641. *Steroids and Walden Inversion. Part XLIX.* Further Observations on the Bromination of 5α-Cholestan-4-one.*

By C. W. Shoppee and Ruth E. Lack.

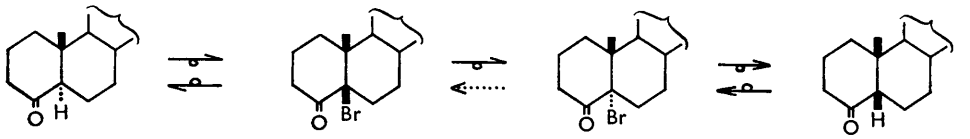
Monobromination of either 5α- or 5β-cholestan-4-one gives a mixture of 5-bromo-5α- and -5β-cholestan-4-one separable into its components by chromatography on silica gel. The material previously described as 3α,5-dibromo-5α-cholestan-4-one is a mixture of 3,3-dibromo-5α-cholestan-4-one and 3α-bromo-5α-cholestan-4-one. 3,3-Dibromo-5α-cholestan-4-one has been prepared from 3α-bromo-5α-cholestan-4-one, whilst 5,6β-dibromo-5α-cholestan-4-one has been made for comparison. 3,3-Dibromo-5α-cholestan-4-one is converted by hydrogen bromide into 3α,5-dibromo-5β-cholestan-4-one.

In Part XLII,[1] monobromination of either 5α- or 5β-cholestan-4-one (I or IV) in acetic acid containing a trace of hydrogen bromide at 20° was reported to give 5-bromo-5α-cholestan-4-one (III), m. p. 145°, $[\alpha]_D$ +66°. We find that this material is a mixture separable by chromatography on silica gel into genuine 5-bromo-5α-cholestan-4-one (III), m. p. 155—157°, $[\alpha]_D$ +89°, and 5-bromo-5β-cholestan-4-one (II), m. p. 115—117°, $[\alpha]_D$ +2°. Axial bromides appear not to be the initial products of bromination,[2] and the reactions (I ⟶ II) and (IV ⟶ III) are kinetically controlled and involve inversion of configuration contrary to our previous conclusions. Reduction of the 5α-bromo-ketone (III)

* Part XLVIII, preceding paper.

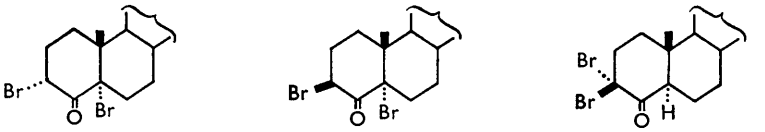
[1] Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630.

with zinc in acetic acid at 100° gives the 5β-ketone (IV) as the major product, accompanied by some of the 5α-ketone (I), probably derived from (IV) by prototropy under the conditions of reduction, since similar reduction of the 5β-bromo-ketone (II) appears to give only the 5α-ketone (I).



(I) (II) (III) (IV)

Dibromination of 5α-cholestan-4-one in acetic acid in the presence of hydrogen bromide at 20° was also reported to give a dibromo-ketone, m. p. 154°. This was regarded as 3α,5α-dibromo-5α-cholestan-4-one (V) rather than the 3β,5α-isomer (VI) because the infrared carbonyl absorption band consisted of two maxima of approximately equal intensity. The doublet could have resulted from a Fermi resonance with a higher frequency overtone, but we were impressed by the apparent analogy with the work of Allinger and Allinger,[3] who obtained curves of similar contour for the infrared carbonyl absorption band of the



(V) (VI) (VII)

equilibrium mixture in carbon tetrachloride solution of the two conformational isomers of 2-bromocyclohexanone (containing axial and equatorial bromine atoms respectively). We therefore suggested that the reputed 3α,5α-dibromo-ketone (V), which is incapable of conformational inversion, existed in carbon tetrachloride solution as an equilibrium mixture of the ring A chair (2 axial bromine atoms) and boat (1 axial and 1 equatorial bromine atom) conformations.

