1193. *Steroids and Walden Inversion. Part LVI.* The Bromination of 5β-Cholestan-3-one*

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Kinetically controlled monobromination of 5β-cholestan-3-one fails to yield the axial 4α-bromo-ketone and gives the equatorial 4β-bromo-ketone. Specimens of the 2β,4β-dibromo-ketone, which are homogeneous by thin-layer chromatography and n.m.r. spectroscopy, give two infrared carbonyl absorption peaks at 1756 and 1733 cm.$^{-1}$, and so appear to contain a small proportion of a second compound suggested to be the 2,2-dibromo-ketone. The 2β,4β-dibromo-ketone by acid-catalysed monobromination affords the 2,2,4β-tribromo-ketone, and by rapid base-catalysed dibromination at 80° the 2,2,4,4-tetrabromo-ketone.

Monobromination of 5β-cholestan-3-one (I) in acetic acid, catalysed by hydrogen bromide, gives, as originally reported by Butenandt and Wolff,[1] the equatorial 4β-bromo-ketone (IV), $\nu_{max.}$ 1733,[2] 1735 cm.$^{-1}$,[3] ($\Delta\nu$ +17, +19). The nuclear magnetic resonance (n.m.r.) spectrum shows the signal for the axial 4α-proton at τ 5·02 as a doublet (J = 12·5 c./sec.) on account of splitting by the single axial 5β-proton; the equatorial 2β-bromo ketone, if formed,[4] can be present only in traces. Kinetically controlled [5] monobromination failed to afford the axial 4α-bromo-ketone † and gave the 4β-bromo-ketone (IV); the axial 4α-position in 5β-steroid 3-ketones is severely hindered by ring B (H-7α, H-9α;

* Part LV, preceding Paper.

† The claim of Holysz (*J. Amer. Chem. Soc.*, 1953, **75**, 4432) to have isolated both 4α- and 4β-bromo-ketones from 5β-pregnane-3,11,20-trione by base-catalysed monobromination in acetic acid, and by toluene-*p*-sulphonic acid-catalysed monobromination in dimethylformamide, rests mainly on somewhat unconvincing infrared spectroscopic evidence—{4α-bromo-ketone: $[\alpha]_D$ + 95°, $\nu_{max.}$ 1704 (CO), 719 (ax. C–Br!) cm.$^{-1}$ (cf. Barton, Page, and Shoppee, *J.*, 1956, 331); 4β-bromo-ketone: $[\alpha]_D$ + 136°, $\nu_{max.}$ 1720 (CO), 714 (eq. C–Br!) cm.$^{-1}$}.

[1] A. Butenandt and A. Wolff, *Ber.*, 1935, **68**, 2091, C. Djerassi and C. R. Scholz, *J. Amer. Chem. Soc.*, 1948, **70**, 417.

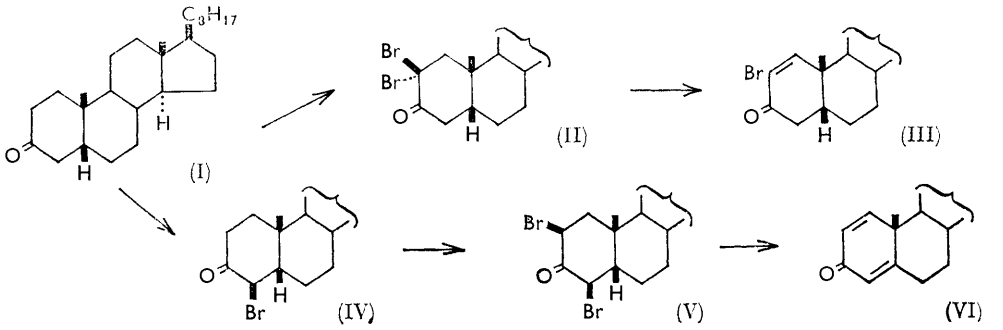
[2] R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828; E. J. Corey, *Experentia*, 1953, **9**, 329.

[3] This Paper.

