Oxidation of Natural Targets by Dioxiranes. 4.[1] High Stereo- and Regioselective Conversion of Vitamin D_2 to Its (*all-R*) Tetraepoxide and C-25 Hydroxy Derivative

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Abstract: Upon reaction with methyl(trifluoromethyl)dioxirane (**1b**) at −40 °C, vitamin D_2 (**2a**) or its 3β-acetyl derivative (**2b**) give in high yield (78−80%) the corresponding tetraepoxide (**3a,b**) as a single diastereoisomer having the 5,6(β);7,8(β);10,19(α);22,23(pseudo-α) configuration. Transformation of tetraepoxide **3a** into its 3β-(*p*-bromobenzoyl) derivative **3c** allowed X-ray diffraction analysis; this permitted us to ascertain that the stereomeric tetraepoxide product has the *R* configuration at all of the seven newly generated stereocenters, i.e. 5*R*,6*R*;7*R*,8*R*;10*R*(19);22*R*,23*R*. The oxidation of 3β-acetyl vitamin D_2 (**2b**) with the less powerful dimethyldioxirane (**1a**) led to the corresponding 5,6(β);7,8(β);10,19(α)-triepoxide **4** as the major product (62%), accompanied by tetraepoxide **3b** (26%). Parallel to vitamin D_3 triepoxide, remarkable site selectivity was monitored in oxyfunctionalization of 3β-acetyl vitamin D_2 tetraepoxide (**3b**) at the side-chain tertiary C-25. Reaction of tetraepoxide **3b** with the powerful dioxirane **1b** at 0 °C left the epoxide groups and remaining C-H functionalities intact, affording the 25-hydroxy derivative **5** in good isolated yield (61%).

Introduction

We have shown that remarkable regio- and stereoselectivities can be attained in applying dioxiranes,[2] such as dimethyldioxirane (**1a**) or methyl(trifluoromethyl)dioxirane (**1b**), to the oxyfunctionalization of several steroids[3] and of vitamin D_3 (cholecalciferol) derivatives.[1] For instance, reaction of 3β-acetyl vitamin D_3 with methyl(trifluoromethyl)dioxirane (**1b**) displayed high diastereoselectivity, affording—among the eight possible diastereoisomers resulting from the three epoxide functionalities introduced—just the corresponding (*all-R*) $\beta\beta\alpha$-triepoxide in high yield.[1] This step, amounting to an effective "masking" of the vitamin D_3 triene system with dioxirane-resistant epoxide moieties, was a necessary preliminar to site-selective C-H functionalization at C-25 leading to the relevant 25-OH derivative.[4]

It is now established that the sequence of hydroxylations which vitamin D_3 (cholecalciferol) undergoes in biological system is triggered by its crucial transformation into its 25-hydroxy derivative in the liver.[5] Similar to the natural vitamin D_3, the unnatural vitamin D_2 (ergocalciferol) must first experience hydroxylation at C-25, then at C-1 before expressing biological activity.[5] With respect to their vitamin D_3 analogues, vitamin D_2 (**2a**) and derivatives present an additional C═C bond with *E* configuration at C-22 as well as a further chiral center at C-24, which renders the synthetic approach more arduous.[6] Because of this additional complexity, it was challenging to explore whether and how the high regio- and stereoselectivities attainable in the dioxirane oxidation of vitamin D_2 (**2a**) change with respect to the vitamin D_3 case.

Results and Discussion

Multiple Epoxidation of Vitamin D_2. Standardized solutions of 0.5−1.0 M methyl(trifluoromethyl)dioxirane (**1b**)[7] in 1,1,1-trifluoropropanone (hereafter, TFP) and of 0.06−0.10 M dimethyldioxirane (**1a**)[8] in acetone could be obtained by following reported procedures.[7,8] We found that careful addition of cold aliquots of **1b** solution during ca. 1.5 h to either vitamin D_2 (**2a**) or to its 3-acetyl derivative (**2b**) at the conditions given in eq 1 resulted in the production of a *single* tetraepoxide diasteroisomer in high yield.

