Neighbouring Group Participation in the Cleavage of Some Steroidal Hydroxy Epoxides†

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Cleavage of steroidal 6β-hydroxy 4α,5α-epoxides by the action of perchloric acid, acetic acid, formic acid, and boron trifluoride–diethyl ether is described. It is shown that, when attack at C-4 by an external nucleophile is inhibited by the inductive effect of a 3-methoxy group, epoxide migration occurs, involving intramolecular nucleophilic attack at C-5 by the adjacent hydroxy group. The product isolated then arises either by rearrangement or by diaxial cleavage of the intermediate isomeric epoxide thus formed. The latter process affords a product derived by overall *cis*-opening of the original oxirane ring.

Isomerisation of a vicinal hydroxy epoxide by intramolecular nucleophilic attack of the hydroxy group upon the adjacent oxiranic centre ('epoxide migration')[1] is well documented in the carbohydrate series[2] and has recently been shown to occur in a suitably disposed steroidal hydroxy epoxide.[3] Thus, when 4α,5-epoxy-3α-methoxy-5α-cholestan-6β-ol (**1**), in which the oxirane ring is *trans* to the axial hydroxy group, is hydrolysed with aqueous perchloric acid overall *cis*-cleavage of the epoxide occurs to afford the triol (**3**). This result is most easily explained by postulating a prior epoxide migration to form the isomeric hydroxy epoxide (**2**), which then undergoes normal diaxial scission.

In contrast to the behaviour of epoxide (**1**), the hydroxy epoxide (**4**), which lacks a methoxy group at C-3, is reported[4] to undergo *trans*-diaxial cleavage upon treatment with methanolic toluene-*p*-sulphonic acid to yield 4β-methoxy-5α-cholestane-5,6β-diol (**5**). In broad general agreement with that observation we have found that, although cleavage of the hydroxy epoxide (**4**) with aqueous perchloric acid in acetone affords a small amount of 5α-cholestane-4α,5,6β-triol (**10**) which presumably arises by an epoxide migration mechanism, the major products are the triol (**6**) (arising by diaxial cleavage of the unrearranged epoxide) and its 4,6-acetonide (**8**). When the cleavage reaction is carried out using butanone as solvent, the acetal (**9**) is obtained. The structures of the triols (**6**) and (**10**) follow from their NMR spectra and from those of the derived acetates (**7**) and (**11**).

It would appear from the foregoing that the epoxide migration observed in the reaction of the hydroxy epoxide (**1**) with perchloric acid may be attributed to the presence of the methoxy group at C-3, the inductive effect of which inhibits cleavage of the C(4)–O bond. Intramolecular nucleophilic attack at C-5 by the 6β-hydroxy group then predominates over attack of external nucleophile at C-4. In support of this view we now report that under a variety of acidic conditions the oxirane ring of 4α,5-epoxy-3β-methoxy-5α-cholestan-6β-ol (**12**) undergoes overall *cis*-cleavage, presumably through an epoxide migration mechanism involving the isomeric hydroxy epoxide (**20**) as an intermediate.

Treatment of compound (**12**) with aqueous perchloric acid using acetone as solvent afforded the 4α,5α,6β-triol (**13**) and its acetonide (**14**).‡ Cleavage of the hydroxy epoxide (**12**) with acetic acid followed a similar course; the product isolated was 4α-acetoxy-3β-methoxy-5α-cholestane-5,6β-diol (**16**), presumably arising from the initially formed tertiary acetate (**17**) by a process of intramolecular *trans*-esterification. The structure of compound (**16**) was confirmed by its preparation from the triol (**13**) by selective acylation. Further acylation of either of the compounds (**13**) or (**16**) gave the diacetate (**18**).

Formic acid cleavage of the hydroxy epoxide (**12**) gave the diformate (**19**), which could be saponified to the triol (**13**). Doubtless the 4α-formoxy group of compound (**19**) arises in an analogous manner to the ester function of compound (**16**); esterification of the 6β-hydroxy group with formic acid is unexceptional. The 5β,6β-epoxide (**20**) thought to be an intermediate in the hydrolysis, acetolysis, and formolysis of compound (**12**) was obtained by isomerisation of the latter with methanolic potassium hydroxide (*cf.* ref. 3). As expected, it was converted into the diformate (**19**) by the action of formic acid.

Overall *cis*-cleavage of the oxirane ring was again observed when compound (**12**) was treated with boron trifluoride–diethyl ether. In this case, the external nucleophile is fluoride ion which, unlike the acetoxy and formoxy groups discussed above, is unable to migrate away from its initial point of attack. The product isolated was 5-fluoro-3β-methoxy-5α-cholestane-4α,6β-diol (**28**). As expected, the derived acetate (**29**) was obtained by the action of boron trifluoride–diethyl ether on the acetate (**21**) of the epoxide migration product (**20**). It is noteworthy that even in the absence of a methoxy group at C-3, epoxide migration predominates over direct attack by a weak nucleophile like fluoride ion. Thus, 4α,5-epoxy-5α-cholestan-6β-ol (**4**) was cleaved with boron trifluoride–diethyl ether to afford the fluoro diol (**30**) arising by overall *cis*-cleavage of the epoxide ring. Both compounds (**28**) and (**30**) underwent selective acetylation of the equatorial 4α-hydroxy group to give the monoacetates (**29**) and (**31**) respectively, when treated with acetic anhydride and pyridine.

Treatment of 4α,5-epoxy-3α-methoxy-5α-cholestan-6β-ol (**32**) [the C-3 epimer of compound (**12**)] with boron trifluoride–diethyl ether resulted in isomerisation to the ketone (**33**). In this case epoxide migration has been followed by rearrangement of

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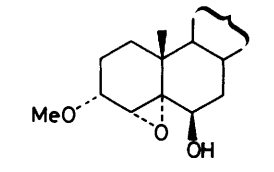
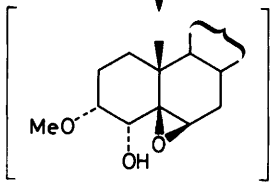
‡ When the 6-deoxy analogue (**22**) of compound (**12**) was treated with perchloric acid under similar conditions the major product was 3β-methoxy-5β-cholestane-4α,5-diol (**23**), identified by dehydration of the derived acetate (**24**) to give 4α-acetoxy-3β-methoxycholest-5-ene (**25**). In this case, also, the inductive effect of the methoxy group inhibits nucleophilic attack at C-4. In the absence of a vicinal *trans*-axial hydroxy group epoxide cleavage occurs by attack of external nucleophile at C-5.

It is to be noted that lithium aluminium hydride reduction of the epoxides (**12**) and (**22**) gave the products (**26**) and (**27**) respectively, arising by normal diaxial cleavage of the oxirane ring, with nucleophilic attack at C-4 and fission of the C(4)–O bond. These contrasting results reflect the greater development of positive charge on the oxiranic carbon atom during acid-catalysed cleavage.



