23. *Studies in the Sterol Group. Part XXXIV. The Dibromination of 6-Ketocholestanyl Acetate.*

By I. M. Heilbron, H. Jackson, E. R. H. Jones, and F. S. Spring.

With the object of preparing steroid ketones containing unsaturated centres in rings A and B [see (II), p. 103] the dibromination of 6-ketocholestanyl acetate has been investigated. Two isomeric dibromides have been isolated and characterised as 5 : 7- and 5′ : 7-dibromo-6-ketocholestanyl acetates. The reactions of these bromides with pyridine and with sodium acetate in alcohol have been examined in detail and several new unsaturated ketones characterised.

When 6-ketocholestanyl acetate is treated with two moles of bromine in ether–acetic acid at 0°, 5-bromo-6-ketocholestanyl acetate (I) (Heilbron, Jones, and Spring, J., 1937, 801) separates and remains in suspension as sole product, even after long standing. If, however, the addition is effected in acetic acid at room temperature, (I) separates immediately and then gradually redissolves. Treatment of the reaction mixture with water after 1 hour gives 5 : 7-*dibromo-6-ketocholestanyl acetate* (III), m. p. 152°, in 40% yield, and after 18 hours similar treatment gives the same yield of the isomeric 5′ : 7-*dibromo-6-ketocholestanyl acetate* (IV), m. p. 129°.

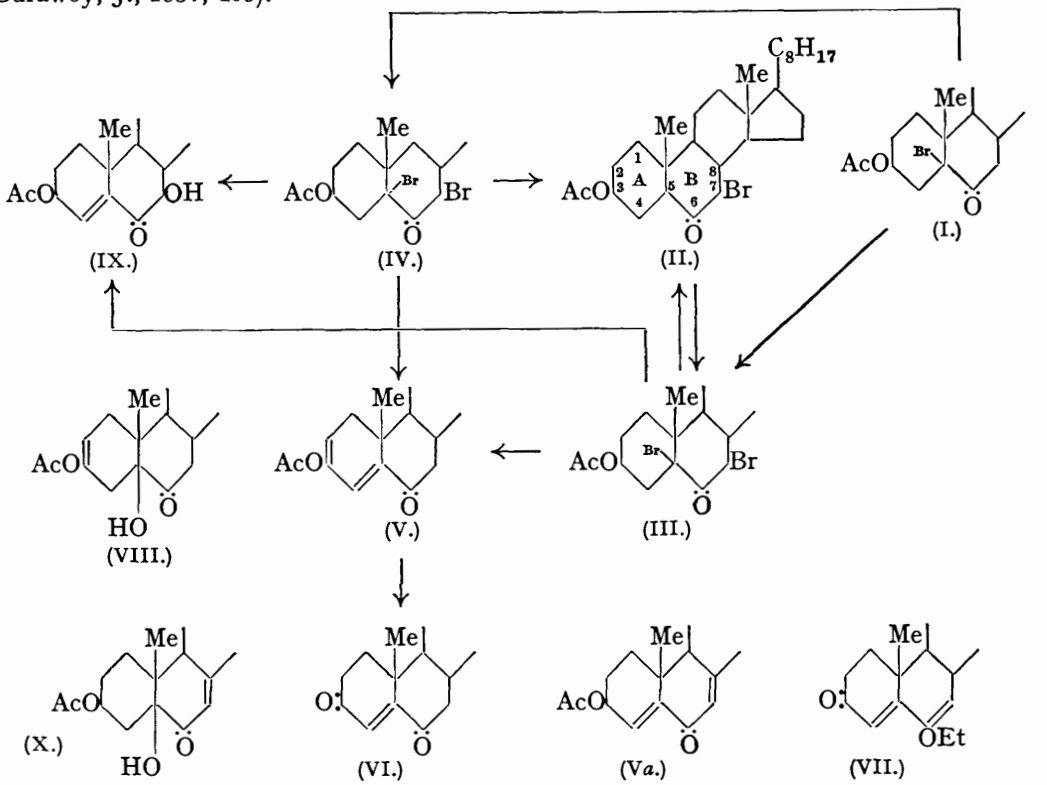
The isomeric 5- and 7-bromo-6-ketocholestanyl acetates (I) and (II) (Heilbron, Jones, and Spring, *loc. cit.*) are stable to bromine in acetic acid and chloroform under a variety of conditions and further bromination can only be effected in the presence of at least one mole of hydrogen bromide. Under suitable reaction conditions the 5-monobromide can be converted into either of the dibromides, but the 7-monobromide gives only the higher-melting isomer (III).

