677. *The 3-Methylcholestanols and their Derivatives.*

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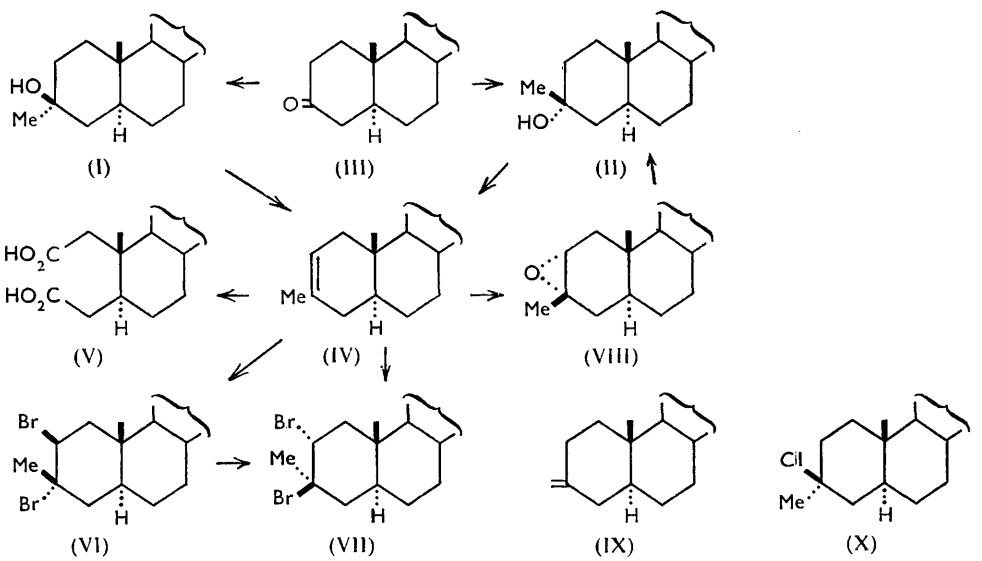
Configurations have been assigned to the two 3-methylcholestanols. 3-Methylcholest-2-ene and 3-methylenecholestane have been prepared and characterised. All four compounds afford in high yield the same 3β-chloro-3α-methylcholestane on treatment with hydrogen chloride. The process is regarded as kinetically rather than thermodynamically controlled. Corresponding experiments with hydrogen bromide afford 3β-bromo-3α-methylcholestane. Reduction of these two halides with lithium and liquid ammonia affords, after protonation, 3β-methylcholestane. Some of the results presented have already been summarised in preliminary form.[1]

Stereochemical aspects of carbonium-ion behaviour in alicyclic systems have not been the subject of extensive investigation. *tert.*-Carbonium ions are, of course, most easily generated and are best suited for study. In aliphatic systems *tert.*-carbonium ions show only weak stereochemical preference [2,3] with a slight excess of inversion over racemisation. The present investigation was initiated in order to determine the stereochemical fate of a *tert.*-carbonium ion generated from a tertiary alcohol, or from the appropriate olefin, in a conformationally unambiguous alicyclic system. The results obtained led us to investigate several other aspects of conformational behaviour in the system chosen.



Two epimeric tertiary alcohols, (I) and (II), were easily obtained [4,5,6] from cholestanone (III) and the methyl Grignard reagent. Both alcohols, which were characterised as their *p*-nitrobenzoates, readily lost water on treatment with acetic acid containing a trace of perchloric acid, to give the known anhydro-derivative.[4,5,6,7] This was proved to be 3-methylcholest-2-ene (IV), for on successive oxidations with osmium tetroxide, lead tetra-acetate, and sodium hypobromite it furnished *seco*cholestane-2 : 3-dioic acid [8] (V).

