Supporting Information

Synthesis of Spongistatin 2 Employing a New Route to the EF Fragment

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I) General Experimental Procedures

All experiments were performed under an argon atmosphere under anhydrous conditions in oven dried glassware unless otherwise stated.

Solvents and reagents: Solvents were distilled under argon prior to use; CH_2Cl_2, MeOH, MeCN and toluene from calcium hydride; Et_2O and THF from calcium hydride and $LiAlH_4$, with triphenyl methane indicator for THF. All solvents were anhydrous reagent grade unless otherwise stated. All chemical reagents used were commercially available from Fischer and Sigma Aldrich.

Chromatography: Thin layer chromatography (TLC) was performed on pre-coated glass-backed Merck Kieselgel 60 F_{254} plates with visualisation effected with ultra-violet irradiation (λ = 254 nm) and/or staining using cerium ammonium molybdate, or vanillin solutions. Flash column chromatography with Merck Kieselgel (230–400 mesh) silica gel performed according to the method employed by W. C. Still et al.[†] All solvents used for chromatographic purification were distilled prior to use with the exception of Et_2O and HPLC grade *n*-hexane, which were used as supplied.

Atom labeling: Labeling is in accord with the natural product numbering system and is indicated on the relevant diagram.

NMR spectroscopy: ^{1}H NMR spectra recorded on Bruker DPX-400, Bruker Avance 500 (with dual cryoprobe) or Bruker DRX-600 operating at 400, 500 and 600 MHz respectively, with deuterated solvent acting as an internal lock. Data is reported in the following manner: chemical shift (in parts per million (ppm)) relative to tetramethylsilane (external standard), number of protons and assignment, chemical, multiplicity and coupling constant *J* (measured in Hz to the nearest 0.1 Hz). ^{13}C NMR spectra recorded on the same DPX-400, Bruker Avance 500 (with dual cryoprobe) or Bruker DRX-600 operating at 100, 125 and 150 MHz respectively with broadband proton decoupling and the deuterium solvent as an internal lock. ^{19}F NMR spectra were recorded on a Bruker Avance 400 (376 MHz) QNP Ultrashield spectrometer with broadband proton decoupling using the deuterated solvent as internal deuterium lock. Chemical shift data are given in parts per million relative to $CFCl_3$ (external standard).

Residual protic solvent also acted as an internal reference ($CDCl_3$; ^{1}H NMR = 7.26 ppm, ^{13}C = 77.1 ppm, C_6D_6; ^{1}H NMR 7.16 ppm, ^{13}C = 128.06 ppm, CD_3CN; ^{1}H NMR 1.94 ppm, ^{13}C = 118.26 ppm).

Structural assignments were made with the aid of DEPT 135, HMQC, HSQC, HMBC, COSY, NOESY and individual nOe experiments in the assignment of signals in ^{1}H and ^{13}C NMR spectra.

[†] W. C. Still, M. Kahn, M. J. Mitra, *J. Org. Chem*. **1978**, *43*, 2923–2925.

Infrared Spectroscopy: Spectra were recorded on a Perkin-Elmer Spectrum One FT-IR ATR (Attenuated Total Reflectance) Spectrometer as a thin film deposited on the ATR. Only selected characteristic peaks are recorded.

Optical rotations: Measured on Perkin Elmer 343 polarimeter and $[\alpha]_D$ values quoted in 10^{-1}degcm^{2}g^{-1} with concentration (*c*) quoted in g(100 mL)$^{-1}$.

Mass Spectroscopy (EI, ESI): High resolution mass spectra (HRMS) recorded on Waters Micromass LCT spectrometer using time of flight with positive electrospray ionisation (ESI^+) or negative electrospray ionisation (ESI^-), an ABI/MDS Sciex Q-STAR Pulsar with ESI^+, or a Bruker BioApex II 4.7e FTICR utilising either ESI^+ or a positive electron ionisation (EI^+) source equipped with a direct insertion probe. The mass reported is that containing the most abundant isotopes (^{35}Cl and ^{79}Br). This was performed at the Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, with each value obtained within 5 ppm of the calculated mass.

Melting points: Determined using an SRS Optimelt MPA 100 automated melting point system, with range quoted to the nearest whole number.

Elemental Analysis: Performed by the Microanalytical Laboratories at the Department of Chemistry, University of Cambridge. All reported values are within ±0.5% of the calculated value.

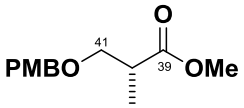
Naming of compounds: Carried out using the computer programme ACD/Name. This software generates the systematic name of chemical structures according to the guidelines specified by the International Union of Pure and Applied Chemistry (IUPAC). As a result the numbering system used in these names does not follow that of the natural product. In order to allow for the straightforward comparison of data, the NMR assignments given follow the natural product numbering system which is shown on the chemical structure.

Structures not shown in the manuscript that have been described in the Supporting Information are numbered with the form S#.

The procedures quoted in this supplementary information are those with the highest yield regardless of scale. For the purpose of synthesising multigram quantities of material, several reaction steps were telescoped and hence the yield for the scale-up procedures is not reported in some instances.

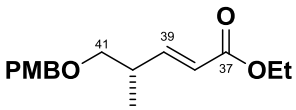
(II) Experimental Data for Compounds

Methyl (2*R*)-3-((4-methoxybenzyl)oxy)-2-methylpropanoate S1



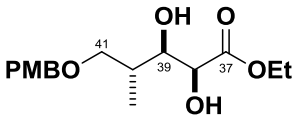
To a stirred solution of methyl-(*R*)-3-hydroxy-2-methyl propionate (**8**) (60 g, 500 mmol) and PMBTCA (212 g, 750 mmol) in CH_2Cl_2 (500 mL) at room temperature was added PPTS (12.5 g, 50 mmol) and the resulting orange mixture stirred at room temperature for 24 h. The reaction was quenched by the addition of solid $NaHCO_3$ (50 g) and petrol (500 mL) and stirred vigorously for 30 min before being cooled to –20 °C overnight. The resulting white precipitate was removed by filtration and washed with petrol/CH_2Cl_2 (1:1, 2 × 100 mL). The combined filtrates were concentrated *in vacuo* to give an orange oil that was filtered through silica eluting with Et_2O (1000 mL) and concentrated *in vacuo* to give the crude product as a dark orange oil. Flash chromatography using petrol/Et_2O (90:10 then 80:20) afforded the title compound **S1** as a yellow oil (121.1 g, quant.); R_f = 0.29 (petrol/EtOAc, 80:20); $[\alpha]_D^{25.0}$ –10.4 (*c* 1.11 in $CHCl_3$); [lit[1] $[\alpha]_D^{20}$ –8.0 (*c* 0.9, CH_2Cl_2)]; IR (film) ν_{max}/cm^{-1} 2950, 2905, 2860, 1736, 1512, 1244, 1085; ^1H (400 MHz), $CDCl_3$: δ = 7.24 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.87 (2H, d, *J* = 8.6 Hz, Ar-*meta*-H), 4.45 (2H, s, OC*H*$_2$-Ar), 3.81 (3H, s, Ar-OC*H*$_3$), 3.69 (3H, s, CO_2CH_3), 3.63 (1H, dd, *J* = 9.1, 7.3 Hz, 41-C*H*$_A$H$_B$), 3.46 (1H, dd, *J* = 9.0, 6.0 Hz, 41-CH$_A$*H*$_B$), 2.81–2.72 (1H, m, 40-C*H*) and 1.17 (3H, d, *J* = 7.1 Hz, 40-CHC*H*$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 175.1 (39-*C*O), 159.1 (Ar-*C*OCH$_3$), 130.2 (Ar-*C*CH$_2$), 129.1 (2C, Ar-*ortho*-C), 113.7 (2C, Ar-*meta*-C), 72.6 (41-CH$_2$), 71.6 (O*C*H$_2$-Ar), 55.1 (CO_2CH_3), 51.5 (Ar-O*C*H$_3$), 40.1 (40-*C*H) and 13.9 (40-CH*C*H$_3$); *m/z* (ESI+) Found $[M+Na]^+$ 261.1109; $C_{13}H_{18}O_4Na$ requires 261.1103, Δ 2.3 ppm.

Ethyl (2*E*,4*S*)-5-((4-methoxybenzyl)oxy)-4-methylpent-2-enoate 9



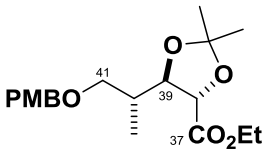
To a stirred solution of ester **S1** (60 g, 250 mmol) in CH_2Cl_2 (100 mL) at –78 °C was added dropwise DIBAL-H (1.0 M in CH_2Cl_2, 375 mL, 375 mmol) over 4 h. The resultant pale yellow solution was stirred at –78 °C for 2 h before being quenched at –78 °C by the dropwise addition of MeOH (25 mL) and warmed to room temperature. To the reaction was added Rochelle's salt (sat. aq, 1000 mL) and the mixture stirred vigorously at room temperature for 24 h before the phases were separated and the aqueous extracted with CH_2Cl_2 (2 × 250 mL). The combined organics were dried (Na_2SO_4), filtered and concentrated *in vacuo* to leave a solution of the intermediate aldehyde in CH_2Cl_2 (approx. 1000 mL total volume). This solution was stirred and cooled to 0 °C before the addition of carbethoxymethylene triphenylphosphorane (263 g, 750 mmol) and then stirred at room temperature overnight. After 24 h the reaction was concentrated *in vacuo* to give a orange/white oil which was filtered through silica eluting with Et_2O/EtOAc (1:1, 2000 mL) and concentrated *in vacuo* to give a dark orange oil containing a white solid. This was diluted with Et_2O (1000 mL) and stirred vigorously for 30 min before the resultant white precipitate was removed by filtration and the filtrate concentrated *in vacuo* to give an orange oil. This material was diluted with petrol/Et_2O (9:1, 1000 mL) and stirred vigorously for 30 min before the resultant white precipitate was removed by filtration and the filtrate concentrated *in vacuo* to give the crude product as an orange oil. Flash chromatography using petrol/Et_2O (90:10 gradient to Et_2O) afforded the title compound **9** as a yellow oil (65.7 g, 94% over 2 steps); R_f = 0.35 (petrol/EtOAc, 80:20); $[\alpha]_D^{25.0}$ –14.4 (*c* 1.02 in $CHCl_3$); [lit[2] $[\alpha]_D^{20}$ –20.0 (*c* 0.75, CH_2Cl_2)]; IR (film) ν_{max}/cm^{-1} 2964, 2937, 2904, 2855, 1714, 1512, 1245, 1033; ^{1}H (400 MHz), $CDCl_3$: δ = 7.24 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.94 (1H, dd, *J* = 15.8, 7.0 Hz, 39-C*H*), 6.87 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 5.85 (1H, d, *J* = 15.8 Hz, 38-C*H*), 4.44 (2H, s, OCH_2-Ar), 4.19 (2H, q, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 3.80 (3H, s, Ar-OCH_3), 3.40–3.32 (2H, m, 41-CH_2), 2.63 (1H, septet, *J* = 6.7 Hz, 40-C*H*), 1.29 (3H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$) and 1.08 (3H, d, *J* = 6.8 Hz, 40-CHCH_3); ^{13}C NMR (150 MHz), $CDCl_3$: δ = 166.7 (37-*C*O), 159.2 (Ar-*C*OCH$_3$), 151.2 (39-*C*H), 130.3 (Ar-*C*CH$_2$), 129.2 (2C, Ar-*ortho*-C), 121.0 (38-*C*H), 113.8 (2C, Ar-*meta*-C), 73.6 (41-*C*H$_2$), 72.8 (OCH$_2$-Ar), 60.2 ($CO_2CH_2CH_3$), 55.2 (Ar-OCH$_3$), 36.8 (40-*C*H), 16.1 (40-CH*C*H$_3$) and 14.3 ($CO_2CH_2CH_3$); *m/z* (ESI+) Found $[M+Na]^+$ 301.1409; $C_{16}H_{22}O_4Na$ requires 301.1416, Δ 2.3 ppm; Elemental analysis found C, 69.10; H, 7.95. $C_{16}H_{22}O_4$ requires C, 69.04; H, 7.97%.

Ethyl 4-deoxy-5-*O*-(4-methoxybenzyl)-4-methyl-D-arabinonate 10



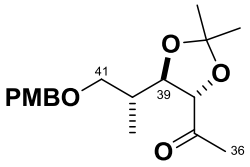
To a stirred mixture of the ester **9** (27.8 g, 100 mmol) in *t*BuOH (500 mL) and H_2O (500 mL) at room temperature was added methanesulfonamide (9.5 g, 100 mmol), potassium hexacyanoferrate (98.0 g, 300 mmol), potassium carbonate (41.0 g, 300 mmol) and $(DHQD)_2$-PHAL (780 mg, 1 mmol). The orange solution was cooled to 4 °C and potassium osmium (VI) oxide hydrate (74 mg, 0.2 mmol) was added and the resulting orange mixture stirred at 4 °C for 48 h. The reaction was quenched by the addition of solid sodium sulfite (150 g) and stirred vigorously at room temperature for 2 h before being diluted with water (500 mL) and extracted with CH_2Cl_2 (3 × 250 mL). The combined organics were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil which was filtered through silica eluting with EtOAc (500 mL) and concentrated *in vacuo* to give a yellow oil (*dr* 94:6). This oil was seeded with pure product and crystallised at room temperature to give a crude off-white solid. The crude product was recrystallised from petrol (60-80)/toluene (1:1, reflux to 0 °C) to afford the title compound **10** as a white crystalline solid (28.6 g, 92%) and single diastereomer; R_f = 0.35 (petrol/EtOAc, 50:50); m.p. = 67–68 °C; $[\alpha]_D^{25.0}$ –20.9 (*c* 1.12 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3511 (br), 2977, 2934, 2905, 2847, 1701, 1515, 1251, 1024; ^1H (400 MHz), $CDCl_3$: δ = 7.23 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.87 (2H, d, *J* = 8.6 Hz, Ar-*meta*-H), 4.46 (2H, s, OCH_2-Ar), 4.34–4.21 (2H, m, $CO_2CH_2CH_3$), 4.18 (1H, d, *J* = 7.8 Hz, 38-C*H*), 3.86–3.81 (1H, obscured m, 39-C*H*), 3.80 (3H, s, Ar-OCH_3), 3.62 (1H, dd, *J* = 9.2, 4.0 Hz, 41-CH_AH_B), 3.51 (1H, app. t, *J* = 9.1, 8.8 Hz, 41-CH_AH_B), 3.11 (2H, app. t, *J* = 3.9 Hz, 2 × O*H*), 2.25–2.13 (1H, m, 40-C*H*), 1.31 (3H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$) and 0.94 (3H, d, *J* = 6.9 Hz, 40-$CHCH_3$); ^{13}C NMR (150 MHz), $CDCl_3$: δ = 173.6 (37-*C*O), 159.5 (Ar-*C*OCH_3), 129.6 (Ar-*C*CH_2), 129.5 (2C, Ar-*ortho*-C), 114.0 (2C, Ar-*meta*-C), 77.5 (39-*C*H), 74.9 (41-*C*H_2), 73.3 (OCH_2-Ar), 71.8 (38-*C*H), 61.8 ($CO_2CH_2CH_3$), 55.4 (Ar-OCH_3), 35.3 (40-*C*H), 14.3 ($CO_2CH_2CH_3$) and 13.7 (40-$CHCH_3$); *m/z* (ESI+) Found $[M+H]^+$ 313.1642; $C_{16}H_{25}O_6$ requires 313.1651, Δ 2.9 ppm; Elemental analysis found C, 61.59; H, 7.64. $C_{16}H_{24}O_6$ requires C, 61.52; H, 7.74%.

Ethyl 4-deoxy-5-*O*-(4-methoxybenzyl)-4-methyl-2,3-*O*-(1-methylethylidene)-D-arabinonate S2



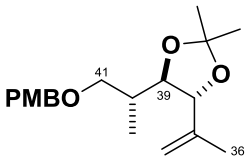
To a stirred suspension of diol **10** (31.2 g, 100 mmol) in 2,2-dimethoxypropane (200 mL, 1.6 mol) at room temperature was added CSA (2.3 g, 10 mmol) and the resulting mixture stirred at room temperature for 5 h. The reaction mixture was diluted with CH_2Cl_2 (500 mL), washed with sat. $NaHCO_{3(aq)}$ (2 × 250 mL), H_2O (250 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a colourless oil. Flash chromatography using petrol/EtOAc (80:20 gradient to 65:35) afforded the title compound **S2** as a colourless oil (33.8 g, 96%); R_f = 0.27 (petrol/EtOAc, 80:20); $[\alpha]_D^{25.0}$ +18.0 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2989, 2938, 2908, 1751, 1513, 1246, 1034; ^1H (400 MHz), $CDCl_3$: δ = 7.25 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.87 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 4.42 (2H, s, OCH_2-Ar), 4.38 (1H, d, *J* = 7.0 Hz, 38-C*H*), 4.25–4.15 (3H, m, 39-C*H* and $CO_2CH_2CH_3$), 3.80 (3H, s, Ar-OCH_3), 3.58 (1H, dd, *J* = 9.2, 5.3 Hz, 41-CH_AH_B), 3.38 (1H, dd, *J* = 9.2, 6.2 Hz, 41-CH_AH_B), 2.15 (1H, septet, *J* = 6.3 Hz, 40-C*H*), 1.45 (3H, s, acetal C(CH_3)$_2$), 1.43 (3H, s, acetal C(CH_3)$_2$), 1.27 (3H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$) and 1.03 (3H, d, *J* = 6.9 Hz, 40-CHCH_3); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 171.4 (37-*C*O), 159.0 (Ar-*C*OCH$_3$), 130.6 (Ar-*C*CH$_2$), 129.0 (2C, Ar-*ortho*-C), 113.7 (2C, Ar-*meta*-C), 110.7 (acetal *C*(CH$_3$)$_2$), 80.8 (39-*C*H), 77.0 (38-*C*H), 72.7 (O*C*H$_2$-Ar), 71.5 (41-*C*H$_2$), 61.2 ($CO_2CH_2CH_3$), 55.2 (Ar-OCH$_3$), 36.6 (40-*C*H), 27.0 (acetal C(*C*H$_3$)$_2$), 25.7 (acetal C(*C*H$_3$)$_2$), 14.1 ($CO_2CH_2CH_3$) and 13.5 (40-CH*C*H$_3$); *m/z* (ESI+) Found $[M+Na]^+$ 375.1778; $C_{19}H_{28}O_6Na$ requires 375.1784, Δ 1.6 ppm; Elemental analysis found C, 64.98; H, 8.04. $C_{19}H_{28}O_6$ requires C, 64.75; H, 8.01%.

1,5-Dideoxy-6-*O*-(4-methoxybenzyl)-5-methyl-3,4-*O*-(1-methylethylidene)-D-fructose S3



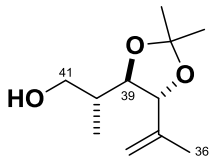
To a solution of ester **S2** (38.5 g, 0.11 mol) in Et_2O (200 mL) at –78 °C was added dropwise MeLi•LiBr complex (1.5 M in Et_2O, 73 mL, 0.11 mol) and the solution stirred at –78 °C for 1 h. The reaction was quenched with sat. $NH_4Cl_{(aq)}$ (250 mL) at –78 °C and warmed to room temperature before being diluted with H_2O (500 mL). The aqueous layer was separated and extracted with Et_2O (3 × 300 mL). The combined organics were dried (Na_2SO_4), filtered and concentrated *in vacuo* give a colourless oil. Flash chromatography using petrol/Et_2O (70:30) afforded the title compound **S3** as a colourless oil (33.5 g, 95%); R_f = 0.36 (petrol/EtOAc, 80:20); $[\alpha]_D^{25.0}$ –17.9 (*c* 1.01 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2988, 2936, 2909, 2862, 1717, 1613, 1513, 1245, 1035; ^1H (600 MHz), $CDCl_3$: δ = 7.24 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.87 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 4.42 (1H, d, *J* = 12.1 Hz, OC*H*$_A$H$_B$-Ar), 4.38 (1H, d, *J* = 12.4 Hz, OCH$_A$*H*$_B$-Ar), 4.25 (1H, d, *J* = 7.2 Hz, 38-C*H*), 4.13 (1H, dd, *J* = 7.1, 5.8 Hz, 39-C*H*), 3.80 (3H, s, Ar-OC*H*$_3$), 3.55 (1H, dd, *J* = 9.2, 5.8 Hz, 41-C*H*$_A$H$_B$), 3.37 (1H, dd, *J* = 9.3, 6.0 Hz, 41-CH$_A$*H*$_B$), 2.24 (3H, s, 36-C*H*$_3$), 2.14 (1H, septet, *J* = 6.4 Hz, 40-C*H*), 1.43 (3H, s, acetal C(C*H*$_3$)$_2$), 1.38 (3H, s, acetal C(C*H*$_3$)$_2$) and 0.99 (3H, d, *J* = 7.0 Hz, 40-CHC*H*$_3$); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 208.4 (37-*C*O), 159.1 (Ar-*C*OCH$_3$), 130.6 (Ar-*C*CH$_2$), 129.2 (2C, Ar-*ortho*-C), 113.7 (2C, Ar-*meta*-C), 109.9 (acetal *C*(CH$_3$)$_2$), 82.9 (38-*C*H), 79.3 (39-*C*H), 72.7 (O*C*H$_2$-Ar), 71.5 (41-*C*H$_2$), 55.2 (Ar-O*C*H$_3$), 36.5 (40-*C*H), 26.9 (acetal C(*C*H$_3$)$_2$), 26.3 (36-*C*H$_3$), 26.2 (acetal C(*C*H$_3$)$_2$) and 13.4 (40-CH*C*H$_3$); *m/z* (ESI+) Found $[M+Na]^+$ 345.1683; $C_{18}H_{26}O_5Na$ requires 345.1678, Δ 1.4 ppm; Elemental analysis found C, 67.03; H, 8.15. $C_{18}H_{26}O_5$ requires C, 67.06; H, 8.13%.

(4*R*,5*R*)-4-((2*R*)-1-(4-Methoxybenzyl)oxy)propan-2-yl)-2,2-dimethyl-5-(prop- 1-en-2-yl)-1,3-dioxolane 11



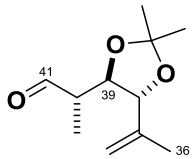
To a stirred suspension of methyl triphenylphosphonium bromide (74.0 g, 208 mmol) in THF (360 mL) at 0 °C was added *n*BuLi (1.6 M in hexane, 117.0 mL, 187 mmol) and the resulting yellow mixture was stirred at 0 °C for 30 min before the addition of a solution of ketone **S3** (33.4 g, 104 mmol) in THF (100 mL). The resulting mixture was allowed to warm to room temperature and stirred for 19 h before being quenched by the addition of silica (100 g) and stirred for 1 h. The resulting slurry was filtered through a pad of silica gel eluting with Et_2O (1000 mL) and concentrated *in vacuo* to give a yellow oil. Flash chromatography using petrol/Et_2O (87.5:12.5) afforded the title compound **11** as a colourless oil (31.8 g, 96%); R_f = 0.48 (petrol/EtOAc, 80:20); $[\alpha]_D^{25.0}$ +0.6 (*c* 1.05 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2985, 2934, 2861, 1613, 1513, 1244, 1036; ^1H (400 MHz), $CDCl_3$: δ = 7.25 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.88 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 5.09 (1H, s, 37-C=CH_AH_B), 4.98 (1H, t, *J* = 1.2 Hz, 37-C=CH_AH_B), 4.44 (1H, d, *J* = 11.6 Hz, OCH_AH_B-Ar), 4.41 (1H, d, *J* = 11.6 Hz, OCH_AH_B-Ar), 4.32 (1H, d, *J* = 8.4 Hz, 38-C*H*), 3.82 (1H, dd, *J* = 8.3, 6.1 Hz, 39-C*H*), 3.80 (3H, s, Ar-OCH_3), 3.59 (1H, dd, *J* = 9.2, 5.5 Hz, 41-CH_AH_B), 3.35 (1H, dd, *J* = 9.1, 6.6 Hz, 41-CH_AH_B), 2.10–2.02 (1H, septet, *J* = 6.5 Hz, 40-C*H*), 1.79 (3H, s, 36-CH_3), 1.42 (3H, s, acetal C(CH_3)$_2$), 1.39 (3H, s, acetal C(CH_3)$_2$) and 0.99 (3H, d, *J* = 7.0 Hz, 40-CHCH_3); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 159.1 (Ar-*C*OCH$_3$), 142.5 (37-*C*), 130.7 (Ar-*C*CH$_2$), 129.1 (2C, Ar-*ortho*-C), 115.6 (37-C=*C*H$_2$), 113.7 (2C, Ar-*meta*-C), 108.0 (acetal *C*(CH$_3$)$_2$), 83.0 (38-*C*H), 79.6 (39-*C*H), 72.7 (O*C*H$_2$-Ar), 71.9 (41-*C*H$_2$), 55.2 (Ar-O*C*H$_3$), 36.3 (40-*C*H), 27.2 (acetal C(*C*H$_3$)$_2$), 27.0 (acetal C(*C*H$_3$)$_2$), 17.1 (36-*C*H$_3$) and 14.0 (40-CH*C*H$_3$); *m/z* (ESI+) Found $[M+Na]^+$ 343.1877; $C_{19}H_{28}O_4Na$ requires 343.1885, Δ 2.3 ppm; Elemental analysis found C, 71.39; H, 8.85. $C_{19}H_{28}O_4$ requires C, 71.22; H, 8.81%.

