*Steroids and Walden Inversion. Part XXVI.** 4β-*Methoxycholest*-5-*ene*, 6β-*Methoxycholest*-4-*ene*, *and Related Compounds.*

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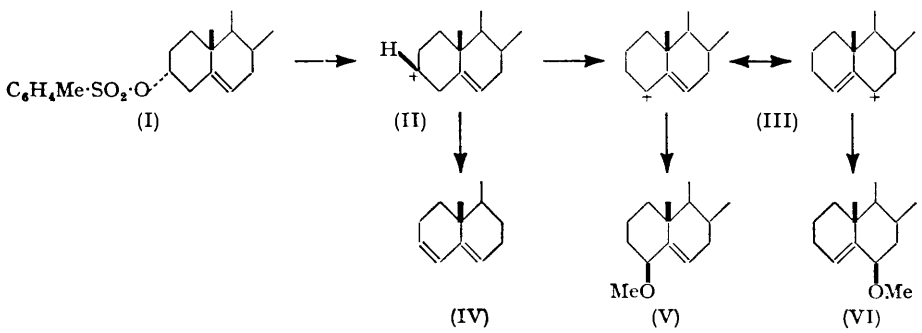
[Reprint Order No. 6339.]

4β-Methoxycholest-5-ene and 6β-methoxycholest-4-ene have been prepared and shown to be identical with the products isolated from the methanolysis of *epi*cholesteryl toluene-*p*-sulphonate by Evans and Shoppee (*J.*, 1953, 540).

Hydrogenation of cholest-5-en-4β-ol, its acetate, and its methyl ether gave by hydrogenolysis only cholestane, whereas hydrogenation of cholest-5-en-4α-ol gave cholestan-4α-ol. Hydrogenation of the epimeric 6-acetoxy- and 6-hydroxycholest-4-enes gave respectively the epimeric 6-acetoxycoprostanes or the epimeric coprostan-6-ols; the latter by cautious oxidation both yielded coprostan-6-one, isomerised by acid, alkali, or alkaline aluminium oxide to cholestan-6-one.

Reduction of 5-hydroxycholestan-4-one with sodium–*n*-propanol gave the expected products, cholestan-4α-ol and cholestane-4α : 5-diol; similar reduction of 5-hydroxycholestan-6-one gave cholestan-6α-ol, and cholestane-5 : 6α-diol accompanied by coprostane-5 : 6α-diol.

The methanolysis of *epi*cholesteryl toluene-*p*-sulphonate (I) has been shown independently by Schmid and Kägi (*Helv. Chim. Acta*, 1952, **35**, 2194) and Evans and Shoppee (*J.*, 1953, 540) to afford cholesta-3 : 5-diene (IV) and two isomeric methyl ethers regarded as 4β-methoxycholest-5-ene (V) and 6β-methoxycholest-4-ene (VI). The observation that the acetolysis of *epi*cholesteryl toluene-*p*-sulphonate exhibits first-order kinetics (Williams and Shoppee, *J.*, 1955, 686) supports, by analogy, Evans and Shoppee's view (*loc. cit.*) that the methanolysis involves a unimolecular heterolysis to give the cation (II), which can achieve neutrality by loss of a proton to give cholesta-3 : 5-diene (IV), or by rearrangement involving hydrogen migration to yield the mesomeric cation (III), and thence the isomeric methyl ethers (V) and (VI).



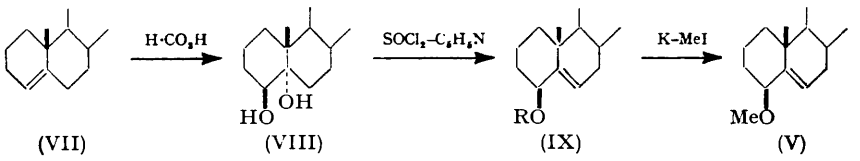
(I) (II) (III) (IV) (V) (VI)

The partial syntheses of these methyl ethers, now reported, confirm Evans and Shoppee's structural conclusions.† The cause of the β-configurational specificity displayed, which recalls that of the 3 : 5-*cyclo*steroid rearrangement, is obscure, but some analogies are provided by the oxidation of cholesterol with sodium dichromate in benzene–acetic acid to 6β-hydroxycholest-4-en-3-one (Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4377; 1954, **76**, 1728), or with selenium dioxide–acetic acid to cholest-5-ene-3β : 4β-diol, which at higher temperatures rearranges to cholest-4-ene-3β : 6β-diol (Rosenheim *et al.*, *J.*, 1937, 377; 1943, 135; Butenandt and Hausmann, *Ber.*, 1937, **70**, 1154; Paige, *J.*, 1943, 437).

* Part XXV, *J.*, 1955, 1891.

† Since this paper was submitted, the partial syntheses of the methyl ethers (V) and (VI) and of related compounds have been described by Becker and Wallis (*J. Org. Chem.*, 1955, **20**, 353).

Hydroxylation of cholest-4-ene (VII) with performic or peracetic acid gave, after mild alkaline hydrolysis, cholestane-4β : 5-diol (VIII), previously obtained by oxidation of cholesta-2 : 4-diene to cholest-2-ene-4β : 5-diol and hydrogenation of the latter (Bergmann and Skau, *J. Org. Chem.*, 1940, **5**, 439). Acetylation with acetic anhydride–pyridine at 20° gave the 4β-monoacetate whilst use of acetyl chloride in boiling chloroform yielded the diacetate; the 4β-monoacetate by dehydration with thionyl chloride–pyridine at 0° gave 4β-acetoxycholest-5-ene (IX; R = Ac), hydrolysed by treatment with lithium aluminium hydride in ether to cholest-5-en-4β-ol (IX; R = H). This by methylation with potassium–



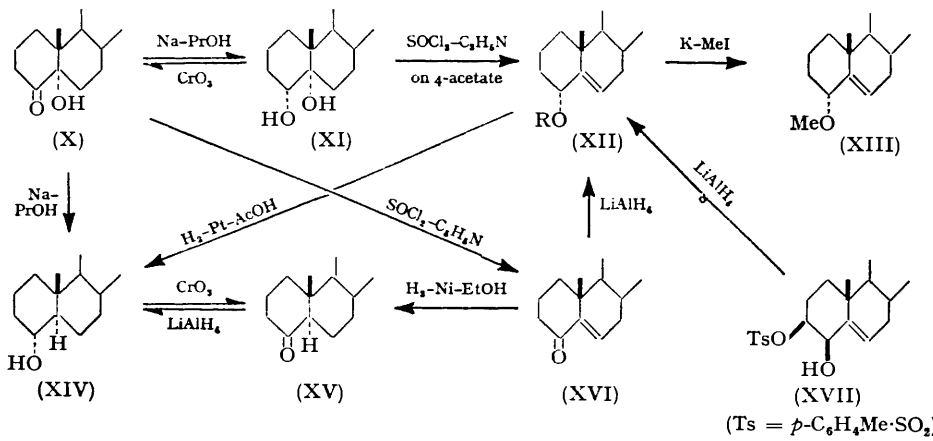
(VII) (VIII) (IX) (V)

M. p. 68°, [−73] [a] *
M. p. 66°, [−73] [b]
M. p. 65°, [−68]

* These and similar figures in brackets are $[\alpha]_D$.

methyl iodide in benzene gave 4β-methoxycholest-5-ene (V), identical with specimens prepared by Schmid and Kägi (*loc. cit.*; ref. *a*) and by Evans and Shoppee (*loc. cit.*; ref. *b*).

Catalytic hydrogenation with platinum in ethyl acetate with or without a trace of perchloric acid, or in ethanol containing a trace of formic acid, of the alcohol or its acetate (IX; R = H or Ac) caused hydrogenolysis and gave only cholestane; hydrogenation of the acetate (IX; R = Ac) with platinum in dioxan gave an unidentified hydrocarbon, m. p. 66°, $[\alpha]_D$ +1°, which is under investigation. Hydrogenation of the methyl ether (V) has already been reported to give cholestane (Evans and Shoppee, *loc. cit.*; Schmid and Kägi, *loc. cit.*).



