Supporting Information for:

Efficient Convergent Synthesis of 1 α ,25-Dihydroxyvitamin D₃ and its Analogues by the Suzuki-Miyaura Coupling

Takeshi Hanazawa, Akiko Koyama, Takeshi Wada, Eiko Morishige, Sentaro Okamoto, and Fumie Sato*

Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama, Kanagawa 226-8501, Japan.

General. ¹H and ¹³C NMR spectra were recorded in CDCl₃ at 300 and 75 MHz, respectively, on a Varian Gemini-2000 spectrometer. Chemical shifts are reported in parts per million (ppm, δ) relative to Me₄Si (δ 0.00), residual CHCl₃ (δ 7.26 for ¹H NMR), or CDCl₃ (δ 77.0 for ¹³C NMR). IR spectra were recorded on an FT-IR spectrometer (JASCO FT/IR-230). Elemental analyses were performed on an Elemental automatic analyzer. All reactions sensitive to oxygen and/or moisture were performed under an argon atmosphere. Dry solvents (THF, ethyl ether, dimethylformamide, CH₂Cl₂, and toluene) were purchased from Kanto Chemicals. Other chemicals are commercially available, unless otherwise indicated, and were used as received.

(S)-8-(Trimethyl-silanyl)-octa-2,7-diyne-1,5-diol (7): To a stirred solution of 3-triethylsilyloxy-1-propyne (18.7 g, 110 mmol) in THF (100 mL) was slowly added *n*-BuLi (63.7 mL, 1.57 M in hexane, 100 mmol) at -78 °C. After stirring for 1 h at the same temperature, a solution of epoxide **5** (7.71 g, 50.0 mmol) in THF (70 mL) and then boron trifluoride etherate (12.6 mL, 100 mmol) were added. The mixture was stirred for 1 h at -78 °C and warmed to room temperature over 30 min. After addition of saturated aqueous NH₄Cl (100 mL), the mixture was extracted with Et₂O (3 x 100 mL). The

combined organic layers were dried over MgSO_4 and concentrated. To a stirred solution of the crude residue in THF (150 mL) was slowly added aqueous 3N HCl (50 mL) at 0 °C. After stirring for 1 h at room temperature, the mixture was diluted with H_2O (100 mL) and extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with saturated aqueous NaHCO_3 (100 mL), dried over MgSO_4 , concentrated and chromatographed on silica gel (hexane- EtOAc) to give **7** (8.61 g, 82 %). ^1H NMR (CDCl_3) δ 4.26 (br s, 2H), 3.86-3.96 (m, 1H), 3.31 (br s, 2H), 2.45-2.60 (m, 4H), 0.15 (s, 9H); ^{13}C NMR (CDCl_3) δ 102.4, 87.6, 81.9, 80.9, 68.5, 50.9, 27.6, 26.3, 0.1; IR (neat) 3350, 2959, 2177, 1424, 1249, 1137, 1027, 840, 760 cm^{-1} ; $[\alpha]_{\text{D}}^{28}$ -14.0 (*c* 2.69, CHCl_3).

Acetic acid (S)-5-hydroxy-8-(trimethyl-silanyl)-octa-2,7-diynyl ester (8): To a solution of **7** (16.5 g, 78.4 mmol) in vinyl acetate (78 mL) was added PPL (42 units/mg, Sigma-Aldrich, 16.5 g). After stirring for 3 days at room temperature, the mixture was filtered through a pad of Celite with Et_2O (200 mL). The filtrate was concentrated and chromatographed on silica gel (hexane- Et_2O) to give **8** (19.0 g, 96 %). ^1H NMR (CDCl_3) δ 4.68 (br s, 2H), 3.87-3.97 (m, 1H), 2.52-2.58 (m, 4H), 2.36 (s, 1H), 2.10 (s, 3H), 0.17 (s, 9H); ^{13}C NMR (CDCl_3) δ 170.2, 102.0, 88.0, 83.1, 76.7, 68.3, 52.6, 27.7, 26.4, 20.9, 0.1; IR (neat) 3462, 2958, 2176, 1748, 1379, 1250, 1028, 845, 761 cm^{-1} ; $[\alpha]_{\text{D}}^{27}$ -0.76 (*c* 2.22, CHCl_3).