(2*R*)-2-((4*R*,5*R*)-2,2-Dimethyl-5-(prop-1-en-2-yl)-1,3-dioxolan-4-yl)propan- 1-ol S4



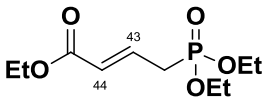
To a vigorously stirred mixture of **11** (16 g, 50 mmol) in CH_2Cl_2 (200 mL) and pH7 buffer (10 mL) was added DDQ (23 g, 100 mmol). The resultant mixture stirred at room temperature for 30 min before being quenched with sat. $NaHCO_{3(aq)}$ (500 mL), diluted with H_2O (3000 mL) and extracted with CH_2Cl_2 (4 × 200 mL). The combined organic extracts were washed with brine (400 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil. The oil was re-dissolved in CH_2Cl_2 (500 mL) and Quadrapure BZA resin (100 g) added. The mixture was stirred at room temperature for 19 h, filtered and the resin washed with CH_2Cl_2 (3 × 300 mL). The combined organics were concentrated *in vacuo* to afford the title compound **S4** as a yellow oil (10.2 g, quant.) that was used directly in the next step without any further purification; R_f = 0.62 (petrol/EtOAc, 50:50); $[\alpha]_D^{25.0}$ = –22.3 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3422 (br), 2984, 2934, 2879, 1370, 1239, 1054; ^1H (400 MHz), $CDCl_3$: δ = 5.06 (1H, s, 37-C=CH_AH_B), 4.97 (1H, s, 37-C=CH_AH_B), 4.22 (1H, d, *J* = 8.2 Hz, 38-C*H*), 3.72 (1H, t, *J* = 7.9 Hz, 39-C*H*), 3.62–3.57 (2H, m, 41-CH_2), 2.87 (1H, s, O*H*), 1.87–1.83 (1H, m, 40-C*H*), 1.74 (3H, s, 36-CH_3), 1.38 (6H, s, 2 × acetal C(CH_3)$_2$) and 0.85 (3H, d, *J* = 7.1 Hz, 40-CHCH_3); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 142.0 (37-*C*), 116.3 (37-C=*C*H_2), 108.5 (acetal *C*(CH$_3$)$_2$), 84.7 (38-*C*H), 82.1 (39-*C*H), 66.6 (41-*C*H_2), 38.4 (40-*C*H), 27.2 (acetal C(*C*H$_3$)$_2$), 26.9 (acetal C(*C*H$_3$)$_2$), 16.9 (36-*C*H$_3$) and 13.3 (40-CH*C*H$_3$); *m/z* (ESI+) Found $[M+Na]^+$ 223.1311; $C_{11}H_{20}O_3Na$ requires 223.1305, Δ 2.7 ppm; Elemental analysis found C, 65.87; H, 9.96. $C_{11}H_{20}O_3$ requires C, 65.97; H, 10.07%

(2*S*)-2-((4*R*,5*R*)-2,2-Dimethyl-5-(prop-1-en-2-yl)-1,3-dioxolan-4-yl)propanal 12



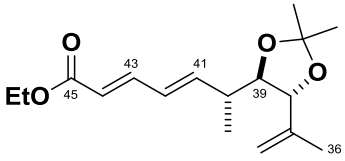
To a stirred solution of alcohol **S4** (10.2 g, 50 mmol) in CH_2Cl_2 (250 mL) at room temperature was added Dess–Martin periodinane (42.4 g, 100 mmol) and the resultant mixture stirred at room temperature for 2 h. The reaction was quenched with sat. $NaHCO_{3(aq)}$ (250 mL) and Na_2SO_3 (250 mL) and stirred for 30 min before being diluted with H_2O (200 mL) and extracted with Et_2O (200 mL) and CH_2Cl_2/Et_2O (1:1, 2 × 200 mL). The combined organics were washed with brine (300 mL), dried (Na_2SO_4), filtered through a plug of florosil eluting with Et_2O (700 mL) and concentrated *in vacuo* to afford the title compound **12** (assumed quant.) as a yellow oil; R_f = 0.45 (petrol/EtOAc, 80:20); IR (film) ν_{max}/cm^{-1} 2986, 2937, 2880, 1726, 1371, 1234, 1051; ^{1}H (600 MHz), $CDCl_3$: δ = 9.74 (1H, s, 41-C*H*O), 5.07 (1H, s, 37-C=CH_AH$_B$), 5.00 (1H, t, *J* = 1.2 Hz, 37-C=CH$_A$$H_B$), 4.27 (1H, d, *J* = 8.6 Hz, 38-C*H*), 3.95 (1H, t, *J* = 7.1 Hz, 39-C*H*), 2.56–2.52 (1H, m, 40-C*H*), 1.76 (3H, s, 36-CH_3), 1.40 (3H, s, acetal C(CH_3)$_2$), 1.37 (3H, s, acetal C(CH_3)$_2$) and 1.11 (3H, dd, *J* = 7.1, 1.1 Hz, 40-CHCH_3); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 203.0 (41-*C*HO), 141.2 (37-*C*), 116.2 (37-C=*C*H$_2$), 109.0 (acetal *C*(CH$_3$)$_2$), 83.5 (38-*C*H), 78.7 (39-*C*H), 48.2 (40-*C*H), 27.0 (acetal C(*C*H$_3$)$_2$), 26.8 (acetal C(*C*H$_3$)$_2$), 16.9 (36-*C*H$_3$) and 10.7 (40-CH*C*H$_3$); *m/z* (ESI+) Found [M+NH$_4$]$^+$ 216.1600; $C_{11}H_{22}O_3N$ requires 216.1594, Δ 2.8 ppm.

(*E*)-ethyl 4-(diethoxyphosphoryl)but-2-enoate 13



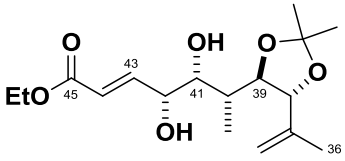
A mixture of ethyl-4-bromocrotonate (200 g, 1.03 mol) and triethylphosphite (183 g, 1.1 mol) were heated to 80 °C under reduced pressure (450 mbar, Büchi) with mixing for 3 h to give a yellow oil which was distilled under reduced pressure (b.p. = 178–180 °C at 2 mmHg) to afford the title compound **13** as a colourless oil (176.0 g, 703 mmol, 68%).[3]

Ethyl (2*E*,4*E*,6*R*)-6-((4*R*,5*R*)-2,2-dimethyl-5-(prop-1-en-2-yl)-1,3-dioxolan-4-yl)hepta-2,4-dienoate 14



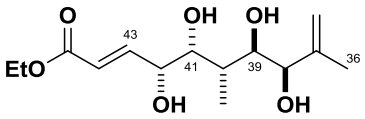
To a stirred solution of phosphonate **13** (16.8 g, 60 mmol) in THF (200 mL) at –78 °C was added LHMDS (1 M in THF, 60 mL, 60 mmol). The resultant orange solution was stirred at –78 °C for 1 h before the addition of a solution of the intermediate aldehyde **12** (assumed quant., 50 mmol) in THF (60 mL). The dark orange solution was allowed to warm to 12 °C slowly over 16 h. The reaction mixture was quenched with sat. $NH_4Cl_{(aq)}$ (200 mL) and H_2O (200 mL). The aqueous layer was separated and extracted with Et_2O (3 × 150 mL). The combined organics were washed with brine (300 mL), dried (Na_2SO_4), filtered through a plug of silica eluting with Et_2O (700 mL) and concentrated *in vacuo* to give an orange oil. Flash chromatography using petrol/Et_2O (95:5 then 90:10) afforded the title compound **14** as a pale yellow oil (11.8 g, 80% over 3 steps from alcohol **S4**, *dr* 95:5); R_f = 0.53 (petrol/EtOAc, 80:20); $[\alpha]_D^{25.0}$ = +24.0 (*c* 1.19 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2983, 2933, 2876, 1713, 1643, 1369, 1227; ^1H (600 MHz), $CDCl_3$: δ = 7.28–7.23 (1H, m, 43-C*H*), 6.20–6.17 (2H, m, 40-C*H* and 41-C*H*), 5.83 (1H, d, *J* = 15.4 Hz, 44-C*H*), 5.03 (1H, s, 37-C=CH_AH$_B$), 4.98 (1H, s, 37-C=CH$_A$$H_B$), 4.21 (2H, q, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 4.12 (1H, d, *J* = 8.6 Hz, 38-C*H*), 3.73 (1H, dd, *J* = 8.6, 4.1 Hz, 39-C*H*), 2.48–2.43 (1H, m, 40-C*H*), 1.77 (3H, s, 36-CH_3), 1.42 (3H, s, acetal C(CH_3)$_2$), 1.38 (3H, s, acetal C(CH_3)$_2$), 1.30 (3H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$) and 1.14 (3H, d, *J* = 7.0 Hz, 40-CHCH_3); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 167.0 (45-*C*O), 144.5 (41-*C*H), 144.3 (43-*C*H), 141.7 (37-*C*), 129.1 (42-*C*H), 120.3 (44-*C*H), 115.1 (37-C=*C*H$_2$), 108.5 (acetal *C*(CH$_3$)$_2$), 82.8 (38-*C*H), 81.5 (39-*C*H), 60.2 ($CO_2CH_2CH_3$), 38.9 (40-*C*H), 27.1 (acetal C(*C*H$_3$)$_2$), 27.0 (acetal C(*C*H$_3$)$_2$), 17.5 (40-CH*C*H$_3$), 17.2 (36-*C*H$_3$) and 14.3 ($CO_2CH_2CH_3$); *m/z* (ESI+) Found $[M+NH_4]^+$ 312.2182; $C_{17}H_{30}O_4N$ requires 312.2169, Δ 4.2 ppm; Elemental analysis found C, 69.38; H, 9.00. $C_{17}H_{26}O_4$ requires C, 69.36; H, 8.90%.

Ethyl (2*E*,8*R*)-2,3,6-trideoxy-6-methyl-7,8-*O*-(1-methylethylidene)-8-*C*-prop-1-en-2-yl-L-*gluco*-oct-2-enonate 15



A mixture of methanesulfonamide (5 g, 50 mmol), AD-mix-β (70 g, 1.4 g/mmol), $K_2OsO_2(OH)_4$ (180 mg, 0.5 mmol), $(DHQD)_2$-PHAL (400 mg, 0.5 mmol) and $NaHCO_3$ (13 g, 150 mmol) in *t*BuOH/H_2O (1:1, 400 mL) were stirred at room temperature for 30 min (almost complete dissolution) before being cooled to 0 °C whereupon the inorganic salts partly crystallised out. To this mixture was added a solution of diene **14** in *t*BuOH/H_2O (1:1, 100 mL) and the resultant orange mixture stirred vigorously at 0 °C for 24 h. The reaction was quenched by the addition of solid Na_2SO_3 (75 g) and stirred vigorously at room temperature for 1 h before being diluted with H_2O (500 mL) and extracted with CH_2Cl_2 (3 × 250 mL). The combined organics were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an orange oil. Flash chromatography using petrol/EtOAc (70:30 gradient to 40:60) afforded the title compound **15** (14.6 g, 89%, *dr* 86:14) as a pale yellow oil; R_f = 0.31 (hexane:EtOAc, 80:20); $[\alpha]_D^{25.0}$ +15.0 (*c* 0.93 in $CHCl_3$); ^{1}H (600 MHz), $CDCl_3$: δ = 6.91 (1H, dd, *J* = 14.3, 3.6 Hz, 43-C*H*), 6.19 (1H, d, *J* = 14.3 Hz, 44-C*H*), 5.11 (1H, br s, 37-C=CH_AH$_B$), 4.96 (1H, br s, 37-C=CH$_A$$H_B$), 4.41–4.38 (1H, br s, O*H*), 4.21–4.19 (1H, m, 42-C*H*), 4.13–4.08 (3H, m, 38-C*H* and $CO_2CH_2CH_3$), 3.83–3.77 (2H, m, 39-C*H* and 41-C*H*), 3.01 (1H, d, *J* = 2.6 Hz, O*H*), 2.93 (1H, d, *J* = 2.6 Hz, 40-C*H*), 2.02 (3H, s, 36-CH_3), 1.43 (3H, s, acetal C(CH_3)$_2$), 1.38 (3H, s, acetal C(CH_3)$_2$), 1.29 (3H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$) and 1.10 (3H, d, *J* = 7.1 Hz, 40-CHCH_3); ^{13}C NMR (125 MHz), $CDCl_3$: δ = 166.1 (45-*C*O), 145.6 (43-*C*H), 141.5 (37-*C*), 122.9 (44-*C*H), 116.1 (37-C=*C*H$_2$), 108.8 (acetal *C*(CH$_3$)$_2$), 83.8 (38-*C*H), 81.3 (39-*C*H), 74.5 (42-*C*H), 71.8 (41-*C*H), 60.4 ($CO_2CH_2CH_3$), 36.9 (40-*C*H), 27.3 (acetal C(*C*H$_3$)$_2$), 26.8 (acetal C(*C*H$_3$)$_2$), 15.2 (36-*C*H$_3$), 14.2 ($CO_2CH_2CH_3$) and 11.7 (40-CH*C*H$_3$); m/z (+ESI) Found $[M+Na]^+$ 351.1749; $C_{17}H_{28}NaO_6$ requires 351.1784.

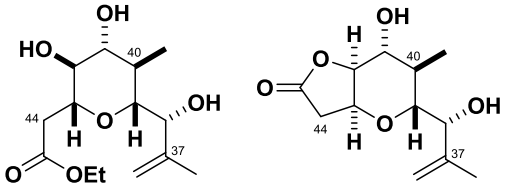
(4*R*,5*R*,6*R*,7*R*,8*R*,*E*)-Ethyl-4,5,7,8-tetrahydroxy-6,9-dimethyldeca-2,9-dienoate 7



To a solution of diol **15** (2.0 g, 6.1 mmol) in EtOH (10 mL) and H_2O (10 mL) was added macroporous toluene sulfonic acid (0.67 g, 3.0 mmol) at ambient temperature. The reaction mixture was refluxed at 82 ^oC for 15 h, allowed to cool to room temperature and filtered. The filtrate was concentrated *in vacuo* to afford the title compound **7** as a pale yellow oil (1.7 g, 98%); R_f 0.31 (CH_2Cl_2/MeOH, 90:10); $[\alpha]_D^{25.0}$ –1.2 (*c* 1.10 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3419 (OH), 2972 (CH), 2925 (CH), 2344, 2086, 1709 (C=O), 1654, 1451, 1371, 1302, 1280, 1178 and 1086; ^1H (600 MHz), $CDCl_3$: δ = 6.83 (1H, dd, *J* = 15.7, 5.5 Hz, 43-C*H*), 6.13 (1H, dd, *J* = 15.7, 1.5 Hz, 44-C*H*), 4.98 (1H, br s, 37-C=CH_AH_B), 4.94 (1H, br s, 37-C=CH_AH_B), 4.27 (1H, obscured t, *J* = 6.6 Hz, 42-C*H*), 4.20 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 4.12 (1H, d, *J* = 5.9 Hz, 38-C*H*), 3.87 (1H, dd, *J* = 7.3, 1.8 Hz, 41-C*H*), 3.61 (1H, t, *J* = 5.1 Hz, 39-C*H*), 3.21 (1H, br s, OH), 1.88−1.79 (1H, m, 40-C*H*), 1.75 (3H, s, 36-CH_3), 1.29 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3) and 1.07 (3H, d, *J* = 7.3 Hz, 40-CHCH_3); ^{13}C (100 MHz), $CDCl_3$: δ = 166.1 (45-*C*O), 145.4 (43-*C*H), 144.2 (37-*C*=CH$_2$), 122.7 (44-*C*H), 114.2 (37-C=*C*H$_2$), 75.9 (38-*C*H), 75.6 (39-*C*H), 74.3 (41-*C*H), 72.1 (42-*C*H), 60.6 ($CO_2CH_2CH_3$), 35.2 (40-*C*H), 18.0 (36-*C*H$_3$), 14.2 ($CO_2CH_2CH_3$) and 11.9 (40-CH*C*H$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 311.1460; $C_{14}H_{24}NaO_6$ requires 311.1471, Δ 3.5 ppm.

Ethyl 2-((2*R*,3*S*,4*R*,5*R*,6*R*)-3,4-dihydroxy-6-((*S*)-1-hydroxy-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate 16

(3a*S*,5*R*,6*R*,7*R*,7a*S*)-7-Hydroxy-5-((*S*)-1-hydroxy-2-methylallyl)-6-methylhexahydro-2*H*-furo[3,2-*b*]pyran-2-one 17



To a pale yellow solution of tetraol **7** (0.50 g, 1.7 mmol) in dry EtOH (25 mL) stirred in a Schlenk tube was added $Zn(OTf)_2$ (127 mg, 350 μmol) at ambient temperature. The Schlenk tube was sealed and the reaction mixture was stirred at 100 ^{o}C for 6 h. The solution was allowed to cool to room temperature, then filtered through a pad of silica and eluted with EtOH (100 mL). The filtrate was concentrated *in vacuo* to afford a pale yellow oil. Flash chromatography using CH_2Cl_2/MeOH (98:2 then 96:4) afforded the title compound **16** as a pale yellow foam (431 mg, 88%). In addition, lactone **17** was isolated as a pale yellow foam (40 mg, 8%).

Triol 16; R_f 0.35 (CH_2Cl_2/MeOH, 90:10); $[\alpha]_D^{25}$ +16.0 (*c* 0.3 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3388 (OH), 2964 (CH), 2925 (CH), 2854 (CH), 1733 (C=O), 1453, 1371, 1307, 1268, 1161, 1096, 1057, 1035, 1004 and 902; ^{1}H (600 MHz), $CDCl_3$: δ = 4.96 (1H, br s, 37-C=CH_AH$_B$), 4.88 (1H, br s, 37-C=CH$_A$$H_B$), 4.17–4.09 (2H, m, OC$H_2CH_3$), 4.07 (1H, br s, 38-C*H*), 3.72−3.64 (1H, m, 43-C*H*), 3.27–3.18 (3H, m, 42-C*H*, 41-C*H*, 39-C*H*), 2.83 (1H, dd, *J* = 15.4, 3.8 Hz, 44-CH_AH$_B$), 2.67 (1H, br s, OH), 2.49 (1H, dd, *J* = 15.4, 8.8 Hz, 44-CH$_A$$H_B$), 2.29 (1H, br s, OH), 1.97–1.88 (1H, m, 40-C*H*), 1.73 (3H, s, 36-CH_3), 1.24 (3H, t, *J* = 7.1 Hz, OCH$_2$CH_3) and 1.07 (3H, d, *J* 6.6, 40-CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 171.5 (C=O), 145.5 (37-*C*=CH$_2$), 111.2 (37-C=*C*H$_2$), 81.5 (41-*C*H or 42-*C*H), 78.7 (39-*C*H), 75.9 (43-*C*H), 75.4 (41-*C*H or 42-*C*H), 73.0 (38-*C*H), 60.7 (O*C*H$_2$CH$_3$), 38.4 (40-*C*H), 38.1 (44-*C*H$_2$), 19.1 (36-*C*H$_3$), 14.1 (OCH$_2$*C*H$_3$) and 12.7 (40-CH*C*H$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 311.1458; $C_{14}H_{24}NaO_6$ requires 311.1471, Δ 4.2 ppm.

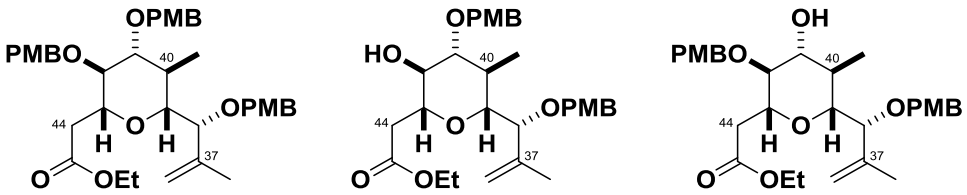
Lactone 17; R_f 0.47 (CH_2Cl_2/MeOH 90:10); $[\alpha]_D^{25}$ –32.7 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} 3424 (OH), 2932 (CH), 1770 (C=O), 1377, 1205, 1168, 1079, 1002, 925 and 732; ^{1}H (600 MHz), $CDCl_3$: δ = 5.05 (1H, br s, 37-C=CH_AH$_B$), 4.99 (1H, br s, 37-C=CH$_A$$H_B$), 4.85−4.79 (1H, m, 43-C*H*), 4.40 (1H, obscured t, *J* = 5.5 Hz, 42-C*H*), 4.20 (1H, d, *J* = 4.4 Hz, 38-C*H*), 3.74 (1H, dd, *J* = 9.9, 6.0 Hz, 41-C*H*), 3.48 (1H, dd, *J* = 8.2, 4.9 Hz, 39-C*H*), 3.28 (1H, br s, OH), 2.76 (1H, dd, *J* = 18.7, 7.1 Hz, 44-CH_AH$_B$), 2.58 (1H, dd, *J* = 18.7, 2.2 Hz, 44-CH$_A$$H_B$), 1.98–1.89 (1H, m, 40-C*H*), 1.76 (3H, s, 36-CH_3) and 1.09 (3H, d, *J* = 6.6 Hz,

40-CHC*H*$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 175.2 (C=O), 144.2 (37-*C*=CH_2), 113.3 (37-C=*C*H_2), 87.8 (42-*C*H), 79.2 (39-*C*H), 75.6 (38-*C*H), 72.6 (41-*C*H), 69.0 (43-*C*H), 35.4 (44-*C*H_2), 33.9 (40-*C*H), 18.5 (36-*C*H_3) and 15.6 (40-CH*C*H_3); *m/z* (+ESI) Found $[M+Na]^+$ 265.1046. $C_{12}H_{18}NaO_5$ requires 265.1052, Δ 2.6 ppm.

Ethyl 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-bis(4-methoxybenzyloxy)-6-((*S*)-1-(4-methoxy benzyloxy) -2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate 18

Ethyl 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3-hydroxy-4-((4-methoxybenzyl)oxy)-6-((*R*)-1-((4-methoxybenzyl)oxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate S5

Ethyl 2-((2*R*,3*S*,4*R*,5*R*,6*R*)-4-hydroxy-3-((4-methoxybenzyl)oxy)-6-((*R*)-1-((4-methoxybenzyl)oxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate S6



To a solution of pyran **16** (20 mg, 70 μmol) in dry toluene (2 mL) stirred in a Schlenk tube, were added 2-(4-methoxybenzyloxy)-4-methylquinoline (0.12 g, 0.42 mmol) and methyl *p*-toluenesulfonate (0.10 mL, 0.42 mmol) at ambient temperature. The Schlenk tube was sealed and the yellow solution was stirred at 40 ºC for 15 h then concentrated under reduced pressure to afford a pale yellow paste. Flash chromatography (crude product was dry-loaded) using petrol/Et_2O (70:30) afforded the title compound **18** (31 mg, 72%) as a pale yellow oil. In addition, two bis-PMB protected regioisomeric products **S5** and **S6** were isolated.

