SUPPORTING INFORMATION

Total Syntheses of Amphidinolide T1, T3, T4 and T5

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General. All reactions were carried out under Ar. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et₂O (Mg-anthracene), CH₂Cl₂ (P₄O₁₀), MeCN, Et₃N, pyridine, DMF (CaH₂), MeOH (Mg), hexane, toluene (Na/K). Flash chromatography: Merck silica gel 60 (230-400 mesh). NMR: Spectra were recorded on a DPX 300, AV 400 or DMX 600 spectrometer (Bruker) in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. IR: Nicolet FT-7199 spectrometer, wavenumbers in cm⁻¹. MS (EI): Finnigan MAT 8200 (70 eV), HRMS: Finnigan MAT 95, Bruker APEX III FT-ICR-MS (7 T magnet). Melting points: Büchi melting point apparatus (uncorrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. All commercially available compounds (Lancaster, Fluka, Aldrich) were used as received unless stated otherwise.

(2S)-(+)-2-Methyl-3-(toluene-4-sulfonyloxy)-propionic acid methyl ester (7). To a solution of compound **6** (10.47 g, 88.63 mmol) in CH₂Cl₂ (125 mL) at 0°C were successively added Et₃N (14.8 mL, 106.3 mmol), DMAP (2.17 g, 17.76 mmol), and TsCl (20.28 g, 106.4 mmol). The mixture was stirred overnight at room temperature. The reaction was quenched with water (100 mL) and the aqueous phase was extracted twice with CH₂Cl₂ (100 mL). The combined organic layers were washed with aq. sat. NaHCO₃ (100 mL) and brine (100 mL) and dried (MgSO₄). Filtration through a pad of silica and evaporation of the solvent afforded a colorless oil which slowly crystallised on standing to give compound **7** (22.71 g, 94%) as white crystals. The product can also

be purified by distillation under vacuum (150 °C at 0.17 mbar). $[\alpha]_{\text{D}}^{25} +9.3^{\circ}$ (*c* 1.5, MeOH); $[\alpha]_{\text{D}}^{17.5} +3.8^{\circ}$ (*c* 2.0, CHCl₃). IR (film): 2955, 1742, 1598, 1460, 1436, 1363, 1208, 1190, 1177, 1097, 977, 947, 845, 816, 754, 667, 555 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.80-7.75 (2H, m), 7.36-7.33 (2H, m), 4.18 (1H, dd, *J* = 9.0 Hz, *J* = 6.0 Hz), 4.05 (1H, dd, *J* = 9.0 Hz, *J* = 6.0 Hz), 3.63 (3H, s), 2.84-2.77 (1H, m), 2.45 (3H, s), 1.17 (3H, d, *J* = 6.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 173.0, 144.9, 132.7, 129.8 (2C), 127.9 (2C), 70.7, 52.0, 39.1, 21.6, 13.5; MS (EI) *m/z* (rel. intensity) 272 (*M*⁺, 11), 187 (6), 172 (8), 155 (70), 117 (55), 91 (100), 85 (23); Anal. calcd. for C₁₂H₁₆O₅S: C, 52.93; H, 5.92; S, 11.77; found: C, 53.04; H, 6.02; S, 11.80.

(2S,3S)-(+)-Toluene-4-sulfonic acid 3-hydroxy-2-methyl-hex-5-enyl ester (8). To a solution of ester **7** (10.0 g, 36.72 mmol) in toluene (50 mL) at -95 °C was slowly added via syringe a solution of DiBAL-H in toluene (1 M, 47.74 mL, 47.74 mmol). The reaction mixture was stirred for 1 h at -95 °C before it was quenched with EtOAc (40 mL) and warmed to room temperature. An aqueous solution of citric acid (1 M, 75 mL) was added and the aqueous phase was extracted 3 times with EtOAc. The combined organic phases were washed with water (100 mL) and brine (100 mL). Drying (MgSO₄), filtration through a pad of celite and evaporation of the solvents afforded the crude aldehyde (*ca.* 10 g) as a colorless oil, which was dissolved in Et₂O (50 mL) at -100 °C and transferred via canula to a solution of (-)-Ipc₂B-allyl in Et₂O (0.86M, 42.7 mL, 36.72 mmol) at -100 °C. It is important to maintain the temperature at -100 °C and to drop the solution of the aldehyde slowly against the cold inside of the flask. The reaction mixture was stirred for 30 min at -100 °C before it was quenched with MeOH (20 mL) and warmed to room temperature. Diethanolamine (5 mL, 52.04 mmol) was then added and stirring continued for 14 h. Water (200 mL) was added and the aqueous phase was extracted with EtOAc (3 × 150 mL). The combined organic layers were successively washed with water, aq. sat. NaHCO₃ and brine before they were dried (Na₂SO₄), filtered and evaporated. Flash chromatography of the crude product with a gradient of solvents (hexane → hexane:Et₂O, 3:2 → hexane:EtOAc, 3:2) afforded alcohol **8** (7.62 g, 73% yield) as a colorless oil. $[\alpha]_{\text{D}}^{20} +3.2^{\circ}$ (*c* 1.1, CHCl₃). IR (film): 3550, 3076, 2977, 2933, 1641, 1598, 1357, 1189, 1176, 1097, 966, 815, 668, 555 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (2H, br d, *J* = 8.0 Hz), 7.34 (2H, d, *J* = 8.0 Hz), 5.82-5.68 (1H, m), 5.13-5.06 (2H, m), 4.07 (1H, dd, *J* = 9.5 Hz, *J* = 7.5 Hz), 3.90 (1H, dd, *J* = 9.5 Hz, *J* = 6.0 Hz), 3.73 (1H, dt, *J* = 7.0 Hz, *J* = 3.5 Hz), 2.44 (3H, s), 2.17 (2H, t, *J* = 7.0 Hz), 1.97-1.88 (1H, m), 1.81 (1H, br. s), 0.87 (3H, d, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 144.8, 134.6, 132.9, 129.8 (2C), 127.8 (2C), 118.1, 72.6, 69.3, 39.0, 37.3, 21.6, 9.6; MS (EI) *m/z* (rel. intensity) 243 (20), 173 (96), 155 (38), 91 (76), 71 (100); HRMS (CI): calcd. for C₁₄H₂₁O₄S, 285.1161; found: 285.1160 (*M*H⁺). Anal. calcd. for C₁₄H₂₀O₄S: C, 59.13; H, 7.09; S, 11.28; found: C, 59.04; H, 7.14; S, 11.34.

(3S,4S)-(+)-1-Cyano-4-hydroxy-3-methyl-hept-6-ene (9). KCN (3.06 g, 46.98 mmol) was added to a solution of tosylate **8** (6.68 g, 23.49 mmol) in dry DMSO (100 mL). The reaction mixture was stirred at 60 °C for 2 h and for 17 h at ambient temperature. It was then cooled with an ice bath, quenched with water (100 mL) and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic phases were washed with water (2 × 100 mL) and brine (100 mL), they were

dried (Na₂SO₄), filtered and evaporated to give a pale yellow oil which was purified by chromatography (hexane:EtOAc: 4:1 → 2:1) to afford nitrile **5** (3.05 g, 93 %) as a colorless oil. $[\alpha]_D^{19} +27.7^\circ$ (*c* 1.1, CHCl₃). IR (KBr): 3431, 3075, 2977, 2929, 2249, 1642, 1425, 1091, 988, 919 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.87-5.73 (1H, m), 5.20-5.13 (2H, m), 3.74-3.68 (1H, m), 2.51 (1H, dd, *J* = 16.5 Hz, *J* = 6.5 Hz), 2.33 (1H, dd, *J* = 16.5 Hz, *J* = 7.5 Hz), 2.31-2.12 (2H, m), 2.05-1.94 (1H, m), 1.85 (1H, br s), 1.06 (3H, d, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 134.2, 119.2, 118.8, 71.6, 38.9, 35.2, 21.4, 13.1; MS (EI) *m/z* (rel. intensity) 139 (0.15), 98 (100), 80 (11), 70 (67), 55 (34), 43 (75); HRMS (CI): calcd. for C₈H₁₄NO: 140.1075; found: 140.1075 (MH⁺); Anal. calcd. for C₈H₁₃NO: C, 69.03; H, 9.41; N, 10.06; found: C, 68.93; H, 9.35; N, 10.14.

(4S,5S)-(+)-5-Allyl-4-methyl-tetrahydrofuran-2-ol (10). A solution of DiBAL-H in CH₂Cl₂ (1 M, 39.01 mL, 39.01 mmol) was added over 10 min to a solution of nitrile **9** (1.81 g, 13.00 mmol) in CH₂Cl₂ (150 mL) at -78 °C and the mixture was allowed to stir at that temperature for 3 h. For work up, the reaction was quenched at -78 °C by addition of EtOAc (10 mL) followed by HCl (2 M, 20 mL). The mixture was then allowed to warm to room temperature, the aqueous layer was extracted with EtOAc (2 × 100 mL) and the combined organic layers were washed with brine (100 mL). Drying (MgSO₄), filtration and evaporation of the solvents afforded a crude oil which was purified by flash chromatography on Florisil (Hexane-EtOAc, 3/1) to yield lactol **10** as a 2.4:1 mixture of anomers (1.68 g, 91 %) as a colorless oil. The anomer ratio evolved to 3:1 upon standing in CDCl₃. Due to its rather low stability, this compound was used immediately in the next step. $[\alpha]_D^{20} -59.1^\circ$ (*c* 1.25, CHCl₃). The NMR signals corresponding to the minor anomer are marked with “Min.”. ¹H NMR (300 MHz, CDCl₃) δ 5.92-5.77 (1H, m), 5.55 (1H, dd, *J* = 5.0 Hz, *J* = 3.0 Hz, Maj.), 5.46 (1H, dd, *J* = 5.0 Hz, *J* = 3.0 Hz, Min.), 5.21-5.05 (2H, m), 4.23 (1H, td, *J* = 8.0 Hz, *J* = 6.0 Hz, Maj.), 3.98 (1H, td, *J* = 8.5 Hz, *J* = 5.5 Hz, Min.), 3.29 (1H, br. s, Min.), 3.06 (1H, br. s, Maj.), 2.56-2.10 (2H, m), 2.05 (1H, dd, *J* = 7.0 Hz, *J* = 3.0 Hz, Min.), 2.00 (1H, dd, *J* = 7.0 Hz, *J* = 3.0 Hz, Maj.), 1.82 (1H, t, *J* = 6.0 Hz, Maj.), 1.78 (1H, t, *J* = 5.5 Hz, Min.), 1.08 (3H, dd, *J* = 7.0 Hz, *J* = 3.0 Hz, Min.), 0.93 (3H, d, *J* = 7.0 Hz, Maj.); ¹³C NMR (75 MHz, CDCl₃) 135.6 (Min.), 135.3, 116.6, 98.5 (Min.), 97.4, 82.2 (Min.), 79.9, 41.8, 41.2 (Min.), 35.9 (Min.), 35.1, 35.0 (Min.), 34.3, 14.8 (Min.), 14.5; MS (EI) *m/z* (rel. intensity) 124 (11), 83 (72), 55 (100), 41 (54); HRMS (CI): calcd. for C₈H₁₅O₂: 143.1072; found: 143.1073 (MH⁺).

(2S,3S)-2-Allyl-5-benzenesulfonyl-3-methyl-tetrahydrofuran (11). A solution of phenylsulfinic acid sodium salt (18.24 g) in sulfuric acid (2 M, 83 mL) was stirred for 20 min. Additional H₂SO₄ (2 M, 100 M) was added and the aqueous phase was extracted with CH₂Cl₂ (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried (MgSO₄), filtered and evaporated to afford PhSO₂H (12.50 g, 99.5%) as a white solid which was immediately used in the next step. To a solution of lactol **10** (1.58 g, 11.11 mmol) in CH₂Cl₂ (100 mL) at 0 °C were added PhSO₂H (12.50 g, 87.92 mmol) and CaCl₂ (2.47 g, 22.22 mmol) and the resulting mixture was stirred for 2 h. The reaction was quenched by addition of a saturated solution of Na₂CO₃ (100 mL) and the aqueous layer was extracted with CH₂Cl₂ (3 × 100 mL). The combined organic layers were filtered through a cotton plug and washed with a sat. solution of Na₂CO₃ (100 mL) and brine (100

mL) before they were dried (Na_2SO_4), filtered and evaporated. The crude product was purified by flash chromatography (hexane:EtOAc, 3:1) to yield sulfone **11** as a colorless oil a (2.58 g, 87%). The anomer ratio, originally 2.5:1, evolved to 1.5:1 upon standing in CDCl_3 over a few days. For analytical purposes, a small sample was repurified to give analytically pure *trans*-isomer as white crystals whose structure was confirmed by single X-Ray crystallography. M.p. 36.5 – 37.5 °C; $[\alpha]_{\text{D}}^{20}$ -120.6° (*c* 2.5, CHCl_3); $[\alpha]_{\text{D}}^{20}$ -150.3° (*c* 1.14, C_6H_6). IR (film): 2969, 2933, 2878, 1642, 1447, 1308, 1288, 1149, 1075, 913, 751, 718, 688, 584 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ 7.93-7.91 (2H, m), 7.63 (1H, tt, $J = 8.5$ Hz, $J = 1.5$ Hz), 7.55-7.52 (2H, m), 5.74 (1H, dddd, $J = 17.0$ Hz, $J = 10.5$ Hz, $J = 7.0$ Hz, $J = 6.5$ Hz), 5.09 (1H, qd, $J = 17.0$ Hz and $J = 1.5$ Hz), 5.05 (1H, qd, $J = 10.5$ Hz, $J = 1.5$ Hz), 4.90 (1H, dd, $J = 8.0$ Hz, $J = 6.5$ Hz), 4.29 (1H, ddd, $J = 8.0$ Hz, $J = 6.0$ Hz, $J = 5.0$ Hz), 2.79 (1H, ddd, $J = 14.0$ Hz, $J = 7.5$ Hz, $J = 6.5$ Hz), 2.45 (1H, m), 2.26 (1H, tddd, $J = 14.5$ Hz, $J = 8.0$ Hz, $J = 6.5$ Hz, $J = 1.5$ Hz), 2.15 (1H, tddd, $J = 14.5$ Hz, $J = 7.0$ Hz, $J = 6.0$ Hz, $J = 1.5$ Hz), 2.03 (1H, ddd, $J = 14.0$ Hz, $J = 8.0$ Hz, $J = 3.0$ Hz), 0.90 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3) 137.2, 134.2, 133.8, 129.3 (2C), 129.0 (2C), 117.1, 92.5, 83.6, 35.1, 34.4, 33.6, 14.2; MS (ESI) m/z : 305 ($\text{M}+\text{K}^+$), 289 ($\text{M}+\text{Na}^+$), 160, 142, 125; Anal. calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_3\text{S}$: C, 63.13; H, 6.81; S, 12.04; found: C, 63.03; H, 6.75; S, 11.95.

(4*S*,5*R*)-(-)-4-Methyl-5-phenyl-3-propionyl-oxazolidin-2-one (12). To a solution of the commercially available oxazolidinone auxiliary (10.0 g, 56.43 mmol) in dry THF (150 mL) at -78 °C was slowly added via syringe pump (ca. 90 min. addition time) a solution of *n*-BuLi (1.6 M, 37 mL, 59.25 mmol). The reaction mixture was stirred at that temperature for 30 min before propionyl chloride (5.74 mL, 62.07 mmol) was introduced and stirring was continued for 2 h (formation of a white precipitate). The reaction was then quenched with sat. aq. NH_4Cl (50 mL). After warming to room temperature, EtOAc (100 mL) was added, the phases were separated, the aqueous layer was extracted with EtOAc (2 × 100 mL), the combined organic phases were washed with aq. sat. Na_2CO_3 (100 mL) and brine (100 mL) before they were dried (MgSO_4), filtered and evaporated. The crude product was purified by flash chromatography (hexane:EtOAc, 2:1) to yield oxazolidinone **12** (13.10 g, 99.5%) as a colorless oil. $[\alpha]_{\text{D}}^{20}$ -51.6° (*c* 2.23, CHCl_3). IR (film): 2983, 2941, 1782, 1705, 1456, 1370, 1348, 1247, 1218, 1200, 1151, 1123, 1079, 1068, 1038, 1011, 982, 948, 767, 701 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.44-7.28 (5H, m), 5.66 (1H, d, $J = 7.5$ Hz), 4.76 (1H, qt., $J = 7.0$ Hz), 3.04-2.87 (2H, m), 1.18 (3H, t, $J = 7.5$ Hz), 0.89 (3H, d, $J = 6.5$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 173.8, 153.0, 133.3, 128.7, 128.6 (2C), 125.6 (2C), 78.9, 54.7, 29.2, 14.5, 8.2; MS (EI) m/z (rel. intensity) 233 (M^+ , 40), 176 (5), 163 (10), 116 (19), 107 (70), 57 (100).

(2'*S*,3'*R*,4*S*,5*R*)-(-)-3-(3-Hydroxy-2,4-dimethyl-pent-4-enoyl)-4-methyl-5-phenyl-oxazolidin-2-one (13). Oxazolidinone **12** (12.55 g, 53.80 mmol) was dried in a round bottom flask by applying three cycles of vacuum/argon. It was then dissolved in freshly distilled CH_2Cl_2 (200 mL) and Et_3N (10.5 mL, 75.30 mmol). The solution was cooled to -78 °C and a solution of freshly purchased Bu_2BOTf (1 M, 59.2 mL, 59.2 mmol) was added via syringe pump over a period of 1 h. The reaction mixture was stirred at -78 °C for 30 min and at ambient temperature for 75 min before it was cooled again to -78 °C. Freshly distilled methacrolein (4.90 mL, 59.21 mmol) was added via

syringe and the resulting solution was stirred at -78 °C for 45 min and at 0 °C for 1 h. The reaction was quenched by the addition of a buffer solution (pH 7, 50 mL) followed by MeOH (50 mL). A mixture of H₂O₂ (30 %, 60 mL) and MeOH (50 mL) was then slowly added at 0 °C (*Caution*: exothermic). Stirring for 1 h at 0 °C was followed by addition of sodium sulfite until no more oxidant was present in the solution (control with iodine paper). The aqueous layer was extracted three times with CH₂Cl₂ (100 mL), the combined organic phases were washed with brine (200 mL), they were dried (Na₂SO₄), filtered and evaporated, and the crude product was purified by flash chromatography (hexane:EtOAc, 3:1 → 2:1) to yield alcohol **13** as a white crystalline product (14.62 g, 90 % yield). m.p. 97-99 °C (Lit.¹ m.p. 97-99 °C); $[\alpha]_D^{20}$ -37.0° (*c* 2.6, CHCl₃); Lit.¹ for enantiomer $[\alpha]_D^{23}$ +38.0° (*c* 1.5, CHCl₃). IR (film): 3505, 2977, 2941, 2859, 1774, 1676, 1361, 1346, 1236, 1202, 1147, 1119, 1066, 1036, 990, 962, 909 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.47-7.37 (3H, m), 7.33-7.30 (2H, m), 5.70 (1H, d, *J* = 7.0 Hz), 5.14-5.13 (1H, m), 5.00-4.99 (1H, m), 4.80 (1H, qt., *J* = 7.0 Hz), 4.45-4.43 (1H, m), 3.99 (1H, dq, *J* = 7.0 Hz, *J* = 3.5 Hz), 2.95 (1H, br s), 1.77 (3H, s), 1.18 (3H, d, *J* = 7.0 Hz), 0.91 (3H, d, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 176.8, 152.6, 143.7, 133.1, 128.8, 128.7 (2C), 125.6 (2C), 111.8, 79.0, 74.0, 54.9, 40.2, 19.4, 14.3, 9.8; MS (EI) *m/z* (rel. intensity) 303 (M⁺, 8), 233 (94), 178 (22), 160 (13), 134 (36), 126 (50), 118 (53), 107 (66), 91 (24), 57 (100); HRMS (CI): calcd. for C₁₇H₂₂NO₄, 304.1549; found: 304.1548 (MH⁺). Anal. calcd. for C₁₇H₂₁NO₄: C, 67.31; H, 6.98; N, 4.62; found: C, 67.25; H, 7.06; N, 4.59.