(1)



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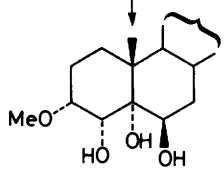

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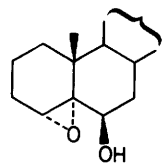

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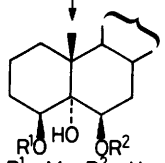
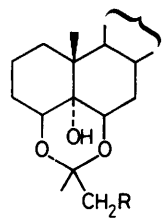


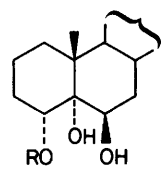
(5) R^1 = Me, R^2 = H
(6) R^1 = R^2 = H
(7) R^1 = R^2 = Ac

+



(8) R = H
(9) R = Ac

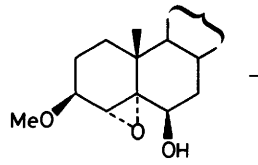
+



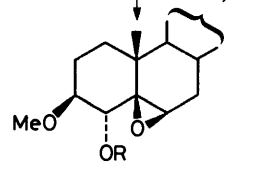
(10) R = H
(11) R = Ac

the resulting 5β,6β-epoxide (**2**) involving hydride migration from C-6α to C-5α.[5] The diastereoisomeric hydroxy epoxide (**34**), in which the vicinal hydroxy and oxirane rings are *cis*, cannot undergo epoxide migration. It has been found that treatment with boron trifluoride–diethyl ether, or with aqueous perchloric acid, causes rearrangement to the ketone (**35**), which is the C-4 epimer of compound (**33**). Formation of this compound is envisaged to proceed by a mechanism which involves a 4α→5α hydride shift[6] [formula (**34**), arrows].

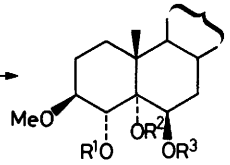
When a solution of the hydroxy ketone (**35**) in benzene was heated under reflux with iodine, aromatisation of ring A



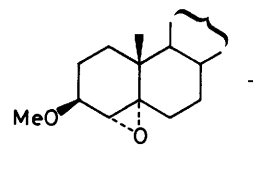
(12)



(20) R = H
(21) R = Ac



(13) R^1 = R^2 = R^3 = H
(14) R^1,R^2 = CMe_2, R^3 = H
(15) R^1,R^2 = CMe_2, R^3 = Ac
(16) R^1 = Ac, R^2 = R^3 = H
(17) R^1 = R^3 = H, R^2 = Ac
(18) R^1 = R^3 = Ac, R^2 = H
(19) R^1 = R^3 = CHO, R^2 = H



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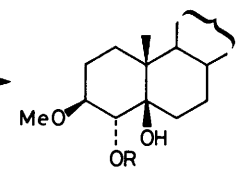
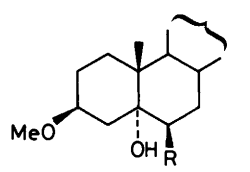
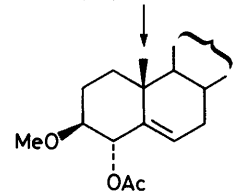


(23) R = H
(24) R = Ac



(26) R = OH
(27) R = H



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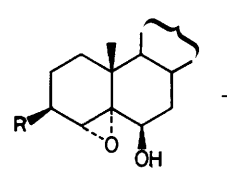
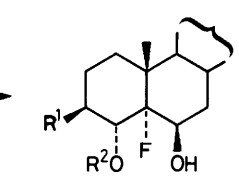
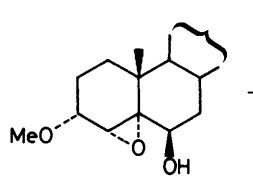


(12) R = OMe
(4) R = H



(28) R^1 = OMe, R^2 = H
(29) R^1 = OMe, R^2 = Ac
(30) R^1 = R^2 = H
(31) R^1 = H, R^2 = Ac



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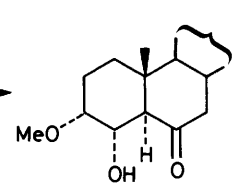
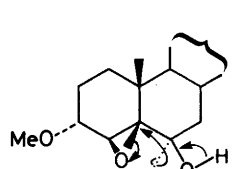
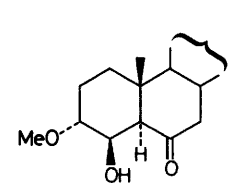


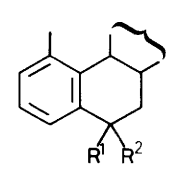
(33)



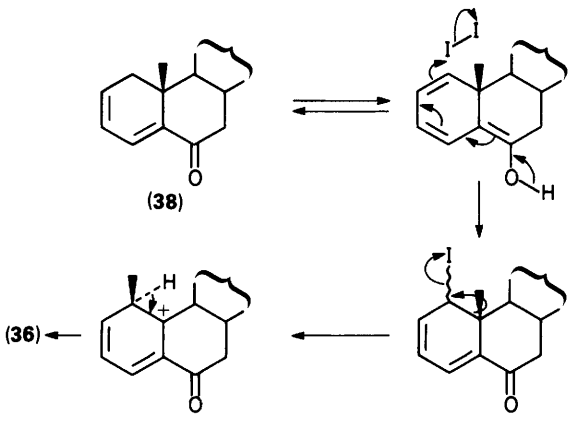
(34)



(35)



(36) R^1,R^2 = O
(37) R^1 = R^2 = H

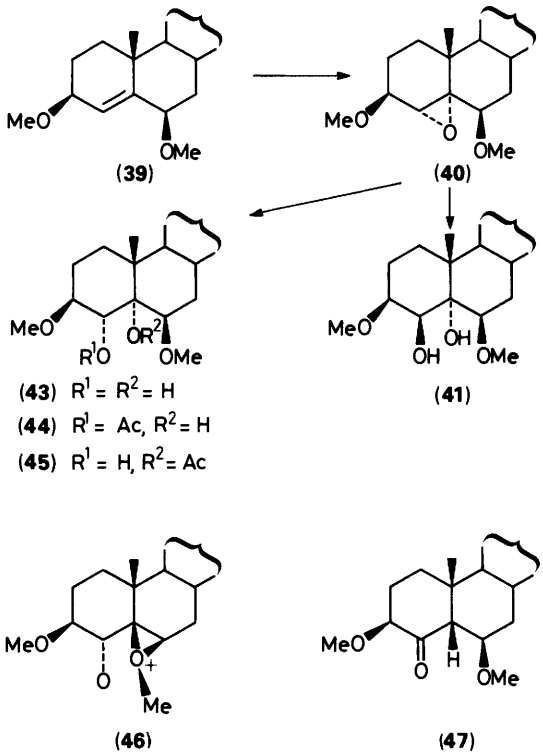


Scheme.

occurred to afford 1-methyl-19-norcholesta-1,3,5(10)-trien-6-one (**36**),[7] the structure of which followed from its NMR spectrum and from its conversion into 1-methyl-19-norcholesta-1,3,5(10)-triene (**37**)[8] upon Wolff-Kishner reduction. The formation of compound (**36**) may proceed by elimination of the elements of water and of methanol to give the dienone (**38**), which could then undergo rearrangement as shown in the Scheme.