Tris-PMB ether 18; R_f 0.30 (petrol/Et_2O, 50:50); $[\alpha]_D^{25}$ +10.0 (*c* 0.2 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2932 (CH), 1734 (C=O), 1612, 1513, 1464, 1363, 1302, 1247, 1173, 1074, 1033 and 821; ^1H (600 MHz), $CDCl_3$: δ = 7.26 (2H, t, *J* = 4.4 Hz, Ar-*ortho*-H), 7.22 (4H, d, *J* = 8.8 Hz, Ar-*ortho*-H), 6.90–6.83 (6H, m, Ar-*meta*-H), 4.97 (1H, s, 37-C=CH_AH_B), 4.93 (1H, s, 37-C=CH_AH_B), 4.81 (1H, d, *J* = 11.0 Hz, OCH_AH_B-Ar), 4.82 (1H, d, *J* = 10.6 Hz, OCH_AH_B-Ar), 4.62 (1H, d, *J* = 12.1 Hz, OCH_AH_B-Ar), 4.54 (1H, d, *J* = 11.0 Hz, OCH_AH_B-Ar), 4.53 (1H, d, *J* = 10.6 Hz, OCH_AH_B-Ar), 4.10 (1H, d, *J* = 12.1 Hz, OCH_AH_B-Ar), 4.10–4.00 (2H, m, OCH_2CH$_3$), 3.80 (9H, s, 3 × Ar-OCH_3), 3.73 (1H, s, 38-C*H*), 3.62 (1H, td, *J* = 9.9, 3.3 Hz, 43-C*H*), 3.27 (1H, obscured t, *J* = 9.3 Hz, 42-C*H*), 3.14 (1H, obscured t, *J* = 9.3 Hz, 41-C*H*), 3.03 (1H, d, *J* = 10.4 Hz, 39-C*H*), 2.70 (1H, dd, *J* = 15.4, 2.7 Hz, 44-CH_AH_B), 2.42 (1H, dd, *J* = 15.4, 9.9 Hz, 44-CH_AH_B), 2.10–1.94 (1H, m, 40-C*H*), 1.75 (3H, s, 36-CH_3), 1.21 (3H, t, *J* = 7.1 Hz, OCH$_2$CH_3) and 0.59 (3H, d, *J* = 6.0 Hz, 40-CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 171.4 (C=O), 159.3 (3C, Ar-*C*OCH$_3$), 148.1 (37-*C*=CH$_2$), 130.6 (Ar-*C*CH$_2$), 130.3 (Ar-*C*CH$_2$), 130.2 (2C, Ar-*ortho*-C), 130.0 (Ar-*C*CH$_2$), 129.7 (2C, Ar-*ortho*-C), 129.5 (2C, Ar-*ortho*-C), 113.9 (2C, Ar-*meta*-C), 113.8 (2C, Ar-*meta*-C) 113.6 (2C, Ar-*meta*-C), 113.4 (37-C=*C*H$_2$), 86.5 (41-*C*H), 84.5 (39-*C*H), 82.1 (42-*C*H), 78.5 (38-*C*H), 76.9 (43-*C*H), 74.9

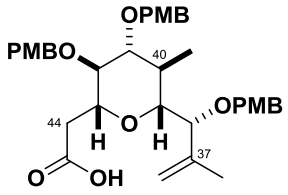
(O*C*H$_2$-Ar), 74.4 (O*C*H$_2$-Ar), 70.1 (O*C*H$_2$-Ar), 60.3 (O*C*H$_2$CH$_3$), 55.3 (3C, Ar-O*C*H$_3$), 37.5 (44-*C*H$_2$), 30.3 (40-*C*H), 19.1 (36-*C*H$_3$), 14.1 (OCH$_2$*C*H$_3$) and 12.2 (40-CH*C*H$_3$); *m/z* (+ESI) Found [M+Na]$^+$ 671.3190; $C_{38}H_{48}NaO_9$ requires 671.3196, Δ 0.9 ppm.

38,41-Bis-PMB ether S5; R_f 0.10 (petrol/Et$_2$O, 50:50); $[\alpha]_D^{25}$ –14.8 (*c* 1.2 in CHCl$_3$); IR (film) ν_{max}/cm^{-1} 3479 (OH), 2959 (CH), 2929 (CH), 2871 (CH), 1737 (C=O), 1612, 1514, 1464, 1366, 1302, 1248, 1173, 1068, 1036 and 822; ^{1}H (600 MHz), CDCl$_3$: δ = 7.28 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 7.23 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.89 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 6.86 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 5.00 (1H, s, 37-C=C*H*$_A$H$_B$), 4.93 (1H, s, 37-C=CH$_A$*H*$_B$), 4.67 (1H, d, *J* = 11.3 Hz, OC*H*$_A$H$_B$-Ar), 4.63 (1H, d, *J* = 12.1 Hz, OCH$_A$*H*$_B$-Ar), 4.57 (1H, d, *J* = 11.3 Hz, OC*H*$_A$H$_B$-Ar), 4.15−4.07 (3H, m, OCH$_A$*H*$_B$-Ar, O*C*H$_2$CH$_3$), 3.81 (6H, s, 2 ×Ar-O*C*H$_3$), 3.76 (1H, s, 38-C*H*), 3.57 (1H, td, *J* = 9.6, 3.6 Hz, 43-C*H*), 3.38 (1H, obscured t, *J* = 8.5 Hz, 42-C*H*), 3.07 (1H, dd, *J* = 10.6, 1.4 Hz, 39-C*H*), 3.02 (1H, obscured t, *J* = 9.3 Hz, 41-C*H*), 2.80 (1H, dd, *J* = 15.6, 3.6 Hz, 44-C*H*$_A$H$_B$), 2.54 (1H, dd, *J* = 15.6, 9.1 Hz, 44-CH$_A$*H*$_B$), 2.27 (1H, s, OH), 2.09–2.02 (1H, m, 40-C*H*), 1.77 (3H, s, 36-C*H*$_3$), 1.23 (3H, t, *J* = 7.1 Hz, OCH$_2$C*H*$_3$) and 0.64 (3H, d, *J* = 6.6 Hz, 40-CHC*H*$_3$); ^{13}C (150 MHz), CDCl$_3$: δ = 171.0 (C=O), 159.4 (Ar-*C*OCH$_3$), 159.3 (Ar-*C*OCH$_3$), 144.0 (37-*C*=CH$_2$), 130.6 (Ar-*C*CH$_2$), 130.2 (2C, Ar-*ortho*-C), 130.0 (Ar-*C*CH$_2$), 129.6 (2C, Ar-*ortho*-C), 114.1 (2C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 113.5 (37-C=*C*H$_2$), 87.2 (41-*C*H), 84.6 (39-*C*H), 78.5 (38-*C*H), 77.0 (43-*C*H), 74.2 (42-*C*H), 73.8 (O*C*H$_2$-Ar), 70.1 (O*C*H$_2$-Ar), 60.4 (O*C*H$_2$CH$_3$), 55.28 (Ar-O*C*H$_3$), 55.27 (Ar-O*C*H$_3$), 37.9 (44-*C*H$_2$), 37.5 (40-*C*H), 19.1 (36-*C*H$_3$), 14.1 (OCH$_2$*C*H$_3$) and 12.4 (40-CH*C*H$_3$); *m/z* (+ESI) Found [M+Na]$^+$ 551.2640; $C_{30}H_{40}NaO_8$ requires 551.2621, Δ 3.4 ppm.

38,42-Bis-PMB ether S6; R_f 0.12 (petrol/Et$_2$O, 50:50); $[\alpha]_D^{25}$ –17.0 (*c* 0.1 in CHCl$_3$); IR (film) ν_{max}/cm^{-1} 3483 (OH), 2957 (CH), 2919 (CH), 2851 (CH, 1734 (C=O), 1614, 1514, 1464, 1367, 1302, 1250, 1174, 1035 and 821; ^{1}H (600 MHz), CDCl$_3$: δ = 7.29−7.19 (4H, m, Ar-*ortho*-H), 6.88 (2H, d, *J* = 8.4 Hz, Ar-*meta*-H), 6.85 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 4.97 (1H, s, 37-C=C*H*$_A$H$_B$), 4.93 (1H, s, 37-C=CH$_A$*H*$_B$), 4.66 (1H, d, *J* = 11.0 Hz, OC*H*$_A$H$_B$-Ar), 4.64 (1H, d, *J* = 12.4 Hz, OCH$_A$*H*$_B$-Ar), 4.56 (1H, d, *J* = 11.0 Hz, OC*H*$_A$H$_B$-Ar), 4.13–4.07 (3H, m, OCH$_A$*H*$_B$-Ar, O*C*H$_2$CH$_3$), 3.80 (6H, s, 2 × Ar-O*C*H$_3$), 3.74 (1H, s, 38-C*H*), 3.61 (1H, td, *J* = 9.9, 2.9 Hz, 43-C*H*), 3.23 (1H, obscured t, *J* = 9.2 Hz, 42-C*H*), 3.13 (1H, obscured t, *J* = 9.2 Hz, 41-C*H*), 3.04 (1H, dd, *J* = 10.3, 1.8 Hz, 39-C*H*), 2.75 (1H, dd, *J* = 15.4, 2.9 Hz, 44-C*H*$_A$H$_B$), 2.53 (1H, dd, *J* = 15.4, 9.9 Hz, 44-CH$_A$*H*$_B$), 1.99–1.87 (1H, m, 40-C*H*), 1.76 (3H, s, 36-C*H*$_3$), 1.22 (3H, t, *J* = 7.3 Hz, OCH$_2$C*H*$_3$) and 0.61 (3H, d, *J* = 6.6 Hz, 40-CHC*H*$_3$); ^{13}C (150 MHz), CDCl$_3$: δ = 171.2 (C=O), 159.5 (Ar-*C*OCH$_3$), 159.4 (Ar-*C*OCH$_3$), 144.0 (37-*C*=CH$_2$), 130.2 (2C, Ar-*ortho*-C), 130.0 (2C, Ar-*C*CH$_2$), 129.7 (2C, Ar-*ortho*-C), 114.1 (2C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 113.4 (37-C=*C*H$_2$), 84.4 (41-*C*H), 82.7 (39-*C*H), 78.3 (38-*C*H), 77.2 (43-*C*H), 76.5 (42-*C*H), 74.5 (O*C*H$_2$-Ar), 70.1 (O*C*H$_2$-Ar), 60.4 (O*C*H$_2$CH$_3$), 55.3 (2C, Ar-O*C*H$_3$), 38.3 (44-*C*H$_2$), 37.8 (40-*C*H), 19.1 (36-*C*H$_3$), 14.1

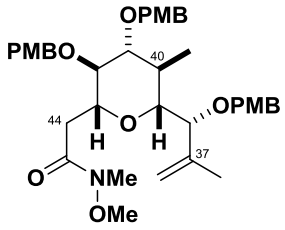
(OCH_2CH_3) and 12.2 (40-$CHCH_3$); *m/z* (+ESI) Found $[M+Na]^+$ 551.2623; $C_{30}H_{40}NaO_8$ requires 551.2621, Δ 0.4 ppm.

2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*R*)-1-(4-methoxy benzyloxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetic acid S7



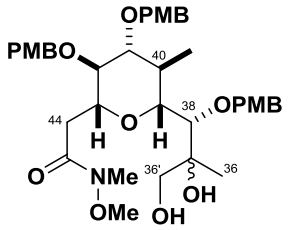
Ester **18** (284 mg, 0.438 mmol) was taken up in THF (15 mL) and cooled to 0 °C. A solution of LiOH•H_2O (0.5 M solution in H_2O, 1.0 mL, 0.482 mmol) and H_2O were added sequentially and the reaction stirred at ambient temperature for 4 days. At this point TLC analysis indicated incomplete conversion to the product and further LiOH•H_2O (20.2 mg, 0.482 mmol) as well as MeOH (2 mL) were added. The stirring reaction was stirred at ambient temperature until complete consumption of the starting material was achieved. The reaction was then cooled to 0 ºC and acidified with ice-cold H_3PO_4 to pH 2–3 and the aqueous layer further extracted with EtOAc (3 × 50 mL). The combined organics were washed with brine (30 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product **S7** (272 mg, quant.) as a thick yellow oil. This material was used directly in the next step without any further purification. R_f 0.24 (petrol/EtOAc, 60:40); $[\alpha]_D^{25}$ +4.8 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2957 (CH), 2929 (CH), 2866 (CH), 2835 (CH), 1717 (C=O), 1612, 1586, 1514, 1464, 1302, 1248, 1174, 1073, 1033, 904, 821 and 758; ^{1}H (600 MHz), $CDCl_3$: δ = 7.27 (2H, d, *J* = 7.7 Hz, Ar-*ortho*-H), 7.23 (4H, dd, *J* = 8.5, 3.3 Hz, Ar-*ortho*-H), 6.91–6.83 (6H, m, Ar-*meta*-H), 5.08 (1H, s, 37-C=CH_AH_B), 5.04 (1H, s, 37-C=CH_AH_B), 4.83 (1H, d, *J* = 8.1 Hz, OCH_AH_B-Ar), 4.81 (1H, d, *J* = 8.1 Hz, OCH_AH_B-Ar), 4.62 (1H, d, *J* = 11.8 Hz, OCH_AH_B-Ar), 4.55 (1H, d, *J* = 10.9 Hz, OCH_AH_B-Ar), 4.54 (1H, d, *J* = 10.9 Hz, OCH_AH_B-Ar), 4.15 (1H, d, *J* = 11.8 Hz, OCH_AH_B-Ar), 3.81 (3H, s, Ar-OCH_3), 3.80 (3H, s, Ar-OCH_3), 3.79 (3H, s, Ar-OCH_3), 3.76 (1H, s, 38-C*H*), 3.54 (1H, td, *J* = 9.3, 3.0 Hz, 43-C*H*), 3.28 (1H, obscured t, *J* = 9.1 Hz, 42-C*H*), 3.18–3.10 (2H, m, 41-C*H*, 39-C*H*), 2.77 (1H, dd, *J* = 15.9, 3.0 Hz, 44-CH_AH_B), 2.50 (1H, dd, *J* = 15.9, 9.1, 44-CH_AH_B), 2.06–2.03 (1H, m, 40-C*H*), 1.74 (3H, s, 36-CH_3) and 0.64 (d, *J* = 6.6 Hz, 40-CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 159.5 (*C*OCH$_3$-Ar), 159.4 (*C*OCH$_3$-Ar), 159.3 (*C*OCH$_3$-Ar), 142.3 (37-*C*=CH$_2$), 130.4 (*C*CH$_2$-Ar), 130.2 (2C, Ar-*ortho*-C), 129.8 (*C*CH$_2$-Ar), 129.74 (2C, Ar-*ortho*-C), 129.71 (*C*CH$_2$-Ar), 129.6 (2C, Ar-*ortho*-C), 114.0 (2C, Ar-*meta*-C), 113.90 (2C, Ar-*meta*-C), 113.86 (37-C=*C*H$_2$) 113.8 (2C, Ar-*meta*-C), 85.9 (39-*C*H or 41-*C*H), 83.1 (39-*C*H or 41-*C*H), 81.6 (42-*C*H), 78.3 (38-*C*H), 75.9 (43-*C*H), 75.1 (O*C*H$_2$-Ar), 74.7 (O*C*H$_2$-Ar), 70.5 (O*C*H$_2$-Ar), 55.29 (2C, Ar-O*C*H$_3$), 55.28 (Ar-O*C*H$_3$), 38.1 (40-*C*H), 36.8 (44-*C*H$_2$), 19.3 (36-*C*H$_3$) and 12.2 (40-CH*C*H$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 643.2891; $C_{36}H_{44}NaO_9$ requires 643.2883, Δ 1.2 ppm.

2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*R*)-1-(4-methoxy benzyloxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S8



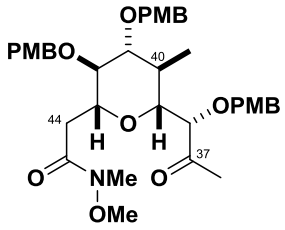
Carboxylic acid **S7** (272 mg, 0.438 mmol) was taken up in CH_2Cl_2 (20 mL) and cooled to 0 ºC. HOBt (119 mg, 0.88 mmol), EDCI·HCl (253 mg, 1.32 mmol), HCl·HN(OMe)Me (215 mg, 2.20 mmol) and Et_3N (0.7 mL, 4.84 mmol) were added sequentially. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. The reaction was re-cooled to 0 ºC and quenched by addition of saturated $NH_4Cl_{(aq)}$ (10 mL) and diluted with H_2O (20 mL). The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organics dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a pale yellow oil. Flash chromatography using petrol/EtOAc (80:20, 70:30 then EtOAc) afforded the title compound **S8** (251 mg, 86% over 2 steps) as a pale yellow oil. R_f 0.45 (petrol/EtOAc, 30:70); $[\alpha]_D^{25}$ +17.2 (*c* 1.4 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2956 (CH), 2925 (CH), 2873 (CH), 2857 (CH), 1658 (C=O), 1612, 1514, 1463, 1302, 1249, 1173, 1075, 1034 and 822; ^1H (600 MHz), $CDCl_3$: δ = 7.27 (2H, d, *J* = 7.1 Hz, Ar-*ortho*-H), 7.22 (4H, dd, *J* = 9.9, 9.1 Hz, Ar-*ortho*-H), 6.89–6.81 (6H, m, Ar-*meta*-H), 4.96 (1H, s, 37-C=CH_AH$_B$), 4.89 (1H, s, 37-C=CH$_A$$H_B$), 4.83 (1H, d, *J* = 11.5 Hz, OCH_AH$_B$-Ar), 4.81 (1H, d, *J* = 11.0 Hz, OCH$_A$$H_B$-Ar), 4.58 (1H, d, *J* = 11.8 Hz, OCH_AH$_B$-Ar), 4.57 (1H, d, *J* = 11.0 Hz, OCH$_A$$H_B$-Ar), 4.54 (1H, d, *J* = 10.8 Hz, OCH_AH$_B$-Ar), 4.10 (1H, d, *J* = 11.8 Hz, OCH$_A$$H_B$-Ar), 3.80 (6H, s, 2 × Ar-OCH_3), 3.79 (3H, s, Ar-OCH_3), 3.74–3.70 (2H, m, 43-C*H*, 38-C*H*), 3.58 (3H, s, NOCH_3), 3.29 (1H, obscured t, *J* = 9.1 Hz, 42-C*H*), 3.16 (1H, obscured t, *J* = 9.9 Hz, 41-C*H*), 3.10 (3H, s, NCH_3), 3.06 (1H, d, *J* = 10.4 Hz, 39-C*H*), 2.76–2.51 (2H, m, 44-CH_2), 2.06–1.98 (1H, m, 40-C*H*), 1.73 (3H, s, 36-CH_3) and 0.62 (3H, d, *J* = 6.6 Hz, 40-CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 172.0 (C=O), 159.22 (2C, Ar-*C*OCH$_3$), 159.18 (Ar-*C*OCH$_3$), 130.7 (37-*C*=CH$_2$), 130.6 (3C, Ar-*C*CH$_2$), 130.1 (2C, Ar-*ortho*-C), 129.7 (2C, Ar-*ortho*-C), 129.5 (2C, Ar-*ortho*-C), 113.82 (2C, Ar-*meta*-C), 113.77 (2C, Ar-*meta*-C), 113.6 (2C, Ar-*meta*-C), 113.4 (37-C=*C*H$_2$), 86.5 (41-*C*H), 84.1 (39-*C*H), 82.3 (42-*C*H), 78.8 (43-*C*H or 38-*C*H), 76.4 (43-*C*H or 38-*C*H), 74.9 (O*C*H$_2$-Ar), 74.2 (O*C*H$_2$-Ar), 70.0 (O*C*H$_2$-Ar), 61.3 (NO*C*H$_3$), 55.27 (Ar-O*C*H$_3$), 55.26 (Ar-O*C*H$_3$), 55.25 (Ar-O*C*H$_3$), 38.5 (40-*C*H), 31.9 (N*C*H$_3$), 29.7 (44-*C*H$_2$), 19.0 (36-*C*H$_3$) and 12.3 (40-CH*C*H$_3$); *m/z* (+ESI) Found $[M+H]^+$ 664.3483; $C_{38}H_{50}NO_9$ requires 664.3486, Δ 0.5 ppm.

2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-2,3-Dihydroxy-1-(4-methoxybenzyloxy)-2-methylpropyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methyacetamdide S9



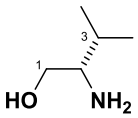
Amide **S8** (0.25 g, 0.38 mmol) was taken up in acetone at ambient temperature. Water (5 mL), NMO (0.13 g, 1.1 mmol) and OsO_4 (2.5 wt% solution in propan-2-ol, 100 μL, 800 μmol) were added sequentially. The reaction was stirred at ambient temperature for 3 days, then quenched by addition of saturated $Na_2SO_{3(aq)}$ (20 mL). The aqueous layer was extracted with EtOAc (3 × 70 mL) and the combined organic layers washed with saturated brine (30 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a yellow oil. Flash chromatography using CH_2Cl_2/MeOH (98:2) afforded the title compound **S9** as a pale yellow opaque oil (260 mg, 98%); R_f 0.17 (neat EtOAc); IR (film) ν_{max}/cm^{-1} 3453 (OH), 2923 (CH), 1647 (C=O), 1613, 1514, 1462, 1302, 1249, 1174, 1076, 1034 and 822; ^1H (600 MHz), $CDCl_3$: δ = 7.30 (6H, d, *J* = 8.4 Hz, Ar-*ortho*-H), 6.93–6.83 (6H, m, Ar-*meta*-H), 4.86 (2H, d, *J* = 11.0 Hz, OCH_AH_B-Ar), 4.61 (4H, m, OCH_AH_B-Ar), 4.09 (1H, br s, OH), 3.81 (3H, s, Ar-OCH_3), 3.80 (6H, s, 2 × Ar-OCH_3), 3.70 (1H, obscured t, *J* = 9.0 Hz, 43-C*H*), 3.63 (1H, d, *J* = 11.0 Hz, 39-C*H*), 3.60−3.50 (2H, m, 36'-CH_2), 3.54 (3H, s, NOCH_3), 3.46 (1H, d, *J* = 11.5 Hz, 38-C*H*), 3.30 (1H, obscured t, *J* = 8.8 Hz, 42-C*H*), 3.25 (1H, obscured t, *J* = 9.5 Hz, 41-C*H*), 3.12 (3H, s, NCH_3), 2.95 (1H, br s, OH), 2.70 (1H, d, *J* = 16.5 Hz, 44-CH_AH_B), 2.54–2.39 (1H, m, 44-CH_AH_B), 2.17–2.02 (1H, m, 40-C*H*), 1.16 (3H, s, 36-CH_3) and 0.97 (3H, d, *J* = 6.6 Hz, 40-CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 159.37 (Ar-*C*OCH$_3$), 159.36 (Ar-*C*OCH$_3$), 159.35 (Ar-*C*OCH$_3$), 130.6 (Ar-*C*CH$_2$), 130.43 (Ar-*C*CH$_2$), 130.40 (Ar-*C*CH$_2$), 129.7 (4C, Ar-*ortho*-C), 129.6 (2C, Ar-*ortho*-C), 113.9 (4C, Ar-*meta*-C), 113.8 (2C, Ar-*meta*-C), 86.9 (41-*C*H), 82.3 (39-*C*H), 77.2 (37-*C*), 75.4 (36'-*C*H$_2$), 75.3 (43-*C*H), 75.2 (42-*C*H or 38-*C*H), 74.4 (42-*C*H or 38-*C*H), 69.8 (3C, O*C*H$_2$-Ar), 61.1 (NO*C*H$_3$), 55.31 (Ar-O*C*H$_3$), 55.29 (Ar-O*C*H$_3$), 55.27 (Ar-O*C*H$_3$), 38.6 (44-*C*H$_2$), 33.7 (N*C*H$_3$), 29.7 (40-*C*H), 22.2 (36-*C*H$_3$) and 13.3 (40-CH*C*H$_3$); *m/z* (+ESI) Found $[M+H]^+$ 720.3392; $C_{38}H_{52}NO_{11}$ requires 720.3360, Δ 4.9 ppm.

