232. *Steroids and Related Compounds. Part IV. The Stereochemical Configuration of the Cholestane-3 : 5 : 6-triols.*

By B. Ellis and V. A. Petrow.

A study of the products obtained on oxidation and bromination of 6-*acetoxy-cholestan-5-ol-3-one* (II, R = Ac), obtained from cholestanetriol I,* has enabled us to determine the configuration of triols I and II and the relative positions of the three hydroxyl groups to each other and to the tertiary methyl group at C_{10}. The results indicate that in triol I the rings I and II have the *trans*-decalin configuration, whereas in triol II they are of the *cis*-decalin type.

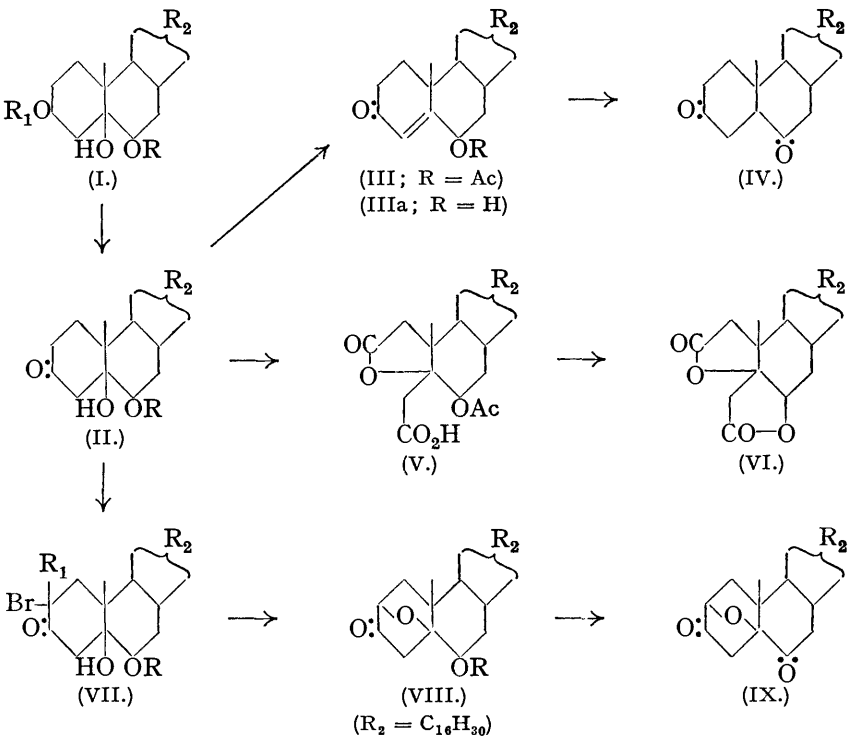
Two isomeric cholestane-3 : 5 : 6-triols have been obtained from cholesterol, triol I by direct oxidation with hydrogen peroxide (Pickard and Yates, J., 1908, **93**, 1678) or by

* *Note on nomenclature* : In analogy to the corresponding ergosterol derivatives it is proposed to differentiate the two cholestane-3 : 5 : 6-triols by the Roman numerals I and II, instead of by the Greek prefixes α and β hitherto in use. The need for this change is indicated in view of the confusion arising out of the simultaneous use of the generally accepted designations (α) and (β) attached to the numbers indicating the position of the hydroxyl groups (Fieser, " A Supplement to the Chemistry of Natural Products Related to Phenanthrene," 1937, p. 399). The symbols (*e.g.*, $C_2\|C_3$) proposed by Sobotka (" The Chemistry of the Steroids," 1938) for the dicarboxylic acids arising on ring cleavage have been adopted. The convention proposed by Linstead (*Chem. and Ind.*, 1937, **56**, 511; J., 1938, 699) has been used in formulæ (X) and (XI), to indicate the position of the substituents above and below the plane of the ring system.

hydrolysis of cholestan-3-ol-5 : 6-oxide I (Westphalen, *Ber.*, 1915, **48**, 1064), and triol II, formed by oxidation with potassium permanganate (Windaus, *Ber.*, 1907, **40**, 257) or with osmic acid (Ushakov and Lutenberg, *Nature*, 1937, **140**, 466). On the evidence of lead tetra-acetate titrations Criegee (*Ber.*, 1932, **65**, 1770) has assigned "*trans*"- and "*cis*"-configurations to the α-glycol groups at $C_5 : C_6$ of the triols I and II respectively; the present communication describes experiments designed to determine the relative positions of the three hydroxyl groups to one another and to the angular methyl group at C_{10}.

