Supporting Information

Synthesis of (–)-Amphidinolide K Fragment C9–C22

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General procedures

Unless specified otherwise, all starting materials and reagents were obtained from commercial suppliers and used without further purification. All reactions were conducted in oven-dried glassware, under dry nitrogen or argon atmosphere with anhydrous solvents, which were dried and distilled before use according to standard procedures. Solvents used for isolation of products and chromatography were glass distilled. Analytical thin-layer chromatography (TLC) was performed on 0.25 mm silica gel plates (F₂₅₄, Merck). Retention factors (*R_f*) are approximate. Flash column chromatography was performed on SDS silica gel 60 (35–70 μ m). ¹H NMR (200 MHz) and ¹³C NMR (50.3 MHz) spectra were recorded on a Varian Gemini-200 spectrometer; ¹H NMR (300 MHz) and ¹³C NMR (75.4 MHz) spectra were recorded on a Varian 300 Unity Plus spectrometer; ¹H NMR (400 MHz) and ¹³C NMR (100.6 MHz) spectra were recorded on a Varian Mercury-400 spectrometer. Chemical shifts (δ) are reported in units of parts per million downfield from tetramethylsilane for ¹H NMR and CDCl₃ (δ 77.0) for ¹³C. All coupling constants (*J*) are reported in hertz; data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Where necessary, 2D experiments were performed to assist in structure elucidation. Optical rotations ($[\alpha]_D$) were measured on a Perkin-Elmer 241MC polarimeter at 20 °C. Infrared spectra were recorded on either a Perkin-Elmer 681 or a Nicolet 510-FT spectrometer; only the more representative frequencies are reported (cm^{–1}). Mass spectra were obtained on a HP-5988-A instrument and only the most representative peaks are reported (*m/z*). High-resolution mass spectra (FAB-HRMS) were obtained by CACTI, Universidade de Vigo.

(*R*)-5-((4-Methoxybenzyloxy)methyl)tetrahydrofuran-2-one (8)*

NaH (ca. 60% dispersion in mineral oil, 614 mg, ca. 14 mmol) was added to a solution of (*R*)-7 (1.1 g, 9.39 mmol) in 7 mL of DMF and 5 mL of THF, under N₂. PMBCl (1.91 mL, 14.1 mmol) was added via syringe and the mixture was stirred for 4 days at room temperature before being quenched with phosphate buffer solution (8 mL). It was then diluted with CH₂Cl₂ (4 x 50 mL), washed with water (3 x 10 mL) and dried (Na₂SO₄). The volatiles were removed under reduced pressure and the residue was purified by

column chromatography on silica gel (1% MeOH in CH₂Cl₂) to afford 2.057 g (94%) of the protected lactone **8** as a yellow oil: R_f (1% MeOH in CH₂Cl₂) 0.32; ¹H NMR (CDCl₃, 300 MHz) δ 7.24 (d, *J* = 8.4, 2 H), 6.88 (d, *J* = 8.4, 2 H), 4.65 (m, 1 H), 4.50 (s, 2 H), 3.81 (s, 3 H), 3.65 (dd, *J* = 10.6, 3.6, 1 H), 3.55 (dd, *J* = 10.6, 4.0, 1 H), 2.75–2.00 (m, 4 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ 177.2, 159.3, 129.8, 129.2, 113.8, 79.0, 73.2, 71.2, 55.2, 28.3, 24.1; MS (CI, NH₃) 254 (M+18, 100); [α]_D –12.5 (CH₂Cl₂, *c* 0.99).

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(*R*)-4-Hydroxy-5-(4-methoxybenzyloxy)pentanoic acid

A solution of **8** (4.5 g, 19.1 mmol) and KOH (3.2 g, 57.3 mmol) in MeOH (147 mL) was heated to reflux for 6 h. When TLC analysis showed complete conversion of the starting material, the mixture was left to return to room temperature and the solvent was removed under vacuum. The residue was diluted with water (20 mL) and 2 N HCl was added to reach pH 4. The aqueous solution was extracted with 100 mL of EtOAc (x 5). The procedure was repeated 5 times. The combined organic extracts were washed with brine (3 x 20 mL), dried (Na₂SO₄) and concentrated under reduced pressure to afford 4.8 g (100%) of the hydroxyacid, which was directly carried to the protection step in order to avoid lactone reformation. Fast purification by silica gel chromatography (10% MeOH in CH₂Cl₂) afforded a yellow oil: R_f (10% MeOH in CH₂Cl₂) 0.34; ¹H NMR (CDCl₃, 300 MHz) δ 7.25 (d, *J* = 8.6, 2 H), 6.88 (d, *J* = 8.6, 2 H), 4.48 (s, 2 H), 3.83 (m, 1 H), 3.81 (s, 3 H), 3.48 (dd, *J* = 9.6, 3.2, 1 H), 3.32 (dd, *J* = 9.6, 7.4, 1 H), 2.51 (m, 2 H), 1.73 (m, 2 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ 178.1, 159.3, 129.8, 129.4, 113.8, 73.8, 73.0, 69.5, 55.2, 30.1, 27.8; MS (CI, NH₃): 255 (M+1, 100); [α]_D –12.3 (CH₂Cl₂, *c* 1.05).

(*R*)-4-(*tert*-Butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)pentanoic acid (9**)**

The hydroxyacid (4.8 g, 19.1 mmol) was dissolved in anhydrous CH₂Cl₂ (135 mL) and TBSCl (6.1 g, 40.1 mmol) and imidazole (5.2 g, 76.4 mmol) were added under N₂ at room temperature. The mixture was stirred for 5 h and then filtered through celite. The filtrate was concentrated and diluted in 40 mL of a MeOH–THF 3:1 mixture. Water (10 mL) containing 1 g of K₂CO₃ was added at 0 °C and the mixture was stirred vigorously for 1 h. After addition of 2 N HCl until pH 4 and extraction with EtOAc (4 x 40 mL), the combined organic extracts were dried (Na₂SO₄) and concentrated under reduced

pressure. The residue was purified (silica gel, 40% EtOAc in hexane) to afford 6.6 g (94%) of acid **9**: R_f (30% EtOAc in hexane) 0.31; 1H NMR ($CDCl_3$, 300 MHz) δ 7.25 (d, J = 8.6, 2 H), 6.87 (d, J = 8.6, 2 H), 4.44 (s, 2 H), 3.85 (m, 1 H), 3.80 (s, 3 H), 3.35 (m, 2 H), 2.42 (m, 2 H), 2.00–1.73 (m, 2 H); 0.87 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 179.7, 159.1, 130.2, 129.2, 113.7, 73.8, 73.0, 70.1, 55.3, 29.6, 25.9, 18.1, –4.4, –4.8; IR (film) 3000 (br), 2900, 2840, 1700, 1510, 1240; MS (FAB) 291 ($M+23$, 100); $[\alpha]_D = -13.6$ (CH_2Cl_2 , c 1.03).