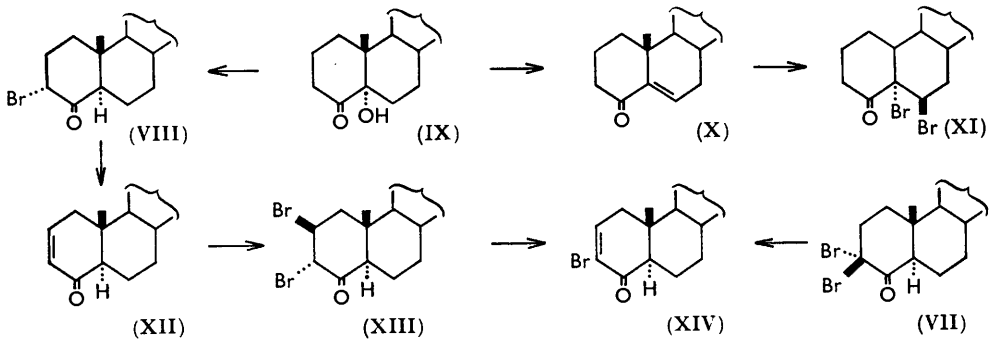
The spectral characteristics of the reputed 3α,5α-dibromo-ketone (V) have been further investigated. In the infrared region, the double peak has been found to be only slightly modified by passing from carbon tetrachloride to tetrahydrofuran as the solvent. Similarly, the ultraviolet absorption maximum at 308 mμ does not alter appreciably when the medium is changed from cyclohexane to acetonitrile. Finally, the optical rotatory dispersion curves are almost identical in cyclohexane and in acetonitrile; Professor G. Ourisson [4] writes: " in other cases, where conformational equilibria have been encountered, the change from non-polar cyclohexane to polar acetonitrile had more dramatic results than the change from cyclohexane to methanol used by Djerassi."

In brief, neither spectral (infrared, ultraviolet) nor rotatory-dispersion evidence indicates the existence of a conformational equilibrium, and we have now shown the reputed 3α,5α-dibromo-ketone (V) to be a mixture of 3,3-dibromo-5α-cholestan-4-one (VII) and 3α-bromo-5α-cholestan-4-one (VIII).

5-Hydroxy-5α-cholestan-4-one [5] (IX), which was shown to give a low yield of 3α-bromo-5α-cholestan-4-one (VIII) on prolonged treatment with hydrogen bromide in chloroform at 20°, affords the pure 3α-bromo-ketone (VIII), in almost quantitative yield, under the same conditions in 5 min. When the time is increased to 30 min., the 3α-bromo-ketone (VIII) is contaminated by an αβ-unsaturated ketone, probably cholest-5-en-4-one [5] (X). It therefore seemed possible that the reputed dibromo-ketone might be

[2] Zimmermann and Mais, *J. Amer. Chem. Soc.*, 1959, **81**, 3644; Djerassi, Finch, Cookson, and Bird, *ibid.*, 1960, **82**, 5488.
[3] Allinger and Allinger, *Tetrahedron*, 1958, **2**, 64.
[4] Ourisson, personal communication.
[5] Shoppee, Jones, Lewis, and Summers, *J.*, 1955, 2876.

derived from cholest-5-en-4-one by addition of bromine. In fact, cholest-5-en-4-one (X) readily undergoes *trans*-diaxial addition of bromine in acetic acid at 20°, but to give a



different substance, 5,6β-dibromo-5-α-cholestan-4-one (XI), exhibiting the spectral characteristics of an axial α-monobromo-ketone. The structure of 3α-bromo-5α-cholestan-4-one (VIII) is confirmed by conversion with boiling collidine under nitrogen into the αβ-unsaturated ketone 5α-cholest-2-en-4-one (XII); this adds bromine to give 2β,3α-dibromo-5α-cholestan-4-one (XIII), which is dehydrobrominated by aluminium oxide to 3-bromo-5α-cholest-2-en-4-one (XIV).

