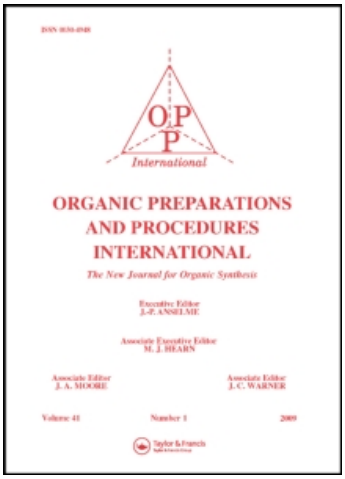

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REGIOSELECTTVE SYNIHESIS OF CHOLESTANE-3β,5α,6α-TRIOL-7-ONE 3-ACETATE AND EIGHT STEREOISOMERIC CHOLESTANE-3β,4,5α,6 AND OF 3β,5α,6,7-TETROL TRIACETATES

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REGIOSELECTIVE SYNTHESIS OF CHOLESTANE-3β,5α,6α-TRIOL-7-ONE 3-ACETATE AND EIGHT STEREOISOMERIC CHOLESTANE-3β,4,5α,6 AND OF 3β,5α,6,7-TETROL TRIACETATES

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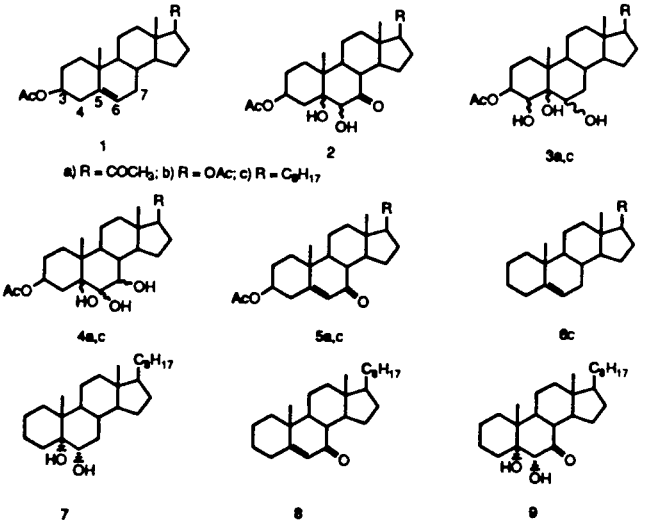
In a previous publication, the oxidation of various steroid-5-enes (1) with potassium permanganate in pyridine-water solution was reported.[1a] Although the structure of the major neutral product was established as 2, the configuration of the C5 and C6 hydroxyl groups was not determined. A second neutral product was tentatively assigned either structure 3a,c or 4a,c. Analogous oxidation of 5a,c also gave 2a,c. In a subsequent study,[2] steroid 6c was oxidized in the same manner to yield 7-9 as the major neutral products. This result, together with the 60 MHz PMR spectra of 2[1b] and of the acetates of 3a,c and 4a,c, suggested that 2-4 also had the trans AB ring juncture and the C5 and C6 hydroxyl groups were cis-α. In order to rigorously establish the stereochemistry of 2c and the structure and stereochemistry of 3c and 4c, nine 5α-cholestane-polyols were synthesized and their respective PMR spectra analyzed.[3]



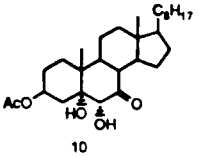
1 2 3a,c

a) R = $COCH_3$; b) R = OAc; c) R = C_8H_{17}

4a,c 5a,c 6c

7 8 9

Oxidation of the known[4] 5c with OsO_4 gave a 74% yield of 10. Analogous oxidation of a similar steroid olefin has been reported in the literature.[5]



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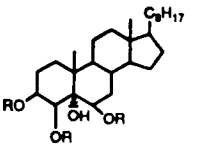
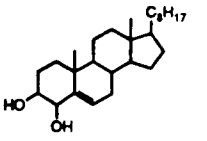


