Synthesis of 11- and 15-Oxygenated Steroids. The Course of 8,14-Dienes Oxidation by Chromic Acid

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3β-Acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one, 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one, and 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione were obtained by oxidizing 3β-acetoxy-5α-cholesta-8,14-diene with various amounts of Jones reagent or performing the reaction under different temperature conditions. The epoxy ketones were also obtained by independent synthesis.

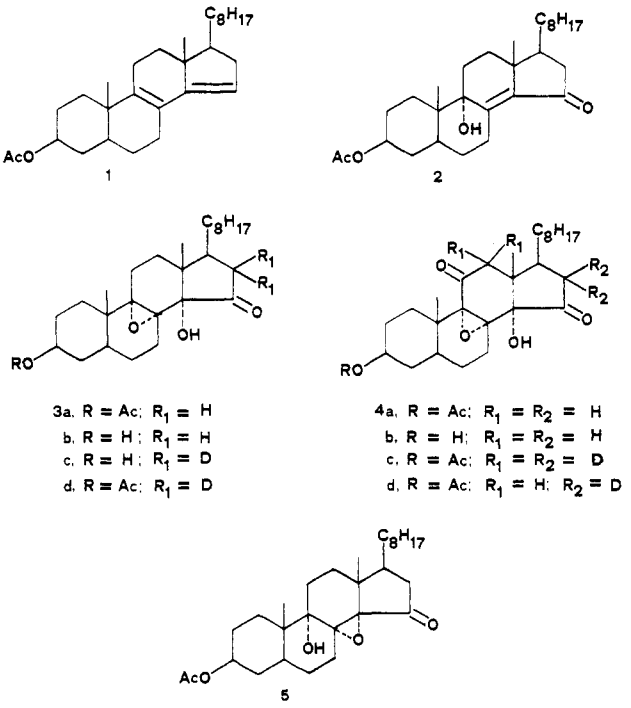
In our previous papers we showed that sterols containing an 8,14-diene system are good starting material for the introduction of oxygenated functions by *m*-chloroperbenzoic acid (MCPBA) or chromic acid oxidation in both 15- and 9α-positions.[1a,c]

In connection with our studies on the synthesis of 15-oxygenated sterols as inhibitors of cholesterol biosynthesis, we reexamined the reactivity of 3β-acetoxy-5α-cholesta-8,14-diene (**1**, Chart I) with chromic acid with the aim of introducing a 15- and an 11-oxygenated function in the steroid nucleus. This idea rose from the observation that the oxidation of **1** with chromic acid at 10 °C affords 3β-acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one (**2**), the allylic hydroxy group of which could be transformed again when subjected to more drastic oxidation conditions. In fact the oxidation of tertiary allylic alcohols with Cr(VI) is a well-known reaction, giving rearranged α,β-unsaturated or α,β-epoxy aldehydes or ketones depending on the chromium species used.[2]

In the case of **2** chromium oxidation could afford 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one (**3a**), the product of epoxidative 1,3-rearrangement. The 8α,9α-oxide ring of **3a** could permit on the end the transformation of the 11-methylene into a keto group by an opening of the oxide ring in the acidic medium of the reaction, formation of an 8α-hydroxy-$\Delta^{9(11)}$-ene system, and oxidative rearrangement of the allylic alcohol to afford 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-cholestan-11,15-dione (**4a**). However the opening of the oxide ring to a 9α-hydroxy-Δ^{7}-ene system with successive formation of an 8α,9α-epoxy 7-ketone in principle could not be excluded. On the other hand, inspection of the Dreiding model of **3a** showed that only the 11α-hydrogen is antiparallel to the C-9α–OH linkage, thus favoring the formation of the 8α-hydroxy-$\Delta^{9(11)}$-ene system by a concerted epoxide ring cleavage and elimination of the 11α-hydrogen.

