127. *Steroids and Walden Inversion. Part XLII.* 5α-Cholestan-4-one and Some Derivatives thereof.*

By C. W. Shoppee, M. E. H. Howden, R. W. Killick, and G. H. R. Summers.

5α-Cholestan-4-one is readily obtained from cholest-4-ene by rearrangement of the derived 4α : 5α-epoxide to 5β-cholestan-4-one and isomerisation of the latter. The 4β : 5β-epoxide has been prepared and by rearrangement gives 5α-cholestan-4-one.

Bromination of the 5-epimeric cholestan-4-ones affords the same 5-bromo-5α-cholestan-4-one, which in the presence of hydrogen bromide affords 3α-bromo-5α-cholestan-4-one, also obtained by the action of hydrogen bromide on 5-hydroxy-5α-cholestan-4-one. Dibromination of 5α-cholestan-4-one gives 3α : 5-dibromo-5α-cholestan-4-one.

The general symmetry of the steroid 4- and 6-positions suggested that recent studies on 5α-cholestan-6-one [1] and the epimeric 5α-cholestan-6-ols [2] should be paralleled by work on 5α-cholestan-4-one and related compounds.

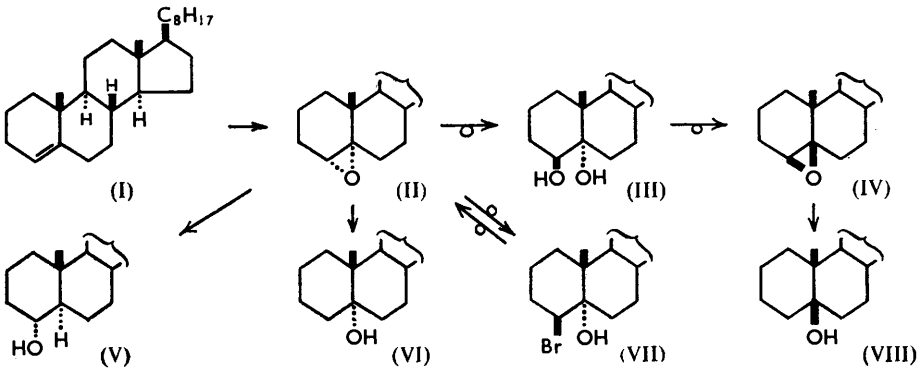
Although 5α-cholestan-4-one (X) was prepared some forty years ago by Windaus [3] from cholest-4-ene (I) by nitration and reduction of the resulting 4-nitrocholest-4-ene with zinc and acetic acid, the yield is poor and the product contaminated with cholest-4-en-3-one and cholest-4-en-6-one. Thus the ketone (X) and its derivatives have been relatively inaccessible and little investigated,[4,5] and we have devised a new and convenient method of preparation.

Cholest-4-ene (I) by treatment with perbenzoic acid gives the 4α : 5α-epoxide (II),[6,7] whose structure follows from its acetolysis [6] to the 4-monoacetate [5,8] of 5α-cholestane-4β : 5-diol (III) and its catalytic hydrogenation [6,7] to a mixture of 5α-cholestan-4α-ol [4,5] (V)

* Part XLI, *J.*, 1959, 345.