11

a) R = H; b) R = Ac



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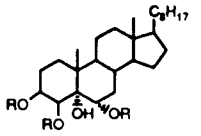
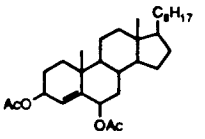
Compound 10 is identical to 2c and thus the permanganate pyridine–water oxidation of steroid-5-enes 1 gave as the major neutral product cis-5α,6α-diol-7-ones. Our next objective was the synthesis of the four isomeric cholestane-3β,4,5α,6-tetrol-3,4,6-triacetates. The known[6] 11a was acetylated to give the desired triacetate 11b. Tetrol 13a was prepared by OsO_4 oxidation of the known 12.[7] The tetrol then was acetylated to give the desired triacetate 13b in 72% yield. The next isomeric tetrol triacetate 15b was synthesized from the known 14.[8] The latter compound was oxidized with OsO_4 and gave 67% of the tetrol diacetate 15a, which then was acetylated at the C4 hydroxyl to yield 74% of the tetrol triacetate 15b. The stereochemistry of the new diol was assigned based on analogy to literature examples.[9] The last compound in the cholestane-3β,4,5α,6-tetrahydroxy series was 17b. It was obtained from the known 16b,[10] which was oxidized with OsO_4 and gave the tetrahydroxy 3,4-diacetate 17a. This compound was then directly acetylated and afforded the desired triacetate 17b in 69% overall yield. Our last objective was the synthesis of the four isomeric cholestane-3β-5α,6,7-tetrol-3,6,7-triacetates. Reaction of the known[10] 18 with OsO_4 gave the tetrol diacetate 19a which was acetylated to yield the tetrol triacetate 19b in 85% overall yield. Reduction of 10 with



13a R = H
b R = Ac



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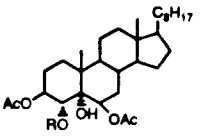
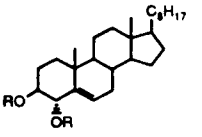
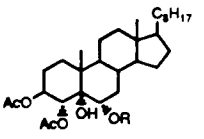


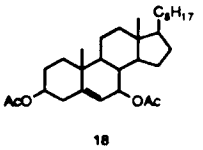
15a R = H
b R = Ac



16a R = H
b R = Ac



17a R = H
b R = Ac



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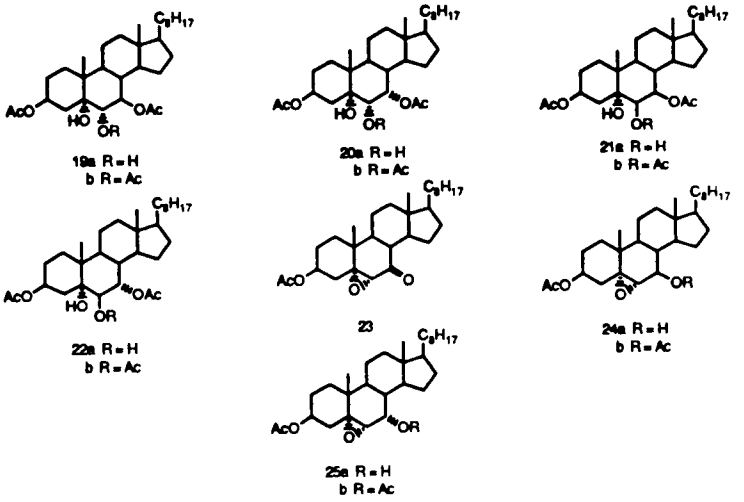
lithium tri(t-butoxy)aluminum hydride and subsequent acetylation of the intermediate alcohol afforded 20b in 61% overall yield. Reduction of the C7 ketone of the known[12] 23 with the above hydride, yielded the C7β alcohol 24a in 73% yield and the C7α alcohol[11] 25a in 15% yield. Both 24a and 25a were acetylated to give their respective diacetates 24b and 25b.[13]



The reaction of epoxide 24b with HIO_4 yielded 21a in 84% yield. Acetylation of 21a gave 21b.[13] The reaction of epoxide (25b) with HIO_4 gave 22a in 32% yield, which was then acetylated and afforded 22b.

