

SUPPORTING INFORMATION FOR

A more reliable synthesis of a Gemini vitamin D analog, a potentially effective chemotherapeutic agent for the treatment of colorectal carcinomes.

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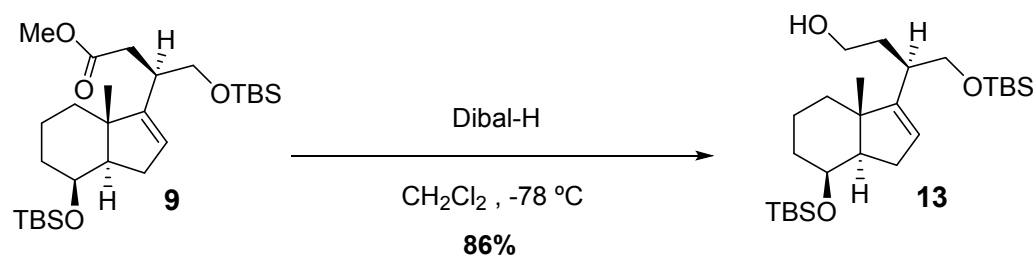
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Experimental procedure

General: Solvents were purified and dried by standard procedures before use. Melting points are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker ARX-400 spectrometer (400 MHz for ^1H NMR, 100.61 MHz for ^{13}C NMR) using TMS as internal standard (Chemical shifts in δ values, J in Hz). Flash chromatography (FC) was performed on silica gel (Merck 60, 230-400 mesh); analytical TLC was performed on plates precoated with silica gel (Merck 60 F254, 0.25mm); mass spectra (FAB, EI) were recorded using FISIONS VG and electron spray ionization (ESI-MS) spectroscopy was recorded using Bruker FTMS APEXIII. Melting points were obtained in open capillary tubes and are not corrected. Optical rotations were obtained using a Jasco P-2000 polarimeter. IR spectra were recorded with a JASCO FT/I(R)-6100 spectrophotometer.

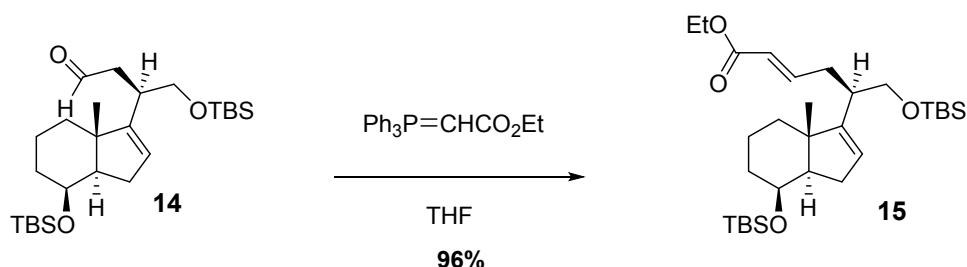
(R)-4-((tert-butyldimethylsilyl)oxy)-3-((3a*S*,7*S*,7a*R*)-7-((tert-butyldimethylsilyl)oxy)-3a-methyl-3a,4,5,6,7,7a-hexahydro-1*H*-inden-3-yl)butan-1-ol (**13**)



To a solution ester **9** (710 mg, 1.43 mmol) in CH_2Cl_2 (2.5 mL) at -78°C was added Dibal-H (5.7 mL, 5.7 mmol, 1M soln in hexane) and the mixture was stirred for 15 h. $t\text{BuOMe}$ (7 mL) and H_2O (1 mL) were added and the mixture allowed to reach room temperature. Stirring was continued till the formation of a white gel before adding H_2O (1 mL) and a 4 M aqueous solution of NaOH (1 mL). Stirring was continued till the formation of a white solid. Na_2SO_4 and silica gel were added and the mixture stirred for 20 min. The solid was separated by filtration and the filtrate was concentrated to afford a residue which was chromatographed on silica gel using 1% EtOAc/Hexane as eluent, affording compound **13** (576 mg, 86%) as a colourless liquid; Rf: 0.45 (10% EtOAc/Hexane); IR (NaCl, cm^{-1}): 3356, 2950, 2927, 2855, 1471, 1253, 1069, 835, 773; $[\alpha]_D^{23} = +13.71$ (c 0.8, CHCl_3); $^1\text{H-NMR}$ (CDCl_3 , δ): 5.39 (1H, s, H-16), 4.11 (1H, s, H-8), 3.70 (1H, m), 3.60 (2H, m), 3.30 (1H, t, $J=9.6$ Hz), 2.26 (2H, m), 1.92 (2H,

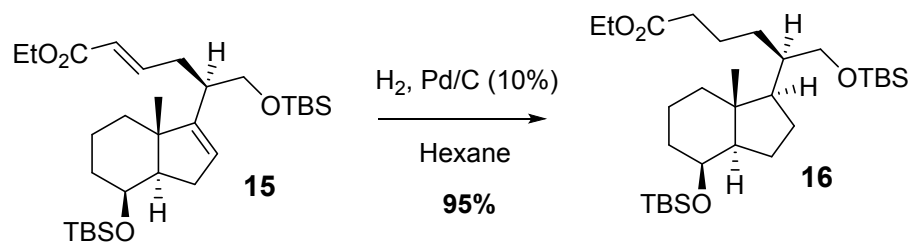
[*m/z*, (%)]: 467.33 (*M*⁺+1, 100); **HRMS (ESI)**: 467.33712 calculated for C₂₆H₅₁O₃Si₂ and found 467.33601.

Ethyl(R,E)-6-((tert-butyldimethylsilyl)oxy)-5-((3*aS*,7*S*,7*aR*)-7-((tert-butyldimethylsilyl)oxy)-3*a*-methyl-3*a*,4,5,6,7,7*a*-hexahydro-1*H*-inden-3-yl)hex-2-enoate (15**)**



