329. *Steroids and Walden Inversion. Part XXXIX.* The Halogenation of 5α-Cholestan-6-one and the Pyrolysis of 5-Chloro-5α-cholestan-6-one.*

By C. W. SHOPPEE, R. H. JENKINS, and G. H. R. SUMMERS.

5-Chloro-5α-cholestan-6-one, prepared from 5-hydroxy-5α-cholestan-6-one and hydrogen chloride, has also been obtained from 5 : 6β-epoxy-5β-cholestane by a configurationally unambiguous method; on pyrolysis at 290°/15 mm. it yields hydrogen chloride (1 mol.) and 5α-cholestan-6-one (~0·5 mol.), with an unidentified compound which appears to contain two steroid nuclei. 5α-Cholestan-6-one by monobromination, and 5-hydroxy-5α-cholestan-6-one by treatment with hydrogen bromide, give a mixture of 5α-bromo-, 7α-bromo-, and 7 : 7-dibromo-5α-cholestan-6-one. 5α-Cholestan-6-one by dibromination in the presence of hydrogen bromide is converted into 5α : 7α-dibromo-5α-cholestan-6-one, which is transformed into 5α : 7β-dibromo-5α-cholestan-6-one.

SOME years ago Dr. H. Grasshof, of Eschwege, West Germany, directed the attention of one of us to some unfinished and unpublished work described in his Inaugural Dissertation.[1] Grasshof converted cholest-5-ene (I) by perbenzoic acid into 5 : 6α-epoxy-5α-cholestane (II), which by acetolysis with potassium acetate in acetic anhydride at ~140° gave 5α-cholestane-5 : 6β-diol 6-acetate [2] (III; R = Ac), m. p. 109°, $[\alpha]_D$ −47° (*c* 1·2 in C_6H_6), hydrolysed by methanolic potassium hydroxide to 5α-cholestane-5α : 6β-diol [2,3,4,5] (III; R = H). Oxidation with chromium trioxide–acetic acid at 15° furnished 5-hydroxy-5α-cholestan-6-one, m. p. 149°, $[\alpha]_D$ −56° (*c* 0·8 in C_6H_6) [3,4,5] (IV), which proved unexpectedly resistant to dehydration; distillation at 300°/15 mm. or heating with acetic anhydride at 165° was without effect, whilst treatment with hydrogen chloride in chloroform at 15° gave a chloro-ketone, m. p. 115°, $[\alpha]_D$ −122° (*c* 0·85 in C_6H_6). Grasshof regarded this as either 5-chloro-5α-cholestan-6-one (VII) or 4ξ-chloro-5α-cholestan-6-one (VIII) formed by dehydration of (IV) to cholest-4-en-6-one and Markovnikov addition of hydrogen chloride thereto. We have prepared 4β-chloro-5α-cholestan-6-one (VIII), m. p. 174°, by addition of hydrogen chloride to cholest-4-en-6-one in chloroform; it is different from Grasshof's chloro-ketone, and we now show that the chloro-ketone is (VII).

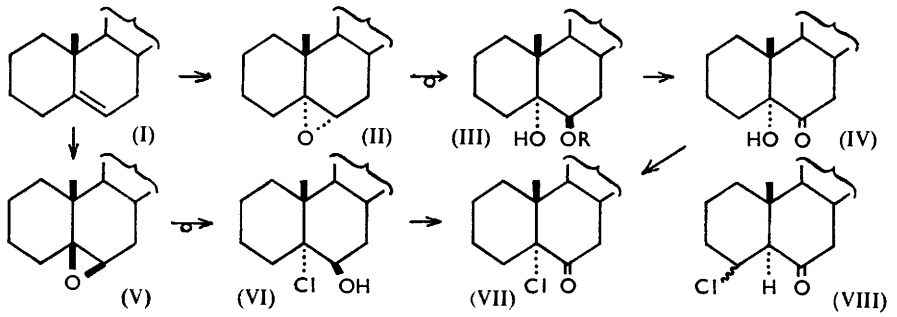
Cholest-5-ene (I) with perbenzoic acid furnished 5 : 6β-epoxy-5β-cholestane [3] (V), converted by hydrogen chloride in chloroform at 15° with diaxial fission and inversion of configuration at $C_{(5)}$ into 5-chloro-5α-cholestan-6β-ol (VI). This was oxidised by chromium trioxide–acetic acid at 15° to 5-chloro-5α-cholestan-6-one (VII), m. p. 115°, $[\alpha]_D$ −120°, identical with Grasshof's compound. Reduction of the chloro-ketone with lithium aluminium hydride in ether at 36°, or with sodium borohydride, gave a gelatinous product and a

* Part XXXVIII, *J.*, 1957, 4364. The paper by Evans and Summers, *J.*, 1957, 906, may be considered a part of this Series.

