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Supporting Information

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Enantioselective Synthesis of Oasomycin A, Part I. Synthesis of the C_1–C_{12} and C_{13}–C_{28} Subunits

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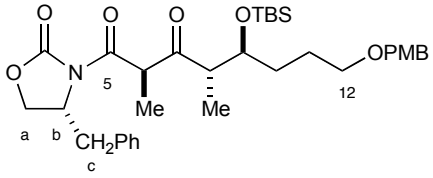
General Information and Materials

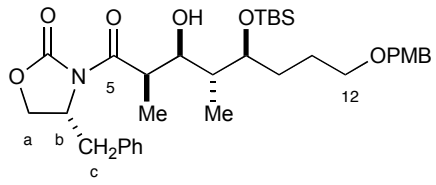
All reactions were carried out under an atmosphere of nitrogen in flame– or oven–dried glassware with magnetic stirring, unless otherwise noted. Air–sensitive reagents and solutions were transferred *via* syringe or cannula and were introduced to the apparatus through rubber septa. Reactions were cooled via external cooling baths: ice water (0 °C), dry ice–acetone (–78 °C), ice–acetone (–10 °C), methanol–liquid nitrogen (–95 °C), or Neslab immersion cooler (–20 → –80 °C). Heating was accomplished by heating mantle or silicon oil bath using a temperature controller. Analytical thin layer chromatography (TLC) was performed on EM Reagent 0.25 mm silica gel 60–F plates. Visualization was accomplished with UV light and exposure to aqueous ceric ammonium molybdate (CAM) solution or anisaldehyde followed by heating. Flash chromatography was performed using EM silica gel 60 (230–240 mesh). Solvents for extraction and chromatography were HPLC grade.

When necessary, solvents and reagents were dried prior to use. Reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), toluene and diethyl ether (Et_2O) were filtered through a column of activated alumina under an argon atmosphere. Methanol (MeOH) was distilled from magnesium methoxide. Benzene, acetonitrile, 2,6–lutidine, pyridine, *N*,*N*–diisopropylethylamine, *N*,*N*–dimethylethylamine, triethylamine, diisopropylamine and chlorotrimethylsilane were distilled from calcium hydride. Optical rotations were measured on a Jasco DIP–0181 digital polarimeter with a sodium lamp and reported as follows: $[\alpha]_D^{25}$ (*c* g/100 ml, solvent). Infrared spectra were recorded on a Perkin Elmer model 1600 FT–IR spectrometer. Mass spectra were obtained on a JEOL AX–505 or SX–102 high resolution magnetic sector mass spectrometer by the Harvard University Mass Spectrometry Laboratory. Electrospray mass spectra were obtained using a LCT mass spectrometer (Micromass Instruments, Beverly, MA). Exact mass measurements were obtained by internal calibration with an appropriate lock mass compound. ^{1}H NMR spectra were recorded on Varian Inova–600 (600 MHz), Inova–500 (500 MHz) or Mercury–400 (400 MHz) spectrometers. Chemical shifts (δ) are reported from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26, C_6D_6: δ 7.15). Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, appt = apparent, br = broad, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were recorded on Varian INOVA–500 (125 MHz) or Mercury–400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0, C_6D_6: δ 128.0). Unless noted otherwise, the reported ^{1}H NMR signals were assigned using standard 2D NMR techniques or by a direct comparison to the ^{1}H NMR spectra of corresponding starting materials.

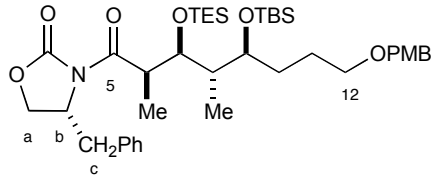


(*2R,4S,5S*)–1–((*R*)–4–benzyl–2–oxooxazolidin–3–yl)–5–(tert–butyldimethylsilyloxy)–8–(4–methoxybenzyloxy)–2,4–dimethyloctane–1,3–dione (3). To a solution of compound **1** (10.0 g, 34.5 mmol) in anhydrous ether (350 mL) at 0 °C was sequentially added dicyclohexylboron chloride (9.08 mL, 41.5 mmol) and dimethylethylamine (4.5 mL, 41.5 mmol). After stirring at 0 °C for 1 h the resulting suspension was cooled to –78 °C and then treated, through a dropwise addition (over 10 min), with a solution of aldehyde **6** in anhydrous ether (10 mL). The reaction mixture was stirred at –78 °C for 2 h then warmed to 0 °C. The reaction mixture was maintained at 0 °C for 1 h then treated sequentially with methanol (40 mL) and NH_4Cl (40 mL of a saturated aqueous solution). After stirring vigorously for 15 min at 0 °C the resulting solution was diluted with water (350 ml) and extracted with ether (3 × 100 mL). The combined organic phases were washed with water (300 mL) and brine (300 mL), then dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford the aldol adduct (*ca*. 14 g, existing as a 84:16 mixture based on ^{1}H NMR spectroscopic analysis of the crude reaction mixture) as pale yellow oil. This material was immediately used, without purification, in the next step of the reaction sequence.

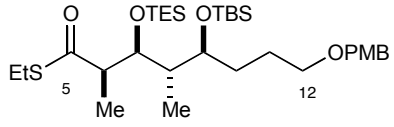
To a solution of the alcohol (1.7 g, 3.4 mmol) in 17 mL of methylene chloride at 0 °C was added 2,6–lutidine (1.2 mL, 10.2 mmol) and TBSOTf (1.2 mL, 5.1 mmol). The reaction mixture was stirred at 0 °C for 30 minutes, before the it was partitioned between 20 mL of water and 20 mL of diethyl ether. The organic layer was separated and washed with 1N HCl, sat. $NaHCO_3$, and brine, dried ($MgSO_4$) and concentrated. The resulting oil was purified by column chromatography (silica, 10% → 14% v/v ethyl acetate/hexanes elution) to yield 1.69 g (79%) of the product **3** as a colorless oil. $[\alpha]_D^{25}$ = –24 (*c* = 2.3, $CHCl_3$); IR (neat): 2945, 2856, 1783, 1720, 1691, 1682, 1612, 1586, 1513, 1461, 1386, 1358, 1248, 1212, 1112, 1034, 835, 776, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ ppm 7.37–7.32 (m, 2H, Ar**H**), 7.31–7.24 (m, 3H, Ar**H**), 7.23–7.19 (m, 2H, Ar**H**), 6.91–6.86 (m, 2H, Ar**H**), 4.84 (q, *J* = 7.3 Hz, 1H, C_6**H**), 4.77 (ddd, *J* = 9.5, 5.1, 3.1 Hz, 1H, $\mathbf{H}_b$), 4.44 (s, 2H, PMBC$\mathbf{H}_2$), 4.27 (t, *J* = 8.5 Hz, 1H, $\mathbf{H}_c$), 4.19 (dd, *J* = 9.1, 2.6 Hz, 1H, $\mathbf{H}_c$), 4.00 (dt, *J* = 8.1, 4.0 Hz, 1H, C_9**H**), 3.81 (s, 3H, ArOC$\mathbf{H}_3$), 3.49–3.36 (m, 2H, $C_{12}\mathbf{H}_2$), 3.29 (dd, *J* = 13.5, 3.2 Hz, 1H, $\mathbf{H}_a$), 2.91 (dd, *J* = 7.9, 7.0 Hz, 1H, C_8**H**), 2.78 (dd, *J* = 13.5, 9.7 Hz, 1H, $\mathbf{H}_a$), 1.75 (m, 1H, C_{11}**H**), 1.68–1.54 (m, 2H, C_{10}**H**, C_{11}**H**), 1.48 (m, 1H, C_{10}**H**), 1.44 (d, *J* = 7.3 Hz, 3H, $C_6C\mathbf{H}_3$), 1.08 (d, *J* = 7.0 Hz, 3H, $C_8C\mathbf{H}_3$), 0.86 (s, 9H, $SiC(C\mathbf{H}_3)_3$), 0.04 (s, 3H, $Si(C\mathbf{H}_3)_2$), –0.03 (s, 3H, $Si(C\mathbf{H}_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 135.1, 130.7, 129.4, 129.2, 129.0, 127.4, 113.7, 77.3, 77.0, 76.8, 73.3, 72.5, 70.3, 66.2, 55.3, 55.2, 53.0, 49.2, 37.9, 29.7, 25.9, 23.4, 18.0, 13.0, 12.4; HRMS (ES) calcd for $C_{34}H_{49}NO_7Si$ $[M+NH_4]^+$ 629.3617. Found 629.3625.



(*R*)–4–benzyl–3–((*2R,3S,4R,5S*)–5–(tert–butyldimethylsilyloxy)–3–hydroxy–8–(4–methoxybenzyloxy)–2,4–dimethyloctanoyl)oxazolidin–2–one (3a). Ketone **3a** (32mg, 0.052 mmol) was dissolved in 0.5 mL of methylene chloride and cooled to –78 °C. 0.54 mL of a $Zn(BH_4)_2$ solution (0.145M in diethyl ether) were added and the reaction mixture was stirred at –78 °C for 45 min. After that the flask was transferred to a –25 °C bath and stirred for 2h. The reaction was quenched by addition of 10% tartaric acid at –25 °C and then allowed to warm to room temperature. The resulting mixture was extracted with ether (2 × 5 mL) and the combined organic phases were washed with brine (5 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale yellow oil. Column chromatography (silica, 17% v/v ethyl acetate/hexanes elution) yielded 22 mg of the *title compound* **3a** (0.036 mmol, 69% yield, 81% brsm).

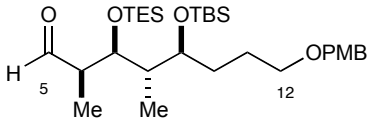


(*R*)–4–benzyl–3–((2R,3S,4S,5S)–5–(tert–butyldimethylsilyloxy)–8–(4–methoxybenzyloxy)–2,4–dimethyl–3–(triethylsilyloxy)octanoyl)oxazolidin–2–one (3b). Alcohol **3a** (418 mg, 0.682 mmol) was dissolved in 7 mL CH_2Cl_2 and cooled to –78 °C. 2, 6–lutidine (480 μL, 4.092 mmol) and TESOTf (360 μL, 1.364 mmol) were added and the reaction mixture was stirred until TLC indicated completion (2h). Saturated $NaHCO_3$ (5 mL) was added and the mixture was extracted with diethyl ether (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residual oil was purified by column chromatography (silica, 12% v/v ethyl acetate/hexanes elution) to yield 435 mg (0.597 mmol, 88% yield) of the *title compound*: $[\alpha]_D^{25}$ = –48.3 (*c* = 3.65, $CHCl_3$); IR (neat): 2954, 2934, 2877, 2856, 1782, 1702, 1612, 1513, 1461, 1384, 1360, 1302, 1247, 1210, 1101, 1037, 1009, 972, 834, 774, 738, 702; ^{1}H NMR ($CDCl_3$) δ ppm 7.38–7.33 (m, 2H, Ar**H**), 7.32–7.19 (m, 5H, Ar**H**), 6.90–6.84 (m, 2H, Ar**H**), 4.65–4.85 (m, 1H, $\mathbf{H}_a$), 4.43 (s, 2H, PMBC$\mathbf{H}_2$), 4.19 (dd, *J* = 8.8, 1.9 Hz, 1H, $\mathbf{H}_c$), 4.14 (t, *J* = 8.3 Hz, 1H, $\mathbf{H}_c$), 4.01 (dd, *J* = 8.3, 3.4 Hz, 1H, $C_9\mathbf{H}$), 3.91–3.82 (m, 2H, $C_6\mathbf{H}$, $C_7\mathbf{H}$), 3.79 (s, 3H, ArOC$\mathbf{H}_3$), 3.51–3.37 (m, 2H, $C_{12}\mathbf{H}_2$), 3.30 (dd, *J* = 13.2, 2.9 Hz, 1H, $\mathbf{H}_a$), 2.77 (dd, *J* = 13.2, 9.8 Hz, 1H, $\mathbf{H}_a$), 1.91–1.73 (m, 2H, $C_8\mathbf{H}$, $C_{11}\mathbf{H}$), 1.57–1.45 (m, 1H, $C_{10}\mathbf{H}$), 1.42–1.33 (m, 2H, $C_{10}\mathbf{H}$, $C_{11}\mathbf{H}$), 1.20 (d, *J*=6.8 Hz, 3H, $C_6C\mathbf{H}_3$), 0.96 (t, *J* = 8.1 Hz, 9H, $Si(CH_2C\mathbf{H}_3)_3$), 0.91–0.87 (m, 12H, $C_8C\mathbf{H}_3$, $SiC(C\mathbf{H}_3)_3$), 0.59 (q, *J* = 8.1 Hz, 6H, $Si(C\mathbf{H}_2CH_3)_3$), 0.04 (d, *J* = 3.9 Hz, 6H, $Si(C\mathbf{H}_3)_2$); ^{13}C NMR (125 MHz) 175.4, 159.0, 152.9, 135.3, 130.9, 129.5, 129.2, 129.0, 127.4, 113.7, 74.2, 72.4, 72.1, 70.6, 65.9, 55.8, 55.3, 44.2, 41.8, 37.6, 27.6, 26.7, 25.9, 18.1, 10.5, 9.7, 7.1, 5.5, –4.5; HRMS (ES) calcd for $C_{40}H_{65}NO_7Si_2$ $[M+NH_4]^+$ 745.4643. Found 745.4644.



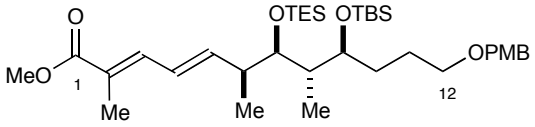
(*2R,3S,4S,5S*)–*S*–ethyl–5–(tert–butyldimethylsilyloxy)–8–(4–methoxybenzyloxy)–2,4–dimethyl–3–(triethylsilyloxy)octanethioate (3c).

Ethanethiol (170 μL, 1.33 mmol) was dissolved in 10 mL THF and cooled to –20°C. Butyllithium (0.53 mL, 2.87M in hexane, 1.53 mmol) was added dropwise. After 10 min. a cloudy solution has formed, to which a solution of oxazolidinone **3b** (927 mg, 1.33 mmol) in 5 mL THF was added by cannula. The reaction mixture was stirred at –20 °C until TLC indicated completion (30 min). The reaction mixture was partitioned between 20 mL of methylene chloride and 20 mL of sat. $NaHCO_3$. The aqueous layer was extracted a second time with 10 mL of methylene chloride. The combined organic layers were dried ($MgSO_4$) and concentrated. The excess Ethanthiol was removed *in vacuo* (stench!). Column chromatography (silica, 9% v/v ethyl acetate/hexanes elution) yielded 815 mg of the *title compound* **3c** (1.33 mmol, quantitative yield): $[\alpha]_D^{25} = -20.6$ (c = 3.6, $CHCl_3$); IR (film): 2954, 1877, 1685, 1614, 1514, 1458, 1387, 1360, 1302, 1248, 1172, 1095, 1038, 1007, 958, 835, 774, 738; ^{1}H NMR ($CDCl_3$) δ ppm 7.34–7.26 (m, 2H, Ar**H**), 6.94–6.89 (m, 2H, Ar**H**), 4.48 (s, 2H, PMBC$\mathbf{H}_2$), 4.11 (dd, J = 8.1, 3.1 Hz, 1H, $C_7\mathbf{H}$), 3.90 (ddd, J = 8.9, 3.4, 3.2 Hz, 1H, $C_9\mathbf{H}$), 3.84 (s, 3H, ArOC$\mathbf{H}_3$), 3.53–3.43 (m, 2H, $C_{12}\mathbf{H}_2$), 2.96–2.85 (m, 2H, $CH_3C\mathbf{H}_2S$), 2.83 (ddd, J = 13.9, 6.8, 2.9 Hz, 1H, $C_6\mathbf{H}$), 1.87–1.77 (m, 2H, $C_8\mathbf{H}$, $C_{11}\mathbf{H}$), 1.61–1.53 (m, 1H, $C_{11}\mathbf{H}$), 1.52–1.46 (m, 1H, $C_{10}\mathbf{H}$), 1.36–1.45 (m, 1H, $C_{10}\mathbf{H}$), 1.29 (t, J = 7.5 Hz, 3H, $C\mathbf{H}_3CH_2S$), 1.20 (d, J = 7.0 Hz, 3H, $C_6C\mathbf{H}_3$), 0.97 (t, J = 7.9 Hz, 9H, $Si(CH_2C\mathbf{H}_3)_3$), 0.92 (s, 9 H, $SiC(C\mathbf{H}_3)_3$), 0.88–0.85 (d, J = 7.0 Hz, 3H, $C_8C\mathbf{H}_3$), 0.69–0.52 (m, 6H, $Si(C\mathbf{H}_2CH_3)_3$), 0.08 (d, J = 3.5 Hz, 6H, $Si(C\mathbf{H}_3)_2$); HRMS (ES) calcd for $C_{32}H_{60}O_5SSi_2$ $[M+NH_4]^+$ 630.4044. Found 630.4036.