With this in mind we treated **2** with Jones reagent (0.66 mol equiv) and isolated a compound of assigned structure **3a**. The same compound was obtained by oxidation of **1** with a major amount of Jones reagent (2 mol equiv) at 10 °C. Elemental analysis and the mass spectrum of the compound are in keeping with the molecular formula $C_{29}H_{46}O_5$. The IR spectra of **3a** and of the parent alcohol **3b** show the appropriate carbonyl absorptions. The ^1H NMR spectrum of **3a** exhibits a signal at δ 3.62 for the alcoholic proton, a double doublet centered at δ 2.75, assigned to the 16-proton ($J_{16\alpha,17\alpha}$ = 8, $J_{16\alpha,16\beta}$ = 18 Hz), and an unresolved two-proton signal at δ 2.35, attributable to the 16β-proton superimposed on the signal of the 7β-proton deshielded by the 15-keto group.[1a,3] Supporting evidence for these assignments was provided by the spectrum of 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one-*16,16-d*$_2$ (**3d**), which lacks the signals attributed to the 16α- and 16β-protons and shows a one-proton signal centered at δ 2.35, corresponding to the 7β-proton. The chemical shifts observed for the C-18 and C-19 angular methyl groups of **3a** are also in good agreement with the calculated values.[3,4] The assignment of the structure was confirmed by independent synthesis of **3a** and of the isomer 3β-acetoxy-8α,14α-epoxy-9α-hydroxy-5α-cholestan-15-one (**5**), whose properties are completely different from those observed for **3a** (Scheme I). Osmilation of **1** afforded 3β-acetoxy-5α-cholest-8-ene-14α,15α-diol (**6**) in high yield as the only product, presumably the result of pref-

Chart I



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(1) (a) Anastasia, M.; Fiecchi, A.; Scala, A. *J. Chem. Soc., Perkin Trans. I* **1979**, 1821. (b) Anastasia, M.; Fiecchi, A.; Gariboldi, P.; Scala, A. *J. Org. Chem.* **1979**, *44*, 4447. (c) Anastasia, M.; Allevi, P.; Fiecchi, A.; Scala, A. *Ibid.* **1981**, *46*, 3265.

(2) (a) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682. (b) Sundararaman, P.; Herz, W. *Ibid.* **1977**, *42*, 813 and references cited therein.

(3) Bhacca, N. W.; Williams, D. H. "Applications of NMR Spectroscopy in Organic Chemistry"; Holden-Day: San Francisco, CA, 1964; Chapters 2 and 6.

(4) Tsuda, M.; Parish, E. J.; Schroepfer, G. J. *J. Org. Chem.* **1979**, *44*, 1282.

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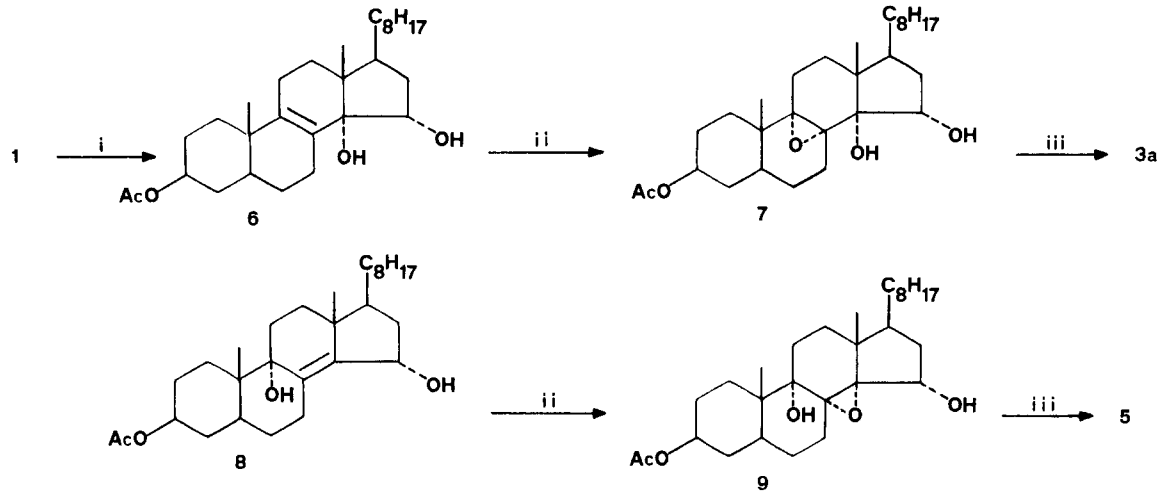
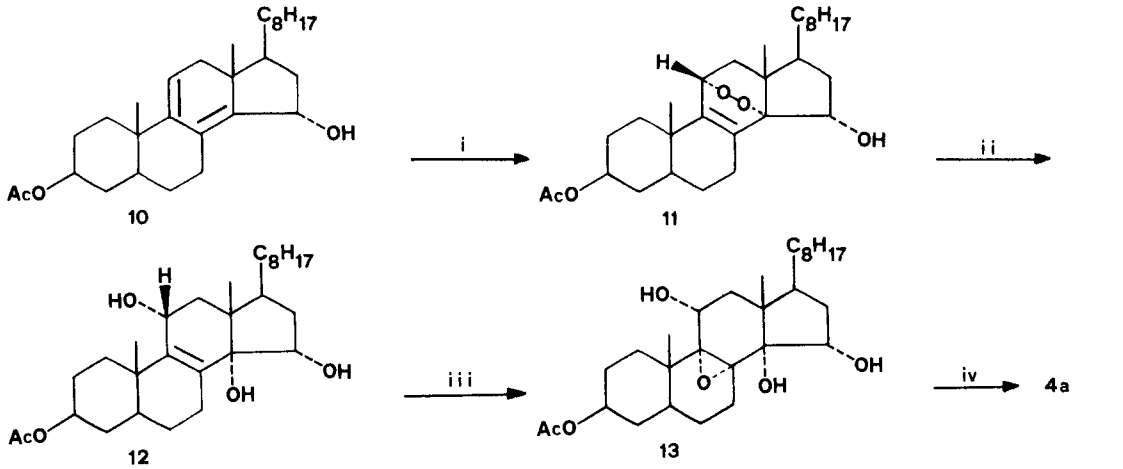
Scheme I[a]