EXPERIMENTAL SECTION

All solvents and reagents were of reagent grade quality and were used without further purification. Melting points were taken on a Thomas Hoover apparatus and were uncorrected. Microanalyses were performed by Baron Consulting Co., Orange, Connecticut, and Meade Laboratories, Amherst, Massachusetts. Thin-layer chromatography was performed on Analtech Silica Gel GF Uniplates. Baker's Analyzed Silica Gel powder (60-200 mesh) was used as is for column chromatography. Approximately 30 g of silica gel was used per g of material. Infrared spectra were taken using a Perkin-Elmer 337 or 247 IR spectrophotometer and KBr discs that contained about 3 mg of sample to 60 mg of KBr. Proton magnetic resonance spectra were obtained on a Varian Associates A60-A or a Bruker WH-270 spectrometer using a solution of sample in 99.8% $CDCl_3$ that contained tetramethylsilane (TMS) as an internal standard, unless stated otherwise. Spectra are reported as shifts in parts per million (ppm) downfield from TMS. Specific rotation measurements are recorded on a Perkin-Elmer 141 polarimeter operating at 589 nm. All measurements are made in a 10 cm microcell on $CHCl_3$ solutions unless stated otherwise.

General Procedure for Osmium Tetroxide Oxidation of Steroid Olefins.- OsO_4, (1.00 g, 3.94 mmol), was added to a stirred solution of 3.84 mmol of steroid olefin in 10.0 ml pyridine at room temperature. The solution was stirred until TLC indicated the disappearance of the olefin. A solution of 1.8 g of $NaHSO_3$ in 30.0 ml H_2O and 20.0 ml pyridine was then added in small portions and the resulting mixture stirred for another 20 hrs. Occasionally, the mixture was heated briefly on the steam bath. The mixture, which contained a water-soluble black osmium modification, was extracted

with 100 mL of CH_2Cl_2. The combined organic layer was then washed successively with 15% HCl solution, saturated $NaHCO_3$ solution, H_2O, brine and dried ($MgSO_4$).

General Procedure for Acetylation of Steroid Alcohols.- A solution of 1.37 mmol of sterol in 2.0 mL pyridine and 20.0 mL acetic anhydride is either stirred at ambient temperature or heated under reflux until TLC indicates a lack of sterol , then diluted with ice-H_2O and cooled to -5°. The crude product was isolated by filtration or by extractive workup using CH_2Cl_2.

Cholestane-3β,5α,6α-triol-7-one 3-acetate 10.- The solvent was evaporated to yield 1.85 (100%) of solid; homogeneous to TLC. Two recrystallizations from 45.0 mL of absolute CH_3OH gives 1.35 g (74%) of shiny plates; mp. 179-180°; mixture mp. 178.5-180.5° with an authentic sample[18]; $[\alpha]_D^{22°}$ = -28.7° (c = 2.38). IR (KBr): 3460, 3413, 1709, 1250 cm^{-1}. PMR: δ 0.67(18-CH_3), 1.29(19-CH_3), 2.0(s, 3H, acetate CH_3), 2.41(s, 1H, disappeared upon addition of D_2O), 3.86(d, J = 3.0Hz), 4.07(d, J = 3.5Hz) [The pair of doublets collapsed upon addition of D_2O and a one proton singlet appeared at 4.07 C6β-H], 4.75-5.35(bc, 1H, 3α-H).

Anal. Calcd. for $C_{29}H_{48}O_5$: C, 73.06; H, 10.10.
Found: C, 73.19; H, 10.31.