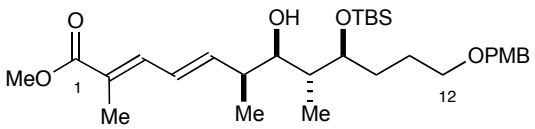


(*2R,3S,4S,5S*)–5–(tert–butyldimethylsilyloxy)–8–(4–methoxybenzyloxy)–2,4–dimethyl–3–(triethylsilyloxy)octanal (4). Thioester **3c** (203 mg, 0.331 mmol) was dissolved in 3 mL of methylene chloride and cooled to –90 °C. At this temperature a 1M solution of DIBALH in toluene was added (761 μL, 0.761 mmol) and the reaction mixture was stirred for 30 min. Methanol (*ca.* 2 mL), pre–cooled to –90 °C were added to quench the reaction, followed by 5 mL of Rochelle's salt saturated solution. 10 mL of diethyl ether were added and the mixture was allowed to warm to rt and stirred for 1h. After separation, the organic layer was washed with 1N NaOH (2 × 10 mL), $NaHCO_3$ (10 mL), and brine (5 mL), dried and concentrated. The residual oil was purified by column chromatography on (silica, 9% v/v etheyl acetates/hexanes elution) to yield 178 mg (0.322 mmol, 97% yield) of the *title compound* **4**: $[\alpha]_D^{25} = -23.6$ (c = 3.2, $CHCl_3$); IR (film): 2955, 2935, 2899, 2878, 1726, 1613, 1513, 1458, 1248, 1098, 1032, 835, 774 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ ppm 9.62 (s, 1 H, RC**H**O), 7.20–7.14 (m, 2H, Ar**H**), 6.81–6.77 (m, 2H, Ar**H**), 4.35 (s, 2H, PMBC$\mathbf{H}_2$), 4.12 (dd, J = 8.5, 2.1 Hz, 1H, $C_7\mathbf{H}$), 3.76 (ddd, J = 7.6, 4.2, 3.2 Hz, 1H, $C_9\mathbf{H}$), 3.71 (s, 3H, ArOC$\mathbf{H}_3$), 3.40–3.31 (m, 2H, $C_{12}\mathbf{H}_2$), 2.37 (ddd, J = 13.8, 6.8, 2.1 Hz, 1H, $C_6\mathbf{H}$), 1.82–1.74 (m, 1H,$C_8\mathbf{H}$), 1.74–1.65 (m, 1H, $C_{11}\mathbf{H}$), 1.49–1.41 (m, 1H, $C_{11}\mathbf{H}$), 1.40–1.27 (m, 2H, $C_{12}\mathbf{H}_2$), 1.02 (d, J = 7.0 Hz, 3H, $C_6C\mathbf{H}_3$), 0.83 (t, J = 8.1 Hz, 9H, $Si(CH_2C\mathbf{H}_3)_3$), 0.79 (s, 9H, $SiC(C\mathbf{H}_3)_3$), 0.73 (d, J = 7.3 Hz, 3H, $C_8C\mathbf{H}_3$), 0.46 (q, J = 8.1 Hz, 6H, $Si(C\mathbf{H}_2CH_3)_3$), –0.05 (d, J =

6.4 Hz, 6H, Si(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.2, 159.1, 130.8, 129.1, 128.3, 113.7, 72.4, 72.2, 72.1, 70.4, 55.3, 50.1, 43.5, 28.0, 26.3, 25.9, 10.3, 7.0, 5.4, –4.3; HRMS (ES) calcd for $C_{30}H_{56}O_5Si_2$ $[M+NH_4]^+$ 570.4010. Found 570.4005.

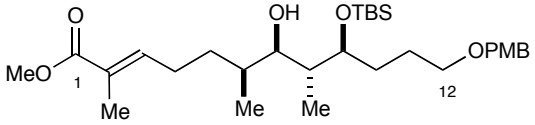


(*2E,4E,6S,7R,8S,9S*)–methyl–9–(tert–butyldimethylsilyloxy)–12–(4–methoxybenzyloxy)–2,6,8–trimethyl–7–(triethylsilyloxy)dodeca–2,4–dienoate (6). (*E*)–methyl 4–(diethoxyphosphoryl)–2–methylbut–2–enoate (2.1 g, 7.59 mmol) was dissolved in 40 mL of THF and cooled to –78 °C. At this temperature a 2.5 M solution of butyllithium in hexane (2.45 mL, 7.59 mmol) was added drop wise and the mixture was stirred for 5 min, before it was transferred to an ice bath. After 30 min. a solution of aldehyde **4** (3.0 g, 5.42 mmol) in 15 mL THF was added by cannula. The reaction mixture was stirred at 0° C until TLC indicated completion (1.5 h). A solution of sat. NH_4Cl was added to quench the reaction and the reaction mixture was extracted with diethyl ether (2 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated. The residual oil was purified by column chromatography (silica, 17% v/v ethyl acetate/hexanes elution) to yield 3.38 g (5.21 mmol, 96% yield) of the *title compound* **6**: $[\alpha]_D^{25} = –12.9$ (*c* = 2.3, $CHCl_3$); IR (film): 2954, 2877, 2856, 1712, 1638, 1613, 1513, 1460, 1436, 1388; 1360, 1248, 1172, 1100, 1065, 1036, 1008, 977, 834, 774, 738; ^{1}H NMR ($CDCl_3$) δ ppm 7.33–7.25 (m, 2H, Ar**H**), 7.20 (d, *J* = 11.4 Hz, 1 H, C_3**H**), 6.93–6.88 (m, 2H, Ar**H**), 6.37 (dd, *J* = 15.1, 11.3 Hz, 1H, C_4**H**), 6.13 (dd, *J* = 15.2, 7.3 Hz, 1H, C_5**H**), 4.47 (s, 2H, PMBC**H**$_2$), 3.92 (ddd, *J* = 8.9, 4.5, 2.5 Hz, 1H, C_9**H**), 3.84 (s, 3H, CO_2C**H**$_3$), 3.80 (s, 3H, ArOC**H**$_3$), 3.62 (dd, *J* = 7.8, 3.4 Hz, 1H, C_7**H**), 3.52–3.43 (m, 2H, C_{12}**H**$_2$), 2.54 (td, *J* = 6.7, 3.1 Hz, 1H, C_6**H**), 1.98 (s, 3H, C_2C**H**$_3$), 1.89–1.83 (m, 1H, C_8**H**), 1.83–1.77 (m, 1H, C_{11}**H**), 1.61–1.51 (m, 1H, C_{11}**H**), 1.50–1.43 (m, 1H, C_{10}**H**), 1.43–1.35 (m, 1H, C_{10}**H**), 1.06 (d, *J* = 6.7 Hz, 3H, C_6C**H**$_3$), 0.97 (t, *J* = 8.1 Hz, 9H, Si(CH_2C**H**$_3$)$_3$), 0.92 (s, 9H, SiC(C**H**$_3$)$_3$), 0.86 (d, *J* = 7.0 Hz, 3H, C_8C**H**$_3$), 0.60 (q, *J* = 7.9 Hz, 6H, Si(C**H**$_2$CH$_3$)$_3$), 0.07 (d, *J* = 1.5 Hz, 6H, Si(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 146.9, 138.6, 130.8, 129.1, 125.1, 113.7, 77.6, 72.4, 72.1, 70.6, 55.2, 51.7, 43.4, 40.7, 28.0, 26.3, 25.9, 18.1, 13.3, 12.6, 10.3, 7.1, 5.5, –4.3, –4.4; HRMS (ES) calcd for $C_{36}H_{64}O_6Si_2$ $[M+NH_4]^+$ 666.4585. Found 666.4573.

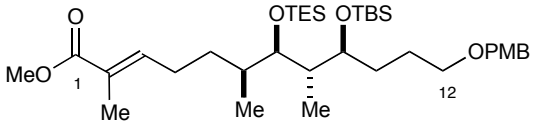


(*2E,4E,6S,7R,8R,9S*)–methyl 9–(tert–butyldimethylsilyloxy)–7–hydroxy–12–(4–methoxybenzyloxy)–2,6,8–trimethyldodeca–2,4–dienoate (6a). Protected diol **6** (192 mg, 0.296 mmol) was dissolved in 3 mL of 1:1 mixture of methanol and CH_2Cl_2. The solution was cooled to –10 °C, treated with camphor sulfonic acid (3.4 mg in 0.5 mL methanol), and stirred until TLC indicated completion (45 min). The reaction mixture was quenched by addition of 10 drops of triethyl amine and was concentrated. The residual oil was purified by colum chromatography (silica, 17% v/v ethyl acetate/hexanes elution) to yield 155 mg

(0.290 mmol, 98% yield) the *title compound* **6a**: $[\alpha]_D^{25}$ = +6.7 (*c* = 2.6, $CHCl_3$); IR (film): 2954, 2856, 1709, 1637, 1612, 1513, 1459, 1437, 1388, 1361, 1249, 1102, 1037, 979, 835, 774, 751; ^{1}H NMR ($CDCl_3$) δ ppm 7.32–7.26 (m, 2H, Ar**H**), 7.23 (d, *J* = 11.1 Hz, 1H, C_3**H**), 6.95–6.87 (m, 2H, Ar**H**), 6.43 (dd, *J* = 15.2, 11.1 Hz, 1H, C_4**H**), 6.22 (dd, *J* = 15.2, 7.3 Hz, 1H, C_5**H**), 4.46 (s, 2H, PMBC$\mathbf{H}_2$), 3.92 (dt, *J* = 6.7, 4.5 Hz, 1H, C_9**H**), 3.83 (s, 3H, $CO_2C\mathbf{H}_3$), 3.78 (s, 3H, ArOC$\mathbf{H}_3$), 3.50–3.46 (m, 3H, C_7**H**, $C_{12}\mathbf{H}_2$), 2.74 (d, *J* = 2.3 Hz, 1H, C_7O**H**), 2.57–2.50 (m, 1H, C_6**H**), 1.97 (s, 3H, $C_2C\mathbf{H}_3$), 1.86–1.80 (m, 1H, C_8**H**), 1.79–1.71 (m, 1H, C_{11}**H**), 1.69–1.61 (m, 1H, C_{11}**H**), 1.61–1.51 (m, 2H, $C_{10}\mathbf{H}_2$), 1.08 (d, *J* = 6.7 Hz, 3H, $C_6C\mathbf{H}_3$), 0.93 (s, 9H, $SiC(C\mathbf{H}_3)_3$), 0.87 (d, *J* = 7.0 Hz, 3H, $C_8C\mathbf{H}_3$), 0.11 (d, *J* = 5.6 Hz, 6H, $Si(C\mathbf{H}_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 159.1, 146.7, 138.8, 130.6, 129.2, 125.3, 113.7, 76.5, 75.1, 72.5, 70.1, 55.2, 51.7, 40.7, 39.5, 29.8, 25.9, 25.4, 18.0, 12.6, 12.4 11.6, –4.39, –4.53.

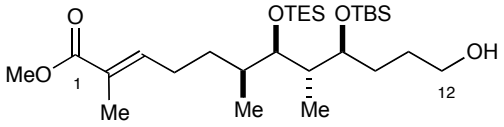


(*6S,7R,8R,9S,E*)–methyl 9–(tert–butyldimethylsilyloxy)–7–hydroxy–12–(4–methoxybenzyloxy)–2,6,8–trimethyldodec–2–enoate (6b). Crabtree's catalyst (34 mg, 0.042 mmol) was dissolved in 0.25 mL of methylene chloride and diluted with 4.75 mL THF. This solution was transferred to a flask containing diene **6a** (426 mg, 0.796 mmol). The flask was flushed with hydrogen and the reaction mixture was stirred for 45 min, at which point 5 mL of a second solution of Crabtree's catalyst (34 mg, 0.042 mmol), prepared as described above, were added and the reaction was allowed to proceed for another 45 min. The reaction mixture was filtered through a plug of silica to remove the catalyst and then concentrated. The residual oil was purified by column chromatography (silica, 15% v/v acetone/hexanes elution) to yield 397 mg (0.739 mmol, 93%) the *title compound* **6c**: $[\alpha]_D^{25}$ = +7.4 (*c* = 2.05, $CHCl_3$); IR (film): 2926, 2854, 1716, 1653, 1614, 1513, 1459, 1437, 1248, 1201, 1097, 1066, 1037, 983, 835, 774; ^{1}H NMR ($CDCl_3$) δ ppm 7.33–7.26 (m, 2H, Ar**H**), 6.94–6.87 (m, 2H, Ar**H**), 6.80 (td, *J* = 7.5, 1.5 Hz, 1H, C_3**H**), 4.46 (s, 2H, PMBC$\mathbf{H}_2$), 3.86 (q, *J* = 5.6 Hz, 1H, C_9**H**), 3.83 (s, 3H, $CO_2C\mathbf{H}_3$), 3.76 (s, 3H, ArOC$\mathbf{H}_3$), 3.48 (t, *J* = 6.4 Hz, 2H, $C_{12}\mathbf{H}_2$), 3.42 (dt, *J* = 9.4, 2.5 Hz, 1H, C_7**H**), 2.92 (d, *J* = 2.9 Hz, 1H, C_7O**H**), 2.23 (q, *J* = 7.4 Hz, 2H, $C_4\mathbf{H}_2$), 1.87 (s, 3H, $C_2C\mathbf{H}_3$), 1.81–1.71 (m, 3H, C_8**H**, $C_{11}\mathbf{H}_2$), 1.70–1.64 (m, 1H, C_{10}**H**), 1.64–1.54 (m, 3H, C_5**H**, C_6**H**, C_{10}**H**), 1.43–1.53 (m, 1H, C_5**H**), 0.93 (s, 9H, $SiC(C\mathbf{H}_3)_3$), 0.89 (d, *J* = 6.7 Hz, 3H, $C_6C\mathbf{H}_3$), 0.78 (d, *J* = 6.7 Hz, 3H, $C_8C\mathbf{H}_3$), 0.12 (d, *J* = 8.2 Hz, 6H, $Si(C\mathbf{H}_3)_2$) ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 159.1, 142.7, 130.6, 129.2, 127.3, 113.7, 76.1, 75.9, 72.4, 70.1, 55.2, 51.6, 40.7, 34.2, 33.2, 30.3, 26.5, 25.9, 25.0, 18.0, 12.6, 12.3, 11.9, –4.4, –4.6; HRMS (ES) calcd for $C_{30}H_{52}O_6Si$ $[M+Na]^+$ 559.3431. Found 599.3423.

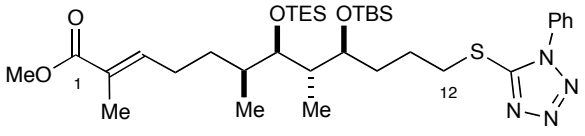


(*6S,7R,8S,9S,E*)–methyl 9–(tert–butyldimethylsilyloxy)–12–(4–methoxybenzyloxy)–2,6,8–trimethyl–7–(triethylsilyloxy)dodec–

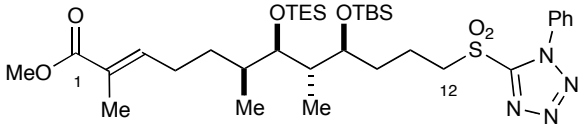
2–enoate (7). Alcohol **6b** (100 mg, 0.186 mmol) was dissolved in 2 mL of methylene chloride and cooled to –78 °C. 2,6–lutidine (65 μL, 0.558 mmol) and TESOTf (63 μL, 0.279 mmol) were added in this order and the mixture was stirred until TLC indicated completion (1 h). 5 ml of a saturated solution of $NaHCO_3$ were added to quench the reaction and the mixture was extracted with diethyl ether (2 × 10 mL). The organic layers were dried and concentrated. The residual oil was purified by column chromatography on silica gel to yield 107 mg (0.164 mmol, 88%): $[\alpha]_D^{25}$ = –12.3 (*c* = 2.1, $CHCl_3$); IR (film): 2954, 2878, 1717, 1613, 1514, 1461, 1436, 1388, 1360, 1248, 1202, 1098, 1066, 1038, 1007, 978, 835, 774, 738; ^{1}H NMR ($CDCl_3$) δ ppm 7.32–7.26 (m, 2H, Ar**H**), 6.94–6.87 (m, 2H, Ar**H**), 6.78 (td, *J* = 7.5, 1.46 Hz, 1H, C_3**H**), 4.47 (s, 2H, PMBC$\mathbf{H}_2$), 3.92 (ddd, *J* = 9.5, 3.4, 2.6 Hz, 1H, C_9**H**), 3.84 (s, 3H, $CO_2C\mathbf{H}_3$), 3.78 (s, 3H, ArOC$\mathbf{H}_3$), 3.53–3.42 (m, 3H, C_7**H**, $C_{12}\mathbf{H}_2$), 2.31–2.22 (m, 1H, C_4**H**), 2.22–2.13 (m, 1H, C_4**H**), 1.88 (s, 3H, $C_2C\mathbf{H}_3$), 1.87–1.80 (m, 2H, C_8**H**, C_{11}**H**), 1.63–1.59 (m, 1H, C_6**H**), 1.59–1.47 (m, 1H, C_{11}**H**), 1.47–1.32 (m, 4H, $C_5\mathbf{H}_2$, $C_{12}\mathbf{H}_2$), 0.99 (t, *J* = 8.1 Hz, 9H, $Si(CH_2C\mathbf{H}_3)_3$), 0.92 (s, 9H, $SiC(C\mathbf{H}_3)_3$), 0.88 (d, *J* = 6.7 Hz, 3H, $C_6C\mathbf{H}_3$), 0.79 (d, *J* = 7.0 Hz, 3H, $C_8C\mathbf{H}_3$), 0.63 (q, *J* = 7.9 Hz, 6H, $Si(C\mathbf{H}_2CH_3)_3$), 0.07 (d, *J* = 2.6 Hz, 6H, $Si(C\mathbf{H}_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 159.0, 142.5, 130.8, 129.1, 127.5, 113.7, 77.8, 72.4, 70.6, 55.3, 51.7, 43.4, 36.0, 33.4, 27.5, 27.0, 26.8, 25.9, 18.1, 12.9, 12.4, 10.2, 7.2, 5.7, –4.3, –4.4; HRMS (ES) calcd for $C_{36}H_{66}O_6Si_2$ $[M+Na]^+$ 673,4296. Found 673.4299.



