androst*-9-*en*-5-*one* (V; R = OH).—17β-Benzoyloxydes-A-androst-9-en-5-one (1·25 g.) was heated under reflux in nitrogen with potassium hydroxide (2 g.) in 85% methanol (30 c.c.) for 90 min. The product was isolated *via* chloroform. Crystallisation from ether–methylene dichloride afforded prisms of the *hydroxy-ketone* (800 mg.), m. p. 169·5—170°, $[\alpha]_D$ −42° (*c* 0·96) (Found: C, 76·8; H, 9·3. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%), $\nu_{max.}$ 3559 (free OH), 3448 (hydrogen-bonded OH), 1664 (C=C–C=O), 1062 cm.$^{-1}$ (OH), $\lambda_{max.}$ 2485 Å (ε 15,700). R.D. in methanol: [*M*] (5890 Å), −450°; (3600), −1100°; (3200), +1100°; (3000), −5000°.

17β-*Acetoxydes*-A-*androst*-9-*en*-5-*one* (V; R = OAc).—A solution of the hydroxy-ketone (680 mg.) in pyridine (20 c.c.) and acetic anhydride (3·5 c.c.) was kept at 20° for 24 hr. The product, isolated *via* ether, was adsorbed on deactivated alumina (60 g.). Light petroleum–benzene (2 : 1) eluted the *acetoxy-ketone* (666 mg.), which after sublimation at 100°/0·01 mm. had m. p. 74—75°, $[\alpha]_D$ −38° (*c* 1·05) (Found: C, 74·1; H, 8·75. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·75%), $\nu_{max.}$ 1742 (OAc), 1672 (C=C–C=O), 1222 cm.$^{-1}$ (OAc), $\lambda_{max.}$ 2475 Å (ε 15,400). R.D. in methanol: [*M*] (5890 Å), +150°; (3570), −600°; (3200), +1300°; (3100), +900°.

Bromination of 5-*Acetoxy*-17β-*benzoyloxy*-10α-*des*-A-*androst*-5-*ene* (VI; R = OBz).—(*a*) Bromine (330 mg., 1·5 mol.) in acetic acid (1 c.c.) was added to a solution of the enol acetate (499 mg.) in collidine–acetic acid (6 c.c.; 1 : 10 v/v) under nitrogen. The mixture was kept in the dark at 20° for 24 hr. The product, isolated *via* chloroform, was adsorbed on silica gel (60 g.). Light petroleum–benzene (3 : 7) eluted a series of solid fractions with continuously increasing rotations from fraction 1, $[\alpha]_D$ −100° (*c* 0·96), to fraction 11, $[\alpha]_D$ +2° (*c* 1·17) (total 500 mg.).

Fractions 1 and 2 were combined (144 mg.) and rechromatographed on silica gel (20 g.). Light petroleum–benzene (1 : 2) eluted three fractions (total 86 mg.) of constant rotation $[\alpha]_D$ −100°, and ether one fraction (40 mg.), $[\alpha]_D$ −60° (*c* 0·98). Crystallisation of the first three fractions from ether–light petroleum afforded 17β-*benzoyloxy*-6β-*bromo*-10α-*des*-A-*androstan*-5-*one* (65 mg.) as needles, m. p. 116—117°, $[\alpha]_D$ −101° (*c* 0·98) (Found: C, 62·75; H, 6·8; Br, 18·8 $C_{22}H_{27}BrO_3$ requires C, 63·0; H, 6·5; Br, 19·1%), $\nu_{max.}$ 1724 (OBz and *ax*-bromo-ketone), 1271 cm.$^{-1}$ (OBz). R.D. in methanol: [*M*] (5890 Å), −300°; (3250), −11,600°; (2850), + 14,300°; (2830), +13,500°.

Fractions 6—11 (total 180 mg.) above were combined and adsorbed on silica gel (20 g.). Light petroleum–benzene (1 : 2) eluted, first, fractions (71 mg.), $[\alpha]_D$ −50° (*c* 0·99), then three fractions (97 mg.) of constant rotation $[\alpha]_D$ +2° (*c* 1·07). Crystallisation of the last three fractions from ether–light petroleum afforded 17β-*benzoyloxy*-6α-*bromo*-10α-*des*-A-*androstan*-5-*one* (70 mg.) as needles, m. p. 128—129°, $[\alpha]_D$ +3° (*c* 0·95) (Found: C, 63·1; H, 6·8; Br, 18·95%), $\nu_{max.}$ 1724 (OBz and *eq*-bromo-ketone), 1271 (OBz), 750 cm.$^{-1}$ (*eq*-bromo-ketone). R.D. in methanol: [*M*] (5890 Å), +300°; (3320), +1720°; (3000), −3260; (2950), −3000°.