3-Methylcholest-2-ene was further characterised by addition of bromine, the major

[1] Barton, *Experientia*, 1955, Suppl. II, p. 121; see also Barnes and Palmer, *Austral. J. Chem.*, 1956, **9**, 105.
[2] Doering and Zeiss, *J. Amer. Chem. Soc.*, 1953, **75**, 4733, and references there cited.
[3] Hughes, Ingold, Martin, and Meigh, *Nature*, 1950, **166**, 679.
[4] Farmer and Kon, *J.*, 1937, 414.
[5] Bolt and Backer, *Rec. Trav. chim.*, 1937, **56**, 1139.
[6] Kuwada and Miyasaka, *J. Pharm. Soc. Japan*, 1938, **58**, 115; *Chem. Abs.*, 1938, **32**, 7474.
[7] Kon and Woolman, *J.*, 1939, 794.
[8] Windaus and Uibrig, *Ber.*, 1914, **47**, 2384.

product being 2β : 3α-dibromo-3β-methylcholestane (VI) and the minor the 2α : 3β-isomer (VII). The configurations are based on the principle of preferred diaxial addition [9] and on the relative rotations {$[\alpha]_D$ +89° for (VI), and −15° for (VII)} as compared with the rotations of 2β : 3α- and 2α : 3β-dibromocholestane [9] ($[\alpha]_D$ +76° and −29° respectively). In agreement with the assigned configurations [9] the 2β : 3α-dibromide (VI) rearranged to the more stable 2α : 3β-isomer (VII) in boiling chloroform solution; also [9] the diaxial compound (VI) was more easily eluted from alumina than the diequatorial isomer (VII). In agreement with the assigned stereochemistry [10] the diaxial isomer (VI) showed infrared bands (in carbon disulphide) at 537 and 547 cm.$^{-1}$ and the diequatorial compound bands at 752 and 804 cm.$^{-1}$.

Configurations were assigned to the two tertiary alcohols (I) and (II) on the following evidence. First, both showed carbon–oxygen stretching frequencies at 940 and 893 cm.$^{-1}$ (in carbon disulphide) in agreement [11] with the presence of equatorial and axial hydroxyl groups respectively. Secondly, treatment of 3-methylcholest-2-ene (IV) with perphthalic acid gave an epoxide which was reduced by lithium aluminium hydride to the alcohol (II). The diaxial epoxide opening rule requires that the hydroxyl group formed by the reduction be axial, that is α-oriented as in (II). The oxide must, therefore, have the α-configuration (VIII) as would be expected.

The behaviour of the two tertiary alcohols (I) and (II) on dehydration with phosphorus oxychloride in pyridine was also in agreement with the assigned configurations. The α-alcohol (II) afforded the olefin (IV) in high yield. The β-alcohol (I), on the other hand, gave an isomeric olefin mixture recognised as substantially (IX) by its infrared spectrum [maxima at 883 (strong) and 1647 cm.$^{-1}$ (medium) in Nujol], by its conversion by osmium tetroxide followed by lead tetra-acetate into cholestanone, and by comparison with the pure compound (IX) obtained from this ketone by the Wittig reaction.[12] The olefin (IX) was further characterised by conversion into two dibromides neither of which was identical with the two dibromides obtained from 3-methylcholest-2-ene (IV). The major dibromide from 3-methylenecholestane has been tentatively formulated as the 3α(axial)-bromide on the basis of preferred diaxial addition [9] and because it was much less stable thermally than its equatorial isomer.

The α-alcohol (II), with the axial hydroxyl group, has four centres coplanar (2β-H, $C_{(2)}$, $C_{(3)}$, and 3α-OH) for elimination towards $C_{(2)}$. The β-alcohol, with the equatorial hydroxyl group, does not, of course, satisfy this geometric requirement. Adequate coplanarity is, however, readily obtained with the aid of a suitable 3-methyl hydrogen atom, thus provoking elimination to give the exocyclic methylene isomer (IX).

Treatment of either of the tertiary alcohols (I) and (II), or of 3-methylcholest-2-ene (IV) or 3-methylenecholestane (IX), with hydrogen chloride in dioxan at room temperature gave in approximately 75% isolated yield the same chloride, m. p. 154—156°, $[\alpha]_D$ +33°. The total yield of the chloride was determined by an isotope dilution method to be 82%. The chloride was identified as 3β-chloro-3α-methylcholestane (X) on the basis of the following evidence. First, the compound showed an infrared frequency (carbon disulphide solution) at 782 cm.$^{-1}$ corresponding [10] to an equatorial (β) bond. Secondly, treatment with collidine gave a product identified by its dibromide as the olefin (IX). The identity was confirmed by stepwise oxidation (see above) to cholestanone. The direction of elimination is consonant with equatorial (β) chlorine, not axial (α) chlorine.