(2'S,3'R,4S,5R)-(-)-3-(3-Methoxymethoxy-2,4-dimethyl-pent-4-enoyl)-4-methyl-5-phenyl-oxazolidin-2-one (14). MOMCl (10.51 mL, 138.4 mmol) was added via syringe over 5 min to a solution of alcohol **13** (14.0 g, 46.13 mmol) in CH₂Cl₂ (200 mL) at 0 °C, followed by the addition of *i*-Pr₂NEt (24.11 mL, 138.4 mmol). The resulting mixture was stirred at 0 °C for 2 h and at ambient temperature for 16 h. Since TLC indicated that the reaction was not complete, additional *i*-Pr₂NEt (4.02 mL, 23.05 mmol) and MOMCl (1.75 mL, 23.05 mmol) were introduced and stirring was continued for another 5 h. The reaction was quenched with sat. aq. Na₂CO₃ (100 mL), the aqueous layer was extracted three times with CH₂Cl₂ (100 mL), the combined organic phases were washed with brine (200 mL), they were dried (MgSO₄), filtered and evaporated, and the residue was purified by flash chromatography (hexane:EtOAc, 4:1) to yield product **14** as a colorless oil (14.88 g, 93 % yield). $[\alpha]_D^{19}$ -78.9° (*c* 1.4, CHCl₃). IR (film): 2940, 1782, 1704, 1456, 1365, 1343, 1233, 1196, 1157, 1120, 1031, 957, 916, 768, 700 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.37 (3H, m), 7.32-7.29 (2H, m), 5.63 (1H, d, *J* = 7.0 Hz), 5.01 (2H, s), 4.69 (1H, qt., *J* = 7.0 Hz), 4.61 (1H, d, *J* = 7.0 Hz), 4.53 (1H, d, *J* = 7.0 Hz), 4.33 (1 H, d, *J* = 7.0 Hz), 4.18-4.09 (1H, m), 3.39 (3H, s), 1.74 (3H, s), 1.26 (3H, d, *J* = 7.0 Hz), 0.91 (3H, d, *J* = 6.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 174.3, 152.8, 142.2, 133.2, 128.7, 128.7 (2C), 125.6 (2C), 114.7, 94.3, 80.3, 79.0, 55.9, 55.3, 40.9, 21.0, 14.2, 12.3; MS (EI) *m/z* (rel. intensity) 347 (M⁺, 0.4), 302 (11), 277 (12), 245 (7), 230 (4), 178 (10), 169 (9), 134 (12), 118 (20), 45 (100); HRMS (CI): calcd. for C₁₉H₂₆NO₅:

¹ Smith, A. B.; Barbosa, J.; Wong, W.; Wood, J. L.; *J. Am. Chem. Soc.* **1995**, *117*, 10777-10778.

348.1811; found: 348.1813 (MH^+); Anal. calcd. for $\text{C}_{19}\text{H}_{25}\text{NO}_5$: C, 65.69; H, 7.25; N, 4.03; found: C, 65.75; H, 7.15; N, 3.98.

(2R,3S)-(-)-3-Methoxymethoxy-2,4-dimethyl-pent-4-en-1-ol (15). LiBH_4 (1.15 g, 52.76 mmol) was added to a solution of compound **14** (14.1 g, 40.59 mmol) in aq. Et_2O (150 mL + 0.2 mL H_2O). After stirring for 2h, the evolution of gas had ceased and the reaction was quenched at 0 °C with aq. NaOH (1 M, 75 mL) and stirring was continued for 1 h. The aqueous layer was then extracted with Et_2O (3 $\times$ 50 mL), the combined organic phases were washed with brine (100 mL), they were dried (MgSO_4), filtered and evaporated, and the residue was purified by flash chromatography (hexane: EtOAc , 7:3) to yield alcohol **15** as a colorless oil (5.52 g, 78 %). $[\alpha]_{\text{D}}^{18}$ -161.8° (c 2.0, CHCl_3). IR (film): 3423, 2933, 2886, 1651, 1453, 1156, 1097, 1034, 904 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.99-4.96 (2H, m), 4.60 (1H, d, J = 6.5 Hz), 4.53 (1H, d, J = 6.5 Hz), 4.01 (1H, d, J = 6.0 Hz), 3.58 (1H, dd, J = 11.0 Hz, J = 7.0 Hz), 3.50 (1H, dd, J = 11.0 Hz, J = 5.5 Hz), 3.40 (3H, s), 2.25 (1H, br s), 1.98-1.89 (1H, m), 1.68 (3H, s), 0.92 (3H, d, J = 7.0 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 143.0, 113.4, 94.6, 81.1, 65.3, 55.8, 37.5, 18.5, 11.7; MS (EI) m/z (rel. intensity): 174 (M^+ , 0.02), 142 (3), 115 (22), 71 (19), 45 (100); HRMS (CI): calcd. for $\text{C}_9\text{H}_{19}\text{O}_3$: 175.1334; found: 175.1335 (MH^+); Anal. calcd. for $\text{C}_9\text{H}_{18}\text{O}_3$: C, 62.04; H, 10.41; found: C, 61.94; H, 10.35. Further elution of the column with EtOAc/MeOH provided the recovered chiral auxillary (5.80 g, 81 %) as white crystals; $[\alpha]_{\text{D}}^{18}$ -160.5° (c 1.1, CHCl_3).

(2R,3S)-(-)-tert-Butyl-(3-methoxymethoxy-2,4-dimethyl-pent-4-enyloxy)-dimethyl-silane (16). Imidazole (3.91 g, 57.39 mmol) and TBDMSCl (8.65 g, 57.39 mmol) were successively added to a solution of alcohol **15** (5.00 g, 28.70 mmol) in dry DMF (100 mL) at 0 °C. After stirring at room temperature for 3 h, the reaction was quenched at 0 °C with aq. sat. NH_4Cl (200 mL) and was diluted with EtOAc (100 mL). The aqueous layer was extracted with EtOAc (3 $\times$ 100 mL), the combined organic layers were washed with water (2 $\times$ 100 mL) and brine (100 mL), they were dried (MgSO_4), filtered and evaporated, and the residue was purified by flash chromatography (hexane: EtOAc , 4:1) to yield product **16** as a colorless oil (7.91 g, 95.5 % yield). $[\alpha]_{\text{D}}^{20}$ -84.3° (c 2.4, CHCl_3). IR (KBr): 3074, 2955, 2929, 2886, 2858, 1652, 1472, 1463, 1254, 1091, 1031, 837, 775 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.97-4.93 (2H, m), 4.63 (1H, d, J = 6.5 Hz), 4.51 (1H, d, J = 6.5 Hz), 3.93 (1H, d, J = 7.0 Hz), 3.53 (1H, dd, J = 10.0 Hz, J = 5.5 Hz), 3.39 (1H, dd, J = 10.0 Hz, J = 6.0 Hz), 3.39 (3H, s), 1.86-1.75 (1H, m), 1.66 (3H, s), 0.99 (3H, d, J = 6.5 Hz), 0.90 (9H, s), 0.03 (3H, s), 0.02 (3H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 142.9, 114.1, 94.0, 80.9, 65.1, 55.7, 37.9, 25.9 (3C), 18.3, 17.9, 12.6, -5.4, -5.5; MS (CI) m/z (rel. intensity) 289 (MH^+ , 21), 244 (45), 227 (100), 132 (36), 95 (14); HRMS (CI): calcd. for $\text{C}_{15}\text{H}_{33}\text{O}_3\text{Si}$: 289.2199; found: 289.2200 (MH^+). Anal. calcd. for $\text{C}_{15}\text{H}_{32}\text{O}_3\text{Si}$: C, 62.45; H, 11.18; Si, 9.73; found: C, 62.51; H, 11.26; Si, 9.76.

(3S,4R)-(-)-5-(tert-Butyl-dimethyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentan-2-one (17). Ozone was bubbled through a solution of olefin **16** (3.00 g, 10.40 mmol) in CH_2Cl_2 (200 mL) at -78°C until the reaction mixture became blue (1 h). At that point, the solution was flushed with

argon until it became colorless (approximately 45 min). PPh₃ (3.00 g, 11.44 mmol) was added and the mixture was stirred at -78 °C for 45 min before it was allowed to reach ambient temperature. Evaporation of the solvent and purification of the crude product by flash chromatography (hexane:EtOAc, 95:5) gave ketone **17** as a colorless oil (2.60 g, 86 %). $[\alpha]_D^{19}$ -6.6° (*c* 2.7, CHCl₃). IR (KBr): 2955, 2930, 2896, 2958, 1718, 1472, 1255, 1155, 1107, 1090, 1040, 839, 777 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.66 (1H, d, *J* = 6.5 Hz), 4.63 (1H, d, *J* = 6.5 Hz), 4.25 (1H, d, *J* = 3.5 Hz), 3.52-3.48 (2H, m), 3.38 (3H, s), 2.17 (3H, s), 2.15-2.07 (1H, m), 0.90 (9H, s), 0.82 (3H, d, *J* = 7.0 Hz), 0.06 (3H, s), 0.05 (3H, s); ¹³C NMR (75 MHz, CDCl₃) δ 209.8, 97.0, 82.3, 64.3, 56.1, 38.5, 27.1, 25.8 (3C), 18.2, 10.7, -5.5 (2C); MS (EI) *m/z* (rel. intensity) 259 (0.4), 247 (3), 233 (1), 201 (8), 171 (11), 145 (9), 115 (8), 89 (15), 73 (13), 45 (100); HRMS (CI): calcd. for C₁₄H₃₁O₄Si: 291.1992; found: 291.1993 (MH⁺). Anal. calcd. for C₁₄H₃₀O₄Si: C, 57.89; H, 10.41; found: C, 57.93; H, 10.34.

(3*S*,4*R*)-(-)-2,5-Bis-(*tert*-butyl-dimethyl-silanyloxy)-3-methoxymethoxy-4-methyl-pent-1-ene (18). Et₃N (1.59 mL, 11.43 mmol) and TBSOTf (2.62 mL, 11.43 mmol) were added to a solution of ketone **17** (1.66 g, 5.71 mmol) in Et₂O (10 mL) at 0 °C in a pear-shaped flask and the resulting mixture was stirred at ambient temperature for 3 h. The stirring was discontinued, causing the separation of two phases. The brown lower phase was removed via syringe and discarded (*Caution*: stench) before a sat. aq. solution of NaHCO₃ (10 mL) was added to the remaining ethereal phase. The aqueous layer was extracted three times with Et₂O (10 mL), the combined organic phases were washed with a brine (100 mL), they were dried (Na₂SO₄), filtered and evaporated, and the crude product was purified by flash chromatography (hexane:EtOAc, 98:2) to yield pure silyl enol ether **18** (2.15 g, 93 % yield) as a colorless oil. $[\alpha]_D^{20}$ -68.9° (*c* 1.03, CHCl₃). IR (film): 2956, 2930, 2887, 2858, 1633, 1472, 1464, 1255, 1156, 1106, 1089, 1040, 836, 813, 778 cm⁻¹; ¹H NMR (300 MHz, C₆D₆) δ 4.80 (1H, d, *J* = 6.5 Hz), 4.52 (1H, d, *J* = 6.5 Hz), 4.47 (1H, br s), 4.34 (1H, d, *J* = 0.5 Hz), 4.25 (1H, d, *J* = 4.5 Hz), 3.75 (1H, dd, *J* = 7.0 Hz, *J* = 9.5 Hz), 3.58 (1H, dd, *J* = 6.0 Hz, *J* = 9.5 Hz), 3.25 (3H, s), 2.31-2.21 (1H, m), 1.15 (3H, d, *J* = 7.0 Hz), 1.01 (9H, s), 0.97 (9H, s), 0.16 (3H, s), 0.15 (3H, s), 0.09 (6H, s); ¹³C NMR (75 MHz, CDCl₃) δ 157.2, 95.3, 92.0, 77.8, 65.7, 55.9, 38.7, 26.4 (3C), 26.1 (3C), 18.7, 18.5, 11.9, -4.2, -4.6, -4.99, -5.00; MS (EI) *m/z* (rel. intensity) 347 (18), 318 (11), 318 (36), 233 (14), 232 (69), 215 (16), 212 (12), 211 (57), 199 (17), 183 (17), 171 (20), 149 (18), 147 (15), 133 (15), 131 (60), 129 (11), 119 (26), 115 (16), 89 (77), 75 (29), 73 (100), 59 (19), 57 (20), 45 (57); HRMS (CI): calcd. for C₂₀H₄₅O₄Si₂: 405.2856; found: 405.2857 (MH⁺); Anal. calcd. for C₂₀H₄₄O₄Si₂: C, 59.35; H, 10.96; Si, 13.88; found: C, 59.30; H, 11.06; Si, 13.75.

(2*S*)-(+)-2-Methyl-pent-4-enoic acid (20). A solution of NaHMDS (10 M in THF, 25 mL, 25 mmol) was added via syringe pump over 25 min to a solution of compound **19** (5.13 g, 21.99 mmol) in THF (70 mL) at -78 ° and the resulting mixture was stirred at that temperature for 2 h. Allylbromid (13 mL, 95.8 mmol) was then introduced and stirring was continued at -78 °C for 1 h and at 0 °C for 16 h. The reaction was quenched with aq. sat. NH₄Cl (120 mL) and diluted with EtOAc (50 mL). The aqueous phase was extracted with EtOAc (3 × 50 mL), the combined organic layers were washed with brine (100 mL), they were dried (Na₂SO₄), filtered and evaporated, and

the crude product was purified by flash chromatography (hexane:EtOAc, 8:1) to yield the corresponding allylation product as a colorless oil which crystallised upon standing (3.60 g, 60 %); m.p. 69-70 °C, Lit.² m.p. 69-70 °C; $[\alpha]_{\text{D}}^{20} +49.9^\circ$ (*c* 2.28, CHCl₃); $[\alpha]_{\text{D}}^{22} +46.2^\circ$ (*c* 2.26, CH₂Cl₂); Lit.² $[\alpha]_{\text{D}}^{20} +47.0^\circ$ (*c* 2.36, CH₂Cl₂). IR (KBr): 3067, 2987, 2931, 2878, 1781, 1767, 1701, 1639, 1539, 1458, 1369, 1349, 1238, 1198, 769, 699 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.47-7.30 (5H, m), 5.81 (1H, tdd, *J* = 17.0 Hz, *J* = 10.0 Hz, *J* = 7.0 Hz), 5.67 (1H, d, *J* = 7.0 Hz), 5.11-5.01 (2H, m), 4.80 (1H, qt., *J* = 7.0 Hz), 3.90 (1H, sex., *J* = 7.0 Hz), 2.50 (1H, m), 2.23 (1H, m), 1.21 (3H, d, *J* = 7.0 Hz), 0.88 (3H, d, *J* = 6.5 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 176.3, 152.7, 135.2, 133.4, 128.7 (2C), 125.6 (2C), 117.1, 78.8, 54.9, 37.9, 37.2, 16.5, 14.6; MS (EI) *m/z* (rel. intensity) 273 (M⁺, 30), 178 (16), 156 (35), 134 (42), 118 (84), 107 (30), 96 (30), 69 (100); Anal. calcd. for C₁₆H₁₉NO₃: C, 70.31; H, 7.01; N, 5.12; found: C, 70.24; H, 7.08; N, 5.15. To a solution of this product (1.00 g, 3.66 mmol) in THF/H₂O (12 mL/3 mL) at 0 °C was slowly added H₂O₂ (30 % aq., 1.66 mL, 14.63 mmol) followed by a solution of LiOH·H₂O (246 mg, 5.85 mmol) in water (2 mL). The mixture was stirred at 0 °C for 1 h before it was quenched with aq. sat. sodium sulfite to destroy excess H₂O₂. Most of the ethereal solvent was evaporated and the pH of the aqueous phase was adjusted to 12-13 upon addition of NaOH (1 M). Extraction with CH₂Cl₂ (3 × 20 mL) removed the chiral auxillary. The aqueous phase was then acidified with HCl (2 M) until pH 1 to 2 was reached and extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with brine (50 mL), they were dried (MgSO₄), filtered and evaporated, and the residue was purified by flash chromatography (hexane:EtOAc, 1:2) to yield acid **20** as a pale yellow oil (387 mg, 93%); the e.e. was determined by chiral GC analysis (Ifadex 7, 25m, H₂ 0.5 bar) to be 96 % [with temperature program: 220/60 1/min 320/10min iso 350: (+): R_t = 26.33 min; (-): R_t = 28.29 min]. $[\alpha]_{\text{D}}^{20} +9.2^\circ$ (*c* 1.42, CHCl₃); Lit.² $[\alpha]_{\text{D}}^{26} +10.52^\circ$ (*c* 1.14, CHCl₃); IR (film): 3081, 2980, 1939, 1708, 1643, 1418, 1287, 1246, 1216, 918 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 11.30 (1H, br s), 5.78 (1H, tdd, *J* = 17.0 Hz, *J* = 10.0 Hz, *J* = 7.0 Hz), 5.14-5.04 (2H, m), 2.57 (1H, sex., *J* = 7.0 Hz), 2.46 (1H, m), 2.22 (1H, m), 1.20 (3H, d, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 182.6, 135.1, 117.1, 39.1, 37.4, 16.3; MS (EI) *m/z* (rel. intensity) 114 (M⁺, 14), 99 (19), 69 (88), 55 (14), 41 (100); HRMS (EI): calcd. for C₆H₁₂O₂: 114.0681; found: 114.0681.

3-Oxo-hexanoic acid *tert*-butyl ester (21). *t*-BuOH (15.1 mL, 157.99 mmol) and a catalytic amount of *t*-BuOK (177 mg, 1.58 mmol) were successively added to a solution of 3-oxo-hexanoic acid ethyl ester (5.00 mL, 31.60 mmol) in benzene (250 mL). The flask was equipped with a Soxhlet apparatus whose upper trap was filled with activated molecular sieves 3Å. The mixture was refluxed for 6 days, cooled to ambient temperature and quenched with aq. sat. NH₄Cl (200 mL). The aqueous layer was extracted with EtOAc (2 × 100 mL), the combined organic phases were washed with brine (100 mL), they were dried (MgSO₄), filtered and evaporated, and the crude product was purified by flash chromatography (hexane:EtOAc, 9:1) to yield an orange oil which was further purified by distillation under vacuum (7 mbar: 86 °C, Lit.³: 3 mbar: 66-67 °C), thus

² Sibi, M. P.; Rheault, T. R. *J. Am. Chem. Soc.* **2000**, *122*, 8873-8879.

³ Dubois, E. J. et al. *Bull. Soc. Chim. Fr.* **1963**, 1491-1496.

affording product **21** as a colorless oil (3.47 g, 59 %). IR (film): 2969, 2936, 2877, 1738, 1716, 1644, 1458, 1410, 1394, 1369, 1320, 1254, 1150, 1065, 956, 844 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.33 (2H, s), 2.51 (2H, t, $J = 7.0$ Hz), 1.67-1.59 (2H, m), 1.47 (9H, s), 0.93 (3H, t, $J = 7.0$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 203.3, 166.5, 81.8, 50.7, 44.8, 28.0 (3C), 16.9, 13.6; MS (EI) m/z (rel. intensity) 186 (M^+ , 0.9), 130 (17), 113 (19), 102 (8), 57 (100). Anal. calcd. for $\text{C}_{10}\text{H}_{18}\text{O}_3$: C, 64.49; H, 9.74; found: C, 64.41; H, 9.68.

