Supporting Information: Experimental Procedures

A Formal Chemoselective Synthesis of Leucascandrolide A

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General

All the reactions were carried out under an argon atmosphere in anhydrous solvent when no water was necessary. CH₂Cl₂ and toluene were distilled from CaH₂ and THF and Et₂O were distilled from Sodium/benzophenone. Flash chromatography was performed with Merck Geduran Si60 silica gel (40–63 μM). Infrared (IR) spectra were recorded on a Bruker TENSOR-27 (IRFT), wavenumbers are indicated in cm⁻¹. ¹H NMR spectra were recorded on

a Bruker AVANCE 400 at 400 MHz and data are reported as follows: chemical shift in ppm from tetramethylsilane with the residual solvent peak as an internal indicator (CDCl_3 δ : 7.26, C_6D_6 δ : 7.16 ppm) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances), integration. ^{13}C NMR spectra were recorded on a Bruker AVANCE 400 at 100 MHz and data are reported as follows: chemical shift in ppm from tetramethylsilane with the solvent as an internal indicator, multiplicity with proton (CDCl_3 δ : 77.0, C_6D_6 δ : 128.0, $\text{C}_5\text{D}_5\text{N}$ δ : 135.5 ppm). Mass spectra with electronic impact (MS-EI) were recorded from a Hewlett-Packard tandem 5890 A GC (12 m capillary column) – 5971 MS (70 eV). High resolution mass spectra (HRMS) were performed by the laboratoire de Structure et Fonction de Molecules Bioactives (Université Pierre et Marie Curie, Paris VI).

Aldehyde 2

To a solution of TBSCl (6.7 g, 42.2 mmol, 1 equiv) and imidazole (5.9 g, 87 mmol, 2 equiv) in dry DMF (30 mL) was added but-3-en-1-ol (4.29 mL, 50 mmol, 1.15 equiv) at rt. The resulting solution was stirred for 16 h and was quenched by addition of a saturated solution of NH_4Cl (60 mL). After stirring for 20 min, the reaction mixture was diluted with pentane (100 mL). The aqueous layer was extracted with Et_2O (40 mL) and the combined organic layers were washed with brine (2x40 mL), dried over MgSO_4 and filtered on a pad of silica gel (pentane/ Et_2O : 9/1). Evaporation of the solvent afforded TBS ether (7.09 g, 89%).

IR(neat), 3100–2800, 1642, 1472, 1096, 986, 909 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) 5.81 (ddt, $J=17.3, 10.3, 6.9$ Hz, 1H), 5.10–4.99 (m, 1H), 3.66 (t, $J=6.8$ Hz, 2H), 2.27 (app qt, $J=6.8, 1.3$ Hz, 2H), 0.89 (s, 9H, *t*Bu), 0.05 (s, 6H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) 135.4 (d), 116.3 (t), 62.8 (t), 37.5 (t), 25.9 (q), 18.3 (s), –5.3 (q) ppm; MS (EI), 145 ($\text{M}-\text{C}_3\text{H}_5^+$, 3), 129 ($\text{M}-t\text{-Bu}^+$, 75), 101 (100), 99 (35), 89 (18), 75 (20), 73 (28).

To a solution of the above olefin (7.09 g, 37.7 mmol, 1 equiv) in dry CH_2Cl_2 (80 mL) at –78 °C was bubbled O_3 until a persistent blue colour appeared. O_2 was then bubbled until the blue color vanished, then under N_2 bubbling, Et_3N (12.1 mL, 87 mmol, 2 equiv) was added and the solution was stirred at rt for 2 h. The reaction mixture was diluted with pentane (100 mL) and

was washed with aqueous 8% H₃PO₄ (2x40 mL). The aqueous layer was extracted with Et₂O (50 mL), and the combined organic layers were washed with a saturated aqueous Na₂CO₃ solution (2x40 mL) and then with brine (40 mL). The organic phase was dried over MgSO₄ and filtered on a plug of silica gel (pentane/Et₂O : 50/50). A careful concentration of the solution afforded the volatile colourless aldehyde **2** (6.01 g, 85%).

IR(neat) 3000-2800, 1727, 1472, 1389, 1253, 1094 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 9.77 (t, *J*=2.1 Hz, 1H, H₁₁), 3.96 (t, *J*=6.0 Hz, 2H, H₉), 2.57 (td, *J*=6.0, 2.1 Hz, 2H), 0.85 (s, 9H), 0.04 (s, 6H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 202.0 (s), 57.3 (t), 46.5 (t), 25.7 (q), 18.2 (s), -5.5 (q) ppm; MS (EI), 131 (M-*t*-Bu⁺, 89), 101 (100), 75 (42), 59 (20).

Alcohol **3**

To a suspension of (*R,R*)-Duthaler complex (17.00 g, 27.8 mmol, 1.4 equiv) in Et₂O (200 mL) at 0 °C was added a solution of 2-butenyl magnesium chloride (45.7 mL, 0.5 M in THF, 22.8 mmol, 1.15 equiv). After 2.5 h at 0 °C, the solution was cooled to -78 °C and a solution of aldehyde **2** (3.74 g, 19.9 mmol, 1.0 equiv) in dry Et₂O (30 mL) at -78 °C was added *via* canula. After 16 h at -78 °C, deionised water (50 mL) was added and the reaction mixture was stirred at rt for 3 days. Celite was added and the mixture was filtered on a pad of Celite (washing with Et₂O). The resulting solution was dried over MgSO₄, filtered, and concentrated. The residue was diluted with pentane, the white precipitate ((*R,R*)-TADDOL) was sonicated, filtered, and dried in vacuo (12.59 g, 97%). Pentane was evaporated and the residue was purified by silica gel chromatography (Petroleum Ether/Et₂O : 9/1) to afford the homoallylic alcohol **3** (4.20 g, 86%).

[α]_D²⁰ -9.7 (*c* 1.10, CHCl₃); IR(neat) 3383, 3000-2800, 1639, 1463, 1255, 1086, 1003 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 5.83 (m, 1H), 5.06 (m, 2H), 3.88 (dt, *J*=10.1, 5.0 Hz, 1H), 3.80 (m, 1H), 3.68 (dt, *J*=7.2, 5.0 Hz), 3.20 (br s, 1H, OH), 2.23 (sext_{app}, *J*=6.8 Hz, 1H), 1.70–1.56 (m, 2H), 1.03 (d, *J*=6.9 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 6H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 140.7 (d), 115.1 (t), 75.1 (d), 62.8 (t), 43.9 (d), 35.5 (t), 25.9 (q), 18.2 (s), 15.7 (q), -5.5 (q) ppm; MS (EI), 189 (M-CH₂=CHCHMe⁺, 37), 145 (11), 131 (46), 105 (52), 101 (35), 95 (100), 89 (38), 75 (93), 73 (41), 67 (23). HRMS (ESI) 267.1750 (calcd for C₁₃H₂₈O₂Si+Na⁺ 267.1751).

