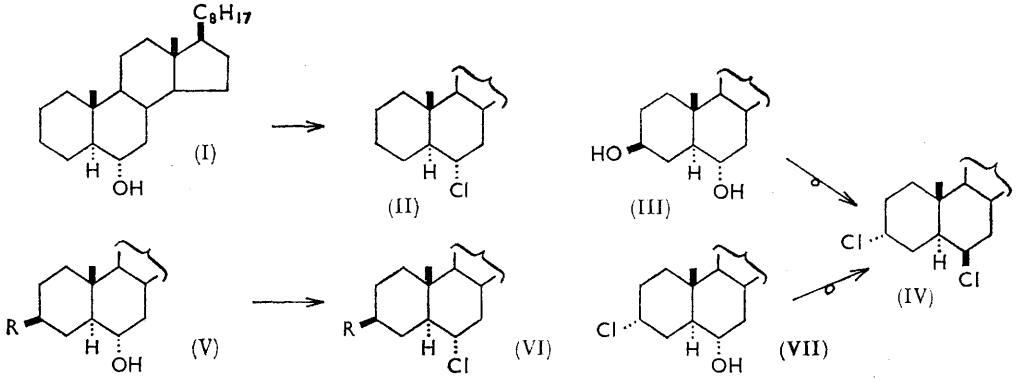
960. *Steroids and Walden Inversion. Part LIII.* Substitution Reactions of the 3β-Acetoxy-, 3α-Acetoxy-, 3β-Chloro-, and 3α-Chloro-5α-cholestan-6α-ols: Some Further Examples of Walden Retention.*

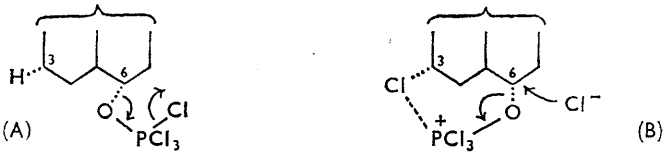
By C. W. Shoppee, Ruth Lack, and Berwyn McLean.

On treatment with phosphorus pentachloride 3β-acetoxy-, 3α-acetoxy-, and 3β-chloro-5α-cholestan-6α-ol undergo substitution with retention of configuration, but 3α-chloro-5α-cholestan-6α-ol undergoes substitution with inversion of configuration.

In Part XLVI [1] we reported two simple examples of Walden retention; thus 5α-cholestan-6α-ol (I) gives 6α-chloro-5α-cholestane (II) on treatment with phosphorus pentachloride, with retention of configuration at the site of substitution, whereas 5α-cholestane-3β,6α-diol (III) yields 3α,6β-dichloro-5α-cholestane (IV), with inversion of configuration at both the centres of substitution.



To explain this remarkable difference in stereochemical behaviour, we suggested that replacement of the 3β-hydroxyl group of the diol (III) proceeded rapidly with inversion, and that the resultant 3α-chlorine atom controlled the orientation of the next-formed 6α-$OPCl_4$ group by intramolecular bonding, thereby preventing the operation of mechanism S_Ni (A: retention), whilst permitting the operation of mechanism S_N2 (B: inversion). If this suggestion is in principle correct, the initial provision of a 3α-chlorine atom should enable the formation of an intermediate of type (B) and lead to inversion of configuration at the seat of substitution, C-6.

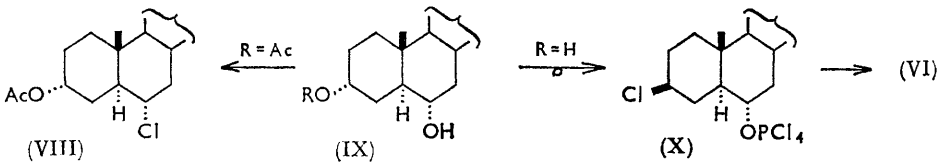


We now record three further simple examples of Walden retention. We have examined the stereochemical course of substitution at C-6 in the reaction of 3β-acetoxy-5α-cholestan-6α-ol (V; R = OAc) and 3β-chloro-5α-cholestan-6α-ol (V; R = Cl) with phosphorus pentachloride. These two saturated secondary alcohols, in which either the 3β-hydroxyl group is protected, or the 3β-chlorine atom is so orientated as to be incapable of intramolecular interaction with a 6α-$OPCl_4$ group, both react with retention of configuration at C-6 to give 3β-acetoxy-6α-chloro-5α-cholestane (VI; R = OAc) and 3β,6α-dichloro-5α-cholestane (VI; R = Cl), respectively.