Cholestane-3β,4β,5α,6β-tetrol 3,4,6-triacetate 11b.- The crude solid was recrystallized twice from 95% alcohol and once from acetone; to yield 119.5 mg (15.5%); mp. 215-215.8°; $[\alpha]_D^{21°}$ = -47.5° (c = 1.77). IR (KBr): 3390, 1754, 1739, 1701, 1299-1198, 1026 cm^{-1}. PMR: δ [60 MHz] 0.69 (18-CH_3), 1.36(19-CH_3), 1.94(s, 3H, acetate CH_3), 2.0(s, 3H, acetate CH_3), 2.07(s, 3H, acetate CH_3), 2.77(s, 1H, 5α-OH; disappeared upon addition of D_2O), 4.89(m, 1H, 6α-H, 5.0Hz wide at half-peak height), 5.22(d, 1H, J = 3.0Hz, 4α-H), 5.3-5.6(bc, 1H, 3α-H); [270 MHz] 0.678(s, 3H, 18-CH_3), 0.864 (d, J = 6.67Hz, 6H, 26,27-CH_3), 0.904(d, J = 6.15Hz, 3H, 21-CH_3), 1.35(s, 3H, 19-CH_3), 1.96(s, 3H, acetate-CH_3), 2.02(s, 3H, acetate-CH_3), 2.09(s, 3H, acetate-CH_3), 2.28(bs, 1H, 5α-OH), 4.84(t, J = 4.95Hz, 1H, 6α-H), 5.19 (d, J = 3.1Hz, 1H, 4α-H), 5.36(m, 3α-H).

Anal. Calcd. for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67; O, 19.9.
Found: C, 69.97; H, 9.44; O, 20.5.

Cholestane-3β,4β,5α,6α-tetrol 13a.- The crude product was recrystallized thrice from absolute CH_3OH to yield 1.4 g (89%) of shiny white flakes; homogeneous to TLC; mp. 286-288° (sealed tube); $[\alpha]_D^{26°}$ = + 32.8° (c = 0.244 pyridine). IR (KBr): 3597, 3077, 1031 cm^{-1}. PMR: δ [60 MHz] (50.0 mg/0.657 g-d^5 pyridine), 0.70(18-CH_3), 1.45(19-CH_3), 4.16-5.0(bc, diminished upon addition of D_2O).

Anal. Calcd. for $C_{27}H_{48}O_4$: C, 74.26; H, 11.08.
Found: C, 74.53; H, 11.27.

Cholestane-3β,4β,5α,6α-tetrol 3,4,6-triacetate 13b.- The crude product was loaded on 6.0 g of silica gel. Elution of the column with benzene and then with 30% ether in benzene gives 78.0 mg (71.5%) of solid; homogeneous to TLC. This solid was crystallized from aqueous CH_3OH to give a gel, which was treated with a small amount of anhydrous powdered $MgSO_4$ and allowed to stand unperturbed, gave 60.0 mg of small translucent needles; mp. 151-152°; $[\alpha]_D^{21°} = +1.8°$ (c = 1.3). IR (KBr): 3333, 1730-1718, 1695, 1282, 1220, 1031 cm^{-1}. PMR: δ [60 MHz] 0.66(18-CH_3), 1.19(19-CH_3), 1.97(s, 3H acetate-CH_3), 2.02(s, 3H, acetate-CH_3), 2.06(s, 3H, acetate-CH_3), 5.0-5.5 (bc, 3H; 3,4,6-methine protons); no change upon addition of D_2O; [270 MHz] 0.644(s, 3H, 18-CH_3), 0.866(dd, J = 6.66,1.03Hz, 6H, 26,27-CH_3), 0.902(d, J = 6.67Hz, 3H, 21-CH_3), 1.18(s, 3H, 19-CH_3), 1.87(s, 1H, 5α-OH), 1.962(s, 3H, acetate-CH_3), 2.02(s, 3H, acetate-CH_3), 2.06(s, 3H, acetate-CH_3), 5.16 (dd, J = 11.3Hz, J=5.64Hz, 1H, 6β-H), 5.22(d, J = 4.10Hz, 1H, 4α-H), 5.31 (m, 1H, 3α-H).

Anal. Calcd. for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67.
Found: C, 70.65; H, 9.88.