[1] H. Grasshof, Inaug.-Diss., Göttingen, 1935.
[2] Heilbron, Shaw, and Spring, *Rec. Trav. chim.*, 1938, **57**, 529.
[3] Ruzicka, Furter, and Thomann, *Helv. Chim. Acta*, 1933, **11**, 332.
[4] Reich, Walker, and Collins, *J. Org. Chem.*, 1951, **16**, 1753.
[5] D. N. Jones, Lewis, Shoppee, and Summers, *J.*, 1955, 2876.

satisfactory chromatographic separation of the 6-epimeric chlorohydrins could not be achieved; reduction with zinc and acetic acid gave 5α-cholestan-6-one [5,6] (X), m. p. 98°, $[\alpha]_D$ −7°.

The axial 5α-chloro-structure of the chloro-ketone (VII) is confirmed by comparison of its ultraviolet and infrared absorption spectra with those of 5α-cholestan-6-one (X) and



its substitution products. The displacement of the absorption maximum toward longer wavelengths by 18 mμ, and the change in intensity (cf. Table 1, where data are for EtOH solutions), correspond well with the average values found for α-bromo-ketones (axial, $\Delta\lambda_{max.}$ +28 mμ, Δ log ε 0·6; equatorial, $\Delta\lambda_{max.}$ −5 mμ, Δ log ε 0) and for a chloro-ketones (axial, $\Delta\lambda_{max.}$ +15 mμ, Δ log ε 0·4; equatorial, $\Delta\lambda_{max.}$ −7 mμ, Δ log ε 0·2) found by Cookson.[7] The displacements of the absorption maxima and the changes in intensity found for 5-bromo-5α-cholestan-6-one (XIII) and for 5-hydroxy-5α-cholestan-6-one (IV) likewise correspond with Cookson's observations [7] in the 3β-acetoxy-5α-cholestan-6-one series.

TABLE 1.

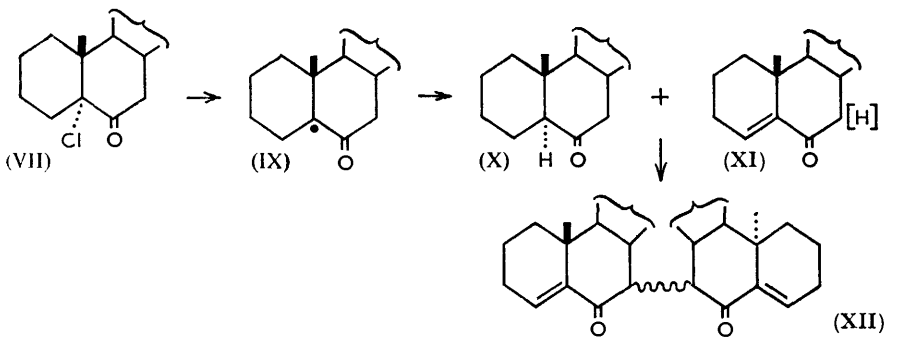
	$\lambda_{max.}$	$\Delta\lambda_{max.}$	log ε	Δ log ε
5α-Cholestan-6-one (X)	284	—	1·6	—
5-Chloro-5α-cholestan-6-one (VII)	302	+18	1·90	0·3
5-Bromo-5α-cholestan-6-one (XIII)	308	+24	2·10	0·5
5-Hydroxy-5α-cholestan-6-one (IV)	305	+21	—	—
3β-Acetoxy-5α-cholestan-6-one	280	—	1·6	—
3β-Acetoxy-5-bromo-5α-cholestan-6-one	308	+28	1·9	0·3
3β-Acetoxy-5-hydroxy-5α-cholestan-6-one	300	+20	1·77	0·17

