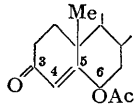
118. *Acyl Migrations in the Sterol Series.*

By M. F. C. Paige.

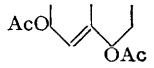
In connection with a project for the conversion of cholesterol into hyodeoxycholic acid and its stereoisomerides a study has been made of possible new methods of preparation of 6(β)-acetoxy-Δ^4-cholesten-3-one (I). In the course of this work an investigation was made of the acyl migrations which take place with 3-monoesters (VII) of *cis*-Δ^5-cholestene-3 : 4-diol. Evidence is adduced that this migration proceeds through the intermediate formation of an orthocarbonate (VIII).

HYODEOXYCHOLIC acid (3 : 6-dihydroxycholanic aid) has been isolated from pigs' bile, and its structure determined (Windaus and Bohne, *Annalen*, 1923, **433**, 278; Windaus, *ibid.*, 1926, **447**, 233; Wieland and Gumlich, *Z. physiol. Chem.*, 1933, **215**, 18). The isolation from the same source of an epimeric 3 : 6-dihydroxycholanic acid was claimed by Kimura (*ibid.*, 1937, **248**, 280). The preparation of hyodeoxycholic acid from a sterol has not yet been recorded, although this bile acid has been degraded stepwise to androsterone (Dalmer *et al.*, *Ber.*, 1935, **68**, 1814). The experiments now described were initiated as part of a project to obtain 3 : 6-dihydroxycholanic acids from cholesterol and to study the configurational relationships between hyodeoxycholic acid and its epimerides, three of which are theoretically possible. In a preliminary investigation of possible routes from cholesterol the issue became somewhat confused by the occurrence of acyl migrations of the type described by Spring and Swain (*Nature*, 1940, **146**, 718; J., 1941, 83) and by Rosenheim (*Nature*, 1941, **147**, 776; Petrow, Rosenheim, and Starling, this vol., p. 135), and it is with these migrations that the present communication is mainly concerned. When the author's experiments were complete Dr. Rosenheim kindly placed at his disposal the typescript of the detailed paper of Petrow, Rosenheim, and Starling, and it is satisfactory that the two lines of approach have led to the same general conclusions as to the mechanism of the migrations.

6(β)-Acetoxy-Δ⁴-cholesten-3-one (I) seemed a suitable intermediate for use in the conversion of cholesterol into the desired bile acids, and attempts were made to obtain this unsaturated ketone by a more convenient method than that of Ellis and Petrow (J., 1939, 1078). As 3(β) : 6(β)-diacetoxy-Δ⁴-cholestene (II) is obtainable in 25% yield by oxidation of cholesteryl acetate with selenium dioxide (Butenandt and Hausmann, *Ber.*, 1937, **70**, 1154), its partial hydrolysis to 6(β)-acetoxy-Δ⁴-cholesten-3(β)-ol (III) would probably afford such a method (compare Marker and Krueger, *J. Amer. Chem. Soc.*, 1940, **62**, 79; Ellis and Petrow, *loc. cit.*). Attempts to effect this partial hydrolysis were unsuccessful, and attention was therefore directed to the production of a mixed ester of the diol corresponding to (II) in which the ester group at position 3 would be more susceptible to hydrolysis than that at position 6. For this purpose a study was made of the oxidation of 3-*O*-carbomethoxy-



(I.)



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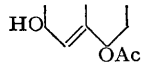
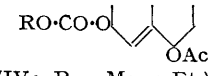
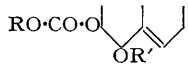


(III.)