We regard the chloride (X) as the more stable epimer because 1-methyl*cyclo*hexyl chloride, where the molecule is free to adopt either conformation for the carbon–chlorine bond, shows only the frequency at 772 cm.$^{-1}$ (carbon disulphide solution) characteristic [10] of equatorial chlorine. In all four carbonium-ion reactions the more stable epimer is, therefore, the major product. The same result is obtained in the addition of hydrogen chloride to cholest-5-ene, the product being 5α-chlorocholestane.[13] Such a conclusion

[9] Alt and Barton, *J.*, 1954, 4284.
[10] Barton, Page, and Shoppee, *J.*, 1956, 331.
[11] Page, *J.*, 1955, 2017, and references there cited.
[12] Wittig and Schollkopf, *Chem. Ber.*, 1954, **87**, 1318.
[13] Bernal, Crowfoot, and Fankuchen, *Phil. Trans.*, 1940, *A*, **239**, 135; Crowfoot in "Vitamins and Hormones," Vol. II, p. 409, Academic Press, New York, 1944.

would, of course, be self-evident if the reactions were reversible and thus subject to thermodynamic control. At least for the chloride (X) this does not seem probable, for the extent of solvolysis of the chloride in 90% aqueous dioxan at 20° was insignificant even after seven days. In contrast the approximate times of half-reaction for the formation of the chloride (X) were as follows: from the α-alcohol (II), 30 min.; from the β-alcohol (I), 4 hr.; from the olefin (IV), 13 min. Since the forward reaction is so fast and the back-reaction under comparable conditions so slow, we reject the idea of thermodynamic control and conclude that the formation of the more stable configuration is indeed a rate-controlled process. There remains the problem of whether the chloride (X) is formed directly from the carbonium ion or through the olefin (IV) after elimination of water. We hope to present a detailed account of this aspect of the problem on a subsequent occasion.

It is of interest to compare the stereospecificity of addition of bromine or chlorine to the ethylenic linkage with that of hydrogen chloride, all additions being of the ionic type. Diaxial addition of halogen is well established [9] and, at least for the case of the 5 : 6-ethylenic linkage of cholesterol and its congeners, the initial halgenonium ion is formed on the less hindered α-side of the molecule, the process of addition being completed non-Markownikoff-wise.[14] It is clear that the addition of hydrogen chloride to 3-methylcholest-2-ene and to cholest-5-ene cannot be of analogous stereochemical form.

Some of the experiments summarised above for hydrogen chloride have been repeated with hydrogen bromide. Thus the tertiary alcohols (I) and (II) and the olefin (IV) gave the same bromide in 75% isolated yield. The bromide is formulated as 3β-bromo-3α-methylcholestane on the basis of its infrared frequency at 780 cm.$^{-1}$ (in carbon disulphide) corresponding to equatorial bromine.[10] * Again one must note the predominant formation of the more stable product.

From some recent comments on the behaviour of carbanions [15,16] one can conclude that the steric requirements of a carbon–carbon bond, a carbanion, and a carbon–hydrogen bond are in that diminishing order. If this is correct then reduction of 3β-chloro- or 3β-bromo-3α-methylcholestane by lithium in liquid ammonia should afford,[15,16] on protonation, 3β-methylcholestane for the steric requirements of CMe should be greater than those of the carbanion. This conclusion was confirmed by experiment although the 3β-methylcholestane obtained had somewhat different properties from those recorded [6,17] in the literature. An authentic specimen was therefore prepared from methyl cholestane-3β-carboxylate [18,19] by reduction with lithium aluminium hydride to 3β-hydroxymethylcholestane, conversion into the toluene-*p*-sulphonate, and further reduction with the same reagent.[20] 3β-Methylcholestane was also obtained by hydrogenation of 3-methylcholest-2-ene (IV).

Experimental

Rotations were taken in $CHCl_3$ solution. Infrared spectra were kindly determined by Dr. J. E. Page of Messrs. Glaxo Laboratories Ltd., and by Dr. G. Eglinton using, unless stated to the contrary, carbon disulphide as solvent. The light petroleum used was of b. p. 40—60°.

