Steroids. Part XXXV.[1] Preparation of the Epimeric 2-Hydroxy-19-nor-5α-cholestanes

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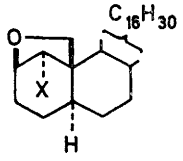
2β,19-Epoxy-5α-cholestane, readily obtained from 5α-cholestan-2β-ol by treatment with lead tetra-acetate, on acetolysis with acetic anhydride catalysed by pyridinium hydrochloride or by boron trifluoride gave a variety of products, from which were derived 5α-cholestan-19-oic acids, 5α-cholest-1- and -2-en-19-aldehydes, and 5α-cholestan-19-ols. 2α-Acetoxy- and 2α-methoxy-5α-cholestan-19-oic acids resisted decarboxylation; the inseparable mixture of 5α-cholest-1- and -2-en-19-als when irradiated underwent decarbonylation to give 19-nor-5α-cholest-1-ene.

An improved preparation of 19-nor-5α-cholest-1-ene from 5α-cholest-1-ene was devised. Conversion of the latter into 1α-bromo-5α-cholestan-2β-ol followed by treatment with lead tetra-acetate gave 1α-bromo-2β,19-epoxy-5α-cholestane. This was converted with zinc–ethanol into 5α-cholest-1-en-19-ol, which was oxidised to 5α-cholest-1-en-19-al with Jones reagent. Irradiation of this aldehyde gave 19-nor-5α-cholest-1-ene, converted by hydroboration (bis-3-methyl-2-butylborane) into 19-nor-5α-cholestan-2α-ol (56%), 19-nor-5α-cholestan-2β-ol (28%), and the isomeric 19-nor-1α-ol (4%) and 19-nor-1β-ol (12%), which were separated by column chromatography, followed by preparative t.l.c.

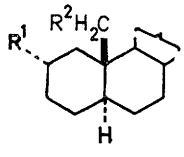
To evaluate the effect of the angular 10β-methyl group on the substitution reactions of the 2-hydroxy-5α-cholestanes,[2] the preparation and substitution reactions [3] of 19-nor-5α-cholestanes have been investigated. Unsuccessful attempts to prepare these alcohols by way of 2β-hydroxy-5α-cholestan-19-oic acid have been described.[4]

2β,19-Epoxy-5α-cholestane (Ia) was prepared (60%) by treatment of 5α-cholestan-2β-ol with lead tetra-acetate in cyclohexane in the presence of calcium



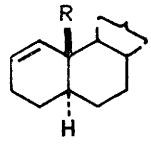
(I)

a; X = H
b; X = Br



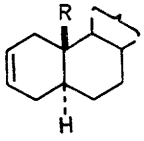
(II)

a; R^1 = Cl, R^2 = OAc
b; R^1 = Cl, R^2 = OH
c; R^1 = R^2 = OAc
d; R^1 = R^2 = OH
e; R^1 = OH, R^2 = OAc
f; R^1 = OAc, R^2 = OH
g; R^1 = OMe, R^2 = OAc
h; R^1 = OMe, R^2 = OH



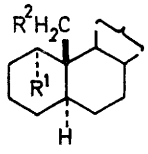
(III)

a; R = CH_2·OAc
b; R = CO_2Me
c; R = CH_2·OH
d; R = CHO
e; R = H
f; R = Me



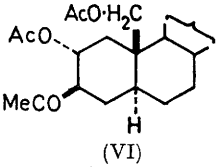
(IV)

a; R = CH_2·OAc
b; R = CO_2Me
c; R = CH_2·OH
d; R = CHO
e; R = CO_2H



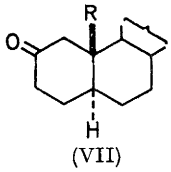
(V)

a; R^1 = R^2 = OAc
b; R^1 = R^2 = OH
(c); R^1 = OH, R^2 = OAc
d; R^1 = OMe, R^2 = OAc
e; R^1 = OMe, R^2 = OH



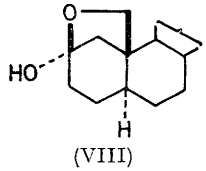
(VI)

carbonate.[5] Acetolysis of the ether linkage with pyridine hydrochloride–acetic anhydride[6] under reflux gave an inseparable mixture of 2α-chloro-5α-cholestan-19-yl acetate (IIa) (65%) and 5α-cholest-1- and 2-en-19-yl acetates (IIIa) and (IVa) (35%), as disclosed by g.l.c.

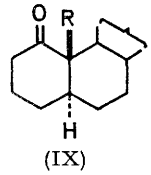


(VII)

a; R = CH_2·OH
b; R = CH_2·OAc
c; R = CO_2H
d; R = CO_2Me
e; R = H

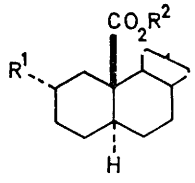


(VIII)



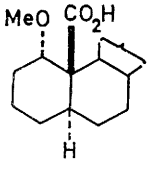
(IX)

a; R = CH_2·OAc
b; R = CH_2·OH
c; R = CO_2H
d; R = CO_2Me

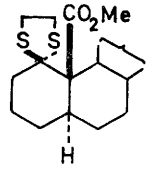


(X)

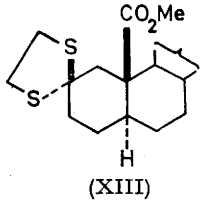
a; R^1 = OAc, R^2 = H
b; R^1 = OMe, R^2 = H



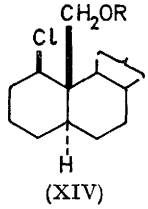
(XI)



(XII)

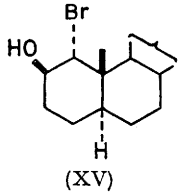


(XIII)



(XIV)

a; R = Ac
b; R = H



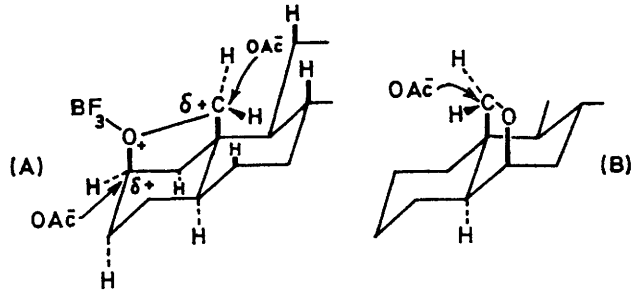
(XV)

These products would be expected to arise by S_N2 attack of chloride ion from the least hindered α [to give (IIa)] side of the molecule and by diaxial elimination from the pyridinium complex (*cf.* ref. 7) of the ether (Ia).

[1] Part XXXIV, C. W. Shoppee and B. C. Newman, *J. Chem. Soc.* (*C*), 1970, 558.
[2] C. W. Shoppee, T. E. Bellas, and R. E. Lack, *J. Chem. Soc.*, 1965, 6450.
[3] C. W. Shoppee and J. C. Coll, *J. Chem. Soc.* (*C*), 1970, 1121.
[4] C. W. Shoppee, T. E. Bellas, J. C. Coll, and R. E. Lack, *J. Chem. Soc.* (*C*), 1969, 2734.
[5] K. Heusler, J. Kalvoda, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, 1962, **45**, 1575; P. N. Rao and J. C. Uroda, *Naturwiss.*, 1963, **50**, 548.
[6] W. G. Dauben and G. J. Fonken, *J. Amer. Chem. Soc.*, 1954, **76**, 4618.
[7] C. R. Naryanan and K. N. Iyer, *Tetrahedron Letters*, 1965, 1369.