Cholestane-3β,4α,5α,6β-tetrol 3,6-diacetate 15a.- The crude product was loaded on 30.0 g of silica gel. Elution of the column with 10% ether in benzene (425.0 mL) gave, after combination, 0.907 g of starting material. Elution with 30% ether in benzene (400.0 mL) gave, after combination, 0.701 g of tetrol diacetate. The product was crystallized once from 80% alcohol and once from n-hexane; to yield 0.437 g (41%) of small hard translucent crystals, mp. 160.6-162°; $[\alpha]_D^{21°} = +4.9°$ (c = 3.0). IR (KBr): 3425, 1795, 1701, 1271, 1222, 1047, 1031 cm^{-1}. PMR: δ [60 MHz] 0.70(18-CH_3), 1.08(19-CH_3), 2.06(s, 3H, acetate-CH_3), 2.11(s, 3H, acetate-CH_3), 2.68(s, 1H, 5α-OH, disappeared upon addition of D_2O), 3.5-3.84[(bc, 2H) changed to a doublet (1H, J = 9.5Hz) centered at 3.67 upon addition of D_2O; 4β-H], 4.75-5.3(bc, 2H, 3α,6α-methine protons).

Anal. Calcd. for $C_{31}H_{52}O_6$: C, 71.50; H, 10.07.
Found: C. 71.40, H, 9.95.

Cholestane-3β,4α,5α,6β-tetrol 3,4,6-triacetate 15b.- The crude solid was collected, washed well with H_2O, and dried. One crystallization from aqueous 2-methoxyethanol gave 80.0 mg (74%) of triacetate; mp. 148-149.2°. IR (KBr): 3484, 1739, 1282-1176, 1030 cm^{-1}. PMR: δ [60 MHz] 0.70(18-CH_3), 1.22(19-CH_3), 1.98(s, 3H, acetate-CH_3), 2.02(s, 6H, two acetate-CH_3), 4.83 (m, 1H, 6β-H, 5.0Hz wide at half-peak height), 4.92-5.55(bc, 2H, 3α,4α-

methine protons); no change upon addition of D_2O; [270 MHz] 0.675(s, 3H, 18-CH_3), 0.859(d, J = 6.92Hz, 6H, 26,27-CH_3), 0.901(d, J = 5.88Hz, 3H, 21-CH_3), 1.21(s, 3H, 19-CH_3), 1.91(s, 1H, 5α-OH), 1.99(s, 3H, acetate CH_3), 2.02(s, 3H, acetate-CH_3), 2.03(s, 3H, acetate-CH_3), 4.82(m, 1H, 6α-H), 5.20(m, 1H, 3α-H), 5.40(d, J = 9.6Hz, 1H, 4β-H).

Anal. Calcd. for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67.
Found: C. 70.19, H, 9.54.

Cholestane-3β,4α,5α,6α-tetrol 3,4,6-triacetate 17b.- The crude solid was loaded onto 60.0 g of silica gel. Elution with benzene and then with 30% ether in benzene gave, after combination, 1.34 g (69%) of white solid. Two crystallizations from CH_3OH gave 0.978 g (51%) of fine white needles; mp. 175-176.5°; $[\alpha]_D^{22°}$ = + 76.9° (c = 1.54). IR (KBr): 3484, 1733, 1299-1205, 1053 cm^{-1}. PMR: δ [60 MHz] 0.66(18-CH_3), 1.07(19-CH_3), 1.99(s, 6H, two acetate-CH_3), 2.03(s, 3H, acetate-CH_3), 2.56(s, 1H, 5α-OH, disappeared upon addition of D_2O), 4.95-5.55(bc, 3H, 3,4,6-methine protons); [270 MHz] 1.06(s, 3H, 19-CH_3), 5.08(dd, 1H, 6β-H), 5.16(bc, 1H, 3α-H), 5.33(d, J = 13.0Hz, 1H, 4β-H).

Anal. Calcd. for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67.
Found: C, 70.66, H, 9.71.