Since dibromination of 6-ketocholestanyl acetate gives (III) in a comparatively short time, it appeared probable that the latter is isomerised on long standing in the presence of hydrogen bromide to (IV). That this view is untenable is shown by the fact that treatment of the dibromide (III) with hydrogen bromide and acetic acid simply reduces it to 7-bromo-6-ketocholestanyl acetate (II), a reaction inhibited by the presence of bromine. Incidentally (IV) is stable to hydrogen bromide at room temperature, but at 100° it is likewise reduced to the 7-monobromide. The conversion of (I) into (III) and (IV) must thus proceed by simultaneous and not consecutive reactions, which probably involve the further bromination of an intermediate ion or radical related to 7-bromo-6-ketocholestanyl acetate. We attribute the fact that only 5′ : 7-dibromo-6-ketocholestanyl acetate (IV) can be isolated after 18 hours to the slow conversion of the less soluble isomer (III) into the very soluble 7-bromo-6-ketocholestanyl acetate (II). We have shown above that the latter reaction is inhibited by bromine and, as anticipated, we have found that treatment of 6-ketocholestanyl acetate with slightly more than two moles of bromine gives only (III) even after 24 hours.

Treatment of either of the dibromides with boiling pyridine gives two products, m. p. 139—140° and 227—229°. The former, which preponderates, has the formula $C_{29}H_{44}O_3$, and on hydrolysis with cold sodium methoxide gives 3 : 6-diketo-Δ^4-cholestene (VI). Of the two possible constitutions (V) and (V*a*) for the compound, m. p. 139—140°, we favour the former (6-*keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene*), since the alternative (V*a*) does not afford a ready interpretation of the behaviour on hydrolysis, nor does the compound give the Tortelli–Jaffé reaction (Heilbron and Spring, *Biochem. J.*, 1930, **24**, 133). The new enol-acetate (V) exhibits a well-defined band at 3170 A., differing from that of the enol-ether of 3 : 6-diketo-Δ^4-cholestene (VII) (Butenandt and Schramm, *Ber.*, 1936, **69**, 2289), which is characterised by a band at 2950 A. This observation affords another example of the different chromophoric effect of a conjugated system according as it is present in a single cyclic system or distributed between two rings.

The product, m. p. 227—229°, has the formula $C_{29}H_{46}O_4$; its formation from either dibromide has therefore involved the elimination of one molecule of hydrogen bromide and replacement of the second halogen atom by a hydroxyl group. In view of the established constitution of the major product (V) an attractive hypothesis appeared to