[a] i, OsO_4; ii, MCPBA; iii, CrO_3·Py.

Scheme II[a]



[a] i, O_2-$h\nu$; ii, H_2-Pd; iii, MCPBA; iv, CrO_3·Py.

erential α attack on the less hindered Δ^{14} double bond. Subsequent epoxidation of **6** with MCPBA afforded 3β-acetoxy-8α,9α-epoxy-5α-cholestane-14α,15α-diol (**7**), which by oxidation with Sarett reagent produced **3a**. Epoxidation with MCPBA of 3β-acetoxy-5α-cholest-8(14)-ene-9α,15α-diol (**8**)[1c] afforded 3β-acetoxy-8α,14α-epoxy-5α-cholestane-9α,15α-diol (**9**), which was then oxidized to the epoxy ketol **5**.

Compound **3a** was also obtained in a one-pot reaction by treatment of an acetone solution of **6** with chromic acid in 8 N sulfuric acid via the apparently direct epoxidation of the Δ^8 double bond and oxidation of the 15α-hydroxy group. On the other hand, we observed that the formation of **3a** is the result of an acidic transposition of **6** to the allylic diol **8**, which in turn suffers oxidation at C-15 and epoxidative rearrangement to **3a**. In fact, the presence of **8** and **2** was observed in the first stages of the reaction by monitoring the reaction by TLC. On the other hand, **6** was quantitatively transformed into **8** on exposure to the oxidation solvent.

The formation of **3a** by oxidation with Jones reagent of **1** or **2** was always accompanied by the formation of a minor amount (10–20%) of a compound now formulated as **4a**. Compound **4a** was the main product when oxidations with Jones reagent were performed at room temperature. Elemental analysis and the mass spectrum of **4a** were in accordance with the molecular formula $C_{29}H_{44}O_6$. The IR spectra of **4a** and of the parent alcohol **4b** showed the presence of a six- and a five-membered ketone. The ^1H NMR spectrum of **4a** shows a doublet at δ 2.71 ($J_{12\alpha,12\beta}$ = 18 Hz), assigned to the 12β-proton (the A part of an AB system), superimposed on a double doublet due to the 16α-proton (as discussed for **3a**) and a doublet at δ 2.24 (J = 18 Hz), assigned to the 12α-proton (the B part of the AB system), superimposed on a complex two-proton signal due to the 1β- and 7β-protons deshielded by the 11- and 15-keto groups and to the 16β-proton. In accordance with these assignments in the spectrum of 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-11,15-dione-*12,12,16,16-d*$_4$ (**4c**), the signals attributed to the enolizable protons completely disappeared while a residual two-proton signal at δ 2.00–2.30 is present, consistent with the assignment of the 1β- and 7β-protons. In addition, the spectrum of 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione-*16,16-d*$_2$ (**4d**) shows a clear doublet at δ 2.71 for the 12β-proton (J = 18 Hz) and at δ 2.03–2.30, a three-proton signal constituted by the doublet of the 12-proton resonance centered at δ 2.24 (J = 18 Hz) superimposed on the signals of 1β- and 7β-protons.

