Some Reactions of 3β-Mesyloxycholestane-5α,6β-diol and Cholest-2-ene-5α,6β-diol Acetates

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Reaction of 3β-mesyloxycholestane-5α,6β-diol 6-monoacetate (**1***e*) with potassium *t*-butoxide gave the 3α,5α-oxycholestan-6β-ol (**4***a*), which rearranged further to 5β,6β-epoxycholestan-3α-ol (**5**). Treatment of **1***c* with triethylamine gave cholest-2-ene-5α,6β-diol diacetate (**7***a*), whereas heating diacetate **1***c* in pyridine–dimethylformamide gave cholestan-3α,5α,6β-triol 3,6-diacetate (**2***a*). Cholest-2-ene-5α,6β-diol diacetate (**7***a*) reacted with *m*-chloroperbenzoic acid to give the α-epoxide **10**. Reaction of **7***a* with aqueous *N*-bromosuccinimide gave 2β-bromo-3α-hydroxy-5α,6β-diacetoxycholestane (**8**). Both epoxide **10** and bromohydrin **8** rearranged in acidic media to the tetrahydrofuran **11**.

La réaction de l'acétate-6 de mésyl-3β cholestane-5α diol-6β (**1***e*) avec le *t*-butylate de potassium, donne l'oxy-5α,3α cholestanol-6β (**4***a*) qui se réarrange ultérieurement en époxy-5β,6β cholestanol-3α (**5**). Le traitement de (**1***c*) avec la triéthylamine, conduit au diacétate de cholestène-2,5α diol-6β (**7***a*), tandis que le chauffage du diacétate (**1***c*) dans un mélange pyridine–diméthylformamide conduit au diacétate-6,3 de cholestanetriol-3α,5α,6β (**2***a*). Le diacétate de cholestène-2,5α diol-6β (**7***a*) réagit avec l'acide *m*-chloroperbenzoique pour donner l'époxyde-α (**10**). La réaction de (**7***a*) avec une solution aqueuse de *N*-bromosuccinimide donne le bromo-2β hydroxy-3α,5α diacétonycholestane-6β (**8**). L'époxyde (**10**) et la bromhydrine (**8**) se réarrangent tous deux en milieu acide en tétrahydrofuranne (**11**).
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In connection with some other work, we required a substantial amount of 2β-hydroxy-3α-bromo-5α,6β-diacetoxycholestane. An obvious precursor for such a compound is the readily available cholestane-3β,5α,6β-triol, which can be obtained by oxidation of cholesterol with hydrogen peroxide in formic acid, followed by hydrolysis (1). Acetylation gave the known triacetate **1***a* (2), which was transformed to the mesylate **1***c* via triol diacetate **1***b* (3). This mesylate was heated under reflux in dimethylformamide containing pyridine in order to form the olefin **7***a*. The product obtained, however, was a cholestanetriol diacetate to which we assigned structure **2***a* (Scheme 1). Partial hydrolysis of this diacetate gave triol monoacetate **2***b*. Chromic acid oxidation of both triol monoacetates **2***b* and **1***d* (4) gave the ketone **3**. Since the stereochemistry at position 3 of alcohol **1***d* is known, the stereochemistry of the hydroxy function of **2***b* must be as depicted.

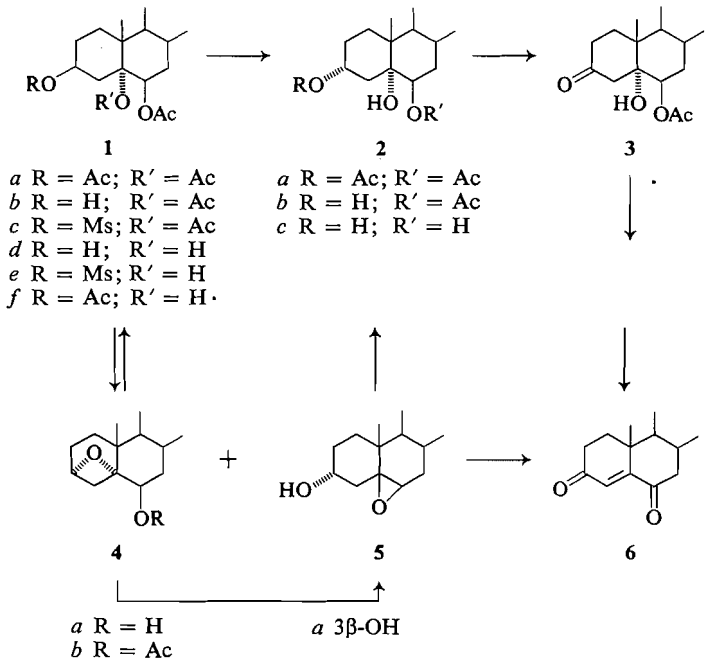
The new compound **2***a* is most likely formed by participation of the 5α-acetate group during the solvolytic reaction. The intermediate acetoxonium ion is then hydrolyzed to give exclusively the 3α-acetate **2***a*.