2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*S*)-1-(4-methoxy benzyloxy)-2-oxopropyl)-5-methyltetrahydro-2H-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide 5



Diol **S9** (0.26 g, 0.38 mmol) was taken up in dry toluene (15 mL) and stirred at ambient temperature. Lead(IV) acetate (0.19 g, 0.42 mmol) was added and a pale yellow precipitate formed. The reaction was stirred at room temperature for 2 h then filtered. The filter cake was washed with toluene and the filtrate was concentrated *in vacuo* to give the crude product as a yellow oil. Flash chromatography using $CHCl_3$/acetone (95:5) afforded the title compound **5** as a white foam (248 mg, 98%); R_f = 0.52 (neat EtOAc); $[\alpha]_D^{25}$ +165.7 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2956 (CH), 2923 (CH), 2852 (CH),1727 (C=O), 1655, 1612, 1586, 1514, 1463, 1248, 1174, 1074, 1033 and 821; ^{1}H (600 MHz), $CDCl_3$: δ = 7.29–7.25 (2H, m, Ar-*ortho*-H), 7.22 (4H, dd, *J* = 8.0, 6.3 Hz, Ar-*ortho*-H), 6.88 (2H, d, *J* = 8.5 Hz, Ar-*meta*-H), 6.85 (4H, dd, *J* = 8.8, 2.7 Hz, Ar-*meta*-H), 4.83 (2H, d, *J* = 10.7 Hz, OCH_AH_B-Ar), 4.72 (1H, d, *J* = 11.5 Hz, OCH_AH_B-Ar), 4.56 (1H, d, *J* = 10.7 Hz, OCH_AH_B-Ar), 4.55 (1H, d, *J* = 10.7 Hz, OCH_AH_B-Ar), 4.22 (1H, d, *J* = 11.5 Hz, OCH_AH_B-Ar), 3.83–3.75 (1H, m, 38-C*H*), 3.80 (3H, s, Ar-OCH_3), 3.79 (3H, s, Ar-OCH_3), 3.78 (3H, s, Ar-OCH_3), 3.74–3.66 (1H, m, 43-C*H*), 3.55 (3H, s, NOCH_3), 3.38 (1H, dd, *J* = 10.4, 1.9 Hz, 39-C*H*), 3.28 (1H, obscured t, *J* = 9.1 Hz, 42-C*H*), 3.20 (1H, obscured t, *J* = 10.4 Hz, 41-C*H*), 3.08 (3H, s, NCH_3), 2.65–2.41 (2H, m, 44-CH_2), 2.14 (3H, s, 36-CH_3), 2.10−2.00 (1H, m, 40-C*H*) and 0.66 (3H, d, *J* = 6.3 Hz, 40-CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 209.6 (37-C=O), 171.5 (45-C=O), 159.5 (Ar-*C*OCH$_3$), 159.24 (Ar-*C*OCH$_3$), 159.21 (Ar-*C*OCH$_3$), 130.4 (Ar-*C*CH$_2$), 130.3 (Ar-*C*CH$_2$), 130.2 (2C, Ar-*ortho*-C), 129.6 (2C, Ar-*ortho*-C), 129.5 (2C, Ar-*ortho*-C), 128.9 (Ar-*C*CH$_2$), 113.80 (2C, Ar-*meta*-C), 113.75 (4C, Ar-*meta*-C), 86.1 (41-*C*H), 82.3 (38-*C*H), 81.9 (39-*C*H), 81.8 (42-*C*H), 76.3 (43-*C*H), 75.0 (O*C*H$_2$-Ar), 74.3 (O*C*H$_2$-Ar), 72.7 (O*C*H$_2$-Ar), 61.2 (NO*C*H$_3$), 55.22 (Ar-O*C*H$_3$), 55.21 (Ar-O*C*H$_3$), 55.18 (Ar-O*C*H$_3$), 37.9 (40-*C*H), 34.2 (44-*C*H$_2$), 32.0 (N*C*H$_3$), 26.8 (36-*C*H$_3$) and 12.2 (40-CH*C*H$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 688.3081; $C_{37}H_{47}NNaO_{10}$ requires 688.3098, Δ 0.3 ppm.

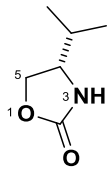
(*S*)-2-Amino-3-methylbutan-1-ol S10



L-valinol

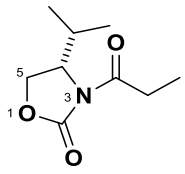
A 2-neck flask was charged with L-valine (50 g, 0.43 mol), $NaBH_4$ (39 g, 1.0 mol) and dry THF (800 mL). A solution of I_2 (120 g, 448 mmol) in dry THF (250 mL) was added slowly at 0 ºC *via* a dropping funnel over the course of 90 min, causing hydrogen gas evolution. The pressure generated by the hydrogen was mitigated by an efficient vent. The white suspension was refluxed for 18 h after iodine addition was complete, then allowed to cool to ambient temperature and MeOH (250 mL) was added slowly *via* a dropping funnel. Methanol addition caused the reaction to turn from a white suspension into a clear solution which was concentrated under reduced pressure to give a white paste. An aqueous solution of KOH (20 wt%, 600 mL), was added and the suspension stirred at room temperature for 4 h. The aqueous layer was extracted with CH_2Cl_2 (3 × 300 mL) and the combined organic layers washed with saturated brine (200 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product as a clear liquid. Vacuum distillation (65–67 ºC, 5 mmHg) afforded the title compound L-valinol **S10** as a clear liquid (21 g, 47%); R_f 0.09 (CH_2Cl_2/MeOH, 90:10); $[\alpha]_D^{25}$ +40.4 (*c* 2.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3353 (OH), 3286 (NH), 2958 (CH), 2934 (CH), 2873 (CH), 1589, 1467, 1388, 1369, 1050, 1009, 922, 873, 827 and 731; ^1H (600 MHz), $CDCl_3$: δ = 3.62 (1H, dd, *J* = 10.8, 3.8 Hz, 1-CH_AH$_B$), 3.27 (1H, dd, *J* = 10.8, 8.8 Hz, 1-CH$_A$*H*$_B$), 2.58–2.51 (1H, m, 2-C*H*), 1.95 (3H, br s, OH, NH_2), 1.60–1.49 (1H, m, 3-C*H*), 0.91 (3H, d, *J* = 7.1 Hz, 4-CH_3) and 0.90 (3H, d, *J* = 7.1 Hz, 4'-CH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 64.67 (1-*C*H$_2$), 58.5 (2-*C*H), 31.5 (3-*C*H), 19.3 (4-*C*H$_3$) and 18.4 (4'-*C*H$_3$). Recorded data are consistent with reported literature values.[4]

(*S*)-4-Isopropyloxazolidin-2-one S11



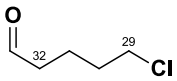
A 2-neck flask equipped with a thermometer and a Vigreux column fitted with a distillation head was charged with L-valinol **S10** (24 g, 0.23 mol), diethylcarbonate (34 mL, 0.28 mol) and sodium ethoxide (0.20 g , 2.3 mmol). The resulting solution was heated at 120–125 ºC causing ethanol to distil off at 100−105 ºC (internal temperature). After approx. 90 min, ethanol distillation ceased and the internal temperature reached 120–125 ºC. The yellow reaction mixture was allowed to cool to 65 ºC and was poured into ice-cold Et_2O (250 mL). A white solid crystallised out in the freezer at –20 ºC and was filtered to afford the title compound **S11** as white crystalline needles (25 g, 98%), m.p. = 68–70 ºC; R_f 0.29 (petrol/EtOAc, 20:80); $[\alpha]_D^{25}$ +13.3 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3264 (NH), 3162 (NH), 2975 (CH), 2961 (CH), 2915 (CH), 2875 (CH), 1745 (C=O), 1722 (C=O), 1699, 1472, 1405, 1245, 1090, 1050, 1009, 936, 769 and 710; ^{1}H (600 MHz), $CDCl_3$: δ = 6.52 (1H, br s, NH), 4.34 (1H, dd, *J* = 9.9, 8.8 Hz, 5-CH_AH$_B$), 4.09 (1H, dd, *J* = 8.8, 6.3 Hz, 5-CH$_A$$H_B$), 3.60 (1H, q, *J* = 6.9 Hz, 4-C*H*), 1.76–1.69 (1H, m, C*H*$(CH_3)_2$), 0.96 (3H, d, *J* = 6.6 Hz, CHCH_3) and 0.89 (3H, d, *J* = 6.9 Hz, CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 160.3 (C=O), 68.6 (5-*C*H$_2$), 58.3 (4-*C*H), 32.7 (*C*H$(CH_3)_2$), 18.0 (CH*C*H$_3$) and 17.6 (CH*C*H$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 152.0682; $C_6H_{11}NNaO_2$ requires 152.0687, Δ 3.3 ppm; Elemental analysis expected: C 55.80, H 8.58, N 10.84; found for $C_6H_{11}NO_2$: C 55.61, H 8.51, N 10.77. Recorded data are consistent with reported literature values.[4]

(*S*)-4-Isopropyl-3-propionyloxazolidin-2-one S12



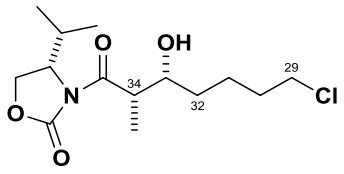
Oxazolidinone **S11** (65 g, 0.51 mol) was taken up in dry THF (500 mL) and cooled to −78 ºC. A solution of *n*BuLi (1.60 M in hexanes, 0.44 L, 0.70 mol) was added dropwise *via* a dropping funnel. The resulting suspension was stirred at –78 ºC for 1 h followed by the dropwise addition of propionyl chloride (53 mL, 0.61 mol). The yellow solution was stirred at −78 ºC for 4 h then quenched by addition of saturated $NH_4Cl_{(aq)}$ (300 mL) and diluted with H_2O (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 300 mL) and the combined organic layers washed with saturated brine (200 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product as a pale yellow liquid. Flash chromatography using petrol/Et_2O (60:40) afforded the title compound **S12** as a pale yellow liquid (90 g, 96%); R_f 0.41 (petrol/Et_2O, 50:50); $[\alpha]_D^{25}$ +86.6 (*c* 1.4 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2967 (CH), 2944 (CH), 2880 (CH), 1777 (C=O), 1702 (C=O), 1388, 1375, 1302, 1245, 1205, 1120, 1071 and 1025; ^{1}H (600 MHz), $CDCl_3$: δ = 4.43 (1H, dt, *J* = 8.2, 3.2 Hz, 4-C*H*), 4.29 (1H, dd, *J* = 9.9, 9.1 Hz, 5-CH_AH_B), 4.21 (1H, dd, *J* = 9.1, 3.2 Hz, 5-CH_AH_B), 3.02–2.87 (2H, m, COCH_2CH$_3$), 2.42–2.34 (1H, m, C*H*(CH$_3$)$_2$), 1.17 (3H, t, *J* = 7.4 Hz, COCH$_2$CH_3), 0.92 (3H, d, *J* = 6.6 Hz, CHCH_3) and 0.88 (3H, d, *J* = 6.9 Hz, CHCH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 203.2 (C=O amide), 174.1 (C=O carbamate), 63.4 (5-*C*H$_2$), 58.4 (4-*C*H), 29.2 (CO*C*H$_2$CH$_3$), 28.4 (*C*H(CH$_3$)$_2$), 18.0 (CH*C*H$_3$), 14.7 (CH*C*H$_3$) and 8.4 (COCH$_2$*C*H$_3$); *m/z* (+ESI) Found $[M+H]^+$ 186.1125; $C_9H_{16}NNaO_3$ requires 186.1130, Δ 3.1 ppm. Recorded data are consistent with reported literature values.[4]

5-Chloropentanal S13



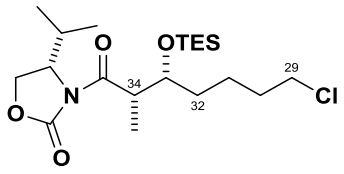
To a solution of 5-chlorovaleronitrile (25 g, 0.21 mol) in dry CH_2Cl_2 (500 mL) cooled to −78 ºC was added DIBAL (1.0 M in CH_2Cl_2, 250 mL, 250 mmol) dropwise *via* a dropping funnel. The reaction was stirred for 2 h then quenched at –78 ºC by addition of HCl (3 N, 500 mL) then allowed to warm to room temperature. The aqueous layer was extracted with CH_2Cl_2 (3 × 300 mL) and the combined organic layers washed with saturated $NaHCO_{3(aq)}$ (300 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as an orange liquid. Vacuum distillation (69–75 ºC, 20 mmHg; lit. b.p. = 60–66 °C, 10 mmHg)[i] afforded the desired product **S13** as a clear liquid (24 g, 96%); R_f 0.41 (petrol/Et_2O, 60:40); IR (film) ν_{max}/cm^{-1} 2954 (CH), 2872 (CH), 2830 (CH), 2725 (CH), 1721 (C=O), 1448, 1411, 1392, 1311, 1279, 1074, 877, 751 and 725; ^1H (400 MHz), $CDCl_3$: δ = 9.77 (1H, s, C*H*O), 3.54 (2H, d, *J* = 6.2 Hz, 29-CH_2), 2.48 (2H, td, *J* = 5.9, 1.3 Hz, 32-CH_2), 1.86–1.74 (4H, m, 31-CH_2, 30-CH_2); ^{13}C (100 MHz), $CDCl_3$: δ = 201.7 (*C*HO), 44.4 (29-*C*H_2), 42.9 (32-*C*H_2), 31.8 (31-*C*H_2 or 30-*C*H_2) and 19.4 (31-*C*H_2 or 30-*C*H_2).

(*S*)-3-((2*S*,3*R*)-7-Chloro-3-hydroxy-2-methylheptanoyl)-4-isopropyloxazolidin-2-one S14



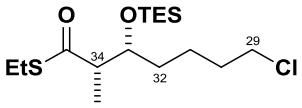
Oxazolidinone **S12** (15 g, 81 mmol) was taken up in dry Et_2O (200 mL) and cooled to −78 ºC. Hünig's base (0.23 L, 0.13 mol) and *n*Bu_2BOTf (0.23 L, 0.11 mol) were added sequentially. The yellow suspension was allowed to warm to 0 ºC and stirred for 90 min then re-cooled to –78 ºC. 5-Chloropentanal (**S13**) (19 mL, 0.16 mmol) was added dropwise and the suspension was stirred for 1 h then allowed to warm to 0 ºC and stirred for a further 3 h. The reaction was quenched by slow addition of pre-mixed pH 7 buffer (50 mL), MeOH (50 mL) and 30% H_2O_2 (25 mL) and allowed to warm to ambient temperature. After stirring for 3 h the yellow suspension was diluted with H_2O (50 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product as a yellow oil. Flash chromatography using petrol/EtOAc (80:20 then 60:40) afforded the title compound **S14** as a clear oil (21.5 g, 86%); R_f 0.20 (petrol/Et_2O, 50:50); $[\alpha]_D^{25}$ +50.8 (*c* 3.6 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3507 (OH), 2960 (CH), 2937 (CH), 2875 (CH), 1779 (C=O), 1695 (C=O), 1386, 1301, 1227 and 1205; ^{1}H (600 MHz), $CDCl_3$: δ = 4.47–4.41 (1H, m, NC*H*), 4.26 (1H, dd, *J* = 9.9, 8.8 Hz, C(O)OCH_AH_B), 4.19 (1H, dd, *J* = 9.3, 2.7 Hz, C(O)OCH$_A$*H*$_B$), 3.93-3.87 (1H, m, 33-C*H*), 3.73 (1H, qd, *J* = 7.3, 2.5 Hz, 34-C*H*), 3.50 (2H, t, *J* = 6.6 Hz, 29-CH_2), 3.04 (1H, s, OH), 2.34–2.26 (1H, m, C*H*$(CH_3)_2$), 1.81–1.71 (2H, m, 30-CH_2), 1.65–1.56 (1H, m, 31-CH_AH_B), 1.56–1.41 (2H, m, 32-CH_AH_B, 31-CH$_A$*H*$_B$), 1.40–1.33 (1H, m, 32-CH$_A$*H*$_B$), 1.21 (3H, d, *J* = 7.3 Hz, 34-CHCH_3), 0.89 (3H, d, *J* = 6.9 Hz, CH(CH_3)$_2$) and 0.84 (3H, d, *J* = 6.9 Hz, CH(CH_3)$_2$); ^{13}C (150 MHz), $CDCl_3$: δ = 177.6 (35-*C*=O), 153.4 (*C*(O)OCH_2), 70.9 (33-*C*H), 63.3 (C(O)O*C*H_2), 58.1 (N*C*H), 44.8 (29-*C*H_2), 42.0 (34-*C*H), 32.9 (32-*C*H_2), 32.3 (30-*C*H_2), 28.3 (*C*H$(CH_3)_2$), 23.3 (31-*C*H_2), 17.8 (CH(*C*H_3)$_2$), 14.6 (CH(*C*H_3)$_2$) and 10.7 (34-CH*C*H_3); *m/z* (+ESI) Found $[M+Na]^+$ 328.1299. $C_{14}H_{24}ClNNaO_4$ requires 328.1292, Δ 2.1 ppm.

(*S*)-3-((2*S*,3*R*)-7-Chloro-2-methyl-3-(triethylsilyloxy)heptanoyl)-4-isopropyl oxazolidin-2-one S15



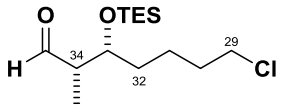
To a solution of alcohol **S14** (25 g, 82 mmol) and imidazole (33 g, 0.49 mol) in dry DMF (60 mL) cooled to 0 ºC was slowly added TESCl (55 mL, 0.33 mol). The reaction was allowed to warm to ambient temperature and stirred for 12 h then re-cooled to 0 ºC. The yellow reaction mixture was quenched by slow addition of saturated $NaHCO_{3(aq)}$ (50 mL) and diluted with H_2O (50 mL). The aqueous layer was extracted with EtOAc (3 × 100 mL) and the combined organic layers washed with saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as a yellow oil. Flash chromatography using petrol/EtOAc (neat petrol then 90:10) afforded the title compound **S15** as a white solid (30.2 g, 88%); R_f 0.66 (petrol/EtOAc, 50:50); $[\alpha]_D^{25}$ +31.4 (*c* 2.2 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2957 (CH), 2915 (CH), 2877 (CH), 1777 (C=O), 1698 (C=O), 1458, 1383, 1364, 1300, 1227, 1201, 1104, 1057, 1014, 991, 964 and 726; ^1H (600 MHz), $CDCl_3$: δ = 4.42–4.38 (1H, m, NC*H*), 4.23 (1H, dd, *J* = 9.6, 9.1 Hz, C(O)OCH_AH_B), 4.20 (1H, dd, *J* = 9.3, 3.0 Hz, C(O)OCH_AH_B), 4.03–3.98 (1H, m, 33-C*H*), 3.88 (1H, obscured quint, *J* = 6.3 Hz, 34-C*H*), 3.52 (2H, td, *J* = 6.9, 2.5 Hz, 29-CH_2), 2.41–2.34 (1H, m, C*H*$(CH_3)_2$), 1.80–1.70 (2H, m, 30-CH_2), 1.56–1.41 (4H, m, 32-CH_2, 31-CH_2), 1.20 (3H, d, *J* = 6.6 Hz, 34-CHCH_3), 0.95 (9H, t, *J* = 8.0 Hz, Si(CH_2CH_3)$_3$), 0.91 (3H, d, *J* = 7.1 Hz, CH(CH_3)$_2$), 0.87 (3H, d, *J* = 7.1 Hz, CH(CH_3)$_2$) and 0.59 (6H, q, *J* = 8.0 Hz, Si(CH_2CH$_3$)$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 175.3 (35-*C*=O), 153.7 (*C*(O)OCH$_2$), 72.7 (33-*C*H), 63.2 (C(O)O*C*H$_2$), 58.6 (N*C*H), 44.9 (29-*C*H$_2$), 42.9 (34-*C*H), 34.8 (32-*C*H$_2$), 32.6 (30-*C*H$_2$), 28.3 (*C*H(CH$_3$)$_2$), 22.2 (31-*C*H$_2$), 18.0 (CH(*C*H$_3$)$_2$), 14.7 (CH(*C*H$_3$)$_2$), 12.9 (34-CH*C*H$_3$), 6.9 (3C, Si(CH_2CH_3)$_3$) and 5.1 (3C, Si(*C*H$_2$CH$_3$)$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 442.2168. $C_{20}H_{38}ClNNaO_4Si$ requires 442.2156, Δ 2.7 ppm.

(2*S*,3*R*)-*S*-Ethyl 7-chloro-2-methyl-3-(triethylsilyloxy)heptanethioate S16



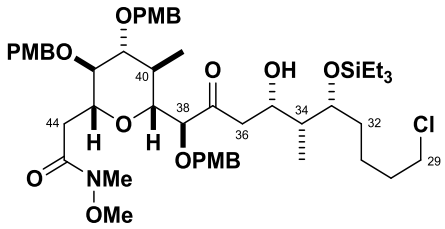
A solution of *n*BuLi (2.5 M in hexanes, 4.0 mL, 9.5 mmol) was added to a solution of EtSH (6.0 mL, 79 mmol) in dry THF (30 mL) cooled to 0 ºC. The resulting white suspension was stirred for 10 min followed by the addition of a solution of oxazolidone **S15** (3.33 g, 7.90 mmol) in THF (5 mL) at 0 ºC. After 30 min the reaction was quenched by addition of saturated $NaHCO_{3(aq)}$ (100 mL). The aqueous layer was extracted with EtOAc (3 ×70 mL) and the combined organic layers washed with saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product as a pale yellow oil. Flash chromatography using petrol/Et_2O (95:5) afforded the title compound **S16** as a pale yellow oil (2.2 g, 80%); R_f 0.63 (petrol/Et_2O, 90:10); $[\alpha]_D^{25}$ +11.9 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2954 (CH), 2912 (CH), 2877 (CH), 1684 (C=O), 1457, 1414, 1378, 1238, 1069, 1004, 956, 726 and 688; ^1H (600 MHz), $CDCl_3$: δ = 3.97 (1H, q, *J* = 6.9 Hz, 33-C*H*), 3.53 (2H, t, *J* = 6.9 Hz, 29-CH_2), 2.86 (2H, q, *J* = 7.4 Hz, SCH_2CH$_3$), 2.71 (1H, obscured quint., *J* = 6.9 Hz, 34-C*H*), 1.76 (2H, obscured quint., *J* = 6.9 Hz, 30-CH_2), 1.57–1.42 (4H, m, 32-CH_2, 31-CH_2), 1.24 (3H, t, *J* = 7.4 Hz, SCH$_2$CH_3), 1.18 (3H, d, *J* = 6.9 Hz, 34-CHCH_3), 0.95 (9H, t, *J* = 8.0 Hz, Si(CH$_2$CH_3)$_3$) and 0.60 (6H, t, *J* = 8.0 Hz, Si(CH_2CH$_3$)$_3$);^{13}C (150 MHz), $CDCl_3$: δ = 202.2 (C=O), 73.5 (33-*C*H), 53.7 (34-*C*H), 44.9 (29-*C*H$_2$), 34.6 (32-*C*H$_2$ or 31-*C*H$_2$), 32.7 (30-*C*H$_2$), 23.1 (S*C*H$_2$CH$_3$), 22.4 (32-*C*H$_2$ or 31-*C*H$_2$), 14.6 (SCH$_2$*C*H$_3$), 13.1 (34-CH*C*H$_3$), 6.9 (3C, Si(CH$_2$*C*H$_3$)$_3$) and 5.2 (3C, Si(*C*H$_2$CH$_3$)$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 375.1552; $C_{16}H_{33}ClNaO_2SSi$ requires 375.1557, Δ 1.3 ppm.