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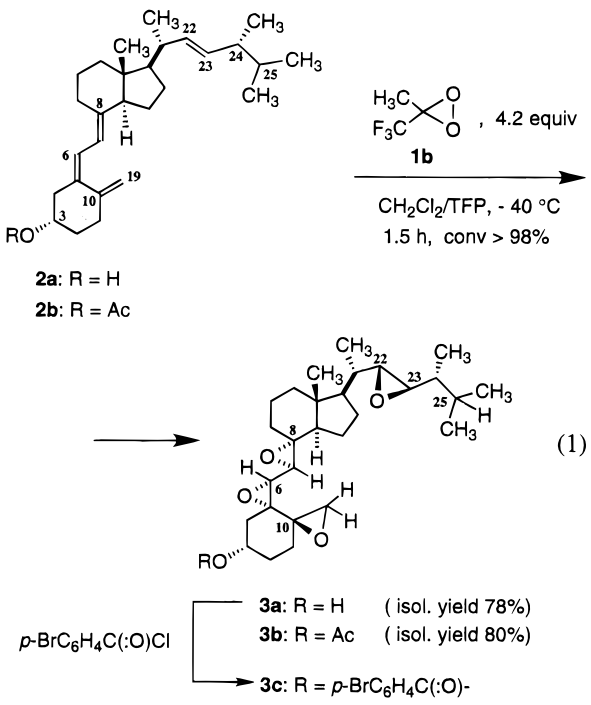


(1)

That the two tetraepoxides had identical stereochemistry was established by the conversion of **3a** into its 3β-acetyl derivative, having ^{1}H and ^{13}C NMR spectra identical with those of **3b**. Next, **3a** was transformed into its *p*-bromobenzoyl derivative **3c** (eq 1). That this derivative has the same stereochemistry as **3b** and **3a** is demonstrated by a comparison of their ^{1}H and ^{13}C NMR spectra, which present strict similarities of chemical shift and coupling constant values for analogous resonances. For instance, the ^{1}H NMR chemical shift and coupling constant 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 **3b**, and δ 2.90, 2.59 ($^2J_{HH}$ = 5.7 Hz) for **3c**; for both **3b** and **3c** (analogous to what was recorded for vitamin D_3 triepoxide[1]), the coupling constant value of the C-6 and C-7 oxiranyl proton resonances ($^3J_{HH}$ = 7.7−7.8 Hz) is indicative of a quasi *syn* (i.e., $\beta\beta$) disposition of the vicinal 5,6- and 7,8-oxirane moieties.[1] The crystalline *p*-bromobenzoyl derivative **3c** was found suitable for X-ray analysis; its structural features are displayed in Figure 1.

The anomalous dispersion contribution of the bromine atoms allowed us to establish the absolute configuration at the *seven* newly generated stereocenters, which is seen to be 5*R*,6*R*;7*R*,8*R*;10*R*(19);22*R*,23*R*.

On the basis of our previous findings concerning dioxirane epoxidation of vitamin D_3 derivatives,[1] high diastereoselectivity (d.e. ≥92%) might perhaps have been expected for the transformation of the analogous triene system of vitamin D_2, leading to a 5,6(β);7,8(β);10,19(α) triepoxide moiety. However, epoxidation at the side-chain $\Delta^{22,23}$ unsaturation in vitamin D_2 must also occur with surprisingly high diastereoselectivity; this is manifested by the production of a single tetraepoxide (**3a** or **3b**) in 78−80% isolated yield (eq 1), with average stereoselectivity of ca. 94%. It is likely that this derives from the well-known sensitivity of dioxirane epoxidation to steric and stereoelectronic alignment effects.[2a,9] On this ground, a rationale for the highly stereoselective production of the mentioned vitamin D_3 $\beta\beta\alpha$-triepoxide was proposed;[1] for the multiple