(S,E)-5-(tert-Butyl-dimethyl-silanyloxy)-8-(trimethyl-silanyl)-oct-2-en-7-yn-1-ol (9): To a mixture of **8** (22.0 g, 87.2 mmol) and imidazole (13.0 g, 191 mmol) in DMF (180 mL) was added TBSCl (14.4 g, 95.6 mmol) at 0 °C. After stirring for 12 h at room

temperature, to this was added saturated aqueous NaHCO_3 (100 mL) at 0 °C. The mixture was extracted with hexane (3 x 100 mL). The combined organic layers were dried over MgSO_4 and concentrated. The resulting pale yellow residue was directly used for the next reaction without purification.

To a solution of the residue thus obtained in Et_2O (200 mL) was slowly added Red-Al (63.3 mL, 3.42 M in toluene, 216 mmol) at 0 °C. After stirring for 1 h at the same temperature, saturated aqueous 1N HCl (200 mL) was added carefully. The mixture was extracted with Et_2O (3 x 100 mL). The combined organic layers were dried over MgSO_4 , concentrated and chromatographed on silica gel (hexane- Et_2O) to give **9** (27.8 g, 97 %). ^1H NMR (CDCl_3) δ 5.68-5.71 (m, 2H), 4.10 (s, 2H), 3.84 (tt, J = 6.0, 6.0 Hz, 1H), 2.21-2.40 (m, 2H), 2.33 (d, J = 6.0 Hz, 2H), 1.38 (s, 1H), 0.88 (s, 9H), 0.14 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (CDCl_3) δ 131.8, 128.5, 104.4, 86.3, 70.8, 63.7, 39.8, 28.4, 25.9, 18.2, 0.2, -4.3, -4.5; IR (neat) 3326, 2956, 2857, 2178, 1472, 1362, 1250, 1101, 1031, 973, 841, 776 cm^{-1} .

(3S,5R)-5-(tert-Butyl-dimethyl-silanyloxy)-8-(trimethyl-silanyl)-oct-1-en-7-yn-3-ol

(2): To a mixture of $\text{Ti}(\text{O}-i\text{-Pr})_4$ (5.00 mL, 17.0 mmol) and 4A molecular sieves (5.56 g) in CH_2Cl_2 (50 mL) was added diisopropyl L-(+)-tartarate (L-(+)-DIPT) (4.28 mL, 20.4 mmol) at -15 °C and the mixture was stirred for 30 min. To this was slowly added a solution of **9** (27.8 g, 85.1 mmol) in CH_2Cl_2 (30 mL). After stirring for 40 min at -15 °C, the mixture was cooled to -30 °C and *t*-BuOOH (TBHP) (49.7 mL, 3.41 M in CH_2Cl_2 , 169 mmol) was added. The resulting mixture was allowed to warm to -20 °C and stirred for 24 h. After addition of methyl sulfide (9.34 mL, 127 mmol) and stirring for 1 h at -20 °C, to the mixture was added 10% tartaric acid (30 mL). The mixture was warmed to room temperature over 1 h and diluted with Et_2O (500 mL). After addition of NaF (55.6 g) and Celite (55.6 g), the mixture was stirred for 1 h, and filtered through a pad of Celite. The resulting filtrate was evaporated to remove solvents. The residue was diluted with Et_2O (300 mL) and aqueous 3N NaOH (85 mL) and was vigorously stirred for 1.5 h at room temperature. After addition of H_2O (300 mL), the mixture was extracted with

Et₂O (3 x 150 mL) and the combined organic layers were dried over MgSO₄ and concentrated *in vacuo* to give the epoxy alcohol as a pale yellow oil, which was subjected to the next reaction without purification.

To a mixture of the epoxide thus obtained and NEt₃ (21.1 mL, 187 mmol) in CH₂Cl₂ (130 mL) was slowly added MsCl (7.88 mL, 102 mmol) at 0 °C. After stirring for 1 h, mixture was quenched by addition of saturated aqueous NaHCO₃ (100 mL) and extracted with CH₂Cl₂ (3 x 90 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure to give a colorless residue, which was subjected to the next reaction without purification.