Grasshof [1] found that on distillation at 290°/15 mm. the chloro-ketone gave a halogen-free ketone, m. p. 96°, $[\alpha]_D$ +5° (*c* 0·7 in C_6H_6) (oxime, m. p. 191—192°), regarded as derived from 4ξ-chloro-5α-cholestan-6-one (VIII) and assigned the structure 5α-cholest-3-en-6-one because its ultraviolet absorption spectrum failed to show the maximum at 240 mμ characteristic of αβ-unsaturated ketones. He found apparent confirmation for his view since the ketone, on treatment with hydrogen and palladium black in acetic acid for several hours, gave 5α-cholestan-6-one, m. p. 98°, $[\alpha]_D$ −9° (*c* 1·0 in C_6H_6) (oxime, m. p. 196—197°), identical with a genuine specimen prepared from 6-nitrocholest-5-ene by Windaus's method.[8]

Because the chloro-ketone has the structure (VII), and not (VIII), we repeated its vacuum-pyrolysis. Hydrogen chloride (0·96 mol.) was eliminated but the principal product (50%) was the saturated compound 5α-cholestan-6-one (X). Grasshof [1] gives no figure for the volume of hydrogen absorbed in his " hydrogenation " with palladium, neither does he appear to have determined the m. p. of a mixture of his pyro-ketone, $[\alpha]_D$ +5°, and its supposed hydrogenation product, $[\alpha]_D$ −9°; clearly they are both 5α-cholestan-6-one,[4,8] m. p. 98°, $[\alpha]_D$ −7°.

[6] Plattner, Petrzilka, and Lang, *Helv. Chim. Acta*, 1944, **27**, 513.
[7] Cookson, *J.*, 1954, 282; Cookson and Dandegaonker, *ibid.*, 1955, 352.
[8] Windaus, *Ber.*, 1920, **53**, 490.

The production of 5α-cholestan-6-one from 5-chloro-5α-cholestan-6-one by vacuum-pyrolysis is surprising and suggests a mechanism involving radicals, *e.g.*, (IX), since dismutation can then lead to a saturated unimolecular product (X) as shown. We



have been unable chromatographically to isolate cholest-4-en-6-one [4] (XI), $\lambda_{max.}$ 243 mμ, log ε 3·80, from the pyrolysis product, although the mother-liquors from the fractions yielding 5α-cholestan-6-one showed an absorption maximum of low intensity at 245 mμ. We have, however, obtained in about 15% yield a highly insoluble substance, m. p. 291°, $[\alpha]_D$ +33°, which may be derived from cholest-4-en-6-one by abstraction of hydrogen and subsequent dimerisation, and possess the structure (XII); the substance (mol. wt. 731) showed in its infrared absorption spectrum peaks at 1613 and 1680 $cm.^{-1}$ which are typical of αβ-unsaturated ketones [cf. cholest-4-en-3-one, 1614 and 1675 $cm.^{-1}$],[9] and in its ultraviolet absorption spectrum a single band with $\lambda_{max.}$ 250 mμ, log ε 4·0, which is consistent with the presence of two identical αβ-unsaturated ketone groupings although the maximum is displaced 8 mμ from that found for cholest-4-en-6-one [4] at 243 mμ (log ε 3·80) (calc. 242 mμ), and a somewhat higher extinction coefficient might have been expected. Owing to its insolubility, ketonic derivatives of the substance (XII?) could not be prepared and it resisted reduction by lithium aluminium hydride, and with platinum oxide in a variety of solvents.

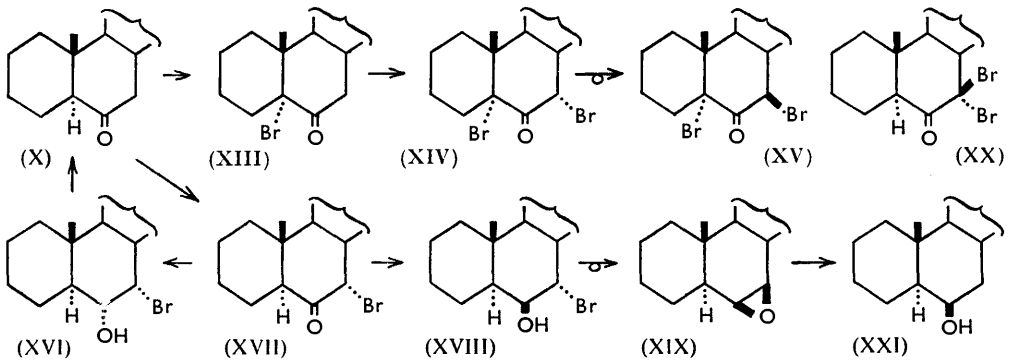
5α-Cholestan-6-one (X) on monobromination in acetic acid at 20°, and 5-hydroxy-5α-cholestan-6-one (IV) on treatment with hydrogen bromide in chloroform at 20°, afforded a mixture of the 5α-bromo-ketone (XIII), the 7α-bromo-ketone (XVII), and the 7 : 7-dibromo-ketone (XX). The 5α-bromo-ketone (XIII; cf. VII) was also prepared from the 5β : 6β-epoxide (V); this on treatment with hydrogen bromide in acetic acid gave 5α-bromo-5α-cholestan-6β-ol (as VI), which could not be obtained crystalline but on treatment with zinc in acetic acid yielded cholest-5-ene (I) and on oxidation with chromium trioxide in acetic acid at 15° gave the 5α-bromo-ketone (XIII). For completeness, it should be stated that the 5α : 6α-epoxide (II) with hydrogen bromide in acetic acid furnished 5α-hydroxy-5α-cholestan-6β-yl bromide (as III with OR replaced by Br), converted by treatment with zinc in acetic acid into cholest-5-ene (I).