Acrylic ester **4**

To a solution of alcohol **3** (4.99 g, 20.4 mmol, 1 equiv) and Et_3N (5.67 mL, 40.8 mmol, 2 equiv) in Et_2O (70 mL) at $-18\text{ }^{\circ}C$ was added dropwise acryloyl chloride (2.25 mL, 26.5 mmol, 1.3 equiv). The mixture was allowed to stir for 2 h, and was quenched by addition of a saturated solution of $NaHCO_3$ and then stirred at rt for 15 min. The aqueous layer was extracted with Et_2O and the organic extracts were washed with aqueous 8% H_3PO_4 and brine, then dried over $MgSO_4$ and filtered on a pad of silica gel. After concentration, the acrylic ester **4** (5.62 g, 92%) was obtained.

$[\alpha]_D^{20} +21.0$ (c 0.98 $CHCl_3$); IR(neat) 3000-2800, 1724, 1638, 1462, 1404, 1255, 1190, 1094 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) 6.38 (dd, $J=17.3, 1.5$ Hz, 1H), 6.10 (dd, $J=17.3, 10.4$ Hz, 1H), 5.81 (dd, $J=10.4, 1.5$ Hz, 1H), 5.76 (m, 1H), 5.09-5.02 (m, 3H), 3.63 (ddd, $J=10.3, 6.7, 5.7$ Hz, 1H), 3.60 (dt $J=10.2, 7.5$ Hz, 1H), 2.23 (sext_{app}, $J=7.0$ Hz, 1H), 1.78 (m, 2H), 1.03 (d, $J=6.9$ Hz, 3H), 0.88 (s, 9H), 0.02 (2s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 165.8 (s), 139.3 (d), 130.3 (t), 128.8 (t), 115.6 (t), 74.2 (d), 59.7 (t), 41.6 (d), 34.3 (t), 25.9 (q), 18.2 (s), 15.6 (q), -5.5 (q) ppm; MS (EI), 243 ($M-CH_2=CH_2CO^+$, 12), 171 (10), 169 (15), 129 (96), 101 (18), 95 (100), 89 (13), 75 (31), 73 (17), 67 (15), 55 (34). HRMS (ESI) 321.1856 (calcd for $C_{16}H_{30}O_3Si+Na^+$ 321.1856).

Lactone **5**

To a solution of ester **4** (5.49 g, 18.4 mmol, 1 equiv) in CH_2Cl_2 at $40\text{ }^{\circ}C$ was added Grubbs catalyst 2nd generation Ru-I (475 mg, 0.55 mmol, 0.03 equiv). After refluxing for 48 h, the solution was allowed to cool to rt and Pd/C 5% (790 mg, 0.37 mmol, 0.02 equiv) was added. The solution was stirred under a gentle bubbling of H_2 for 8 h and was left overnight under H_2 atmosphere. The black suspension was filtered on Celite and was concentrated *in vacuo*. The

residue was purified by silica gel chromatography (Petroleum Ether/ Et₂O : 7/3) to afford the lactone **5** (3.50 g, 70%).

$[\alpha]_D^{20} +60.0$ (c 0.58, CHCl₃); IR(neat) 3000-2800, 1733, 1462, 1250, 1208, 1087, 1035, 1001, 833 cm⁻¹; MS (EI), 215 (M-*t*Bu⁺, 37), 197 (59), 185 (100), 171 (9), 129 (26), 123 (38), 95 (28), 75 (71); ¹H NMR (CDCl₃, 400 MHz) 4.10 (td, *J*=9.5, 2.4 Hz, 1H), 3.81 (ddd, *J*=10.2, 8.4, 5.0 Hz, 1H), 3.78 (ddd, *J*=10.2, 6.6, 4.5 Hz, 1H), 2.61 (ddd, *J*=17.7, 6.8, 4.8 Hz, 1H), 2.46 (ddd, *J*=17.7, 9.7, 7.0 Hz, 1H), 1.99-1.87 (m, 2H), 1.81-1.66 (m, 2H), 1.55 (m, 1H), 1.02 (d, *J*=6.6 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 171.7 (s), 82.7 (d), 58.6 (t), 36.7 (t), 32.5 (d), 29.5 (t), 27.8 (t), 25.9 (q), 18.2 (s), 17.5 (q), -5.4 (q) ppm; HRMS (ESI) 295.1700 (calcd for C₁₄H₂₈O₃Si+Na⁺ 295.1700).

Acetate **6**

To a solution of lactone **5** (11.96 mmol, 3.24 g, 1 equiv) in dry CH₂Cl₂ (75 mL) at -78 °C was added dropwise DIBAL-H (16.74 mL, 1.0 M in hexanes, 16.74 mmol, 1.4 equiv) and the solution was stirred for 1.5 h at -78 °C. Pyridine (4.74 g, 60 mmol, 5 equiv), DMAP (4.36 g, 36 mmol, 3 equiv), and finally Ac₂O (6.12 g, 60 mmol, 5 equiv) were then added. The reaction mixture was stirred for 30 min at -78 °C and then warmed to 0 °C. The reaction was quenched by addition of a saturated aqueous solution of potassium sodium tartrate. After 10 min, a saturated aqueous NaHCO₃ solution was added. After stirring for 20 min, the aqueous layer was extracted with Et₂O and the combined organic layers were washed with a saturated aqueous NaHCO₃ solution, with a saturated aqueous CuSO₄ solution, and finally with brine. The organic layer was dried over MgSO₄, filtered on a plug of silica gel (4 cm, Et₂O/Petroleum Ether : 50/50), and concentrated to afford the unstable acetate **6** (3.76 g, 98%) in a 12/1 ratio.

¹H NMR (C₆D₆, 400 MHz) 5.70 (dd, *J*=9.3, 3.0 Hz, 1H), 3.90 (ddd, *J*=9.8, 8.4, 5.7 Hz, 1H), 3.80 (ddd, *J*=9.8, 6.7, 4.3 Hz, 1H), 3.21 (td, *J*=9.5, 2.3 Hz, 1H), 1.90 (dddd, *J*=13.9, 8.4, 6.8, 2.3 Hz, 1H), 1.65 (s, 3H, Ac), 1.60 (m, 1H), 1.54 (m, 1H), 1.48 (tdd, *J*=12.5, 9.5, 4.2 Hz, 1H), 1.40 (m, 1H), 1.15 (m, 1H), 0.88 (dddd, 13.4, 12.5, 11.9, 5.2 Hz, 1H), 1.00 (s, 9H, *t*-Bu), 0.58 (d, *J*=6.6 Hz, 3H), 0.13 (s, 3H) 0.09 (s, 3H) ppm; ¹³C NMR (C₆D₆, 100 MHz) 168.6 (s), 94.8 (d), 79.2 (t), 59.6 (d), 36.7 (t), 34.4 (t), 31.4 (t), 30.8 (t), 26.2 (q), 20.73 (q), 18.5 (s), 17.1 (q), -5.2 (q) ppm.