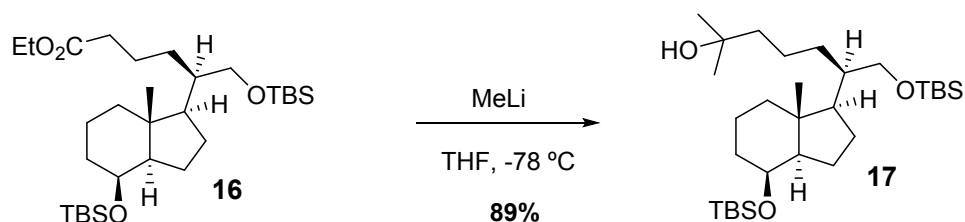
To a solution of aldehyde **14** (252 mg, 0.54 mmol) in THF (4 mL) was added $\text{Ph}_3\text{P}=\text{CHCO}_2\text{Et}$ (375 mg, 1.07 mmol) and the mixture was stirred at room temperature for 20 h. The solvent was rotary evaporated to afford a residue which was chromatographed on silica gel using 1% EtOAc/Hexane as eluent, affording compound **15** (276 mg, 96%) as a colourless liquid, *R*_f: 0.56 (5% EtOAc/Hexane); **IR (ATR, cm⁻¹)**: 2952, 2927, 2854, 1723, 1463, 1255, 1080, 835, 774; [*α*]_D²⁷ = -16.95 (c 0.5, CHCl₃); **¹H-NMR (CDCl₃, δ)**: 6.94 (1H, m, H-23), 5.81 (1H, d, *J*=16.1 Hz, H-24), 5.40 (1H, s, H-16), 4.19 (2H, q, *J*=7.1 Hz, CH₂-OEt), 4.10 (1H, s, H-8), 3.61 (1H, m, H-21), 3.27 (1H, dd, *J*=10.0/8.1 Hz, H-21), 2.67 (1H, m), 2.27 (3H, m), 1.89 (2H, m), 1.76-1.41 (6H, m), 1.28 (3H, t, *J*=7.1 Hz, CH₃-OEt), 0.99 (3H, s, CH₃-18), 0.91 (9H, s, CH₃-*t*Bu), 0.90 (9H, s, CH₃-*t*Bu), 0.05 (3H, s, CH₃-Si), 0.04 (3H, s, CH₃-Si), 0.04 (3H, s, CH₃-Si), 0.03 (3H, s, CH₃-Si); **¹³C-NMR (CDCl₃, δ)**: 166.64 (C=O), 153.86 (C-17), 148.67 (CH-23), 123.96 (CH-24), 122.11 (CH-16), 68.91 (CH-8), 66.53 (CH₂-21), 59.97 (CH₂-OEt), 54.75 (CH-14), 46.67 (C-13), 39.78 (CH-20), 35.51 (CH₂), 34.69 (CH₂), 34.53 (CH₂), 31.04 (CH₂), 25.93 (CH₃-*t*Bu), 25.78 (CH₃-*t*Bu), 18.91 (CH₃-18), 18.28 (C-*t*Bu), 18.00 (C-*t*Bu), 17.99 (CH₂), 14.25 (CH₃-OEt), -4.86, -5.16, -5.29, -5.35; **MS (ESI) [*m/z*, (%)]**: 559.36 (*M*⁺+Na, 17), 537.37 (*M*⁺+1, 68), 405.28 (*M*⁺-OTBS); **HRMS (ESI)**: 537.37899 calculated for C₃₀H₅₇O₄Si₂, found 537.37766.

Ethyl(R)-6-((tert-butyldimethylsilyl)oxy)-5-((1*R*,3*aR*,4*S*,7*aR*)-4-((tert-butyldimethylsilyl)oxy)-7*a*-methyloctahydro-1*H*-inden-1-yl)hexanoate (16**)**



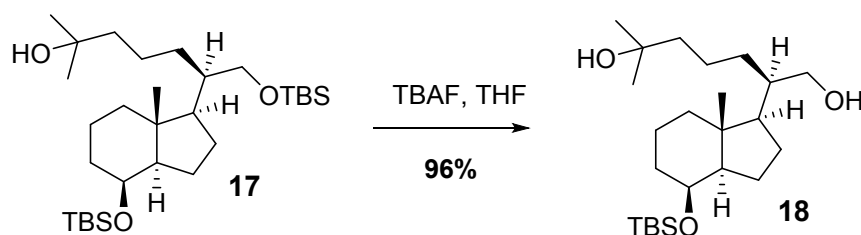
To a mixture of diene **15** (138 mg, 0.25 mmol) in hexane (2 mL) was added a catalytic amount of Pd/C (10%) and the suspension was stirred for 13 h at room temperature under H_2 . The mixture was then filtered through celite and the filtrate was rotatory evaporated to afford a residue which was chromatographed on silica gel using 1% EtOAc/Hexane as eluent, affording compound **16** (132 mg, 95%) as a colourless liquid, Rf: 0.55 (5% AcOEt/Hexano); IR (ATR, cm^{-1}): 2951, 2928, 2856, 1738, 1462, 1387, 1251, 1090, 835; $[\alpha]_{\text{D}}^{23} = -27.09$ (c 1.0, CHCl_3); ^1H - NMR (CDCl_3 , δ): 4.13 (2H, q, $J=7.1$ Hz, $\text{CH}_2\text{-OEt}$), 4.00 (1H, s, CH-8), 3.66 (1H, dd, $J=10.1/3.7$ Hz, H-21), 3.49 (1H, dd, $J=10.1/6.0$ Hz, H-21), 2.26 (2H, m, H-24), 1.86-1.28 (16H, m), 1.26 (3H, t, $J=7.2$ Hz, $\text{CH}_3\text{-OEt}$), 1.13 (1H, m), 0.92 (3H, s, $\text{CH}_3\text{-18}$), 0.90 (18H, s, $\text{CH}_3\text{-}^t\text{Bu}$), 0.04 (6H, s, $\text{CH}_3\text{-Si}$), 0.02 (3H, s, $\text{CH}_3\text{-Si}$), 0.01 (3H, s, $\text{CH}_3\text{-Si}$); ^{13}C - NMR (CDCl_3 , δ): 173.83 (C=O), 69.43 (CH-8), 62.82 ($\text{CH}_2\text{-21}$), 60.06 ($\text{CH}_2\text{-OEt}$), 52.97 (CH-14), 50.80 (CH-17), 41.94 (C-13), 41.77 (CH-20), 40.24 (CH_2), 35.01 (CH_2), 34.48 (CH_2), 28.80 (CH_2), 26.41 (CH_2), 25.94 ($\text{CH}_3\text{-}^t\text{Bu}$), 25.81 ($\text{CH}_3\text{-}^t\text{Bu}$), 22.94 (CH_2), 21.64 (CH_2), 18.22 (C- ^tBu), 18.01 (C- ^tBu), 17.70 (CH_2), 14.26 ($\text{CH}_3\text{-18}$), 14.04 ($\text{CH}_3\text{-OEt}$), -4.80 ($\text{CH}_3\text{-Si}$), -5.16 ($\text{CH}_3\text{-Si}$), -5.38 ($\text{CH}_3\text{-Si}$), -5.47 ($\text{CH}_3\text{-Si}$); MS (ESI) $[\text{m/z}, (\%)]$: 541.40 ($\text{M}^+ + 1$, 100); HRMS (ESI): 541.41029 calculated for $\text{C}_{30}\text{H}_{61}\text{O}_4\text{Si}_2$, found 541.40849.