The steric configuration of rings I and II in the 3-keto-steroids has been correlated with the reactivity of the adjacent methylene groups at C_2 and C_4. Oxidation of the ketones in which rings I and II are of the *trans*-decalin (cholestanone) type leads to the $C_2\|C_3$ diacids, and bromination to the 2-bromo-derivatives (Butenandt and Wolff, *Ber.*, 1935, **68**, 2091). Where this configuration is of the *cis*-decalin (coprostanone) type, the $C_3\|C_4$ diacids and the 4-bromo-compounds (Butenandt and Wolff, *loc. cit.*) are obtained. We have now examined the application of these principles to the corresponding ketone obtainable from triol I, which was prepared by the following series of reactions.

Partial saponification of 3 : 6-diacetoxycholestan-5-ol (I, R = R_1 = Ac) (Pickard and Yates, *loc. cit.*) with alcoholic potassium hydroxide at room temperature led to the formation of a *triol monoacetate*, $C_{29}H_{48}O_4$, m. p. 144°. Its constitution as *6-acetoxycholestane-3 : 5-diol* (I; R = Ac, R_1 = H) was proved by its conversion on benzoylation into 3-benzoyloxy-6-acetoxycholestan-5-ol (I; R = Ac, R_1 = Bz) (Petrow, J., 1937, 1077). On oxidation with chromic acid it gave *6-acetoxycholestan-5-ol-3-one*, $C_{29}H_{48}O_4$, m. p. 161—162° (II, R = Ac). The acetate (II, R = Ac) underwent facile dehydration, either with sodium



acetate–acetic anhydride or by the Darzens method, to *6-acetoxy-Δ⁴-cholesten-3-one* (III), $C_{29}H_{46}O_3$, m. p. 101·5°, which was hydrolysed by cold alcoholic potassium hydroxide to *Δ⁴-cholesten-6-ol-3-one* (IIIa), m. p. 192°; this was characterised by its semicarbazone, m. p. 221° (cf. Dane, Wang, and Schulte, *Z. physiol. Chem.*, 1936, **245**, 80), and oxidised by Kiliani's chromic acid mixture to Δ⁴-cholestene-3 : 6-dione. The constitutions assigned to (III) and (IIIa) were confirmed by their isomerisation on treatment with hot alcoholic

hydrochloric acid into cholestane-3 : 6-dione (IV) (cf. Butenandt and Schramm, *Ber.*, 1936, **69**, 2289; Heilbron, Jones, and Spring, J., 1937, 801). This compound was also obtained directly from 6-acetoxycholestan-5-ol-3-one by saponification with sodium methoxide, hydrolysis of the C_6 acetoxy-group being accompanied by dehydration to (IIIa) and rearrangement to (IV).

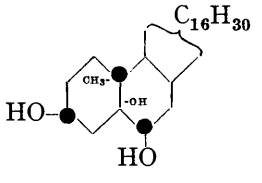
Oxidation of 6-acetoxycholestan-5-ol-3-one with chromic acid led, probably by way of the intermediary $C_2||C_3$ diacid, to the monobasic *6-acetoxy-lactonic acid*, $C_{29}H_{46}O_6$, m. p. 218°, to which the constitution (V) has been assigned. This structure was confirmed by the conversion of (V) on treatment with 0·5% alcoholic potassium hydroxide at room temperature into the neutral *dilactone* (VI), $C_{27}H_{42}O_4$, m. p. 165°, which required two equivalents of potassium hydroxide on titration.