Bromination of 3α-bromo-5α-cholestan-4-one (VIII) in acetic acid in the presence of hydrogen bromide again gave the reputed 3α,5α-dibromo-ketone, m. p. 150—155°, Δν 0° and +18 cm.$^{-1}$, Δλ + 23 mμ; although fractional crystallisation or chromatography on neutral aluminium oxide was ineffective, chromatography on silica gel in pentane achieved a separation into a new compound 3,3-dibromo-5α-cholestan-4-one (VII), m. p. 179—181°, $[\alpha]_D$ −58°, Δν + 17 cm.$^{-1}$, Δλ + 20 mμ, and unaltered 3α-bromo-ketone (VIII). The *gem*-dibromo-structure (VII), with one bromine atom axial and one bromine atom equatorial, is consistent with the spectral characteristics quoted, and is proved by the rotatory dispersion curve, which shows a negative Cotton effect.[6] This circumstance excludes 3β,5-dibromo-5α-cholestan-4-one (VI), since this structure requires a positive Cotton effect.[6] The structure of 3,3-dibromo-5α-cholestan-4-one (VII) is confirmed by dehydrobromination with refluxing collidine under nitrogen to 3-bromo-5α-cholest-2-en-4-one (XIV).

Treatment of 3α-bromo-5α-cholestan-4-one (VIII) with a large excess of bromine in acetic acid in the presence of hydrogen bromide at 20° gave a product, m. p. 160—165°, unchanged by recrystallisation, exhibiting a single infrared band at 1730 cm.$^{-1}$ with a shoulder at 1713 cm.$^{-1}$, consisting of a 3 : 1 mixture of the 3,3-dibromo-ketone (VII) and the 3α-bromo-ketone (VIII), and separable into its components by chromatography on silica gel in pentane.

In an attempt to avoid acid-catalysed enolisation and possible rearrangement of the first-formed dibromo-ketone, base-catalysed bromination of 3α-bromo-5α-cholestan-4-one was examined. This method, although successfully employed [7] to afford pure 2,2-dibromo-5α-cholestan-3-one from 2α-bromo-5α-cholestan-3-one, gave after 20 hr. a product, m. p. 128—130°, $\nu_{max.}$ 1712s, 1729w cm.$^{-1}$, shown by analysis to be a 1 : 3 mixture of the 3,3-dibromo-ketone (VII) and the 3α-bromo-ketone (VIII), which could not be separated by crystallisation. Prolonged base-catalysed bromination gave a similar product, m. p. 130—135°, $\nu_{max.}$ 1712s, 1730w cm.$^{-1}$, which was separated by chromatography on silica gel in pentane into its components (VII) and (VIII).

The 3,3-dibromo-ketone (VII) and the 3α-bromo-ketone (VIII) appear to form a series of solid solutions, since bromination of the latter under varying conditions gave a series of products, incapable of separation by fractional crystallisation or by chromatography

[6] Djerassi and Klyne, *J. Amer. Chem. Soc.*, 1957, **79**, 1506.
[7] Crowne, Evans, Green, and Long, *J.*, 1956, 4351.

on neutral aluminium oxide, showing an approximately linear variation in m. p. with analytical composition [percentage of (VII) 0, 24·9, 58·9, 74·2, 100; m. p. 120°, 129°, 152°, 163°, 180°] and in the ratio of the intensities of the two infrared peaks at 1710 and 1729 cm.$^{-1}$.

It appears that dibromination of 5α-cholestan-4-one gives initially the 5α-bromo-ketone (accompanied by the 5β-bromo-ketone as a minor product), which is rapidly converted by hydrogen bromide, by reduction and rebromination under thermodynamic control, into the 3α-bromo-ketone; this then undergoes slow incomplete bromination to give the 3,3-dibromo-ketone. The sequence, 5α-Br ⟶ 3α-Br ⟶ 3,3-Br_2, in the 5α-cholestan-4-one series recalls that found, 5α-Br ⟶ 7α-Br ⟶ 7,7-Br_2, in the 5α-cholestan-6-one series;[8] we are unable to account for the absence of the 3α,5α-dibromo-4-ketone since the 5α,7α-dibromo-6-ketone (also a *cis*-2,6-dibromocyclohexanone) was obtained without difficulty.

Physical properties of the 5-cholestan-4-ones and their bromo-derivatives.