Silyl Enol Ether 7

To a solution of 4-methyl-pentyne (5.88 mL, 50 mmol, 1 equiv) in Et₂O (150 mL) at –78 °C, was added dropwise *n*-BuLi (24.4 mL, 2.15 M in hexanes, 52.5 mmol, 1.05 equiv) and the solution was stirred at –78 °C for 1.5 h. Then a freshly prepared solution of ZnBr₂ (60 mL, 1.2 M in Et₂O, 1.45 equiv, 72 mmol) was added and the reaction mixture was stirred to 0 °C for 30 min. The solution was transferred *via canula* to a solution of AcCl (7.85 g, 2 equiv, 100 mmol) in Et₂O (60 mL) at –78 °C and the solution was allowed to stir at rt for 1h. The ethereal solution was carefully concentrated under vacuum and diluted with a mixture of pentane /Et₂O (8/2 , 30 mL). This solution was filtered on a short silica gel column containing a Celite layer upside (Pentane/Et₂O : 8/2). After careful evaporation of the solvent, the methyl propargylic ketone (4.71 g, 76%) was obtained.

IR(neat) 3000-2800, 2207, 1675, 1358, 1226, 1196 cm⁻¹, MS (EI), 124 (M^{•+}, 3), 109 (M–Me⁺, 100), 82 (81), 79 (9), 67(22); ¹H NMR (CDCl₃, 400 MHz) 2.30 (s, 3H), 2.23 (d, *J*=6.7 Hz, 2H), 1.88 (m, *J*=6.7 Hz, 1H), 0.98 (d, *J*=6.7 Hz, 6H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 184.8 (s), 93.1 (s), 82.2 (s), 32.7 (q), 27.9 (t), 27.5 (d), 21.9 (q) ppm;

To a solution of the above methyl propargylic ketone (3.54 g, 28.5 mmol, 1 equiv) in THF (100 mL) at –78 °C was added LiHMDS (7.55 g, 45.2 mmol, 1.6 equiv) in THF (20 mL). After 20 min, TMSCl (4.13 mL, 34.2 mmol, 1.2 equiv) was added dropwise and the solution was stirred for 30 min at 0 °C. The solution was concentrated under vacuum until the precipitation of the salts and was diluted with pentane (150 mL). The resulting suspension was filtered on Celite (washing with pentane) and was concentrated under vacuum. Distillation of the residue (43-50°C, 0.5 mbar) afforded the TMS enol ether **7** (4.81 g, 86%).

IR(neat) 3000-2800, 1605, 1286, 1251, 911, 839, 760, 674 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 4.76 (d, *J*=0.4 Hz, 1H), 4.75 (d, *J*=0.4 Hz, 1H), 1.93 (d, *J*=6.5 Hz, 2H), 1.61 (m, *J*=6.7 Hz, 1H), 0.82 (d, *J*=6.7 Hz, 6H), 0.24 (s, 9H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 140.3 (s), 101.4 (t), 87.9 (s), 80.0 (s), 28.3 (t), 28.1 (d), 22.0 (q), 0.3 (q) ppm; MS (EI), 196 (M^{•+}, 29), 181 (M–Me⁺, 27), 153 (M–*i*Pr⁺, 58), 154 (79), 139 (M–CH₂*i*Pr⁺, 100), 75(63), 73 (36).

***trans*-Tetrahydropyran 8**

To a solution of the freshly prepared silyl enol ether **7** (4.66 g, 23.8 mmol, 2 equiv) and freshly prepared acetate **6** (3.76 g, 11.9 mmol, 1.0 equiv) in CH_2Cl_2 (160 mL) at $-78\text{ }^\circ C$ was added a solution of $ZnCl_2$ (26.2 mL, 1.0 M in Et_2O , 26.18 mmol, 2.2 equiv). The reaction mixture was allowed to warm to rt and was quenched by addition of a saturated solution of $NaHCO_3$, and was diluted with Et_2O . The aqueous layer was extracted with Et_2O and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica gel chromatography (Petroleum Ether/ Et_2O : 95/5 to 90/10) to afford the *trans*-tetrahydropyran **8** (4.03 g, 89%)-(*Trans/Cis* THP : 13/1 by GC).

$[\alpha]_D^{20} +44.9$ (c 0.92, $CHCl_3$); IR(neat) 3000-2800, 2210, 1673, 1462, 1251, 1165, 1083 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) 4.60 (dddd, $J=7.7, 6.4, 5.0, 4.6$ Hz, 1H), 3.70 (ddd, $J=10.0, 7.5, 5.1$ Hz, 1H), 3.61 (m, 1H), 3.36 (ddd, $J=8.7, 7.3, 3.7$ Hz, 1H), 2.90 (dd, $J=15.1, 7.7$ Hz), 2.66 (dd, $J=15.1, 6.4$ Hz, 1H), 2.26 (d, $J=6.6$ Hz, 2H), 1.90 (m, $J=6.7$ Hz, 1H), 1.82-1.64 (m, 4H), 1.54-1.28 (m, 3H), 1.01 (d, $J=6.7$ Hz, 6H), 0.93 (d, $J=6.7$, 3H), 0.88 (s, 9H), 0.04 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 185.8 (s), 93.6 (s), 81.8 (s), 73.8 (d), 67.7 (d), 60.1 (t), 48.6 (t), 35.8 (t), 33.6 (d), 28.0 (t), 27.6 (d), 27.5 (t), 26.6 (t), 26.0 (q), 22.0 (q), 18.3 (s), 18.2 (q), -5.3 (2q) ppm; MS (EI), 323 ($M-tBu^+$, 27), 293 (58), 199 (100), 175 (10), 143 (37), 139 (14), 131 (19), 109 (41), 107 (34), 99 (25), 81 ($M-C_7H_9O$, 15), 75 (48). HRMS (ESI) 403.2640 (calcd for $C_{22}H_{40}O_3Si+Na^+$ 403.2639).

Propargylic alcohol **9**

To a solution of the propargylic ketone **8** (732 mg, 1.93 mmol, 1 equiv) in a mixture of CH_2Cl_2 (4 mL) and H_2O (4 mL), were added $HCOONa$ (1.31 g, 19.3 mmol, 10 equiv), $n-Bu_4Cl$ (96 mg, 0.579 mmol, 0.3 equiv) and Noyori's catalyst $Ru(R,R)\text{-II}$ (12.3 mg, 0.0193 mmol, 0.01 equiv). The solution was stirred for 24 h at rt and two new portions of catalyst (2x0.01 equiv) were added after 24 h and after 48 h of stirring. After 72 h, the aqueous layer was extracted with Et_2O , and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel chromatography (AcOEt/Petroleum ether: 8/92) to afford the propargylic alcohol **9** (558 mg, 76%).