In the foregoing brominations the 5-bromo-5α-cholestan-6-one (XIII) is formed initially and converted in the presence of hydrogen bromide, by reduction and re-bromination [7] under thermodynamic control,[10] into 7α-bromo-5α-cholestan-6-one (XVII). On reduction with sodium borohydride, the 7α-bromo-ketone (XVII) gave a mixture of the 7α-bromo-6α- (XVI) and the 7α-bromo-6β-alcohol (XVIII); under the usual alkaline conditions of the reaction, these were in part dehydrobrominated, and passed respectively into 5α-cholestan-6-one (X) and 6β : 7β-epoxy-5α-cholestane (XIX), which was reduced by

[9] R. N. Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[10] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.

lithium aluminium hydride to 5α-cholestan-6β-ol (XXI). The 7α-bromo-6α-alcohol (XVI) afforded cholest-6-ene [11] when treated with zinc and acetic acid.

Dibromination of 5α-cholestan-6-one (X) in acetic acid afforded as the initial product of kinetic control 5 : 7α-dibromo-5α-cholestan-6-one (XIV) (a *cis*-2 : 6-dibromo*cyclo*hexan-1-one of fixed diaxial conformation). In the presence of hydrogen bromide the 5α : 7α-dibromo-ketone passed into the thermodynamically more stable 5α : 7β-dibromo-5α-cholestan-6-one (XV) (a *trans*-2 : 6-dibromo*cyclo*hexan-1-one of fixed axial–equatorial conformation), a crystalline material of m. p. 40° which is accordingly difficult to purify.



The formation, in small amounts, of the 7 : 7-dibromo-ketone (XX) appears to involve a relatively fast bromination of the axial 7α-hydrogen atom in the labile 7β-bromo-epimeride of (XVII), which is expected to be present to the extent of 2% in the equilibrium mixture. The stability of the 7 : 7-dibromo-ketone (XX) in the presence of hydrogen bromide is interesting. Since 2 : 2-dibromo-5α-cholestan-3-one is rapidly converted by dry hydrogen bromide into 2α : 4α-dibromo-5α-cholestan-3-one, conversion of the 7 : 7-dibromo-ketone into the 5α : 7β-dibromo-ketone (XV) might have been expected. The stability of the 7 : 7-dibromo-ketone (XX) may arise from the circumstance that the axial 7α-bromine atom is subject to repulsive 1 : 3-interaction with only three axial hydrogen atoms, whereas in the 5α : 7β-dibromo-ketone (XV) the axial 5α-bromine atom is subject to four such repulsive 1 : 3-interactions.

The structures assigned to the above bromo-ketones are supported by the values found in the ultraviolet absorption spectra for $\Delta\lambda_{max.}$ and $\Delta \log \varepsilon$,[7] and for the displacement

TABLE 2.