(*b*) Bromine (84 mg., 1·1 mol.) in carbon tetrachloride (0·54 c.c.) was added to a stirred ice-cold solution of the enol acetate (200 mg.) and epichlorohydrin (0·2 c.c.) in carbon tetrachloride (15 c.c.). The solution was stirred for a further 10 min. and then worked up *via* chloroform. The residual oil was adsorbed on silica gel (25 g.). Light petroleum–benzene (1 : 2) eluted 17β-benzoyloxy-6β-bromo-10α-des-A-androstan-5-one (199 mg.), m. p. 116—117°, $[\alpha]_D$ −100° (*c* 1·03).

17β-*Benzoyloxy*-10α-*des*-A-*androst*-6-*en*-5-*one* (IX; R = OBz).—17β-Benzoyloxy-6β-bromo-10α-des-A-androstan-5-one (300 mg.) was added to a suspension of lithium carbonate (400 mg.) in boiling dimethylformamide (20 c.c.) and heated under reflux for 5 hr. The product, isolated *via* ether, was adsorbed on deactivated alumina (25 g.). Light petroleum–benzene (5 : 2) eluted the *keto-benzoate* (218mg.) which crystallised from ether–light petroleum as plates, m. p. 119—120°, $[\alpha]_D$ +9° (*c* 1·05) (Found: C, 78·2; H, 7·8. $C_{23}H_{26}O_3$ requires C, 78·1; H, 7·7%), $\nu_{max.}$ 1715 (OBz), 1675 (C=C–C=O), 1267 (OBz), 810 cm.$^{-1}$ (*cis*-disubstituted C=C), $\lambda_{max.}$ 2295 Å (ε 24,700). R.D. in methanol: [*M*] (5890 Å), −700°; (3680), +1250°; (3100), −1050°; (3050), −650°; (2950), −1100°.

5,17β-*Diacetoxydes*-A-*androst*-5(10)-*ene* (III; R = OAc).—A solution of 17β-acetoxy-10α-des-A-androstan-5-one (4·1 g.) in carbon tetrachloride (46 c.c.) was treated with acetic anhydride (3·05 c.c.) and 60% perchloric acid (0·09 c.c.) and kept at 20° for 24 hr. Isolation *via* ether afforded an oil (4·72 g.), which was adsorbed on deactivated alumina (400 g.). Elution with light petroleum–benzene (4 : 1) gave an oil (2·3 g.) which slowly solidified; the *enol acetate* was further purified by sublimation at 100°/0·01 mm. and formed a wax, m. p. 39—44°, $[\alpha]_D$ +50° (*c* 1·01) (Found: C, 71·1; H, 8·6. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%), $\nu_{max.}$ 1739 and 1208 (enol acetate), 1727 and 1235 (17β-acetate), and 1681 cm.$^{-1}$ (C=C). R.D. in methanol: [*M*] (5890 Å), +50°; (5000), +100°; (4000), +250°; (3000), +750°; (2750), +1075°. Further elution with benzene afforded unchanged starting material (1·4 g.).

5,17β-*Diacetoxy*-10α-*des*-A-*androst*-5-*ene* (VI; R = OAc).—The solvent was fractionally distilled at 96° from a solution of 17β-acetoxy-10α-des-A-androstan-5-one (5·7 g.) and toluene-*p*-sulphonic acid (870 mg.) in isopropenyl acetate (125 c.c.). After 7 hr. (50 c.c. of distillate) the remaining solvent was removed at 20 mm. The product isolated *via* ether was adsorbed on deactivated alumina. Elution with light petroleum–benzene (4 : 1) afforded the *enol acetate* (2·81 g.); a specimen purified by sublimation at 100°/0·01 mm. was a waxy solid, m. p. 78—81°, $[\alpha]_D$ −4° (*c* 0·97) (Found: C, 71·1; H, 8·7. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%), $\nu_{max.}$ 1745 and 1208 (enol acetate), 1727 and 1235 (17β-acetate), and 1681 cm.$^{-1}$ (C=C). R.D. in methanol: [*M*] (5890 Å), −50°; (5000), −50°; (4000), −25°; (3000), 0°.

Further elution with benzene afforded unchanged starting material (3·3 g.).

17β-*Acetoxy*-10β-*bromo*-10α-*des*-A-*androstan*-5-*one* (IV; R = OAc).—Bromine (255 mg.) in carbon tetrachloride (2 c.c.) was added to a stirred ice-cold solution of 5,17β-diacetoxydes-A-androst-5(10)-ene (510 mg.) and epichlorohydrin (0·2 c.c.) in carbon tetrachloride (20 c.c.). The solution was stirred for a further 10 min. and the product (701 mg.), isolated *via* chloroform, was adsorbed on silica gel (60 g.). Light petroleum–benzene (1 : 2) eluted the *bromo-ketone* (453 mg.), which crystallised from ether as prisms (420 mg.), m. p. 130—131° (decomp.), $[\alpha]_D$ +132° (*c* 0·95) (Found: C, 57·3; H, 7·1; Br, 22·1. $C_{17}H_{25}BrO_3$ requires C, 57·1; H, 7·05; Br, 22·4%), $\nu_{max.}$ 1730 and 1236 (OAc), 1709 cm.$^{-1}$ (*ax*-bromo-ketone), $\lambda_{max.}$ 3070 Å (ε 120). R.D. in methanol: [*M*] (5890 Å), +75°; (3300), +11,700°; (2800), −13,200°; (2700), −12,500°.