(R)-7-((tert-butyldimethylsilyl)oxy)-6-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-2-methylheptan-2-ol (17)



To a solution of ester **16** (262 mg, 0.48 mmol) in THF (4 mL) at -78 °C was added MeLi·LiBr (1.5 mL, 2.42 mmol, 1.5 M solution in ethyl ether) and the mixture was stirred for 5 h. H₂O (5 mL) was added and the product extracted with CH₂Cl₂ (3 x 10 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 5% EtOAc/Hexane as eluent, affording alcohol **17** (227 mg, 89%) as a colourless liquid, R_f: 0.31 (10% AcOEt/Hexano); **IR** (ATR, cm⁻¹): 3357, 2948, 2927, 2855, 1471, 1251, 1085, 834, 773; [α]_D²⁵ = -8.56 (c 0.5, CHCl₃); **¹H-NMR** (CDCl₃, δ): 4.01 (1H, s, CH-8), 3.67 (1H, dd, *J*=9.9/3.6 Hz, H-21), 3.52 (1H, dd, *J*=9.9/5.5 Hz, H-21), 1.87-1.24 (20H, m), 1.22 (6H, s, CH₃-26/CH₃-27), 0.93 (3H, s, CH₃-18), 0.90 (18H, s, CH₃-^tBu), 0.04 (6H, s, CH₃-Si), 0.02 (3H, s, CH₃-Si), 0.01 (3H, s, CH₃-Si); **¹³C-NMR** (CDCl₃, δ): 71.06 (C-25), 69.47 (CH-8), 62.79 (CH₂-21), 52.99 (CH-14), 50.94 (CH-17), 44.71 (CH₂), 41.97 (CH-20), 41.96 (C-13), 40.28 (CH₂), 34.51 (CH₂), 29.76 (CH₂), 29.25 (CH₃-26/CH₃-27), 29.21 (CH₃-26/CH₃-27), 26.55 (CH₂), 25.95 (CH₃-^tBu), 25.83 (CH₃-^tBu), 22.98 (CH₂), 20.87 (CH₂), 18.25 (C-^tBu), 18.03 (C-^tBu), 17.73 (CH₂), 14.06 (CH₃-18), -4.78 (CH₃-Si), -5.14 (CH₃-Si), -5.34 (CH₃-Si), -5.46 (CH₃-Si); **MS (ESI) [*m/z*, (%)]**: 509.42 (M⁺-OH, 100), 527.42 (M⁺+1, 47); **HRMS (ESI)**: 527.43103 calculated for C₃₀H₆₃O₃Si₂, found 527.42979.

(R)-2-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-6-methylheptane-1,6-diol (18)

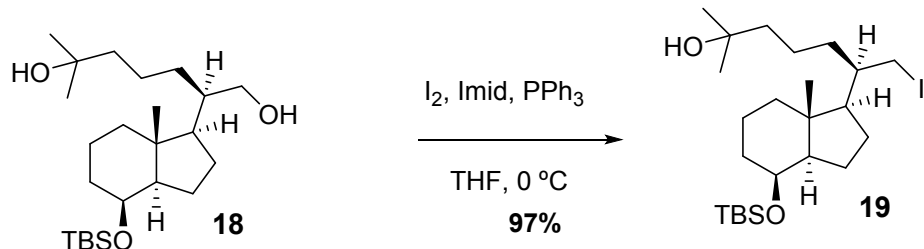


To a solution of **17** (220 mg, 0.418 mmol) in THF (4 mL) was added tetra-*n*-butylammonium fluoride (TBAF) (835 μ L of a 1 M solution in THF, 0.835 mmol) and the mixture was stirred at room temperature for 19 h, quenched with an aqueous saturated solution of NH₄Cl (3 mL) and the product extracted with EtOAc (3 x 15 mL). The combined organic phases were dried, filtered and evaporated

to give a residue which was chromatographed on silica gel using 50% EtOAc/Hexane as eluent, affording diol **18** (165 mg, 96%) as a white solid (mp: 105-109°C), Rf: 0.10 (30% EtOAc/Hexane);

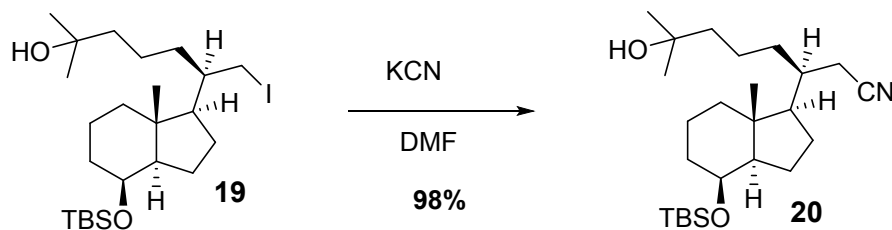
IR (ATR, cm⁻¹): 3348, 2948, 2928, 2856, 1471, 1251, 1022, 937, 835; **[α]²⁵_D**= -7.85 (c 1.00, CHCl₃); **¹H- NMR (CDCl₃, δ):** 4.01 (1H, s, H-8), 3.73 (1H, dd, *J*=11.1/3.3 Hz, H-21), 3.64 (1H, dd, *J*=11.2/5.2 Hz, H-21), 1.96-1.25 (21H, m), 1.22 (6H, s, CH₃-26/CH₃-27), 0.94 (3H, s, CH₃-18), 0.90 (9H, s, CH₃-^{*t*}Bu), 0.02 (3H, s, CH₃-Si), 0.01 (3H, s, CH₃-Si); **¹³C- NMR (CDCl₃, δ):** 71.03 (C-25), 69.35 (CH-8), 62.57 (CH₂-21), 52.98 (CH-14), 50.87 (CH-17), 44.21 (CH₂), 41.91 (C-13), 41.87 (CH-20), 40.12 (CH₂), 34.41 (CH₂), 29.69 (CH₂), 29.37 (CH₃-26/CH₃-27), 29.32 (CH₃-26/CH₃-27), 26.71 (CH₂), 25.81 (CH₃-^{*t*}Bu), 22.89 (CH₂), 20.74 (CH₂), 18.02 (CH₂), 17.68 (C-^{*t*}Bu), 13.96 (CH₃-18), -4.79 (CH₃-Si), -5.15 (CH₃-Si); **MS (ESI) [m/z, (%)]:** 395.33 (M⁺-OH, 100), 435.32 (M⁺+Na, 22); **HRMS (ESI):** 435.32649 calculated for C₂₄H₄₈NaO₃Si₂, found 435.32554.