(X) (XI) (XII) (XIII)

(XIV) (XV) (XVI) (XVII)

(Ts = *p*-$C_6H_4Me{\cdot}SO_2$)

Hydroxylation of cholest-4-ene (VII) with osmium tetroxide gave cholestane-4α : 5-diol (XI). The 4α-monoacetate of this, obtained by acetic anhydride–pyridine at 20°, was dehydrated by thionyl chloride–pyridine at 0° or on attempted acetylation with acetyl chloride and dimethylaniline in boiling chloroform, affording 4α-acetoxycholest-5-ene (XII; R = Ac), which by contrast with the 4β-epimeride (IX; R = Ac), slowly decomposed at 100° into cholesta-3 : 5-diene and acetic acid, probably by ionic elimination [*E*1], since the 4β-epimeride (IX; R = Ac), by evaporation of an ethereal solution containing 1 drop of 10N-hydrochloric acid, gave cholesta-3 : 5-diene and acetic acid. The 4α-monoacetate (XII; R = Ac) by hydrolysis with lithium aluminium hydride in ether gave cholest-5-en-4α-ol (XII; R = H; OH, equatorial)]. This substance was

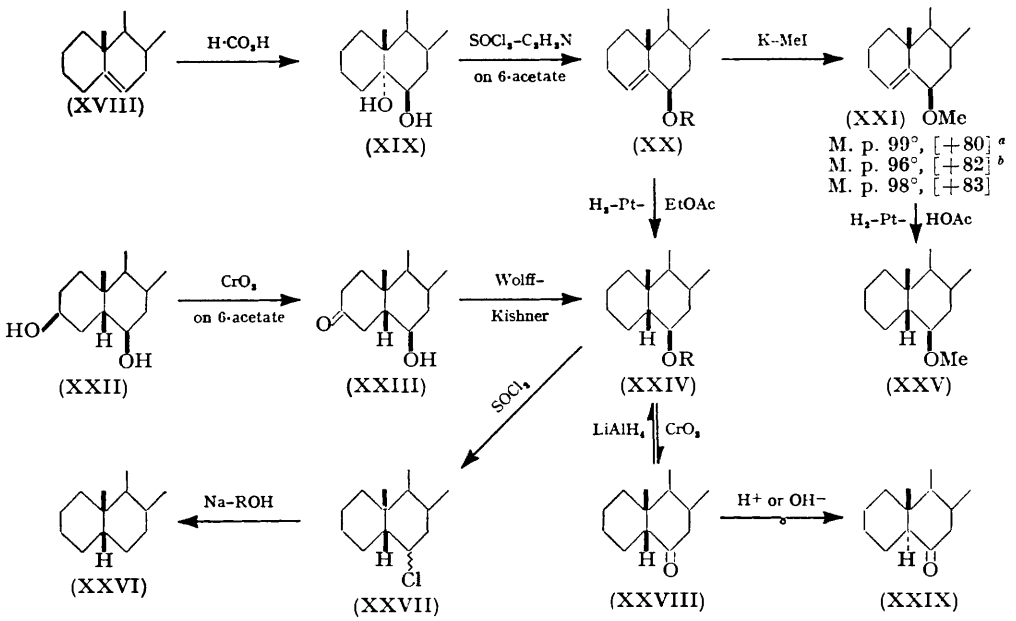
identical with the product of the reduction of 4β-hydroxycholest-5-en-3β-yl toluene-*p*-sulphonate (XVII; 4-OH, axial) with lithium aluminium hydride (Karrer, Sareen, Asmis, and Schwyzer, *Helv. Chim. Acta*, 1951, **34**, 1022); these authors proved the configuration at $C_{(4)}$ of their product by hydrogenation in presence of platinum–acetic acid to cholestan-4α-ol (XIV) [wrongly described in their paper as cholestan-4β-ol] (Tschesche and Hagedorn, *Ber.*, 1935, **68**, 2251; Fürst and Scotoni, *Angew. Chem.*, 1951, **63**, 196; Barton and Rosenfelder, *J.*, 1951, 1032). Methylation with potassium–methyl iodide in benzene gave 4α-methoxycholest-5-ene (XIII), m. p. 85—86° (Schmid and Kägi, *loc. cit.*).

Oxidation of cholestane-4β : 5-diol (VIII) with *N*-bromosuccinimide furnished 5-hydroxycholestan-4-one (X), which by reduction with lithium aluminium hydride gave cholestane-4β : 5-diol, but by reduction with sodium–*n*-propanol gave a mixture of cholestane-4α : 5-diol (XI) and cholestan-4α-ol (XIV), readily separated chromatographically. The latter substance was oxidised by chromium trioxide to cholestan-4-one (XV), which was identical with a specimen prepared from cholest-4-ene (VII) by conversion into 4-nitrocholest-4-ene and reduction of this with zinc–acetic acid (Windaus, *Ber.*, 1920, **53**, 488); by reduction with lithium aluminium hydride it gave cholestan-4β-ol (88%) accompanied by cholestan-4α-ol (XIV) (7%). 5-Hydroxycholestan-4-one (X) was readily dehydrated with thionyl chloride–pyridine at 0° to cholest-5-en-4-one, $\lambda_{max.}$ 242 mμ (log ε 3·85) (XVI), which showed the low extinction characteristic of a cisoid system, and has previously been prepared with $\lambda_{max.}$ 241 mμ (log ε 3·86) from 2α-bromocholestan-3-one by treatment with potassium acetate in acetic acid at 210° (Butenandt and Ruhenstroth-Bauer, *Ber.*, 1944, **77**, 397; cf. Ruzicka, Plattner, and Aeschbacher, *Helv. Chim. Acta*, 1938, **21**, 866). By reduction with Raney nickel in ethanol containing a trace of formic acid cholest-5-en-4-one (XVI) gave cholestan-4-one (XV), and by reduction with lithium aluminium hydride cholest-5-en-4α-ol (XII : R = H).

Cholest-5-ene (XVIII) was hydroxylated with performic acid according to the directions of Reich, Walker, and Collins (*J. Org. Chem.*, 1951, **16**, 1753) to give cholestane-5 : 6β-diol (XIX), which with acetic anhydride–pyridine at 20° gave the 6β-monoacetate and with acetyl chloride in boiling chloroform the diacetate. The 6β-monoacetate on dehydration with thionyl chloride–pyridine at 0° was smoothly converted into 6β-acetoxycholest-4-ene (XX; R = Ac). The 6β-acetate (XX; R = Ac) was unchanged when heated briefly at 100°, but evaporation of an ethereal solution containing 1 drop of 10N-hydrochloric acid yielded acetic acid and cholesta-4 : 6-diene, which is known to rearrange under these conditions to cholesta-3 : 5-diene. It has been observed that 6β-acetates of the *allo*pregnane series (Herzog and Ehrenstein, *J. Org. Chem.*, 1951, **16**, 1050), of the pregn-4-ene series (Balant and Ehrenstein, *ibid.*, 1952, **17**, 1587; Florey and Ehrenstein, *ibid.*, 1954, **19**, 1331), and of the cholest-4-ene series (Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4377; Sondheimer, Kaufmann, Romo, Martinez, and Rosenkranz, *ibid.*, p. 4712) are epimerised at $C_{(6)}$ by hydrogen chloride at 0° in chloroform containing 0·7% of ethanol (but not in pure chloroform); 6β-acetoxycholest-4-ene (XX; R = Ac) was not epimerised by this treatment. 6β-Acetoxycholest-4-ene resisted hydrolysis with hot methanolic potassium hydroxide although by treatment with lithium aluminium hydride in ether it gave cholest-4-en-6β-ol (XX; R = H). The alcohol and potassium–methyl iodide in benzene gave 6β-methoxycholest-4-ene (XXI), identical with the preparations by Schmid and Kägi (*loc. cit.*; ref. *a*) and Evans and Shoppee (*loc. cit.*; ref. *b*). Hydrogenation of 6β-methoxycholest-4-ene with platinum in ethyl acetate–acetic acid gave 6β-methoxycoprostane (XXV), m. p. 64—65°, $[\alpha]_D$ +10°, which was different from 6β-methoxycholestane, double m. p. 52°/77°, $[\alpha]_D$ +14°, prepared from cholestan-6β-ol by methylation with potassium and methyl iodide in boiling benzene.

Hydrogenation of cholest-4-en-6β-ol (XX; R = H) with platinum in ethyl acetate containing perchloric acid (a trace) gave cholestane and coprostan-6β-ol (XXIV; R = H), characterised as the acetate, which showed the infrared spectral pattern associated with an axial steroid acetate with bands at 1730 and 1242 cm.$^{-1}$. Hydrogenation of 6β-acetoxycholest-4-ene (XX; R = Ac) with platinum in ethyl acetate in the presence of a trace of perchloric acid gave cholestane and coprostan-6β-yl acetate (XXIV; R = Ac). The stereochemical course of the hydrogenations (XX ⟶ XXIV) was proved in three ways.

