Preparation of Some Unsaturated Side-Chain Derivatives of Cholesterol

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Cholesta-5,22(*E*),25-trien-3β-ol (**6**), cholesta-5,25-dien-3β-ol (**7**), 5α-cholest-25-en-3β-ol (**8**), cholesta-5,22(*E*),24-trien-3β-ol (**9**), and cholesta-5,22(*E*)-dien-3β-ol were prepared from the product obtained by reaction of 3β-acetoxychola-5,23-dien-22-ol with an *N,O*-ketene acetal.

Cholesterol derivatives with unsaturated side chains are commonly prepared with organometallic or Wittig reagents and suitable C_{19}–C_{24} carbonyl derivatives.[1] More recently, allylic rearrangements[2,3] and the ene reaction[4,5] were used to generate specific chirality at C_{20}. A Claisen rearrangement was extensively used by Sucrow and co-workers to prepare (24*R*)- and (24*S*)-24-ethyl sterols with Δ^{25} unsaturation in the side chain.[6a-d] In this paper we describe an application of this rearrangement to the synthesis of a number of cholesterol derivatives.

Our starting material was (20*S*,22*R*,*S*)-3β-acetoxychola-5,23-dien-22-ol (**2**) prepared from (20*S*)-3β-acetoxybisnorchol-5-en-22-al (**1**) and vinylmagnesium bromide.[7] Alcohol **2** reacted readily with 1-methoxy-1-(dimethylamino)-1-propene[8] in refluxing benzene to give (22*E*,25*R*,*S*)-*N*,*N*-dimethyl-3β-acetoxycholesta-5,22-dien-26-amide (**3**, Scheme I). Amide **3** was then stepwise hydrogenated in neutral and acid solutions to the Δ^5 (**4**) and saturated (**5**) amides, respectively.

The three amides were reduced with LAH in THF to hydroxyamines **3a**–**5a** and these in turn oxidized to the *N*-oxides **3b**–**5b** with H_2O_2 in MeOH. From here our methodology diverged from that of Sucrow et al.

Pyrolysis of **3b** in Me_2SO[6a-d] gave poor yields of the desired sterol (**6**); the main product of the reactions was amine **3a**.[9] Pyrolysis in pyridine improved the yield of **6** but still gave appreciable amine. Addition of solid alkali[10] to the hot pyridine prior to addition of the *N*-oxides inhibited amine formation and provided the desired unsaturated sterols in good yield and without epimerization at C_3. The alkali of choice for conversion of **3b** to **6** was $Ba(OH)_2$; pyrolysis of *N*-oxides **4b** to 5,25-cholestadienol (**7**) and **5b** to 25-cholestenol (**8**) went smoothly and more rapidly with KOH. The use of KOH in the pyrolysis of **3b** led to various quantities of a byproduct that was shown to be 5,22(*E*),24-cholestatrienol (**9**) and which formed by alkaline isomerization of the 5,22(*E*),25-triene. The reaction of **6** with KOH in hot pyridine was then used to prepare **9**.

5,22(*E*),25-Cholestatrienol (**6**) was previously reported to have been synthesized by isomerization of cholesta-4,22(*E*),25-trien-3-one (prepared by a Wittig synthesis) to the 5,22(*E*),25-trienone followed by LAH reduction and purification by preparative TLC.[11] Since the melting point that we observed for **6** [119–120 °C (air), 121.5-122.5 (in vacuo, corr)] was so different from the one reported[11] (140 °C), we believe the latter to be an isomer, possibly the 20-iso derivative,[1] of **6**. All of our chromatographic and spectral data agree with the assigned structure.

The physical and spectroscopic properties that we observed for 5,22(*E*),24-cholestatrienol (**9**) and its acetate were in accord with those given by Hutchins et al.,[12] and those of 5,25-cholestadienol (**7**) and its acetate corresponded well to literature values.[13] 25-Cholestenol (**8**) has not been reported before either as a synthetic or naturally occurring sterol.