(R)-6-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-7-iodo-2-methylheptan-2-ol(19)



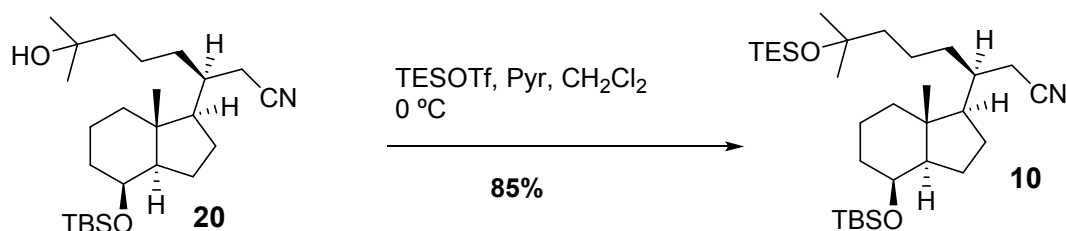
To a solution of diol **18** (165 mg, 0.4 mmol) in THF (4 mL) at room temperature were added sequentially PPh₃ (157 mg, 0.6 mmol) and imidazole (82 mg, 1.2 mmol). After cooling the mixture to 0 °C, I₂ (142 mg, 0.56 mmol) was added and stirring continued for 20 min. The reaction was quenched with an aqueous saturated solution of NaHCO₃ (10 mL) and the product extracted with EtOAc (3x20 mL). The organic phase was washed with a 10% aqueous solution of Na₂S₂O₃ (10 mL) and brine (10 mL), dried over Na₂SO₄, filtered and concentrated to give a residue which was chromatographed on silica gel using 20% EtOAc/Hexane as eluent, affording iodide **19** (202 mg, 97%) as a colourless liquid, Rf: 0.9 (50% AcOEt/Hexano); **IR (ATR, cm⁻¹):** 3357, 2948, 2928, 2856, 1470, 1251, 1070, 836, 773; **[α]²⁴_D**= -6.32 (c 0.25, CHCl₃); **¹H- NMR (CDCl₃, δ):** 3.99 (1H, s, H-8), 3.46 (1H, dd, *J*=10.0/3.2 Hz, H-

21), 3.35 (1H, dd, $J=10.0/4.4$ Hz, H-21), 1.88-1.22 (20H, m), 1.21 (6H, s, CH₃-26/27), 0.91 (3H, s, CH₃-18), 0.89 (9H, s, CH₃-^{*t*}Bu), 0.01 (3H, s, CH₃-Si), 0.00 (3H, s, CH₃-Si); **¹³C-NMR (CDCl₃, δ):** 70.87 (C-25), 69.30 (CH-8), 53.13 (CH-17), 52.74 (CH-14), 43.92 (CH₂), 42.08 (C-13), 40.50 (CH₂), 39.64 (CH-20), 34.28 (CH₂), 33.49 (CH₂), 29.34 (CH₃-26/CH₃-27), 29.31 (CH₃-26/CH₃-27), 26.43 (CH₂), 25.83 (CH₃-^{*t*}Bu), 22.74 (CH₂), 20.24 (CH₂), 18.01 (C-^{*t*}Bu), 17.65 (CH₂), 17.43 (CH₂), 13.94 (CH₃-18), -4.75 (CH₃-Si), -5.13 (CH₃-Si); **MS (ESI) [m/z, (%)]:** 505.23 (M⁺-OH, 100); **HRMS (ESI):** 505.23331 calculated for C₂₄H₄₆IO₂Si, found 505.23471.



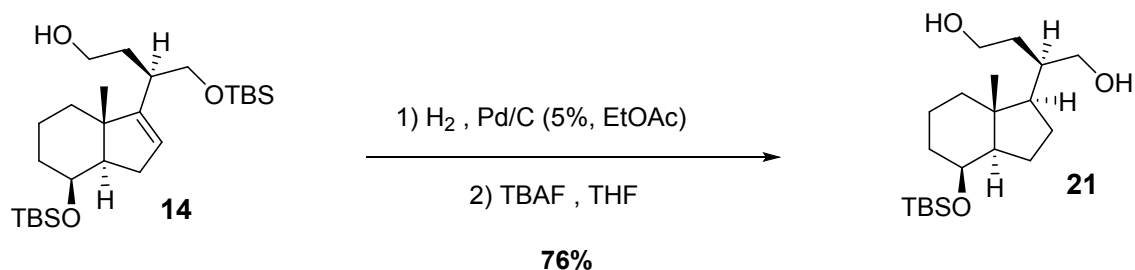
17.55 (CH₂), 13.90 (CH₃-18), -4.79 (CH₃-Si), -5.17 (CH₃-Si); **MS (ESI) [m/z, (%)]**: 444.32 (M+Na⁺, 24), 404.33 (M⁺-OH, 100); **HRMS (ESI)**: 444.32683 calculated for C₂₅H₄₇NNaO₂Si, found 444.32591.

(S)-3-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-7-methyl-7-((triethylsilyl)oxy)octanenitrile (10)