* Part LII, *J.*, 1963, 3366.

[1] Shoppee, Howden, and Lack, *J.*, 1960, 4874.

On the contrary, 3α-chloro-5α-cholestan-6α-ol (VII), in which a 3α-chlorine atom is present in the correct orientation for intramolecular bonding with a 6α-$OPCl_4$ group, reacts with phosphorus pentachloride with inversion at C-6, to afford 3α,6β-dichloro-5α-cholestane (IV) with some cholesta-3,5-diene. The van der Waals radii of chlorine and phosphorus (1·8, 1·9 Å) appear to be sufficiently large to permit bonding, of mixed electrovalent–covalent character, as envisaged in (B) without severe deformation of the chair conformation of ring A.* Both of the possible boat conformations of ring A (apices at C-3 and C-10, or at C-2 and C-5) from examination of Dreiding models appear to lead to increased distances between the 3α- and 6α-substituents.



3α-Acetoxy-5α-cholestan-6α-ol (IX; R = Ac) by treatment with phosphorus pentachloride underwent substitution with retention of configuration, to give 3α-acetoxy-6α-chloro-5α-cholestane (VIII). It seems, therefore, that the shorter C–O bond length (1·43 Å) and the lesser van der Waals radius of oxygen (1·40 Å), as compared with chlorine (C–Cl, 1·77 Å; Cl, 1·80) render the unshared electrons of the oxygen atom incapable of effective intramolecular bonding with a 6α-$OPCl_4$ group. 5α-Cholestane-3α,6α-diol (IX; R = H) reacted with phosphorus pentachloride to give, with retention of configuration at C-6, presumably by way of the 3β-chloro-intermediate (X), 3β,6α-dichloro-5α-cholestane (VI; R = Cl) accompanied by various unsaturated compounds [2] as disclosed by qualitative thin-layer chromatography on silica.

Hydroboration of cholesteryl acetate by a modification of the method of Brown and Subba Rao [3] gave a mixture of 3β-acetoxy-5α-cholestan-6α-ol (V; R = OAc) and 5α-cholestane-3β,6α-diol (V; R = OH). The former yielded a separable mixture of cholesteryl acetate and 3β-acetoxy-6α-chloro-5α-cholestane (VI; R = OAc), when treated with either thionyl chloride or phosphorus pentachloride, with no trace of the inverted product, 3β-acetoxy-6β-chloro-5α-cholestane.

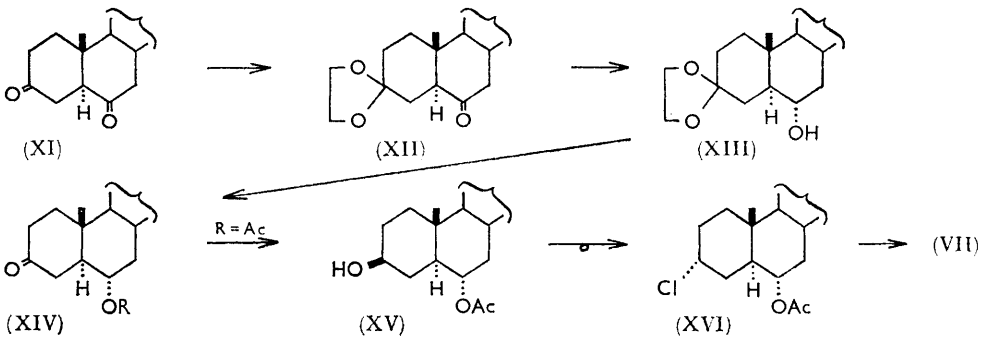
Similarly, hydroboration of cholesteryl chloride gave an 80% yield of 3β-chloro-5α-cholestan-6α-ol (V; R = Cl) which, on treatment with phosphorus pentachloride, gave a mixture of cholesteryl chloride and 3β,6α-dichloro-5α-cholestane (VI; R = Cl). A separation was achieved by column chromatography on silica gel.

