Oxidation of Natural Targets by Dioxiranes. 3.[1] Stereoselective Synthesis of (all-*R*)-Vitamin D_3 Triepoxide and of Its 25-Hydroxy Derivative

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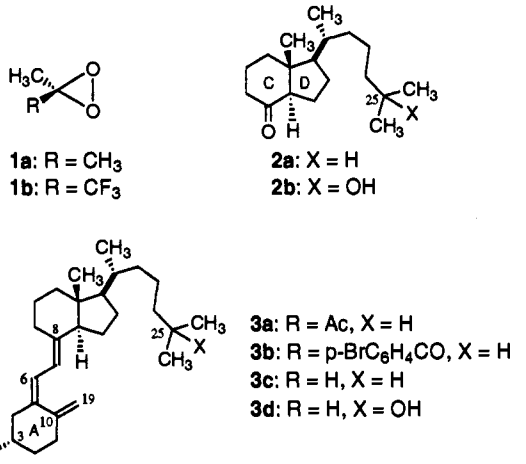
Abstract: In applying dimethyldioxirane (**1a**) and methyl(trifluoromethyl)dioxirane (**1b**) to the oxyfunctionalization of vitamin D_3 and of its 3-acyl derivatives, remarkable selectivities could be attained. Thus, reaction of 3β-acetylvitamin D_3 (**3a**) and of 3β-(*p*-bromobenzoyl)vitamin D_3 (**3b**) with dioxirane **1b** in CH_2Cl_2 at –40 °C displayed high diastereoselectivity, giving the corresponding *all-R* triepoxides **4a** and **4b**, in 85% and 83% isolated yield, respectively; X-ray crystallographic analysis allowed us to determine unambiguously the 5*R*,6*R*,7*R*,8*R*,10*R* stereochemistry of **4b**. In reacting with **1b** under the adopted conditions, vitamin D_3 itself (**3c**) also gave the corresponding *all-R* triepoxide **4c** (72% isolated yield); here, chemoselectivity is demonstrated by the fact that the unmasked secondary alcohol moiety at C-3 was left unaffected. Steric effects and intermolecular dipolar directing effects, exercised over the incoming oxidant by the epoxide functionalities sequentially introduced, are thought to dictate the high diastereoselectivity observed in the formation of triepoxides **4a–c**. By contrast, treatment of **3a** with dimethyldioxirane (**1a**) at –40 °C gave just the corresponding 7,8-epoxide **5** as the major product (yield 60%). High site selectivity was achieved in the subsequent oxyfunctionalization of triepoxide **3a** with excess methyl(trifluoromethyl)dioxirane (**1b**) in CH_2Cl_2 at 0 °C, which afforded the corresponding C-25 hydroxy derivative (**6**) in 82% isolated yield.

Introduction

The advent[2a] of dioxiranes on the scene of new synthetic reagents has led to the intensive utilization of these versatile oxidants;[2,3] recently, the combination of high reactivity, selectivity, neutral pH, and ease of product isolation presented by these new reagents has spurred their application to the oxyfunctionalization of non-natural[4] as well as natural targets.[1-3,5] For instance, we have successfully applied dimethyldioxirane (**1a**), and the more powerful methyl(trifluoromethyl)dioxirane (**1b**), to the regio-selective, stereoselective, and site-selective oxidation of steroids.[1,5a] Also, the direct oxyfunctionalization at C-25 of the side chain of cholestane derivatives could be achieved in high yield under mild conditions using dioxiranes.[1]

In the same study, we reported the analogous high-yield transformation of the Windaus–Grundmann ketone **2a** into its C-25 hydroxy derivative **2b**. This is significant, since **2b** can act as a precursor of the C,D-ring/side-chain fragment in convergent synthetic approaches to 25-hydroxycholecalciferol (**3d**);[6] the latter is an obligatory metabolic intermediate in the formation of the physiologically important 1α,25-dihydroxycholecalciferol, the hormonally active form of vitamin D_3 (**3c**).[6,7]