(*R*)-4-Benzyl-3-((*R*)-4-(*tert*-butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)-pentanoyl)oxazolidin-2-one (10**)**

At 0 °C, under N_2 , Et_3N (2.1 mL, 14.9 mmol) and pivaloyl chloride (1.8 mL, 14.9 mmol) were added to a solution of **9** (4.9 g, 13.4 mmol) in 89 mL of anhydrous THF and the mixture was stirred at this temperature for 3 h. In a separate dry flask, at –78 °C and under N_2 , BuLi (1.6 M in hexanes, 10 mL, 16.1 mmol) was added to a solution of non-natural oxazolidinone (2.7 g, 15.4 mmol), containing a small amount of Ph_3CH as an indicator, in 33 mL of THF. Stirring was maintained at –78 °C until colour change, and then the second mixture was added dropwise via cannula to the first one, cooled down to –78 °C. After stirring for 2 h, the reaction was quenched with phosphate buffer (10 mL) and extracted with EtOAc (4 x 50 mL). The combined organic extracts were washed with brine (2 x 10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified (silica gel, 25% EtOAc in hexane) to afford 6.7 g (95%) of **10** as a yellow oil: R_f (30% EtOAc in hexane) 0.40; 1H NMR ($CDCl_3$, 300 MHz) δ 7.26 (m, 7 H), 6.87 (d, J = 8.6, 2 H), 4.65 (m, 1 H), 4.46 (s, 2 H), 4.14 (m, 2 H), 3.92 (m, 1 H), 3.80 (s, 3 H), 3.40 (m, 2 H), 3.30 (dd, J = 13.3, 9.7, 1 H), 3.00 (m, 2 H), 2.72 (m, 1 H), 1.80 (m, 1 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 173.2, 159.3, 135.4, 129.4, 129.2, 128.9, 127.3, 113.7, 74.2, 73.0, 70.3, 66.1, 55.2, 55.1, 37.9, 31.6, 28.9, 27.0, 25.9, 18.1, –4.4, –4.8; IR (film) 2910, 2850, 1780, 1510; MS (FAB) 550 ($M+23$, 50), 528 ($M+1$, 70); $[\alpha]_D -14.1$ (CH_2Cl_2 , c 1.05).

(*R*)-4-Benzyl-3-((*R*)-4-(*tert*-butyldimethylsilyloxy)-5-hydroxypentanoyl)oxazolidin-2-one

To a solution of **10** (3.7 g, 7.03 mmol) in CH_2Cl_2 (70 mL) and water (0.5 mL) at 0 °C was added DDQ (1.9 g, 8.44 mmol) in two portions. The mixture was vigorously stirred

for 30 minutes at 0 °C and 2 h at room temperature, and then was quenched with 10 mL of sat. NaHCO₃ at 0 °C. The mixture was extracted thoroughly with CH₂Cl₂ (5 x 50 mL), the combined organic extracts were washed with sat. NaHCO₃ (2 x 10 mL) and brine (2 x 20 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The residue was purified (silica gel, 30% EtOAc in hexane) to afford 2.7 g (93%) of the primary alcohol: R_f (30% EtOAc in hexane) 0.32; ¹H NMR (CDCl₃, 300 MHz) δ 7.36 (m, 5 H), 4.67 (m, 1 H), 4.18 (m, 2 H), 3.88 (m, 1 H), 3.58 (dd, *J* = 11.2, 4.5, 1 H), 3.51 (dd, *J* = 11.2, 4.7, 1 H), 3.31 (dd, *J* = 13.3, 3.2, 1 H), 3.01 (m, 2 H), 2.74 (dd, *J* = 13.3, 9.8, 1 H), 1.92 (m, 2 H), 0.92 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ 173.4, 153.6, 129.6, 129.2, 127.6, 77.6, 77.2, 76.9, 71.8, 66.4, 66.2, 55.4, 38.1, 31.6, 28.1, 26.1, 18.3, -4.3, -4.4; IR (film) 2930 (br), 1786, 1702, 1389, 1211, 838; MS (FAB) 550 (M+23, 50), 408 (M+1, 100); [α]_D -13.1 (CH₂Cl₂, *c* 1.12).

Ethyl (2*E*,4*R*)-7-((*R*)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl)-4-(*tert*-butyldimethylsilyloxy)-7-oxohept-2-enoate (11)

Freshly distilled DMSO (0.54 mL, 6.02 mmol) was added dropwise to a cooled (-78 °C) solution of oxalyl chloride (0.25 mL, 3.01 mmol) in anhydrous CH₂Cl₂ (26 mL). Five minutes later, a solution of primary alcohol (942 mg, 2.31 mmol) in CH₂Cl₂ (45 mL + 6 mL wash) was slowly added via cannula and the mixture was stirred at -78 °C for 30 minutes. Et₃N (1.93 mL, 0.59 mmol) was added and stirring continued for 15 minutes in the dry ice-acetone bath and for another 30 minutes while slowly warming to room temperature. It was then quenched with 10 mL of phosphate buffer solution and extracted with CH₂Cl₂ (3 x 40 mL). The combined organic extracts were washed with water (2 x 10 mL) and brine (2 x 20 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The resulting 937 mg (2.31 mmol, 100%) of the pure aldehyde were dissolved in anhydrous DME (24 mL) and added via cannula at room temperature and under N₂ to a mixture of triethyl phosphonoacetate (0.5 mL, 2.43 mmol) and BuLi (1.6 M in hexanes, 1.5 mL, 2.43 mmol) in anhydrous DME (4.8 mL) stirred during 20 minutes before the addition. Stirring was continued for 5 h at room temperature, then the reaction was quenched with 10 mL of sat. NaHCO₃ at 0 °C, left to warm to room temperature, and extracted with 3 x 40 mL of CH₂Cl₂. The combined extracts were washed with brine (2 x 10 mL), dried (Na₂SO₄), and concentrated. The residue was purified (silica gel, 30% EtOAc in hexane) to provide 989 mg (90%) of **11** as a pale yellow oil: R_f (30% EtOAc in hexane) 0.40; ¹H NMR (CDCl₃, 400 MHz) δ 7.35–7.20 (m, 5 H), 6.93 (dd, *J* = 15.6, 4.7, 1 H), 6.01 (dd, *J* = 15.6, 1.6, 1 H), 4.65 (m, 1 H), 4.46 (m, 1 H), 4.19 (q, *J* = 7.1, 2 H), 4.17 (m, 2 H), 2.31 (dd, *J* = 13.3, 3.5, 1 H), 3.02 (m, 2 H), 2.74 (dd, *J* = 13.3, 9.8, 1 H), 2.01 (br m, 1 H), 1.87 (br m, 1 H), 1.30 (t, *J* = 7.1, 3 H), 0.93 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H); ¹³C NMR (CDCl₃, 100.6 MHz) δ 172.7, 166.4, 153.2, 149.9, 135.2, 129.3, 128.9, 127.2, 120.4, 70.3, 66.1, 60.3, 55.1, 37.8, 31.2, 30.9, 25.7, 18.1, 14.1, -4.6, -4.9; MS (FAB) 498.3 (M+23), 476.4 (M+1); HRMS (FAB) calc. for C₂₅H₃₈NO₆Si (M+1) 476.2468, found 476.2476; [α]_D -13.0 (CHCl₃, *c* 1.05).

