431. *Steroids and Walden Inversion. Part LIV.* The Grignard Oxygenation of Epicholesteryl Bromide and Partial Synthesis of 3α-Hydroxycholest-6-ene*

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Grignard oxygenation of a sample of epicholesteryl bromide furnished alcohols derived from epicholesteryl bromide and also from 3α-bromo-5α-cholest-6-ene. The partial synthesis of 3α-hydroxy-5α-cholest-6-ene is described. A re-investigation of the methods of preparation of epicholesteryl chloride and bromide has been made.

An exploratory examination, made in 1953 by Dr. R. J. Stephenson, of the Grignard carboxylation of a reputedly pure specimen of epicholesteryl bromide yielded an acid, which differed from cholest-5-ene-3α- and -3β-carboxylic acid.[1] As appears from the sequel, this acid [m. p. 200°, $[\alpha]_D$ −44°, methyl ester, m. p. 82°, $[\alpha]_D$ −42°] is probably 5α-cholest-6-ene-3α-carboxylic acid. It seemed that investigation of Grignard oxygenation[2] of epicholesteryl bromide should precede re-examination of the carboxylation reaction because numerous sterols are available as reference compounds, whereas few steroid nuclear carboxylic acids are known. In a preliminary investigation, made in 1953 by Dr. R. J. Stephenson, the Grignard oxygenation of epicholesteryl bromide[3] appeared to yield neither cholesterol nor epicholesterol but two other unsaturated alcohols, m. p 156—158°, $[\alpha]_D$ −59°, and m. p. 126—132°, $[\alpha]_D$ −53°.

The original small-scale preparation of chromatographically purified epicholesteryl bromide (I) from 3α-bromo-5α-cholestan-6β-ol (II) had m. p. 103—105°, $[\alpha]_D$ −5°;[3] larger-scale dehydrations of the noncrystalline 3α-bromo-5α-cholestan-6β-ol (II) with phosphorus oxychloride–pyridine at 0—15° gave a product, m. p. 104° after purification by crystallisation, which was regarded as pure epicholesteryl bromide, and was used for Grignard oxygenation. The material was not chromatographically purified, and only subsequently was its specific rotation found to be −40°; as the results of its Grignard oxygenation indicate, the preparation consisted of a mixture of epicholesteryl bromide (I) and 3α-bromo-5α-cholest-6-ene (III).

Grignard oxygenation furnished a complex mixture of unsaturated alcohols only partially resolved by absorption chromatography into two main fractions. One main

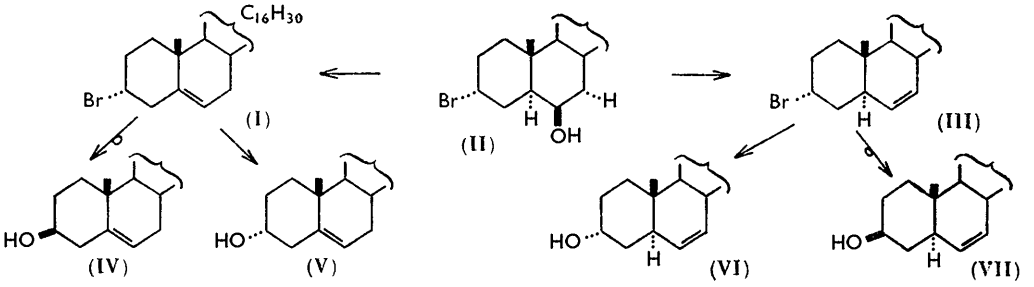
* Part LIII, C. W. Shoppee, R. E. Lack, and B. McLean, *J.*, 1964, 4996.

[1] C. W. Shoppee, *Chem. and Ind.*, 1954, 759; cf. G. Roberts, C. W. Shoppee, and R. J. Stephenson, *J.*, 1954, 2705.

[2] G. Roberts and C. W. Shoppee, *J.*, 1954, 3418.

