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SYNTHESIS OF 1,3-DIEPI-ED-71, A BIOLOGICALLY IMPORTANT DIASTEREOMER OF 1α,25-DIHYDROXY-2β-(3-HYDROXYPROP-OXY)VITAMIN D_3 (ED-71)*

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Abstract – The synthesis of biologically important 1,3-diepi-ED-71, a diastereomer of 1α,25-dihydroxy-2β-(3-hydroxypropoxy)vitamin D_3 (ED-71) at the 1-position and 3-position of the A-ring using Trost's coupling methodology is described.

INTRODUCTION

Active vitamin D_3, 1α,25-dihydroxyvitamin D_3 (1,25$(OH)_2D_3$, **1**), is well recognized as a potent regulator of cell proliferation and differentiation processes while also possessing regulatory effects on calcium and phosphorus metabolism.[1] Various analogs of 1,25$(OH)_2D_3$ (**1**) have been synthesized in attempts to separate differentiation-induction and antiproliferation activities from calcemic activity with the aim of obtaining useful drugs for the medical treatment of psoriasis, secondary hyperparathyroidism, cancer, etc.[2] There is also intense interest in obtaining analogs more potent than 1,25$(OH)_2D_3$ (**1**) in regulating calcium and phosphorus metabolism with the objective of treating bone diseases such as osteoporosis. 1α,25-Dihydroxy-2β-(3-hydroxylpropoxy)vitamin D_3 (ED-71, **2**), an analog of 1,25$(OH)_2D_3$ (**1**), which possesses a hydroxypropoxy substituent at the 2-position of the A-ring of **1**, is such an analog that shows potent effects on bone therapy (Figure 1).[3-7] Phase III clinical studies of ED-71 (**2**) as a promising

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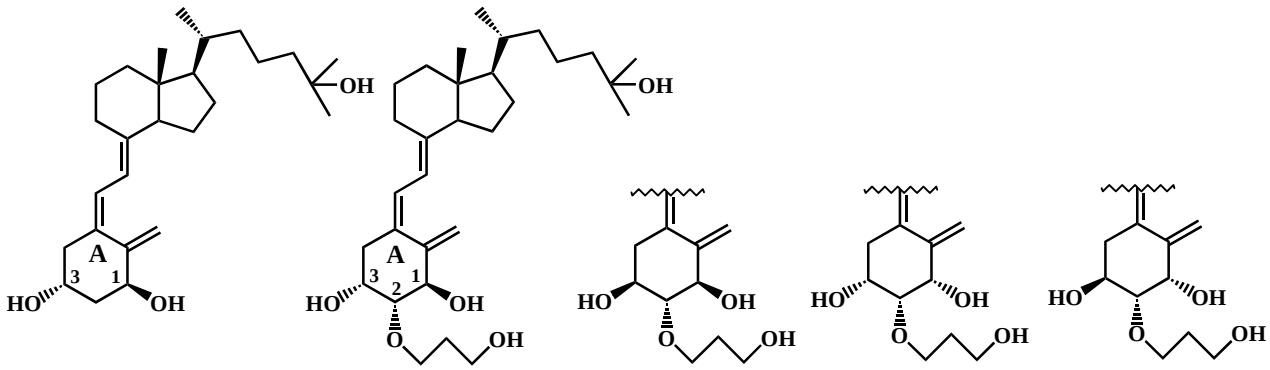
**This paper is dedicated to the memory of the late Dr. Masatomo Hamana, Professor Emeritus, Kyushu University.*

candidate for the treatment of osteoporosis and bone fracture prevention are now being successfully conducted in Japan and will be completed soon.[8,9]



(1) 1,25(OH)$_2$D$_3$ **(2) ED-71** **(3) 3-epi-ED-71** **(4) 1-epi-ED-71** **(5) 1,3-diepi-ED-71**