To a mixture of the crude mesylate and NaHCO₃ (2.13 g, 25.4 mmol) in dry acetone (200 mL) was added NaI (38.2 g, 255 mmol) at room temperature. After stirring for 20 h, the mixture was concentrated by rotary evaporation and then diluted with saturated aqueous Na₂S₂O₃ (200 mL). After extraction with Et₂O (3 x 100 mL), the combined organic layers were dried over MgSO₄ and concentrated *in vacuo* to give the corresponding iodide, which was directly used for the next reaction without purification.

To a mixture of zinc powder (16.6 g, 254 mmol, activated by washing with diluted HCl and drying *in vacuo*) in MeOH (20 mL) was added acetic acid (0.273 mL, 4.77 mmol). To this mixture, a solution of the crude iodide, prepared above, in MeOH (40 mL) was added under sonication. After 1 h of sonication, acetic acid (4.83 mL, 84.9 mmol) was added. The mixture was filtered with NH₄Cl (200 mL) and CH₂Cl₂ (200 mL) and extracted with CH₂Cl₂ (2 x 200 mL). The combined organic layers were dried over MgSO₄, concentrated and chromatographed on silica gel (hexane-Et₂O) to give **2** (22.0 g, 78 % from **9**). ¹H NMR (CDCl₃) δ 5.81-5.93 (m, 1H), 5.26 (dt, *J* = 17.1, 1.5 Hz, 1H), 5.09 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.38-4.46 (m, 1H), 4.10-4.18 (m, 1H), 2.92 (s, 1H), 2.77 (d, *J* = 6.6 Hz, 2H), 1.83 (ddd, *J* = 3.3, 5.7, 14.4 Hz, 1H), 1.75 (ddd, *J* = 3.6, 9.3, 14.4 Hz, 1H), 0.89 (s, 9H), 0.13 (s, 9H), 0.12 (s, 6H); ¹³C NMR (CDCl₃) δ 140.9, 113.9, 103.4, 87.0, 69.5, 69.4, 42.0, 28.2, 25.9, 18.0, 0.1, -4.4, -4.7; IR (neat) 3447, 2957, 2858, 2178, 1647, 1472, 1362, 1251, 1099, 924, 839, 777 cm⁻¹. [α]_D²⁷ -26.3 (*c* 4.77, CHCl₃)

(Z)-(1S,2S,5R)-2-Bromomethyl-3-[bromo-(trimethyl-silanyl)-methylene]-5-(tert-butyl-dimethyl-silanyloxy)-cyclohexanol (10): To a solution of **2** (1.63 g, 4.99 mmol) in Et₂O (50 mL) was added dropwise *i*-PrMgCl (2.51 mL, 1.99 M in Et₂O, 4.99 mmol) at 0 °C. After stirring for 10 min at the same temperature, Ti(O-*i*-Pr)₄ (2.95 mL, 10.0 mmol) was added. The resulting mixture was cooled to –78 °C and *i*-PrMgCl (10.1 mL, 1.99 M in Et₂O, 20.1 mmol) was added slowly. After stirring for 30 min at –78 °C, the resulting yellow mixture was warmed to –50 °C over 30 min and stirred for 3 h at this temperature. After cooling to –78 °C, to this was slowly added a solution of NBS (4.90 g, 27.5 mmol) in THF (30 mL) and the mixture was allowed to warm to room temperature. After stirring for 1 h at room temperature, saturated aqueous NH₄Cl (60 mL) was added. The mixture was extracted with Et₂O (3 x 50 mL), washed with saturated aqueous NaHCO₃ (80 mL) and H₂O (60 mL), dried over MgSO₄, concentrated and chromatographed on silica gel (hexane-Et₂O) to give **10** (1.26 g, 51 %). ¹H NMR (CDCl₃) δ 4.36-4.40 (m, 1H), 3.92-4.04 (m, 1H), 3.65-3.71 (m, 1H), 3.41 (d, *J* = 1.2 Hz, 1H), 3.38 (d, *J* = 4.5 Hz, 1H), 2.82 (dd, *J* = 4.8, 14.1 Hz, 1H), 1.94-2.50 (m, 1H), 1.97 (dd, *J* = 11.1, 14.1 Hz, 1H), 1.65 (s, 1H), 1.63 (ddd, *J* = 2.7, 10.5, 13.8 Hz, 1H), 0.88 (s, 9H), 0.30 (s, 9H), 0.06 (s, 6H); ¹³C NMR (CDCl₃) δ 147.2, 129.7, 69.2, 66.6, 51.7, 39.9, 37.5, 31.3, 25.8, 18.1, 1.3, –4.4; IR (neat) 3447, 2954, 2857, 1472, 1361, 1251, 1095, 876, 839, 776 cm^{–1}; [α]_D²⁷ 0.50 (*c* 2.96, CHCl₃); Anal. Calcd. for C₁₇H₃₄Br₂O₂Si₂: C, 41.98; H, 7.05. Found: C, 42.31; H, 6.85.