Since the 5α-acetoxy group seemed to interfere in the desired elimination reaction, we next prepared the 5α-hydroxy-3β-mesylate **1***e*. The compound could be readily obtained by partial hydrolysis of the known cholestan-3β,5α,6β-triol 3,6-diacetate **1***f* (4). Mesylation of the monoacetate **1***d* gave the desired mesylate **1***e* in good yield. Treatment of **1***e* with pyridine in dimethylformamide gave a low yield of the desired olefin **7**. Treatment of **1***e* with potassium *t*-butoxide in *t*-butanol gave two isomeric ethers **4***a* and **5**. Ether **4***a* was an intermediate in the formation of **5**, since it could be converted to **5** by submitting it to the reaction conditions.

Oxetane **4***a* (ν 3420 cm^{-1}, *m/e* 402) exhibited peaks in the n.m.r. at 4.6 p.p.m. (3β-H) and 4.0 p.p.m. (6α-H, $w_{1/2}$ 6 Hz) the latter signal being shifted to 5.17 p.p.m. upon acetylation. The two protons at C-4 appeared as a four-line system centered at 2.65 p.p.m. in both oxetane **4***a* and its acetate **4***b*. Treatment of **4***b* with methanesulfonic acid in ether regenerated the mesylate **1***e*, thereby confirming the structure of oxetane **4***a*.

Epoxide **5** had an i.r. and mass spectrum very similar to that of its 3-epimer **5***a*, which was obtained by treatment of triacetate **1***a* with potassium hydroxide in ethanol (5). Both **5** and **5***a* gave **6** upon Sarett oxidation (6).

[1]Revision received July 16, 1973.



SCHEME 1

The n.m.r. spectra of both **5** and **5***a* were identical except for the position of the 3-hydrogen, which appeared in **5** as a signal at 4.25 p.p.m. ($w_{1/2}$ 10 Hz) and in **5***a* at 3.7 p.p.m. ($w_{1/2} \sim$ 18–20 Hz). This indicated that the hydroxy group in **5** is axial, and its 3-epimer **5***a* equatorial. There is no doubt that the 3-hydroxy group in **5** is α, since treatment of **5** with acid gave the known triol **2***c* (1). Equally, there is no doubt about the stereochemistry of the 3β-hydroxy group in **5***a*, since it was derived from cholesterol by a simple sequence. The 5β,6β-epoxide in **5** and **5***a* must therefore impose on ring B of the steroid molecule a boat-like conformation.

The elimination of methanesulfonic acid was finally achieved upon heating mesylate **1***e* with triethylamine to give **7** (17) in approximately 70% yield. Monoacetate **7** could be converted to diacetate **7***a* by heating **7** with acetyl chloride and *N*,*N*-dimethylaniline (7).

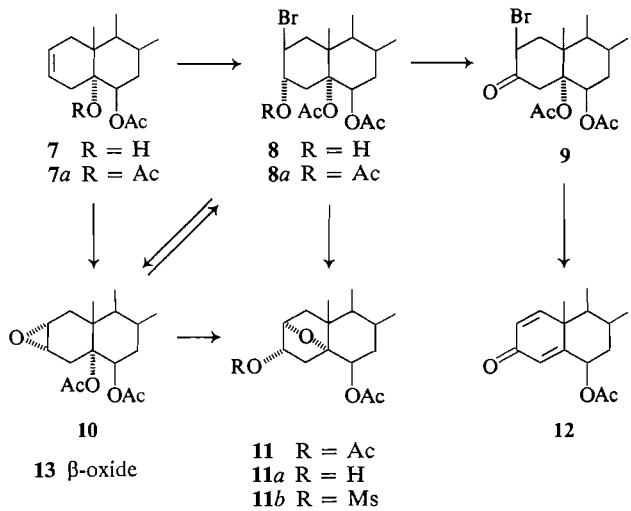
The desired 3α-bromocholestan-2β,5α,6β-triol-5,6-diacetate can in principle be obtained by epoxidation of olefin **7***a*, followed by treatment of the epoxide with hydrobromic acid, if the preferential side of the electrophilic attack is β, or by the action of hypobromous acid on olefin **7***a*, if the preferential side of attack is α (8). At the outset, it was difficult to assess whether the steric hindrance due to the 5α-acetate group would alter the well-known rule of preferential α-side attack in electrophilic reactions on steroids.