[3] C. W. Shoppee and G. H. R. Summers, *J.*, 1952, 1790.

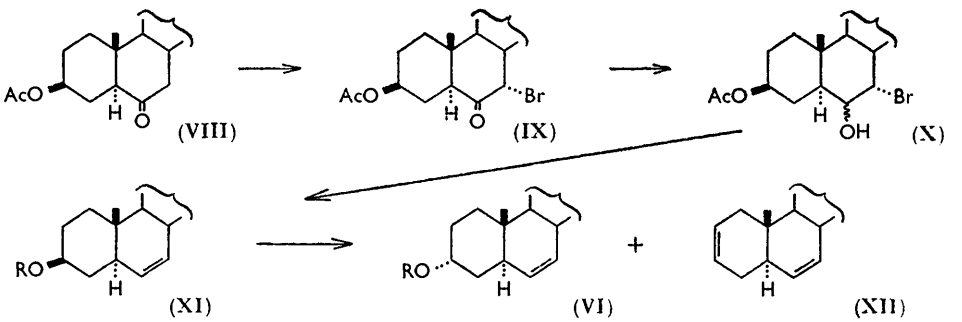
fraction, m. p. 160°, $[\alpha]_D$ −64°, −68°, consisted of a mixture of cholesterol (IV) and 5α-cholest-6-en-3α-ol (VI), m. p. 162°, $[\alpha]_D$ −88°, which by hydrogenation gave 5α-cholestan-3α-ol and by oxidation 5α-cholest-6-en-3-one, but which could not be separated by column chromatography.



The other main fraction, m. p. 144°, $[\alpha]_D$ −64°, gave no depression with cholesterol, m. p. 148°, $[\alpha]_D$ −39°, whilst the derived acetate, m. p. 110°, $[\alpha]_D$ −61° after further chromatography, gave no depression with cholesteryl acetate, m. p. 113°, $[\alpha]_D$ −43°; this fraction thus contained cholesterol (IV), isolated by conversion into the dibromide and debromination of the purified dibromide, and characterised by oxidation to cholest-4-en-3-one and by hydrogenation to 5α-cholestan-3β-ol, accompanied by a more lævorotatory companion, which we believe to be 5α-cholest-6-en-3β-ol (VII), m. p. 124°, $[\alpha]_D$ −88°,[4-6] but which we were unable to isolate.

A partial separation of the Grignard oxygenation product was achieved by use of digitonin, which removed the 3β-hydroxy-steroids (IV, VII) as insoluble digitonides and afforded, after column chromatography, 5α-cholest-6-en-3α-ol (VI), m. p. 160°, $[\alpha]_D$ −85°. This was characterised by Oppenauer oxidation to 5α-cholest-6-en-3-one,[4] by hydrogenation of the acetate to 5α-cholestan-3α-yl acetate, and by direct comparison with a synthetic specimen. Epicholesterol (V) could not be isolated.

A partial synthesis of 5α-cholest-6-en-3α-ol (VI) was carried out as follows. 6-Oxo-5α-cholestan-3β-yl acetate (VIII) was converted into the 7α-bromo-derivative (IX),[7,8] which was reduced with sodium borohydride[6] to a mixture of the epimeric 7α-bromo-6α-hydrin and the 7α-bromo-6β-hydrin represented by (X); treatment with zinc–acetic



acid gave 5α-cholest-6-en-3β-yl acetate (XI; R = Ac),[7] hydrolysed by potassium hydroxide or by use of lithium aluminium hydride to 5α-cholest-6-en-3β-ol (XI; R = H).[4-6] Conversion into the toluene-*p*-sulphonate (XI; R = Ts), and acetolysis afforded

[4] D. H. R. Barton and W. J. Ronsenfelder, *J.*, 1949, 2459.
[5] O. Wintersteiner and M. Moore, *J. Amer. Chem. Soc.* 1950, **72**, 1923.
[6] D. R. James, R. W. Rees, and C. W. Shoppee, *J.*, 1955, 1370.
[7] I. M. Heilbron, E. R. H. Jones, and F. S. Spring, *J.*, 1937, 801.
[8] D. R. James and C. W. Shoppee, *J.*, 1954, 4224.