	$\lambda_{max.}$	$\Delta\lambda_{max.}$	log ε	Δ log ε	$\nu_{max.}$	$\Delta\nu_{max.}$
5α-Cholestan-6-one (X)	284	—	1·6	—	1711	—
5α-Chloro-5α-cholestan-6-one (VII)	302	+18	1·9	0·3	1715 †	+ 4
5α-Bromo-5α-cholestan-6-one (XIII)	308	+24	2·1	0·5	1712	+ 1
7α-Bromo-5α-cholestan-6-one (XVII)	308	+24	2·18	0·6	1711	0
5α : 7α-Dibromo-5α-cholestan-6-one (XIV)	334	+50	2·1	0·5	1713	+ 2
5α : 7β-Dibromo-5α-cholestan-6-one (XV)	— *	—	— *	—	1725	+14
7 : 7-Dibromo-5α-cholestan-6-one (XX)	292	+ 8	1·70	0·1	1725	+14
3β-Acetoxy-5α-cholestan-6-one	280	—	1·6	—	1711	—
3β-Acetoxy-5α-bromo-5α-cholestan-6-one	308	+28	2·1	0·5	1711	0
3β-Acetoxy-7α-bromo-5α-cholestan-6-one	310	+30	2·2	0·6	1713	+ 2
3β-Acetoxy-5α : 7α-dibromo-5α-cholestan-6-one	340	+60	2·2	0·6	1708	− 3
3β-Acetoxy-5α : 7β-dibromo-5α-cholestan-6-one	305	+25	2·1	0·5	1727	+16

The values of $\nu_{max.}$ for (X), (XIV), and (XV) in $CHCl_3$ were 1702, 1704, and 1716 cm.$^{-1}$. * No definite peak, but an inflection at ~315 mμ. † Since this paper was written $\nu_{max.}$ for (VII) in CS_2 has been reported as 1718 cm.$^{-1}$ ($\Delta\lambda = 4$) by Cummins and Page (*J.*, 1957, 3847), who have also measured the frequency of the low-frequency "halogen-sensitive" band at 756 cm.$^{-1}$ and so confirmed the axial conformation of the C–Cl linkage.

$\Delta\nu_{max.}$ of the carbonyl stretching frequency [9,10] in the infrared absorption spectra. These values are collected in Table 2, which also gives the values for the 3β-acetoxy-analogues ($\lambda_{max.}$ are for EtOH solutions, $\nu_{max.}$ for CCl_4).

[11] Reichstein and Shoppee, *Discuss. Faraday Soc.*, 1949, **7**, 205.

Experimental

For general experimental directions, see *J.*, 1957, 4364. Ultraviolet absorption spectra were determined for EtOH solutions in a Hilger Uvispek spectrophotometer; infrared absorption spectra were measured on a Perkin-Elmer Model 21 double-beam instrument. $[\alpha]_D$ are in $CHCl_3$, unless otherwise stated. Alumina was Spence type H (activity ~II).

5 : 6β-*Epoxy*-5β-*cholestane* (V).—Cholest-5-ene (m. p. 90°; 5 g.) in benzene (150 c.c.) was treated with a benzene solution of perbenzoic acid (1·2 mol.) at 0° for 3·5 days. The product, isolated in the usual way, was chromatographed on aluminium oxide (150 g.) in pentane. Elution with pentane (4 × 75 c.c.) gave 5 : 6β-epoxy-5β-cholestane (300 mg.), m. p. 58° (lit.,[3] m. p. 53°) after crystallisation from ethanol; further elution with pentane and benzene–pentane (1 : 9) gave 5 : 6α-epoxy-5α-cholestane, m. p. 80°.

5-*Chloro*-5α-*cholestan*-6β-*ol* (VI).—The 5β : 6β-epoxide (V) (83 mg.) in chloroform (10 c.c.) was treated with dry hydrogen chloride at 15° for 1 hr., and the solution left overnight. The usual working up afforded an oil, which on crystallisation from acetone–methanol gave 5-*chloro*-5α-*cholestan*-6β-ol (70 mg.), m. p. 108—109°, $[\alpha]_D$ −22° (*c* 0·7) [Found (after drying at 40°/0·01 mm. for 12 hr.): C, 76·95; H, 11·2. $C_{27}H_{47}OCl$ requires C, 76·8; H, 11·0%].

5-*Chloro*-5α-*cholestan*-6-*one* (VII).—(*a*) The 5α-chloro-6β-alcohol (VI) (61 mg.) in 1 : 2 ether–acetic acid (6 c.c.) was oxidised with a 2% solution of chromium trioxide in acetic acid (1·0 c.c. ≡ 2 g.-atoms of O) at 15° for 18 hr. Excess of chromium trioxide was destroyed by addition of methanol, the solution diluted with water, and the precipitate filtered off, washed with water, and dried. Recrystallisation from acetone–methanol gave 5-chloro-5α-cholestan-6-one (40 mg.), m. p. 116°, $[\alpha]_D$ −102° (*c* 0·7) [Found (after drying at 55°/0·01 mm. for 10 hr.): C, 76·9; H, 10·7. Calc. for $C_{22}H_{45}OCl$: C, 77·0; H, 10·7%].