[4] V. R. Mattox and E. C. Kendall, *J. Biol. Chem.*, 1950, **185**, 593; 1951, **188**, 287, footnote 6.

the C-6/7, and C-10/9 bonds), and it seems probable therefore that the equatorial 4β-bromine atom is introduced directly [5] or by way of a quasi-boat intermediate (ends at C-2 and C-5) with reversion to the chair conformation.[5,6]

Base-catalysed monobromination of 5β-cholestan-3-one, which fails with 5α-cholestan-3-one,[7] gave 49% of the 4β-bromo-ketone (IV). This compound was also obtained in ~43% yield by use of phenyltrimethylammonium tribromide [8] in tetrahydrofuran at 20°, and in ~24% yield by use of cupric bromide [9] in refluxing methanol.



Dibromination of 5β-cholestan-3-one in acetic acid, catalysed by hydrogen bromide, originally thought to give the 4,4-dibromo-ketone,[10-12] furnished [13] 90% of the diequatorial 2β,4β-dibromo-ketone (V), m. p. 136—137°, $[\alpha]_D$ +10°, $\nu_{max.}$ 1756 cm.$^{-1}$,[13] [Δν +40), converted by dehydrobromination with collidine into cholesta-1,4-dien-3-one (VI).[13,14] This compound was, however, accompanied by 2-bromo-5β-cholest-1-en-3-one (III), derived from ~8% of the 2,2-dibromo-ketone (II), either present in admixture with the 2β,4β-dibromo-ketone, or formed therefrom by rearrangement.[13] Acid-catalysed monobromination in acetic acid of the 4β-bromo-ketone (I) also affords the 2β,4β-dibromo-ketone (V), m. p. 137—138°, in 70% yield.

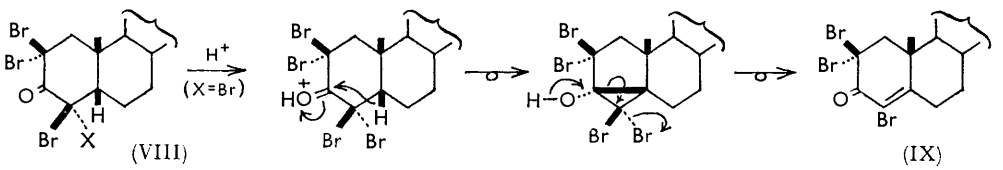
Specimens of the 2β,4β-dibromo-ketone, prepared by either method, give n.m.r. spectra exhibiting a signal for one proton, attached to a carbon atom bearing a bromine atom, as a quartet centred at τ 5·18 (J = 5·0 and 14·6 c./sec.), due to the axial 2α-proton with splitting by the equatorial 1α-proton and the axial 1β-proton, and a signal, for one proton attached to a carbon atom bearing a bromine atom, as a doublet at τ 4·92 (J = 11·4 c./sec.), due to the axial 4α-proton with splitting by the single axial 5β-proton. The infrared (i.r.) absorption spectra, however, disclose two carbonyl stretching frequencies, $\nu_{max.}$ 1756s and 1733w cm.$^{-1}$, although thin-layer chromatography on silica gel in pentane gave only one spot, and column chromatography on silica, not unexpectedly, failed to achieve any separation. Since the analytical figures corresponded to a dibromo-ketone, the compound responsible for the maximum at 1733 cm.$^{-1}$ (Δν +17) must contain one equatorial bromine atom, and can only be the 4,4-, 2β,4α-, 2α,4β-, or 2,2-dibromo-ketone, unless some of the 2β,4β-dibromoketone exists as the energetically improbable boat conformation (ends at C-2 and C-5) with the 4β-bromide atom boat-equatorial and the 2β-bromide atom as a flagpole.

The axial 4α-bromine atom in the 4,4- and 2β,4α-isomers is subject to 1,3 and 1,4 steric

[5] R. Mauli, H. J. Ringold, and C. Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 5494.
[6] J. Vals and E. Toromanoff, *Bull. Soc. chim. France*, 1961, 758.
[7] C. W. P. Crowne, R. M. Evans, G. F. H. Green, and A. G. Long, *J.*, 1956, 4351.
[8] A. Marquet, M. Dvolaitzky, H. B. Kajan, L. Mamlok, C. Ouannes, and J. Jacques, *Bull. Soc. chim. France*, 1961, 1822.
[9] E. R. Glazier, *J. Org. Chem.*, 1962, **27**, 2937.
[10] A. Butenandt, G. Schramm, A. Wolff, and H. Kudzsus, *Ber.*, 1936, **69**, 2779.
[11] L. Ruzicka, W. Bosshard, W. H. Fischer, and H. Wirz, *Helv. Chim. Acta*, 1936, **19**, 1147.
[12] H. H. Inhoffen, G. Stoeck, and I. U. Nebel, *Annalen*, 1949, **563**, 135.
[13] C. Djerassi and G. Rosenkranz, *Experientia*, 1951, **7**, 93.
[14] H. H. Inhoffen, G. Kolling, G. Koch, and I. U. Nebel, *Chem. Ber.*, 1951, **84**, 361.