(Z)-(2S,3S,5R)-2-Bromomethyl-1-[bromo-(trimethyl-silanyl)-methylene]-3,5-bis-(tert-butyl-dimethyl-silanyloxy)-cyclohexane (11): To a mixture of **10** (1.70 g, 3.51 mmol), imidazole (0.47 g, 6.90 mmol) and DMF (5 mL) were added TBSCl (0.573 g, 3.80 mmol) at 0 °C. After stirring for 12 h at room temperature, to this was added saturated aqueous NaHCO₃ (20 mL). The mixture was extracted with hexane (3 x 20 mL) and the combined organic layers were dried over MgSO₄, concentrated and chromatographed on silica gel (hexane-Et₂O) to give **11** (2.02 g, 96 %) as a colorless oil.

^1H NMR (CDCl_3) δ 4.34-4.38 (m, 1H), 3.97-4.08 (m, 1H), 3.57-3.63 (m, 1H), 3.38 (d, J = 3.9 Hz, 1H), 3.35 (d, J = 8.4 Hz, 1H), 2.79 (dd, J = 4.5, 13.8 Hz, 1H), 1.92 (dd, J = 10.8, 13.8 Hz, 1H), 1.82-1.90 (m, 1H), 1.58 (ddd, J = 2.4, 10.5, 12.9 Hz, 1H), 0.89 (s, 9H), 0.86 (s, 9H), 0.29 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (CDCl_3) δ 148.0, 128.5, 69.3, 66.9, 51.6, 40.1, 38.1, 31.6, 25.9, 25.7, 18.2, 17.9, 1.3, -4.5, -4.6, -4.9; IR (neat) 2953, 2857, 1471, 1361, 1252, 1100, 1018, 837, 775 cm^{-1} ; $[\alpha]^{27}_{\text{D}}$ 14.2 (c 2.85, CHCl_3); Anal. Calcd. for $\text{C}_{23}\text{H}_{48}\text{Br}_2\text{O}_2\text{Si}_3$: C, 45.99; H, 8.05. Found: C, 46.11; H, 7.86.

(Z)-(3S,5R)-1-Bromomethylene-3,5-bis-(tert-butyl-dimethyl-silanyloxy)-2-methylene-cyclohexane (1): To a solution of **11** (1.70 g, 2.84 mmol) in toluene (5.6 mL) was added DBU (1.68 mL, 11.2 mmol) at 0 $^{\circ}\text{C}$. The reaction mixture was stirred at 70 $^{\circ}\text{C}$ for 20 h. After addition of saturated aqueous NaHCO_3 (15 mL), the mixture was extracted with hexane (3 x 10 mL) and the combined organic layers were dried over MgSO_4 and concentrated to give the crude diene product as a yellow oily residue.