The preparation of the hitherto unknown 3α-chloro-5α-cholestan-6α-ol (VII) proved more difficult. Since the proposed mechanism for the chlorination of 5α-cholestane-3β,6α-diol (III) proceeds by the rapid substitution of the 3β-hydroxyl group by a 3α-chlorine atom, an attempt was made to isolate the intermediate 3α-chloro-5α-cholestan-6α-ol (VII) by treatment of the diol (III) with one equivalent of phosphorus pentachloride. However, at 20° no reaction was observed, whilst at 80° a mixture of unchanged material and 3α,6β-dichloro-5α-cholestane (IV) was obtained. This result is in agreement with the formation of a proposed intermediate (B) in which bimolecular substitution at C-6 would be facilitated by the positive charge on phosphorus. An attempt partially to dehydrochlorinate 3α,6β-dichloro-5α-cholestane (IV) by treatment with collidine for 3 hours at 180° was unsuccessful, and pure specimens of epicholesteryl chloride were difficult to obtain on a

* Severe deformation of ring A must occur in 3α,5α-epoxycholestane, produced in 54% yield from 5α-cholestane-3β,5-diol 3-toluene-*p*-sulphonate and potassium t-butoxide, cf. Clayton, Henbest, and Smith, *J.*, 1957, 1982.

[2] Shoppee and Summers, *J.*, 1952, 1790.
[3] Brown and Subba Rao, *J. Amer. Chem. Soc.*, 1956, **78**, 5694; *J. Org. Chem.*, 1957, **22**, 1135.

large scale by the published routes.[2,4] Dehydration of 3α-chloro-5α-cholestan-6β-ol [2] with phosphorus oxychloride in pyridine gave a crystalline product, m. p. 111—113°, $[\alpha]_D$ −42°, which was not homogeneous on thin-layer chromatography and is a mixture of 3α-chlorocholest-5-ene and 3α-chloro-5α-cholest-6-ene.[5] Treatment of this impure epicholesteryl chloride with diborane followed by alkaline hydrogen peroxide gave two products, probably 3α-chloro-5β-cholestan-5-ol and 3α-chloro-5β-cholestan-6β-ol, both containing an equatorial chlorine atom ($\nu_{max.}$ 752 cm.$^{-1}$),[6] indicating that β-addition to the Δ^5-double bond had occurred, as a result of hindrance by the axial 3α-chlorine atom to the α-approach of the reagent, as opposed to the desired α-addition.

