704. *Steroids. Part XVI.* The Bromination of Some 3-Keto-steroids Methylated in Ring-A.*

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Monobromination, under kinetic control, of 2β-, 4α-, and 4β-methyl-5α-cholestan-3-one gives equatorial bromo-derivatives. The 2β-methyl ketone gives the same 2α-bromo-derivative as had been obtained from the 2α-methyl epimer; both the 4α- and the 4β-methyl ketone give 2α-bromo-4α-methyl-5α-cholestan-3-one.

A study of di- and tri-bromination of the three ketones has been made, and the bromination products of 4-methylcholest-4-en-3-one have been prepared for comparison.

Recent investigations by Djerassi and his co-workers [1-3] of the monobromination of 2α-methyl-3-oxo- and 19-nor-2α-methyl-3-oxo-steroids demonstrate that the stereochemical course of such brominations is considerably more complicated than envisaged originally by Corey,[4] and that modification is required of the currently accepted stereochemical picture of the halogenation of cyclohexanones.

* Part XV, *J.*, 1962, 2233.

[1] Djerassi, Finch, Cookson, and Bird, *J. Amer. Chem. Soc.*, 1960, **82**, 5488; Djerassi, Finch, and Mauli, *ibid.*, 1959, **81**, 4997.

[2] Mauli, Ringold, and Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 5494.

[3] Villoti, Ringold, and Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 5693.

[4] Corey, *Experientia*, 1953, **9**, 329; *J. Amer. Chem. Soc.*, 1954, **76**, 175.

Djerassi *et al.*[3] concluded that, in the presence of steric inhibition, the product of kinetic control is the equatorial and not the axial bromo-ketone, whilst in the absence of such steric factors appreciable amounts of the equatorial epimers may accompany the axial bromo-ketones. Consistently, chlorination under apparent kinetic control of the Δ^6-enol of 3β-acetoxy-5α-cholestan-7-one has been found [5] to give only the equatorial 6α-chloro-ketone; and chlorination of 5α-cholestan-7-one has been shown [6] to give only the equatorial 6α-chloro-ketone, whilst only equatorial bromo-ketones have been obtained from 4,4-dimethyl-5α-cholestan-3-one [7] and 5α-cholestan-1-one.[7,8]

Kinetically controlled bromination of 2α-methyl-5α-cholestan-3-one (I) or its Δ^2-enol acetate (IV; R = Ac) gave [9] a monobromo-ketone shown by its optical rotatory dispersion [1] to be 2α-bromo-2β-methyl-5α-cholestan-3-one (II), in which ring A exists in the boat conformation. The greater stability of the boat conformation is due to the presence of the angular 10β-methyl group,[10] since in brominations of the analogous 19-nor-steroids [3] the boat conformation is not encountered. Djerassi *et al.*[1,3] regard the bromination of 2α-methyl-5α-cholestan-3-one (I) as proceeding by rearward (α) equatorial bromination of an intermediate of chair-like conformation,[11] followed by conformational change of ring A to the boat form.

It was of interest, therefore, to examine the bromination of 2β-, 4α-, and 4β-methyl-5α-cholestan-3-one. 2β-Methyl-5α-cholestan-3-one (III) was prepared by the method of Mazur and Sondheimer,[9] by hydrogenation of 2-methyl-5α-cholest-1-en-3-one. It was found, however, more convenient to prepare the intermediate 2α-methyl-5α-cholestan-3-one by the method of Djerassi *et al.*[1]. Kinetically controlled monobromination of 2β-methyl-5α-cholestan-3-one * (III) yielded 2α-bromo-2β-methyl-5α-cholestan-3-one (II) with ring A in the boat conformation, identical with the product derived from 2α-methyl-5α-cholestan-3-one (I) under similar conditions. This would be the expected result if bromination proceeds by rearside (α) attack by way of the Δ^2-enol (IV; R = H). No pure product was isolated on attempted dibromination of the ketone (III).