The rightly popular Lythgoe-type coupling of C,D-ring units,[6,7] such as **2b**, with the appropriate conjugate base of A-ring phosphine oxides is a reliable method to achieve the synthesis of hydroxy derivatives of vitamin D_3. As an alternative approach, however, we wished to explore the applicability of dioxiranes to the C-25 hydroxylation of suitable vitamin D_3 derivatives; indeed, this would complement our recent efforts directed toward the mentioned selective oxyfunctionalization in the cholestane steroid

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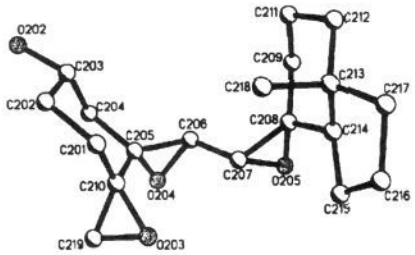


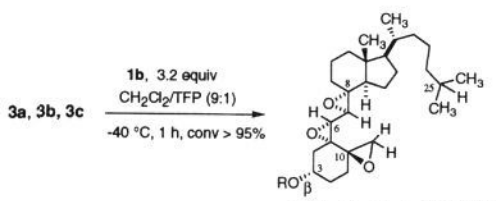
Figure 1. Computer-generated view of X-ray structure of triepoxide **4b**. For clarity, the *p*-bromobenzoyl group attached to O202 and the side chain departing from C-17 (C217 in the figure) have been omitted. Selected bond lengths (Å) are as follows: C(5)–C(10), 1.502(37); C(5)–C(6), 1.494(31); C(5)–O(4), 1.421(24); C(6)–O(4), 1.456(25); C(6)–C(7), 1.493(31); C(7)–O(5), 1.475(24); C(7)–C(8), 1.489(30); C(8)–O(5), 1.477(24); C(10)–C(19), 1.405(35); C(10)–O(3), 1.434(31); C(19)–O(3), 1.385(30).

series, featuring a biomimetic[7] highly site-selective hydroxylation at the side-chain C-25.[8]

Results and Discussion

Before attempting the side-chain oxyfunctionalization of vitamin D_3, we thought it appropriate to achieve prior protection of its 3-OH functionality and of the triene system. In fact, it is known that dioxirane epoxidations,[2,3] as well as transformation of secondary alcohol moieties into carbonyls,[9] occur much faster than O-insertion into "unactivated" C–H bonds of hydrocarbons.[10]

Along these lines, (+)-vitamin D_3 (cholecalciferol, **3c**) was preliminarily transformed into its 3β-acetyl derivative **3a**[11] using Ac_2O/py. By following reported protocols,[2] dimethyldioxirane (**1a**) solutions in acetone and methyl(trifluoromethyl)dioxirane (**1b**) in 1,1,1-trifluoropropanone (hereafter, TFP) were obtained. Then, reaction of the acetate **3a** with dioxirane **1b** (in only slight excess over stoichiometric) at low temperature produced the corresponding 5,6:7,8:10(19)-triepoxide **4a** in high yield and with practically complete substrate conversion at the conditions given in eq 1.



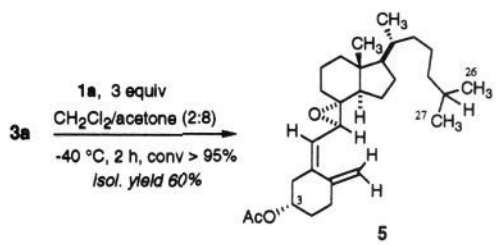
(1)

Likewise, oxidation of p-bromobenzoyl derivative **3b** (obtained upon treatment of **3c** with *p*-BrC_6H_4COCl/py) by dioxirane **1b** under the same conditions afforded a *single* diastereoisomeric triepoxide, i.e. **4b** (eq 1). The structural features of the latter were established by an X-ray crystallographic study; the anomalous dispersion contribution of the bromine atoms made it possible to confirm the absolute structure. The central portion of molecule **4b** is pictured in Figure 1, showing the triepoxide region. Its stereochemistry is seen to be 5,6(β):7,8(β):10(19)-(α), i.e. 5*R*,6*R*,7*R*,8*R*,10*R*.[12] Thus, in a single operation, *five* new stereocenters are efficiently generated.