(*b*) 5-Hydroxy-5α-cholestan-6-one (IV) (m. p. 150°; 5 g.) in chloroform (100 c.c.) was treated with dry hydrogen chloride at 20° for 1 hr.; working up in the usual way afforded an oil, which crystallised readily from acetone to give 5-chloro-5α-cholestan-6-one (4 g.), m. p. and mixed m. p. 116°, $[\alpha]_D$ −104° (*c* 1·2). The infrared spectra of the two preparations were identical.

Pyrolysis of 5-*Chloro*-5α-*cholestan*-6-*one* (VII).—The chloro-ketone (4·60 g.) was distilled at 295°/10 mm. and the distillate re-distilled at 295°/10 mm. into a second receiver; the gaseous products were passed into 0·1N-sodium hydroxide (200 c.c.) and subsequent titration showed that 0·96 mol. of hydrogen chloride had been evolved. The final distillate was chromatographed on aluminium oxide (140 g.) in light petroleum. Elution with light petroleum and with benzene–light petroleum (1 : 9) furnished 5α-cholestan-6-one [5,8] (2·0 g.), m. p. and mixed m. p. 98°, $[\alpha]_D$ −7° (*c* 1·0); the mother-liquors gave further small quantities of the saturated ketone, but cholest-4-en-6-one could not be isolated although an absorption maximum of low intensity at 245 mμ was observed. Elution with benzene gave an oil, which on crystallisation from chloroform–ethyl acetate yielded a *substance* (XII?) (650 mg.), m. p. 291°, $[\alpha]_D$ +33° (*c* 0·8), $\lambda_{max.}$ 250 mμ (log ε 4·0), $\nu_{max.}$ (in $CHCl_3$) 1613 and 1680 $cm.^{-1}$ [Found (after drying at 80°/0·01 mm. for 6 hr.): C, 84·0, 84·4; H, 9·8, 10·1; O, 5·2%; *M* (Rast), 731. $C_{54}H_{88}O_2$ requires C, 84·3; H, 11·5; O, 4·2%; *M*, 768], giving a yellow colour with tetranitromethane–chloroform and a negative Beilstein test. In another experiment, the chloro-ketone (3 g.) gave 5α-cholestan-6-one (1·8 g. crude; 1·5 g. pure) and the dimer (XII?) (360 mg.). Pyrolysed in an atmosphere of nitrogen, the chloro-ketone (3 g.) gave 5α-cholestan-6-one (1·3 g.) and the dimer (XII?) (400 mg.).

4β-*Chloro*-5α-*cholestan*-6-*one* (VIII).—Cholest-4-en-6-one (m. p. 108°; 0·5 g.) in chloroform (20 c.c.) was treated with dry hydrogen chloride for 0·75 hr.; working up in the usual way afforded an oil which crystallised readily from acetone to give 4β-*chloro*-5α-*cholestan*-6-*one* (490 mg.) as needles, m. p. 173—174° [Found (after drying at 25°/0·01 mm. for 8 hr.): C, 76·85; H, 10·7. $C_{27}H_{45}OCl$ requires C, 77·0; H, 10·7%].

5α-*Bromo*-5α-*cholestan*-6-*one* (XIII).—(*a*) The 5β : 6β-epoxide (V) (100 mg.) in acetic acid was treated with a 5% solution of hydrogen bromide in acetic acid (2 c.c.) at 15° for 1 hr. The solution was worked up in the usual way, giving an oil. This crude 5-bromo-5α-cholestan-6β-ol in acetic acid (10 c.c.) was refluxed with zinc for 1 hr., to give cholest-5-ene, m. p. and mixed m. p. 88—90° (from acetone–methanol); the residue of the crude bromohydrin in acetic acid (3 c.c.) was oxidised with a 2% solution of chromium trioxide in acetic acid (2 c.c.) at 15° for 18 hr. Excess of the reagent was destroyed by methanol, the solution diluted and extracted

with ether, and the product isolated in the usual manner, to furnish an oil, which crystallised from acetone–methanol. 5-Bromo-5α-cholestan-6-one (40 mg.) had m. p. and mixed m. p. 101°, $[\alpha]_D$ −146° (*c* 1·2).