repulsions, and should undergo ready *trans*-diaxial elimination with the tertiary 5β-hydrogen atom; specimens of the above 2β,4β-dibromo-ketone showed no tendency, as revealed by ultraviolet (u.v.) spectroscopy, to lose hydrogen bromide under mild conditions. Numerous attempts were made to prepare the unknown 4,4-dibromo-ketone from the 4β-bromo-ketone (IV). Kinetically controlled [5] monobromination at 20° gave 32% of 2β,4β-dibromo-ketone (V), m. p. 134—136°, $\nu_{max.}$ 1756 and 1733 cm.$^{-1}$; in a repetition, the total bromination product was heated briefly with collidine, and gave 24% of the starting material (IV), and 19% of 2α-bromocholest-4-en-3-one [15] (presumably derived from the 2β,4β-dibromo-ketone by elimination at C-4 and inversion at C-2), but no 4-bromocholest-4-en-3-one.[16] Base-catalysed monobromination did not occur at 20° or 40°, and at 80° gave unsaturated non-crystalline material; bromination did not proceed with phenyltrimethylammonium tribromide [8] in tetrahydrofuran at 20° or with cupric bromide [9] in refluxing methanol during 2 hr. An attempt to prepare 2α,4β-dibromo-5β-cholestan-3-one by acid-catalysed monobromination of the 4β-bromo-ketone (I) in dioxan at 25° [17] gave 77% of a product, m. p. 134—136°, whose n.m.r. spectrum showed only the pattern expected for the 2β,4β-dibromo-ketone (V), and whose i.r. spectrum again exhibited two carbonyl stretching frequencies, $\nu_{max.}$ 1756 and 1733 cm.$^{-1}$. It is suggested that the compound responsible for the peak at 1733 cm.$^{-1}$ is the 2,2-dibromo-ketone (II). If some 8% of the 2β-bromo-ketone were present in specimens of the 4β-bromo-ketone, its presence would not easily be recognised by n.m.r. spectroscopy. The 2,2-dibromo-ketone could be formed by bromination at C-2 of 5β-cholestan-3-one, since the 2α-position, in contrast to the 4α-position, is hindered only by H-9α and the C-10/9 bond, but production of the 2,2-dibromo-ketone by monobromination of the 4β-bromo-ketone must involve rearrangement. An attempt to isolate the 2,2-dibromo-ketone postulated to be present, by formation of the 4-piperonylidene derivative, failed; the material recovered still showed two peaks at $\nu_{max.}$ 1756 and 1733 cm.$^{-1}$.

Attempted tribromination of 5β-cholestan-3-one (I) in chloroform–acetic acid at 20° during two weeks gave 13% of 2,2,4-tribromocholest-4-en-3-one [11,15,18,19] (IX), m. p. 179—181°, $\nu_{max.}$ 1705 cm.$^{-1}$, identified by mixed m. p. and i.r. spectra, and possibly produced from some initially formed 2,2,4,4-tetrabromo-ketone (VIII; X = Br) by the reaction sequence:



Although the 2β,4β-dibromo-ketone [V] was unaltered by brief treatment with bromine in acetic acid at 20°, monobromination in chloroform–acetic acid at 20° for two weeks,[20] followed by careful chromatography, gave the 2,2,4β-tribromo-ketone (VIII; X = H), m. p. 62—65°, $\nu_{max.}$ 1752 cm.$^{-1}$ ($\Delta\nu$ +36), whose n.m.r. spectrum showed a signal for one proton on carbon attached to bromine as a doublet at τ 4·20 (J = 12·5 c./sec.), due to the 4α-proton, and signals for two protons at τ 6·62 and 7·46 forming an AB quartet (J_{AB} = 17 c./sec.), due to the 1α- and 1β-protons. Further chromatography gave later fractions containing unchanged 2β,4β-dibromo-ketone, and 2α,4-dibromocholest-4-en-3-one,[18] $\lambda_{max.}$ 266 mμ, which were identified by comparison of R_F values with those of authentic samples.