Having demonstrated that in the acid-catalysed cleavage of a 4α,5α-epoxide, fission of the C(4)–O bond is inhibited by the inductive effect of a 3-methoxy group (and that, if a 6β-hydroxy group is also present, alternative pathways involving neighbouring hydroxy group participation and epoxide migration are followed), it was of interest to investigate the mode of cleavage of a 4α,5α-epoxide in which the oxirane ring was flanked on both sides by methoxy groups. Accordingly, 3β,6β-dimethoxy-4α,5-epoxy-5α-cholestane (**40**) was prepared by oxidation of 3β,6β-dimethoxycholest-4-ene (**39**) with *m*-chloroperoxybenzoic acid.

Cleavage of the oxirane ring of compound (**40**) in acetone



solution, with aqueous perchloric acid, proceeded very slowly; this may be attributed to the inductive effects of the methoxy groups which inhibit scission of both oxiranic C–O bonds. The major product (52% yield) was 3β,6β-dimethoxy-5α-cholestane-4β,5-diol (**41**). It appears therefore that, when both C(4)–O and C(5)–O bond fission are inhibited, normal diaxial opening of the epoxide, with placement of the incoming nucleophile at the 4β-position, can compete effectively. The minor product (29% yield) is formulated as the C-4 epimer (**43**), thought to arise by intramolecular nucleophilic attack by the axial 6β-methoxy group on the protonated epoxide to give the oxonium ion (**46**) which subsequently is hydrolysed to afford the observed product.

A similar mechanism may be invoked to account for the formation of the acetate (**44**) when the epoxide (**40**) is cleaved with acetic acid. The structure of compound (**44**) follows from its NMR spectrum and from its saponification to the diol (**43**). In this case, the intermediate oxonium ion (**46**) has undergone acetolysis to give the 5α-acetoxy compound (**45**), which has then undergone intramolecular *trans*-esterification to afford the isomeric hydroxy-acetate (**44**).

Reaction of the dimethoxy epoxide (**40**) with boron trifluoride–diethyl ether gave the ketone (**42**) in poor yield as the only product isolated. Its formation by cleavage of the oxiranic C–O bond at the more substituted carbon, followed by hydride migration to the positively charged centre with retention of configuration, is unexceptional.[9]

Experimental

M.p.s were measured on a Kofler hot-stage apparatus. IR spectra (Nujol mulls unless stated otherwise) were recorded on a Perkin-Elmer 157G or a Pye Unicam SP1000 spectrophotometer. NMR spectra were measured on a Perkin-Elmer R12, a Varian Associates A60-A, or a Bruker FX90 instrument, with deuteriochloroform as solvent unless stated otherwise. Mass spectra were measured on an A.E.I. MS902 spectrometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter for solutions in chloroform. Merck Kieselgel GF_{254} was used for TLC and column chromatography. Light petroleum refers to the fraction of boiling range 60–80 °C. Ether refers to diethyl ether. Solutions in organic solvents were dried with anhydrous sodium sulphate or magnesium sulphate.

Reaction of 4α,5-*Epoxy*-5α-*cholestan*-6β-*ol* (**4**) *with Aqueous Perchloric Acid.*—(a) *In acetone solution.* A solution of 4α,5-epoxy-5α-cholestan-6β-ol (**4**) (166 mg) in acetone (6 ml) was treated at room temperature with aqueous perchloric acid (7%, 0.5 ml) for 2 days. Ether was then added and the reaction mixture was washed with aqueous sodium hydrogen carbonate and water, and then dried and evaporated under reduced pressure to give a gum which was chromatographed [10 g column; benzene–ether (3:1) as eluant]. The first fraction gave 5α-*cholestane*-4β,5,6β-*triol* 4β,6β-*acetonide* (**8**) (126 mg), m.p. 59–63 °C (ex. methanol); $[\alpha]_D^{20}$ +14.7° (*c* 9.20) [Found: C, 75.55; H, 11.4%; M^+, 445.3680. $C_{30}H_{52}O_3 \cdot CH_3OH$ requires C, 75.6; H, 11.4%; $C_{29}H_{49}O_3$ ($M - CH_3$) requires *m/z* 445.3682]; ν_{max} 3 400 cm^{-1}; δ_H 1.45 (9 H, s, 10-CH_3 and CH_3 groups of acetonide), and 3.71 (2 H, m, $W_{\frac{1}{2}}$ 7 Hz, 4α-H and 6α-H).

The second fraction afforded 5α-*cholestane*-4β,5,6β-*triol* (**6**) (23 mg), m.p. 213–215 °C (ex. aqueous acetone); $[\alpha]_D^{20}$ +13.1° (*c* 1.08) (Found: C, 77.95; H, 11.4%; M^+, 420.3598. $C_{27}H_{48}O_3$ requires C, 77.1; H, 11.5%; *M*, 420.3603); δ_H(pyridine solution) 1.91 (3 H, s, 10-CH_3) and 4.40 (2 H, m, $W_{\frac{1}{2}}$ 8 Hz, 4α-H, 6α-H). The derived *diacetate* (**7**) (62 mg) was obtained by treating the triol (**6**) (176 mg) with acetic anhydride (5 ml) and pyridine (5 ml) at 100 °C for 2 h, m.p. 168–169 °C (ex. aqueous methanol); $[\alpha]_D^{20}$ +1.6° (*c* 3.15) (Found: C 73.7; H, 10.25. $C_{31}H_{52}O_5$ requires C, 73.75; H, 10.4%); δ_H 1.38 (3 H, s, 10-CH_3), 2.07 (6 H,

s, 2 × OAc), and 4.92 (2 H, m, $W_{\frac{1}{2}}$ 6 Hz, 4α-H, 6α-H); *m/z* 444 (M^+ − AcOH).

The final fraction gave 5α-*cholestane*-4α,5,6β-*triol* (**10**) (18 mg), m.p. 196–198 °C (ex. aqueous acetone); $[\alpha]_D^{20}$ +4.5° (*c* 1.75) (Found: C, 77.2; H, 11.45. $C_{27}H_{48}O_3$ requires C, 77.1; H, 11.5%); ν_{max} 3 490 and 3 200 cm^{-1}; δ_H(pyridine solution) 1.09 (3 H, s, 10-CH_3), 2.22–2.61 (2 H, m, 2 × OH, both exchangeable with D_2O), 3.91 (1 H, m, $W_{\frac{1}{2}}$ 7 Hz, 6α-H), and 4.19 (1 H, m, $W_{\frac{1}{2}}$ 14 Hz, 4β-H); *m/z* 420 (M^+). (Since our preliminary publication this compound has been described also by other workers.[10]) Treatment with acetic anhydride and pyridine at room temperature for 2 h afforded 4α-*acetoxy*-5α-*cholestane*-5,6β-*diol* (**11**), m.p. 138–40 °C (ex. aqueous methanol); $[\alpha]_D^{20}$ +46.5° (*c* 2.20) (Found: C, 76.0; H, 10.75. $C_{29}H_{50}O_4$ requires C, 75.3; H, 10.9%); ν_{max} 3 520, 3 440, 1 690, and 1 280 cm^{-1}; δ_H 1.18 (3 H, s, 10-CH_3), 2.10 (3 H, s, OAc), 3.42 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 6α-H), and 5.42 (1 H, dd, *J* 8 Hz and 6 Hz, 4β-H); *m/z* 462 (M^+).