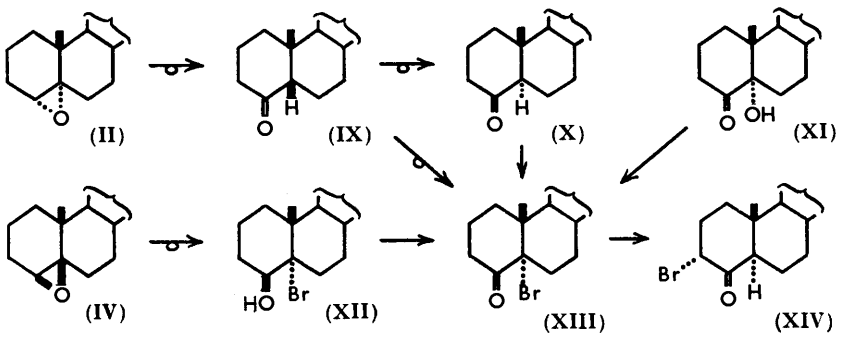
[1] Shoppee, Jenkins, and Summers, *J.*, 1958, 1657.
[2] Shoppee and Summers, *J.*, 1952, 3361; Shoppee and Howden, *Chem. and Ind.*, 1958, 414.
[3] Windaus, *Ber.*, 1920, **53**, 488.
[4] Tschesche and Hagedorn, *Ber.*, 1935, **68**, 2251; Barton and Rosenfelder, *J.*, 1951, 1048.
[5] Shoppee, D. N. Jones, Lewis, and Summers, *J.*, 1955, 2876.
[6] Heilbron, Shaw, and Spring, *Rec. Trav. chim.*, 1938, **57**, 529.
[7] Plattner, Petrzilka, and Lang, *Helv. Chim. Acta*, 1944, **27**, 523.
[8] Bergmann and Skau, *J. Org. Chem.*, 1940, **5**, 439.

and -5-ol [7,9] (VI). The 4α : 5α-epoxide (II) resists reduction with lithium aluminium hydride in ether at 35°, but is smoothly converted in refluxing dioxan into 5α-cholestan-5-ol (VI) (Henbest and Wilson [10] state that the 4α : 5α-epoxide is reduced with this hydride to 5α-cholestan-5-ol but give no experimental details), and by diaxial fission with hydrogen bromide gives the 4β-bromo-5α-alcohol (VII), partially reconverted into the epoxide by treatment with aluminium oxide.



The 4β : 5β-epoxide (IV) is readily prepared from the diacetate [5] of 5α-cholestane-4β : 5-diol (III) by treatment with hot ethanolic potassium hydroxide; it is reduced by lithium aluminium hydride in ether at 36°, presumably by bimolecular substitution [11] [S_N2] with inversion of configuration at $C_{(4)}$, and so with diaxial fission, to 5β-cholestan-5-ol (VIII) in nearly quantitative yield.

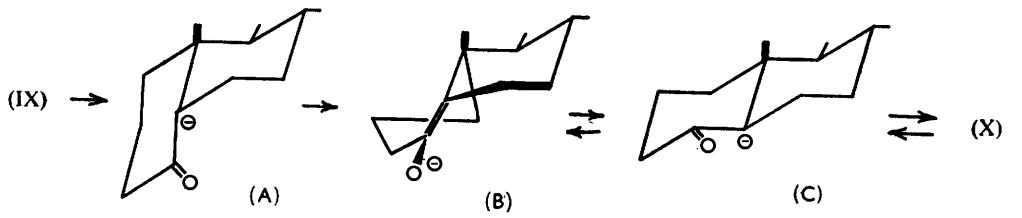
Pinacolic rearrangement of substituted ethylene oxides to ketones can be accomplished by use of acids [12] or electrophilic reagents such as boron trifluoride [13,14] or ferric chloride.[13] Thus the 4α : 5α-epoxide (II) is rearranged by brief treatment with boron trifluoride with inversion of configuration at the migration terminus to give 5β-cholestan-4-one [15] (IX),



readily isomerised by treatment with acid, alkali, or aluminium oxide [5] to the more thermodynamically stable 5α-cholestan-4-one (X). Since this work was done, the same reaction sequence (II ⟶ IX ⟶ X) has been described independently by Henbest and Wrigley.[16]

[9] Fudge, Shoppee, and Summers, *J.*, 1954, 958.
[10] Henbest and Wilson, *J.*, 1957, 1960.
[11] Cram, *J. Amer. Chem. Soc.*, 1952, **74**, 2149, 2152.
[12] Lagrave, *Ann. Chim.* (*France*), 1927, **8**, 363.
[13] Heusser, Eichenberger, Kurath, Dällenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106; Heusser, Anliker, Eichenberger, and Jeger, *ibid.*, 1952, **35**, 936.
[14] Heusler and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 398; Bladon, Henbest, E. R. H. Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.
[15] Stevenson and Fieser, *J. Amer. Chem. Soc.*, 1956, **78**, 1409.
[16] Henbest and Wrigley, *J.*, 1957, 4596.