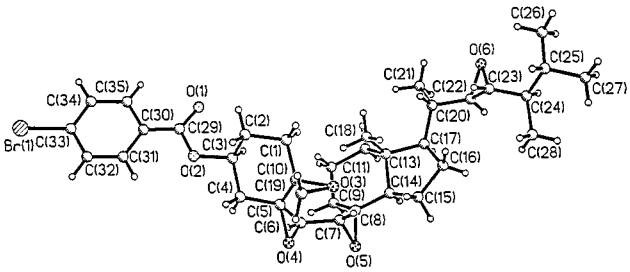
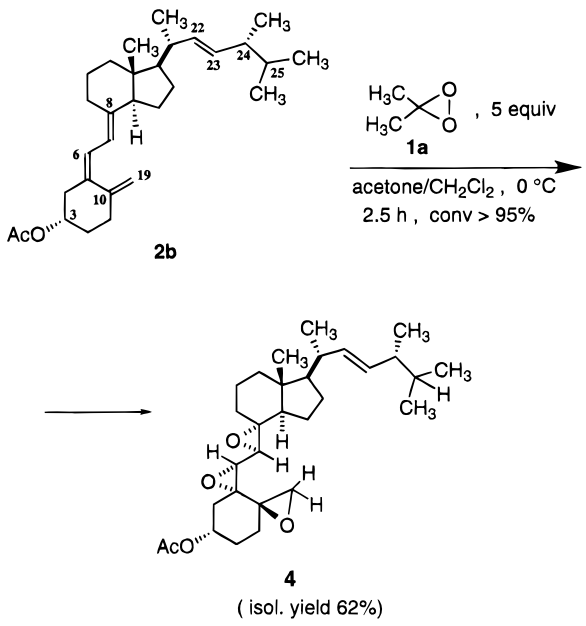


Figure 1. Computer-generated view of X-ray structure of tetraepoxide **3c**. Selected bond lengths (Å) are as follows: O(3)−C(10), 1.420(10); O(3)−C(19), 1.491(13); O(4)−C(5), 1.453(10); O(4)−C(6), 1,461(10); O(5)−C(7), 1.434(10); O(5)−C(8), 1.457(10); O(6)−C(22), 1.441(10); O(6)−C(23), 1.439(11); C(10)−C(19), 1.524(14); C(5)−C(6), 1.478(13); C(7)−C(8), 1.457(12); C(22)−C(23), 1.430(12). Mean C−O in epoxide groups: 1.45(2). Mean C−C [excluding C(10)−C(19)]: 1.46(2).

epoxidation of vitamin D_2, it can likewise be applied to a preliminary stereoselective generation of the vicinal 5,6(β);7,8(β);10,19(α) triepoxide moiety. In fact, ^{1}H- and ^{13}C-monitoring of the reaction between **2a** or **2b** with dioxirane **1b** unexpectedly revealed that epoxidation at $\Delta^{22,23}$ occurs last. Actually, using the less powerful dimethyldioxirane (**1a**) the epoxidation of **2b** could be stopped short of epoxidation at the side-chain C═C at the conditions given in eq 2, affording triepoxide **4** in >60% yield alongside the above described tetraepoxide **3a** (yield 26%). The intermediate triepoxide could be isolated and fully characterized.



(2)

With the epoxidation in the side chain of vitamin D_2 taking place at the end of the sequence involving the introduction of four oxirane functionalities, a rationale for the high diastereoselectivity recorded at $\Delta^{22,23}$ might be advanced as represented in Figure 2.

Given that the unsaturation brings about a certain conformational rigidity of the side chain, it is seen that only one face of the residual C═C π system is relatively unencumbered to dioxirane attack in a *spiro* stereo arrangement.[2a,9] Concurrent with this, the given stereoselective epoxidation could be explained in terms of allylic strain and "matched" induction by the C-20 and C-24 stereocenters.[10]

Selective Side-Chain Oxyfunctionalization at C-25. This crucial oxyfunctionalization at the side-chain was performed using 3β-acetyl vitamin D_2 tetraepoxide **3b** as starting material;

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(10) We thank a reviewer for the suggestion of this rationale.