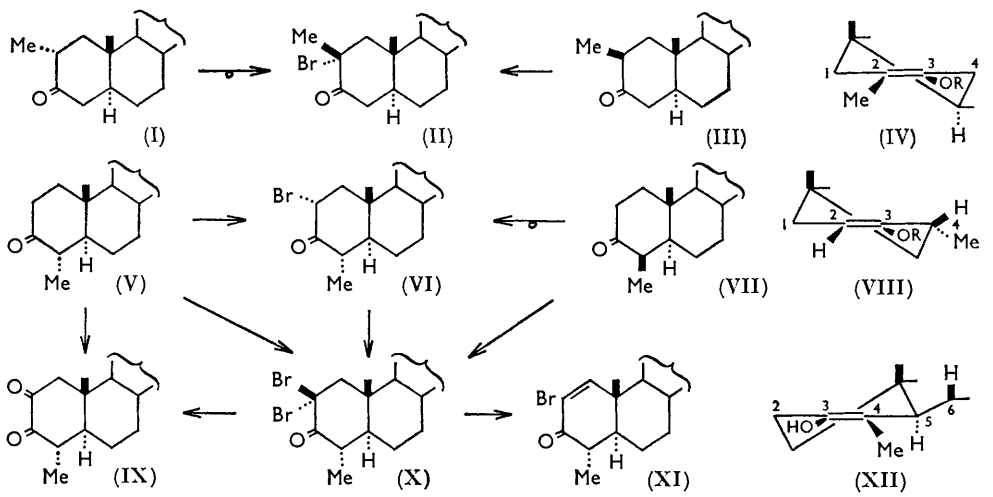
Several methods have recently been reported [12,13] for introduction of steroid 4-methyl groups; we have found the most satisfactory route to 4α- and 4β-methyl-5α-cholestan-3-one to be Atwater's modification [14] of the procedure of Woodward *et al.*[15] for the 4,4-dimethylation of cholest-4-en-3-one. This procedure gave fair yields of the monoalkylated product, which could be separated cleanly from the dimethylated and unmethylated material by chromatography on silica gel to give a 40% yield of 4-methylcholest-4-en-3-one. Reduction of this ketone with lithium in liquid ammonia gave 4α-methyl-5α-cholestan-3-one (V) [9] in high yield, and hydrogenation in ethanol with a palladium–charcoal catalyst followed by crystallisation gave 4β-methyl-5α-cholestan-3-one (VII).[9] The positive Cotton curves found for both ketones (V) and (VII) had amplitudes which agreed with those already reported.[16]

* The chair conformation of 2β-methyl-5α-cholestan-3-one (III) has the same 2β-methyl–10β-methyl interaction as the chair conformation of the bromo-ketone (II); (III) may therefore exist in the boat conformation, a circumstance which would not be disclosed by optical rotatory dispersion spectroscopy.

[5] Corey and Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 6269.
[6] Shoppee and Lack, *J.*, 1960, 4864.
[7] Sigg and Tamm, *Helv. Chim. Acta*, 1960, **43**, 1402.
[8] Shoppee, Roy, and Goodrich, *J.*, 1961, 1583.
[9] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.
[10] Barton, Lewis, and McGhie, *J.*, 1957, 2907.
[11] Johnson, Baver, Margrave, Frisch, Dreger, and Hubbard, *J. Amer. Chem. Soc.*, 1961, **83**, 606.
[12] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753.
[13] Ireland and Marshall, *J. Amer. Chem. Soc.*, 1959, **81**, 6336; Fugimoto, *ibid.*, 1951, **73**, 1856; Heard and Ziegler, *ibid.*, p. 4036; Woodward, Sondheimer, Taub, Heusler, and McLamore, *ibid.*, 1952, **74**, 4223; Sondheimer and Mazur, *ibid.*, 1957, **79**, 2906; Kirk and Petrow, *J.*, 1961, 114.
[14] Atwater, *J. Amer. Chem. Soc.*, 1960, **82**, 2847.
[15] Woodward, Patchett, Barton, Ives, and Kelly, *J. Amer. Chem. Soc.*, 1954, **76**, 2852; *J.*, 1957, 1131.
[16] Djerassi, Halpern, Halpern, and Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 4001.