Chloro-compounds have previously been isolated [8] during similar reactions with pyridine hydrochloride. The acetolysis products (IIa), (IIIa), and (IVa) were inseparable by column chromatography, and attempts to isolate the 2α-chloro-19-acetate (IIa) as the derived 2α-chloro-19-ol (IIb) resulted in an internal S_N2 substitution to regenerate the ether (Ia). The chloro-compound (IIa) was separated from the olefins (IIIa) and (IVa) by epoxidation of the olefinic compounds followed by column chromatography, and showed i.r. absorption (CS_2) at 744 cm.$^{-1}$ (Cl,*eq*).[9]

Boron trifluoride-catalysed acetolysis [10,11] of the 2β,19-epoxide (Ia) at 50° produced the 2α,19-diacetate (IIc) and the 1α,19-diacetate (Va), separated by column chromatography from the olefins (IIIa) and (IVa). The formation of the 2α-acetate (IIc) and the olefins (IIIa) and (IVa) by the mechanism proposed by Narayanan and Iyer [12] would be expected after consideration of steric interactions. Boron trifluoride complexing of the 2β,19-epoxide (Ia) generates partial positive charges at C-2 and C-19 (A); however, owing to hindrance to S_N2 attack by acetate ion at C-19, nucleophilic attack occurs at C-2 to give the 2α,19-diacetate (IIc). Elimination of the axial 1α- or 3α-protons, in a concerted process with cleavage of the C-2 oxygen bond, reasonably



accounts for the formation of the olefins (IIIa) and (IVa). 1α,19-Diacetoxy-5α-cholestane (Va) appears to arise from the boron trifluoride-catalysed addition of acetic acid to the olefin (IIIa), directed by participation of the 19-acetoxy-group [13] involving a six-membered transition state in which the acetate carbonyl group stabilises the carbonium ion intermediate at C-1; this permits approach of the acetate ion from the α-side of the molecule. However, when 19-acetoxy-5α-cholest-1-ene (IIIa) was treated with boron trifluoride–acetic anhydride, no reaction occurred; under the same conditions 19-acetoxy-5α-cholest-2-ene (IVa) gave the 3β-acyl compound (VI). It appears that the formation of the 1α,19-diacetate (Va) requires conditions only present during the acetolytic cleavage of the ether.

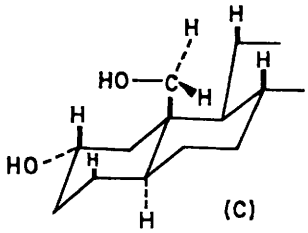
Cleavage of 3β,17β-diacetoxy-6β,19-epoxy-5α-androstane (B) with boron trifluoride–acetic anhydride afforded [14] only 3β,6β,17β,19-tetra-acetoxy-5α-androstane; the ether (Ia) afforded no 2β,19-diacetate. In the 2β,19-ether (A) attack by acetate ion at C-19 is hindered by the 8β-hydrogen atom, the 11β-hydrogen atom, and the 13β-methyl group, whereas in the 6β,19-ether (B) free approach by an acetate ion to C-19 is allowed, to afford only the 6β,19-diacetate.

The mixture of the 2α,19-diacetate (IIc) and the 1α,19-diacetate (Va) was hydrolysed with methanolic potassium hydroxide to give the corresponding diols (IId) and (Vb), which were separated by preparative t.l.c. or by column chromatography on acetic acid-washed alumina. Reacetylation of each of the diols (IId) and (Vb) gave the related diacetates (IIc) and (Va). It has been reported [15] that oxidation of 5α-cholestane-2β,19-diol with *N*-bromosuccinimide in aqueous pyridine–t-butyl alcohol gives mainly 19-hydroxy-5α-cholestan-2-one (VIIa), m.p. 171—173°, $[\alpha]_D$ +38° $\nu_{max.}$ (KBr) 3333 and 1697 cm.$^{-1}$, after 1 hr. at 50°; we confirmed this. However, the epimeric 5α-cholestane-2α,19-diol (IId), when oxidised under the same conditions, was almost unchanged after 1 hr. as indicated by t.l.c. on silica, whereas prolonged treatment under the same conditions for 24 hr. at 50° afforded 2β,19-epoxy-5α-cholestan-2α-ol (VIII), m.p. 176—178°, $\nu_{max.}$ (Nujol) 3750 and 1000 cm.$^{-1}$. The 2β,19-diol is apparently more readily oxidised than the 2α,19-diol (IId) because there is a considerable decrease of steric strain [16] in formation of the 2-ketone; oxidation of the 2α-epimer is not similarly facilitated by steric factors.

Partial hydrolysis of the 2α,19-diacetate (IIc) with potassium hydroxide (1 mol.) in a large excess of methanol at 55—60° for 1 hr. gave 19-acetoxy-5α-cholestan-2α-ol (IIe), separated by preparative t.l.c. from some unchanged diacetate (IIc) and the diol (IId). Oxidation of the monoacetate (IIe) with Jones reagent [17] afforded the 2-ketone (VIIb), which on hydrolysis gave the hemiacetal (VIII). The o.r.d. curve of the 2-oxo-19-acetate (VIIb) confirmed the presence of the 2-carbonyl group.[18] Partial acetylation of the 2α,19-diol (IId) gave a mixture of 19-acetoxy-5α-cholestan-2α-ol (IIe) and 2α-acetoxy-5α-cholestan-19-ol (IIf). The formation of both the monoacetates (IIe and f) in the acetylation of the diol (IId), and of only the monoacetate (IIe) in the hydrolysis of the

[8] Dr. L. N. Mander, Univ. of Adelaide, personal communication.
[9] D. H. R. Barton, J. E. Page, and C. W. Shoppee, *J. Chem. Soc.*, 1956, 331.
[10] B. Kamber, G. Cainelli, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, 1960, **43**, 347.
[11] A. Bowers, E. Denot, L. C. Ibanez, M. E. Cabezas, and H. J. Ringold, *J. Org. Chem.*, 1962, **27**, 1862.
[12] C. R. Naryanan and K. N. Iyer, *J. Org. Chem.*, 1965, **30**, 1734; R. D. Youssefyeh and Y. Mazur, *Tetrahedron Letters*, 1962, 1287.
[13] S. Winstein and R. E. Buckles, *J. Amer. Chem. Soc.*, 1964, **64**, 2780, 2787.
[14] A. Bowers, L. C. Ibanez, M. E. Cabezas, and H. J. Ringold, *Chem. and Ind.*, 1960, 1299.
[15] M. E. Wolff and T. Morioka, *J. Org. Chem.*, 1965, **30**, 2553.
[16] R. Filler, *Chem. Rev.*, 1963, **63**, 21.
[17] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.
[18] C. Djerassi, 'Optical Rotatory Dispersion,' McGraw-Hill, New York, 1960, 42; P. Crabbé, 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry,' Holden-Day, San Francisco, 1965, 36.

diacetate (IIc) can be rationalised by consideration of the steric requirements of the 2α- and 19-substituents.



(C)

It has been proposed [19] that the 19-hydroxy-group exists preferentially in the conformation (C), in which it lies above C-1, since in all other conformations it suffers steric interaction with the 2β, 4β-, 6β-, 8β-, or 11β-hydrogen atoms. In this conformation, approach by an acetylium ion to the oxygen atom with production of the 19-acetate would not be more hindered than approach to the equatorial 2α-oxygen atom; thus formation of both monoacetates (IIe and f) would be expected. Alkaline hydrolysis, however, involves nucleophilic attack of hydroxide anion on an acetate carbonyl group, and equatorial acetates are readily hydrolysed.[20] Thus the equatorial 2α-acetoxy-group is hydrolysed in preference to the more hindered 19-acetoxy-group to give the 19-monoacetate (IIe) as the major product.

Partial acetylation of the 1α,19-diol (Vb) with acetic anhydride in pyridine at 20° for 24 hr. afforded 19-acetoxy-5α-cholestan-1α-ol (Vc), which, when treated with Jones reagent,[17] gave the 1-ketone (IXa). This was hydrolysed to the alcohol (IXb), which was identified by its o.r.d. curve.[18] The 19-monoacetate (Vc) was also obtained by partial hydrolysis of the 1α,19-diacetate (Va) with potassium hydroxide (1 mol.) in a large volume of methanol at 55—60°. Formation of these products can be rationalised as follows: in the preferred conformation [as (C)] the 19-hydroxy-group is not hindered to acetylation, whereas the axial 1α-hydroxy-group suffers 1,3-diaxial interactions with the 3α-, 5α-, 7α-, and 9α-hydrogen atoms. The C-19 acetoxy-group has been shown to be resistant to mild alkaline hydrolyses [*cf.* (IIc)]; thus the 1α-acetoxy-group is preferentially hydrolysed to give the 19-monoacetate (Vc).