[15] C. W. Shoppee, R. E. Lack, and J. Scott, *J.*, 1962, 2233.
[16] D. N. Kirk, D. K. Patel, and V. Petrow, *J.*, 1956, 627.
[17] G. Muller, R. Joly, G. Nominé, and D. Bertin, *Bull. Soc. chim. France*, 1956, 1457.
[18] C. W. Shoppee, P. J. Havlicek, and R. E. Lack, *J.*, 1964, 4992.
[19] H. H. Inhoffen and W. Becker, *Chem. Ber.*, 1952, **85**, 181.
[20] B. Ellis and V. Petrow, *J.*, 1953, 3869.

The 2,2,4,4-tetrabromo-ketone (VIII; X = Br) was obtained by rapid base-catalysed dibromination at 80° of the 2β,4β-dibromo-ketone (V). The compound, m. p. 58—61°, $\nu_{max.}$ 1756 cm.$^{-1}$ ($\Delta\nu$ +40), also showed a small i.r. peak at 1680 cm.$^{-1}$ and u.v. absorption at 265 mμ, due to traces of 2,2,4-tribromocholest-4-en-3-one (IX) into which it tended to pass, possibly by sequence (A), on recrystallisation or chromatography. The n.m.r. spectrum, however, showed no protons attached to the same carbon atom as bromine, and no vinyl proton. Base-catalysed tetrabromination at 80° of 5β-cholestan-3-one (I) gave a mixture of the 2β,4β-dibromo-ketone (V), the 2,2,4,4-tetrabromo-ketone (VIII; X = Br), and its decomposition product (IX), which could not be completely separated by column chromatography, but were identified by thin-layer chromatography. Polybromination of 5β-cholestan-3-one in chloroform–acetic acid at 20° for three weeks gave only 2,2,4-tribromocholest-4-en-3-one (IX), which crystallised from the solution; in chloroform at 20° for five weeks, the products were the unsaturated 2,2,4-tribromo-ketone (IX), and possibly 2,2,4,6β-tetrabromocholest-4-en-3-one. Irradiation of 2,2,4-tribromocholest-4-en-3-one (IX) with *N*-bromosuccinimide in refluxing carbon tetrachloride gave, after column chromatography, fractions consisting of the starting material mixed with a substance possessing the same R_F value, on thin-layer chromatography, as the postulated unsaturated 2,2,4,6β-tetrabromo-ketone; further column chromatography failed to yield the 2,2,4,6β-tetrabromo-ketone.

The i.r. absorption maxima and the significant n.m.r. signals for the bromo-5β-cholestan-3-ones are given in the Table. The consistent values of the increments $\Delta\nu$ for the introduction of equatorial 2β- and 4β-bromine atoms suggest that, in contrast to the 5α-series,[21] there is little distortion of ring A in the 5β-series, although some twisting may occur in the tetrabromo-ketone (VIII; X = Br). Similarly, successive introduction at C-2 and C-4 of bromine atoms lying at 90° or 109° to the C-19 angular methyl group produces but little shift in the n.m.r. signal given by that group.

Infrared and n.m.r. absorptions of bromo-5β-cholestan-3-ones

Compound	$\nu_{max.}$ (cm.$^{-1}$)	$\Delta\nu$	C-19 (Me) (τ)	1-H (τ)	2-H (τ)	4-H (τ)
(I)	1716	—	8·99	—	—	—
(IV)	1735	+19	8·92	—	—	5·02[D] [c]
(V)	1756	+40	8·91	—	5·18[Q] [b]	4·92[D] [d]
(VIII; X = H)	1752	+36	8·91	7·03[Q] [a]	—	4·20[D] [e]
(VIII; X = Br)	1755	+39	8·90	—	—	—

Q = quartet. D = doublet.

$J_{H:H}$: *a* = 16·0 and 50·0, *b* = 5·0 and 14·6, *c* = 12·5, *d* = 11·4, *e* = 12·5 c./sec.