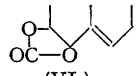
cholesterol with selenium dioxide in acetic acid and acetic anhydride solution. From the results of Butenandt and Hausmann (*loc. cit.*; cf. Rosenheim and Starling, J., 1937, 377) it was anticipated that this would give the desired mixed ester (IV; R = Me) in addition to the 3-*O*-carbomethoxy-derivative of *cis*-Δ⁵-cholestene-3 : 4-diol and/or its 4-acetate (type V). When the oxidation was carried out in acetic anhydride solution there was formed a mixture of products from which the only pure compound isolated was 3-O-*carbomethoxy*-4-*acetoxycholesterol* (V; R = Me; R′ = COMe). The 3 : 6-ester (the product of an allylic rearrangement) was not isolated, but was evidently formed, as hydrolysis of the uncrystallisable residues yielded a small amount of Δ⁴-cholestene-3 : 6-diol.



(IV; R = Me or Et.)



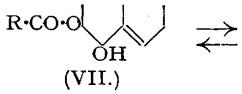
(V; R = Me or Et, R′ = H or COMe.)



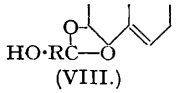
(VI.)

When 3-*O*-carbomethoxycholesterol was oxidised with selenium dioxide in acetic acid solution, the 4-acetoxy-derivative (V; R = Me, R′ = COMe), m. p. 161°, was again isolated, together with a second crystalline product, m. p. 173°. As in the former experiment, the formation of the desired 3 : 6-ester was shown only by the isolation of the 3 : 6-diol after hydrolysis. The compound, m. p. 173°, like 3-*O*-carbomethoxy-4-acetoxycholesterol, gave *cis*-Δ⁵-cholestene-3 : 4-diol on hydrolysis, but was evidently not the 4-hydroxy-derivative of 3-*O*-carbomethoxycholesterol, as it could not be acetylated or benzoylated. This compound was shown, by its independent preparation from *cis*-Δ⁵-cholestene-3 : 4-diol and carbonyl chloride, to be the *carbonate* (VI) of the 3 : 4-diol. The selenium dioxide oxidation of 3-*O*-carbethoxycholesterol in acetic anhydride solution gave 3-O-*carbethoxy*-4-*acetoxycholesterol* (V; R = Et; R′ = COMe) together with a compound of the type sought, namely, 3-O-*carbethoxy*-6-*acetoxy*-Δ⁴-*cholesten*-3-*ol* (IV; R = Et). The structure of the latter compound was shown by its hydrolysis to Δ⁴-cholestene-3 : 6-diol. When the oxidation was carried out in acetic acid solution, the same two products were isolated, together with the carbonate (VI).

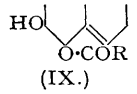
The formation of the carbonate (VI) of the 3 : 4-diol is of interest in connection with the mechanism of the acyl migrations described by Rosenheim (*loc. cit.*), who found that the 3-monoacetate (VII; R = Me) of *cis*-Δ⁵-cholestene-3 : 4-diol is converted into the 4-monoacetate (IX; R = Me) by warming its solution in



(VII.)



(VIII.)



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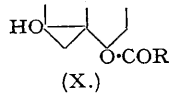

(X.)

acetic acid to 90°. Rosenheim regarded this as proceeding through the intermediate cyclic acetal (VIII; R = Me), but also drew attention to an alternative mechanism involving the intermediate formation of a

labile pentacyclic compound (X; R = Me) related to *i*-cholesterol. It would appear that the first product of oxidation of 3-*O*-carbomethoxycholesterol in acetic acid solution is its 4-hydroxy-derivative (V; R = Me, R′ = H), which then rearranges to the orthocarbonate (VIII; R = OMe). In this case, however, the intermediate (VIII) becomes stabilised by loss of methyl alcohol to give the carbonate (VI), rather than by further rearrangement to the 4-monoester (IX; R = OMe). In support of this interpretation it was found that the 3-*O*-carbomethoxy- and the 3-*O*-carbethoxy-derivative of *cis*-Δ^5-cholestene-3 : 4-diol were transformed into the carbonate (VI) by boiling acetic or propionic acid.