$[\alpha]_D^{20} +134.7$ (c 1.15, $CHCl_3$); IR(neat) 3431, 3000-2800, 1462, 1253, 1141, 1089, 1054, 835, 775 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) 4.56 (m, 1H), 4.23 (m, 1H), 3.78-3.66 (m, 2H), 3.55 (m, 1H), 3.27 (d, $J=7.0$, 1H, OH), 2.12 (m, 1H), 2.09 (dd, $J=6.6$, 2.0 Hz, 2H), 1.92-1.66 (m, 4H), 1.64-1.43 (m, 4H), 1.37 (m, 1H), 0.99 (d, $J=6.5$ Hz, 3H), 0.98 (d, $J=7.0$, 6H), 0.89 (s, 9H), 0.05 (2s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 84.2 (s), 82.0 (s), 73.9 (d), 68.3 (d), 60.7 (d), 59.8 (t), 40.1 (t), 35.3 (t), 32.8 (d), 28.0 (d), 27.9 (t), 27.6 (t), 26.0 (t), 25.9 (q), 22.0 (q), 18.3 (s), 18.2 (q), -5.3 (q), -5.4 (q) ppm; MS (EI), 364 ($M-18^+$, 0.1), 325 ($M-tBu^+$, 1), 217 (26), 199 (38), 143(31), 125 (32), 107 (49), 105 (36), 101 (30), 99 (100), 95 (39), 81 (33), 75(75), 55 (23). HRMS (ESI) 405.2795 (calcd for $C_{22}H_{42}O_3Si+Na^+$ 405.2795).

Compound 10

To a solution of propargyl alcohol **9** (522 mg, 1.367 mmol, 1 equiv) in THF (15 mL) was added dropwise a Red-Al[®] solution (3.3 mL, 70% in toluene, 10.9 mmol, 8 equiv). After 18 h at 30 °C, the reaction mixture was quenched at 0 °C by a dropwise addition of a saturated solution of potassium sodium tartrate and the reaction mixture was stirred 30 min at rt. The aqueous layer was extracted with AcOEt (4x40 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum.

To a solution of the above residue in CH₂Cl₂ (25 mL) was added 2,6-lutidine (650 μL, 5.47 mmol, 4 equiv). The solution was cooled to -18 °C and TBSOTf (941 μL, 4.10 mmol, 3 equiv) was added dropwise. The solution was stirred for 2 h at 0 °C and the reaction was quenched with a saturated aqueous solution of NaHCO₃. The organic layer was extracted with Et₂O and the combined organic extracts were washed with H₃PO₄ 8% and brine, dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified by silica gel chromatography to afford the allylic TBS ether **10** (624 mg, 92%).

IR(neat) 3000-2800, 1463, 1254, 1089, 1053, 971, 938, 833, 774 cm⁻¹, $[\alpha]_D^{20} +36.6$ (c 1.02, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) 5.52 (dt, *J*=15.1, 7.0 Hz, 1H), 5.41 (dd, *J*=15.1, 6.5 Hz, 1H), 4.16 (ddd, *J*=9.5, 6.5, 3.0 Hz, 1H), 4.01 (m, 1H), 3.78 (ddd, *J*=9.8, 7.8, 4.8 Hz, 1H), 3.69 (dt, *J*=9.8, 7.3 Hz, 1H), 3.29 (td, *J*=9.0, 3.0 Hz, 1H), 1.98-1.86 (m, 3H), 1.86-1.72 (m, 2H), 1.68-1.56 (m, 3H), 1.46-1.24 (m, 4H), 0.86-0.91 (m, 9H), 0.90 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 6H), 0.03 (s, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 135.4 (d), 128.5 (d), 72.3 (d), 70.4 (d), 68.1 (d), 60.5 (t), 41.6 (t), 40.1 (t), 36.6 (t), 34.8 (d), 29.0 (t), 28.4 (d), 27.4 (t), 26.0 (q), 25.9 (q), 22.4 (q), 22.3 (q), 18.3 (q), 18.3 (s), 18.2 (s), -4.0 (q), -4.7 (q), -5.2 (2q) ppm; MS (EI), 441 (M-*t*Bu⁺, 11), 331 (12), 309 (15), 239 (24), 227 (95), 217 (24), 199 (21), 187 (27), 171 (45), 131 (29), 107 (35), 99 (39), 89 (31), 75 (100), 73 (65). HRMS (ESI) 521.3812 (calcd for C₂₈H₅₈O₃Si₂+Na⁺ 521.3817).

Primary alcohol **11**

To a solution of compound **10** (3.04 g, 6.09 mmol, 1 equiv) in MeOH (183 mL), was added NH_4F (4.50 g, 122 mmol, 20 equiv) and the reaction was stirred for 4 h at 60 °C. The reaction was quenched by addition of an aqueous solution saturated $NaHCO_3$ (50 mL) and brine (50 mL), and diluted with Et_2O (150 mL). The aqueous layer was extracted with Et_2O (4x50mL), dried over $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography (Petroleum Ether/ $AcOEt$: 92/8 to 50/50) to afford the unreacted starting material (103 mg, 4%), the mono-protected alcohol **11** (1.88 g, 80%), and the diol **11'** (211 mg, 13%).

$[\alpha]_D^{20} +34.3$ (c 0.81, $CHCl_3$); IR(neat) 3442, 3000-2800, 1461, 1250, 1070, 1006, 970, 938, 833, 774 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) 5.53 (dt, $J=15.3$, 7.0 Hz, 1H, H_{19}), 5.41 (ddt, $J=15.1$, 6.5, 1.3 Hz, 1H, H_{18}), 4.19-4.08 (m, 2H), 3.79 (ddd, $J=10.8$, 6.5, 3.7 Hz, 1H), 3.75 (ddd, $J=10.8$, 7.5, 3.5 Hz, 1H), 3.40 (td, $J=9.0$, 3.0 Hz, 1H), 1.99 (ddd, $J=14.3$, 9.5, 3.3 Hz, 1H), 1.94-1.80 (m, 4H), 1.54-1.72 (m, 3H), 1.51- 1.37 (m, 3H), 1.36-1.20 (m, 2H), 0.89 (d, $J=6.7$ Hz, 3H), 0.88 (d, $J=6.5$ Hz, 3H), 0.87 (s, 9H), 0.84 (d, $J=6.8$ Hz, 3H), 0.07 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 135.1 (d), 129.1 (d), 76.2 (d), 70.8 (d), 69.0 (d), 61.6 (t), 41.5 (t), 39.4 (t), 35.2 (d), 34.8 (t), 29.1 (t), 28.4 (d), 27.3 (t), 25.9 (q), 22.4 (q), 22.3 (q), 18.2 (s), 18.1 (q), -3.9 (q), -4.9 (q) ppm; MS (EI), 327 ($M-tBu^+$, 0.4), 227 (4), 217 (3), 199 (3), 187 (2), 171 (2), 143 (2), 131 (6), 125 (5), 99 (10), 75 (100). HRMS (ESI) 405.2952 (calcd for $C_{22}H_{44}O_3Si+Na^+$ 407.2952).