Kinetically controlled monobromination of 4α-methyl-5α-cholestan-3-one (V) yielded 2α-bromo-4α-methyl-5α-cholestan-3-one (VI), identical with that obtained [9] by bromination of the Δ^2-enol acetate (VIII; R = Ac). Further bromination of the monobromo-ketone (VI) or dibromination of the ketone (V) afforded 2,2-dibromo-4α-methyl-5α-cholestan-3-one (X). Both the bromo-ketones (VI) and (X) were stable to hydrogen bromide.

The structure of the dibromo-ketone (X) was established when treatment with boiling collidine under nitrogen readily afforded 2-bromo-4α-methylcholest-1-en-3-one (XI), $\lambda_{max.}$



256 mμ, whilst treatment with refluxing ethanolic potassium hydroxide gave 4α-methyl-5α-cholestane-2,3-dione (IX), with spectral properties similar to those reported [17] for friedelane-2,3-dione and identical with the product of oxidation of 4α-methyl-5α-cholestan-3-one (V) by selenium dioxide. The dibromo-ketone (X) must exist in the chair conformation since the shape and amplitude of its positive Cotton curve correspond with those reported [18] for 2,2-dibromo-5α-cholestan-3-one.

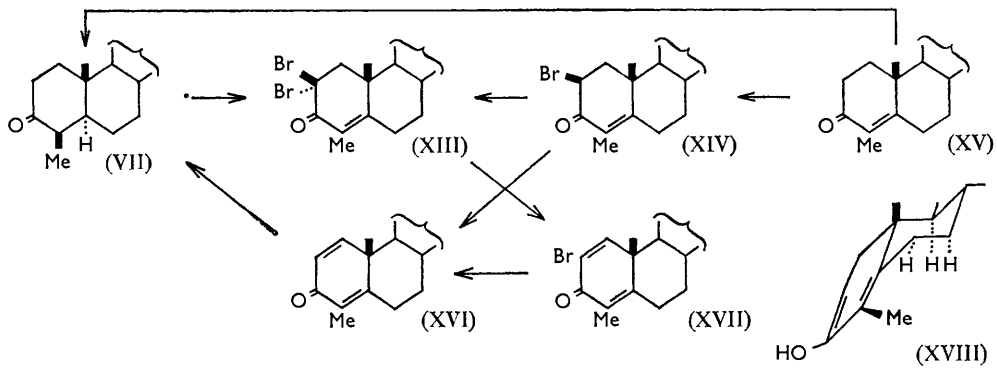
4β-Methyl-5α-cholestan-3-one (VII), on monobromination under kinetic control, gave a single monobromo-ketone, which surprisingly was identified as 2α-bromo-4α-methyl-5α-cholestan-3-one (VI), whilst the product of dibromination was again 2,2-dibromo-4α-methyl-5α-cholestan-3-one (X). These results suggest that the 1,3-diaxial interactions of the 4β-methyl and 10β-methyl groups in the ketone (VII) cause Δ^3-enolisation to give compound (XII), which because of the 10β-methyl and 6β-hydrogen interaction [19] is then rapidly isomerised to the more stable Δ^2-enol (VIII; R = H).

4β-Methyl-5α-cholestan-3-one (VII) is readily epimerised to the 4α-methyl ketone (V) by brief treatment in refluxing acidic ethanol [9] and by potassium t-butoxide under the conditions of methylation,[12] whilst hydrogenation of 4-methylcholest-4-en-3-one with platinum in acetic acid [20] gave only 4α-methyl-5α-cholestan-3-one instead of the 4β-methyl compound expected as a result of rearside *cis*-addition.