The isolation of the carbonate in these rearrangements of the 3-*O*-carbomethoxy- and -carbethoxy-compounds affords strong evidence that the mechanism of the acyl migration in 3-monoesters of cholestenediol is as formulated above (VII $\rightleftharpoons$ VIII $\rightleftharpoons$ IX). Additional evidence was furnished by the rearrangement of the 3-monoacetate by hot propionic acid; this gave the 4-monoacetate, and not the propionate which would be anticipated from an intermolecular mechanism involving intermediate formation of (X). Moreover, the rearrangement in propionic acid took place to a smaller extent than in the more strongly acidic acetic acid; even in acetic acid it was incomplete in 6 hours, indicating an equilibrium reaction (compare Petrow, Rosenheim, and Starling *loc. cit.*).

In an attempt to reverse the change and transform the carbonate (VI) into the 3-monoacetate (VII : R = Me) and/or its isomer (IX; R = Me) the carbonate was treated with methylmagnesium iodide (compare Tschitschibabin, *Ber.*, **1905**, **38**, 561). The attempt failed on account of the reducing action of the Grignard reagent, which led to Δ^4-cholestene as the only isolable product.

The mixed esters of *cis*-Δ^5-cholestene-3 : 4-diol formed by the action of selenium dioxide on 3-*O*-carbomethoxy- or -carbethoxy-cholesterol in acetic anhydride were hydrolysed to the 3 : 4-diol, and their structures were confirmed by the preparation of the same esters by carbomethoxylation or carbethoxylation of the diol, followed by acetylation of the mono-esters. It is known that monoacylations of this diol take place on the hydroxyl group at C_3 (Rosenheim and Starling, *loc. cit.*; Petrow and Starling, J., **1940**, **63**; Rosenheim, *loc. cit.*; compare Spring and Swain, J., **1941**, **83**). The same esters (V; R = Me or Et, R′ = COMe) were also formed by treatment of the 4-monoacetate (IX; R = Me) in pyridine solution with methyl and ethyl chloroformate.

Marker and Rohrmann (*J. Amer. Chem. Soc.*, **1939**, **61**, 3022) oxidised cholesteryl acetate in benzene–acetic acid solution with selenium dioxide and isolated two compounds which they regarded as polymorphic forms of 4-hydroxycholesteryl acetate. Reinvestigation of this reaction showed that one of Marker's products is 4-acetoxycholesterol, so the two compounds are structural isomerides. A similar conclusion regarding these " polymorphs " was independently reached by Petrow, Rosenheim, and Starling (*loc. cit.*).

In connection with the original objective of the investigation the catalytic hydrogenation of 6(β)-acetoxy-Δ^4-cholesten-3-one (I) was examined, with palladium, followed by platinum. It was hoped in this way to obtain 6-acetoxy*epi*coprostanol. However, although hydrogen was rapidly absorbed, a crystalline product could not be isolated. Reduction of the acetoxy-ketone (I) with sodium and amyl alcohol gave a resinous product, from which was isolated, after benzoylation, the dibenzoate of cholestane-3(β) : 6(α)-diol. This diol was also formed by similar reduction of cholesterol α- and β-oxides. Hydrogenation of the benzoate of cholesterol β-oxide could not be effected with Adams's platinum oxide catalyst. The slow catalytic hydrogenation of cholesterol α-oxide with palladium in acetic acid was described by Stavely (*J. Amer. Chem. Soc.*, **1942**, **64**, 2723). Reduction of Δ^4-cholestene-3 : 6-diol with sodium and amyl alcohol gave a hydrocarbon, m. p. 79—80°, which on catalytic hydrogenation took up one molecule of hydrogen to give cholestane. This product was not Δ^5-cholestene. Its m. p. corresponds with that given in the literature for Δ^4-cholestene, the formation of which involves reduction of both hydroxyl groups of the diol.

Experimental.