(2*S*)-2,5-Dihydroxy-1-tosyloxypentane

To a solution of the tosyl furanone **13** (716 mg, 2.65 mmol) in THF (10 mL) at $-78\text{ }^{\circ}\text{C}$, DIBALH (10.6 mL of a 1.0 M solution in hexanes, 10.6 mmol) was added. Upon complete addition, the solution was left to warm to room temperature. After 1.5 h, TLC showed complete consumption of the starting material. The reaction mixture was cooled to $0\text{ }^{\circ}\text{C}$, quenched with phosphate buffer solution (10 mL) and solid sodium potassium tartrate, and extracted with CH_2Cl_2 (3 x 30 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated. Flash chromatography of the resulting residue (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) furnished (2*S*)-2,5-dihydroxy-1-tosyloxypentane (690 mg, 2.52 mmol, 95%): R_f (5% MeOH in CH_2Cl_2) 0.33; ^1H NMR (CDCl_3 , 200 MHz) δ 7.80 (d, $J = 8.4$, 2 H), 7.36 (d, $J = 8.4$, 2 H), 3.95 (m, 3 H), 3.65 (m, 2 H), 2.45 (s, 3 H), 1.80 - 1.20 (m, 4 H); ^{13}C NMR (CDCl_3 , 50.3 MHz) δ 145.0, 132.4, 129.9, 127.9, 73.7, 69.1, 62.4, 29.9, 28.5, 21.1; IR (film) 3367 (br), 2940, 1346, 1168, 962; MS (CI, NH_3) 292 ($\text{M}+18$); $[\alpha]_D +3.3$ (CHCl_3 , c 1.05).

(2*S*)-5-(*tert*-Butyldimethylsilyloxy)-2-hydroxy-1-tosyloxypentane (**14**)

Et_3N (0.84 mL, 6.03 mmol) was added to a solution of (2*S*)-2,5-dihydroxy-1-tosyloxypentane (1.498 g, 5.46 mmol), *tert*-butyldimethylsilyl chloride (910 mg, 6.04 mmol) and DMAP (30 mg, 0.24 mmol) in CH_2Cl_2 (24 mL). After stirring at room temperature for 5 h, the reaction mixture was diluted with CH_2Cl_2 (50 mL), and washed with water (2 x 10 mL) and aqueous saturated NH_4Cl (2 x 10 mL). The organic extracts were dried (Na_2SO_4), filtered, and concentrated. The resulting yellow oil was purified by flash chromatography (2% MeOH in CH_2Cl_2) to yield the secondary alcohol **14** (1.954 g, 92%) as a yellow oil: R_f (CH_2Cl_2) 0.20; ^1H NMR (CDCl_3 , 200 MHz) δ 7.80 (d, $J = 8.4$, 2 H), 7.36 (d, $J = 8.4$, 2 H), 3.95 (m, 2 H), 3.85 (m, 1 H), 3.62 (m, 2 H), 3.35 (br s, 1 H), 2.45 (s, 3 H), 1.60 (m, 4 H); 0.88 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (CDCl_3 , 50.3 MHz) δ 144.8, 132.7, 129.8, 127.9, 73.5, 69.1, 63.2, 30.6, 28.6, 25.9, 21.7, 18.3, -5.4; MS (CI, NH_3) 388 (M); $[\alpha]_D +2.5$ (CHCl_3 , c 1.06).

(2*S*)-5-*tert*-Butyldimethylsilyloxy-1,2-epoxypentane (**15**)*

NaH (ca. 60% dispersion in mineral oil, 55 mg, ca. 1.26 mmol) was added to a solution of **14** (306 mg, 0.79 mmol) in THF (3 mL). After stirring for 2 h at room temperature, the reaction was quenched by addition of sodium phosphate buffer (5 mL). The resulting mixture was extracted with CH_2Cl_2 (3 x 10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue obtained was purified by flash chromatography (75% CH_2Cl_2

in hexane) to afford **15** (161 mg, 0.74 mmol, 95%) as a light yellow oil: R_f (CH_2Cl_2) 0.65; ^1H NMR (CDCl_3 , 200 MHz) δ 3.61 (m, 2 H), 2.93 (m, 1 H), 2.75 (dd, $J = 5.1$, $J = 4.1$, 1 H), 2.48 (dd, $J = 5.1$, $J = 2.5$, 1 H), 1.62 (m, 4 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (CDCl_3 , 50.3 MHz) δ 62.6, 52.2, 47.1, 29.1, 25.9, 18.3, -5.3; IR (film) 2954, 2926, 2862, 1467, 1247, 1090, 827; MS (CI, NH_3): 217 ($\text{M}+1$); $[\alpha]_D -4.8$ (CHCl_3 , c 0.98).

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(4*S*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)oct-6-en-4-ol (**16**)

Using (*E*)-1-propenyl-1-lithium and CuCN :

(*E*)-1-Bromo-1-propene (560 μL , 6.52 mmol) was slowly added to a suspension of lithium (455 mg, 65.6 mmol) in Et_2O (2.6 mL) at 0 °C. After stirring for 1 h at this temperature, the suspension was filtered under Ar and the resulting solution was added to a suspension of CuCN (296 mg, 3.30 mmol) in THF (1.4 mL) at -78 °C, then left to rise to room temperature. The yellow cuprate solution obtained was then cooled to -78 °C and a solution of **15** (180 mg, 0.83 mmol) in Et_2O (2 mL) was added. The reaction mixture was stirred for 1 h at -78 °C and 1 h at 0 °C. The reaction mixture was quenched with a 10% NH_4OH solution in saturated NH_4Cl (10 mL) and extracted with $t\text{BuOMe}$ (3 x 30 mL). The combined organic extracts were dried (MgSO_4), filtered, and concentrated. Purification by flash column chromatography (CH_2Cl_2) afforded **16** (213 mg, 0.82 mmol, 99%) as a colourless oil.

Using (*E*)-1-propenyl-1-lithium and lithium [cyano(2-thienyl)cuprate]:

(*E*)-1-Bromo-1-propene (1.78 mL, 20.7 mmol) was slowly added to a suspension of lithium (386 mg, 55.1 mmol) in Et_2O (8.3 mL) at 0 °C. After stirring for 1.5 h at this temperature, the suspension was filtered under Ar and the resulting solution was added (+ 4 mL Et_2O wash) to a stirred yellow solution of $\text{Li}_2[\text{Cu}(\text{CN})(2\text{-thienyl})]$ (0.23 M in THF, 78 mL, 17.9 mmol) in THF (36 mL) at -78 °C. Stirring continued for 30 minutes at -78 °C (the mixture turned orange and then yellow again) and a solution of **15** (3.0 g, 13.8 mmol) in Et_2O (9.2 mL) was added dropwise. The reaction mixture was stirred for 1 h at -78 °C and 3 h at 0 °C, quenched with a 10% NH_4OH solution in saturated NH_4Cl (20 mL), and extracted with Et_2O (4 x 50 mL). The combined organic extracts were washed with brine (2 x 20 mL), dried (Na_2SO_4), filtered and concentrated. Purification by flash column chromatography (10–20% EtOAc in hexane) afforded 3.2 g of **16** (90%) as a colourless oil: R_f (CH_2Cl_2) 0.23; ^1H NMR (CDCl_3 , 300 MHz) δ 5.47 (m, 2 H), 3.62 (m, 3 H), 2.45 (br s, 1 H), 2.15 (m, 2 H), 1.67 (m, 6 H), 1.45 (m, 1 H), 0.89 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) δ 128.4, 127.4, 70.9, 63.4,

40.7, 33.7, 29.1, 25.9, 18.0, -5.4; IR (film) 3500–3200, 2910, 2840, 1250, 1090, 825; MS (CI, NH₃) 259 (M+1); [α]_D -3.6 (CHCl₃, *c* 1.00).

