1a. Purification by preparative TLC yielded 100 mg of aldehyde 6 and 7.7 mg of ketone 8.

Aldehyde 6: $C_{20}H_{26}O_7$; oil; IR (film) ν_{max} 2860 and 2715 (aldehyde C-H), 1765 (γ-lactone), 1720 (aldehyde), 1670 and 1650 cm^{-1} (double bonds); mass spectrum, *m/e* 378 (M^+), 349 (M - CHO), 346 (M - CH_3OH), 335 [M - $(CH_3)_2CH$], 332 (M - C_2H_4O), 308 [M - $(CH_3)_2C{=}C{=}O$], 276 [M - CH_3OH - $(CH_3)_2C{=}C{=}O$], 258 (M - CH_3OH - isobutyric acid), 71 [$(CH_3)_2CHC{\equiv}O^+$, base peak], 43 ($CH_3C{\equiv}O^+$).

Ketone 8: $C_{20}H_{26}O_7$; oil; IR (film) ν_{max} 1750 (γ-lactone), 1735 (ester), 1720 (ketone), 1650 cm^{-1} (double bond); mass spectrum, *m/e* 378 (M^+), 346 (M - CH_3OH), 332 (M - 46), 321 (M - 57), 294 (M - 84), 276 [M - CH_3OH - $(CH_3)_2C{=}C{=}O$], 258 (M - CH_3OH - isobutyric acid), 71 [$(CH_3)_2CHC{\equiv}O^+$, base peak], 43 ($CH_3C{\equiv}O^+$).

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Registry No. **1a**, 74562-62-2; **1b**, 74562-63-3; **1c**, 74562-64-4; **1d**, 74562-65-5; **2a**, 74562-66-6; **2c**, 74577-77-8; **2d**, 74562-67-7; **3**, 67927-54-2; **4**, 67927-56-4; **5**, 74562-68-8; **6**, 74562-69-9; **7**, 74577-78-9; **8**, 74577-79-0; **9**, 74562-70-2; **10**, 74562-71-3.

Inhibitors of Sterol Biosynthesis. Synthesis of 9α-Fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one and Related Compounds[1]

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9α-Fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one has been prepared in 90% yield by treatment of 3β,9α-dihydroxy-5α-cholest-8(14)-en-15-one with HF-pyridine. These two compounds are potent inhibitors of sterol biosynthesis in animal cells in culture and the former compound has significant hypocholesterolemic action in animals. The latter compound was prepared in 78% yield by treatment of the $\Delta^{8,14}$-ethyl enol ether derivative of 3β-(benzoyloxy)-5α-cholest-8(14)-en-15-one with perchloryl fluoride and in 86% yield by hydrolysis of 3β-(benzoyloxy)-9α-hydroxy-5α-cholest-8(14)-en-15-one. The latter 9α-hydroxy ester was prepared by oxidation of the $\Delta^{8(14)}$-ethyl enol ether of 3β-(benzoyloxy)-5α-cholest-8(14)-en-15-one with either perchloryl fluoride or with *m*-chloroperbenzoic acid or by oxidation of 3β-(benzoyloxy)-5α-cholesta-8,14-diene with Jones reagent. 9α-Fluoro-5α-cholest-8(14)-ene-3,15-dione and 9α-hydroxy-5α-cholest-8(14)-ene-3,15-dione were prepared in high yield by oxidation of the corresponding 3β-hydroxysterols with pyridinium chlorochromate.

3β-Hydroxy-5α-cholest-8(14)-en-15-one (1) (Scheme I) is a potent inhibitor of sterol biosynthesis in L cells and in primary cultures of fetal mouse liver cells.[2,3] Moreover, this compound and a number of its derivatives have been shown to have significant hypocholesterolemic activity upon oral or subcutaneous administration to animals.[4-7]