2α-Acetoxy-5α-cholestan-19-oic acid (Xa) was prepared by oxidation of the 19-alcohol (IIf) with excess of Jones reagent.[17] The 19-acetoxy-1α-ol (Vc) and the 19-acetoxy-2α-ol (IIe) were each treated with diazomethane in the presence of boron trifluoride [21] to give the corresponding 19-acetoxy-1- and 2-methoxy-derivatives (Vd) and (IIg), which were hydrolysed and oxidised [17] to give the 1α- and 2α-methoxy-19-oic acids (XI) and (Xb). However, attempts to decarboxylate the acids (XI) and (Xb) by irradiation with t-butyl hypoiodite [22] were unsuccessful. 2β-Methoxy-5α-cholestan-19-oic acid has also been shown [2] to resist decarboxylation under the same conditions, although these conditions have been used successfully for less hindered tertiary carboxylic acids.[22]

Following these unsuccessful attempts to prepare 19-nor-steroids by decarboxylation, the photochemical decarbonylation [23] of the 1-en-19-al (IIId) was examined. The 2α,19-diol (IId) and the 1α,19-diol (Vb) were treated with excess of chromic acid in acetone for 5 hr. to give the 2-oxo-19-acid (VIIc) and the 1-oxo-19-acid (IXc) respectively, which were converted into the methyl esters (VIId) and (IXd) by treatment with diazomethane. The 1- and 2-thioacetals (XII) and (XIII) were prepared by treatment of the 1- and 2-oxo-19-methyl esters (IXd) and (VIId) with ethanedithiol and boron trifluoride.[24] On treatment with deactivated Raney nickel in acetone,[25] the thioacetal (XIII) was converted into a mixture of methyl 5α-cholest-1- and 2-en-19-oates (IIIb) and (IVb); on similar treatment the thioacetal (XII) gave only the Δ^1-isomer (IIIb), converted with lithium aluminium hydride into the Δ^1-alcohol (IIIc), which was oxidised with Jones reagent [17] to the Δ^1-aldehyde (IIId). The mixture of methyl esters (IIIb) and (IVb) was converted by reduction with lithium aluminium hydride into a mixture and 5α-cholest-1- and -2-en-19-ols and these alcohols were oxidised with Jones reagent [17] to the corresponding mixture of 19-als (IIId) and (IVd). This mixture of Δ^1- and Δ^2-aldehydes was irradiated [23] to give, after column chromatography on silica, 19-nor-5α-cholest-1-ene (IIIe) and unchanged 5α-cholest-2-en-19-al (IVd), which after several months had spontaneously transformed into the acid (IVe).

Attempts to dehydrate 19-acetoxy-5α-cholestan-1α-ol (Vc) by treatment with thionyl chloride in pyridine [25] gave only 1β-chloro-5α-cholestan-19-yl acetate (XIVa), which was hydrolysed to the corresponding 1β-chloro-19-alcohol (XIVb), $\nu_{max.}$ (CS_2) 756 $cm.^{-1}$ (Cl*eq*).[9] The formula of the 1β-chloro-19-ol (XIVb) was confirmed by its mass spectrum, which showed a molecular ion at *m/e* 422 and the appropriate isotope abundances for one chlorine atom. The absence of elimination was unexpected since 5α-cholestan-1α-ol is known to afford olefinic products,[26] although in the presence of pyridine the S_Ni mechanism is suppressed in favour of the synchronous covalent S_N2 mechanism.[27]

An improved yield of 19-nor-5α-cholest-1-ene (IIIe) was obtained from 5α-cholest-1-ene, which was prepared from 5α-cholest-1-en-3-one [28] by treatment with lithium

[19] R. R. Fraser, M. Kaufman, P. Morand, and G. Govil, *Canad. J. Chem.*, 1969, **47**, 403.
[20] D. H. R. Barton, *J. Chem. Soc.*, 1953, 1027.
[21] O. C. Musgrave, R. Templeton, and H. D. Munro, *J. Chem. Soc.* (*C*), 1968, 250.
[22] D. H. R. Barton, H. P. Faro, E. P. Serebryakov, and N. F. Woolsey, *J. Chem. Soc.*, 1954, 2438.
[23] J. Irate, J. Hill, K. Schaffner, and O. Jeger, *Proc. Chem. Soc.*, 1963, 114.
[24] L. F. Fieser, *J. Amer. Chem. Soc.*, 1954, **76**, 1945.
[25] E. S. Allen and S. Bernstein, *J. Amer. Chem. Soc.*, 1955, **77**, 1028.
[26] C. W. Shoppee, R. E. Lack, S. C. Sharma, and L. R. Smith, *J. Chem. Soc.* (*C*), 1967, 1155.
[27] J. Kenyon, A. G. Lipscombe, and H. Phillips, *J. Chem. Soc.*, 1930, 415.
[28] G. F. H. Green and A. G. Long, *J. Chem. Soc.*, 1961, 2532.

aluminium hydride and active aluminium trichloride.[29] The major by-product was formed by saturation of the Δ^1-double bond; this could have occurred because the aluminium trichloride was insufficiently active. Treatment of the olefin (IIIf) with *N*-bromosuccinimide–perchloric acid in aqueous t-butyl alcohol,[30] afforded 1α-bromo-5α-cholestan-2β-ol (XV) in 70% yield after column chromatography on silica or deactivated alumina. The 1α-bromo-2β-ol (XV) in benzene was treated with a foil-wrapped vessel with lead tetra-acetate–calcium carbonate[31] under reflux for 3 days to give 1α-bromo-2β,19-epoxy-5α-cholestane (Ib) in 60% yield. The presence of bromine was confirmed by the mass spectral isotopic abundances of the molecular ions (M^+, m/e 464; $M+2$, m/e 466). Treatment of the 1α-bromo-ether (Ib) with zinc in ethanol[32] afforded 5α-cholest-1-en-19-ol (IIIc), which was oxidised with Jones reagent[17] to 5α-cholest-1-en-19-al (IIId), which readily furnished a good yield of 19-nor-5α-cholest-1-ene (IIIe) on irradiation in ethanol.[23]

Hydroboration of 5α-cholest-1-ene with bis-3-methyl-2-butylborane[33,34] gave 5α-cholestan-2α-ol (XVIa) in 70% yield, with no trace of the epimeric 2β-ol (XVIIa) or the 1-ols (XVIIIa) and (XIXa). In the case of 5α-cholest-2-ene and 5α-cholest-3-ene, only alcohols of α-configuration[34] were obtained, indicating that the 10β-methyl group severely hinders the β face of ring A. In the absence of the 10β-methyl group both the α and β faces of ring A would be accessible to the hindered dialkylborane,[33,34] with α approach possibly being more favoured because of the influence of the rather distant 13β-methyl group and the 17β-alkyl side chain. In agreement with these considerations, 19-nor-5α-cholest-1-ene (IIIe) afforded 19-nor-5α-cholestan-2α-ol (XVIb) (56%) and the 2β-ol (XVIIb) (28%), with small amounts of the 1α-ol (XVIIIb) (4%) and the 1β-ol (XIXb) (12%) as estimated by g.l.c. These alcohols were separated by column chromatography on deactivated alumina followed by preparative t.l.c. on silica, and were identified by the shape and position of the n.m.r. C*H*·OH signal (see Table). Both the 19-nor-2α-ol (XVIb) and the 19-nor-2β-ol (XVIIb) on oxidation[17] gave 19-nor-5α-cholestan-2-one (VIIe), identified by its o.r.d. curve.[18]

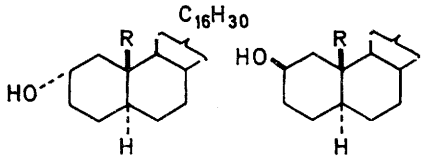
All the structures assigned were confirmed by n.m.r. spectroscopy (see Table). The signal for the 1β-proton

N.m.r. data (τ values; J and W_H in Hz)