(2*S*,3*R*)-7-Chloro-2-methyl-3-(triethylsilyloxy)heptanal 19



To a suspension of 30% Pd/C (0.5 g) in dry CH_2Cl_2 (40 mL) was added Et_3SiH (2.2 mL, 1.4 mmol). The suspension was stirred for 10 min under the evolution of hydrogen gas. Subsequently, a solution of thioester **S16** (1.4 g, 3.9 mmol) in dry THF (5 mL) was added slowly and the suspension was stirred at ambient temperature for 1 h. The reaction mixture was filtered through a pad of celite and the filtrate concentrated *in vacuo* to give the crude product as a pale yellow oil. Flash chromatography using petrol/EtOAc (98:2) afforded the title compound **19** as a clear oil (1.1 g, 97%); R_f 0.36 (petrol/Et_2O, 90:10); $[\alpha]_D^{25}$ +43.5 (*c* 0.9 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2955 (CH), 2912 (CH), 2877 (CH), 1726 (CO), 1458, 1239, 1103, 1032, 1006, 809, 774, 724 and 673; ^1H (600 MHz), $CDCl_3$: δ = 9.78 (1H, s, C*H*O), 4.14−4.08 (1H, m, 33-C*H*), 3.53 (2H, t, *J* = 6.6 Hz, 29-CH_2), 2.49–2.42 (1H, m, 34-*C*H), 1.78 (2H, m, 30-CH_2), 1.59–1.36 (4H, m, 32-CH_2, 31-CH_2), 1.07 (3H, d, *J* = 6.6 Hz, 34-CHCH_3), 0.95 (9H, t, *J* = 8.0 Hz, Si(CH_2CH_3)$_3$) and 0.60 (6H, t, *J* = 8.0 Hz, Si(CH_2CH_3)$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 205.1 (d, *C*HO), 72.1 (33-*C*H), 51.4 (34-*C*H), 44.8 (29-*C*H_2), 33.9 (32-*C*H_2 or 31-*C*H_2), 32.5 (30-*C*H_2), 23.1 (32-*C*H_2 or 31-*C*H_2), 7.9 (34-CH*C*H_3), 6.8 (3C, Si(CH_2CH_3)$_3$) and 5.1 (3C, Si(CH_2CH_3)$_3$); *m/z* (+ESI) Found $[M+Na]^+$ 315.1536; $C_{14}H_{29}ClNaO_2Si$ requires 315.1523, Δ 4.1 ppm.

2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((1*S*,4*S*,5*R*,6*R*)-10-Chloro-4-hydroxy-1-(4-methoxybenzyloxy)-5-methyl-2-oxo-6-(triethylsilyloxy)decyl)-3,4-bis(4-methoxybenzyl oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide 20



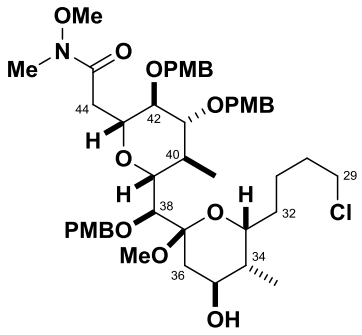
Methyl ketone **5** (0.68 g, 1.0 mmol) was taken up in dry Et_2O (5 mL) under argon and cooled to –78 °C. A solution of Cy_2BCl (1.0 M in hexanes, 1.5 mL, 1.5 mmol) and Et_3N (0.30 mL, 2.0 mmol) were added sequentially. The reaction was allowed to warm to 0 °C and stirred for 3 h upon which a pale yellow slurry formed. The suspension was then re-cooled to –78 °C and a solution of aldehyde **19** (0.88 g, 3.0 mmol) in dry Et_2O (2.5 mL) was added. The reaction mixture was stirred for 18 h at −78 °C and then allowed to warm slowly to 0 °C and stirred for a further 1 h. The slurry was quenched by addition of $NH_4Cl_{(aq)}$ (20 mL) and allowed to warm to room temperature. The aqueous layer was extracted with EtOAc (3 × 60 mL) and the combined organic layers dried ($MgSO_4$), filtered and concentrated *in vacuo*. Silica gel was added and the yellow solution was stirred at room temperature for 30 min, then filtered and the filter cake washed with additional EtOAc (3 × 30 mL). The filtrate was concentrated under reduced pressure to afford the crude product as a yellow oil. Flash chromatography using petrol/EtOAc (70:30) afforded the title compound **20** as a pale yellow oil (789 mg, 82%); R_f 0.28 (petrol/EtOAc, 50:50); $[\alpha]_D^{25}$ +7.2 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3432 (OH), 2953 (CH), 2875 (CH), 1725 (C=O), 1613, 1514, 1463, 1302, 1249, 1174, 1078, 1034, 821 and 740; ^1H (600 MHz), $CDCl_3$: δ = 7.30–7.24 (2H, m, Ar-*ortho*-H), 7.21 (4H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.88 (2H , d, *J* = 8.2 Hz, Ar-*meta*-H), 6.84 (4H, dd, *J* = 8.5, 1.4 Hz, Ar-*meta*-H), 4.82 (1H, d, *J* = 11.3 Hz, OCH_AH_B-Ar), 4.81 (1H, d, *J* = 10.7 Hz, OCH_AH_B-Ar), 4.75 (1H, d, *J* = 11.5 Hz, OCH_AH_B-Ar), 4.55 (2H, d, *J* = 10.7 Hz, OCH_AH_B-Ar), 4.23 (1H, dd, *J* = 6.0, 2.7 Hz, 35-C*H*), 4.21 (1H, d, *J* = 11.8 Hz, OCH_AH_B-Ar), 3.87 (1H, d, *J* = 1.9 Hz, 38-C*H*), 3.83 (1H, d, *J* = 4.7 Hz, 33-C*H*), 3.80 (3H, s, Ar-OCH_3), 3.79 (3H, s, Ar-OCH_3), 3.78 (3H, s, Ar-OCH_3), 3.66 (1H, td, *J* = 9.1, 2.5 Hz, 43-C*H*), 3.59–3.49 (2H, m, 39-C*H*, 29-CH_2), 3.57 (3H, s, NOCH_3), 3.27−3.19 (2H, m, 42-C*H*, 41-C*H*), 3.09 (3H, s, NCH_3), 2.85 (1H, dd, *J* = 16.2, 9.3 Hz, 36-CH_AH_B), 2.64–2.45 (2H, m, 44-CH_2), 2.35 (1H, dd, *J* = 16.2, 2.5 Hz, 36-CH_AH_B), 2.04–2.00 (1H, m, 40-C*H*), 1.77 (2H, obscured quint, *J* = 7.1 Hz, 30-CH_2), 1.63–1.50 (3H, m, 34-C*H*, 32-CH_2), 1.50–1.37 (2H, m, 31-CH_2), 0.97 (9H, t, *J* = 8.0 Hz, Si(CH_2CH_3)$_3$), 0.92 (3H, d, *J* = 6.9 Hz, 34-CHCH_3), 0.65 (3H, d, *J* = 6.3 Hz, 40-CHCH_3) and 0.07 (6H, q,

J = 8.0 Hz, Si(C*H*$_2$CH$_3$)$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 209.7 (C=O ketone), 172.0 (C=O amide), 159.5 (Ar-*C*OCH$_3$), 159.3 (Ar-*C*OCH$_3$), 159.2 (Ar-*C*OCH$_3$), 130.5 (Ar-*C*CH$_2$), 130.4 (Ar-*C*CH$_2$), 130.3 (2C, Ar-*ortho*-C), 129.7 (2C, Ar-*ortho*-C), 129.5 (2C, Ar-*ortho*-C), 129.2 (Ar-*C*CH$_2$), 113.9 (2C, Ar-*meta*-C), 113.8 (2C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 86.1 (41-*C*H or 42-*C*H), 81.9 (38-*C*H), 81.9 (41-*C*H or 42-*C*H), 80.1 (39-*C*H), 75.72 (43-*C*H), 75.68 (33-*C*H), 75.1 (O*C*H$_2$-Ar), 74.3 (O*C*H$_2$-Ar), 72.1 (O*C*H$_2$-Ar), 69.2 (35-*C*H), 61.3 (NO*C*H$_3$), 55.28 (Ar-O*C*H$_3$), 55.26 (Ar-O*C*H$_3$), 55.25 (Ar-O*C*H$_3$), 45.4 (36-*C*H$_2$), 45.0 (29-*C*H$_2$), 42.0 (34-*C*H), 37.9 (40-*C*H), 34.1 (44-*C*H$_2$), 33.5 (32-*C*H$_2$), 32.9 (30-*C*H$_2$), 32.0 (N*C*H$_3$), 22.8 (31-*C*H$_2$), 12.2 (40-CH*C*H$_3$), 8.5 (34-CH*C*H$_3$), 7.0 (3C, Si(CH$_2$*C*H$_3$)$_3$) and 5.4 (3C, Si(*C*H$_2$CH$_3$)$_3$); *m/z* (+ESI) Found $[M+H]^+$ 958.4922; $C_{51}H_{77}ClNO_{12}Si$ requires 958.4904, Δ 1.4 ppm.

The relative stereochemistry of the β-hydroxyl ketone formed from the aldol reaction was determined by analysis of the 36-CH$_A$H$_B$ coupling constants (ABX pattern) using the technique described by Roush.[†] A 34,35-*syn* (or Felkin) stereochemistry was inferred.

[†] W. R. Roush, T. D. Bannister, M. D. Wendt, M. S. Van Nieuwenhze, D. J. Gustin, G. J. Dilley, G. C. Lane, K. A. Scheidt and W. J. Smith III, *J. Org. Chem*. 2002, **67**, 4284.

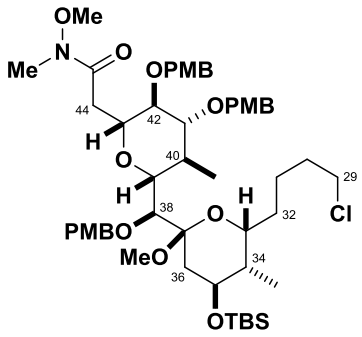
2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*R*,6*R*)-6-(4-Chlorobutyl)-4-hydroxy-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S17



Aldol adduct **20** (1.43 g, 1.49 mmol) was taken up in dry MeOH (30 mL) at ambient temperature. Trimethylorthoformate (3.0 mL, 27.4 mmol) and PPTS (67 mg, 0.27 mmol) were added sequentially and the resulting reaction mixture was stirred for 20 min. The reaction was cooled to 0 ºC and quenched by addition of saturated $NaHCO_{3(aq)}$ (50 mL) and the mixture extracted with EtOAc (3 × 70 mL). The combined organic layers washed with saturated brine (200 mL), dried (Na_2SO_4 and 10 drops of Et_3N as stabiliser), filtered and concentrated under reduced pressure to give the crude product as an opaque oil. Flash chromatography using petrol/acetone/Et_3N (60:40:1) afforded the title compound **S17** as a colourless oil (1.14 g, 89%); R_f 0.16 (petrol/acetone, 60:40); $[\alpha]_D^{25}$ +24.8 (*c* 1.0 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 3522 (OH), 2956 (CH), 2929 (CH), 2875 (CH), 1720 (C=O), 1656, 1612, 1586, 1513, 1463, 1302, 1248, 1173, 1085, 1064, 1030, 849, 821 and 731; ^{1}H (600 MHz), $CDCl_3$: δ = 7.28 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 7.23 (4H, d, *J* = 9.3 Hz, Ar-*ortho*-H), 6.91–6.81 (6H, m, Ar-*meta*-H), 4.82 (1H, d, *J* = 11.5 Hz, OC*H*$_A$H$_B$-Ar), 4.80 (1H, d, *J* = 11.0 Hz, OCH$_A$*H*$_B$-Ar), 4.77 (1H, d, *J* = 11.3 Hz, OC*H*$_A$H$_B$-Ar), 4.64 (1H, d, *J* = 11.3 Hz, OCH$_A$*H*$_B$-Ar), 4.56 (1H, d, *J* = 11.3 Hz, OC*H*$_A$H$_B$-Ar), 4.53 (1H, d, *J* = 10.7 Hz, OCH$_A$*H*$_B$-Ar), 4.06–4.00 (1H, m, 33-C*H*), 3.81 (3H, s, Ar-OC*H*$_3$), 3.80 (3H, s, Ar-OC*H*$_3$), 3.79 (3H, s, Ar-OC*H*$_3$), 3.80−3.70 (1H, m, 43-C*H*), 3.68 (1H, br s, 35-C*H*), 3.60 (2H, obscured td, *J* = 6.9, 2.7 Hz, 29-C*H*$_2$), 3.56 (3H, s, NOC*H*$_3$), 3.48 (1H, s, 38-C*H*), 3.24 (1H, obscured t, *J* = 9.1 Hz, 42-C*H*), 3.17 (3H, s, OC*H*$_3$ *ketal*), 3.16–3.09 (2H, m, 41-C*H*, 39-C*H*) 3.13 (3H, s, NC*H*$_3$), 2.72–2.62 (1H, m, 44-C*H*$_A$H$_B$), 2.62–2.51 (1H, m, 44-CH$_A$*H*$_B$), 2.15 (1H, dd, *J* = 15.1, 3.6 Hz, 36-C*H*$_A$H$_B$), 1.93–1.73 (5H, m, 40-C*H*, 36-CH$_A$*H*$_B$, 31-C*H*$_A$H$_B$, 30-C*H*$_2$), 1.72−1.64 (2H, m, 34-C*H*, 32-C*H*$_A$H$_B$), 1.59–1.49 (1H, m, 31-CH$_A$*H*$_B$), 1.46−1.39 (1H, m, 32-CH$_A$*H*$_B$), 0.87 (3H, d, *J* = 7.4 Hz, 34-CHC*H*$_3$) and 0.49 (3H, d, *J* = 6.9 Hz, 40-CHC*H*$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 171.8 (C=O), 159.3 (*C*OCH$_3$-Ar), 159.2 (*C*OCH$_3$-Ar), 159.1 (*C*OCH$_3$-Ar), 131.0 (2C, Ar-*ortho*-C), 130.5 (*C*CH$_2$-Ar) 130.4 (*C*CH$_2$-Ar), 129.6 (2C, Ar-*ortho*-C), 129.5

(2C, Ar-*ortho*-C), 129.0 (*C*CH_2-Ar), 113.8 (2C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 113.6 (2C, Ar-*meta*-C), 103.8 (37-*C*), 86.5 (41-*C*H), 82.2 (42-*C*H), 79.6 (39-*C*H), 76.2 (43-*C*H), 74.9 (O*C*H_2-Ar), 74.2 (O*C*H_2-Ar), 73.5 (38-*C*H), 73.1 (O*C*H_2-Ar), 70.5 (35-*C*H), 67.2 (33-*C*H), 61.2 (NO*C*H_3), 55.24 (2C, Ar-O*C*H_3), 55.20 (Ar-O*C*H_3), 47.3 (O*C*H_3 *ketal*), 45.0 (29-*C*H_2), 38.5 (34-*C*H), 37.2 (40-*C*H), 34.1 (44-*C*H_2), 33.6 (N*C*H_3), 32.6 (30-*C*H_2), 32.3 (32-*C*H_2), 31.9 (36-*C*H_2), 23.5 (31-*C*H_2), 12.4 (40-CH*C*H_3) and 10.6 (34-CH*C*H_3); *m/z* (+ESI) Found $[M+Na]^+$ 880.4029; $C_{46}H_{64}ClNNaO_{12}$ requires 880.4015, Δ 1.6 ppm.

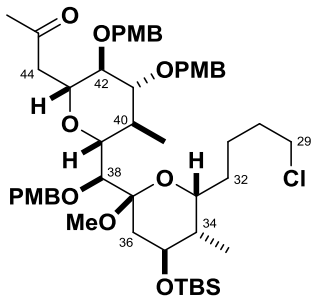
2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S18



A solution of TBSOTf (2.76 mL, 12.0 mmol) and 2,6-lutidine (3.98 mL, 34.3 mmol) in dry THF (15 mL) was cooled to –78 ºC and added dropwise to a solution of alcohol **S17** (1.47 g, 1.71 mmol) in dry THF (13 mL) at –78 ºC. The reaction was stirred for 30 min, then quenched by addition of saturated $NH_4Cl_{(aq)}$ (40 mL). The mixture was extracted with Et_2O (3 × 80 mL) and the combined organic layers dried ($MgSO_4$ and 10 drops of Et_3N as stabiliser), filtered and concentrated under reduced pressure to give the crude product as a yellow oil. Flash chromatography using petrol/Et_2O/Et_3N (55:45:1, 50:50:0 then 45:55:0) afforded the title compound **S18** as a white foam (1.64 g, 99%); R_f 0.48 (petrol/acetone, 60:40); $[\alpha]_D^{25}$ +58.4 (*c* 1.2 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2951 (CH), 2936 (CH), 2859 (CH), 1660, 1613, 1514, 1465, 1302, 1249, 1092, 1080, 1034, 836, 824 and 777; ^{1}H (600 MHz), $CDCl_3$: δ = 7.29–7.25 (2H, m, Ar-*ortho-H*), 7.23 (4H, dd, *J* = 8.8, 3.3 Hz, Ar-*ortho-H*), 6.89–6.82 (6H, m, Ar-*meta-H*), 6.83 (1H, d, *J* = 11.0 Hz, OC*H*$_A$H$_B$-Ar), 6.78 (1H, d, *J* = 11.0 Hz, OCH$_A$*H*$_B$-Ar), 6.77 (1H, d, *J* = 11.0 Hz, OC*H*$_A$H$_B$-Ar), 4.62 (1H, d, *J* = 11.0 Hz, OCH$_A$*H*$_B$-Ar), 4.58 (1H, d, *J* = 11.0 Hz, OC*H*$_A$H$_B$-Ar), 4.51 (1H, d, *J* = 10.7 Hz, OCH$_A$*H*$_B$-Ar), 4.16–4.11 (1H, m, 33-C*H*), 3.83–3.77 (1H, m, 43-C*H*), 3.80 (6H, s, 2 × Ar-OC*H*$_3$), 3.79 (3H, s, Ar-OC*H*$_3$), 3.73 (1H, d, *J* = 2.2 Hz, 35-C*H*), 3.59 (2H, t, *J* = 6.6 Hz, 29-C*H*$_2$), 3.52 (3H, s, NOC*H*$_3$), 3.50–3.44 (1H, s, 38-C*H*), 3.26–3.21 (2H, m, 42-C*H*, 39-C*H*), 3.17 (1H, d, *J* = 9.9 Hz, 41-C*H*), 3.12 (3H, s, OC*H*$_3$ *ketal*), 3.05 (3H, s, NC*H*$_3$), 2.74–2.61 (2H, m, 44-C*H*$_2$), 2.03 (1H, dd, *J* = 15.6, 3.0 Hz, 36-C*H*$_A$H$_B$), 1.89–1.82 (2H, m, 30-C*H*$_2$), 1.81–1.68 (2H, m, 40-C*H*, 31-C*H*$_A$H$_B$), 1.67–1.59 (2H, m, 32-C*H*$_A$H$_B$, 36-CH$_A$*H*$_B$), 1.57–1.44 (2H, m, 31-CH$_A$*H*$_B$, 34-C*H*), 143–1.35 (1H, m, 32-CH$_A$*H*$_B$), 0.89 (9H, s, SiC(C*H*$_3$)$_3$), 0.86 (3H, d, *J* = 7.1 Hz, 34-CHC*H*$_3$), 0.58 (3H, d, *J* = 6.3 Hz, 40-CHC*H*$_3$), 0.09 (3H, s, SiC*H*$_3$) and 0.02 (3H, s, SiC*H*$_3$); ^{13}C (150 MHz), $CDCl_3$: δ = 171.6 (C=O), 159.2 (2C, Ar-*C*OCH$_3$), 159.0 (Ar-*C*OCH$_3$), 130.83 (Ar-*C*CH$_2$), 130.79 (Ar-*C*CH$_2$), 130.7 (Ar-*C*CH$_2$), 130.7 (2C, Ar-*ortho*-C), 129.6 (2C, Ar-*ortho*-C), 129.1 (2C, Ar-*ortho*-C), 113.8 (2C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 113.6 (2C, Ar-

meta-C), 102.4 (37-*C*), 86.4 (41-*C*H), 83.2 (42-*C*H), 79.0 (39-*C*H) 75.4 (43-*C*H), 74.8 (O*C*H_2-Ar), 74.6 (O*C*H_2-Ar), 74.0 (O*C*H_2-Ar), 73.7 (38-*C*H), 70.5 (35-*C*H), 66.7 (33-*C*H), 61.2 (NO*C*H_3), 55.28 (2C, Ar-O*C*H_3), 55.25 (Ar-O*C*H_3), 47.2 (O*C*H_3 *ketal*), 45.0 (29-*C*H_2), 38.9 (34-*C*H), 38.0 (40-*C*H), 34.9 (44-*C*H_2), 32.7 (30-*C*H_2), 32.2 (32-*C*H_2), 30.9 (N*C*H_3), 29.9 (36-*C*H_2), 25.8 (3C, SiC(*C*H_3)$_3$), 23.5 (31-*C*H_2), 18.0 (Si*C*(CH$_3$)$_3$), 12.7 (40-CH*C*H_3), 10.2 (34-CH*C*H_3), –4.5 (Si*C*H_3) and −5.1 (Si*C*H_3); *m/z* (+ESI) Found $[M+Na]^+$ 994.4844; $C_{52}H_{78}ClNNaO_{12}Si$ requires 994.4874, Δ 3.0 ppm.

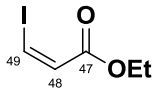
1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)propan-2-one 21



Dry Ce(III)Cl (1.7 g, 6.8 mmol) was taken up in dry THF (20 mL) and sonicated for 2 h at ambient temperature. The white suspension was cooled to –78 ºC and a solution of MeLi.Et_2O (1.6 M, 3.0 mL, 5.0 mmol) was added dropwise. The resulting brown suspension was stirred for 2 h at –78 ºC and a solution of amide **S18** (0.53 g, 0.55 mmol) in dry THF (10 mL) was slowly added. The reaction mixture was stirred at –78 ºC for 18 h then quenched by addition of saturated $NH_4Cl_{(aq)}$ (20 mL) and Et_3N (2 mL). The suspension was filtered through a pad of celite and the filter cake washed with Et_2O (3 × 50 mL). The aqueous layer was re-extracted with Et_2O (2 × 50 mL) and the combined organic layers dried (Na_2SO_4 and 10 drops of Et_3N as stabiliser), filtered and concentrated *in vacuo* to give the crude product as a pale yellow oil. Flash chromatography using HPLC grade hexane/EtOAc/Et_3N (90:10:1 then 85:15:1) afforded the title compound **21** as a white foam (500 mg, quant.); R_f 0.72 (petrol:EtOAc, 60:40); $[\alpha]_D^{25}$ +19.0 (*c* 0.3 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2953 (CH), 2933 (CH), 2857 (CH), 1719 (C=O), 6131, 1515, 1461, 1360, 1302, 1249, 1173, 1082, 1034, 835 and 775; ^1H (600 MHz), $CDCl_3$: δ = 7.27 (2H, d, *J* = 8.2 Hz, Ar-*ortho*-H), 7.22 (4H, dd, *J* = 12.4, 8.5 Hz, Ar-*ortho*-H), 6.90–6.83 (6H, m, Ar-*meta*-H), 4.86–4.73 (3H, m, OCH_AH_B-Ar), 4.69 (1H, d, *J* = 11.5 Hz, OCH_AH_B-Ar), 4.52 (1H, d, *J* = 11.8 Hz, OCH_AH_B-Ar), 4.50 (1H, d, *J* = 11.0 Hz, OCH_AH_B-Ar), 4.18–4.11 (1H, m, 33-C*H*), 3.80 (6H, s, 2 × Ar-OCH_3), 3.79 (3H, s, Ar-OCH_3), 3.75-3.67 (2H, m, 43-C*H*, 35-C*H*), 3.60 (2H, obscured td, *J* = 7.7, 1.7 Hz, 29-CH_2), 3.46 (1H, s, 38-C*H*), 3.22 (1H, d, *J* = 10.5 Hz, 39-C*H*), 3.18 (1H, obscured t, *J* = 9.1 Hz, 42-C*H*), 3.15–3.10 (1H, m, 41-C*H*), 3.13 (3H, s, OCH_3 *ketal*), 2.63 (1H, dd, *J* = 15.9, 4.1 Hz, 44-CH_AH_B), 2.57 (1H, dd, *J* = 15.9, 8.0 Hz, 44-CH_AH_B), 2.13–2.01 (1H, m, 36-CH_AH_B), 2.07 (3H, s, 46-CH_3), 1.91−1.81 (2H, m, 30-CH_2), 1.79–1.69 (3H, m, 40-C*H*, 31-CH_2), 1.69–1.60 (1H, m, 32-CH_AH_B), 1.58–1.49 (2H, m, 34-CH_AH_B, 36-CH_AH_B), 1.49–1.44 (1H, m, 34-CH_AH_B), 1.44–1.35 (1H, m, 32-CH_AH_B), 0.89 (9H, s, SiC(CH_3)$_3$), 0.87 (3H, d, *J* = 7.1 Hz, 34-CHCH_3), 0.45 (3H, d, *J* = 6.3 Hz, 40-CHCH_3), 0.07 (3H, s, SiCH_3) and 0.01 (3H, s, SiCH_3);

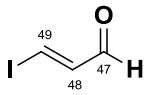
^{13}C (150 MHz), $CDCl_3$: δ = 206.1 (C=O), 159.4 (Ar-*C*OCH_3), 159.23 (Ar-*C*OCH_3), 159.20 (Ar-*C*OCH_3), 131.0 (2C, Ar-*ortho*-C), 130.6 (Ar-*C*CH_2), 130.5 (Ar-*C*CH_2), 130.5 (Ar-*C*CH_2), 129.5 (2C, Ar-*ortho*-C), 129.4 (2C, Ar-*ortho*-C), 113.83 (2C, Ar-*meta*-C), 113.80 (2C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 102.5 (37-*C*), 86.6 (41-*C*H), 82.0 (42-*C*H), 79.8 (39-*C*H), 75.5 (43-*C*H), 74.7 (38-*C*H), 74.2 (O*C*H_2-Ar), 74.1 (O*C*H_2-Ar), 73.3 (O*C*H_2-Ar), 70.2 (35-*C*H), 66.8 (33-*C*H), 55.28 (2C, Ar-O*C*H_3), 55.27 (Ar-O*C*H_3), 47.3 (O*C*H_3 *ketal*), 46.3 (44-*C*H_2), 45.0 (29-*C*H_2), 38.5 (34-*C*H), 38.0 (40-*C*H), 32.7 (30-*C*H_2), 32.3 (32-*C*H_2), 30.6 (46-*C*H_3), 30.5 (36-*C*H_2), 25.8 (3C, SiC(*C*H_3)$_3$), 23.5 (31-*C*H_2), 18.0 (Si*C*$(CH_3)_3$), 12.5 (40-CH*C*H_3), 10.2 (34-CH*C*H_3), −4.7 (Si*C*H_3) and –5.1 (Si*C*H_3); *m/z* (+ESI) Found $[M+Na]^+$ 949.4708; $C_{51}H_{75}NaClO_{11}Si$ requires 949.4665, Δ 4.5 ppm.