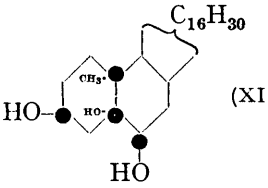
Bromination of 6-acetoxycholestan-5-ol-3-one yielded a *monobromide*, $C_{29}H_{47}O_4Br$, m. p. 186°, together with small amounts of a *dibromide*, $C_{29}H_{46}O_4Br_2$, m. p. 218°. The monobromide has been assigned the constitution of *2-bromo-6-acetoxycholestan-5-ol-3-one* (VII; R = Ac, R_1 = H). The alternative position for the bromine atom at C_4 is excluded by the following series of reactions: The monobromide underwent debromination and immediate dehydration on treatment with 0·5% methyl-alcoholic potassium hydroxide to give *cholestan-6-ol-3-one-2 : 5-oxide* (VIII, R = H), $C_{27}H_{44}O_2$, m. p. 182°, which yielded a *monoacetate* (VIII, R = Ac), $C_{29}H_{46}O_4$, m. p. 84°, on acetylation. On oxidation with chromic acid cholestan-6-ol-3-one-2 : 5-oxide passed into *cholestane-3 : 6-dione-2 : 5-oxide* (IX), $C_{27}H_{42}O_3$, m. p. 116°, characterised by a *bisdinitrophenylhydrazone*, m. p. 171°. The two compounds (VIII, R = H) and (IX) were stable both to alcoholic hydrochloric acid and to lead tetra-acetate. These transformations are unambiguously interpreted on the basis of the formulæ assigned to them, since the only alternative formulation, a $C_{4:5}$ oxide arising from a C_4 bromide, is not in agreement with the stability of (VIII), a *trans*-annular oxide (cf. Bergmann, Hirschmann, and Skau, *J. Org. Chem.*, 1939, **4**, 29) of the type occurring in terpenes (*e.g.*, cineole).

The dibromide liberates bromine on warming with sodium iodide in benzene–alcohol solution, and is probably 2 : 2-*dibromo-6-acetoxycholestan-5-ol-3-one* (VII; R = Ac, R_1 = Br).

On the assumption that the rules valid for the behaviour of 3-keto-steroids on bromination and oxidation (see above) are not invalidated when a hydroxyl group is substituted for the hydrogen atom at C_5, the experimental results described seem to justify the conclusion that the rings I and II in cholestane-3 : 5 : 6-triol I possess the *trans*-decalin configuration. The hydroxyl group at C_3 in cholesterol and the two triols is in the *cis*-position to the tertiary methyl group at C_{10} and, since the hydroxyl groups at C_5 and C_6 in triol I are in the *trans*-position to each other (Criegee, *loc. cit.*), it follows that the stereochemical configuration of this triol is cholestane-3(β) : 5(α) : 6(β)-triol (X).

(X.)





(XI.)

The isomerism between the two triols is known to be due to the different steric positions of the hydroxyl group at C_5: on oxidation with chromic acid they yield different cholestan-5-ol-3 : 6-diones (I and II), but both these oxidation products are dehydrated to Δ^4-cholestene-3 : 6-dione (Windaus, *loc. cit.*). Since it has now been established that in triol I the hydroxyl group at C_5 is in a *trans*-position to the C_{10} methyl group, it follows that in triol II the C_5 hydroxyl group is in a *cis*-position to the methyl group at C_{10}, and, being a *cis*-glycol at $C_{5:6}$ (Criegee, *loc. cit.*), its stereochemical configuration is established as coprostane-3(β) : 5(β) : 6(β)-triol (XI).

In the experimental part the preparation of certain derivatives of the two triols is

described, whose stereochemical configuration can now be satisfactorily interpreted on the basis of the above results.

Coprostan-5(β)-ol-3 : 6-dione is identical with " cholestan-5-ol-3 : 6-dione II ", the oxidation product of triol II (Windaus, *loc. cit.*), and has now been obtained by oxidation of cholestane-3 : 5-diol-6-one (Heilbron, Jones, and Spring, *loc. cit.*). The latter compound belongs therefore to series II and inversion has taken place either during its formation from 5-bromo-3-acetoxycholestan-6-one or in the formation of the latter (cf. Heilbron, Jackson, Jones, and Spring, J., 1938, 102). We have further obtained cholestane-3(β) : 5(α)-diol-6-one by partial oxidation of triol I with chromic acid and identified it by its monoacetate (Pickard and Yates, *loc. cit.*). The latter substance is dehydrated by boiling with thionyl chloride in pyridine solution (Darzens' reaction) to 3(β)-acetoxy-Δ^4-cholesten-6-one (cf. Heilbron, Jones, and Spring, *loc. cit.*). Attempts to dehydrate it with potassium hydrogen sulphate in acetic anhydride solution (cf. Part III, this vol., p. 998) led unexpectedly to the formation of 3(β) : 5(α)-diacetoxycholestan-6-one, previously obtained by oxidation of cholesteryl acetate with chromic acid (Mauthner and Suida, *Monatsh.*, 1896, **17**, 594; Schenck, *Z. physiol. Chem.*, 1936, **243**, 119).