Treatment of olefin **7***a* with 1 equiv. of *N*-bromosuccinimide in aqueous dioxane (9) gave bromohydrin **8** as a major product (Scheme 2). The position of the hydroxy group in **8** was established by oxidation of **8** to **9**, which was then dehydrobrominated with lithium carbonate in dimethylformamide (10) to dienone **12**.

The formation of the *trans*-diequatorial bromohydrin bearing the hydroxy group at C-3 could be excluded because of the strong deshielding of the C-19 methyl group in bromohydrin **8**. It therefore seemed that attack of olefin **7***a* by the bromonium ion took place preferentially from the β-side, presumably because of the steric hindrance due to the 5α-acetoxy group.

Since the bromonium ion seemed to have attacked the double bond preferentially from the β-side of the molecule, it was anticipated that epoxidation would lead to the formation of 2β,3β-epoxycholestane-5α,6β-diol diacetate **13**, which could then be converted to the desired bromohydrin by means of hydrobromic acid.

Treatment of olefin **7***a* with *m*-chloroperbenzoic acid gave in good yield the α-epoxide **10**.



SCHEME 2

The stereochemistry of the epoxide **10** was deduced from the chemical shift of the C-19 methyl group, which remained at the same position as in the starting material. Furthermore, it was identical to the epoxide obtained by base treatment of bromohydrin **8** (11). The reason for a reversal of the preferential side of attack by bromonium ion and by peracid are not clear.

Treatment of the α-epoxide **10** with hydrogen bromide gave, in addition to the expected bromohydrin **8**, a new diacetoxy oxide, to which we assigned structure **11**. The same compound **11** was obtained by treating bromohydrin **8** with *p*-toluenesulfonic acid. The formation of this type of furan has been described recently by H. Tanida and co-workers (12) and by T. Komeno and co-workers (13, 14).[2]

The assignment of structure **11** is supported by its n.m.r. spectrum and decoupling experiments. A peak at 5.32 p.p.m. was assigned to the 6α-H, a double doublet at 4.7 p.p.m. (1H, $J = 7, J = 3$ Hz) to the 3β-H, a doublet at 4.35 p.p.m. (1H, $J = 7$ Hz) to the 2β-H, a four-lines pattern centered at 2.6 p.p.m. (2H, $J = 13$, $J = 7$ Hz) to the methylene protons at C-4, and a sharp signal at 2.0 p.p.m. (6H) was assigned to the acetates at C-3 and -6. The presence of an ABX system was further verified by spin decoupling analysis[3] of the splitting pattern produced by the protons giving rise to signals at 4.7, 4.35, and 2.6 p.p.m.

The formation of **11** may best be rationalized in terms of migration of acetate from 5α to 3α followed by a displacement of the 2β-bromide by the 5α-alcohol. The driving force in this reaction is quite clearly a relief of steric strain between the C-19 methyl group and the β-bromide (14).

The compound **11** was characterized by hydrolysis to the monoacetate **11***a*, ν 3400 and 1760 cm^{-1} and its mesylate **11***b*, ν 1750, 1640, and 1350 cm^{-1}; M^+ 538.

Experimental

All melting points are uncorrected. I.r. spectra were recorded on a Perkin–Elmer 257 grating i.r. spectrophotometer using potassium bromide pellets, unless otherwise stated. Nuclear magnetic resonance spectra were recorded on a Varian T-60 spectrometer using deuterochloroform as solvent and tetramethylsilane as an internal standard. Chemical shifts are reported in p.p.m. Mass spectra were taken on a AEI MS902 spectrometer operating at 75 eV. All t.l.c. was carried out on silica gel HF 254 plates. Analyses were performed by Beller Laboratories, 34 Gottingen, Theaterstrasse 23, Germany.

