Tetrahedron. Vol. 29, pp. 239 to 243. Pergamon Press 1973. Printed in Great Britain

3β-METHOXY-5α-CHOLESTANE-4β,5-DIOL AND RELATED COMPOUNDS[1]

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(*Received in the UK* 22 *August* 1972; *Accepted for publication* 10 *September* 1972)

Abstract—The major product of acid-catalysed hydrolysis of 4α,5-epoxy-3β-methoxy-5α-cholestane (**5**) has been shown to be the allylic alcohol **9** (R = H) and not diol **10** as previously reported. A preparation of the latter compound, and of a number of cholestane derivatives with oxygen substituents in rings A and B, is described.

The major product arising by sulphuric acid-catalysed cleavage of 4α,5-epoxy-3β-methoxy-5α-cholestane (**5**) has been reported[2] to be 3β-methoxy-5α-cholestane-4β,5-diol (**10**). We now present evidence that this compound is in fact 3β-methoxycholest-5-en-4α-ol (**9**; R = H), and describe a valid preparation of diol **10** and of a number of other derivatives of cholestane with oxygen substituents in rings A and B, required by us in connection with another project.

Epoxidation of 3β-methoxycholest-4-ene (**4**) with *m*-chloroperbenzoic acid gave, in addition to the required α-epoxide (**5**), a small amount of the hitherto undescribed 4β,5-epoxy-3β-methoxy-5β-cholestane (**2**). The structure of the latter compound followed from its NMR spectrum (which exhibited a doublet at τ 7·10, *J* 3·5 Hz, for the epoxidic proton[3]) and from its reconversion into the starting olefin (**4**) by treatment with LAH and dehydration of the 3β-methoxy-5β-cholestan-5-ol (**1**) thus formed with $SOCl_2$ and pyridine. Treatment of β-epoxide **2** with NaOMe afforded 3β,4α-dimethoxy-5β-cholestan-5-ol (**3**).

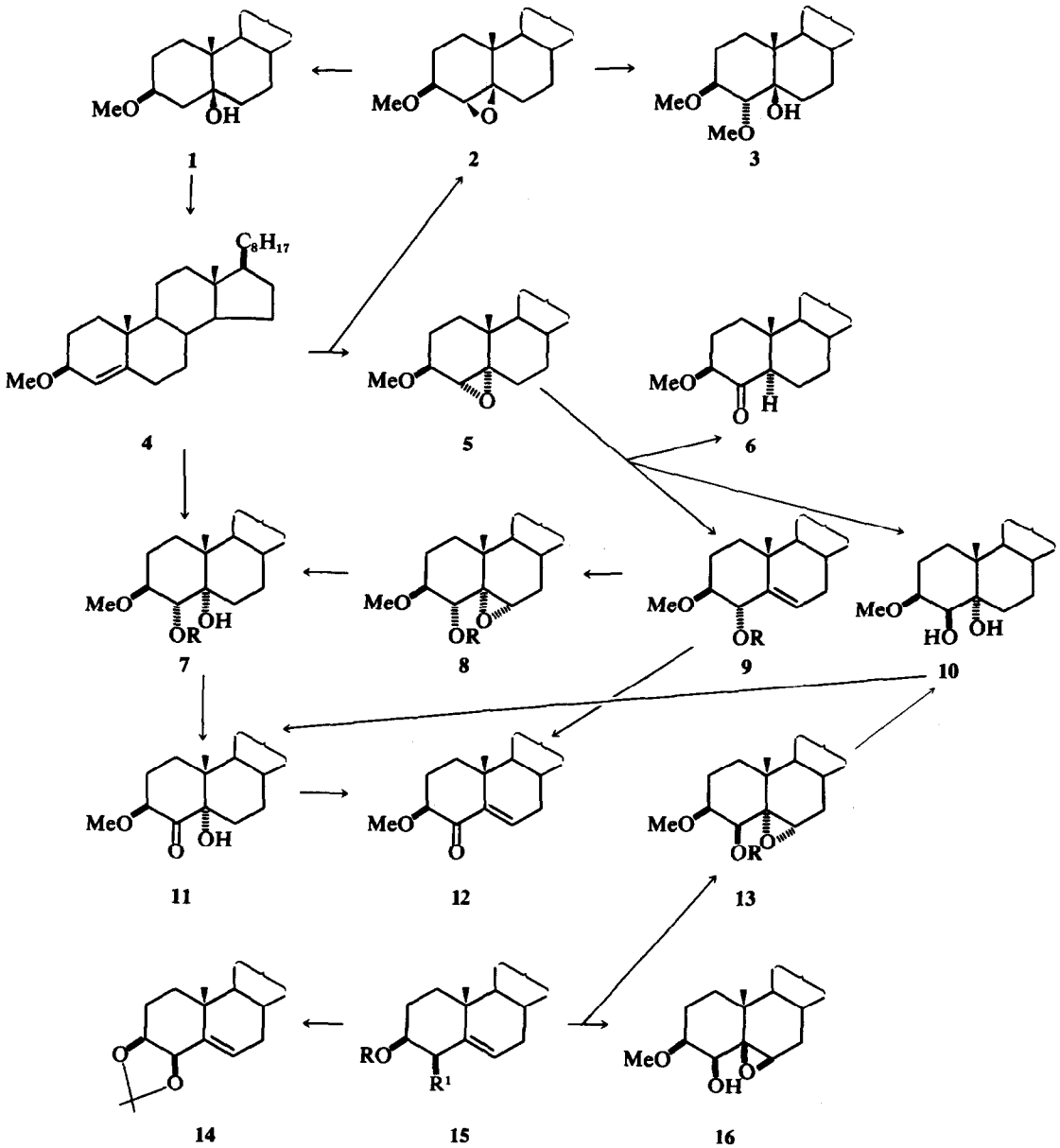
Cleavage of the α-epoxide (**5**) with H_2SO_4 gave as major product (75%) a compound with physical constants in reasonable agreement with those previously described.[2] Microanalysis, however, indicated a molecular formula of $C_{28}H_{48}O_2$ rather than $C_{28}H_{50}O_3$ (as required by structure **10** previously assigned[2]) and the NMR spectrum (experimental) and chemical properties of the compound showed that it is to be formulated as 3β-methoxycholest-5-en-4α-ol (**9**; R = H).