(*6S,7R,8S,9S,E*)–methyl–9–(tert–butyldimethylsilyloxy)–12–hydroxy–2,6,8–trimethyl–7–(triethylsilyloxy)dodec–2–enoate (7a). PMB alcohol **7** (68 mg, 0.097 mmol) was dissolved in 1 mL of methylene chloride. To this solution, pH 7.0 buffer (0.5 mL) followed by DDQ (44 mg, 0.194 mmol) was added. The reaction mixture was stirred for 1 h and then $NaHCO_{3(sat.)}$ (5 mL) was added and the mixture was extracted with methylene chloride (2 × 10 mL). The combined organic layers were dried and concentrated. The residual oil was purified by column chromatography (silica, 20% v/v diethyl ether/hexanes then 40% v/v ethyl acetate/hexanes elution) to yield 46 mg (0.088 mmol, 91% yield) of the *title compound* **7a**: $[\alpha]_D^{25}$ = –14.4 (*c* = 2.25, $CHCl_3$); IR (film): 2955, 2878, 1718, 1649, 1461, 1436, 1387, 1256, 1120, 1094, 1057, 1027, 1007, 977, 836; ^{1}H NMR ($CDCl_3$) δ ppm 6.75 (td, *J* = 7.5, 1.46 Hz, 1H, C_3**H**), 3.91 (ddd, *J* = 9.3, 3.6, 2.6 Hz, 1H, C_9**H**), 3.74 (s, 3H, $CO_2C\mathbf{H}_3$), 3.62–3.67 (m, 2H, C_{12}**H**), 2.28–2.19 (m, 1H, C_4**H**), 2.19–2.10 (m, 1H, C_4**H**), 1.84 (s, 3H, $C_2C\mathbf{H}_3$), 1.84–1.80 (m, 1H, C_8**H**), 1.76 (m, 1H, C_{12}O**H**), 1.63–1.56 (m, 1H, C_6**H**), 1.55–1.45 (m, 3H, C_5**H**, $C_{11}\mathbf{H}_2$), 1.44–1.32 (m, 3H, C_5**H**, $C_{10}\mathbf{H}_2$), 0.97 (t, *J* = 7.9 Hz, 9H, $Si(CH_2C\mathbf{H}_3)_3$), 0.89 (s, 9H, $SiC(C\mathbf{H}_3)_3$), 0.85 (d, *J* = 6.7 Hz, 3H, $C_6C\mathbf{H}_3$), 0.77 (d, *J* = 7.0 Hz, 3H, $C_8C\mathbf{H}_3$), 0.60 (q, *J* = 7.9 Hz, 6H, $Si(C\mathbf{H}_2CH_3)_3$), 0.05 (d, *J* = 3.2 Hz, 6H, $Si(C\mathbf{H}_3)_2$), ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 142.4, 127.5, 77.9, 72.4, 63.4, 51.7, 43.3, 36.0, 33.4, 29.8, 27.1, 27.0, 25.9, 18.1 12.9, 12.4, 10.2, 7.2, 5.7, –4.3, –4.4; HRMS (ES) calc. for $C_{28}H_{58}O_5Si_2$ $[M+Na]^+$ 553,3720. Found 533.3731.

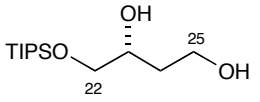


(*6S,7R,8S,9S,E*)–methyl 9–(tert–butyldimethylsilyloxy)–2,6,8–trimethyl–12–(1–phenyl–1*H*–tetrazol–5–ylthio)–7–(triethylsilyloxy)dodec–2–enoate (7b). Alcohol **7a** (59 mg, 0.111 mmol), 1–phenyl–1*H*–tetrazole–5–thiol (24 mg, 0.133 mmol), and triphenlyphosphine (35 mg, 0.133 mmol) were dissolved in 1 mL THF. To this mixture DEAD (35μL, 0.222 mmol) was added drop wise and the yellow mixture was stirred for 1h. The reaction mixture was concentrated and the residual yellow oil was purified by column chromatography (silica, 14% v/v ethyl acetate/hexanes elution) to yield 76 mg (0.110 mmol, 99% yield) of the *title compound* **7b**: $[\alpha]_D^{25} = -12.0$ (*c* = 2.45, $CHCl_3$); IR (film): 2953, 2934, 2878, 1715, 1500, 1461, 1413, 1386, 1257, 1047, 1007, 966, 836, 774, 739; ^{1}H NMR ($CDCl_3$) δ ppm 7.62–7.51 (m, 5H, Ar**H**), 6.74 (td, *J* = 7.5, 1.5 Hz, 1H, C_3**H**), 3.90 (ddd, *J* = 9.6, 3.6, 2.1 Hz, 1H, C_9**H**), 3.74 (s, 3H, CO_2C**H**$_3$), 3.45–3.52 (m, 1H, C_{12}**H**), 3.44–3.37 (m, 2H, C_7**H**, C_{12}**H**), 2.27–2.18 (m, 1H, C_4**H**), 2.18–2.09 (m, 1H, C_4**H**), 2.08–1.98 (m, 1H, C_{11}**H**), 1.84 (s, 3H, C_2C**H**$_3$), 1.83–1.79 (m, 1H, C_8**H**), 1.79–1.71 (m, 1H, C_{11}**H**), 1.62–1.54 (m, 1H, C_6**H**), 1.54–1.39 (m, 3H, C_5**H**, C_{10}**H**$_2$), 1.39–1.31 (m, 1H, C_5**H**), 0.93 (t, *J* = 7.9 Hz, 9H, $Si(CH_2C$**H**$_3)_3$), 0.86 (s, 9H, $SiC(C$**H**$_3)_3$), 0.84 (d, *J* = 6.7 Hz, 3H, C_6C**H**$_3$), 0.76 (d, *J* = 7.0 Hz, 3H, C_8C**H**$_3$), 0.61–0.52 (m, 6H, $Si(C$**H**$_2CH_3)_3$), 0.02 (d, *J* = 5.9 Hz, 6H, $Si(C$**H**$_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 160.3, 154.4, 142.3, 133.8, 127.6, 123.8, 77.9, 71.9, 51.7, 43.3, 36.1, 34.1, 33.3, 30.0, 26.9, 26.0, 25.8, 18.0, 12.9, 12.4, 10.2, 7.1, 5.7, –4.3, –4.5; HRMS (ES) calc. for $C_{35}H_{62}N_4O_4SSi_2$ $[M+H]^+$ 691.4109. Found 691.4113.

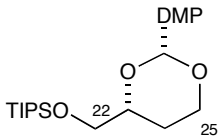


(*6S,7R,8S,9S,E*)–methyl 9–(tert–butyldimethylsilyloxy)–2,6,8–trimethyl–12–(1–phenyl–1*H*–tetrazol–5–ylsulfonyl)–7–(triethylsilyloxy)dodec–2–enoate (8). Sulfide **7b** (169 mg, 0.245 mmol) was dissolved in 2.5 mL ethanol. 284 μL of a 0.19M solution of ammonium molybdate in 30% H_2O_2 were added and the mixture was stirred over night. The reaction was quenched by addition of water and the mixture was extracted with ethyl acetate (2 × 5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residual oil was purified by column chromatography (silica, 15% diethyl ether/methylene chloride elution) to yield 151 mg (0.209 mmol, 85% yield) of the *title compound*: $[\alpha]_D^{25} = -10.1$ (*c* = 1.54, $CHCl_3$); IR (film): 2954, 2879, 2866, 1716, 1648, 1498, 1461, 1436, 1388, 1345, 1259, 1153, 1076, 1008, 967, 836, 774, 740, 688; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.77–7.70 (m, 2H, Ar**H**), 7.69–7.60 (m, 3H, Ar**H**), 6.78 (td, *J* = 7.5, 1.5 Hz, 1H, C_3**H**), 3.97 (ddd, *J* = 9.7, 3.4, 2.3 Hz, 1H, C_9**H**), 3.86–3.75 (m, 2H, C_{12}**H**$_2$), 3.77 (s, 3H, CO_2C**H**$_3$), 3.43 (dd, *J* = 8.8, 2.1 Hz, 1H, C_7**H**), 2.31–2.23 (m, 1H, C_{11}**H**), 2.22–2.13 (m, 2H, C_4**H**), 1.99–1.89 (m, 1H, C_{11}**H**), 1.88 (s, 3H, C_2C**H**$_3$), 1.89–1.83 (m, 1H, C_8**H**), 1.64–1.56 (m, 2H, C_5**H**, C_6**H**), 1.56–1.48 (m, 2H, C_5**H**, C_{10}**H**), 1.43–1.34 (m, 1H, C_{10}**H**), 1.00 (t, *J* = 7.9 Hz, 9H, $Si(CH_2C$**H**$_3)_3$),

0.90 (s, 9H, SiC(C**H**$_3$)$_3$), 0.89 (d, *J* = 7.0 Hz, 3H, C$_6$C**H**$_3$), 0.81 (d, *J* = 7.0 Hz, 3H, C$_8$C**H**$_3$), 0.66–0.59 (m, 6H, Si(C**H**$_2$CH$_3$)$_3$), 0.06 (d, *J* = 11.4 Hz, 6H, Si(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 142.2, 131.4, 129.7, 127.6, 125.0, 77.9, 71.9, 56.4, 51.7, 43.1, 36.2, 33.1, 29.6, 26.9, 25.8, 19.4, 18.0, 13.1, 12.4, 10.2, 7.2, 5.7, –4.2, –4.5; HRMS (ES) calcd for $C_{35}H_{62}N_4O_6SSi_2$ $[M+NH_4]^+$ 740,4272. Found 740.4252.

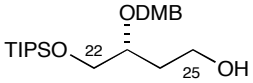


(*R*)–4–(triisopropylsilyloxy)butane–1,3–diol (17a). To the precooled to 0 ºC solution of $LiAlH_4$ (370 mg, 9.80 mmol) in diethyl ether (15.0 mL) the solution of *D*–Malic acid derivative **17** (1.52 g, 4.55 mmol) in diethyl ether (5.0 mL) was added over 10 min period. The reaction mixture was stirred for 50 min, sequentially treated with ethyl acetate (3 mL) and methanol (3 mL), and then 1 M solution of tartaric acid (15 mL) was added. The obtained solution was stirred for 15 min, extracted with methylene chloride (3 × 30 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a yellow oil. Subjection of this material to flash chromatography (silica, 33% → 100% v/v ethyl acetate/hexane elution) afforded, after concentration of the appropriate fractions (R_f 0.6, 50% v/v ethyl acetate/hexanes), the *title compound* **17a** (0.90 g, 75% yield): $[\alpha]_D^{25}$ = –0.7 (*c* = 8.85, $CHCl_3$); IR (film) 3375, 2937, 2870, 1464, 1380, 1251, 1116, 1066, 1004 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (ddd, *J* = 10.5, 6.5, 4.0 Hz, 1H, C$_{23}$**H**), 3.79 (t, *J* = 5.5 Hz, 2H, C$_{25}$**H**$_2$), 3.66 (dd, *J* = 10.0, 4.5 Hz, 1H, C$_{22}$**H**), 3.53 (dd, *J* = 10.0, 7.0 Hz, 1H, C$_{22}$**H**), 2.94 (s, OH), 1.66 (d, J_{AB}= 6.0 Hz, 1H, C$_{24}$**H**), 1.64 (d, J_{AB}= 6.0 Hz, 1H, C$_{24}$**H**), 1.07 (m, 3H, SiC**H**(CH$_3$)$_2$), 1.06 (d, *J* = 5.6, 18H, SiCH(C**H**$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.7, 67.4, 60.9, 34.7, 17.9, 11.8; HRMS (ESI): Exact mass calcd for $C_{13}H_{30}O_3Si$ $[M+H]^+$: 263.2042. Found: 263.2039.

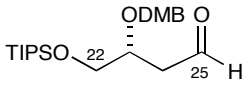


(((2*R*,4*R*)–2–(3,4–dimethoxyphenyl)–1,3–dioxan–4–yl)methoxy)triisopropylsilane (18). To the solution of diol **17a** (2.3 g, 8.78 mmol) and 3,4–dimethoxybenzylidene acetal (2.46 mL, 13.2 mmol) in methylene chloride (44.0 mL) CSA (165 mg, 0.702 mmol) was added. The reaction mixture was stirred for 45 min, treated with triethyl amine (*ca.* 0.2 mL), and concentrated under reduced pressure to afford a yellow oil. Subjection of this material to flash chromatography (silica, 17% v/v diethyl ether/pentane elution) afforded, after concentration of the appropriate fractions (R_f 0.8, 50% v/v ethyl acetate/hexanes), the *title compound* **18** (3.4 g, 94% yield): $[\alpha]_D^{25}$ = –2.1 (*c* = 5.58, $CHCl_3$); IR (film) 2943, 2866, 1596, 1519, 1464, 1409, 1374, 1265, 1139, 1109, 1031 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.06 (d, *J* = 2.0 Hz, 1H, Ar**H**), 7.02 (dd, *J* = 8.5, 2.0 Hz, 1H, Ar**H**), 6.84 (d, *J* = 8.3 Hz, 1H, Ar**H**), 5.48 (s, 1H, OC**H**O), 4.30 (ddd, *J* = 11.0, 5.0, 1.0 Hz, 1H, C$_{23}$**H**), 3.98 (td, *J* = 12.2, 2.5 Hz, 1H, C$_{25}$**H**), 3.95 (m, 1H, C$_{25}$**H**), 3.91 (m, 1H, C$_{22}$**H**), 3.90 (s, 3H, ArOC**H**$_3$), 3.86 (s, 3H, ArOC**H**$_3$), 3.70 (dd, *J* = 9.5, 6.3 Hz, 1H, C$_{24}$**H**), 1.85 (tdd, *J* = 13.0, 11.5, 5.0 Hz, 1H, C$_{24}$**H**), 1.70 (dq, *J* = 13.0, 1.5 Hz, 1H, SiC**H**(CH$_3$)$_2$), 1.09 (m, 3H), 1.06 (d, *J* = 5.6, 18H, SiCH(C**H**$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 148.8, 131.5, 118.7, 110.6,

109.0, 101.1, 77.7, 67.0, 66.4, 55.9, 55.8, 28.4, 18.0, 11.9; HRMS (ESI): Exact mass calcd for $C_{22}H_{38}O_5Si$ $[M+H]^+$: 411.2567. Found: 411.2562.

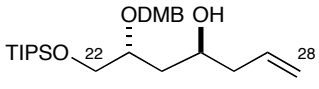


(*R*)–3–(3,4–dimethoxybenzyloxy)–4–(triisopropylsilyloxy)butan–1–ol (18a). To the precooled to –78 ºC solution of acetal **17** (4.5 g, 11.0 mmol) in methylene chloride (60 mL) the solution of DIBALH (1.0 M, 24.1 mL, 24.1 mmol) in hexanes was added. The reaction mixture was warmed to –24 ºC stirred for 45 min, then warmed to room temperature and sequentially treated with ethyl acetate (5 mL) and tartaric acid (1 M, 10 mL). The aqueous phase was then washed with methylene chloride (2 × 15 mL), and the combined organic phase was then washed with $NaHCO_{3(sat.)}$ (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a yellow oil. Subjection of this material to flash chromatography (silica, 50% → 75% v/v diethyl ether/pentane elution) afforded, after concentration of the appropriate fractions (R_f 0.1, 25% v/v ethyl acetate/hexanes), the *title compound* **18a** (3.60 g, 80% yield): $[\alpha]_D^{25}$ = +27.2 (*c* = 2.44, $CHCl_3$); IR (film) 3462, 2939, 2855, 1590, 1512, 1460, 1266, 1239, 1161, 1134 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.88 (s, 1H, Ar**H**), 6.86 (dd, *J* = 10.2, 1.8 Hz, 1H, Ar**H**), 6.82 (d, *J* = 7.9 Hz, 1H, Ar**H**), 4.72 (d, J_{AB} = 11.1 Hz, 1H, DMPC**H**H), 4.53 (d, J_{AB} = 11.2 Hz, 1H, DMPCH**H**), 3.87 (s, 3H, DMPOC**H**$_3$), 3.86 (s, 3H, DMPOC**H**$_3$), 3.83 (td, *J* = 7.8, 4.2 Hz, 1H, C_{23}**H**), 3.74 (t, *J* = 5.9 Hz, 2H), 3.70 (m, 2H), 1.87–1.81 (m, 1H, C_{24}**H**), 1.80–1.76 (m, 1H, C_{24}**H**), 1.10 (m, 3H, SiC**H**$(CH_3)_2$), 1.06 (d, *J* = 6.2, 18H, SiCH(C**H**$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 148.7, 131.0, 120.5, 111.2, 110.9, 78.9, 72.3, 65.9, 60.5, 55.9, 55.8, 34.4, 18.0, 11.9; **HRMS** (ESI): Exact mass calcd for $C_{22}H_{40}O_5Si$ $[M+H]^+$: 413.2723. Found: 413.2729.