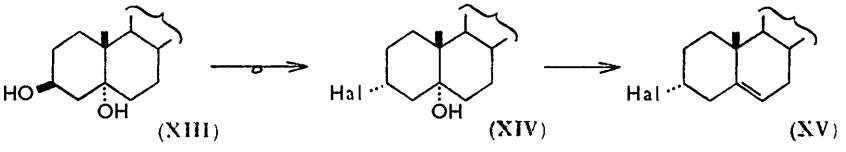
5α-cholesta-2,6-diene (XII) [4] and 3α-acetoxy-5α-cholest-6-ene (VI; R = Ac), hydrolysed by treatment with lithium hydride to 5α-cholest-6-en-3α-ol (VI; R = H)

The properties of the Grignard oxygenation product and the synthetic material, and of their oxidation and reduction products, are shown in the Table.

	Cholest-6-en-3α-ol	3α-Acetoxy-cholest-6-ene	Cholest-6-en-3-one	3α-Acetoxy-cholestane	Cholestan-3α-ol
Oxygenation product	m. p. 160° $[\alpha]_D$ −75°	m. p. 94—96° $[\alpha]_D$ −51°	m. p. 118° $[\alpha]_D$ −70°	m. p. 92—94° $[\alpha]_D$ +30°	m. p. 185—187° $[\alpha]_D$ +29°
Synthetic material	m. p. 162° $[\alpha]_D$ −88°	m. p. 98° $[\alpha]_D$ −56°	m. p. 116—117° $[\alpha]_D$ −76°	m. p. 94—96° $[\alpha]_D$ +33°	m. p. 182—185° $[\alpha]_D$ +30°

We reported recently [9] that as judged by the specific rotation pure specimens of epicholesteryl chloride, m. p. 107°, $[\alpha]_D$ −3°, were difficult to obtain on a large scale by dehydration of 3α-chloro-5α-cholestan-6β-ol.[3] Thus Eckert and Le Fèvre [10] obtained material, m. p. 107—108°, $[\alpha]_D$ −42°, and McLean [11] obtained preparations, m. p. 106°, $[\alpha]_D$ −50°, one of which was shown by thin-layer chromatography on silica gel to contain a small amount of a second chloro-compound, believed by analogy to be 3α-chloro-5α-cholest-6-ene. In a re-investigation, dehydration of 3α-chloro-5α-cholestan-6β-ol with phosphoryl chloride–pyridine at 20° yielded a product, m. p. 107°, $[\alpha]_D$ −50°, giving three spots (R_F, 0·47, 0·56, and 0·65) in a thin-layer chromatogram on silica gel in hexane; separation of the three components on a silica gel column was not attempted because of the proximity of the R_F values. We have observed that treatment of 5α-stan-6β-ols with thionyl chloride frequently leads not to substitution, but causes dehydration to give unsaturated hydrocarbons.[12] When 3α-chloro-5α-cholestan-6β-ol was dissolved in thionyl chloride and the solution stirred at 20° for 0·5 hr., the reaction product gave two spots (R_F 0·46 and 0·65) by thin-layer chromatography on silica gel in hexane. The compound with R_F 0·65 was identified as cholesta-3,5-diene; this was readily separated by column chromatography on silica gel in hexane to give pure homogeneous epicholesteryl chloride, m. p. 114—117°, $[\alpha]_D$ −45°, R_F 0·46.