Experimental.

Microanalyses were made by Dr. G. Weiler and Dr. F. B. Strauss. All the rotations were measured in chloroform solution in a 2 dm. tube. Melting points are corrected.

6-*Acetoxycholestane*-3 : 5-*diol* (I; R_1 = H, R = Ac).—To a solution of 3 : 6-diacetoxycholestan-5-ol (112 g.) in absolute alcohol (8 l.) was added dropwise with mechanical stirring during 2 days a solution of potassium hydroxide (12·5 g.; equiv. to 1·05 mols.) in absolute alcohol (670 ml.). After a further 24 hours the solution was acidified with a few drops of acetic acid, concentrated to half volume in a vacuum, and warmed, and sufficient water added to produce a turbidity. On cooling, 6-*acetoxycholestane*-3 : 5-*diol* separated in long silky needles containing water of crystallisation, m. p. 132—133°, $[\alpha]_D^{19°}$ −26·4 (*c*, 2·94) (Found : C, 71·1; H, 10·4; loss in weight on drying, 3·9. $C_{29}H_{50}O_4,H_2O$ requires C, 72·5; H, 10·8; H_2O, 3·8%). After drying at 125° for 1 hour the m. p. was raised to 143—144°. Yield, 85%.

On benzoylation (0·5 g. in 3 ml. of pyridine and 1 ml. of benzoyl chloride for 18 hours at room temperature) it gave 3-benzoyloxy-6-acetoxycholestan-5-ol, m. p. 164° alone or in admixture with an authentic specimen (Petrow, Part I, *loc. cit.*).

6-*Acetoxycholestan*-5-*ol*-3-*one* (II, R = Ac).—A solution of 6-acetoxycholestane-3 : 5-diol (20 g.) in glacial acetic acid (180 ml.) was treated for 3 minutes at 100° with a solution of chromic acid (6 g.) in acetic acid (50 ml. of 80%). The neutral fraction of the oxidation product, after two crystallisations from aqueous alcohol, yielded pearly plates of 6-*acetoxycholestan*-5-*ol*-3-*one*, m. p. 161—162°, $[\alpha]_D^{19°}$ −10·2° (*c*, 2·7) (Found : C, 75·5; H, 10·5. $C_{29}H_{48}O_4$ requires C, 75·6; H, 10·4%). Yield, 75%.

6-*Acetoxy*-Δ^4-*cholesten*-3-*one* (III).—(*a*) 6-Acetoxycholestan-5-ol-3-one (1 g.) in dry pyridine (10 ml.) was treated with thionyl chloride (0·32 ml.; 2 mols.), added dropwise at room temperature with shaking. The mixture, after refluxing for 10 minutes, was poured into water, and the product extracted with ether. On crystallisation from acetone–methyl alcohol, 6-*acetoxy*-Δ^4-*cholesten*-3-*one* was obtained in flat needles, m. p. 101·5°, $[\alpha]_D^{19°}$ + 36° (*c*, 3·195) (Found : C, 78·3; H, 10·2. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·4%).

(*b*) 6-Acetoxycholestan-5-ol-3-one (5 g.) was refluxed for 10 hours with acetic anhydride (75 ml.). Crystallisation of the product from acetone–methyl alcohol yielded 6-*acetoxy*-Δ^4-*cholesten*-3-*one*, identical with the compound prepared by method (*a*) in m. p., mixed m. p., and optical rotation. Yield, 60%.

Δ^4-*Cholesten*-6-*ol*-3-*one*, prepared by treating the acetate (1 g.) with 100 ml. of 1% methyl-alcoholic potassium hydroxide for 60 hours at room temperature, formed hard needles from aqueous acetone, m. p. 192° (Found : C, 81·0; H, 10·8. $C_{27}H_{44}O_2$ requires C, 81·0; H, 11·0%) (semicarbazone, m. p. 221°; cf. Dane, Wang, and Schulte, *loc. cit.*).