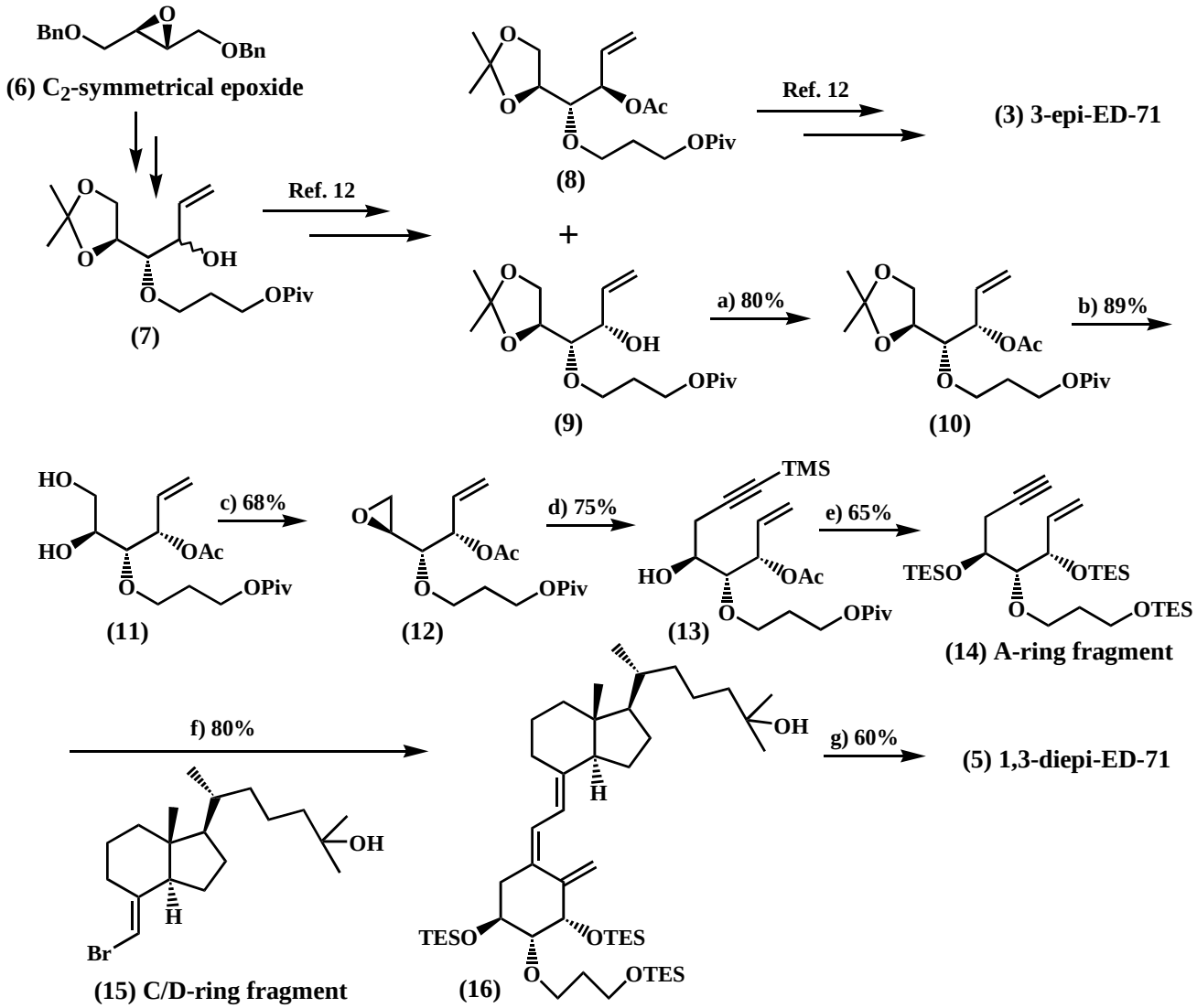
Figure 1. Structures of the active vitamin D$_3$, ED-71 and diastereomers

Recently, it was reported that the epimerization of 1,25(OH)$_2$D$_3$ (**1**) at the 3-position of the A-ring plays a major role in parathyroid hormone (PTH) synthesis and secretion. Epimerized 3-epi-1,25(OH)$_2$D$_3$ shows equipotent and prolonged activities in comparison to **1** at suppressing PTH secretion.[10,11] During our clinical development of ED-71 (**2**), serum PTH in osteoporotic patients, however, did not change significantly upon treatment with **2**.[9] We assumed that a bulky hydroxylpropoxy substituent at the 2-position of the A-ring would interfere with epimerization of ED-71 (**2)** at the adjacent and sterically hindered 3-position leading to lack of epimerized 3-epi-ED-71 (**3**) in parathyroid glands, which could explain why ED-71 (**2**) showed weak potency in PTH suppression during clinical studies. We, therefore, previously executed the synthesis and the biological evaluation of 3-epi-ED-71 (**3**) (Figure 1).[12]