Monobromination in acetic acid containing a trace of hydrogen bromide at 20° of either 5β- or 5α-cholestan-4-one (IX or X) gives the same 5-bromo-5α-cholestan-4-one (XIII), $[\alpha]_D$ +66°, whose ultraviolet and infrared absorption spectra ($\Delta\lambda_{max.}$ +25 mμ, log ε +0·4; $\Delta\nu_{max.}$ 0) demonstrate the uniquely axial character of the bromine atom. Corey [17] has suggested that axial bromides are the initial products of bromination of ketones; replacement of the axial 5-hydrogen atoms in the ketones (IX) and (X) might therefore appear to lead to epimeric 5-bromo-ketones. The mechanism of the bromination process, however,



permits the energy difference associated with the *cis*- and *trans*-A/B-ring fusions to operate; if we write the carbanions (A, C) theoretically derivable from the ketones (IX, X), then the enolic anion (B) is formed irreversibly from (A) but reversibly from (C). Formation from 5β-cholestan-4-one (IX) of 5-bromo-5α-cholestan-4-one (XIII) shows that the reaction is thermodynamically controlled, and provides a further example of the generalisation that carbanion reductions (protonation,[18] carboxylation,[19] bromination) yield the more thermodynamically stable product.

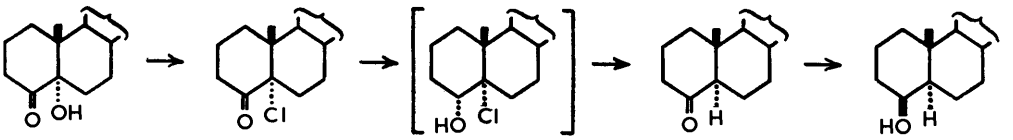
Reduction of the 5α-bromo-ketone (XIII) with sodium borohydride in methanol at 20° yielded a non-crystalline product containing little, if any, of the 5α-bromo-4β-alcohol (XII) and consisting largely or exclusively of the epimeric 5α-bromo-4α-alcohol, since treatment with hot methanolic potassium hydroxide gave a good yield of 5α-cholestan-4-one (X), unaccompanied by the 4β : 5β-epoxide (IV). The crystalline 5α-bromo-4β-alcohol (XII) is obtained from the 4β : 5β-epoxide (IV) by diaxial fission with hydrogen bromide at 20°; the reaction appears to involve protonation, to furnish the conjugate acid of the 4β : 5β-epoxide, the positive pole of which then facilitates bimolecular substitution by a bromine anion at $C_{(5)}$ with inversion of configuration. Oxidation of the 5α-bromo-4β-alcohol (XII) with chromium trioxide–acetic acid at 20° yields the 5α-bromo-ketone (XIII). An attempt to convert the 5α-bromo-ketone (XIII) into the 4β : 5β-epoxide (IV) by treatment with a deficit (0·25 mol.) of lithium aluminium hydride in ether [16,20] failed, possibly on account of the small scale of the experiment.

The 5α-bromo-ketone (XIII) is isomerised by hydrogen bromide in acetic acid at 20° to 3α-bromo-5α-cholestan-4-one (XIV), $[\alpha]_D$ −78°, whose structure follows from its ultraviolet and infrared absorption spectra (Δλ +25 mμ, Δlog ε +0·4; Δν +3 $cm.^{-1}$). The 3α-bromo-ketone (XIV) is also obtained from 5-hydroxy-5α-cholestan-4-one (XI) by treatment with hydrogen bromide in chloroform at 20°, probably as the result of initial formation of the 5α-bromo-ketone (XIII) and subsequent rearrangement. Both the 5α- (XIII) and the 3α-bromo-ketone (XIV) on reduction with zinc–acetic acid regenerate the parent ketone (X).