Our initial goal in this study was to prepare *trans*-22-dehydrocholesterol (**10**) for work with *Drosophila*. We had previously prepared **10** by the conventional Wittig reaction, but separation of this compound from 30% of its Δ^{22} cis isomer as acetates was tedious on a gram scale.[14] The ketene acetal route described here appeared useful in that it gives only *trans*-22-dehydrosterols.[15] However, unlike the facile hydrogenations of the (24*R*)- and (24*S*)-24-ethyl $\Delta^{22(E),25}$ side chains over a soluble rhodium catalyst to the corresponding $\Delta^{22(E)}$ derivatives,[6c,d] absence of an alkyl group at C_{24} in triene **6** makes its Δ^{22} bond much more susceptible to reduction, and it was difficult to get good conversion of **6** to **10** over this catalyst. A small amount of **6** was reduced to **10** over a commercial Ni catalyst, but the reaction had to be stopped before all the **6** had been converted to **10** because cholesterol (**11**; by reduction of the Δ^{22} bond) was already apparent by argentation TLC. Reductions of **7** to **11** and **8** to cholestanol (**12**) for structure corroboration and confirmation of the normal configuration at C_{20} were straightforward.

Experimental Section

Melting points were taken in air or in vacuo in capillary tubes with a Thomas-Hoover apparatus and are corrected. IR spectra were obtained with a Perkin-Elmer 398 (2.5% solutions in CS_2), UV spectra with a Beckamn DU-8 (EtOH), ^1H NMR spectra with a Bruker WM-250 ($CDCl_3$), mass spectra with a Varian MAT 311 A (direct inlet, 70 eV), optical rotations with a Rudolph DP-06-01

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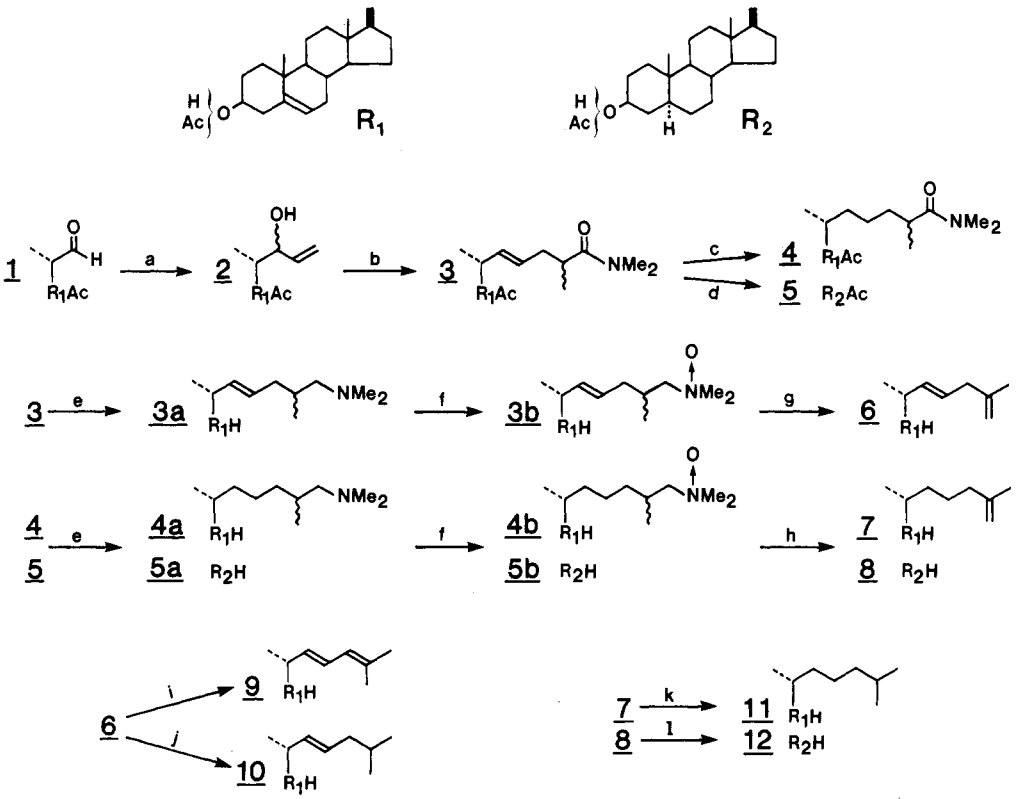
Scheme I[a]