(*b*) *In butanone solution.* A solution of 4α,5-epoxy-5α-cholestan-6β-ol (**4**) (418 mg) in butanone (10 ml) was treated with aqueous perchloric acid (7%; 0.5 ml) at room temperature for 12 h and then worked up as described in the preceding experiment. Chromatography [20 g column; benzene–ether (19:1) as eluant] gave 5α-*cholestane*-4β,5,6β-*triol* 4β,6β-*butanonide* (**9**) (257 mg), m.p. 51–53 °C (ex. methanol); $[\alpha]_D^{20}$ +16.0° (*c* 4.45) [Found: C, 76.7; H, 10.8%; *m/z* 459.3827. $C_{31}H_{54}O_3{\cdot}CH_3OH$ requires C, 75.9; H, 11.5%; $C_{30}H_{51}O_3$ ($M - CH_3$) requires *m/z* 459.3838]; ν_{max} 3 400 cm^{-1}; δ_H 1.42 (6 H, s, 10-CH_3 and acetal methyl group), and 3.75 (2 H, m, $W_{\frac{1}{2}}$ 8 Hz, 4α-H, 6α-H). Further elution with benzene–ether (7:3) gave the previously described 5α-cholestane-4β,5,6β-triol (**6**) (112 mg) and 5α-cholestane-4α,5,6β-triol (**10**) (27 mg).

Reaction of 4α,5-*Epoxy*-3β-*methoxy*-5α-*cholestan*-6β-*ol* (**12**) *with aqueous Perchloric Acid in Acetone.*—A solution of 4α,5-epoxy-3β-methoxy-5α-cholestan-6β-ol (**12**)[3] (122 mg) in acetone (25 ml) was treated with perchloric acid (6%; 1.5 ml) at room temperature for 12 h and then heated under reflux for 2 h. Chloroform was added and the mixture was washed successively with aqueous sodium hydrogen carbonate and water, and then dried and evaporated under reduced pressure to give a gum which was chromatographed [10 g column; benzene–ether (7:3) as eluant]. The early fractions gave 3β-*methoxy*-5α-*cholestane*-4α,5,6β-*triol* 4α,5-*acetonide* (**14**) (42 mg) as a gum which could not be induced to crystallise; $[\alpha]_D^{20}$ +1.5° (*c* 1.88) (Found: C, 75.65; H, 11.1. $C_{31}H_{54}O_4$ requires C, 75.85; H, 11.1%); ν_{max}(film) 3 450 cm^{-1}; δ_H 1.10 (3 H, s, 10-CH_3), 1.42 (6 H, s, acetonide methyl groups), 1.81 (1 H, m, $W_{\frac{1}{2}}$ 5 Hz, OH, exchangeable with D_2O), 3.40 (3 H, s, OCH_3), 3.40–3.85 (1 H, m, 3α-H), 4.01 (1 H, t, *J* 2.5 Hz, 6α-H), and 4.27 (1 H, d, *J* 4 Hz, 4β-H); *m/z* 490 (M^+) and 475 ($M^+ - CH_3$). The derived *acetate* (**15**) was obtained as a gum by treatment of the acetonide (**14**) with acetic anhydride and pyridine overnight at room temperature; $[\alpha]_D^{20}$ −27.4° (*c* 2.10) (Found: C, 74.4; H, 10.6. $C_{33}H_{56}O_5$ requires C, 74.4; H, 10.5%); ν_{max} 1 740 and 1 240 cm^{-1}; δ_H 1.09 (3 H, s, 10-CH_3), 1.49 (6 H, s, acetonide methyl groups), 3.41 (3 H, s, OCH_3), 3.45–3.80 (1 H, m, 3α-H), 3.93 (1 H, d, *J* 4 Hz, 4β-H), and 5.13 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 6α-H).

The later fractions afforded 3β-methoxy-5α-cholestane-4α,5,6β-triol (**13**) (69 mg), m.p. 206–207 °C (ex. methanol), identical (TLC, IR, NMR, m.p., and mixed m.p.) with an authentic sample prepared as previously described.[3] This compound (24 mg) was also obtained when a solution of the acetonide (**14**) (27 mg) in acetone (10 ml) was heated under reflux for 13 h with aqueous perchloric acid (6%; 3 ml).

4α-*Acetoxy*-3β-*methoxy*-5α-*cholestane*-5,6β-*diol* (**16**).—(*a*) A solution of 4α,5-epoxy-3β-methoxy-5α-cholestan-6β-ol (**12**) (217 mg) in acetic acid (5 ml) was heated under reflux for 9 h. Ether was added to the cooled solution, which was then washed successively with aqueous sodium hydroxide and water, dried, and evaporated under reduced pressure. Chromatography of the residue (30 g column; chloroform as eluant) gave 4α-*acetoxy*-3β-*methoxy*-5α-*cholestane*-5,6β-*diol* (**16**) (153 mg), m.p. 200–205 °C (ex. aqueous methanol); $[\alpha]_D^{20}$ +55.5° (*c* 5.19) (Found: C, 73.2; H, 10.6. $C_{30}H_{52}O_5$ requires C 73.1; H, 10.65%); ν_{max} 3 470, 1 703, and 1 270 cm^{-1}; δ_H 1.21 (3 H, s, 10-CH_3), 2.18 (3 H, s, OAc), 3.36 (3 H, s, OCH_3), 3.36–3.90 (2 H, m, 3α-H, 6α-H), and 5.26 (1 H, d, *J* 9 Hz, collapsing to a singlet on irradiation at δ 3.59, 4β-H); *m/z* 492 (M^+).

(*b*) 3β-Methoxy-5α-cholestane-4α,5,6β-triol (**13**) (72 mg) was treated with acetic anhydride (1.5 ml) and pyridine (3 ml) overnight at room temperature to give, after the usual work-up procedure, the acetate (**16**), identical with the sample obtained as described in (*a*).

4α,6β-*Diacetoxy*-3β-*methoxy*-5α-*cholestan*-5-*ol* (**18**).—(*a*) 4α-Acetoxy-3β-methoxy-5α-cholestane-5,6β-diol (**16**) (90 mg) was treated with acetic anhydride (4 ml) and pyridine (4 ml) at 100 °C for 24 h to give, after the usual work-up procedure, the *diacetate* (**18**), m.p. 73–76 °C (ex. aqueous acetone) (Found: C, 70.95; H, 10.05. $C_{32}H_{54}O_6{\cdot}\frac{1}{2}H_2O$ requires C, 70.7; H, 10.1%); ν_{max} 3 400, 1 738, 1 720, and 1 245 cm^{-1}; δ_H 1.12 (3 H, s, 10-CH_3), 1.96 (3 H, s, OAc), 2.01 (3 H, s, OAc), 3.28 (3 H, s, OCH_3), 3.30–3.60 (1 H, m, 3α-H), 4.76 (1 H, m, $W_{\frac{1}{2}}$ 5 Hz, 6α-H), and 5.30 (1 H, d, *J* 9.5 Hz, 4β-H).