Δ^4-*Cholestene*-3 : 6-*dione*.—Kiliani's chromic acid mixture (2 ml.) was added dropwise with mechanical stirring during 1½ hours to a solution of Δ^4-cholesten-6-ol-3-one (300 mg.) in benzene (8 ml.) and acetic acid (2 ml.) at 15°, and the stirring continued for a further 30 minutes. A few drops of alcohol were added to remove the excess of chromic acid and the benzene layer was separated, washed with water and dilute sodium hydroxide solution, and dried over sodium sulphate. On removal of the benzene and crystallisation of the solid residue from 85% alcohol,

Δ^4-cholestene-3 : 6-dione (210 mg.) was obtained, m. p. 122—123° (Found : C, 81·5; H, 10·8. Calc. for $C_{27}H_{42}O_2$: C, 81·3; H, 10·6%), not depressed in admixture with an authentic specimen. The dione was further characterised by the preparation of the monophenylhydrazone, m. p. 280—281° (Mauthner and Suida, *Monatsh.*, 1896, **17**, 579), and of the enol ether, m. p. 165—166° (Windaus, *loc. cit.*).

Cholestane-3 : 6-*dione*.—(*a*) 6-Acetoxy-Δ^4-cholesten-3-one (200 mg.) in absolute alcohol (5 ml.) was refluxed for 30 minutes with 10 drops of concentrated hydrochloric acid. The crystalline deposit (150 mg.) separated from acetone in tablets of cholestane-3 : 6-dione, m. p. 169—170°, not depressed in admixture with an authentic specimen. Similar treatment of Δ^4 -cholesten-6-ol-3-one likewise gave the 3 : 6-dione.

(*b*) 6-Acetoxycholestan-5-ol-3-one was refluxed for 1 hour with excess of 5% sodium methoxide solution. The product, isolated with ether and crystallised from acetone, gave cholestane-3 : 6-dione in short hard needles, m. p. 170—171° (Found : C, 80·5; H, 11·0. Calc. for $C_{27}H_{44}O_2$: C, 81·0; H, 11·0%), alone or in admixture with an authentic specimen.

6-*Acetoxy-lactonic Acid*, $C_{29}H_{46}O_6$ (V).—The acidic fractions from the oxidations of 135 g. of 6-acetoxycholestane-3 : 5-diol (above) (6·1 g.) were extracted with light petroleum (b. p. 60—80°). The insoluble fraction separated from acetone–light petroleum in iridescent spangles of the 6-*acetoxy-lactonic acid*, m. p. 217—218° (sintering at 185°), $[\alpha]_D^{20°}$ −10·4° (*c*, 1·68) (Found : C, 71·5; H, 9·4; *M*, by titration, 480. $C_{29}H_{46}O_6$ requires C, 71·0; H, 9·4%; *M*, for monobasic acid, 490). On refluxing with 0·5% alcoholic potassium hydroxide, 0·2450 g. were neutralised by 0·0753 g. of potassium hydroxide, equivalent to 2·7 mols. The dipotassium salt was sparingly soluble in alcohol. The acid did not absorb bromine in chloroform, and did not react with 2 : 4-dinitrophenylhydrazine. With concentrated sulphuric acid it gave a yellow coloration slowly changing to deep orange.

Dilactone, $C_{27}H_{42}O_4$ (VI).—The lactonic acid (V) (500 mg.) was treated for 18 hours at room temperature with 30 ml. of 0·5% alcoholic potassium hydroxide. The *dilactone*, isolated by acidification with acetic acid and extraction with ether, formed needles from light petroleum–acetone, m. p. 165° (sintering at 155°) (Found : C, 75·6; H, 9·5. $C_{27}H_{42}O_4$ requires C, 75·4; H, 9·8%). Yield, 60%. On refluxing with 0·5% alcoholic potassium hydroxide, 0·150 g. were neutralised by 0·038 g. of potassium hydroxide, equivalent to 1·98 mols.