[a] (a) ViMgBr; (b) $CH_3CH{=}C(OMe)NMe_2$; (c) H_2, Pt, EtOAc; (d) H_2, Pd/C, HOAc, EtOAc; (e) $LiAlH_4$, THF; (f) H_2O_2, MeOH; (g) py, $Ba(OH)_2$, 105 °C; (h) py, KOH, 100 °C; (i) py, KOH, 120 °C; (j) H_2, Ni, EtOAc; (k) H_2, $(Ph_3P)_3RhCl$, EtOH–C_6H_6; (l) H_2, Pd/C, EtOAc.

polarimeter (C_3, $CHCl_3$), and acetylations with pyridine–Ac_2O at room temperature.

Chromatography. GC retention times (in minutes) were determined with a 2 m long × 3 mm id, 5% OV-101 column at 250 °C, and a Sr^{90} detector. Relative retention time (RRT) with respect to **11**: **3a**, 1.95; **4a**, 2.13; **5a**, 2.16; **6**, 0.97; **7**, 1.07; **8**, 1.09; **9**, 1.18; **10**, 0.97; **12**, 1.02.

TLC was performed with Merck aluminum-backed silica gel plates (0.25 mm) (Sigel) and with these plates dipped in 10% $AgNO_3$ in 80% EtOH, air-dried, and activated at 110 °C for 20 min (Ag^+ Sigel) in five solvent systems: (1) Sigel, 6:4 hexane–EtOAc, one development; (2) Sigel, 6:4 MeOH–Et_2O, one development; (3) Ag^+ Sigel, 99:1 $CHCl_3$–Me_2CO, 2.5-h development; (4) Ag^+ Sigel, 19:1 $CHCl_3$–Me_2CO, 2-h development; (5) Ag^+ Sigel, 5:2 hexane–benzene, 4-h development. RRT (with respect to **11ac**; ac = steryl acetates): **6ac**, 0.11; **7ac**, 0.17; **8ac**, 0.32; **9ac**, 0.28; **10ac**, 0.65; **12ac**, 1.22. In systems 3–5 the top 1 cm of the plate protruded through a slit in an aluminum foil cover of the TLC tank to allow for continuous development. Sigel (100 mesh)–Celite (2:1) was used for column chromatography.

Ketene Acetal. 1-(Dimethylamino)-1-methoxy-1-propene was refluxed over and distilled from Ca turnings under N_2: bp 117–121 °C; n^{25}_D 1.4261 (lit.[8] bp 117–118 °C; n^{20}_D 1.4250).

(25*R*,*S*)-3β-Acetoxy-*N*,*N*-dimethylcholesta-5,22-dien-26-amide (3). Ketene acetal (20 mL) was added to 5 g of (22*R*,*S*)-**2** in 100 mL of dry benzene and refluxed under N_2 until the reaction was complete (TLC system 1). The solution was washed several times with H_2O, dried (Na_2SO_4), and evaporated. The residue was applied to a silica gel column (150 g) and eluted with 4:1 petroleum ether–Et_2O, and **3** crystallized from hexane: yield 5.28 g (86%); mp 125–133 °C (in vacuo); IR 1730, 1240 (OAc), 1650 (amide), 970 (trans Δ^{22}), 903, 800 (Δ^5); NMR δ 0.68 (3 H, s, C_{18}), 0.99 (3 H, d, C_{21}), 1.02 (3 H, s, C_{19}), 1.08 (3 H, d, C_{27}), 2.03 (3 H, s, CH_3CO), 2.32 (2 H, d, C_4), 2.71 (1 H, sextet, C_{25}), 2.94, 3.04 (6 H, 2 s, NMe_2), 4.60 (1 H, m, C_3), 5.28 (2 H, m, $C_{22,23}$), 5.37 (1 H, d, C_6); mass spectrum, *m*/*e* (relative intensity) 483 (M^+, 36), 468 (M – Me, 4.3), 423 (M – HOAc,27), 408 (M – Me – HOAc, 10.2), 253 (M – HOAc – (SC + 2 H), 7.1), 168 (SC, 100), 102 (CHMe-$CONMe_2$ + 2H, 17.4), 72 ($CONMe_2$, 90.2). Anal. Calcd for $C_{31}H_{49}O_3N$ (mol wt 483.7): C, 76.97; H, 10.21; N, 2.90. Found: C, 76.74; H, 10.35; N, 2.70.