5-Hydroxy-5α-cholestan-4-one (XI) on treatment with hydrogen chloride in chloroform at 20° furnished a chloro-ketone, which we regard as 5-chloro-5α-cholestan-4-one (XV; Cl, axial) by analogy with the conversion with hydrogen chloride of 5-hydroxy-5α-cholestan-6-one into 5-chloro-5α-cholestan-6-one,[1] and because the hydrogen halides are incapable of causing rearrangement of α-chloro-ketones, *e.g.*, (XV) ⟶ (XIV with Cl for Br).[21] The

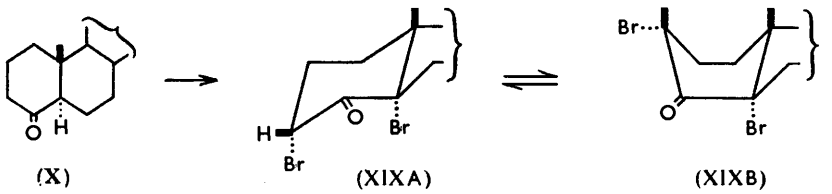
[17] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301; 1954, **76**, 175.
[18] Barton, *Experientia*, 1955, **11**, Suppl. II, 121; Barton and Robinson, *J.*, 1954, 3045.
[19] Roberts and Shoppee, *J.*, 1954, 3418.
[20] E. R. H. Jones, Henbest, Wagland, and Wrigley, *J.*, 1955, 2477.
[21] Ellis and Petrow, *J.*, 1953, 3869; Beereboom and Djerassi, *J. Org. Chem.*, 1954, **19**, 1196.

infrared carbonyl absorption maximum of (XV) shows a displacement of 9 cm.$^{-1}$, compared with that of 4 cm.$^{-1}$ for 5-chloro-5α-cholestan-6-one,[1,22] for which we cannot account;



(XI) (XV) (XVI) (X) (XVII)

however, the ultraviolet absorption is consistent with formula (XV). The chloro-ketone is reduced by sodium borohydride in methanol at 20° to a mixture of 5α-cholestan-4-one



(X) (XIXA) (XIXB)

(X) and -4β-ol (XVII). The ketone may be formed by the easy dehydrochlorination of an intermediate 5α-chloro-4α-alcohol (XVI), or may result from removal of chlorine by attack of BH_4^- on the halogen of the 5α-chloro-ketone [20] to give initially the carbanion (C), of 5α-cholestan-4-one (X). The alcohol is produced by further reduction of the ketone (X), which with lithium aluminium hydride in ether at 15° gives 90% of the 4β-alcohol (XVII) accompanied by 7% of the 4α-alcohol.[5]

[*Amended, October 29th*, 1958.] Dibromination of 5α-cholestan-4-one (X) in acetic acid at 20° gave a dibromo-ketone, reduced by zinc and ethanol to the parent ketone, which we regard as 3α : 5-dibromo-5α-cholestan-4-one (XIX). The carbonyl absorption band was composed of two maxima at 1709 and 1722 cm.$^{-1}$ of nearly equal intensity, which could not completely be resolved. Allinger and Allinger [24] have recently described curves of similar contour for the carbonyl absorption of 2-bromo*cyclo*hexanone; they attribute the twin peaks to an equilibrium in solution of the two (chair) conformational isomers [$\nu_{max.}$ 1742 (bromine equatorial), 1730 (bromine axial); cf. *cyclo*hexanone, $\nu_{max.}$ 1730 cm.$^{-1}$; both in carbon tetrachloride]. We suggest that the 3α : 5α-dibromo-ketone (XIX) exists in solution as an equilibrium mixture of the chair conformation (XIXA) and the boat conformation (XIXB).