Tribromination of 4β-methyl-5α-cholestan-3-one (VII) or monobromination of the dibromo-ketone (X) in acetic acid in the presence of hydrogen bromide gave 2,2-dibromo-4-methylcholest-4-en-3-one (XIII), identical with a sample prepared by dibromination of 4-methylcholest-4-en-3-one (XV) and probably formed by elimination of hydrogen bromide

[17] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041; Shoppee and Johnston, *J.*, 1962, 498.
[18] Djerassi, Osiecki, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 1216.
[19] Corey and Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505.
[20] Meakins and Rodig, *J.*, 1956, 4679.

from an unstable intermediate 2,2,4β-tribromo-ketone. Monobromination of 4-methylcholest-4-en-3-one (XV) with bromine in acetic acid in the presence of hydrogen bromide gave 2β-bromo-4-methylcholest-4-en-3-one (XIV), whilst further bromination gave 2,2-dibromo-4-methylcholest-4-en-3-one (XIII); both these ketones (XIII) and (XIV) were stable to hydrogen bromide. Dehydrobromination of the ketone (XIV) with lithium bromide and lithium carbonate in dimethylformamide [21] gave 4-methylcholesta-1,4-dien-3-one (XVI), which was hydrogenated with palladium–charcoal in ethanol to give 4β-methyl-5α-cholestan-3-one (VII), identical with the sample prepared by similar hydrogenation of 4-methylcholest-4-en-3-one (XV). Dehydrogenation of 2,2-dibromo-4-methylcholest-4-en-3-one gave an oil, having spectral properties consistent with its being 2-bromo-4-methylcholesta-1,4-dien-3-one (XVII) and converted by zinc in acetic acid into 4-methylcholesta-1,4-dien-3-one (XVI).



The formation of axial 2β-bromo-4-methylcholest-4-en-3-one (XIV) appears at first sight to be a departure from the view of Djerassi *et al.*[3] that " in the presence of steric inhibition, the kinetic product is the equatorial and not the axial bromo-ketone." However, examination of a model indicates that in the enol form (XVIII) of the ketone (XV), as a result of distortion of the shape of both rings A and B, the rearward equatorial approach of bromine would be more hindered by the equatorial 6α-hydrogen atom and the axial 7α-hydrogen and 9α-hydrogen atoms than would be the forward axial approach of bromine by the 10β-methyl group, and this possibly explains the exclusive formation of 2β-bromo-4-methylcholest-4-en-3-one.

Experimental

For general experimental directions see *J.*, 1959, 345. M. p.s were determined on a Kofler block and are corrected. $[\alpha]_D$ refer to chloroform solutions at room temperature. Ultraviolet absorption spectra were determined for cyclohexane solutions unless otherwise stated, on a 4000A Perkin–Elmer model spectrophotometer. Infrared absorption spectra were measured in carbon tetrachloride solution by use of a Perkin–Elmer model 221 spectrophotometer. Chromatography was effected on silica gel (Davison 40—200 mesh) or aluminium oxide (Spence's type H, activity II). Analytical samples were dried at 20°/0·5 mm. for 2—8 hr.

2β-*Methyl*-5α-*cholestan*-3-*one*.—2α-Methyl-5α-cholestan-3-one was prepared by hydrogenolysis of 2-hydroxymethylene-5α-cholestan-3-one [20] as described by Djerassi *et al.*,[1] and its monobromo-derivative [9] was treated with collidine to give 2-methyl-5α-cholest-1-en-3-one. Hydrogenation [9] in ethanol in the presence of palladium–charcoal gave 2β-methyl-5α-cholestan-3-one, m. p. 95—97°, $[\alpha]_D$ +80° (*c* 1·0). The m. p. was depressed by *ca.* 10° on admixture with 2α-methyl-5α-cholestan-3-one.