Cholestane-3β,5α,6α,7β-tetrol 3,6,7-triacetate 19b.- The crude solid was collected, washed well with H_2O, and dried, yield 1.8 g (85%); homogeneous to TLC. Two crystallizations from n-hexane gave 0.894 g (42%) of hard white crystals; mp. 190.6-191.2°; $[\alpha]_D^{22°}$ = + 7.9° (c = 3.05). IR (KBr): 3413, 1802-1681, 1282, 1202, 1031 cm^{-1}. PMR: δ [60 MHz] 0.68(18-CH_3), 1.11(19-CH_3), 1.93(s, 3H, acetate-CH_3), 2.0(s, 6H, two acetate-CH_3), 2.98 (s, 1H, 5α-OH, diappeared upon addition of D_2O), 4.8-5.4(bc, 3H; 3α,6β,7α-methine protons); [270 MHz] 0.672(s, 3H, 18-CH_3), 0.854(d, J = 6.63Hz, 6H, 26,27-CH_3), 0.902(d, J = 6.62Hz, 3H, 21-CH_3), 1.11(s, 3H, 19-CH_3), 1.94(s, 3H, acetate-CH_3), 2.00(s, 3H, acetate-CH_3), 2.04(s, 3H, acetate-CH_3), 3.49 (bs, 1H, 5α-OH), 4.98(d, J = 8.7Hz, 1H, 6β-H), 5.09(m, 1H, 3α-H), 5.21(dd, 1H, 7α-H).

Anal. Calcd. for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67.
Found: C. 70.65; H, 9.91.

Cholestane-3β,5α,6α,7α-tetrol 3,6,7-triacetate 20b.- A solution of 0.391 g (0.82 mmol) of 10 and 1.68 g lithium tri(t-butoxy) aluminum hydride in 30.0 mL anhydrous THF was stirred for 12.5 days at room temperature. After hydrolysis at 0° by the dropwise addition of 13.0 mL of 5% H_2SO_4, the mixture was extracted with ether. After acetlyation, the crude triacetate was isolated by extraction with ether. The crude product was loaded on

100.0 g of aluminum oxide. Elution of the column first with hexane and then with benzene gave, after combination and two recrystallizations from n-hexane, 0.282 g (61%) of fine white needles; mp. 221.5-222.5°; $[\alpha]_D^{22°}$ = + 16.9° (c = 1.01). IR (KBr): 3472, 1739, 1282-1195, 1040, 1026 cm^{-1}. PMR: δ [60 MHz] 0.67(18-CH_3), 1.08(19-CH_3), 1.99(s, 3H, acetate-CH_3), 2.02 (s, 3H, acetate-CH_3), 2.10(s, 3H, acetate- CH_3), 3.13(s, 1H, 5α-OH; disappeared upon addition of D_2O), 4.95(d, 1H, J = 4.0Hz; 6β-H), 5.0-5.5(bc, 2H; 3α,7β-methine protons); [270 MHz] 0.652(s, 3H, 18-CH_3), 0.853(dd, J = 6.67,1.54Hz, 6H, 26,27-CH_3), 0.902(d, J = 6.67Hz, 3H, 21-CH_3), 1.08(s, 3H, 19-CH_3), 2.00(s, 3H, acetate-CH_3), 2.03(s, 3H, acetate-CH_3), 2.12(s, 3H, acetate-CH_3), 3.14(s, 1H, 5α-OH), 4.90(d, J = 3.6Hz, 1H, 6β-H), 5.11(m, 1H, 3-H), 5.31(dd, 1H, 7β-H).

Anal. Calcd. for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67
Found: C, 70.56; H, 9.54

Cholestane-3β,5α,6β,7β-tetrol 3,7-diacetate 21a.- A stirred solution of 569.0 mg (1.13 mmol) of 24b and 522.0 mg periodic acid dihydrate in 40.0 mL THF was boiled under reflux for 1.5 hours. The solution was then decanted from some solid, diluted with 100.0 mL of ether, and worked up to yield 659.0 mg of white solid. The crude product was loaded onto 20.0 g of silica gel. Elution with hexane and then with 30% ether in hexane gave a small amount of inhomogeneous solid. Elution with 50% ether in hexane (500.0 mL) gave, after combination, 497.0 mg (84%) of white solid; homogeneous to TLC. Two crystallizations of this solid from 10% aqueous CH_3OH afforded 247.0 mg (42%) of crystals as a mat of fine white needles; mp. (sealed tube) 210-211°; $[\alpha]_D^{21°}$ = + 23.3° (c = 1.79). IR (KBr): 3401, 1739, 1250, 1026 cm^{-1}. PMR: δ [60 MHz] 0.70(18-CH_3), 1.19(19-CH_3), 2.02 (s, 3H, acetate-CH_3), 2.05(s, 3H, acetate-CH_3), 2.66(s, 1H, 5α-OH, disappeared on addition of D_2O), 3.55-3.78[m, 1H, 6α-H; changed to a doublet (J = 4.0Hz) centered at 3.67 upon addition of D_2O; 6α-H split by 7α-H], 4.93-5.4(bc, 2H, 3α and 7α-methine protons).