3-Methylcholestan-3α- and -3β-ol.—Cholestanone, m. p. 128—129°, $[\alpha]_D$ +39° (*c* 1·21), (5·2 g.) in dry ether (50 ml.) was added to methylmagnesium iodide [prepared from methyl iodide (4·8 g.) and magnesium (1·02 g.) in dry ether (18 ml.)] with good stirring during 30 min. and the resulting solution refluxed for 2 hr. The product, in 3 : 2 light petroleum–benzene (50 ml.), was chromatographed over neutralised alumina (75 g.) (27 fractions). Elution with the same

* Some of the infrared bands shown to be characteristic [10] for equatorial and axial chlorine and bromine may correspond to polarised or coupled C–H deformation modes rather than to carbon–halogen stretching frequencies. Such a change in the assumed origin of these bands would not, of course, influence the purely empirical correlation [10] with the conformation of the halogen. We thank Dr. G. Eglinton for this helpful comment.

[14] Fieser, *Experientia*, 1950, **6**, 312; Barton, Miller, and Young, *J.*, 1951, 2598.
[15] Barton and Robinson, *J.*, 1954, 3045.
[16] Roberts and Shoppee, *J.*, 1954, 3418.
[17] Baker, Minckler, and Petersen, *J. Amer. Chem. Soc.*, 1955, **77**, 3644.
[18] Corey and Sneen, *ibid.*, 1953, **75**, 6234.
[19] Roberts, Shoppee, and Stephenson, *J.*, 1954, 2705.
[20] Schmid and Karrer, *Helv. Chim. Acta*, 1949, **32**, 1371.

solvent mixture, with benzene and with 9 : 1 benzene–ether (19 fractions in all) gave 3β-methylcholestan-3α-ol (2·90 g.), m. p. (from ethyl acetate–methanol) 126—127°, $[\alpha]_D$ +28° (*c* 1·68). Elution with 1 : 1 benzene–ether and with ether alone (8 fractions in all) afforded 3α-methylcholestan-3β-ol (2·19 g.), m. p. (from acetic acid) 147—149°, $[\alpha]_D$ +34° (*c* 1·24). Kuwada and Miyasaka [6] reported m. p. 125° and 147—148° respectively.

The two alcohols were characterised as follows. The alcohol (1·0 g.) in dry ether (50 ml.) was stirred for 1 hr. with a solution of phenyl-lithium prepared from bromobenzene (782 mg.) and excess of lithium wire in dry ether (150 ml.) with stirring for 2 hr. *p*-Nitrobenzoyl chloride (2·0 g.) in dry ether (25 ml.) was added and the solution left overnight. Crystallisation of the product from ethyl acetate–methanol afforded 3β-*methylcholestan*-3α-*yl* p-*nitrobenzoate*, needles, m. p. 159—160°, $[\alpha]_D$ +20° (*c* 1·03) (Found: C, 76·45; H, 9·45. $C_{35}H_{53}O_4N$ requires C, 76·2; H, 9·7%). The derivative from the β-alcohol was only obtained crystalline with difficulty (gel) by chromatography over neutralised alumina (45 g.) in benzene. Crystallisation from acetic acid gave 3α-*methylcholestan*-3β-*yl* p-*nitrobenzoate*, needles, m. p. 194°, $[\alpha]_D$ +30° (*c* 1·75) (Found: C, 76·3; H, 9·7%).

3-*Methylcholest*-2-*ene*.—The two stereoisomeric alcohols behaved in the same way on treatment with acetic acid–perchloric acid. The alcohol (40 mg.) in " AnalaR " acetic acid (2 ml.) with addition of perchloric acid (70%; two drops) was heated on the steam-bath for 30 min. The product was filtered through alumina in light petroleum and crystallised from the same solvent, then having m. p. 82—83°, $[\alpha]_D$ +74° (*c* 1·32), +74° (*c* 1·39). The olefin can be conveniently prepared by the same treatment of the mixed alcohols from the Grignard reaction on cholestanone.