The alcohol (**9**; R = H) afforded 3β,4α-dimethoxycholest-5-ene (**9**; R = Me) by treatment with MeI and Ag_2O, and gave the derived acetate (**9**; R = Ac), which could be reconverted into the parent alcohol by LAH reduction. Treatment of the appropriate olefins (**9**) with *m*-chloroperbenzoic acid gave epoxides **8** (R = Me and R = Ac), and saponification of the latter afforded epoxyalcohol **8** (R = H). Confirmation of these structures was obtained by reduction of the oxides **8** (R = H and R = Ac) with LAH to give, in each case, 3β-methoxy-5α-cholestane-4α,5-diol (**7**; R = H), identical with material obtained by hydroxylation of 3β-methoxy cholest-4-ene (**4**) with OsO_4. Glycol **7** (R = H) gave the derived methanesulphonate (**7**; R = Ms) and acetate (**7**; R = Ac) and was recovered from the latter by reduction with LAH. Methylation of diol **7** (R = H) with MeI and Ag_2O afforded 3β,4α-dimethoxy-5α-cholestan-5-ol (**7**; R = Me), which was also prepared from methoxy-epoxide **8** (R = Me) by reduction with LAH.

Chromatography of the mother liquors remaining after crystallisation of the major product (**9**; R = H) arising from the sulphuric acid-catalysed cleavage of the epoxide (**5**) gave, in very small yield, 3β-methoxy-5α-cholestan-4-one (**6**) and the expected product, 3β-methoxy-5α-cholestane-4β,5-diol (**10**).

A more satisfactory preparation of diol **10** was afforded by hydride cleavage of 5,6α-epoxy-3β-methoxy-5α-cholestan-4β-ol (**13**; R = H) or its derived acetate (**13**; R = Ac). These epoxides were obtained by the action of *m*-chloroperbenzoic acid on the corresponding olefins **15** (R = Me, R′ = OH and R = Me, R′ = OAc) respectively; in the case of the former, some of the β-epoxide (**16**) was also obtained as minor product. A mixture of **15** (R = Me, R′ = OH and R = Me, R′ = OAc)* was obtained by oxidation of 3β-methoxycholest-5-ene **15**; R = Me, R′ = H) with SeO_2 in AcOH;[2] however, the configuration at C_4 of these compounds had not previously been defined unambiguously. In the present work, alcohol **15** (R = Me, R′ = OH) was obtained also by selective methylation of 3β,4β-dihydroxycholest-5-ene (**15**; R = H, R′ = OH) with MeI and Ag_2O, thus confirming the previous assignment. A preparation of the related acetonide (**14**) is described in the experimental.