Anal. Calcd. for $C_{31}H_{52}O_6$: C, 71.50; H, 10.07
Found: C. 71.24; H, 10.07

Cholestane-3β,5α,6β,7β-tetrol 3,6,7-triacetate 21b.- The crude solid was loaded onto 30.0 g of silica gel. Elution of the column with hexane, then with 50% ether in hexane gave, after combination, 0.637 g (98%) of tetrol triacetate as an oil; homogeneous to TLC. PMR: δ [60 MHz] 0.71(18-CH_3), 1.17(19-CH_3), 1.90(s, acetate-CH_3), 2.03(s, acetate-CH_3), 2.08(s, acetate-CH_3), 3.65(s, 1H, 5α-OH, disappeared upon addition of D_2O), 4.87-5.55(bc, 3H, 3α, 6α and 7α-methine protons); [270 MHz] 0.720(s, 3H, 18-CH_3), 0.850

(dd, J = 6.67,1.54Hz, 6H, 26,27-CH_3), 0.900(d, J = 6.67Hz, 3H, 21-CH_3), 1.15(s, 3H, 19-CH_3), 1.90(s, 3H, acetate-CH_3), 2.03(s, 3H, acetate-CH_3), 2.08(s, 3H, acetate-CH_3), 3.26(s, 1H, 5α-OH), 5.03(d, J = 3.7Hz, 6α-H), 5.21(m, 1H, 7α-H), 5.26(m, 1H, 3α-H).

Cholestane-3β,5α,6β,7α-tetrol 3,7-diacetate 22a.- A solution of 0.185 g (0.368 mmol) of diacetate[13] 25b and 0.571 g periodic acid dihydrate in 20.0 mL THF was boiled under reflux for 3.0 hours, then permitted to cool to room temperature. The solution was decanted from a little insoluble solid. To this solution was added 40.0 mL ether and the resulting solution worked up to yield a solid. This solid was loaded onto 10.0 g of silica gel. Elution of the column with hexane and then with 20% ether in hexane gave inhomogeneous oils and then some starting material. Elution with 40% ether in hexane gave, after combination, 0.062 g (32%) of white solid, homogeneous to TLC. One crystallization of this solid from 12.0 mL n-hexane gave 0.035 g (18%), mp. 226.5-228.0° (sealed tube); $[\alpha]_D^{22°}$ = + 23.3° (c = 1.79). IR (KBr): 3390, 1709, 1379, 1258 cm^{-1}. PMR: δ [60 MHz] 0.69(18-CH_3), 1.18(19-CH_3), 2.02(acetate-CH_3), 2.10(acetate-CH_3), 2.51-2.83(m, 2H, 5α and 6β-OH), 3.43-3.67(m, 1H, 6α-H), [addition of D_2O caused the absorption at 2.51-2.83 to disappear and the one at 3.43-3.67 to change to a doublet (J = 2.0Hz) centered at 3.55], 4.79-5.01(m, 1H, 7β-H), 5.01-5.6(bc, 1H, 3α-H).

Anal. Calcd. for $C_{31}H_{50}O_6$: C, 71.50; H, 10.07.
Found: C, 71.24; H, 10.07.