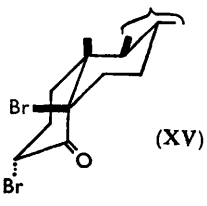
	Compound	M. p.	$[\alpha]_D$	$\lambda_{max.}$ (cm.$^{-1}$)	Δλ	$\lambda_{max.}$ (mμ)	Δλ
(I)	5α-Cholestan-4-one	100°	+27°	1712	—	285	—
(IV)	5β-Cholestan-4-one	110	+40	1713	—	285	—
(II)	5α-Bromo-5α-ketone	155	+89	1713	−1	310	+25
(III)	5β-Bromo-5β-ketone	115	+2	1713	0	310	+25
(VIII)	3α-Bromo-5α-ketone	121	−72	1712	0	309	+24
(VII)	3,3-Dibromo-5α-ketone	179	−58	1729	+15	305	+20
(XV)	3α,5β-Dibromo-5β-ketone	109	—	1728	+16	309	+24

Compound	Cotton curve sign and molar amplitude ($10^{-2}a$)	Molar dispersion contribn. of subst. (Δa)	Position λ* (mμ) of 1st trough (peak)	Δλ*	Halogen confign.
(I)	−94° [a]	—	307·5 [a]	—	—
(IV)	+22 [b]	—	300 [b]		
(II)	+149	+243° (5α-Br)	332	+24·5	*ax*
(III)	−213	−235 (5β-Br)	335	+35	*ax*
(VIII)	−202	−108 (3α-Br)	332	+24·5	*ax*
(VII)	−194	−100 (3α-Br)	325	+17·5	*eq, ax*
(XV)	−110	−132 (5β-Br)	331	+31	*eq, ax*

Δλ* is the difference (in mμ) between the position of the first trough (peak) of the compound and of its parent ketone.

[a] Djerassi, Closson, and Lippman, *J. Amer. Chem. Soc.*, 1956, **78**, 3163. [b] Djerassi, Riniker, and Riniker, *ibid.*, p. 6362; Mouli, Ringold, and Djerassi, *ibid.*, 1960, **82**, 5494.

Finally, extended bromination (6 days) of 3α-bromo-5α-cholestan-4-one (VIII) in anhydrous acetic acid–chloroform in the presence of hydrogen bromide at 20° afforded a new dibromo-ketone, whose spectral characteristics by comparison with those of 5α-cholestan-4-one reveal differences, Δν + 16 cm.$^{-1}$ and Δλ + 24 mμ, indicative of one axial bromine atom and one equatorial bromine atom. The compound was thought to be 3β,5-dibromo-5α-cholestan-4-one (VI), derived from the first-formed 3,3-dibromo-5α-cholestan-4-one (VII) by debromination with hydrogen bromide and rebromination,[7,9] and should then give a positive Cotton curve. The compound, however, shows a simple negative Cotton curve, and must therefore be 3α,5-dibromo-5β-cholestane (XV). The molar dispersion contribution, $\Delta a = -132°$, of the axial 5β-bromine atom in compound (XV) is consistent with that found, $\Delta a = -235°$, for the 5β-bromine atom in compound (III); further proof of structure by dehydrobromination was prevented by lack of material, but it is hoped to undertake this in the future. Compounds (VI) and (XV) are spectroscopically indistinguishable; their differentiation further illustrates the analytical power of optical rotatory dispersion measurements.



(XV)

[8] Shoppee, Jenkins, and Summers, *J.*, 1958, 1657.
[9] Cookson and Dandegaonkar, *J.*, 1955, 352; James and Shoppee, *J.*, 1958, 1064.

The physical properties of the cholestan-4-ones and their bromo-derivatives are summarised in the Table.

Experimental

For general directions see *J.*, 1959, 630. $[\alpha]_D$ are for $CHCl_3$ solutions; ultraviolet absorption spectra were measured for EtOH solutions on a Hilger Uvispek spectrophotometer; infrared absorption spectra were determined for CCl_4 solutions on a Perkin–Elmer model 21 double-beam instrument or an Infrachord spectrophotometer. Analytical samples were dried at 20°/0·1 mm. for 2—4 hr.