On the other hand, it was also reported that the epimerization of 1,25(OH)$_2$D$_3$ (**1**) at the 1-position of the A-ring renders **1** devoid of activity as an agonist for transcaltachia concerning non-genomic intestinal calcium absorption. Therefore, 1-epi-1,25(OH)$_2$D$_3$ might be considered a potent stereospecific antagonist of **1** stimulating transcaltachia response.[13] Considering the structure-activity relationship between **1** and 1-epi-1,25(OH)$_2$D$_3$, we have previously synthesized 1-epi-ED-71 (**4**) and compared its biological activity to that of ED-71 (**2**) (Figure 1).[14]

To further explore structure-activity-relationships between ED-71 (**2**) and related analogs, we focused significant attention to the diastereomer of **2** at both 1- and 3-positions of the A-ring. In this paper, we describe the synthesis of structurally and biologically relevant 1,3-diepi-ED-71 (**5**), a member that completes the set all possible A-ring diastereomers at the 1-position and the 3-position of ED-71 (**2**). This analog, in combination with others, is anticipated to enhance our understanding of the mode-of-action

of medicinally important **2** (Figure 1).



Scheme 1: Synthesis of 1,3-diepi-ED-71. Reagents and conditions: a) $Ac_2O/Et_3N/DMAP/CH_2Cl_2$, rt. b) 60% AcOH, rt. c) PPh_3/DEAD/dioxane, reflux. d) HC≡CTMS/*n*-BuLi/BF_3-OEt_2/THF, -78 °C. e) 1) 10 M NaOH/MeOH, rt. 2) TESOTf/Et_3N/CH_2Cl_2, -40 °C. f) $(PPh_3)_4Pd/Et_3N$/toluene, reflux. g) 46% HF/MeCN, rt.

RESULTS AND DISCUSSION

The synthesis of 1,3-diepi-ED-71 (**5**) was envisioned using Trost's methodology involving palladium-catalyzed coupling between A-ring fragment (**14**) and C/D-ring fragment (**15**) (Scheme 1).[15,16] The synthesis of A-ring fragment (**14**) started from alcohol (**9**) which was developed in our previous synthesis of 3-epi-ED-71 (**3**) from C_2 symmetrical (2*R*,3*R*)-2,3-bis(benzyloxymethyl)oxirane (**6**).[17] Lipase-catalyzed acetylation[18] of **7** produced **9** as the unreacted (*S*)-isomer together with (*R*)-acetate (**8**). Alcohol (**9**) possesses the requisite stereochemistry at positions 1, 2 and 3 of the A-ring that comprises **5**.

Acetylation of **9** gave acetate (**10**) in 80% yield from which diol (**11**) was obtained in 89% yield after deprotection of the acetonide moiety using 60% acetic acid. Mitsunobu reaction of **11** with diethyl azodicarboxylate (DEAD) and triphenylphosphine in boiling toluene afforded epoxide (**12**) in 68% yield.[19] Reaction of **12** with lithium trimethylsilylacetylide in the presence of boron trifluoride diethyl etherate at -78 °C gave the enyne (**13**) in 75% yield, which was then converted to A-ring fragment (**14**) by saponification with 10 M sodium hydroxide and subsequent protection of the hydroxyl groups as their triethylsilyl (TES) ether in 65% overall yield.

With A-ring fragment (**14**) in hand, we next coupled it to C/D-ring fragment (**15**) using the Trost's methodology.[15,16] Thus, A-ring fragment (**14**) was coupled with C/D-ring fragment (**15**), which was readily secured by our method[20] from commercially available 25-hydroxyvitamin D_3, in the presence of tetrakis(triphenylphosohine)palladium(0) [$(Ph_3P)_4Pd$] and triethylamine in boiling toluene to produce the desired coupling product (**16**) in 80% yield. Desilylation of **16** with 46% hydrofluoric acid in acetonitrile at room temperature gave rise to 1,3-diepi-ED-71 (**5**) in 60% yield (Scheme 1).

CONCLUSION

Based on the Trost's coupling methodology involving A-ring fragment (**14**) and C/D-ring fragment (**15**), we successfully completed the synthesis of 1,3-diepi-ED-71 (**5**). This ED-71 analog is epimeric at both 1- and 3-positions of A-ring and completes the full complement of A-ring 1- and 3-positional diastereomers. The detailed biological properties of **5** in comparison with ED-71 (**2**), 3-epi-ED-71 (**3**) and 1-epi-ED-71 (**4**) are currently under investigation and will be reported elsewhere.