17β-*Acetoxy*-6β-*bromo*-10α-*des*-A-*androstan*-5-*one* (VIII; R = OAc).—Bromine (255 mg.) in carbon tetrachloride (2 c.c.) was added to a stirred ice-cold solution of 5,17β-diacetoxy-10α-des-A-androst-5-ene (510 mg.) and epichlorohydrin (0·2 c.c.) in carbon tetrachloride (20 c.c.). The solution was stirred for a further 10 min. and the product (685 mg.) isolated *via* chloroform was adsorbed on silica gel (60 g.). Light petroleum–benzene (1 : 2) eluted the *bromo-ketone* (526 mg.), which crystallised from ether as prisms (424 mg.), m. p. 133—134° (decomp.), $[\alpha]_D$ −193° (*c* 0·97) (Found: C, 57·3; H, 7·1; Br, 22·4%), $\nu_{max.}$ 1730 and 1235 (OAc), 1709 cm.$^{-1}$ (*ax*-bromo-ketone), $\lambda_{max.}$ 3080 Å (ε 140). R.D. in methanol: [*M*] (5890 Å), −600°; (3300), −14,500°; (2800), +16,000°, (2780), +15,800°.

Dehydrobromination of 17β-*Acetoxy*-10β-*bromo*-10α-*des*-A-*androstan*-5-*one* (IV; R = OAc).—The bromo-ketone (367 mg.) was heated at 80° for 2 hr. with a suspension of lithium carbonate (1 g.) in dimethylformamide (20 c.c.). The product (298 mg.), isolated *via* ether, solidified. Sublimation at 100°/0·01 mm. gave 17β-acetoxydes-A-androst-9-en-5-one, m. p. 74—75°, $[\alpha]_D$ −38° (*c* 1·01), identical with the material obtained as above.

17β-*Acetoxy*-10α-*des*-A-*androst*-6-*en*-5-*one* (IX; R = OAc).—17β-Acetoxy-6β-bromo-10α-des-A-androstan-5-one (620 mg.) was added to a suspension of lithium carbonate (2 g.) in boiling dimethylformamide (40 c.c.) and heated under reflux for 2 hr. The product (499 mg.), isolated *via* ether, was adsorbed on deactivated alumina (40 g.). Light petroleum–benzene (1 : 1) eluted the conjugated *ketone* (391 mg.), which sublimed at 100°/0·01 mm., to give a solid,

m. p. 66—68°, $[\alpha]_D$ −78° (*c* 0·95) (Found: C, 73·8; H, 8·8. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·75%), $\nu_{max.}$ 1742 and 1239 (OAc), 1686 (C=C–C=O), 813 cm.$^{-1}$ (*cis*-disubstituted C=C), $\lambda_{max.}$ 2290 Å (ε 10,900). R.D. in methanol: [*M*] (5890 Å), −650°; (3880), −50°; (2780), −4400°.

Alkali-treatment of 10α-*Des*-A-*cholest*-6-*en*-5-*one* (IX; R = C_8H_{17}).—The ketone (100 mg.) was heated under reflux with potassium hydroxide (200 mg.) in 90% methanol (10 c.c.) under nitrogen for 90 min. Isolation *via* ether afforded an oil (98 mg.), $\nu_{max.}$ 1715 (C=O), 1675 (C=C–C=O), and 810 cm.$^{-1}$ (*cis*-disubstituted C=C), $\lambda_{max.}$ 2290 Å (ε 4800). These constants suggest a 50% conversion of 10α-des-A-cholest-6-en-5-one into 10α-des-A-cholest-7-en-5-one.

Alkaline Hydrolysis of 17β-*Benzoyloxy*-10α-*des*-A-*androst*-6-*en*-5-*one* (IX; R = OBz).—The keto-benzoate (240 mg.) was heated under reflux with potassium hydroxide (500 mg.) in 85% methanol (12 c.c.) under nitrogen for 90 min. Isolation *via* chloroform gave an oil (160 mg.), $\nu_{max.}$ 3546 and 1047 (OH), 1715 (C=O), 1675 (C=C–C=O) and 810 cm.$^{-1}$ (*cis*-disubstituted C=C), $\lambda_{max.}$ 2290 Å (ε 5000). The product, probably a mixture of 17β-hydroxy-10α-des-A-androst-6-ene-5-one (*ca.* 50%) and its βγ-isomer, could not be resolved chromatographically.

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