Experimental

For general directions see *J.*, 1959, 345; $[\alpha]_D$ are for chloroform solutions; u.v. absorption spectra were measured in 1% ethanol solutions with a Perkin-Elmer 4000A spectrophotometer, whilst i.r. absorption spectra were determined for carbon tetrachloride solutions with a Perkin-Elmer 221 double-beam instrument. N.m.r. spectra were recorded on a Varian D.P. 60 instrument at 60 Mc./sec. with deuterochloroform as solvent and tetramethylsilane as internal reference. Silica gel (Davis) or alumina (Spence type H, activity ~II) was used for chromatography.

5β-*Cholestan*-3-*one* (I) (cf. ref. 22).—Cholest-4-en-3-one (13 g.) in ethanol (200 ml.) containing potassium hydroxide (0·5 g.) was hydrogenated with 10% palladium–charcoal (0·5 g.) until absorption ceased. After filtration, neutralisation with acetic acid, and removal of ethanol *in vacuo*, the residue was worked up in the usual way to give 5β-cholestan-3-one (10·4 g.), m. p. 58—60° (from acetone–ethanol).

[21] C. W. Shoppee, T. E. Bellas, R. E. Lack, and S. Sternhell, *J.*, 1965, 2483.

[22] L. Ruzicka, H. Brüngger, E. Eichenberger, and J. Meyer, *Helv. Chim. Acta*, 1934, **17**. 1414; cf. H. Grasshof, *Z. physiol. Chem.*, 1934, **223**, 250.

4β-*Bromo*-5β-*cholestan*-3-*one* (IV).—(*a*) The ketone (I) (11·5 g.) was dissolved in acetic acid (250 ml.) and a few drops of 4N-hydrogen bromide in acetic acid were added, followed by bromine in acetic acid (30·2 ml. of 5% v/v solution: 1·0 mol.); decolourisation occurred in a few minutes. The product (14 g.), isolated in the usual manner, was chromatographed on silica (1100 g.) in pentane; elution with ether–pentane (3 : 97) gave 4β-bromo-5β-cholestan-3-one (10·8 g.), m. p. 111—113° (from aqueous ethanol), $[\alpha]_D$ + 40°, $\nu_{max.}$ 1735 cm.$^{-1}$, τ 5·02 (doublet, J = 12·5 c./sec.) [Found (after drying at 25°/0·3 mm. for 12 hr.): C, 69·55; H, 9·8. Calc. for $C_{27}H_{45}BrO$: C, 69·65; H, 9·75%].

(*b*) The ketone (I) (375 mg.) dissolved in acetic acid (10 ml.) at 20°, was treated with a solution of hydrogen bromide in acetic acid (1 drop), and then titrated with a solution of bromine in acetic acid (10 ml.; 0·5% v/v solution; 1·05 mol.) during 20 min.[5] A solution of sodium hydrogen sulphite was added, and the product extracted with ether. The usual isolation procedure furnished an oil (470 mg.), which was chromatographed on silica (30 g.) in pentane. Elution with ether–pentane (1 : 49; 9 × 30 ml.) gave 4β-bromo-5β-cholestan-3-one (203 mg.), m. p. 106—108°, whose i.r. spectrum was identical with that of an authentic sample. Further elution with ether–pentane gave unchanged 5β-cholestan-3-one (135 mg.), m. p. 55—57°.

(*c*) The ketone (I) (300 mg.), dissolved in acetic acid (20 ml.) at 80°, was treated with a solution of anhydrous potassium acetate (1 g.) in acetic acid (9 ml.) at 80°, followed by bromine in acetic acid (4·0 ml. of 1% v/v solution; 1·0 mol.). After 15 min. at 80° the colour had disappeared, the solution was cooled, and the product (266 mg.) isolated with ether in the usual fashion. Chromatography on silica (17 g.) in pentane, and elution with ether–pentane (3 : 97; 6 × 20 ml.), gave 4β-bromo-5β-cholestan-3-one (108 mg.), m. p. and mixed m. p. 110—112°; further elution with the same eluant (3 × 20 ml.) gave the ketone [I] (68 mg.), m. p. and mixed m. p. 55—57°.