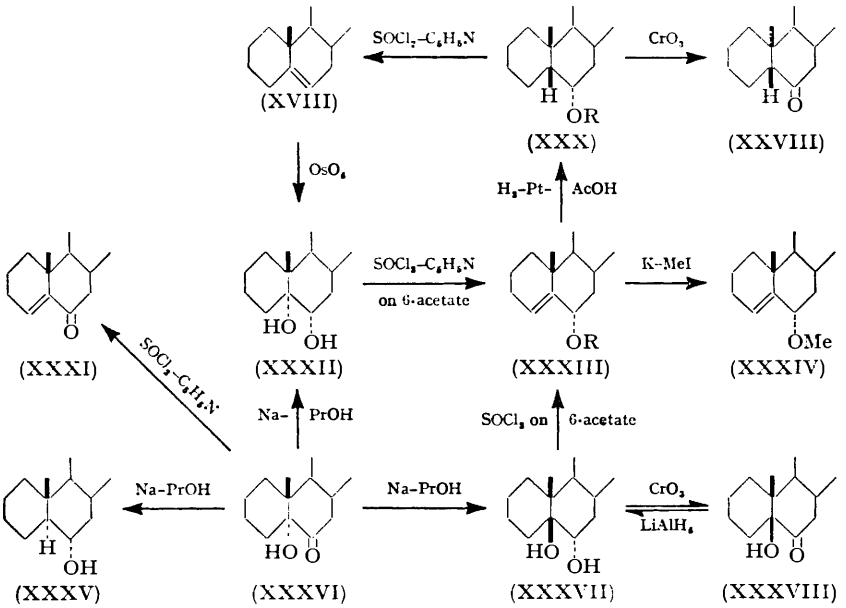
First, the 6-monoacetate of coprostane-3β : 6β-diol (Prelog and Tagmann, *Helv. Chim. Acta*, **1944**, **27**, 1880) was oxidised with chromium trioxide in acetic acid at 20° to the 3-oxo-6β-yl acetate which by alkaline hydrolysis gave 6β-hydroxycoprostan-3-one (XXIII); this by modified Wolff–Kishner reduction furnished coprostan-6β-ol (XXIV; R = H). Secondly, by cautious oxidation with chromium trioxide in acetic acid at 20° coprostan-6β-ol afforded coprostan-6-one (XXVIII), m. p. 133—134°, $[\alpha]_D$ −44°, the infrared absorption spectrum of which showed a band at 1705 cm.$^{-1}$ [6-membered-ring ketone of the A/B-*cis*-series (cf. R. N. Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956)]; coprostan-6-one, when reduced with lithium aluminium hydride, regenerated coprostan-6β-ol, and by treatment with acid or alkali or by contact with moist alkaline aluminium oxide, underwent keto–enol prototropy with inversion of configuration at $C_{(5)}$, to give the more thermodynamically stable cholestan-6-one (XXIX), m. p. 96°, $[\alpha]_D$ −2° (cf. Windaus, *Ber.*, 1920, **53**, 488). Thirdly, coprostan-6β-ol with thionyl



chloride in pyridine gave (probably with retention of configuration) 6ξ-chlorocoprostane (XXVII), reduced by sodium in boiling pentyl alcohol to coprostane (XXVI). The formation of cholestane in the above hydrogenations is noteworthy, and suggests the occurrence to some degree of hydrogenolysis of the 6β-substituent before reduction of the 4 : 5-double bond; the rôle played by the 6β-substituent in the production of compounds of the coprostane series does not appear readily explicable (cf. Brewster, *J. Amer. Chem. Soc.*, 1954, **76**, 6361, 6364, 6368; Fukushima and Gallagher, *ibid.*, 1955, **77**, 139).

Cholest-5-ene (XVIII) by hydroxylation with osmium tetroxide gave cholestane-5 : 6α-diol (XXXII), converted by acetic anhydride–pyridine at 20° into the 6α-monoacetate; use of acetyl chloride–dimethylaniline in boiling chloroform gave the diacetate, which failed to crystallise but by hydrolysis with lithium aluminium hydride regenerated the 5α : 6α-diol (XXXII). The 6α-monoacetate was dehydrated by thionyl chloride–pyridine to 6α-acetoxycholest-4-ene (XXXIII; R = Ac), which gave a yellow colour with tetranitromethane in chloroform (cf. Djerassi, Rosenkranz, *et al.*, *J. Org. Chem.*, 1951, **16**, 192), and which by hydrolysis with potassium hydroxide or lithium aluminium hydride afforded cholest-4-en-6α-ol (XXXIII; R = H). The 6α-acetate (XXXIII; R = Ac) was stable to thermal treatment, but gave cholesta-3 : 5-diene under mild acidic conditions. The allylic alcohol (XXXIII; R = H) was also obtained from cholest-4-en-6-one (XXXI) by reduction with lithium aluminium hydride. Cholest-4-en-6α-ol (XXXIII; R = H)

on attempted methylation with potassium–methyl iodide in boiling benzene yielded cholesta-3 : 5-diene; further experimentation showed that methylation at 30—35° gave, after chromatographic purification, 6α-methoxycholest-4-ene (XXXIV) as an oil, $[\alpha]_D$ +20°, which did not crystallise and decomposed at ~70° to furnish cholesta-3 : 5-diene. This ready elimination * of the 6α-methoxyl group (equatorial) in (XXXIV) contrasts with the relative stability of the 6β-methoxyl group (axial) in (XXI), recalls the ready elimination of the 4α-acetoxyl group (equatorial) in (XI; R = Ac) in contrast to the relative stability of the 4β-acetoxyl group (axial) in (IX; R = Ac), and suggests an ionic mechanism [*E*1]. Cholest-4-en-6α-ol (XXXIII; R = H) by hydrogenation with platinum in ethyl acetate in the presence of a trace of perchloric acid gave some cholestane and coprostan-6α-ol (XXX; R = H); similarly, 6α-acetoxycholest-4-ene (XXXIII; R = Ac) by hydrogenation with platinum in ethyl acetate–acetic acid afforded cholestane accompanied by 6α-acetoxycoprostane (XXX; R = Ac). The stereochemical course of these hydrogenations was established by cautious oxidation of coprostan-6α-ol (XXX; R = H) with chromium trioxide in acetic acid at 20° to coprostan-6-one (XXVIII), identical with that obtained previously from coprostan-6β-ol (XXIV; R = H). The production of cholestane is again to be noted, and suggests hydrogenolysis of the 6α-substituent before reduction of the 4 : 5-double bond.



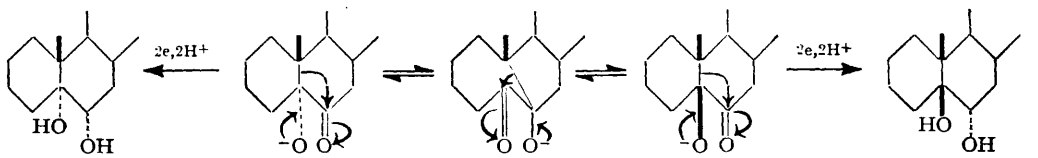
Whereas coprostan-6β-ol (XXIV; OH, axial), on treatment with thionyl chloride–pyridine, underwent substitution to give 6ξ-chlorocoprostane (XXVII), similar treatment of coprostan-6α-ol (XXX; OH, equatorial) gave coprostan-6α-yl sulphite, accompanied by elimination to yield cholest-5-ene (XVIII) in 35% yield. In coprostan-6α-ol, the 6α-hydroxyl group and the 5β-hydrogen atom are both equatorial to ring B, so that although *trans*-orientated these entities cannot be coplanar.

Oxidation of cholestane-5 : 6β-diol (XIX) with *N*-bromosuccinimide (cf. Reich, Walker, and Collins, *loc. cit.*) gave 5-hydroxycholestan-6-one (XXXVI). This ketol was reduced by lithium aluminium hydride to cholestane-5 : 6β-diol (XIX), but with sodium–*n*-propanol to a mixture, separated chromatographically, of cholestan-6α-ol (XXXV) (Tschesche, *Ber.*, 1932, **65**, 1842; Shoppee and Summers, *J.*, 1952, 3361), cholestane-5 : 6α-diol (XXXII), and coprostane-5 : 6β-diol (XXXVII). The last-named by mild oxidation with chromium

* Whilst Fieser (*J. Amer. Chem. Soc.*, 1953, **75**, 4377) observed that both 6α- and 6β-acetoxycholest-4-en-3-one are smoothly converted into cholest-4-en-3-one by treatment with zinc–acetic acid, we find that 6α-acetoxycholest-4-ene is unaltered by this reagent.

trioxide–acetic acid at 20° gave 5-hydroxycoprostan-6-one (XXXVIII), reconverted into the diol (XXXVII) by reduction with lithium aluminium hydride. The non-crystalline 6α-monoacetate of the diol (XXXVII) was dehydrated with thionyl chloride–pyridine at 0° to 6α-acetoxycholest-4-ene (XXXIII; R = Ac); thus the diols (XXXII) and (XXXVII) differ only in configuration at $C_{(5)}$, and their molecular rotations, despite vicinal action, are consistent with these structures.