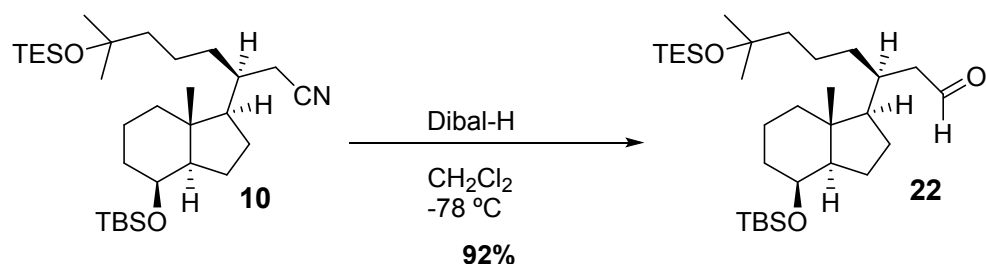
To a solution of alcohol **20** (159 mg, 0.37 mmol) in CH₂Cl₂ (3 mL) at 0°C were added sequentially pyridine (0.3 ml, 3.77 mmol) and triethyl silyl triflate (TESOTf) (0.25 ml, 1.13 mmol) and the mixture was stirred overnight at room temperature. The reaction was quenched with a 10% aqueous solution of NaHCO₃ (5 mL) and the product extracted with EtOAc (3 x 15 ml). The combined organic phases were dried over Na₂SO₄, filtered and concentrated to give a residue which was chromatographed on silica gel using hexane as eluent, affording nitrile **10** (173 mg, 85%) as a colourless liquid, R_f: 0.96 (30% AcOEt/Hexano); **IR (ATR, cm⁻¹):** 2951, 2927, 2855, 2243, 1461, 1250, 1017, 835, 742; **[α]_D²⁴:** -3.76 (c 0.5, CHCl₃); **¹H-NMR (CDCl₃, δ):** 4.03 (1H, s, H-8), 2.51 (2H, d, *J*=4.2 Hz, H-21), 1.91-1.23 (19H, m), 1.21 (6H, s, CH₃-26/27), 0.97 (9H, t, *J*=7.9 Hz, CH₃-OTES), 0.94 (3H, s, CH₃-18), 0.91 (9H, s, CH₃-*t*Bu), 0.59 (6H, q, *J*=7.9 Hz, CH₂-OTES), 0.04 (3H, s, CH₃-Si), 0.02 (3H, s, CH₃-Si); **¹³C-NMR (CDCl₃, δ):** 118.68 (CN), 73.14 (C-25), 69.23 (CH-8), 53.11 (CH-17), 52.73 (CH-14), 45.00 (CH₂), 41.99 (C-13), 40.19 (CH₂), 36.48 (CH-20), 34.16 (CH₂), 32.33 (CH₂), 29.92 (CH₃-26/27), 29.86 (CH₃-26/27), 26.87 (CH₂), 25.80 (CH₃-*t*Bu), 22.78 (CH₂), 20.77 (CH₂), 20.11 (CH₂), 18.02 (C-*t*Bu), 17.58 (CH₂), 13.92 (CH₃-18), 7.12 (CH₃-OTES), 6.80 (CH₂-OTES), -4.79 (CH₃-Si), -5.17 (CH₃-Si); **MS (ESI) [m/z, (%)]:** 536.42 (M⁺+1, 100), 405.33 (M⁺-OTES, 67); **HRMS (ESI):** 536.43136 calculated for C₃₁H₆₂NO₂Si₂, found 536.42945.

(R)-2-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)butane-1,4-diol (21)



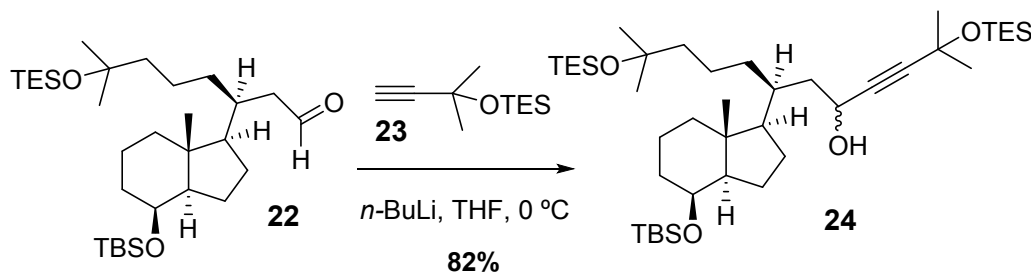
To a solution of alkene **14** (31 mg, 0.065 mmol) in ethyl acetate (2 mL) was added a catalytic amount of Pd/C (10%) and the suspension was stirred for 6 h at room temperature under H₂. The mixture was then filtered through celite and the filtrate was rotatory evaporated to afford a residue which was taken up with THF (2 ml). TBAF (130 μ L of a 1 M solution in THF, 0.13 mmol) was added and the mixture was stirred at room temperature for 4 h, quenched with an aqueous saturated solution of NH₄Cl (3 mL) and the product extracted with EtOAc (3 x 5 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 50% EtOAc/Hexane as eluent, affording diol **21** (17 mg, 76%) as a white solid (mp: 117-119°C), R_f: 0.12 (50% EtOAc/Hexane); **IR (ATR, cm⁻¹)**: 3298, 2956, 2923, 2853, 1463, 1377, 1026, 836; **[α]_D²¹** = -7.93 (c 0.95, CHCl₃); **¹H-NMR (CDCl₃, δ)**: 4.03 (1H, s, H-8), 3.79 (2H, m), 3.65 (2H, m), 2.79 (2H, s, OH), 1.94-1.52 (8H, m), 1.47-1.15 (7H, m), 0.97 (3H, s, CH₃-18), 0.91 (9H, s, CH₃-^tBu), 0.03 (3H, s, CH₃-Si), 0.02 (3H, s, CH₃-Si); **¹³C-NMR (CDCl₃, δ)**: 69.32 (CH-8), 64.38 (CH₂-21), 60.70 (CH₂-23), 52.97 (CH-14), 50.61 (CH-17), 41.96 (C-13), 41.05 (CH-20), 40.22 (CH₂), 34.35 (2 CH₂), 26.92 (CH₂), 25.81 (CH₃-^tBu), 22.89 (CH₂), 18.03 (C-^tBu), 17.68 (CH₂), 13.88 (CH₃-18), -4.78 (CH₃-Si), -5.15 (CH₃-Si); **MS (ESI) [m/z, (%)]**: 379.2 (M+Na⁺, 18), (M⁺+1, 100), 357.2 (M⁺, 24), 339.2 (M⁺-OH, 71); **HRMS (ESI)**: 357.28195 calculated for C₂₀H₄₁O₃Si, found 357.28123.