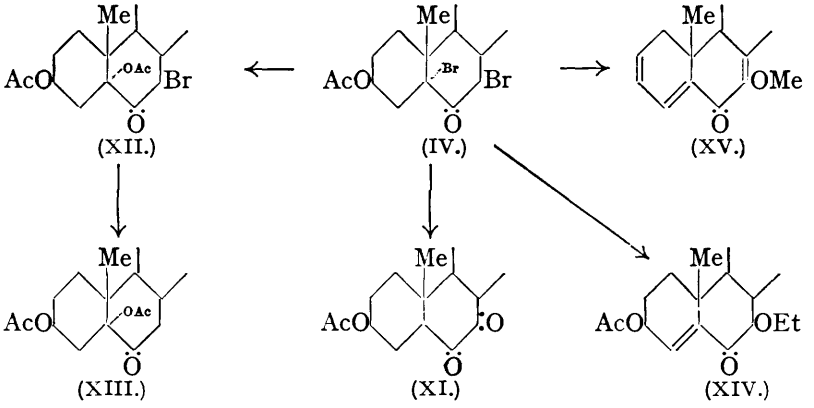
be that the second product is 5-hydroxy-6-keto-3-acetoxy-Δ^2-cholestene (VIII). This is excluded, however, since on hydrolysis it fails to give either of the known 3 : 6-diketo-5-hydroxycholestanes. Of the two remaining constitutions, 7-hydroxy-6-keto-3-acetoxy-Δ^4-cholestene (IX) and 5-hydroxy-6-keto-3-acetoxy-Δ^7-cholestene (X), the former is correct, since the compound gives a *benzoate*, m. p. 136—137°, and does not exhibit the typical light absorption properties and Tortelli–Jaffé reaction characteristic of (X) (cf. Burawoy, J., 1937, 409).



In contrast to the reaction with boiling pyridine a marked difference is observed on treatment of the two dibromides with this reagent (or with pyridine and silver nitrate) at room temperature. Whereas the dibromide (IV) gives halogen-free mixtures from which no crystalline product has as yet been isolated, both (III) and 5- and 7-bromo-6-ketocholestanyl acetates are recovered unchanged. The dibromide (III) and the two monobromides are also unchanged after heating with sodium acetate in alcohol, whereas the dibromide (IV) gives a mixture from which 6 : 7-diketocholestanyl acetate (XI) has been isolated, together with two other compounds, m. p. 198° and 119—120°. The product, m. p. 198°, which is obtained as sole product by treatment of (IV) with potassium acetate in acetic acid, has been characterised as *7-bromo-6-keto-3 : 5'-diacetoxycholestane* (XII), since on treatment with aluminium amalgam it gives a 6-keto-3 : 5-diacetoxycholestane (XIII), m. p. 169°, the identity of which was established by comparison with an authentic specimen prepared by the method of Schenck (*Z. physiol. Chem.*, 1936, **243**, 119). An interesting stereochemical point emerges from the isolation of this diacetoxy-ketone from the dibromide (IV). We have previously shown (Heilbron, Jones, and Spring, *loc. cit.*) that hydrolysis of 5-bromo-6-ketocholestanyl acetate gives a 3 : 5-dihydroxy-6-ketocholestane, m. p. 138°. This differs from the dihydroxy-ketone, m. p. 232°, prepared by hydrolysis of the 6-keto-3 : 5-diacetoxycholestane described above,*

* Attempts to hydrolyse the two dibromides to the corresponding trihydroxy-ketones were unsuccessful.

and consequently the two dihydroxy-ketones must differ solely in the orientation of the groups associated with C_5. According to the nomenclature adopted by us, the dihydroxy-ketone, m. p. 138°, will be 3 : 5- and the isomer m. p. 232°, 3 : 5′-dihydroxy-6-keto-cholestane. It proves, therefore, that the orientation of the halogen atom in 5-bromo-6-ketocholestanyl acetate relative to the angular methyl group at C_{10} is the same as that of the C_5 halogen atom in the dibromide (III) and opposite to that in (IV), and consequently we designate (III) as 5 : 7-dibromo-6-ketocholestanyl acetate and (IV) as 5′ : 7-dibromo-6-ketocholestanyl acetate, a notation which has a relative and not an absolute significance.



The product, m. p. 119—120°, has the formula $C_{31}H_{50}O_4$; it contains an ethoxy-group and exhibits general absorption in the ultra-violet region of the spectrum (figure) similar to that shown by the unsaturated hydroxy-ketone (IX). These facts suggest the constitution 6-*keto*-3-*acetoxy*-7-*ethoxy*-Δ^4-*cholestene* (XIV) for the compound; with either cold alcoholic potassium hydroxide or a hot solution of sodium methoxide in methyl alcohol it gives 3-*hydroxy*-6-*keto*-7-*ethoxy*-Δ^4-*cholestene*, m. p. 113°.