That triepoxide **4a** has the same stereochemistry as **4b** is indicated by its ^1H and ^{13}C NMR spectra, which present strict similarities of chemical shift and coupling constant values for analogous resonances. For instance, for both **4a** and **4b**, the magnitude of the coupling constant relative to the C-6 and C-7 oxiranyl proton resonances ($^3J_{HH}$ = 7.7–7.8 Hz) speaks for a quasi *syn* (i.e., $\beta\beta$) disposition of the vicinal 5,6- and 7,8-oxirane moieties, with a dihedral angle Φ close to 175°.[13] Furthermore, the ^1H NMR parameters for the exocyclic $C^{19}H_aH_b$ system are quite similar, i.e. δ 2.87, 2.57 ($^2J_{HH}$ = 5.7 Hz) for **4a** and δ 2.90, 2.59 ($^2J_{HH}$ = 5.7 Hz) for **4b**.

In order to determine whether the high chemo- and stereoselectivity attained in triepoxide formation critically depends upon acyl protection of the 3-OH functionality, vitamin D_3 itself (**3c**) was made to react with dioxirane **1b**. Under the given controlled conditions, practically no oxidation of the secondary 3-OH functionality to carbonyl was found to occur; furthermore, the *all-R* triepoxide diastereomer was again isolated as the main reaction product (eq 1). The identity and diastereomeric purity of **4c** could be established from its ^1H and ^{13}C NMR spectra, as well as upon its conversion into **4a** by treatment with Ac_2O/py.

In the above reactions, it is remarkable that a single vicinal triepoxide diastereoisomer is isolated in good yield (eq 1). Apparently, the series of *three* consecutive epoxidations at the triene system of substrate proceeds with a high degree of stereocontrol.[14] Most likely, the sequence initiates with epoxidation at the more electron-rich unsaturated $\Delta^{7,8}$ moiety; this should be forced to occur at the β face, due to effective steric shielding by the flagpole 18α-CH_3. Indeed, we find that treatment of **3a** with 3 equiv of dimethyldioxirane (**1a**) at –40 °C results in the formation of 3β-acetyl-7,8(β)-epoxyvitamin D_3 (**5**) as the major product (yield 60%).[15]



(2)

It is worthy of note that the analogous 3β-(3,5-dinitrobenzoyl) derivative of vitamin D_2 (ergocalciferol) has been reported to react with monoperphthalic acid, also yielding the 7,8-epoxide.[15a] Furthermore, epoxidation of vitamin D_3 (**3c**) with *m*-chloroperbenzoic acid seemingly also occurs at the $\Delta^{7,8}$ unsaturated end of the triene system.[15c]

Once granted obligatory initial formation of the 7,8(β)-epoxide, however, further stringent stereoelectronic requirements—and possibly intermolecular dipolar directing effects[1] exercised by epoxide functionalities over the incoming oxidant[16]—must dictate the stereocontrolled synthesis of just one out of the remaining four possible[17] stereoisomers.

(8) Steroidal numbering.

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(14) Of the two remaining unsaturated sites (i.e., $\Delta^{5,6}$ and $\Delta^{10,19}$) available for epoxidation, each has two possible facial selectivities, for a total of four outcomes; a single diastereomer is formed in two sequential epoxidations with an overall yield of 85%. Thus, the average stereoselectivity is $100 \times (0.85)^{1/4}$ = 96%.

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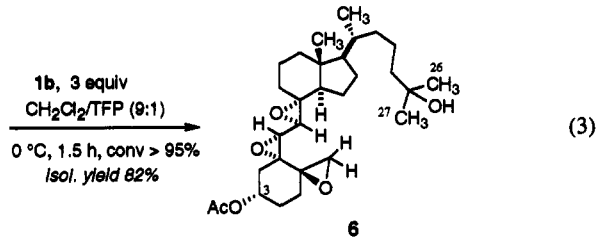
Finally, the reaction of triepoxide **4a** with dioxirane **1b** was found to be highly chemoselective and site-selective, producing the desired C-25 hydroxy derivative **6** in high yield, under remarkably mild conditions (eq 3).



(3)

This transformation can be monitored readily; in fact, in the ^{13}C NMR spectra of **6**, most telling is the appearance of a resonance at 71.06 ppm due to the C^{25}-OH. In the ^1H NMR spectra, the $C^{26}H_3$ and $C^{27}H_3$ resonances—a well defined 1:1 doublet (δ 0.83, $^3J_{HH}$ = 6.8 Hz) for **4a**—give a sharp singlet (δ 1.18) for **6**, owing to removal of the C-25 proton.