(25*R*,*S*)-3β-Acetoxy-*N*,*N*-dimethylcholest-5-en-26-amide (4). A solution of 2.09 g of **3** in 100 mL of EtOAc (free of acid) was reduced over 75 mg of PtO_2 until H_2 absorption stopped (TLC system 3). After removal of catalyst and solvent, the residue was crystallized from petroleum ether to yield **4**: 1.99 g (95%); mp 112.5–119.5 °C(in vacuo) IR similar to that of **3** but lacking a 970-cm^{-1} band (trans Δ^{22}); NMR δ 0.67 (3 H, s, C_{18}), 0.90 (3 H, d, C_{21}), 1.02 (3 H, s, C_{19}), 1.04 (3 H, d, C_{27}), 2.03 (3 H, s, CH_3CO), 2.32 (2 H, d, C_4), 2.69 (1 H, m, C_{25}), 2.96, 3.05 (6 H, 2 s, NMe_2), 4.60 (1 H, m, C_3), 5.37 (1 H, d, C_6); mass spectrum, *m*/*e* (relative intensity) 485 (M^+, 0.6), 425 (M – HOAc, 100), 410 (M – Me – HOAc, 11.3), 255 (M – HOAc – SC, 15.4), 170 (SC, 7.4), 101 ($CHMeCONMe_2$ + 1 H, 90.6), 72 ($CONMe_2$, 26.2).

(25*R*,*S*)-3β-Acetoxy-*N*,*N*-dimethyl-5α-cholestan-26-amide (5). A solution of 2 g **3** in 100 mL of 3:1 EtOAc–HOAc was hydrogenated over 0.5 g of 10% Pd/C overnight (TLC system 3). After removal of catalyst and solvents, the residue was taken up in ether, washed ($NaHCO_3$ and H_2O), and again evaporated. Crystallization of the residual solid from petroleum ether gave **5**: 1.59 g (79%); mp 109.5–111.5 °C (in vacuo); IR similar to that of **4** but lacking 903 and 800-cm^{-1} bands (Δ^5); NMR δ 0.64 (3 H, s, C_{18}), 0.81 (3 H, s, C_{19}), 0.88 (3 H, d, C_{21}), 1.09 (3 H, d, C_{27}), 2.02 (3 H, s, CH_3CO), 2.69 (1 H, sextet, C_{25}), 2.95, 3.05 (6 H, 2 s, NMe_2), 4.68 (1 H, m, C_3); mass spectrum, *m*/*e* (relative intensity) 487 (M^+, 11.1), 412 (M – Me – HOAc, 5.8), 170 (SC, 8.0), 101 (CHMe-$CONMe_2$ + 1 H, 100), 72 ($CONMe_2$, 20).

(22*E*,25*R*,*S*)-26-(Dimethylamino)cholesta-5,22-dien-3β-ol (3a). A solution of 10 g of **3** in 200 mL of THF was added dropwise over 1 h to a refluxing, mechanically stirred slurry of 5 g of $LiAlH_4$ in 250 mL of THF in a 2-L three-necked flask. After 1 h of additional refluxing, the reaction mixture was sampled (TLC system 2) and the condenser moved to a distillation position for recovery of most of the dry THF. After cooling, the residue was decomposed with wet ether and just enough water to form an inorganic sludge. The solution was decanted, treated with 10 mL of concentrated HCl in 25 mL of EtOH and allowed to stand overnight to form the ether- and water-insoluble **3a**·HCl. The

ether layer was washed with water and discarded; the aqueous layer and precipitated **3a**·HCl were combined, made alkaline with excess aqueous NaOH, and ether extracted. Evaporation of solvent left 9 g of crude product which was crystallized from acetone to yield **3a**: 7.0 g (81%); mp 103.5–104.5 °C (in vacuo).