Stimulated by these findings we sought the preparation of the 9α-fluoro derivative of 1. Our initial efforts toward this goal concentrated on the attempted 9α-fluorination of an enol ether of the α,β-unsaturated $\Delta^{8(14)}$-15-one derivative. Electrophilic fluorination by perchloryl fluoride to form a carbon-fluorine bond has found extensive use.[8,9] While treatment of enamines of Δ^4-3-ketosteroids with perchloryl fluoride has been reported to give products of mono- and difluorination at carbon atom 4,[10-13] the application of the same reaction to enol ethers and enol ethers of Δ^4-3-ketosteroids has been reported to give 6-fluorinated derivatives.[13-15] Accordingly, we sought to adopt the fluorination of the enol ethers of the Δ^4-3-ketosteroids to the case of the enol ether of $\Delta^{8(14)}$-15-ketosteroids. The ethyl enol ether (3) of 3β-(benzoyloxy)-5α-cholest-8(14)-en-15-one (2) and the enol ether (4) of 3β-hydroxy-5α-cholest-8(14)-en-15-one (1) were prepared in high yields by treatment of 2 and 1 with triethyl orthoformate and an acid catalyst, an adaptation of procedures described previously for the preparation of enol ethers of Δ^4-3-ketosteroids.[16,17] Treatment of 3 and 4 with perchloryl fluoride at -35 to -40 °C did not give the desired 9α-fluoro-$\Delta^{8(14)}$-15-ones as significant products but gave as the major products the corresponding 9α-hydroxy-$\Delta^{8(14)}$-15-one com-

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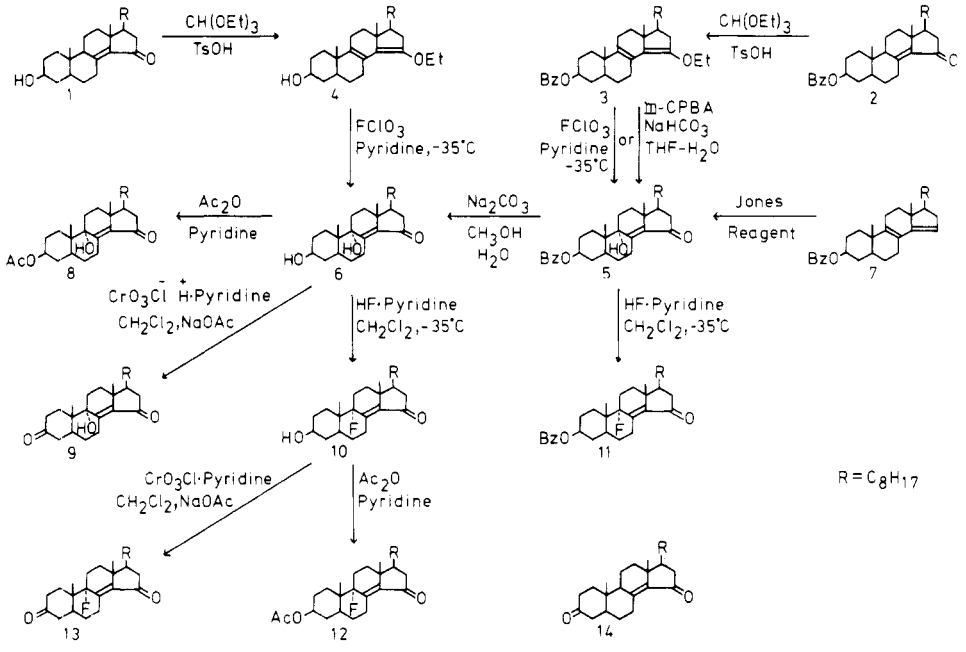
Scheme I. Chemical Syntheses of Various 9α-Hydroxy and 9α-Fluoro Derivatives of $\Delta^{8(14)}$-15-Ketosterols



pounds **5** and **6**, respectively. **5** was shown to be identical with the same compound prepared by treatment of **3** with *m*-chloroperbenzoic acid[18] and also identical with **5** prepared by Jones oxidation of 3β-(benzoyloxy)-5α-cholesta-8,14-diene (**7**).[19]

5α-Cholest-8(14)-ene-3β,9α-diol (**6**) was also prepared, in 87% yield, by alkaline hydrolysis of its benzoate ester **5**. **6**, prepared in this fashion, was found to be identical with **6** prepared directly by perchloryl fluoride treatment of 15-ethyl-5α-cholesta-8,14-dien-3β-ol **4**. **6** was further characterized by its conversion, in 86% yield, to its corresponding 3β-acetate derivative (**8**)[21] and by its conversion, in 89% yield, to its corresponding 3-keto derivative (**9**) by oxidation with pyridinium chlorochromate.[21]