Since axial α-bromine atoms do not affect the frequency of the adjacent carbonyl absorption maximum, structure (XIXA) should absorb at ~1712 cm.$^{-1}$ [Δν −3 cm.$^{-1}$; cf. 5 : 7α-dibromo-5α-cholestan-6-one [1] (Δν +2 cm.$^{-1}$) and its 3β-acetoxy-derivative [25] (Δν −3 cm.$^{-1}$)]; a boat-equatorial α-bromine atom increases the frequency of the adjacent carbonyl absorption maximum,[26] so that structure (XIXB) should absorb at ~1722 cm.$^{-1}$ [Δν +10 cm.$^{-1}$]. The ultraviolet absorption spectrum of (XIX) showed a maximum at 312 mμ, log ε 2·1 [(XIXB) bromine axial: Δλ +27 mμ, Δ log ε +0·6] with some indication of a point of inflexion at ~340 mμ [(XIXA) : 2 bromine atoms diaxial : Δλ ~+55 mμ].

The existence of an equilibrium (XIXA ⇌ XIXB) may reasonably be attributed to reduction of the large steric repulsion of the diaxial 3α- and 5α-bromine atoms in (XIXA) at the expense of some increase of dipolar repulsion between the equatorial 3α-bromine–carbon bond and the 4-carbonyl group and of the steric repulsion of the 3β-hydrogen atom and the 10β-methyl group in (XIXB).

[22] Cummins and Page, *J.*, 1957, 3847.
[23] Henbest and Hallsworth, *J.*, 1957, 4604.
[24] Allinger and Allinger, *Tetrahedron*, 1958, **2**, 64.
[25] Cookson, *J.*, 1954, 282.
[26] Barton, Lewis, and McGhie, *J.*, 1957, 2907.

Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ are in $CHCl_3$; ultraviolet absorption spectra were determined on a Hilger Uvispek spectrophotometer in EtOH and infrared absorption spectra on a Perkin-Elmer Model 21 double-beam instrument, or a Grubb-Parsons double-beam grating instrument, in CCl_4.

5α-Cholestan-5-ol.—4α : 5-Epoxy-5α-cholestane [m. p. 100—101° (from ethanol), $[\alpha]_D$ +80° (*c* 1·1)] (235 mg.) in dioxan (30 c.c.) was refluxed with lithium aluminium hydride (200 mg.) for 4 hr. The usual isolation procedure gave 5α-cholestan-5-ol (158 mg., 68%), m. p. 106—108°, $[\alpha]_D$ +12° (*c* 1·8), $\nu_{max.}$ 3605 cm.$^{-1}$ (OH), after two crystallisations from aqueous acetone [Found: (after drying at 50°/0·5 mm. for 48 hr.): C, 83·5; H, 12·4. Calc. for $C_{27}H_{48}O$: C, 83·4; H, 12·4%].

4β-Bromo-5α-cholestan-5-ol.—4α : 5-Epoxy-5α-cholestane (246 mg.) in acetic acid (5 c.c.) and a little ether was treated with a 2% solution of hydrogen bromide in acetic acid (7·5 c.c.) at 20° for 2 hr. The solution was poured into sodium hydrogen carbonate solution, and worked up to give the *4β-bromo-5α-alcohol* (270 mg.), m. p. 108° [Found: Br, 17·0. $C_{27}H_{47}OBr$ requires Br, 17·1%], which decomposed on attempted crystallisation from ethanol or acetone. Chromatography on alkaline aluminium oxide gave some 4α : 5-epoxy-5α-cholestane, m. p. and mixed m. p. 97—99°.

4β : 5-Epoxy-5β-cholestane.—5α-Cholestane-4β : 5α-diol diacetate (m. p. 157—158°, cf. lit.,[5] 147—148°; 1·6 g.) in ethanol (80 c.c.) was refluxed with potassium hydroxide (2 g.) for 2·5 hr. The usual isolation procedure gave a yellow oil, whose pentane solution by filtration through deactivated aluminium oxide and evaporation, and crystallisation from ether–methanol gave *4β : 5-epoxy-5β-cholestane*, m. p. 60—62°, $[\alpha]_D$ +3·5° (*c* 1·45) [Found (after drying at 20°/0·02 mm. for 2 hr.): C, 84·0; H, 11·9. $C_{27}H_{46}O$ requires C, 83·9; H, 12·0%].