(25*R*,*S*)-26-(Dimethylamino)cholest-5-en-3β-ol (4a) and (25*R*,*S*)-26-(Dimethylamino)-5α-cholestan-3β-ol (5a). Comparable reductions of 5 g of **4** gave 3.6 g (82%) of **4a** [mp 120–137 °C (in vacuo)] and of 3.9 g of **5** gave 2.8 g (82%) of **5a**, mp 110–117.5 °C (in vacuo).

(22*E*,25*R*,*S*)-26-(Dimethylamino)cholesta-5,22-dien-3β-ol *N*-Oxide (3b). A solution of 2.0 g of **3a** and 3.5 mL of 30% H_2O_2 in 45 mL of MeOH was refluxed overnight (TLC system 2) and evaporated to dryness at <45 °C in vacuo. The residual sticky solid was refluxed with 100 mL of ether, the ether decanted, and the residue dried from 100% EtOH and in vacuo at <40 °C to give **3b**: 2.1 g; mp 150–157 °C dec (air).

(25*R*,*S*)-26-(Dimethylamino)cholest-5-en-3β-ol *N*-Oxide (4b) and (25*R*,*S*)-26-(Dimethylamino)-5α-cholestan-3β-ol *N*-Oxide (5b). Hydroxy amines **4a** (3.40 g) and **5a** (2.40 g) were oxidized in the same way to yield 3.55 g of **4b** [mp 150–155 °C dec (air)] and 2.85 g of **5b**, mp 145–150 °C dec (air).

Cholesta-5,22(*E*),25-trien-3β-ol (6). (A) Large-Scale Runs in Pyridine. Four preparations of **3b** (17.6, 17.5, 15.7, and 18 g) were each refluxed for 4–7 h in 350 mL of dry pyridine under N_2. TLC of each (system 1 and 2) showed that substantial amounts of amine **3a** had formed during the pryolysis after **3b** was no longer evident in the reaction mixtures. The solutions were evaporated to dryness and the residues applied to 400 g of silica gel columns and eluted with 5:1 petroleum ether–ether to give 5.76 (38%), 6 (40%), 7.8 (57%), and 5.5 g (35%) of crude trienol **6**, respectively. These fractions were combined with material prepared in the same way from 45 g of less pure *N*-oxide **3b** and extensively worked up by crystallization and further chromatography to yield the following fractions of **6**: 16.6 g, mp 119–120 °C (in vacuo); 4.4 g, mp 94–110 °C; 6 g, mp 90–110 °C; overall yield of about 28%.

(B) Smaller Scale Run in Pyridine with $Ba(OH)_2$. Amine oxide **3b** (0.50 g) was added to a slurry of 5 g of $Ba(OH)_2 \cdot 8\ H_2O$ in 20 mL of pyridine that had been stirred in an oil bath at 105 °C for 1 h, and stirring at that temperature was continued for 12 h (TLC systems 1, 2, and 4). After cooling and addition of dilute HCl, the mixture was ether extracted. The ether phase was washed (dilute HCl, H_2O) and evaporated, and the residue was applied to a 25-g silica gel column and eluted with 9:1 petroleum ether–ether (TLC system 1) to yield **6**: 0.29 g (67%); mp 121.5–122.5 °C (in vacuo; MeOH); $[\alpha]^{25}_D$ −62.1° [lit.[11] mp 140 °C (MeOH)]. Anal. Calcd for $C_{27}H_{42}O$ (mol wt 382.60): C, 84.75; H, 11.06. Found: C, 84.81; H, 10.88.

6 Acetate: mp 109–110 °C (air), 111–111.5 °C (in vacuo; MeOH); $[\alpha]^{25}_D$ −63.3°; no UV absorption >220 nm; IR 3060, 1645, 885 (C=CH_2), 1760, 1240 (OAc), 970 (trans Δ^{22}), 903, 800 cm^{-1} (Δ^5); NMR δ 0.70 (3 H, s, C_{18}), 1.02 (3 H, s, C_{19}), 1.02 (3 H, d, C_{21}), 1.70 (3 H, s, C_{27}), 2.03 (3 H, s, CH_3CO), 2.32 (2 H, d, C_4), 2.64 (2 H, d, C_{24}), 4.60 (1 H, m, C_3), 4.69, 4.70 (2 H, 2 s, C_{26}), 5.29 (2 H, m, $C_{22,23}$), 5.37 (1 H, d, C_6); mass spectrum, *m/e* (relative intensity) 364 (M − HOAc, 68.5), 349 (M − Me − HOAc, 7), 255 (M − HOAc − SC, 33.4), 109 (SC, 71.2), 107 (SC − 2H, 37.2), 81 (SC − $C_{20,21}$, 100).