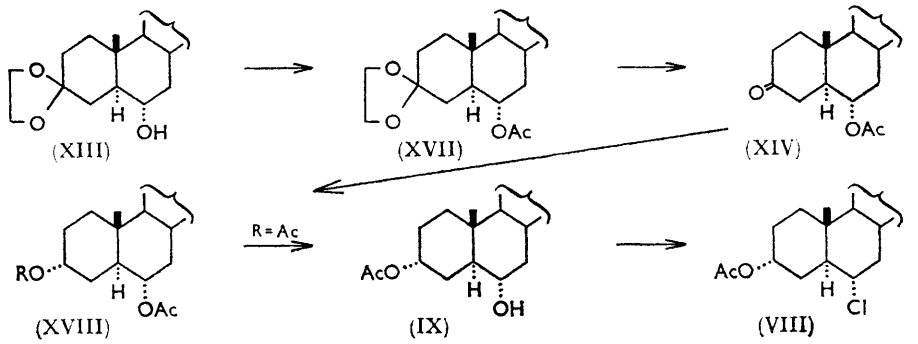


3α-Chloro-5α-cholestan-6α-ol (VII) was finally prepared by an indirect route. Monoketalisation of 5α-cholestane-3,6-dione (XI) in benzene with one equivalent of ethylene glycol gave 3,3-ethylenedioxy-5α-cholestan-6-one (XII) exhibiting a negative Cotton curve typical of a 6-oxo-5α-steroid.[7] This ketone (XII) was reduced with sodium in ethanol to 3,3-ethylenedioxy-5α-cholestan-6α-ol (XIII) which gave 6α-hydroxy-5α-cholestan-3-one (XIV: R = H) on acid hydrolysis. This hydroxy-ketone was not identical with an authentic sample of 6β-hydroxy-5α-cholestan-3-one,[8] prepared by sodium borohydride reduction of 3,3-ethylenedioxy-5α-cholestan-6-one, and readily formed an acetyl derivative (XIV; R = Ac). Reduction of this acetate with sodium borohydride in methanol gave the required 6α-acetoxy-5α-cholestan-3β-ol (XV), converted by treatment with phosphorus pentachloride into 3α-chloro-5α-cholestan-6α-yl acetate (XVI), which was hydrolysed to 3α-chloro-5α-cholestan-6α-ol (VII). Treatment of compound (VII) with phosphorus pentachloride gave an oily product, unsaturated to tetranitromethane, but exhibiting infrared absorption identical with that of 3α,6β-dichloro-5α-cholestane (IV). The unsaturated material could not be separated by column chromatography, but was removed by treatment of the mixture with perbenzoic acid [9] to give pure 3α,6β-dichloro-5α-cholestane, identical with the sample prepared by treatment of 5α-cholestan-3β,6α-diol (III) with phosphorus pentachloride.

3α-Acetoxy-5α-cholestan-6α-ol (IX) was prepared in the following way. The ketal (XIII) was acetylated to furnish the acetate (XVII); removal of the protecting ketal group by gentle hydrolysis with toluene-*p*-sulphonic acid in acetone gave 6α-acetoxy-5α-cholestan-3-one (XIV). Hydrogenation of the 3-ketone (XIV) with platinum oxide in di-n-butyl ether at 60—70° gave 6α-acetoxy-5α-cholestan-3α-ol (XVIII; R = H), which was separated from the 3β-isomer by chromatography on alumina. The derived diacetate (XVIII; R = Ac) was converted into the required 3α-acetoxy-5α-cholestan-6α-ol (IX) by preferential hydrolysis of the equatorial 6α-acetoxyl group by slow addition of 1 equivalent

[4] Fudge, Shoppee, and Summers, *J.*, 1954, 958.
[5] Shoppee, Holley, and Newsoroff, *J.*, in the press.
[6] Barton, Page, and Shoppee, *J.*, 1956, 331.
[7] Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960, p. 43.
[8] Marker and Krueger, *J. Amer. Chem. Soc.*, 1940, **62**, 79.
[9] Roberts, Shoppee, and Stevenson, *J.*, 1954, 2705.

of potassium hydroxide in ethanol over 30 hours. The 3α-monoacetate (IX) with phosphorus pentachloride gave a crude product, purified on silica gel to give 3α-acetoxy-6α-chloro-5α-cholestane (VIII) containing an equatorial chlorine atom ($\nu_{max.}$ 768, 737 cm.$^{-1}$).



These results support the proposed mechanism (B) for the substitution of 5α-cholestane-3β,6α-diol (III) with inversion at both C-3 and C-6. The retention of configuration at C-6 observed when 5α-cholestan-6α-ol, and 3β-acetoxy- and 3β-chloro-5α-cholestan-6α-ol, are treated with phosphorus pentachloride has been attributed [1] to the steric inhibition by the axial 10-methyl group of 6β-attack by a chlorine anion. It is therefore proposed to examine the chlorination of 3-substituted 5α-cholestan-6α-ols in the 19-nor-series, in which such steric inhibition should be absent.

Experimental

For general directions see *J.*, 1959, 345; $[\alpha]_D$ refer to chloroform solutions at room temperature. Infrared spectra were determined in $CHCl_3$ solution on a Perkin-Elmer model 211 double-beam instrument. Analytical samples were dried at 70°/0·5 mm.