(3R)-3-Hydroxy-hexanoic acid tert-butyl ester (22). *Preparation of the catalyst:* $[\text{RuCl}_2\text{COD}]_n$ (100 mg, 0.36 mmol) and *R*-BINAP (245 mg, 0.39 mmol) were placed in a 50 mL Schlenk tube which was subjected to three high-vacuum/argon cycles. Freshly distilled toluene (20 mL, degassed) and Et_3N (0.8 mL) were added via syringe, the system was sealed. a safety metal grid was installed, and the closed vessel was refluxed (oil bath 140 $^\circ\text{C}$) for 4 h at which time a deeply red colored solution had formed. The heating was discontinued and the mixture was slowly cooled to *ca.* 5 $^\circ\text{C}$, vigorously stirred and opened under argon. The toluene was slowly removed in vacuo and the remaining deep red, air-sensitive solid was dissolved in freshly distilled THF (15 mL) and used immediately in the next step. *Hydrogenation:* An oven-dried 250 mL autoclave was charged with ester **21** (1.25 g, 6.71 mmol), MeOH (40 mL) and the freshly prepared solution of the Ru-BINAP catalyst (0.05 equiv.) in THF. The autoclave was closed, filled with H_2 (10 bar) and heated to 90-95 $^\circ\text{C}$ over 17 hr. After venting of the autoclave, the reaction mixture was evaporated and the residue was purified by flash chromatography (hexane:EtOAc, 7:1) to yield alcohol **22** as a colorless oil (1.04 g, 83%). The e.e. was determined to be 98 % by chiral GC analysis [30 m TBDMS- β -CD, H_2 0.8 bar, temperature program: 200/60 1/min 100 5/min 180 iso 10 min; (–)-isomer: $R_t = 44.53$ min; (+)-isomer: $R_t = 44.72$ min]. $[\alpha]_D^{20} -25.1^\circ$ (*c* 1.4, CHCl_3) [data of enantiomer with 94% ee:⁴ $[\alpha]_D^{20} +23.0^\circ$ (*c* 1, CHCl_3)]. IR (film): 3442, 2961, 2933, 2874, 1729, 1715, 1393, 1368, 1257, 1155 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.99-3.94 (1H, m), 3.06 (1H, d, $J = 4.0$ Hz), 2.42 (1H, dd, $J = 16.0$ Hz, $J = 3.5$ Hz), 2.31 (1H, dd, $J = 16.0$ Hz, $J = 8.5$ Hz), 1.54-1.35 (4H, m), 1.47 (9H, s), 0.93 (3H, t, $J = 7.0$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 172.6, 81.2, 67.8, 42.3, 38.6, 28.1 (3C), 18.6, 14.0; MS (EI) m/z (rel. intensity) 145 (9), 127 (11), 115 (9), 97 (11), 89 (10), 73 (9), 57 (100); HRMS (CI): calcd. for $\text{C}_{10}\text{H}_{21}\text{O}_3$: 189.1491; found: 189.1490 (MH^+). Anal. calcd. for $\text{C}_{10}\text{H}_{20}\text{O}_3$: C, 63.80; H, 10.71; C, 63.95; H, 10.66.

(2'S,3R)-(+)-3-(2-Methyl-pent-4-enoyloxy)-hexanoic acid tert-butyl ester (23). DMAP (1.67 g, 13.67 mmol) and EDCI (2.62 g, 13.67 mmol) were added to a solution of acid **20** (96 % e.e., 520 mg, 4.56 mmol) and alcohol **22** (98 % e.e., 858 mg, 4.56 mmol) in dry CH_2Cl_2 (40 mL). The mixture was stirred at ambient temperature for 16 h before it was quenched with water (40 mL). The aqueous phase was extracted three times with CH_2Cl_2 (25 mL) and the combined organic layers were washed with brine (50 mL). Drying (MgSO_4), filtration and evaporation of the solvents afforded a colorless residue which was purified by flash chromatography (hexane:EtOAc, 4:1) to provide ester **23** as a colorless oil (1.13 g, 87 % yield). The d.e. was determined by chiral HPLC

⁴ Duthaler, R. O.; Herold, P.; Lotterbach, W.; Oertle, K.; Riediker, M. *Angew. Chem., Int. Ed. Engl.* **1989**, 28, 495.

analysis (250 mm Chiralpack AD, 4.6 mm i. D. n-Heptan:2-Propanol = 95:5, 0.5 mL/min, 298 K, 1.1 Mpa, UV, 220 nm) to be de = 96.4. $[\alpha]_{\text{D}}^{20} +11.7^{\circ}$ (*c* 2.1, CHCl₃); IR (KBr): 3079, 2976, 2936, 2876, 1736, 1642, 1549, 1368, 1160, 916 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.82-5.68 (1H, m), 5.27-5.18 (1H, m), 5.10-5.01 (2H, m), 2.50-2.37 (4H, m), 2.23-2.12 (1H, m), 1.68-1.47 (2H, m), 1.44 (9H, s, ^tBu), 1.41-1.23 (2H, m), 1.14 (3H, d, *J* = 7.0 Hz), 0.92 (3H, t, *J* = 7.5 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 175.3, 169.6, 135.5, 116.8, 80.7, 70.3, 40.6, 39.3, 37.7, 36.1, 28.0 (3C), 18.4, 16.6, 13.8; MS (EI) *m/z* (rel. intensity) 284 (M⁺, 4), 228 (15), 211 (16), 170 (5), 114 (86), 97 (98), 69 (78), 57 (100), 41 (49); HRMS (CI): calcd. for C₁₆H₂₉O₄: 285.2066; found: 285.2064 (MH⁺). Anal. calcd. for C₁₆H₂₈O₄: C, 67.57; H, 9.92; found: C, 67.41; H, 9.86.

(2'S,3R)-(+)-3-(2-Methyl-pent-4-enoyloxy)-hexanoic acid (24a). To a solution of ester **23** (1.20 g, 4.22 mmol) in CH₂Cl₂ (20 mL) at 0 °C were added Et₃SiH (0.45 mL, 2.83 mmol) and trifluoroacetic acid (4.20 mL, 54.85 mmol). The mixture was stirred at room temperature for 1.5 h before the solvent was evaporated. Remaining trifluoroacetic acid was removed by repeated azeotropic distillation with toluene, and the residue was subjected to flash chromatography (hexane:EtOAc, 3:1, see Note) to afford acid **24a** (960 mg, quant.) as a colorless oil. The d.e. was determined by chiral HPLC analysis (250 mm Chiralcel OD-R, 4.5 mm i. D. Acetonitrile / 0.1 % TFA = 30/70 (v/v), 0.5 mL/min, 298 K, 3.4 MPa, UV, 220 nm, detector RI) to be de = 98 %. $[\alpha]_{\text{D}}^{20} +5.3^{\circ}$ (*c* 1.16, CHCl₃). IR (film): 3000, 2964, 1937, 1737, 1715, 1643, 1460, 1438, 1416, 1381, 1180, 917 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.45 (1H, br s), 5.74 (1H, tdd, *J* = 17.0 Hz, *J* = 10.0 Hz, *J* = 7.0 Hz), 5.27-5.19 (1H, m), 5.10-5.00 (2H, m), 2.69-2.36 (4H, m), 2.21-2.11 (1H, m), 1.70-1.51 (2H, m), 1.43-1.28 (2H, m), 1.14 (3H, d, *J* = 7.0 Hz), 0.93 (3H, t, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 176.1, 175.5, 135.3, 116.8, 69.8, 39.3, 39.3, 38.8, 37.6, 36.0, 18.3, 16.5, 13.7; MS (EI) *m/z* (rel. intensity) 228 (M⁺, 2), 210 (1), 133 (5), 114 (34), 97 (50), 69 (100), 41 (40); HRMS (EI): calcd. for C₁₂H₂₀O₄: 228.13626; found: 228.1363. Anal. calcd. for C₁₂H₂₀O₄: C, 63.14; H, 8.83; found: C, 63.06; H, 8.78.

(3S,4R,2'R,4'S,5'S)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-5-(tert-butyl-dimethylsilyloxy)-3-methoxymethoxy-4-methyl-pentan-2-one (25). Sulfone **11** (329 mg, 1.23 mmol) and silyl enol ether **18** (500 mg, 1.23 mmol) were dried *separately* using three cycles of high-vacuum / argon and were dissolved in freshly distilled CH₂Cl₂ (5 mL each). The solution of sulfone **11** was then added to the flask containing **18** at -78 °C, followed by the addition of SnCl₄ (144 μL, 1.23 mmol) via syringe. The resulting mixture was stirred at -78 °C for 90 min before it was quenched with a sat. aq. NH₄Cl (10 mL). The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL), the combined organic layers were washed with water (25 mL) and brine (25 mL), they were dried (Na₂SO₄), filtered and evaporated, and the crude product was purified by flash chromatography (hexane:EtOAc, 98:2) to yield ketone **21** as a colorless oil (471 mg, 86%). $[\alpha]_{\text{D}}^{20} -39.3^{\circ}$ (*c* 0.87, C₆H₆). IR (KBr): 2957, 2931, 2895, 2858, 1722, 1642, 1471, 1464, 1385, 1255, 1156, 1091, 1036, 838, 777 cm⁻¹; ¹H NMR (600 MHz, C₆D₆) δ 5.84 (1H, dddd, *J* = 17.0 Hz, *J* = 10.5 Hz, *J* = 7.5 Hz, *J* = 6.0 Hz), 5.05 (1H, qd, *J* = 17.0 Hz, *J* = 2.0 Hz), 5.01 (1H, qtd, *J* = 10.5

Hz, $J = 2.0$ Hz), 4.64 (1H, m), 4.63 (1H, d, $J = 6.5$ Hz), 4.60 (1H, d, $J = 6.5$ Hz), 4.40 (1H, d, $J = 3.5$ Hz), 3.78 (1H, ddd, $J = 8.0$ Hz, $J = 5.5$ Hz, $J = 5.0$ Hz), 3.56 (1H, dd, $J = 10.0$ Hz, $J = 8.5$ Hz), 3.45 (1H, dd, $J = 10.0$ Hz, $J = 5.5$ Hz), 3.22 (3H, s), 2.85 (1H, dd, $J = 16.5$ Hz, $J = 7.0$ Hz), 2.33 (1H, dd, $J = 16.5$ Hz, $J = 6.0$ Hz), 2.26-2.20 (2H, m), 1.99 (1H, dddd, $J = 13.5$ Hz, $J = 7.5$ Hz, $J = 6.0$ Hz, $J = 1.5$ Hz), 1.91 (1H, m), 1.65 (1H, ddd, $J = 12.5$ Hz, $J = 7.0$ Hz, $J = 3.5$ Hz), 1.50 (1H, ddd, $J = 12.5$, $J = 7.5$ Hz, $J = 7.0$ Hz), 0.96 (9H, br s), 0.92 (3H, d, $J = 7.0$ Hz), 0.71 (3H, d, $J = 7.0$ Hz), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (125 MHz, C_6D_6) δ 208.7, 136.2, 116.1, 97.1, 82.2, 80.7, 73.2, 64.9, 55.8, 46.5, 40.3, 38.2, 36.2, 35.5, 26.1 (3C), 18.4, 14.0, 11.0, -5.3, -5.4; MS (EI) m/z (rel. intensity) 414 (12), 201 (23), 171 (37), 145 (39), 125 (100), 115 (14), 107 (32), 101 (11), 89 (24), 83 (21), 81 (41), 79 (9), 73 (18), 55 (15), 45 (82); HRMS (CI): calcd. for $\text{C}_{22}\text{H}_{43}\text{O}_5\text{Si}$: 415.2880; found: 415.2878 (MH^+); Anal. calcd. for $\text{C}_{22}\text{H}_{42}\text{O}_5\text{Si}$: C, 63.73; H, 10.21; found: C, 63.61; H, 10.12.

(2*S*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-5-(tert-butyl-dimethyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentan-2-ol (26). A solution of L-Selectride (1 M, 1.41 mL, 1.41 mmol) was added to a solution of ketone **25** (325 mg, 0.788 mmol) in THF (5 mL) at -78°C . The mixture was stirred at -78°C for 90 min, before it was quenched with a sat. solution of Rochelle's salts (20 mL) and allowed to stirred for 16 hr at room temperature. The aqueous phase was extracted with EtOAc (3×20 mL), the combined organic layers were washed with brine (25 mL) before being dried (Na_2SO_4), filtered, and evaporated. The crude product was purified by flash chromatography (hexane:EtOAc, 7:1) to yield the alcohol **26** as a colorless oil (237 mg, 72%). $[\alpha]_{\text{D}}^{20} -39.5^\circ$ (c 1.08, C_6H_6). IR (film): 3466, 3074, 2956, 2929, 2857, 1642, 1471, 1463, 1385, 1256, 1151, 1092, 1034, 915, 837, 776 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 5.89 (1H, tdd, $J = 17.0$ Hz, $J = 10.0$ Hz, $J = 7.0$ Hz), 5.08 (1H, dd, $J = 17.0$ Hz, $J = 1.5$ Hz), 5.02 (1H, dd, $J = 10.0$ Hz, $J = 1.5$ Hz), 4.69 (1H, d, $J = 6.5$ Hz), 4.62 (1H, d, $J = 6.5$ Hz), 4.63-4.59 (1H, m), 4.16 (1H, ddd, $J = 9.5$ Hz, $J = 7.0$ Hz, $J = 2.5$ Hz), 3.85 (1H, td, $J = 8.5$ Hz, $J = 5.5$ Hz), 3.66 (1H, dd, $J = 7.0$ Hz, $J = 3.0$ Hz), 3.59 (1H, dd, $J = 10.0$ Hz, $J = 8.0$ Hz), 3.52 (1H, dd, $J = 10.0$ Hz, $J = 5.5$ Hz), 3.13 (3H, s), 2.35-2.29 (1H, m), 2.10-2.03 (1H, m), 2.00-1.65 (2H, m), 1.69 (1H, ddd, $J = 13.5$ Hz, $J = 9.0$ Hz, $J = 2.5$ Hz), 1.61-1.57 (2H, m), 1.57 (1H, ddd, $J = 13.5$ Hz, $J = 9.5$ Hz, $J = 3.5$ Hz), 0.97 (9H, s), 0.95 (3H, d, $J = 7.0$ Hz), 0.77 (3H, d, $J = 7.0$ Hz), 0.06 (6H, br s); ^{13}C NMR (100 MHz, C_6D_6) δ 136.3, 116.1, 99.0, 85.5, 80.4, 74.2, 69.9, 65.6, 55.6, 40.9, 40.8, 37.9, 36.3, 35.7, 26.1, 18.4, 14.1, 10.9, -5.3, -5.4; MS (EI) m/z (rel. intensity) 343 (10), 327 (18), 297 (15), 203 (28), 169 (25), 145 (21), 125 (87), 107 (27), 81 (5), 45 (100); HRMS (CI): calcd. for $\text{C}_{22}\text{H}_{45}\text{O}_5\text{Si}$: 417.3036; found: 417.3038 (MH^+). Anal. calcd. for $\text{C}_{22}\text{H}_{44}\text{O}_5\text{Si}$: C, 63.42; H, 10.64; found: C, 63.29; H, 10.58.

(2*R*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-5-(tert-butyl-dimethyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentan-2-ol (27). A 3-necked flask was charged with ketone **25** (1.484 g, 3.58 mmol) and Et_2O (80 mL). LiI (4.79 g, 35.8 mmol) was added and the resulting mixture was stirred for 5 min at -40°C before it was cooled to -100°C and LiAlH_4 (272 mg, 7.16 mmol) was added in one portion. After stirring for 1h, additional LiAlH_4 (408 mg, 10.74 mmol) was introduced. The mixture was stirred for 4 h before it was carefully quenched with sat.

aq. Na₂SO₄. The precipitate was filtered off and was carefully washed with EtOAc, the filtrate was evaporated and the residue was purified by flash chromatography (hexane-EtOAc, 10/1 → 4/1) to yield alcohol **27** (1.04 g, 70%) and, as a second fraction, alcohol **26** (159 mg, 11%) as a colorless oil each. Data of compound **27**: $[\alpha]_D^{20}$ -2.4° (*c* 0.5, C₆H₆). IR (KBr): 3480, 3076, 2958, 2929, 2897, 2858, 1642, 1471, 1463, 1255, 1149, 1092, 1034, 918, 837, 776 cm⁻¹; ¹H NMR (300 MHz, C₆D₆) δ 5.71 (1H, tdd, *J* = 7.0 Hz, *J* = 10.0 Hz, *J* = 17.0 Hz), 5.05-4.95 (2H, m), 4.78 (1H, d, *J* = 6.5 Hz), 4.74 (1H, d, *J* = 6.5 Hz), 4.14 (1H, tdt, *J* = 3.0 Hz, *J* = 7.5 Hz, *J* = 10.0 Hz), 4.05 (1H, ddd, *J* = 2.0 Hz, *J* = 6.5 Hz, *J* = 10.0 Hz), 3.81 (1H, dd, *J* = 3.5 Hz, *J* = 6.5 Hz), 3.70 (1H, td, *J* = 6.0 Hz, *J* = 8.5 Hz), 3.66 (1H, dd, *J* = 8.0 Hz, *J* = 10.0 Hz), 3.59 (1H, dd, *J* = 6.5 Hz, *J* = 10.0 Hz), 3.24 (3H, s), 2.49-2.36 (1H, m), 2.17-2.07 (1H, m), 1.97-1.88 (2H, m), 1.85-1.77 (1H, m), 1.61 (1H, td, *J* = 10.0 Hz, *J* = 14.0 Hz), 1.44 (2H, dd, *J* = 5.0 Hz, *J* = 7.5 Hz), 1.17 (3H, d, *J* = 7.0 Hz), 0.99 (9H, s), 0.67 (3H, d, *J* = 7.0 Hz), 0.10 (3H, s), 0.09 (3H, s); ¹³C NMR (75 MHz, C₆D₆) δ 135.6, 116.5, 98.7, 82.9, 80.6, 78.0, 72.6, 66.0, 55.7, 40.9, 39.90, 37.2, 35.5, 35.4, 26.1 (3C), 18.4, 13.9, 11.6, -5.2, -5.3; MS (EI) *m/z* (rel. intensity) 385 (3), 327 (22), 297 (25), 203 (35), 169 (34), 125 (100), 81 (53), 45 (98); HRMS (CI): calcd. for C₂₂H₄₅O₅Si: 417.3036; found: 417.3035 (MH⁺); Anal. calcd. for C₂₂H₄₄O₅Si: C, 63.42; H, 10.64; Si, 6.74; found: C, 63.32; H, 10.58; Si, 6.65.

(2R,3S,4S,2'R,4'S,5'S)-(-)-[5-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-4-(4-methoxybenzyloxy)-3-methoxymethoxy-2-methyl-pentyloxy]-tert-butyl-dimethyl-silane (28a). HBr (48 %, 1.69 mL, 10.08 mmol) was added to p-methoxybenzyl alcohol (1.25 mL, 10.08 mmol) and the resulting mixture was stirred for 20 min. The reaction was quenched at 0°C with sat. aq. NaHCO₃ (20 mL) and diluted with Et₂O (20 mL). The aqueous phase was extracted with Et₂O (3 × 20 mL), the combined organic layers were washed with brine (50 mL), they were dried (Na₂SO₄), filtered and evaporated to give p-MeOC₆H₄CH₂Br (1.61 g, 80%) as a pale yellow oil which was used directly in the next step. To a solution of alcohol **26** (100 mg, 0.24 mmol) in DMF (1 mL) at 0 °C was added p-MeOC₆H₄CH₂Br (70 μ L, 0.48 mmol) followed by a solution of KHMDS (1 M in THF, 0.48 mL, 0.48 mmol). The mixture was stirred at rt for 16 h before it was quenched with aq. sat. NH₄Cl (5 mL) and Et₂O (5 mL). The aqueous phase was extracted three times with Et₂O (5 mL), the combined organic layers were washed with brine (20 mL), they were dried (Na₂SO₄), filtered and evaporated, and the crude product was purified by flash chromatography (CH₂Cl₂) to yield compound **28a** as a colorless oil (99 mg, 77%). $[\alpha]_D^{20}$ -94.8° (*c* 1.2, C₆H₆). IR (KBr): 3074, 2954, 2931, 2857, 1641, 1613, 1514, 1464, 1249, 1091, 1038, 837, 776 cm⁻¹; ¹H NMR (300 MHz, C₆D₆) δ 7.36 (2H, d, *J* = 8.5 Hz), 6.83 (2H, d, *J* = 8.5 Hz), 5.89 (1H, dddd, *J* = 17.0 Hz, *J* = 10.0 Hz, *J* = 7.0 Hz, *J* = 6.5 Hz), 5.13-5.02 (2H, m), 4.90 (1H, d, *J* = 6.5 Hz), 4.80 (1 H, d, *J* = 11.0 Hz), 4.75 (1H, d, *J* = 6.5 Hz), 4.68 (1H, d, *J* = 11.0 Hz), 4.40 (1H, m), 4.09 (1H, ddd, *J* = 10.0 Hz, *J* = 6.5 Hz, *J* = 2.0 Hz), 3.93 (1H, dd, *J* = 6.5 Hz, *J* = 3.5 Hz), 3.84-3.78 (1H, m), 3.58 (1H, dd, *J* = 9.5 Hz, *J* = 6.5 Hz), 3.31 (6H, s), 2.34-2.24 (1H, m), 2.19-2.11 (1H, m), 2.11-2.00 (1H, m), 2.00-1.91 (1H, m), 1.83 (1H, ddd, *J* = 13.5 Hz, *J* = 10.0 Hz, *J* = 2.5 Hz), 1.58 (1H, ddd, *J* = 13.5 Hz, *J* = 10.0 Hz, *J* = 3.0 Hz), 1.50 (2H, dd, *J* = 7.0 Hz, *J* = 5.0 Hz), 1.15 (3H, d, *J* = 7.0 Hz), 1.01 (9H, s), 0.76 (3H, d, *J* = 7.0 Hz), 0.12 (3H, s), 0.11 (3H, s); ¹³C NMR (75 MHz, C₆D₆) δ 159.6, 136.5,

132.0, 129.6 (2C), 116.1, 114.0 (2C), 98.5, 80.3, 79.8, 78.9, 73.6, 73.4, 66.5, 55.8, 54.8, 40.7, 39.4, 37.4, 36.3, 35.8, 26.2 (3C), 18.6, 14.2, 12.1, -5.1 (2C); MS (ESI pos.) m/z : 575 ($M+K^+$), 559 ($M+Na^+$); HRMS (CI): calcd. for $C_{30}H_{52}O_6Si$: 537.3611; found: 537.3610 (MH^+).