Ethyl (2*Z*)-3-iodoprop-2-enoate S19



To ethyl propiolate (15.5 mL, 153 mmol) was added glacial AcOH (150 mL) and lithium iodide hydrate (22.5 g, 168 mmol) in one portion. The mixture was heated to 70 °C and maintained at this temperature for 16 h. The reaction was cooled to room temperature and poured onto H_2O (50 mL) and neutralized with solid K_2CO_3 until no CO_2 gas was evolved. The mixture was extracted with Et_2O (3 × 70 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to give a brown oil. Flash chromatography using petrol/Et_2O (90:10) afforded the title compound **S19** as a pink oil (3.34 g, 97%); IR (film) ν_{max}/cm^{-1} 3067, 2982, 2940, 2909, 1719, 1599, 1475, 1465, 1445, 1390, 1366, 1322, 1272, 1232, 1192, 1160, 1096, 1024, 942; ^1H (400 MHz), $CDCl_3$: δ = 7.43 (1H, d, *J* = 8.9 Hz, 49-C*H*), 6.89 (1H, d, *J* = 8.9 Hz, 48-C*H*), 4.25 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 1.32 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C (150 MHz), $CDCl_3$: δ = 164.6 (47-*C*O), 130.0 (48-*C*H), 94.5 (49-*C*H), 60.8 ($CO_2CH_2CH_3$), 14.2 ($CO_2CH_2CH_3$); *m/z* (+ESI) Found $[M+Na]^+$ 226.9564; $C_5H_8O_2I$ requires 226.9564, Δ 2.3 ppm. Recorded data are consistent with those previously reported.[5]

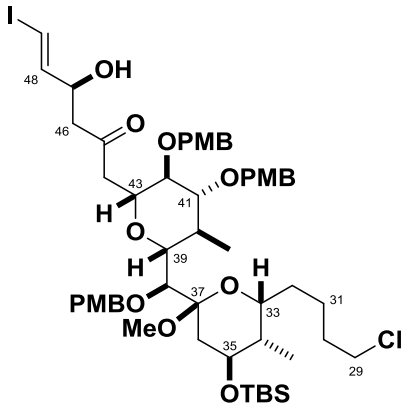
(2*E*)-3-Iodoprop-2-enal 22



To a solution of ester **S19** (7.5 g, 33.2 mmol) in CH_2Cl_2 (75 mL) at –78 °C was added DIBAL-H (1 M solution in CH_2Cl_2, 38.2 mL, 38.2 mmol) dropwise over 35 min. The mixture was stirred at –78 °C for a further 10 min at which point it was warmed to 0 °C and maintained at this temperature for 15 min. The reaction was quenched by the dropwise addition of MeOH (5.8 mL). Following dilution with Et_2O (300 mL), Rochelle's salt (1 M solution, 200 mL) was added and stirring continued for 1 h at room temperature. The mixture was extracted with Et_2O (2 × 300 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow oil. The oil was re-dissolved in Et_2O (10 mL) and cooled to –20 °C resulting in a light yellow solid precipitate. The supernatant was carefully removed using a syringe, and the residual solvent removed under vacuum. The title compound **22** was isolated as yellow solid (2.24 g, 37%); ^1H (400 MHz), $CDCl_3$: δ = 9.23 (1H, d, *J* = 7.3 Hz, 47-C*H*O), 8.01 (1H, d, *J* = 15.0 Hz, 49-C*H*) 7.17 (1H, dd, *J* = 15.0, 7.3 Hz, 48-C*H*).

The product was found to be unstable when isolated in neat form, preventing full characterization. Upon isolation Et_2O (5 mL), THF (1.5 mL) and CaH_2 were added quickly, and this mixture used directly in the following aldol reaction with **21**.[6]

(4*S*,5*E*)-1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-4-hydroxy-6-iodohex-5-en-2-one 23



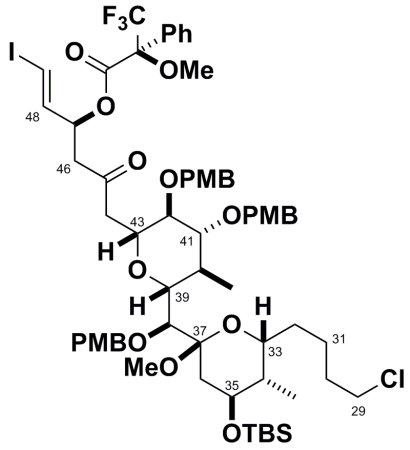
To a solution of ketone **21** (1.02 g, 1.1 mmol) in Et_2O (16.6 mL) at room temperature was added CaH_2 in one portion and the mixture stirred for 1 h. The reaction was cooled to –55 °C and Et_3N (1.22 mL, 8.8 mmol) and Cy_2BCl (1 M solution in hexane, 4.4 mL, 4.4 mmol) added sequentially resulting in a pale yellow precipitate. The reaction was allowed to warm to 0 °C and stirred for 5 h. After being re-cooled to –70 °C, aldehyde **22** (2.24 g, 12.3 mmol)[†] was added dropwise over 10 min as a solution in Et_2O (5 mL) and THF (1.5 mL) containing CaH_2 (See previous procedure for **22**). The contents of the flask were then rinsed with Et_2O (2 × 3 mL) and the washings added dropwise. The reaction was stirred for 4 h during which time the temperature rose to 10 °C. The mixture was then re-cooled to –18 °C and stirred for 16 h at this temperature and quenched by the addition of saturated $NH_4Cl_{(aq)}$ (15 mL). The resulting mixture was extracted with Et_2O (3 × 50 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as an orange oil. Flash chromatography using petrol/Et_2O (88:12 to 0:100) afforded the title compound **23** as a pale yellow oil (124 mg, 65%) and single diastereomer (dr>95:5 by ^{1}H NMR); R_f 0.25 (petrol/Et_2O, 40:60); $[\alpha]_D^{25.5}$ = +15.0 (*c* 0.74 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2953, 2928, 2857, 1713, 1661, 1612, 1586, 1513, 1463, 1442, 1380, 1360, 1342, 1302, 1247, 1173, 1092, 1075, 1031, 965, 950, 912, 834, 821, 774; ^{1}H (400 MHz), $CDCl_3$: δ = 7.30–7.21 (6H, m, Ar-*ortho*-H),

[†] A large excess of vinyl iodide **22** was required due to its poor solubility in Et_2O.

6.91–6.84 (6H, m, Ar-*meta*-H), 6.34 (1H, dd, *J* = 14.4, 5.1 Hz, 48-C*H*), 6.23 (1H, dd, *J* = 14.4, 1.0 Hz, 49-C*H*), 4.84 (1H, d, *J* = 10.9 Hz, OC$H_A$$H_B$-Ar), 4.79 (1H, d, *J* = 11.2 Hz, OC$H_A$$H_B$-Ar), 4.78 (1H, d, *J* = 10.5 Hz, OC$H_A$$CH_B$-Ar), 4.65 (1H, d, *J* = 11.2 Hz, OC$H_A$$H_B$-Ar), 4.62 (1H, d, *J* = 10.9 Hz, OC$H_A$$H_B$-Ar), 4.53 (1H, d, *J* = 10.5 Hz, OC$H_A$$H_B$-Ar), 4.39–4.33 (1H, m, 47-C*H*), 4.17–4.11 (1H, m, 33-C*H*), 3.81 (9H, s, 3 × Ar-OCH_3), 3.80–3.76 (1H, m, 35-C*H*), 3.67 (1H, ddd, *J* = 9.2, 6.2, 5.0 Hz, 43-C*H*), 3.60 (2H, t, *J* = 6.5 Hz, 29-CH_2), 3.50 (1H, s, 38-C*H*), 3.26 (1H, t, *J* = 9.2 Hz, 42-C*H*), 3.24 (1H, d, *J* = 10.1 Hz, 39-C*H*), 3.13 (3H, s, OCH_3 *ketal*), 3.12 (1H, dd, *J* = 9.6, 9.2 Hz, 41-C*H*), 2.70 (1H, dd, *J* = 15.1, 5.0 Hz, 44-C$H_A$$H_B$), 2.60 (1H, dd, *J* = 14.3, 6.2 Hz, 44-C$H_A$$H_B$), 2.59 (1H, dd, *J* = 17.0, 2.5 Hz, 46-C$H_A$$H_B$), 2.45 (1H, dd, *J* = 17.0, 9.4 Hz, 46-C$H_A$$H_B$), 2.07 (1H, dd, *J* = 15.1, 3.7 Hz, 36-C$H_A$$H_B$), 1.87 (2H, app br. quintet, *J* = 7.0 Hz, 30-CH_2), 1.80–1.70 (2H, m, 40-C*H*, 31-C$H_A$$H_B$), 1.70–1.63 (1H, m, 32-C$H_A$$H_B$), 1.60 (1H, br. d, *J* = 15.1 Hz, 36-C$H_A$$H_B$), 1.57–1.47 (2H, m, 31-C$H_A$$H_B$, 34-C*H*), 1.44–1.36 (1H, m, 32-C$H_A$$H_B$), 0.91–0.87 (3H, obscured d, 34-CHCH_3), 0.90 (9H, s, SiC(CH_3)$_3$), 0.54 (3H, d, *J* = 6.4 Hz, 40-CHCH_3), 0.07 (3H, s, SiCH_3) and 0.03 (3H, s, SiCH_3); ^{13}C (101 MHz), $CDCl_3$: δ = 208.5 (C=O), 159.5 (*C*OCH$_3$-Ar), 159.3 (2C, *C*OCH$_3$-Ar), 146.3 (48-*C*H), 130.9 (2C, Ar-*ortho*-C), 130.5 (2C, *C*CH$_2$-Ar), 130.4 (*C*CH$_2$-Ar), 129.5 (2C, Ar-*ortho*-C), 129.4 (2C, Ar-*ortho*-C), 113.9 (4C, Ar-*meta*-C), 113.8 (2C, Ar-*meta*-C), 102.3 (37-C), 86.6 (41-*C*H), 81.7 (42-*C*H), 79.6 (39-*C*H), 77.4 (49-*C*H), 75.1 (43-*C*H), 74.8 (O*C*H$_2$-Ar), 74.4 (38-*C*H), 74.2 (O*C*H$_2$-Ar), 73.8 (O*C*H$_2$-Ar), 70.3 (35-*C*H), 69.9 (47-*C*H), 67.0 (33-*C*H), 55.4 (2C, Ar-O*C*H$_3$), 55.3 (Ar-O*C*H$_3$), 49.6 (46-*C*H$_2$), 47.1 (CO*C*H$_3$ *ketal*), 46.2 (44-*C*H$_2$), 45.1 (29-*C*H$_2$), 38.7 (40-*C*H), 38.1 (34-*C*H), 32.8 (30-*C*H$_2$), 32.3 (32-*C*H$_2$), 30.4 (36-*C*H$_2$), 25.8 (3C, SiC(*C*H$_3$)$_3$), 23.6 (31-*C*H$_2$), 18.1 (Si*C*(CH$_3$)$_3$), 12.6 (40-CH*C*H$_3$), 10.4 (34-CH*C*H$_3$), –4.5 (Si*C*H$_3$) and –4.9 (Si*C*H$_3$); *m/z* (+ESI) 1131.3875; $C_{54}H_{78}O_{12}SiClINa$ requires 1131.3888, Δ 1.2 ppm.

The absolute stereochemistry of the 47-CH hydroxyl group was determined by Mosher ester analysis.[7]

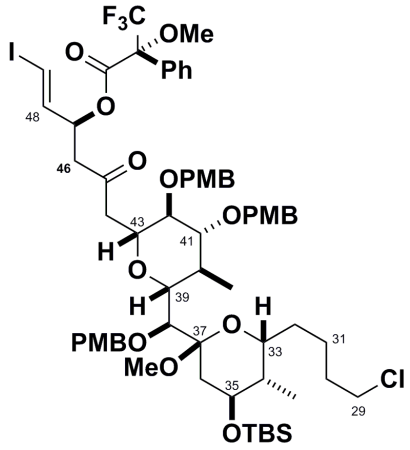
(1*E*,3*S*)-6-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-1-iodo-5-oxohex-1-en-3-yl (2*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate S20



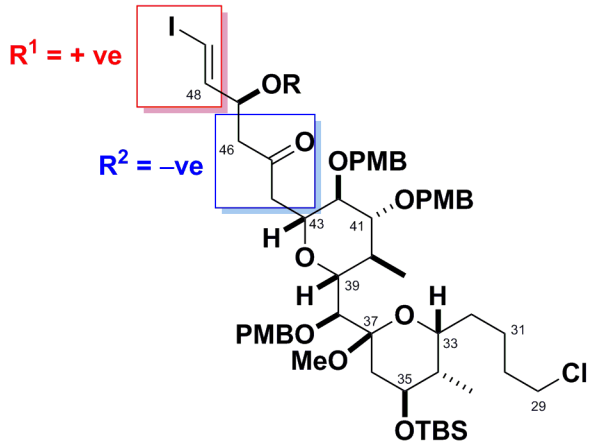
The configuration of the newly formed 47-CH stereocentre was determined by conversion to the corresponding (*S*)- and (*R*)-Mosher ester derivatives using the procedure described by Hoye.[7]

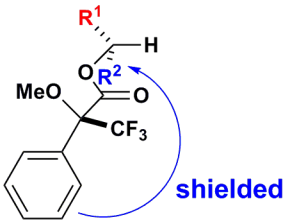
R_f 0.25 (hexane/Et_2O, 50:50); ^{1}H (500 MHz), $CDCl_3$: δ = 7.46–7.35 (5H, m, Ar-Mosher's), 7.31–7.19 (6H, m, Ar-*ortho*-H), 6.90–6.84 (6H, m, Ar-*meta*-H), 6.38–6.36 (2H, m, 48-C*H*, 49-C*H*), 5.73–5.69 (1H, m, 47-C*H*), 4.81 (1H, d, *J* = 11.0 Hz, OCH_AH$_B$-Ar), 4.77 (1H, d, *J* = 11.0 Hz, OCH$_A$$H_B$-Ar), 4.76 (1H, d, *J* = 10.6 Hz, OCH_AH$_B$-Ar), 4.63 (1H, d, *J* = 11.2 Hz, OCH_AH$_B$-Ar), 4.58 (1H, d, *J* = 11.0 Hz, OCH$_A$$H_B$-Ar), 4.51 (1H, d, *J* = 10.6 Hz, OCH$_A$$H_B$-Ar), 4.15–4.11 (1H, m, 33-C*H*), 3.81 (3H, s, Ar-OCH_3), 3.80 (6H, s, 2 × Ar-OCH_3), 3.78–3.75 (1H, m, 35-C*H*), 3.63–3.57 (2H, 38-C*H*, 43-C*H*), 3.60 (2H, t, *J* = 6.5 Hz, 29-CH_2), 3.48 (3H, s, OCH_3 Mosher's), 3.24–3.16 (2H, m, 39-C*H*, 42-C*H*), 3.12 (3H, s, OCH_3 *ketal*), 3.13–3.07 (1H, obscured m, 41-C*H*), 2.73 (2H, d, *J* = 7.5 Hz, 46-CH_2), 2.57 (1H, dd, *J* = 14.5, 5.0 Hz, 44-CH_AH$_B$), 2.46 (1H, dd, *J* = 15.0, 5.5 Hz, 44-CH$_A$$H_B$), 2.07 (1H, dd, *J* = 15.0, 4.0 Hz, 36-CH_AH$_B$), 1.90–1.83 (2H, m, 30-CH_2), 1.78–1.68 (3H, m, 40-C*H*, 31-CH_2), 1.67–1.60 (1H, m, 32-CH_AH$_B$), 1.60–1.50 (1H, obscured m, 36-CH$_A$$H_B$), 1.51–1.45 (1H, m, 34-C*H*), 1.43–1.38 (1H, m, 32-CH$_A$$H_B$), 0.89 (9H, s, SiC(C$H_3$)$_3$), 0.83 (3H, d, *J* = 7.0 Hz, 34-CHCH_3), 0.52 (3H, d, *J* = 6.5 Hz, 40-CHCH_3), 0.05 (3H, s, SiCH_3) and 0.00 (3H, s, SiCH_3); ^{19}F (376 MHz), $CDCl_3$: δ = –71.69.

(1*E*,3*S*)-6-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-1-iodo-5-oxohex-1-en-3-yl (2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate S21



R_f 0.31 (hexane/Et_2O, 50:50); ^1H (500 MHz), $CDCl_3$: δ = 7.45–7.37 (5H, m, Ar-Mosher's), 7.26–7.20 (6H, m, Ar-*ortho*-H), 6.90–6.85 (6H, m, Ar-*meta*-H), 6.15–6.13 (2H, m, 48-C*H*, 49-C*H*), 5.64–5.59 (1H, m, 47-C*H*), 4.84 (1H, d, *J* = 11.0 Hz, OC$H_A$$H_B$-Ar), 4.76 (2H, app d, *J* = 10.7 Hz, OCH_2-Ar), 4.62 (1H, d, *J* = 11.1 Hz, OCH_AH_B-Ar), 4.60 (1H, d, *J* = 11.0 Hz, OCH_AH_B-Ar), 4.51 (1H, d, *J* = 10.6 Hz, OCH_AH_B-Ar), 4.14–4.10 (1H, m, 33-C*H*), 3.82 (3H, s, Ar-OCH_3), 3.80 (6H, s, 2 × Ar-OCH_3), 3.76–3.73 (1H, m, 35-C*H*), 3.65–3.58 (2H, 38-C*H*, 43-C*H*), 3.60 (2H, t, *J* = 6.6 Hz, 29-CH_2), 3.48 (3H, s, OCH_3 Mosher's), 3.25–3.19 (2H, m, 39-C*H*, 42-C*H*), 3.12 (3H, s, OCH_3 *ketal*), 3.14–3.09 (1H, obscured m, 41-C*H*), 2.73 (2H, d, *J* = 6.6 Hz, 46-CH_2), 2.64 (1H, dd, *J* = 14.5, 5.5 Hz, 44-C$H_A$$H_B$), 2.50 (1H, dd, *J* = 14.5, 4.9 Hz, 44-CH_AH_B), 2.07 (1H, dd, *J* = 15.0, 3.8 Hz, 36-C$H_A$$H_B$), 1.90–1.83 (2H, m, 30-$CH_2$), 1.78–1.68 (3H, m, 40-C*H*, 31-CH_2), 1.67–1.60 (1H, m, 32-C$H_A$$H_B$), 1.60–1.50 (1H, obscured m, 36-CH_AH_B), 1.51–1.45 (1H, m, 34-C*H*), 1.42–1.37 (1H, m, 32-CH_AH_B), 0.88 (9H, s, SiC(CH_3)$_3$), 0.86 (3H, d, *J* = 7.2 Hz, 34-CHCH_3), 0.55 (3H, d, *J* = 6.5 Hz, 40-CHCH_3), 0.03 (3H, s, SiCH_3) and 0.00 (3H, s, SiCH_3); ^{19}F (376 MHz), $CDCl_3$: δ = –71.66.





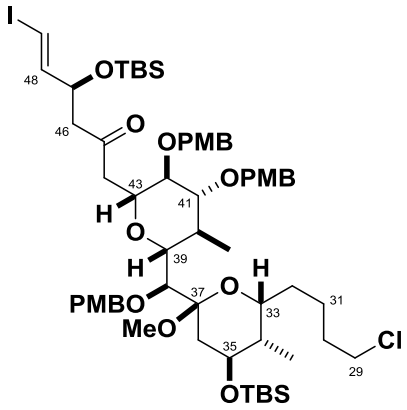
R = 2-methoxy-2-phenyl-2(trifluoromethyl)acetic acid

H	δ (*S*)-ester S20 (ppm)[a]	δ (*R*)-ester S21 (ppm)[a]	Δδ (δ_S-δ_R)-ester × 400 (Hz)
C49H	6.37	6.14	+115
C48H	6.37	6.14	+115
C46H_2	2.73	2.73	0
C44$H_A$$H_B$	2.46	2.50	–20
C44$H_A$$H_B$	2.57	2.64	–35

[a]For chemical shifts quoted as a multiplet in the above procedures, the midpoint of the range has been taken.

Based on the model proposed by Mosher,[7] the C47-CH stereocentre was assigned the **(*S*)-configuration**.