To a mixture of the crude residue thus obtained and DMF (6 mL) was added Cs_2CO_3 (3.69 g, 11.3 mmol). The reaction mixture was stirred at room temperature for 12 h. After addition of saturated aqueous NaHCO_3 (30 mL), the mixture was extracted with hexane (3 x 15 mL) and the combined organic layers were dried over MgSO_4 , concentrated and chromatographed on silica gel (hexane- Et_2O) to give **1** (1.16 g, 91 %) as a colorless oil. ^1H NMR (CDCl_3) δ 6.03 (d, J = 1.5 Hz, 1H), 5.34 (d, J = 1.5 Hz, 1H), 5.16 (d, J = 1.5 Hz, 1H), 4.39-4.44 (m, 1H), 4.14-4.21 (m, 1H), 2.41 (ddd, J = 1.5, 3.6, 13.5 Hz, 1H), 2.23 (dd, J = 6.3, 13.5 Hz, 1H), 1.73-1.87 (m, 2H), 0.91 (s, 9H), 0.88 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (CDCl_3) δ 146.3, 140.4, 112.1, 100.8, 70.7, 66.8, 44.7, 44.5, 25.9, 25.8, 18.4, 18.2, -4.6, -4.66, -4.71, -5.0; IR (neat) 2950, 1621, 1471, 1361, 1253, 1082, 1006, 776 cm^{-1} ; $[\alpha]^{27}_{\text{D}}$ -9.10 (c 3.69, CHCl_3); Anal. Calcd. for $\text{C}_{20}\text{H}_{39}\text{BrO}_2\text{Si}_2$: C, 53.67; H, 8.78. Found: C, 53.39; H, 8.80.

1 α ,25-Dihydroxyvitamin D₃ from **1 and **3**:** To a mixture of boronate **3**¹ (0.160 g, 0.336 mmol), aqueous 3N KOH (0.11 mL) and THF (0.3 mL) was added dropwise a mixture of bromide **1** (89.5 mg, 0.200 mmol), PdCl₂(dppf) (12.3mg, 0.00167 mmol) and THF (0.3 mL) at room temperature. The resulting mixture was stirred for 24 h at 60 °C. After addition of Et₂O (20 mL), the mixture was washed with aqueous 1N HCl (10 mL) and brine (10 mL), dried over MgSO₄, concentrated and purified by passing through a short silica gel column with 1 % ether in hexane to provide the corresponding coupling product. To a solution of the coupling product thus obtained in THF (5 mL) was added TBAF (1 mL, 1 M in THF, 1.0 mmol). After stirring for 24 h at room temperature, the solvents were removed under reduced pressure. The residue was diluted with H₂O (10 mL) and then extracted with EtOAc (5 x 10 mL). The combined organic layers were dried over MgSO₄, concentrated and chromatographed on silica gel (hexane-ethyl acetate) to give 1 α ,25-Dihydroxyvitamin D₃ (68.3 mg) in 82 % yield, the spectral data (¹H NMR, IR) and [α]_D value of which were identical to those reported²: ¹³C NMR (CDCl₃) δ 147.5, 143.0, 132.8, 124.8, 116.9, 111.7, 71.1, 70.8, 66.8, 56.5, 56.4, 45.9, 45.3, 44.4, 42.9, 40.5, 36.4, 36.1, 29.4, 29.3, 29.1, 27.7, 23.7, 22.3, 20.9, 18.9, 12.1; [α]_D³⁰ 47.2 (*c* 1.29, EtOH) [Lit., [α]_D²⁴ 47.7 (*c* 0.50, EtOH)].²

Retiferol from 1 and 12: Retiferol (55.1 mg) was obtained in 78 % yield starting from **1** (94 mg, 0.21 mmol) and **12** (0.130 g, 0.306 mmol) under similar reaction conditions described for synthesis of 1 α ,25-dihydroxyvitamin D₃ from **1** and **3**. The ¹H NMR spectroscopic spectra were in full agreement with those reported.³ ¹³C NMR (CDCl₃) δ 147.3, 135.4, 133.4, 129.4, 126.6, 112.0, 71.13, 71.09, 66.7, 45.1, 44.2, 42.9, 37.5, 36.4, 33.1, 32.6, 29.8, 29.3, 26.8, 21.8, 19.8; IR (neat) 3373, 2925, 1653, 1458, 1375, 1052, 908, 842, 759 cm⁻¹; [α]_D²⁷ 14.7 (*c* 0.65, CHCl₃).