3-Methylcholest-2-ene (233 mg.) in dry dioxan (10 ml.) was treated with osmium tetroxide (210 mg.) in the same solvent (10 ml.) and left at room temperature in the dark for 3 days. The osmate was cleaved by saturation with hydrogen sulphide and, after filtration, the dioxan was removed *in vacuo*. The residue was taken up in " AnalaR " acetic acid (30 ml.) with addition of lead tetra-acetate (740 mg.) in the same solvent (20 ml.) and left for one day (uptake 1·0 mol. of tetra-acetate). The product in dry dioxan (20 ml.) was treated with sodium hypobromite solution (2·0 ml.) [prepared by adding bromine (2 ml.) to ice-cold water (26·5 ml.) containing sodium hydroxide (6·3 g.)], and the solution stirred for 5 hr. at room temperature. The acidic fraction of the product was crystallised from ether–light petroleum, to give *seco*cholestane-2 : 3-dioic acid (34 mg.), identified by m. p., mixed m. p. and rotation {$[\alpha]_D$ +35° (*c* 0·85)}. The authentic specimen, prepared by chromic acid oxidation of cholestanol according to Windaus and Uibrig,[8] had m. p. 196—198°, $[\alpha]_D$ +35° (*c* 0·95).

3-Methylcholest-2-ene (412 mg.) in carbon tetrachloride (20 ml.) was titrated with bromine (15% w/w; in carbon tetrachloride). Removal of the solvent *in vacuo* at room temperature and chromatography over alumina in light petroleum (development with the same solvent) gave two dibromides. Eluted more easily was 2β : 3α-*dibromo*-3β-*methylcholestane* (440 mg.), needles (from ethyl acetate–methanol), m. p. 106—108° (decomp.), $[\alpha]_D$ +89° (*c* 1·23) (Found: C, 62·25; H, 8·65; Br, 29·15. $C_{28}H_{48}Br_2$ requires C, 61·75; H, 8·9; Br, 29·35%). Eluted with more difficulty was 2α : 3β-*dibromo*-3α-*methylcholestane*, m. p. (from ethyl acetate–methanol) 160—162°, $[\alpha]_D$ −15° (*c* 0·82) (Found: C, 61·7; H, 9·05; Br, 29·4%). The 2β : 3α-dibromide (220 mg.) in chloroform (35 ml.) was refluxed for 97 hr. (no further change in rotation). Removal of the chloroform *in vacuo* and crystallisation from ethyl acetate–methanol gave the 2α : 3β-dibromide, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −16° (*c* 1·03)}.

2α : 3α-*Epoxy*-3β-*methylcholestane*.—3-Methylcholest-2-ene (500 mg.) was treated with 3 mols. of perphthalic acid in ether overnight at room temperature (uptake of 1 mol.). Filtration of the product in light petroleum over silica gel gave 2α : 3α-*epoxy*-3β-*methylcholestane*, m. p. (from alcohol) 133—135°, $[\alpha]_D$ +47° (*c* 1·17) (Found: C, 83·85; H, 11·65. $C_{28}H_{48}O$ requires C, 83·95; H, 12·1%). This epoxide (1·4 g.) in ether (100 ml.) was reduced with an excess of lithium aluminium hydride (2·8 g.) in the same solvent (100 ml.) under reflux for 40 hr. Crystallisation from ethanol gave 3β-methylcholestan-3α-ol, identified by m. p. and mixed m. p.

3-*Methylenecholestane* (IX).—Triphenylmethylphosphonium bromide [12] (2·77 g.) was treated with phenyl-lithium (651 mg.) in dry ether (46 ml.) with shaking for 3 hr. To this solution there was added cholestanone (3·0 g.), and the solution was refluxed overnight. After being washed with water, the ethereal solution was dried (Na_2SO_4) and evaporated *in vacuo*. The residue was refluxed with excess of lithium aluminium hydride in ether. After being worked up in the usual way the product was filtered in light petroleum through alumina (50 g.). Elution with the same solvent (150 ml.) afforded 3-*methylenecholestane* (1·6 g.), needles (from ethyl acetate–methanol), m. p. 65—66°, $[\alpha]_D$ +23° (*c* 2·16 in CCl_4) (Found: C, 87·7; H, 12·45. $C_{28}H_{48}$