With potassium acetate in *n*-butyl alcohol, 5′ : 7-dibromo-6-ketocholestanyl acetate yields a product which exhibits an intense ferric chloride coloration. Repeated crystallisation of this crude product from methyl alcohol gives 6-*keto*-7-*methoxy*-$\Delta^{2:4:7}$-*cholestatriene* (XV), m. p. 119—121°, which shows a well-defined absorption maximum at 3150 A. The formation of this enol-ether has obviously involved the methylation of an intermediate 6 : 7-diketone, since neither the enol-ether nor the material recovered from the combined mother-liquors gives any reaction with ferric chloride.

Experimental.

Great difficulty has been experienced in the preparation of 6-ketocholestanyl acetate according to the directions available in the literature. A method which we have developed and found suitable for the preparation of relatively large quantities of the saturated keto-acetate is appended. A suspension of cholesterol (20 g.) in acetic acid (80 c.c.) was treated with 30 drops of a mixture of nitric acid (80 c.c.; *d* 1·50) and fuming nitric acid (50 c.c.; Kahlbaum; *d* 1·515) with stirring at room temperature. The mixture was now cooled (ice–salt), and the remainder of the acid added during 1 hour with rapid stirring, which was continued for a further 30 minutes. The separated solid (20 g.) was collected, dried in air, and crystallised from acetic acid, from which 6-nitrocholesteryl nitrate was obtained in needles, m. p. 128°. A mixture of the nitro-ester (28 g.), zinc dust (50 g.), acetic acid (400 c.c.), and water (75 c.c.) was heated on the steam-bath for 2 hours, care being taken to prevent the reaction becoming vigorous. The mixture was then heated under reflux for a further 10 hours and largely diluted with water. The product, isolated by means of ether, was hydrolysed by heating under reflux with a mixture of hydrochloric acid (85 c.c.) and alcohol (300 c.c.) for 1½ hours. The solid (16—18 g.), m. p. 136—138°, which separated on cooling was crystallised from alcohol, from which 6-ketocholestanol separated in needles, m. p. 140—141°. A solution of this (15 g.) in pyridine (30 c.c.) was treated with acetic anhydride (15 c.c.), and the mixture heated on the steam-bath for 1 hour. Water was added, the

solution cooled, and the crystalline solid (15 g.), m. p. 122—124°, collected. After one crystallisation from alcohol this gave 6-ketocholestanyl acetate in prisms, m. p. 128—129°.

5 : 7-*Dibromo*-6-*ketocholestanyl Acetate* (III).—(a) 6-Ketocholestanyl acetate (6·0 g.) in acetic acid (40 c.c.) was treated at 23° with 1 drop of hydrogen bromide in acetic acid (50%) and then with a solution of bromine in acetic acid (88 c.c.; 5%; 2 mols.), added during 3 minutes with shaking. The 5-bromo-6-ketocholestanyl acetate which at first separated gradually redissolved and after 75 minutes the solution was clear and the bromine absorption complete. After warming and dilution with water (20 c.c.) crystallisation was induced by scratching. The separated solid (3·4 g.) was crystallised from aqueous acetone, from which 5 : 7-*dibromo*-6-*ketocholestanyl acetate*, m. p. 152°, $[\alpha]_D^{20°}$ — 140° (l = 1, c = 0·6 in chloroform), separated in aggregates of fine needles. The dibromide was dimorphous, separating on prolonged standing from either acetic acid or acetone in magnificent rhombic crystals; the two forms were readily interconvertible (Found: C, 57·7; H, 7·3. $C_{29}H_{46}O_3Br_2$ requires C, 57·8; H, 7·7%). It reacted neither with sodium iodide in alcohol nor with *o*-phenylenediamine (cf. 2 : 4-dibromocholestanone; Ruzicka, Bosshard, and Wirz, *Helv. Chim. Acta*, 1936, **19**, 1147; Inhoffen, *Ber.*, 1937, **70**, 1695).