(*b*) 6β-Acetoxy-3β-methoxy-5α-cholestane-4α,5-diol (**16**) (51 mg) was treated with pyridine (3 ml) and acetic anhydride (1.5 ml) at room temperature for 24 h. After the usual work-up procedure the 4α,6β-diacetate (**18**) was obtained, identical with a sample prepared as described in (*a*).

5,6β-*Epoxy*-3β-*methoxy*-5β-*cholestan*-4α-*ol* (**20**).—4α,5-Epoxy-3β-methoxy-5α-cholestan-6β-ol (**12**) (660 mg) was heated under reflux with methanolic potassium hydroxide (10%; 25 ml) for 1.5 h. Water was added and the mixture was extracted with ether. The extract was washed with water, dried, and evaporated under reduced pressure to give a residue, shown by TLC to consist of two components, of which the minor one was starting material (**12**). Part of this mixture (593 mg) was chromatographed [60 g column; benzene–methanol (49:1) as eluant] to give 5,6β-*epoxy*-3β-*methoxy*-5β-*cholestan*-4α-*ol* (**20**) (451 mg), m.p. 183–185 °C (ex. methanol–ether); $[\alpha]_D^{20}$ +21° (*c* 5.65) (Found: C, 77.4; H, 11.2. $C_{28}H_{48}O_3$ requires C, 77.7; H, 11.2%); ν_{max} 3 385 cm^{-1}; δ_H 1.00 (3 H, s, 10-CH_3), 2.41 (1 H, m, $W_{\frac{1}{2}}$ 5 Hz, OH, exchangeable with D_2O), 3.00–3.45 (1 H, m, 3α-H), 3.46 (3 H, s, OCH_3), 3.58 (1 H, m, $W_{\frac{1}{2}}$ 5 Hz, 6α-H), and 3.93 (1 H, d, *J* 8 Hz, 4β-H); *m/z* 432 (M^+). The derived *acetate* (**21**) was obtained by treatment of the epoxy-alcohol (**20**) (64 mg) with acetic anhydride (2 ml) and pyridine (2 ml) at 100 °C for 1 h; m.p. 127–130 °C (ex. aqueous acetone) (Found: C, 76.0; H, 10.6. $C_{30}H_{50}O_4$ requires C, 75.9; H, 10.6%); ν_{max} 1 740 and 1 240 cm^{-1}; δ_H 1.06 (3 H, s, 10-CH_3), 2.05 (3 H, s, OAc), 3.36 (3 H, s, OCH_3), 3.20–3.55 (2 H, m, 3α-H, 6α-H), and 5.34 (1 H, d, *J* 9 Hz, 4β-H).

4α,6β-*Diformyloxy*-3β-*methoxy*-5α-*cholestane*-5-*ol* (**19**).—(*a*) A solution of 4α,5-epoxy-3β-methoxy-5α-cholestan-6β-ol (**12**) (119 mg) in formic acid (5 ml) was heated under reflux for 2 h. Ether was added to the cooled solution, which was then washed successively with dilute aqueous sodium hydroxide and water, dried, and evaporated under reduced pressure. The residue was chromatographed on a preparative TLC plate [chloroform–methanol (24:1) as eluant] to give 4α,6β-*diformyloxy*-3β-*methoxy*-5α-*cholestane*-5-*ol* (**19**) (99 mg), m.p. 183–185 °C (ex. aqueous methanol); $[\alpha]_D^{20}$ +21.7° (*c* 1.80) (Found: C, 71.35; H, 9.95. $C_{30}H_{50}O_6$ requires C, 71.0; H, 9.95%);

ν_{max} 3 580, 1 745, 1 695, and 1 180 cm^{-1}; δ_H 1.19 (3 H, s, 10-CH_3), 3.31 (3 H, s, OCH_3), 3.31–3.80 (2 H, m, 3α-H, OH), 4.97 (1 H, m, $W_{\frac{1}{2}}$ 5 Hz, 6α-H), 5.29 (1 H, d, *J* 9 Hz, collapsing to a singlet on irradiation at δ 3.55, 4β-H), 8.01 (1 H, s, formate), and 8.14 (1 H, s, formate); *m/z* 506 (M^+).

(*b*) A solution of 5,6β-epoxy-3β-methoxy-5β-cholestan-4α-ol (**20**) (59 mg) in formic acid (2 ml) was heated under reflux for 2 h. The crude product was isolated in the usual way and chromatographed [8 g column; benzene–methanol (4:1) as eluant] to give the triol diformate (**19**) (60 mg), identical with the sample obtained as described in (*a*).

Treatment of the diformate (**19**) (144 mg) with methanolic potassium hydroxide (3%; 10 ml) at room temperature overnight gave 3β-methoxy-5α-cholestane-4α,5,6β-triol (**13**) (105 mg) identical with an authentic sample prepared as previously described.[3]

3β-*Methoxy*-5β-*cholestane*-4α,5-*diol* (**23**).—A solution of 4α,5-epoxy-3β-methoxy-5α-cholestane (**22**) (667 mg) in acetone (30 ml) was treated with aqueous perchloric acid (7%;3 ml) at room temperature for 3 days. Ether was added and the reaction mixture was washed successively with dilute aqueous sodium hydroxide and water and then dried and evaporated under reduced pressure. The resulting gum was chromatographed [35 g column; benzene–methanol (19:1) as eluant] to give, from the early fractions, unchanged starting material (94 mg) and from later fractions 3β-*methoxy*-5β-*cholestane*-4α,5-*diol* (**23**) (492 mg), m.p. 155–160 °C (ex. aqueous acetone); $[\alpha]_D^{20}$ +16.8° (*c* 3.80) (Found: C, 77.4; H, 11.55. $C_{28}H_{50}O_3$ requires C, 77.35; H, 11.6%); ν_{max} 3 350 cm^{-1}; δ_H 0.95 (3 H, s, 10-CH_3), 2.33 (1 H, m, $W_{\frac{1}{2}}$ 9 Hz, OH, exchangeable with D_2O), 3.38 (3 H, s, OCH_3), 3.24–3.47 (1 H, m, 3α-H), 3.60–3.90 (2 H, m, 4β-H, OH; simplifies to 1 H, d, *J* 3.5 Hz, at δ 3.78 on D_2O addition); *m/z* 416 ($M^+ - H_2O$). The derived *acetate* (**24**) was obtained by treatment of the diol (**23**) (120 mg) with acetic anhydride (3 ml) and pyridine (3 ml) at 100 °C for 1.5 h; m.p. 95–96 °C (ex. methanol); $[\alpha]_D^{20}$ +14.3° (*c* 3.45) (Found: C, 75.15; H, 11.15. $C_{30}H_{52}O_4$ requires C, 75.6; H, 11.0%); ν_{max} 3 500, 1 735, and 1 238 cm^{-1}; δ_H 0.96 (3 H, s, 10-CH_3), 2.08 (3 H, s, OAc), 3.37 (1 H, m, $W_{\frac{1}{2}}$ 7 Hz, 3α-H), 3.43 (3 H, s, OCH_3), 3.50–3.90 (1 H, m, OH, exchangeable with D_2O), and 5.01 (1 H, d, *J* 2.5 Hz, 4β-H).