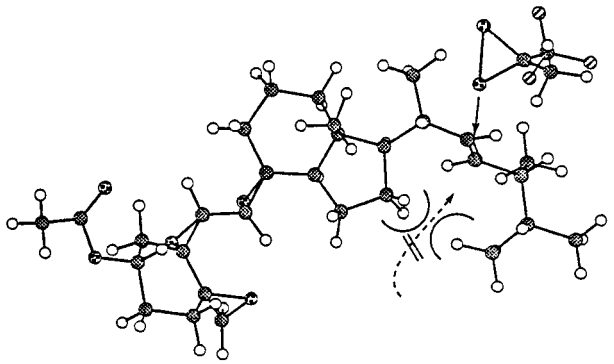
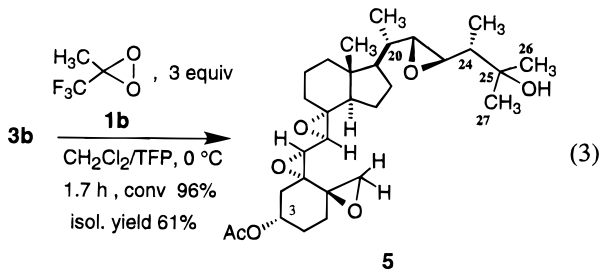


Figure 2. Likely transition state for face-selective dioxirane attack at the side-chain C=C of 3β-acetyl vitamin D_2 triepoxide (**4**); the stereoformula of the latter was minimized using implemented MM2 force field (CambridgeSoft Corp. software, Chem3D Pro. v.3.3 output).

protection of the secondary C-OH functionality at C-3 was deemed essential in order to avoid its facile oxidation to carbonyl by the dioxirane.[11] As it is seen by inspection of eq 3,



(3)

employing the powerful dioxirane **1b** we could achieve in satisfactory yield the site-selective conversion of **3b** into its key C-25(OH) derivative **5**. This transformation is easily monitored since the ^{1}H NMR multiplicity of the C-26 and C-27 methyl resonances (doublet) in **3b** is removed on going to **5**, and a distinct C-25(OH) signal (δ 73.46) becomes apparent in the ^{13}C NMR of the latter.

This surprisingly high site selectivity for dioxirane O-insertion at the tertiary C25-H parallels that already recorded for the analogous triepoxide of vitamin D_3. In the case at hand this might seem even more amazing since, besides the tertiary C-20, the vitamin D_2 derivative **3b** presents an additional tertiary C-H at C-24. However, here oxidation at the C-24 and C-20 carbon−hydrogen bond might be discouraged because of inductive deactivation by the proximal 22,23-epoxide moiety.[10]

On the other hand, a precedent for the given site-selective C-25 hydroxylation could be found in the distinct preference usually displayed by dioxiranes in attacking tertiary C-H centers bearing geminal methyl groups as compared to the other tertiary C-H positions available in target molecules such as some cholestane derivatives.[3] We have already described in detail a suitable FMO model[12] that provides a distinctive rationale for the stringent steric and stereoelectronic requirements which are likely to dictate the high stereoselectivity of dioxirane O-insertion at C-H bonds.[2a,13]

In view of the versatility of the epoxide moiety as a precursor to diverse functionalities, the efficient access to the tetraepoxide of vitamin D_2 in high diastereomeric purity and to its C-25(OH) derivative reported herein show promise to pave the road to the synthesis of a number of interesting derivatives of this target molecule. Thus, further work in this promising area is warranted.

Experimental Section

General 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 and routinely redistilled 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 0.06−0.10 M dimethyldioxirane (**1a**) in acetone[8] and of 0.5−1.0 M methyl(trifluoromethyl)dioxirane (**1b**) in TFP[7] were obtained by adopting procedures, equipment, and precautions which have been already described in detail.[2b,7,8] Commercial (Fluka) (5*Z*,7*E*,22*E*)-3β-hydroxy-9,10-secoergosta-5,7,10(19),22-tetraene (**2a**, vitamin D_2) was employed as starting material after further purification by column chromatography (silica gel, petroleum ether/Et_2O 4:1). High-resolution 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.