(2*R*,3*S*,4*S*,2'*R*,4'*S*,5'*S*)-5-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-4-(4-methoxy-benzyloxy)-3-methoxymethoxy-2-methyl-pentan-1-ol (28). To a solution of silyl ether **28a** (97 mg, 0.18 mmol) in THF was added TBAF in three portions (1 M in THF, 199 μ L, 0.199 mmol each). After stirring for 1.5 h, the solvent was evaporated and the crude product was subjected to flash chromatography (hexane-EtOAc, 3/1) providing alcohol **28** as a colorless oil (71 mg, 93%); $[\alpha]_D^{20}$ -113.4° (c 2.26, C_6H_6). IR (KBr): 3470, 3074, 2959, 2941, 1641, 1613, 1514, 1464, 1249, 1091, 1036, 916, 822 cm^{-1} ; 1H NMR (400 MHz, C_6D_6) δ 7.29 (2H, d, J = 8.0 Hz), 6.81 (2H, d, J = 8.5 Hz), 5.87 (1H, dddd, J = 17.0 Hz, J = 10.5 Hz, J = 8.0 Hz, J = 7.0 Hz), 5.10-5.01 (2H, m), 4.85 (1H, d, J = 6.5 Hz), 4.68 (1H, d, J = 11.0 Hz), 4.66 (1H, d, J = 11.0 Hz), 4.54 (1H, d, J = 6.5 Hz), 4.37-4.30 (1H, m), 4.07 (1H, ddd, J = 10.5 Hz, J = 7.0 Hz, J = 2.5 Hz), 3.79 (1H, td, J = 8.5 Hz, J = 5.5 Hz), 3.76 (1H, dd, J = 7.0 Hz, J = 5.0 Hz), 3.63 (2H, d, J = 7.0 Hz), 3.31 (3H, s), 3.16 (3H, s), 2.30-2.22 (1H, m), 2.07-1.90 (3H, m), 1.68 (1H, ddd, J = 14.0 Hz, J = 10.0 Hz, J = 2.5 Hz), 1.56 (1H, ddd, J = 14.0 Hz, J = 10.5 Hz, J = 3.0 Hz), 1.49-1.42 (2H, m), 0.95 (3H, d, J = 7.0 Hz), 0.76 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 159.8, 136.5, 131.6, 129.7 (2C), 116.1, 114.1 (2C), 98.9, 81.6, 80.4, 79.2, 74.0, 73.3, 65.6, 55.8, 54.8, 40.6, 38.9, 37.4, 36.3, 35.7, 14.3, 12.1; MS (EI) m/z (rel. intensity) 166 (8), 125 (17), 122 (10), 121 (100), 101 (6), 81 (4), 45 (15); HRMS (CI): calcd. for $C_{24}H_{39}O_6$: 423.2747; found: 423.2742 (MH^+). Anal. calcd. for $C_{24}H_{38}O_6$: C, 68.22; H, 9.06; found: C, 68.13; H, 9.07.

(-)-(2*S*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-2-(5-allyl-4-methyl-tetrahydrofuran-2-yl-methyl)-3-methoxymethoxy-4-methyl-tetrahydrofuran (29). PPh_3 (65 mg, 0.248 mmol) and imidazole (17 mg, 0.248 mmol) were dried in a round bottomed flask by three vacuum/argon cycles. Freshly distilled CH_2Cl_2 (1 mL) was added, followed by the addition of I_2 (63 mg, 0.248 mmol) and a solution of the alcohol **28** (70 mg, 0.166 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 4 h, the solvent was evaporated and the crude product was purified by flash chromatography (hexane-EtOAc, 6/1) to yield tetrahydrofuran **29** as a colorless oil (16 mg, 34%). $[\alpha]_D^{20}$ -23.0° (c 0.88, $CHCl_3$). IR (KBr): 3076, 2960, 2931, 2877, 1641, 1459, 1384, 1150, 1093, 1043, 918 cm^{-1} ; 1H NMR (600 MHz, $CDCl_3$) δ 5.80 (1H, dddd, J = 17.0 Hz, J = 10.0 Hz, J = 7.0 Hz, J = 6.5 Hz), 5.09 (1H, qappd, J = 17.0 Hz, J = 1.5 Hz), 5.01 (1H, dtd, J = 10.0 Hz, J = 2.0 Hz, J = 1.0 Hz), 4.67 (1H, d, J = 7.0 Hz), 4.60 (1H, d, J = 7.0 Hz), 4.25 (1H, m), 4.09 (1H, dd, J = 8.5 Hz, J = 7.0 Hz), 3.97 (1H, td, J = 8.5 Hz, J = 4.5 Hz), 3.89 (1H, ddd, J = 7.2 Hz, J = 7.0 Hz, J = 5.0 Hz), 3.72 (1H, dd, J = 4.0 Hz, J = 2.0 Hz), 3.35 (3H, s), 3.29 (1H, dd, J = 8.5 Hz, J = 5.5 Hz), 2.31 (1H, m), 2.29 (1H, m), 2.24 (1H, m), 2.15 (1H, m), 1.78 (2H, m), 1.74 (2H, m), 1.04 (3H, d, J = 7.0 Hz), 0.92 (3H, d, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 116.3, 95.7, 84.6, 80.4, 78.3, 74.7, 73.2, 55.6, 40.7, 40.3, 36.5, 35.8, 35.2, 17.1, 14.0; MS (ESI pos.) m/z 307 ($M+Na^+$); HRMS (CI): calcd. for $C_{16}H_{29}O_4$: 285.2066; found: 285.2064 (MH^+). The relative stereochemistry was confirmed by NOE analysis (NMR 600 MHz).

(2*S*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-5-(*tert*-butyl-dimethyl-silanyloxy)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentane (30).

KHMDS (1.15 g, 5.76 mmol) and TBDPSCl (1.5 mL, 5.76 mmol) were successively added to a solution of compound **26** (2 g, 4.8 mmol) in THF (10 mL) at 0°C. The mixture was stirred overnight at ambient temperature, before it was quenched with aq. sat. NH₄Cl and repeatedly extracted with CH₂Cl₂. The organic layer was dried over Na₂SO₄, filtered and evaporated, and the residue was purified by flash chromatography (hexanes:EtOAc, 30:1 then 6:1) to give recovered **26** (350 mg 18%) and compound **30** as colorless oil. (2.0 g, 77%). $[\alpha]_D^{20}$ -9.3° (*c* 0.385, CHCl₃). IR (film): 3072, 3050, 2957, 2930, 2889, 2857, 1642, 1472, 1428, 1255, 1110, 1088, 1037, 914, 836, 776, 703, 611, 506 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.74-7.70 (4H, m), 7.42-7.36 (6H, m), 5.71 (1H, ddt, *J* = 17.4 Hz, *J* = 10.2 Hz, *J* = 6.3 Hz), 5.00 (1H, ddd, *J* = 17.2 Hz, *J* = 3.6 Hz, *J* = 1.6 Hz), 4.95 (1H, ddd, *J* = 10.2 Hz, *J* = 2.2 Hz, *J* = 1.2 Hz), 4.44 (2H, s), 4.10 (1H, dd, *J* = 7.5 Hz, *J* = 4.3 Hz), 3.93 (1H, ddd, *J* = 12.5 Hz, *J* = 8.1 Hz, *J* = 4.5 Hz), 3.70 (1H, dd, *J* = 5.9 Hz, *J* = 5.1 Hz), 3.68 (1H, dd, *J* = 9.9 Hz, *J* = 5.3 Hz), 3.35 (1H, dd, *J* = 9.4 Hz, *J* = 4.4 Hz), 3.28 (1H, dd, *J* = 9.9 Hz, *J* = 5.3 Hz), 3.25 (3H, s), 2.08 (2H, m), 2.03 (1H, m), 1.99 (1H, m), 1.83 (1H, ddd, *J* = 13.6 Hz, *J* = 8.7 Hz, *J* = 4.4 Hz), 1.50 (1H, m), 1.35 (1H, m), 1.30 (1H, m), 1.06 (9H, s), 0.94 (3H, d, *J* = 6.7 Hz), 0.89 (9H, s), 0.72 (3H, d, *J* = 7.0 Hz), 0.03 (3H, s), 0.02 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ 136.3 (4C), 134.7 (2C), 129.6, 127.7 (4C), 127.5 (2C), 115.9, 97.6, 81.0, 80.0, 73.1, 72.8, 66.4, 55.9, 40.3, 40.1, 36.5, 35.9, 35.5, 27.3 (3C), 26.1 (3C), 19.6, 18.5, 14.0, 13.4, -5.2 (2C); MS (EI) *m/z* (rel. intensity): 654 (11), 597 (13), 407 (32), 337 (16), 213 (12), 205 (22), 199 (15), 195 (10), 183 (10), 151 (10), 135 (21), 125 (100), 115 (5), 109 (12), 107 (33), 97 (9), 91 (14), 89 (20), 81 (49), 79 (9), 73 (21), 55 (12), 45 (26), 43 (12); HRMS (CI): calcd. for C₃₈H₆₃O₅Si₂: 655.4214, found: 655.4210 (MH⁺). Anal. calcd. for C₃₈H₆₂O₅Si₂: C, 69.67; H, 9.54; Si, 8.57; found: C, 69.78; H, 9.54; Si, 8.50.

(2*S*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentan-5-ol (31).

p-TsOH (377 mg, 1.98 mmol) was added to a solution of compound **30** (1.0 g, 1.53 mmol) in MeOH (10 mL) and water (1 mL). After stirring for 1 h, the mixture was poured into water and extracted 3 times with ether. The combined organic layers were dried with Na₂SO₄, filtered and concentrated, and the residue was purified by flash chromatography (hexanes:EtOAc, 6:1) to give product **31** as a colorless oil (595 mg, 73%). $[\alpha]_D^{20}$ -30.5° (*c* 0.2, CHCl₃). IR (film): 3450, 3072, 3048, 2960, 2931, 2891, 2857, 1642, 1589, 1471, 1427, 1387, 1152, 1105, 1034, 915, 822, 739, 703, 612, 508 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.92-7.84 (4H, m), 7.28-7.21 (6H, m), 5.76 (1H, dddd, *J* = 17.5 Hz, *J* = 10.5 Hz, *J* = 7.5 Hz, *J* = 6.5 Hz), 5.06-4.97 (2H, m), 4.50 (1H, ddd, *J* = 8.0 Hz, *J* = 5.0 Hz, *J* = 3.0 Hz), 4.44 (1H, d, *J* = 6.5 Hz), 4.36 (1H, d, *J* = 6.5 Hz), 4.20-4.13 (1H, m), 3.69-3.53 (4H, m), 3.09 (3H, s), 2.24-2.18 (1H, m), 2.16-2.09 (1H, m), 1.98-1.89 (2H, m), 1.86-1.76 (2H, m), 1.37-1.32 (2H, m), 1.22 (9H, s), 1.00 (3H, d, *J* = 7.0 Hz), 0.63 (3H, d, *J* = 7.0 Hz); ¹³C NMR (100 MHz, C₆D₆) δ 136.7 (2C), 136.6 (2C), 136.5, 134.7, 134.1, 130.1, 130.0, 128.3-127.8 (4C), 115.9, 97.9, 82.2, 80.3, 73.5, 73.1, 66.5, 55.7, 40.7, 40.4, 36.7, 36.2, 35.9, 27.5 (3C), 19.8, 14.8, 13.4; MS (EI) *m/z* (rel. intensity) 451 (13),

407 (31), 253 (17), 221 (15), 199 (29), 183 (13), 151 (9), 135 (19), 125 (100), 115 (3), 107 (37), 97 (13), 91 (12), 81 (59), 79 (12), 55 (16), 45 (36), 43 (17); MS (ESI pos.) m/z 563 ($M+Na^+$); HRMS (CI): calcd. for $C_{32}H_{49}O_5Si$: 541.3349; found: 541.3351 (MH^+). Anal. calcd. for $C_{32}H_{48}O_5Si$: C, 71.07; H, 8.95; found: C, 70.94; H, 8.87.

(2*S*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-5-iodo-pentane (32a). A two-necked, flame-dried, 25 mL flask was charged with compound **31** (457 mg, 0.85 mmol) in toluene (8.5 mL), followed by addition of imidazol (431 mg, 1.7 mmol), triphenylphosphine (333 mg, 1.27 mmol) and iodine (431 mg, 1.7 mmol). The flask was protected from light and the resulting mixture was stirred for 1 h. For work-up, the red-brown mixture was quenched with aq. sat. $Na_2S_2O_3$, the aqueous layer was extracted with EtOAc, the recombined organic layers were washed with brine, dried with Na_2SO_4 , filtered and evaporated. Flash chromatography of the residue (hexanes:EtOAc, 30:1) afforded product **32a** as a colorless oil (444 mg, 80%). $[\alpha]_D^{20}$ -31° (c 2.0, C_6H_6). IR (film): 3071, 3048, 2960, 2932, 2891, 2857, 2823, 1642, 1589, 1472, 1463, 1427, 1149, 1105, 1034, 915, 822, 739, 703, 612, 507 cm^{-1} ; 1H NMR (400 MHz, C_6D_6) δ 7.88-7.84 (4H, m), 7.31-7.21 (6H, m), 5.79 (1H, ddt, $J = 17.4$ Hz, $J = 10.2$ Hz, $J = 6.3$ Hz), 5.03 (1H, dd, $J = 17.2$ Hz, $J = 1.6$ Hz), 5.00 (1H, dd, $J = 10.1$ Hz, $J = 0.9$ Hz), 4.36 (1H, d, $J = 6.6$ Hz), 4.31 (1H, d, $J = 6.6$ Hz), 4.41 (1H, t, $J = 4.0$ Hz), 4.18 (1H, m), 3.68 (1H, dt, $J = 8.0$ Hz, $J = 5.4$ Hz), 3.44 (1H, t, $J = 4.5$ Hz), 3.35 (1H, dd, $J = 9.6$ Hz, $J = 4.2$ Hz), 3.07 (3H, s), 2.94 (1H, dd, $J = 9.9$ Hz, $J = 9.2$ Hz), 2.29 (1H, dddd, $J = 17.6$ Hz, $J = 10.5$ Hz, $J = 4.4$ Hz, $J = 2.2$ Hz), 2.16 (1H, ddd, $J = 14.2$ Hz, $J = 7.9$ Hz, $J = 6.4$ Hz), 1.96 (1H, ddd, $J = 14.0$ Hz, $J = 7.1$ Hz, $J = 6.1$ Hz), 1.90 (1H, m), 1.86 (1H, m), 1.59 (1H, ddd, $J = 13.8$ Hz, $J = 8.5$ Hz, $J = 3.0$ Hz), 1.39 (1H, ddd, $J = 12.2$ Hz, $J = 6.6$ Hz, $J = 3.1$ Hz), 1.30 (1H, dt, $J = 12.2$ Hz, $J = 7.6$ Hz), 1.20 (9H, s), 1.15 (3H, d, $J = 6.7$ Hz), 0.66 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 136.6 (2C), 136.5 (2C), 134.6, 134.5, 130.1, 130.0 (2C), 127.9 (4C), 116.0, 97.8, 83.1, 80.3, 73.5, 73.4, 55.7, 40.7, 40.3, 36.8, 36.2, 35.9, 27.5 (3C), 19.8, 17.2, 14.7, 14.1; MS (EI) m/z (rel. intensity): 650 (6), 593 (13), 409 (26), 407 (72), 333 (16), 309 (21), 253 (12), 243 (11), 225 (12), 213 (32), 199 (51), 183 (35), 181 (13), 151 (8), 135 (29), 125 (100), 115 (7), 107 (33), 97 (10), 91 (27), 81 (63), 79 (11), 55 (19), 45 (73), 43 (12); HRMS (CI): calcd. for $C_{32}H_{48}IO_4Si$: 651.2367; found: 655.2371 (MH^+). Anal. calcd. for $C_{32}H_{47}IO_4Si$: C, 59.07; H, 7.28; found: C, 58.91; H, 7.21.

(-)-2-Methyl-pent-4-enoic acid-[(2*S*, 3*S*, 4*R*, 2'*R*, 4'*S*, 5'*S*)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-6-one]-undec-8-yl ester (33). A 10 mL flame-dried Schlenk tube was charged at room temperature with Zn-Cu couple (19 mg, 0.288 mmol), a 0.4 mL toluene solution of compound **28** (125 mg, 0.192 mmol), DMA (29 μ L, 0.317 mmol) and $TMSCl$ (6 μ L, 0.048 mmol). After stirring for 1 h, the mixture was warmed to $50^\circ C$ and stirring was continued for 3-4 h. A second Schlenk tube was charged with $Pd_2(dba)_3$ (5.3 mg, 5.76 μ mol), $P(furyl)_3$ (2.7 mg, 11.52 μ mol) and toluene (0.4 mL) to give a red homogeneous solution, which turned green upon addition of a solution of freshly prepared acid chloride **24b** [from acid **24a** (44 mg, 0.192 mmol) and oxalyl chloride in CH_2Cl_2 /DMF] in toluene (0.4 mL).