Compound **4a** was prepared by an independent route (Scheme II). 3β-Acetoxy-5α-cholesta-8(14),9(11)-dien-15α-ol (**10**)[1c] and molecular oxygen were reacted with intense lighting[5] and a sensitizer to afford 3β-acetoxy-

(5) Laubach, G. D.; Schreiber, E. C.; Agnello, E. J.; Lightfoot, E. N.; Brunings, K. J. *J. Am. Chem. Soc.* **1953**, *75*, 1514.

11α,14α-epidioxy-5α-cholest-8-en-15α-ol (**11**). Assignment of structure **11** to this compound is based on the expected addition of oxygen to the α face of the molecule, on the spectral evidence, and on chemical transformations. Elemental analysis and the mass spectrum of **11** are in keeping with the formula $C_{29}H_{46}O_5$. The IR spectrum shows no ketonic carbonyl absorption. The ^1H NMR spectrum displays a broad multiplet for the protons at C-3, C-11, and C-15. Consistent with the peroxide structure, **11** readily liberated iodine from an acidified iodide solution.[6] Compound **11** was hydrogenated to 3β-acetoxy-5α-cholest-8-ene-11α,14α,15α-triol (**12**) in the presence of pyridine-deactivated palladium on carbon. In these conditions hydrogen does not attack either the allylic oxygen substituents or the Δ^8 double bond. The spectral properties establish the identity of this compound. Treatment of **12** with MCPBA affords 3β-acetoxy-8α,9α-epoxy-5α-cholestane-11α,14α,15α-triol (**13**), which was oxidized with Sarett reagent to a compound possessing the same chemicophysical properties of **4a**.

The results obtained in the chromic acid oxidation of **1** show that 8,14-dienes are good starting material for introducing oxygenated functions in the C and D rings of steroids by simple Jones oxidations. As far as the mechanism of the oxidations is concerned, the previously suggested[1a] monoepoxidation of the Δ^8 or the Δ^{14} double bond appears to be the starting step of the reaction. In fact, Jones oxidation of 3β-acetoxy-8α,9α-epoxy-5α-cholest-14-ene (**14**)[1c] and of 3β-acetoxy-14α,15α-epoxy-5α-cholest-8-ene (**15**)[1c] (Chart II) affords in good yield the ketol **2** by intermediary formation of **8**. Compound **2** then suffers transpositive epoxidation to the epoxy ketol **3a**. Different mechanisms are reported in order to clarify transpositive oxidations of allylic alcohols, which also appear to be reasonable in the present case.[2b]

The introduction of the 11-keto group in **3a** with formation of **4a** is well clarified by the formation of a $\Delta^{9(11)}$-8α-hydroxy system in the opening of the oxide ring of **3a** and successive oxidative rearrangement. However, all efforts to isolate the supposed intermediate allylic alcohol were unsuccessful, and in the absence of other proofs this proposed mechanism should be considered only as the most reasonable one.

Experimental Section

All melting points are uncorrected. Infrared spectra were recorded for solutions in chloroform or as Nujol mulls, and absorptions are reported in reciprocal centimeters; NMR spectra were recorded on a Varian HA-100 from chloroform-*d* solutions and are reported in δ relative to Me_4Si. Optical rotations were taken from chloroform solutions. The mass spectra were determined on a Varian MAT 112 S spectrometer by direct inlet methods. The progress of all reactions and column chromatographies (silica 230–400 mesh) was monitored by TLC on silica gel (HF_{254}) plates. Hexane–ethyl acetate mixtures were used as developing solvents, and spots were detected by spraying with 70% sulfuric acid followed by heating.

Synthesis of 3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one (3a) by Chromic Oxidation. A. 3β-Acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one (**2**, 1 g) in acetone (75 mL) was oxidized with Jones reagent[7] (0.55 mL). After 30 min at 10 °C the reaction product was recovered by extraction with dichloromethane and chromatographed to afford first 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one (**3a**, 660 mg): mp 143–144 °C (methanol); $[\alpha]^{20}_D$ +80°; IR 3420, 1745, 1720 cm^{-1}; ^1H NMR δ 0.91 (s, 3 H, 18-CH_3; calcd[3,4] 0.874), 1.05 (s, 3 H, 19 CH_3; calcd[3,4] 1.066), 2.01 (s, 3 H, CH_3COO), 2.35 (overlapping, 2 H, 7β- and 16β-H), 2.75 (dd, 1 H, 16α-H, $J_{16\alpha,17\alpha}$ = 8 Hz, $J_{16\alpha,16\beta}$ = 18 Hz), 3.62 (m, 1 H, OH), 4.70 (m, 1 H, 3α-H); mass spectrum, *m/z* (relative intensity) 474 (14, M^+), 396 (19), 263 (9), 290 (100), 237 (90).