3β-*Acetoxy*-5α-*cholestan*-6α-*ol.*—Cholesteryl acetate (2 g.) and boron trifluoride etherate (5 ml.) were added to diethylene glycol dimethyl ether (diglyme) (20 ml.). A solution of sodium borohydride (1·0 g.) in diglyme (100 ml.) was added dropwise during 30 min. and the mixture set aside for 2 hr. A 12% solution of sodium hydroxide in ethanol (15 ml.) was added, followed by dropwise addition of 30% hydrogen peroxide (15 ml.) under nitrogen. Dilution with water and ether extraction gave a product (1·8 g.), which was chromatographed on alumina (60 g.) in pentane to give unchanged cholesteryl acetate (1·1 g.) on elution with pentane. Elution with benzene–pentane (2 : 3) gave the *cholestanol* (670 mg.), m. p. 127—128° (Found: C, 78·25; H, 11·15. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%). Increasing the reaction time to 18 hr. resulted in the hydrolysis of the 3β-acetoxyl group to give 5α-cholestane-3β,6α-diol.

Chlorination of 3β-*Acetoxy*-5α-*cholestan*-6α-*ol.*—(*a*) 3β-Acetoxy-5α-cholestan-6α-ol (200 mg.) was treated with thionyl chloride (5 ml.) at 20° for 30 min. The mixture was poured into water to give a solid (165 mg.), which was chromatographed on silica gel (10 g.) in pentane. Elution with pentane gave 3β-*acetoxy*-6α-*chloro*-5α-*cholestane* (125 mg.), m. p. 213°, $[\alpha]_D$ +17° (*c.* 1·0), $\nu_{max.}$ (CS_2) 770, 730 cm.$^{-1}$ (Found: C, 75·2; H, 10·8. $C_{29}H_{49}ClO_2$ requires C, 74·9; H, 10·6%).

(*b*) 3β-Acetoxy-5α-cholestan-6α-ol (200 mg.) was treated with resublimed phosphorus pentachloride (150 mg.) in benzene at 80° for 2 hr. The usual working up gave an oil, which was chromatographed on silica gel (15 g.) in pentane. Elution with pentane gave an oil (35 mg.), whilst elution with ether–pentane (1 : 50) gave 3β-acetoxy-6α-chloro-5α-cholestane (115 mg.), m. p. 205—207°, identical with the sample prepared under (*a*). Elution with ether gave unchanged 3β-acetoxy-5α-cholestan-6α-ol (85 mg.), m. p. and mixed m. p. 127—128°.

3β-*Chloro*-5α-*cholestan*-6α-*ol.*—Cholesteryl chloride (5 g.) and boron trifluoride etherate (12 ml.) in diglyme (40 ml.) were treated with a solution of sodium borohydride (2·0 g.) in diglyme (300 ml.) added dropwise during 20 min. and the mixture was set aside overnight. A 12% solution of sodium hydroxide in ethanol (35 ml.) was added, followed by dropwise

addition under nitrogen of 30% hydrogen peroxide (35 ml.). Dilution with water and ether extraction gave a crude product (4·7 g.), which was chromatographed on alumina (150 g.) in pentane. Elution with pentane (4 × 150 ml.) gave unchanged cholesteryl chloride (43 mg.), whilst use of ether–benzene (4 : 5; 25 × 150 ml.) gave 3β-*chloro*-5α-*cholestan*-6α-*ol* (4·0 g.), m. p. 116—118° (from methanol), $[\alpha]_D$ +52° (*c* 1·0), $\nu_{max.}$ (CS_2) 775 cm.$^{-1}$ (Found: C, 76·8; H, 11·2. $C_{27}H_{47}ClO$ requires C, 76·7; H, 11·1%).

3β-*Chloro*-5α-*cholestan*-6α-*yl Acetate*.—3β-Chloro-5α-cholestan-6α-ol (140 mg.) was treated with pyridine–acetic anhydride (2 : 1; 2 ml.) at 20° for 24 hr. The usual woring up gave an oil which was chromatographed on alumina (5 g.) in pentane. Elution with pentane gave the *acetate* (120 mg.), m. p. 97—99° (from methanol–acetone), $[\alpha]_D$ +25° (*c* 1·0), $\nu_{max.}$ 1722, 1260, 758 cm.$^{-1}$ (Found: C, 75·3; H, 10·8. $C_{29}H_{49}ClO_2$ requires C, 74·9; H, 10·55%).