Homoallylic alcohol **12**

To a solution of the primary alcohol **11** (2.12 g, 5.52 mmol, 1 equiv) in CH_2Cl_2 (110 mL) was added dropwise the Dess-Martin Periodinane reagent (24.0 mL, 15 wt% in CH_2Cl_2 , 11.04 mmol, 2 equiv) at 0 °C. The solution was stirred for 2 h at rt, and the reaction was quenched by the addition of a saturated aqueous solution of K_2CO_3 (20 mL), an aqueous solution of 10% $Na_2S_2O_3$ (20 mL) and water (20 mL). The reaction mixture was stirred for 30 min, and then diluted with pentane (100 mL). The aqueous layer was extracted with Et_2O (2x50 mL), and the combined organic extracts were washed with a saturated solution of $NaHCO_3$ (20 mL) and brine (30 mL). The organic solution was dried over $MgSO_4$, filtered over a small pad of silica gel (3 cm, washing Et_2O), and concentrated under vacuum to obtain the crude aldehyde, which was used in the next step without further purification.

To a suspension of (*R,R*)-Duthaler complex (4.73 g, 7.73 mmol, 1.4 equiv) in Et_2O (60 mL) at 0 °C was added a solution of allyl magnesium chloride (3.3 mL, 0.5 M in THF, 6.62 mmol, 1.2 equiv). After 2.5 h at 0 °C, the solution was cooled to -78 °C and a solution of the above crude aldehyde in dry Et_2O (10 mL) was added *via* syringe. After 16 h at -78 °C, deionised water (20 mL) was added and the reaction mixture was stirred at rt for 3 days. Celite was added and the mixture was filtered on Celite (washing with Et_2O). The resulting solution was dried over $MgSO_4$, filtered, and concentrated. The residue was diluted with pentane, the white precipitate ((*R,R*)-TADDOL) was sonicated, filtered, and dried in vacuo (2.5 g). Pentane was evaporated and the residue was purified by silica gel chromatography (Petroleum Ether/ Et_2O : 95/5 to 7/3) to afford the homoallylic alcohol **12** (1.87 g 80%) and (*R,R*)-TADDOL (0.95 g, 95% in total).

$[\alpha]_D^{20} +31.4$ (*c* 0.51, $CHCl_3$); IR(neat) 3446, 3000-2800, 1641, 1462, 1383, 1251, 1141, 1070, 1053, 972, 912, 835, 776 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) 5.83 (ddt, *J*=17.1, 10.3, 7.1 Hz, 1H), 5.53 (dt, *J*=15.3, 7.0 Hz, 1H), 5.41 (ddt, *J*=15.1, 7.0, 1.2 Hz, 1H), 5.13-5.06 (m, 2H),

4.19 (ddd, $J=9.5, 7.0, 3.1$ Hz, 1H), 4.12 (m, 1H), 3.97 (m, 1H), 3.49 (dt, $J=9.4, 5.3$ Hz, 1H), 3.16 (d, $J=3.5$ Hz, 1H, OH), 2.29 (dtt, $J=13.9, 7.0, 1.3$ Hz, 1H), 2.22 (m, 1H), 2.00 (ddd, $J=14.2, 9.8, 3.3$ Hz, 1H), 1.92-1.81 (m, 3H), 1.67 (dd, $J=5.8, 5.1$, 2H), 1.66-1.56 (m, 2H), 1.55-1.42 (m, 2H), 1.38 (ddd, $J=14.2, 9.5, 4.0$ Hz, 1H), 1.35-1.20 (m, 1H), 0.89 (d, $J=6.6$ Hz, 3H), 0.88 (d, $J=6.6$ Hz, 3H), 0.87 (s, 9H), 0.82 (d, $J=6.5$ Hz, 3H), 0.06 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) 135.2 (d), 135.1 (d), 128.9 (d), 117.3 (t), 73.2 (d), 70.7 (d), 69.0 (d), 67.8 (t), 42.1 (t), 41.5 (t), 39.1 (t), 38.1 (t), 34.5 (d), 29.2 (t), 28.3 (d), 27.5 (t), 25.9 (q), 22.4 (q), 22.3 (q), 18.2 (s), 18.1 (q), -4.0 (q), -4.8 (q) ppm; MS (EI), 367 ($\text{M}-t\text{Bu}^+$, 3), 257 (36), 239 (12), 227 (33), 187 (18), 165 (20), 145 (42), 131 (35), 99 (39), 95 (58), 75 (100). HRMS (ESI) 447.3265 (calcd for $\text{C}_{25}\text{H}_{48}\text{O}_3\text{Si}+\text{Na}^+$ 447.3263).

Methyl Ether 13

To a solution of the homoallylic alcohol **12** (1.80 g, 4.37 mmol, 1 equiv) in Et_2O (8 mL) was added MeI (12.4 g, 87.40 mmol, 20 equiv), Drierite[®] (2 g), and freshly prepared Ag_2O (3.04 g, 13.11 mmol, 3 equiv). After 20 h of vigorous stirring at 20 °C, the brown reaction mixture was filtered on a pad of Celite, concentrated, and the residue was purified by silica gel chromatography (Petroleum Ether/ Et_2O : 96/4) to afford the methyl ether **13** (1.79 g, 96%).

$[\alpha]_D^{20} +48.0$ (c 0.55, CHCl_3); IR(neat) 3000-2800, 1642, 1462, 1252, 1096, 1074, 971, 911, 835, 776 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) 5.80 (ddt, $J=17.2, 10.1, 7.1$ Hz, 1H), 5.54 (dt, $J=15.3, 7.1$ Hz, 1H), 5.42 (ddt, $J=15.3, 6.7, 1.2$ Hz, 1H), 5.03-5.12 (m, 2H), 4.20 (ddd, $J=9.2, 6.9, 3.0$ Hz, 1H), 4.05 (m, 1H), 3.57 (m, 1H), 3.38 (m, 1H), 3.38 (s, 3H), 2.29 (m, 2H), 1.99 (ddd, $J=14.1, 9.5, 3.3$ Hz, 1H), 1.91 (m, 2H), 1.80 (m, 1H), 1.70 (ddd, $J=14.4, 10.1, 2.1$ Hz, 1H), 1.66-1.53 (m, 2H), 1.48-1.25 (m, 5H), 0.89 (s, 9H), 0.88 (d, $J=6.6$ Hz, 3H), 0.87 (d, $J=6.6$ Hz, 3H), 0.86 (d, $J=6.1$ Hz, 3H), 0.08 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) 135.3 (d), 134.5 (d), 128.5 (d), 117.2 (t), 76.4 (d), 71.4 (d), 70.4 (d), 68.4 (d), 56.5 (q), 41.5 (t), 40.0 (t), 38.5 (t), 37.8 (t), 35.4 (d), 29.2 (t), 28.3 (d), 27.5 (t), 25.9 (q), 22.4 (q), 22.2 (q), 18.3 (q), 18.2 (s), -3.9 (q), -4.6 (q) ppm; MS (EI), 438 (M^+ , 0.1), 381 ($\text{M}-t\text{Bu}^+$, 7), 349

(9), 257 (9), 239 (10), 230 (11), 229 (60), 227 (75), 187 (50), 171 (31), 147 (37), 131 (40), 95 (40), 85 (100), 75 (73), 73 (44). HRMS (ESI) 461.3419 (calcd for $C_{26}H_{50}O_3Si+Na^+$ 461.3421).