[Characteristic data of acid chloride **24b**: ^1H NMR (400 MHz, C_6D_6) δ 5.72 (1H, tdd, $J = 17.0$ Hz, $J = 10.0$ Hz, $J = 7.0$ Hz), 5.27-5.17 (1H, m), 5.00 (1H, m), 4.96 (1H, m), 2.59 (1H, ddd, $J = 22.2$ Hz, $J = 11.0$ Hz, $J = 5.5$ Hz), 2.40 (1H, m), 2.36-2.31 (2H, m), 2.00 (1H, m), 1.32-1.22 (1H, m), 1.04-1.00 (7H, m), 0.68 (3H, t, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 174.6, 170.5, 135.8, 117.0, 69.2, 49.9, 39.5, 38.0, 35.7, 18.7, 18.4, 16.6, 13.7]. The mixture of the acid chloride and the palladium catalyst was then added via canula to the solution of the organozinc reagent (final concentration of *ca.* 0.2 M), and the resulting mixture was stirred overnight. For work up, the reaction was quenched with aq. sat. NH_4Cl and the mixture was filtered through a pad of Celite which was carefully rinsed with EtOAc. The combined filtrates were successively washed with aq. sat. NH_4Cl and brine, they were dried with Na_2SO_4 , filtered and evaporated. Flash chromatography of the residue (hexanes:EtOAc, 15:1) afforded product **33** as a colorless oil (60 mg, 40%). $[\alpha]_{\text{D}}^{20}$ -21.1° (*c* 1.35, CHCl_3). IR (film): 3073, 2961, 2933, 2876, 1733, 1642, 1589, 1428, 1180, 1146, 1110, 1035, 965, 916, 822, 740, 704, 612, 505 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.74-7.70 (4H, m), 7.41-7.34 (6H, m), 5.72 (2H, m), 5.24 (1H, qt, $J = 5.8$ Hz), 5.07-4.94 (4H, m), 4.37 (1H, d, $J = 6.6$ Hz), 4.33 (1H, d, $J = 6.6$ Hz), 4.16 (1H, dd, $J = 8.0$ Hz, $J = 4.0$ Hz), 3.96 (1H, m), 3.72 (1H, ddd, $J = 7.9$ Hz, $J = 5.7$ Hz, $J = 5.3$ Hz), 3.23 (3H, s), 3.15 (1H, dd, $J = 5.7$ Hz, $J = 4.6$ Hz), 2.74 (1H, dd, $J = 17.1$ Hz, $J = 3.6$ Hz), 2.63 (1H, dd, $J = 16.3$ Hz, $J = 7.0$ Hz), 2.49 (1H, dd, $J = 16.4$ Hz, $J = 5.9$ Hz), 2.47-2.35 (3H, m), 2.20 (1H, dd, $J = 17.1$ Hz, $J = 3.9$ Hz), 2.12 (1H, m), 2.10-1.97 (2H, m), 2.08 (1H, m), 1.77 (1H, ddd, $J = 13.7$ Hz, $J = 9.3$ Hz, $J = 3.7$ Hz), 1.58-1.53 (1H, m), 1.50 (1H, m), 1.47-1.42 (2H, m), 1.37-1.29 (3H, m), 1.12 (3H, d, $J = 6.8$ Hz), 1.07 (9H, s), 0.92 (3H, t, $J = 7.3$ Hz), 0.83 (3H, d, $J = 6.6$ Hz), 0.74 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 207.0, 175.4, 136.3 (2C), 136.2 (2C), 135.7, 134.4, 134.2, 129.7, 127.7 (2C), 127.6 (4C), 116.9, 115.9, 97.6, 83.6, 80.0, 73.0, 73.1, 70.1, 55.9, 48.5, 47.6, 40.4, 39.9, 39.5, 37.9, 36.5, 35.9, 35.5, 29.2, 27.3 (3C), 19.6, 18.6, 16.7, 16.3, 14.1, 14.0; MS (EI) m/z (rel. intensity) 734 (7), 563 (40), 501 (13), 407 (45), 333 (23), 303 (38), 267 (10), 213 (65), 183 (12), 151 (15), 125 (100), 107 (35), 97 (35), 81 (52), 79 (11), 69 (23), 55 (22), 45 (37), 43 (17); HRMS (ESI pos.): calcd. for $\text{C}_{44}\text{H}_{66}\text{NaO}_7\text{Si}$: 757.4476; found: 757.4472 ($\text{M}+\text{Na}^+$). Anal. calcd. for $\text{C}_{44}\text{H}_{66}\text{O}_7\text{Si}$: C, 71.89; H, 9.05; found: C, 71.89; H, 9.12. A second fraction was eluted (36 mg) which consisted of a mixture of **32a** (7%) and **32b** (28%), respectively.

(1S,6S,9R,13R,14S,17R,19S)-(-)-15-tert-butylidiphenylsilyloxy-14-methoxymethoxy-6,13,19-trimethyl-9-propyl-8,20-dioxa-bicyclo[15.2.1]eicosane-3-en-7,11-dione (35). A solution of compound **33** (165 mg, 0.225 mmol) and the ruthenium catalyst **34** (9.5 mg, 0.011 mmol) in CH_2Cl_2 (45 mL) was refluxed for 2 h. For work up, the reaction was quenched with a few drops of ethylvinyl ether before all volatiles were stripped off under reduced pressure. Flash chromatography of the residue (hexanes:EtOAc, 12.5:1 then 10:1) afforded product **35** as a pale pink syrup (137 mg, 86 %, *E:Z* = 6:1). $[\alpha]_{\text{D}}^{20}$ -80.5° (*c* 0.515, CHCl_3). IR (film): 3071, 2961, 2932, 2858, 1736, 1716, 1589, 1428, 1378, 1241, 1156, 1110, 1032, 917, 741, 704, 613, 503 cm^{-1} ; ^1H NMR (600 MHz, CD_2Cl_2) δ 7.79 (2H, m), 7.71 (2H, m), 7.43 (1H, m), 7.42 (1H, m), 7.39 (2H, m), 7.37 (2H, m), 5.34 (1H, ddd, $J = 15.4$ Hz, $J = 7.6$ Hz, $J = 4.0$ Hz), 5.25 (1H, ddd, $J = 15.4$ Hz, $J = 8.2$ Hz, $J =$

5.2 Hz), 5.22 (1H, dtd, $J = 10.1$ Hz, $J = 6.2$ Hz, $J = 3.3$ Hz), 4.88 (1H, d, $J = 6.8$ Hz), 4.63 (1H, d, $J = 6.7$ Hz), 3.93 (1H, ddd, $J = 8.6$ Hz, $J = 4.6$ Hz, $J = 2.9$ Hz), 3.65 (1H, ddd, $J = 10.2$ Hz, $J = 4.5$ Hz, $J = 2.1$ Hz), 3.38 (3H, s), 3.26 (1H, dd, $J = 8.6$ Hz, $J = 1.9$ Hz), 3.06 (1H, dtd, $J = 10.0$ Hz, $J = 7.3$ Hz, $J = 1.6$ Hz), 2.76 (1H, dd, $J = 18.2$ Hz, $J = 8.6$ Hz), 2.74 (1H, dd, $J = 15.4$ Hz, $J = 10.2$ Hz), 2.60 (1H, dqdd, $J = 8.6$ Hz, $J = 6.9$ Hz, $J = 4.0$ Hz, $J = 1.9$ Hz), 2.38 (1H, dqd, $J = 10.9$ Hz, $J = 6.9$ Hz, $J = 4.0$ Hz), 2.36 (1H, dd, $J = 15.4$ Hz, $J = 3.4$ Hz), 2.24 (1H, dd, $J = 18.2$ Hz, $J = 4.0$ Hz), 2.12 (1H, dtd, $J = 14.4$ Hz, $J = 5.2$ Hz, $J = 4.0$ Hz), 2.06 (1H, ddd, $J = 14.4$ Hz, $J = 10.8$ Hz, $J = 8.2$ Hz), 1.93 (1H, m), 1.92 (1H, ddd, $J = 14.4$ Hz, $J = 7.6$ Hz, $J = 2.0$ Hz), 1.88 (1H, ddd, $J = 15.7$ Hz, $J = 10.0$ Hz, $J = 4.6$ Hz), 1.85 (1H, m), 1.53 (1H, m), 1.48 (1H, m), 1.38 (1H, ddd, $J = 15.5$ Hz, $J = 2.5$ Hz, $J = 1.9$ Hz), 1.47-1.42 (2H, m), 1.29 (2H, m), 1.28 (1H, m), 1.12 (1H, d, $J = 6.9$ Hz), 1.05 (1H, m), 1.04 (9H, s), 0.90 (3H, t, $J = 7.4$ Hz), 0.84 (3H, d, $J = 6.9$ Hz), 0.59 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 208.4, 174.3, 136.7 (2C), 136.6 (2C), 135.4, 134.1, 130.2, 130.0, 129.8, 128.0 (2C), 127.9 (2C), 127.8, 99.3, 85.6, 79.3, 76.0, 75.1, 71.0, 55.8, 50.2, 46.6, 44.7, 42.7, 40.8, 38.2, 36.7, 36.7, 34.0, 27.3 (3C), 27.2, 19.4, 18.6, 18.2, 14.6, 14.3, 14.1; MS (EI) m/z (rel. intensity): 706 (10), 661 (18), 649 (74), 617 (27), 587 (25), 579 (21), 477 (29), 419 (26), 407 (13), 389 (56), 379 (18), 377 (11), 371 (9), 309 (13), 293 (15), 277 (10), 267 (41), 247 (11), 211 (52), 199 (85), 195 (20), 193 (31), 175 (13), 169 (95), 165 (18), 147 (16), 139 (32), 135 (61), 123 (14), 105 (15), 99 (32), 97 (61), 95 (24), 93 (28), 91 (17), 81 (29), 71 (20), 69 (38), 55 (30), 45 (100), 43 (22); HRMS (EI): calcd. for $\text{C}_{42}\text{H}_{62}\text{O}_7\text{Si}$: 706.4265; found: 757.4272 ($\text{M}+\text{Na}^+$). Anal. calcd. for $\text{C}_{42}\text{H}_{62}\text{O}_7\text{Si}$: C, 71.35; H, 8.84; found: C, 71.26; H, 8.73.

(1S,6S,9R,13R,14S,17R,19S)-(-)-15-tert-butylidiphenylsilyloxy-14-methoxymethoxy-6,13,19-trimethyl-9-propyl-8,20-dioxabicyclo[15.2.1]eicosane-7,11-dione (36). Pd on charcoal (7 mg, 6.5 μmol) was added to a solution of compound **35** (37 mg, 0.0523 mmol) in EtOAc (2 mL) and the resulting mixture was stirred under an atmosphere of H_2 (1 atm) for 5 h. The catalyst was then filtered off through a pad of Celite and the filtrate was evaporated to give product **36** as a white solid (32 mg, 86%). M.p. 118-121°C. $[\alpha]_{\text{D}}^{20}$ -64.9° (c 1.7, CHCl_3). IR (film): 3072, 2962, 2934, 2860, 1722 (br), 1590, 1463, 1429, 1379, 1257, 1160, 1110, 1064, 941, 742, 704, 615, 501 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.74-7.71 (4H, m), 7.40-7.37 (6H, m), 5.36 (1H, ddt, $J = 14.9$ Hz, $J = 6.3$ Hz, $J = 2.7$ Hz), 4.92 (1H, d, $J = 6.8$ Hz), 4.65 (1H, d, $J = 6.7$ Hz), 3.99 (1H, ddd, $J = 9.4$ Hz, $J = 4.0$ Hz, $J = 2.5$ Hz), 3.72 (1H, ddd, $J = 9.9$ Hz, $J = 4.1$ Hz, $J = 1.8$ Hz), 3.41 (3H, s), 3.22 (1H, d, $J = 9.7$ Hz), 2.91 (1H, dd, $J = 19.0$ Hz, $J = 10.1$ Hz), 2.89 (1H, m), 2.78 (1H, dd, $J = 15.1$ Hz, $J = 11.3$ Hz), 2.60 (1H, m), 2.36 (1H, dd, $J = 15.0$ Hz, $J = 2.7$ Hz), 2.33 (1H, m), 2.22 (1H, dd, $J = 19.1$ Hz, $J = 2.6$ Hz), 1.81 (1H, m), 1.95 (1H, ddd, $J = 15.6$ Hz, $J = 10.6$ Hz, $J = 4.4$ Hz), 1.60-1.55 (3H, m), 1.47 (1H, m), 1.45 (1H, m), 1.35-1.23 (7H, m), 1.29 (1H, m), 1.22-1.18 (1H, m), 1.11 (3H, d, $J = 6.9$ Hz), 1.07 (9H, s), 0.97 (1H, m), 0.92 (3H, t, $J = 7.3$ Hz), 0.87 (3H, d, $J = 6.9$ Hz), 0.55 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 208.5, 174.8, 136.4 (4C), 135.3, 133.7, 129.7, 129.5, 127.8 (2C), 127.7 (2C), 99.3, 85.5, 76.5, 76.0, 74.9, 70.9, 55.6, 50.7, 46.2, 44.8, 42.7, 41.0, 36.6 (2C), 36.2, 30.7, 27.5, 27.4 (3C), 26.6, 19.2, 18.4, 18.2, 14.3, 14.1, 14.0; MS (ESI pos.) m/z

(rel. intensity) 747 ($M+K^+$, 13), 731 ($M+Na^+$, 100), 677 (20), 570 (24), 391 (10); Anal. calcd. for $C_{42}H_{64}O_7Si$: C, 71.15; H, 9.10; found: C, 71.10; H, 9.02.

(2*S*,3*S*,4*R*,2'*S*,4'*S*,5'*S*)-6-[5-(2-*tert*-butyldiphenylsilyloxy-3-methoxymethoxy-4-methyl-[1]-undec-7-en-6-one)-3-methyl-tetrahydrofuran-2-yl]-hexanoic acid (37). IR (film): 3500-2600, 3071, 3048, 2959, 2929, 2856, 1736, 1706, 1676, 1629, 1590, 1427, 1152, 1105, 1034, 978, 963, 916, 822, 739, 703, 612 cm^{-1} . Characteristic NMR data: 1H NMR (400 MHz, $CDCl_3$) δ 7.75-7.71 (4H, m), 7.43-7.34 (6H, m), 6.77 (1H, dt, $J = 15.9$ Hz, $J = 6.9$ Hz), 6.07 (1H, d, $J = 15.9$ Hz), 4.45 (1H, d, $J = 6.7$ Hz), 4.41 (1H, d, $J = 6.7$ Hz), 4.16 (1H, dt, $J = 7.5$ Hz, $J = 4.0$ Hz), 3.90 (1H, m), 3.64 (1H, m), 3.27 (3H, s), 3.23 (1H, dd, $J = 5.6$ Hz, $J = 4.5$ Hz), 2.86 (1H, dd, $J = 15.9$ Hz, $J = 3.0$ Hz), 2.49-2.44 (2H, m), 2.38 (1H, dd, $J = 15.9$ Hz, $J = 10.0$ Hz), 2.17 (2H, qd, $J = 7.2$ Hz, $J = 0.2$ Hz), 2.00 (2H, m), 1.78 (1H, ddd, $J = 13.7$ Hz, $J = 9.0$ Hz, $J = 4.0$ Hz), 1.28 (3H, d, $J = 7.0$ Hz), 1.08 (9H, s), 0.95 (3H, d, $J = 7.4$ Hz), 0.87 (3H, d, $J = 6.3$ Hz), 0.71 (3H, d, $J = 7.0$ Hz); MS (ESI pos.) m/z : 731 ($M+Na^+$, 100).

(1*S*,6*S*,9*R*,13*R*,14*S*,17*R*,19*S*)-(-)-15-*tert*-butyldiphenylsilyloxy-14-methoxymethoxy-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxabicyclo[15.2.1]eicosane-7-one (39). Neat $TiCl_4$ (15 μL , 0.141 mmol) was added via syringe to a solution of Nysted's reagent **38** (347 mg, 0.152 mmol) in THF (0.5 mL) at $0^\circ C$, followed by a solution of ketone **36** (11 mg, 0.0141 mmol). The cooling bath was removed and the mixture was refluxed for 2 h. For work up, the dark brown slurry was diluted with EtOAc, the mixture was filtered through a short pad of deactivated neutral alumina (10 g of Al_2O_3 for 1 mL of water), the filtrate was evaporated and the residue was purified by flash chromatography (hexanes:EtOAc, 22.5/1) to give product **39** as a colorless oil (7 mg, 64%). $[\alpha]_D^{20}$ -20.8° (c 0.43, $CHCl_3$). IR (film): 3072, 3049, 2960, 2932, 2857, 1729, 1642, 1589, 1428, 1251, 1157, 1109, 1035, 915, 740, 703, 613, 503 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.80-7.72 (4H, m), 7.42-7.39 (6H, m), 5.11 (1H, qt, $J = 5.8$ Hz), 4.97 (1H, s), 4.87 (1H, s), 4.85 (1H, d, $J = 6.7$ Hz), 4.64 (1H, d, $J = 6.7$ Hz), 4.00 (1H, ddd, $J = 7.1$ Hz, $J = 4.8$ Hz, $J = 4.4$ Hz), 3.57 (1H, m), 3.40 (1H, m), 3.39 (3H, s), 3.27 (1H, m), 2.43-2.39 (2H, m), 2.28 (1H, dd, $J = 14.4$ Hz, $J = 6.0$ Hz), 2.20 (1H, dd, $J = 14.3$ Hz, $J = 5.4$ Hz), 1.96-1.93 (2H, m), 1.84 (1H, m), 1.57-1.45 (6H, m), 1.37-1.29 (8H, m), 1.22-1.18 (2H, m), 1.14 (3H, d, $J = 6.8$ Hz), 1.04 (9H, s), 0.90 (3H, t, $J = 7.3$ Hz), 0.91 (3H, d, $J = 6.6$ Hz), 0.59 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 144.0, 136.4 (4C), 135.3, 133.9, 129.7, 129.6, 127.8 (2C), 127.7 (2C), 115.4, 99.8, 84.7, 78.2, 74.4, 74.2, 72.4, 55.8, 43.8, 42.7, 41.3, 40.5, 39.9, 36.4, 35.5, 34.8, 31.2, 30.7, 27.4 (3C), 19.3, 18.7, 18.1, 15.4, 14.3, 14.1; MS (EI) m/z (rel. intensity) 706 (5), 649 (16), 617 (22), 419 (31), 401 (20), 389 (34), 371 (10), 267 (8), 213 (48), 205 (11), 199 (49), 195 (100), 183 (22), 177 (21), 167 (58), 161 (17), 149 (82), 139 (20), 107 (28), 105 (17), 95 (78), 93 (25), 91 (14), 71 (14), 69 (31), 55 (34), 45 (56), 43 (20); HRMS (CI, *i*-Bu): calcd. for $C_{43}H_{67}O_6Si$: 707.4706; found: 707.4712 (MH^+).

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¹H NMR spectrum (400 MHz) of compound **39** in CDCl₃

(1S,6S,9R,13R,14S,17R,19S)-(-)-15-hydroxy-14-methoxymethyl-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxabicyclo[15.2.1]eicosane-7-one (40). A solution of TASF (63 mg, 0.229 mmol) in MeCN (3.75 mL) was added to silyl ether **39** (34 mg, 0.048 mmol) and the resulting mixture was refluxed for 22 h. The reaction was quenched with brine and EtOAc. Dilution with water, extraction of the aqueous layer with EtOAc, drying of the combined organic phases over Na₂SO₄, evaporation of the solvent and flash chromatography (hexanes:EtOAc, 4:1) of the residue afforded product **40** as a colorless oil (19 mg, 84%). $[\alpha]_D^{20}$ -5.5° (*c* 0.84, CHCl₃). IR (film): 3477, 3072, 2960, 2934, 2874, 1728, 1642, 1461, 1379, 1348, 1279, 1252, 1210, 1154, 1076, 1033, 964, 918, 906, 804, 737 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.02 (1H, qt, *J* = 6.1 Hz), 4.88 (1H, s), 4.85 (1H, s), 4.76 (1H, d, *J* = 6.5 Hz), 4.68 (1H, d, *J* = 6.5 Hz), 4.30 (1H, ddd, *J* = 15.3 Hz, *J* = 7.4 Hz, *J* = 4.3 Hz), 3.83 (2H, m), 3.42 (3H, s), 3.28 (1H, dd, *J* = 6.3 Hz, *J* = 3.1 Hz), 2.46 (1H, m), 2.32 (1H, dd, *J* = 14.3 Hz, *J* = 6.4 Hz), 2.24 (1H, dd, *J* = 13.2 Hz, *J* = 6.1 Hz), 2.20 (1H, m), 2.18 (1H, dd, *J* = 14.6 Hz, *J* = 5.5 Hz), 1.98 (1H, m), 1.93 (1H, m), 1.75 (2H, m), 1.62-1.55 (3H, m), 1.54-1.39 (3H, m), 1.35-1.23 (7H, m), 1.13 (3H, d, *J* = 6.9 Hz), 0.94 (3H, d, *J* = 6.5 Hz), 0.91 (3H, t, *J* = 7.4 Hz), 0.88 (3H, d, *J* = 7.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 176.2, 144.2, 115.0, 99.0, 85.7, 78.9, 74.3, 73.0, 71.0, 56.2, 42.3, 41.8, 40.5, 40.3, 39.8, 36.5, 35.8, 34.2, 33.1, 28.8, 26.2, 25.7, 18.7, 17.3, 14.7, 14.5, 14.1; MS (EI) *m/z* (rel. intensity): 468 (6), 436 (13), 423 (48), 406 (11), 390 (4), 379 (8), 269 (6), 257 (37), 251 (7), 239 (25), 221 (11), 213 (31), 211 (4), 195 (47), 193 (5), 167 (81), 166 (6), 150 (19), 149 (47), 138 (13), 112 (5), 110 (13), 107 (27), 95 (100), 94 (11), 55 (46), 45 (80); HRMS (CI, *i*-Bu): calcd. for C₂₇H₄₉O₆: 469.3529; found: 469.3529 (MH⁺).