Anal. Calcd for $C_{29}H_{46}O_5$: C, 73.37; H, 9.76. Found: C, 73.40; H, 9.50.

Saponification of **3a** with methanolic potassium hydroxide gave the parent alcohol **3b**: mp 130–131 °C (methanol); IR 3500, 3350, 1745 cm^{-1}; ^1H NMR δ 1.05 (s, 3 H, 18-CH_3), 1.13 (s, 3 H, 19-CH_3).

Anal. Calcd for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 74.80; H, 10.42.

Further elution yielded 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione (**4a**, 100 mg): mp 205–206 °C (from methanol); $[\alpha]^{21}_D$ +69°; IR 3400, 1745, 1720, 1710 cm^{-1}; ^1H NMR δ 1.06 (s, 3 H, 18-CH_3), 1.12 (s, 3 H, 19-CH_3), 2.00 (s, 3 H, CH_3COO), 2.00–2.30 (overlapping, 4 H, 1β-, 7β-, 12α-, 16β-H), 2.60–2.80 (overlapping, 2 H, 12β- and 16α-H), 3.32 (s, 1 H, OH), 4.70 (m, H, 3α-H); mass spectrum, *m/z* (relative intensity) 488 (3, M^+), 429 (50), 324 (53), 291 (27), 232 (46).

Anal. Calcd for $C_{29}H_{44}O_6$: C, 71.28; H, 9.07. Found: C, 71.40; H, 10.00.

Saponification of **4a** with methanolic potassium hydroxide gave the parent alcohol **4b**: mp 154–156 °C; IR 3400, 1745, 1710 cm^{-1}; ^1H NMR δ 1.05 (s, 3 H, 18-CH_3), 1.13 (s, 3 H, 19-CH_3).

Anal. Calcd for $C_{27}H_{42}O_5$: C, 72.60; H, 9.48. Found: C, 72.50; H, 9.60.

B. 3β-Acetoxy-5α-cholesta-8,14-diene (1, 1 g) in acetone (75 mL) was oxidized with Jones reagent (1.8 mL) at 10 °C. After 30 min, the usual workup and chromatography afforded compound **3a** (590 mg; mp 143–144 °C) and compound **4a** (70 mg; mp 205–206 °C), both having the same NMR and mass spectra reported for the compounds obtained above.

C. 3β-Acetoxy-5α-cholest-8-ene-14α,15α-diol (**6**, 500 mg) in acetone (45 mL) was oxidized with Jones reagent (0.55 mL) at 10 °C. After 30 min at 10 °C, the usual workup and chromatography afforded **3a** (300 mg) and **4a** (50 mg) both identical with those obtained above (mp, NMR, and mass spectra). Formation of **8** was observed (TLC) in the first stages of the reaction.

3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one-*16,16-d*$_2$ (3d). A solution of the acetate **3a** (200 mg) in methanol-*d* (25 mL) containing sodium methoxide (200 mg) was heated overnight under reflux in a nitrogen atmosphere. The solvent was then distilled, fresh methanol-*d* (25 mL) was added, and the above procedure was repeated. The residue was dissolved in dichloromethane, washed with water, and dried. Evaporation of the solvent gave the dideuterated compound **3c**: mp 130–131 °C (methanol); mass spectrum, *m/z* (relative intensity) 450 (4, M^+), 389 (44), 281 (38), 210 (100).

Acetylation of **3c** afforded **3d**: mp 143–144 °C; ^1H NMR δ 0.91 (s, 3 H, 18-CH_3), 1.05 (s, 3 H, 19-CH_3), 2.01 (s, 3 H, CH_3COO), 2.35 (m, 1 H, 7β-H), 3.36 (s, 1 H, OH); mass spectrum, *m/z* (relative intensity) 476 (14, M^+), 398 (19), 365 (9), 290 (100), 237 (90).