EXPERIMENTAL

Anhydrous THF was purchased from Kanto Chemical Co., Inc., MeOH and EtOH were distilled from sodium, toluene was distilled from phosphorus pentoxide, and CH_2Cl_2 and Et_3N were distilled from calcium hydride. All other purchased solvents and reagents were used without further purification. All reactions were carried out under an atmosphere of argon unless otherwise noted. Celite 545 was purchased from Nacarai Tesque Inc. All extracts were dried over magnesium sulfate and evaporated under reduced pressure with a rotary evaporator. Chromatographic purification was carried out with Silica Gel 60N Cat. No. 37560-84 purchased from Kanto Chemical Co., Inc., flash column chromatography with Silica Gel 60N Cat. No. 37563-84 from Kanto Chemical Co., Inc., and preparative thin layer chromatography (TLC) with Merck Kieselgel 60 PFR_{254} Art. 1.05744.0009 or Art. 1.05715.0009.

Optical rotations were measured with JASCO DIP-370 polarimeter. ^1H and ^{13}C NMR spectra were

recorded on VARIAN Gemini-300 and Gemini-400 spectrometers using $CDCl_3$ as a solvent. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane or calibrated from $CHCl_3$. Infrared (IR) spectra were obtained using JASCO FT/IR-5300, JEOL JIR-6000, and Hitachi 270-30 spectrophotometers. Mass spectra (MS) were measured with JEOL JMS-DX303 instrument. High resolution mass spectra (HRMS) were recorded on JEOL JMS-AX-500 and VG Auto Spec Q instruments.

3-[(1*S*,2*S*)-2-Acetoxy-1-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-enyloxy]propyl pivalate (10): To a stirred solution of **9** (2.7 g, 8.18 mmol) in CH_2Cl_2 (20 mL) at rt, was added Et_3N (4.58 mL, 32.7 mmol), 4-*N*,*N*-dimethylaminopyridine (DMAP) (0.05 g, 0.41 mmol) and Ac_2O (1.56 mL, 16.4 mmol). The resulting mixture was stirred at the same temperature for 20 h. To the stirred mixture, was added H_2O (20 mL). The mixture was extracted with AcOEt (100 mL), washed with 0.5 M HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and saturated aqueous NaCl (30 mL), evaporated and chromatographed on silica gel. Elution with *n*-hexane-AcOEt (7:1 then 1:1) gave **10** (2.42 g, 80%) as a colorless oil. $[\alpha]_D^{25}$ -5.5° (*c* 2.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.93 (1H, ddd, *J*=7.28, 11.9, 17.4 Hz), 5.30 (1H, d, *J*=17.4 Hz), 5.29 (1H, d, *J*=11.9 Hz), 5.18 (1H, dd, *J*=3.6, 6.7 Hz), 4.12 (2H, t, *J*=6.7 Hz), 4.08 (1H, t, *J*= 7.1 Hz), 3.98 (1H, t, *J*=7.3 Hz), 3.79-3.70 (3H, m), 3.42 (1H, dd, *J*= 3.6, 7.3 Hz), 2.09 (3H, s), 1.92 (2H, t, *J*=5.6 Hz), 1.40 (3H, s), 1.35 (3H, s), 1.20 (9H, s). ^{13}C NMR ($CDCl_3$): δ 178.2, 169.5, 132.4, 119.0, 109.0, 82.3, 76.6, 74.8, 68.8, 65.8, 61.3, 38.6, 29.3, 27.1, 26.4, 25.4, 21.0. IR (neat): ν 2976, 1736, 1471, 1373, 1232, 1161, 1070 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{32}O_7$ (M^+) 372.2149, found 372.2137.