The conversion of 5-hydroxycholestan-6-one (XXXVI) into coprostane-5 : 6α-diol (XXXVII) is noteworthy. It does not involve prior formation of cholestane-5 : 6α-diol (XXXII) and inversion of configuration at $C_{(5)}$ thereof, because both cholestane-5 : 6α-diol and cholestan-5-ol are unchanged by extended treatment with sodium in boiling *n*-propanol; it therefore involves fission either of the $C_{(5)}$–O bond, or, more probably, of the $C_{(5)}$–$C_{(4)}$ or $C_{(5)}$–$C_{(10)}$ bond * in a reversible α-ketol change (Shoppee, *J.*, 1928, 1662; Wendler and Taub, *Chem. and Ind.*, 1955, 505) :



(XXXII) (XXXVI) (XXXVIII) (XXXVII)

Reduction of the carbonyl group of the epimeric α-ketols (XXXVI) and (XXXVIII) by the dissolving sodium gives, *via* the appropriate carbanions $^{-}C_{(6)}$–$O^{-}\}Na^{+}$ (cf. Birch, *Quart. Rev.*, 1952, **4**, 69; Barton and Robinson, *J.*, 1954, 3045), cholestane-5 : 6α-diol (XXXII) and coprostane-5 : 6α-diol (XXXVII) respectively.

Experimental

For general experimental directions, see *J.*, 1955, 1891. $[\alpha]_D$ are in $CHCl_3$ unless otherwise stated. Ultraviolet absorption spectra were determined in EtOH on a Unicam SP 500 spectrometer with corrected scale and infrared absorption spectra in CS_2 on a Perkin–Elmer double-beam instrument.

Cholestane-4β : 5-*diol* (VIII).—Cholest-4-ene (6·6 g.) was rapidly stirred with 98% formic acid (105 c.c.) and benzene (10 c.c.) whilst hydrogen peroxide (100-vol.; 12 c.c.) was slowly added at 30—45° during 6 hr. The solution was poured into water and extracted with ether, and the ethereal extract dried and evaporated; the residual oil was refluxed with 5% methanolic potassium hydroxide (100 c.c.) for 2·5 hr., and the mixture worked up in the usual way. The product (6·6 g.) was chromatographed on aluminium oxide (200 g.) in pentane; elution with pentane gave cholest-4-ene (1·8 g.), whilst use of ether–benzene (1 : 1; 5 × 100 c.c.) gave cholestane-4β : 5-diol, m. p. 171—172°, $[\alpha]_D$ +27° (*c*, 1·9). The 4β-monoacetate was obtained by use of acetic anhydride in pyridine at 20° for 16 hr. and crystallised from acetone in needles, m. p. 175—176°, $[\alpha]_D$ +38° (*c*, 1·5). The 4β : 5α-diol (120 mg.) was refluxed with acetyl chloride (1·5 c.c.) and dimethylaniline (1·0 c.c.) in purified chloroform (25 c.c.); 4β : 5α-diacetoxycholestane (80 mg.), isolated in the usual way, was an oil but chromatography on aluminium oxide (3 g.) and elution with benzene–pentane (3 : 7) gave 4β : 5-*diacetoxycholestane*, m. p. 147—148°, $[\alpha]_D$ +60° (*c*, 1·7), after recrystallisation from aqueous acetone [Found (after drying at 100°/0·01 mm. for 3 hr.) : C, 76·7; H, 10·8. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%].

4β-*Acetoxycholest*-5-*ene* (IX; R = Ac).—4β-Acetoxycholestan-5-ol (150 mg.) by treatment with thionyl chloride (0·5 c.c.) in pyridine (2 c.c.) at 0° furnished a product, which after chromatography on aluminium oxide by elution with benzene–pentane (1 : 4) yielded 4β-*acetoxycholest*-5-*ene*, m. p. 108°, $[\alpha]_D$ −70° (*c*, 1·1), after recrystallisation from acetone–methanol (1 : 9) [Found (after drying at 90°/0·01 mm. for 2 hr.) : C, 81·4; H, 11·3. $C_{29}H_{48}O_2$ requires C, 81·25; H, 11·3%), giving a yellow colour with tetranitromethane–chloroform.

Cholest-5-*en*-4β-*ol* (IX; R = H).—4β-Acetoxycholest-5-ene (350 mg.), dissolved in ether (20 c.c.), was refluxed with a solution of lithium aluminium hydride (400 mg.) in ether (30 c.c.) for 0·5 hr. The solid product (320 mg.) was isolated in the usul way and by recrystallisation

* We are grateful to a Referee for drawing our attention to the possibly analogous cases of the conversion of purpurogallin into purpurogallone and of humulone into humulic acid.

from methanol yielded *cholest-5-en-4β-ol*, m. p. 132°, $[\alpha]_D$ −59° (*c*, 0·44) [Found (after drying at 100°/0·01 mm. for 3 hr.) : C, 84·0; H, 12·2. $C_{27}H_{46}O$ requires C, 83·8; H, 12·0%], giving a yellow colour with tetranitromethane–chloroform.

4β-Methoxycholest-5-ene (V).—Cholest-5-en-4β-ol (150 mg.) was heated with " molecular " potassium (~100 mg.) in benzene (25 c.c.) for 1 hr., and then with methyl iodide (5 c.c.) for 3 hr. The product was isolated in the usual way and purified by chromatography on aluminium oxide prepared in pentane; elution with pentane furnished 4β-methoxycholest-5-ene, m. p. 65°, $[\alpha]_D$ −68° (*c*, 0·5), after crystallisation from acetone, giving a yellow colour with tetranitromethane–chloroform and identical with specimens prepared by Evans and Shoppee (*loc. cit.*) and by Schmid and Kägi (*loc. cit.*).

Hydrogenation of Cholest-5-en-4β-ol and its Acetate.—(*a*) The acetate (70 mg.), dissolved in ethyl acetate (10 c.c.), was hydrogenated with platinum oxide (50 mg.) for 2 hr.; the product (68 mg.) consisted solely of cholestane, m. p. and mixed m. p. 77—78° after crystallisation from acetone.

(*b*) The stenol (70 mg.), dissolved in ethanol (15 c.c.) containing 98% formic acid (1 c.c.), was hydrogenated with Raney nickel for 3 hr.; the product consisted of cholestane, m. p. and mixed m. p. 79°, after crystallisation from acetone.

Cholestane-4α : 5-diol (XI).—Cholest-4-ene (1 g.) was treated with a solution of osmium tetroxide (1 g.) in ether (25 c.c.) containing pyridine (2 c.c.) for 2·5 days; lithium aluminium hydride (1·4 g.) was then added and the solution refluxed for 2 hr. The product, isolated in the usual way, was an oil (650 mg.) which was chromatographed on aluminium oxide in pentane. Elution with pentane gave cholest-4-ene (550 mg.), m. p. and mixed m. p. 78° after crystallisation from acetone; elution with ether–benzene (3 : 7) gave *cholestane-4α : 5-diol* (50 mg.), m. p. 135°, $[\alpha]_D$ +14° (*c*, 0·83) [Found (after drying at 100°/0·01 mm. for 3 hr.) : C, 80·1; H, 11·8. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·95%]. The *4α-monoacetate*, obtained by use of acetic anhydride in pyridine at 20° for 18 hr., had m. p. 149°, $[\alpha]_D$ +35° (*c*, 1·28) after recrystallisation from methanol [Found (after drying at 100°/0·01 mm. for 3 hr.) : C, 77·9; H, 11·3. $C_{29}H_{50}O_3$ requires C, 77·95; H, 11·3%].

4α-Acetoxycholest-5-ene (XII; R = Ac).—(*a*) Cholestane-4α : 5-diol 4-monoacetate (420 mg.) was treated with thionyl chloride (1 c.c.) in pyrdine (10 c.c.) at 0° for 0·5 hr. to afford, after processing in the usual way, *4α-acetoxycholest-5-ene*, m. p. 123°, $[\alpha]_D$ −27° (*c*, 0·65), after crystallisation from acetone [Found (after drying at 60°/0·01 mm. for 3 hr.) : C, 81·0; H, 11·2. $C_{29}H_{48}O_2$ requires C, 81·2; H, 11·3%], giving a yellow colour with tetranitromethane–chloroform. The acetate (150 mg.) when heated at 100° for 10 min., evolved acetic acid; chromatography of the resultant oil on aluminium oxide (4·5 g.) in pentane, with elution by pentane (3 × 15 c.c.), gave cholesta-3 : 5-diene (70 mg.), m. p. and mixed m. p. 77°, after recrystallisation from acetone, whilst elution with benzene–pentane (1 : 9; 4 × 15 c.c.) gave the unchanged acetate (69 mg.), m. p. and mixed m. p. 120—123° after recrystallisation from acetone.