Bromination of 5α-Cholestan-4-one.—5α-Cholestan-4-one (700 mg.), in acetic acid (100 ml.) containing a trace of hydrogen bromide, was treated at 20° with bromine (320 mg., 1·05 mol.) in acetic acid. After 10 min. water was added, and the precipitate filtered off, washed with water, and dried. The product, m. p. 122—145°, was chromatographed on Davison silica gel (100—200 mesh; W. R. Grace & Co., Baltimore, Ind., U.S.A.); the column was prepared from the silica gel (75 g.) made into a slurry with ether–pentane (1 : 19), which was then washed free from ether with pentane. Elution with pentane (3 × 30 ml.) gave *5-bromo-5β-cholestan-4-one* (120 mg.) (from methanol), m. p. 115—117° (mixed m. p. with 3α-bromo-5α-cholestan-4-one depressed to 85—90°), $[\alpha]_D$ +2°, 0° (*c* 1·0), $\nu_{max.}$ 1713 cm.$^{-1}$, $\lambda_{max.}$ 310 (log ε 1·75), rotatory dispersion: $[\alpha]_{335}$ − 1910° (trough), $[\alpha]_{288}$ + 2670° (peak) (*c* 0·01 in MeOH at 20°) (Found: C, 69·4; H, 10·0. $C_{27}H_{45}BrO$ requires C, 69·6; H, 9·7%). Further elution with ether–pentane (1 : 99, 5 × 50 ml.) gave *5-bromo-5α-cholestan-4-one* (600 mg.), m. p. 155—157°, $[\alpha]_D$ +89° (*c* 1·0), $\nu_{max.}$ 1713 cm.$^{-1}$, $\lambda_{max.}$ 310 mμ (log ε 1·9), rotatory dispersion: $[\alpha]_{332}$ +1520° (peak), $[\alpha]_{288}$ −1680° (trough) (*c* 0·01 in MeOH at 20°), after recrystallisation from acetone (Found: C, 69·35; H, 9·6%). Subsequent elution with ether–pentane (1 : 19; 2 × 50 ml.) gave unchanged 5α-cholestan-4-one (157 mg.), m. p. and mixed m. p. 99—100°.

Reduction of 5-Bromo-5α-cholestan-4-one.—5-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (20 ml.) was treated with zinc dust (200 mg.) at 100° for 2 hr. The usual isolation gave crystals, m. p. 75—85°, which were chromatographed on silica gel (10 g.). Elution with ether–pentane (2 : 98; 3 × 25 ml.) gave 5β-cholestan-4-one (52 mg.), m. p. and mixed m. p. 108—109° (from methanol). Further elution with the same solvent (2 × 25 ml.) gave material, m. p. 85—95° (19 mg.), probably a mixture of 5β- and 5α-cholestan-4-one. Yet further elution with the same solvent (2 × 25 ml.) gave 5α-cholestan-4-one (11 mg.), m. p. and mixed m. p. 98—99°.

Reduction of 5-Bromo-5β-cholestan-4-one.—5-Bromo-5β-cholestan-4-one (20 mg.) in acetic acid (10 ml.) was treated with zinc dust (40 mg.) at 100° for 2 hr. The usual working up gave 5α-cholestan-4-one (14 mg.), m. p. and mixed m. p. 98—99° (mixed m. p. with 5β-cholestan-4-one depressed to 85—89°).

3α-Bromo-5α-cholestan-4-one.—(*a*) 5-Hydroxy-5α-cholestan-4-one [5] (m. p. 158—159°; 1 g.) in chloroform (20 ml.) was treated with a stream of dry hydrogen bromide at 20° for 0·5 hr. The usual isolation procedure gave an oil, which was chromatographed on aluminium oxide (30 g.; Woelm, neutral) in pentane. Elution with pentane (6 × 25 ml.) gave 3α-bromo-5α-cholestan-4-one (220 mg.), m. p. 117—120°, $[\alpha]_D$ −75° (*c* 0·85), $\nu_{max.}$ 1713 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ (log ε 2·0), after recrystallisation from acetone. Further elution with benzene–pentane gave crystalline fractions, m. p. 82—85°, with $\nu_{max.}$ 1712 (C=O), 1685 (C=C–C=O), and 1610 (C=C) cm.$^{-1}$, probably a mixture of a monobromo-ketone and an unsaturated ketone.