(*b*) 5α-Cholestan-6-one (500 mg.) in ether–acetic acid (1 : 1; 20 c.c.) was treated with a 10% solution of bromine in acetic acid (2 c.c., 1·1 mol.) and a few drops of a solution of hydrogen bromide in acetic acid, and kept at 15° for 1 hr. The colourless solution, after the usual working up, yielded 5-bromo-5α-cholestan-6-one (300 mg.), m. p. and mixed m. p. 101°, $[\alpha]_D$ −145° (*c* 1·2) (from acetone–methanol) [Found (after drying at 40°/0·01 mm. for 10 hr.): C, 69·4; H, 9·7. Calc. for $C_{27}H_{45}OBr$: C, 69·6; H, 9·75%]. Henbest and Wrigley [11a] give m.p. 101—102°, $[\alpha]_D$ −134°.

5-Bromo- (XIII), *7α-Bromo-* (XVII), *and 7 : 7-Dibromo-5α-cholestan-6-one* (XX).—5-Hydroxy-5α-cholestan-6-one (IV) (3 g.) in chloroform (100 c.c.) was treated with dry hydrogen bromide at 20° for 2 hr. and left overnight. Working up in the usual way gave an oil, which was chromatographed on aluminium oxide (90 g.) in light petroleum. Elution with light petroleum afforded an oil, which crystallised from ethanol, to give *7α-bromo-5α-cholestan-6-one* (1·3 g.), m. p. 82°, $[\alpha]_D$ +51° (*c* 1·1) [Found (after drying at 20°/0·01 mm. for 12 hr.): C, 69·5; H, 9·8. $C_{27}H_{45}OBr$ requires C, 69·6; H, 9·75%]. Elution with benzene–light petroleum (1 : 9) gave material which crystallised readily from ethanol, to yield 5-bromo-5α-cholestan-6-one (600 mg.), m. p. and mixed m. p. 101°. Elution with benzene–light petroleum (1 : 4) gave an oil (600 mg.), from which by repeated recrystallisation there was obtained *7 : 7-dibromo-5α-cholestan-6-one* (45 mg.), m. p. 167—168°, $[\alpha]_D$ −28° (*c* 0·85) [Found (after drying at 40°/0·01 mm. for 10 hr.): C, 60·4; H, 7·9. $C_{27}H_{44}OBr_2$ requies C, 59·6; H, 8·15%].

Reduction of 7α-Bromo-5α-cholestan-6-one (XVII).—To a solution of the 7α-bromo-ketone (830 mg.) in ether (100 c.c.) was added one of sodium borohydride (350 mg.) in methanol (50 c.c.), and the mixture kept at 15° for 18 hr. The product, isolated in the usual way, was an oil which was chromatographed on neutralised aluminium oxide [11] (28 g.) in light petroleum. Elution with light petroleum furnished an oil (130 mg.) which crystallised from ethanol, to give *6β : 7β-epoxy-5α-cholestane*, m. p. 106—108°, $[\alpha]_D$ −10° (*c* 1·05) [Found (after drying at 40°/0·01 mm. for 12 hr.): C, 83·3; H, 11·8. $C_{27}H_{46}O$ requires C, 83·8; H, 12·0%]. Elution with benzene–light petroleum (1 : 4 and 3 : 7) gave an oil (90 mg.), which by crystallisation from ethanol afforded 5α-cholestan-6-one, m. p. and mixed m. p. 98°. Elution with benzene–light petroleum (1 : 1), and with benzene, gave an oil (200 mg.), which by crystallisation from ethanol gave *7α-bromo-6α-hydroxy-5α-cholestane* (XVI), m. p. 168°, $[\alpha]_D$ −13° (*c* 1·0) [Found (after drying at 60°/0·01 mm. for 6 hr.): C, 68·9; H, 9·9. $C_{27}H_{47}OBr$ requires C, 69·3; H, 10·15%]. Finally, elution with ether–benzene mixtures and with ether gave material (90 mg.), which on crystallisation from ethanol gave an unidentified substance, m. p. 233—235°, $[\alpha]_D$ −20° (*c* 1·0) [Found (after drying at 60°/0·01 mm. for 6 hr.): C, 79·5; H, 11·2%].