(*d*) The ketone (I) (250 mg.), dissolved in tetrahydrofuran (3 ml.) at 20°, was treated with a solution of phenyltrimethylammonium tribromide [8] (92 mg.) in tetrahydrofuran (2 ml.); immediate decolourisation occurred, and phenyltrimethylammonium bromide was precipitated. After 1 hr. at 20°, a 5% solution of sodium hydrogen carbonate was added, and the solution extracted with ether. The resultant oil (349 mg.) was chromatographed on silica (20 g.) in pentane; elution with ether–pentane (6 × 25 ml.) gave 4β-bromo-5β-cholestan-3-one (82 mg.), m. p. and mixed m. p. 110—112°, and further similar elution (3 × 25 ml.) gave a mixture of the 4β-bromo-ketone and the ketone (I) (31·5 mg.), followed (5 × 25 ml.) by the ketone (I) (92 mg.), m. p. and mixed m. p. 57°.

(*e*) The ketone (I) (500 mg.) was refluxed with cupric bromide [9] (583 mg., 2 mol.) in methanol (80 ml.) for 24 hr. Filtration and vacuum-evaporation gave a brown paste; water was added and organic material extracted with chloroform. The resultant yellow oil (450 mg.) was shown by thin-layer chromatography on silica (20 g.) in pentane to contain six compounds. Column chromatography on silica (20 g.) in pentane, and elution with ether–pentane (3 : 97; 5 × 30 ml.), gave 4β-bromo-5β-cholestan-3-one (142 mg.), m. p. and mixed m. p. 110—112°; further elution with ether–pentane (3 : 97, 4 : 96; 5 × 30 ml.) gave a mixture of compounds (184 mg.), $\lambda_{max.}$ 261 mμ.

2β,4β-*Dibromo*-5β-*cholestan*-3-*one* (V).—(*a*) The ketone (I) was dibrominated according to the directions of Djerassi and Rosenkranz; [13] the product, m. p. 137—138°, $[\alpha]_D$ + 10° (from acetone–ethanol), showed $\nu_{max.}$ 1756 and 1733 cm.$^{-1}$.

(*b*) The 4β-bromo-ketone (IV) (1·64 g.) in acetic acid (80 ml.) was treated with a few drops of a 4N-solution of hydrogen bromide in acetic acid, followed by a solution of bromine in acetic acid (3·8 ml. of 5% v/v solution; 1·05 mol.). Decolourisation was complete after 20 min. at 20°, and crystals began to form. After 1 hr., the crystals (1·6 g.) were filtered off and recrystallised from acetone–ethanol to give 2β,4β-dibromo-5β-cholestan-3-one (1·3 g.), m. p. 137—138°, $\nu_{max.}$ 1756s, 1733w cm.$^{-1}$, τ 5·18 (quartet; J = 5·0 and 14·6 c./sec.) and τ 4·92 (doublet; J = 11·4 c./sec.) [Found (after drying at 20°/0·5 mm. for 18 hr.): C, 59·4; H, 8·2. Calc. for $C_{27}H_{44}Br_2O$: C, 59·55; H, 8·15%].

(*c*) The 4β-bromo-ketone (IV) (300 mg.) was brominated according to the procedure of Muller, Joly, Nominé, and Bertin [17] in dioxan (5 ml.) at 20°; a few drops of a 4N-solution of hydrogen bromide in acetic acid were added, followed by a solution of bromine in acetic acid (3·5 ml. of 1% v/v solution; 1·05 mol.). Decolourisation occurred in a few minutes, and the product was extracted with ether, and isolated as directed.[17] The resultant solid (290 mg.), by crystallisation from acetone–ethanol, gave 2β,4β-dibromo-5β-cholestan-3-one, m. p. and

mixed m. p. 134—136°, $\nu_{max.}$ 1756, 1733 cm.$^{-1}$, τ 5·18 (quartet: J = 5·0 and 14·6 c./sec.), τ 4·92 (doublet: J = 11·4 c./sec.).

Attempted Separation of 2,2-*Dibromo*-5β-*cholestan*-3-*one as the* 4-*Piperonylidene Derivative.*—2β,4β-Dibromo-5β-cholestan-3-one ($\nu_{max.}$ 1756 and 1733 cm.$^{-1}$, suspected to contain a small proportion of 2,2-dibromo-5β-cholestan-3-one) (300 mg.), was dissolved in hexane (10 ml.) and treated with piperonal (91 mg., 1·1 mol.) and a solution of hydrogen chloride in ethanol (saturated at 0°).[23] The mixture was shaken at 20° for 40 hr.; ethanol was then removed at 30°/10 mm., and the residue mixed with a little water. The solid was filtered off, dried *in vacuo* (209 mg.), and chromatographed on silica (18 g.) in pentane. Elution with ether–pentane (1 : 99; 4 × 30 ml.) gave 2β,4β-dibromo-5β-cholestan-3-one (133 mg.), m. p. and mixed m. p. 134—137°, $\nu_{max.}$ 1756 and 1733 cm.$^{-1}$; further elution with the same eluant (7 × 30 ml.) gave impure 2β,4β-dibromo-5β-cholestan-3-one (54 mg.), but use of other ether–pentane mixtures failed to yield a piperonylidene compound.