Compound	10β-Me	19-CH_2	(J_{AB})	1β-H	(W_H)	2β-H	(W_H)	COMe	Vinyl H	OMe	Miscellaneous
(Ib)	9·39	6·11, 6·25	(8)	5·69							5·75 (1β-H) (W_H 5)
(IIa)	9·38	5·68, 5·88	(12)	7·40	(12)	6·20	(13)	7·90			
(IIc)	9·35	5·80 (A_2)		7·60	(12)	5·22	(25)	7·90, 8·00			
(IId)	9·34	6·12, 6·40	(11)	7·58	(12)	6·25	(24)				8·00 (1α-H)
(IIe)	9·35	5·72, 5·96	(12)	7·60	(12)	6·27	(15)	7·90			
(IIf)	9·32	6·12, 6·29	(12)	7·60	(12)	5·20	(25)	8·00			
(IIg)	9·34	5·74, 5·90	(12)	7·50	(12)	6·80	(25)	7·93		6·68	
(IIh)	9·31	6·11, 6·39	(12)	7·44	(12)	6·68	(20)			6·68	
(IIIa) and (IVa)	9·34	5·65, 5·89	(12)						4·15		
(IIIc)	9·34	6·22, 6·35	(12)						4·15		
(IIId)	9·30								4·15		0·15 (CHO)
(IIIe)	9·35								4·35		
(IIIb) and (IVb)	9·34	5·65, 5·89	(12)						4·50	6·45	
(IVc)	9·31	6·25 (A_2)		7·45	(12)				4·35		
(IVd)	9·38			7·35	(14)				4·35		0·15 (CHO)
(IVe)	9·42			7·20	(15)				4·35		
(Va)	9·35	5·75 (A_2)		4·98	(5)			7·95			
(Vb)											
(Vc)	9·35	5·70 (A_2)		5·90	(6)			7·92			
(Vd)	9·37	5·74 (A_2)		6·58	(7)			7·99		6·73	
(Ve)	9·32	6·13 (A_2)		6·50	(8)					6·55	
(VI)	9·38	5·79 (A_2)		7·60	(12)	5·00	(16)	7·90, 8·01			6·80 (W_H 12) (3α-H) 7·82 (COMe)
(VIIb)	9·35	5·78 (A_2)		7·35	(14)			8·05			
(VIII)	9·40	6·23, 6·09	(8)	7·90	(12)						
(Xa)	9·38			7·30	(12)	4·95	(22)	7·98			0·40 (CO_2H)
(Xb)	9·38			7·20	(12)	6·65	(B)			6·69	0·40 (CO_2H)
(XI)	9·40			6·50	(6)					6·69	
(XII)	9·44									6·32	6·73 (S·$[CH_2]_2$·S)
(XIII)	9·44									6·33	6·72 (S·$[CH_2]_2$·S)
(XIVa)	9·36	5·62, 5·78	(12)					7·92			6·20 (W_H 20) (1α-H)
(XIVb)	9·36	6·08, 6·18	(12)								6·20 (W_H 20) (1α-H)
(XVIb)	9·32					6·50	(25)				
(XVIIb)	9·36										5·89 (W_H 8) (2α-H)
(XIXb)	9·34										6·40 (W_H 30) (1α-H)

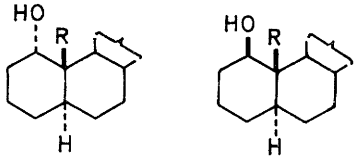
[29] J. Broome, B. R. Brown, A. Roberts, and A. M. S. White, *J. Chem. Soc.*, 1960, 1406.
[30] H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1959, 4136.
[31] A. Bowers, R. Villotti, J. A. Edwards, E. Denot, and O. Halpern, *J. Amer. Chem. Soc.*, 1962, **84**, 3204.
[32] R. M. Moriarty and T. D. J. D'Silva, *Tetrahedron*, 1965, **21**, 547.
[33] H. C. Brown, 'Hydroboration,' Benjamin, New York, 1962, p. 20 and ch. 13.
[34] F. Sondheimer and M. Nussim, *J. Org. Chem.*, 1961, **26**, 630.

was observable in the spectra of almost all the 2,19-di-substituted 5α-cholestanes[4,35] in the range τ 6·9—7·8 as a broad doublet, J_{gem} 10 Hz. The assignment



(XVI) a; R=Me b; R=H

(XVII) a; R=Me b; R=H



(XVIII) a; R=Me b; R=H

(XIX) a; R=Me b; R=H

of axial or equatorial configuration to a substituent was based on the shape of the signal of the proton attached to the same carbon atom.[36]

EXPERIMENTAL

For general experimental directions see *J. Chem. Soc.*, 1959, 345. M.p.s were determined with a Kofler hot-stage apparatus. U.v. (solutions in ethanol) and i.r. absorption spectra (solutions in carbon tetrachloride) were measured with Perkin-Elmer 4000A and 221 spectrophotometers, respectively. N.m.r. spectra were measured with Varian A60 and HA 100 instruments, with deuteriochloroform as solvent and tetramethylsilane as internal reference. O.r.d. curves were measured for solutions in methanol at 22°, with a Jasco model ORD/UV-5 recorder. Column chromatography was performed on alumina (Spence type H, activity II), or on alumina deactivated by washing with 2N-acetic acid, or on silica (Davison, 100—200 mesh). T.l.c. was carried out on silica plates in ether–hexane (1 : 4) and the plates were developed by spraying with conc. sulphuric acid and heating. Preparative t.l.c. was carried out on silica plates in ether–hexane (1 : 4); the plates were sprayed with berberine hydrochloride and examined under u.v. light. G.l.c. was performed with an F and M 400 instrument fitted with a disc integrator, on a column [1·75 m. × 3 mm. (diam.)] packed with 1% silicone rubber (nitrile) XE 60 on acid-washed (100–140 mesh) silanised Gas Chrom P at 260°; the injection port and detector temperature were *ca.* 60° higher than the column temperature, and helium was used as the carrier gas at a flow rate of 75 ml./min. Mass spectra were measured with an A.E.I. MS9 double-focus spectrometer.

2β,19-*Epoxy-5α-cholestane* (Ia).—5α-Cholestan-2β-ol (10 g.) in cyclohexane (300 ml.) with calcium carbonate (4·0 g.), was heated under reflux with lead tetra-acetate (50 g.) for 24 hr.[5] to give 2β,19-epoxy-5α-cholestane (Ia) (6·5 g.), m.p. 92—93° (from methanol) (lit.,[5] 93—95°).

Acetolysis of the Ether (Ia) *with Acetic Anhydride–Pyridine Hydrochloride.*—The ether (Ia) (1·2 g.) in acetic anhydride (10 ml.) was treated with freshly prepared pyridine hydrochloride (1 g.) under reflux for 24 hr. to give, after the usual isolation procedure, a product (800 mg.) homogeneous by t.l.c. but shown by g.l.c. to be a mixture of 19-acetoxy-2α-chloro-5α-cholestane (IIa) (65%) with the 19-acetoxy-olefins (IIIa) and (IVa) (35%). This mixture (750 mg.) in methanol (30 ml.) was heated with potassium hydroxide (500 mg.) for 1 hr. to give a mixture of the ether (Ia) and the 19-hydroxy-olefins (IIc) and (IVc), which could only partially be separated by chromatography on silica in hexane and was acetylated by treatment with acetic anhydride (30 ml.) and pyridine (0·5 ml.) at 140°. The product (420 mg.) was placed on an alumina column (20 g.) in hexane and eluted with ether–hexane (1 : 19) to give mixed 19-acetoxy-olefins (IIIa) and (IVa) (250 mg.), $\nu_{max.}$ (Nujol) 1755, 1240, and 1040 cm.$^{-1}$, τ 9·34 (13β-Me), 5·65, 5·89 (J_{AB} 12 Hz, 19-CH_2), and 4·15 (two vinyl H). Elution with ether–hexane (1 : 4) gave 2β,19-epoxy-5α-cholestane (Ia) (120 mg.), m.p. mixed m.p. 92°.

19-*Acetoxy-2α-chloro-5α-cholestane* (IIa).—The mixture of the chloride (IIa) and the 19-acetoxy-olefins (IIIa) and (IVa) isolated from the reaction just described was treated in chloroform (50 ml.) at 0° with excess of *m*-chloroperbenzoic acid (500 mg.) for 20 hr. The crude product, dissolved in hexane, was placed on an acetic acid-washed alumina column (50 g.); elution with ether–hexane (1 : 19) gave 19-*acetoxy-2α-chloro-5α-cholestane* (IIa) (60 mg.), m.p. 99—100° from ether–methanol, $\nu_{max.}$ (CS_2) 1738 and 744 (Cl*eq*) cm.$^{-1}$, τ 9·38 (13β-Me), 5·68 and 5·88 (J_{AB} 12 Hz, 19-CH_2), 6·20 ($W_H > 20$ Hz, 2β-H) [Found: Cl, 7·5%; *M* (mass spectrometry), 464, 466. $C_{29}H_{49}ClO_2$ requires Cl, 7·6%; *M*, 465], *m/e* 464 (97%), 404 (89), 391 (100), and 368 (53) [isotopic abundances 464 (100%), 465 (32), 466 (38), and 467 (10)].