(S)-1-(Trimethyl-silanyl)-oct-7-en-1-yn-4-ol (13): To a suspension of CuCN (45 mg, 0.50 mmol) in THF (30 mL) was slowly added allylmagnesium bromide (15 mL, 1.0 M in Et₂O, 15 mmol) at -20 °C. The resulting brown slurry was stirred for 10 min and a solution of **5** (1.54 g, 10.0 mmol) in THF (15 mL) was slowly added at -20 °C. The stirring was continued for 0.5 h at -20 °C. After addition of saturated aqueous NH₄Cl (60 mL), the mixture was extracted with Et₂O (3 x 30 mL), dried over MgSO₄, concentrated and chromatographed on silica gel (hexane-Et₂O) to give **13** (1.52 g, 77 %) as a pale yellow oil. ¹H NMR (CDCl₃) δ 5.74-5.89 (m, 1H), 4.94-5.08 (m, 2H), 3.69-3.79 (m, 1H), 2.45 (dd, *J* = 5.1, 16.8 Hz, 1H), 2.34 (dd, *J* = 6.9, 16.8 Hz, 1H), 2.11-2.22 (m, 2H), 2.07 (s, 1H), 1.57-1.65 (m, 2H), 0.14 (s, 9H); ¹³C NMR (CDCl₃) δ 138.2, 115.0, 103.1, 87.6, 69.2, 35.2, 29.7, 28.8, -0.1; IR (neat) 3368, 2959, 2176, 1653, 1642, 1419, 1250, 1081, 1020, 913, 844, 760, 699 cm⁻¹; Anal. Calcd. for C₁₁H₂₀OSi: C, 67.28; H, 10.27. Found: C, 67.54; H, 10.35.

(Z)-(1S,4S)-4-Bromomethyl-3-[bromo-(trimethyl-silanyl)-methylene]-cyclohexyloxy-*t*-butyl-dimethylsilane: The titled compound (0.754 g, 1.60 mmol) was

obtained in 59 % yield starting from **13** (0.533 g, 2.71 mmol) under similar reaction conditions described for synthesis of **11** from **2**. ^1H NMR (CDCl_3) δ 4.04-4.08 (m, 1H), 3.57-3.63 (m, 1H), 3.37-3.46 (m, 2H), 2.67 (d, $J = 15.0$ Hz, 1H), 2.06 (dd, $J = 3.0, 15.0$ Hz, 1H), 2.00 (dt, $J = 4.5, 13.2$ Hz, 1H), 1.76-1.85 (m, 1H), 1.65 (tt, $J = 3.3, 13.5$ Hz, 1H), 1.43-1.53 (m, 1H), 0.87 (s, 9H), 0.28 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (CDCl_3) δ 148.1, 127.0, 67.3, 44.3, 37.5, 33.8, 27.6, 25.9, 21.4, 18.2, 1.5, -4.6; IR (neat) 2954, 2857, 1589, 1472, 1361, 1251, 1096, 1030, 960, 838, 775, 693 cm^{-1} ; Anal. Calcd. for $\text{C}_{17}\text{H}_{34}\text{Br}_2\text{OSi}_2$: C, 43.40; H, 7.28. Found: C, 43.36; H, 7.29.

(Z)-(S)-3-(Bromomethylene-4-methylene-cyclohexyloxy)-tert-butyl-dimethyl-silane (14): **14** (0.265 g, 0.834 mmol) was obtained in 74 % yield starting from (Z)-(1*S*,4*S*)-4-bromomethyl-3-[bromo-(trimethyl-silanyl)-methylene]-cyclohexyloxy-*t*-butyl-dimethylsilane (0.530 g, 1.13 mmol) under similar reaction conditions described for synthesis of **1** from **11**. ^1H NMR (CDCl_3) δ 5.98 (s, 1H), 5.15 (s, 1H), 5.09 (s, 1H), 3.80-3.88 (m, 1H), 2.40-2.49 (m, 2H), 2.08-2.25 (m, 2H), 1.79-1.89 (m, 1H), 1.52-1.65 (m, 1H), 0.88 (s, 9H), 0.056 and 0.052 (s, each 3H); ^{13}C NMR (CDCl_3) δ 143.1, 141.5, 113.6, 99.0, 69.5, 45.4, 35.7, 31.8, 25.9, 18.2, -4.6; IR (neat) 2929, 2857, 1617, 1472, 1361, 1252, 1094, 836, 774 cm^{-1} ; Anal. Calcd. for $\text{C}_{14}\text{H}_{25}\text{BrOSi}$: C, 52.99; H, 7.94. Found: C, 53.20; H, 7.94.