(*b*) Cholestane-4α : 5-diol (275 mg.), refluxed with acetyl chloride (2 c.c.) and dimethylaniline (2 c.c.) in chloroform (15 c.c.), underwent partial acetylation accompanied by dehydration, to yield 4α-acetoxycholest-5-ene (100 mg.), m. p. and mixed m. p. 120—123° with the specimen prepared by method (*a*), after recrystallisation from acetone, and cholestane-4α : 5-diol 4-monoacetate (139 mg.), m. p. and mixed m. p. 148° after recrystallisation from methanol. Separation was effected by chromatography on aluminium oxide (8 g.) and elution with pentane and benzene–pentane (1 : 4).

Cholest-5-en-4α-ol (XII; R = H).—(*a*) 4α-Acetoxycholest-5-ene (150 mg.) was hydrolysed by treatment with lithium aluminium hydride in ether to give, after the usual working up, cholest-5-en-4α-ol (120 mg.), m. p. 144—145°, $[\alpha]_D$ −50° (*c*, 0·55), after recrystallisation from acetone–pentane, identical with a specimen prepared by the method of Karrer, Sareen, Asmis, and Schwyzer (*loc. cit.*).

(*b*) Cholest-5-en-4-one (41 mg.) was treated with a solution of lithium aluminium hydride (60 mg.) in ether (20 c.c.) for 0·5 hr. The usual working up gave cholest-5-en-4α-ol (40 mg.), m. p. and mixed m. p. 144—145°, after crystallisation from acetone–pentane.

4α-Methoxycholest-5-ene (XIII). Cholest-5-en-4α-ol, by methylation in an atmosphere of nitrogen with potassium and methyl iodide in boiling benzene, gave 4α-methoxycholest-5-ene, m. p. 86° after crystallisation from ether–methanol (cf. Schmid and Kägi, *loc. cit.*).

Cholestan-4α-ol (XIV).—Cholest-5-en-4α-ol (50 mg.) was hydrogenated with platinum oxide (25 mg.) in ethyl acetate (5 c.c.) containing acetic acid (5 c.c.) to give, after the usual working up, cholestan-4α-ol, m. p. 188—189°, after recrystallisation from acetone.

5-Hydroxycholestan-4-one (X).—Cholestane-4β : 5-diol (3 g.), dissolved in a mixture of ether

(65 c.c.), methanol (12 c.c.), and water (11 c.c.), was treated with *N*-bromosuccinimide (2 g.); after 40 min. ether was added, and the solution washed with water, sodium metabisulphite solution, and water, dried, and evaporated. The solid residue (2·9 g.) by recrystallisation from methanol gave the *ketol*, m. p. 159°, $[\alpha]_D$ +55° (*c*, 1·4) [Found (after drying at 100°/0·01 mm. for 3 hr.): C, 80·8; H, 11·1. $C_{27}H_{46}O_2$ requires C, 80·55; H, 11·5%].

Reduction of 5-Hydroxycholestan-4-one (X) *with Lithium Aluminium Hydride.*—The ketol (25 mg.) was reduced with lithium aluminium hydride (50 mg.) in ether at 15°. Working up gave a solid (25 mg.), which by recrystallisation from ether–pentane yielded cholestane-4β : 5-diol, m. p. and mixed m. p. 172°.

Reduction of 5-Hydroxycholestan-4-one (X) *with Sodium and Propanol.*—Sodium (7 g.) was added gradually to a solution of the ketol (1·4 g.) in boiling propan-1-ol (100 c.c.); after refluxing for 3 hr., the solution was poured into water, propanol largely removed in a vacuum, and a solid (1·34 g.) isolated in the usual manner. Crystallisation from acetone–methanol (1 : 5) gave cholestan-4α-ol (390 mg.), m. p. 188°, $[\alpha]_D$ +6° (*c*, 0·8), characterised by preparation, with acetic anhydride in pyridine at 20°, of the *acetate*, m. p. 110°, $[\alpha]_D$ +14·5° (*c*, 1·0), after crystallisation from acetone [Found (after drying at 65°/0·01 mm. for 3 hr.): C, 80·85; H, 11·45. $C_{29}H_{50}O_2$ requires C, 80·85; H, 11·6%]. The material from the acetone–methanol mother-liquor failed to crystallise and was chromatographed on aluminium oxide (50 g.); elution with benzene gave cholestan-4α-ol (400 mg.), m. p. 188°, whilst use of ether–benzene (1 : 9) gave cholestane-4α : 5-diol (376 mg.), m. p. 133—135°, identical with the preparation described above.

Cholestan-4-one (XV).—Cholestan-4α-ol (150 mg.) was dissolved in acetic acid (10 c.c.) and oxidised with chromium trioxide (300 mg.) in 90% acetic acid (3 c.c.). After 48 hr. at 20°, the solution was evaporated at 30—35°/10 mm., and the product isolated in the usual way, to yield cholestan-4-one, m. p. 96°, $[\alpha]_D$ +27° (*c*, 0·6), after crystallisation from methanol; Barton and Rosenfelder (*J.*, 1951, 1032) record m. p. 94—96°.

Reduction of Cholestan-4-one with Lithium Aluminium Hydride.—Cholestan-4-one (308 mg.) was treated with lithium aluminium hydride (107 mg.) in ether at 15° for 1 hr. The product, an oil, was chromatographed on aluminium oxide (9 g.) in pentane; elution with pentane yielded cholestan-4-one (9 mg.), m. p. and mixed m. p. 96°, and elution with benzene gave cholestan-4β-ol (265 mg.), m. p. 135°, $[\alpha]_D$ +31° (*c*, 0·9), after crystallisation from methanol, whilst elution with ether–benzene (1 : 4) furnished cholestan-4α-ol (22 mg.), m. p. 188—190°, after recrystallisation from acetone.

Cholest-5-en-4-one (XVI).—5-Hydroxycholestan-4-one (150 mg.), dissolved in pyridine (5 c.c.), was treated with thionyl chloride (0·5 c.c.) at 0°; after 0·5 hr., at 20°, the solution was poured into water and worked up in the usual way. The product (110 mg.) was purified by chromatography on aluminium oxide (3 g.); elution with pentane gave cholest-5-en-4-one, m. p. 111°, $[\alpha]_D$ −34° (*c*, 0·54), $\lambda_{max.}$ 242 mμ (log ε 3·85), after recrystallisation from acetone, giving a yellow colour with tetranitromethane–chloroform. Butenandt and Ruhenstroth-Bauer (*loc. cit.*) give m. p. 111—112°, $[\alpha]_D$ −32°, $\lambda_{max.}$ 241 mμ (log ε 3·86).

Cholestane-5 : 6β-diol (XIX).—Cholest-5-ene was hydroxylated with performic acid according to the directions of Reich, Walker, and Collins (*loc. cit.*), to give, after chromatographic purification and crystallisation from aqueous ethanol, cholestane-5 : 6β-diol, double m. p. 60° and 125°, $[\alpha]_D$ −3° (*c*, 0·9); the 6β-monoacetate, prepared by acetic anhydride in pyridine at 20°, had m. p. 112—114°. Cholestane-5 : 6β-diol (120 mg.) was refluxed with acetyl chloride (2 c.c.) and dimethylaniline (2 c.c.) in purified chloroform (20 c.c.) for 4 hr.; the usual working-up gave an oil (122 mg.), which was purified by elution from aluminium oxide with pentane, to give 5 : 6β-*diacetoxycholestane*, m. p. 76°, $[\alpha]_D$ −33° (*c*, 0·9), after crystallisation from acetone [Found (after drying at 60°/0·01 mm. for 3 hr.): C, 76·3; H, 10·7. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%].