Bromination of 2β-*Methyl*-5α-*cholestan*-3-*one*.—The ketone (III) (200 mg.) in acetic acid (25 ml.) was treated with one drop of a saturated solution of hydrogen bromide in acetic acid

[21] Holysz, *J. Amer. Chem. Soc.*, 1953, **75**, 4432; Joly and Warnant, *Bull. Soc. chim. France*, 1958, 367.

and then dropwise with a solution of bromine (85 mg.) and anhydrous sodium acetate (43 mg.) in acetic acid (10 ml.). Decolorisation of bromine was immediate. Water was added and the mixture extracted with ether. Working up in the usual way gave a crystalline residue (231 mg.), which was chromatographed on silica gel (10 g.) in pentane. Elution with ether–pentane (1 : 99) and crystallisation from ether–methanol yielded 2α-bromo-2β-methyl-5α-cholestan-3-one (182 mg.), m. p. and mixed m. p. 137—139°, $[\alpha]_D$ −25° (*c* 1·0), $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 312 mμ. 2β-Methyl-5α-cholestane was recovered unchanged (188 mg.; m. p. 95—97°) on repetition of the above procedure without the bromine. Attempted dibromination of the ketone (III) by the above procedure yielded oils which could not be further purified by chromatography on silica gel or by direct crystallisation.

4-*Methylcholest*-4-*en*-3-*one by Direct Methylation of Cholest*-4-*en*-3-*one*.—(Modification of the procedure described by Atwater.[14]) A hot solution of potassium t-butoxide (from 300 mg. of potassium) in t-butyl alcohol (10 ml.) was added to a refluxing solution of cholest-4-en-3-one (1 g.) in dry benzene (30 ml.). The refluxing mixture was then treated during 2·5 hr. with methyl iodide (3 ml.) in benzene (75 ml.) and t-butyl alcohol (75 ml.). After a further 1 hour's refluxing, the turbid solution was cooled and water (0·5 ml.) was added. The mixture was evaporated to dryness under reduced pressure, ether was added, and the insoluble matter was filtered off. The filtrate was evaporated to dryness and the residue in benzene solution was chromatographed on a column of silica gel (100 g.) prepared in benzene. Elution with benzene and crystallisation from chloroform–methanol gave 4,4-dimethylcholest-5-en-3-one (485 mg.), m. p. 172—174°. Elution with ethyl acetate–benzene (1 : 99) and crystallisation from methanol afforded 4-methylcholest-4-en-3-one (415 mg.), m. p. 101—103°, $[\alpha]_D$ +112° (*c* 0·9). Elution with ethyl acetate–benzene (1 : 19), and crystallisation from methanol, furnished unchanged cholest-4-en-3-one (150 mg.), m. p. 79—81°.

4α-*Methyl*-5α-*cholestan*-3-*one*.—A solution of 4-methylcholest-4-en-3-one was reduced by lithium in liquid ammonia by the method of Mazur and Sondheimer,[9] giving 4α-methyl-5α-cholestan-3-one, m. p. 121—123°, $[\alpha]_D$ +26° (*c* 1·5). Optical rotatory dispersion: in MeOH, $[M]$ +2820° (305 mμ, peak), −2900° (267·5, shortest wavelength measured); $10^{-2}a$ +57.

4β-*Methyl*-5α-*cholestan*-3-*one*.—4-Methylcholest-4-en-3-one was hydrogenated in ethanol in the presence of palladium–charcoal catalyst by the method of Mazur and Sondheimer,[9] giving 4β-methyl-5α-cholestan-3-one, m. p. 126—127°, $[\alpha]_D$ +38° (*c* 1·0). Optical rotatory dispersion: in MeOH, $[M]$ +7880° (305 mμ, peak), −500° (270, shortest wavelength measured); $10^{-2}a$ +84. The m. p. on admixture with a sample of 4α-methyl-5α-cholestan-3-one was 105—110°.