Dehydrobromination and Dehypobromination of the 7α-Bromo-6α-alcohol (XVI).—(*a*) The bromohydrin (40 mg.) was dissolved in a solution of potassium hydroxide (150 mg.) in methanol (8 c.c.) and the solution refluxed for 5 hr. The solution was diluted and the resulting precipitate filtered off, washed with water, and dried. Recrystallisation from ethanol gave 5α-cholestan-6-one, m. p. and mixed m. p. 98°.

(*b*) The bromohydrin (65 mg.) was refluxed with zinc dust (300 mg.) in acetic acid (15 c.c.) for 6 hr.; the warm solution was filtered off, acetic acid largely removed at 10 mm., and the product extracted with ether. The usual procedure gave an oil, which crystallised from acetone to give 5α-cholest-6-ene,[12] m. p. 86—87°, $[\alpha]_D$ −91° (*c* 1·07).

5α-Cholestan-6β-ol (XXI).—The 6β : 7β-epoxide (50 mg.) in ether (15 c.c.) was added to a solution of lithium aluminium hydride (30 mg.) in ether (10 c.c.), and the mixture refluxed for 4 hr. Excess of the reagent was decomposed with ice and 2N-sulphuric acid, and the product isolated in the usual way. The resulting oil crystallised with difficulty from methanol, to give 5α-cholestan-6β-ol, m. p. 78—82°, mixed m. p. with authentic 5α-cholestan-6β-ol,[13] 80—82°.

5 : 7α-Dibromo-5α-cholestan-6-one (XIV).—5α-Cholestan-6-one (670 mg.) was dissolved in acetic acid (40 c.c.) and treated with a 10% solution of bromine in acetic acid (6·2 c.c., 2·2 mol.). After 2 hr. at 15°, the colourless solution was worked up in the usual way, to give an oil, which was chromatographed on neutralised aluminium oxide [11] (20 g.). Elution with light petroleum

[11a] Henbest and Wrigley, *J.*, 1958, 4596.
[12] Fischer, Lardelli, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 1577.
[13] Shoppee and Summers, *J.*, 1952, 1786, 3361.

gave an oil (240 mg.), which crystallised with difficulty from ethanol, to give 5 : 7α-*dibromo*-5α-*cholestan*-6-*one*, m. p. 115°, $[\alpha]_D$ −101° (*c* 0·9) [Found (after drying at 40°/0·01 mm. for 8 hr.): C, 60·0; H, 8·3. $C_{27}H_{44}OBr_2$ requires C, 59·55; H, 8·15%]. Elution with benzene–light petroleum furnished some 5α-cholestan-6-one (negative Beilstein test).

5 : 7β-*Dibromo*-5α-*cholestan*-6-*one* (XV).—5α-Cholestan-6-one (460 mg.) in acetic acid (50 c.c.) was treated with a 10% solution of bromine in acetic acid (4 c.c., 2·2 mol.), and with a solution of hydrogen bromide in acetic acid (0·5 c.c.) at 15°. After being kept overnight at 20°, the colourless solution was diluted with water (50 c.c.), and the precipitate filtered off, washed with water, and dried, to afford 5 : 7β-dibromo-5α-cholestan-6-one, m. p. ~40°, $[\alpha]_D$ −12° (*c* 0·8), which could not satisfactorily be crystallised but gave satisfactory analytical figures [Found (after drying at 15°/0·01 mm. for 18 hr.): C, 59·3; H, 8·05. $C_{27}H_{44}OBr_2$ requires C, 59·55; H, 8·15%].

5-*Hydroxy*-5α-*cholestan*-6β-*yl Chloride and Bromide*.—5 : 6α-Epoxy-5α-cholestane in chloroform was treated with dry hydrogen chloride at 15° for 1 hr., and the solution set aside overnight. The usual isolation furnished material, which on crystallisation from acetone gave 5-*hydroxy*-5α-*cholestan*-6β-*yl chloride*, m. p. 119°, $[\alpha]_D$ −6° (*c* 1·2) [Found (after drying at 20°/0·01 mm. for 7 hr.): C, 76·45; H, 11·2. $C_{27}H_{47}OCl$ requires C, 76·8; H, 11·0%]. Use of hydrogen bromide similarly gave 5-*hydroxy*-5α-*cholestan*-6β-*yl bromide*, m. p. 109—110°, $[\alpha]_D$ −11° (*c* 1·35), after crystallisation from acetone [Found (after drying at 20°/0·01 mm. for 6 hr.): C, 69·5; H, 10·05. $C_{27}H_{47}OBr$ requires C, 69·5; H, 9·95%].

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