Conclusion

The feat of high diastereoselectivity in the triepoxidation of vitamin D_3 and its derivatives using dioxiranes is remarkable; in fact, it presents one more case speaking for the potential in synthesis of this new class of powerful and yet selective oxidants. Equally notable seems the finding that, once the 3-OH functionality and the triene moiety of these derivatives are protected, the key site-selective C-25 oxyfunctionalization[1] can be performed efficiently. Indeed, selective deoxygenation[6a,18] of all three epoxide functionalities of **6** (with retention of the original triene geometry) and hydrolysis would give 25-hydroxycholecalciferol (**3d**) in a novel synthetic approach that is alternative to current methods. Efforts in this direction are underway in our laboratories.

Experimental Section

Equipment and Methods. Melting points were not corrected. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM 500 or on a Varian XL 200 spectrometer. The ^1H NMR are referenced to residual isotopic impurity $CHCl_3$ (7.26 ppm) of the solvent $CDCl_3$ and/or to TMS; the ^{13}C NMR spectra are referenced with respect to the middle peak of $CDCl_3$ solvent (77.0 ppm). Mass spectra were run on a VG ZAB 2F instrument; accurate mass measurements (±0.005) were performed by the peak matching technique at 10 000 resolving power, with 10% valley definition. The FT-IR or IR spectra were recorded on a Perkin-Elmer Model 1710 or Model 681 instrument, interfaced with a Model 7350 data station. Optical rotations were measured employing a Perkin-Elmer Model 241 MC spectropolarimeter. The GLC analyses were performed on a Perkin-Elmer Model 3800 chromatograph, equipped with an Epson Model FX 850 data station, using a SE 30 capillary column (30 m × 0.25 μm i.d.). In most of the cases, column flash chromatography was carried out using silica gel (eluent petroleum ether/Et_2O or *n*-hexane/Et_2O), and TLC was performed on precoated silica gel plates (Kieselgel 60, Merck F 254). The X-ray structure determination was carried out at Brown University using a Siemens P4 diffractometer (Mo Kα radiation, at 298 K). The XSCANS software collected data automatically and determined the unit cell; this contained two crystallographically independent molecules, both having the same configuration (see supplementary material).

Materials. All solvents, starting materials, and compounds used as reference standards in product analyses were of the highest purity commercially available; further purification, whenever appropriate, was achieved by following conventional methods. Purified methylene chloride, acetone, and 1,1,1-trifluoro-2-propanone (TFP) (bp 22 °C) solvents were stored over 5-Å molecular sieves at 2–5 °C, routinely redistilled, and flushed with dry N_2 prior to use. Curox triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (a gift by Peroxid-Chemie GmbH, Münich, Germany) was our source of potassium peroxymonosulfate; it was used as received for the synthesis of dioxiranes **1a** and **1b**. Solutions of 0.08–0.16 M dimethyldioxirane (**1a**)[2b-d] in acetone and of 0.8–1.0 M methyl(trifluoromethyl)dioxirane (**1b**)[2e] in TFP were obtained by adopting procedures, equipment, and precautions which have been already described in detail.[2,3] Commercial (Fluka) (5*Z*,7*E*)-3β-hydroxy-9,10-secocholesta-5,7,10(19)-triene (**3d**, vitamin D_3) was employed as starting material.