Dehydration of 4α-*Acetoxy*-3β-*methoxy*-5β-*cholestan*-5-*ol* (**24**).—4α-Acetoxy-3β-methoxy-5β-cholestan-5-ol (**24**) (113 mg) was treated with thionyl chloride (0.3 ml) and pyridine (5 ml) at 0 °C for 10 min. The reaction mixture was diluted with water and extracted with ether. The extract was washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried and evaporated under reduced pressure. Chromatography of the residual gum [10 g column; benzene–methanol (99:1) as eluant] afforded 4α-acetoxy-3β-methoxycholest-5-ene (**25**) (97 mg); identical with a sample prepared as previously described.[11]

Lithium Aluminium Hydride Reduction of 4α,5-*Epoxy*-3β-*methoxy*-5α-*cholestan*-6β-*ol* (**12**).—A solution of the epoxide (**12**) (34 mg) in ether (2 ml) was stirred with lithium aluminium hydride (30 mg) at room temperature for 3 days. Excess of reducing agent was destroyed by the addition of water and the mixture was extracted with ether. The extract was washed with water, dried, and evaporated under reduced pressure to give, after recrystallisation from methanol, 3β-methoxy-5α-cholestane-5,6β-diol (**26**), m.p. 150–152 °C, identical with an authentic sample prepared as previously described.[12]

Lithium Aluminium Hydride Reduction of 4α,5-*Epoxy*-3β-*methoxy*-5α-*cholestane* (**22**).—A solution of the epoxide (**22**) (119 mg) in ether (5 ml) was stirred with lithium aluminium hydride at room temperature for 15 h and then heated under reflux for a further hour. Work-up as described in the preceding experiment gave 3β-methoxy-5α-cholestan-5-ol (**27**) (117 mg), m.p. 133–134 °C (lit.,[13] 133–136 °C); ν_{max} 3 400 cm^{-1}; δ_H 1.00 (3 H, s, 10-CH_3), 3.36 (3 H, s, OCH_3), and 3.45–3.85 (1 H, m, 3α-H).

5-*Fluoro*-3β-*methoxy*-5α-*cholestane*-4α,6β-*diol* (**28**).—A solution of 4α,5-epoxy-3β-methoxy-5α-cholestan-6β-ol (**12**) (124 mg) in dry ether (5 ml) was treated with boron trifluoride–diethyl ether (0.5 ml) for 15 h at room temperature. More ether was added and the solution was washed with water, dried, and evaporated under reduced pressure. Chromatography of the residue [12 g column; benzene–ether (7:3) as eluant] gave 5-*fluoro*-3β-*methoxy*-5α-*cholestane*-4α,6β-*diol* (**28**) (108 mg), m.p. 165–167 °C; $[\alpha]_D^{20}$ +25.5° (*c* 2.03) (Found: 74.4; H, 10.9; F, 4.3. $C_{28}H_{49}FO_3$ requires C, 74.2; H, 10.9; F, 4.2%); ν_{max} 3 400 cm^{-1}; δ_H 1.17 (3 H, s, 10-CH_3), 2.55 (2 H, m, $W_{\frac{1}{2}}$ 7 Hz, 2 × OH, exchangeable with D_2O), 3.45 (3 H, s, OCH_3), 3.25–3.65 (1 H, m, 3α-H), 4.02 (1 H, dd, *J* 28 Hz and 10 Hz, collapsing to 1 H, d, *J* 10 Hz on irradiation at the ^{19}F signal frequency, 4β-H); the ^{19}F NMR spectrum exhibited a doublet, *J* 28 Hz, 1 300.5 Hz upfield from reference signal given by C_6F_6. Treatment of the diol (**28**) (76 mg) with acetic anhydride (2 ml) and pyridine (2 ml) at room temperature for 2 h afforded the derived 4α-*acetate* (**29**), which crystallised from aqueous acetone as needles, m.p. 150–152 °C; $[\alpha]_D^{20}$ +63.9° (*c* 5.87) (Found: C, 72.85; H, 10.45; F, 3.9. $C_{30}H_{51}O_4F$ requires C, 72.7; H, 10.05; F, 3.85%); ν_{max} 3 560, 1 725, and 1 260 cm^{-1}; δ_H 1.20 (3 H, s, 10-CH_3), 2.16 (3 H, s, OAc), 3.20 (1 H, m, $W_{\frac{1}{2}}$ 15 Hz, OH, exchangeable with D_2O), 3.36 (3 H, s, OCH_3), 3.30–3.75 (1 H, m, 3α-H), 3.63 (1 H, m, $W_{\frac{1}{2}}$ 11 Hz, 6α-H), and 5.20 (1 H, dd, *J* 28 Hz and 9.5 Hz, collapsing to 1 H, d, *J* 9.5 Hz on irradiation at the ^{19}F signal frequency, 4β-H); the ^{19}F NMR spectrum exhibited a doublet, *J* 28 Hz, 1 044 Hz upfield from reference signal given by C_6F_6.

The same acetate (**29**) (187 mg) was obtained when a solution of 4α-acetoxy-5,6β-epoxy-3β-methoxy-5β-cholestane (**21**) (461 mg) in ether (7 ml) was treated at room temperature with boron trifluoride–diethyl ether (0.5 ml) for 15 h. The product was isolated as described above in the conversion of the epoxy alcohol (**12**) into the fluoro-diol (**28**).