Chlorination of 3β-*Chloro*-5α-*cholestan*-6α-*ol*.—(*a*) 3β-Chloro-5α-cholestan-6α-ol (100 mg.) was treated with thionyl chloride (0·1 ml.) at 60° for 10 min. The excess of thionyl chloride was decomposed by the addition of water, and the resultant oil was chromatographed on alumina (3 g.). Elution with pentane (6 × 3 ml.) gave material, m. p. 110—113° (from acetone–methanol), $\nu_{max.}$ (CS_2) 773, 760, and 738 cm.$^{-1}$, unsaturated to tetranitromethane (Found: C, 76·1; H, 11·2. Calc. for $C_{27}H_{46}Cl_2$; C, 73·5; H, 10·4%. Calc. for $C_{27}H_{45}Cl$; C, 80·2; H, 11·1%). Trial thin-layer chromatography on silica gel in pentane disclosed cholesteryl chloride, R_F 0·55, as the minor product and 3β,6α-dichloro-5α-cholestane, R_F 0·32, as the major product. An ethereal solution of the mixture (28 mg.) was applied to silica gel plates (layer thickness, 3—4 mm., width, 10 cm.), the solvent allowed completely to evaporate, and the chromatogram run in pentane to yield two bands, at 3—6 and 7—10 cm. from the baseline. The first band, by extraction with ether, gave 3β,6α-dichloro-5α-cholestane (9 mg.), m. p. 117° (after softening), which was homogeneous on further thin-layer chromatography. The second band yielded an oil (7 mg.) giving two spots on thin-layer chromatography.

(*b*) 3β-Chloro-5α-cholestan-6α-ol (150 mg.) by treatment with phosphorus pentachloride (100 mg.; freshly sublimed) in benzene (20 ml.) at 80° for 1 hr. gave a mixture of cholesteryl chloride and 3β,6α-dichloro-5α-cholestane, showing the same infrared absorption and R_F values as preparation (*a*). Chromatography on silica gel (10 g.) in hexane, and elution with hexane gave cholesteryl chloride, m. p. and mixed m. p. 97°, $\nu_{max.}$ (CS_2) 760 cm.$^{-1}$; further elution with hexane gave 3β,6α-*dichloro*-5α-*cholestane*, m. p. 113—115° (from acetone–methanol), $\nu_{max.}$ (CS_2) 773, 758, 737 cm.$^{-1}$ (Found: C, 73·3; H, 10·4. $C_{27}H_{46}Cl_2$ requires C, 73·45; H, 10·4%).

Chlorination of 5α-*Cholestane*-3β,6α-*diol*.—The 3β,6α-diol (100 mg.; dried azeotropically with benzene) was heated with phosphorus pentachloride (52 mg.; 1 equiv.) in benzene (10 ml.) at 80° for 1 hr. The product was chromatographed on alumina (3 g.) in pentane. Elution with pentane gave 3α,6β-dichloro-5α-cholestane, m. p. 128°, $\nu_{max.}$ 714 cm.$^{-1}$, whilst further elution with methanol–chloroform (1 : 20) gave unchanged 5α-cholestane-3β,6α-diol (41 mg.).

3,3-*Ethylenedioxy*-5α-*cholestan*-6-*one*.—5α-Cholestane-3,6-dione (6·5 g.), dissolved in benzene (300 ml.) was heated with ethylene glycol (1 ml.) and toluene-*p*-sulphonic acid (170 mg.) in a Dean–Stark water separator at 80° for 8 hr. The product, isolated in the usual way, was chromatographed on alumina (180 g.) in hexane. Elution with benzene–hexane (1 : 1; 3 × 180 ml.) gave an oil (580 mg.), probably a mixture of the 3,3:6,6-bisketal and the 3,3-ketal. Further elution with benzene–hexane (1 : 1, 15 × 180 ml.) gave 3,3-ethylenedioxy-5α-cholestan-6-one (3·0 g.), m. p. 124—126° (from methanol), $\nu_{max.}$ 1714 cm.$^{-1}$, optical rotatory dispersion in dioxan: [ϕ] 1870° (266 mμ, peak), −1000° (315 mμ, trough), 0° (589 mμ, 600 mμ) (Found: C, 78·5; H, 10·6. $C_{29}H_{48}O_3$ requires C, 78·2; H, 10·9%). Further elution with benzene gave unchanged 5α-cholestane-3,6-dione (2·1 g.).