3-[(2*S*,3*S*,4*S*)-4-Acetoxy-1,2-dihydroxyhex-5-en-3-yloxy]propyl pivalate (11): A mixture of **10** (2.3 g, 6.18 mmol) and 60% AcOH (77 mL) was stirred at rt for 17 h, diluted with $NaHCO_3$ (66 g) and H_2O, extracted with CH_2Cl_2 (300 mL), washed with saturated NaCl, evaporated and chromatographed on silica gel. Elution with *n*-hexane-AcOEt (2:1 then 0:1) gave **11** (1.82 g, 89%) as a colorless oil. $[\alpha]_D^{27}$ +5.7° (*c* 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.91 (1H, ddd, *J*=6.6, 11.1, 17.4 Hz), 5.48 (1H, ddt, *J*=6.6, 4.4, 1.5 Hz), 5.35 (1H, dt, *J*=17.2, 1.2 Hz), 5.31 (1H, dt, *J*=10.8, 1.2 Hz), 4.25 (1H, dt, *J*=11.1, 5.7 Hz), 4.11 (1H, dt, *J*=11.1, 5.7 Hz), 3.84 (1H, dt, *J*= 9.3, 5.7 Hz), 3.74-3.68 (1H, m), 3.54 (1H, dt, *J*= 9.3, 6.0 Hz), 3.46 (1H, t, *J*=4.7 Hz), 2.79 (1H, br), 2.20 (1H, br), 2.11 (3H, s), 1.91 (2H, quint, *J*=6.6 Hz), 1.20 (9H, s). ^{13}C NMR ($CDCl_3$): δ 178.6, 169.9, 132.4, 119.1, 80.6, 74.3, 71.0, 68.7, 63.5, 61.0, 38.8, 29.5, 27.2, 21.1. IR (neat): ν 3468, 2967, 1742, 1480, 1372, 1240, 1166 cm^{-1}. HRMS (EI) calcd for $C_{16}H_{28}O_7$ (M^+) 332.1835,

found 332.1821.

3-[(1*S*,2*S*)-2-Acetoxy-1-((*S*)-oxiran-2-yl)but-3-enyloxy]propyl pivalate (12): To a stirred solution of **11** (1.70 g, 5.12 mmol) in dioxane (50 mL), was added PPh_3 (1.65 g, 7.67 mmol) and DEAD (3.49 mL, 7.67 mmol). The resulting mixture was stirred at 130 °C for 7.5 h. Additional PPh_3 (1.65 g, 7.67 mmol) and DEAD (3.49 mL, 7.67 mmol) were added. The resulting mixture was stirred at 130 °C for 10 h, evaporated and chromatographed on silica gel. Elution with *n*-hexane-AcOEt (10:1 then 3:1) gave **12** (1.10 g, 68%) as a colorless oil. $[\alpha]_D^{24}$ -8.4° (*c* 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 5.91 (1H, ddd, *J*=6.6, 10.2, 17.1 Hz), 5.42-5.38 (1H, m), 5.33 (1H, dt, *J*=17.1, 1.4 Hz), 5.29 (1H, dt, *J*=10.2, 1.4 Hz), 4.16 (1H, t, *J*=7.1 Hz), 3.80 (1H, dt, *J*=7.1, 10.1 Hz), 3.61 (1H, dt, *J*=7.1, 10.1 Hz), 3.02-3.00 (2H, m), 2.79 (1H, dd, *J*=3.0, 5.1 Hz), 2.58 (1H, dd, *J*=3.0, 5.1 Hz), 2.10 (3H, s), 1.91 (2H, t, *J*=7.1 Hz), 1.19 (9H, s). ^{13}C NMR ($CDCl_3$) δ: 178.4, 169.8, 132.7, 118.6, 82.6, 74.3, 67.1, 64.2, 61.2, 52.0, 43.4, 38.7, 29.1, 27.1, 21.0. IR (neat): ν 3642, 2975, 1814, 1747, 1241, 1167 cm^{-1}. HRMS (EI) calcd for $C_{16}H_{26}O_6$ (M^+) 314.1729, found 314.1710.