(5*Z*,7*E*)-3β-Acetoxy-9,10-secocholesta-5,7,10(19)-triene (3a)[11] was obtained upon reaction of vitamin D_3 (**3c**) with Ac_2O/py (yield 85%): colorless viscous oil; ^1H NMR (200 MHz, $CDCl_3$) δ 6.21 (d, J = 11.1 Hz, 1 H, C^6H), 6.02 (d, J = 11.4 Hz, 1 H, C^7H), 5.05 (m, 1 H, $C^{19}H_a$), 4.93 (m, 1 H, C^3H), 4.83 (d, J = 2.3 Hz, 1 H, $C^{19}H_b$), 2.03 (s, 3 H, CH_3CO), 0.91 (d, J = 6.0 Hz, 3 H, $C^{21}H_3$), 0.864 (d, J = 6.6 Hz, 3 H, $C^{26}H_3$), 0.860 (d, J = 6.6 Hz, 3 H, $C^{27}H_3$), 0.54 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.63 (CH_3CO), 144.61, 142.48, 134.28, 122.43, 117.44, 112.70, 71.78 (C^3), 56.57, 56.35, 45.90, 42.13, 40.53, 39.49, 36.12 (C^{20} and C^{22}), 32.18, 31.96, 29.05, 28.01, 27.66, 23.86, 23.56, 22.82 (C^{26}), 22.55 (C^{27}), 22.21, 21.41 (CH_3CO), 18.83, 11.97 (C^{18}); IR (neat) 2955, 2875, 1742 (C=O), 1466, 1444, 1379, 1244, 1124, 1034, 957, 899 cm^{-1}.

(5*Z*,7*E*)-3β-((*p*-Bromobenzoyl)oxy)-9,10-secocholesta-5,7,10(19)-triene (3b) was synthesized upon reaction of **3c** with p-BrC_6H_4COCl/py (yield 82%): after column chromatography, mp 49–51 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87–7.52 (m, AA'XX' system, 4 H, ArH), 6.23 (d, J = 11.2 Hz, 1 H, C^6H), 6.04 (d, J = 11.2 Hz, 1 H, C^7H), 5.18 (m, 1 H, C^3H), 5.08 (m, 1 H, $C^{19}H_a$), 4.87 (d, J = 2.3 Hz, 1 H, $C^{19}H_b$), 0.91 (d, J = 6.4 Hz, 3 H, $C^{21}H_3$), 0.86 (d, J = 6.6 Hz, 3 H, $C^{26}H_3$), 0.85 (d, J = 6.6 Hz, 3 H, $C^{27}H_3$), 0.54 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.19 (C=O), 144.54, 142.55, 134.02, 131.61, 131.12, 129.61, 127.87, 122.68, 117.43, 112.84, 72.64 (C^3), 56.61, 56.37, 45.93, 42.17, 40.54, 39.50, 36.13 (C^{20} and C^{22}), 32.19, 31.99, 29.07, 28.00, 27.66, 23.87, 23.57, 22.81 (C^{26}), 22.55 (C^{27}), 22.24, 18.85, 11.99 (C^{18}); FTIR (KBr) 2949, 2867, 1719 (C=O str), 1591, 1477, 1397, 1272, 1115, 1102, 1069, 1013, 847, 757 cm^{-1}.

Dioxirane Oxidation of Substrates 3a–c and 4a—General Procedure. The reactions were carried out under the conditions given in eqs 1–3. An aliquot (usually from 2 to 20 mL) normally containing 3 equiv of standardized[2] cold solution of methyl(trifluoromethyl)dioxirane (**1b**) (ca. 1 M in TFP) or of dimethyldioxirane (**1a**) (ca. 0.1 M in acetone) was added in two or three portions during 10–30 min to a stirred solution of 1 equiv of the substrate (200–900 mg) in CH_2Cl_2 (5–20 mL), kept at the given temperature (–40 or 0 °C). After the reaction was complete (TLC monitoring), product isolation was achieved upon removal of solvent *in vacuo*, followed by column chromatography. Whenever appropriate, the products thus isolated were further purified by recrystallization and identified as reported below.

3β-Acetoxy-5,6:7,8:10(19)-triepoxy-9,10-secocholestane (4a): mp 53–55 °C, white laths (acetone); ^1H NMR (200 MHz, $CDCl_3$) δ 4.81 (m, 1 H, C^3H), 3.44 (d, J = 7.8 Hz, 1 H, C^7H), 2.87 (d, J = 5.7 Hz, 1 H, $C^{19}H_a$), 2.80 (d, J = 7.8 Hz, 1 H, C^6H), 2.57 (d, J = 5.7 Hz, 1 H, $C^{19}H_b$), 2.02 (s, 3 H, CH_3CO), 0.89 (d, J = 6.0 Hz, 3 H, $C^{21}H_3$), 0.83 (d, J = 6.8 Hz, 6 H, $C^{26}H_3$, $C^{27}H_3$), 0.74 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.20 (C=O), 70.18 (C^3), 65.56, 63.59, 59.79, 56.61, 55.97, 55.86, 53.87, 50.50, 45.57, 40.30, 39.35, 35.96, 35.56 (C^{20} and C^{22}), 30.64, 30.30, 29.43, 27.95, 27.28, 23.78, 22.90, 22.79 (C^{26}), 22.52 (C^{27}), 21.17 (CH_3CO), 19.99, 18.74, 13.08 (C^{18}); IR (KBr) 2961, 2936, 1744 (C=O str), 1466, 1381, 1243, 1099, 1043, 966, 922, 872 cm^{-1}; $[\alpha]_D$ +82.3° (*c* 0.38, acetone); HRMS (EI, 70 eV) calcd for $C_{29}H_{46}O_5$ 474.3345, found m/z 474.3340 (M_x).