The other published route [13] to epicholesteryl chloride by conversion of 5α-cholestane-3β,5-diol (XIII) with phosphoryl chloride–pyridine at 10—15° into 3α-chloro-5α-cholestan-5-ol (XIV; Hal = Cl), and dehydration of this by brief treatment with thionyl chloride–pyridine has been re-examined. The 3α-chloro-5α-ol (XIV; Hal = Cl) so prepared was shown by thin-layer chromatography on silica gel in hexane to be contaminated with cholesta-3,5-diene (R_F values, 0·08 and 0·65), which was removed by column chromatography on silica gel in hexane. The purified 3α-chloro-5α-ol (XIV; Hal = Cl), m. p. 124°, by brief dehydration with thionyl chloride–pyridine at 0—20° gave by chromatography on a column of silica gel in hexane cholesta-3,5-diene and pure homogeneous epicholesteryl (XV; Hal = Cl), m. p. 116°, $[\alpha]_D$ −46°.



(XIII) (XIV) (XV)

The preparation of epicholesteryl bromide has also been re-investigated. 3β-Hydroxy-5α-cholestan-6-one by treatment with phosphoryl bromide–pyridine at 40—50° gave 3α-bromo-5α-cholestan-6-one,[3] reduced by lithium aluminium hydride in ether to 3α-bromo-5α-cholestan-6β-ol [3] (II), which could not be induced to crystallise. Dehydration of (II)

[9] C. W. Shoppee, R. E. Lack, and B. McLean, *J.*, 1964, 4996.
[10] J. M. Eckert and R. J. W. Le Fèvre, *J.*, 1962, 1081.
[11] B. McLean, M.Sc. Thesis, Sydney, 1962.
[12] C. W. Shoppee, M. E. H. Howden, and R. E. Lack, *J.*, 1960, 4874.
[13] A. J. Fudge, C. W. Shoppee, and G. H. R. Summers, *J.*, 1954, 958.

with phosphoryl chloride–pyridine at 0—20° gave by column chromatography on silica in hexane, with control of each fraction by thin-layer chromatography, cholesta-3,5-diene, pure homogeneous epicholesteryl bromide (I), m. p. 112—115°, $[\alpha]_D$ −37°, and 3α-bromo-5α-cholest-6-ene (III), m. p. 70—71°, $[\alpha]_D$ −52°, the n.m.r. spectrum of which confirmed this structure, showing a signal for the 10-methyl group at τ 9·26 (cf. 5α-cholestane, τ 9·24, but cholest-5-ene, τ 9·00), a signal for the two vinylic protons 6H, 7H as a multiplet centred at τ 4·63, and a signal for the one equatorial proton 3β-H at τ 5·25.

Treatment of 5α-cholestane-3β,5-diol (XIII) with phosphoryl bromide at 0—20° gave cholesta-3,5-diene and cholesteryl bromide; this result indicates that dehydration of the tertiary hydroxyl group here precedes substitution of the secondary hydroxyl group, which then occurs with retention of configuration. At −60 to 0°, the product consisted mainly of an ether-insoluble phosphate accompanied by a small amount of ether-soluble material, giving three spots on thin-layer chromatography corresponding to cholesta-3,5-diene, and possibly epicholesteryl bromide and cholesteryl bromide.

Experimental

For general directions see *J.*, 1959, 345. $[\alpha]_D$ refer to $CHCl_3$ solutions at 20°. Ultraviolet absorption spectra were determined in EtOH on a Unicam S.P. 500 spectrophotometer with corrected scale, or on a Perkin-Elmer 4000 Å spectrophotometer. Infrared spectra in CCl_4 were measured with a Perkin-Elmer 221 spectrophotometer, whilst n.m.r. spectra were obtained in $CDCl_3$ solutions using a 60 Mc. Varian A60 spectrometer with tetramethylsilane as internal reference. Spence type H alumina or Davison silica gel was used for chromatography.

Grignard Oxygenation of Reputed Epicholesteryl Bromide.—3α-Bromo-5α-cholestan-6-one (m. p. 174—176°) was reduced with lithium aluminium hydride in ether at 0°,[3] or with sodium borohydride in methanol at 15°, to the non-crystalline 3α-bromo-5α-cholestan-6β-ol, which was dehydrated with phosphoryl chloride-pyridine at 0° and 15°; [3] the product, dissolved in pentane, was filtered through alumina, the filtrate evaporated, and the resulting solid crystallised from acetone to give epicholesteryl bromide (contaminated with 3α-bromo-5α-cholest-6-ene), m. p. 104—106°, $[\alpha]_D$ −40° (*c* 2·0).