(4*S*,6*E*)-1-*tert*-Butyldimethylsilyloxy-4-*tert*-butyldiphenylsilyloxy-6-octene

tert-Butyldiphenylsilylchloride (3.6 mL, 13.8 mmol) was added to a solution of **16** (2.4 g, 9.20 mmol), imidazole (1.6 g, 22.9 mmol) and DMAP (56 mg, 0.46 mmol) in CH₂Cl₂ (84 mL). After stirring for 5 h at room temperature, the reaction mixture was quenched with 10 mL of sat. NH₄Cl and the volatiles were removed under vacuum. The residue was diluted with 10 mL of water and extracted with Et₂O (3 x 50 mL). The organic extracts were washed with water (2 x 10 mL) and brine (2 x 10 mL), dried over Na₂SO₄, and concentrated. The residue was purified (silica gel, 5% Et₂O in hexane) to afford 4.2 g (92%) of the fully protected compound: R_f (5% Et₂O in hexane) 0.50; ¹H NMR (CDCl₃, 300 MHz) δ 7.68 (m, 4 H), 7.39 (m, 6 H), 5.30 (m, 2 H), 3.75 (m, 1 H), 3.47 (m, 2 H), 2.13 (m, 2 H), 1.60–1.20 (m, 7 H), 1.06 (s, 9 H), 0.88 (s, 9 H), 0.02 (s, 6 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ 136.0, 135.9, 134.7, 129.4, 127.4, 127.3, 127.2, 73.0, 63.3, 39.8, 32.2, 28.1, 27.1, 25.9, 19.4, 18.0, -5.3; IR (film): 2950, 2920, 2850, 1425, 1250, 1105, 830, 700; MS (CI, NH₃) 513 (M+17); [α]_D -9.9 (CHCl₃, *c* 0.99).

(4*S*,6*E*)-4-*tert*-Butyldiphenylsilyloxy-6-octen-1-ol (17**)**

A solution of the protected compound (347 mg, 0.70 mmol), pyridinium *p*-toluenesulfonate (88 mg, 0.35 mmol) in absolute EtOH (4 mL) was stirred at room temperature for 8 h. Purification by flash chromatography (CH₂Cl₂) of the residue obtained after removal of the solvent afforded compound **17** (254 mg, 0.66 mmol, 95%) as a colorless oil: R_f (30% EtOAc in hexane) 0.35; ¹H NMR (CDCl₃, 300 MHz) δ 7.68 (m, 4 H), 7.37 (m, 6 H), 5.29 (m, 2 H), 3.77 (dddd, *J* = 15.5, 10.1, 5.0, 1.5, 1 H), 3.47 (m, 2 H), 2.14 (m, 2 H), 1.83 (br s, 1 H), 1.57 (d, *J* = 5.0, 3 H), 1.54–1.45 (m, 4 H), 1.07 (s, 9 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ 136.2, 134.7, 129.4, 127.7, 127.5, 73.3, 63.3, 39.9, 32.5, 28.2, 27.3, 19.6, 18.3; IR (film) 3200 (br), 2910, 2830, 1250, 1100, 830; MS (CI, NH₃) 384 (M+1, 100); [α]_D -10.4 (CHCl₃, *c* 1.15).

(4*S*,6*E*)-4-(*tert*-Butyldiphenylsilyloxy)oct-6-enal (18**)**

Freshly distilled DMSO (0.15 mL, 1.70 mmol) was added dropwise to a cooled (-78°C) solution of distilled oxalyl chloride (70 μL , 0.85 mmol) in anhydrous CH_2Cl_2 (7 mL). Five minutes later, a solution of the primary alcohol **17** (250 mg, 0.65 mmol) in CH_2Cl_2 (12 mL + 3 mL wash) was slowly added via cannula and the mixture was stirred at -78°C for 30 minutes. Et_3N (0.54 mL, 3.92 mmol) was added and stirring continued for 15 minutes in the dry ice–acetone bath and for another 30 minutes while slowly warming to room temperature. It was then quenched with phosphate buffer solution (5 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with water (2 x 10 mL) and brine (2 x 10 mL), dried (Na_2SO_4), and concentrated under reduced pressure, to afford pure aldehyde **18** (248 mg, 100%), directly used for the aldol reactions.

The primary alcohol **17** (133 mg, 0.35 mmol) was dissolved in 3.5 mL of anhydrous CH₂Cl₂ and the solution was cooled to 0 °C. Dess–Martin periodinane (221 mg, 0.52 mmol) was added under Ar and the mixture was stirred for 1 h at 0 °C and another 2 h at room temperature. It was then filtered through silica gel (CH₂Cl₂) and the filtrate was concentrated under reduced pressure to afford 127 mg (95%) of pure aldehyde **18**, which was directly used for the aldol reactions.

[illegible]

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129.3, 128.9, 127.2, 113.6, 74.3, 72.9, 71.5, 71.2, 69.9, 66.0, 55.9, 55.2, 45.0, 43.3, 38.0, 31.6, 25.9, 25.8, 24.6, 23.6, 21.7, 18.2, -4.2, -4.8; IR (film) 3523 (br), 2954, 2919, 2848, 1773, 1688, 1510; MS (CI, NH₃) 614 (M+1).

(2*R*,4*S*,5*S*)-2-*tert*-Butyldimethylsilyloxy-5-hydroxy-4-hydroxymethyl-1-(4-methoxy)benzyloxy-7-methyloctane

MeOH (40 μ L, 0.99 mmol) and then LiBH₄ (22 mg, 0.99 mmol) were added to a solution of **19** (506 mg, 0.83 mmol) in THF (7 mL) at 0 °C. The reaction flask was then purged with N₂ and stirred for 5 h at 0 °C and 7 h at room temperature. The reaction mixture was quenched with 5 mL of 1 M aqueous solution of sodium potassium tartrate and stirred for 20 minutes at room temperature. The mixture was partitioned between water and CH₂Cl₂ and the aqueous layer was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic phases were dried (Na₂SO₄), filtered, and concentrated. The residue was purified by flash column chromatography (35% EtOAc in hexane) to yield the corresponding diol (341 mg, 0.77 mmol, 94%) as a colourless oil: R_f (35% EtOAc in hexane) 0.33; ¹H NMR (CDCl₃, 200 MHz) δ 7.25 (d, *J* = 8.4, 2 H), 6.87 (d, *J* = 8.4, 2 H), 4.44 (s, 2 H), 3.91 (m, 2 H), 3.81 (s, 3 H), 3.71 (m, 2 H), 3.40 (m, 2 H), 1.86–1.09 (m, 6 H), 0.93 (d, *J* = 6.6, 3 H), 0.90 (d, *J* = 6.6, 3 H), 0.88 (s, 9 H), 0.06 (s, 6 H); ¹³C NMR (CDCl₃, 50.3 MHz) δ 159.1, 130.1, 129.3, 113.7, 74.2, 73.6, 73.0, 69.6, 65.2, 55.3, 43.0, 40.6, 30.1, 25.9, 24.6, 23.5, 22.1, 18.1, -4.2, -4.8; IR (film) 3388 (br), 2954, 2919, 2862, 1617, 1510, 1460, 1247, 1033, 827; MS (CI, NH₃) 441 (M+1).