Synthesis of 3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione (4a) by Chromic Oxidation. A. 3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one (**3a**, 1 g) in acetone (75 mL) was oxidized with Jones reagent (0.90 mL). After 30 min at 25 °C, the reaction product was recovered by extraction with dichloromethane and chromatographed to yield **4a** [(390 mg) mp 205–206 °C; $[\alpha]^{21}_D$ +69°] identical with that obtained above (IR, NMR, and mass spectrum).

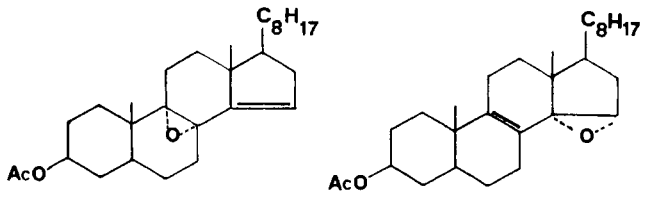
B. 3β-Acetoxy-5α-cholesta-8,14-diene (1, 500 mg) in acetone (45 mL) was oxidized with Jones reagent (1.5 mL) at 25 °C for 30 min to yield after chromatography compound **4a** (160 mg) identical with that obtained above (mp, IR, NMR, and mass spectrum).

C. 3β-Acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one (**2**, 500 mg) in acetone (45 mL) was oxidized with Jones reagent (1.10 mL) at 25 °C for 30 min to afford **4a** (165 mg) identical with that obtained above (mp, NMR, IR, and mass spectrum).

3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione-*12,12,16,16-d*$_4$ (4c) and 3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione-*16,16-d*$_2$ (4d). The acetate **4a** (100 mg) was heated to reflux in methanol-*d* (12 mL) under nitrogen. Sodium methoxide (100 mg) was added and heating under reflux continued overnight. The methanol-*d* was

(6) Bergmann, W.; McLean, M. J. *Chem. Rev.* **1941**, *28*, 367.
(7) Bowden, K.; Heilbron, I. M.; Jones, E. H. R.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39.

Chart II



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again removed by distillation and the product taken up in anhydrous dichloromethane (10 mL) and washed with deuterium oxide (3 × 2 mL). Drying and concentration yielded a crude product (98 mg) which was acetylated with acetic anhydride in pyridine to afford the acetate **4c** (80 mg): mp 205–206 °C; ^{1}H NMR δ 1.06 (s, 3 H, 18-CH_3), 1.12 (s, 3 H, 19-CH_3), 2.00 (s, 3 H, CH_3COO), 2.00–2.30 (overlapping, 2 H, 1β- and 7β-H), 3.32 (s, 1 H, OH), 4.70 (m, 1 H, 3α-H); mass spectrum, m/z 492 (M^+).

The dideuterated compound **4d** was obtained by oxidation of the dideuterated compound **3d** with Jones reagent. **4d** shows the following: mp 205–206 °C (methanol); ^{1}H NMR δ 1.06 (s, 3 H, 18-CH_3), 1.12 (s, 3 H, 1-CH_3), 2.00 (s, 3 H, CH_3COO), 2.03–2.30 (overlapping, 3 H, 1β-, 7β-, 12α-H), 2.71 (d, 1 H, 12β-H, J = 18 Hz); mass spectrum, m/z 490 (M^+).

Synthesis of 3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-15-one (3a, (Scheme I). 3β-Acetoxy-5α-cholesta-8,14-diene (**1**, 1.1 g) dissolved in diethyl ether (10 mL) was added to a solution of osmium tetraoxide (1 g) in diethyl ether (50 mL) containing pyridine (5 mL), and the mixture was allowed to stand at room temperature in the dark for 72 h. The base was eliminated by washing with dilute hydrochloric acid, and the diethyl ether–dichloromethane extract was shaken with potassium hydroxide (3 g) and D-mannitol (3 g) in water (30 mL). The product was isolated with the usual washing and drying procedures. After chromatography the product was crystallized from methanol to afford 3β-acetoxy-5α-cholest-8-ene-14α,15α-diol (**6**, 700 mg): mp 138–139 °C (hexane); $[\alpha]^{20}_D$ +29°; ^{1}H NMR δ 0.73 (s, 3 H, 18-CH_3; calcd^{3,4} 0.717), 1.01 (s, 3 H, 19-CH_3; calcd^{3,4} 0.958), 2.02 (s, 3 H, CH_3COO), 2.72 (d, 1 H, 15α-OH, J = 12 Hz), 4.10 (m, 1 H, 15β-H), 4.70 (m, 1 H, 3α-H); mass spectrum, m/z (relative intensity) 460 (3, M^+), 442 (20), 427 (5), 382 (4), 367 (50), 349 (9), 311 (40), 275 (100).