6β-*Acetoxycholest-4-ene* (XX; R = Ac).—6β-Acetoxycholestan-5-ol (1 g.) was dissolved in pyridine (15 c.c.) and treated with thionyl chloride (2 c.c.) at 0°; the mixture was kept at 20° for 0·5 hr., poured into water, and worked up in the usual way. The resultant oil (900 mg.) by elution from aluminium oxide with pentane afforded 6β-*acetoxycholest-5-ene*, m. p. 76—77°, $[\alpha]_D$ +74° (*c*, 0·9), after recrystallisation from methanol [Found (after drying at 60°/0·01 mm. for 2 hr.): C, 81·5; H, 11·2. $C_{29}H_{48}O_2$ requires C, 81·3; H, 11·3%], giving a yellow colour with tetranitromethane–chloroform. The acetate (20 mg.) was unchanged (m. p. and mixed m. p. 75—76°) by treatment with dry hydrogen chloride in chloroform (25 c.c.) containing ethanol (0·2 c.c.) at −5° for 1 hr.

Cholest-4-en-6α-ol (XX; R = H).—6β-Acetoxycholest-4-ene (700 mg.) was hydrolysed by treatment with lithium aluminium hydride in ether; working up in the usual way furnished an

oil, which crystallised from acetone, to give *cholest-4-en-6β-ol*, m. p. 86—87°, $[\alpha]_D$ +62° (*c*, 0·9) [Found (after drying at 60°/0·01 mm. for 2 hr.) : C, 83·2; H, 11·7. $C_{27}H_{46}O$ requires C, 83·8; H, 11·9%], giving a yellow colour with tetranitromethane–chloroform.

6β-*Methoxycholest-4-ene* (XXI).—Cholest-4-en-6β-ol (216 mg.) was heated in an atmosphere of nitrogen with " molecular " potassium (~200 mg.) in benzene for 1 hr., and then with methyl iodide (5 c.c.) for 3 hr. The product obtained by working up was purified by elution from aluminium oxide with pentane, to yield 6β-methoxycholest-4-ene, m. p. 97—98°, $[\alpha]_D$ +83° (*c*, 0·7) [Found (after drying at 60°/0·01 mm. for 2 hr.) : C, 83·5; H, 11·8. $C_{28}H_{48}O$ requires C, 83·9; H, 12·0%], giving a yellow colour with tetranitromethane in chloroform, and identical with the material isolated by Evans and Shoppee (*loc. cit.*).

6β-*Methoxycoprostane* (XXV).—6β-Methoxycholest-4-ene (77 mg.), dissolved in ethyl acetate (10 c.c.) containing acetic acid (2 c.c.), was shaken with platinum oxide (62 mg.) in hydrogen for 1 hr.; after working up and removal of traces of solvents and moisture by repeated evaporation with benzene in a vacuum, the residual oil (75 mg.) failed to crystallise. Chromatography on a long column of aluminium oxide (5 g.; activated at 250—310° for 1 hr.) prepared in pentane, and elution with pentane (2 × 5 c.c.) gave cholestane (7 mg.), m. p. and mixed m. p. 78—79°; further elution with pentane (6 × 5 c.c.) gave 6β-*methoxycoprostane* (67 mg.), m. p. 64—65°, $[\alpha]_D$ +9°, +11° (*c*, 0·4, 0·6), after recrystallisation from acetone [Found (after drying at 20°/0·01 mm. for 3 hr.) : C, 83·6; H, 12·6. $C_{28}H_{52}O$ requires C, 83·5; H, 12·5%].

6β-*Methoxycholestane*.—Cholestan-6β-ol (106 mg.), prepared by the method of Shoppee and Summers (*J.*, 1952, 3361), was methylated with potassium and methyl iodide in boiling benzene. The product, purified by elution from aluminium oxide with benzene–pentane (1 : 9), yielded 6β-methoxycholestane (40 mg.), double m. p. 52° and 77°, $[\alpha]_D$ +14° (*c*, 1·7) after recrystallisation from acetone [Found (after drying at 20°/0·01 mm. for 4 hr.) : C, 83·3; H, 12·2%].

Coprostan-6β-ol (XXIV; R = H).—(*a*) Cholest-4-en-6β-ol (750 mg.) was hydrogenated with platinum oxide (100 mg.) in ethyl acetate (20 c.c.) containing <1% of 60% perchloric acid. The product was purified by chromatography on aluminium oxide (22 g.) prepared in pentane; repeated elution with pentane gave cholestane (300 mg.), m. p. and mixed m. p. 80°, after recrystallisation from acetone. Elution with ether–benzene (1 : 4; 6 × 50 c.c.) gave *coprostan-6β-ol* (375 mg.), $[\alpha]_D$ +21° (*c*, 1·1) [Found (after distillation at 130°/0·01 mm.) : C, 83·3; H, 12·35. $C_{27}H_{48}O$ requires C, 83·4; H, 12·45%], which did not crystallise. The *acetate*, prepared by use of acetic anhydride in pyridine at 20°, crystallised readily from acetone–methanol in plates, m. p. 109—111°, $[\alpha]_D$ +22° (*c*, 0·55) [Found (after drying at 70°/0·01 mm. for 4 hr.) : C, 80·5; H, 11·85. $C_{29}H_{50}O_2$ requires C, 80·85; H, 11·7%], and exhibited infrared absorption bands at 1730 and 1242 cm.$^{-1}$. The acetate was also obtained by hydrogenation of 6β-acetoxycholest-4-ene (170 mg.) in ethyl acetate (15 c.c.) containing 60% perchloric acid (3 drops) with platinum oxide (101 mg.); the resultant oil (171 mg.) by chromatography on aluminium oxide and elution with pentane gave cholestane (30 mg.), m. p. and mixed m. p. 77—78°, whilst use of benzene–pentane (1 : 9) gave a solid (135 mg.) which by crystallisation from methanol gave coprostan-6β-yl acetate, m. p. and mixed m. p. 108—110°.

(*b*) Coprostane-3β : 6β-diol, prepared following Prelog and Tagmann's directions (*loc. cit.*), was converted into the diacetate, m. p. 137—139°, $[\alpha]_D$ +13°. The diacetate (2 g.) was refluxed with potassium hydroxide (5 g.) in methanol (750 c.c.) for 2 hr.; the solution was cooled, acidified to Congo-red with concentrated hydrochloric acid, neutralised with aqueous ammonia, concentrated in a vacuum, and allowed to cool. The concentrate was diluted with water and extracted with ether, and the ethereal extract dried and evaporated. The product was dissolved in benzene (40 c.c.), pentane (360 c.c.) added, and the solution set aside for 30 min.; coprostane-3β : 6β-diol (530 mg.), m. p. and mixed m. p. 198—200°, was removed by filtration, and the filtrate chromatographed on a column of aluminium oxide (60 g.) prepared in pentane. Elution with chloroform gave 6β-*acetoxycoprostan-3β-ol* (1·13 g.), m. p. 144°, $[\alpha]_D$ +11° (*c*, 0·9), after recrystallisation from acetone [Found (after drying at 55°/0·01 mm. for 6 hr.) : C, 78·0; H, 11·3. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%], whilst elution with methanol yielded coprostane-3β : 6β-diol (200 mg.), m. p. and mixed m. p. 198—200° after recrystallisation from ethyl acetate. 6β-Acetoxycoprostan-3β-ol (1 g.), dissolved in acetic acid (75 c.c.), was treated with chromium trioxide (200 mg.) in 96% acetic acid (25 c.c.) for 16 hr. at 20°. After evaporation at 30—35°/10 mm., the usual working-up gave an oil (972 mg.) which crystallised and then had m. p. 104—109°; purification by elution from aluminium oxide (30 g.) with benzene–pentane mixtures and recrystallisation from ethanol afforded 6β-*acetoxycoprostan-3-one*, m. p. 113—115°, $[\alpha]_D$ +20° (*c*, 2·57) [Found (after drying at 90°/0·01 mm. for 6 hr.) : C, 78·5; H, 11·1.

$C_{29}H_{48}O_3$ required C, 78·3; H, 10·9%]. The acetate (300 mg.) was refluxed with hydrazine (1 c.c.) and potassium hydroxide (600 mg.) in ethanol (25 c.c.) for 30 min.; ethylene glycol (20 c.c.) was added, aqueous ethanol (28 c.c.) removed by distillation, and the temperature raised to 196°. After refluxing at 196° for 3 hr., the mixture was allowed to cool, poured into water, and worked up in the usual manner. The resultant brown oil (231 mg.) was chromatographed on neutralised aluminium oxide (8 g.) in pentane; elution with benzene gave a colourless oil (211 mg.). To remove any ketonic material, the oil was dissolved in ethanol–acetic acid (9 : 1; 25 c.c.) and refluxed with Girard's reagent T (200 mg.) for 0·5 hr.; the cooled mixture was poured into water and extracted with ether, and the ethereal extract washed with 2N-sodium carbonate, dried, and evaporated. The product was chromatographed on neutralised aluminium oxide (6 g.) in pentane; repeated elution with pentane gave an oil (18 mg.), which did not crystallise and was discarded, whilst elution with benzene–pentane gave coprostan-6β-ol (180 mg.) as a colourless oil, $[\alpha]_D$ +21°; this did not crystallise, but by acetylation as usual at 25° for 14 hr. gave coprostan-6β-yl acetate, m. p. 100—105°, which after recrystallisation from acetone–methanol had m. p. and mixed m. p. 109—111°, $[\alpha]_D$ +22·5°.