*In the present work the m.p. recorded for the acetate (**15**; R = Me, R′ = OAc) differs significantly from that previously reported (experimental).



Oxidation of either of the diols 7 (R = H) or **10** with CrO_3 gave 3β-methoxy-5-hydroxy-5α-cholestan-4-one (**11**) as a stable crystalline compound (ν_{max} CCl_4 1730 cm^{-1}), clearly not identical with the unstable gummy solid (ν_{max} $CHCl_3$ 1705 cm^{-1}) previously formulated as **11**.[2] Dehydration of ketol **11** with $SOCl_2$ and pyridine yielded 3β-methoxycholest-5-en-4-one (**12**); this compound was also obtained by CrO_3 oxidation of allylic alcohol **9** (R = H).

EXPERIMENTAL

M.ps were measured on a Kofler block and are uncorrected. IR spectra were recorded on a Grubb-Parsons DB-1, a Perkin-Elmer 125, or a Unicam SP200. UV spectra were recorded on a Unicam SP 800. NMR spectra were measured on a Varian A60 using $CDCl_3$ as solvent unless stated otherwise. Chemical shifts are given in τ using TMS as internal reference, and coupling constants (*J*) in Hz. Unless specified to the contrary, alumina was Spence's grade O, deactivated, when stated, with water. Petrol refers to the fraction of b.p. 60–80°.

Epoxidation of 3β-methoxycholest-4-ene (**4**). 3β-Methoxycholest-4-ene (2·4 g) was treated with *m*-chloroperbenzoic acid (2·4 g) in ether (75 ml) at room temp for 16 h. The mixture was washed successively with 10% aq. Na_2SO_3, dilute $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated *in vacuo*. The resulting gum (2·3 g) was chromatographed on alumina (175 g) using 60% benzene-

40% petrol as eluant. From the early fractions there was obtained 4α,5-epoxy-3β-methoxy-5α-cholestane (5) (1·92 g), m.p. 51–54°, $[\alpha]_D$ + 50° (*c*, 1·14) (lit.[4] m.p. 58–59°, $[\alpha]_D$ + 57°); NMR (CCl_4): 6·40–6·80 (1H, m, 3-H), 6·62 (3H, s, OMe), 7·23 (1H, s, 4-H), 8·92 (3H, s, 10-Me). Material obtained in this way was sufficiently pure for further reactions.

The later fractions afforded *4β,5-epoxy-3β-methoxy-5β-cholestane* (2) (230 mg) as needles, m.p. 78–79°, $[\alpha]_D$ − 41° (*c*, 1·00) after recrystallisation from MeOH; NMR (CCl_4): 6·45–6·86 (1H, m, 3-H), 6·66 (3H, s, OMe), 7·10 (1H, d, *J* 3·5, 4-H), 8·96 (3H, s, 10-Me). (Found: C, 80·3; H, 11·4. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%).

Conversion of 4β,5-epoxy-3β-methoxy-5β-cholestane (2) *into 3β-methoxycholest-4-ene* (4). A solution of 4β,5-epoxy-3β-methoxy-5β-cholestane (2) (15 mg) and LAH (15 mg) in ether (2 ml) was heated under reflux for 30 min. EtOAc was added to destroy excess hydride, and the product ether extracted. $SOCl_2$ (0·2 ml) was added dropwise at 0° to a solution of the product (14 mg) in pyridine (1 ml). After 3 min at room temp the mixture was poured into ice-water and the product was ether extracted. In this way, 3β-methoxycholest-4-ene (13 mg) was obtained, m.p. 72–3° after crystallisation from MeOH, m.m.p. undepressed.[4] The identity of the product was confirmed by comparing its IR spectrum and TLC behaviour with those of an authentic specimen.