(1S,6S,9R,13R,14S,17R,19S)-(+)-14-methoxymethyl-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxabicyclo[15.2.1]eicosane-7,15-dione (40b). Dess-Martin periodinane (26 mg, 0.061 mmol) was added to a solution of alcohol **40** (19 mg, 0.018 mmol) in CH₂Cl₂ (1.5 mL). After stirring for 3 h, the mixture was diluted with ether and quenched with aq. sat. Na₂S₂O₃ and aq. sat. NaHCO₃. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layers were washed with brine, dried over Na₂SO₄ and filtered. Evaporation of the solvents followed by a purification of the residue by flash chromatography (hexanes:EtOAc, 7:1) afforded the title compound as a colorless oil (17.6 mg, 93%). $[\alpha]_D^{20}$ $+48.2^\circ$ (*c* 1.35, CHCl₃). IR (film): 3074, 2960, 2936, 2875, 1726, 1643, 1460, 1379, 1282, 1252, 1218, 1154, 1059, 1040, 916 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 5.34 (1H, ddt, *J* = 7.9 Hz, *J* = 5.3 Hz, *J* = 5.1 Hz), 5.00 (1H, s), 4.89 (1H, s), 4.68 (1H, d, *J* = 6.8 Hz), 4.63 (1H, d, *J* = 6.8 Hz), 4.62 (1H, m), 4.16 (1H, d, *J* = 2.4 Hz), 3.77 (1H, ddd, *J* = 10.5 Hz, *J* = 7.5 Hz, *J* = 2.8 Hz), 3.30 (3H, s), 2.52-2.45 (2H, m), 2.42 (1H, dd, *J* = 15.1 Hz, *J* = 8.8 Hz), 2.28 (2H, d, *J* = 5.1 Hz), 2.24 (1H, dd, *J* = 13.1 Hz, *J* = 4.1 Hz), 2.09 (1H, dd, *J* = 15.0 Hz, *J* = 3.0 Hz), 1.80 (1H, m), 1.65-1.20 (15H, m), 1.15 (3H, d, *J* = 6.5 Hz), 1.08 (3H, d, *J* = 6.9 Hz), 0.88 (3H, t, *J* = 7.3 Hz), 0.68 (3H, d, *J* = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 207.4, 175.0, 144.1, 115.9, 97.3, 84.3, 78.5, 73.3, 71.8, 56.1, 46.5, 42.0, 41.5, 40.0, 39.9, 36.7, 35.8, 35.2, 31.4, 29.9, 27.0, 26.2, 19.2, 18.2, 14.9, 14.2, 14.1; MS (EI) *m/z* (rel. intensity): 466 (12), 438 (4), 421 (12), 406 (11), 377 (20), 300 (13), 283 (22), 269 (22), 255 (17), 237 (25), 213 (34), 195 (66), 171 (25), 168 (20), 167 (94), 166 (18), 149 (80), 138 (15), 110 (11), 107 (23), 95 (100), 93 (20), 83

(40), 71 (14), 67 (19), 55 (37), 45 (77), 43 (20); HRMS (EI): calcd. for C₂₇H₄₆O₆: 466.3294; found: 466.3292.

Amphidinolide T1 (1). DOWEX-50WX4 resin (40 mg) was added to a solution of ketone **40b** (10 mg, 0.0214 mmol) in 2.5 mL of MeOH and the resulting suspension was refluxed for 10 h. The resin was filtered off through a short pad of silica, the filtrate was evaporated and the residue was purified by flash chromatography (hexanes:EtOAc, 6:1) to give amphidinolide T1 as a colorless oil (4.6 mg, 52%). The ¹H and ¹³C NMR data were identical to those reported in the literature (ref.⁴ in the text, see also Table S-1 and spectrum). [α]_D²⁰ +42.0° (*c* 0.30, CHCl₃). MS (EI) *m/z* (rel. intensity): 422 (9), 404 (4), 394 (10), 257 (12), 239 (14), 213 (13), 195 (28), 167 (100), 149 (45), 141 (24), 138 (17), 137 (19), 107 (14), 97 (15), 95 (79), 93 (12), 79 (8), 69 (29), 68 (11), 67 (18), 55 (35), 43 (21); HRMS (EI): calcd. for C₂₅H₄₂O₅, 422.3032; found: 422.3037.

Table S-1. Comparison of the ¹³C NMR data of amphidinolide T1 (**1**)

Position	Literature	(1)
1	174.9	175.0
2	41.7	41.9
3	35.1	35.2
4	26.8	26.9
5	26.2	26.3
6	29.7	29.8
7	78.6	78.5
8	36.5	36.6
9	39.7	39.8
10	73.6	73.7
11	45.0	45.1
12	212.0	212.1
13	78.2	78.2
14	32.0	32.0
15	41.2	41.3
16	143.5	143.6
17	40.1	40.1
18	71.7	71.8
19	35.7	35.7
20	19.1	19.2
21	13.9	14.0
22	18.0	18.2
23	14.0	14.1
24	13.7	13.9
25	116.1	116.3

 ^1H NMR spectrum (400 MHz) of amphidinolide T1 (**1**) in C_6D_6

(1*S*,6*S*,9*R*,13*R*,14*S*,17*R*,19*S*)-(+)-15-*tert*-butyldiphenylsilyloxy-14-hydroxy-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxo-bicyclo[15.2.1]eicosane-7-one (41). Bu₄NBr (27 mg, 0.0848 mmol) was added to a solution of TMSCl (11 μ L, 0.0848 mmol) in CH₂Cl₂ (0.5 mL) at 0°C. After stirring for 45 min, a solution of compound **39** (15 mg, 0.0212 mmol) in CH₂Cl₂ (0.5 mL) was introduced and the mixture was stirred overnight at 5°C. For work up, the mixture was quenched with aq. sat. NaHCO₃, the aqueous layer was extracted with CH₂Cl₂, the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and evaporated. Purification of the residue by flash chromatography (hexanes:EtOAc, 20:1 then 17.5:1) afforded product **41** as a colorless oil (12 mg, 85%). $[\alpha]_D^{20}$ +4.5° (*c* 0.65, CHCl₃). IR (film): 3448, 3070, 3050, 2959, 2930, 2856, 1726, 1589, 1462, 1428, 1112, 1076, 739, 702, 608, 506 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.73-7.69 (4H, m), 7.43-7.35 (6H, m), 5.09 (1H, qt, *J* = 5.9 Hz), 4.88 (1H, s), 4.85 (1H, s), 3.97 (1H, m), 3.64 (1H, m), 3.42 (1H, dd, *J* = 6.3 Hz, *J* = 3.5 Hz), 3.34 (1H, ddd, *J* = 17.6 Hz, *J* = 9.8 Hz, *J* = 2.8 Hz), 2.39 (1H, m), 2.30 (1H, dd, *J* = 13.9 Hz, *J* = 7.9 Hz), 2.23 (2H, d, *J* = 5.4 Hz), 2.00 (1H, dd, *J* = 13.8 Hz, *J* = 7.1 Hz), 1.91 (1H, m), 1.84 (1H, ddd, *J* = 13.7 Hz, *J* = 6.8 Hz, *J* = 3.2 Hz), 1.57-1.46 (8H, m), 1.35-1.25 (8H, m), 1.12 (3H, d, *J* = 6.9 Hz), 1.06 (9H, s), 0.91 (3H, d, *J* = 6.9 Hz), 0.90 (3H, t, *J* = 6.9 Hz), 0.63 (3H, d, *J* = 7.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 177.4, 144.3, 136.2 (4C), 134.5, 133.5, 129.9, 129.8, 127.9 (2C), 127.7 (2C), 114.7, 78.3, 76.2, 75.0, 74.5, 72.5, 43.1, 41.7, 40.5, 40.0, 36.2, 35.7, 34.8, 32.6, 29.7, 27.2 (3C), 19.6, 18.8, 17.9, 14.4, 14.1, 14.1; MS (EI) *m/z* (rel. intensity): 662 (5), 605 (28), 389 (28), 371 (15), 283 (12), 267 (6), 205 (17), 199 (100), 197 (14), 195 (8), 183 (16), 177 (19), 167 (23), 161 (15), 149 (54), 139 (22), 137 (38), 107 (22), 105 (12), 95 (53), 93 (20), 69 (34), 55 (34), 43 (21); HRMS (EI): calcd. for C₄₁H₆₂O₅Si: 662.4367; found: 662.4376.

(1*S*,6*S*,9*R*,13*R*,17*R*,19*S*)-(+)-15-*tert*-butyldiphenylsilyloxy-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxo-bicyclo[15.2.1]eicosane-7,14-dione (41b). Dess-Martin periodinane was added to a solution of alcohol **41** (12 mg, 0.018 mmol) in CH₂Cl₂ (1 mL) and the resulting mixture was stirred for 3 h. For work up, the mixture was diluted with ether and the reaction was quenched with aq. sat. Na₂S₂O₃ and aq. sat. NaHCO₃. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layers were washed with brine, dried with Na₂SO₄ and filtered. Evaporation of the solvents followed by a purification of the residue by flash chromatography (hexanes:EtOAc, 20:1) afforded the title compound as a colorless oil (10 mg, 83%). $[\alpha]_D^{20}$ +5.8° (*c* 0.43, CHCl₃). IR (film): 3072, 3049, 2960, 2931, 2856, 1727, 1644, 1589, 1428, 1259, 1158, 1111, 1018, 740, 702, 613 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.67-7.65 (4H, m), 7.40-7.32 (6H, m), 4.90 (1H, qt, *J* = 6.3 Hz), 4.78 (1H, m), 4.73 (1H, m), 4.60 (1H, dd, *J* = 6.8 Hz, *J* = 3.5 Hz), 4.15 (1H, ddd, *J* = 15.2 Hz, *J* = 7.5 Hz, *J* = 2.9 Hz), 3.72 (1H, m), 2.58 (1H, m), 2.38 (1H, m), 2.32 (1H, dd, *J* = 14.4 Hz, *J* = 5.0 Hz), 2.21 (1H, dd, *J* = 14.0 Hz, *J* = 6.8 Hz), 2.18 (1H, m), 2.05 (1H, dd, *J* = 14.1 Hz, *J* = 6.3 Hz), 1.85 (1H, ddd, *J* = 14.6 Hz, *J* = 8.1 Hz, *J* = 3.5 Hz), 1.81 (1H, m), 1.80 (1H, dd, *J* = 14.4 Hz, *J* = 9.6 Hz), 1.73 (1H, ddd, *J* = 14.6 Hz, *J* = 6.8 Hz, *J* = 3.7 Hz), 1.67 (1H, ddd, *J* = 12.4 Hz, *J* = 7.2 Hz, *J* = 3.1 Hz), 1.60-1.53 (2H, m), 1.49-1.45 (2H, m), 1.35-1.25 (7H, m), 1.12 (3H, d, *J* = 7.0 Hz), 1.07 (9H, s), 0.88 (3H, t, *J* = 7.3 Hz), 0.80 (3H, d, *J* = 7.0 Hz), 0.48 (3H, d, *J* = 7.4 Hz); ¹³C

NMR (100 MHz, CDCl_3) δ 212.1, 176.0, 142.9, 136.4 (2C), 136.2 (2C), 134.1 (2C), 129.7 (2C), 127.7 (2C), 127.6 (2C), 114.9, 78.6, 75.3, 73.6, 72.2, 41.3, 41.1 (2C), 41.0, 40.2, 38.1, 36.1, 35.8, 34.2, 29.1, 27.2 (3C), 19.7, 18.6, 17.9, 16.0, 14.2, 14.1; MS (EI) m/z (rel. intensity): 660 (6), 603 (19), 387 (100), 377 (13), 369 (15), 281 (11), 267 (12), 199 (48), 197 (14), 195 (58), 183 (17), 177 (11), 175 (17), 139 (18), 135 (27), 105 (7), 95 (32), 93 (10), 69 (21), 67 (15), 55 (25), 43 (15); HRMS (EI): calcd. for $\text{C}_{41}\text{H}_{60}\text{O}_5\text{Si}$: 660.4210; found: 660.4213.

Amphidinolide T4 (4). HF/pyridine complex (~ 0.1 mL) was added via a teflon syringe to a solution of silyl ether **41b** (10 mg, 0.015 mmol) in MeCN (0.5 mL). After stirring overnight, the mixture was poured into water and the aqueous phase was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexanes:EtOAc, 10:1 then 7:1) to give amphidinolide T4 as a colorless oil (5.5 mg, 87%). The ^1H and ^{13}C NMR data were identical to those reported in the literature (ref. ⁴ in the Text; see also Table S-2 and spectrum). $[\alpha]_{\text{D}}^{20} -3.0^\circ$ (c 0.12, CHCl_3). IR (film): 3456 (br), 2993, 2874, 1725, 1071 cm^{-1} ; MS (EI) m/z (rel. intensity): 422 (6), 404 (11), 394 (32), 257 (65), 255 (8), 239 (64), 221 (18), 213 (34), 195 (48), 167 (17), 165 (16), 149 (17), 138 (56), 110 (15), 95 (100), 93 (16), 79 (13), 68 (31), 67 (37), 56 (12), 55 (62), 43 (44), 41 (38); HRMS (EI): calcd. for $\text{C}_{25}\text{H}_{42}\text{O}_5$, 422.3032; found: 422.3040.

Table S-2. Comparison of the ^{13}C NMR data of amphidinolide T4 (**4**)

Position	Literature	(4)
1	175.5	175.4
2	41.0	41.0
3	33.9	33.8
4	26.7	26.6
5	26.1	26.0
6	28.8	28.7
7	79.4	79.3
8	36.2	36.1
9	40.3	40.2
10	74.7	74.6
11	40.2	40.1
12	75.0	74.9
13	215.6	215.7
14	39.6	39.5
15	38.5	38.4
16	143.2	143.1
17	40.9	40.8
18	72.0	71.9
19	35.6	35.5
20	18.8	18.7
21	14.0	13.9
22	18.1	18.0
23	14.2	14.1
24	16.0	15.9
25	115.5	115.4

¹H NMR spectrum (400 MHz) of amphidinolide T4 (**4**) in C₆D₆

(2R,3S,4R,2'R,4'S,5'S)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-5-(tert-butyl-dimethyl-silanyloxy)-2-(tert-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentane (42). The procedure for the preparation of compound **30** was applied analogously to substrate **27** (0.09 g, 0.22 mmol). Purification by flash chromatography (hexanes:EtOAc, 20:1) afforded product **42** as a colorless oil (116 mg, 82%). $[\alpha]_{\text{D}}^{20}$ -4.2° (c 0.12, CHCl_3). IR (film): 3072, 3050, 2957, 2930, 2892, 2857, 1642, 1472, 1428, 1389, 1256, 1105, 1091, 1036, 917, 837, 776, 739, 702, 612, 506 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73-7.70 (4H, m), 7.44-7.33 (6H, m), 5.67 (1H, ddt, $J = 17.2$ Hz, $J = 10.2$ Hz, $J = 7.0$ Hz), 5.00 (1H, ddd, $J = 16.6$ Hz, $J = 3.1$ Hz, $J = 1.3$ Hz), 4.95 (1H, ddd, $J = 10.2$ Hz, $J = 1.9$ Hz, $J = 0.9$ Hz), 4.77 (1H, d, $J = 6.4$ Hz), 4.60 (1H, d, $J = 6.3$ Hz), 4.00-3.90 (2H, m), 3.76 (1H, dd, $J = 3.9$ Hz, $J = 3.0$ Hz), 3.54 (1H, q, $J = 6.4$ Hz), 3.47 (1H, dd, $J = 9.7$ Hz, $J = 7.0$ Hz), 3.38 (1H, dd, $J = 9.7$ Hz, $J = 6.1$ Hz), 3.36 (3H, s), 2.10-1.90 (4H, m), 1.76 (1H, dt, $J = 14.2$ Hz, $J = 6.6$ Hz), 1.55 (1H, dt, $J = 14.0$ Hz, $J = 6.3$ Hz), 1.32-1.20 (1H, m), 1.14-1.05 (1H, m), 1.07 (9H, s), 0.96 (3H, d, $J = 6.9$ Hz), 0.89 (9H, s), 0.71 (3H, d, $J = 7.0$ Hz), 0.03 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ 136.3 (2C), 136.1, 135.7, 134.7, 134.0, 129.7 (2C), 129.6, 127.6 (4C), 116.1, 96.8, 80.0, 79.9, 73.6, 73.1, 66.1, 56.0, 41.0, 39.9, 37.1, 35.6, 35.1, 27.3 (3C), 26.1 (3C), 19.6, 18.4, 14.1, 12.7, -5.3 (2C); MS (EI) m/z (rel. intensity): 654 (10), 597 (7), 407 (18), 337 (13), 213 (13), 205 (24), 199 (16), 195 (8), 183 (11), 151 (8), 135 (25), 125 (100), 115 (7), 109 (10), 107 (41), 97 (12), 91 (13), 89 (31), 81 (76), 79 (13), 73 (36), 55 (20), 45 (38), 43 (14); HRMS (ESI pos.): calcd. for $\text{C}_{38}\text{H}_{62}\text{O}_5\text{Si}_2\text{Na}$: 677.4034; found: 677.4032 ($\text{M}+\text{Na}^+$). Anal. calcd. for $\text{C}_{38}\text{H}_{62}\text{O}_5\text{Si}_2$: C, 69.67; H, 9.54; found: C, 69.73; H, 9.47.

(2R,3S,4R,2'R,4'S,5'S)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-2-(tert-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-pentan-5-ol (43). Prepared according to the procedure for the synthesis of compound **31** using substrate **42** (2.65 g, 4.05 mmol). Purification by flash chromatography (hexanes:EtOAc, 4:1) afforded product **43** as a white solid (1.898 g, 87%). M.p. = 60-61°C. $[\alpha]_{\text{D}}^{20}$ -6.4° (c 0.155, CHCl_3). IR (film): 3449, 3072, 3049, 2960, 2932, 2892, 2858, 1642, 1472, 1428, 1389, 1110, 1034, 916, 822, 740, 703, 611, 506 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.72-7.67 (4H, m), 7.42-7.34 (6H, m), 5.68 (1H, ddt, $J = 17.2$ Hz, $J = 10.2$ Hz, $J = 6.9$ Hz), 5.01 (1H, ddd, $J = 17.0$ Hz, $J = 3.3$ Hz, $J = 1.9$ Hz), 4.95 (1H, ddd, $J = 10.3$ Hz, $J = 2.0$ Hz, $J = 1.0$ Hz), 4.78 (1H, d, $J = 6.4$ Hz), 4.54 (1H, d, $J = 6.4$ Hz), 4.06-3.98 (2H, m), 3.78 (1H, t, $J = 3.7$ Hz), 3.62-3.57 (1H, m), 3.50-3.44 (2H, m), 3.38 (3H, s), 2.10-1.96 (4H, m), 1.75 (1H, dt, $J = 14.2$ Hz, $J = 6.6$ Hz), 1.60 (1H, dt, $J = 14.0$, $J = 6.3$ Hz), 1.35-1.30 (1H, m), 1.23-1.19 (1H, m), 1.06 (9H, s), 0.92 (3H, d, $J = 6.9$ Hz), 0.74 (3H, d, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 136.4 (2C), 136.2, 135.7, 134.4, 133.8, 129.8, 129.7 (2C), 127.7 (2C), 127.6 (2C), 116.3, 97.1, 81.0, 80.2, 73.4, 72.7, 65.9, 56.1, 40.8, 39.9, 36.9, 35.6, 35.1, 27.2 (3C), 19.5, 14.1, 12.5; MS (EI) m/z (rel. intensity) 540 (1), 451 (9), 407 (27), 253 (38), 223 (15), 221 (6), 199 (36), 183 (16), 151 (9), 135 (20), 125 (100), 117 (3), 107 (37), 97 (12), 91 (11), 81 (70), 79 (13), 55 (23), 45 (62), 43 (23); HRMS (ESI pos.): calcd. for $\text{C}_{32}\text{H}_{48}\text{O}_5\text{SiNa}$: 563.3169; found: 563.3170 ($\text{M}+\text{Na}^+$). Anal. calcd. for $\text{C}_{32}\text{H}_{48}\text{O}_5\text{Si}$: C, 71.07; H, 8.95; found: C, 71.02; H, 8.86.