Elution with ether gave an epoxide mixture which was not further investigated.

Acetolysis of the Ether (Ia) *with Acetic Anhydride–Boron Trifluoride.*—The ether (Ia) (2·5 g.) in acetic anhydride (120 ml.) at 25° was treated with boron trifluoride–ether complex (10 drops) for 3 min.; the mixture was quenched with ice and worked up as usual to give an oil (2·3 g.), shown by t.l.c. and by g.l.c. at 248° to be a mixture of the 2α,19-diacetate (IIc), 1α,19-diacetate (Va), and the olefins (IIIa) and (IVa). The oil (2·3 g.) in hexane was placed on an alumina column (100 g.); elution with ether–hexane (1 : 19) gave the mixed olefins (IIIa) and (IVa) (1·1 g.), identical with the mixture obtained before; further elution with ether–hexane (1 : 4) gave a mixture of the diacetates (IIc) and (Va). This mixture of diacetates (1 g.) in methanol (50 ml.) was hydrolysed under reflux with potassium hydroxide (0·5 g.) for 1 hr. to give the mixed diols (IId) and (Vb) (850 mg.). Extraction of the mixture with ether–hexane (1 : 19) gave the less soluble 5α-*cholestane-2α,19-diol* (IId) (600 mg.), m.p. 198—200° (from acetonitrile), $\nu_{max.}$ (Nujol) 3510, 3420, and 3300 (OH) cm.$^{-1}$, τ 9·34 (13β-Me), 6·12 and 6·40 (J_{AB} 11 Hz, 19-CH_2), and 6·25 (2β-H) [Found: C, 79·9; H, 11·9%; *M* (mass spectrometry), 404. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·9%; *M* 404], *m/e* 404 (10%), 386 (15), 373 (25), and 355 (100).

[35] N. Bhacca, M. E. Wolff, and R. Kwok, *J. Amer. Chem. Soc.*, 1962, **84**, 4976.

[36] A. Hassner and C. Heathcock, *J. Org. Chem.*, 1964, **29**, 1350.

The ether–hexane extracts were combined and introduced on to a deactivated acetic acid-washed alumina column (50 g.); elution with ether–hexane (3 : 17, 1 : 4) gave 5α-*cholestane*-1α,19-*diol* (Vb) (200 mg.), m.p. 163—165° (from acetonitrile), $\nu_{max.}$ (Nujol) 3350 (OH) cm.$^{-1}$, τ 9·32 (13β-Me), 6·03 and 6·21 (J_{AB} 12 Hz, 19-CH_2), 5·85 (W_H 6 Hz, 1β-H) [Found: C, 79·4; H, 12·05%; *M* (mass spectrometry), 404. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·9%; *M* 404], *m/e* 404 (10%), 386 (15), 373 (25), and 355 (100). Further elution, with ether, afforded the diol (IId), m.p. 199°, identical with the sample already described.

2α,19-*Diacetoxy*-5α-*cholestane* (IIc).—The 2α,19-diol (IId) (500 mg.) in acetic anhydride (20 ml.) was heated with a trace of pyridine at 80° for 1 hr. The usual work-up gave 2α,19-diacetoxy-5α-cholestane (IIc) (475 mg.) as an oil, $\nu_{max.}$ 1738 and 1240 (OAc) cm.$^{-1}$, τ 9·35 (13β-Me), 7·90 and 8·00 (2 × COMe), 5·80 (19-CH_2), and 5·22 (2β-H) [Found: *M* (mass spectrometry), 488. $C_{31}H_{52}O_4$ requires *M*, 488], *m/e* 488 (10%), 428 (90), 368 (100), and 355 (70).

1α,19-*Diacetoxy*-5α-*cholestane* (Vc).—The 1α,19-diol (Vb) (100 mg.) in acetic anhydride (5 ml.) was heated with a trace of pyridine at 80° for 2 hr. The usual isolation procedure gave 1α,19-diacetoxy-5α-cholestane (90 mg.) as an oil, $\nu_{max.}$ 1740 and 1230 (OAc) cm.$^{-1}$, τ 9·35 (13β-Me), 7·95 (COMe), 5·75 (19-CH_2), and 4·98 (W_H 8 Hz, 1β-H) [Found: *M* (mass spectrometry), 488. $C_{31}H_{52}O_4$ requires *M*, 488], *m/e* 488 (10%), 428 (40), 415 (20), 368 (100), 355 (70).

Oxidation of the 2α,19-*Diol* (IId) *with* N-*Bromosuccinimide*.—A solution of *N*-bromosuccinimide (700 mg.), pyridine (0·3 ml.), and water (0·3 ml.) in t-butyl alcohol (30 ml.) was added to the diol (IId) (250 mg.) in t-butyl alcohol at 50° and the mixture was kept at 50° for 24 hr. Preparative t.l.c. of a portion of the product (50 mg.) on silica in ether–hexane (1 : 1) gave 2β,19-*epoxy*-5α-*cholestan*-2α-*ol* (VIII) (30 mg.), m.p. 176—178° (from acetonitrile), $\nu_{max.}$ (Nujol) 3750 and 1000 cm.$^{-1}$, τ 9·40 (13β-Me), 7·90 (1β-H), 6·23 and 6·09 (J_{AB} 8 Hz, 19-CH_2) [Found: *M* (mass spectrometry), 402·3503. $C_{27}H_{46}O_2$ requires *M*, 402·3498].

Selective Hydrolysis of 2α,19-*Diacetoxy*-5α-*cholestane* (IIc).—The diacetate (IIc) (1·1 g.) in methanol (400 ml.) was stirred with potassium hydroxide (130 mg., 1·05 mol.) at 55—60° for 2 hr. The pH of the solution was adjusted to 5 and methanol was removed in a vacuum. The product was placed on a deactivated acetic acid-washed alumina column in ether–hexane (1 : 9). Elution with this solvent mixture gave unchanged diacetate (IIc) (580 mg.); use of ether–hexane (3 : 17) afforded 19-*acetoxy*-5α-*cholestan*-2α-*ol* (IIe) (320 mg.), m.p. 89—91° (from acetonitrile), $\nu_{max.}$ 3615 (OH), 1740, and 1230 (OAc) cm.$^{-1}$, τ 9·35 (13β-Me), 7·90 (COMe), 5·72 and 5·96 (J_{AB} 12 Hz, 19-CH_2), and 6·27 (2β-H) [Found: C, 76·7; H, 10·9%; *M* (mass spectrometry), 446·3758. $C_{29}H_{50}O_3$ requires C, 77·9; H, 10·7%; *M*, 446·3760], *m/e* 446 (7%), 428 (10), and 386 (100). Elution with ether gave the 2α,19-diol (IId).

19-*Acetoxy*-5α-*cholestan*-2-*one* (VIIb).—The monoacetate (IIf) (80 mg.) in acetone (20 ml.) was titrated with 8N-chromic acid.[17] The usual work-up gave 19-*acetoxy*-5α-*cholestan*-2-*one* (VIIb) (67 mg.), m.p. 99—101° (from acetonitrile), $\nu_{max.}$ 1748 (OAc) and 1718 (C=O) cm.$^{-1}$, τ 9·35 (13β-Me), 8·05 (COMe), and 5·78 (19-CH_2), o.r.d.: $[\phi]_{302}$ +3670°pk, $[\phi]_{275}$ −1728°tr [Found: *M* (mass spectrometry), 444. $C_{29}H_{48}O_3$ requires *M*, 444], *m/e* 444 (45%), 384 (100), and 371 (60).

The 2-ketone (VIIb) (60 mg.) in methanol (20 ml.) was heated with potassium hydroxide (50 mg.) in water (1 ml.) under reflux for 1 hr. to give the hemiacetal (VIII) (50 mg.), m.p. and mixed m.p. 176—178° (from acetonitrile).