3β,4α-Dimethoxy-5β-cholestan-5-ol (3). 4β,5-Epoxy-3β-methoxy-5β-cholestane (2) (31 mg) and methanolic NaOMe (17·5 ml, 1·7 molar) were heated under reflux for 2 days. The mixture was shaken with water and ether extracted. The extract was water washed, dried (Na_2SO_4), and evaporated *in vacuo* to afford a gum which was chromatographed on alumina (10 g, 5% deactivated). Elution with benzene gave *3β,4α-dimethoxy-5-hydroxy-5β-cholestane* (28 mg), m.p. 128–29°, $[\alpha]_D$ − 25° (*c*, 1·13); NMR: 4·63 and 4·70 (each 3H, s, 2 × OMe), 8·93 (3H, s, 10-Me) (Found: C, 77·8; H, 11·5. $C_{29}H_{52}O_3$ requires C, 77·6; H, 11·7%).

Acid-catalysed cleavage of 4α,5-epoxy-3β-methoxy-5α-cholestane (5). Dilute H_2SO_4 (3 ml, 2N) was added to a solution of 4α,5-epoxy-3β-methoxy-5α-cholestane (930 mg) in dioxan (30 ml), and the mixture heated under reflux for 1 hr, poured into water and ether extracted. The extract was water washed, dried (Na_2SO_4) and evaporated *in vacuo* to give a solid residue (920 mg) which was crystallised from acetone to afford *3β-methoxycholest-5-en-4α-ol* (700 mg) which was further purified by chromatography on alumina (49 g). Elution with 3% MeOH-97% Et_2O gave the product (680 mg) as needles, m.p. 175–177° from MeOH, $[\alpha]_D$ − 15° (*c*, 0·99); $\nu_{max}^{CCl_4}$ cm^{-1} 3595; NMR (CCl_4): 4·25 (1H, m, 6-H), 6·04 (1H, d, *J* 9, with further splitting, 4-H), 6·64 (3H, s, OMe), 7·20 (1H, m, 3-H), 7·45 (1H, s, OH), 9·00 (3H, s, 10-Me). (Found: C, 80·95; H, 11·45. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%).

Treatment with Ac_2O and pyridine at room for 16 h gave the derived *acetate* (9; R = Ac), recrystallised from aqueous acetone as needles, m.p. 114–15°, $[\alpha]_D$ − 2·5° (*c*, 0·99); ν_{max}^{nujol} cm^{-1} 1245, 1754. (Found: C, 78·95; H, 10·95. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). The acetate (9; R = Ac) (50 mg) was readily cleaved back to the alcohol (9; R = H) (31 mg) with LAH (61 mg) when a solution of the two in ether (3 ml) was heated under reflux for 30 min.

The residue obtained by evaporation of the mother liquor remaining after isolation of the alcohol (9; R = H) as a product of hydrolysis of the epoxide (5) was chromatographed on alumina (Woelm, Grade 5). In this way very small amounts of two other compounds were obtained in a homogeneous state. The first of these, thought to be 3β-methoxy-5α-cholestan-4-one (6) had m.p. 85–92°, $[\alpha]_D$ − 20° (*c*, 0·62); $\nu_{max}^{CHCl_3}$ cm^{-1} 1720. (Found: C, 80·45; H, 11·5. Calc. for $C_{28}H_{48}O_2$: C, 80·7; H, 11·6%) (lit.[2] m.p. 92–93°, $[\alpha]_D$ − 24°). The other was 3β-methoxy-5α-cholestane-4β,5-diol (10), the identity of which was established by direct comparison with an authentic specimen obtained by LAH reduction of 5,6α, epoxy-3β-methoxy-5α-cholestan-4β-ol as described below.

3β,4α-Dimethoxycholest-5-ene (9; R = Me). 3β-Methoxycholest-5-en-4α-ol (9; R = H) (325 mg) was heated under reflux in benzene (30 ml) for 16 hr with Ag_2O (1·11 g) and MeI (15 ml) to afford, after filtration and removal of solvent, a gum (321 mg). Several crystallisations from MeOH gave *3β,4α-dimethoxycholest-5-ene* as needles, m.p. 104–107°, $[\alpha]_D$ + 10·5° (*c*, 1·35); $\nu_{max}^{CCl_4}$ cm^{-1} 850. (Found: C, 80·85; H, 11·65. $C_{29}H_{50}O_2$ requires C, 80·85; H, 11·7%).