requires C, 87·4; H, 12·6%). This hydrocarbon (89·5 mg.) in carbon tetrachloride (10 ml.) containing one drop of " AnalaR " pyridine was titrated with bromine (3·36% w/v) in the same solvent. After removal of the solvent *in vacuo* at room temperature the oily product was chromatographed over silica gel (2·0 g.) in light petroleum (5 ml.). Elution with the same solvent (30 ml.) gave 3α-*bromo*-3β-*bromomethylcholestane* (91·7 mg.), flat needles (from ethyl acetate), m. p. 116—118°, $[\alpha]_D$ +38° (*c* 1·65) (Found : C, 62·25; H, 8·8; Br, 29·45. $C_{28}H_{48}Br_2$ requires C, 61·75; H, 8·9; Br, 29·35%). Further elution with the same solvent (15 ml. and 45 ml.) gave respectively a mixture (16·8 mg.) and then 3β-*bromo*-3α-*bromomethylcholestane* (16·6 mg.), needles (from ethyl acetate), m. p. 124—126°, $[\alpha]_D$ +23° (*c* 1·14) (Found : C, 61·35; H, 9·05; Br, 29·6%). The two dibromides gave a marked depression in m. p. on admixture.

Conversion of 3-*Methylenecholestane into Cholestanone.*—3-Methylenecholestane (162 mg.) in dry dioxan (5 ml.) was treated with osmium tetroxide (139 mg.) in the same solvent (5 ml.) at room temperature for 48 hr. The osmium tetroxide complex was cleaved with hydrogen sulphide,[21] and the product crystallised from ethanol, to furnish the *glycol*, blades, m. p. 208—209°, $[\alpha]_D$ +29° (*c* 0·71) (Found : C, 79·85; H, 12·45. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·1%). In an identical experiment the total glycol in ethanol (10 ml.) and dioxan (35 ml.) was treated with periodic acid (308 mg.) in water (5 ml.) for 16 hr. (uptake of 1 mol. of oxidant). After being worked up in the usual way the product was filtered in benzene through alumina (3 g.). Elution with the same solvent gave cholestanone (130 mg., 80%), identified by m. p., mixed m. p., and rotation.

3β-*Methylcholestane.*—(a) *From cholestane*-3β-*carboxylic acid.* Methyl cholestane-3β-carboxylate [18,19] (1·2 g.) in dry ether (50 ml.) was reduced with a large excess of lithium aluminium hydride in the same solvent under reflux for 6 hr. Crystallisation of the product from ethyl acetate–methanol gave 3β-*hydroxymethylcholestane*, needles, m. p. 151—152°, $[\alpha]_D$ +28° (*c* 1·28) (Found : C, 83·65; H, 12·35. $C_{28}H_{50}O$ requires C, 83·5; H, 12·5%). This alcohol (1·1 g.) in dry pyridine (30 ml.) was treated with toluene-*p*-sulphonyl chloride (3·0 g.) in the same solvent (20 ml.) overnight at room temperature, to furnish the *toluene*-p-*sulphonate*, m. p. (from chloroform–methanol) 113—114°, $[\alpha]_D$ +22° (*c* 1·02) (Found : C, 74·65; H, 9·9. $C_{35}H_{56}O_3S,\frac{1}{2}CH_4O$ requires C, 74·4; H, 10·2%). This toluene-*p*-sulphonate (496 mg.) in ether (50 ml.) was reduced with a large excess of lithium aluminium hydride under reflux for 72 hr. to 3β-methylcholestane (350 mg.), m. p. (from chloroform–methanol) 105—106°, $[\alpha]_D$ +28° (*c* 1·76). For this compound Baker, Minckler, and Petersen [17] reported m. p. 97—98°, $[\alpha]_D$ +11°.

(b) *From* 3-*methylcholest*-2-*ene.* The olefin (223 mg.) in 1 : 1 ethyl acetate–acetic acid (60 ml.) was hydrogenated over platinum, to give 3β-methylcholestane (200 mg.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +27° (*c* 1·23)}.

(c) *From* 3β-*chloro*-3α-*methylcholestane.* The chloro-compound (see below) (140 mg.) in dry ether (30 ml.) was added during 10 min. to a solution of lithium (150 mg.) in liquid ammonia at −60° and the solution stirred for 5 hr. Excess of ammonium chloride was added and ammonia left to evaporate. Crystallisation from chloroform–methanol gave 3β-methylcholestane (100 mg.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +28° (*c* 0·84)}. In a second experiment 3β-chloro-3α-methylcholestane (102 mg.) in 1 : 1 ether–acetic acid (60 ml.) was treated with excess of zinc dust during 18 hr. at room temperature (good stirring). Chromatography of the product over silica gel (3·0 g.) in light petroleum gave 3β-methylcholestane (26 mg.), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +28° (*c*, 0·89)}, and negative Beilstein test, as well as unchanged starting material (66 mg.), identified by m. p., mixed m. p., and positive Beilstein test.