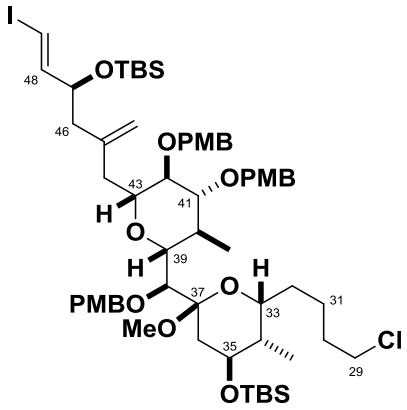
(4*S*,5*E*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-6-iodohex-5-en-2-one S22



To a solution of alcohol **23** (784 mg, 0.71 mmol) in dry DMF (37 mL) was added imidazole (3.61 g, 53.03 mmol) in one portion. The reaction was cooled to 0 °C and TBSCl (2.13 g, 14.15 mmol) added in one portion. The mixture allowed to warm to room temperature slowly over 16 h. The reaction was cooled to 0 °C and quenched by the sequential addition of MeOH (4 mL) and saturated $NH_4Cl_{(aq)}$ (2 mL). The resulting mixture was extracted with Et_2O (3 × 50 mL) and the combined organic layers washed with 10% $LiCl_{(aq)}$ solution (100 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a yellow oil. Flash chromatography using petrol/Et_2O/Et_3N (75:25:1 then 66:33:1) afforded the title compound **S22** as a colourless oil (1.8 g). The product was used directly in the next step of the reaction sequence; R_f 0.45 (petrol/Et_2O, 60:40); $[\alpha]_D^{28.0}$ = +12.3 (*c* 2.4 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2952, 2928, 2855, 1717, 1612, 1586, 1514, 1463, 1443, 1361, 1342, 1302, 1248, 1172, 1092, 1078, 1033, 943, 911, 835, 776; ^1H (600 MHz), $CDCl_3$: δ = 7.29 (2H, d, *J* = 8.2 Hz, Ar-*ortho*-H), 7.26–7.21 (4H, m, Ar-*ortho*-H), 6.90–6.82 (6H, m, Ar-*meta*-H), 6.43 (1H, dd, *J* = 14.4, 5.7 Hz, 48-C*H*), 6.19 (1H, d, *J* = 14.4 Hz, 49-C*H*), 4.82 (1H, d, *J* = 10.9 Hz, OC$H_A$$H_B$-Ar), 4.80 (1H, d, *J* = 11.3 Hz, OC$H_A$$H_B$-Ar), 4.76 (1H, d, *J* = 10.5 Hz, OC$H_A$$H_B$-Ar), 4.67 (1H, d, *J* = 11.3 Hz, OCH$_A$$H_B$-Ar), 4.57 (1H, d, *J* = 10.9 Hz, OCH$_A$$H_B$-Ar), 4.50 (1H, d, *J* = 10.5 Hz, OCH$_A$$H_B$-Ar), 4.47 (1H, app q, *J* = 6.0 Hz, 47-C*H*), 4.17–4.11 (1H, m, 33-C*H*), 3.80 (9H, s, 3 × Ar-OCH_3), 3.76–3.72 (1H, m, 35-C*H*), 3.69–3.63 (1H, m, 43-C*H*), 3.60 (2H, t, *J* = 6.6 Hz, 29-CH_2), 3.47 (1H, s, 38-C*H*), 3.22 (1H, d, *J* = 10.3 Hz, 39-C*H*), 3.18 (1H, t, *J* = 9.0 Hz, 42-C*H*), 3.15–3.08 (1H, m, 41-C*H*), 3.12 (3H, s, OCH_3 *ketal*), 2.64 (1H, dd, *J* = 15.4, 4.4 Hz, 44-C$H_A$$H_B$), 2.57 (1H, dd, *J* = 16.4, 6.7 Hz, 46-C$H_A$$H_B$), 2.52 (1H, dd, *J* = 15.4, 6.4 Hz, 44-CH$_A$$H_B$), 2.44 (1H, dd, *J* = 16.4,

6.1 Hz, 46-CH_AH_B), 2.07 (1H, dd, *J* = 15.2, 3.5 Hz, 36-CH_AH_B), 1.87 (2H, app br. quintet, *J* = 6.8 Hz, 30-CH_2), 1.79–1.69 (2H, m, 31-CH_AH_B, 40-C*H*), 1.69–1.62 (1H, m, 32-CH_AH_B), 1.60 (1H, br. d, *J* = 15.2 Hz, 36-CH_AH_B), 1.57–1.51 (1H, m, 31-CH_AH_B), 1.51–1.45 (1H, m, 34-*C*H), 1.45–1.37 (1H, m, 32-CH_AH_B), 0.90 (9H, s, SiC(CH_3)$_3$), 0.88 (3H, d, *J* = 7.3 Hz, 34-CHCH_3), 0.84 (9H, s, SiC(CH_3)$_3$), 0.47 (3H, d, *J* = 6.4 Hz, 40-CHCH_3), 0.08 (3H, s, SiCH_3), 0.02 (3H, s, SiCH_3), 0.01 (3H, s, SiCH_3) and 0.00 (3H, s, SiCH_3); ^{13}C (101 MHz), $CDCl_3$: δ = 205.3 (C=O), 159.4 (*C*OCH_3-Ar), 159.3 (*C*OCH_3-Ar), 159.2 (*C*OCH_3-Ar), 147.9 (48-*C*H), 131.0 (2C, Ar-*ortho*-C), 130.7 (*C*CH_2-Ar), 130.6 (2C, *C*CH_2-Ar), 129.6 (2C, Ar-*ortho*-C), 129.4 (2C, Ar-*ortho*-C), 113.9 (4C, Ar-*meta*-C), 113.8 (2C, Ar-*meta*-C), 102.4 (37-C), 86.6 (41-*C*H), 81.9 (42-*C*H), 79.8 (39-*C*H), 76.6 (49-*C*H), 75.1 (43-*C*H), 74.7 (O*C*H_2-Ar), 74.3 (38-*C*H), 74.1 (O*C*H_2-Ar), 73.5 (O*C*H_2-Ar), 71.3 (47-*C*H), 70.3 (35-*C*H), 66.9 (33-*C*H), 55.3 (2C, Ar-O*C*H_3), 55.2 (Ar-O*C*H_3), 51.0 (46-*C*H_2), 47.2 (CO*C*H_3 *ketal*), 46.6 (44-*C*H_2), 45.1 (29-*C*H_2), 38.6 (40-*C*H), 38.1 (34-*C*H), 32.8 (30-*C*H_2), 32.3 (32-*C*H_2), 30.6 (36-*C*H_2), 25.9 (3C, SiC(*C*H_3)$_3$), 25.8 (3C, SiC(*C*H_3)$_3$), 23.6 (31-*C*H_2), 18.1 (Si*C*(CH_3)$_3$), 18.0 (Si*C*(CH_3)$_3$), 12.5 (40-CH*C*H_3), 10.4 (34-CH*C*H_3), –4.4 (Si*C*H_3), –4.6 (Si*C*H_3), –4.9 (Si*C*H_3) and –5.0 (Si*C*H_3); *m/z* (+ESI) 1245.4769; $C_{60}H_{92}O_{12}Si_2ClINa$ requires 1245.4758, Δ 0.9 ppm.

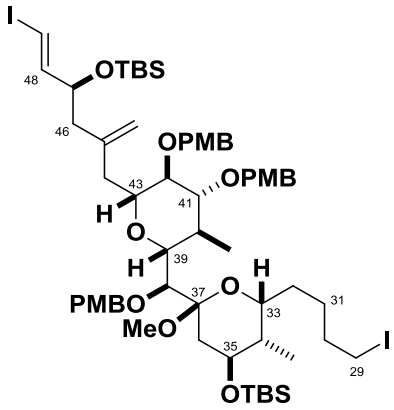
tert-Butyl(((1*E*,3*S*)-5-(((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((_tert_-butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)methyl)-1-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane S23



Activated Zn dust (8.83 g, 135 mmol) and Pb(II)I_2 (622 mg, 1.35 mmol) were suspended in dry THF (35 mL) under argon. Trimethylsilyl chloride (1.06 mL, 8.4 mmol) was added and a Zn-particle aggregation was observed. The suspension was stirred at room temperature for 90 min then cooled to 0 °C and CH_2I_2 (6.04 mL, 75.0 mmol) was added. A vigorous exotherm was observed following the addition. The suspension was allowed to warm to room temperature and stirred for 60 min. The reaction was re-cooled to 0 °C and $TiCl_4$ (1.0 M in CH_2Cl_2, 14.4 mL, 14.4 mmol) was added. The resulting brown/green slurry was allowed to warm to room temperature. After stirring for 3 h, a solution of ketone **S22** (1.8 g) in THF (23 mL) was added *via* cannula over 20 min with rinsing with THF (2 × 6 mL). The resulting suspension stirred for 1 h after which, the reaction mixture was added to an ice-cold 1 M aqueous solution of Rochelle's salt (300 mL) and stirred for 30 min. The resulting white suspension was extracted with Et_2O (3 × 100 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a pale yellow oil. Flash chromatography using petrol/Et_2O (100:0 then 75:25) afforded the title compound **S23** as a yellow oil (794 mg). The product was used directly in the next step of the reaction sequence; R_f 0.55 (petrol/Et_2O, 60:40); $[\alpha]_D^{28.0}$ = +15.7 (*c* 1.4 in $CHCl_3$); ^{1}H (600 MHz), $CDCl_3$: δ = 7.31 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 7.24 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 7.23 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.87 (6H, app d, *J* = 8.3 Hz, Ar-*meta*-H), 6.47 (1H, dd, *J* = 14.3, 5.7 Hz, 48-C*H*), 6.10 (1H, d, *J* = 14.4 Hz, 49-C*H*), 4.91 (1H, br. s, 45-C=CH_AH_B), 4.85–4.79 (2H, m, OCH_2-Ar), 4.82 (br. s, 45-C=CH_AH_B), 4.77 (1H, d, *J* = 10.4 Hz, OCH_AH_B-Ar), 4.72 (1H, d, *J* = 11.4 Hz, OCH_AH_B-Ar), 4.52 (1H, d, *J* = 10.8 Hz, OCH_AH_B-Ar), 4.51 (1H, d, *J* = 10.5 Hz, OCH_AH_B-Ar), 4.17–4.11 (2H, m, 33-C*H*, 47-C*H*),

3.80 (9H, s, 3 × Ar-OC*H*$_3$), 3.77–3.73 (1H, m, 35-C*H*), 3.60 (2H, br. t, *J* = 6.5 Hz, 29-C*H*$_2$), 3.46 (1H, s, 38-C*H*), 3.28 (1H, t, *J* = 9.1 Hz, 43-C*H*), 3.16 (1H, dd, *J* = 9.4, 9.1 Hz, 42-C*H*), 3.11 (1H, d, *J* = 10.6 Hz, 39-C*H*), 3.10 (3H, s, OC*H*$_3$ *ketal*), 3.07 (1H, dd, *J* = 9.9, 9.4 Hz, 41-C*H*), 2.44 (1H, d, *J* = 14.7 Hz, 44-C*H*$_A$H$_B$), 2.27 (1H, dd, *J* = 13.4, 6.4 Hz, 46-C*H*$_A$H$_B$), 2.20–2.13 (2H, m, 44-CH$_A$*H*$_B$, 46-CH$_A$*H*$_B$), 2.10 (1H, dd, *J* = 15.5, 3.6 Hz, 36-C*H*$_A$H$_B$), 1.87 (2H, app br. quintet, *J* = 6.8 Hz, 30-C*H*$_2$), 1.78–1.70 (2H, m, 31-C*H*$_A$H$_B$, 40-C*H*), 1.70–1.57 (2H, m, 32-C*H*$_A$H$_B$, 36-CH$_A$*H*$_B$), 1.58–1.48 (1H, m, 31-CH$_A$*H*$_B$), 1.48–1.36 (2H, m, 32-CH$_A$*H*$_B$, 34-*C*H), 0.90–0.85 (3H, obscured d, 34-CHC*H*$_3$), 0.88 (9H, s, SiC(C*H*$_3$)$_3$), 0.86 (9H, s, SiC(C*H*$_3$)$_3$), 0.41 (3H, d, *J* = 6.4 Hz, 40-CHC*H*$_3$), 0.03 (3H, s, SiC*H*$_3$), 0.00 (6H, s, SiC*H*$_3$) and –0.02 (3H, s, SiC*H*$_3$); ^{13}C (101 MHz), CDCl$_3$: δ = 159.4 (*C*OCH$_3$-Ar), 159.3 (*C*OCH$_3$-Ar), 159.2 (*C*OCH$_3$-Ar), 148.5 (48-*C*H), 141.9 (45-C), 131.3 (2C, Ar-*ortho*-C), 130.7 (2C, *C*CH$_2$-Ar), 130.6 (*C*CH$_2$-Ar), 129.6 (2C, Ar-*ortho*-C), 129.4 (2C, Ar-*ortho*-C), 115.8 (C45-C=*C*H$_2$), 113.9 (4C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 102.6 (37-C), 86.9 (41-*C*H), 82.6 (42-*C*H), 79.7 (39-*C*H), 78.2 (43-*C*H), 75.9 (49-*C*H), 74.6 (O*C*H$_2$-Ar), 74.5 (O*C*H$_2$-Ar), 73.9 (38-*C*H), 73.8 (47-*C*H), 73.0 (O*C*H$_2$-Ar), 70.2 (35-*C*H), 66.8 (33-*C*H), 55.3 (3C, Ar-OCH$_3$), 47.2 (CO*C*H$_3$ *ketal*), 45.1 (29-*C*H$_2$), 44.7 (46-*C*H$_2$), 38.5 (40-*C*H), 38.0 (44-*C*H), 37.5 (34-*C*H), 32.7 (30-*C*H$_2$), 32.3 (32-*C*H$_2$), 30.4 (36-*C*H$_2$), 25.9 (3C, SiC(*C*H$_3$)$_3$), 25.8 (3C, SiC(*C*H$_3$)$_3$), 23.5 (31-*C*H$_2$), 18.2 (Si*C*(CH$_3$)$_3$), 17.9 (Si*C*(CH$_3$)$_3$), 12.6 (40-CH*C*H$_3$), 10.3 (34-CH*C*H$_3$), –4.4 (Si*C*H$_3$), –4.6 (Si*C*H$_3$), –4.7 (Si*C*H$_3$), and –4.8 (Si*C*H$_3$); *m/z* (+ESI) 1243.5022; $C_{61}H_{94}O_{11}Si_2ClINa$ requires 1243.4966, Δ 4.5 ppm.

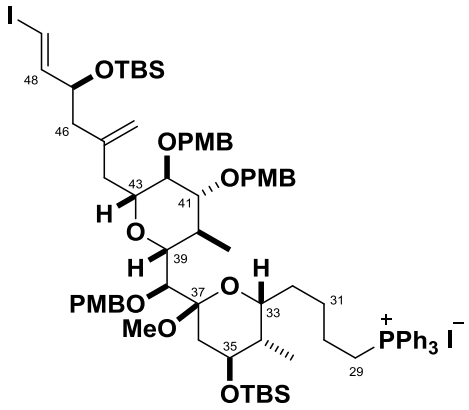
tert-Butyl(((1*E*,3*S*)-5-(((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-iodobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)methyl)-1-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane S24



To a solution of vinyl iodide **S23** (794 mg) in a Biotage® microwave vial under argon was added acetone (21 mL), NaI (3.90 g, 26.0 mmol), $NaHCO_3$ (1.09 g, 13.0 mmol), Na_2SO_3 (819 mg, 6.5 mmol) and 1-iodopropane (1.27 mL, 13.0 mmol). The vial was sealed and the reaction heated to 67 °C and maintained at this temperature for 15 h, after which it was cooled to room temperature. The reaction was quenched with H_2O (20 mL) and diluted with Et_2O (20 mL). The layers were separated and the aqueous further extracted with Et_2O (3 × 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as an orange viscous oil. Flash chromatography using petrol/Et_2O/Et_3N (75:25:1) afforded the title compound **S24** as a yellow oil (687 mg, 74% over 3 steps); R_f 0.55 (petrol/Et_2O, 60:40); $[\alpha]_D^{27.0}$ = +15.7 (*c* 1.6 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2948, 2928, 2855, 1612, 1586, 1513, 1463, 1441, 1360, 1302, 1247, 1215, 1172, 1073, 1034, 940, 907, 898, 833, 774; ^1H (600 MHz), $CDCl_3$: δ = 7.32 (2H, d, *J* = 8.4 Hz, Ar-*ortho*-H), 7.24 (2H, d, *J* = 8.3 Hz, Ar-*ortho*-H), 7.23 (2H, d, *J* = 8.2 Hz, Ar-*ortho*-H), 6.89–6.85 (6H, app d, *J* = 8.3 Hz, Ar-*meta*-H), 6.46 (1H, dd, *J* = 14.3, 5.6 Hz, 48-C*H*), 6.09 (1H, dd, *J* = 14.3, 0.7 Hz, 49-C*H*), 4.91 (1H, br. s, 45-C=CH_AH_B), 4.84–4.79 (3H, m, OCH_2-Ar, 45-C=CH_AH_B), 4.77 (1H, d, *J* = 10.5 Hz, OCH_AH_B-Ar), 4.72 (1H, d, *J* = 11.4 Hz, OCH_AH_B-Ar), 4.52 (1H, d, *J* = 10.4 Hz, OCH_AH_B-Ar), 4.50 (1H, d, *J* = 10.2 Hz, OCH_AH_B-Ar), 4.15–4.10 (2H, m, 33-C*H*, 47-C*H*), 3.81 (3H, s, Ar-OCH_3), 3.80 (6H, br. s, 2 × Ar-OCH_3), 3.77–3.73 (1H, m, 35-C*H*), 3.45 (1H, br. s, 38-C*H*), 3.30–3.21 (3H, m, 29-CH_2, 43-C*H*), 3.16 (1H, dd, *J* = 9.2, 8.9 Hz, 42-C*H*), 3.13–3.09 (1H, m, 39-C*H*), 3.10 (3H, s, OCH_3 *ketal*), 3.07 (1H, dd, *J* = 10.0, 9.2 Hz, 41-C*H*), 2.44 (1H, br. d, *J* = 14.7 Hz, 44-CH_AH_B), 2.27 (1H, dd, *J* = 12.0, 6.3 Hz, 46-CH_AH_B), 2.19–2.13 (2H, m, 44-CH_AH_B, 46-CH_AH_B), 2.11 (1H, dd, *J* = 15.5, 3.6 Hz, 36-CH_AH_B),

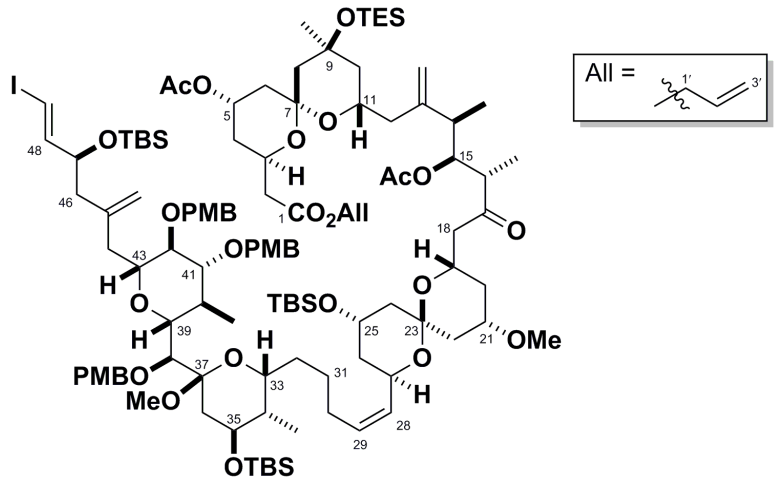
1.91 (2H, app br. quintet, J = 7.2 Hz, 30-CH_2), 1.77–1.71 (1H, m, 40-CH), 1.70–1.60 (3H, m, 31-CH_2, 36-C$H_A H_B$), 1.51–1.34 (3H, m, 32-CH_2, 34-CH), 0.91–0.82 (3H, obscured d, 34-CHCH_3), 0.88 (9H, s, SiC(CH_3)$_3$), 0.86 (9H, s, SiC(CH_3)$_3$), 0.40 (3H, d, J = 6.4 Hz, 40-CHCH_3), 0.02 (3H, s, SiCH_3), 0.00 (6H, s, 2 × SiCH_3) and –0.02 (3H, s, SiCH_3); ^{13}C (101 MHz), $CDCl_3$: δ = 159.4 (*C*OCH$_3$-Ar), 159.3 (*C*OCH$_3$-Ar), 159.2 (*C*OCH$_3$-Ar), 148.5 (48-*C*H), 142.0 (45-C), 131.2 (2C, Ar-*ortho*-C), 130.8 (2C, *C*CH$_2$-Ar), 130.7 (*C*CH$_2$-Ar), 129.6 (2C, Ar-*ortho*-C), 129.4 (2C, Ar-*ortho*-C), 115.4 (C45-C=*C*H$_2$), 113.9 (4C, Ar-*meta*-C), 113.7 (2C, Ar-*meta*-C), 102.6 (37-C), 87.0 (41-*C*H), 82.6 (42-*C*H), 79.7 (39-*C*H), 78.2 (43-*C*H), 75.8 (49-*C*H), 74.6 (O*C*H$_2$-Ar), 74.5 (O*C*H$_2$-Ar), 74.1 (38-*C*H), 73.8 (47-*C*H), 73.2 (O*C*H$_2$-Ar), 70.2 (35-*C*H), 66.8 (33-*C*H), 55.3 (3C, Ar-O*C*H$_3$), 47.2 (CO*C*H$_3$ *ketal*), 44.7 (46-*C*H$_2$), 38.5 (40-*C*H), 38.0 (34-*C*H), 37.9 (44-*C*H), 33.6 (30-*C*H$_2$), 30.8 (36-*C*H$_2$), 30.4 (32-*C*H$_2$), 27.2 (31-*C*H$_2$), 25.9 (3C, SiC(*C*H$_3$)$_3$), 25.8 (3C, SiC(*C*H$_3$)$_3$), 18.2 (Si*C*(CH$_3$)$_3$), 18.0 (Si*C*(CH$_3$)$_3$), 12.6 (40-CH*C*H$_3$), 10.3 (34-CH*C*H$_3$), 7.0 (29-CH$_2$), –4.4 (Si*C*H$_3$), –4.6 (Si*C*H$_3$), –4.7 (Si*C*H$_3$) and –4.8 (Si*C*H$_3$); *m/z* (+ESI) 1335.4302; $C_{61}H_{94}O_{11}Si_2I_2Na$ requires 1335.4322, Δ 1.5 ppm.

(4-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-bis((4-methoxybenzyl)oxy)-3-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)butyl)(triphenyl)phosphonium iodide 3



To a solution of primary iodide **S24** (54 mg, 41.1 μmol) in a Biotage® microwave vial under argon was added MeCN (503 μL), DIPEA (36 μL, 0.206 mmol) and PPh_3 (54 mg, 0.206 mmol). The vial was sealed and the reaction heated to 90 °C for 48 h. The reaction was cooled to room temperature and concentrated *in vacuo* to give the crude product as a brown solid which was used directly in the next step of the reaction.