5,6α-Epoxy-3β-methoxy-5α-cholestan-4α-ol acetate (8; R = Ac). (a) 3β-Methoxycholest-5-en-4α-ol acetate (9; R = Ac) (400 mg) in ether (30 ml) was treated with *m*-chloroperbenzoic acid (400 mg) at room temp for 16 hr. Working up in the usual way gave gum (400 mg) which was chromatographed on alumina (25 g, Woelm grade 3). Elution with 85% benzene-15% petrol gave, after recrystallisation from aqueous acetone, the *epoxide* (8; R = Ac) as needles (220 mg), m.p. 114–18°, $[\alpha]_D$ + 3·9° (*c*, 1·00); $\nu_{max}^{CCl_4}$ cm^{-1} 1235, 1737; NMR: 4·61 (1H, d, *J* 10, 4-H), 6·60 (3H, s, OMe), 7·02 (1H, d, *J* 4·5, 6-H), 7·92 (3H, s, OAc), 8·87 (3H, s, 10-Me). (Found: C, 76·1; H, 10·6. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%). (b) Treatment of 5,6α-epoxy-3β-methoxy-5α-cholestan-4α-ol (8; R = H) (23 mg) with Ac_2O and pyridine at room temp for three hr gave acetate 8 (R = Ac) (20 mg), identical with material obtained as described in (a).

5,6-Epoxy-3β-methoxy-5α-cholestan-4α-ol (8; R = H). A solution of 5,6α-epoxy-3β-methoxy-5α-cholestan-4α-ol acetate (8; R = Ac) (166 mg) and $NaHCO_3$ (124 mg) in a mixture of MeOH (35 ml) and water (1·75 ml) was heated under reflux for 75 min. MeOH (*ca.* 20 ml) was then distilled from the reaction, and the resulting slurry worked up in the usual way to give *5,6α-epoxy-3β-methoxy-5α-cholestan-4α-ol* as a white solid (160 mg) which recrystallised from MeOH as needles, m.p. 136–38°, $[\alpha]_D$ − 30° (*c*, 0·61); NMR: 6·66 (3H, s, OMe), 6·78 (1H, d, *J* 4·5, 6-H), 8·98 (3H, s, 10-Me). (Found: C, 77·75; H, 10·8. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%).

3β,4α-Dimethoxy-5,6α-epoxy-5α-cholestane (8; R = Me). 3β,4α-Dimethoxycholest-5-ene (9; R = Me) (168 mg) in ether (25 ml) was treated with *m*-chloroperbenzoic acid (168 mg) at room temp for 17 hr. The mixture was worked up in the usual way to give a gum (168 mg). Chromatography on alumina (10 g) using benzene as eluant gave, from the later fractions, *3β,4α-dimethoxy-5,6α-epoxy-5α-cholestane* (80 mg), m.p. 105–8°, $[\alpha]_D$ + 26° (*c*, 0·62); NMR: 6·58 (3H, s, OMe), 6·78 (1H, d, *J* 4·5, 6-H), 8·98 (3H, s, 10-Me). (Found: C, 78·05; H, 11·2. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%).

The earlier fractions gave an isomeric *compound* (60 mg), m.p. 82–87°, $[\alpha]_D$ + 5·2° (*c*, 0·21). (Found: C, 77·8; H, 11·2. $C_{29}H_{50}O_3$ requires C, 78·0; H, 11·3%).

3β-Methoxy-4α-cholestane-4α,5-diol (7; R = H). (a) 5,6α-Epoxy-3β-methoxy-5α-cholestan-4α-ol acetate (8; R = Ac) (225 mg) and LAH (225 mg) in ether (10 ml) were heated under reflux for 30 min. Work up in the usual way gave *3β-methoxy-5α-cholestane-4α,5-diol* (200 mg)

which crystallised from aq. acetone as needles, m.p. 156–159°, $[\alpha]_D$ +42° (*c*, 0·71); NMR: 6·3–6·7 (2H, m, 3- and 4-H), 6·61 (3H, s, OMe), 7·40 and 8·13 (each 1H, s, 2× OH), 9·08 (3H, si, 10-Me). (Found: C, 77·45; H, 11·4. $C_{28}H_{50}O_3$ requires C, 77·35; H, (11·6%).

The derived *acetate* (7; R = Ac) was obtained by treatment with Ac_2O and pyridine at room temp. M.p. 156–157°, $[\alpha]_D$ +60° (*c*, 2·05); NMR: 4·92 (1H, d, *J* 9, 4-H), 6·65 (3H, s, OMe), 7·89 (3H, s, OAc), 8·98 (3H, s, 10-Me). (Found: C, 75·65; H, 10·8. $C_{30}H_{52}O_4$ requires C, 75·6; H, 11·0%). The acetate (7; R = Ac) (20 mg) was reduced back to the alcohol (7; R = H) (18 mg) by heating its solution in ether (3 ml) under reflux with LAH (20 mg) for 30 min. The m.p. of the product, 158–159°, was undepressed on admixture with an authentic sample of the alcohol (7; R = H).