(C) Comparison of *N*-Oxide Pyrolysis in Pyridine with and without $Ba(OH)_2$. *N*-Oxide **3b**, obtained from 3 g of amide **3**, was stirred with (10 h) and without (13 h) 5 g of $Ba(OH)_2 \cdot H_2O$ in 75 mL of pyridine under N_2 at 105 °C. After a workup as in B, a 62% yield of trienol **6** and 26 mg of amine **3a** were obtained from the pyrolysis with $Ba(OH)_2$, and a 28% yield of **6** and 400 mg of **3a** were obtained without the alkali (quantitative GLC).

Cholesta-5,25-dien-3β-ol (7). Amine oxide **4b** (1.70 g) was added to a mixture of 1.9 g of KOH and 60 mL of pyridine that had been stirred 1 h at 100 °C, and pyrolysis was continued under these conditions for 4.5 h (TLC systems 1 and 2). Half of the pyridine was evaporated in vacuo and the crude product worked up as above to give **7**: 0.98 g (67%); mp 135–136 °C (MeOH); $[\alpha]^{25}_D$ −40.2° (lit.[13] mp 135–136 °C; $[\alpha]^{25}_D$ −44°).

7 Acetate: mp 112–113 °C (in vacuo; MeOH); $[\alpha]^{25}_D$ −41.3° (lit.[13] 113–114 °C; $[\alpha]^{25}_D$ 40°); IR similar to that of the **6** acetate but lacking the 970-cm^{-1} band (transΔ^{22}); NMR δ 0.68 (3 H, s, C_{18}), 0.92 (3 H, d, C_{21}), 1.02 (3 H, s, C_{19}), 1.71 (3 H, s, C_{27}), 2.03 (3 H, s, CH_3CO), 2.32 (2 H, d, C_4), 4.60 (1 H, m, C_3), 4.66, 4.68 (2 H, 2 s, C_{26}), 5.37 (1 H, d, C_6); mass spectrum, *m/e* (relative intensity) 366 (M − HOAc, 100), 351 (M − Me − HOAc, 16.1), 255 (M − HOAc − SC, 12.2), 253 (M − HOAc − SC − 2H, 15.4), 111 (SC, 22.3), 109 (SC − 2H, 31.8), 81 (SC − $C_{20,21}$ − 2H, 81.1).

5α-Cholest-25-en-3β-ol (8). Amine oxide **5b** (1.0 g) was pyrolyzed as above for **4b** and worked up in the same way to yield **8**: 0.64 g (74%); mp 110–111, 124–124.5 °C (in vacuo, double fusion, MeOH); $[\alpha]^{25}_D$ +24°. Anal. Calcd for $C_{27}H_{46}O$ (mol wt 386.64): C, 83.87; H, 11.99. Found: C, 84.01; H, 12.19.

8 Acetate: mp 119–120 °C (in vacuo; MeOH); $[\alpha]^{25}_D$ +12°; IR similar to that of **7** acetate but lacking 903, 800-cm^{-1} bands (Δ^5); NMR δ 0.65 (3 H, s, C_{18}), 0.82 (3 H, s, C_{19}), 0.91 (3 H, d, C_{21}), 1.71 (3 H, s, C_{27}), 2.02 (3 H, s, CH_3CO), 4.68 (1 H, m, C_3), 4.67, 4.68 (2 H, 2 s, C_{26}); mass spectrum, *m/e* (relative intensity) 428 (M^+, 63.6), 413 (M − Me, 20.8), 368 (M − HOAc, 6.1), 353 (M − Me − HOAc, 14.6), 315 (M − SC − 2H, 62), 257 (M − HOAc − SC, 12.9), 255 (M − HOAc − SC − 2H, 46.6), 111 (SC, 11.8), 109 (SC − 2H, 47.6), 81 (SC − $C_{20,21}$ − 2H, 100).