(*a*) This material (550 mg.) was refluxed in ether with magnesium (50 mg.) and methylmagnesium iodide [prepared from magnesium (125 mg.) and methyl iodide (0·25 ml.)] for 20 hr. Oxygen was then passed through the warm ethereal solution for 0·5 hr., and ice-cold 2N-sulphuric acid added: the product, isolated in the usual way, was chromatographed on alumina (10 g.) in pentane. Elution with pentane gave hydrocarbon(s) (170 mg.), probably cholesta-3,5-diene; use of benzene–pentane (2 : 8 and 3 : 7) yielded only traces of oil. Elution with benzene–pentane (4 : 6) gave a solid (140 mg.), yielding impure 5α-cholest-6-en-3α-ol, m. p. 160°, $[\alpha]_D$ −64° (*c* 1·4) by repeated crystallisation from acetone. Benzene–pentane (1 : 1) furnished negligible amounts of material; use of benzene afforded cholesterol, contaminated with a more lævorotatory compound (which could not be separated by crystallisation), m. p. 144°, $[\alpha]_D$ −64° (*c* 1·3), after crystallisation from methanol, giving a yellow colour with tetranitromethane and no m. p. depression with cholesterol, m. p. 148°, $[\alpha]_D$ −39°, and yielding by acetylation, chromatography on alumina, and crystallisation from acetone, impure cholesteryl acetate, m. p. 108—110°, $[\alpha]_D$ −61° (*c* 0·6), which gave no depression with cholesteryl acetate, m. p. 113°, and by Oppenauer oxidation gave cholest-4-en-3-one, m. p. 81°, $[\alpha]_D$ +91°, $\lambda_{max.}$ 241, log ε 4·2. The above impure 5α-cholest-6-en-3α-ol (50 mg.) by hydrogenation with platinum oxide-acetic acid gave 5α-cholestan-3α-ol, m. p. and mixed m. p. 184°, $[\alpha]_D$ +21° (*c* 0·6); similar hydrogenation of the above contaminated cholesterol gave 5α-cholestan-3β-ol, m. p. and mixed m. p. 142°, $[\alpha]_D$ +22° (*c* 0·8), characterised as the acetate, m. p. and mixed m. p. 110—111°.

(*b*) In a similar experiment the reputed epicholesteryl bromide (1·5 g.) gave impure 5α-cholest-6-en-3α-ol (230 mg.), m. p. 161°, $[\alpha]_D$ −68° (*c* 1·8); from acetone, m. p. 160°, $[\alpha]_D$ −69° (*c* 2·7), after further crystallisation from acetone, and impure cholesterol (230 mg.), m. p. 136—140°, from acetone; m. p. 137—140°, $[\alpha]_D$ −60° (*c* 2·7) after recrystallisation from ether–methanol. A portion of the latter was treated with bromine in ether, and gave cholesterol dibromide, m. p. 120°, $[\alpha]_D$ −39° (*c* 1·45) from ether–methanol, which by debromination with zinc–acetic acid furnished cholesterol, m. p. and mixed m. p. 146—148°, $[\alpha]_D$ −41° (*c* 1·2).