3β-Hydroxy-5,6;7,8;10,19;22,23-tetraepoxy-9,10-secoergostane (3a). A cold solution of dioxirane **1b** (0.51 M in TFP, 24.5 mL, 12.5 mmol) was added during 1 h in three equal portions to a solution of **2a** (1.18 g, 3.0 mmol) in CH_2Cl_2 (5 mL) kept at −40 °C; TLC monitoring revealed that the starting material was consumed after ca. 1.5 h. Removal of the solvent in vacuo, followed by flash column chromatography (silica gel, petroleum ether/Et_2O (3:7)) afforded the tetraepoxide, as white laths (1.07 g, 2.3 mmol, yield 78%): mp 196−199 °C, colorless crystals (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (m, 1 H), 3.44 (d, J = 7.8 Hz, 1 H), 2.84 (dd, J = 5.7 Hz, J = 1.6 Hz [long-range coupling], 1 H), 2.76 (d, J = 7.8 Hz, 1 H), 2.56−2.54 (m, 2 H), 2.41 (d, J = 7.9 Hz, J = 2.3 Hz (long-range coupling), 1 H), 0.95 (d, J = 6.9 Hz, 3 H), 0.93 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.88 (d, J = 6.8 Hz, 3 H), 0.72 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.84, 65.38, 63.68, 63.49, 60.23, 60.09, 60.06, 56.25, 56.01, 53.44, 50.59, 45.78, 43.92, 42.18, 39.17, 38.24, 33.87, 31.05, 30.61, 29.60, 25.90, 22.80, 20.40, 20.16, 19.44, 15.97, 13.60, 13.10; IR (KBr) 3409, 1442, 1358 cm^{-1}; $[\alpha]_D$ +32.2° (*c* 0.43, acetone); HRMS (EI, 70 eV) calcd for $C_{28}H_{44}O_5$ *m/z* 460.3177, found *m/z* 460.3208 (M_x).

Treatment of **3a** with Ac_2O/pyridine, followed by flash column chromatography (silica gel, petroleum ether/Et_2O (9:1)), afforded acetate **3b** indistinguishable with material produced as described below.

3β-Acetoxy-5,6;7,8;10,19;22,23-tetraepoxy-9,10-secoergostane (3b). By following the same procedure, reaction of dioxirane **1b** (0.734 M in TFP, 13.8 mL, 10.2 mmol) with **2b** (1.06 g, 2.42 mmol) in CH_2Cl_2 (4 mL) at −40 °C afforded, after column chromatography (silica gel, petroleum ether/Et_2O (9:1)), the tetraepoxide as colorless crystals (0.973 g, 1.94 mmol, yield 80%): mp 62−65 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.81 (m, 1 H), 3.45 (d, J = 7.8 Hz, 1 H), 2.87 (dd, J = 5.7 Hz, J = 1.5 Hz (long-range coupling), 1 H), 2.80 (d, J = 7.8 Hz, 1 H), 2.57 (d, J = 5.6 Hz, 1 H), 2.54 (m, 2 H), 2.03 (s, 3 H), 0.97 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.90 (d, J = 6.7 Hz, 6 H), 0.74 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.20, 70.18, 65.46, 63.74, 63.45, 60.20, 59.80, 56.31, 55.89, 55.84, 53.46, 50.48, 45.85, 42.25, 40.25, 39.20, 38.34, 31.10, 30.67, 30.28, 29.43, 25.99, 22.87, 21.18, 20.45, 20.22, 19.50, 16.05, 13.67, 13.14; FT-IR (KBr) 1741, 1463, 1379 cm^{-1}; $[\alpha]_D$ +40.9° (*c* 0.69, acetone); HRMS (EI, 70 eV) calcd for $C_{30}H_{46}O_6$ *m/z* 502.3282, found *m/z* 502.3304 (M_x).