Kinetically Controlled Monobromination of 4α-*Methyl*-5α-*cholestan*-3-*one*.—4α-Methyl-5α-cholestan-3-one (400 mg.) in acetic acid (25 ml.) was treated with one drop of a saturated solution of hydrogen bromide in acetic acid and then dropwise with a solution of bromine (170 mg.) and anhydrous sodium acetate (85 mg.) in acetic acid (20 ml.). Dilution with water, extraction with ether, and working up in the usual way gave a crystalline product (465 mg.). Two crystallisations from ether–methanol yielded 2α-bromo-4α-methyl-5α-cholestan-3-one, m. p. 110—111°, $\nu_{max.}$ 1735 cm.$^{-1}$, $\lambda_{max.}$ 287 mμ. Optical rotatory dispersion: in methanol, $[M]$ +3400° (310 mμ, peak), −1810° (280, shortest wavelength measured); $10^{-2}a$ +52. 2α-Bromo-4α-methyl-5α-cholestan-3-one (25 mg.) was recovered unchanged after 5 days at 25° in chloroform (50 ml.) containing five drops of a saturated solution of hydrogen bromide in chloroform.

Kinetically Controlled Dibromination of 4α-*Methyl*-5α-*cholestan*-3-*one*.—The ketone (V) (400 mg.) was treated as above with bromine (340 mg.) and anhydrous sodium acetate (170 mg.) in acetic acid (40 c.c.). Dilution with water, extraction with ether, and working up in the usual way gave a product (523 mg.), which was chromatographed on silica gel (20 g.) in pentane. Elution with pentane and crystallisation from ether–methanol yielded 2,2-*dibromo*-4α-*methyl*-5α-*cholestan*-3-*one* (418 mg.), m. p. 134—135°, $\nu_{max.}$ 1735 cm.$^{-1}$, $\lambda_{max.}$ 316 mμ (Found: C, 60·45; H, 8·35. $C_{28}H_{46}Br_2O$ requires C, 60·2; H, 8·3%). Optical rotatory dispersion: in MeOH, $[M]$ +10,600° (330—327·5 mμ, peak), −12,200° (280, shortest wavelength measured); $10^{-2}a$ +228.

Elution with ether–pentane (1 : 99) gave 2α-bromo-4α-methyl-5α-cholestan-3-one (85 mg.), m. p. 110—111° (from ether–methanol). The dibromo-ketone (X) (25 mg.) was recovered unchanged after 5 days at 25° in chloroform (5 ml.) containing five drops of a saturated solution of hydrogen bromide in chloroform.

Bromination of 2α-*Bromo*-4α-*methyl*-5α-*cholestan*-3-*one*.—The bromo-ketone (VI) (480 mg.) in acetic acid (35 ml.) was treated with one drop of a saturated solution of hydrogen bromide in acetic acid, followed by bromine (165 mg.) in acetic acid (5 ml.). Dilution with water,

extraction with ether, and recrystallisation from ether–methanol gave 2,2-dibromo-4α-methyl-5α-cholestan-3-one (485 mg.), m. p. 135°.

2-Bromo-4α-methyl-5α-cholest-1-en-3-one.—2,2-Dibromo-4α-methyl-5α-cholestan-3-one (100 mg.) was treated with *s*-collidine (5 ml.) under nitrogen at 180° for 30 min. The usual working-up gave an oil which was chromatographed on silica gel (8 g.) in pentane. Elution with ether–pentane (1 : 99) gave *2-bromo-4α-methyl-5α-cholest-1-en-3-one* (35 mg.) (from methanol), m. p. 117—118°, $\lambda_{max.}$ (in EtOH), 255 mμ (Found: C, 70·4; H, 9·7. $C_{28}H_{45}BrO$ requires C, 70·4; H, 9·5%).

4α-Methyl-5α-cholestane-2,3-dione.—(*a*) 2,2-Dibromo-4α-methyl-5α-cholestan-3-one (100 mg.) was refluxed with 20% ethanolic potassium hydroxide (50 ml.) for 1 hr. Dilution with water and acidification with 2N-hydrochloric acid gave a product which was chromatographed on aluminium oxide (3 g.) in ether. Elution with methanol afforded *4α-methyl-5α-cholestane-2,3-dione* (61 mg.) (from aqueous methanol), m. p. 121—124°, $\lambda_{max.}$ 275 mμ, $\nu_{max.}$ 1665 and 1640 cm.$^{-1}$ (Found: C, 81·25; H, 11·0. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%).