(2*R*,4*S*,5*S*)-2-*tert*-Butyldimethylsilyloxy-5-hydroxy-1-(4-methoxy)benzyloxy-7-methyl-4-(trityloxymethyl)octane (20**)**

A solution of the above diol (180 mg, 0.41 mmol) and trityl chloride (137 mg, 0.49 mmol) in pyridine (3 mL) was heated at 70 °C for 12 h. The solvent was concentrated under vacuum and the residue was purified by flash column chromatography (CH₂Cl₂) over silica gel deactivated with 2.5% of Et₃N. Compound **20** (279 mg, 0.41 mmol, 100%) was isolated as a colourless oil: R_f (CH₂Cl₂) 0.35; ¹H NMR (CDCl₃, 300 MHz) δ 7.50–7.20 (m, 17 H), 6.87 (d, *J* = 8.4, 2 H), 4.41 (s, 2 H), 3.82 (s, 3 H), 3.80 (m, 2 H), 3.45 (m, 1 H), 3.35 (m, 1 H), 3.23 (m, 2 H), 3.00 (br s, 1 H), 2.00–1.00 (m, 6 H), 0.88

(m, 15 H), -0.06 (s, 3 H), -0.05 (s, 3 H); ^{13}C NMR (CDCl_3 , 50.3 MHz) δ 159.2, 147.7, 129.2, 129.1, 128.6, 127.8, 127.0, 113.7, 87.1, 74.2, 72.8, 71.4, 70.3, 66.0, 55.2, 42.4, 40.3, 32.3, 25.9, 24.5, 23.7, 21.7, 18.1, -4.3 , -4.7 ; IR (film) 3531 (br), 2954, 2919, 2855, 1609, 1503, 1439, 1247; MS (FAB) 705 ($M+23$).

(2*R*,4*S*,5*S*)-2-*tert*-Butyldimethylsilyloxy-5-methanesulfonyloxy-1-(4-methoxy)-benzyloxy-7-methyl-4-(trityloxymethyl)octane

Mesyl chloride (23 μL , 0.30 mmol) was added to a solution of **20** (102 mg, 0.15 mmol) in pyridine (1 mL) at 0 $^{\circ}\text{C}$. After stirring for 5 h at room temperature, the solvent was removed under vacuum and the residue was purified by flash column chromatography (15% EtOAc in hexane) using deactivated silica gel (2.5% Et_3N). The mesyloxy intermediate (113 mg, 0.15 mmol, 99%) was isolated as a colorless oil: R_f (15% EtOAc in hexane) 0.54; ^1H NMR (CDCl_3 , 300 MHz) δ 7.50–7.20 (m, 17 H), 6.87 (d, $J = 8.4$, 2 H), 5.20 (m, 1 H), 4.37 (s, 2 H), 3.80 (s, 3 H), 3.67 (m, 1 H), 3.38–3.28 (m, 2 H), 3.22 (dd, $J = 6.2$, $J = 3.8$, 1 H), 3.01 (t, $J = 8.8$, 1 H), 2.60 (s, 3 H), 1.80–1.25 (m, 6 H), 1.00 (d, $J = 6.0$, 3 H), 0.96 (d, $J = 6.2$, 3 H), 0.85 (s, 9 H), 0.01 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) δ 143.7, 129.2, 128.8, 127.9, 127.8, 127.2, 127.1, 113.7, 83.1, 74.5, 72.9, 69.4, 62.4, 55.3, 41.1, 38.3, 38.1, 31.2, 25.8, 24.5, 22.6, 22.2, 18.0, -4.3 , -4.7 ; IR (film) 2954, 2926, 2855, 1602, 1510, 1353, 1247, 1168; MS (FAB) 783 ($M+23$); $[\alpha]_D -18.03$ (CHCl_3 , c 1.68).

(2*R*,3*S*,5*R*)-2-Isobutyl-5-(4-methoxy)benzyloxymethyl-3-(trityloxymethyl)-tetrahydrofuran (21**)**

A solution of the above mesylate (42 mg, 0.06 mmol) and TBAF $\cdot 3\text{H}_2\text{O}$ (36 mg, 0.11 mmol) in THF (1 mL) was stirred for 12 h at room temperature. The residue obtained after removal of the solvent was purified by column chromatography (5% EtOAc in hexane) using deactivated silica gel (2.5% Et_3N). Tetrahydrofuran **21** (30 mg, 95%) was isolated as a yellow oil: R_f (5% EtOAc in hexane) 0.63; ^1H NMR (CDCl_3 , 300 MHz) δ 7.45–7.20 (m, 17 H), 6.85 (d, $J = 8.7$, 2 H), 4.48 (d, $J = 11.7$, 1 H), 4.02 (m, 2 H), 3.79 (s, 3 H), 3.33 (d, $J = 3.8$, 2 H), 3.05 (m, 2 H), 2.53 (m, 1 H), 1.65 (m, 1 H), 1.20–0.90 (m, 4 H), 0.81 (d, $J = 6.9$, 6 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) δ 144.2, 129.3, 128.7,

127.9, 127.7, 127.2, 126.9, 113.7, 85.5, 78.8, 77.2, 73.2, 72.9, 63.1, 55.3, 41.9, 39.3, 32.2, 29.7, 24.9, 23.6; IR (film) 2919, 2848, 1602, 1503, 1446, 1247; MS (FAB) 551 (M+1); $[\alpha]_D -19.48$ (CHCl₃, *c* 1.55).

(*R*)-4-Benzyl-3-((2*R*,3*S*,6*S*,8*E*)-2-((*R*)-2-(*tert*-butyldimethylsilyloxy)-3-(4-methoxybenzyloxy)propyl)-6-(*tert*-butyldiphenylsilyloxy)-3-hydroxy-8-decenoyl)oxazolidin-2-one (22**)**

Using the titanium enolate of 10:

To a cooled ($-90\text{ }^{\circ}\text{C}$) solution of **10** (163 mg, 0.30 mmol) in anhydrous CH₂Cl₂ (3 mL) was added Et^{*i*}Pr₂N (5 μL , 0.03 mmol) under Ar and then 358 μL (0.36 mmol) of a 1.0 M TiCl₄ solution in CH₂Cl₂, followed by another 57 μL (0.33 mmol) of Et^{*i*}Pr₂N. The mixture was stirred for 10 minutes at $-90\text{ }^{\circ}\text{C}$, and then slowly warmed to $0\text{ }^{\circ}\text{C}$ and stirring continued for 45 minutes. The mixture was again cooled to $-78\text{ }^{\circ}\text{C}$ and aldehyde **18** (148 mg, 0.39 mmol, dissolved in 0.5 mL of anhydrous CH₂Cl₂) was slowly added via cannula. Stirring was maintained for 10 minutes at $-78\text{ }^{\circ}\text{C}$, 30 minutes at $0\text{ }^{\circ}\text{C}$ and 5 h at room temperature before quenching with 2 mL of phosphate buffer at $0\text{ }^{\circ}\text{C}$. The mixture was allowed to warm to room temperature and extracted with CH₂Cl₂ (3 x 20 mL). The organic extracts were washed with water and brine (2 x 10 mL), dried over Na₂SO₄, and concentrated under vacuum. Silica gel chromatography (20% EtOAc in hexane) afforded 135 mg (50%) of **22**, while 25 mg (15%) of **10** were recovered.