The observed course of the reactions with the perchloryl fluoride (i.e., oxidation at C-9 rather than fluorination) is not without precedent. For example, Osawa and Neeman[15] have observed that treatment of the enol acetate derivative of testosterone acetate with perchloryl fluoride gave not only the expected 6α-fluoro and 6β-fluoro derivatives of testosterone acetate but also the corresponding 6α-hydroxy and 6β-hydroxy compounds. The same workers[22] also reported that perchloryl fluoride treatment of indene gave a mixture of both fluorinated and oxygenated products. Perchloryl fluoride, in the presence of aluminum chloride, has also been reported to give perchloryl derivatives upon reaction with a variety of aromatics.[23] Perchlorylbenzene gave phenol upon alkaline hydrolysis.[23] While the mechanism(s) involved in the observed formation of the 9α-hydroxysteroids upon treatment of the $\Delta^{8,14}$-15-enol ethers was not established, the possibilities of an electrophilic hydroxylation or of the formation of an intermediary 9-perchloryl derivative which undergoes subsequent hydrolysis appear worthy of consideration.

While treatment of the ethyl enol ether derivative of either **1** or **2** with perchloryl fluoride did not give the corresponding 9α-fluoro-$\Delta^{8(14)}$-15-keto compounds directly, the availability of the 9α-hydroxy compounds provided the key precursors for the synthesis of the desired 9α-fluoro-$\Delta^{8(14)}$-15-keto compounds. By adaptation of the method of Ambles and Jacquesy[24] for the preparation of 5α-fluorosterols from the corresponding 5α-hydroxysterols, the syntheses of 9α-fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one (**10**) and 3β-(benzoyloxy)-9α-fluoro-5α-cholest-8(14)-en-15-one (**11**) from the corresponding 9α-hydroxysterols were effected in very high (~91%) yields.[25] **10** was further characterized by conversion to its 3β-acetoxy derivative (**12**) and by oxidation to give the corresponding 3,15-dione (**13**).

3β,9α-Dihydroxy-5α-cholest-8(14)-en-15-one (**6**), 9α-fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one (**10**), and 9α-fluoro-5α-cholest-8(14)-ene-3,15-dione (**13**) have been found to be potent inhibitors of sterol synthesis in L cells.[26] The concentrations required to cause a 50% inhibition of the synthesis of digitonin-precipitable sterols from labeled acetate were comparable to those required to cause a 50% reduction in the levels of the regulatory enzyme HMG-CoA reductase in the same cells. Moreover, **10** has been found to have marked hypocholesterolemic activity upon oral administration to normal rats.[27]

Experimental Section

General Methods and Materials. Procedures and conditions for the recording of melting points (mp), infrared (IR) spectra,

(18) An adaptation of the method of Kirk and Miles (*J. Chem. Soc. D*, 518 (1970)) for the preparation of 6β-hydroxyandrost-4-ene-3,17-dione from the enol acetate of androst-4-ene-3,17-dione.

(19) An adaptation of the recently published synthesis of 3β-acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one (**8**) by Anastasia, Fiecchi, and Scala.[20]

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(21) The melting point and UV data on **8** and **9** compared favorably with those reported for the same compounds prepared by Jones oxidation of 3β-acetoxy-5α-cholesta-8,14-diene and 5α-cholesta-8,14-dien-3β-ol, respectively.[20]

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ultraviolet (UV) spectra (ethanol solvent), and low-resolution mass spectral analyses and for thin-layer chromatography (TLC) have been detailed previously.[28] Proton magnetic resonance (^{1}H NMR) spectra were determined on a Varian EM-390 spectrometer at 90 MHz with tetramethylsilane (Me_4Si) as an internal standard. Peaks are reported as parts per million (δ) downfield from the Me_4Si standard. High-resolution mass spectra were recorded on a Varian CH-5 spectrometer (courtesy of Professor C. C. Sweeley). Medium-pressure liquid chromatography (medium-pressure LC; 60 psi) was performed on columns (100 × 2.5 cm) of silica gel (0.032–0.063 mm). Ordinary column chromatography employed silica gel (60–200 mesh) on, unless otherwise stated, columns which were 60 × 1.5 cm. Organic extracts of reaction mixtures were routinely washed with water, dried over anhydrous $MgSO_4$, and evaporated to dryness under reduced pressure.