(2*R*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-Allyl-4-methyl-tetrahydrofuran-2-yl)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-5-iodo-pentane (44a). Prepared according to the procedure for the synthesis of compound **32a** using substrate **43** (1.838 g, 3.40 mmol). Flash chromatography (hexanes:EtOAc, 15:1) afforded product **44a** as a colorless oil (1.97 g, 89%). $[\alpha]_{\text{D}}^{20}$ -4.4° (c 0.165, CHCl_3). IR (film): 3071, 3048, 2960, 2931, 2893, 2857, 1642, 1472, 1427, 1389, 1152, 1110, 1034, 918, 822, 740, 703, 611, 506 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73-7.68 (4H, m), 7.45-7.35 (6H, m), 5.69 (1H, ddt, $J = 17.2$ Hz, $J = 10.2$ Hz, $J = 7.0$ Hz), 5.01 (1H, ddd, $J = 17.2$ Hz, $J = 3.5$ Hz, $J = 1.5$ Hz), 4.97 (1H, ddd, $J = 10.2$ Hz, $J = 2.0$ Hz, $J = 1.0$ Hz), 4.81 (1H, d, $J = 6.5$ Hz), 4.60 (1H, d, $J = 6.5$ Hz), 4.03 (1H, dt, $J = 7.2$ Hz, $J = 6.8$ Hz), 3.91 (1H, dt, $J = 5.8$ Hz, $J = 3.4$ Hz), 3.70 (1H, dd, $J = 4.3$ Hz, $J = 3.5$ Hz), 3.58 (1H, qd, $J = 6.4$ Hz, $J = 1.5$ Hz), 3.37 (3H, s), 3.25 (1H, dd, $J = 9.3$ Hz, $J = 5.9$ Hz), 3.05 (1H, dd, $J = 9.7$ Hz, $J = 6.6$ Hz), 2.10-1.90 (4H, m), 1.76 (1H, ddd, $J = 14.2$ Hz, $J = 7.8$ Hz, $J = 5.8$ Hz), 1.56 (1H, dt, $J = 14.2$, $J = 6.0$ Hz), 1.30 (1H, dt, $J = 12.4$ Hz, $J = 7.3$ Hz), 1.23-1.15 (1H, m), 1.07 (9H, s), 1.02 (3H, d, $J = 6.7$ Hz), 0.74 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 136.4, 136.3 (2C), 135.8, 134.3, 133.6, 129.9 (2C), 129.8, 127.7 (4C), 116.3, 97.3, 83.0, 80.2, 73.3, 72.5, 56.2, 40.7, 40.1, 37.2, 35.6, 35.1, 27.3 (3C), 19.5, 16.6, 14.1, 12.5; MS (EI) m/z (rel. intensity): 650 (9), 593 (13), 409 (14), 407 (40), 363 (17), 333 (16), 309 (13), 253 (6), 243 (17), 225 (8), 213 (26), 205 (16), 199 (32), 183 (23), 181 (8), 150 (9), 135 (20), 125 (89), 115 (3), 107 (32), 97 (9), 91 (18), 81 (66), 79 (12), 45 (100), 43 (23); HRMS (ESI pos.): calcd. for $\text{C}_{32}\text{H}_{47}\text{IO}_4\text{SiNa}$: 673.2186; found: 673.2194 ($\text{M}+\text{Na}^+$). Anal. calcd. for $\text{C}_{32}\text{H}_{47}\text{IO}_4\text{Si}$: C, 59.07; H, 7.28; found: C, 59.14; H, 7.22.

2-Methyl-pent-4-enoic acid-[(2*R*,3*S*,4*R*,2'*R*,4'*S*,5'*S*)-(-)-1-(5-allyl-4-methyl-tetrahydrofuran-2-yl)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-methoxymethoxy-4-methyl-6-one]-undec-8-yl ester (45) and 2-methyl-pent-4-enoic acid-[(2*R*,3*S*,1'*R*,4'*S*,5'*S*)-(1)-[1-(2-*tert*-butyldiphenylsilyloxy)-3-methoxymethoxy-3-isopropyl-prop-1-yl]-5-methyl-7-oxa-norborn-2-yl]-2-one]-hept-4-yl ester (46). Prepared according to the procedure for the synthesis of compound **33** starting from substrate **44a** (350 mg). After flash chromatography we obtained 253 mg of a polar fraction containing coupling products of the same molecular weight (3/2 ratio) which was further purified by preparative HPLC (125 mm, Nucleosil 100-5-C18/A, 4.5 mm i. D.; Methanol:water, 9:1) to give products **45** (84 mg) and **46** (49 mg). Data of compound **45**: $[\alpha]_{\text{D}}^{20}$ -36.1° (c 4.2, CHCl_3). IR (film): 3073, 2961, 2933, 2876, 1733, 1642, 1589, 1428, 1180, 1146, 1110, 1035, 965, 916, 822, 740, 704, 612, 505 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73-7.67 (4H, m), 7.42-7.36 (6H, m), 5.67 (1H, ddt, $J = 17.0$ Hz, $J = 10.2$ Hz, $J = 7.0$ Hz), 5.21 (1H, dt, $J = 6.8$ Hz, $J = 6.0$ Hz), 5.07-4.95 (4H, m), 4.75 (1H, d, $J = 6.5$ Hz), 4.55 (1H, d, $J = 6.5$ Hz), 4.10 (1H, qt, $J = 7.0$ Hz), 3.88 (1H, dt, $J = 5.8$ Hz, $J = 3.1$ Hz), 3.59 (1H, q, $J = 6.3$ Hz), 3.47 (1H, dd, $J = 4.3$ Hz, $J = 3.3$ Hz), 3.36 (3H, s), 2.63 (1H, dd, $J = 16.4$ Hz, $J = 6.9$ Hz), 2.46 (1H, dd, $J = 16.4$ Hz, $J = 5.9$ Hz), 2.47-2.35 (3H, m), 2.32 (1H, m), 2.18 (1H, dd, $J = 16.3$ Hz, $J = 8.4$ Hz), 2.15 (1H, m), 2.10-1.95 (3H, m), 1.79 (1H, ddd, $J = 13.8$ Hz, $J = 7.1$ Hz, $J = 6.3$ Hz), 1.61 (1H, dt, $J = 14.0$ Hz, $J = 6.1$ Hz), 1.54-1.49 (2H, m), 1.37-1.19 (4H, m), 1.12 (3H, d, $J = 6.8$ Hz), 1.07 (9H, s), 0.90 (3H, t, $J = 7.3$ Hz), 0.87 (3H, d, $J = 6.7$ Hz), 0.74 (3H, d, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 207.0, 175.4, 136.5 (2C), 136.3

(2C), 135.8, 135.6, 134.4, 133.8, 129.8, 129.7, 127.6 (4C), 116.9, 116.2, 97.0, 83.6, 80.1, 73.5, 72.6, 70.1, 56.0, 48.6, 47.4, 40.8, 40.0, 39.5, 37.9, 36.4, 35.6, 35.1, 30.1, 27.2 (3C), 19.5, 18.5, 16.7, 15.6, 14.1, 14.0; MS (EI) m/z (rel. intensity) 734 (5), 563 (39), 533 (18), 531 (11), 503 (10), 501 (29), 485 (10), 407 (57), 405 (10), 389 (9), 363 (8), 333 (55), 303 (33), 285 (16), 283 (17), 219 (36), 213 (65), 201 (19), 199 (51), 197 (19), 191 (19), 183 (25), 181 (12), 173 (14), 151 (18), 135 (45), 125 (100), 107 (38), 97 (58), 91 (12), 81 (57), 79 (14), 69 (33), 55 (34), 45 (54), 43 (22), 41 (22); HRMS (CI): calcd. for $C_{44}H_{66}NO_7Si$: 757.4922; found: 757.4917 ($M+NH_4^+$).

Data of compound **46**: 2 diastereomers (ratio 8:3), 1H NMR (600 MHz, $CDCl_3$) Major isomer: δ 7.72 (2H, m), 7.66 (2H, m), 7.39 (2H, m), 7.35 (2H, m), 7.34 (2H, m), 5.72 (1H, ddt, $J = 17.1$ Hz, $J = 10.2$ Hz, $J = 6.9$ Hz), 5.17 (1H, dt, $J = 6.8$ Hz, $J = 5.7$ Hz), 5.04 (1H, m), 5.01 (1H, m), 4.73 (1H, d, $J = 6.5$ Hz), 4.55 (1H, d, $J = 6.5$ Hz), 4.10 (1H, qd, $J = 4.0$ Hz, $J = 1.2$ Hz), 3.95 (1H, t, $J = 5.1$ Hz), 3.47 (1H, dd, $J = 6.3$ Hz, $J = 1.0$ Hz), 3.31 (3H, s), 2.58 (1H, dd, $J = 16.3$ Hz, $J = 7.0$ Hz), 2.47-2.36 (3H, m), 2.33 (1H, dd, $J = 17.1$ Hz, $J = 4.2$ Hz), 2.17-2.11 (2H, m), 2.02-1.92 (3H, m), 1.80 (1H, m), 1.73 (1H, m), 1.54 (1H, m), 1.51 (2H, m), 1.39 (1H, t, $J = 11.7$ Hz), 1.29 (2H, m), 1.11 (3H, d, $J = 6.9$ Hz), 1.04 (9H, s), 1.03 (3H, d, $J = 6.6$ Hz), 0.91 (3H, m), 0.90 (1H, m), 0.76 (3H, d, $J = 7.0$ Hz), 0.18 (1H, dd, $J = 12.3$ Hz, $J = 6.2$ Hz); Characteristic signals of the minor diastereomer: δ 4.74 (1H, d, $J = 6.5$ Hz), 4.58 (1H, d, $J = 6.5$ Hz), 4.16 (1H, qd, $J = 4.0$ Hz, $J = 1.2$ Hz), 3.97 (1H, t, $J = 5.0$ Hz), 3.49 (1H, dd, $J = 6.3$ Hz, $J = 1.0$ Hz), 2.63 (1H, dd, $J = 16.3$ Hz, $J = 6.8$ Hz), 1.10 (3H, d, $J = 6.9$ Hz), 0.77 (3H, d, $J = 7.2$ Hz), 0.37 (1H, dd, $J = 12.7$ Hz, $J = 6.0$ Hz); ^{13}C NMR (150 MHz, $CDCl_3$) Major isomer: δ 207.1, 175.3, 136.3 (2C), 136.1 (2C), 135.5, 134.4, 133.6, 129.7, 129.6, 127.5 (2C), 127.4 (2C), 116.8, 96.5, 85.8, 84.9, 79.7, 73.3, 69.7, 55.8, 47.5, 46.6, 42.4, 40.6, 39.3, 37.7, 36.8, 36.3, 35.2, 32.7, 29.0, 27.1 (3C), 21.0, 19.3, 18.4, 16.6, 15.3, 13.8; Minor isomer: δ 206.3, 175.3, 136.3 (2C), 136.2 (2C), 135.4, 134.9, 133.9, 129.6, 129.5, 127.5 (2C), 127.4 (2C), 116.8, 96.6, 87.0, 85.1, 79.8, 73.0, 69.9, 55.8, 47.5, 47.0, 44.5, 43.5, 39.4, 37.1, 37.0, 36.3, 35.2, 33.5, 28.8, 27.0 (3C), 21.1, 19.3, 19.2, 18.5, 16.6, 14.9, 13.8.

(2R,3S,1'R,4'S,5'S)-1-(2-tert-butylidiphenylsilyloxy-3-methoxymethoxy-3-isopropyl-prop-1-yl)-2-iodomethyl-5-methyl-7-oxa-norbornane (47). A solution of the iodo derivative **44a** (134 mg, 0.21 mmol), hexamethylditin (0.31 mL, 0.2 M solution in benzene, 0.062 mmol), and AIBN (4 mg, 0.021 mmol) in benzene (0.7 mL) was refluxed for 16 h before evaporating the solvents. The crude product was filtrated through silica using pentane followed by hexanes:EtOAc = 1:1 as the eluents. This tin-free sample (131 mg) was submitted to a separation by HPLC to give 50 mg of product **44a** and 12 mg of **47** as colorless syrup each. Product **47** consists of an equimolar mixture of two diastereomers. IR (film) 3071, 3048, 2958, 2931, 2857, 1589, 1472, 1427, 1389, 1147, 1111, 1035, 918, 822, 740, 703, 612, 506 cm^{-1} ; Characteristic data: 1H NMR (400 MHz, $CDCl_3$) δ 7.73-7.68 (4H, m), 7.45-7.35 (6H, m), 4.79 (1H, d, $J = 6.5$ Hz), 4.76 (1H, d, $J = 6.5$ Hz), 4.61 (1H, d, $J = 6.5$ Hz), 4.59 (1H, d, $J = 4.59$ Hz), 4.16 (1H, m), 4.14 (1H, m), 4.05 (1H, t, $J = 5.1$ Hz), 4.00 (1H, t, $J = 5.2$ Hz), 3.50 (1H, m), 3.48 (1H, m), 3.36 (3H, s), 3.35 (3H, s), 3.23 (1H, dd, $J = 9.0$ Hz, $J = 3.9$ Hz), 2.77 (1H, dd, $J = 11.6$ Hz, $J = 9.5$ Hz), 2.69 (1H, dd, $J = 12.5$ Hz, $J = 9.0$ Hz), 2.67 (1H, dd, $J = 9.0$ Hz, $J = 3.4$ Hz), 2.07 (1H, dd, $J = 15.1$ Hz, $J = 7.6$ Hz), 2.03-1.95 (4H, m), 1.90-

1.80 (4H, m) 1.71 (1H, dd, $J = 15.1$ Hz, $J = 4.8$ Hz), 1.66 (1H, dd, $J = 15.5$, $J = 4.0$ Hz), 1.41 (1H, dd, $J = 11.9$ Hz, $J = 11.6$ Hz), 1.36 (1H, dd, $J = 12.6$ Hz, $J = 5.5$ Hz), 1.27 (1H, m), 1.18 (1H, m), 1.09 (9H, s), 1.08 (9H, s), 1.07 (3H, d, $J = 6.7$ Hz), 1.04 (3H, d, $J = 6.7$ Hz), 0.92 (3H, d, $J = 6.8$ Hz), 0.90 (3H, d, $J = 6.8$ Hz), 0.84 (3H, d, $J = 7.0$ Hz), 0.79 (3H, d, $J = 7.0$ Hz), 0.48 (1H, dd, $J = 12.9$ Hz, $J = 5.9$ Hz), 0.18 (1H, dd, $J = 12.2$ Hz, $J = 6.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 136.5 (2C), 136.4, 136.3 (2C), 136.2, 135.8, 133.7, 129.9, 129.8, 129.7, 127.8, 127.7, 127.6, 127.5, 96.7, 87.7, 85.3, 83.5, 79.6, 79.5, 73.4, 72.9, 56.0, 52.6, 50.3, 41.2, 37.6, 37.4, 36.8, 35.2, 34.9, 33.0, 32.5, 29.3, 29.0, 27.3 (3C), 27.2 (3C), 21.2, 21.1, 19.5, 19.0, 15.5, 15.0, 13.8, 5.5; MS (EI) m/z (rel. intensity): 650 (5), 563 (9), 533 (65), 531 (20), 507 (11), 403 (10), 333 (32), 309 (10), 283 (100), 267 (26), 263 (12), 243 (11), 239 (24), 237 (10), 235 (30), 213 (68), 205 (33), 199 (73), 197 (41), 188 (11), 187 (22), 183 (54), 181 (18), 163 (11), 145 (12), 139 (17), 135 (96), 133 (19), 131 (11), 123 (19), 105 (21), 93 (14), 91 (19), 85 (17), 81 (22), 79 (11), 57 (11), 55 (12), 45 (62), 43 (10); HRMS (ESI pos.): calcd. for $\text{C}_{32}\text{H}_{47}\text{IO}_4\text{SiNa}$: 673.2186; found: 673.2186 ($\text{M}+\text{Na}^+$).

H607007

AIS-CB-171-01

¹H NMR spectrum (600 MHz) of compound 46 in CDCl₃; mixture of diastereomers.

ATS-CB-219-40

¹H NMR spectrum (400 MHz) of compound **47** in CDCl₃; mixture of diastereomers

(1*S*,6*S*,9*R*,13*R*,14*S*,17*R*,19*S*)-(-)-15-*tert*-butyldiphenylsilyloxy-14-methoxymethoxy-6,13,19-trimethyl-9-propyl-8,20-dioxo-bicyclo[15.2.1]eicosane-3-en-7,11-dione (48). A solution of compound **45** (80 mg, 0.109 mmol) and the ruthenium complex **34b** (18.5 mg, 0.022 mmol) in toluene (22 mL) was refluxed for 10 min. The reaction was quenched with a few drops of ethylvinyl ether and all volatiles were stripped off under reduced pressure. Flash chromatography (hexanes:EtOAc, 10:1) of the residue afforded product **48** as a pale pink syrup (63 mg, 82%, *E*:*Z* = 7:3). The *E*/*Z* ratio was determined by HPLC analysis (150 mm, YMC-Pack ODS-A, Methanol:H₂O, 95:5). [(*Z*): Rt=14.29 min; (*E*): Rt=13.01 min]. [α]_D²⁰ -36.8° (*c* 0.785, CHCl₃). IR (film): 3071, 3048, 2961, 2933, 2858, 1730, 1589, 1462, 1428, 1379, 1153, 1111, 1032, 920, 741, 703, 613, 506, 486 cm⁻¹; MS (EI) *m/z* (rel. intensity): 706 (3), 661 (11), 649 (28), 617 (18), 587 (23), 477 (30), 419 (65), 401 (11), 389 (35), 379 (8), 377 (10), 371 (10), 277 (13), 267 (20), 211 (47), 199 (69), 195 (16), 193 (34), 175 (16), 169 (91), 165 (18), 163 (16), 147 (18), 139 (32), 135 (62), 129 (12), 123 (25), 105 (18), 99 (36), 97 (56), 93 (30), 91 (18), 81 (31), 71 (24), 69 (45), 55 (36), 45 (100), 43 (32); HRMS (CI): calcd. for C₄₂H₆₂O₇SiNa: 729.4163; found: 729.4164 (M+Na⁺).