(*c*) In another experiment using the reputed epicholesteryl bromide (2 g.), the oxygenation

product was introduced on to alumina in pentane, and the column eluted with pentane until free from hydrocarbon(s). The mixed alcohols, eluted from the column with ether and dissolved in warm ethanol (50 ml.), were treated with a solution of digitonin (3 g.) in warm ethanol; water (15 ml.) was added, and, after the mixture had been kept for 1 hr., the precipitate was filtered off, and washed with 96% ethanol, and with ether. The filtrate was evaporated in a vacuum, the solid residue repeatedly extracted with ether, and the combined extracts evaporated. The resulting 3α-ols were chromatographed on alumina in pentane; elution with benzene–pentane (1 : 1) gave eleven fractions, m. p. 150—160°, which were united (262 mg.) and by repeated crystallisation from acetone afforded 5α-cholest-6-en-3α-ol, m. p. and mixed m. p. 160°, $[\alpha]_D$ −75° (*c* 1·2). This was characterised (i) by oxidation with aluminium isopropoxide–acetone in refluxing benzene to give, after chromatography on alumina in pentane and elution with benzene–pentane (1 : 4), 5α-cholest-6-en-3-one, m. p. 118°, $[\alpha]_D$ −70° (*c* 0·6) [lit.,[4] m. p. 116—117°, $[\alpha]_D$ −76°, −80°], and (ii) by acetylation with acetic anhydride–pyridine at 20° for 16 hr. as the acetate, m. p. and mixed m. p. 98°, $[\alpha]_D$ −51° (*c* 0·9), which was rapidly hydrogenated with platinum oxide in ethyl acetate containing a trace of 60% perchloric acid to yield, after crystallisation from ethanol, 5α-cholestan-3α-yl acetate, m. p. and mixed m. p. 92–94°, $[\alpha]_D$ +30° (*c* 1·6), hydrolysed by treatment with lithium aluminium hydride in ether to 5α-cholestan-3α-ol, m. p. and mixed m. p. 185°, $[\alpha]_D$ +20° (*c* 0·4), from acetone.

Partial Synthesis of 5α-Cholest-6-en-3α-ol.—7α-Bromo-6-oxo-5α-cholestan-3β-yl acetate [7,8] (m. p. 145—147°) was reduced with sodium borohydride in methanol to a mixture of the 7α,6α- and 7α,6β-bromohydrins,[6] converted by zinc–acetic acid into 3β-acetoxy-5α-cholest-6-ene, m. p. 107° (lit.,[6] 108°), which was hydrolysed with hot methanolic potassium hydroxide, or by treatment with lithium aluminium hydride, to 5α-cholest-6-en-3β-ol, m. p. 124° (lit.,[6] 124—126°). This alcohol (200 mg.) in pyridine (10 ml.) was treated with toluene-*p*-sulphonyl chloride (400 mg.) at 39° for 16 hr.; the reaction mixture was diluted with ether, poured into ice-cold 2N-hydrochloric acid, and the ethereal extract worked up in the usual way to give 3β-*toluene*-p-*sulphonoxycholest*-6-*ene*, m. p. 142°, $[\alpha]_D$ −87° (*c* 1·0) after crystallisation from acetone [Found (after drying at 60°/0·02 mm. for 2 hr.): C, 75·25; H, 9·6. $C_{34}H_{52}O_3S$ requires C, 75·5; H, 9·6%]. The toluene-*p*-sulphonate (250 mg.) was heated with freshly fused potassium acetate (2 g.) in acetic acid (13 ml.) at 100° for 3 hr., and the product, isolated in the usual way, hydrolysed by treatment with lithium aluminium hydride in ether. The resulting material was chromatographed on alumina (7·5 g.) in pentane; elution with pentane gave cholesta-2,6-diene, m. p. 72°, $[\alpha]_D$ 0° (lit.,[4] m. p. 72°, $[\alpha]_D$ 0°), after recrystallisation from acetone, whilst elution with ether gave *cholest*-6-*en*-3α-*ol*, m. p. 162°, $[\alpha]_D$ −88°, −86° (*c* 0·8, 0·95) [Found (after drying at 60°/0·02 mm. for 2 hr.): C, 83·8; H, 12·1. $C_{27}H_{46}O$ requires C, 83·9; H, 12·0%]. The *acetate*, prepared by use of acetic anhydride–pyridine at 15°, had m. p. 98°, $[\alpha]_D$ −56° (*c* 1·0) after recrystallisation from ether–methanol [Found (after drying at 40°/0·02 mm. for 2 hr.): C, 81·1; H, 11·4. $C_{29}H_{48}O_2$ requires C, 81·2; H, 11·3%].