3β-(Benzoyloxy)-5α-cholest-8(14)-en-15-one (**2**),[29-33] 5α-cholest-8(14)-ene-3,15-dione (**14**),[34] and 3β-hydroxy-5α-cholest-8(14)-en-15-one (**1**)[3,4] were prepared as described previously. 3β-(Benzoyloxy)-5α-cholesta-8,14-diene (**7**) was prepared by treatment of 5α-cholesta-8,14-dien-3β-ol with benzoyl chloride and pyridine. The latter sterol (mp 120.5 °C [lit. mp 116–117 °C,[35] 113.5–114.5 °C,[36] and 119–120 °C[37]] was prepared from 7-dehydrocholesterol by the method of Fieser and Ourisson.[35] Jones reagent was prepared as described by Djerassi et al.[38] Perchloryl fluoride was purchased from Ozark-Mahoning Company (Tulsa, OK). HF–pyridine (70% HF in pyridine), *m*-chloroperbenzoic acid, and pyridinium chlorochromate were obtained from Aldrich Chemical Company (Milwaukee, WI).

3β-(Benzoyloxy)-15-ethoxy-5α-cholesta-8,14-diene (3) from 3β-(Benzoyloxy)-5α-cholest-8(14)-en-15-one (2). To **2** (6.00 g, 11.9 mmol) in dry dioxane (60 mL) was added *p*-toluenesulfonic acid monohydrate (480 mg) and triethyl orthoformate (12 mL) and the mixture was stirred at 25 °C for 24 h. Water (400 mL) containing triethylamine (15 mL) was slowly added and the resulting mixture was poured into ether (1000 mL). The crude brown product (~95% pure on TLC) was subjected to silica gel column chromatography (solvent, a mixture of triethylamine (2%) and hexane (20%) in toluene) and recrystallization three times from acetone–water to give **3** (5.32 g, 84% yield): mp 164.5–166.0 °C; IR ν_{max} 1720, 1630, 1285, 1122, 722 cm^{-1}; ^{1}H NMR 0.85 (s, 3 H, C-19-CH_3), 1.01 (s, 3 H, C-19-CH_3), 3.80 (q, 2 H, ethoxy), 4.94 (m, 1 H, C-3-H), 7.77 (m, 5 H, aromatic); mass spectrum, *m/z* 532 (100%, M), 517 (51%, M – CH_3), 487 (2%, M – OCH_2CH_3), 419 (7%, M – side chain), 410 (9%, M – benzoic acid), 395 (23%, M – CH_3 – benzoic acid), 297 (3%, M – side chain – benzoic acid), 251 (9%); high-resolution mass spectrum, 532.3889 (calcd for $C_{36}H_{52}O_3$ 532.3917); UV λ_{max} 254 nm (ϵ 18500), 232 (20300). The product showed a single component on TLC in two solvent systems.

15-Ethoxy-5α-cholesta-8,14-dien-3β-ol (4) from 3β-Hydroxy-5α-cholest-8(14)-en-15-one (1). **1** (6.00 g, 15.0 mmol) in dry dioxane (60 mL) was treated with *p*-toluenesulfonic acid monohydrate (480 mg) and triethyl orthoformate (12 mL) as described above, and the reaction mixture was processed as described above. Silica gel column chromatography gave **4** (5.26 g, 82% yield) as a light yellow glass which resisted all attempts at crystallization: IR ν_{max} 3440, 1645, 1060 cm^{-1}; ^{1}H NMR 0.82 (s, 3 H, C-19-CH_3), 0.97 (s, 3 H, C-18-CH_3), 3.62 (m, 1 H, C-3-H), 3.80 (q, 2 H, ethoxy); mass spectrum, *m/z* 428 (92%, M), 413 (100%, M – CH_3), 398 (10%, M – CH_3 – CH_3), 395 (5%, M – CH_3 – H_2O), 382 (7%, M – OCH_2CH_3), 315 (22%, M – side chain), 285 (5%, M – CH_3 – side chain), 251 (10%); high-resolution mass spectrum, 428.3649 (calcd for $C_{29}H_{48}O_2$ 428.3655); UV λ_{max} 254 nm (ϵ 15300). The product showed a single component on TLC in two solvent systems.