6α-*Acetoxy*-5α-*cholestan*-3-*one*.—3,3-Ethylenedioxy-5α-cholestan-6-one (2·9 g.) was dissolved in boiling ethanol, and the solution saturated with sodium. The usual working up gave an oil, which was dissolved in acetone and treated with toluene-*p*-sulphonic acid (500 mg.) at 55° for 0·5 hr. The solid product (2·8 g.), isolated in the normal manner, was chromatographed on alumina (78 g.) in hexane. Elution with ether–benzene (1 : 1; 8 × 100 ml.) furnished crude 6α-hydroxy-5α-cholestan-3-one, m. p. 160° (after softening from 145°). Acetylation with boiling acetic anhydride (10 ml.) for 15 min., isolation of the product, chromatography thereof on alumina (90 g.) in hexane, and elution with benzene gave the *acetate* (1·4 g.), m. p. 133—134° (from methanol), $[\alpha]_D$ +63° (*c* 1·0), $\nu_{max.}$ 1720, 1695, and 1263 cm.$^{-1}$ (Found: C, 78·4; H, 11·0. $C_{29}H_{48}O_3$ requires C, 78·4; H, 10·8%).

6α-*Acetoxy*-5α-*cholestan*-3β-*ol*.—6α-Acetoxy-5α-cholestan-3-one (1·25 g.) in methanol (40 ml.)

was treated with a solution of sodium borohydride (400 mg.) in methanol (50 ml.) at 20° for 1 hr. The usual isolation procedure gave an oil (1·2 g.), which was chromatographed on alumina (40 g.) in benzene. Elution with ether yielded the *ester* (0·84 g.), m. p. 90—95° (from methanol), $[\alpha]_D$ +35° (*c* 1·0), $\nu_{max.}$ 1726, 1263 cm.$^{-1}$ (Found: C, 77·7; H, 11·35. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%).

Chlorination of 3α-*Chloro*-5α-*cholestan*-6α-*ol*.—The cholestanol (840 mg.) was refluxed with phosphorus pentachloride (1 g.; freshly sublimed) in benzene (100 ml.) for 1 hr. The usual isolation procedure yielded 3α-chloro-5α-cholestan-6α-yl acetate (850 mg.), $\nu_{max.}$ (CS_2) 720 cm.$^{-1}$, as an oil which was hydrolysed with methanolic 0·5N-potassium hydroxide (40 ml.) under reflux for 1 hr. The product (570 mg.), isolated in the usual fashion, was chromatographed on alumina (30 g.) in hexane. Elution with ether–benzene (1 : 3; 17 × 30 ml.) gave 3α-chloro-5α-cholestan-6α-ol (275 mg.), $\nu_{max.}$ (CS_2) 720 cm.$^{-1}$, as an oil, which could not be induced to crystallise because of contamination with unsaturated material [5α-cholest-2-en-6α-ol(?)] giving a yellow colour with tetranitromethane. Thin-layer chromatography on silica gel in ether–pentane (1 : 3) disclosed the presence of two compounds, with R_F 0·47 and 0·56.

3α-Chloro-5α-cholestan-6α-ol (270 mg.) was refluxed with phosphorus pentachloride (300 mg.; freshly sublimed) in benzene (40 ml.) for 1 hr. The normal working up gave an oil (200 mg.) which was chromatographed on alumina (9 g.) in pentane. Elution with pentane (10 × 10 ml.) gave an oil (190 mg.), $\nu_{max.}$ (CS_2), 714 cm.$^{-1}$, whose infrared spectrum was identical with that of an authentic specimen of 3α,6β-dichloro-5α-cholestane, but which could not be induced to crystallise. The presence of unsaturated material, indicated by a yellow colour with tetranitromethane, was confirmed by thin-layer chromatography on alumina in pentane, which showed a strong spot, R_F 0·57, and a weak spot, R_F 0·67; this was removed as follows. Crude 3α,6β-dichloro-5α-cholestane (103 mg.) in chloroform (5 ml.) was treated with a chloroform solution of perbenzoic acid (1 ml.; 0·025 g./ml.) at 20° for 2 days. The usual working up gave an oil (100 mg.); chromatography on alumina (3 g.) in pentane, and elution with pentane (4 × 3 ml.) gave 3α,6β-dichloro-5α-cholestane (17 mg.), m. p. and mixed m. p. 128—130° (from acetone), $\nu_{max.}$ (CS_2) 714 cm.$^{-1}$, giving no colour with tetranitromethane and a single spot, R_F 0·57, on a thin-layer chromatogram on alumina in pentane (Found: C, 73·0; H, 10·7. Calc. for $C_{27}H_{46}Cl_2$: C, 73·4; H, 10·4%).