(*b*) The hydroxy-ketone (1 g.), as in (*a*), with hydrogen bromide for 5 min., gave 3α-bromo-5α-cholestan-4-one (1·05 g.), m. p. 121—122°, $[\alpha]_D$ −72° (*c* 0·9), $\nu_{max.}$ 1712 cm.$^{-1}$, $\nu_{max.}$ 309 mμ (log ε 2·0), rotatory dispersion: $[\alpha]_{332}$ −1770° (trough), $[\alpha]_{282}$ +2580° (peak) (*c* 0·01 in MeOH at 20°), after recrystallisation from acetone (Found: C, 69·6; H, 9·8%). Reduction with zinc in acetic acid gave 5α-cholestan-4-one (910 mg.), m. p. and mixed m. p. 100—101°, $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 285 mμ.

(*c*) 5-Bromo-5α-cholestan-4-one (m. p. 155—157°; 20 mg.) in acetic acid (5 ml.) containing a trace of hydrogen bromide was left at 20° for 0·75 hr. The usual procedure gave 3α-bromo-5α-cholestan-4-one (from acetone) (18 mg.), m. p. and mixed m. p. 117°, $[\alpha]_D$ −70° (*c* 0·85).

5α-Cholest-2-en-4-one.—3α-Bromo-5α-cholestan-4-one (1 g.) was heated with 2,4,6-collidine (20 ml.) under nitrogen at 160° for 4 hr. The customary procedure afforded an oil, which was chromatographed on aluminium oxide (30 g.) in pentane. Elution with benzene–pentane

(1 : 4; 2 × 50 ml.) gave an oil, $\nu_{max.}$ 1712 and 1689 cm.$^{-1}$; further elution with benzene–pentane (2 : 3; 4 × 50 ml.) gave 5α-*cholest*-2-*en*-3-*one* (735 mg.), double m. p. 73°/93°, $\nu_{max.}$ 1689 cm.$^{-1}$, $\lambda_{max.}$ 239 mμ (log ε 4·01), after recrystallisation from methanol (Found: C, 84·5; H, 11·8. $C_{27}H_{44}O$ requires C, 84·55; H, 11·5%).

5,6β-*Dibromo*-5α-*cholestan*-4-*one*.—Cholest-5-en-4-one [4] [100 mg., m. p. 111°, $\nu_{max.}$ 1685 cm.$^{-1}$, $\lambda_{max.}$ 241 mμ (log ε 3·9)] in acetic acid (5 ml.) was treated with bromine (42 mg., 1·06 mol.) in acetic acid (2 ml.). Decolorisation was immediate, and after 5 min. the product was poured into water and extracted with ether, to give 5,6β-*dibromo*-5α-*cholestan*-4-*one* (from ethanol) (120 mg.), m. p. 88°, $[\alpha]_D$ −13° (*c* 0·9), $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 308 mμ (Found: C, 59·8; H, 8·35. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%).