3β-(Benzoyloxy)-9α-hydroxy-5α-cholest-8(14)-en-15-one (5) by Treatment of 3β-(Benzoyloxy)-15-ethoxy-5α-cholesta-8,14-diene (3) with Perchloryl Fluoride. **3** (4.00 g, 7.5 mmol) in dry pyridine (75 mL) was cooled to −35 to −40 °C in a dry ice–acetone bath and a slow stream of perchloryl fluoride was bubbled through the stirred solution for 20 min. After nitrogen was bubbled through the solution for 5 min, the mixture was poured into water and extracted with ether (1000 mL) containing CH_2Cl_2 (10%). The extract was washed successively with water, cold 5% HCl, 5% $NaHCO_3$, and water. The crude product, a light yellow solid, showed a major (~70%) component with an R_f of 0.13 upon TLC (solvent, 10% ethyl acetate in hexane). Silica gel column (100 × 2.0 cm) chromatography (30% ethyl acetate in hexane) and recrystallization from 10% ethyl acetate in hexane at −15 °C gave **5** (1.19 g, 30% yield): mp 202.5–203.5 °C; IR ν_{max} 3490 (sharp), 1720, 1630, 1285, 1122, 722 cm^{-1}; ^{1}H NMR 0.87 (s, 3 H, C-19-CH_3), 0.98 (s, 3 H, C-18-CH_3), 4.00 (m, 1 H, C-7β-H), 4.98 (m, 1 H, C-3-H), 7.76 (m, 5 H, aromatic); mass spectrum, *m/z* 520 (18%, M), 502 (100%, M – H_2O), 487 (12%, M – CH_3 – H_2O), 486 (4%), 460 (13%), 389 (6%, M – H_2O – side chain), 380 (28%, M – H_2O – benzoic acid), 365 (30%, M – CH_3 – H_2O – benzoic acid), 335 (34%), 267 (31%, M – H_2O – side chain – benzoic acid), 213 (37%); high-resolution mass spectrum, 520.3556 (calcd for $C_{34}H_{48}O_4$ 520.3552); high-resolution mass spectrum on ion at *m/z* 502, 502.3445 (calcd for $C_{34}H_{46}O_3$ 502.3447); UV λ_{max} 254 nm (ϵ 14000), 232 (17300). Anal. Calcd for $C_{34}H_{48}O_4$: C, 77.16; H, 9.06. Found: C, 78.27; H, 9.39. The product showed a single component on TLC in two solvent systems. **Caution**: *The reactions were repeated several times as described above. However, on one occasion the reastion was accompanied by a very violent explosion Accordingly, we do not recommend the use of perchloryl fluoride for the preparation of* **5** *or* **6**.

3β-(Benzoyloxy)-9α-hydroxy-5α-cholest-8(14)-en-15-one (5) by Treatment of 3β-(Benzoyloxy)-15-ethoxy-5α-cholesta-8,14-diene (3) with *m*-Chloroperbenzoic Acid. To **3** (400 mg, 0.75 mmol) in a mixture of dioxane (20 mL) and a saturated solution of $NaHCO_3$ (2 mL) were added, with stirring at room temperature, a solution of *m*-chloroperbenzoic acid (130 mg) in a mixture of dioxane (20 mL) and a saturated solution of $NaHCO_3$ (2 mL) slowly over 2 h. The reaction mixture was poured into water and extracted with ether (1000 mL) containing $CHCl_3$ (20%). The crude product, a light yellow solid, showed a major (~85%) component with an R_f of 0.13 upon TLC (10% ethyl acetate in hexane). Silica gel column (100 × 2.0 cm) chromatography (5% ether in toluene) and recrystallization from 10% ethyl acetate in hexane at −15 °C gave **5** (306 mg, 78% yield): mp 202.5–203.5 °C; UV λ_{max} 254 nm (ϵ 14100), 232 (17300). The product showed a single component on TLC in three solvent systems with the same chromatographic mobility and IR, ^{1}H NMR and mass spectra as those of **5** prepared from **3** by using perchloryl fluoride.

3β-(Benzoyloxy)-9α-hydroxy-5α-cholest-8(14)-en-15-one (5) by Jones Oxidation of 3β-(Benzoyloxy)-5α-cholesta-8,14-diene (7). To **7** (3.50 g, 7.16 mmol) in benzene (100 mL) was added acetone (250 mL). After the solution was cooled to 10 °C, Jones reagent (5 mL) was slowly added over 45 min to the stirred solution. The mixture was poured into 5% NaCl and extracted with ether containing CH_2Cl_2 (5%). The combined extracts were successively washed with water, 5% $NaHCO_3$, and water. Analysis by TLC indicated one major (~85%) product. Silica gel column chromatography (4% ether in toluene) and recrystallization from 10% ethyl acetate in hexane at −15 °C gave **5** (3.11 g, 83% yield): mp 202.5–203.5 °C; UV λ_{max} 254 nm (ϵ 14000), 232 (17200). The compound had the same IR, ^{1}H NMR, and mass spectra and chromatographic mobility on TLC as those of **5** prepared by the two methods outlined above.