(d) *From* 3β-*bromo*-3α-*methylcholestane.* The bromo-compound (see below) (97·7 mg.) in dry ether (20 ml.) was slowly (10 min.) dropped with stirring into a solution of lithium (101 mg.) in liquid ammonia (25 ml.) and left with stirring for 2 hr. Protonation with ammonium chloride and working up in the usual way gave a crystalline residue (76·3 mg.). One crystallisation from ethyl acetate–methanol gave 3β-methylcholestane (61 mg.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +27° (*c* 1·12)}.

Dehydration of the 3-*Methylcholestanols.*—3β-Methylcholestan-3α-ol (see above) (240 mg.) in dry pyridine (25 ml.) and redistilled phosphorus oxychloride (290 ml.) was left for 24 hr. at room temperature. Crystallisation of the product from chloroform–methanol afforded 3-methylcholest-2-ene (200 mg.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +70° (*c* 1·29)}.

The same dehydration procedure was applied to 3α-methylcholestan-3β-ol. The resulting

[21] Barton and Elad, *J.*, 1956, 2085.

olefin (194 mg.) was chromatographed over silica gel (50 g.) in light petroleum. All fractions melted indefinitely between 56° and 63° and had rotations close to 40°. A typical mixture had m. p. (from ethyl acetate–methanol) 57—59°, $[\alpha]_D$ +44° (*c* 0·85) (Found: C, 87·1; H, 12·25. Calc. for $C_{28}H_{48}$: C, 87·4; H, 12·6%). In order to characterise the olefin mixture the following experiments were performed. The mixture (1·4 g.) in carbon tetrachloride (25 ml.) was titrated with bromine (15% w/v) in the same solvent. The resulting mixture of dibromides was chromatographed over silica gel in light petroleum, elution being with the same solvent. The first eluted dibromide (1·2 g.), plates (from ethyl acetate–methanol), had m. p. 114° (decomp.), $[\alpha]_D$ +44° (*c* 1·12), and was identified (m. p. and mixed m. p.) as 3α-bromo-3β-bromomethylcholestane. The second eluted dibromide (260 mg.) formed needles (from ethyl acetate–methanol), m. p. 124—126° (decomp.), $[\alpha]_D$ +23° (*c* 1·14), and was identified (m. p. and mixed m. p.) as 3β-bromo-3α-bromomethylcholestane.

The olefin mixture (400 mg.) in dry dioxan was treated with osmium tetroxide (400 mg.) in the same solvent (5 ml.) and left in the dark at room temperature for 2 days. After saturation with hydrogen sulphide and filtration, the dioxan was removed *in vacuo* and the residue in " AnalaR " acetic acid (25 ml.) was oxidised with lead tetra-acetate (1·0 g.) in the same solvent (25 ml.) at room temperature for 4 hr. (1 mol. uptake). The product (360 mg.) was chromatographed over neutralised alumina (8 g.) in light petroleum. Elution with 1 : 4 benzene–light petroleum gave cholestanone (192 mg., pure), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +40° (*c*, 1·20)}.

3β-*Chloro*-3α-*methylcholestane*.—3-Methylcholest-2-ene (265 mg.), 3-methylenecholestane (250 mg.), 3β-methylcholestan-3α-ol (210 mg.), and 3α-methylcholestan-3β-ol (245 mg.) were treated separately with dry hydrogen chloride in dioxan (23% w/v; 25 ml.) for 8 days at room temperature and then for 3 days at 0°. All four solutions deposited pure 3β-*chloro*-3α-*methylcholestane*, m. p. 154—156°, unchanged on crystallisation from light petroleum, $[\alpha]_D$ +32° (*c* 0·92), +33° (*c* 1·02), +33° (*c* 0·93), and +33° (*c* 1·05) respectively (Found: C, 79·9; H, 11·6. $C_{28}H_{49}Cl$ requires C, 79·85; H, 11·7%). Concentration of the mother-liquors *in vacuo* at room temperature gave further crops of the chloride, the total yields being 76, 70, 76, and 70% respectively. The experiments were repeated, the mixtures being left for 24 hr. only at room temperature, with the same results.