3β-Mesyloxy-5α,6β-diacetoxycholestane (1c)

Cholestane-3β,5α,6β-triol 5,6-diacetate (**1***b*) (200 mg) in pyridine (3 ml) was cooled to 0°. Mesyl chloride (0.5 ml) was added and the mixture was stirred at 0° for 3 h and poured into ice-water. The precipitate was crystallized from methanol, m.p. 75–78°; ν_{max} 1740, 1380, 1350, 1320, and 1230 cm^{-1}; δ 4.8 (3α-H) and 6.0 p.p.m. (6α-H).

Anal. Calcd. for $C_{32}H_{54}O_7S$: C, 65.95; H, 9.34; S, 5.49. Found: C, 65.82; H, 9.21; S, 5.38.

3β-Mesyloxy-5α-hydroxy-6β-acetoxycholestane (1e)

1*d* (200 mg) in pyridine (3 ml) was cooled to −5°.

[2]We wish to thank the referee for drawing our attention to these papers.

[3]The spin decoupling analysis was performed by Mr. R. Simoneau, the Pulp and Paper Research Institute, McGill University, Montreal, Que.

Methanesulfonyl chloride (1 ml) was added and the mixture was stirred at 0° for 5 h. The mixture was poured into ice-water and the precipitate collected was crystallized from chloroform–ether, m.p. 162–166°. Recrystallization from methanol raised the m.p. to 167–168°; ν 3440, 1715, 1370, 1355, and 1330 cm^{-1}.

Anal. Calcd. for $C_{30}H_{52}O_6S$: C, 66.73; H, 9.69; S, 5.92. Found: C, 66.70; H, 9.86; S, 5.99.

Cholestane-3α,5α,6β-triol 3,6-Diacetate (2a)

1*c* (120 mg) was warmed in *N,N*-dimethylformamide (3 ml) and pyridine (1 ml) for 16 h at 102°. The mixture was poured into ice-water and extracted with chloroform (5 × 35 ml). The chloroform solution was washed with 5% hydrochloric acid. The organic layer was dried and evaporated to give a yellow gum. Preparative t.l.c. (ether–hexane 3:1) permitted the isolation of a major band, R_f 0.5, which was extracted with ether. The oil (72 mg) obtained was crystallized from ether–hexane, m.p. 86–88° (lit. (15) 86°); ν_{max} 1730 and 3450 cm^{-1}; δ 4.75 (3α-H), 5.3 (6α-H), and 2.15 p.p.m. (two acetates).

Anal. Calcd. for $C_{31}H_{52}O_5$: C, 73.76; H, 10.38. Found: C, 73.63; H, 10.31.

Partial Hydrolysis of Cholestane-3α,5α,6β-triol 3,6-Diacetate (2a)

A mixture of **2***a* (300 mg), sodium bicarbonate (330 mg), and methanol (30 ml) was stirred at room temperature and the reaction was monitored by t.l.c. After approximately 6 h, the mixture was extracted with ether (5 × 40 ml). The ethereal layer was washed with water (3 × 50 ml) and dried with anhydrous sodium sulfate. Evaporation of solvent gave **2***b* as crystals, m.p. 175–180°; ν_{max} 3480, 3420, and 1720 cm^{-1}, δ 3.8 (3β-H) and 5.3 p.p.m. (6α-H). Recrystallization from methanol twice gave needles, m.p. 181–182°.

Anal. Calcd. for $C_{29}H_{52}O_5.H_2O$: C, 72.45; H, 10.90. Found: C, 72.30; H, 10.37.

Partial Hydrolysis of Cholestane-3β,5α,6β-triol 3,6-Diacetate (1f)

This partial hydrolysis was carried out as described for **2***a*. Two crystallizations from methanol gave needles of **1***d*, m.p. 144–145° (lit. (4) 146°).

Oxidation of Cholestane-3α,5α,6β-triol 6-Acetate (2b) and of 1d

Triol acetate **2***b* (72 mg) was submitted to a Sarett oxidation (6). Crystallization of the reaction product from methanol gave **3**, m.p. 161° (lit. (4) 157–158°). This product was identical to the product of oxidation of **1***d* (mixed m.p., t.l.c., and comparison of i.r. spectra).