(S)-3-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-7-methyl-7-((triethylsilyl)oxy)octanal (22)



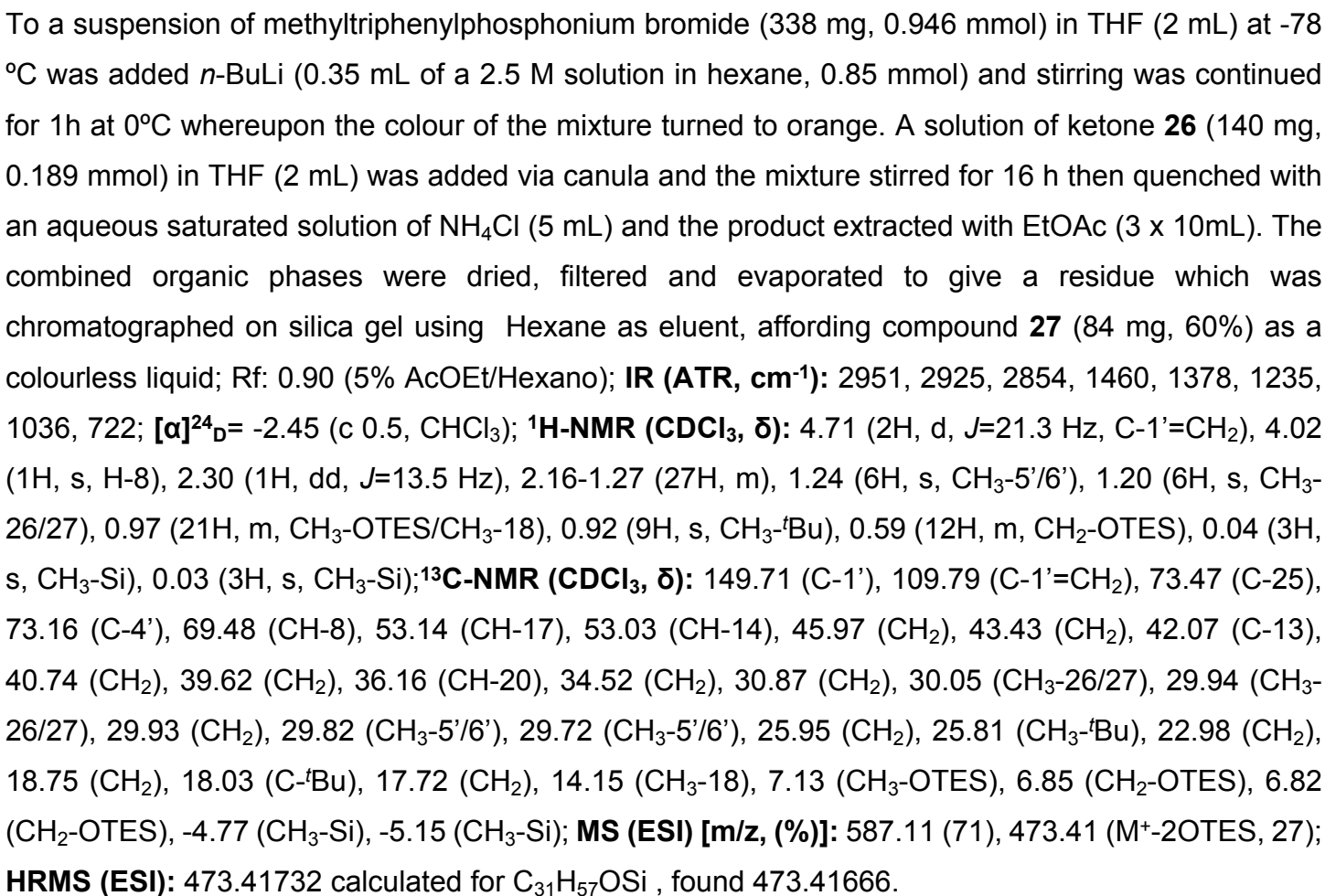
To a solution of nitrile **10** (173 mg, 0.32 mmol) in CH₂Cl₂ (3 mL) at -78 °C was added dropwise Dibal-H (0.9 mL, 0.9 mmol, 1M sln in hexane) and the mixture was stirred for 13 h. NeOH (5 ml) and an aqueous saturated solution of NH₄Cl (2.5 ml) were added and the product was extracted with CH₂Cl₂ (3 x 20 ml). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 2% EtOAc/Hexane as eluent, affording aldehyde **22** (156 mg, 92%) as a colourless liquid; Rf: 0.57 (5% AcOEt/Hexano); **IR (ATR, cm⁻¹):** 2950, 2929, 2874, 1706, 1469, 1251, 1028, 723; **[α]²⁵_D** = -21.10 (c 0.5, CHCl₃); **¹H-NMR (CDCl₃, δ):** 9.78 (1H, s, CHO), 4.01 (1H, s, H-8), 2.58 (1H, ddd, *J*=16.6/4.4/1.9 Hz, H-21), 2.42 (1H, ddd, *J*=16.6/7.5/3.1 Hz, H-21), 1.96 (1H, m), 1.83 (3H, m), 1.69 (1H, m), 1.58 (1H, m), 1.46-1.23 (12H, m), 1.20 (3H, s, CH₃-26/27), 1.19 (3H, s, CH₃-26/27), 0.96 (3H, m, CH₃-18), 0.95 (9H, t, *J*=7.9 Hz, CH₃-OTES), 0.90 (9H, s, CH₃-*t*Bu), 0.57 (6H, q, *J*=7.9 Hz, CH₂-OTES), 0.03 (3H, s, CH₃-Si), 0.02 (3H, s, CH₃-Si); **¹³C-NMR (CDCl₃, δ):** 203.30 (CHO), 73.24 (C-25), 69.29 (CH-8), 53.68 (CH-17), 52.89 (CH-14), 46.35 (CH₂), 45.41 (CH₂), 42.23 (C-13), 40.59 (CH₂), 34.78 (CH-20), 34.31 (CH₂), 33.08 (CH₂), 30.02 (CH₃-26/27), 29.74 (CH₃-26/27), 26.72 (CH₂), 25.79 (CH₃-*t*Bu), 22.79 (CH₂), 20.29 (CH₂), 18.01 (C-*t*Bu), 17.61 (CH₂), 14.18 (CH₃-18), 7.11 (CH₃-OTES), 6.80 (CH₂-OTES), -4.80 (CH₃-Si), -5.17 (CH₃-Si); **MS (ESI) [m/z, (%)]:** 537.41 (M⁺, 60), 407.33 (M⁺-OTES, 100); **HRMS (ESI):** 537.41538 calculated for C₃₁H₆₁O₃Si₂, found 537.41382.

(10S)-10-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-3,3,16,16-tetraethyl-5,5,14,14-tetramethyl-4,15-dioxo-3,16-disilaooctadec-6-yn-8-ol (24).