(5*R*,6*R*,7*R*,8*R*,10*R*)-3β-((*p*-Bromobenzoyl)oxy)-5,6:7,8:10(19)-triepoxy-9,10-secocholestane (4b): mp 171–172 °C, colorless crystals (acetone/MeOH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.84–7.53 (m, AA'XX' system, 4 H, ArH), 5.06 (m, 1 H, C^3H), 3.45 (d, J = 7.7 Hz, 1 H, C^7H), 2.90 (d, J = 5.5 Hz, 1 H, $C^{19}H_a$), 2.84 (d, J = 7.7 Hz, 1 H, C^6H), 2.59 (d, J = 5.7 Hz, 1 H, $C^{19}H_b$), 0.89 (d, J = 6.3 Hz, 3 H, $C^{21}H_3$), 0.823 (d, J = 6.5 Hz, 3 H, $C^{26}H_3$), 0.819 (d, J = 6.5 Hz, 3 H, $C^{27}H_3$), 0.76 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.00 (C=O), 131.80, 131.08, 128.78, 128.41, 71.08 (C^3), 65.59, 63.60, 59.77, 56.65, 55.97, 55.86, 53.89, 50.54, 45.60, 40.38, 39.37, 35.98, 35.58 (C^{20} and C^{22}), 30.68, 30.39, 29.67, 27.95, 27.28, 23.80, 22.95, 22.78 (C^{26}), 22.52 (C^{27}), 20.02, 18.76, 13.13 (C^{18}); FTIR (KBr) 2953, 2868, 1722 (C=O), 1593, 1466, 1398, 1379, 1311, 1278, 1106, 1072, 1012, 924, 871, 846, 756 cm^{-1}; $[\alpha]_D$ +101° (*c* 0.30, acetone); X-ray structure, see Figure 1.

3β-Hydroxy-5,6:7,8:10(19)-triepoxy-9,10-secocholestane (4c): mp 184–186 °C, colorless crystals (CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 3.85 (m, 1 H, C^3H), 3.44 (d, J = 8.0 Hz, 1 H, C^7H), 2.87 (dd, ^2J = 5.5 Hz, J = 1.5 Hz (long-range coupling), 1 H, $C^{19}H_a$), 2.78 (d, J = 7.5

(17) That is, the ($\alpha\beta\alpha$)-, ($\alpha\beta\beta$)-, ($\beta\beta\alpha$)-, and ($\beta\beta\beta$)-5,6:7,8:10(19)-triepoxide.

(18) Martin, M. G.; Ganem, B. *Tetrahedron Lett.* **1984**, *25*, 251.

Hz, 1 H, C^6H), 2.57 (d, J = 5.5 Hz, 1 H, $C^{19}H_b$), 0.89 (d, J = 6.5 Hz, 3 H, $C^{21}H_3$), 0.832 (d, J = 6.6 Hz, 3 H, $C^{26}H_3$), 0.827 (d, J = 6.6 Hz, 3 H, $C^{27}H_3$), 0.74 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 68.96 (C^3), 65.54, 63.62, 60.05, 56.58, 56.10, 56.01, 53.87, 50.67, 45.55, 44.02, 39.35, 35.95, 35.57 (C^{20} and C^{22}), 33.96, 30.64, 29.62, 27.95, 27.27, 23.77, 22.90, 22.80 (C^{26}), 22.53 (C^{27}), 20.00, 18.74, 13.11 (C^{18}); IR (KBr) 3440 (OH), 2953, 2873, 1466, 1374, 1270, 1117, 1093, 1064, 962, 922, 869 cm^{-1}; $[\alpha]_D$ +54.0° (c 0.60, acetone). Treatment of **4c** with Ac_2O/py, followed by flash column chromatography (silica gel, petroleum ether/Et_2O 8:2), afforded acetyl derivative **4a** in 75% isolated yield.