Bromination of 3α-*Bromo*-5α-*cholestan*-4-*one in the Presence of Hydrogen Bromide*.—(*a*) 3α-Bromo-5α-cholestan-4-one (200 mg.) in acetic acid (30 ml.) and chloroform (3 ml.) was treated with bromine (74 mg., 1·06 mol.) and a trace of hydrogen bromide at 20° for 18 hr. After removal of the excess of bromine with aqueous sodium hydrogen sulphite, the solution was worked up in the usual manner to give crystals, m. p. 140—150° (a few crystals remain at 160°). Recrystallisation from ethanol gave material (150 mg.), m. p. 150—155°, $[\alpha]_D$ −63° (*c* 0·9), $\nu_{max.}$ (in CCl_4) 1712, 1730 cm.$^{-1}$ (equal intensities), $\nu_{max.}$ (in Nujol) 1710, 1726 cm.$^{-1}$, $\lambda_{max.}$ 308 mμ, rotatory dispersion: $[\alpha]_{600}$ +25°, $[\alpha]_{500}$ +45°, $[\alpha]_{400}$ +325°, $[\alpha]_{340}$ +970°, $[\alpha]_{329}$ +500°, $[\alpha]_{308}$ −500°, $[\alpha]_{285}$ −1250°, $[\alpha]_{260}$ −1060° (*c* 0·7—0·07 in *cyclo*hexane at 20°), $[\alpha]_{600}$ +25°, $[\alpha]_{500}$ +45°, $[\alpha]_{400}$ +320°, $[\alpha]_{336}$ +920°, $[\alpha]_{327}$ +500°, $[\alpha]_{308}$ −500°, $[\alpha]_{285}$ −1250°, $[\alpha]_{260}$ −1060° (*c* 0·7—0·07 in methyl cyanide at 20°) (Found: C, 63·7; H, 8·65. Calc. for $C_{27}H_{45}BrO$: C, 69·7; H, 9·65. Calc. for $C_{27}H_{44}Br_2O$: C, 59·55; H, 8·15%). This corresponds to 50% of mono- and 50% of di-bromo-ketone, which could not be separated by recrystallisation or by chromatography on neutral aluminium oxide. This mixture (100 mg.) was chromatographed on a column of Davison silica gel (30 g.) prepared as described above. Elution with pentane (10 × 10 ml.) gave 3,3-*dibromo*-5α-*cholestan*-4-*one* (25 mg.), m. p. 179—181°, $[\alpha]_D$ −58° (*c* 0·95), $\nu_{max.}$ 1730 cm.$^{-1}$, $\lambda_{max.}$ 305 mμ (log ε 2·1), rotatory dispersion: $[\alpha]_{700}$ −543°, $[\alpha]_{325}$ −1585°, $[\alpha]_{275}$ +1920°, $[\alpha]_{262·5}$ +1736°, $[\alpha]_{255}$ +2090° (*c* 0·0249 in dioxan at 24°), after recrystallisation from acetone (Found: C, 59·25; H, 8·2. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%). Further elution with pentane containing only a few drops of ether gave a product, m. p. 150—154°, whilst elution with ether–pentane (1 : 99; 2 × 20 ml.) gave unchanged 3α-bromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 119—120°, after recrystallisation from acetone.

(*b*) 3α-Bromo-5α-cholestan-4-one (100 mg.) in chloroform (2 ml.), acetic acid (20 ml.), and a trace of hydrogen bromide was treated with bromine (140 mg., 4·0 mol.) at 20° for 18 hr. The usual isolation gave crystals (92 mg.), m. p. 160—165°, $\nu_{max.}$ 1730s, 1713w cm.$^{-1}$ (Found: C, 62·15; H, 8·65%). These figures correspond to 74% of dibromo-ketone. The mixture (80 mg.) was chromatographed on silica gel, as above, to give 3,3-dibromo-5α-cholestan-4-one (from acetone) (20 mg.), m. p. and mixed m. p. 178—179°, $\nu_{max.}$ 1730 cm.$^{-1}$, $\lambda_{max.}$ 304 mμ, after recrystallisation. Further elution gave unchanged 3α-bromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 119—120°, after recrystallisation from acetone.

Bromination of 3α-*Bromo*-5α-*cholestan*-4-*one in the Presence of Potassium Acetate*.—(*a*) 3α-Bromo-5α-cholestan-4-one (150 mg.) in acetic acid (15 ml.) containing potassium acetate (1 g.) was treated with bromine (55 mg., 1·06 mol.) at 90° for 1 hr. and 20° for 18 hr. After decolorisation with sodium hydrogen sulphite, the usual isolation gave crystals (95 mg.), m. p. 128—130°, $\nu_{max.}$ 1729w, 1712s cm.$^{-1}$ (Found: C, 67·15; H, 9·4%). This corresponds to 75% of mono- and 25% of dibromo-ketone, which could not be separated by recrystallisation.

(*b*) The product from (*a*), m. p. 128—130° (100 mg.), in acetic acid (20 ml.) was further treated with potassium acetate (1 g.) and bromine (140 mg., 4 mol.) in chloroform (5 ml.) for 24 hr. at 20°. The usual working up gave crystals (80 mg.), m. p. 130—135°, $\nu_{max.}$ 1730w, 1712s cm.$^{-1}$, which were separated by chromatography on silica gel, as previously described, into 3,3-dibromo-5α-cholestan-4-one (10 mg.), m. p. and mixed m. p. 179—180°, and unchanged 3α-bromo-5α-cholestan-4-one (25 mg.), m. p. and mixed m. p. 119—120°.