3β-Methoxy-5α-cholestane-4α-5-diol 4-methanesulphonate (7; R = SO_2Me) (150 mg) was obtained by treatment of alcohol 7 (R = H) (160 mg) in pyridine (32 ml) with MesCl (3·2 ml) at 0° for 16 hr and crystallised from petrol as needles, m.p. 198–199°, $[\alpha]_D$ +67° (*c*, 0·53); NMR (CCl_4): 5·55 (1H, d, *J* 10, 4-H), 6·65 (3H, s, OMe), 6·99 (3H, s, OSO_2Me), 9·00 (3H, s, 10-Me). (Found: C, 68·1; H, 10·15; S, 6·40. $C_{29}H_{52}O_5S$ requires C, 67·9; H, 10·2; S, 6·25%).

(b) 3β-Methoxycholest-4-ene (4) (200 mg) was treated with OsO_4 (140 mg) in pyridine (0·25 ml) at room temp for 14 days. The mixture was evaporated *in vacuo* and the residue taken up in $CHCl_3$ (10 ml). The $CHCl_3$ solution was shaken for 3 hr with a mixture of mannitol (2 g), KOH (2 g) and water (20 ml), washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to give a crude product (196 mg), from which, by chromatography on alumina (10 g, Woelm grade 5) a pure sample (33 mg) of 3β-methoxy-5α-cholestane-4α,5-diol was obtained, m.p. 157–60°, undepressed on admixture with an authentic sample prepared as described in (a), and giving a superposable IR spectrum.

3β,4α-Dimethoxy-5α-cholestan-5-ol (7; R = Me). (a) 3β-Methoxy-5α-cholestane-4α,5-diol (7; R = H) (50 mg) and Ag_2O (180 mg) were heated under reflux with MeI (8 ml) and benzene (16 ml) for 16 hr. Work up in the usual way afforded a gum (50 mg), which crystallised from MeOH to give *3β,4α-dimethoxy-5α-cholestan-5-ol* as needles, m.p. 147–148°, $[\alpha]_D$ +71° (*c*, 0·51). (Found: C, 78·4; H, 11·8. $C_{29}H_{52}O_3$ requires: C, 77·6; H, 11·7%).

(b) A solution of 3β,4α-dimethoxy-5,6α-epoxy-5α-cholestane (8; R = Me) (34 mg) and LAH (32 mg) in ether (2·5 ml) was heated under reflux for 30 min. The product (33 mg) was isolated in the usual way and recrystallised once from MeOH to give 3β,4α-dimethoxy-5α-cholestan-5-ol, m.p. 147–148°, identical (m.m.p., IR, TLC) with material obtained as described in (a).

3β,4β-Dihydroxycholest-5-ene-3,4-acetonide (14). To a solution of 3β,4β-dihydroxycholest-5-ene (15; R = H, R′ = OH) (170 mg) in acetone (25 ml) was added anhyd $CuSO_4$ (1·7 g, dried at 150° for 4 hr in high vacuum) and the mixture heated under reflux for 24 hr. The mixture was poured into water, and ether extracted. The extract was water washed, dried (Na_2SO_4) and evaporated *in vacuo* to yield *3β,4β-dihydroxycholest-5-ene-3,4-acetonide* (165 mg), which crystallised from MeOH as needles, m.p. 131–132°, $[\alpha]_D$ −7·5° (*c* 0·99); NMR (CCl_4): 4·35 (1H, m, 6-H), 5·71 (1H, d, *J* 6, 4-H), 5·96 (1H, m, 3-H), 8·58 and 8·75 (each 3H, s, CMe_2), 8·89 (3H, s, 10-Me). (Found: C, 81·75; H, 11·25. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·25%).