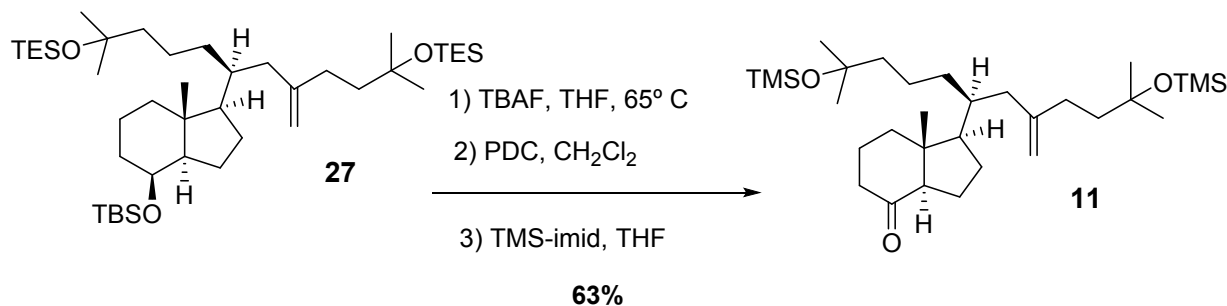


To a solution of alkyne **23** (373 mg, 1.88 mmol) in THF (2 mL) at -78 °C was added dropwise *n*-BuLi (0.7 mL, 1.74 mmol, 2.5 M in hexane) and the mixture left stirring at 0°C for 2 h, before adding a solution of aldehyde **22** (156 mg, 0.29 mmol) in THF (2 mL). After stirring at the same temperature for 15 h, an aqueous saturated solution of NH₄Cl (5 mL) was added and the product extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over Na₂SO₄, filtered and evaporated to give a residue which was chromatographed on silica gel using 3% EtOAc/Hexane as eluent, affording alcohol **24** (176 mg, 82%) as a colourless liquid, R_f: 0.62/0.59 (10% EtOAc /Hexano); **IR (ATR, cm⁻¹)**: 3392, 2953, 2930, 2884, 2858, 1251; **¹H-NMR (CDCl₃, δ)**: 4.43 (1H, dd, *J*=9.1/4.3 Hz, H-1'), 4.03 (1H, s, H-8), 2.02-1.52 (10H, m), 1.50 (3H, s, CH₃-5'/6'), 1.49 (3H, s, CH₃-5'/6'), 1.46-1.24 (14H, m), 1.22 (6H, s, CH₃-26/27), 0.97 (21H, m, CH₃-18, CH₃-OTES), 0.91 (9H, s, CH₃-^{*t*}Bu), 0.70 (6H, q, *J*=7.9 Hz, CH₂-OTES), 0.59 (6H, q, *J*=7.9 Hz, CH₂-OTES), 0.03 (3H, s, CH₃-Si), 0.02 (3H, s, CH₃-Si); **¹³C-NMR (CDCl₃, δ)**: 89.62 (C-2'), 84.01 (C-3'), 73.37 (C-25), 69.42 (CH-8), 66.12 (C-4'), 60.41 (CH-1'), 53.33 (CH-17), 53.08 (CH-14), 45.91 (CH₂), 42.10 (CH₂), 40.75 (CH₂), 40.05 (CH₂), 34.67 (CH-20), 34.49 (CH₂), 33.09 (CH₃-5'/6'), 33.06 (CH₃-5'/6'), 30.92 (CH₂), 29.97 (CH₃-26/27), 29.89 (CH₃-26/27), 26.18 (CH₂), 25.81 (CH₃-^{*t*}Bu), 22.87 (CH₂), 19.04 (CH₂), 18.03 (C-^{*t*}Bu), 17.72 (CH₂), 14.03 (CH₃-18), 7.13 (CH₃-OTES), 6.99 (CH₃-OTES), 6.84 (CH₂-OTES), 6.11 (CH₂-OTES), -4.78 (CH₃-Si), -5.15 (CH₃-Si); **MS (ESI) [*m/z*, (%)]**: 759.55 (M+Na⁺, 17), 719.56 (M⁺-OH, 3), 587.46 (70), 455.37 (100); **HRMS (ESI)**: 759.55696 calculated for C₄₂H₈₄NaO₄Si₃, found 759.55560.

(10S)-10-((1R,3aR,4S,7aR)-4-((tert-butyldimethylsilyl)oxy)-7a-methyloctahydro-1H-inden-1-yl)-3,3,16,16-tetraethyl-5,5,14,14-tetramethyl-4,15-dioxo-3,16-disilaooctadecan-8-ol (25)

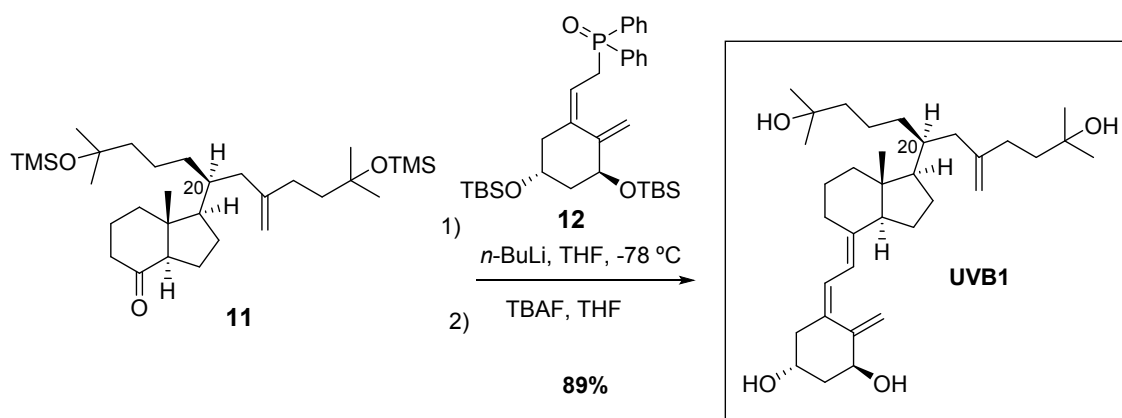


(1R,3aR,7aR)-7a-methyl-1-((S)-2,2,4,4,13,13,15,15-octamethyl-10-methylene-3,14-dioxo-2,15-disilaheptadecan-8-yl)octahydro-4H-inden-4-one (11)