Diol 14

To a solution of olefin **13** (1.78 g, 4.06 mmol, 1 equiv) and *N*-methyl morpholine-*N*-oxide (4.26 mmol, 435 mg, 1.05 equiv) in a mixture of *t*-BuOH (40 mL) and H₂O (20 mL) at 0 °C was added a solution of OsO₄ (2.57 mL, 2.5 wt % in *t*-BuOH, 0.203 mmol, 0.05 equiv) and the solution was stirred at 0 °C for 18 h. After 30 min at rt, the reaction mixture was quenched by addition of Na₂S₂O₃ and the solution was stirred for 30 min. The solution was diluted with EtOAc and the aqueous layer was extracted with EtOAc. The organic layer was finally washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (Petroleum Ether/ EtOAc : 50/50) to afford diol **14** (1.169 g, 61%) in a 1:1 ratio of diastereoisomers, and the unreacted starting material **13** (561 mg, 32%).

IR(neat) 3398, 3000-2800, 1461, 1380, 1251, 1075, 971, 938, 835, 776 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 5.52 (dt, *J*=15.3, 6.9 Hz, 1H), 5.42 (dd, *J*=15.3, 6.8, Hz 1H), 4.18 (m, 1H), 4.03 (m, 1.5H), 3.89 (m, 0.5H), 3.78 (m, 0.5H), 3.71 (m, 0.5H), 3.61 (m, 1H), 3.46 (m, 1H), 3.41 (s, 1.5H), 3.38 (s, 1.5H), 3.42-3.30 (m, 1H), 2.32 (m, 0.5H), 2.08-1.16 (m, 15.5H), 0.92-0.84 (m, 18H), 0.06 (s, 1.5H), 0.07 (s, 1.5H), 0.03 (s, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 135.1 (2d), 129.0 (d), 128.9 (d), 77.5 (d), 76.6 (d), 72.6 (d), 72.2 (d), 70.8 (d), 70.7 (d), 70.6 (d), 69.5 (d), 68.8 (d), 68.7 (d), 67.0 (2t), 57.1 (q), 56.2 (q), 41.5 (2t), 40.1 (t), 40.0 (t), 38.6 (t), 38.3 (t), 37.4 (d), 35.5 (d), 35.4 (d), 35.0 (d), 29.1 (t), 29.0 (t), 28.4 (2d), 27.3 (2t), 25.9 (2q), 22.4 (2q), 22.3 (2q), 18.3 (2s), 18.2 (2q), -3.9 (2q), -4.6 (2q) ppm; HRMS (ESI) 495.34727 (calcd for $C_{26}H_{52}O_5Si+Na^+$ 495.34762).

Homoallylic alcohol **15**

To a solution of diol **14** (1.15 g, 2.44 mmol, 1 equiv) and *n*-Bu₄NCl (121 mg, 0.732 mmol, 0.3 equiv) in THF (20 mL), was added a saturated aqueous solution of NaIO₄ (20 mL, 0.6 M in H₂O, 12.2 mmol, 5 equiv) and the reaction mixture was stirred for 30 min at rt. Celite was added and the reaction mixture was filtered on a pad of celite washing with Et₂O. The ethereal solution was dried over MgSO₄, filtered on a pad of silica gel eluting with Et₂O and concentrated. The crude aldehyde was used in the next step without further purification.

To a suspension of (*R,R*)-Duthaler complex (3.9 mmol, 2.39 g, 1.6 equiv) in Et₂O (28 mL) at 0 °C was added a solution of allyl magnesium chloride (1.71 mL, 2.0 M in THF, 3.42 mmol, 1.4 equiv). After 2.5 h at 0 °C, the solution was cooled to -78 °C and a solution of the above crude aldehyde in dry Et₂O (10 mL) was added *via* syringe. After 16 h at -78 °C, deionised water (15 mL) was added and the reaction mixture was stirred at rt for 3 days. Celite was added and the mixture was filtered on Celite (washing with Et₂O). The resulting solution was dried over MgSO₄, filtered, and concentrated. The residue was diluted with pentane, the white precipitate ((*R,R*)-TADDOL) was sonicated and filtered. Pentane was evaporated and the residue was purified by silica gel chromatography (Toluene/Et₂O : 95/5 to 90/10) to afford the homoallylic alcohol **15** (918 mg, 78%).

$[\alpha]_D^{20}$ +26.4 (*c* 0.69, CHCl₃); ; IR(neat) 3436, 3000-2800, 1641, 1462, 1382, 1252, 1073, 1073, 970, 911, 834, 775 cm⁻¹, ¹H NMR (CDCl₃, 400 MHz) 5.83 (ddt, *J*=17.3, 10.2, 7.1 Hz, 1H), 5.52 (dt, *J*=15.3, 7.1 Hz, 1H), 5.40 (ddt, *J*=15.3, 6.9, 1.2 Hz, 1H), 5.14-5.06 (m, 2H), 4.19 (ddd, *J*=9.0, 7.0, 3.5 Hz, 1H), 4.03 (m, 1H), 3.83 (dtd, *J*=9.3, 6.1, 2.5 Hz, 1H), 3.70 (m, 1H), 3.34 (m, 1H), 3.37 (s, 3H), 3.20 (br s, 1H, OH), 2.23 (m, 2H), 1.97-1.74 (m, 5H), 1.69 (ddd, *J*=14.4, 9.4, 7.7 Hz, 1H), 1.66-1.54 (m, 3H), 1.53-1.40 (m, 3H), 1.38-1.25 (m, 2H), 0.99-0.86 (m, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 135.1 (d), 134.9 (d), 128.9 (d), 117.4 (t), 77.8 (d), 72.4 (d), 70.7 (d), 69.8 (d), 68.7 (d), 56.1 (q), 42.3 (t), 41.5 (t), 40.8 (t), 40.0 (t), 38.8 (t), 35.4 (d), 29.0 (t), 28.4 (d), 27.3 (t), 25.9 (q), 22.4 (q), 22.2 (q), 18.3 (s), 18.2 (q), -3.9 (q), -4.6 (q) ppm. MS (EI), 283 (5), 227 (7), 209

(4), 199 (3), 187 (4), 171 (4), 145 (7), 131 (7), 95 (9), 75 (100). HRMS (ESI) 505.3679 (calcd for $C_{28}H_{54}O_4Si+Na^+$ 505.3684).

Triol 16

To a solution of olefin **15** (857 mg, 1.77 mmol, 1 equiv) and *N*-methyl morpholine *N*-oxide (198.6 mg, 1.95 mmol, 1.1 equiv) in a mixture of *t*-BuOH (20 mL) and H₂O (10 mL) at 0 °C was added a solution of OsO₄ (900 μL, 2.5 wt% in *t*-BuOH, 0.071 mmol, 0.04 equiv) and the solution was stirred at 0 °C for 18 h. After 30 min at rt, the reaction mixture was quenched by addition of Na₂S₂O₃ and the solution was stirred for 30 min. The solution was diluted with EtOAc and the aqueous layer was extracted with. The organic layer was washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (Petroleum Ether/ EtOAc : 20/80 to 0/100) to afford the diol **16** (603 mg, 66%) in a 1:1 ratio of diastereoisomers and the unreacted starting material (149 mg, 17%).