Reaction of 3β-Mesyloxy-5α-hydroxy-6β-acetoxycholestane (1e) with Potassium t-Butoxide

1*e* (500 mg) was heated under reflux for 4 h in a nitrogen atmosphere in 50 ml of *t*-butanol containing 300 mg of potassium. The reaction mixture was poured into ice-water. Neutralization with dilute hydrochloric acid and extraction with ether gave an oil (410 mg). Preparative t.l.c. (petroleum ether – ether 1:1) permitted the isolation of two bands.

(*a*) From the band with lowest R_f was obtained 100 mg of **5**, m.p. 120–126°. Recrystallization from methanol gave plates, m.p. 144–146°; ν_{max} 3420, 3320, 1350, and 1240 cm^{-1}; δ 4.2 (1H broad, 3β-H) and 3.1 p.p.m. (1H, J = 3 Hz, 6α-H). The mass spectrum showed a molecular ion at *m/e* 402.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.41; H, 11.38.

(*b*) The band with R_f 0.4 gave 210 mg of **4***a*, m.p. 119–123°. Recrystallization from methanol gave 170 mg of **4***a*, m.p. 121–122°; ν_{max} 3450 cm^{-1}; δ 4.05 (1H, triplet 6α-H) and 4.7 p.p.m. (1H, multiplet C_3—H). Mass spectrum provided confirmation of the expected molecular weight of 402.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.51; H, 11.32.

3α,5α-Oxycholestan-6β-ol Acetate (4b)

Acetylation of **4***a* (65 mg) in the usual manner gave 82 mg of the acetoxy oxetane **4***b* as an oil. Attempt to crystallize **4***b* failed; ν_{max} 1746 and 1242 cm^{-1}; δ 4.6 (1H, broad C_3—H), 5.15 (1H, multiplet 6α-H), 2.5–2.9 (4H, 2 multiplets), and 2.1 p.p.m. (3H, CH_3CO). The mass spectrum confirmed the expected molecular weight of 444.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.12; H, 10.79.

Acid Treatment of 5β,6β-Epoxycholestan-3α-ol (5)

To 35 mg of epoxide **5** in 5 ml of chloroform was added 2 drops of 71% perchloric acid. The mixture was refluxed for 10 min. Anhydrous magnesium sulfate was added and the organic layer was then evaporated to dryness to give a solid. The solid residue was dissolved in 1 ml of pyridine and 0.5 ml of acetic anhydride was added. The mixture was left overnight at room temperature. Removal of solvents *in vacuo* gave crystals of **2***a*, m.p. 85–86°. It was identical with **2***a* obtained from **1***c* (mixed m.p. and comparison of t.l.c. behavior and i.r. spectra).

Reaction of 3α,5α-Oxycholestan-6β-ol Acetate (4b) with Methanesulfonic Acid

To oxetane **4***b* (22 mg) in 5 ml of ether was added 3 drops of methanesulfonic acid and the reaction mixture was stirred at 25° for 4 h. Exactly 4 ml of 10% sodium bicarbonate solution was added to the stirring mixture. The organic layer was separated, dried with 1 g of anhydrous magnesium sulfate, and evaporated giving 19 mg of solid **1***e* which was crystallized from ether, m.p. 169–170°. It was identical with **1***e*, obtained from **1***d* (mixed m.p., comparison of i.r. spectra and t.l.c. mobility).

Reaction of 3α,5α-Oxycholestan-6β-ol Acetate (4b) with Base

A mixture of oxetane **4***b* (22 mg), potassium *t*-butoxide (22 mg), and dry tetrahydrofuran (5 ml) was refluxed for 24 h under a nitrogen atmosphere. The mixture was evaporated to dryness under reduced pressure and the semi-solid was stirred at room temperature with 10 ml of ether. The solid residue was filtered and the filtrate was evaporated to dryness. The gum obtained was shown to contain two compounds, which were identified as hydroxy oxetane **4***a* and epoxide **5** by comparing R_f values and i.r. spectra.

Sarett Oxidation of 5β,6β-Epoxycholestan-3α-ol (5) and of 5β,6β-Epoxycholestan-3β-ol (5a)

A solution of 64 mg of **5** in 1.2 ml of pyridine was mixed with 120 mg of chromium trioxide in 1.2 ml of pyridine and allowed to stand at room temperature

overnight. The mixture was poured into ice-water and extracted with three portions of benzene–ether 1:1. The extract was passed through celite to break the emulsion. This was dried and evaporated under high vacuum to give a gum. Crystallization from hexane gave leaflets of **6**, m.p. 120–124°; λ_{max} (EtOH) 254 mμ (lit. (4) m.p. 125°, λ_{max} 253 mμ). This product was identical with the product obtained from **3** (t.l.c., mixed m.p.).