Using the boron enolate of 10:

A solution of the enolate precursor **10** (277 mg, 0.52 mmol) in anhydrous CH₂Cl₂ (2 mL) under Ar was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with Et₃N (102 μL , 0.73 mmol) and Bu₂BOTf (1.0 M solution in CH₂Cl₂, 0.68 mL, 0.68 mmol). The resulting yellow mixture was stirred during 30 minutes at $-78\text{ }^{\circ}\text{C}$ and another 90 minutes at $0\text{ }^{\circ}\text{C}$. It was then cooled to $-78\text{ }^{\circ}\text{C}$ and aldehyde **18** (260 mg, 0.68 mmol in 1 mL + 0.5 mL of anhydrous CH₂Cl₂) was added slowly via cannula. The mixture was stirred for 30 minutes at $-78\text{ }^{\circ}\text{C}$ and 5 h at $0\text{ }^{\circ}\text{C}$. The reaction was quenched with a mixture of phosphate buffer and MeOH 1:2 (3 mL) and the biphasic mixture was kept under vigorous stirring during 12 h. It was then extracted with EtOAc (3 x 30 mL). The combined extracts were washed with water (2 x 10 mL) and brine (2 x 10 mL), dried (Na₂SO₄), and concentrated under reduced pressure. Silica gel column chromatography of the residue (40% EtOAc in hexane) afforded 52 mg (20%) of recovered **10** and 389 mg (75%) of **22** as a colorless oil: R_f (20% EtOAc in hexane) 0.40; ¹H NMR (CDCl₃, 300 MHz) δ 7.67 (m, 4 H), 7.37 (m, 9 H), 7.26 (d, *J* = 8.7, 2 H), 7.23 (m, 2 H), 6.85 (d, *J* = 8.7, 2 H), 5.26 (m, 2 H), 4.61 (m, 1 H), 4.46 (s, 2 H), 4.13 (m, 1 H), 4.12 (m, 2 H),

3.87 (m, 1 H), 3.79 (m, 1 H), 3.76 (s, 3 H), 3.74 (m, 1 H), 3.40 (m, 3 H), 2.55 (dd, $J = 13.1, 10.7$, 1 H), 2.19 (m, 1 H), 2.10 (m, 2 H), 1.60 (m, 2 H), 1.56 (d, $J = 5.0$, 3 H), 1.49 (m, 3 H), 1.04 (s, 9 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) δ 174.5, 159.3, 153.6, 136.1, 129.6, 129.5, 129.2, 127.7, 127.6, 113.9, 74.8, 73.7, 73.5, 73.1, 70.1, 66.2, 56.2, 55.4, 45.2, 40.1, 38.2, 32.5, 31.5, 29.9, 27.3, 26.1, 25.9, 19.6, 18.2, 18.3, $-3.8, -4.5$; MS (FAB) 908.5 ($M+1$); $[\alpha]_{\text{D}} -8.8$ (CHCl_3 , c 1.12).

Ethyl (2*E*,4*R*,6*R*,7*S*,10*S*,12*E*)-6-((*R*)-4-benzyl-2-oxo-1,3-oxazolidine-3-carbonyl)-4-(*tert*-butyldimethylsilyloxy)-10-(*tert*-butyldiphenylsilyloxy)-7-hydroxytetradeca-2,12-dienoate (23**)**

*Using the titanium enolate of **11**:*

To a cooled ($-90\text{ }^{\circ}\text{C}$) solution of **11** (250 mg, 0.53 mmol) in anhydrous CH_2Cl_2 (5.3 mL) was carefully added $\text{Et}^i\text{Pr}_2\text{N}$ (9 μL , 0.05 mmol) under Ar and then 632 μL (0.63 mmol) of a 1.0 M TiCl_4 solution in CH_2Cl_2 , followed by another 101 μL (0.58 mmol) of $\text{Et}^i\text{Pr}_2\text{N}$. The mixture was stirred for 10 minutes at $-90\text{ }^{\circ}\text{C}$ and then slowly warmed to $0\text{ }^{\circ}\text{C}$, where stirring was continued for 45 minutes. The mixture was cooled down to $-78\text{ }^{\circ}\text{C}$ and aldehyde **18** (261 mg, 0.68 mmol, dissolved in 1 mL + 0.5 mL wash of anhydrous CH_2Cl_2) was slowly added via cannula. After stirring for 10 minutes at $-78\text{ }^{\circ}\text{C}$ and 2 h at $0\text{ }^{\circ}\text{C}$, the mixture was quenched with 5 mL of phosphate buffer, allowed to warm to room temperature and extracted with CH_2Cl_2 (3 x 30 mL). The organic extracts were washed with water and brine (2 x 10 mL), dried over Na_2SO_4 , and concentrated under vacuum. Silica gel chromatography (20% EtOAc in hexane) afforded 274 mg (61%) of **23**, while 38 mg (15%) of **11** were recovered.

*Using the boron enolate of **11**:*

A solution of the enolate precursor **11** (435 mg, 0.92 mmol) in anhydrous CH_2Cl_2 (4.6 mL) under Ar was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with Et_3N (178 μL , 1.28 mmol) and Bu_2BOTf (1.0 M solution in CH_2Cl_2 , 1.2 mL, 1.19 mmol). The resulting pink-orange mixture was stirred during 30 minutes at $-78\text{ }^{\circ}\text{C}$ and another 90 minutes at $0\text{ }^{\circ}\text{C}$, and eventually turned pale yellow. It was then cooled to $-78\text{ }^{\circ}\text{C}$ and aldehyde **18** (418 mg, 1.1 mmol in 1.5 mL + 0.5 mL of anhydrous CH_2Cl_2) was added slowly via cannula. The mixture was stirred during 30 minutes at $-78\text{ }^{\circ}\text{C}$ and 2 h at $0\text{ }^{\circ}\text{C}$. The reaction was quenched with a 1:2 mixture of phosphate buffer and MeOH (5 mL) and the biphasic mixture was stirred vigorously for 12 h. It was then extracted with EtOAc (3 x 50 mL). The combined extracts were washed with water (2 x 10 mL) and brine (2 x 10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Silica gel column chromatography of the residue (2% EtOAc in CH_2Cl_2 as the eluent) afforded 65 mg

(15%) of recovered **11** and 669 mg (85%) of **23** as a white foam: R_f (20% EtOAc in hexane) 0.42; ^1H NMR (CDCl_3 , 400 MHz) δ 7.67 (m, 4 H), 7.41–7.32 (m, 8 H), 7.27–7.23 (m, 3 H), 6.91 (dd, $J = 15.7, 5.6$, 1 H), 5.98 (dd, $J = 15.7, 1.0$, 1 H), 5.29 (m, 2 H), 4.19 (q, $J = 7.1$, 2 H), 4.13 (d, $J = 4.7$, 2 H), 4.09 (m, 1 H), 3.78 (m, 1 H), 3.73 (m, 1 H), 3.45 (dd, $J = 13.0, 3.0$, 1 H), 2.58 (dd, $J = 13.0, 10.9$, 1 H), 2.17 (ddd, $J = 13.7, 10.6, 3.5$, 1 H), 2.11 (m, 2 H), 1.88 (d, $J = 4.6$, 1 H), 1.61 (m, 1 H), 1.57 (d, $J = 5.1$, 3 H), 1.51 (m, 1 H), 1.47 (m, 1 H), 1.29 (t, $J = 7.1$, 3 H), 1.04 (s, 9 H), 0.92 (s, 9 H), 0.03 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (CDCl_3 , 100.6 MHz) δ 173.8, 166.3, 153.3, 150.3, 135.9, 135.5, 134.3, 134.3, 129.5, 129.4, 129.3, 128.9, 127.5, 127.4, 127.4, 127.3, 127.0, 120.4, 73.3, 73.2, 70.2, 66.0, 60.3, 56.1, 45.0, 39.9, 38.0, 33.4, 32.2, 29.6, 27.0, 25.8, 19.3, 18.0, 17.9, 14.2, –4.2, –5.0; IR 2919, 2848, 1602; MS (FAB) 878.6 ($M+23$), 856.6 ($M+1$); HRMS (FAB) calc. for $\text{C}_{49}\text{H}_{70}\text{NO}_8\text{Si}_2$ ($M+1$) 856.4640, found 856.4673; $[\alpha]_D -10.7$ (CH_2Cl_2 , c 1.37).