Bornate (16): To a solution of alkenylbromide **15** (0.449 g, 1.32 mmol), prepared according to the reported procedure⁴, in Et_2O (4.0 mL) was added *t*-BuLi (2.07 mL, 1.40

M in pentane, 2.90 mmol) at $-78\text{ }^{\circ}\text{C}$. After stirring for 1 h at $-78\text{ }^{\circ}\text{C}$, to this was added $\text{B}(\text{O}-i\text{-Pr})_3$ (1.0 mL, 2.0 M in Et_2O , 2.0 mmol) at $-78\text{ }^{\circ}\text{C}$. The resulting mixture was allowed to warm to room temperature over 4 h, and then saturated aqueous NH_4Cl (10 mL) and EtOAc (10 mL) were added. The mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over MgSO_4 and concentrated under reduced pressure. The residue was dissolved in EtOAc (1.2 mL), and to this were added pinacol (187 mg, 1.58 mmol) and MgSO_4 (1.2 g). The resulting mixture was stirred at room temperature for 12 h, filtered, concentrated *in vacuo* and chromatographed on silica gel (hexane- Et_2O with a trace amount of Et_3N) to give **16** (0.39 g) in 76 % yield. ^1H NMR (CDCl_3) δ 4.90 (s, 1H), 3.14-3.19 (m, 1H), 1.07-2.06 (m, 19H), 1.26 (s, 12H), 0.91 (d, $J = 6.3\text{ Hz}$, 3H), 0.86 (d, $J = 6.6\text{ Hz}$, 3H), 0.85 (d, $J = 6.6\text{ Hz}$, 3H), 0.54 (s, 3H); ^{13}C NMR (CDCl_3) δ 166.2, 115.9 (br s), 82.5, 58.1, 56.9, 46.3, 40.5, 39.5, 36.14, 36.10, 33.3, 28.1, 27.5, 25.0, 24.9, 24.4, 23.9, 22.9, 22.6, 22.4, 19.0, 12.2; IR (neat) 2952, 2862, 1636, 1468, 1340, 1215, 1146, 975, 866, 736 cm^{-1} ; $[\alpha]_{\text{D}}^{27}$ 80.4 (c 2.27, CHCl_3).

Vitamin D₃ from 14 and 16: Vitamin D₃ (56.3 mg) was obtained in 70 % yield starting from **14** (66.6 mg, 0.209 mmol) and **16** (0.130 g, 0.335 mmol) under similar reaction conditions described for synthesis of $1\alpha,25$ -dihydroxyvitamin D₃ from **1** and **3**. The spectroscopic data (^1H and ^{13}C NMR and IR) of vitamin D₃ thus obtained were in full agreement with those measured using commercial vitamin D₃.⁵

References

1. Hanazawa, T.; Wada, T.; Masuda, T.; Okamoto, S.; Sato, F. *Org. Lett.* **2001**, *3*, 3975.
2. Baggiolini E. G., Iacobelli J. A., Hennessy B. M., Batcho A. D., Sereno J. F., Uskokovic M. R. *J. Org. Chem.* **1986**, *51*, 3098.
3. Kutner, A.; Zhao, H.; Fitak, H.; Wilson, S. R. *Bioorganic Chem.* **1995**, *23*, 22.

4. Trost, B. M.; Dumas, J.; Villa, M. *J. Am. Chem. Soc.* **1992**, *114*, 9836.

5. Purchased from Tokyo Kasei Kogyo Co., LTD.