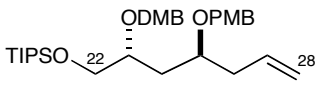


(*R*)–3–(3,4–dimethoxybenzyloxy)–4–(triisopropylsilyloxy)butanal (19). To the precooled to –10 ºC solution of alcohol **18a** (1.32 g, 3.20 mmol) and triethylamine (1.56 mL, 11.2 mmol) in methylene chloride/DMSO (2:1, 13.5 mL) the solution of SO_3•Py (1.7g, 11.2 mmol) in DMSO (4.5 mL) was added. The reaction mixture was stirred for 45 min and treated with water (10 mL), warmed to room temperature and then partitioned between brine (10 mL) and ethyl acetate (10 mL). The separated organic phase was then washed with $Na_2SO_{3(sat.)}$ (5 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford crude oil. Subjection of this material to flash chromatography (silica, 25% v/v diethyl ether/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.6, 33% v/v ethyl acetate/hexanes), the *title compound* **19** (1.07 g, 81% yield): ^1H NMR (600 MHz, $CDCl_3$) δ 9.78 (t, *J* = 2.0 Hz, 1H, C**H**O), 6.86 (s, 1H, Ar**H**), 6.85 (dd, *J* = 7.9, 1.8 Hz, 1H, Ar**H**), 6.81 (d, *J* = 7.9 Hz, 1H, Ar**H**), 4.62 (d, J_{AB} = 11.4 Hz, 1H, DMPC**H**H), 4.53 (d, J_{AB} = 11.1 Hz, 1H, DMPC**H**H), 4.02 (dtd, *J* = 7.2, 6.4, 5.0 Hz, 1H, C_{23}**H**), 3.88 (s, 3H, DMPOC**H**$_3$), 3.87 (s, 3H, DMPOC**H**$_3$), 3.84 (dd, *J* = 9.3, 5.0 Hz, 1H, C_{22}**H**),

3.68 (dd, J = 10.2, 6.4 Hz, 1H, C_{22}**H**), 2.56 (ddd, J = 16.7, 5.0, 1.8 Hz, 1H, C_{24}**H**), 2.66 (ddd, J = 16.4, 7.3, 2.3 Hz, 1H, C_{24}**H**), 1.11 (m, 3H, SiC**H**$(CH_3)_2$), 1.05 (d, J = 6.2, 18H, SiCH(C**H**$_3)_2$).

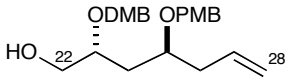


(4*S*,6*R*)–6–(3,4–dimethoxybenzyloxy)–7–(triisopropylsilyloxy)hept–1–en–4–ol (20). To the precooled to –92 ºC solution of aldehyde **19** (2.50 g, 6.01 mmol), $AlMe_2Cl$ (1.39 mL, 15.0 mmol) was added and the obtained solution was stirred for 15 min. The obtained bright yellow reaction mixture was then treated with allyltrimethylsilane (1.88 mL, 12.0 mmol). After 50 min, additional allyltrimethylsilane (1.88 mL, 12.0 mmol) was added, and the obtained solution was stirred for 1.5 h and then quenched with cold (–78 ºC) methanol (*ca.* 4 mL) following by the solution of Roche salt (10 mL). The obtained mixture was allowed to warm to room temperature, and then vigorously stirred for additional 15 min. The resulting mixture was then between ethyl acetate (20 mL) and the solution of Roche salt (40 mL). The organic phase was then washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford crude oil. Subjection of this material to flash chromatography (silica, 25% ethyl acetate/hexanes elution) afforded, after the concentration of the appropriate fractions (R_f 0.2, 25% v/v ethyl acetate/hexanes), the *title compound* **20** (2.14 g, 79%, 9:1 mixture of diastereomers). The separation of the major isomer by MPLC (silica, 25% ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions diastereomerically enriched compound **20** (1.58 g, 17:1 dr) together with the recovered mixture of diastereomers (0.5 g, 6:1 dr): $[\alpha]_D^{25}$ = +21.0 (c = 3.00, $CHCl_3$); IR (film) 3497, 2943, 2866, 1593, 1517, 1465, 1420, 1264, 1239, 1158, 1138, 1092, 1030 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.89 (s, 1H, Ar**H**), 6.88 (dd, J = 8.3, 1.8 Hz, 1H, Ar**H**), 6.82 (d, J = 7.9 Hz, 1H, Ar**H**), 5.81 (ddt, J = 13.8, 10.2, 6.6 Hz, 1H, C_{27}**H**), 5.10–5.07 (m, 2H, C_{28}**H**$_2$), 4.67 (d, J_{AB} = 11.1 Hz, 1H, DMPC**H**H), 4.55 (d, J_{AB} = 11.2 Hz, 1H, DMPC**H**H), 3.91 (ddd, J = 9.0, 5.4, 2.4 Hz, 1H, C_{23}**H**), 3.87 (s, 3H, DMPOC**H**$_3$), 3.87 (s, 3H, DMPOC**H**$_3$), 3.83 (dd, J = 9.7, 4.4 Hz, 1H, C_{22}**H**), 3.77 (m, 1H, C_{25}**H**), 3.70 (dd, J = 9.7, 5.6 Hz, 1H, C_{22}**H**), 2.25–2.20 (m, 2H, C_{26}**H**$_2$), 1.71 (ddd, J = 14.0, 7.2, 2.4 Hz, 1H, C_{24}**H**), 1.65 (ddd, J = 13.8, 9.6, 4.2 Hz, 1H, C_{24}**H**), 1.13–1.08 (m, 3H, SiC**H**$(CH_3)_2$), 1.06 (d, J = 6.2, 18H, SiCH(C**H**$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 148.7, 135.0, 131.0, 124.9, 120.6, 117.4, 111.3, 110.9, 72.5, 67.8, 65.9, 55.9, 55.8, 42.2, 38.1, 18.0, 11.9; HRMS (ESI) Found: ($M+H^+$), 453.3038, $C_{26}H_{46}O_4Si$ requires ($M+H^+$), 453.3038



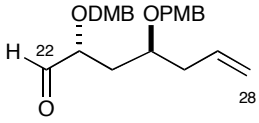
((2*R*,4*S*)–2–(3,4–dimethoxybenzyloxy)–4–(4–methoxybenzyloxy)hept–6–enyloxy)triisopropylsilane (20a). To the precooled to –14 ºC solution of alcohol **20** (1.58 g, 3.51 mmol) and TBAI (647 mg, 1.80 mmol) in DMF/THF (1:2, 36 mL) the solution of NaHMDS in toluene (0.90 M, 4.7 mL, 4.21 mmol) was added. The obtained yellow solution was stirred for 18 min and then treated with solution of PMBBr in toluene (2.89 M, 1.7 mL, 4.91 mmol). After 15 min, the formation of

a precipitate was noted, and the solution was stirred for additional 1h 50 min, quenched with $NH_4Cl_{(sat.)}$ (10 mL) and 1M NaOH (10 mL), and stirred at rt for additional 15 min. The obtained mixture was then partitioned between ethyl acetate (20 mL) and 1:1 mixture of brine and water (40 mL). The organic phase was then washed with brine (40 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford crude oil. Subjection of this material to flash chromatography (silica, 33% diethyl ether/pentane elution) afforded, after concentration of the appropriate fractions (R_f 0.6, 25% v/v ethyl acetate/hexanes), the *title compound* **20a** (1.63 g, 81% yield): $[\alpha]_D^{25}$ = +59.0 (*c* = 1.08, $CHCl_3$); IR (film) 2941, 2882, 1611, 1514, 1466, 1248, 1136, 1093, 1066, 1030 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.5 Hz, 2H, PMP**H**), 6.87–6.82 (m, 4H, Ar**H**), 6.78 (d, *J* = 7.9 Hz, 1H, DMP**H**), 5.83 (ddt, *J* = 14.4, 10.2, 6.6 Hz, 1H, C_{27}**H**), 5.09–5.04 (m, 2H, C_{28}**H**$_2$), 4.70 (d, J_{AB} = 11.1 Hz, 1H, ArC**H**H), 4.50 (d, J_{AB} = 11.1 Hz, 1H, ArC**H**H), 4.37 (d, J_{AB} = 11.4 Hz, 1H, ArC**H**H), 4.22 (d, J_{AB} = 11.1 Hz, 1H, ArC**H**H), 3.85 (m, 1H, C_{23}**H**), 3.85 (s, 3H, DMPOC**H**$_3$), 3.84 (s, 3H, DMPOC**H**$_3$), 3.78 (m, 1H), 3.77 (s, 3H, PMPOC**H**$_3$), 3.76–3.70 (m, 2H), 2.34 (t, *J* = 6.3 Hz, 2H, C_{26}**H**), 1.67 (ddd, *J* = 12.0, 9.7, 2.1 Hz, 1H, C_{24}**H**), 1.60 (ddd, *J* = 9.4, 6.5, 2.9 Hz, 1H, C_{24}**H**), 1.13–1.08 (m, 3H, SiC**H**$(CH_3)_2$), 1.06 (d, *J* = 5.3, 18H, SiCH$(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 148.9, 148.5, 134.7, 131.8, 131.0, 139.2, 120.4, 117.1, 113.7, 111.4, 110.9, 74.8, 72.5, 70.4, 67.0, 55.9, 55.7, 55.3, 38.6, 37.4, 18.0, 11.9. HRMS (ESI): Exact mass calcd for $C_{33}H_{52}O_6Si$ $[M+NH_4]^+$: 590.3877. Found: 590.3864.

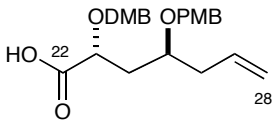


(2*R*,4*S*)–2–(3,4–dimethoxybenzyloxy)–4–(4–methoxybenzyloxy)hept–6–en–1–ol (20b). To the precooled to 0 ºC solution of **20a** (1.63 g, 2.85 mmol) in THF (29 mL) solid TBAF (1.04g, 3.98 mmol) was added. The obtained yellow solution was stirred for 1 h and then treated with an additional TBAF (300 mg, 1.15 mmol). After an additional hour of stirring, the reaction mixture was quenched with $NH_4Cl_{(sat.)}$ (10 mL), and warmed to rt. The aqueous phase was extracted with ethyl acetate (3 × 15 mL), and the combined organic phase was then washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford crude oil. Subjection of this material to flash chromatography (silica, 50% → 66% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.15, 50% v/v ethyl acetate/hexanes), the *title compound* **20b** (977 mg, 82% yield): $[\alpha]_D^{25}$ = +56.7 (*c* = 7.30, $CHCl_3$); IR (film) 3448, 3071, 2938, 2889, 2860, 2836, 1611, 1514, 1460, 1248, 1158, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 9.0 Hz, 2H, PMP**H**), 6.87–6.80 (m, 5H, Ar**H**), 5.83 (ddt, *J* = 14.0, 9.5, 6.5 Hz, 1H, C_{27}**H**), 5.12–5.08 (m, 2H, C_{28}**H**$_2$), 4.55 (d, J_{AB} = 11.0 Hz, 1H, ArCH**H**), 4.48 (d, J_{AB} = 11.0 Hz, 1H, ArCH**H**), 4.38 (d, J_{AB} = 11.3 Hz, 1H, ArCH**H**), 4.26 (d, J_{AB} = 10.8 Hz, 1H, ArCH**H**), 3.87 (m, 1H, C_{23}**H**), 3.86 (s, 3H, DMPOC**H**$_3$), 3.85 (s, 3H, DMPOC**H**$_3$), 3.77 (s, 3H, PMPOC**H**$_3$), 3.69 (dt, J = 8.0, 4.0 Hz, 1H, C_{22}**H**), 3.67–3.63 (m, 1H, C_{25}**H**), 3.49 (dd, *J* = 11.5, 5.0 Hz, 1H, C_{22}**H**), 2.38–2.36 (m, 2H, C_{26}**H**), 2.00 (s, OH), 1.81 (ddd, *J* = 14.5, 8.5, 3.0 Hz, 1H, C_{24}**H**), 1.71 (ddd, *J* = 14.5, 10.0, 4.0 Hz, 1H, C_{24}**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 148.9, 148.6, 134.1, 131.0, 130.4, 129.4, 120.2, 117.5, 114.0, 113.7, 111.1,

110.9, 76.6, 74.7, 71.6, 70.4, 64.4, 55.8, 55.7, 55.1, 38.2, 36.9; HRMS (ESI): Exact mass calcd for $C_{24}H_{32}O_6$ $[M+NH_4]^+$: 434.2543. Found: 434.2532.

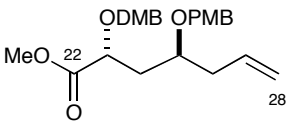


(2*R*,4*S*)–2–(3,4–dimethoxybenzyloxy)–4–(4–methoxybenzyloxy)hept–6–enal (21). To the precooled to –15 ºC solution of alcohol **20b** (0.900 g, 2.16 mmol) and triethylamine (0.90 mL, 6.49 mmol) in methylene chloride/DMSO (2:1, 9 mL) the solution of SO_3•Py (1.0g, 6.49 mmol) in DMSO (3 mL) was added. The reaction mixture was stirred for 1 h and treated with water (10 mL), warmed to room temperature and then partitioned between brine (10 mL) and ethyl acetate (15 mL). The separated organic phase was then washed with $Na_2SO_{3(sat.)}$ (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford crude oil. Subjection of this material to flash chromatography (silica, 50% → 75% v/v diethyl ether/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.4, 50% v/v ethyl acetate/hexanes), the *title compound* **21** (848 g, 95% yield): $[\alpha]_D^{25}$ = +84.0 (*c* = 3.75, $CHCl_3$); IR (film) 3074, 2990, 2936, 2836, 2740, 1729, 1611, 1514, 1466, 1247, 1158, 1139, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.58 (d, *J* = 2.0 Hz, 1H, C**H**O), 7.19 (d, *J* = 8.5 Hz, 2H, PMP**H**), 6.87–6.79 (m, 5H, Ar**H**), 5.80 (ddt, *J* = 14.0, 10.0, 7.5 Hz, 1H, C_{27}**H**), 5.09 (dd, *J* = 16.0, 1.4 Hz, 1H, C_{28}**H**), 5.07 (d, *J* = 10.5 Hz, 1H, C_{28}**H**), 4.52 (d, J_{AB} = 11.0 Hz, 1H, ArCH**H**), 4.51 (d, J_{AB} = 11.0 Hz, 1H, ArCH**H**), 4.30 (d, J_{AB} = 11.3 Hz, 1H, ArCH**H**), 4.20 (d, J_{AB} = 10.8 Hz, 1H, ArCH**H**), 4.01 (ddd, *J* = 10.0, 5.5, 2.0 Hz, 1H, C_{23}**H**), 3.52 (s, 3H, DMPOC$\mathbf{H}_3$), 3.50 (s, 3H, DMPOC$\mathbf{H}_3$), 3.31 (s, 3H, PMPOC$\mathbf{H}_3$), 3.70–3.66 (m, 1H, C_{25}**H**), 2.39–2.35 (m, 2H, $C_{26}\mathbf{H}_2$), 1.85 (ddd, *J* = 14.5, 10.0, 3.5 Hz, 1H, C_{24}**H**), 1.71 (ddd, *J* = 14.8, 10.5, 3.0 Hz, 1H, C_{24}**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 159.4, 149.2, 149.2, 134.1, 130.6, 130.1, 129.7, 121.1, 118.0, 114.0, 111.8, 111.3, 80.9, 73.9, 72.9, 70.9, 56.1, 55.5, 55.4, 38.5, 38.4; HRMS (ESI): Exact mass calcd for $C_{24}H_{30}O_6$ $[M+NH_4]^+$: 432.2386. Found: 432.2383.

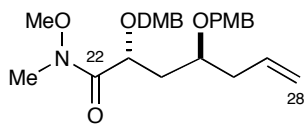


(2*R*,4*S*)–2–(3,4–dimethoxybenzyloxy)–4–(4–methoxybenzyloxy)hept–6–enoic acid (21a). To the precooled to 0 ºC solution of aldehyde **21** (1.00 g, 2.42 mmol) and 2–methyl–2–butene (2.6 mL, 24.2 mmol) in *t*–BuOH/H_2O (7:5, 24 mL) the solution of $NaClO_2$ (480 mg, 5.31 mmol) and NaH_2PO_4 (733 mg, 5.31 mmol) in water (2 mL) was added dropwise. The solution was warmed to room temperature, stirred for 45 min and then partitioned between water (10 mL) and ethyl acetate (15 mL). The aqueous phase was separated and extracted with ethyl acetate (2 × 15 mL). The combine organic phase was then dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford carboxylic acid **21a** (1.04 g, > 99% yield) that was proceeded to the next step without further purification: $[\alpha]_D^{25}$ = +81.0 (*c* = 5.25, $CHCl_3$); IR (film) 3278, 3078, 3011, 2933, 2833, 1750, 1717, 1611, 1517, 1461, 1422, 1250, 1144, 1106, 1028 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.5 Hz, 2H, PMP**H**), 6.88 (d,

J = 1.8 Hz, 1H, DMP**H**), 6.85 (d, *J* = 8.4 Hz, 2H, PMP**H**), 6.83 (m, 1H, DMP**H**), 6.79 (d, *J* = 8.2 Hz, 1H, DMP**H**), 5.80 (ddt, *J* = 14.4, 10.2, 7.8 Hz, 1H, C_{27}**H**), 5.09 (dd, *J* = 15.0, 1.8 Hz, 1H, C_{28}**H**), 5.07 (d, *J* = 7.8 Hz, 1H, C_{28}**H**), 4.58 (d, J_{AB} = 11.1 Hz, 1H, ArCH**H**), 4.53 (d, J_{AB} = 11.1 Hz, 1H, ArCH**H**), 4.21 (d, *J* = 10.8 Hz, 2H, ArC$\mathbf{H}_2$), 4.20 (dd, J = 10.2, 2.6 Hz, 1H, C_{23}**H**), 3.86 (s, 3H, DMPOC$\mathbf{H}_3$), 3.84 (s, 3H, DMPOC$\mathbf{H}_3$), 3.76 (s, 3H, PMPOC$\mathbf{H}_3$), 3.72 (m, 1H, C_{25}**H**), 2.38–2.33 (m, 2H, $C_{26}\mathbf{H}_2$), 1.97 (ddd, *J* = 14.4, 10.2, 3.0 Hz, 1H, C_{24}**H**), 1.88 (ddd, *J* = 12.6, 10.2, 2.4 Hz, 1H, C_{24}**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 159.1, 148.9, 148.9, 133.8, 130.4, 129.7, 129.3, 120.9, 117.7, 113.7, 111.6, 110.9, 74.4, 73.8, 72.6, 70.6, 55.8, 55.8, 55.2, 38.1, 38.0; HRMS (ESI): Exact mass calcd for $C_{24}H_{30}O_7$ $[M+NH_4]^+$: 448.2335. Found: 448.2322.