(1*S*,6*S*,9*R*,13*R*,14*S*,15*R*,17*R*,19*S*)-(-)-15-*tert*-butyldiphenylsilyloxy-14-methoxymethoxy-6,13,19-trimethyl-9-propyl-8,20-dioxo-bicyclo[15.2.1]eicosane-7,11-dione (49). Prepared as described for product **36** using substrate **48** (25 mg, 0.035 mmol). Colorless syrup (25 mg, 99%). [α]_D²⁰ -26.8° (*c* 0.715, CHCl₃). IR (film): 3071, 3049, 2960, 2933, 2874, 2858, 1730, 1589, 1462, 1427, 1383, 1255, 1167, 1154, 1111, 1034, 918, 822, 741, 703, 613, 504, 483 cm⁻¹; ¹H NMR (300 MHz, toluene d₈, recorded at 353 K) δ 7.85-7.71 (4H, m), 7.28-7.19 (6H, m), 5.15 (1H, dt, *J* = 12.5 Hz, *J* = 5.9 Hz), 4.89 (1H, d, *J* = 6.2 Hz), 4.58 (1H, d, *J* = 6.2 Hz), 4.35 (1H, dt, *J* = 9.1 Hz, *J* = 3.1 Hz), 4.17 (1H, m), 3.71 (1H, dd, *J* = 5.0 Hz, *J* = 2.9 Hz), 3.55 (1H, ddd, *J* = 10.4 Hz, *J* = 6.1 Hz, *J* = 2.3 Hz), 3.27 (3H, s), 2.68-2.60 (2H, m), 2.45-2.37 (3H, m), 2.02 (2H, m), 1.87 (2H, m), 1.73-1.62 (3H, m), 1.59-1.51 (2H, m), 1.49-1.40 (2H, m), 1.36-1.21 (8H, m), 1.19 (9H, s), 1.11 (3H, d, *J* = 6.5 Hz), 1.10 (3H, d, *J* = 6.9 Hz), 0.84 (3H, t, *J* = 7.3 Hz), 0.70 (3H, d, *J* = 7.0 Hz); MS (EI) *m/z* (rel. intensity): 663 (9), 651 (27), 621 (8), 619 (16), 589 (20), 437 (6), 421 (49), 403 (9), 391 (33), 379 (5), 373 (13), 355 (6), 293 (8), 279 (9), 267 (14), 225 (10), 213 (47), 199 (44), 195 (43), 169 (100), 151 (20), 139 (24), 135 (33), 123 (18), 99 (23), 97 (39), 95 (21), 81 (20), 69 (34), 55 (28), 45 (73). HRMS (CI): calcd. for C₄₂H₆₄O₇SiNa: 731.4319; found: 731.4309 (M+Na⁺).

^1H NMR spectrum (300 MHz) of **49** in toluene- d_8 at $T = 303\text{ K}$ (top) and 353 K (bottom)

(1*S*,6*S*,9*R*,13*R*,14*S*,15*R*,17*R*,19*S*)-(-)-15-*tert*-butyldiphenylsilyloxy-14-hydroxy-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxa-bicyclo[15.2.1]eicosane-7-one (50). Ketone **49** (12.5 mg, 0.0175 mmol) was processed according to the procedure described for the preparation of product **39**. Flash chromatography (hexanes:EtOAc, 10/1) afforded product **50** as a colorless oil (6.5 mg, 55%). $[\alpha]_D^{20}$ -34.3° (c 0.64, CHCl₃). IR (film): 3478, 3071, 3049, 2960, 2932, 2857, 1728, 1643, 1620, 1461, 1428, 1381, 1259, 1181, 1167, 1110, 1076, 1018, 894, 822, 740, 703, 612, 503 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.82-7.72 (4H, m), 7.24-7.19 (6H, m), 5.32 (1H, m), 5.16 (1H, s), 4.99 (1H, s), 4.49 (1H, q, J = 7.7 Hz, J = 16.6 Hz), 4.20 (1H, m), 4.03 (1H, d, J = 8.4 Hz), 3.81 (1H, s), 3.51 (1H, m), 2.81 (1H, dd, J = 8.7 Hz, J = 14.9 Hz), 2.55 (2H, m), 2.46 (1H, m), 2.21 (1H, dd, J = 14.6 Hz, J = 5.2 Hz), 2.07 (1H, dd, J = 14.7 Hz, J = 5.3 Hz), 1.19 (9H, s), 1.15 (3H, d, J = 6.9 Hz), 1.02 (3H, d, J = 6.8 Hz), 0.87 (3H, t, J = 7.3 Hz), 0.66 (3H, d, J = 7.1 Hz); ¹³C NMR (100 MHz, C₆D₆) δ 145.7, 136.4, 135.2, 134.1, 130.1, 129.9, 128.1, 127.8, 112.9, 81.4, 72.9, 72.4, 71.4, 42.0, 41.3, 40.3, 40.3, 39.6, 36.2, 35.9, 34.7, 33.1, 29.7, 27.5 (3C), 27.1, 26.6 (2C), 19.7, 19.0, 17.7, 14.2, 14.1, 13.6, 13.5; MS (EI) m/z (rel. intensity): 662 (5), 607 (4), 605 (26), 584 (6), 421 (6), 406 (19), 389 (27), 377 (5), 371 (16), 365 (7), 343 (13), 337 (4), 308 (6), 289 (7), 287 (7), 283 (24), 199 (100), 195 (49), 167 (28), 149 (92), 139 (24), 137 (22), 107 (22), 95 (50), 69 (22), 55 (25); HRMS (CI): calcd. for C₄₁H₆₂O₅Si: 662.4367; found: 662.4370.

(1*S*,6*S*,9*R*,13*R*,15*R*,17*R*,19*S*)-(-)-15-*tert*-butyldiphenylsilyloxy-6,13,19-trimethyl-11-methylene-9-propyl-8,20-dioxa-bicyclo[15.2.1]eicosane-7,14-dione (51). Dess-Martin periodinane (12 mg, 0.028 mmol) was added to a solution of alcohol **50** (12 mg, 0.018 mmol) in CH₂Cl₂ (3mL) and the resulting mixture was stirred for 1.5 h. For work up, the mixture was diluted with ether and the reaction was quenched with aq. sat. Na₂S₂O₃ and aq. sat. NaHCO₃. The aqueous layer was extracted with CH₂Cl₂, the combined organic phases were washed with brine, dried over Na₂SO₄ and filtered. Evaporation of the solvents followed by flash chromatography (hexanes:EtOAc, 10:1) of the residue afforded product **51** as a colorless oil (10.6 mg, 88%). $[\alpha]_D^{20}$ -37.8° (c 0.53, CHCl₃). IR (film): 3072, 3049, 2961, 2933, 2873, 2858, 1726, 1646, 1589, 1460, 1428, 1382, 1257, 1111, 1073, 1020, 902, 822, 741, 703, 613, 504 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.89-7.83 (4H, m), 7.29-7.20 (6H, m), 5.06 (1H, m), 4.91 (1H, s), 4.89 (1H, s), 4.82 (1H, q, J = 3.7 Hz), 3.54 (1H, m), 3.47 (1H, m), 2.52 (1H, d, J = 13.8 Hz), 2.43 (1H, m), 2.32 (1H, dd, J = 13.7 Hz, J = 7.9 Hz), 2.05 (1H, dd, J = 13.8 Hz, J = 5.6 Hz), 1.24 (9H, s), 1.18 (3H, d, J = 6.7 Hz), 1.10 (3H, d, J = 6.9 Hz), 0.84 (3H, t, J = 7.3 Hz), 0.61 (3H, d, J = 7.0 Hz), 0.28 (6H, s); ¹³C NMR (100 MHz, C₆D₆) δ 213.6, 175.0, 143.7, 136.4 (2C), 134.6 (2C), 130.0 (2C), 127.9 (4C), 114.2, 80.1, 75.8, 72.5, 71.6, 42.4, 41.8, 41.3, 40.0, 39.3, 38.5, 36.5, 35.8, 34.9, 30.5, 27.7, 27.4 (3C), 26.1, 19.8, 18.8, 18.0, 15.7, 14.2, 14.1; MS (EI) m/z (rel. intensity): 605 (7), 604 (20), 603 (42), 585 (8), 575 (5), 437 (6), 419 (6), 393 (7), 387 (100), 377 (23), 375 (6), 369 (27), 359 (8), 341 (5), 333 (5), 313 (5), 299 (6), 289 (10), 281 (21), 255 (6), 240 (12), 237 (9), 229 (5), 225 (11), 224 (8), 221 (8), 203 (12), 201 (13), 199 (68), 197 (18), 195 (94), 183 (25), 182 (23), 177 (23), 175 (25), 173 (7), 167 (12), 165 (7), 159 (8), 149 (33), 139 (32), 135 (38), 123 (21), 95 (52), 69 (33), 55 (41); HRMS (CI): calcd. for C₄₁H₆₀O₅SiNa: 683.4108; found: 683.4102 (M+Na⁺).

Amphidinolide T3 (3). HF-pyridine complex (~ 0.1 mL) was added via a teflon syringe to a solution of silyl ether **51** (10.6 mg, 0.0159 mmol) in MeCN (1 mL). After stirring for 24 h, the mixture was poured into water and the aqueous phase was extracted three times with EtOAc. The combined organic layers were washed with brine, dried with Na₂SO₄, filtered and evaporated, and the residue was purified by flash chromatography on silica gel (hexanes:EtOAc, 20:1, then 10:1) to give amphidinolide T3 as a colorless oil (3.3 mg, 55% based on the recovered starting material). The ¹H and ¹³C NMR were identical to those reported in the literature (see ref.⁴ in the Text; see also Table S-3 and spectrum). [α]_D²⁰ –40.0° (*c* 0.075, CHCl₃). MS (EI) *m/z* (rel. intensity): 422 (4), 404 (6), 394 (29), 297 (5), 296 (6), 284 (8), 257 (59), 239 (59), 221 (16), 213 (29), 195 (40), 186 (8), 167 (25), 149 (18), 138 (63), 110 (15), 95 (100), 79 (12), 68 (31), 67 (37), 55 (61), 43 (39), 41 (38); HRMS (CI): calcd. for C₂₅H₄₂O₅Na, 445.2930, found: 445.2931 [(M+Na)⁺].

Table S-3. Comparison of the ¹³C data of amphidinolide T3 (**3**)

Position	Literature	(3)
1	174.9	174.8
2	41.2	41.2
3	34.6	34.6
4	26.5	26.5
5	26.5	26.5
6	29.7	29.7
7	79.2	79.2
8	36.3	36.3
9	39.3	39.9
10	76.1	76.1
11	39.3	39.3
12	76.3	76.3
13	215.7	215.7
14	38.4	38.4
15	41.4	41.4
16	143.3	143.3
17	40.6	40.6
18	72.1	72.1
19	35.9	35.9
20	18.8	18.8
21	14.1	14.1
22	17.7	17.8
23	14.2	14.2
24	15.5	15.5
25	114.7	114.7

¹H NMR spectrum (400 MHz) of amphidinolide T3 (**3**) in C₆D₆

Crystal Structure Determination

Figure 1. Molecular crystal structure of compound **11**. Anisotropic displacement parameters are drawn at the 50 % probability level.

Table S-4. Crystal data and structure refinement.

Empirical formula	C ₁₄ H ₁₈ O ₃ S	
Color	colorless	
Formula weight	266.34 g · mol ⁻¹	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2₁2₁2₁, (no. 19)	
Unit cell dimensions	a = 8.6145(2) Å	α = 90°.
	b = 8.85250(10) Å	β = 90°.
	c = 18.0214(2) Å	γ = 90°.
Volume	1374.31(4) Å ³	
Z	4	
Density (calculated)	1.287 Mg · m ⁻³	
Absorption coefficient	0.233 mm ⁻¹	
F(000)	568 e	
Crystal size	0.31 x 0.28 x 0.08 mm ³	
θ range for data collection	3.23 to 27.50°.	
Index ranges	-6 ≤ h ≤ 11, -6 ≤ k ≤ 11, -13 ≤ l ≤ 23	
Reflections collected	5201	

Independent reflections	2996 [$R_{\text{int}} = 0.0233$]	
Reflections with $I > 2\sigma(I)$	2949	
Completeness to $\theta = 27.50^\circ$	98.0 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9816 and 0.9312	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2996 / 0 / 163	
Goodness-of-fit on F^2	1.162	
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0252$	$wR^2 = 0.0750$
R indices (all data)	$R_1 = 0.0257$	$wR^2 = 0.0756$
Absolute structure parameter	-0.03(5)	
Largest diff. peak and hole	0.251 and -0.295 e · Å ⁻³	

Table S-5. Atomic coordinates and equivalent isotropic displacement parameters (Å²).
 U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
S(1)	-0.1595(1)	-0.3533(1)	-0.8942(1)	0.018(1)
O(1)	-0.0453(1)	-0.4597(1)	-0.8672(1)	0.027(1)
C(1)	-0.1146(1)	-0.1729(1)	-0.8516(1)	0.016(1)
O(2)	-0.1757(1)	-0.3310(1)	-0.9732(1)	0.024(1)
C(2)	0.0384(1)	-0.1088(2)	-0.8837(1)	0.019(1)
O(3)	-0.2348(1)	-0.0706(1)	-0.8679(1)	0.017(1)
C(3)	-0.0065(1)	0.0549(2)	-0.9034(1)	0.018(1)
C(4)	-0.1776(1)	0.0345(1)	-0.9238(1)	0.017(1)
C(5)	-0.2827(2)	0.1720(2)	-0.9224(1)	0.021(1)
C(6)	-0.4426(2)	0.1322(2)	-0.9494(1)	0.024(1)
C(7)	-0.5703(2)	0.1530(2)	-0.9111(1)	0.035(1)
C(8)	0.0200(2)	0.1625(2)	-0.8383(1)	0.023(1)
C(10)	-0.3437(2)	-0.4012(1)	-0.8581(1)	0.017(1)
C(11)	-0.4764(2)	-0.3479(2)	-0.8936(1)	0.020(1)
C(12)	-0.6206(2)	-0.3857(2)	-0.8651(1)	0.025(1)
C(13)	-0.6318(2)	-0.4733(2)	-0.8013(1)	0.028(1)
C(14)	-0.4990(2)	-0.5253(2)	-0.7659(1)	0.029(1)
C(15)	-0.3532(2)	-0.4903(2)	-0.7947(1)	0.023(1)

Table S-6. Bond lengths [Å] and angles [°].

S(1)-O(2)	1.4448(9)	S(1)-O(1)	1.4461(10)
S(1)-C(10)	1.7659(13)	S(1)-C(1)	1.8139(13)
C(1)-O(3)	1.4060(14)	C(1)-C(2)	1.5471(17)
C(1)-H(1)	1.0000	C(2)-C(3)	1.5409(18)
C(2)-H(2A)	0.9900	C(2)-H(2B)	0.9900
O(3)-C(4)	1.4570(14)	C(3)-C(8)	1.5286(18)
C(3)-C(4)	1.5298(16)	C(3)-H(3)	1.0000
C(4)-C(5)	1.5169(17)	C(4)-H(4)	1.0000
C(5)-C(6)	1.5021(17)	C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900	C(6)-C(7)	1.312(2)
C(6)-H(6)	0.9500	C(7)-H(7A)	0.9500
C(7)-H(7B)	0.9500	C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800	C(8)-H(8C)	0.9800
C(10)-C(15)	1.3916(17)	C(10)-C(11)	1.3929(18)
C(11)-C(12)	1.3853(18)	C(11)-H(11)	0.9500
C(12)-C(13)	1.390(2)	C(12)-H(12)	0.9500
C(13)-C(14)	1.388(2)	C(13)-H(13)	0.9500
C(14)-C(15)	1.394(2)	C(14)-H(14)	0.9500
C(15)-H(15)	0.9500		
O(2)-S(1)-O(1)	119.13(6)	O(2)-S(1)-C(10)	107.98(6)
O(1)-S(1)-C(10)	109.32(6)	O(2)-S(1)-C(1)	108.47(6)
O(1)-S(1)-C(1)	106.64(6)	C(10)-S(1)-C(1)	104.32(5)
O(3)-C(1)-C(2)	108.25(10)	O(3)-C(1)-S(1)	108.77(8)
C(2)-C(1)-S(1)	110.30(8)	O(3)-C(1)-H(1)	109.8
C(2)-C(1)-H(1)	109.8	S(1)-C(1)-H(1)	109.8
C(3)-C(2)-C(1)	102.54(9)	C(3)-C(2)-H(2A)	111.3
C(1)-C(2)-H(2A)	111.3	C(3)-C(2)-H(2B)	111.3
C(1)-C(2)-H(2B)	111.3	H(2A)-C(2)-H(2B)	109.2
C(1)-O(3)-C(4)	107.86(9)	C(8)-C(3)-C(4)	113.63(10)
C(8)-C(3)-C(2)	111.79(11)	C(4)-C(3)-C(2)	100.76(10)
C(8)-C(3)-H(3)	110.1	C(4)-C(3)-H(3)	110.1
C(2)-C(3)-H(3)	110.1	O(3)-C(4)-C(5)	107.47(10)
O(3)-C(4)-C(3)	103.59(9)	C(5)-C(4)-C(3)	118.48(11)
O(3)-C(4)-H(4)	109.0	C(5)-C(4)-H(4)	109.0
C(3)-C(4)-H(4)	109.0	C(6)-C(5)-C(4)	110.72(11)
C(6)-C(5)-H(5A)	109.5	C(4)-C(5)-H(5A)	109.5
C(6)-C(5)-H(5B)	109.5	C(4)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	108.1	C(7)-C(6)-C(5)	124.49(13)
C(7)-C(6)-H(6)	117.8	C(5)-C(6)-H(6)	117.8
C(6)-C(7)-H(7A)	120.0	C(6)-C(7)-H(7B)	120.0

H(7A)-C(7)-H(7B)	120.0	C(3)-C(8)-H(8A)	109.5
C(3)-C(8)-H(8B)	109.5	H(8A)-C(8)-H(8B)	109.5
C(3)-C(8)-H(8C)	109.5	H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5	C(15)-C(10)-C(11)	121.40(12)
C(15)-C(10)-S(1)	119.43(10)	C(11)-C(10)-S(1)	119.16(9)
C(12)-C(11)-C(10)	118.96(12)	C(12)-C(11)-H(11)	120.5
C(10)-C(11)-H(11)	120.5	C(11)-C(12)-C(13)	120.23(12)
C(11)-C(12)-H(12)	119.9	C(13)-C(12)-H(12)	119.9
C(14)-C(13)-C(12)	120.54(13)	C(14)-C(13)-H(13)	119.7
C(12)-C(13)-H(13)	119.7	C(13)-C(14)-C(15)	119.86(12)
C(13)-C(14)-H(14)	120.1	C(15)-C(14)-H(14)	120.1
C(10)-C(15)-C(14)	119.00(13)	C(10)-C(15)-H(15)	120.5
C(14)-C(15)-H(15)	120.5		

Table S-7. Anisotropic displacement parameters ($\text{\AA}^2$). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S(1)	0.019(1)	0.014(1)	0.020(1)	-0.001(1)	0.003(1)	0.002(1)
O(1)	0.023(1)	0.018(1)	0.040(1)	0.001(1)	0.001(1)	0.006(1)
C(1)	0.019(1)	0.014(1)	0.016(1)	-0.001(1)	0.000(1)	0.003(1)
O(2)	0.029(1)	0.025(1)	0.018(1)	-0.005(1)	0.006(1)	-0.004(1)
C(2)	0.016(1)	0.019(1)	0.022(1)	-0.002(1)	0.000(1)	0.002(1)
O(3)	0.016(1)	0.015(1)	0.019(1)	0.002(1)	0.003(1)	0.002(1)
C(3)	0.013(1)	0.021(1)	0.020(1)	0.001(1)	0.001(1)	0.000(1)
C(4)	0.016(1)	0.018(1)	0.016(1)	0.002(1)	0.000(1)	0.000(1)
C(5)	0.019(1)	0.017(1)	0.026(1)	0.005(1)	-0.002(1)	0.001(1)
C(6)	0.022(1)	0.027(1)	0.024(1)	0.005(1)	-0.006(1)	0.003(1)
C(7)	0.021(1)	0.051(1)	0.032(1)	0.004(1)	-0.004(1)	0.003(1)
C(8)	0.019(1)	0.019(1)	0.030(1)	-0.002(1)	-0.004(1)	-0.001(1)
C(10)	0.020(1)	0.015(1)	0.016(1)	-0.001(1)	0.002(1)	-0.001(1)
C(11)	0.024(1)	0.021(1)	0.016(1)	0.001(1)	0.002(1)	0.003(1)
C(12)	0.021(1)	0.027(1)	0.026(1)	-0.004(1)	0.001(1)	0.004(1)
C(13)	0.029(1)	0.029(1)	0.028(1)	-0.002(1)	0.009(1)	-0.004(1)
C(14)	0.037(1)	0.030(1)	0.021(1)	0.006(1)	0.004(1)	-0.006(1)
C(15)	0.027(1)	0.021(1)	0.020(1)	0.003(1)	-0.003(1)	-0.001(1)