5β-Cholestan-5-ol.—4β : 5-Epoxy-5β-cholestane (200 mg.) was refluxed in ether with excess of lithium aluminium hydride for 0·5 hr. The usual isolation procedure gave an oil, which was chromatographed on a column of aluminium oxide (6 g.) prepared in pentane. Elution with ether gave a colourless oil (180 mg.), which by crystallisation from pentane and recrystallisation from methanol gave 5β-cholestan-5-ol, m. p. 82—84°, $[\alpha]_D$ +35° (*c* 0·9) (lit.,[23] m. p. 81—82°, $[\alpha]_D$ +37°).

5-Bromo-5α-cholestan-4β-ol.—4β : 5-Epoxy-5β-cholestane (350 mg.) in acetic acid (6 c.c.) and a little ether was treated with a 2% solution of hydrogen bromide in acetic acid (8 c.c.) at 20° for 2 hr. The crystalline product was filtered off, dried, and recrystallised from acetone, to afford *5-bromo-5α-cholestan-4β-ol*, m. p. 104—106°, $[\alpha]_D$ +40° (*c* 0·8) [Found (after drying at 20°/0·02 mm. for 2 hr.): C, 69·3; H, 10·1. $C_{27}H_{47}OBr$ requires C, 69·35; H, 10·1%].

5β-Cholestan-4-one.—4α : 5-Epoxy-5α-cholestane (300 mg.; dried by azeotropic distillation with benzene at 10 mm.) in benzene (15 c.c.) was treated with a solution of boron trifluoride–ether complex (0·3 c.c.) in benzene at 20° for 3 min. After addition of ice-cold sodium hydrogen carbonate solution, the benzene solution was separated, washed with water, dried, and evaporated at 10 mm. to yield 5β-cholestan-4-one (150 mg.), m. p. 109°, $[\alpha]_D$ +40° (*c* 1·0), after recrystallisation from acetone (lit.,[15,23] m. p. 109—110°, 108—110°, $[\alpha]_D$ +40·5°, +38°, +44°).

5α-Cholestan-4-one.—(*a*) 4β : 5-Epoxy-5β-cholestane (100 mg.), on brief treatment in benzene with boron trifluoride–ether as above, gave 5α-cholestan-4-one (60 mg.), m. p. and mixed m. p. 96—98° (from acetone).

(*b*) 5β-Cholestan-4-one [crude product from rearrangement of 4α : 5-epoxy-5α-cholestane (3 g.) with boron trifluoride–ether] was refluxed in methanol with a trace of sodium methoxide for 0·5 hr. After partial removal of methanol in a vacuum, the residue was diluted, and extracted with ether to give, after the usual working up, 5α-cholestan-4-one (1·3 g.), m. p. and mixed m. p. 96—98° with a genuine specimen prepared by Windaus's method,[3] after crystallisation from acetone. The ketone exhibited $\lambda_{max.}$ 285 mμ (log ε 1·7), $\nu_{max.}$ 1712 cm.$^{-1}$.

5-Bromo-5α-cholestan-4-one.—(*a*) 5α-Cholestan-4-one (250 mg.) in acetic acid (30 c.c.) was treated with bromine (110 mg., 1·06 mol.) in acetic acid (2 c.c.) and a few drops of a solution of hydrogen bromide in acetic acid, and kept at 20° for 0·5 hr. The colourless solution, after the usual working up and two recrystallisations from ethanol, yielded *5-bromo-5α-cholestan-4-one* (100 mg.), m. p. 143—145°, $[\alpha]_D$ +66° (*c* 1·6), $\lambda_{max.}$ 307 mμ (log ε 2·1), $\lambda_{max.}$ 1712 cm.$^{-1}$ (in $CHCl_3$, 1706 cm.$^{-1}$) [Found (after drying at 20°/1 mm. for 17 hr.): C, 69·6; H, 9·7.