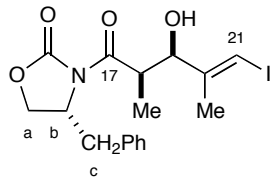


(2*R*,4*S*)–methyl 2–(3,4–dimethoxybenzyloxy)–4–(4–methoxybenzyloxy)hept–6–enoate (21b). To the solution of carboxylic acid **21a** (1.06 g, 2.46 mmol) in PhH/MeOH (1:5, 10 mL) the solution of $TMSCHN_2$ (1 M, 2.46 mL, 2.46 mmol) was added dropwise. After the liberation of nitrogen stopped, acetic acid (*ca.* 0.1 mL) was added to neutralize the excess of $TMSCHN_2$, and the obtained solution was concentrated under reduced pressure to afford a yellow oil. Subjection of this material to flash chromatography (silica, 50% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.5, 50% v/v ethyl acetate/hexanes), the *title compound* **21b** (1.06 g, 97% yield): $[\alpha]_D^{25}$ = +81.5 (*c* = 8.75, $CHCl_3$); IR (film) 3071, 3005, 2940, 2906, 2829, 1748, 1605, 1569, 1511, 1462, 1418, 1357, 1324, 1247, 1203, 1137, 1110, 1030 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.5 Hz, 2H, PMP**H**), 6.87 (d, *J* = 1.46 Hz, 1H, DMP**H**), 6.84 (d, *J* = 8.7 Hz, 2H, PMP**H**), 6.83 (m, 1H, DMP**H**), 6.79 (d, *J* = 7.9 Hz, 1H, DMP**H**), 5.80 (ddt, *J* = 14.4, 10.2, 7.2 Hz, 1H, C_{27}**H**), 5.09–5.06 (m, 2H, $C_{28}\mathbf{H}_2$), 4.55 (d, J_{AB} = 10.8 Hz, 1H, ArCH**H**), 4.51 (d, J_{AB} = 10.8 Hz, 1H, ArCH**H**), 4.20 (d, J_{AB} = 10.8 Hz, 1H, ArCH**H**), 4.18 (d, J_{AB} = 10.8 Hz, 1H, ArCH**H**), 4.21 (dd, *J* = 10.0, 3.2 Hz, 1H, C_{23}**H**), 3.86 (s, 3H, DMPOC$\mathbf{H}_3$), 3.84 (s, 3H, DMPOC$\mathbf{H}_3$), 3.77 (s, 3H, PMPOC$\mathbf{H}_3$), 3.71 (s, 3H, $CO_2C\mathbf{H}_3$), 3.70 (m, 1H, C_{25}**H**), 2.34 (t, *J* = 6.15 Hz, 2H, C_{26}**H**), 1.94–1.82 (m, 2H, C_{24}**H**). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 159.1, 148.9, 148.7, 134.0, 130.6, 130.0, 129.2, 120.8, 117.6, 113.7, 111.6, 110.8, 74.8, 73.8, 72.4, 70.6, 55.8, 55.7, 55.2, 51.7, 38.2, 38.1; HRMS (ESI): Exact mass calcd for $C_{25}H_{32}O_7$ $[M+NH_4]^+$: 462.2492. Found: 462.2511.



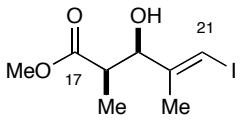
(2*R*,4*S*)–2–(3,4–dimethoxybenzyloxy)–*N*–methoxy–4–(4–methoxybenzyloxy)–*N*–methylhept–6–enamide (22). The solution of methyl ester **21b** (1.05 g, 2.36 mmol) azeotroped with benzene (2 × 10 mL) and (MeO)MeNH•HCl (627 mg, 6.42 mmol) in THF (21.4 mL) was cooled to –13 ºC. The solution of *i*–PrMgCl (1.00 M, 11.6 mL, 11.6 mmol) was then added dropwise over 6 min period. The disappearance of the salt was noticed, and the obtained solution was stirred for 45 min before being quenched with pH 7 buffer (3 mL), warmed to room temperature, and

partitioned between ethyl acetate (20 mL) and $NaHSO_4$ (1 M, 20 mL). The aqueous phase was then washed with ethyl acetate (2 × 10 mL), and the combined organic phase was washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a colorless oil. Subjection of this material to flash chromatography (silica, 50% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.3, 50% v/v ethyl acetate/hexanes), the *title compound* **22** (1.03 g, 92% yield): $[\alpha]_D^{25}$ = +68.0 (*c* = 6.55, $CHCl_3$); IR (film) ν_{max} 3072, 2999, 2936, 2836, 1672, 1612, 1514, 1465, 1427, 1420, 1247, 1148, 1082, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 6.3 Hz, 2H, PMP**H**), 6.90 (d, *J* = 2.0 Hz, 1H, DMP**H**), 6.83 (dd, *J* = 7.8, 2.0 Hz, 1H, DMP**H**), 6.80 (d, *J* = 8.3 Hz, 2H, PMP**H**), 6.76 (d, *J* = 8.4 Hz, 1H, DMP**H**), 5.80 (ddt, *J* = 14.0, 10.0, 7.0 Hz, 1H, C_{27}**H**), 5.08–5.02 (m, 2H, C_{28}**H**$_2$), 4.54 (m, 1H, C_{23}**H**), 4.52 (d, *J* = 10.2 Hz, 1H, ArCH**H**), 4.50 (d, *J* = 10.7 Hz, 1H, ArCH**H**), 4.17 (d, *J* = 11.1 Hz, 1H, ArCH**H**), 4.16 (d, *J* = 10.7 Hz, 1H, ArCH**H**), 3.83 (s, 3H, DMPOC**H**$_3$), 3.80 (s, 3H, DMPOC**H**$_3$), 3.75 (s, 3H, PMPOC**H**$_3$), 3.73 (m, 1H, C_{25}**H**), 3.51 (s, 3H, NC**H**$_3$), 3.15 (3H, NOC**H**$_3$), 2.37–2.26 (m, 2H, C_{26}**H**$_2$), 1.86 (ddd, *J* = 14.0, 10.5, 2.5 Hz, 1H, C_{24}**H**), 1.73 (t, *J* = 11.7 Hz, 1H, C_{24}**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 159.0, 148.6, 134.2, 130.9, 130.3, 129.0, 120.7, 117.4, 113.5, 111.7, 110.7, 74.6, 71.9, 71.5, 70.7, 61.3, 55.8, 55.7, 55.2, 38.5, 37.9, 32.3; HRMS (ESI): Exact mass calcd for $C_{26}H_{35}NO_7$ $[M+H]^+$: 474.2492. Found: 474.2489.

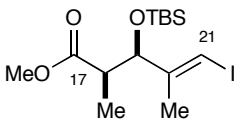


(*R*)-4-benzyl-3-((2*R*,3*R*,*E*)-3-hydroxy-5-iodo-2,4-dimethylpent-4-enoyl)oxazolidin-2-one (10). A solution of propionyl oxazolidinone **14** (10.7 g, 45.9 mmol) in anhydrous CH_2Cl_2 (153 mL) maintained at –10 °C was treated with *n*–Bu_2BOTf (12.2 mL, 48.2 mmol) and NEt_3 (8.5 mL, 64.2 mmol) whilst keeping the temperature of the reaction mixture below 0 °C. After stirring for 1 h the resulting light yellow solution was cooled to –78 °C and treated, dropwise and *via* cannula, with a solution of *E*–3–iodo–2–methylprop–2–enal (**33**) (9.9 g, 50.5 mmol) in methylene chloride (20 mL + 2 × 5 mL rinse). The reaction mixture was stirred at –78 °C for 1 h, then slowly warmed to 0 °C and stirred for an additional 2 h. The resulting mixture was treated with a solution of MeOH/pH 7.0 buffer (100 mL of a 2:1 v/v solution) followed by the careful addition of MeOH/H_2O_2 (30% aqueous solution)(100 mL of a 2:1 v/v solution). The heterogeneous mixture was stirred rapidly at 0 °C for 1 h before being concentrated under reduced pressure. The resulting slurry was concentrated and then dissolved in ether (400 mL) and washed with $NaHCO_3$ (100 mL of a saturated aqueous solution). The separated aqueous solution was extracted with ether (2 × 50 mL) and the combined organic phases were washed with brine (1 × 100 mL), then dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a solid. Subjection of this material to flash chromatography (silica, 10 → 40% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.3, 30% v/v ethyl acetate/hexanes), the *title compound* **38** (12.8 g, 65%) as a clear colorless oil that crystallized upon standing: $[\alpha]_D^{25}$ = –33 (*c* = 0.5, $CHCl_3$); IR (film) 2921, 1777, 1692, 1383, 1209, 1108, 1002, 762, 702 cm^{-1}; ^1H NMR (500 MHz) δ 7.34 (m, 2H, Ar**H**), 7.29 (m, 1H,

Ar**H**), 7.21 (m, 2H, Ar**H**), 6.43 (s, 1H, C_{21}**H**), 4.70 (m, 1H, C_b**H**), 4.51 (m, 1H, C_{19}**H**), 4.22 (m, 2H, C_a**H**$_2$), 4.00 (qd, J = 7.0, 3.0 Hz, 1H, C_{18}**H**), 3.27 (dd, J = 13.5, 3.0 Hz, 1H, C_c**H**), 3.17 (d, J = 3.0 Hz, 1H), 2.82 (dd, J = 13.5, 9 Hz, 1H, C_c**H**), 1.81 (s, 3H, C_{20}C**H**$_3$), 1.19 (d, J = 7.0 Hz, 3H, C_{18}C**H**$_3$); ^{13}C NMR (100 MHz) δ 176.6, 152.9, 145.6, 134.8, 129.4, 129.0, 127.5, 79.3, 75.1, 66.3, 55.1, 40.0, 37.9, 21.5, 10.7; HRMS (ES+): Exact mass calcd for $C_{17}H_{19}INO_3$ $[MH–H_2O]^+$: 412.0410. Found: 412.0405.

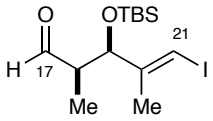


(2*R*,3*R*,*E*)-methyl 3-hydroxy-5-iodo-2,4-dimethylpent-4-enoate (11a).[2] A solution of compound **10** (15.8 g, 36.8 mmol) in anhydrous methylene chloride (245 mL), maintained at –25 °C, was treated with a cold (0 °C) solution of sodium methoxide (101 mL of a 0.4 M solution in MeOH) over 15 min. After being stirred for a further 15 min the reaction mixture was treated with amberlite™ acidic resin. The resin was collected by filtration and subsequently washed with CH_2Cl_2 (100 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford an oil. Subjection of this material to flash chromatography (silica, 5 → 50% v/v EtOAc/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.5, 30% v/v ethyl acetate/hexanes), the title compound **11a** (10.8 g, 97%) as a clear, colorless oil: $[\alpha]_D^{25}$ = +17 (c = 0.6, $CHCl_3$); IR (film) 3477, 2982, 2949, 1722, 1613, 1454, 1435, 1347, 1261, 1202, 1172, 1037, 789 cm^{-1}; ^{1}H NMR (500 MHz) δ 6.39 (d, J = 1.0 Hz, 1H, C_{21}**H**), 4.48 (app. t, J = 3.5 Hz, 1H, C_{19}**H**), 3.72 (s, 3H, COOC**H**$_3$), 2.75 (d, J = 3.5 Hz, 1H, O**H**), 2.73 (m, 1H, C_{18}**H**), 1.79 (s, 3H, C_{20}C**H**$_3$), 1.13 (d, J = 7.5 Hz, 3H, C_{18}C**H**$_3$); ^{13}C NMR (100 MHz) δ 175.8, 145.9, 79.3, 75.7, 52.0, 42.1, 21.1, 10.5.

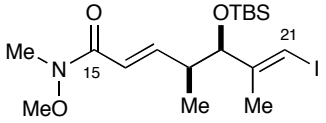


(2*R*,3*R*,*E*)-methyl 3-(*tert*-butyldimethylsilyloxy)-5-iodo-2,4-dimethylpent-4-enoate (11b).[2] TBSOTf (16.7 mL, 72.9 mmol) was added to a stirred solution of compound **11a** (13.8 g, 48.6 mmol) and 2,6–lutidine (14.2 mL, 121.5 mmol) in anhydrous CH_2Cl_2 (243 mL) maintained at –10 °C. After 2 h the reaction mixture was treated with methanol (20 mL) and diluted with ether (400 mL), then washed with HCl (100 mL of a 1 M aqueous solution), $NaHCO_3$ (100 mL of a 5% aqueous solution) and brine (100 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford an oil. Subjection of this material to flash chromatography (silica, 3 → 10% v/v ether/hexanes elution) provided, after concentration of the appropriate fractions (R_f 0.9, 30% v/v ethyl acetate/hexanes), the title compound **11b** (18.8 g, 97%) as a clear, colorless liquid: $[\alpha]_D$ = +13 (c = 1.0, $CHCl_3$); IR (film) 2942, 2857, 1740, 1461, 1434, 1361, 1256, 1196, 1166, 1078, 879, 837, 776 cm^{-1}; ^{1}H NMR (500 MHz) δ 6.19 (s, 1H, C_{21}**H**), 4.35 (d, J = 7.0 Hz, 1H, C_{19}**H**), 3.63 (s, 3H, COOC**H**$_3$), 2.63 (dq, J = 7.0 Hz, 1H, C_{18}**H**), 1.79 (s, 3H, C_{20}C**H**$_3$), 1.14 (d, J = 7.0 Hz, 3H, C_{18}C**H**$_3$), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.03 (s, 3H,

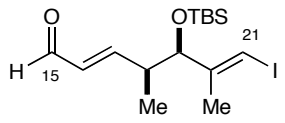
SiC**H**$_3$), –0.03 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz) δ 174.3, 148.5, 78.9, 78.6, 51.6, 44.8, 25.6, 19.8, 18.1, 12.0, –4.9, –5.4; HRMS (ES+): Exact mass calcd for $C_{14}H_{27}IO_3Si$ [M+Na]$^+$: 421.0672. Found: 421.0682.



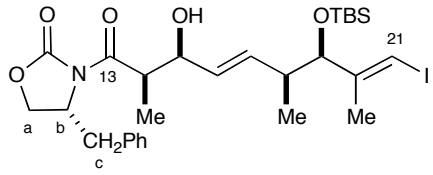
(2*R*,3*R*,*E*)-3-(*tert*-butyldimethylsilyloxy)-5-iodo-2,4-dimethylpent-4-enal (11c).[2] DIBALH (28.7 mL of a 1 M solution in toluene, 28.7 mmol) was added, dropwise, to a stirred solution of methyl ester **11b** (7.63 g, 19.15 mmol) in toluene (192 mL) maintained at –90 °C. The reaction was allowed to warm to –80 °C over 1 h then treated sequentially with MeOH (10 mL) and tartaric acid (100 mL of a 1 M aqueous solution) and allowed to warm to room temperature. The resulting mixture was extracted with ether (3 × 100 mL) and the combined organic phases were washed with brine (1 × 200 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale–yellow oil. Subjection of this material to flash chromatography (silica, 5 → 20% v/v diethyl ether/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.9, 30% v/v ethyl acetate/hexanes), the title compound **11c** (6.84 g, 97%) as a clear, colorless liquid: $[\alpha]_D^{25}$ = +33 (*c* = 1.0, $CHCl_3$); IR (film) 2943, 2873, 2711, 1727, 1467, 1361, 1254, 1144, 1083, 1034, 838, 776, 682 cm^{-1}; ^{1}H NMR (500 MHz) δ 9.68 (d, *J* = 1.5 Hz, 1H, C**H**O), 6.28 (s, 1H, C_{21}**H**), 4.55 (d, *J* = 4.5 Hz, 1H, C_{19}**H**), 2.50 (qdd, *J* = 7.0, 4.5, 1.5 Hz, 1H, C_{18}**H**), 1.79 (s, 3H, C_{20}C**H**$_3$), 1.06 (d, *J* = 7.0 Hz, 3H, C_{18}C**H**$_3$), 0.87 (s, 9H, (C**H**$_3$)$_3$CSi), 0.04 (s, 3H, SiC**H**$_3$), –0.01 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz) δ 203.3, 147.3, 79.1, 76.1, 50.2, 25.6, 20.9, 18.0, 8.07, –4.8, –5.4.