(5*R*,6*R*,7*R*,8*R*,10*R*)-3β-((*p*-Bromobenzoyl)oxy)-5,6;7,8;10,19;22,23-tetraepoxy-9,10-secoergostane (3c) was obtained upon reaction of **3a** with *p*-BrC_6H_4COCl/pyridine (yield 71%); after column chromatography (silica gel, petroleum ether/Et_2O (7:3)): mp 203−206 °C, colorless crystals (acetone/EtOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85−7.54 (m, *AA′XX′* system, 4 H), 5.05 (m, 1 H), 3.46 (d, J = 7.7 Hz, 1 H), 2.90 (dd, J = 5.7 Hz, J = 1.4 Hz, 1 H), 2.84 (d, J = 7.7 Hz, 1 H), 2.59 (d, J = 5.7 Hz, 1 H), 2.55 (dd, J = 7.0 Hz, J = 2.3 Hz, 1 H), 2.41 (dd, J = 7.9 Hz, J = 2.3 Hz, 1 H), 0.97 (d, J = 6.8 Hz, 3 H), 0.93 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.89 (d, J = 6.8 Hz, 3 H), 0.76 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.23, 131.71, 131.69,

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(13) Kuck, D.; Schuster, A.; Fusco, C.; Fiorentino, M.; Curci, R. *J. Am. Chem. Soc.* **1994**, *116*, 2375.

131.07, 131.00, 128.69, 128.33, 71.00, 65.38, 63.63, 63.39, 60.13, 59.69, 56.27, 55.81, 55.75, 53.40, 50.44, 45.78, 42.15, 40.24, 39.15, 38.26, 31.02, 30.62, 30.27, 29.36, 25.90, 22.82, 20.35, 20.15, 19.41, 15.98, 13.56, 13.10; IR (KBr) 1704, 1575, 1444, 1367 cm^{-1}; $[\alpha]_D$ +81.7° (*c* 0.42, acetone); X-ray structure, see Figure 1.

(22*E*)-(5*R*,6*R*,7*R*,8*R*,10*R*)-3*β*-Acetoxy-5,6;7,8;10(19)-triepoxy-9,10-secoergosta-22-ene (4). A cold solution of dioxirane **1a** (0.07 M in acetone, 51 mL, 3.6 mmol) was added during 1.5 h in three portions to a solution of **2b** (318 mg, 0.72 mmol) in CH_2Cl_2 (2 mL) at 0 °C; TLC and GC monitoring revealed that the starting material was completely consumed after ca. 2.5 h. Removal of the solvent in vacuo, followed by flash column chromatography (silica gel, petroleum ether/Et_2O (9:1)) afforded tetraepoxide **3b** (95 mg, 0.19 mmol, yield 26%) and triepoxide **4** (273 mg, 0.56 mmol, yield 78%): mp 124−127 °C, colorless crystals; ^1H NMR (500 MHz, $CDCl_3$) δ 5.15 (d, J = 9.6 Hz, 1 H), 5.14 (d, J = 10.3 Hz, 1 H), 4.82 (m, 1 H), 3.45 (d, J = 7.8 Hz, 1 H), 2.88 (dd, J = 1.7 Hz, J = 5.7 Hz, 1 H), 2.81 (d, J = 7.8 Hz, 1 H), 2.58 (d, J = 5.7 Hz, 1 H), 2.03 (s, 3 H), 0.99 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.8 Hz, 3 H), 0.80 (d, J = 6.8 Hz, 3 H), 0.78 (d, J = 6.8 Hz, 3 H), 0.76 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.21, 135.24, 132.25, 70.20, 65.56, 63.58, 59.81, 56.43, 55.96, 55.90, 53.96, 50.50, 45.47, 42.75, 40.32, 39.99, 39.26, 33.06, 30.64, 30.32, 29.45, 27.47, 22.91, 21.14, 21.01, 20.00, 19.91, 19.62, 17.52, 13.37; IR (KBr) 1744, 1461, 1378 cm^{-1}; $[\alpha]_D$ +105.3° (*c* 0.43, acetone); HRMS (EI, 70 eV) calcd for $C_{30}H_{46}O_5$ *m/z* 486.3345, found *m/z* 486.3312 (M_x).