5-*Fluoro*-5α-*cholestane*-4α,6β-*diol* (**30**).—A solution of 4α,5-epoxy-5α-cholestan-6β-ol (**4**) (216 mg) in ether (5 ml) was treated with boron trifluoride–diethyl ether (0.5 ml) at room temperature for 20 h. The reaction mixture was worked up as described in the preceding experiment to give 5-*fluoro*-5α-*cholestane*-4α,6β-*diol* (**30**) (108 mg), m.p. 194–195 °C (ex. aqueous acetone); $[\alpha]_D^{20}$ +7.2° (*c* 3.30) (Found: C, 76.35; H, 11.25; F, 4.65. $C_{27}H_{47}FO_2$ requires C, 76.7; H, 11.2; F, 4.5%); ν_{max} 3 550 and 3 420 cm^{-1}; δ_H 1.10 (3 H, s, 10-CH_3), 2.49 (2 H, m, $W_{\frac{1}{2}}$ 13 Hz, 2 × OH, exchangeable with D_2O), 3.60–4.40 (1 H, m, 4β-H), and 4.26 (1 H, m, $W_{\frac{1}{2}}$ 13 Hz, 6α-H). Treatment of the diol (**30**) (70 mg) with acetic anhydride (2 ml) and pyridine (2 ml) overnight at room temperature gave, after the usual work-up procedure, the derived 4α-*acetate* (**31**) (56 mg), m.p. 119–120 °C (ex. methanol); $[\alpha]_D^{20}$ +58 °C (*c* 3.95) (Found: C, 74.65; H, 10.6; F, 4.25. $C_{29}H_{49}FO_3$ requires C, 75.0; H, 10.55; F, 4.1%); ν_{max} 3 500, 1 710, and 1 265 cm^{-1}; δ_H 1.21 (3 H, s, 10-CH_3), 2.14 (3 H, s, OAc), 3.10 (1 H, m, $W_{\frac{1}{2}}$ 12 Hz, OH, exchangeable with D_2O), 3.72 (1 H, m, $W_{\frac{1}{2}}$ 11 Hz, 6α-H), 5.00–5.67 (1 H, dt, *J* 27 Hz, 9 Hz, 6 Hz, 4β-H); the ^{19}F NMR spectrum exhibited a doublet, *J* 27 Hz, 1 336 Hz upfield from the reference signal given by C_6F_6.

4α-*Hydroxy*-3α-*methoxy*-5α-*cholestan*-6-*one* (**33**).—A solution of 4α,5-epoxy-3α-methoxy-5α-cholestan-6β-ol (**32**) (62 mg) in ether (5 ml) at 0 °C was treated with boron trifluoride–diethyl ether (0.5 ml), and the reaction mixture was allowed to warm to room temperature. After 2 h, water was added and the reaction

mixture was extracted with ether. The extract was washed with water, dried, and evaporated under reduced pressure. The residual gum was chromatographed [8 g column; benzene–ether (1:1) as eluant] to give 4α-*hydroxy*-3α-*methoxy*-5α-*cholestan*-6-*one* (**33**) (26 mg), m.p. 123–125 °C (ex. aqueous methanol); $[\alpha]_D^{20}$ −31.2 (*c* 2.75) (Found: C, 77.9; H, 11.25. $C_{28}H_{48}O_3$ requires C, 77.7; H, 11.2%); ν_{max} 3 550 and 1 700 cm^{-1}; δ_H 0.77 (3 H, s, 10-CH_3), 2.73 (1 H, d, *J* 10 Hz, 5α-H), 3.40 (3 H, s, OCH_3) 3.60 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, 3β-H), and 4.03 (1 H, dd, *J* 10 Hz and 3 Hz, 4β-H). Later fractions gave unchanged starting material (**32**) (9 mg).

4β-*Hydroxy*-3α-*methoxy*-5α-*cholestan*-6-*one* (**35**).—(*a*) A solution of 4β,5-epoxy-3α-methoxy-5β-cholestan-6β-ol (**34**) (277 mg) in ether (5 ml) was treated with boron trifluoride–diethyl ether (0.5 ml) for 48 h at room temperature. Aqueous sodium hydrogen carbonate was added and the mixture was extracted with ether. The extract was washed with water, dried, evaporated under reduced pressure, and the residual gum was chromatographed [16 g column, benzene–ether (9:1) as eluant] to afford 4β-*hydroxy*-3α-*methoxy*-5α-*cholestan*-6-*one* (**35**) (75 mg), m.p. 105–109 °C (ex. aqueous methanol); $[\alpha]_D^{20}$ +38.7° (*c* 1.65) (Found: C, 78.05; H, 11.15. $C_{28}H_{48}O_3$ requires C, 77.7; H, 11.2%); ν_{max} 3 460 and 1 700 cm^{-1}; δ_H 1.01 (3 H, s, 10-CH_3), 2.50 (1 H, d, *J* 2 Hz collapsing to a singlet on irradiation at δ 4.22, 5α-H), 3.34 (3 H, s, OCH_3), 3.30–3.60 (2 H, m, 3β-H, OH; simplifies to 1 H, m, $W_{\frac{1}{2}}$ 10 Hz at δ 3.40, upon addition of D_2O), 4.22 (1 H, t, *J* 3 Hz, collapsing to a doublet, *J* 3 Hz, on irradiation at δ 2.50, 4α-H).

(*b*) A solution of 4β-5-epoxy-3α-methoxy-5β-cholestan-6β-ol (**34**) (338 mg) in acetone (5 ml) containing aqueous perchloric acid (7%;1 ml) was heated under reflux for 3 h. The reaction mixture was worked up and chromatographed as described in (*a*) to give the hydroxy ketone (**35**) (83 mg), identical with a sample prepared as described above. Unchanged starting material (84 mg) was obtained from later chromatographic fractions.

1-*Methyl*-19-*norcholesta*-1,3,5(10)-*trien*-6-*one* (**36**).—A solution of 4β-hydroxy-3α-methoxy-5α-cholestan-6-one (**35**) (79 mg) in benzene (5 ml) was heated under reflux with iodine (550 mg) for 4.5 h. Aqueous sodium sulphite was added and the mixture was extracted with ether. The extract was washed with water, dried, evaporated under reduced pressure, and the residual gum was chromatographed on a preparative TLC plate using benzene as eluant to give 1-methyl-19-norcholesta-1,3,5(10)-trien-6-one (**36**) (39 mg), m.p. 96–97 °C (ex. aqueous methanol). [Since this work was completed other workers[7] have obtained this compound from other sources and have recorded a m.p. of 140 °C]; $[\alpha]_D^{20}$ +46.9° (*c* 3.45) (Found: C, 84.95; H, 10.4%; M^+, 380.3067. Calc. for $C_{27}H_{40}O$: C, 85.2; H, 10.5%; *M*, 380.3079); λ_{max} 262 (ε, 15 600); ν_{max} 1 680, 1 595, 1 580, 800, and 750 cm^{-1}; δ_H 0.73 (3 H, s, 13-CH_3), 2.38 (3 H, s, 1-CH_3), 7.05–7.35 (2 H, m, 2-H, 3-H), and 7.90 (1 H, dd, *J* 8 Hz and 3 Hz, 4-H); *m/z* 380 (M^+), 365 ($M^+ - CH_3$), and 352 ($M^+ - CO$).

1-*Methyl*-19-*norcholesta*-1,3,5(10)-*triene* (**37**).—A solution of 1-methyl-19-norcholesta-1,3,5(10)-trien-6-one (**36**) (30 mg) and potassium hydroxide (300 mg) in diethylene glycol (15 ml) and hydrazine hydrate (0.4 ml) was heated under reflux for 5 h. Water and hydrazine were then distilled from the reaction mixture during 3 h at 200 °C. Ether was added to the cooled solution and the reaction mixture was washed several times with water, and then dried, evaporated, and chromatographed (10 g column; light petroleum as eluant) to give 1-methyl-19-norcholesta-1,3,5(10)-triene (**37**) (21 mg) as an oil, $[\alpha]_D^{20}$ +144° (*c* 2.05) (lit.,[8] +149°) (Found: M^+, 366.3286. Calc. for $C_{27}H_{42}$: *M*, 366.3280); ν_{max}(film) 1 575 cm^{-1}; λ_{max} 266 nm (ε, 249) [lit.,[8] λ_{max} 266 nm (ε, 269)]; δ_H 0.75 (3 H, s, 13-CH_3), 2.29 (3 H, s, 1-CH_3), 2.72 (3 H, m, $W_{\frac{1}{2}}$ 10 Hz, benzylic protons), and 6.83 (3 H, s, aromatic protons); *m/z* 366 (M^+) and 351 ($M^+ - CH_3$).