Ethyl (2*E*,4*R*,6*S*,7*S*,10*S*,12*E*)-4-(*tert*-butyldimethylsilyloxy)-10-(*tert*-butyldiphenylsilyloxy)-7-hydroxy-6-(hydroxymethyl)tetradeca-2,12-dienoate

To a cooled ($-20\text{ }^\circ\text{C}$) solution of **23** (500 mg, 0.58 mmol) in anhydrous THF (11.7 mL) and anhydrous MeOH (52 μL) was added LiBH_4 (2 M solution in THF, 0.86 mL, 2.2 mmol) under Ar. The reaction mixture was stirred for 1 h at $-20\text{ }^\circ\text{C}$ and another 3 h at room temperature, before being quenched with 6 mL of phosphate buffer solution and extracted with Et_2O (3 x 100 mL). The combined organic extracts were washed with water (2 x 15 mL) and brine (2 x 10 mL), dried with Na_2SO_4 , and concentrated under reduced pressure. Column chromatography using silica gel and 30–40% EtOAc in hexane as eluent provided 360 mg (90%) of the desired diol as a colorless oil: R_f (30 % EtOAc in hexane) 0.37; ^1H NMR (CDCl_3 , 400 MHz) δ 7.67 (m, $J = 4$ H), 7.44–7.35 (m, 6 H), 6.88 (dd, $J = 15.6, 4.9$, 1 H), 5.97 (dd, $J = 15.6, 1.6$, 1 H), 5.29 (m, 2 H), 4.44 (m, 1 H), 4.20 (m, 2 H), 3.74 (m, 2 H), 3.63 (m, 2 H), 2.71 (br s, 1 H), 2.33 (m, 1 H), 2.12 (m, 2 H), 1.81 (m, 1 H), 1.64 (m, 2 H), 1.59 (d, $J = 4.5$, 2 H), 1.52–1.41 (m, 3 H), 1.30 (t, $J = 7.1$ Hz, 3 H), 1.05 (s, 9 H), 0.92 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (CDCl_3 , 100.6 MHz) δ 166.6, 150.5, 136.2, 136.2, 134.7, 129.8, 127.8, 127.4, 120.7, 76.2, 70.5, 73.4, 65.3, 60.7, 40.7, 40.1, 32.5, 30.0, 29.5, 27.3, 26.1, 19.6, 18.4, 18.3, 14.5, –4.0, –4.7; MS (FAB) 705 ($M+23$), 683 ($M+1$); HRMS (FAB) calc. for $\text{C}_{39}\text{H}_{63}\text{O}_6\text{Si}_2$ ($M+1$) 683.4158, found 683.4164; $[\alpha]_D +4.1$ (CH_2Cl_2 , c 0.75).

Ethyl (2*E*,4*R*,6*S*,7*S*,10*S*,12*E*)-4-(*tert*-butyldimethylsilyloxy)-10-(*tert*-butyldiphenylsilyloxy)-7-hydroxy-6-(trityloxymethyl)tetradeca-2,12-dienoate (24a**)**

In a solution containing the above diol (113 mg, 0.17 mmol) in anhydrous pyridine (1.5 mL), trityl chloride (60 mg, 0.22 mmol) was added in two portions, under N₂. The resulting yellow mixture was stirred at 70 °C for 12 h and then allowed to cool to room temperature. Pyridine was removed under reduced pressure (helped by addition of toluene) and the residue was purified (silica gel deactivated with 2.5% Et₃N) using 20% EtOAc in hexane as eluent, to afford 160 mg (100%) of alcohol **24a**: R_f (30 % EtOAc in hexane) 0.64; ¹H NMR (CDCl₃, 400 MHz) δ 7.64 (m, 4 H), 7.40–7.23 (m, 21 H), 6.80 (dd, *J* = 15.6, 5.3, 1 H), 5.87 (dd, *J* = 15.6, 1.1, 1 H), 5.28 (m, 2 H), 4.21 (m, 2 H), 3.95 (m, 1 H), 3.73 (m, 1 H), 3.62 (m, 1 H), 3.34 (dd, *J* = 9.3, 3.3, 1 H), 3.13 (dd, *J* = 9.3, 5.9, 1 H), 2.78 (d, *J* = 3.7, 1 H), 2.07 (m, 2 H), 1.84 (m, 1 H), 1.56 (m, 5 H), 1.48–1.36 (m, 2 H), 1.30 (t, *J* = 7.1, 3 H), 1.26 (m, 2 H), 1.03 (s, 9 H), 0.82 (s, 9 H), –0.09 (s, 3 H), –0.16 (s, 3 H); ¹³C NMR (CDCl₃, 100.6 MHz) δ 166.7, 151.1, 143.8, 136.2, 134.7, 129.7, 128.9, 128.2, 127.7, 127.4, 120.3, 87.5, 75.2, 73.5, 70.0, 64.9, 60.6, 39.9, 39.6, 33.6, 32.7, 27.3, 26.1, 29.1, 19.6, 18.3, 14.5, –4.0, –4.6; [α]_D –10.2 (CH₂Cl₂, *c* 0.97).

Ethyl (2*E*,4*R*,6*S*,7*S*,10*S*,12*E*)-4-(*tert*-butyldimethylsilyloxy)-10-(*tert*-butyldiphenylsilyloxy)-7-(methanesulfonyloxy)-6-(trityloxymethyl)tetradeca-2,12-dienoate

To a solution of alcohol **24a** (160 mg, 0.17 mmol) in anhydrous pyridine (1.3 mL), was added MsCl (26 μL, 0.33 mmol) at room temperature, under N₂. The mixture was stirred for 5 h and pyridine was removed under reduced pressure. The residue was filtered through silica gel (25% EtOAc in hexane) to afford 167 mg (99%) of the mesyloxy intermediate: R_f (30% EtOAc in hexane) 0.51; ¹H NMR (CDCl₃, 400 MHz) δ 7.64 (m, 4 H), 7.37 (m, 10 H), 7.28 (m, 11 H), 6.76 (dd, *J* = 15.6, 5.2, 1 H), 5.89 (dd, *J* = 15.5, 1.3, 1 H), 5.28 (m, 1 H), 4.84 (m, 1 H), 4.20 (m, 2 H), 4.08 (m, 1 H), 3.70 (m, 1 H), 3.32 (dd, *J* = 9.5, 4.6, 1 H), 3.04 (dd, *J* = 9.5, 6.9, 1 H), 2.64 (s, 3 H), 2.13 (m, 1 H), 2.09 (m, 2 H), 1.72 (m, 1 H), 1.57 (d, *J* = 4.6, 1 H), 1.46 (m, 3 H), 1.29 (t, *J* = 7.1, 3 H), 1.25 (m, 2 H), 1.04 (s, 9 H), 0.82 (s, 9 H), –0.08 (s, 3 H), –0.10 (s, 3 H); ¹³C NMR (CDCl₃, 100.6 MHz) δ 166.5, 150.4, 143.8, 136.1, 136.1, 129.8, 128.9, 128.2, 128.1,

127.8, 127.7, 127.4, 120.8, 87.1, 84.7, 72.9, 69.9, 61.9, 60.6, 39.9, 38.7, 38.4, 34.7, 32.1, 29.9, 27.3, 26.0, 19.6, 18.2, 14.5, -4.2, -4.7; $[\alpha]_D -11.0$ (CH_2Cl_2 , c 1.14).