Monoacetylation of the 2α,19-*Diol* (IId).—The diol (IId) (800 mg.) in pyridine (50 ml.) was heated with acetic anhydride (0·20 ml., 1 mol.) at 100° for 15 hr. The cooled mixture was diluted with N-hydrochloric acid (100 ml.) and the precipitate was filtered off, dried, and extracted with boiling hexane; the insoluble residue (450 mg.) was unchanged diol (IId). The hexane extract was placed on a column of deactivated acetic acid-washed alumina and eluted with ether–hexane (1 : 9) to give 2α-*acetoxy*-5α-*cholestan*-19-*ol* (IIf) (135 mg.), m.p. 153—154° (from acetonitrile), $\nu_{max.}$ 3633 (OH) and 1730 (OAc) cm.$^{-1}$, τ 9·32 (13β-Me), 8·07 (COMe), 6·12 and 6·29 (J_{AB} 12 Hz, 19-CH_2), 5·2 (W_H 25 Hz, 2β-H) [Found: *M* (mass spectrometry), 446·3762. $C_{29}H_{50}O_3$ requires *M*, 446·3760], *m/e* 446 (10%), 428 (26), 386 (100), 373 (50), and 355 (50). Further elution with the same solvent and with ether–hexane (1 : 7) afforded the 19-monoacetate (IIe) (150 mg.), m.p. and mixed m.p. 89—91°. Elution with ether afforded the unchanged diol (IId) (20 mg.).

Selective Acetylation of 5α-*Cholestane*-1α,19-*diol* (Vb).—The diol (Vb) (150 mg.) in pyridine (10 ml.) was treated with acetic anhydride (10 drops) and left at 20° overnight. After isolation in the usual way, the product was placed on a deactivated acetic acid–washed alumina column (20 g.) in ether–hexane (1 : 9). Elution with this solvent mixture afforded the 1α,19-diacetate (Va) (20 mg.); elution with ether–hexane (3 : 17) then gave 19-*acetoxy*-5α-*cholestan*-1α-*ol* (Vc) (50 mg.), m.p. 70—72° (from acetonitrile), $\nu_{max.}$ 3622 (OH) and 1740 (OAc) cm.$^{-1}$, τ 9·35 (13β-Me), 7·93 (COMe), 5·70 (19-CH_2), and 5·90 (W_H 6 Hz, 1β-H) [Found: *M* (mass spectrometry), 446·3755. $C_{29}H_{50}O_3$ requires 446·37607] *m/e* 446 (90%), 386 (75), and 373 (100).

The 19-monoacetate (Vc) was also prepared by treatment of the diacetate (Va) (500 mg.) in methanol (500 ml.) with potassium hydroxide (60 mg., 1 mol.), at 55—60° for 2 hr. The product (450 mg.) in hexane was placed on a column of acetic acid-washed alumina and eluted with hexane to yield the unchanged diacetate (Va) (280 mg.). Elution with ether–hexane (1 : 9, 3 : 17) gave the monoacetate (Vc) (150 mg.), m.p. and mixed m.p. 71°.

19-*Hydroxy*-5α-*cholestan*-1-*one* (IXb).—The 19-monoacetate (Vc) (100 mg.) in acetone (20 ml.) was titrated with Jones reagent [17] and after the usual work-up gave 19-acetoxy-5α-cholestan-1-one (IXa) (85 mg.), which was dissolved in methanol (50 ml.) and treated with potassium hydroxide (100 mg.) for 1 hr. The usual isolation procedure afforded 19-*hydroxy*-5α-*cholestan*-1-*one* (IXb) (70 mg.), m.p. 144—146° (from acetonitrile), $\nu_{max.}$ 3590 (OH) and 1717 (CO) cm.$^{-1}$ [Found: *M* (mass spectrometry), 402. $C_{27}H_{46}O_2$ requires *M*, 402], *m/e* 402 (100%), 386 (10), and 371 (20), o.r.d.: $[\phi]_{305}$ +232°pk, $[\phi]_{275}$ +116°tr.

2α-*Acetoxy*-5α-*cholestan*-19-*oic Acid* (Xa).—The 2α-monoacetate (IIf) (220 mg.) in acetone (20 ml.) was titrated with 8N-chromic acid until a permanent colouration was obtained; an equal volume of the reagent was then added and the mixture was set aside at 20° for 5 hr. The usual work-up afforded 2α-*acetoxy*-5α-*cholestan*-19-*oic acid* (Xa), m.p. 185—187°, $\nu_{max.}$ 3600—2500 (OH), 1740 (OAc), and 1691 (CO) cm.$^{-1}$, τ 9·38 (13β-Me), 7·98 (COMe), 7·30 *J* 12 Hz, 1β-H), and 4·95 (W_H 22 Hz, 2β-H) [Found: *M* (mass spectrometry), 460·3548. $C_{29}H_{48}O_4$ requires *M*, 460·3552], *m/e* 460 (10%), 415 (50), 400 (100), 260 (50), and 245 (100).

1α-*Methoxy*-5α-*cholestan*-19-*oic Acid* (XI).—The 19-monoacetate (Vc) (150 mg.) in ether (15 ml.) was stirred with excess of ethereal diazomethane solution at 0°. Boron trifluoride–ether complex (0·5 ml.) was carefully added, and the mixture was left at 0° for 1 hr. After the usual isolation procedure, the product, in hexane, was filtered through a short column of alumina (5 g.) to give 19-acetoxy-1α-methoxy-5α-cholestane (Vd) (80 mg.) as an oil, $\nu_{max.}$ 1739 (CO) cm.$^{-1}$, τ 9·37 (13β-Me), 7·99 (OAc), 5·74 (19-CH_2), and 6·58 (W_H 7 Hz, 1β-H). Elution with more polar solvents gave the unchanged 19-monoacetate (Vc) (65 mg.). The 1α-methoxy-19-acetate (Vd) (60 mg.) in methanol (10 ml.) was heated under reflux with potassium hydroxide (200 mg.) for 1 hr. and the product was worked up to afford 1α-methoxy-5α-cholestan-19-ol (Ve) (45 mg.), as an oil, $\nu_{max.}$ 3620 (OH) cm.$^{-1}$, 9·32 (13β-Me), 6·67 (OMe), 6·13 (19-CH_2), and 6·50 (W_H 8 Hz, 1β-H). This alcohol (Va) (40 mg.) in acetone (20 ml.) was treated with excess of Jones reagent [17] at 20° to furnish 1α-*methoxy*-5α-*cholestan*-19-*oic acid* (XI) (20 mg.), m.p. 153—155°, $\nu_{max.}$ 3600—2500 (HO · · · H), and 1695 (CO) cm.$^{-1}$, τ 9·40 (13β-Me), 6·69 (OMe), and 6·50 (W_H 6 Hz, 1β-H) [Found: *M* (mass spectrometry), 432·3603. $C_{28}H_{48}O_3$ requires *M*, 432·3603].

2α-*Methoxy*-5α-*cholestan*-19-*ol* (IIh).—The 19-monoacetate (IIe) (300 mg.) in ether (20 ml.) was treated with excess of ethereal diazomethane (60 ml.) at 0°; boron trifluoride–ether complex (0·5 ml.) was then added slowly with stirring. After the usual work-up, the product, dissolved in hexane, was filtered through a short column of alumina (5 g.) to give 19-acetoxy-2α-methoxy-5α-cholestane (IIg) (69 mg.), as an oil, $\nu_{max.}$ 1740, 1230 (OAc), and 1100 (OMe) cm.$^{-1}$, τ 9·34 (13β-Me), 7·93 (COMe), 6·68 (4H, OMe and 2β-H), and 5·74 and 5·90 (J_{AB} 12 Hz, 19-CH_2). This methoxy-acetate (500 mg.) in methanol (50 ml.) was refluxed with potassium hydroxide (550 mg.) for 1 hr. to give 2α-*methoxy*-5α-*cholestan*-19-*ol* (IIh) (450 mg.), m.p. 66—68° (from acetonitrile), $\nu_{max.}$ 3630 (OH), 3450 (OH · · · H), and 1095 (OMe) cm.$^{-1}$, τ 9·31 (13β-Me), 6·11 and 6·39 (J_{AB} 12 Hz, 19-CH_2), 6·68 (OMe and 2β-H), and 7·44 (*J* 12 Hz, 1β-H) [Found: *M* (mass spectrometry), 418·3813. $C_{28}H_{50}O_2$ requires *M*, 418·3811], *m/e* 418 (15%), 400 (20), 386 (100), and 355 (100).