$C_{27}H_{45}OBr$ requires C, 69·6; H, 9·7%]. Another preparation had m. p. 144—147°. The material from the mother-liquor of various preparations, by chromatography on aluminium oxide (Woelm, neutral) in hexane, elution with benzene–hexane (1 : 9), and recrystallisation from ethanol, gave a polymorphic form of *5-bromo-5α-cholestan-4-one*, m. p. 125—128°, $[\alpha]_D$ +60° (*c* 1·1), λ_{max} 1712 cm.$^{-1}$ [Found (after drying at 20°/1 mm. for 6 hr.): C, 70·0; H, 9·6%]; elution with benzene–hexane (1 : 4 and 1 : 2) gave 5α-cholestan-4-one, m. p. and mixed m. p. 95°; elution with ether–benzene gave non-crystalline material.

(*b*) 5-Bromo-5β-cholestan-4-one (250 mg.) in acetic acid (30 c.c.) was treated dropwise with a solution of bromine (1·06 mol.) in acetic acid as under (*a*). After 0·5 hr. the solution was worked up by dilution and extraction with ether to give the 5α-bromo-ketone, m. p. and mixed m. p. 144° (from acetone).

(*c*) 5-Bromo-5α-cholestan-4β-ol (m. p. 104—106°; 100 mg.) in acetic acid (2 c.c.) was oxidised with a 2% solution of chromium trioxide in acetic acid (1·5 c.c.) at 20° for 3 hr. The crystalline product was filtered off, washed with a little acetic acid, dried briefly in a vacuum, and recrystallised from acetone or from ethanol, to give 5-bromo-5α-cholestan-4-one, m. p. ~127° after change of crystal form and partial melting at 110—114°, $[\alpha]_D$ +63° (*c* 1·1), $\nu_{max.}$ 1712 cm.$^{-1}$. In a repetition, the material which crystallised from the reaction mixture appeared to be a solvated form, m. p. <80° with partial transformation into plates, m. p. ~132°, $[\alpha]_D$ +60° (*c* 1·1), $\nu_{max.}$ 1712 cm.$^{-1}$, the infrared absorption spectrum being identical with that of the product of m. p. ~127° and that of the forms of m. p. 145° and 125° described under (*a*).

Reduction of 5-Bromo-5α-cholestan-4-one with Sodium Borohydride.—The bromo-ketone (520 mg.) in 98% methanol (30 c.c.) was treated with sodium borohydride (300 mg.) at 20° overnight. The usual isolation procedure furnished an oil (510 mg.), which was chromatographed on a column of aluminium oxide (15 g.) prepared in hexane. Elution with benzene–hexane gave halogen-free oils. Elution with benzene and ether–benzene gave halogen-containing oils, which were united (207 mg.) and refluxed with 2% methanolic potassium hydroxide for 4 hr.; the usual working up gave an oil (160 mg.), which by chromatography on aluminium oxide (5 g.) in hexane and elution with hexane (5 × 16 c.c.) gave 5α-cholestan-4-one (132 mg.), m. p. and mixed m. p. 96—98°, $\nu_{max.}$ 1713 cm.$^{-1}$.

3α-Bromo-5α-cholestan-4-one.—(*a*) 5-Bromo-5α-cholestan-4-one (123 mg.) in acetic acid (12·5 c.c.) was treated with a 50% solution of hydrogen bromide in acetic acid (2·5 c.c.) at 20° for 40 hr. After addition of water, the product was isolated with ether and chromatographed on aluminium oxide (3·5 g.) in hexane. Elution with hexane gave 3α-bromo-5α-cholestan-4-one, m. p. 115°.