3β,9α-Dihydroxy-5α-cholest-8(14)-en-15-one (6) by Treatment of 15-Ethoxy-5α-cholesta-8,14-dien-3β-ol (4) with Per-

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chloryl Fluoride. 4 (4.00 g, 9.3 mmol) in dry pyridine (75 mL) was treated with perchloryl fluoride in the same manner as described above for the 3β-benzoate ester. TLC analysis (50% ethyl acetate in hexane) of the noncrystalline yellow residue obtained upon workup of the reaction mixture indicated one major component (~70%) with an R_f of 0.25. The crude product was subjected to medium-pressure LC on a silica gel column (40% ethyl acetate in hexane) and recrystallization from acetone–water to give **6** (1.34 g, 35% yield): mp 214.5–215.5 °C; IR ν_{max} 3470, 1700, 1621, 1095, 1045, 1023 cm^{-1}; ^{1}H NMR 0.80 (s, 3 H, C-19-CH_3), 0.97 (s, 3 H, C-18-CH_3), 3.64 (m, 1 H, C-3-H), 3.98 (m, 1 H, C-7β-H); mass spectrum, *m/z* 416 (14%, M), 401 (3%, M – CH_3), 398 (100%, M – H_2O), 383 (20%, M – H_2O – CH_3), 380 (10%, M – H_2O – H_2O), 365 (26%, M – CH_3 – H_2O – H_2O), 356 (18%), 290 (10%), 285 (27%, M – H_2O – side chain), 267 (17%, M – H_2O – H_2O – side chain), 258 (30%), 231 (42%), 177 (27%); high-resolution mass spectrum, 416.3288 (calcd for $C_{27}H_{44}O_3$ 416.3290); high-resolution mass spectrum on ion at *m/z* 398, 398.3185 (calcd for $C_{27}H_{42}O_2$ 398.3185); UV λ_{max} 254 nm (ε 13 500). Anal. Calcd for $C_{27}H_{44}O_3$: C, 77.84; H, 10.64. Found: C, 77.70; H, 10.55. The product showed a single component on TLC in two solvent systems. **Caution**: *These reactions were repeated several times as described above. However, on one occasion the reaction was accompanied by a very violent explosion. Accordingly, we do not recommend the use of perchloryl fluoride for the preparation of 5 or 6.*

3β,9α-Dihydroxy-5α-cholest-8(14)-en-15-one (6) from 3β-(Benzoyloxy)-9α-hydroxy-5α-cholest-8(14)-en-15-one (5). To **5** (2.00 g, 3.84 mmol) in methanol (665 mL) was added a saturated aqueous solution of Na_2CO_3 (35 mL). After the mixture was stirred for 36 h at 35 °C, water was added and, after the mixture was cooled, the resulting precipitate was collected, dried, and subjected to silica gel column chromatography (40% ethyl acetate in toluene) and recrystallization from acetone–water to give **6** (1.37 g, 86% yield), mp 214.5–215.5 °C. The IR, ^{1}H NMR, and mass spectra and chromatographic properties were identical with those obtained for **6** prepared directly from **4**.

9α-Hydroxy-5α-cholest-8(14)-ene-3,15-dione (9) from 3β,9α-Dihydroxy-5α-cholest-8(14)-en-15-one (6). To **6** (250 mg, 0.60 mmol) in CH_2Cl_2 (20 mL) were added pyridinium chlorochromate (750 mg) and sodium acetate (250 mg). After being stirred for 30 min, the mixture was poured into a saturated NaCl solution and thoroughly extracted with CH_2Cl_2. The crude product was subjected to silica gel column chromatography (25% ethyl acetate in toluene) and recrystallization from acetone–water to give **9** (222 mg, 89% yield): 204.0–205.5 °C [lit.[20] mp 204–205 °C]; IR ν_{max} 3435, 1728, 1698, 1628, 1229 cm^{-1}; ^{1}H NMR 1.00 (s, 3 H, C-18-CH_3, calcd δ 1.01), 1.05 (s, 3 H, C-19-CH_3, calcd δ 1.04), 3.96 (m, 1 H, C-7β-H); mass spectrum, *m/z* 414 (8%, M), 396 (100%, M – H_2O), 381 (32%, M – CH_3 – H_2O), 354 (20%), 283 (38%, M – H_2O – side chain), 270 (70%); UV λ_{max} 254 nm (ε 12 600) [lit.[20] λ_{max} 254 nm (ε 12 600)]. The product showed a single component on TLC in three solvent systems.