Bromination of 5-*Bromo*-5α-*cholestan*-4-*one*.—(*a*) 5-Bromo-5α-cholestan-4-one (m. p. 155—157°; 100 mg.) in acetic acid (30 ml.) was treated with bromine (37 mg., 1·05 mol.) and a trace of hydrogen bromide at 20° for 0·75 hr. The product, isolated by precipitation with water, had m. p. 155—160°, $\nu_{max.}$ 1728 and 1710 cm.$^{-1}$ (equal intensities), and was chromatographed on silica gel as above, to give by elution with pentane 3,3-dibromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 179—180°, $\nu_{max.}$ 1729 cm.$^{-1}$, $\lambda_{max.}$ 305 mμ, after recrystallisation from

acetone; further elution with ether–pentane (1 : 100) and recrystallisation from acetone gave 3α-bromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 117—119°, $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ.

(*b*) 5-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (50 ml.) was treated with bromine (74 mg., 2·1 mol.) at 20° for 24 hr. Addition of water gave unchanged 5-bromo-5α-cholestan-4-one (78 mg.).

(*c*) 5-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (50 ml.) was treated with 1 drop of a saturated solution of hydrogen bromide in acetic acid and then dropwise with bromine (37 mg., 1·05 mol.) and anhydrous sodium acetate (18 mg.) in acetic acid (10 ml.). After 4 hr. at 20° the bromine was not decolorised, and dilution with water gave unchanged 5-bromo-5α-cholestan-4-one (80 mg.), m. p. and mixed m. p. 154—155° (from acetone).

3-*Bromo*-5α-*cholest*-2-*en*-4-*one*.—(*a*) 5α-Cholest-2-en-4-one (50 mg.) in chloroform (20 ml.) was treated with bromine (22 mg., 1·05 mol.) in chloroform at 20°. The usual working up gave 2β,3α-*dibromo*-5α-*cholestan*-4-*one* (55 mg.) (from acetone), m. p. 185—187°, $\lambda_{max.}$ 310 mμ (log ε 1·5) (Found: C, 59·65; H, 8·0. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%). Chromatography of the 2β,3α-dibromo-ketone (500 mg.) on aluminium oxide (Spence, type H, activity ~II; 15 g.) and elution with benzene–pentane (1 : 9; 4 × 30 ml.) furnished 3-*bromo*-5α-*cholest*-2-*en*-4-*one* (345 mg.), m. p. 131—132°, $\nu_{max.}$ 1702 cm.$^{-1}$, $\lambda_{max.}$ 265 mμ (log ε 3·91), after recrystallisation from acetone (Found: C, 70·0; H, 9·15. $C_{27}H_{43}BrO$ requires C, 69·95; H, 9·35%).

(*b*) 3,3-Dibromo-5α-cholestan-4-one (50 mg.) was heated with 2,4,6-collidine (5 ml.) under nitrogen at 160° for 0·5 hr. The product, isolated in the usual way, was chromatographed on aluminium oxide (Spence, type H; 1·5 g.); elution with benzene–pentane (1 : 9) yielded 3-bromo-5α-cholest-2-en-4-one (from acetone), m. p. 131—132° alone or mixed with the sample prepared as in (*a*).

3β,5-*Dibromo*-5α-*cholestan*-4-*one*.—3α-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (20 ml.) and dry chloroform (5 ml.) was treated with bromine (55 mg., 1·5 mol.) in acetic acid (5 ml.) and a 50% solution of hydrogen bromine in acetic acid (1 ml.) for 44 hr. at 20°. After being worked up in the usual manner, the brown oil crystallised slowly from ethanol, to give 3α,5-*dibromo*-5β-*cholestan*-4-*one* (60 mg.), m. p. 109°, $\nu_{max.}$ 1728 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ (log ε 1·9), optical rotatory dispersion: $[\alpha]_{700}$ 0°, $[\alpha]_{589}$ −16°, $[\alpha]_{331}$ −1730°, $[\alpha]_{314}$ 0°, $[\alpha]_{280}$ +287°, $[\alpha]_{257}$ +199° (*c* 0·075 in MeOH at 27°) (Found: C, 59·3; H, 8·1. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%). A mixed m. p. with 3α-bromo-5α-cholestan-4-one was 85—90°.

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