3-[(3*S*,4*R*,5*S*)-3-Acetoxy-5-hydroxy-8-(trimethylsilyl)oct-1-en-7-yn-4-yloxy]propyl pivalate (13): To a stirred solution of trimethylsilylacetylene (0.25 mL, 1.5 mmol) in THF (13 mL) at -78 °C, was added *n*-BuLi (1.6 M solution in THF, 0.93 mL, 1.5 mmol), and stirring was continued at -78 °C for 30 min. BF_3-Et_2O (0.25 mL, 1.5 mmol) was added to this mixture and, 30 min later, a solution **12** (100 mg, 0.30 mmol) in THF (1 mL) was added at the same temperature. The resulting mixture was stirred at -78 °C for 4 h, and at rt for 10 h. The mixture was quenched with saturated aqueous $NaHCO_3$ (1 mL), extracted with CH_2Cl_2 (60 mL), evaporated and chromatographed on silica gel. Elution with *n*-hexane-AcOEt (7:1 then 0:1) gave **13** (93.4 mg, 75%) as a colorless oil. $[\alpha]_D^{24}$ +9.4° (*c* 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.90 (1H, ddd, *J*=5.8, 10.2, 17.2 Hz), 5.49 (1H, t, *J*=5.8 Hz), 5.21 (1H, d, *J*=17.3 Hz), 5.15 (1H, d, *J*=10.8 Hz), 4.19-4.08 (3H, m), 3.81-3.77 (2H, m), 3.62 (1H, dt, *J*=4.5, 8.2 Hz), 3.52 (1H, q, *J*=4.5 Hz), 2.51 (2H, dd, *J*=4.5, 6.0 Hz), 2.10 (3H, s), 1.90 (2H, quint, *J*=6.4 Hz), 1.19 (9H, s), 0.13 (9H, s). ^{13}C NMR ($CDCl_3$): δ 178.4, 169.7, 133.0, 118.7, 102.8, 87.5, 81.0, 73.9, 69.0, 61.1, 38.7, 29.4, 27.2, 25.3, 21.0, -0.03. IR (neat): ν 3508, 2966, 2175, 1811, 1734, 1471, 1371, 1242, 1163, 1113 cm^{-1}. HRMS (FAB) calcd for $C_{21}H_{36}O_6Si$ (M^+) 412.2282, found 412.2299.

(3*S*,4*R*,5*S*)-4-(3-(Triethylsilyloxy)propoxy)-3,5-bis(triethylsilyloxy)oct-1-en-7-yne (14): To a stirred

solution of **13** (424 mg, 1.03 mmol) in MeOH (5 mL) at rt, was added 10 M NaOH (7 mL). The resulting mixture was stirred at rt for 20 h and evaporated. The residue was extracted with THF, dried over $MgSO_4$ and evaporated to give the crude product (209.2 mg). To a stirred mixture of the crude product (209.2 mg) in CH_2Cl_2 (21 mL) at -40°C, were added Et_3N (2.24 mL, 15.7 mmol) and triethylsilyl trifluoromethanesulfonate (TESOTf) (1.10 mL, 7.84 mmol). The resulting mixture was stirred at the same temperature for 15 h, quenched with H_2O (3.5 mL), extracted with CH_2Cl_2 (30 mL), evaporated and chromatographed on silica gel. Elution with *n*-hexane-AcOEt (20:1) gave **14** (372.5 mg, 65%) as a colorless oil. $[\alpha]_D^{26}$ -2.6° (*c* 0.50, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.95 (1H, ddd, *J*=6.8, 10.5, 17.7 Hz), 5.20 (1H, d, *J*=17.7 Hz), 5.12 (1H, d, *J*=10.5 Hz), 4.30 (1H, dd, *J*=3.6, 6.8 Hz), 3.87 (1H, dd, *J*=5.4, 11.4 Hz), 3.77-3.59 (4H, m), 3.35 (1H, dd, *J*=3.6, 5.1 Hz), 2.49 (1H, ddd, *J*=2.7, 5.4, 16.8 Hz), 2.35 (1H, ddd, *J*=2.4, 5.8, 16.8 Hz), 1.95 (1H, t, *J*=2.6 Hz), 1.77 (2H, quint, *J*=6.5 Hz), 1.25 (2H, s), 0.89 (27H, s), 0.04-0.03 (18H, m). ^{13}C NMR ($CDCl_3$): δ 138.9, 115.9, 85.1, 82.1, 74.5, 71.7, 69.8, 69.5, 60.5, 33.6, 25.9, 25.7, 24.1, 18.2, -2.95, -4.12, -4.72, -5.31. IR (neat): ν 3314, 2930, 2858, 1468, 1362, 1254, 1097 cm^{-1}. HRMS (FAB) calcd for $C_{29}H_{60}O_4Si_3$ (M^+) 556.3799, found 556.3801.