Cholesta-5,22(*E*)-dien-3β-yl Acetate (10 Acetate). Trienol **6** (0.3 g) in 50 mL of EtOAc was reduced over 3 g of Unichema Prikat 9906 Ni catalyst overnight (GC, TLC system 4) to a mixture of ~1:20:5 cholesterol (**11**), **10**, and **6**. The products were acetylated and eluted from a 100 g of 20% $AgNO_3$–silica gel column with 7:3 hexane–benzene (TLC system 5) to yield 0.11 g of **10** acetate: mp and mmp 129–130 °C (in vacuo; EtOH); GC and TLC (system 5) identical with those of **10** acetate prepared by a Wittig reaction.[14]

Cholest-5-en-3β-ol (11). Dienol **7** (50 mg) was reduced over chlorotris(triphenylphosphine)rhodium in 10 mL of 3:1 benzene–EtOH overnight. Evaporation of the solvent and elution from a 10% $AgNO_3$–silica gel column with 7:3 hexane–benzene gave **11**: mp and mmp 148–149 °C (in vacuo); GC and TLC (system 4) identical with those of an authentic sample.

5α-Cholestan-3β-ol (12). Sterol **8** (25 mg) was reduced over 15 mg of 10% Pd/C in 10 mL of EtOAc, and the product was worked up in the usual way to give **12**: mp 139.5–141 °C; mmp 141–142.5 °C (in vacuo; MeOH); GC and TLC (system 4) identical with those of an authentic sample.

Cholesta-5,22(*E*),24-trien-3β-yl Acetate (9 Acetate). Trienol **6** (2.5 g) was added to a mixture of 2.5 g of KOH and 125 mL of pyridine that had been stirred under N_2 at 120 °C for 1 h. After 7 h, when **6** was no longer evident (TLC system 4), 85 mL of solvent was removed in vacuo, and the product was worked up with ether and dilute HCl, acetylated under N_2, purified on a 200-g column of 20% $AgNO_3$–silica gel with 19:1 petroleum ether–ether (TLC system 5, one development), and crystallized from MeOH to yield **9** acetate: 1.91 g (69%); mp 146–148.5 (air), 149–150 °C (in vacuo); $[\alpha]^{25}_D$ −65.1°; UV (EtOH) ϵ_{237} 31 400 (lit.[12] mp 133–135 °C (air); $[\alpha]^{25}_D$ −62°; UV (C_6H_{12}) ϵ_{240} 30 500); IR identical with published spectrum;[12] NMR methyl signals identical with published values,[12] in addition to δ 2.32 (2 H, d, C_4) 4.60 (1 H, m, C_3), 5.37 (1 H, d, C_6), 5.40 (1 H, dd, C_{24}), 5.75 (1 H, d, C_{24}), 6.13 (1 H, dd, C_{23}); mass spectrum identical with published spectrum.[12]

Cholesta-5,22(*E*),24-trien-3β-ol (9). The acetate was hydrolyzed under N_2 in ethanolic KOH to give **9**: mp 137–142 (air), 144–145 °C (in vacuo; MeOH); $[\alpha]^{25}_D$ − 55.1°; UV (EtOH) $\epsilon_{237.5}$ 29 100 (lit.[12] mp 133–135 (air); $[\alpha]^{25}_D$ −56°; UV (MeOH) ϵ_{240} 32 500).

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Registry No. 2, 80907-91-1; **3**, 80925-45-7; **3a**, 80907-92-2; **3b**, 80907-93-3; **4**, 80907-94-4; **4a**, 80907-95-5; **4b**, 80907-96-6; **5**, 80907-97-7; **5a**, 80907-98-8; **5b**, 80907-99-9; **6**, 34714-34-6; **6** acetate, 80925-46-8; **7**, 15240-13-8; **7** acetate, 10525-24-3; **8**, 80908-00-5; **8** acetate, 80908-01-6; **9**, 23656-66-8; **9** acetate, 25819-82-3; **10**, 34347-28-9; **10** acetate, 26033-11-4; **11**, 57-88-5; **12**, 80-97-7; ketene acetal, 816-05-7.