Anal. Calcd for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found: C, 75.41; H, 10.32.

The unsaturated diol **6** (480 mg) dissolved in diethyl ether was treated with *m*-chloroperbenzoic acid (400 mg) in diethyl ether (10 mL) at room temperature for 3 h. The usual workup and crystallization from methanol afforded 3β-acetoxy-8α,9α-epoxy-5α-cholestane-14α,15α-diol (**7**, 400 mg): mp 149–150 °C; $[\alpha]^{22}_D$ +16°; ^{1}H NMR δ 0.76 (s, 3 H, 18-CH_3; calcd^{3,4} 0.832), 1.06 (s, 3 H, 19-CH_3; calcd^{3,4} 1.066), 2.00 (s, 3 H, CH_3COO), 2.82 (d, 1 H, 15α-OH, J = 12 Hz), 3.75 (s, 1 H, 14α-OH), 4.10 (m, 1 H, 15β-H), 4.65 (m, 1 H, 3α-H); mass spectrum, m/z (relative intensity) 476 (2, M^+), 458 (4), 440 (6), 345 (8), 290 (18), 248 (25), 237 (100), 223 (88), 211 (50).

Anal. Calcd for $C_{29}H_{48}O_5$: C, 73.06; H, 10.15. Found: C, 73.10; H, 10.20.

Compound **7** (400 mg) dissolved in pyridine (2 mL) was treated with chromium trioxide (250 mg) and pyridine (8 mL) at room temperature. The usual workup afforded 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestan-15-one (**3a**, 380 mg, mp 143–44 °C; $[\alpha]^{20}_D$ +80°) with physical and spectroscopic properties identical with those of the compound described above.

Synthesis of 3β-Acetoxy-8α,9α-epoxy-9α-hydroxy-5α-cholestan-15-one (5). A solution of 3β-acetoxy-5α-cholest-8(14)-ene-9α,15α-diol (**8**,[1c] 500 mg) in diethyl ether (35 mL) was added to a stirred solution of *m*-chloroperbenzoic acid (250 mg) in diethyl ether (5 mL). The mixture was stirred for 2 h, and then the organic layer was washed, dried, and evaporated to give a solid residue which was crystallized from diisopropyl ether to afford 3β-acetoxy-8α,14α-epoxy-5α-cholestane-9α,15α-diol (**9**, 400 mg): mp 154–155 °C; $[\alpha]^{21}_D$ +50°; ^{1}H NMR δ 0.94 (2 s, 6 H, 18- and 19-CH_3), 2.00 (s, 3 H, CH_3COO), 4.30 (m, 1 H, 15β-H), 4.70 (m, 1 H, 3α-H); mass spectrum, m/z (relative intensity) 461 (1, M^+ – CH_3), 416 (1), 380 (3), 345 (2), 275 (3), 235 (5), 209 (100).

Anal. Calcd for $C_{29}H_{48}O_5$: C, 73.06; H, 10.15. Found: C, 73.10; H, 9.61.

Epoxy diol **9** (200 mg) in pyridine (2 mL) was oxidized with chromium trioxide (100 mg) in pyridine to afford after the usual workup 3β-acetoxy-8α,14α-epoxy-9α-hydroxy-5α-cholestan-15-one (**5**, 170 mg): mp 154–156 °C (diisopropyl ether); $[\alpha]^{20}_D$ +106°; ^{1}H NMR δ 0.94 (s, 3 H, 19-CH_3; calcd^{3,4} 0.960), 1.00 (s, 3 H, 18-CH_3; calcd^{3,4} 1.002); mass spectrum, m/z (relative intensity) 474 (33, M^+), 456 (17), 396 (45), 343 (17), 290 (75), 246 (100), 225 (66).

Anal. Calcd for $C_{29}H_{46}O_5$: C, 73.37; H, 9.76. Found: C, 73.45; H, 10.00.