Cholestane-3β,5α,6β,7α-tetrol 3,6,7-triacetate 22b.- The crude solid was loaded onto 5.0 g of silica gel. Elution with hexane and then with 30% ether in hexane gave, after combination, 0.053 g (79%) of oil, homogeneous to TLC. PMR: δ [60 MHz] 0.71(18-CH_3), 1.16(19-CH_3), 2.01(s, acetate-CH_3), 2.10(s, 6H, two acetate-CH_3), 2.96(s, 1H, 5α-OH, disappeared upon addition of D_2O), 4.81(m, 2H, 6α and 7β-H), 4.94-5.3(bc, 3H, 3α-H); [270 MHz] 0.693(s, 3H, 18-CH_3), 0.860(d, J = 6.67Hz, 6H, 26,27-CH_3), 0.912(d, J = 6.67Hz, 3H, 21-CH_3), 1.16(s, 3H, 19-CH_3), 2.00(s, 3H, acetate-CH_3), 2.10 (s, 3H, acetate-CH_3), 2.12(s, 3H, acetate-CH_3), 2.96(s, 1H, 5α-OH), 4.79 (d, J = 2.0Hz, 1H, 6α-H), 4.86(t, 1H, 7β-H), 5.18(m, 1H, 3α-H).

Cholestan-5α,6α-oxide-3β,7β-diol 3-acetate 24a and Cholestan-5α,6α 3β,7α-diol 3-acetate 25a.- A solution of 3.3 g (7.2 mmol) of 23 and 4.0 g of lithium tri(t-butoxy) aluminum hydride in 100.0 mL of anhydrous THF was stirred at 0° for 13.0 hours. The solution was then hydrolyzed by the dropwise addition of a 10% acetic acid solution during the course of 20 minutes. The resulting mixture was extracted with 100 mL CH_2Cl_2 and the

combined organic layer washed well with saturated $NaHCO_3$, then brine, dried (Na_2SO_4) and the solvent evaporated to yield 3.3 g (99%) of white solid. The crude product was loaded onto 150.0 g of silica gel. Elution with benzene and then with 5% ether in benzene gave a small quantity of starting material. Elution with 10% ether in benzene gave, after combination, 0.48 g (14.5%) of alcohol 25a, 0.1 g of an alcohol mixture, and 2.40 g (72.5%) of alcohol 24a. Alcohol 24a when crystallized from 80% aqueous ethanol gave long translucent fine needles; mp. 124-125° (137-138°); $[\alpha]_D^{22°} = -9.4°$ (c = 1.3). IR (KBr): 3509, 1730, 1261, 1227, 1042, 800 cm^{-1}. PMR: δ [60 MHz] 0.66(18-CH_3), 1.12(19-CH_3), 2.0(s, 3H, 3-acetate-CH_3), 2.85(s, 1H, 6β-H), 3.5-3.85(bc, 1H, 7α-H), 4.51-5.2(bc, 1H, 3α-H) [addition of D_2O caused no change in the spectrum].

Anal. Calcd. for $C_{29}H_{48}O_4$: C, 75.61; H, 10.50.
Found: C, 75.78; H, 10.38.

Alcohol, 25a, when crystallized twice from 80% aqueous CH_3OH yielded clusters of white fine needles; mp. 140-141.5°; $[\alpha]^{22°} = -78.6°$ (c = 1.3). IR (KBr): 3509, 1730, 1261, 1227, 1041, 800 cm^{-1}. PMR: δ [60 MHz] 0.62(18-CH_3), 1.08(19-CH_3), 2.0(s, 3H, acetate-CH_3), 3.22(d, 1H, J=4.5Hz, 6β-H), 3.67-3.97(bc, 1H, 7β-H), 4.51-5.2(bc, 1H, 3α-H) [addition of D_2O caused no change in the spectrum].

Anal. Calcd. for $C_{29}H_{48}O_4$: C, 75.61; H, 10.50.
Found: C, 75.81; H, 10.68.

Cholestan-5α,6α-oxide-3β,7β-diol 3,7-Diacetate 24b.- The crude product was crystallized twice from aqueous CH_3OH to yield 0.15 g (80%) of fine needles, mp. 120-121°; $[\alpha]_D^{21°} = +4.1°$ (c = 3.5). IR (KBr): 1724, 1250, 800 cm^{-1}. PMR: δ [60 MHz] 0.65(18-CH_3), 1.14(19-CH_3), 2.02(s, 3H, 3- acetate-CH_3), 2.07(s, 3H, acetate-CH_3), 2.77(s, 1H, 6β-H), 4.67-4.92(d, J = 6.5Hz, 7α-H), 4.92-5.4(bc, 1H, 3α-H).

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03.
Found: C, 73.87; H, 10.12.

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