Oxidation of the 3β-epimer of **5**, using the same procedure, gave the same dione **6**.

Cholest-4-en-3,6-dione (6)

To **3** (15 mg) dissolved in 3 ml of absolute ethanol, was added 22 mg of solid potassium hydroxide and the mixture was refluxed for 2 h. Evaporation to near dryness and ether extraction gave 11 mg of a solid. The solid was dissolved in 3 ml of acetone, the mixture was cooled to 5° and 1 ml of Jones' reagent (16) was added dropwise. The reaction mixture was allowed to stir at 5° for 1.5 h. Isopropanol (5 ml) was added and the mixture was extracted with ether to give 7 mg of a pale yellow gum. Attempts to crystallize from hexane failed. T.l.c. mobility, i.r. and u.v. spectra of the product proved its identity as **6**.

5α-Hydroxy-6β-acetoxycholest-2-ene (7)

3β-Mesyloxy-5α-hydroxy-6β-acetoxycholestane (**1***e*) (40 g) was refluxed under nitrogen for 38 h with 120 ml of triethylamine. Excess solvent was evaporated completely under reduced pressure. This gave a gum which was chromatographed on alumina (1 kg, activity III). Elution with 1000 ml of petroleum ether gave an impure oil fraction (2.8 g) which was not further characterized. Elution with petroleum ether – benzene 8:1 and 7:1 gave 7 (26.2 g) as an oil, ν_{max} 3500, 3030, 1740, 1660, and 1240 cm^{-1}; δ 5.6 (vinyl protons, 2H), 4.8 (1H, multiplet 6α-H), and 2.0 p.p.m. (CH_3CO, 3H); *m/e* 444, 402, 384, 366.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.12; H, 10.81.

5α,6β-Diacetoxycholest-2-ene (7a)

A mixture of 7 (2.3 g), dry chloroform (50 ml), dimethylaniline (20 ml), and acetyl chloride (12 ml) was heated under reflux in a nitrogen atmosphere for 30 h. This was diluted with 500 ml of chloroform and the mixture was washed with 5–10% cold hydrochloric acid solution (5 × 250), with water and dried with anhydrous magnesium sulfate. Evaporation of the organic solvent gave a light blue gum (3.4 g). This was chromatographed on alumina (200 g, activity III). Petroleum ether (400 ml) eluted 1.1 g of dimethylaniline. Elution with petroleum ether – benzene 8:1 (2.4 l) gave 1.4 g of diacetate **7***a* (17) as a solid. Recrystallization from hexane gave needles, m.p. 136–137°; ν_{max} 3030, 1725, 1625, 1250, 1230, and 1210 cm^{-1}; δ 5.95 (multiplet 6α-H), 5.6 (unsymmetric triplet 2 vinyl H), and 2.1 and 2 p.p.m. (2 acetates). The mass spectrum confirmed the expected molecular weight of 486.

Anal. Calcd. for $C_{31}H_{50}O_4$: C, 76.50; H, 10.36. Found: C, 76.55; H, 10.29.

2β-Bromo-3α-hydroxy-5α,6β-diacetoxycholestane (8)

To a mixture of the olefin **7***a* (100 mg) in 2.5 ml of dioxane was added a solution of 60 mg of *N*-bromosuccinimide in 1 ml of water and 1 ml of 5% perchloric acid. The mixture was stirred at room temperature for 2.5 h. Water was added and the product was isolated by filtration. The filtrate was washed with cold water and dried; 112 mg of a fine powder, m.p. 126–129° was obtained. T.l.c. of this compound indicated one spot (chloroform–methanol 95:5 and hexane–ether 1:1). Recrystallization from acetone gave 36 mg of **8** as cubes, m.p. 132–134°; ν_{max} 3480, 1745, 1712, 1245, and 1045; δ 6 (6α-H), 4.43 (multiplet, 2α-H, 3β-H), and 2.1 and 2.2 p.p.m. (singlets, 2 acetates). A second crop of 40 mg of **8**, m.p. 128–131° was further obtained. Evaporation of the solvent from the mother liquor gave 26 mg of a gum. Attempts to recrystallize failed.

Anal. Calcd. for $C_{31}H_{51}O_5Br$: C, 63.80; H, 8.74; Br, 13.70. Found: C, 63.84; H, 8.88; Br, 13.78.