2-*Bromo*-6-*acetoxycholestan*-5-*ol*-3-*one* (VII; R = Ac, R_1 = H).—6-Acetoxycholestan-5-ol-3-one (10 g.) in glacial acetic acid (250 ml.) was treated at 35° with 30 ml. of bromine–acetic acid (equiv. to 3·5 g. of bromine). Decoloration was complete in 5 minutes. Water was added, and the precipitated material dried and extracted with light petroleum (200 ml.; b. p. 60—80°). The insoluble portion was crystallised from aqueous acetone and gave 2-*bromo*-6-*acetoxycholestan*-5-*ol*-3-*one* in needles, m. p. 186°, $[\alpha]_D^{21°}$ +3·6° (*c*, 2·055) (Found : Br, 15·4. $C_{29}H_{47}O_4Br$ requires Br, 14·8%). Yield, 40%. The light petroleum extract deposited a microcrystalline powder (2 g.) on long standing, identified as the dibromo-derivative (see below).

The 2-bromo-compound was recovered unchanged after refluxing for 1 hour with pyridine.

Cholestan-6-*ol*-3-*one*-2 : 5-*oxide* (VIII, R = H).—A suspension of 2-bromo-6-acetoxycholestan-5-ol-3-one (5 g.) in methyl-alcoholic potassium hydroxide (140 ml.; 1·5%) was mechanically stirred for 1 hour at 55—60°. The deep orange solution was treated with water (300 ml.), and the precipitate extracted with ethyl acetate (300 ml.). The solvent was removed under reduced pressure, the residue treated with light petroleum, and the insoluble portion repeatedly crystallised from aqueous acetone. *Cholestan*-6-*ol*-3-*one*-2 : 5-*oxide* formed soft needles, m. p. 181—182° (Found : C, 77·5; H, 10·5. $C_{27}H_{44}O_3$ requires C, 77·9; H, 10·6%). Yield, 20—30%. It gave no colour with ferric chloride and was unaffected by lead tetra-acetate (Criegee, *loc. cit.*). It was recovered unchanged after refluxing for 3 hours with 10% alcoholic hydrochloric acid. With concentrated sulphuric acid it gave a crimson coloration.

6-*Acetoxycholestan*-3-*one*-2 : 5-*oxide* (VIII, R = Ac).—Cholestan-6-ol-3-one-2 : 5-oxide (170 mg.) in dry pyridine (1 ml.) was treated with acetic anhydride (0·5 ml.) for 18 hours at room temperature. The product, crystallised from methyl alcohol (norit), gave small plates of 6-*acetoxycholestan*-3-*one*-2 : 5-*oxide*, m. p. 84° (Found : C, 75·8; H, 9·9. $C_{29}H_{46}O_4$ requires C, 76·0; H, 10·0%). On saponification at 55—60° with 2·5% methyl-alcoholic potassium hydroxide the original ketol-oxide, m. p. 182°, was recovered.

Cholestane-3 : 6-*dione*-2 : 5-*oxide* (IX).—Cholestan-6-ol-3-one-2 : 5-oxide (600 mg.) in benzene (20 ml.) was shaken at room temperature for 6 hours with chromic acid (0·5 g.) in acetic acid (20 ml.; 95%), and the neutral fraction of the oxidation product crystallised from aqueous acetone. *Cholestane*-3 : 6-*dione*-2 : 5-*oxide* formed large pearly plates, m. p. 115—116° (Found : C, 78·2; H, 10·0. $C_{27}H_{42}O_3$ requires C, 78·2; H, 10·1%). Yield, 60%.

The *bisdinitrophenylhydrazone*, prepared by treating a solution of the dione (50 mg.) and 2 : 4-dinitrophenylhydrazine (50 mg.) in absolute alcoholic solution (10 ml.) with 2 drops of concentrated hydrochloric acid and refluxing the mixture for 2 minutes, formed large flat plates, m. p. 171°, from acetone–chloroform (Found : N, 15·0. $C_{39}H_{50}O_9N_8$ requires N, 14·5%).

2 : 2-*Dibromo-6-acetoxycholestan-5-ol-3-one* (VII; R = Ac, R_1 = Br).—(*a*) 6-Acetoxycholestan-5-ol-3-one (1 g.) in acetic acid (25 ml.) was treated at room temperature with 2 drops of hydrobromic acid and 10 ml. of bromine–acetic acid (0·7 g. of bromine; 2 mols.). Decoloration of the bromine was accompanied by separation of the dibromide (1 g.) in needles, which were removed after 30 minutes. 2 : 2-*Dibromo-6-acetoxycholestan-5-ol-3-one* formed silky needles from aqueous acetone, m. p. 218° (decomp.), $[\alpha]_D^{19°}$ +70·9° (*c*, 1·975) (Found : Br, 25·9. $C_{29}H_{46}O_4Br_2$ requires Br, 25·9%).