(2*E*,4*S*,5*R*,6*E*)-5-(*tert*-butyldimethylsilyloxy)-7-iodo-*N*-methoxy-*N*,4,6-trimethylhepta-2,6-dienamide (11d). A solution of compound **11c** (4.27 g, 11.6 mmol) in methylene chloride (58 mL) maintained at 0 °C was treated with *N*–methoxy–*N*–methyl–2–(triphenylphosphoranylidene)acetamide (6.32 g, 17.4 mmol) under an atmosphere of argon. The reaction was stirred at this temperature for 1 h then allowed to warm to room temperature and stirred for a further 16 h before the reaction mixture was concentrated under reduced pressure. Subjection of this material to flash chromatography (silica, 5 → 30% v/v ethyl acetate/hexanes elution) provided, after concentration of the appropriate fractions (R_f 0.5, 30% v/v ethyl acetate/hexanes), the *title compound* **11d** (5.0 g, 95%) as a clear, colorless liquid: $[\alpha]_D^{25}$ = +29 (*c* = 1.2, $CHCl_3$); IR (film) 2956, 2873, 1666, 1634, 1466, 1415, 1379, 1258, 1071, 1005, 776, 673 cm^{-1}; ^{1}H NMR (300 MHz) d 6.81 (dd, *J* = 15.5, 8.4 Hz, 1H, C_{17}**H**), 6.36 (dd, *J* = 15.5, 1 Hz, 1H, C_{16}**H**), 6.14 (app. t, *J* = 1.0 Hz, 1H, C_{21}**H**), 4.00 (d, *J* = 6.6 Hz, 1H, C_{19}**H**), 3.68 (s, 3H, NOC**H**$_3$), 3.23 (s, 3H, NC**H**$_3$), 2.53 (m, 1H, C_{18}**H**), 1.75 (d, *J* = 1.0 Hz, 3H, C_{20}C**H**$_3$), 1.06 (d, *J* = 7.2 Hz, 3H, C_{18}C**H**$_3$), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.03 (s, 3H, SiC**H**$_3$), –0.04 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz) d 166.5, 148.6, 118.5, 80.5, 79.1, 61.7, 41.6, 32.3, 25.7, 20.2, 18.1, 15.1, –4.9, –5.2; HRMS (ES+): Exact mass calcd for $C_{17}H_{32}INO_3Si$ [M+H]$^+$: 454.1274. Found: 454.1276.

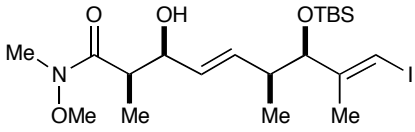


(2*E*,4*S*,5*R*,6*E*)-5-(*tert*-butyldimethylsilyloxy)-7-iodo-4,6-dimethylhepta-2,6-dienal (13). DIBALH (7.74 mL of a 1 M solution in toluene, 7.74 mmol) was added, dropwise, to a stirred solution of compound **11d** (2.34 mg, 5.16 mmol) in THF (26 mL), maintained at –78 °C, over 10 min. The reaction was stirred for a further 45 min and then treated sequentially with MeOH (2 mL) and tartaric acid (20 mL of a 1 M aqueous solution). After warming to room temperature the resulting mixture was extracted with ether (3 × 100 mL) and the combined organic phases were washed with brine (1 × 100 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale–yellow oil. Subjection of this material to flash chromatography (silica, 5 → 25% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.8, 30% v/v ethyl acetate/hexanes), the *title compound* **13** (1.95 g, 96%) as a clear, colorless liquid: $[\alpha]_D^{25}$ = +16 (*c* = 1.0, $CHCl_3$); IR (film) 2929, 2873, 1693, 1471, 1258, 1074, 1026, 976, 862, 837, 776, 674 cm^{-1}; ^1H NMR (400 MHz) δ 9.49 (d, *J* = 8.0 Hz, 1H, C**H**O), 6.70 (dd, *J* = 15.6, 7.6 Hz, 1H, C_{16}**H**), 6.20 (app. t, *J* = 1.2 Hz, 1H, C_{21}**H**), 6.11 (ddd, *J* = 15.6, 7.6, 0.8 Hz, 1H, C_{17}**H**), 4.04 (d, *J* = 6.0 Hz, 1H, C_{19}**H**), 2.63 (m, 1H, C_{18}**H**), 1.74 (d, *J* = 1.2 Hz, 3H, $C_{20}C\mathbf{H}_3$), 1.09 (d, *J* = 6.4 Hz, 3H, $C_{18}C\mathbf{H}_3$), 0.88 (s, 9H, $(C\mathbf{H}_3)_3CSi$), 0.03 (s, 3H, $SiC\mathbf{H}_3$), –0.03 (s, 3H, $SiC\mathbf{H}_3$); ^{13}C NMR (100 MHz) δ 193.7, 159.3, 148.2, 132.3, 80.2, 79.2, 41.5, 25.6, 20.1, 18.1, 14.4, –4.9, –5.3.

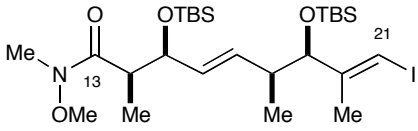


(*R*)-4-benzyl-3-((2*R*,3*S*,4*E*,6*S*,7*R*,8*E*)-7-(*tert*-butyldimethylsilyloxy)-3-hydroxy-9-iodo-2,6,8-trimethylnona-4,8-dienoyl)oxazolidin-2-one (15). A solution of acyl–oxazolidinone **14** (1.05 g, 4.51 mmol) in anhydrous methylene chloride (11 mL) maintained at –78 °C was treated with *n*–Bu_2BOTf (1.14 mL, 4.74 mmol) and NEt_3 (0.84 mL, 6.32 mmol). The reaction mixture was held at this temperature for 15 min before warming to 0 °C for a further 15 min. The reaction mixture was then cooled to –78 °C and treated, dropwise and *via* cannula, with a solution of compound **13** (1.78 g, 4.51 mmol) in methylene chloride (3 mL + with 2 × 1 mL rinse). The reaction mixture was stirred at –78 °C for 30 min, then slowly warmed to –20 °C and stirred for an additional 3 h. The resulting mixture was treated with a solution of MeOH/pH 7 buffer (7 mL of a 2:1 v/v solution) followed by the careful addition of MeOH/H_2O_2 (30% aqueous solution) (7 mL of a 2:1 v/v solution). The heterogeneous mixture was stirred rapidly at 0 °C for 1 h before being diluted with ether (100 mL) and washed with $NaHCO_3$ (50 mL of a saturated aqueous solution). The separated aqueous solution was extracted with ether (3 × 50 mL) and the combined organic phases were washed with brine (1 × 50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a solid. Subjection of this material to flash chromatography (silica, 10→40% v/v ethyl acetate/hexanes

elution) afforded, after concentration of the appropriate fractions (R_f 0.4, 30% v/v ethyl acetate/hexanes), the *title compound* **15** (2.38 g, 84%) as a clear colorless liquid: $[\alpha]_D^{25}$ = –25 (*c* = 1.1, $CHCl_3$); IR (film) 2956, 2856, 1780, 1694, 1385, 1251, 1210, 1071, 1006, 970, 863, 837, 775, 702 cm^{-1}; ^1H NMR (500 MHz) δ 7.34 (m, 2H, Ar**H**), 7.30 (m, 1H, Ar**H**), 7.21 (m, 2H, Ar**H**), 6.10 (s, 1H, C_{21}**H**), 5.49 (m, 2H, C_{16}**H**, C_{17}**H**), 4.70 (m, 1H, C_b**H**), 4.42 (m, 1H, C_{15}**H**), 4.20 (m, 2H, C_a**H**$_2$), 3.78 (m, 2H, C_{14}**H**, C_{19}**H**), 3.27 (dd, *J* = 13.5, 3.5 Hz, 1H, C_c**H**), 2.82 (dd, *J* = 13.5, 9.0 Hz, 1H, C_3**H**), 2.71 (d, *J* = 3.0 Hz, 1H, O**H**), 2.34 (dq, *J* = 7 Hz, 1H, C_{18}**H**), 1.75 (s, 3H, $C_{20}C$**H**$_3$), 1.21 (d, *J* = 7.0 Hz, 3H, $C_{14}C$**H**$_3$), 1.04 (d, *J* = 6.5 Hz, 3H, $C_{18}C$**H**$_3$), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.03 (s, 3H, SiC**H**$_3$), –0.04 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz) δ 176.4, 153.1, 149.4, 135.0, 134.8, 129.4, 129.0, 128.9, 127.4, 81.6, 78.7, 72.5, 66.1, 55.1, 42.7 41.4, 37.7, 25.7, 19.7, 18.2, 16.4, 11.3, –4.9, –5.1; HRMS (ES+): Exact mass calcd for $C_{28}H_{42}INO_5Si$ $[M+Na]^+$: 650.1775. Found: 650.1769.

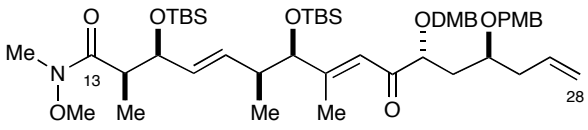


(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*)-7-(*tert*-butyldimethylsilyloxy)-3-hydroxy-9-iodo-*N*-methoxy-*N*,2,6,8-tetramethylnona-4,8-dienamide (15a). A suspension of *N,O*–dimethylhydroxylamine hydrochloride (279 mg, 2.86 mmol) in THF (4.8 mL) maintained at 0 °C was treated, dropwise, with a solution of trimethylaluminum (1.44 mL of a 2 M solution in toluene, 2.88 mmol) with concomitant evolution of gas. The resulting solution was maintained at this temperature for 30 min after which time a solution of compound **15** (852 mg, 1.36 mmol) in THF (2 mL) was added dropwise and *via* cannula. After 2 h at 0 °C the reaction mixture was carefully treated with HCl (2 mL of a 1 M aqueous solution). The separated aqueous layer was extracted with ether (3 × 10 mL) and the combined organic phases were washed with brine (1 × 10 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale–yellow oil. Subjection of this material to flash chromatography (silica, 5 → 40% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.3, 30% v/v ethyl acetate/hexanes), the *title compound* **15** (661 mg, 95%) as a clear, colorless oil: $[\alpha]_D^{25}$ = –6 (*c* = 1.1, $CHCl_3$); IR (film) 3450, 2957, 2874, 1640, 1462, 1388, 1257, 1069, 996, 837, 776, 672 cm^{-1}; ^1H NMR (400 MHz) δ 6.04 (s, 1H, C_{21}**H**), 5.43 (m, 2H, C_{16}**H**, C_{17}**H**), 4.32 (m, 1H, C_{15}**H**), 3.89 (m, 1H, O**H**), 3.82 (d, *J* = 8.0 Hz, 1H, C_{19}**H**), 3.70 (s, 3H, NOC**H**$_3$), 3.19 (s, 3H, NC**H**$_3$), 2.85 (m, 1H, C_{14}**H**), 2.30 (m, 1H, C_{18}**H**), 1.72 (d, *J* = 0.8 Hz, 3H, $C_{20}C$**H**$_3$), 1.15 (d, *J* = 6.8 Hz, 3H, $C_{14}C$**H**$_3$), 1.03 (d, *J* = 6.8 Hz, 3H, $C_{18}C$**H**$_3$), 0.86 (s, 9H, (C**H**$_3$)$_3$CSi), 0.01 (s, 3H, SiC**H**$_3$), –0.06 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz) δ 177.9, 149.7, 134.0, 129.8, 81.8, 78.1, 72.4, 61.7, 41.7, 39.9, 31.9, 25.7, 19.6, 18.2, 16.7, 10.5, –4.9, –5.2; HRMS (ES+): Exact mass calcd for $C_{20}H_{38}INO_4Si$ $[M+H]^+$: 512.1693. Found: 512.1696.



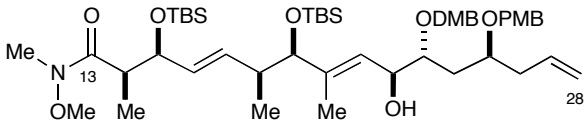
(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*)-3,7-bis(*tert*-butyldimethylsilyloxy)-9-iodo-*N*-methoxy-*N*,2,6,8-tetramethylnona-4,8-dienamide (16). TBSOTf (1.45

mL, 6.33 mmol) was added to a stirred solution of compound **15a** (2.16 g, 4.22 mmol) and 2,6–lutidine (1.23 mL, 10.55 mmol) in anhydrous methylene chloride (21 mL) maintained at –10 °C. After 30 min the reaction mixture was treated with methanol (5 mL) and diluted with ether (100 mL), then washed with HCl (50 mL of a 1 M aqueous solution), $NaHCO_3$ (50 mL of a saturated aqueous solution) and brine (50 mL) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford an oil. Subjection of this material to flash chromatography (silica, 7% v/v ether/hexanes elution) provided, after concentration of the appropriate fractions (R_f 0.8, 30% v/v ethyl acetate/hexanes), the title compound **16** (2.61 g, 99%) as a white solid: $[\alpha]_D^{25} = -5$ (*c* = 1.4, $CHCl_3$); IR (film) 2957, 2929, 2856, 1666, 1471, 1255, 1066, 1003, 836, 775 cm^{-1}; ^1H NMR (400 MHz) δ 6.04 (s, 1H, C_{21}**H**), 5.50 (dd, *J* = 16.0, 7.2 Hz, 1H, C_{16}**H**), 5.34 (dd, *J* = 16.0, 8.0 Hz, 1H, C_{17}**H**), 4.16 (app. t, *J* = 7.2 Hz, 1H, C_{15}**H**), 3.78 (d, *J* = 7.2 Hz, 1H, C_{19}**H**), 3.66 (s, 3H, NOC**H**$_3$), 3.15 (s, 3H, OC**H**$_3$), 2.93 (m, 1H, C_{14}**H**), 2.29 (h, *J* = 7.2 Hz, 1H, C_{18}**H**), 1.71 (d, *J* = 1.2 Hz, 3H, C_{20}C**H**$_3$), 1.11 (d, *J* = 7.2 Hz, 3H, CHC**H**$_3$), 1.01 (d, *J* = 6.8 Hz, 3H, CHC**H**$_3$), 0.87 (s, 9H, (C**H**$_3$)$_3$CSi), 0.86 (s, 9H, (C**H**$_3$)$_3$CSi), 0.02 (s, 3H, SiC**H**$_3$), 0.01 (s, 3H, SiC**H**$_3$), –0.02 (s, 3H, SiC**H**$_3$), –0.06 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz) δ 149.6, 132.4, 131.8, 81.9, 79.0, 75.1, 61.4, 42.7, 41.3, 32.3, 25.9, 25.7, 19.6, 18.2, 18.1, 16.9, 14.1, –3.9, –4.7, –4.9, –5.2; HRMS (ES+): Exact mass calcd for $C_{26}H_{52}INO_4Si_2$ $[M+H]^+$: 626.2558. Found: 626.2558.



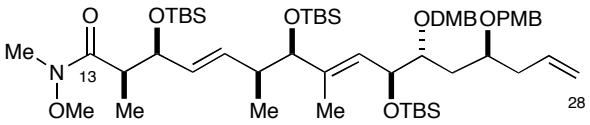
(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*,11*R*,13*S*)–3,7–bis(*tert*–butyldimethylsilyloxy)–11–(3,4–dimethoxybenzyloxy)–*N*–methoxy–13–(4–methoxybenzyloxy)–*N*,2,6,8–tetramethyl–10–oxohexadeca–4,8,15–trienamide (23). The vinyl iodide **16** (1.25 g, 1.37 mmol) was azeotroped with benzene (2 x 10 mL), dissolved in diethyl ether (7 mL) and cooled to –78 ° C. The solution of *n*–BuLi (2.80 M, 0.550 mL, 1.55 mmol) was then added over 3 min period, and the obtained solution was stirred for additional 5 min. At this point, the solution of $MgBr_2$ (0.496 M in 3:1 ether/toluene, 3.76 mL, 1.86 mmol) was added over 5 min period. The obtained yellowish solution was then stirred for 5 min, during which the formation of a white precipitate was noticed, and THF (3 mL) was then introduced. The reaction medium was stirred for additional 20 min, and the precooled to –78 ºC solution of Weinreb amide **22** (660 mg, 1.39 mmol) in diethyl ether/THF (7mL/4mL) was canulated over. After 5 min, the reaction mixture was warmed to –20 ºC (white solid disappeared), stirred for 50 min then warmed to 0 ºC, stirred for additional 5 min and quenched with $NH_4Cl_{(sat.)}$ (1 mL). The solution was partitioned between water (20 mL) and ethyl acetate (10 mL), and the aqueous phase was then extracted with ethyl acetate (2 × 10 mL). The combined organic phase was washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford colorless foam. Subjection of this material to flash chromatography (silica, 33% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.25, 33% v/v ethyl acetate/hexanes), the

title compound **23** (1.14 g, 91% yield): $[\alpha]_D^{25}$ = +27 (*c* = 4.95, $CHCl_3$); IR (film) 2944, 2857, 1659, 1612, 1515, 1464, 1420, 1388, 1363, 1250, 1138, 1074, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.4 Hz, 2H, PMP**H**), 6.86–6.81 (m, 4H, Ar**H**), 6.77 (d, *J* = 8.4 Hz, 1H, DMP**H**), 6.44 (s, 1H, C_{21}**H**), 5.78 (ddt, *J* = 14.4, 10.0, 6.8 Hz, 1H, C_{27}**H**), 5.46 (m, 2H, C_{16}**H**, C_{17}**H**), 5. 04 (m, 2H, C_{28}**H**$_2$), 4.51 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.48 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.20 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.15 (dd, *J* = 7.2, 6.0 Hz, 1H, C_{15}**H**), 4.10 (d, J_{AB} = 11.5 Hz, 1H, ArCH**H**), 4.07 (dd, *J* = 10.4, 3.2 Hz, 1H, C_{19}**H**), 3.84 (s, 3H, DMPOC**H**$_3$), 3.83 (s, 3H, DMPOC**H**$_3$), 3.76 (s, 3H, PMPOC**H**$_3$), 3.75 (m, 1H, C_{23}**H**), 3.72 (m, 1H, C_{25}**H**), 3.62 (s, 3H, NOC**H**$_3$), 3.12 (s, 3H, NC**H**$_3$), 2.98 (m, 1H, C_{14}**H**), 2.31 (t, *J* = 6.4 Hz, 2H, C_{26}**H**$_2$), 2.31 (m, 1H, C_{18}**H),** 2.09 (s, 3H, C_{20}C**H**$_3$), 1.70 (m, 2H, C_{24}**H**$_2$), 1.10 (d, *J* = 7.0 Hz, 3H, C_{14}C**H**$_3$), 0.95 (d, *J* = 6.6 Hz, 3H, C_{18}C**H**$_3$), 0.87 (s, 9H, (C**H**$_3$)$_3$CSi), 0.86 (s, 9H, (C**H**$_3$)$_3$CSi), 0.027 (s, 3H, SiC**H**$_3$), 0.025 (s, 3H, SiC**H**$_3$), –0.023 (s, 3H, SiC**H**$_3$), –0.076 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 161.4, 159.1, 148.9, 148.6, 134.2, 133.5, 131.9, 130.8, 130.5, 129.2, 120.6, 119.1, 117.4, 113.7, 111.4, 110.8, 81.9, 81.5, 77.3, 75.4, 74.1, 72.0, 70.8, 61.4, 55.8, 55.8, 55.2, 42.4, 41.5, 38.5, 37.7, 32.2, 25.9, 25.8, 18.1, 16.4, 15.6, 14.2, –3.8, –4.4, –4.7, –5.0; HRMS (ESI): Exact mass calcd for $C_{50}H_{81}NO_{10}Si_2$ $[M+H]^+$: 912.5477. Found: 912.5455.