Methylation of 3β,4β-dihydroxycholest-5-ene (15; R = H, R′ = OH). To a solution of 3β,4β-dihydroxycholest-5-ene (415 mg) in MeI (50 ml) was added Ag_2O (1·25 g) and the mixture heated under reflux for 17 hr. The mixture was filtered, and evaporated *in vacuo* to give a gum (365 mg) which was chromatographed on alumina (30 g, Woelm grade 4) using 20% benzene-80% petrol as eluant. The early fractions afforded a small amount (14 mg) of a product identified as 3β,4β-dimethoxycholest-5-ene (15; R = Me, R′ = OMe) from its NMR spectrum. M.p. 125–127°, $[\alpha]_D$ −72° (*c*, 0·75), after 5 recrystallisations from MeOH; NMR: 4·38 (1H, m, 6-H), 6·28 (1H, d, *J* 3 with further splitting, 4-H), 6·60 and 6·78 (each 3H, s, 2× OMe), 8·88 (3H, s, 10-Me).

The later fractions gave 3β-methoxycholest-5-en-4β-ol (15; R = Me, R′ = OH) (260 mg) which crystallised from MeOH as needles, m.p. 160–62°, undepressed on admixture with an authentic specimen[2] and giving identical IR and NMR spectra. NMR: 4·29 (1H, m, 6-H), 5·74 (1H, d, *J* 3, 4-H), 6·58 (3H, s, OMe), 6·7–7·1 (1H, m, 3-H), 7·47 (1H, s, OH), 8·78 (3H, s, 10-Me).

The derived acetate (15; R = Me. R′ = OAc) was obtained by treatment with Ac_2O and pyridine at room temp, and was crystallised from MeOH, m.p. 140–141° (lit.[2] 123–125°). NMR: 4·18 (1H, m, 6-H), 4·40 (1H, d, *J* 3, 4-H), 6·66 (3H, s, OMe), 6·8–7·1 (1H, m, 3-H), 7·98 (3H, s, OAc), 8·90 (3H, s, 10-Me). The structure of the acetate was confirmed by reduction with ethereal LAH (heating under reflux for 30 min) to give back the alcohol (15; R = Me, R′ = OH) in quantitative yield.

Epoxidation of 3β-methoxycholest-5-en-4β-ol (15; R = Me, R′ = OH). 3β-Methoxycholest-5-en-4β-ol (500 mg) and *m*-chloroperbenzoic acid (500 mg) were dissolved in ether (150 ml) and left at room temp for 5 days. After combination with another 3 exactly similar mixtures the product was isolated in the usual way as a white solid (2·05 g), which was chromatographed on alumina (130 g, 5% deactivated) using 90% benzene-10% petrol as eluant. The early fractions gave *5,6α-epoxy-3β-methoxy-5α-cholestan-4β-ol* (13; R = H) (1·67 g), which crystallised from MeOH as needles; m.p. 164–66°, $[\alpha]_D$ −40° (*c*, 1·03); NMR: 6·40–6·75 (2H, partly obscured by OMe signal, 3- and 4-H), 6·62 (3H, s, OMe), 6·95 (1H, d, *J* 3·5 6-H), 7·61 (1H, s, OH), 8·76 (3H, s, 10-Me). (Found: C, 77·5; H, 11·15. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%).

The later fractions afforded *5,6β-epoxy-3β-methoxy-5β-cholestan-4β-ol* (16), which crystallised from MeOH as needles, m.p. 140–141°, $[\alpha]_D$ −17·5° (*c*, 1·02); NMR: 6·45–6·9 (3H, complex signal, 3-, 4-, and 6-H), 6·60 (3H, s, OMe), 8·84 (3H, s, 10-Me). (Found: C, 77·35; H, 10·8. $C_{28}H_{48}O_3$ required C, 77·7; H, 11·2%).

5,6α-Epoxy-3β-methoxy-5α-cholestan-4β-ol acetate (13; R = Ac). (a) 5,6α-Epoxy-3β-methoxy-5α-cholestan-4β-ol (13; R = H) (230 mg) was treated with Ac_2O and pyridine at room temp for 3 days to give the derived *acetate* (13; R = Ac), which crystallised from MeOH as needles (200 mg), m.p. 129–130°, $[\alpha]_D$ −51° (*c*, 0·92); NMR (CCl_4): 5·59 (1H, d, *J* 3, 4-H), 6·78 (3H, s, OMe), 6·95 (1H, d, *J* 3, 6-H), 7·96 (3H, s, OAc), 8·91 (3H, s, 10-Me). (Found: C, 76·1; H, 10·65. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

(b) The same product (13; R = Ac) was obtained, together with some unchanged starting material (which was separated by chromatography on grade 4 alumina using petrol as eluant), when 3β-methoxycholest-5-en-4β-ol acetate (15; R = Me, R′ = OAc) (70 mg) in ether (7 ml) was treated with *m*-chloroperbenzoic acid (70 mg) at room temp for 5 days.