In order to determine the total yield of chloride in the above experiments an isotope dilution method was employed. 3-Methylcholest-2-ene was converted into the chloride as above but with deuterium chloride instead of hydrogen chloride. The ordinary chloride has a strong infrared band (carbon disulphide solution) at 783 cm.$^{-1}$ whereas the deuterated material shows no absorption at this frequency. It is simple, therefore, to analyse mixtures of the two substances. 3-Methylcholest-2-ene (90·0 mg.) and the deuterated 3β-chloro-3α-methylcholestane (10·95 mg.) were treated with hydrogen chloride in dioxan as above. The first crop of chloride, m. p. 154—156°, $[\alpha]_D$ +33° (*c* 1·05), was shown to contain 12·0% of labelled chloride. The true yield of 3β-chloro-derivative from the 3-methylcholest-2-ene is, therefore, 82%. The method of analysis is, of course, only valid provided that there is no exchange between ordinary chloride and deuterated chloride. This was checked in two ways: (*a*) the ordinary chloride was treated with deuterium chloride in dioxan, and (*b*) the deuterated chloride was treated with hydrogen chloride in the same solvent. Infrared examination of the product (see above) showed that in each case there was no exchange.

In order to determine the approximate times of half-reaction the following experiments were carried out. 3-Methylcholest-2-ene (92 mg.) in hydrogen chloride–dioxan (23% w/v; 25 ml.) was kept at room temperature (20°) and the reaction followed polarimetrically. The initial rotation was +75° (8 min. after dissolution) {cf. $[\alpha]_D$ for 3-methylcholest-2-ene: +80° (*c* 0·88 in dioxan)}. After 120 min. the rotation was constant at 37°. The time of half-reaction was 14 min. 3β-Methylcholestan-3α-ol (108 mg.) was treated in the same way for 30 min. The product was chromatographed over silica gel (5 g.) in light petroleum. Elution with this solvent gave 3-methylcholest-2-ene (2·2 mg.), identified by m. p., mixed m. p., and negative Beilstein test. Further elution with the same solvent furnished the chloride (60 mg., 53%), identified by m. p., mixed m. p., and positive Beilstein test. Elution with benzene afforded unchanged starting material (48 mg.). 3α-Methylcholestan-3β-ol (103 mg.), treated in the same way for 2 hr., gave 3-methylcholest-2-ene (8 mg.), the chloride (29 mg., 27%), and unchanged alcohol (68 mg.).

3β-Chloro-3α-methylcholestane (100 mg.) in dioxan (65 ml.) and water (5 ml.) was left for 7 days at 20°. The solvent was removed *in vacuo* at room temperature to give back starting material (100 mg.) unchanged (m. p., mixed m. p., and positive Beilstein test).

Treatment of 3β-Chloro-3α-methylcholestane with Collidine.—The chloride (171 mg.) in dry redistilled collidine (5 ml.) was heated under reflux for 3 hr. The product was treated with osmium tetroxide and then with lead tetra-acetate, as described for the processing of the dehydration product of 3α-methylcholestan-3β-ol, to give cholestanone (57 mg.), identified by m. p., mixed m. p., and rotation $\{[\alpha]_D +40°$ (*c*, 1·23)$\}$. In a second experiment the chloride (34 mg.), treated as above with collidine, furnished a product which on titration with bromine gave 3α-bromo-3β-bromomethylcholestane (30 mg.), identified by m. p., mixed m. p., and rotation $\{[\alpha]_D +44°$ (*c* 0·75)$\}$. This dibromide was worked up as before (see above).

3β-Bromo-3α-methylcholestane.—3-Methylcholest-2-ene (203 mg.), 3β-methylcholestan-3α-ol (200 mg.), and 3α-methylcholestan-3β-ol (203 mg.) were treated separately with dry hydrogen bromide in dioxan (25% w/v; 25 ml.) at room temperature (20°) for 7 days. In each case *3β-bromo-3α-methylcholestane* crystallised in pure condition (76, 73, and 74% respectively). It had m. p. 138—139°, unchanged on recrystallisation from cold dry light petroleum, $[\alpha]_D +35°$ (*c* 1·09) (Found: C, 72·1; H, 10·35; Br, 16·8. $C_{28}H_{49}Br$ requires C, 72·25; H, 10·6; Br, 17·15%). The infrared spectra of all three preparations were identical.

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