3β-Acetoxy-9α-hydroxy-5α-cholest-8(14)-en-15-one (8) from 3β,9α-Dihydroxy-5α-cholest-8(14)-en-15-one (6). To **6** (500 mg, 1.20 mmol) in dry pyridine (15 mL) was added acetic anhydride (15 mL). After standing at room temperature for 24 h under nitrogen, the reaction mixture was processed in a standard fashion. The crude product, a white solid (502 mg), was recrystallized twice from acetone–water to give **8** (476 mg, 86% yield): mp 194.0–195.5 °C [lit.[20] mp 194–195 °C]; IR ν_{max} 3475 (sharp), 1739, 1694, 1622, 1380, 1250, 1038 cm^{-1}; ^{1}H NMR 0.81 (s, 3 H, C-18-CH_3, calcd δ 0.82), 0.96 (s, 3 H, C-18-CH_3, calcd δ 0.97), 1.90 (s, 3 H, methyl of acetoxy), 3.96 (m, 1 H, C-7β-H), 4.86 (m, 1 H, C-3-H); mass spectrum, *m/z* 458 (21%, M), 440 (100%, M – H_2O), 425 (14%, M – CH_3 – H_2O), 398 (73%, M – CH_3COOH), 380 (M – H_2O – CH_3COOH), 365 (47%, M – CH_3 – H_2O – CH_3COOH), 345 (5%, M – side chain), 327 (14%, M – H_2O – side chain), 285 (17%, M – CH_3COOH – side chain), 207 (45%, M – H_2O – CH_3COOH – side chain); high-resolution mass spectrum, 458.3396 (calcd for $C_{29}H_{46}O_4$ 458.3396); UV λ_{max} 254 nm (ε 13 800) [lit.[20] 254 nm (ε 13 000)]. The product showed a single component on TLC in two solvent systems.

9α-Fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one (10) from 3β,9α-Dihydroxy-5α-cholest-8(14)-en-15-one (6). **6** (2.00 g, 4.80 mmol) in CH_2Cl_2 (30 mL) was slowly added to a cooled (–35 °C), stirred mixture of CH_2Cl_2 (20 mL) and HF–pyridine (20 mL). After being stirred for 30 min, the mixture was poured into water and thoroughly extracted with ether. Chromatography on a silica gel column (15% ethyl acetate in toluene) and recrystallization from acetone–water gave **10** (1.82 g, 90.5 % yield): mp 139.5–140.5 °C; IR ν_{max} 3480, 1710, 1630, 1232, 1098, 890 cm^{-1}; ^{1}H NMR 0.80 (s, 3 H, C-19-CH_3), 0.96 (s, 3 H, C-18-CH_3), 3.70 (m, 1 H, C-3-H), 3.90 (m, 1 H, C-7β-H); mass spectrum, *m/z* 418 (12%, M), 403 (3%, M – CH_3), 398 (100%, M – HF), 380 (8%, M – HF – H_2O), 365 (27%, M – HF – H_2O – CH_3), 356 (21%), 285 (35%, M – HF – side chain), 258 (27%), 243 (18%), 231 (41%); high-resolution mass spectrum, 418.3247 (calcd for $C_{27}H_{43}O_2F$ 418.3246); UV λ_{max} 248 nm (ε 13 600). The product showed a single component on TLC in three solvent systems with the same chromatographic behavior as that of its 9α-protio analogue (**1**).

3β-Acetoxy-9α-fluoro-5α-cholest-8(14)-en-15-one (12) from 9α-Fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one (10). **10** (200 mg, 0.48 mmol) was dissolved in a 1:1 mixture (30 mL) of acetic anhydride and pyridine. After standing at 25 °C for 2 h under nitrogen, the reaction mixture was processed in a standard fashion. The crude product was subjected to silica gel column chromatography (5% ether in toluene) and recrystallization from methanol–water to give **12** (191 mg, 87% yield): mp 162.5–163.0 °C; IR ν_{max} 1746, 1718, 1641, 1260, 1095, 1039 cm^{-1}; ^{1}H NMR 0.83 (s, 3 H, C-19-CH_3), 0.96 (s, 3 H, C-18-CH_3), 1.99 (s, 3 H, methyl of acetoxy), 3.95 (m, 1 H, C-7β-H), 4.70 (m, 1 H, C-3-H); mass spectrum, *m/z* 460 (1%, M), 440 (100%, M – HF), 425 (12%, M – HF – CH_3), 398 (17%), 380 (19%, M – HF – CH_3COOH), 365 (36%, M – CH_3 – HF – CH_3COOH), 327 (9%, M – HF – side chain), 273 (46%), 267 (29%, M – HF – CH_3COOH – side chain); high resolution mass spectrum, 460.3352 (calcd for $C_{29}H_{45}O_3F$ 460.3352); UV λ_{max} 248 nm (ε 13 700). The compound showed a single component on TLC in three solvent systems.