Acetylation of **8** with pyridine – acetic anhydride gave acetate **8** m.p. 173–177°; ν_{max} 2980, 2880, 1750, 1740, 1730, 1265, 1250, 1230, and 1040 cm^{-1}; δ 6 (6α-H), 5.5 (multiplet 3β-H), 4.5 (multiplet 2α-H), and 2.1 p.p.m. (3 acetate peaks).

Anal. Calcd. for $C_{33}H_{53}O_6Br$: Br, 12.81. Found: Br, 12.72.

6β-Acetoxycholesta-1,4-dien-3-one (12)

Bromohydrin **8** (78 mg) in 5 ml of acetic acid was allowed to stand at 25° for 1 day with a mixture of 42 mg of chromic oxide in 2 ml of acetic acid. Excess of chromic acid was destroyed by addition of methanol and the solution was diluted with cold water. Extraction with ether and evaporation gave bromoketone **9** as an oil. Crude **9** was heated at 110° with *N,N*-dimethylformamide (2 ml), lithium carbonate (45 mg), and lithium bromide (17 mg) in a nitrogen atmosphere for 30 h. The reaction mixture was acidified with 5% hydrochloric acid and extracted with chloroform, and the organic solution washed with 5% hydrochloric acid and with water. Evaporation under reduced pressure gave 55 mg of an oil. Preparative t.l.c. (hexane–ether 2:1) permitted the isolation of 45 mg of **12** as a colorless oil, λ_{max} (MeOH) 247 mμ (ε 9800); ν_{max} ($CHCl_3$) 2940, 2860, 1735, 1665, 1620, and 1200 cm^{-1}; δ 7.2 and 6.35 (AB quartet, 1-H, 2-H), 6.42 (singlet, 4-H), 5.6 (multiplet, 6α-H), and 2.18 p.p.m. (6-acetate); *m/e* 440.

Anal. Calcd. for $C_{29}H_{44}O_3$: C, 79.04; H, 10.07. Found: C, 78.69; H, 10.01.

2α,3α-Epoxy-5α,6β-diacetoxycholestane (10)

Olefin **7***a* (300 mg) in 5 ml methylene chloride was stirred at room temperature for 5 h with 200 mg of 85% *m*-chloroperbenzoic acid in 5 ml methylene chloride. After addition of 10% aqueous sodium sulfite solution, the organic layer was washed with 5% aqueous sodium bicarbonate solution and water, and dried. Evaporation gave 340 mg of an oil which solidified upon standing. Recrystallization from methanol gave 195 mg of epoxydiacetate **10**, m.p. 191–193°. Preparative t.l.c. permitted the isolation of 37 mg of **10**, m.p. 188–191° and 12 mg of a solid which was not further characterized. ν_{max} 1740, 1725, 1370, 1250, 1220, 1040, and 1025 cm^{-1}; δ 5.75 (multiplet 6α-H), 3.25 (singlet, 2H), 2.1 and 2 (2 singlets, 2 acetates), and 1.1 p.p.m. (singlet 19-CH_3); *m/e* 502.

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 73.80; H, 10.24.

Reaction of 2α,3α-epoxy-5α,6β-diacetoxycholestane (10) with Hydrobromic Acid

Epoxide **10**, m.p. 192–194° (242 mg) in 10 ml of dioxane was stirred with approximately 0.3 ml of 48% hydro-

bromic acid and 0.12 ml of water for 2.5 h at room temperature. The mixture was poured into water and the precipitate (270 mg) was purified by preparative t.l.c. (ethyl acetate – cyclohexane 1:4) (*1*). The band at R_f 0.4 gave 134 mg of bromohydrin **8**, m.p. 139°, which was identical to **8** obtained from the *N*-bromosuccinimide reaction of *7a* (t.l.c., i.r., mixed m.p.) (*2*). The band at R_f 0.55 gave 130 mg of furan **11** which was crystallized from methanol, m.p. 142–145°; ν_{max} 2940, 2860, 1730, 1240, 1210, and 1030 cm^{-1}; δ 5.32 (6α-H), 4.7 (double doublets, collapses upon irradiation at 2.6 p.p.m., 3β-H), 4.38 (doublet, 2β-H), 2.6 (2 doublets, collapse upon irradiation at 4.7 p.p.m., 4α and 4β-H), and 2.0 p.p.m. (3,6-diacetates, 6H); *m/e* 502.