(5*Z*,7*E*)-(1*S*,2*R*,3*S*)-1,3-Bis(triethylsilyloxy)-2-(3-*tert*-butyldimethylsilyloxypropoxy)-25-hydroxy-9,10-secocholesta-5,7,10(19)-triene (16): To a stirred mixture of **14** (11 mg, 0.030 mmol) and **15** (11 mg, 0.021 mmol) in toluene (0.4 mL) at rt, was added Et_3N (0.24 mL, 1.719 mmol). To the degassed resulting mixture, was added $(Ph_3P)_4Pd$ (7 mg, 0.006 mmol). The resulting mixture was refluxed for 2 h, diluted with Et_2O, filtrated with Celite, evaporated and chromatographed on silica gel. Elution with *n*-hexane-AcOEt (20:1) gave **16** (14.0 mg, 80%) as a yellow oil. $[\alpha]_D^{22}$ +8.4° (*c* 0.45, MeOH). ^{1}H NMR (CD_3OD): δ 6.16 (1H, d, *J*=11.2 Hz), 6.00 (1H, *d*, *J*=11.2 Hz), 5.20 (1H, s), 4.43 (1H, s), 4.00-4.01 (1H, m), 3.59-3.71 (5H, m), 2.77 (1H, d, *J*=12.2 Hz), 2.50 (1H, d, *J*=12.2 Hz), 2.05 (1H, dd, *J*=5.8, 13.1 Hz), 1.95-1.97 (2H, m), 1.86 (1H, m), 1.68-1.72 (1H, m), 1.59-1.62 (1H, m), 1.38 (4H, m), 1.23-1.29 (2H, m), 1.11 (6H, s), 0.83-0.85 (30H, m), 0.48 (3H, s), 0.05-0.00 (27H, m). ^{13}C NMR (CD_3OD): δ 148.1, 142.2, 136.1, 124.3, 118.9, 86.3, 75.2, 71.5 (2), 69.2, 61.5, 58.0, 57.6, 47.1, 45.3, 42.0, 37.8, 37.5, 34.7, 30.1, 29.3, 29.1, 28.8, 26.6, 26.5 (2), 26.4, 24.7, 23.3, 21.9, 19.4, 19.3, 19.2, 18.9, 12.2, -4.4, -4.5, -4.6, -5.1. IR (neat): ν 3358, 2952, 2857, 1467, 1380, 1252, 1099, 1005 cm^{-1}. HRMS (FAB) calcd for $C_{48}H_{92}O_5Si$ (M^+) 833.4976, found 833.6309.

(5*Z*,7*E*)-(1*S*,2*R*,3*S*)-2-(3-Hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol (5): To a stirred mixture of **16** (11.0 mg, 0.013 mmol) in MeCN (0.3 mL) at rt, was added 46% HF (3.4 μL). The resulting mixture was stirred at room temperature for 17 h, basified with saturated aqueous $NaHCO_3$, extracted with AcOEt and evaporated. The residue was purified by preparative TLC developed with AcOEt to give **5** (3.84 mg, 60%) as a colorless oil. $[\alpha]_D^{22}$ -18.3° (*c* 0.12, MeOH). ^{1}H NMR (CD_3OD): δ 6.25 (1H, d, *J*=11.2 Hz), 5.99 (1H, d, *J*=11.2 Hz), 5.24 (1H, s), 4.88 (1H, s), 4.32 (1H, d, *J*=3.0 Hz), 3.87-3.88 (1H, m), 3.67-3.70 (1H, m), 3.56-3.60 (3H, m), 2.76 (1H, dd, *J*=3.4, 11.2 Hz), 2.51 (1H, dd, *J*=4.9, 13.6 Hz), 2.07 (1H, dd, *J*=6.8, 13.2 Hz), 1.87-1.95 (2H, m), 1.79-1.82 (1H, m), 1.72 (2H, quint, *J*=5.8 Hz), 1.58 (2H, d, *J*=11.2 Hz), 1.31-1.41 (7H, m), 1.19-1.26 (4H, m), 1.07 (6H, s), 0.87 (3H, d, *J*=6.8 Hz), 0.77-0.80 (1H, m), 0.47 (3H, s). ^{13}C NMR (CD_3OD): δ 147.1, 134.6, 125.2, 119.0, 115.0, 85.8, 73.0, 71.5, 69.4, 68.6, 60.4, 58.0, 57.6, 45.3, 42.4, 41.9, 37.8, 33.7, 30.8, 30.0, 29.3, 29.1, 28.7, 24.7, 23.4, 21.9, 19.4, 12.3. IR (neat): ν 3359, 2941, 1375, 1076 cm^{-1}. HRMS (FAB) calcd for $C_{30}H_{50}O_5$ (M^+) 490.3658, found 490.3648.

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