3*β*-Acetoxy-5,6;7,8;10(19);22,23-tetraepoxy-9,10-secoergostan-25-ol (5). A cold solution of dioxirane **1b** (0.68 M in TFP, 5.1 mL, 3.5 mmol) was added during ca. 1.5 h in three equal portions to a solution of **3b** (585 mg, 1.2 mmol) in CH_2Cl_2 (5 mL) at 0 °C; TLC monitoring revealed that the starting material was completely consumed after ca. 1.7 h. Removal of the solvent in vacuo, followed by flash column chromatography (silica gel, petroleum ether/Et_2O (1:4)) afforded the 25-hydroxy derivative **5** (367 mg, 0.71 mmol, yield 61%): mp 92−95 °C, white laths (acetone); ^1H NMR (500 MHz, $CDCl_3$) δ 4.79 (m, 1 H), 3.43 (d, J = 7.8 Hz, 1 H), 2.86 (dd, J = 5.7 Hz, J = 1.6 Hz [long-range coupling], 1 H), 2.79 (d, J = 7.8 Hz, 1 H), 2.70 (dd, J = 8.9 Hz, J = 2.2 Hz, 1 H), 2.56 (d, J = 5.7 Hz, 1 H), 2.39 (dd, J = 8.2 Hz, J = 2.2 Hz, 1 H), 2.01 (s, 3 H), 1.21 (s, 3 H), 1.15 (s, 3 H), 1.06 (d, J = 6.4 Hz, 3 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.72 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.17, 73.46, 70.08, 65.40, 63.33, 63.11, 62.93, 59.78, 55.89, 55.84, 53.97, 53.44, 50.50, 46.50, 45.80, 40.19, 39.16, 39.15, 30.53, 30.21, 29.43, 27.57, 26.96, 25.71, 22.79, 21.08, 20.27, 16.95, 13.13, 12.74; IR (KBr) 3456, 1741, 1461, 1379 cm^{-1}; $[\alpha]_D$ +42.4° (*c* 0.46, acetone); HRMS (EI, 70 eV) calcd for $C_{30}H_{46}O_7$ *m/z* 518.3244, found *m/z* 518.3242 (M_x).

X-ray Diffraction Structure Determination of Tetraepoxide 3c. X-ray data collection was carried out using a Siemens P4 single-crystal diffractometer (Mo Kα radiation, at 298 K) controlled by XSCANS version 2.1 software.[14a] ω scans were used for data collection, at variable speeds from 10 to 60 deg/min. Three standard reflections were measured after every 97 reflections; a 6.8% decrease in standard intensities was observed and corresponding corrections were made. Data reduction included profile fitting and a semiempirical absorption correction, maximum and minimum transmissions 0.470 and 0.430. The crystal used for data collection gave reflection profiles with rather high backgrounds, and did not diffract strongly at higher scattering angles, so only about 4000 reflections were measured and only 1488 had structure factors greater than 4 σ. The structure was determined by direct methods and refined initially by use of programs in the SHELXTL PC version 5.1 package,[14b] which were also used for all figures. Hydrogen atoms were introduced in ideal positions, each riding on the atom to which it is bonded; each was refined with isotropic temperature factor 20% greater than that of the ridden atom. The bromine and oxygen atoms were refined with anisotropic displacement parameters, whereas the carbon atoms were treated as isotropic in order to limit the total number of parameters. Final refinement on F2 was carried out using SHELXL 93.[15] No constraints or restraints were applied to atomic positions except for the hydrogen atoms. Although the data are of less than ideal accuracy, the molecular conformation is unequivocally determined and the structure of the given enantiomer **3c** is confirmed.

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Supporting Information Available: Thermal ellipsoid and unit cell diagrams, summary of X-rays diffraction data, tables of atomic coordinates, bond lengths and angles, anisotropic thermal parameters, H-atom coordinates, and isotropic displacement coefficients for tetraepoxide **3c** (8 pages). See any current masthead page for ordering and internet access instructions.

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(14) (a) Siemens Industrial Automation, Inc.; Analytical Instrumentation Business Unit, Madison, WI. (b) Siemens Analytical X-Ray Instruments, Inc.; Madison, WI.

(15) Sheldrick, G. M. *SHELXL 93. Program for the refinement of crystal structures*; University of Göttingen, Germany, 1993.