2α-*Methoxy*-5α-*cholestan*-19-*oic Acid* (Xb).—The 2α-methoxy-19-ol (IIh) (170 mg.) in acetone (30 ml.) was treated with excess of Jones reagent [17] at 20° for 5 hr. After work-up, the product (130 mg.) was dissolved in ether and acetonitrile was added until the solution became turbid; the product gave 2α-*methoxy*-5α-*cholestan*-19-*oic acid* (Xb) (80 mg.), m.p. 160—162° (from acetonitrile), $\nu_{max.}$ 3600—2500 (HO · · · H) and 1705 (CO) cm.$^{-1}$ τ 9·38 (13β-Me), 7·20 (*J* 12 Hz, 1β-H), 6·65 (OMe and 2β-H), and 0·40 (CO_2H) [Found: C, 77·8; H, 11·4%; *M* (mass spectrometry), 432·3603. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%; *M*, 432·3603], *m/e* 432 (100%), 400 (50), 386 (40), and 356 (50).

Methyl 2,2-*Ethylenedithio*-5α-*cholestan*-19-*oate* (XIII).—The 2α,19-diol (IId) (250 mg.) in acetone (20 ml.) was treated with excess of Jones reagent [17] at 20° for 5 hr., then extracted with ether. The dried extract was treated at 0° with excess of diazomethane. Unused reagent was decomposed with acetic acid (1 ml.) after 1 hr.; work-up then gave the 2-oxo-ester (VIId), (165 mg.), m.p. and mixed m.p. 117—118° (lit.,[2] 117°). This ester (VIId) (150 mg.) was treated at 20° with ethanedithiol (0·5 ml.) followed by boron trifluoride–ether complex (5 drops). Excess of reagent was removed by vacuum distillation and the solid residue was purified by preparative t.l.c. on silica in ether–hexane (1 : 3) to give *methyl* 2,2-*ethylenedithio*-5α-*cholestan*-19-*oate* (XIII) (85 mg.), m.p. 125—126° (from methanol), $\nu_{max.}$ 1725 (CO) cm.$^{-1}$, τ 9·44 (13β-Me), 6·72 (S·$[CH_2]_2$·S), and 6·33 (OMe) [Found: *M* (mass spectrometry), 506·3250. $C_{30}H_{50}O_2S_2$ requires *M*, 506·3252], *m/e* 506 (90%), 447 (100), and 353 (10).

Methyl 1,1-*Ethylenedithio*-5α-*cholestan*-19-*oate* (XII).—The 1α,19-diol (Vb) (100 mg.) in acetone (20 ml.) was treated with excess of Jones reagent at 20° to give, after methylation with ethereal diazomethane, methyl 1-oxo-5α-cholestan-19-oate (IXd) (85 mg.) as an oil, $\nu_{max.}$ 1735 and 1715 cm.$^{-1}$ (CO), τ 9·38 (13β-Me) and 6·25 (OMe). The 1-oxo-ester (IXd) (80 mg.) was treated with ethanedithiol (0·25 ml.) and boron trifluoride–ether complex (5 drops) to give, after preparative t.l.c. on silica in ether–hexane (1 : 3), *methyl* 1,1-*ethylenedithio*-5α-*cholestan*-19-*oate* (XII) (65 mg.), m.p. 64—65° (from methanol), $\nu_{max.}$ 1720 cm.$^{-1}$ (CO), τ 9·44 (13β-Me), 6·72 (S·$[CH_2]_2$·S), and 6·32 (OMe) [Found: *M* (mass spectrometry), 506·3250. $C_{30}H_{50}O_2S_2$ requires *M*, 506·3252] *m/e* 506 (100%), 446 (25), and 353 (20).

Desulphurisation of the 2,2-*Thioacetal* (XIII).—Raney nickel (W_1; 250 mg.) was heated in acetone (20 ml.) under reflux for 20 hr.; the 2,2-thioacetal (XIII) (50 mg.) in acetone (10 ml.) was added, and heating was continued for 2 hr. The cooled solution was filtered, and the catalyst was washed with ether and with chloroform. The crude product was purified by preparative t.l.c. on silica in ether–hexane (1 : 19) to give methyl 5α-cholest-1- and -2-en-19-oates (IIIb) and (IVb) (100 mg.), whose i.r. and n.m.r. spectra were identical with those of an authentic sample.

5α-*Cholest*-1-*en*-19-*ol* (IIIc).—The 1,1-thioacetal (XII) (50 mg.) in acetone (5 ml.) was added to a suspension of deactivated Raney nickel (W_1; 200 mg.) in acetone (20 ml.) and the mixture was refluxed for 7 hr. The crude product was treated with lithium aluminium hydride in refluxing ether for 1 hr., and purified by preparative t.l.c. on silica to give 5α-*cholest*-1-*en*-19-*ol* (IIIc) (30 mg.), m.p. 63—64° (from acetonitrile), $\nu_{max.}$ 3625 cm.$^{-1}$ (OH), τ 9·34 (13β-Me), 6·22 and 6·35 (J_{AB} 12 Hz 19-CH_2), and 4·15 (two vinyl H) [Found: *M* (mass spectrometry), 386·3546. $C_{27}H_{46}O$ requires *M*, 386·3548].

5α-*Cholest*-1- and -2-*en*-19-*als* (IIId) *and* (IVd).—The mixture of 1- and 2-en-19-ols (IIIc) and (IVc) (170 mg.) in acetone (50 ml.) were titrated with Jones reagent; [17] the mixture was quickly quenched with methanol to give the mixed 5α-cholest-1- and 2-en-19-als (IIId) and (IVd) (150 mg.), $\nu_{max.}$ 1730 cm^{-1} (CHO) τ 9·35 (13β-Me), 4·3 (vinyl H), and 0·15 (CHO).

Photochemical Decarbonylation of 5α-*Cholest*-1-*en*-19-*al*.—The mixture of 5α-cholest-1- and -2-en-19-als (IIId) and (IVd) (150 mg.) in ethanol (50 ml.) in a Pyrex flask was irradiated in a Barton box (external probe) with a 125 w (Phillips) HPK mercury lamp for 6 hr. Ethanol was removed *in vacuo*, and the resultant oil was placed on a silica column (10 g.) in pentane. Elution with pentane afforded 19-*nor*-5α-*cholest*-1-*ene* (IIIe) (25 mg.) as an oil, τ 9·35 (13β-Me) and 4·35 (two vinyl H) [Found: *M* (mass spectrometry), 356·3442. $C_{26}H_{44}$ requires *M*, 356·3443]. Further elution with pentane and with ether–pentane (1 : 99) afforded 5α-*cholest*-2-*en*-19-*al* (IVd) (100 mg.), m.p. 85—88° (from methanol), $\nu_{max.}$ 1730 cm.$^{-1}$ (CHO), 7·36 (J_{AB} 14 Hz, 1β-H) and 4·35 (two vinyl H) [Found: C, 82·8;

H, 11·3%; *M* (mass spectrometry), 384. $C_{27}H_{44}O$ requires C, 84·3; H, 11·5%; *M*, 384], *m/e* 384 (70%), 356 (100%). This aldehyde (IVd) was unchanged on further irradiation for 6 hr.

Aerial Oxidation of 5α-Cholest-2-en-19-al (IVd).—A solution of the aldehyde (IVd) in methanol was left to evaporate for 2 months. The product was crystallised from methanol, then from acetonitrile, and finally twice from methanol to give *5α-cholest-2-en-19-oic acid* (IVe), m.p. 202—204°, $\nu_{max.}$ 3600—2500 (HO···H) and 1690 (CO) cm.$^{-1}$, τ 9·42 (13β-Me), 7·20 (*J* 15 Hz, 1β-H), and 4·35 (two vinyl H) [Found: *M* (mass sprctrometry), 400. $C_{27}H_{44}O_2$ requires *M*, 400], *m/e* 400 (100%) and 354 (95).

2β,19-Epoxy-5α-cholestan-3α-ol.—The 2-en-19-al (IVd) (60 mg.) in chloroform (20 ml.) was treated with *m*-chloroperbenzoic acid (100 mg.) at 0° for 20 hr. The crude product was refluxed with lithium aluminium hydride (100 mg.) in ether for 1 hr. to give 2β,19-epoxy-5α-cholestan-3α-ol, m.p. and mixed m.p. 197—199° (lit.,[15] 197—199°).