A. *Selenium Dioxide Oxidations.*—*3-O-Carbomethoxycholesterol in acetic anhydride solution.* A solution of 3-*O*-carbomethoxycholesterol (4·6 g.) (Robberecht, *Bull. Soc. chim.*, 1938, **47**, 597) in acetic anhydride (100 c.c.) was treated dropwise at 105—110° with a solution of selenium dioxide (2·5 g.) in water (5 c.c.). The temperature was maintained at 105—110° for 2 hours, and the cooled solution decomposed with cold water. The product was extracted with acetone, and the extract slowly added to well-stirred 10% aqueous potassium cyanide, stirring being continued for 4 hours. This served to complete the removal of selenium. The oxidation products were extracted with ether, and the dried extract freed from solvent. Trituration of the residual brown gum with cold alcohol gave crystals which, after two recrystallisations from alcohol, formed a colourless, microcrystalline powder, m. p. 160·5—161° (Found: C, 74·1; H, 9·6. $C_{31}H_{50}O_5$ requires C, 74·1; H, 10·0%). This compound, 3-O-*carbomethoxy-4-acetoxycholesterol* (V; R = Me, R′ = COMe), was unaffected by 1 hour's boiling with acetic anhydride and was hydrolysed by boiling 5% methyl-alcoholic potash to *cis*-Δ^5-cholestene-3 : 4-diol, m. p. 174° alone or mixed with an authentic specimen.

This mixed ester was also obtained by two other methods. (*a*) Pure pyridine (5 c.c.) was added dropwise, with shaking, to an ice-cooled solution of 4-hydroxycholesterol (1 g.) in anhydrous ether (20 c.c.), benzene (20 c.c.), and methyl chloroformate (5 c.c.). After 2 hours at room temperature the solution was filtered from pyridine hydrochloride, and solvents removed under reduced pressure. Water was added to the residue, and the resulting solid crystallised several times from alcohol, giving thin colourless plates of 3-O-*carbomethoxy-4-hydroxycholesterol*, m. p. 157·5—159·5° (Found: C, 75·5; H, 10·7. $C_{29}H_{48}O_4$ requires C, 75·65; H, 10·4%). This (200 mg.) was acetylated by boiling for 1 hour with acetic anhydride (5 c.c.); the cooled solution was poured into ice-water, kept overnight, and the product crystallised from alcohol. The resulting microcrystalline powder had m. p. 160·5—161°, not depressed by the 4-acetoxy-derivative formed by oxidation of 3-*O*-carbomethoxycholesterol. Benzoylation of 3-*O*-carbomethoxy-4-hydroxycholesterol, with benzoyl chloride in pyridine at 100°, gave 3-O-*carbomethoxy-4-benzoyloxycholesterol*, rectangular platelets (from acetone–alcohol), m. p. 173—174° (Found: C, 76·5; H, 9·2. $C_{36}H_{52}O_5$ requires C, 76·6; H, 9·2%).

(*b*) The 4-monoacetate of *cis*-Δ^5-cholestene-3 : 4-diol (prepared by rearrangement of the 3-monoacetate in acetic

acid at 90°) (0·33 g.) was treated in the manner described above with methyl chloroformate (3·5 c.c.) and pyridine (6 c.c.). The same mixed ester, m. p. 160·5—161°, was obtained.

The gum formed in the above selenium dioxide oxidation, after removal of the mixed ester, m. p. 161°, was hydrolysed with boiling methyl-alcoholic potash. The resulting crystals, recrystallised from acetone–chloroform, formed colourless fine needles, m. p. 256—257°, and were shown by mixed m. p. to consist of Δ^4-cholestene-3 : 6-diol.