Synthesis of 3β-Acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione (4a, Scheme II). A solution of 3β-acetoxy-5α-cholesta-8(14),9(11)-dien-15α-ol (**10**,[1c] 370 mg) in pyridine (20 mL) and hematoporphyrin (10 mg) was irradiated with a single photospot flood lamp under a fine stream of oxygen for 10 min. A bath temperature of 10–20 °C was maintained throughout. The usual workup followed by chromatography afforded 3β-acetoxy-11α,14α-epidioxy-5α-cholest-8-en-15α-ol (**11**, 250 mg): glass; ^{1}H NMR δ 0.70 (s, 3 H), 0.93 (s, 3 H), 2.00 (s, 3 H, CH_3COO), 4.50–4.70 (overlapping, 3 H, 3α-, 11β-, and 15β-H); mass spectrum, m/z (relative intensity) 474 (8, M^+), 427 (8), 387 (8), 329 (8), 275 (100), 265 (31).

Anal. Calcd for $C_{29}H_{46}O_5$: C, 73.37; H, 9.76. Found: C, 73.50; H, 9.60.

The peroxide **11** (100 mg) dissolved in ethanol (6 mL) containing pyridine (15 μL) was hydrogenated over 10% palladium on carbon (30 mg). After 2 h, 1 mol of hydrogen had been absorbed and hydrogen uptake ceased. Concentration of the filtered reaction mixture under reduced pressure afforded 3β-acetoxy-5α-cholest-8-ene-11α,14α,15α-triol (**12**, 75 mg): mp 155–157 °C (methanol); $[\alpha]^{20}_D$ +70°; ^{1}H NMR δ 0.65 (s, 3 H, 18-CH_3; calcd^{3,4} 0.742), 0.93 (s, 3 H, 19-CH_3; calcd^{3,4} 1.075), 2.00 (s, 3 H, CH_3COO), 4.20–4.40 (overlapping, 2 H, 11β- and 15β-H), 4.70 (m, 1 H, 3α-H); mass spectrum, m/z (relative intensity) 458 (31, $M^+ - H_2O$), 398 (10), 365 (10), 327 (50), 290 (100), 260 (30), 213 (58).

Anal. Calcd for $C_{29}H_{48}O_5$: C, 73.06; H, 10.15. Found: C, 73.41; H, 10.43.

The triol **12** (70 mg) dissolved in 1:1 dichloromethane–diethyl ether (10 mL) was treated with *m*-chloroperbenzoic acid (40 mg) in the presence of 0.5 M aqueous sodium bicarbonate (10 mL). After 2 h the organic layer was washed with water, dried, and evaporated to give a solid residue which was crystallized to afford 3β-acetoxy-8α,9α-epoxy-5α-cholestane-11α,14α,15α-triol (**13**, 50 mg): mp 150–151 °C (from diisopropyl ether); $[\alpha]^{21}_D$ +14°; ^{1}H NMR δ 0.80 (s, 3 H, 1-CH_3; calcd^{3,4} 0.857), 1.13 (s, 3 H, 19-CH_3; calcd^{3,4} 1.183), 2.01 (s, 3 H, CH_3COO), 4.20–4.30 (overlapping, 2 H, 11β- and 15β-H), 4.70 (m, 1 H, 3α-H); mass spectrum, m/z 492 (M^+).

Anal. Calcd for $C_{29}H_{48}O_6$: C, 70.69; H, 9.82. Found: C, 70.80; H, 10.00.

Compound **13** (100 mg) in pyridine (5 mL) was oxidized with chromium trioxide (100 mg) and pyridine (1 mL) to yield 3β-acetoxy-8α,9α-epoxy-14α-hydroxy-5α-cholestane-11,15-dione (**4a**, 90 mg; mp 205–206 °C; $[\alpha]^{21}_D$ +69°) with physical and spectroscopic properties identical with those of the compound described above.

Oxidation of 3β-Acetoxy-8α,9α-epoxy-5α-cholest-14-ene (14) and 3β-Acetoxy-14α,15α-epoxy-5α-cholest-8-ene (15) with Jones Reagent. Oxidation of **14** (500 mg) in acetone (45 mL) with Jones reagent (0.28 mL) at 10 °C for 1 min affords 3β-acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one (**2**, 380 mg; mp 194–195 °C; $[\alpha]^{20}_D$ +153°) with physical and spectroscopic properties identical with those reported previously.[1c] Similar oxidation of **15** (500 mg) afforded **2** (360 mg) with same chemicophysical properties.

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