(b) 5-Bromo-6-ketocholestanyl acetate (500 mg.) in acetic acid (7 c.c.) was treated with bromine in acetic acid (3·5 c.c.; 5%; 1·2 mols.) and hydrogen bromide in acetic acid (0·3 c.c.; 50%). The mixture was maintained at 30° for 30 minutes, largely diluted with water, and the solid collected. Successive crystallisation from acetic acid and aqueous acetone gave 5 : 7-dibromo-6-ketocholestanyl acetate (200 mg.), m. p. 152°, identical with the specimen prepared by method (a).

(c) A mixture of 7-bromo-6-ketocholestanyl acetate (3·0 g.) and aliquot proportions of bromine and hydrogen bromide solutions in acetic acid was set aside at 23° for 40 hours. Subsequent procedure as described under (b) gave 5 : 7-dibromo-6-ketocholestanyl acetate (800 mg.), m. p. 152°, not depressed by admixture with an authentic specimen. Careful examination of the mother-liquors failed to yield any other homogeneous product.

5′ : 7-*Dibromo*-6-*ketocholestanyl Acetate* (IV).—(a) 6-Ketocholestanyl acetate (3·0 g.) in acetic acid (20 c.c.) was treated with a solution of bromine in acetic acid (22 c.c.; 5%; 1 mol.) at 23°, a drop of hydrogen bromide solution in acetic acid being added to induce reaction. The bromine addition was effected at such a rate that free bromine was not present in the solution, the addition extending over 3 minutes. The mixture was then treated with a further mol. of bromine in acetic acid, added rapidly with stirring, and set aside for 18 hours at room temperature. After warming and dilution with water, crystallisation was induced by scratching. The crude solid was recrystallised from acetic acid, from which 5′ : 7-*dibromo*-6-*ketocholestanyl acetate* separated in lustrous plates, m. p. 129°, $[\alpha]_D^{20°}$ — 51·1° (l = 1, c = 2·78 in chloroform). It was more soluble in the common organic solvents than the isomeric 5 : 7-dibromide, but less soluble than 7-bromo-6-ketocholestanyl acetate (Found: C, 57·6; H, 7·4. $C_{29}H_{46}O_3Br_2$ requires C, 57·8; H, 7·7%).

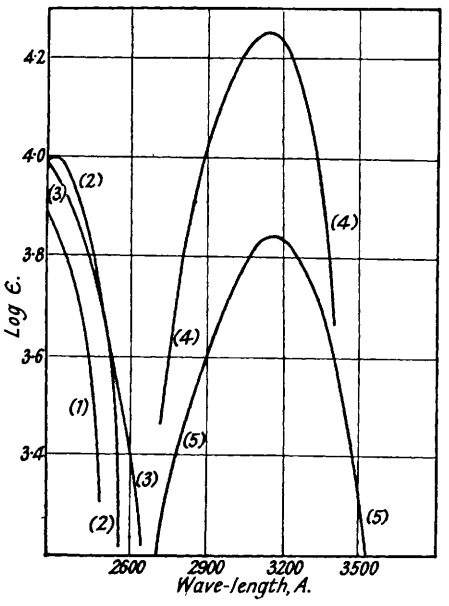
(b) A mixture of 5-bromo-6-ketocholestanyl acetate (1·0 g.), acetic acid (18 c.c.), bromine in acetic acid (6·6 c.c.; 5%; 1·1 mols.), and hydrogen bromide in acetic acid (0·3 c.c.; 50%) was heated on the steam-bath for 15 minutes, and the reaction mixture poured into water. After 12 hours, the clear solution was decanted from the hard resin, and the latter taken up in hot acetic acid. A small amount of insoluble oil was removed, and the solution cooled. The solid separating was recrystallised from acetic acid, yielding 5′ : 7-dibromo-6-ketocholestanyl acetate (100 mg.), m. p. 129°, not depressed on admixture with the specimen prepared by method (a).