Oxidation of 3-O-*carbomethoxycholesterol in acetic acid solution.* 3-*O*-Carbomethoxycholesterol (21 g.) was dissolved in acetic acid (200 c.c.) at 100°, and mixed with a solution prepared by addition of acetic acid (200 c.c.), heated to 100°, to a solution of selenium dioxide (10 g.) in water (5 c.c.). After 5 minutes' boiling, sodium acetate (60 g.) was added, and boiling continued for a further 5 minutes. The hot solution was filtered from selenium, cooled, poured into half-saturated brine (1000 c.c.), and extracted with ether. The extracts were washed with sodium carbonate solution and with water and dried (sodium sulphate), and the ether removed. Trituration of the residue with cold methyl alcohol gave a crystalline material (2·7 g., m. p. 126—139°), from which two pure products were separated by fractional crystallisation from alcohol. The less soluble product was shown to be 3-*O*-carbomethoxy-4-acetoxycholesterol, m. p. 161°; the more soluble product crystallised from alcohol in colourless leaflets, m. p. 173—173·5°, and was the *carbonate* (VI) of *cis*-Δ^5-cholestene-3 : 4-diol (Found: C, 78·7, 78·4; H, 11·1, 10·7. $C_{28}H_{44}O_3$ requires C, 78·5; H, 10·3%). This compound was unaffected by boiling acetic anhydride or by benzoyl chloride in pyridine (48 hours at room temperature). Its structure was shown by its hydrolysis to *cis*-Δ^5-cholestene-3 : 4-diol, and by its preparation from this diol (0·5 g.) in dry pyridine (6 c.c.) and benzene (10 c.c.) by heating in a sealed tube at 70° for 2 hours with carbonyl chloride in toluene (8·8 c.c.; 12·5%). The cooled solution was poured into water and extracted with ether, and the extract washed with dilute hydrochloric acid and then sodium carbonate solution. Removal of the ether gave a crystalline residue, from which the carbonate (VI) (0·37 g.) was obtained by crystallisation from alcohol (charcoal).

The uncrystallisable residue from the above oxidation was hydrolysed with 5% methyl-alcoholic potash, and again gave Δ^4-cholestene-3 : 6-diol.

Oxidation of 3-O-*carbethoxycholesterol in acetic anhydride solution.* This was carried out with 3-*O*-carbethoxycholesterol (Robberecht, *loc. cit.*) (2·38 g.), the oxidation and working up being carried out as in the corresponding treatment of the carbomethoxy-compound. The crystalline material (0·86 g.) obtained by trituration with alcohol of the crude brown gum was separated, by fractional crystallisation from acetone, into less soluble, long, colourless needles, m. p. 163—163·5°, and more soluble rosettes of colourless elongated platelets (from alcohol), m. p. 121—122·5°. The higher-melting compound was shown to be 3-O-*carbethoxy*-4-*acetoxycholesterol* (V; R = Et, R′ = COMe) (Found: C, 73·6; H, 9·8. $C_{32}H_{52}O_5$ requires C, 74·4; H, 10·1%). It was unaffected by boiling acetic anhydride, and was hydrolysed by boiling 5% methyl-alcoholic potash to *cis*-Δ^5-cholestene-3 : 4-diol. This mixed ester was also prepared by the following two methods: (*a*) The diol (1 g.) was converted into 3-O-*carbethoxy*-4-*hydroxycholesterol* (V; R = Et, R′ = H) by treatment with ethyl chloroformate and pyridine as in the corresponding treatment with methyl chloroformate. The 3-monoester formed small, elongated, rectangular plates, m. p. 130·5—131° (Found: C, 76·0; H, 10·7. $C_{30}H_{50}O_4$ requires C, 76·0; H, 10·55%). Acetylation with boiling acetic anhydride (1 hour) gave 3-*O*-carbethoxy-4-acetoxycholesterol, m. p. 162·5—163°, identical with that obtained from the selenium dioxide oxidation. Benzoylation of the 3-monoester (200 mg.) with benzoyl chloride (1 c.c.) in pyridine (5 c.c.) (2 hours at 100°) gave 3-O-*carbethoxy*-4-*benzoyloxycholesterol*, colourless elongated platelets (from alcohol), m. p. 131—131·5° (Found: C, 76·4; H, 9·25. $C_{37}H_{54}O_5$ requires C, 76·8; H, 9·3%). The m. p. was strongly depressed by admixture with the monoester.