3α-*Chlorocholest*-5-*ene.*—(*a*) 3α-Chloro-5α-cholestan-6β-ol [3] (double m. p. 95°/106—111°; 640 mg.), dissolved in pyridine (6·4 ml.), was treated dropwise with phosphoryl chloride (0·77 ml.) at 0—5° and the mixture left overnight at 20°. The usual working up gave a colourless crystalline product (230 mg.), m. p. 92—105°, from acetone; recrystallisation from acetone gave material, m. p. 98—107°, $[\alpha]_D$ −42° (*c* 1·0), giving three spots by thin-layer chromatography on silica in hexane, and consisting of a mixture of cholesta-3,5-diene (R_F 0·65), 3α-chloro-5α-cholest-6-ene (R_F 0·56), and 3α-chlorocholest-5-ene (R_F 0·47).

(*b*) 3α-Chloro-5α-cholestan-6β-ol (500 mg.) was dissolved in thionyl chloride (2·5 ml.) kept at 20°, and the solution stirred at 20° for 0·5 hr. The product, isolated in the usual way, was dissolved in hexane and filtered through a column of silica; the filtrate by evaporation in a vacuum gave an oil, showing two spots (R_F 0·46, 0·65) by thin-layer chromatography on silica in hexane. The spot R_F 0·65 was identified with cholesta-3,5-diene. The oil was chromatographed on a column of silica (50 g.) in hexane, and the column eluted with hexane (5 ml. eluates); each fraction was examined by thin-layer chromatography on silica in hexane. Combination of those fractions giving a single spot (R_F 0·46) gave 3α-chlorocholest-5-ene (43 mg.), m. p. 114—117°, $[\alpha]_D$ −45° (*c* 1·0), R_F 0·46 [Found (after drying at 20°/0·5 mm. for 24 hr.): C, 79·6; H, 11·2. Calc. for $C_{27}H_{45}Cl$: C, 79·5; H, 11·2%].

(*c*) Cholesterol was converted by treatment with *m*-chloroperbenzoic acid into 5,6α-epoxy-5α-cholestan-3β-ol, m. p. 137—140°, which by reduction with lithium aluminium hydride in ether gave 5α-cholestane-3β,5-diol, m. p. 224° from ethanol, R_F 0·03 on silica in ether–hexane

(1 : 1), after chromatographic purification on a column of silica and elution with methanol following prior removal of cholesterol (R_F 0·37) by elution with ether–hexane mixtures. The 3β,5α-diol by treatment with phosphoryl chloride–pyridine [13] yielded a product, m. p. 114—116°, contaminated with cholesta-3,5-diene and giving two spots (R_F 0·12, 0·68) by thin-layer chromatography on silica in hexane. Column chromatography on silica by elution with ether–hexane (1 : 19) gave 3α-chloro-5α-cholestan-5-ol, m. p. 120° from ether–methanol (lit.,[13] m. p. 118—119°). The chloro-alcohol (200 mg.), dissolved in pyridine (5 ml.) was treated with thionyl chloride (1 ml.) at 0°; after 10 min. at 15°, the mixture was poured on to ice and worked up in the usual way. The resultant oil slowly crystallised but gave two spots (R_F 0·52, 0·72) by thin-layer chromatography on silica in hexane; the mixture was chromatographed on a column of silica in hexane, and each hexane (5 ml.) eluate examined by thin-layer chromatography. Cholesta-3,5-diene (90 mg.), m. p. 79—80°, was eluted first, followed by 3α-chlorocholest-5-ene (40 mg.), m. p. and mixed m. p. 114—116°, $[\alpha]_D$ −46° (*c* 1·0) from acetone [Found (after drying at 20°/0·5 mm. for 24 hr.): C, 80·1; H, 11·3. Calc. for $C_{27}H_{45}Cl$: C, 79·5; H, 11·2%).