Coprostan-6-one (XXVIII).—Coprostan-6β-ol [420 mg.; preparation (*a*)] was dissolved in acetic acid (15 c.c.) and treated with a 2% solution of chromium trioxide in acetic acid (9 c.c.) at 20° for 18 hr. After evaporation at 30—35°/10 mm., and isolation in the usual way the product (390 mg.) crystallised rapidly, and by recrystallisation from acetone gave *coprostan-6-one*, m. p. 133°, $[\alpha]_D$ −44° (*c*, 1·05) [Found (after drying at 70°/0·01 mm. for 4 hr.): C, 84·0; H, 11·95. $C_{27}H_{46}O$ requires C, 84·0; H, 12·0%]. Similarly coprostan-6β-ol [52 mg.; preparation (*b*)] by oxidation gave a product (50 mg.), m. p. 125—130°, which, thrice recrystallised from acetone, furnished coprostan-6-one, m. p. and mixed m. p. 133°. The ketone by reduction with lithium aluminium hydride in ether gave a non-crystalline product, which by acetylation as usual at 20° for 16 hr. gave coprostan-6β-yl acetate, m. p. and mixed m. p. 109—111°.

Coprostan-6-one (20 mg.) was refluxed with 1·5% methanolic potassium hydroxide (5 c.c.) for 0·5 hr.; after saturation with carbon dioxide, evaporation in a vacuum, and addition of water, the product was extracted with ether. The resultant oil (20 mg.) crystallised and by recrystallisation from acetone yielded cholestan-6-one, m. p. and mixed m. p. 95—96°, $[\alpha]_D$ −2°. Coprostan-6-one (20 mg.) was refluxed with acetic acid (1 c.c.) containing concentrated hydrochloric acid (1 drop) for 0·5 hr.; the mixture was diluted with water and extracted with ether. The ethereal extract was washed with water and with 2N-sodium carbonate, dried, and evaporated, to give cholestan-6-one, m. p. and mixed m. p. 95—96°. Coprostan-6-one (20 mg.), dissolved in moist benzene (5 c.c.), was introduced on a column of aluminium oxide (1 g.) prepared in pentane; after 16 hr. elution with benzene gave cholestan-6-one, m. p. and mixed m. p. 95—96°.

Reaction of Coprostan-6β-ol with Thionyl Chloride: *6ξ-Chlorocoprostane* (XXVII).—Coprostan-6β-ol (100 mg.), dissolved in pyridine (10 c.c.), was treated with thionyl chloride (0·5 c.c.) at 0°, and the mixture set aside at 20° for 0·5 hr. The usual working-up gave an oil (82 mg.), which was purified by filtration of a pentane solution through a column of aluminium oxide; the product on crystallisation from acetone gave *6ξ-chlorocoprostane*, m. p. 85°, $[\alpha]_D$ −59° (*c*, 1·2) [Found (after drying at 50°/0·01 mm. for 3 hr.): C, 79·45; H, 11·4. $C_{27}H_{47}Cl$ requires C, 79·65; H, 11·6%].

Reduction of 6ξ-Chlorocoprostane with Sodium and Pentyl Alcohol.—6ξ-Chlorocoprostane (80 mg.) was dissolved in pentyl alcohol (25 c.c.), and sodium (1 g.) gradually added to the refluxing solution. After 3 hr., the solution was worked up in the usual way, yielding coprostane, m. p. and mixed m. p. 70—71°.

Cholestane-5 : 6α-diol (XXXII).—Cholest-5-ene (1·03 g.), in ether (50 c.c.) was treated with osmium tetroxide (1 g.) in ether (10 c.c.) containing pyridine (2 c.c.); after 63 hr. at 20°, ether was removed by evaporation and the product refluxed with aqueous-ethanolic sodium sulphite for 3 hr. The solution was then filtered through charcoal, evaporated to dryness in a vacuum, and shaken with ether and 3N-sodium hydroxide containing mannitol; the ethereal layer was separated, washed with water, dried, and evaporated, to give *cholestane-5 : 6α-diol* (950 mg.), m. p. 180—181°, $[\alpha]_D$ +15° (*c*, 1·0), after recrystallisation from acetone [Found (after drying at 100°/0·01 mm. for 2 hr.): C, 80·1; H, 11·85. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·95%]. The *6α-monoacetate*, prepared as usual at 20° and purified by filtration of a benzene–pentane solution through a layer of aluminium oxide, had m. p. 117—118°, $[\alpha]_D$ +24° (*c*, 1·0), after recrystallisation from acetone–methanol [Found (after sublimation at 120°/0·01 mm.): C, 78·0; H, 11·2. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%]. The 5 : 6α-diol with refluxing acetyl chloride and dimethylaniline in purified chloroform gave 5 : 6α-diacetoxycholestane as an oil, $[\alpha]_D$

+43° (*c*, 0·9), which did not crystallise, although hydrolysis with lithium aluminium hydride in ether regenerated the 5 : 6α-diol, m. p. and mixed m. p. 180—181°.

6α-*Acetoxycholest-4-ene* (XXXIII; R = Ac).—6α-Acetoxycholestan-5-ol (420 mg.) in pyridine (5 c.c.) was treated with thionyl chloride (1·0 c.c.) at 0°; after 0·5 hr. at 20°, the product was isolated in the usual way and purified by chromatography on aluminium oxide. Elution with pentane gave 6α-*acetoxycholest-4-ene*, m. p. 95—98°, $[\alpha]_D$ +78·5° (*c*, 0·5), after crystallisation from acetone [Found (after drying at 60°/0·01 mm. for 3 hr.) : C, 80·95; H, 11·4. $C_{29}H_{48}O_2$ requires C, 81·25; H, 11·3%], giving a yellow colour with tetranitromethane in chloroform. In a second run, 6α-acetoxycholestan-5-ol (346 mg.) on treatment with thionyl chloride (1·3 c.c.) in pyridine (5 c.c.) at 0°, gave 6α-acetoxycholest-4-ene (310 mg.), m. p. 95—98°, after recrystallisation from methanol.

Cholest-4-en-6α-ol (XXXIII; R = H).—(*a*) 6α-Acetoxycholest-4-ene (410 mg.) was refluxed with 5% methanolic potassium hydroxide (25 c.c.) for 1 hr.; after saturation with carbon dioxide and evaporation in a vacuum, the usual procedure gave *cholest-4-en-6α-ol* (390 mg.), m. p. 139—140°, $[\alpha]_D$ +64° (*c*, 0·55), after recrystallisation from acetone [Found (after drying at 100°/0·01 mm. for 2 hr.) : C, 83·55; H, 11·8. $C_{27}H_{46}O$ requires C, 83·8; H, 12·0%], giving a yellow colour with tetranitromethane–chloroform.

(*b*) 6α-Acetoxycholest-4-ene (230 mg.) in ether (25 c.c.) was treated with excess of lithium aluminium hydride at 36° for 2 hr. The usual working up afforded a solid, m. p. 136—140°, which by recystallisation from acetone–methanol yielded cholest-4-en-6α-ol, m. p. 140—143°, mixed m. p. 140—142°.

(*c*) Cholest-4-en-6-one (XXXI) (121 mg.) in ether (25 c.c.) was treated with excess of lithium aluminium hydride at 36° for 30 min. The usual processing furnished a solid (118 mg.), m. p. 115—125°. Elution from aluminium oxide (6 g.) with benzene gave a little oil (discarded), whereafter elution with ether gave cholest-4-en-6α-ol (92 mg.), m. p. and mixed m. p. 140—141°. In a second experiment, cholest-4-en-6-one (120 mg.) was treated with lithium aluminium hydride in ether (20 c.c.) for 15 min. at 36°. The product, isolated in the usual way, by crystallisation from acetone–methanol gave cholest-4-en-6α-ol (110 mg.), m. p. 139—142°, mixed m. p.140—141°.