(*b*) A solution of 4α-methyl-5α-cholestan-3-one (100 mg.) in hot ethanol (20 ml.) was added to a refluxing solution of freshly sublimed selenium dioxide (1 g.) in water (5 ml.) and ethanol (45 ml.). After 15 min. the cooled solution was filtered. The filtrate was diluted with water and extracted with ether, giving 4α-methyl-5α-cholestane-2,3-dione (78 mg.), m. p. and mixed m. p. 121—124°.

Monobromination of 4β-Methyl-5α-cholestan-3-one.—The ketone (VII) (200 mg.) in acetic acid (12 ml.) was treated with one drop of a saturated solution of hydrogen bromide in acetic acid and then dropwise with a solution of bromine (85 mg.) and anhydrous sodium acetate (43 mg.) in acetic acid (10 ml.). After 10 min. water was added and the product obtained by ether-extraction was chromatographed on silica gel in pentane. Elution with ether–pentane (1 : 99) gave 2α-bromo-4α-methyl-5α-cholestan-3-one, m. p. 111—112°, $\lambda_{max.}$ 287 mμ, $\nu_{max.}$ 1735 cm.$^{-1}$ (Found: C, 70·2; H, 9·9. Calc. for $C_{28}H_{47}BrO$: C, 70·1; H, 9·9%). Optical rotatory dispersion: in MeOH, [*M*] +3000° (310 mμ, peak), −2700° (280 mμ, trough); $10^{-2}a$ +57. This sample had the same infrared absorption as the sample previously isolated.

Dibromination of 4β-Methyl-5α-cholestan-3-one.—The ketone (VII) (200 mg.) was treated under kinetic control, as above, with bromine (170 mg.) and sodium acetate (85 mg.) in acetic acid (20 ml.). The usual isolation gave a solid which was chromatographed on silica gel (2 g.) in pentane. Elution with pentane gave 2,2-dibromo-4α-methyl-5α-cholestan-3-one, m. p. 135—136°. The infrared absorption was identical with that of the sample obtained by dibromination of 4α-methyl-5α-cholestan-3-one. Optical rotatory dispersion: in MeOH, [*M*] +9600° (327·5 mμ, peak), −11,300° (280 mμ, trough); $10^{-2}a$ +209.

2β-Bromo-4-methylcholest-4-en-3-one.—4-Methylcholest-4-en-3-one (400 mg.) in acetic acid (25 ml.) was treated with bromine (165 mg.) in acetic acid (5 ml.) in the presence of 1 drop of a saturated solution of hydrogen bromide in acetic acid. The bromine was decolorised immediately. *2β-Bromo-4-methylcholest-4-en-3-one*, isolated by dilution with water, had m. p. 128—129° (from methanol: 375 mg.), $\lambda_{max.}$ (in cyclohexane) 255, (in EtOH) 261 mμ, $\nu_{max.}$ 1675 cm.$^{-1}$ (Found: C, 70·7; H, 9·75. $C_{28}H_{45}BrO$ requires C, 70·4; H, 9·5%). Optical rotatory dispersion: in MeOH, [*M*] +380 (390 mμ, peak); −20,900 (310 mμ; shortest wavelength recorded). The product (25 mg.) was recovered unchanged after 5 days at 25° in chloroform (5 ml.) containing 5 drops of a saturated solution of hydrogen bromide in chloroform.