¹H NMR (CDCl₃, 400 MHz) 5.51 (dt, *J*=15.2, 6.8 Hz, 1H), 5.40 (dd, *J*=15.2, 7.0 Hz, 1H), 4.24-3.94 (m, 4H), 3.73-3.60 (m, 2.5H), 3.60-3.46 (m, 1.5H), 3.38 (s, 1.5H), 3.37 (s, 1.5H), 3.31 (m, 1H), 1.96-1.28 (m, 18H), 0.91-0.85 (m, 9H), 0.88 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) 135.0 (d), 129.1 (d), 129.1 (d), 78.9 (d), 78.6 (d), 77.2 (d), 77.4 (d), 73.0 (d), 72.9 (d), 70.9 (d), 70.8 (d), 69.0 (d), 68.9 (d), 68.9 (3d), 66.7 (t), 56.2 (q), 56.1 (q), 41.5 (t), 40.0 (3t), 38.5 (t), 38.3 (t), 35.5 (2d), 29.0 (2t), 28.3 (d), 27.2 (2t), 25.9 (q), 22.4 (q), 22.3 (q), 18.3 (2s), 18.2 (q), -3.9 (2q), -4.6 (2q) ppm; IR(neat) 3368, 3000-2800, 1461, 1381, 1251, 1075, 971, 836, 776 cm⁻¹. HRMS (ESI) 539.3733 (calcd for $C_{28}H_{56}O_6Si+Na^+$ 447.3738).

Homoallylic alcohol **17**

To a solution of **16** (595 mg, 1.153 mmol, 1 equiv) and *n*-Bu₄NCl (57 mg, 0.346 mmol, 0.3 equiv) in a mixture of THF (20 mL) and H₂O (10 mL) was added a solution of NaIO₄ (10 mL, 0.6 M in H₂O, 5.77 mmol, 5 equiv) and the reaction mixture was stirred for 30 min at rt. Celite was added and the reaction mixture was filtered on a pad of Celite eluting with Et₂O. The ethereal solution was dried over Na₂SO₄, filtered on a pad of silica gel eluting with Et₂O and concentrated. The crude aldehyde was used in the next step without further purification. To solution of allylTMS (4 mmol, 634 μ L) in CH₂Cl₂ (10 mL) was added SnCl₄ (4 mmol, 460 μ L) and the solution was stirred 18 h at rt to make a solution of allylSnCl₃ (0.36 M).

To a solution of the above crude aldehyde in CH₂Cl₂ (3 mL) at -78°C was added allylSnCl₃ (4.75 mL, 0.36 M in CH₂Cl₂, 1.73 mmol, 1 equiv) and the solution was stirred for 1 h at -78°C . The reaction mixture was quenched by the addition of MeOH (0.5 mL), and stirred 30 min at -78°C . A saturated aqueous solution of NH₄Cl was then added (3 mL) with apparition of a white precipitate. After warming at rt, the white mixture was filtered on Celite and the aqueous layer was extracted with Et₂O, dried over Na₂SO₄ and concentrated. The residue was purified on a silica gel chromatography (Petroleum ether/AcOEt : 75/25) to afford the diol **17** (448 mg, 74%).

$[\alpha]_D^{20} +25.8$ (*c* 0.87, CHCl₃); IR(neat) 3400, 3000-2800, 1642, 1461, 1407, 1382, 1251, 1075, 971, 913, 835, 776 cm^{-1} ; ¹H NMR (CDCl₃, 400 MHz) 5.83 (ddt, *J*=17.1, 10.3, 7.1 Hz, 1H), 5.51 (dt, *J*=15.3, 7.1Hz, 1H), 5.40 (dd, *J*=15.3, 6.9 Hz, 1H), 5.13-5.05 (m, 2H), 4.19 (ddd, *J*=9.0, 7.4, 3.5 Hz, 1H), 4.07-3.99 (m, 2H), 3.92 (m, 1H), 3.66 (m, 1H), 3.35 (s, 3H), 3.28-3.37 (m, 1H), 2.30-2.15 (m, 2H), 1.96-1.70 (m, 6H), 1.40-1.67 (m, 8H), 1.39-1.25 (m, 2H), 0.87 (s, 9H), 0.90-0.85 (m, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 135.1 (d), 134.9 (d), 129.0 (d), 117.4 (t), 78.1 (d), 72.8 (d), 71.8 (d), 71.6 (d), 70.8 (d), 68.9 (d), 56.1 (q), 42.8 (t), 42.2 (t), 42.1 (d), 41.5 (t), 39.9 (t), 38.4 (t), 35.5 (d), 29.0 (t), 28.3 (d), 27.2

(t), 25.9 (q), 22.4 (q), 22.2 (q), 18.3 (q), 18.1 (s), -3.9 (q), -4.6 (q); HRMS (ESI) 549.3938 (calcd for $C_{30}H_{58}O_5Si+Na^+$ 549.3946).

Unsaturated ester **18**

To a solution of olefin **17** (0.195 mmol, 102.5 mg, 1 equiv) and methyl acrylate (1.95 mmol, 168 mg, 10 equiv) in CH_2Cl_2 (1 mL) was added Grubbs-Hoveyda catalyst Ru-**III** (18.3 mg, 29.5 μ mol, 0.15 equiv). After stirring for 18 h, the reaction mixture was concentrated in vacuo and the residue was purified by silica gel chromatography (Petroleum ether/AcOEt : 70/30) to afford the unsaturated ester **18** (96.0 mg, 84%).

$[\alpha]_D^{20} +16.2$ (c 1.04, $CHCl_3$); 1H NMR ($CDCl_3$, 400 MHz) 7.00 (dt, $J=15.7, 7.4$ Hz, 1H), 5.89 (d, $J=15.7$ Hz, 1H), 5.50 (dt, $J=15.2, 7.0$ Hz, 1H), 5.40 (dd, $J=15.2, 7.0$ Hz, 1H), 4.30-4.13 (m, 2H), 4.08-3.98 (m, 3H), 3.72 (s, 3H), 3.67 (m, 1H), 3.35 (s, 3H), 3.27 (m, 1H), 2.45-2.28 (m, 2H, H_4), 1.96-1.68 (m, 6H), 1.66-1.40 (m, 8H), 1.35-1.20 (m, 2H), 0.90-0.83 (m, 9H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 166.8 (s), 145.6 (t), 135.0 (d), 129.0 (d), 123.1 (d), 78.3 (d), 72.9 (d), 71.9 (d), 71.0 (d), 70.8 (d), 68.9 (d), 56.0 (q), 51.4 (q), 42.9 (t), 42.1 (d), 41.5 (t), 40.4 (t), 39.9 (t), 38.2 (t), 35.5 (d), 29.0 (t), 28.3 (d), 27.2 (t), 25.9 (q), 22.4 (q), 22.2 (q), 18.3 (q), 18.1 (s), -3.9 (q), -4.7 (q); IR(neat) 3433, 3000-2800, 1726, 1658, 1461, 1436, 1365, 1251, 1075, 972, 938, 835, 776 cm^{-1} . HRMS (ESI) 607.3993 (calcd for $C_{32}H_{60}O_7Si+Na^+$ 607.4001).