To a solution of **27** (184 mg, 0.25 mmol) in THF (3 mL) was added TBAF (750 μ L of a 1 M solution in THF, 0.75 mmol) and the mixture was stirred at 65°C for 7 days. The solvent was rotatory evaporated and the residue taken up with CH₂Cl₂ (3 mL). Pyridinium dichromate (PDC) (277 mg, 0.75 mmol) was added and the brown suspension stirred at room temperature for 3 h and the solvent rotatory evaporated. The residue was dissolved in THF (2 mL) and 1-(trimethylsilyl)imidazole (TMS-Im) (0.36 mL, 2.5 mmol) added and the mixture stirred at room temperature for 12 h. After solvent evaporation the crude was chromatographed on silica gel using 10% EtOAc/Hexane as eluent, affording **11** (84 mg, 63%) as a colourless liquid; R_f: 0.76 (10% AcOEt/Hexano); **IR (NaCl, cm⁻¹)**: 2985, 2956, 2903, 2835, 1707, 1587, 1212, 1194, 987, 927, 773, 608; **[α]²²_D**: +21.80 (c 1.00, CHCl₃); **¹H-NMR (CDCl₃, δ)**: 4.73 (2H, d, J=14.1 Hz, C-1'=CH₂), 2.45 (1H, dd, J=11.1/7.5 Hz, H-14), 2.18 (3H, m), 1.92 (6H, m), 1.58 (8H, m), 1.30 (6H, m), 1.20 (6H, s, CH₃-26, CH₃-27, CH₃-5', CH₃-6'), 1.18 (6H, s, CH₃-26, CH₃-27, CH₃-5', CH₃-6'), 0.64 (3H, s, CH₃-18), 0.06 (18H, s, TMS); **¹³C-NMR (CDCl₃, δ)**: 211.85 (CO), 148.84 (C-1'), 110.43 (C-1'=CH₂), 73.91 (C-25/C-4'), 73.58 (C-25/C-4'), 61.73 (CH-14), 53.02 (CH-17), 49.84 (C-13), 45.42 (CH₂), 43.04 (CH₂), 40.90 (CH₂), 39.81 (CH₂), 38.73 (CH₂), 36.19 (CH-20), 30.92 (CH₂), 29.90 (CH₃-26/CH₃-27/CH₃-5'/CH₃-6'), 29.80 (CH₃-26/CH₃-27/CH₃-5'/CH₃-6'), 29.74 (CH₂), 29.69 (CH₃-26, CH₃-27, CH₃-5', CH₃-6'), 25.62 (CH₂), 23.95 (CH₂), 19.01 (CH₂), 18.90 (CH₂), 12.83 (CH₃-18), 2.60 (CH₃-Si), 2.54 (CH₃-Si); **MS (FAB⁺) [m/z, (%)]**: 559.40 (M+Na⁺, 26), 537.40 (M⁺+1, 100); **HRMS (FAB⁺)**: 559.4098 calculated for C₃₁H₆₀O₃Si₂Na, found 559.4093.

(1R,3S,Z)-5-(2-((1R,3aS,7aR,E)-1-((S)-2,11-dihydroxy-2,11-dimethyl-8-methylenedodecan-6-yl)-7a-methyloctahydro-4H-inden-4-ylidene)ethylidene)-4-methylenecyclohexane-1,3-diol (UVB1)



To a solution of phosphine oxide **12** (150 mg, 0.257 mmol) in THF (2 mL) was added dropwise $n\text{-BuLi}$ (100 μL of a 2.5 M solution in THF, 0.25 mmol) at $-78\text{ }^{\circ}\text{C}$ and the deep red mixture was stirred for 1 h. A solution of ketone **11** (17 mg, 0.03 mmol) in THF (1.5 mL) was added at the same conditions via cannula and stirred for 15 h. A saturated aqueous solution of NH_4Cl (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 5 mL). The organic phase was dried over Na_2SO_4 , filtered and the solvent removed under reduced pressure. The residue was taken up with THF (2 mL) and TBAF (0.5 mL of a 1 M solution in THF, 0.5 mmol) was added. The mixture was stirred for 21 h and the solvent removed under reduced pressure. The residue was chromatographed on silica gel using EtOAc as eluent, affording **UVB1** (14 mg, 89%) as a white solid; m.p: 78.5°C ; Rf: 0.40 (EtOAc); IR (NaCl , cm^{-1}): 3721, 3376, 3364, 2914, 2851, 2201, 1200, 1159, 1024, 835; $[\alpha]^{25}_{\text{D}} = +8.10$ (c 0.4, CHCl_3); $^1\text{H-NMR}$ (CDCl_3 , δ): 6.33 (1H, d, $J=11.2$ Hz, H-6), 6.00 (1H, d, $J=11.2$ Hz, H-7), 5.29 (1H, s, H-19), 4.97 (1H, s, H-19), 4.72 (2H, d, $J=24.0$ Hz, C-1'=CH₂), 4.37 (1H, d, $J=3.9$, H-1), 4.18 (1H, d, $J=3.1$ Hz, H-3), 2.74 (1H, m), 2.49 (2H, dd, $J=50.7/12.4$ Hz), 2.24 (3H, m), 1.92 (10H, m), 1.56 (10H, m), 1.34 (7H, m), 1.17 (12H, m, CH₃-26/CH₃-27/CH₃-5'/CH₃-6'), 0.89 (1H, m), 0.54 (3H, s, CH₃-18); $^{13}\text{C-NMR}$ (CDCl_3 , δ):

149.1 (C-10), 147.7 (C-10), 142.6 (C-8), 133.2 (C-5), 124.7 (CH-6), 117.1 (CH-7), 111.6 (CH₂-19), 110.4 (C-1'=CH₂), 71.0 (C-25/C-4'), 70.8 (C-25/C-4'), 70.5 (CH-1), 66.6 (CH-3), 56.1 (CH-14), 52.8 (CH-17), 45.7 (C-13), 45.1 (CH₂), 44.5 (CH₂), 42.7 (CH₂), 41.8 (CH₂), 40.2 (CH₂), 39.5 (CH₂), 37.0 (CH-20), 30.8 (CH₂), 29.9 (CH₂), 29.4 (CH₃-26/CH₃-27/CH₃-5'/CH₃-6'), 29.2 (CH₃-26/CH₃-27/CH₃-5'/CH₃-6'), 29.3 (CH₃-26/CH₃-27/CH₃-6'/CH₃-7'), 29.1 (CH₂), 28.9 (CH₃-26/CH₃-27/CH₃-5'/CH₃-6'), 25.9 (CH₂), 23.5 (CH₂), 22.1 (CH₂), 18.73 (CH₂), 12.3 (CH₃-18); **MS (ESI) [m/z, (%)]**: 529.42 (M⁺+1, 100), 511.40 (29), 493.39 (25); **HRMS (ESI)**: 529.42514 calculated for C₃₄H₅₇O₄ ; found 529.42557.