Ethyl (*E*)-3-((2*R*,4*S*,5*R*)-5-((3*S*,5*E*)-3-(*tert*-butyldiphenylsilyloxy)hept-5-enyl)-4-(trityloxymethyl)tetrahydrofuran-2-yl)propenoate (2a**)**

A solution of the mesylate (70 mg, 0.07 mmol) in anhydrous THF (1.1 mL) was cooled to 0 °C and TBAF·3H₂O (44 mg, 0.14 mmol) was added under N₂. The mixture was stirred at 0 °C for 30 minutes and allowed to warm to room temperature overnight (12 h). When TLC suggested the completion of both steps of the reaction, the mixture was directly purified using silica gel and 25% EtOAc in hexane as the eluent, to give 55 mg (95%) of target compound **2a** as a pale yellow oil: R_f (20% EtOAc in hexane) 0.40; ¹H NMR (CDCl₃, 400 MHz) δ 7.59 (m, 4 H), 7.39 (m, 9 H), 7.25 (m, 12 H), 6.81 (dd, J = 15.6, 5.1, 1 H), 5.89 (dd, J = 15.6, 1.5, 1 H), 5.22 (m, 2 H), 4.40 (dddd, J = 12.5, 7.2, 5.1, 1.5, 1 H), 4.18 (q, J = 7.1, 2 H), 3.79 (ddd, J = 9.6, 6.8, 3.1, 1 H), 3.58 (m, 1 H), 3.06 (dd, J = 8.9, 6.3, 1H), 2.91 (dd, J = 8.9, 1.2, 1H), 2.53 (m, 1 H), 2.27 (m, 1 H), 2.00 (m, 2 H), 1.68–1.60 (m, 1 H), 1.54 (m, 3 H), 1.52–1.49 (m, 1 H), 1.40–1.35 (m, 1 H), 1.27 (t, J = 7.1, 3 H), 1.25–1.20 (m, 1 H), 0.99 (s, 9 H), 0.90–0.80 (m, 1 H); ¹³C NMR (CDCl₃, 100.6 MHz) δ 166.4, 148.5, 144.0, 135.9, 135.8, 129.4, 128.5, 127.7, 127.9, 127.3, 127.3, 126.9, 119.9, 86.5, 81.3, 76.9, 73.2, 62.7, 60.2, 42.5, 39.9, 35.5, 33.2, 29.6, 27.0, 19.3, 17.9, 14.2; $[\alpha]_D -9.8$ (CH_2Cl_2 , c 1.07).

Ethyl (2*E*,4*R*,6*R*,7*S*,10*S*,12*E*)-4-(*tert*-butyldimethylsilyloxy)-10-(*tert*-butyldiphenylsilyloxy)-7-hydroxy-6-((2-pyridylselenyl)methyl)tetradeca-2,12-dienoate (24b**)**

PMe₃ (1.0 M in THF, 0.6 mL, 0.6 mmol) and PySeSePy (51 mg, 0.16 mmol) were quickly added to a dry vial containing the diol (80 mg, 0.12 mmol) at room temperature and under Ar. Two hours later, the reaction was diluted with water (0.5 mL) and extracted with Et₂O (3 x 10 mL). The combined organic extracts were washed with brine (2 x 5 mL), dried with Na₂SO₄, and concentrated under reduced pressure to afford 96 mg of pure **24b** as an intense yellow oil: R_f (30 % EtOAc in hexane) 0.48; ¹H NMR

(CDCl₃, 400 MHz) δ 8.36 (m, 1 H), 7.65 (m, 4 H), 7.44 (m, 2 H), 7.39–7.29 (m, 6 H), 7.04 (m, 1 H), 6.89 (dd, J = 15.6, 5.1, 1 H), 5.96 (dd, J = 15.6, 1.4, 1 H), 5.26 (m, 2 H), 4.63 (m, 1 H), 4.20 (m, 2 H), 3.75 (m, 2 H), 3.33 (m, 1 H), 3.22 (m, 1 H), 2.34 (m, 1 H), 2.07 (m, 2 H), 1.76 (m, 2 H), 1.61 (m, 2 H), 1.55 (d, J = 3.7, 3 H), 1.47–1.38 (m, 2 H), 1.29 (t, J = 7.1, 3 H), 1.03 (s, 9 H), 0.91 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ¹³C NMR (CDCl₃, 100.6 MHz) δ 173.6, 166.4, 156.2, 150.9, 149.8, 135.9, 134.5, 129.3, 127.3, 128.5, 127.3, 125.7, 120.4, 120.0, 73.3, 71.1, 69.9, 69.0, 60.3, 40.6, 39.6, 36.1, 32.8, 29.7, 27.0, 25.8, 19.3, 17.9, 14.2, –4.2, –4.8; MS (FAB) 823.4 (M+1); HRMS (FAB) calc. for C₄₄H₆₆NO₅SeSi₂ (M+1) 824.3639, found 824.3648; [α]_D –6.8 (CH₂Cl₂, c 0.97).

Ethyl (*E*)-3-((2*R*,4*R*,5*R*)-5-((3*S*,5*E*)-3-(*tert*-butyldiphenylsilyloxy)hept-5-enyl)-4-((2-pyridyl)selenyl)methyl)tetrahydrofuran-2-yl)propenoate (2b**)**

To a solution of alcohol **20b** (23 mg, 0.03 mmol) in anhydrous pyridine (0.3 mL) was added MsCl (6 μ L, 0.06 mmol) at room temperature and under N₂. The mixture was stirred for 5 h and pyridine was removed under reduced pressure. The residue was filtered through silica gel (1% MeOH in CH₂Cl₂) affording 25 mg (99%) of the mesyloxy intermediate, which was directly dissolved in 0.3 mL of THF and cooled to 0 °C. TBAF·3H₂O (21 mg, 0.07 mmol) was added under Ar and the mixture was stirred at 0 °C for 2 h, then left to warm to room temperature overnight. When TLC analysis showed both deprotection and cyclization were completed, the mixture was directly purified by silica gel column (20% EtOAc in hexane) to provide 18 mg (95%) of target compound **2b**: R_f (20% EtOAc in hexane) 0.53; ¹H NMR (CDCl₃, 400 MHz) δ 8.40 (m, 1H), 7.70 (m, 4 H), 7.40 (m, 8 H), 7.00 (m, 1 H), 6.91 (dd, J = 15.6, 5.2, 1 H), 5.98 (dd, J = 15.6, 1.6, 1 H), 5.32 (m, 2 H), 4.40 (m, 1 H, 1 H), 4.19 (q, J = 7.1, 2 H), 3.84–3.72 (m, 2 H), 3.20 (m, 1 H), 2.91 (m, 1 H), 2.55 (m, 1 H), 2.30 (m, 1 H), 2.16 (m, 2 H), 1.80 (m, 1 H), 1.57 (m, 3 H), 1.46 (m, 1 H), 1.26 (t, J = 7.1, 3 H), 1.25–1.20 (m, 3 H), 1.07 (s, 9 H); ¹³C NMR (CDCl₃, 100.6 MHz) δ 166.7, 150.2, 148.7, 136.2, 136.2, 135.0, 129.8, 129.7, 129.6, 127.9, 127.7, 127.3, 125.6, 120.5, 120.3, 82.7, 73.5, 60.5, 42.8, 40.4, 38.2, 33.2, 32.1, 27.3, 26.7, 26.1, 22.9, 19.6, 18.2, 14.3; MS (FAB) 691 (M+1); HRMS (FAB) calc. for C₃₈H₅₀NO₄SeSi (M+1) 692.2669, found 692.2630; [α]_D –7.4 (CH₂Cl₂, c 1.02).

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24a

2a

24b

2b