(*b*) 2-Bromo-6-acetoxycholestan-5-ol-3-one (1 g.) in acetic acid (10 ml.) was treated at room temperature with 1 drop of hydrobromic acid and 0·35 g. of bromine dissolved in 5 ml. of acetic acid. After 2 hours the dibromide (0·75 g.) was removed and purified as above; m. p. 218°, not depressed in admixture with a sample prepared by method (*a*).

The dibromide liberated bromine when warmed with sodium iodide in benzene–alcohol solution.

Coprostan-5(β)-ol-3 : 6-dione.—200 Mg. of cholestane-3 : 5-diol-6-one II (Heilbron, Jones, and Spring, *loc. cit.*) in 5 ml. of acetic acid were treated with 150 mg. of chromic acid in 5 ml. of 90% acetic acid. After 24 hours at room temperature the crystalline deposit was filtered off. Coprostan-5(β)-ol-3 : 6-dione formed prisms from glacial acetic acid, m. p. 253° alone or in admixture with an authentic specimen (Windaus, *loc. cit.*).

3-Acetoxycholestan-5-ol-6-one.—Cholestane-3 : 5 : 6-triol I (21 g.) in glacial acetic acid (600 ml.) was treated with a solution of chromic acid (3·7 g.) in acetic acid (100 ml. of 94%), added dropwise with mechanical stirring at room temperature. Half the oxidising agent was added during 4½ hours, the mixture kept overnight, and the remainder added during 6 hours. The product, isolated by dilution with water and extraction with benzene, was refluxed with acetic anhydride (100 ml.) for 45 minutes. 3-Acetoxycholestan-5-ol-6-one (15 g.) crystallised on cooling. It was purified from glacial acetic acid and formed plates, m. p. 238°, $[\alpha]_D^{23°}$ −56·2° (*c*, 2·49) (Found : C, 75·2; H, 10·6. Calc. for $C_{29}H_{48}O_4$: C, 75·6; H, 10·4%), alone or in admixture with an authentic specimen. Hydrolysis with sodium methoxide solution yielded cholestane-3 : 5-diol-6-one I, m. p. 237° alone or in admixture with an authentic specimen.

Darzens Dehydration of 3-Acetoxycholestan-5-ol-6-one I.—Thionyl chloride (0·2 ml.) was added with shaking to 3-acetoxycholestan-5-ol-6-one (0·67 g.) dissolved in pyridine (10 ml.), and the mixture refluxed for 10 minutes. The product, isolated with ether, formed hexagonal plates from methyl alcohol, m. p. 110°, identified with 3(β)-acetoxy-Δ^4-cholesten-6-one by mixed m. p.

3(β) : 5(α)-Diacetoxycholestan-6-one.—(*a*) 3-Acetoxycholestan-5-ol-6-one I (25 g.) and potassium hydrogen sulphate (6 g.) were heated with acetic anhydride (125 ml.) for 15 minutes on the water-bath. The product was poured into saturated brine, and the mixture kept overnight. The crystalline precipitate was collected and purified from aqueous acetone (norit). 3(β) : 5(α)-Diacetoxycholestan-6-one (Schenck, *loc. cit.*) formed needles, m. p. 169—170°, $[\alpha]_D^{22°}$ −11° (*c*, 2·5) (Found : C, 74·1; H, 10·0. Calc. for $C_{31}H_{50}O_5$: C, 74·0; H, 10·0%). Yield, 35%. On saponification it gave cholestane-3 : 5-diol-6-one I, m. p. 237° alone or in admixture with an authentic specimen.

(*b*) 3-Acetoxycholestan-5-ol-6-one I (1 g.) in acetic anhydride (15 ml.) was refluxed for 10½ hours. On cooling, unchanged material (300 mg.) separated and was removed. Water was added to the filtrate and the precipitated solids were crystallised from aqueous alcohol The product was identified as 3(β) : 5(α)-diacetoxycholestan-6-one by m. p. and mixed m. p. with a sample prepared by method (*a*).

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