6α-*Methoxycholest-4-ene* (XXXIV).—Cholest-5-en-6α-ol (64 mg.) by methylation in an atmosphere of nitrogen with potassium and methyl iodide in boiling benzene gave only cholesta-3 : 5-diene (40 mg.), m. p. and mixed m. p. 76—78° after crystallisation from acetone. The stenol (175 mg.) was converted into the potassium derivative by vigorous agitation with " molecular " potassium in benzene at 30—35°; methyl iodide (5 c.c.) was added and shaking continued at 35° for 3 hr. The usual working-up gave a product, which by chromatography on aluminium oxide (5 g.) and elution with pentane yielded an oil (65 mg.), which failed to crystallise on inoculation with cholesta-3 : 5-diene. The oil was rechromatographed on a long column of aluminium oxide (activated at 250—310° for 1 hr.) prepared in pentane; elution with pentane (4 × 100 c.c.) furnished cholesta-3 : 5-diene (29 mg.), m. p. and mixed m. p. 79—80°, after crystallisation from acetone, but elution with benzene–pentane (1 : 9; 3 × 10 c.c.) gave 6α-methoxycholest-4-ene (35 mg.), $[\alpha]_D$ +20° (*c*, 1·16), which did not cystallise and at 70° decomposed to give cholesta-3 : 5-diene.

Coprostan-6α-ol (XXX; R = H).—(*a*) Cholest-4-en-6α-ol (225 mg.) was hydrogenated with platinum oxide (55 mg.) in ethyl acetate (21 c.c.) containing 60% perchloric acid (1 drop). The theoretical amount of hydrogen was absorbed in 15 min. and the product purified by chromatography on a column of aluminium oxide (5 g.) prepared in pentane; elution with pentane gave cholestane (15 mg.), m. p. and mixed m. p. 79°, after crystallisation from acetone. Elution with ether–benzene (1 : 9) gave coprostan-6α-ol, $[\alpha]_D$ +18° (*c*, 0·7), which did not crystallise, whilst the acetate, $[\alpha]_D$ +23° (*c*, 1·57), prepared as usual at 20°, also failed to crystallise after chromatography on aluminium oxide, elution with pentane, and distillation in a high vacuum.

(*b*) 6α-Acetoxycholest-4-ene (68 mg.) was hydrogenated with platinum oxide (48 mg.) in ethyl acetate (10 c.c.) containing acetic acid (5 c.c.) for 1 hr. The usual working-up gave an oil (67 mg.) which was chromatographed on chromium oxide (2 g.) prepared in pentane. Elution with pentane yielded cholestane (9 mg.), m. p. and mixed m. p. 78° after crystallisation from acetone, whilst elution with benzene–pentane (1 : 9) gave 6α-acetoxycoprostane (XXX; R = Ac) (56 mg.) as an oil, $[\alpha]_D$ +23° (*c*, 1·0), hydrolysed by methanolic potassium hydroxide to coprostan-6α-ol, an oil, $[\alpha]_D$ +18° (*c*, 0·7).

Coprostan-6α-ol (130 mg.) in acetic acid (2 c.c.) was oxidised with chromium trioxide (50 mg.) in 98% acetic acid (2 c.c.) at 20° to coprostan-6-one, m. p. and mixed m. p. 132—134° after two recrystallisations from acetone.

Reaction of Coprostan-6α-ol (XXX; R = H) *with Thionyl Chloride.*—Coprostan-6α-ol (150 mg.) in pyridine (10 c.c.) was treated with thionyl chloride (0·75 c.c.) at 0°; the mixture, after 0·5 hr. at 20°, was worked up in the usual way. The resultant oil was chromatographed on aluminium oxide (6 g.) in pentane; elution with pentane (2 × 5 c.c.) gave cholest-5-ene (37 mg.), m. p. and mixed m. p. 94—95°, after crystallisation from acetone. Further elution with pentane yielded a viscous oil (105 mg.), which gave no colour with tetranitromethane in chloroform, contained sulphur, and probably consisted of coprostan-6α-yl sulphite.

5-Hydroxycholestan-6-one (XXXVI).—Prepared from cholestane-5 : 6β-diol by oxidation with *N*-bromosuccinimide, the ketol had m. p. 153° (cf. Reich, Walker, and Collins, *loc. cit.*).

Dehydration.—This material (1·07 g.) was treated in pyridine (20 c.c.) with thionyl chloride (4 c.c.) at 0°; the solution at once became deep-red, and after 0·5 hr. at 20° was poured into ice and 3N-hydrochloric acid. The product, isolated in the usual way and purified by elution from aluminium oxide (100 g.) with pentane, gave cholest-4-en-6-one (450 mg.), m. p. 106—108° after recrystallisation from acetone–methanol, giving a yellow colour with tetranitromethane–chloroform.

Reduction of 5-Hydroxycholestan-6-one (XXXVI).—(*a*) *With lithium aluminium hydride.* The ketol (30 mg.) was treated with lithium aluminium hydride in ether (5 c.c.) at 36° for 0·5 hr.; the product, isolated in the usual way and crystallised from aqueous acetone, gave cholestane-5 : 6β-diol, m. p. and mixed m. p. 123—125°.

(*b*) *With sodium and propan-1-ol.* The ketol (1·1 g.) in boiling propanol (90 c.c.) was treated gradually with sodium (7 g.), and the solution refluxed for 4 hr. The usual working-up gave an oil (1·05 g.), which was chromatographed on aluminium oxide (35 g.) prepared in pentane. Elution with benzene–pentane (1 : 1; 5 × 100 c.c.) yielded cholestan-6α-ol (283 mg.), m. p. 130°, $[\alpha]_D$ +37° (*c*, 0·5), after recrystallisation from acetone; it was characterised as the acetate, m. p. 78—79°, $[\alpha]_D$ +74° (*c*, 0·6). Elution with ether–benzene (1 : 1; 4 × 100 c.c.) gave cholestane-5 : 6α-diol, m. p. and mixed m. p. 180—181°, after recrystallisation from acetone; this was characterised as the 6α-monoacetate, m. p. and mixed m. p. 117—118° (from acetone–methanol). Finally, elution with ether afforded *coprostane-5 : 6α-diol*, m. p. 141—142°, $[\alpha]_D$ +31° (*c*, 0·8), after recrystallisation from acetone [Found (after drying at 100°/0·01 mm. for 2 hr.): C, 80·1; H, 12·1. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·95%]; acetylation as usual at 20° gave 6α-acetoxycoprostan-5-ol, $[\alpha]_D$ +33° (*c*, 0·9) after chromatographic purification, which did not crystallise.

5-Hydroxycoprostan-6-one (XXXVIII).—Coprostane-5 : 6α-diol (35 mg.) in acetic acid (6 c.c.) was treated with chromium trioxide (20 mg.) in 98% acetic acid (1·0 c.c.) at 20° for 12 hr. The usual working-up afforded an oil, which crystallised on trituration with acetone and on recrystallisation from acetone gave *5-hydroxycoprostan-6-one*, m. p. 102—103°, $[\alpha]_D$ −18° (*c*, 0·6) [Found (after drying at 70°/0·01 mm. for 3 hr.): C, 78·5; H, 11·35. $C_{27}H_{46}O_2,\frac{1}{2}H_2O$ requires C, 78·75; H, 11·5%]. The ketol, on reduction with lithium aluminium hydride in ether, regenerated coprostane-5 : 6α-diol, m. p. and mixed m. p. 139—141°.

Dehydration of 6α-Acetoxycoprostan-5-ol to 6α-Acetoxycholest-4-ene (XXXIII; R = Ac).—6α-Acetoxycoprostan-5-ol (57 mg.), dissolved in pyridine (1 c.c.), was treated with thionyl chloride (0·25 c.c.) at 0°; after 0·5 hr. at 20°, the mixture was worked up in the usual manner. The product was chromatographed on a column of aluminium oxide (1·5 g.) prepared in pentane; elution with pentane gave 6α-acetoxycholest-4-ene, m. p. and mixed m. p. 92—93°.

Attempted Epimerisation of Cholestane-5 : 6α-diol (XXXII) *and Cholestan-5-ol.*—(*a*) The 5α : 6α-diol (67 mg.) was dissolved in boiling propan-1-ol (50 c.c.), and sodium (5 g.) was gradually added; after 4 hours' refluxing, working up gave cholestane-5 : 6α-diol (65 mg.), m. p. and mixed m. p. 175—176°.

(*b*) Cholestan-5-ol (83 mg.), prepared by the method of Plattner, Petrzilka, and Lang (*Helv. Chim. Acta*, 1944, **27**, 513), was dissolved in boiling propanol, and sodium (5 g.) was gradually added; after 4 hours' refluxing, working-up afforded cholestan-5-ol (78 mg.), m. p. and mixed m. p. 97—99°.

Two of us (D. N. J., J. R. L.) acknowledge the financial support of the Department of Scientific and Industrial Research. We thank Glaxo Laboratories Ltd. for gifts of cholesterol and for determination of the infrared spectra.

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