Cis tetrahydropyran 20

To a solution of the unsaturated ester **18** (46.9 mg, 80 μ mol, 1 equiv) in THF (10 mL) at 0 °C was added *t*-BuOK (80 μ mol, 1 mg, 0.1 equiv), and the solution was stirred for 1 h. A second portion of *t*-BuOK (0.1 equiv) was then added and the reaction was stirred for 1 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated to afford the THP ring **19** in a 3/1 (*cis*-**19** / *trans*-**19**) ratio.

To a solution of the above crude residue in THF (10 mL), TBAF (1.6 mL, 1.6 mmol, 1.0 M in THF, 20 equiv) was added and the reaction mixture was stirred for 24 h. The reaction was quenched by addition saturated $NaHCO_3$ solution, extracted with AcOEt, dried over Na_2SO_4 , filtered and concentrated. The residue was first purified by silica gel chromatography (AcOEt) to afford a mixture of the two diastereoisomers *cis*-**20** and *trans*-**20** THP (19.8 mg, 52%, *cis/trans*: 3/1). This mixture was purified by silica gel chromatography (Petroleum ether/AcOEt : 20/80) to obtain *cis*-**20** THP isomer (14.8 mg, 38%)¹ and *trans*-**20** THP isomer (5.0 mg).

$[\alpha]_D^{20} = +21.3$ (c 0.075, $CHCl_3$); IR(neat) 3338, 3000-2800, 1737, 1460, 1379, 1256, 1164, 1087, 1047 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) 5.65 (dtd, $J=15.3, 7.2, 1.0$ Hz, 1H), 5.49 (ddt, $J=15.3, 6.2, 1.1$ Hz, 1H), 4.35 (m, 1H), 4.26-4.18 (m, 2H), 4.00 (m, 1H), 3.85 (m, 1H), 3.66 (s, 3H), 3.60 (m, 1H), 3.53 (m, 1H), 3.30 (s, 3H), 3.20 (br s, 1H, OH), 2.50 (dd, $J=15.1, 8.5$ Hz, 1H), 2.37 (dd, $J=15.1, 4.9$ Hz, 1H), 1.95-1.16 (m, 18H), 1.00 (d, $J=6.6$ Hz, 3H), 0.87 (d, $J=6.6$ Hz, 3H), 0.86 (s, $J=6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 171.9 (s), 134.5 (d), 129.2 (d), 74.8 (d), 73.2 (d), 68.9 (d), 68.6 (d), 68.4 (d), 66.9 (d), 64.5 (d), 56.4 (q), 51.7 (q), 41.6 (t), 41.1 (t), 40.6 (t), 40.2 (t), 38.7 (t), 38.1 (t), 37.9 (t), 33.3 (d, C_{12}), 28.3 (d), 27.7 (t), 26.2 (t), 22.3 (q), 22.2 (q), 18.5 (q) ppm; HRMS (ESI) 493.3130 (calcd for $C_{25}H_{48}O_3Si + Na^+$ 493.3141).

¹ Spectral data of *cis*-**20** agreed with Crimmins' group, see: Crimmins, M. T.; Siliphaivanh, P. *Org. Lett.* **2003**, 5, 4641.

Macrolide 1

To a solution of the ester **20** (10.0 mg, 21.3 μ mol, 1 equiv) in Et₂O (5 mL) was added TMSOK (8.2 mg, 64 μ mol, 3 equiv). After stirring for 16 h, the reaction mixture was diluted with CH₂Cl₂ and quenched by addition of an aqueous solution of KHSO₄ 0.1 N until pH=2. The aqueous layer was extracted with CH₂Cl₂ (6x30 mL), then combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated. The crude carboxylic acid was dried by azeotropic removal of water with toluene (2x20 mL) and was used in the next step without further purification.

To a solution of the above carboxylic acid in toluene (100 mL) was added Et₃N (130 μ L, 937 μ mol, 44 equiv), followed by 2,4,6 trichlorobenzoyl chloride (133 μ L, 852 μ mol, 40 equiv), and DMAP (25.8 mg, 213 μ mol, 10 equiv). After stirring for 1 h at rt, a second portion of DMAP (10 equiv), was added and the reaction was stirred for 48 h. The reaction mixture was quenched by addition of a saturated aqueous solution of NaHCO₃ (30 mL) and water (20 mL). After stirring for 20 min, the aqueous layer was extracted with AcOEt (20 mL), and the combined organic layers were washed with aqueous KHSO₄ 0.1N (30 mL). The last acidic aqueous phase was extracted with AcOEt (20 mL) and the combined organic phases were washed with brine (30 mL), dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel chromatography (AcOEt/Petroleum Ether: 50/50) to afford the leucascandrolide A macrolactone **1** (7.0 mg, 75%) as an oil.

$[\alpha]_D^{20}$ +58.5 (*c* 0.205, EtOH) ; IR(neat) 3429, 3000-2800, 1738, 1461, 1385, 1272, 1238, 1195, 1167, 1142, 1111, 1076, 1034, 1004, 964 cm⁻¹; ¹H NMR (C₅D₅N, 400 MHz) 6.38 (br s, 1H, OH), 5.81-5.70 (m, 2H), 5.53 (dd, *J*=15.4, 6.9 Hz, 1H), 4.62 (t_{app}, *J*=11.6 Hz, 1H), 4.41 (m, 1H), 4.17 (t_{app}, *J*=11.3 Hz, 1H), 4.05 (d_{app}, *J*=10.9, 1H), 3.91 (t_{app}, *J*=10.5 Hz, 1H), 3.74 (t_{app}, *J*=10.7 Hz, 1H), 3.36 (s, 3H), 2.67 (dd, *J*=12.9, 3.8 Hz, 1H), 2.57-2.42 (m, 2H), 2.10 (app t, *J*=12.5 Hz, 1H), 1.95-1.13 (m, 14H), 1.06 (d, *J*=7.0 Hz, 3H), 1.12-0.99 (m, 2H), 0.77 (d, *J*=6.6 Hz, 3H), 0.76 (d, *J*=6.6 Hz, 3H); ¹³C NMR (C₅D₅N, 100 MHz) 170.3 (s), 131.9 (t),

131.5 (d), 73.9 (d), 73.8 (d), 70.9 (d), 69.9 (d), 69.7 (d), 63.8 (d), 63.1 (d), 56.7 (q), 43.9 (t), 43.4 (t), 41.7 (t), 39.9 (t), 39.6 (t), 39.5 (t), 35.9 (t), 31.4 (t), 28.3 (d), 27.4 (t), 24.2 (t), 22.3 (q), 22.2 (q), 18.4 (q); HRMS (ESI) 461.2870 (calcd for $\text{C}_{25}\text{H}_{42}\text{O}_6 + \text{Na}^+$ 461.2874).