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 73.80; H, 9.68.

Reaction of 2β-Bromo-3α-hydroxy-5α,6β-diacetoxycholestane (8) with p-Toluenesulfonic Acid

A mixture of bromohydrin **8** (130 mg) in 8 ml of methylene chloride and a few crystals of *p*-toluenesulfonic acid in 0.25 ml of tetrahydropyran was allowed to stand overnight. The solvent was removed *in vacuo* and the resulting oil reacetylated with acetic anhydride and pyridine. Evaporation and extraction with methylene chloride gave an oil which solidified after some time. The t.l.c. mobility, n.m.r. and i.r. spectra of this oil were identical to those of **11** obtained from epoxide **10**.

Partial Hydrolysis of 2α,5α-Oxy-3α,6β-diacetoxycholestane (11)

3,6-Diacetate **11** (23 mg) was stirred at −4° for 0.5 h with 3 ml of 5% ethanolic potassium hydroxide. Ether extraction gave 18 mg of an oil **11***a*, ν (NaCl) 3400 cm^{-1} (—OH), 1760 cm^{-1} (—OAc); δ 5.4 (m, 1H, 6α-H), 4.38 (d, 1H, J = 6 Hz, 2β-H), 3.9 (m, 1H, 3β-H), and 2.05 p.p.m. (s, 3H, acetate); M^+ 460.

Anal. Calcd. for $C_{29}H_{50}O_5$: C, 72.76; H, 10.53. Found: C, 72.52; H, 10.32.

3α-Mesyloxy-2α,5α-oxy-6β-acetoxycholestane (11b)

Hydroxy-furan **11***a* (45 mg) was stirred at 2° for 4.5 h with a few drops of mesyl chloride in pyridine (3 ml). Work-up as usual gave 62 mg of mesylate **11***b*. Attempts on recrystallization failed. ν 1740 (—OAc), 1370, 1320, and 1260 cm^{-1} (—SO_2—); δ 5.4 (m, 1H, 6α-H), 4.8 (d, 1H, J = 6 Hz, 2β-H), 4.6 (m, 1H, 3β-H), 3.1 (s, 3H, CH_3SO_2—), and 2.1 p.p.m. (s, 3H, CH_3CO—); *m/e* 538, 478, 442, 400, and 382.

Anal. Calcd. for $C_{30}H_{50}O_6S$: C, 66.88; H, 9.36; S, 5.94. Found: C, 66.72; H, 9.40; S, 5.92.

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1. L. Fieser and S. Rajagopalan. J. Am. Chem. Soc. **71**, 3938 (1949).
2. L. Fieser and M. Fieser. Steroids. Reinhold Publishing Corp., N.Y. 1959. p. 198.
3. M. J. Coppen, M. P. Hartshorn, and D. N. Kirk. J. Chem. Soc. 576 (1966).
4. B. Ellis and V. Petrow. J. Chem. Soc. 1078 (1939).
5. A. T. Rowland and H. R. Nace. J. Am. Chem. Soc. **82**, 2833 (1960).
6. G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett. J. Am. Chem. Soc. **75**, 425 (1953).
7. F. Bladon. J. Chem. Soc. 4883 (1952).
8. I. Roberts and G. E. Kimball. J. Am. Chem. Soc. **59**, 947 (1937).
9. H. L. Slates and N. L. Wendler, J. Am. Chem. Soc. **78**, 3749 (1956).
10. R. Joly, J. Warnant, G. Nomine, and D. Bertin. Bull. Soc. Chim. 366 (1958).
11. C. W. Shoppee, D. N. Jones, and G. H. R. Summers. J. Chem. Soc. 3100 (1957).
12. T. Tsuji, T. Komeno, H. Itani, and H. Tanida. J. Org. Chem. **36**, 1648 (1971).
13. T. Komeno and M. Kishi. Tetrahedron, **27**, 1517 (1971).
14. T. Komeno, H. Itani, H. Iwakura, and K. Nabeyama. Chem. Pharm. Bull. **18**(6), 1145 (1970).
15. Y. Urushibara and K. Mori. Bull. Chem. Soc. Jap. **31**, 1068 (1958).
16. A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin. J. Chem. Soc. 2555 (1953).
17. T. Komeno, H. Itani, H. Iwakura, and K. Nabeyama. Chem. Pharm. Bull. (Tokyo), **18**, 1145 (1970).