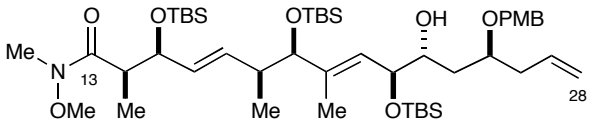
(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*,10*S*,11*R*,13*S*)–3,7–bis(*tert*–butyldimethylsilyloxy)–11–(3,4–dimethoxybenzyloxy)–10–hydroxy–*N*–methoxy–13–(4–methoxybenzyloxy)–*N*,2,6,8–tetramethylhexadeca–4,8,15–trienamide (24). Ketone **23** (1.15 g, 1.26 mmol) was azeotroped with benzene (2 x 10 mL), dissolved in methylene chloride (44 mL) and cooled to –78 ºC. The solution of $Zn(BH_4)_2$ (0.10 M, 24 mL, 2.4 mmol) was then introduce over 10 min period. The reaction mixture was warmed to –35 ºC, stirred for 50 min, quenched with acetone (1 mL) then $NH_4Cl_{(sat.)}$ was added (20 mL) and the solution was warmed to room rt. The mixture was then stirred for 12 h and then partitioned between water (30 mL) and ethyl acetate (40 mL). The organic phase was washed with $NaHCO_{3(sat.)}$ (10 mL), brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford colorless oil. The oil was redissolved in ethyl acetate (15 mL) and acetic acid (0.2 mL) and concentrated under reduced pressure. Subjection of this material to flash chromatography (silica, 33% → 50% v/v ethyl acetate/hexanes elution) afforded, after the concentration of the appropriate fractions (R_f 0.2, 33% v/v ethyl acetate/hexanes), the *title compound* **24** (1.05 g, 91% yield): $[\alpha]_D^{25}$ = +22.3 (*c* = 3.16, $CHCl_3$); IR (film) 3450, 2956, 2914, 2857, 1665, 1660, 1642, 1639, 1611, 1575, 1465, 1420, 1364, 1250, 1059, 1004 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.8 Hz, 2H, PMP**H**), 6.85–6.78 (m, 5H, Ar**H**), 5.81 (ddt, *J* = 14.2, 10.2, 7.3 Hz, 1H, C_{27}**H**), 5.48–5.40 (m, 3H, C_{16}**H,** C_{17}**H,** C_{21}**H**), 5.08 (dd, *J* = 15.2, 1.5 Hz, 1H, C_{28}**H**), 5.04 (dd, J = 10.2, 1.6 Hz, 1H, C_{28}**H**), 4.57 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.54 (m, 1H, C_{22}**H**), 4.52 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.34 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.22 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.13 (m,

1H, C_{15}**H**), 3.84 (s, 3H, DMPOC**H**$_3$), 3.84 (s, 3H, DMPOC**H**$_3$), 3.84 (m, 1H, C_{23}**H**), 3.76 (s, 3H, PMPOC**H**$_3$), 3.70 (d, J = 6.3 Hz, 1H, C_{19}**H**), 3.67 (m, 1H, C_{25}**H**), 3.63 (s, 3H, NOC**H**$_3$), 3.12 (s, 3H, NC**H**$_3$), 3.01 (m, 1H, C_{14}**H**), 2.37–2.29 (m, 2H, C_{26}**H**$_2$), 2.26 (m, 1H, C_{18}**H**), 1.69 (ddd, J = 14.6, 10.3, 2.4 Hz, 1H, C_{24}**H**), 1.61 (s, 3H, C_{20}C**H**$_3$), 1.56 (ddd, J = 14.6, 10.2, 2.4 Hz, 1H, C_{24}**H**), 1.11 (d, J = 6.8 Hz, 3H, CHC**H**$_3$), 0.96 (d, J = 6.4 Hz, 3H, CHC**H**$_3$), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.86 (s, 9H, (C**H**$_3$)$_3$CSi), 0.030 (s, 3H, SiC**H**$_3$), 0.015 (s, 3H, SiC**H**$_3$), –0.003 (s, 3H, SiC**H**$_3$), –0.040 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 159.0, 148.9, 148.5, 141.0, 134.6, 134.5, 131.5, 131.1, 131.0, 129.4, 124.8, 120.2, 117.2, 113.7, 113.7, 111.1, 110.9, 81.2, 78.9, 76.0, 74.7, 72.3, 70.2, 69.7, 61.4, 55.9, 55.8, 55.2, 42.3, 42.0, 38.4, 35.2, 32.1, 25.9, 18.2, 18.2, 16.1, 14.4, 13.8, –3.8, –4.3, –4.6, –5.0; HRMS (ESI): Exact mass calcd for $C_{50}H_{81}NO_{10}Si_2$ $[M+H]^+$: 914.5628. Found: 914.5623.

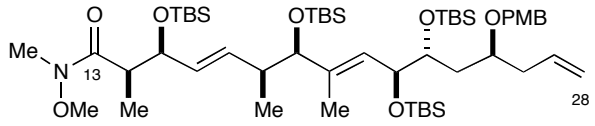


(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*,10*S*,11*R*,13*S*)–3,7,10–tris(*tert*–butyldimethylsilyloxy)–11–(3,4–dimethoxybenzyloxy)–*N*–methoxy–13–(4–methoxybenzyloxy)–*N*,2,6,8–tetramethylhexadeca–4,8,15–trienamide (25). The solution of **24** (0.93 g, 1.02 mmol) in THF (11.0 mL) was cooled to 0 ºC. Then, 2,6–lutidine (0.423 mL, 3.82 mmol) followed by TBSOTf (0.372 mL, 1.63 mmol) was introduced. The mixture was stirred for 15 min, diluted with water (5 mL) and ethyl acetate (10 mL). The organic phase was washed separated and then washed with 1 M HCl (5 mL), $NaHCO_{3(sat.)}$ (5 mL), and brine (5 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford colorless oil. Subjection of this material to flash chromatography (silica, 17% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.6, 30% v/v ethyl acetate/hexanes), the *title compound* **25** (969 mg, 95% yield): $[\alpha]_D^{25}$ = +44.0 (c = 2.05, $CHCl_3$); IR (film) 2956, 2913, 2873, 1664, 1612, 1590, 1515, 1464, 1420, 1388, 1361, 1249, 1057 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, J = 8.3 Hz, 2H, PMP**H**), 6.88 (s, 1H, DMP**H**), 6.87–6.75 (m, 4H, Ar**H**), 5.81 (ddt, J = 14.2, 10.2, 7.3 Hz, 1H, C_{27}**H**), 5.59 (dd, J = 15.6, 7.3 Hz, 1H, C_{16}**H**), 5.46 (dd, J = 15.1, 7.8 Hz, 1H, C_{17}**H**), 5.45 (d, J = 8.8 Hz, 1H, C_{21}**H**), 5. 08–5.03 (m, 2H, C_{28}**H**$_2$), 4.75 (d, J_{AB} = 11.7 Hz, 1H, ArCH**H**), 4.50 (dd, J = 8.8, 2.0 Hz, 1H, C_{23}**H**), 4.49 (d, J_{AB} = 11.2 Hz, 1H, ArC**H**$_2$), 4.27 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 4.18 (t, J = 7.8Hz, 1H, C_{15}**H**), 4.16 (d, J_{AB} = 11.2 Hz, 1H, ArCH**H**), 3.84 (s, 3H, DMPOC**H**$_3$), 3.84 (s, 3H, DMPOC**H**$_3$), 3.81 (d, J = 4.5 Hz, 1H, C_{19}**H**), 3.76 (s, 3H, PMPOC**H**$_3$), 3.66 (d, J = 10.5 Hz, 1H, C_{23}**H**), 3.64 (m, C_{25}**H**) 3.63 (s, 3H, NOC**H**$_3$), 3.12 (s, 3H, NOC**H**$_3$), 3.02 (m, 1H, C_{14}**H**), 2.37–2.29 (m, 2H, C_{26}**H**$_2$), 2.26 (h, J = 6.0 Hz, 1H, C_{18}**H**), 1.59 (m, 1H, C_{24}**H**), 1.57 (s, 3H, C_{20}C**H**$_3$), 1.47 (dd, J = 13.2, 10.3 Hz, 1H, C_{24}**H**), 1.13 (d, J = 7.0 Hz, 3H, CHC**H**$_3$), 0.90 (d, J = 8.0 Hz, 3H, CHC**H**$_3$), 0.89 (s, 9H, (C**H**$_3$)$_3$CSi), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.87 (s, 9H, (C**H**$_3$)$_3$CSi), 0.063 (s, 3H, SiC**H**$_3$), 0.021 (s, 3H, SiC**H**$_3$), 0.021 (s, 3H, SiC**H**$_3$), 0.017 (s, 3H, SiC**H**$_3$), –0.009 (s, 3H, SiC**H**$_3$), –0.041 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 159.0, 148.8, 148.2, 137.2, 134.9, 134.8, 132.2, 131.2,

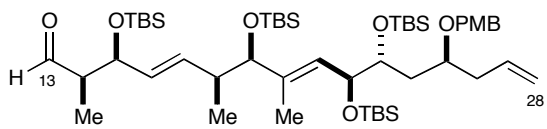
131.0, 129.2, 126.6, 120.0, 117.0, 113.6, 111.2, 110.8, 80.5, 80.2, 77.2, 75.8, 74.8, 72.7, 72.2, 70.4, 61.3, 55.9, 55.7, 55.2, 42.5, 41.6, 38.7, 36.4, 25.9, 25.9, 25.9, 18.2, 18.2, 18.2, 14.8, 14.0, 13.8, –3.8, –4.3, –4.5, –4.5, –4.7, –4.8; HRMS (ESI): Exact mass calcd for $C_{56}H_{97}NO_{10}Si_3$ $[M+NH_4]^+$: 1045.6764. Found: 1045.6754.



(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*,10*S*,11*R*,13*S*)–3,7,10–tris(*tert*–butyldimethylsilyloxy)–11–hydroxy–*N*–methoxy–13–(4–methoxybenzyloxy)–*N*,2,6,8–tetramethylhexadeca–4,8,15–trienamide (25a). The solution of **25** (995 mg, 0.970 mmol) in methylene chloride/pH 7 buffer (18:1, 9.8 mL) was cooled to 0 ºC, and DDQ (234 mg, 1.05 mmol) was added. The obtained green solution was stirred for 20 min (color change to grey/pink), diluted with $NaHCO_{3(sat.)}$ (3 mL) and Na_2SO_3 (1M, 3 mL), and stirred for additional 10 min. The aqueous phase was then washed with methylene chloride (2 × 10 mL), and the combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford colorless foam. Subjection of this material to flash chromatography (silica, 40% → 50% v/v diethyl ether/pentane elution) afforded, after concentration of the appropriate fractions (R_f 0.75, 30% v/v ethyl acetate/hexanes), the *title compound* **25a** (624 mg, 73% yield) as well as the corresponding *p*-methoxyphenyl acetal side-product (*ca.* 60 mg, 7%). **25a**: $[\alpha]_D^{25}$ = +13.0 (*c* = 2.95, $CHCl_3$); IR (film) 3484, 2943, 2895, 2857, 1668, 1660, 1638, 1618, 1514, 1460, 1388, 1364, 1250, 1068, 1004 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.8 Hz, 2H, PMP**H**), 6.76 (d, *J* = 8.8 Hz, 2H, PMP**H**), 5.74 (ddt, *J* = 14.5, 10.0, 7.0 Hz, 1H, C_{27}**H**), 5.50 (dd, *J* = 15.5, 6.7 Hz, 1H, C_{17}**H**), 5.34 (dd, *J* = 15.8, 7.5 Hz, 1H, C_{16}**H**), 5.22 (d, *J* = 8.5 Hz, 1H, C_{21}**H**), 4.99 (*appt* d, *J* = 14.0 Hz, 1H, C_{28}**H**), 4.95 (*appt* d, *J* = 11.3 Hz, 1H, C_{28}**H**), 4.47 (d, J_{AB} = 10.7 Hz, 1H, PMPCH**H**), 4.38 (d, J_{AB} = 11.1 Hz, 1H, PMPCH**H**), 4.16 (dd, *J* = 8.8, 4.4 Hz, 1H, C_{22}**H**), 4.08 (t, *J* = 7.8 Hz, 1H, C_{15}**H**), 3.71 (m, 1H), 3.69 (s, 3H, PMPOC**H**$_3$), 3.69 (m, 1H), 3.68 (d, *J* = 5.5 Hz, 1H, C_{19}**H**), 3.54 (s, 3H, NOC**H**$_3$), 3.02 (s, 3H, NC**H**$_3$), 2.98 (m, 1H, C_{14}**H**), 2.56 (s, OH), 2.31–2.20 (m, 2H, C_{26}**H**$_2$), 2.16 (dq, *J* = 6.6, 6.5 Hz, 1H, C_{18}**H**), 1.53 (ddd, *J* = 15.0, 10.0, 2.0 Hz, 1H, C_{24}**H**), 1.47 (s, 3H, C_{20}C**H**$_3$), 1.40 (ddd, *J* = 13.5, 10.5, 2.5 Hz, 1H, C_{24}**H**), 1.04 (d, *J* = 7.0 Hz, 3H, C_{14}C**H**$_3$), 0.84 (d, *J* = 7.0 Hz, 3H, C_{18}C**H**$_3$), 0.80 (s, 9H, (C**H**$_3$)$_3$CSi), 0.78 (s, 9H, (C**H**$_3$)$_3$CSi), 0.78 (s, 9H, (C**H**$_3$)$_3$CSi), –0.042 (s, 3H, SiC**H**$_3$), –0.057 (s, 3H, SiC**H**$_3$), –0.062 (s, 3H, SiC**H**$_3$), –0.069 (s, 3H, SiC**H**$_3$), –0.075 (s, 3H, SiC**H**$_3$), –0.12 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 159.1, 138.6, 134.9, 134.6, 131.1, 131.1, 129.3, 126.3, 117.0, 113.7, 81.1, 77.2, 75.8, 75.6, 72.8, 71.9, 71.2, 61.4, 55.2, 42.6, 41.3, 39.0, 36.9, 25.9, 25.8, 25.8, 18.2, 18.2, 18.1, 15.3, 14.1, 13.4, –3.8, –4.2, –4.3, –4.7, –4.7, –4.8; HRMS (ESI): Exact mass calcd for $C_{47}H_{87}NO_8Si_3$ $[M+NH_4]^+$: 895.6083. Found: 895.6056.