(5*Z*)-(7*R*,8*R*)-3β-Acetoxy-7,8-epoxy-9,10-secocholesta-5,10(19)-diene (5): viscous oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.17 (d, J = 9.3 Hz, 1 H, C^6H), 5.01 (m, 1 H, $C^{19}H_a$), 4.94 (m, 1 H, C^3H), 4.81 (d, J = 2.3 Hz, 1 H, $C^{19}H_b$), 3.85 (d, J = 9.3 Hz, 1 H, C^7H), 2.01 (s, 3 H, CH_3CO), 0.89 (d, J = 6.4 Hz, 3 H, $C^{21}H_3$), 0.84 (d, J = 6.6 Hz, 3 H, $C^{26}H_3$), 0.83 (d, J = 6.6 Hz, 3 H, $C^{27}H_3$), 0.66 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.64 (CH_3CO), 144.46, 144.31, 121.50, 112.62, 71.18 (C^3), 65.54, 56.57, 56.31, 54.06, 45.87, 41.98, 39.41, 36.04, 35.57, 31.87, 31.72, 30.70, 27.97, 27.37, 23.79, 22.79 (C^{26}), 22.53 (C^{27}), 22.25, 21.34 (CH_3CO), 19.96, 18.74, 12.61 (C^{18}); IR (neat) 2957, 2942, 1739 (C=O), 1640, 1466, 1446, 1378, 1245, 1165, 1082, 1049, 1035, 959, 916, 877 cm^{-1}; $[\alpha]_D$ +24.3° (c 0.50, acetone); HRMS (EI, 70 eV) calcd for $C_{29}H_{46}O_3$ 442.3435, found m/z 442.3395 (M_x).

3β-Acetoxy-5,6:7,8:10(19)-triepoxy-9,10-secocholestan-25-ol (6): mp 61–63 °C, colorless leaflets (acetone); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.80 (m, 1 H, C^3H), 3.45 (dd, ^3J = 7.8 Hz, J = 1.4 Hz (long-range coupling), 1 H, C^7H), 2.88 (dd, ^2J = 5.6 Hz, J = 1.4 Hz (long-range coupling), 1 H, $C^{19}H_a$), 2.81 (d, J = 7.8 Hz, 1 H, C^6H), 2.58 (d, J = 5.6 Hz, 1 H, $C^{19}H_b$), 2.03 (s, 3 H, CH_3CO), 1.18 (s, 6 H, $C^{26}H_3$, $C^{27}H_3$), 0.91 (d, J = 5.9 Hz, 3 H, $C^{21}H_3$), 0.75 (s, 3 H, $C^{18}H_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.25 (C=O), 71.06 (C^{25}), 70.18 (C^3), 65.54, 63.60, 59.81, 56.52, 55.99, 55.87, 53.84, 50.52, 45.58, 44.26, 40.28, 39.32, 36.24, 35.57, 30.63, 30.29, 29.43, 29.33 (C^{26}), 29.21 (C^{27}), 27.30, 22.90, 21.16 (CH_3CO), 20.71, 19.98, 18.72, 13.07 (C^{18}); FTIR (KBr) 3500 (OH), 2960, 2868, 1740 (C=O), 1467, 1380, 1240, 1166, 1148, 1099, 1039, 963, 948, 923, 867 cm^{-1}; $[\alpha]_D$ +66.4° (c 1.02, acetone); HRMS (EI, 70 eV) calcd for $C_{29}H_{46}O_6$ 490.3294, found m/z 490.3264 (M_x).

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Supplementary Material Available: Thermal ellipsoid and unit cell diagrams, summary of X-ray diffraction data, and tables of atomic coordinates, bond lengths and angles, anisotropic thermal parameters, H atom coordinates, and isotropic displacement coefficients for triepoxide **4b** (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.