2,2,4β-*Tribromo*-5β-*cholestan*-3-*one* (VIII; X = H).—The 2β,4β-dibromo-ketone (V) (316 mg.), dissolved in chloroform (3 ml.) and acetic acid (3 ml.) was treated with bromine in acetic acid (3·5 ml. of 1% v/v solution; 1·2 mol.) at 20° for 2 weeks. Dilution with water, extraction with ether, and the usual working up gave an oil (374 mg.), which was chromatographed on silica (25 g.) in pentane. Elution with ether–pentane (0·6: 99·4; 5 × 30 ml.) gave 2,2,4β-*tribromo*-5β-*cholestan*-3-*one* (33 mg.), m. p. 62—65°, $\nu_{max.}$ 1756 cm.$^{-1}$, τ 6·62, 7·46 (AB-quartet, J_{AB} = 17 c./sec.) and 4·20 (doublet: J = 12·5 c./sec.) after crystallisation from aqueous ethanol [Found (after drying at 20°/0·2 mm. for 15 hr.): C, 52·05; H, 6·75. $C_{27}H_{43}BrO$ requires C, 52·0; H, 6·95%]. Further elution with ether–pentane mixtures gave fractions containing mixtures (200 mg.) of the 2,2,4-tribromo-ketone, 2α,4-dibromocholest-4-en-3-one, and unchanged 2β,4β-dibromo-ketone, which were identified, by comparison of R_F values on thin-layer chromatography, with those of authentic samples.

2,2,4,4-*Tetrabromo*-5β-*cholestan*-3-*one* (VIII; X = Br).—(*a*) The 2β,4β-dibromo-ketone (V) (250 mg.), dissolved in acetic acid (20 ml.) at 80°, was treated with a solution of anhydrous potassium acetate (2 g.) in acetic acid (12 ml.) at 80°, followed by bromine in acetic acid (4·7 ml. of 1% v/v solution; 2 mol.). After 8 min. at 80° decolourisation was complete; the solution was cooled in ice, and water added. The product was filtered off, dried roughly on porous porcelain, and then at 20°/0·1 mm. for 1 hr. Chromatography on silica (5 g.) in pentane and elution with pentane (1 × 30 ml.) gave 2,2,4,4-*tetrabromo*-5β-*cholestan*-3-*one* (55 mg.), m. p. 58—61°, $\nu_{max.}$ 1756 cm.$^{-1}$, after rapid recrystallisation from hexane–methanol, but showing $\nu_{max.}$ 1680 and $\lambda_{max.}$ 262 mμ due to traces of unsaturated material [?2,2,4-tribromo-cholest-4-en-3-one (IX)] [Found (after drying at 20°/0·3 mm. for 15 hr.): C, 46·7; H, 6·8. $C_{27}H_{42}Br_4O$ requires C, 46·2; H, 6·1%]. The n.m.r. spectrum showed no protons on carbon attached to bromine, and no vinyl proton.

(*b*) The 5β-ketone (I) (500 mg.) was treated at 80°, as above, in acetic acid in presence of potassium acetate with bromine (4 mol.). The product, by column chromatography on silica (30 g.) in pentane, gave by elution with pentane (2 × 50 ml.) a mixture (143 mg.) of the 2,2,4,4-tetrabromo-ketone (VIII; X = Br) and 2,2,4-tribromocholest-4-en-3-one (IX), identified by thin-layer chromatography; further elution with pentane (4 × 50 ml.) furnished 2,2,4-tribromocholest-4-en-3-one (IX) (90 mg.), m. p. and mixed 179—180°, whilst elution with ether–pentane (1 : 199; 4 × 50 ml.) yielded 2β,4β-dibromo-5β-cholestan-3-one (V) (47 mg.), m. p. and mixed m. p. 135—137°.

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[23] C. W. Shoppee, *Helv. Chim. Acta*, 1944, **27**, 426.