3α-Bromo-5α-cholestan-6-one.—3β-Hydroxy-5α-cholestan-6-one,[14] by treatment with phosphoryl bromide in pyridine at 40—50° for 1 hr. and at 20° for 2 hr., after the usual isolation procedure and column chromatography on silica in hexane gave: (i) by elution with ether–hexane (1 : 9), 5α-cholest-2-en-6-one, m. p. 107°, from acetone, $\lambda_{max.}$ 284 mμ, log ε 1·67, $\nu_{max.}$ 1710 cm.$^{-1}$ (lit.,[3,15–17] m. p. 104—106°, $\lambda_{max.}$ 285 mμ, log ε 1·7) [Found: C, 84·1; H, 11·6. Calc. for $C_{27}H_{44}O$: C, 84·3; H, 11·5%]; (ii) by elution with ether–hexane (2 : 8), 3α-bromo-5α-cholestan-6-one, m. p. 176°, from acetone, $\nu_{max.}$ 1710, 700 cm.$^{-1}$ (lit.,[3] m. p. 173°); and (iii) by elution with ether–hexane (1 : 1), unchanged 3β-hydroxy-5α-cholestan-6-one, m. p. and mixed m. p. 148° (lit.,[14] m. p. 148–149°).

3α-Bromocholest-5-ene and 3α-Bromo-5α-cholest-6-ene.—3α-Bromo-5α-cholestan-6-one (600 mg.) was reduced with excess of lithium aluminium hydride (1·8 g.) in ether at 0° for 0·5 hr. The usual working up gave 3α-bromo-5α-cholestan-6β-ol (500 mg.). The colourless oil, dissolved in pyridine (10 ml.) at 0°, was treated dropwise with phosphoryl chloride (1 ml.) and left at 20° overnight. The product (470 mg.), obtained by the usual working up, gave by thin-layer chromatography on silica in hexane, three spots, R_F 0·72, 0·64, and 0·55. Column chromatography on silica (100 g.) in hexane and elution with hexane [with control of each fraction (30 × 5 ml.) by thin-layer chromatography] gave: (i) cholesta-3,5-diene (110 mg., R_F 0·72), m. p. 79—80°, $\lambda_{max.}$ 234 mμ; (ii) 3α-bromo-5α-cholest-6-ene (20 mg., R_F 0·69); (iii) 3α-bromocholest-5-ene (60 mg., R_F 0·55); and (iv) a mixture (155 mg., R_F 0·64, 0·52). Similar column chromatography of the mixture (vi) gave cholesta-3,5-diene (30 mg.) formed by elimination of hydrogen bromide on the column, 3α-bromo-5α-cholest-6-ene (93 mg.), and 3α-bromocholest-5-ene (20 mg.). Fractions from the above chromatograms containing identical compounds were combined and recrystallised from acetone to furnish pure homogeneous 3α-bromocholest-5-ene, m. p. 112—115°, $[\alpha]_D$ −37° (*c* 1·0) [Found (after drying at 20°/0·1 mm. for 24 hr.): C, 72·8, 72·9; H, 10·05, 10·2. Calc. for $C_{27}H_{45}Br$: C, 72·1; H, 10·1%], and *3α-bromo-5α-cholest-6-ene*, m. p. 70—71°, $[\alpha]_D$ −52° (*c* 1·2), for which a good analysis could not be obtained [Found (after drying at 20°/0·1 mm. for 24 hr.): C, 70·7; H, 9·7%], but the n.m.r. spectrum of which exhibited peaks at τ 9·26 [10β-Me], τ 5·25 [3β-H], and a multiplet centred at τ 4·63 [H-6, H-7].

We thank Miss B. McLean, M.Sc., for a preliminary re-examination of the preparation of epicholesteryl chloride during the tenure of a Commonwealth Research Scholarship.

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