5α-Cholest-2-en-19-ol (IVc).—The aldehyde (IVd) (150 mg.) in refluxing ether (50 ml.) was treated with lithium aluminium hydride (500 mg.) for 2 hr. to give *5α-cholest-2-en-19-ol* (IVc), m.p. 83—84° (from ether–methanol), $\nu_{max.}$ 3630 (OH), 3500—3100 (HO···H), and 1650 (C=C) cm.$^{-1}$, 9·31 (13β-Me), 6·25 (19-CH_2), 7·45 (1β-H), and 4·35 (two vinyl H) [Found: *M* (mass spectrometry), 386·3546. $C_{27}H_{46}O$ requires *M*, 386·3546], *m/e* 386 (35%), 368 (25), and 355 (100).

Attempted Dehydration of 19-Acetoxy-5α-cholestan-1α-ol (Vc).—The alcohol (Vc) (100 mg.) in pyridine (5 ml.) was treated with thionyl chloride (0·5 ml.) at −5° for 18 hr. to give, after separation by preparative t.l.c. on silica in benzene, 19-acetoxy-1β-chloro-5α-cholestane (XIVa) (20 mg.), $\nu_{max.}$ (CS_2) 1738 (OAc), 800, and 756 (Cl*eq*) cm.$^{-1}$, τ 9·36 (13β-Me), 7·92 (COMe), 5·62 and 5·78 (J_{AB} 12 Hz, 19-CH_2), and 6·2 (W_H 20 Hz 1α-H). Unchanged alcohol (Vc) (43 mg.) was recovered. The 1β-chloride (XIVa) (20 mg.) in methanol (10 ml.) was heated under reflux with potassium hydroxide (100 mg.) to give *1β-chloro-5α-cholestan-19-ol* (XIVb), m.p. 124—126° (from methanol), $\nu_{max.}$ (CS_2) 3600 (OH) and 756 (Cl*eq*) cm.$^{-1}$, τ 9·36 (13β-Me), 6·08 and 6·18 (J_{AB} 12 Hz, 19-CH_2), and 6·20br (1α-H) [Found: *M* (mass spectrometry), 422. $C_{27}H_{47}ClO$ requires *M*, 422], *m/e* 422 (100%), 391 (100), 386 (95), and 355 (54) [isotopic abundances: 422 (100%), 423 (27), 424 (33), and 425 (10)].

Addition of Acetic Anhydride to the Olefin (IVa).—(*a*) The olefin (IVa) (150 mg.) in acetic anhydride (20 ml.) and acetic acid (10 drops) was treated with boron trifluoride–ether complex (10 drops) for 10 min. at 20°. The product, isolated in the usual way, was purified by preparative t.l.c. to give unchanged olefin (IVa) (95 mg.) and *2β,19-diacetoxy-3β-acetyl-5α-cholestane* (VI) (35 mg.), m.p. 156—158° (from methanol), $\nu_{max.}$ 1732 (CO) cm.$^{-1}$, τ 9·38 (13β-Me), 7·90 and 8·01 (OAc), 7·82 (Ac), 5·79 (19-CH_2), 5·00 (W_H 25 Hz, 2β-H), and 6·80 (W_H 12 Hz, 3α-H) [Found: *M* (mass spectrometry), 530. $C_{33}H_{54}O_5$ requires *M*, 530], *m/e* 530 (1%), 470 (80), 410 (100), 397 (80), and 377 (50).

(*b*) The mixture of Δ^1- and Δ^2-19-acetates (IIIa) and (IVa) with acetic anhydride (50 ml.) and acetic acid (10 drops) gave the unchanged mixed olefins (IIIa) and (IVa) together with the 3β-acetyl compound (VI) already described, after purification by preparative t.l.c.

1α-Bromo-2β,19-epoxy-5α-cholestane (Ib).—The bromohydrin (XV)[30] (1 g.) in benzene (50 ml.) was heated under reflux with calcium carbonate (500 mg.) and lead tetra-acetate (5 g.) for 72 hr. After the usual work-up, the crude product was placed on a silica column (80 g.) in hexane. Elution with ether–hexane (1 : 19) afforded *1α-bromo-2β,19-epoxy-5α-cholestane* (Ib) (650 mg.), m.p. 89—90° (from acetone), $\nu_{max.}$ 1005 cm.$^{-1}$ (–O–), τ 9·39 (13β-Me), 6·25 and 6·11 (J_{AB} 8 Hz, 19-CH_2), 5·75 (W_H 12 Hz, 2α-H), and 5·69 (W_H 6 Hz, 1β-H) [Found: *M* (mass spectrometry), 464·2658. $C_{27}H_{45}BrO$ requires *M*, 464·2654], *m/e* 464 (50%), 420 (10), 386 (25), and 355 (100) [isotopic abundances: 464 (100%), 465 (25), 466 (100), and 467 (20%)].

19-Nor-5α-cholest-1-ene (IIIe).—The epoxy-bromide (Ib) (1 g.) in ethanol (50 ml.) was heated under reflux with zinc dust (10 g.) for 24 hr. to give 5α-cholest-1-en-19-ol (IIIe) (700 mg.), m.p. 63—64°, identical with the sample already described.

Hydroboration of 19-Nor-5α-cholest-1-ene (IIIe).—A solution of lithium aluminium hydride (0·5 g.) in ether (30 ml.) was added dropwise to a solution of 2-methylbut-2-ene (2·5 g.) and boron trifluoride–ether complex (2·5 g.) in ether (40 ml.) at 0° during 1 hr. 19-Nor-5α-cholest-1-ene (IIIe) (500 mg.) in ether (20 ml.) was added, and the mixture was left at 20° for 4 hr. The product, isolated by addition of excess of a saturated solution of sodium sulphate, was dissolved in tetrahydrofuran and treated with hydrogen peroxide (30%) (10 ml.) in 2N-sodium hydroxide (15 ml.) at 0° for 1 hr. The product was filtered through a column of alumina (deactivated by washing with dilute acetic acid) to give unchanged olefin (IIIe) (200 mg.) and a mixture of the four 19-nor-alcohols (XVIb), (XVIIb), (XVIIIb), and (XIXb). Three of these were separated by preparative t.l.c. on silica in ether–benzene (1 : 19). The alcohols, in order of polarity, had the following properties: *19-nor-5α-cholestan-2β-ol* (XVIIb) (60 mg.), m.p. 135—137° (from methanol), $\nu_{max.}$ 3680 (OH) and 3600—3400 (HO···H) cm.$^{-1}$ τ 9·36 (13β-Me) and 5·89 (W_H 8 Hz, 2α-H) [Found: *M* (mass spectrometry), 374·3549. $C_{26}H_{46}O$ requires *M*, 374·3548]; *19-nor-5α-cholestan-2α-ol* (XVIb) (120 mg.), m.p. 165—170° (from methanol), $\nu_{max.}$ 3690 (OH) and 3600—3200 (HO···H) cm.$^{-1}$, τ 9·32 (13β-Me) and 6·5 (W_H 25 Hz, 2β-H)[Found: *M* (mass spectrometry), 374·3552. $C_{26}H_{46}O$ requires *M*, 374·3548]; *19-nor-5α-cholestan-1β-ol* (XIXb) (5 mg.), m.p. 98—105° (from methanol), τ 9·34 (3β-Me), 6·4 (W_H *ca.* 30 Hz 1α-H) [Found: *M* (mass spectrometry), 374·3552. $C_{26}H_{46}O$ requires *M*, 374·3548].

Oxidation of the Alcohols (XVIb) *and* (XVIIb).—The 19-nor-2β-ol (XVIIb) (20 mg.) in acetone (10 ml.) was treated with Jones reagent[17] to give, after the usual isolation procedure, *19-nor-5α-cholestan-2-one* (VIIe) (11 mg.), m.p. 73—75° (from methanol), $\nu_{max.}$ 1715 cm.$^{-1}$, o.r.d. $[\phi]_{304}$ +3440°pk (trough not observed but form of curve closely similar to that of 5α-cholestan-2-one) [Found: *M* (mass spectrometry), 372·3393. $C_{26}H_{44}O$ requires *M*, 372·3392]. The 19-nor-2α-ol (XVIb) (20 mg.) was oxidised similarly to give the 19-nor-2-one (VIIe), m.p. and mixed m.p. 73—75°, i.r. spectrum identical with that of the sample obtained before.

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