3β,6β-*Dimethoxy*-4α,5-*epoxy*-5α-*cholestane* (**40**).—A solution of 3β,6β-dimethoxycholest-4-ene (**39**) (521 mg) and *m*-chloroperoxybenzoic acid (300 mg) was left at room temperature for 15 h. Ether was then added and the reaction mixture was washed successively with aqueous sodium sulphite, dilute aqueous sodium hydroxide, and water, and then dried, and evaporated under reduced pressure to give 3β,6β-*dimethoxy*-4α,5-*epoxy*-5α-*cholestane* (**40**) (520 mg), m.p. 102–103 °C (ex. methanol); $[\alpha]_D^{20}$ +20.7° (*c* 4.40) (Found: C, 77.75; H, 11.2. $C_{29}H_{50}O_3$ requires C, 77.95; H, 11.3%); δ_H 1.26 (3 H, s, 10-CH_3), 2.73 (1 H, t, *J* 2.5 Hz, 6α-H), 3.07 (1 H, s, 4β-H), 3.35 (3 H, s, OCH_3), 3.44 (3 H, s, OCH_3), and 3.40–3.70 (1 H, m, 3α-H).

Reaction of 3β,6β-*Dimethoxy*-4α,5-*epoxy*-5α-*cholestane* (**40**) *with Aqueous Perchloric Acid*.—A solution of 3β,6β-dimethoxy-4α,5-epoxy-5α-cholestane (**40**) (111 mg) in acetone (5 ml) was heated under reflux with aqueous perchloric acid (70%; 0.4 ml) for 5 days. Aqueous sodium hydrogen carbonate was added to the cooled solution, which was extracted with ether. The extract was washed with water, dried, evaporated under reduced pressure, and the residual gum was chromatographed [8g column; benzene–ether (1:1) as eluant] to give, from the early fractions 3β,6β-*dimethoxy*-5α-*cholestane*-4α,5-*diol* (**43**) (34 mg), m.p. 139–140 °C (ex. aqueous acetone); $[\alpha]_D^{20}$ +7.1° (*c* 1.90) (Found: C, 75.0; H, 11.3. $C_{29}H_{52}O_4$ requires C, 74.95; H, 11.3%); ν_{max} 3 480 cm^{-1}; δ_H 1.02 (3 H, s, 10-CH_3), 1.95 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, OH, exchangeable with D_2O), 2.50 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, OH, exchangeable with D_2O), 3.27 (3 H, s, OCH_3), 3.37 (3 H, s, OCH_3), 3.37 (1 H, m, 6α-H), 3.40–3.80 (1 H, m, 3α-H), and 3.93 (1 H, d, *J* 10 Hz, 4β-H); *m/z* 464 (M^+).

Later fractions gave 3β,6β-*dimethoxy*-5α-*cholestane*-4β,5-*diol* (**41**) (60 mg), m.p. 181–182 °C (ex. aqueous acetone); $[\alpha]_D^{20}$ −31.4° (*c* 4.10) (Found; C, 74.95; H, 11.2. $C_{29}H_{52}O_4$ requires C, 74.95; H, 11.3%); ν_{max} 3 490 and 3 420 cm^{-1}; δ_H 1.36 (3 H, s, 10-CH_3), 3.37 (3 H, s, OCH_3), 3.39 (1 H, m, 6α-H), 3.41 (3 H, s, OCH_3), 3.45–3.80 (1 H, m, 3α-H), 4.01 (1 H, d, *J* 3.5 Hz, 4α-H), and 4.34 (1 H, m, $W_{\frac{1}{2}}$ 4 Hz, OH, exchangeable with D_2O); *m/z* 464 (M^+).

4α-*Acetoxy*-3β,6β-*dimethoxy*-5α-*cholestan*-5-*ol* (**44**).—A solution of 3β,6β-dimethoxy-4α,5-epoxy-5α-cholestane (**40**) (84 mg) in acetic acid was heated under reflux for 6 days. Ether was added to the cooled reaction mixture, and the solution was washed successively with dilute aqueous sodium hydroxide and water, and then dried and evaporated under reduced pressure. The residual gum was chromatographed [8 g column; benzene–ether (4:1) as eluant] to afford 4α-*acetoxy*-3β,6β-*dimethoxy*-5α-*cholestan*-5-*ol* (**44**) (27 mg), m.p. 203–205 °C (ex. methanol); $[\alpha]_D^{20}$ +31° (*c* 1.85) (Found: C, 74.1; H, 10.35. $C_{31}H_{54}O_5$ requires C, 73.75; H, 10.4%); ν_{max} 3 590, 1 750, and 1 235 cm^{-1}; δ_H 1.09 (3 H, s, 10-CH_3), 2.09 (3 H, s, OAc), 3.02 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 6α-H), 3.13 (3 H, s, OCH_3), 3.30 (3 H, s, OCH_3), 3.40–3.80 (1 H, m, 3α-H), and 5.46 (1 H, d, *J* 10 Hz, 4β-H); *m/z* 506 (M^+). Saponification of the acetate (**44**) (23 mg) by heating under reflux for 30 min its solution in methanolic potassium hydroxide (5%; 5 ml) gave 3β,6β-dimethoxy-5α-cholestane-4α,5-diol (**43**), identical with a sample prepared as described in the preceding experiment.

3β,6β-*Dimethoxy*-5β-*cholestan*-4-*one* (**42**).—A solution of 3β,6β-dimethoxy-4α,5-epoxy-5α-cholestane (**40**) (199 mg) in ether (5 ml) was treated with boron trifluoride–diethyl ether (0.5 ml) at room temperature for 3 days. Water was then added and

the reaction mixture was extracted with ether. The extract was washed with water, dried, and evaporated under reduced pressure. The residual gum was chromatographed (12 g column; benzene as eluant) to give 3β,6β-*dimethoxy*-5β-*cholestan*-4-*one* (**42**) (40 mg), m.p. 63–66 °C (Found: C, 77.95; H, 11.15. $C_{29}H_{50}O_3$ requires C, 77.95; H, 11.3%); ν_{max} 1 710 cm^{-1}; δ_H 1.21 (3 H, s, 10-CH_3), 2.95 (1 H, m, $W_{\frac{1}{2}}$ 4.5 Hz, 5β-H), 3.26 (6 H, s, 2 × OCH_3), 3.35 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, 6α-H), and 3.80 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, 3α-H); *m/z* 446 (M^+). Further elution of the column with benzene–ether (97:3) gave unchanged starting material (**40**) (54 mg).

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