(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*,10*S*,11*R*,13*S*)–3,7,10,11–tetrakis(*tert*–butyldimethylsilyloxy)–*N*–methoxy–13–(4–methoxybenzyloxy)–*N*,2,6,8–tetramethylhexadeca–4,8,15–trienamide (25b). The solution of **25a** (566 mg, 0.645 mmol) in methylene chloride (6.5 mL) was cooled to 0 ºC. Then, 2,6–lutidine (0.143 mL, 1.29 mmol) followed by TBSOTf (0.191 mL, 0.838 mmol) was introduced. The mixture was stirred for 15 min, diluted with water (5 mL) and ethyl acetate (10 mL). The organic phase was washed separated and then washed with 1 M HCl (5 mL), $NaHCO_{3(sat.)}$ (5 mL), and brine (5 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford colorless oil. Subjection of this material to flash chromatography (silica, 10% v/v ethyl acetate/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.8, 30% v/v ethyl acetate/hexanes), the *title compound* **25b** (622 mg, 97% yield): $[\alpha]_D^{25}$ = +22.0 (*c* = 4.50, $CHCl_3$); IR (film) 2944, 2930, 2857, 1666, 1624, 1514, 1467, 1385, 1368, 1250, 1072, 1006 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.8 Hz, 2H, PMP**H**), 6.85 (d, *J* = 8.8 Hz, 2H, PMP**H**), 5.79 (ddt, *J* = 17.1, 10.2, 7.1 Hz, 1H, C_{27}**H**), 5.62 (dd, *J* = 15.4, 7.6 Hz, 1H, C_{17}**H**), 5.45 (dd, J = 15.6, 7.8 Hz, 1H, C_{16}**H**), 5.36 (d, *J* = 8.8 Hz, 1H, C_{21}**H**), 5.09 (*appt* dd, *J* = 16.0, 2.0 Hz, 1H, C_{28}**H**), 5.06 (*appt* dd, *J* = 9.0, 1.7 Hz, 1H, C_{28}**H**), 4.59 (d, J_{AB} = 10.5 Hz, 1H, PMPC**H**H), 4.37 (d, J_{AB} = 10.7 Hz, 1H, PMPC**H**H), 4.29 (dd, *J* = 9.2, 1.7 Hz, 1H, C_{22}**H**), 4.22 (t, *J* = 7.7 Hz, 1H, C_{15}**H**), 3.97 (d, *J* = 9.0 Hz, 1H, C_{23}**H**), 3.87 (d, *J* = 3.0 Hz, 1H, C_{19}**H**), 3.79 (s, 3H, PMPOC**H**$_3$), 3.78–3.66 (m, 1H, C_{25}**H**), 3.64 (s, 3H, NOC**H**$_3$), 3.13 (s, 3H, NC**H**$_3$), 2.99 (m, 1H, C_{14}**H**), 2.40 (dtdt, *J* = 9.8, 6.8, 3.9, 1.3 Hz, 1H, C_{26}**H**), 2.30 (qt, *J* = 7.3, 1.5 Hz, 1H, C_{26}**H**), 2.26 (dqd, *J* = 7.1, 6.5, 2.9 Hz, 1H, C_{18}**H**), 1.55 (s, 3H, C_{20}C**H**$_3$), 1.58–1.55 (m, 1H, C_{24}**H**), 1.46 (ddd, *J* = 14.2, 9.8, 2.4 Hz, 1H, C_{24}**H**), 1.14 (d, *J* = 7.5 Hz, 3H, C_{14}C**H**$_3$), 0.90 (s, 9H, (C**H**$_3$)$_3$CSi)), 0.89 (s, 9H, (C**H**$_3$)$_3$CSi), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.88 (s, 9H, (C**H**$_3$)$_3$CSi), 0.87 (m, 3H, C_{14}C**H**$_3$), 0.14 (s, 3H, SiC**H**$_3$), 0.055 (s, 3H, SiC**H**$_3$), 0.042 (s, 3H, SiC**H**$_3$), 0.032 (s, 3H, SiC**H**$_3$), 0.024 (s, 3H, SiC**H**$_3$), 0.008 (s, 3H, SiC**H**$_3$), 0.001 (s, 3H, SiC**H**$_3$), –0.038 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 159.0, 136.7, 135.0, 134.6, 131.2, 131.0, 129.0, 126.3, 117.2, 113.7, 80.3, 77.2, 75.7, 75.4, 74.7, 74.2, 70.3, 61.3, 55.3, 42.6, 42.4, 38.9, 38.5, 32.2, 26.3, 26.0, 26.0, 25.9, 18.4, 18.3, 18.2, 18.2, 14.8, 14.4, 13.8, –3.2, –3.8, –4.2, –4.6, –4.7, –4.9, –5.1; HRMS (ESI): Exact mass calcd for $C_{53}H_{101}NO_8Si_4$ $[M+NH_4]^+$: 1009.6948. Found: 1009.6962.



(2*R*,3*S*,4*E*,6*S*,7*R*,8*E*,10*S*,11*R*,13*S*)–3,7,10,11–tetrakis(*tert*–butyldimethylsilyloxy)–13–(4–methoxybenzyloxy)–2,6,8–trimethylhexadeca–4,8,15–trienal (26). The solution of **25b** (410 mg, 0.413 mmol) in toluene (8.3 mL) was cooled to –78 ºC. The solution of DIBALH (1 M, 1.03 mL, 1.03 mmol) was then introduced over 5 min period. The mixture was stirred for 2 h, quenched with precooled to –78 ºC acetone (1 mL) and warmed to rt. Then, the saturated Rochelle's salt solution (10 mL) was added, and the solution was stirred for 45 min, and then extracted with ethyl acetate (2 × 25 mL). The organic phase

was washed with brine (5 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford colorless oil. Subjection of this material to flash chromatography (silica, 14% v/v diethyl ether/hexanes elution) afforded, after concentration of the appropriate fractions (R_f 0.5, 20% v/v diethyl ether/hexanes), the *title compound* **26** (346 mg, 90% yield): $[\alpha]_D^{25}$ = +6.2 (*c* = 7.15, $CHCl_3$); IR (film) 2956, 2930, 2913, 2857, 2708, 1728, 1641, 1614, 1515, 1472, 1389, 1368, 1250, 1082, 1046 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.62 (s, 1H, C**H**O), 7.13 (d, *J* = 8.8 Hz, 2H, PMP**H**), 6.74 (d, *J* = 8.8 Hz, 2H, PMP**H**), 5.68 (ddt, *J* = 14.2, 10.3, 6.8 Hz, 1H, C_{27}**H**), 5.52 (dd, *J* = 15.3, 7.1 Hz, 1H, C_{17}**H**), 5.29 (dd, *J* = 15.6, 8.2 Hz, 1H, C_{16}**H**), 5.24 (d, *J* = 8.8 Hz, 1H, C_{21}**H**), 4.97 (m, 2H, C_{28}**H**$_2$), 4.47 (d, *J* = 10.7 Hz, 1H, PMPCH**H**), 4.36 (dd, *J* = 7.3, 3.9 Hz, 1H, C_{15}**H**), 4.34 (d, *J*= 10.7 Hz, 1H, PMPCH**H**), 4.24 (d, *J* = 7.3 Hz, 1H, C_{22}**H**), 3.87 (d, *J* = 8.8 Hz, 1H, C_{23}**H**), 3.75 (d, *J* = 4.9 Hz, 1H, C_{19}**H**), 3.69 (s, 3H, PMPOC**H**$_3$), 3.58 (m, 1H, C_{25}**H**), 2.30 (m, 1H, C_{26}**H**), 2.22 (m, 2H, C_{18}**H**, C_{26}**H**), 1.46 (s, 3H, C_{20}C**H**$_3$), 1.49 (m, 1H, C_{24}**H**), 1.37 (ddd, *J* = 11.7, 9.8, 2.0 Hz, 1H, C_{24}**H**), 0.93 (d, *J* = 6.8 Hz, 3H, C_{14}C**H**$_3$), 0.82 (d, *J* = 7.8 Hz, 3H, C_{18}C**H**$_3$) 0.80 (s, 9H, (C**H**$_3$)$_3$CSi), 0.80 (s, 9H, (C**H**$_3$)$_3$CSi), 0.79 (s, 9H, (C**H**$_3$)$_3$CSi), 0.76 (s, 9H, (C**H**$_3$)$_3$CSi), 0.45 (s, 3H, SiC**H**$_3$), –0.041 (s, 3H, SiC**H**$_3$), –0.053 (s, 3H, SiC**H**$_3$), –0.059 (s, 3H, SiC**H**$_3$), –0.062 (s, 3H, SiC**H**$_3$), –0.088 (s, 3H, SiC**H**$_3$), –0.092 (s, 3H, SiC**H**$_3$), –0.122 (s, 3H, SiC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 159.0, 136.2, 135.6, 134.5, 131.1, 129.8, 129.0, 127.2, 117.2, 113.7, 80.8, 75.4, 74.7, 74.2, 74.0, 70.3, 55.3, 53.1, 42.2, 38.9, 38.5, 26.2, 26.0, 25.9, 25.8, 18.4, 18.3, 18.2, 18.1, 15.3, 14.0, 8.3, –3.2, –3.8, –4.3, –4.4, –4.6, –4.7, –5.0, –5.1; LRMS (ESI): Exact mass calcd for $C_{53}H_{101}NO_8Si_4$ $[M+NH_4]^+$: 950.7. Found: 950.0.

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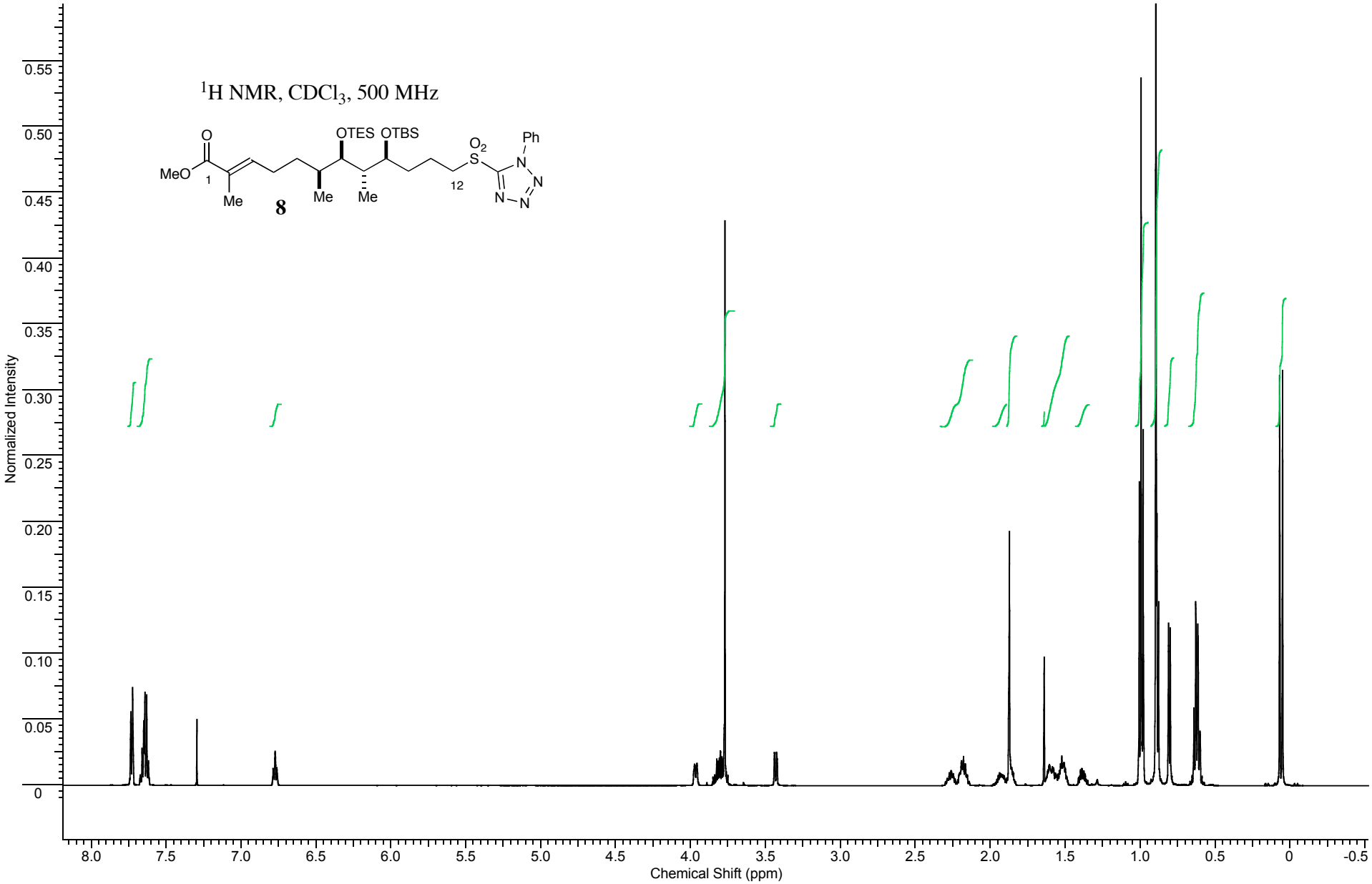
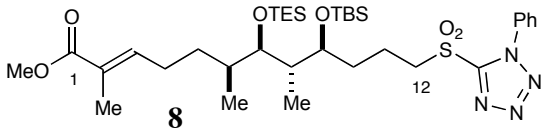
[1] D. D. Perrin, and W. L. Armarego, Purification of Laboratory Chemicals; 3rd ed., Pergamon Press, Oxford, 1988.

[2] R. Baker, J. L. Castro, *J. Chem. Soc. Perkin Trans. 1* **1990**, 47–65.

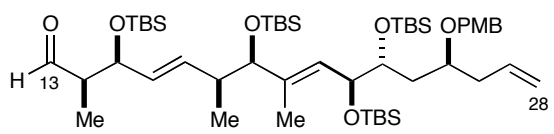

^{1}H NMR, $CDCl_3$, 500 MHz
MeO
O
1
Me
Me
OTES
OTBS
Me
12
O_2
S
Ph
N
N
N
N
8
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)

^{13}C NMR, $CDCl_3$, 125 MHz

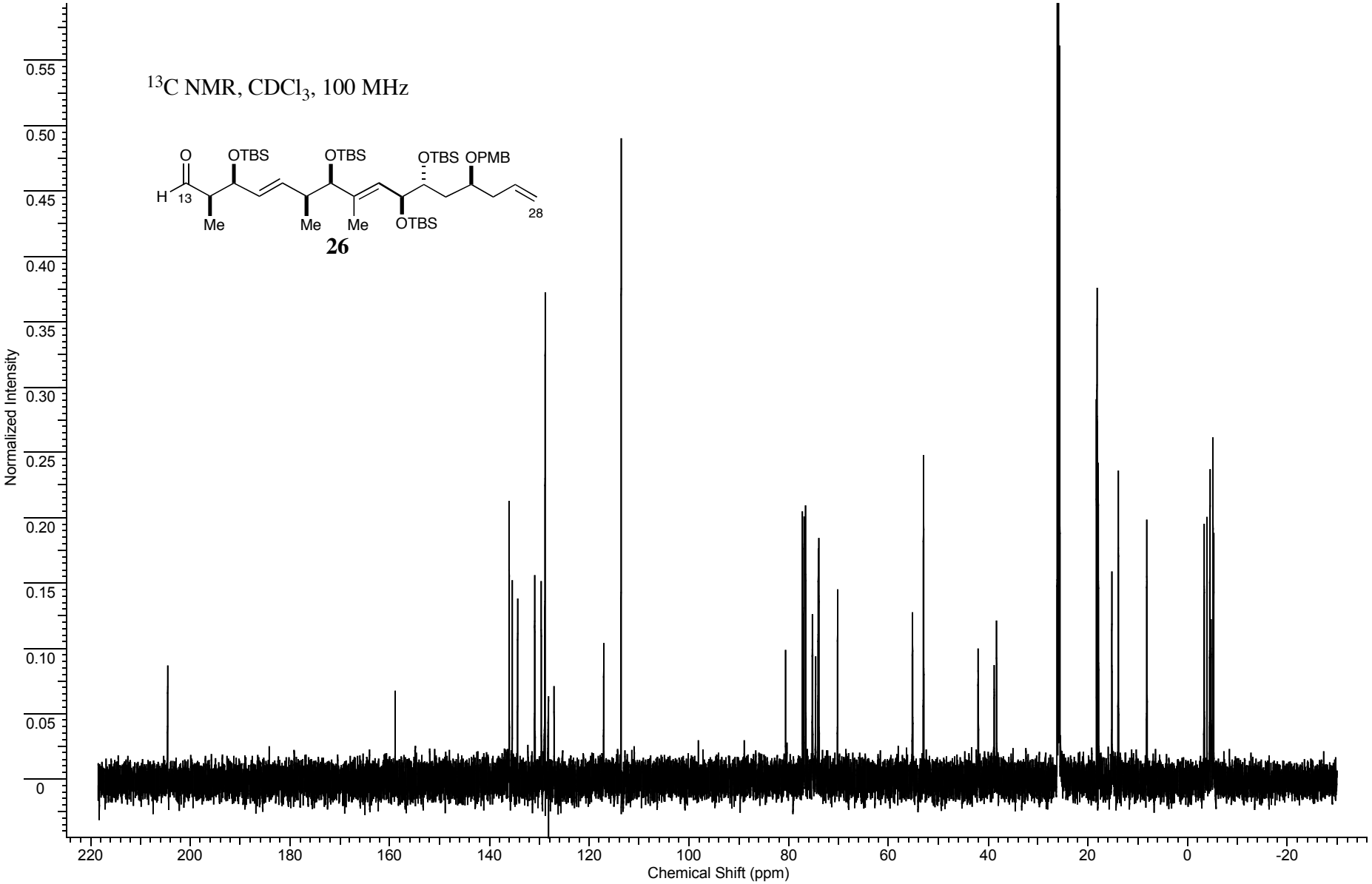


8

^{1}H NMR, $CDCl_3$, 500 MHz



26


^{13}C NMR, $CDCl_3$, 100 MHz
O
OTBS
OTBS
OTBS
OPMB
H
13
Me
Me
Me
OTBS
28
26
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)