2,2-Dibromo-4-methylcholest-4-en-3-one.—(*a*) 4-Methylcholest-4-en-3-one (400 mg.) in acetic acid (25 ml.) containing one drop of a saturated solution of hydrogen bromide in acetic acid was treated with bromine (330 mg.) in acetic acid (10 ml.). After 10 min. the product was isolated by dilution with water and extraction with ether as crystals (518 mg.), which were chromatographed on silica gel (25 g.) in pentane. Elution with pentane and crystallisation from methanol gave *2,2-dibromo-4-methylcholest-4-en-3-one* (410 mg.), m. p. 133—135°, $\lambda_{max.}$ (in cyclohexane) 260, (in EtOH) 365 mμ, $\nu_{max.}$ 1695 cm.$^{-1}$ (Found: C, 60·3; H, 7·85. $C_{28}H_{44}Br_2O$ requires C, 60·4; H, 7·95%). Optical rotatory dispersion: in MeOH, [*M*] +1420° (380 mμ, peak), −25,500° (310, shortest wavelength measured). Elution with ether–pentane (1 : 99) afforded 2β-bromo-4-methylcholest-4-en-3-one (89 mg.), m. p. and mixed m. p. 128—129°. The dibromo-ketone (XIV) (25 mg.) was recovered unchanged after 5 days at 25° in chloroform (5 ml.) containing 5 drops of a saturated solution of hydrogen bromide in chloroform.

(*b*) 4β-Methyl-5α-cholestan-3-one (200 mg.) in acetic acid (18 ml.) was treated with one drop of a saturated solution of hydrogen bromide in acetic acid and bromine (255 mg.) in acetic acid

(10 ml.) for 4 hr. Dilution with water, and ether-extraction of the product, chromatography on silica gel (20 g.) in pentane, and elution with ether–pentane (1 : 99) gave 2,2-dibromo-4-methylcholest-4-en-3-one (215 mg.), m. p. and mixed m. p. 129—130°.

Dehydrobromination of 2β-Bromo-4-methylcholest-4-en-3-one.—2β-Bromo-4-methylcholest-4-en-3-one (100 mg.) in dimethylformamide (5 ml.) was treated with lithium bromide (100 mg.) and lithium carbonate (100 mg.) for 18 hr. with stirring at 95°. The cooled solution was poured into 2N-sulphuric acid (150 ml.). Extraction with ether and working-up in the usual way gave a yellow oil, which was chromatographed on aluminium oxide (3 g.) in pentane. Elution with ether–pentane (1 : 9), and crystallisation from aqueous methanol, gave *4-methylcholesta-1,4-dien-3-one* (61 mg.), m. p. 85—86°, $\lambda_{max.}$ (in cyclohexane) 245, (in EtOH) 250 mμ, $\nu_{max.}$ 1665 cm.$^{-1}$ (Found: C, 84·65; H, 11·5. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%).

Hydrogenation of 4-Methylcholesta-1,4-dien-3-one.—4-Methylcholesta-1,4-dien-3-one (40 mg.) in ethanol (100 ml.) was hydrogenated in the presence of 10% palladium–charcoal (5 mg.) until uptake of hydrogen was complete (10 min.). Filtration, evaporation to dryness *in vacuo*, and three crystallisations of the residue from ether–methanol gave 4β-methyl-5α-cholestan-3-one (21 mg.), m. p. 126—127°, identical with the product obtained from hydrogenation of 4-methylcholest-4-en-3-one by Mazur and Sondheimer.[9]

Dehydrobromination of 2,2-Dibromo-4-methylcholest-4-en-3-one.—The dibromo-ketone (XIII) (100 mg.) in dimethylformamide (5 ml.) was treated with lithium bromide (100 mg.) and lithium carbonate (100 mg.) for 18 hr. with stirring at 95°. Working-up as before gave a yellow oil which was chromatographed on aluminium oxide (3 g.) in pentane. Elution with ether–pentane (1 : 9) gave a colourless viscous oil (60 mg.), $\nu_{max.}$ 1665 cm.$^{-1}$, $\lambda_{max.}$ 255 mμ. The oil (20 mg.) in acetic acid (10 ml.) was treated with zinc dust (40 mg.) at 95° for 2 hr. Filtration and evaporation of the filtrate *in vacuo* gave an oil which was chromatographed on aluminium oxide (600 mg.) in pentane. Elution with ether–pentane (1 : 9) and crystallisation from aqueous methanol afforded 4-methylcholesta-1,4-dien-3-one (12 mg.), m. p. and mixed m. p. 85—86°.

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