7-*Bromo*-6-*ketocholestanyl Acetate from* 5 : 7- *and* 5′ : 7-*Dibromo*-6-*ketocholestanyl Acetates*.—(a) 5 : 7-Dibromo-6-ketocholestanyl acetate (700 mg.) in acetic acid (32 c.c.) was set aside at 22° for 24 hours with a solution of hydrogen bromide in acetic acid (1·25 c.c.; 50%; 2·0 mols.). The solid precipitated by dilution with water was crystallised from acetone, giving 7-bromo-6-ketocholestanyl acetate (300 mg.), m. p. 144—145°, unaltered on admixture with an authentic specimen.

(b) A solution of 5′ : 7-dibromo-6-ketocholestanyl acetate (500 mg.) in acetic acid (5 c.c.) was heated on the steam-bath for 15 minutes with a solution of hydrogen bromide in acetic acid (1·0 c.c.; 50%; 1·1 mols.), the mixture showing a play of colour, passing through green to brown. Precipitation with water gave an oil, which was isolated with ether and taken up in acetic acid. After long standing in a vacuum over potassium hydroxide, 7-bromo-6-ketocholestanyl acetate (120 mg.) separated, which, after a single recrystallisation from acetic acid, had m. p. 144—145°, unaltered on admixture with an authentic specimen.

6-*Keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene* (V).—A solution of either 5 : 7- or 5′ : 7-dibromo-6-ketocholestanyl acetate (3·0 g.) in anhydrous pyridine (75 c.c.) was heated under reflux for 6½ hours. Water was added to the hot solution until it became cloudy and the solid separating on cooling (1·2 g.) was crystallised from acetic acid, from which **6-*keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene*** separated in pale yellow, flat needles, m. p. 139—140°, $[\alpha]_D^{20°}$ + 27° (l = 1, c = 0·6 in chloroform) (Found: C, 79·4; H, 10·1. $C_{29}H_{44}O_3$ requires C, 79·0; H, 10·0%). *Light absorption in alcohol* (figure): Maximum, 3170 A.; log ε = 3·8.

3 : 6-*Diketo*-Δ^4-*cholestene* (VI).—A solution of 6-keto-3-acetoxy-$\Delta^{2:4}$-cholestadiene (100 mg.) in methyl alcohol (10 c.c.) was treated with a solution of sodium methoxide in methyl alcohol (3 c.c.; 10%), and the mixture set aside at 22° for 18 hours. The solution was acidified with dilute acetic acid, and the crude solid twice crystallised from methyl alcohol, 3 : 6-diketo-Δ^4-cholestene (50 mg.) being obtained, m. p. 122—123°, unaltered on admixture with an authentic specimen.



(1) 7-*Hydroxy*-6-*keto*-3-*acetoxy*-Δ^4-*cholestene* (IX).
(2) 6-*Keto*-3-*acetoxy*-7-*ethoxy*-Δ^4-*cholestene* (XIV).
(3) 3-*Hydroxy*-6-*keto*-7-*ethoxy*-Δ^4-*cholestene*.
(4) 6-*Keto*-7-*methoxy*-$\Delta^{2:4:7}$-*cholestatriene* (XV).
(5) 6-*Keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene* (V).