6α-*Acetoxy*-5α-*cholestan*-3α-*ol*.—6α-Acetoxy-5α-cholestan-3-one (3·1 g.) was hydrogenated with platinum oxide (430 mg.) in di-n-butyl ether (100 ml.) containing 48% hydrobromic acid (0·5 ml.) at 60—70° until absorption ceased. Filtration from the catalyst and complete evaporation of the filtrate at 100°/0·2 mm. gave a product, shown by trial thin-layer chromatography to consist mainly of the 3α-ol accompanied by some 3β-ol. The epimers were separated by chromatography on alumina (90 g.) in hexane. Elution with ether–benzene (3 : 7) gave 6α-*acetoxy*-5α-*cholestan*-3α-*ol* (1·75 g.), m. p. 117—120° (from methanol) (Found: C, 77·6; H, 11·1. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%). The 3α,6α-diacetate was obtained, by use of acetic anhydride–pyridine at 20° overnight and purification by chromatography on silica gel (140 g.) in hexane and elution with benzene, as an oil (1·57 g.) which could not be induced to crystallise.

3α-*Acetoxy*-5α-*cholestan*-6α-*ol*.—3α,6α-Diacetoxy-5α-cholestane (1·57 g.), dissolved in ethanol (125 ml.) was treated with a solution of potassium hydroxide (0·18 g.; 1 mol.) in ethanol (50 ml.) added dropwise with stirring at 20° during 3 days. After removal of ethanol at 40°/10 mm., the usual working up gave a product which was chromatographed on alumina (50 g.) in hexane. Elution with ether–benzene (1 : 4) at first gave 6α-acetoxy-5α-cholestan-3α-ol (0·1 g.), followed by mixtures of 6α-acetoxy-5α-cholestan-3α-ol and 3α-acetoxy-5α-cholestan-6α-ol (0·24 g.), and finally by 3α-*acetoxy*-5α-*cholestan*-6α-*ol* (0·32 g.), m. p. 87—90° (from methanol) (Found: C, 77·7; H, 11·1. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%). Elution with chloroform gave 5α-cholestane-3α,6α-diol (0·32 g.), m. p. 219—222° (from methanol) (Found: C, 80·4; H, 12·3. Calc. for $C_{27}H_{48}O_2$: C, 80·15; H, 12·0%).

Chlorination of 3α-*Acetoxy*-5α-*cholestan*-6α-*ol*.—3α-Acetoxy-5α-cholestan-6α-ol (100 mg.) dissolved in benzene (20 ml.) was heated with phosphorus pentachloride (100 mg.; freshly sublimed) under reflux for 1 hr. The usual isolation procedure gave material, which was chromatographed on silica gel (10 g.) in hexane. Elution with benzene–hexane (1 : 1) gave 3α-*acetoxy*-6α-*chloro*-5α-*cholestane* (48 mg.) m. p. 125—131° (from methanol–acetone), $\nu_{max.}$ 1736 (OAc), 768, and 737 cm.$^{-1}$, affording a single spot on thin-layer chromatography on silica gel (Found: C, 74·3; H, 10·6. $C_{29}H_{49}ClO_2$ requires C, 74·2; H, 10·45%).

Chlorination of 5α-*Cholestane*-3α,6α-*diol*.—The diol (105 mg.) in benzene (30 ml.) was heated under reflux with phosphorus pentachloride (210 mg.; freshly sublimed) for 1 hr. The usual isolation procedure gave an oil, which furnished six spots on thin-layer chromatography on silica gel. Two spots had, respectively, the same R_F values as cholesteryl chloride and 3β,6α-dichloro-5α-cholestane; the mixture could not be separated by column chromatography.

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Department of Organic Chemistry,
The University of Sydney, Australia. [*Received, March 25th,* 1964.]