(*b*) The 4-monoacetate of *cis*-Δ^5-cholestene-3 : 4-diol was esterified with ethyl chloroformate in pyridine under the standard conditions (see above) and gave the same 3-*O*-carbethoxy-4-acetoxycholesterol.

The compound, m. p. 121—122·5°, isolated from the products of oxidation of 3-*O*-carbethoxycholesterol, gave on hydrolysis with boiling 5% methyl-alcoholic potash Δ^4-cholestene-3 : 6-diol, m. p. 256—257°. This product was evidently 3-O-*carbethoxy*-6-*acetoxy*-Δ^4-*cholesten*-3-*ol* (IV; R = Et) (Found: C, 74·6; H, 10·2. $C_{32}H_{52}O_5$ requires C, 74·4; H, 10·1%).

Oxidation of 3-O-*carbethoxycholesterol in acetic acid solution.* 3-*O*-Carbethoxycholesterol (4·28 g.) was oxidised with selenium dioxide (2 g.) as described for the corresponding experiment with the carbomethoxy-compound. The crude mixture of products was obtained by slow crystallisation, during 6 weeks, from acetic acid. Fractional crystallisation from acetone of the resulting solid gave (*a*) 3-*O*-carbethoxy-4-acetoxycholesterol, m. p. 163°, (*b*) the carbonate (VI), m. p. 173°; this was obtained by crystallisation from ligroin of the material from the acetone liquors of (*a*); (*c*) 3-*O*-carbethoxy-6-acetoxy-Δ^4-cholesten-3-ol, m. p. 115—117·5°, not depressed by the pure material, m. p. 121—122·5°. This was obtained by further crystallisation from acetone and ligroin, of the material from the liquors of (*b*).

B. *Rearrangement of* 3-*Monoesters* (VII) *of* cis-Δ^5-*Cholestene*-3 : 4-*diol.*—(*a*) A saturated solution of the 3-monoacetate (3 g.) in acetic acid at 90° was maintained at this temperature for an hour. The crystals which separated on cooling were collected; fractional crystallisation from methyl alcohol of these, and of the crystals obtained from the acetic acid liquors by vacuum concentration, gave the 4-monoacetate (IX; R = Me) (1·9 g.), m. p. 161—163°. Treatment of this with benzoyl chloride in pyridine gave the 4-acetate-3-benzoate, m. p. 165·5—166·5°, identical with a specimen prepared by acetylation of the 3-monobenzoate formed by selenium dioxide oxidation of cholesteryl benzoate (Rosenheim and Starling, J., 1937, 380).

(*b*) A solution of the 3-monoacetate (1 g.) in propionic acid (5 c.c.) was heated at 100° for an hour. The first crops of crystals obtained were largely unchanged 3-monoacetate. The more soluble material from the liquors was obtained as a gum which gave, with benzoyl chloride in pyridine, the above-mentioned 4-acetate-3-benzoate, m. p. 165·5—166·5°.

(*c*) A solution of 3-*O*-carbomethoxy-4-hydroxycholesterol (V; R = Me, R′ = H) (200 mg.) in glacial acetic acid (10 c.c.) and water (0·5 c.c.) was boiled for an hour. The product, after several recrystallisations from alcohol, gave the glycol carbonate (VI), m. p. 173°. When the experiment was carried out at 90°, some carbonate was formed but much of the carbomethoxy-compound was unchanged.

(*d*) The carbonate was also formed when a solution of the 3-*O*-carbomethoxy-compound (100 mg.) in propionic acid (10 c.c.) and water (0·5 c.c.) was boiled for an hour.

(*e*) A solution of 3-*O*-carbethoxy-4-hydroxycholesterol (400 mg.) in glacial acetic acid (20 c.c.) and water (1 c.c.) was boiled for 30 minutes. The glycol carbonate (180 mg.) was again isolated.