7-*Hydroxy*-6-*keto*-3-*acetoxy*-Δ^4-*cholestene* (IX).—The pyridine mother-liquor from 6-keto-3-acetoxy-$\Delta^{2:4}$-cholestadiene was largely diluted with water and extracted with ether. The extract was washed with dilute sulphuric acid and water, dried, and the solvent removed. Repeated crystallisation of the solid residue from acetic acid gave **7-*hydroxy*-6-*keto*-3-*acetoxy*-Δ^4-*cholestene*** (450 mg.), m. p. 227—229°, in flat needles sparingly soluble in alcohol and in acetic acid. This compound, which is the sole product of treatment of the 5′ : 7-dibromide with a boiling solution of silver nitrate in pyridine, fails to give a coloration with tetranitromethane in chloroform, ferric chloride in alcohol, antimony trichloride in chloroform, or with the Tortelli–Jaffé reagent (Found: C, 75·9; H, 10·0; *M*, 400 $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1%; *M*, 458). *Active hydrogen determination* (Zerewitinoff): The unsaturated ketone (6·61 mg.) evolved 0·30 c.c. of methane, measured at 30° and 763 mm., corresponding to 0·9 atom of active hydrogen per mole. *Microhydrogenation*: The unsaturated ketone (4·780 mg.), when shaken in acetic acid with palladium–barium sulphate, absorbed 0·255 c.c. of hydrogen at 20° and 753 mm., corresponding to $\overline{1}\cdot1$. *Light absorption in alcohol* (figure): At 2280 A., log ε = 3·9. A solution of the keto-alcohol (40 mg.) in anhydrous pyridine (1·0 c.c.) and benzoyl chloride (0·5 c.c.) was heated on the steam-bath for 3 hours. The oil obtained on dilution with water and ether extraction crystallised from methyl alcohol. After three recrystallisations from ether–methyl alcohol the *monobenzoate* was obtained in glistening needles, m. p. 136—137° (Found: C, 78·7; H, 9·2. $C_{35}H_{50}O_4$ requires C, 78·6; H, 9·4%).

3 : 7-*Dihydroxy*-6-*keto*-Δ^4-*cholestene*.—7-Hydroxy-6-keto-3-acetoxy-Δ^4-cholestene (50 mg.) was heated under reflux with a solution of sodium methoxide in methyl alcohol (15 c.c.; 5%) for 30 minutes. The solid separating on dilution with water was thrice crystallised from aqueous methyl alcohol, giving **3 : 7-*dihydroxy*-6-*keto*-Δ^4-*cholestene*** in felted needles, m. p. 220—222°. The dihydroxy-ketone was very soluble in methyl alcohol, from which it separated in long flat prisms (Found: C, 78·1; H, 10·7. $C_{27}H_{44}O_3$ requires C, 77·8; H, 10·7%).

7-*Bromo*-6-*keto*-3 : 5′-*diacetoxycholestane* (XII).—A solution of 5′ : 7-dibromo-6-ketocholestanyl acetate (1·0 g.) and freshly fused potassium acetate (2·0 g.) in acetic acid (400 c.c.) was heated on the steam-bath for 1½ hours. Water (5 c.c.) was added and the solid which separated was crystallised from acetic acid, yielding **7-*bromo*-6-*keto*-3 : 5′-*diacetoxycholestane*** (400 mg.) in prisms, m. p. 198° (decomp.), sparingly soluble in methyl alcohol, but moderately soluble in ether, acetone, and acetic acid (Found: C, 63·7; H, 8·2. $C_{31}H_{49}O_5Br$ requires C, 64·0; H, 8·5%).

6-*Keto*-3-*acetoxy*-7-*ethoxy*-Δ^4-*cholestene* (XIV).—A solution of 5′ : 7-dibromo-6-ketocholes-

tanyl acetate (3·0 g.) in absolute alcohol (220 c.c.) was heated under reflux for 1 hour with freshly fused sodium acetate (4·5 g.). The hot solution was diluted with water until just cloudy; on cooling, 7-bromo-6-keto-3 : 5′-diacetoxycholestane (500 mg.) separated, which after three crystallisations from methyl alcohol had m. p. 198°, not depressed on admixture with an authentic specimen. The original mother-liquor was gradually diluted with water, whereby a small quantity of oil separated. Further dilution of the decanted solution gave a solid (600 mg.), m. p. 100—103°, slow crystallisation of which from methyl alcohol gave a mixture of small hard nodules and large plates. The mixture was separated mechanically, recrystallisation of the nodules from methyl alcohol giving a further quantity of 7-bromo-6-keto-3 : 5′-diacetoxycholestane. The large plates were thrice recrystallised from alcohol; *6-keto-3-acetoxy-7-ethoxy-*Δ^4*-cholestane* (300 mg.) was then obtained, m. p. 119—120°. With tetranitromethane in chloroform the ether gave a yellow coloration; it sublimed unchanged at 140°/10^{-3} mm. (Found : C, 76·5; H, 10·4; OEt, 8·4. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4; OEt, 9·2%). *Light absorption in alcohol* (figure) : At 2300 A., log $\varepsilon = 3{\cdot}9$.