9α-Fluoro-5α-cholest-8(14)-ene-3,15-dione (13) from 9α-Fluoro-3β-hydroxy-5α-cholest-8(14)-en-15-one (10). To **10** (500 mg, 1.19 mmol) in CH_2Cl_2 (40 mL) were added sodium acetate (0.5 g) and pyridinium chlorochromate (1.5 g). After being stirred for 30 min, the mixture was poured into a saturated solution of NaCl and thoroughly extracted with CH_2Cl_2. Chromatography on a silica gel column (5% ethyl acetate in toluene) and recrystallization from acetone–water gave **13** (418 mg, 84% yield): mp 155.0–156.5 °C; IR ν_{max} 1722, 1708, 1630, 1220, 895 cm^{-1}; ^{1}H NMR 0.98 (s, 6 H, C-19-CH_3 and C-18-CH_3), 3.90 (m, 1 H, C-7β-H); mass spectrum, *m/z* 416 (5%, M), 401 (2%, M – CH_3), 396 (100%, M – HF), 381 (31%, M – HF – CH_3), 354 (19%), 283 (39%, M – HF – side chain), 256 (21%), 241 (22%), 229 (65%); high-resolution mass spectrum, 416.3090 (calcd for $C_{27}H_{41}O_2F$ 416.3090); UV λ_{max} 248 nm (ε 13 700). The product showed a single component on TLC in three solvent systems with the same chromatographic behavior as that of its 9α-protio analogue (**14**).

3β-(Benzoyloxy)-9α-fluoro-5α-cholest-8(14)-en-15-one (11) from 3β-(Benzoyloxy)-9α-hydroxy-5α-cholest-8(14)-en-15-one (5). **5** (1.00 g, 1.92 mmol) in CH_2Cl_2 (10 mL) was slowly added to a cooled (–35 °C) mixture of HF–pyridine (10 mL) and CH_2Cl_2 (10 mL). After being stirred for 30 min, the mixture was poured into water and thoroughly extracted with ether. Silica gel column chromatography (toluene) and recrystallization from acetone–water gave **11** (0.92 g, 91% yield): mp 152.5–153.5 °C; IR ν_{max} 1722, 1645, 1605, 1589, 1278, 1115, 1030, 722 cm^{-1}; ^{1}H NMR 0.84 (s, 3 H, C-19-CH_3), 0.94 (s, 3 H, C-18-CH_3), 3.96 (m, 1 H, C-7β-H), 4.93 (m, 1 H, C-3-H), 7.70 (m, 5 H, aromatic); mass spectrum, *m/z* 522 (4%, M), 502 (100%, M – HF), 487 (11%, M – CH_3 – HF), 460 (13%), 389 (6%, M – HF – side chain), 380 (24%, M – HF – benzoic acid), 367 (39%, M – HF – side chain – benzoic acid), 365 (30%), 335 (34%), 213 (37%); high-resolution mass spectrum, 522.3508 (calcd for $C_{34}H_{47}O_3F$ 522.3509); UV λ_{max} 248 nm (ε 14 100), 232 (17 100). The compound showed a single component on TLC in three solvent systems with the same chromatographic behavior as an authentic sample of its 9α-protio analogue (**2**).

Registry No. **1**, 50673-97-7; **2**, 7654-37-7; **3**, 74498-81-0; **4**, 73765-12-5; **5**, 74498-82-1; **6**, 73765-13-6; **7**, 74524-23-5; **8**, 72584-37-3; **9**, 72584-38-4; **10**, 73765-14-7; **11**, 74498-83-2; **12**, 74498-84-3; **13**, 73765-15-8; triethyl orthoformate, 122-51-0.