C. *Additional Experiments.—Action of methylmagnesium iodide on the carbonate* (VI). A solution of the carbonate (0·5 g.) in ether (20 c.c.) was added to ethereal methylmagnesium iodide (2 mols.), and the whole kept overnight in an atmosphere of dry hydrogen. The product was poured into ice-water and acidified with hydrochloric acid, and the ethereal extract washed, dried, and freed from solvent. The residue crystallised from alcohol in colourless needles, m. p. 77—78° after several recrystallisations from methyl alcohol. The m. p. was not depressed by admixture with Δ^4-cholestene, prepared by reduction of Δ^4-cholestene-3 : 6-diol (see below).

Reduction of 6(β)-*acetoxy*-Δ^4-*cholesten*-3-*one* (I). Sodium (5 g.) was added during 40 minutes to a boiling solution of the ketone (1 g.) (Ellis and Petrow, J., 1939, 1081) in amyl alcohol (40 c.c.). Boiling was continued for 3 hours, during which more amyl alcohol (20 c.c.) was added. The cooled reaction mixture was decomposed with water, the amyl alcohol layer separated, and the aqueous liquors extracted with ether. The ethereal extract was combined with the amyl

alcohol solution, and the whole washed and freed from solvents. The resulting pale yellow viscous residue could not be crystallised and was treated (48 hours at room temperature) with benzoyl chloride (4 c.c.) in pyridine (10 c.c.). The product was isolated in the usual way as a gum which, triturated with acetone, gave a solid. Recrystallisation from acetone–chloroform and then ethyl acetate gave 3(β) : 6(α)-cholestanediol dibenzoate (0·12 g.), m. p. 213—214·5°, alone or mixed with an authentic sample prepared from cholesterol α-oxide (Urushibara, *Bull. Chem. Soc. Japan*, 1941, **16**, 182). Hydrolysis of the dibenzoate gave the free diol, m. p. 218—219·5°.

Reduction of Δ^4*-cholestene-3 : 6-diol.* Sodium (10 g.) was added during an hour to a boiling solution of the diol (2 g.) in amyl alcohol (100 c.c.), boiling being continued for 3 hours. The product, isolated as described in the preceding case, was an almost colourless gum, an alcoholic solution of which deposited long needles when cooled. Recrystallisation gave pure Δ^4-cholestene (1·4 g.), m. p. 79—80°. The m. p. was depressed by admixture with coprostenone or Δ^5-cholestene. Catalytic hydrogenation with palladium-black gave cholestane, m. p. 77—78°, not depressed by an authentic specimen of cholestane, of m. p. 79—80°.

Cholesteryl benzoate α- and β-oxides (compare Spring and Swain, J., 1939, 1356; Chakravorty and Levin, *J. Amer. Chem. Soc.*, 1942, **64**, 2317). A solution of monoperphthalic acid (24 g.) in ether (1 l.) was added dropwise during 90 minutes to a stirred solution of cholesteryl benzoate (40 g.) in ether (450 c.c.) and chloroform (300 c.c.), the temperature being kept at −5°. After 12 hours at 0° and 4 days at room temperature, the excess of peracid was extracted with sodium carbonate solution. The washed and dried ether–chloroform solution was evaporated, and the crystalline residue recrystallised several times from ethyl acetate, giving pure cholesteryl benzoate α-oxide (22 g.), m. p. 168°, hydrolysed to cholesterol α-oxide, m. p. 142—143°. The material from the ethyl acetate liquors was recrystallised repeatedly from ethyl acetate–methyl alcohol, giving cholesteryl benzoate β-oxide (10·5 g.), m. p. 150°. Hydrolysis gave the β-oxide.

Cholesterol α-oxide (1·8 g.) was obtained by oxidation of cholesterol (2 g.) with monoperphthalic acid.

Reduction of cholesterol oxides. This was carried out in the usual way with sodium and amyl alcohol. By treatment of the crude resinous product from the β-oxide with acetone there was obtained a small yield of cholestane-3(β) : 6(α)-diol. Benzoylation of the gum from the acetone liquors gave the dibenzoate of this diol.

The same diol (0·11 g.) was obtained by similar reduction of cholesterol α-oxide (1 g.).

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