6 : 7-*Diketocholestanyl Acetate from* 5′ : 7-*Dibromo-6-ketocholestanyl Acetate.*—The mother-liquor obtained after the removal of the solid, m. p. 100—103° (above), was again gradually diluted with water. A further quantity of the ether, m. p. 119—120°, was obtained and subsequently a solid, m. p. 110—128°, which gave an intense green-violet coloration with alcoholic ferric chloride solution. After two crystallisations from aqueous acetone the latter gave 6 : 7-diketocholestanyl acetate (100 mg.), m. p. 156—157°, which showed no depression on admixture with an authentic specimen and was characterised by the formation of the quinoxaline derivative, m. p. 186—187°.

6-Keto-3 : 5′-diacetoxycholestane (XIII).—A solution of 7-bromo-6-keto-3 : 5′-diacetoxycholestane (70 mg.) in ether (70 c.c.) was treated at 20° with aluminium amalgam (2 g.), water being periodically added to the reaction mixture during 3 hours. After filtration and removal of solvent the product (40 mg.), which readily solidified on grinding with methyl alcohol, was twice crystallised from the same solvent, 6-keto-3 : 5′-diacetoxycholestane separating in long hard needles, m. p. 169—170°, not depressed when mixed with an authentic specimen (Found : C, 74·2; H, 10·2. Calc. for $C_{31}H_{50}O_5$: C, 74·0; H, 10·0%).

3-Hydroxy-6-keto-7-ethoxy-Δ^4*-cholestene.*—6-Keto-3-acetoxy-7-ethoxy-Δ^4-cholestene (50 mg.) in methyl alcohol (5 c.c.) was heated under reflux for 30 minutes with a solution of sodium methoxide in methyl alcohol (5 c.c.; 10%). The crude material separating on dilution with water was thrice crystallised from aqueous methyl alcohol, from which *3-hydroxy-6-keto-7-ethoxy-*Δ^4*-cholestene* separated in hair-like needles, m. p. 113° (Found : C, 78·5; H, 10·8. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%). *Light absorption in alcohol* (figure) : At 2300 A., log $\varepsilon = 4{\cdot}0$.

6-Keto-7-methoxy-$\Delta^{2:4:7}$*-cholestatriene* (XV).—A solution of 5′ : 7-dibromo-6-ketocholestanyl acetate (1·6 g.) in dry *n*-butyl alcohol (80 c.c.) was heated under reflux for 7 hours with freshly fused potassium acetate (3·0 g.). The product, isolated by means of ether, gave an intense coloration with alcoholic ferric chloride. Crystallisation was effected from methyl alcohol containing a little acetone, and recrystallisation from ether–methyl alcohol yielded clusters of needles, m. p. 116—118°, still giving an intense red coloration with ferric chloride. Two further crystallisations from methyl alcohol gave *6-keto-7-methoxy-*$\Delta^{2:4:7}$*-cholestatriene* in fine needles, m. p. 119—121°, which did not give a ferric chloride coloration (Found : C, 81·9; H, 10·7. $C_{28}H_{42}O_2$ requires C, 81·9; H, 10·3%). *Light absorption in alcohol* (figure) : Maximum, 3150 A.; log $\varepsilon = 4{\cdot}2$.

Our thanks are due to the Rockefeller Foundation for a grant, to the University of Wales for a Fellowship (E. R. H. J.), to Messrs. Tootal Broadhurst Lee and Co., Ltd., for a scholarship (H. J.), and to Imperial Chemical Industries, Ltd., for their continued assistance.

THE UNIVERSITY, MANCHESTER. [*Received, November 20th,* 1937.]