3β-Methoxy-5α-cholestane-4β,5-diol (**10**). A solution of 5,6α-epoxy-3β-methoxy-5α-cholestan-4β-ol (**13**; R = H) (150 mg) in ether (12 ml) was heated under reflux with LAH (150 mg) for 30 min. The mixture was worked up in the usual way to afford *3β-methoxy-5α-cholestane-4β,5-diol* (145 mg), which crystallised from MeOH as needles, m.p. 158–160°, $[\alpha]_D$ + 18° (*c*, 0·84); NMR: 6·1–6·6 (1H, m, 3-H), 6·30 (1H, poorly resolved d, *J* 3, 4-H), 6·60 (3H, s, OMe), 7·65 (1H, s, OH), 8·85 (3H, s, 10-Me). (Found: C, 77·55; H, 11·35. $C_{28}H_{50}O_3$ requires C, 77·35; H, 11·6%).

The same product was obtained when the acetate (**13**; R = Ac) was similarly reduced with LAH.

5-Hydroxy-3β-methoxy-5α-cholestan-4-one (**11**). (a) Jones' reagent[5] (0·05 ml) was added dropwise at 0° to 3β-methoxy-5α-cholestane-4β,5-diol (**10**) (30 mg) in acetone (15 ml). The mixture was allowed to stand at room temp for 3 min, then poured into water and ether extracted. The ether solution was water washed, dried (Na_2SO_4), and evaporated *in vacuo* to afford *5-hydroxy-3β-methoxy-5α-cholestan-4-one* (25 mg), which crystallised from MeOH as needles, m.p. 178–180° $[\alpha]_D$ + 7° (*c*, 0·28); $\nu_{max}^{CCl_4}$ cm^{-1} 3511, 3485, 1730; NMR (CCl_4): 5·62 (1H, m, 3-H), 6·70 (3H, s, OMe), 8·03 (1H, s, OH), 9·26 (3H, s, 10-Me). (Found: C, 77·7; H, 11·1. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%).

(b) 3β-Methoxy-5α-cholestane-4α,5-diol (7; R = H) (30 mg) was oxidised as described in (a) to give ketone **11**, the identity of which was established by m.p., m.m.p., TLC and by a comparison of its IR spectrum with that exhibited by a sample obtained as described in (a).

3β-Methoxycholest-5-en-4-one (**12**). (a) Jones' reagent[5] (0·04 ml.) was added dropwise at 0° to a solution of 3β-methoxycholest-5-en-4α-ol (**9**; R = H) (50 mg) in acetone (23 ml). The mixture was left at room temp for 15 min, then worked up in the usual way to give 3β-methoxycholest-5-en-4-one (45 mg) which crystallised from MeOH-acetone as needles, m.p. 112–15°, $[\alpha]_D$ − 85° (*c*, 0·8) (lit.[2] m.p. 118–19° $[\alpha]_D$ − 85°); $\nu_{max}^{CCl_4}$ cm^{-1} 1703, 1635 (lit.[2] $\nu_{max}^{CHCl_3}$ cm^{-1} 1685); λ_{max}^{EtOH} 242 nm. (log ε, 3·86) [lit. $\lambda_{max}^{CCl_4}$ 241 nm (log ε, 3·78)].

(b) To 5-hydroxy-3β-methoxy-5α-cholestan-4-one (**11**) (5 mg) in dry pyridine (6 drops) at 0° was added $SOCl_2$ (4 drops). After 5 min at room temp, the mixture was worked up to afford 3β-methoxycholest-5-en-4-one, identical (m.p., m.m.p., TLC) with material obtained as described in (a).

Acknowledgement—We thank the S.R.C. for the award of a Research Studentship (to T.H.C.).

REFERENCES

[1]T. H. Campion and G. A. Morrison, *Tetrahedron Letters* 1 (1968)
[2]B. R. Brown and D. M. L. Sandbach, *J. Chem. Soc.* 5313 (1963)
[3]Cf. A. D. Cross, *J. Am. Chem. Soc.* **84**, 3206 (1962)
[4]H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.* 1958 (1957)
[5]R. G. Curtis, Sir I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 1953, 457.