(*b*) 5-Hydroxy-5α-cholestan-4-one [5] (m. p. 159°; 500 mg.) in chloroform was treated with a stream of dry hydrogen bromide at 20° for 2 hr. Next morning the dark red solution gave by the usual isolation procedure an oil, which was chromatographed on aluminium oxide (15 g.; Woelm, neutral) in pentane. Elution with pentane (2 × 50 c.c.) gave two crystalline fractions (213 mg., 27 mg.), which were united and repeatedly recrystallised from acetone, to yield *3α-bromo-5α-cholestan-4-one* (95 mg.), m. p. 117—119° (remelt 117—120°), $[\alpha]_D$ −78° (*c* 0·8), $\nu_{max.}$ 1715 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ (log ε 2·0) [Found (after drying at 20°/0·05 mm. for 16 hr.): C, 69·1; H, 9·6. $C_{27}H_{45}OBr$ requires C, 69·6; H, 9·7%]. Further elution with pentane (2 × 50 c.c.) gave two oily fractions, which on reduction with zinc in acetic acid gave 5α-cholestan-4-one.

3α : 5-Dibromo-5α-cholestan-4-one.—5α-Cholestan-4-one (300 mg.) in acetic acid (30 c.c.) was treated with a solution of bromine (255 mg., 2·05 mol.) in acetic acid in the presence of a little hydrogen bromide at 20°. After 2 hr. dropwise addition of a little water gave a precipitate of needles; after 15 min. the crystals were filtered off, washed with water, and dried. Two recrystallisations from acetone gave *3α : 5-dibromo-5α-cholestan-4-one* (124 mg.), m. p. 151—154° (decomp.), $\lambda_{max.}$ 312 mμ (log ε 2·1), $\nu_{max.}$ 1710 cm.$^{-1}$ and 1720 cm.$^{-1}$ [Found (after drying at 25°/0·2 mm. for 24 hr.): C, 61·1; H, 8·6. $C_{27}H_{44}OBr_2$ requires C, 61·4; H, 8·4%]. Another preparation had m. p. 154—155°, $\nu_{max.}$ 1709 and 1722 cm.$^{-1}$.

5-Chloro-5α-cholestan-4-one.—5-Hydroxy-5α-cholestan-4-one [5] (m. p. 159°; 990 mg.) in chloroform (10 c.c.) was treated with a stream of dry hydrogen chloride at 20° for 1 hr. The dark orange solution was evaporated completely in a vacuum, to give an oil which was chromatographed on aluminium oxide (30 g.; Woelm, acid) prepared in hexane. Elution with hexane (4 × 100 c.c.) gave crystalline fractions, which were united (711 mg.) and recrystallised from acetone, to yield *5-chloro-5α-cholestan-4-one*, m. p. 136—138°, $[\alpha]_D$ +105° (*c* 1·3), $\lambda_{max.}$ 301 mμ,

log ε 2·0, $\nu_{max.}$ 1721 cm.$^{-1}$ [Found (after drying at 20°/0·05 mm. for 16 hr.): C, 77·1; H, 10·4. $C_{27}H_{45}OCl$ requires C, 77·0; H, 10·7%]. Elution with ether and chloroform gave some starting material.

Reduction of 5-Chloro-5α-cholestan-4-one with Sodium Borohydride.—The 5α-chloro-ketone (800 mg.) in methanol (25 c.c.) and a little ether was treated with sodium borohydride (125 mg.) at 20° overnight. The usual isolation procedure gave an oil, which was chromatographed on aluminium oxide (15 g.; Woelm, neutral) prepared in hexane. Elution with hexane (3 × 50 c.c.) gave starting material (93 mg.), m. p. 136; use of benzene–hexane (1 : 4; 6 × 50 c.c.) gave material (total, 518 mg.), which crystallised from acetone–methanol to yield 5α-cholestan-4-one, m. p. and mixed m. p. 96—98°, $\nu_{max.}$ 1710 cm.$^{-1}$. Elution with benzene (2 × 50 c.c.) gave oils. Use of ether (50 c.c.) gave 5α-cholestan-4β-ol (195 mg.), m. p. 132° [lit.,[4] m. p. 132°] after crystallisation from methanol; its infrared absorption spectrum was identical with that of a genuine specimen.

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UNIVERSITY COLLEGE, SWANSEA.
DEPARTMENT OF ORGANIC CHEMISTRY, THE UNIVERSITY,
SYDNEY, AUSTRALIA.

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