Prop-2-en-1-yl ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-bis((4-methoxybenzyl)oxy)-3-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetate 25

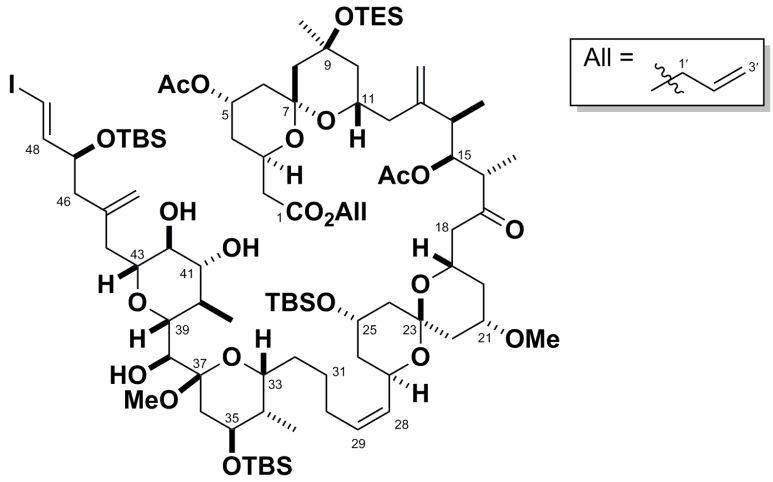


To a solution of phosphonium iodide **3** (64.7 mg, 41.1 μmol) in THF (0.6 mL) at room temperature was added CaH_2 and the mixture stirred for 1 h. A solution of the aldehyde coupling partner **24**[8] (60 mg, 54.5 μmol) in THF (0.4 mL) was made, and dried by stirring with CaH_2 for 2 h. The phosphonium iodide mixture was cooled to –78 °C and LiHMDS (1 M solution in THF, 123 μL, 0.123 mmol) added dropwise resulting in a bright orange solution. The solution was allowed to warm to –20 °C over 1 h 15 min after which it was re-cooled to –70 °C and the aldehyde (**24**) solution added dropwise *via* syringe with further rinsing with THF (0.4 mL). The reaction was allowed to warm to 10 °C over 4 h and the resulting red solution quenched by the addition of sat. aq. NH_4Cl (2 mL). The mixture was extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a pale yellow oil containing brown solid. Flash chromatography using petrol/Et_2O/Et_3N (45:55:1, 40:60 then 25:75) afforded the title compound **25** as a pale yellow oil (50 mg, 56% over 2 steps); R_f 0.25 (petrol/Et_2O, 40:60); $[\alpha]_D^{26.0}$ = –12.9 (*c* 0.8 in C_6H_6); IR (film) ν_{max}/cm^{-1} 2953, 2929, 2857, 1735, 1669, 1612, 1586, 1514, 1462, 1432, 1362, 1301, 1248, 1173, 1159, 1142, 1094, 1064, 1029, 1004, 936, 908, 888, 834, 774; ^1H (600 MHz), C_6D_6: δ = 7.43 (2H, d, *J* = 8.4 Hz, Ar-*ortho*-H), 7.35 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 7.26 (2H, d, *J* = 8.5 Hz, Ar-*ortho*-H), 6.87–6.80 (6H, m, Ar-*meta*-H), 6.62 (1H, dd, *J* = 14.3, 5.9 Hz, 48-C*H*), 6.22 (1H, d, *J* = 14.3

Hz, 49-C*H*), 5.84–5.78 (1H, m, 2′-C*H*), 5.79–5.71 (1H, m, 28-C*H*), 5.67–5.59 (2H, m, 15-C*H*, 27-C*H*), 5.58–5.50 (1H, m, 29-C*H*), 5.19 (1H, br. s, 13′-C=CH_AH$_B$), 5.17 (1H, obscured dd, *J* = 15.9, 1.3 Hz, 3′-C=CH_AH$_B$), 5.09 (1H, br. s, 45-C=CH_AH$_B$), 5.06–5.00 (4H, m, 3′-C=CH$_A$$H_B$, 5-C*H*, 45-C=CH$_A$$H_B$, OC$H_AH_B$-Ar), 4.97 (1H, br. s, 13′-C=CH$_A$$H_B$), 4.96 (1H, d, *J* = 11.0 Hz, OCH$_A$$H_B$-Ar), 4.93 (1H, d, *J* = 11.1 Hz, OCH_AH$_B$-Ar), 4.75 (1H, d, *J* = 11.0 Hz, OCH$_A$$H_B$-Ar), 4.62 (1H, d, *J* = 10.9 Hz, OCH_AH$_B$-Ar), 4.53 (1H, d, *J* = 11.4 Hz, OCH$_A$$H_B$-Ar), 4.51–4.45 (3H, m, 1′-C=CH_2, 3-C*H*), 4.40–4.31 (2H, m, 11-C*H*, 33-C*H*), 4.26–4.14 (2H, m, 19-C*H*, 47-C*H*), 3.98–3.94 (1H, m, 35-C*H*), 3.93–3.89 (1H, m, 25-C*H*), 3.70 (1H, br. s, 38-C*H*), 3.52 (1H, app t, *J* = 8.3, 7.9 Hz, 43-C*H*), 3.38–3.34 (2H, m, 39-C*H*, 42-C*H*), 3.36 (3H, s, Ar-OCH_3), 3.33 (3H, s, Ar-OCH_3), 3.32 (3H, s, Ar-OCH_3), 3.29–3.23 (1H, m, 21-C*H*), 3.21 (3H, s, OCH_3 *ketal*), 3.21–3.14 (1H, m, 41-C*H*), 3.12–3.08 (1H, m, 18-CH_AH$_B$), 3.05 (3H, s, 21-CHOCH_3), 2.93 (1H, dq, *J* = 9.6, 7.1 Hz, 16-C*H*), 2.83–2.72 (2H, m, 14-C*H*, 18-CH$_A$$H_B$), 2.69–2.62 (2H, m, 2-C$H_AH_B$, 44-C$H_AH_B$), 2.57–2.50 (3H, m, 12-CH_AH$_B$, 36-CH_AH$_B$, 46-CH_AH$_B$), 2.47–2.33 (5H, m, 12-CH$_A$$H_B$, 20-C$H_AH_B$, 30-C$H_2$, 46-CH$_A$$H_B$), 2.31–2.25 (2H, m, 2-CH$_A$$H_B$, 44-CH$_A$$H_B$), 2.21–2.07 (3H, m, 22-CH_AH$_B$, 24-CH_AH$_B$, 40-C*H*), 2.02–1.95 (1H, m, 36-CH$_A$$H_B$), 1.94 (3H, s, COC$H_3$), 1.94–1.88 (1H, m, 6-C$H_AH_B$), 1.86–1.80 (1H, m, 32-CH_AH$_B$), 1.79 (3H, s, COCH_3), 1.79–1.66 (4H, m, 4-CH_AH$_B$, 22-CH$_A$$H_B$, 31-C$H_2$), 1.66–1.56 (4H, m, 8-C$H_AH_B$, 26-C$H_2$, 34-C*H*), 1.52–1.37 (2H, m, 10-CH_AH$_B$, 32-CH$_A$$H_B$), 1.27 (3H, d, *J* = 6.7 Hz, 14-CHCH_3), 1.19 (3H, d, *J* = 6.9 Hz, 16-CHCH_3), 1.24–1.14 (2H, m, 4-CH$_A$$H_B$, 6-CH$_A$$H_B$), 1.13–1.10 (1H, m, 24-CH$_A$$H_B$), 1.07–0.98 (36H, m, 8-CH$_A$$H_B$, 9-CC$H_3$, 10-CH$_A$$H_B$, 20-CH$_A$$H_B$, 34-CHC$H_3$, 3 × SiCH$_2CH_3$, 2 × SiC(C$H_3$)$_3$), 0.95 (9H, s, SiC(C$H_3$)$_3$), 0.79 (3H, d, *J* = 6.4 Hz, 40-CHCH_3), 0.60 (6H, q, *J* = 7.8 Hz, SiCH_2CH$_3$), 0.24 (3H, s, SiCH_3), 0.14 (3H, s, SiCH_3), 0.08 (3H, s, SiCH_3), 0.07 (6H, s, 2 × SiCH_3) and 0.02 (3H, s, SiCH_3); ^{13}C (150 MHz), C$_6$D$_6$: δ = 209.7 (17-*C*O), 170.3 (*C*OCH$_3$), 170.2 (1-*C*O$_2$All), 168.8 (*C*OCH$_3$), 159.9 (*C*OCH$_3$-Ar), 158.8 (2C, *C*OCH$_3$-Ar), 149.2 (48-*C*H), 148.0 (13-*C*), 142.9 (45-*C*), 132.7 (2′-*C*H), 132.3 (28-*C*H), 131.7 (*C*CH$_2$-Ar), 131.5 (*C*CH$_2$-Ar), 131.4 (*C*CH$_2$-Ar), 131.0 (29-*C*H), 130.9 (2C, Ar-*ortho*-C), 129.5 (4C, Ar-*ortho*-C), 117.9 (3′-*C*H$_2$), 115.8 (45-C*C*H$_2$), 114.2 (2C, Ar-*meta*-C), 114.1 (4C, Ar-*meta*-C), 113.8 (13-C*C*H$_2$), 103.0 (37-*C*), 98.4 (23-*C*), 97.1 (7-*C*), 87.2 (41-*C*H, weak), 83.3 (39-*C*H), 79.9 (42-*C*H), 78.6 (43-*C*H), 76.3 (49-*C*H), 76.1 (38-*C*H), 74.9 (15-*C*H), 74.3 (47-*C*H), 73.9 (21-*C*H), 71.1 (35-*C*H), 70.7 (9-*C*), 67.6 (33-*C*H), 67.0 (5-*C*H), 66.7 (19-*C*H), 65.3 (25-*C*H), 65.0 (1′-*C*H$_2$), 64.3 (11-*C*H), 62.3 (27-*C*H), 61.2 (3-*C*H), 55.2 (21-CHO*C*H$_3$), 54.9 (Ar-O*C*H$_3$), 54.8 (2C, Ar-O*C*H$_3$), 51.2 (18-*C*H$_2$), 48.0 (16-*C*H), 47.9 (8-*C*H$_2$), 47.3 (CO*C*H$_3$ *ketal*), 45.6 (10-*C*H$_2$), 45.5 (2C, 12-*C*H$_2$, 20-*C*H$_2$), 44.6 (22-*C*H$_2$), 43.2 (46-*C*H$_2$), 40.8 (2-*C*H$_2$), 39.5 (26-*C*H$_2$), 39.2 (40-*C*H), 38.9 (14-*C*H), 38.8 (44-*C*H$_2$), 38.1 (6-*C*H$_2$), 38.0 (34-*C*H), 34.9 (24-*C*H$_2$), 34.4 (4-*C*H, 9-C*C*H$_3$, 31-*C*H$_2$), 32.2 (36-*C*H$_2$), 28.8 (30-*C*H$_2$), 26.9 (32-*C*H$_2$), 26.2 (6C, SiC(*C*H$_3$)$_3$), 26.1 (3C, SiC(*C*H$_3$)$_3$), 21.4 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 18.4 (3C, Si*C*(CH$_3$)$_3$), 13.7 (16-CH*C*H$_3$), 13.4 (40-CH*C*H$_3$), 12.2 (14-CH*C*H$_3$), 10.7 (34-CH*C*H$_3$), 7.7 (3C, SiCH$_2$*C*H$_3$), 7.3 (3C, Si*C*H$_2$CH$_3$), –4.1 (Si*C*H$_3$), –4.3 (Si*C*H$_3$), –4.4 (Si*C*H$_3$), –

4.5 (Si*C*H$_3$), –4.7 (Si*C*H$_3$), –4.8 (Si*C*H$_3$); *m/z* (+ESI) 2200.0806; $C_{113}H_{181}O_{25}Si_4INa$ requires 2200.0906, Δ 4.5 ppm.

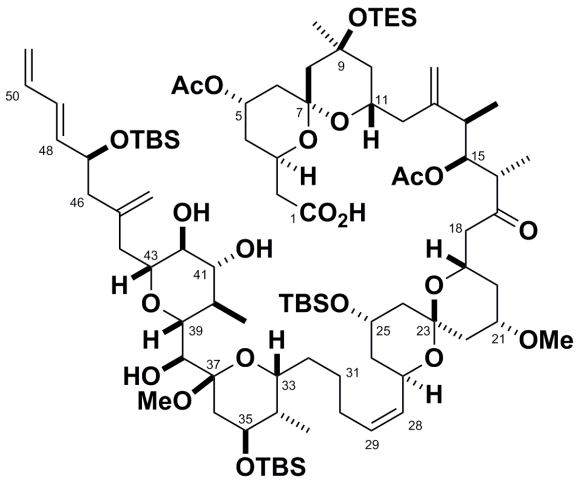
Prop-2-en-1-yl ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*S*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-dihydroxy-3-methyltetrahydro-2*H*-pyran-2-yl)(hydroxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetate S25



To a solution of **26** (124 mg, 0.057 mmol) in CH_2Cl_2 (3.34 mL)/pH 7 phosphate buffer (334 μL) at 0 °C was added DDQ (155 mg, 0.684 mmol). The reaction mixture was maintained between 0 °C and 10 °C for 45 min, after which 10% $Na_2S_2O_{3(aq)}$ (3 mL) was added and the mixture allowed to warm to room temperature. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organics dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a yellow oil. Flash chromatography using CH_2Cl_2/acetone (90:10 then 80:20) afforded the title compound **S25** as a pale yellow oil (74 mg, 71%); R_f 0.60 (CH_2Cl_2/acetone, 80:20); $[\alpha]_D^{25.6}$ = –8.5 (*c* 0.6 in C_6H_6); IR (film) ν_{max}/cm^{-1} 3480, 2952, 2930, 2857, 1735, 1461, 1433, 1417, 1407, 1370, 1364, 1249, 1231, 1175, 1159, 1142, 1093, 1076, 1059, 1027, 1004, 938, 907, 889, 834, 774; ^{1}H (600 MHz), C_6D_6: δ = 6.63 (1H, dd, *J* = 14.4, 6.0 Hz, 48-C*H*), 6.27 (1H, d, *J* = 14.4 Hz, 49-C*H*), 5.79 (1H, m, 2′-C*H*), 5.72 (1H, app t, *J* = 9.9, 9.1 Hz, 28-C*H*), 5.66–5.58 (2H, m, 15-C*H*, 27-C*H*), 5.53–5.47 (1H, m, 29-C*H*), 5.21 (1H, s, 13-C=CH_AH$_B$), 5.19 (1H, d, *J* = 10.6 Hz, 3′-C=CH_AH$_B$), 5.06 (1H, d, *J* = 10.5 Hz, 3′-C=CH$_A$$H_B$), 5.03–4.96 (4H, m, 5-C*H*, 13-C=CH$_A$$H_B$, 45-C=C$H_AH_B$, 45-C=CH$_A$$H_B$), 4.53 (1H, td, *J* = 13.3, 5.6 Hz, 1′-C=CH_AH$_B$), 4.50–4.45 (2H, m, 1′-

C=CH$_A$*H$_B$*, 3-C*H*), 4.38–4.32 (1H, app t, *J* = 9.4, 8.7 Hz, 11-C*H*), 4.32–4.28 (33-C*H*), 4.22 (1H, app q, *J* = 6.3 Hz, 47-C*H*), 4.19 (1H, app t, *J* = 10.3 Hz, 19-C*H*), 3.92 (2H, br. s, 25-C*H*, 35-C*H*), 3.81 (1H, br. s, 38-C*H*), 3.36 (1H, td, *J* = 9.4, 2.0 Hz, 43-C*H*), 3.32 (1H, br. d, *J* = 10.3 Hz, 39-C*H*), 3.29–3.23 (1H, m, 21-C*H*), 3.17 (3H, s, OC*H*$_3$ *ketal*), 3.11 (1H, dd, *J* = 18.5, 2.4 Hz, 18-C*H*$_A$H$_B$), 3.07 (3H, s, 21-CHOC*H*$_3$), 3.06–3.04 (1H, obscured m, 42-C*H*), 3.02–2.99 (1H, m, 16-C*H*), 2.95 (1H, app t, *J* = 9.8, 9.1 Hz, 41-C*H*), 2.85–2.79 (2H, m, 14-C*H*, 18-CH$_A$*H$_B$*), 2.72–2.65 (2H, 2-C*H*$_A$H$_B$, 44-C*H*$_A$H$_B$), 2.54 (1H, br. d, *J* = 12.3 Hz, 12-C*H*$_A$H$_B$), 2.47–2.40 (2H, m, 12-CH$_A$*H$_B$*, 46-C*H*$_A$H$_B$), 2.42–2.34 (1H, m, 20-C*H*$_A$H$_B$), 2.35–2.29 (3H, m, 30-C*H*$_2$, 46-CH$_A$*H$_B$*), 2.29 (1H, dd, *J* = 16.1, 7.3 Hz, 2-CH$_A$*H$_B$*), 2.25–2.16 (2H, m, 36-C*H*$_A$H$_B$, 44-CH$_A$*H$_B$*), 2.12 (2H, app t, *J* = 15.9, 12.7 Hz, 22-C*H*$_A$H$_B$, 24-C*H*$_A$H$_B$), 1.97 (3H, s, COC*H*$_3$), 1.98–1.96 (1H, m, 40-C*H*), 1.91 (1H, d, *J* = 14.9 Hz, 6-C*H*$_A$H$_B$), 1.83 (3H, s, COC*H*$_3$), 1.81–1.71 (6H, m, 4-C*H*$_A$H$_B$, 22-CH$_A$*H$_B$*, 31-C*H*$_2$, 32-C*H*$_A$H$_B$, 36-CH$_A$*H$_B$*), 1.66–1.55 (4H, m, 8-C*H*$_A$H$_B$, 26-C*H*$_A$H$_B$, 26-CH$_A$*H$_B$*, 34-C*H*), 1.50–1.39 (2H, m, 10-C*H*$_A$H$_B$, 32-CH$_A$*H$_B$*), 1.30 (3H, d, *J* = 6.8 Hz, 14-CHC*H*$_3$), 1.27–1.24 (1H, m, 6-CH$_A$*H$_B$*), 1.21 (3H, d, *J* = 6.9 Hz, 16-CHC*H*$_3$), 1.19–1.11 (2H, m, 4-CH$_A$*H$_B$*, 24-CH$_A$*H$_B$*), 1.10–0.95 (48H, m, 8-CH$_A$*H$_B$*, 9-CC*H*$_3$, 10-CH$_A$*H$_B$*, 20-CH$_A$*H$_B$*, 34-CHC*H*$_3$, 40-CHC*H*$_3$, 3 × SiCH$_2$C*H*$_3$, 3 × SiC(C*H*$_3$)$_3$), 0.61 (6H, q, *J* = 7.9 Hz, SiC*H*$_2$CH$_3$), 0.22 (3H, s, SiC*H*$_3$), 0.13 (3H, s, SiC*H*$_3$), 0.10 (6H, s, 2 × SiC*H*$_3$), 0.09 (3H, s, SiC*H*$_3$) and 0.06 (3H, s, SiC*H*$_3$); ^{13}C (150 MHz), C$_6$D$_6$: δ = 209.8 (17-*C*O), 170.4 (2C, 1-*C*O$_2$All, *C*OCH$_3$), 168.8 (*C*OCH$_3$), 149.2 (48-*C*H), 148.0 (13-*C*), 142.9 (45-*C*), 132.7 (2′-*C*H), 132.2 (28-*C*H), 131.2 (29-*C*H), 118.0 (3′-*C*H$_2$), 115.8 (45-*C*H$_2$), 113.9 (13-*C*H$_2$), 101.2 (37-*C*), 98.4 (23-*C*), 97.1 (7-*C*), 79.1 (41-*C*H), 78.4 (39-*C*H), 78.0 (43-*C*H), 76.4 (49-*C*H), 75.7 (42-*C*H), 74.9 (15-*C*H), 74.8 (47-*C*H), 73.9 (21-*C*H), 71.0 (35-*C*H), 70.7 (38-*C*H), 70.6 (9-*C*), 67.6 (33-*C*H), 67.0 (5-*C*H), 66.6 (19-*C*H), 65.3 (25-*C*H), 65.1 (1′-*C*H$_2$), 64.2 (11-*C*H), 62.1 (27-*C*H), 61.2 (3-*C*H), 55.2 (21-CHO*C*H$_3$), 51.1 (18-*C*H$_2$), 48.0 (16-*C*H), 47.9 (8-*C*H$_2$), 47.4 (CO*C*H$_3$ *ketal*), 45.6 (10-*C*H$_2$), 45.2 (46-*C*H$_2$), 44.5 (22-*C*H$_2$), 43.2 (12-*C*H$_2$), 40.8 (2-*C*H$_2$), 39.5 (44-*C*H$_2$), 39.1 (2C, 26-*C*H$_2$, 40-*C*H), 38.8 (2C, 6-*C*H$_2$, 34-*C*H), 38.1 (20-*C*H$_2$), 38.0 (14-*C*H), 35.0 (24-*C*H$_2$), 34.3 (4-*C*H$_2$), 33.2 (31-*C*H$_2$), 32.2 (9-C*C*H$_3$), 30.8 (36-*C*H$_2$), 28.8 (30-*C*H$_2$), 26.8 (32-*C*H$_2$), 26.2 (6C, SiC(*C*H$_3$)$_3$), 26.1 (3C, SiC(*C*H$_3$)$_3$), 21.5 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 18.4 (3C, Si*C*(CH$_3$)$_3$), 13.7 (16-CH*C*H$_3$), 13.3 (40-CH*C*H$_3$), 12.3 (14-CH*C*H$_3$), 10.6 (34-CH*C*H$_3$), 7.7 (3C, SiCH$_2$*C*H$_3$), 7.3 (3C, Si*C*H$_2$CH$_3$), –4.2 (Si*C*H$_3$), –4.3 (Si*C*H$_3$), –4.5 (Si*C*H$_3$), –4.6 (Si*C*H$_3$), –4.7 (Si*C*H$_3$) and –4.8 (Si*C*H$_3$); *m/z* (+ESI) 1839.9204; C$_{89}$H$_{157}$O$_{22}$Si$_4$INa requires 1839.9181, Δ 1.3 ppm.

((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(Acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*S*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-2-methylideneocta-5,7-dien-1-yl)-4,5-dihydroxy-3-methyltetrahydro-2*H*-pyran-2-yl)(hydroxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetic acid 26

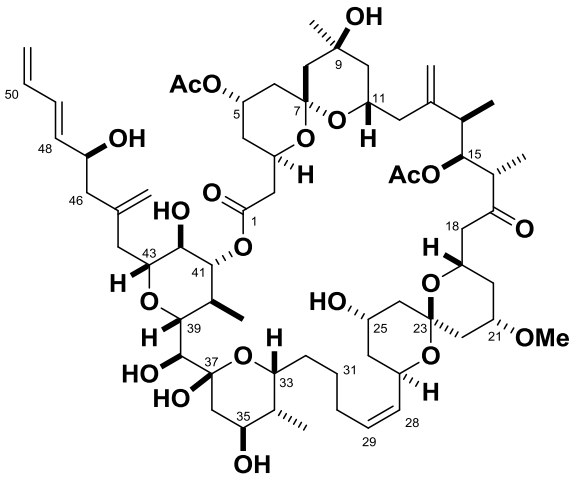


To solution of vinyl iodide **S25** (11.6 mg, 6.4 μmol) in DMF (0.8 mL) and THF (0.8 mL) at room temperature was added tributyl(vinyl)tin (9.4 μL, 32 μmol), $AsPh_3$ (0.8 mg, 2.6 μmol) and morpholine (5.6 μL, 64 μmol) sequentially. The resulting mixture was degassed for 15 min using argon after which Pd_2dba_3 (0.6 mg, 0.64 μmol) was added in one portion to give a yellow solution. The reaction was stirred in the absence of light for 1 h 30 min at which point additional Pd_2dba_3 (0.6 mg, 0.64 μmol) was added and the stirring continued for a further 1 h 45 min. The mixture was diluted with Et_2O (5 mL), washed with 10% $LiCl_{(aq)}$ solution (5 mL) and the layers separated. The aqueous was further extracted with Et_2O (3 × 5 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a yellow oil. Flash chromatography using hexane/EtOAc (100:0, 70:30, 100:0) then CH_2Cl_2/MeOH (99:1, 98:2, 97:3, 95:5) afforded the title compound **26** as a white foam (9.0 mg, 84%); R_f 0.28 (CH_2Cl_2/MeOH, 95:5); $[\alpha]_D^{25.5}$ = +4.2 (*c* 0.33 in CH_2Cl_2); IR (film) ν_{max}/cm^{-1} 3420, 2956, 2928, 2856, 1735, 1720, 1461, 1433, 1413, 1370, 1256, 1229, 1184, 1143, 1095, 1074, 1060, 1026, 1004, 906, 892, 833, 800, 774; ^{1}H (500 MHz), CD_3CN: δ = 6.37–6.30 (1H, m, 50-C*H*), 6.18 (1H, dd, *J* = 15.5, 15.2 Hz, 49-C*H*), 5.69 (1H, dd, *J* = 15.2, 6.4 Hz, 48-C*H*), 5.47–5.41 (1H, m, 29-C*H*), 5.34 (1H, app t, *J* = 8.7, 8.3 Hz, 28-C*H*), 5.21–5.15 (2H, m, 27-C*H*, 51-CH_AH_B), 5.13 (1H, dd, *J* = 10.1, 2.3 Hz, 15-C*H*), 5.04 (1H, dd,

J = 10.1, 1.5 Hz, 51-CH$_A$*H$_B$*), 4.93 (1H, br. s, 13-C=C*H$_A$*H$_B$), 4.92–4.89 (1H, m, 5-C*H*), 4.85 (2H, br. s, 13-C=CH$_A$*H$_B$*, 45-C=C*H$_A$*H$_B$), 4.82 (1H, br. s, 45-C=C*H$_A$*H$_B$), 4.32 (1H, app q, *J* = 6.5 Hz, 47-C*H*), 4.26–4.15 (2H, m, 3-C*H*, 11-C*H*), 4.12 (1H, br. t, *J* = 3.1 Hz, 25-C*H*), 4.08–4.03 (1H, m, 33-C*H*), 3.90 (1H, tt, *J* = 11.3, 2.4 Hz, 19-C*H*), 3.77–3.75 (1H, m, 35-C*H*), 3.60 (1H, br. s, 38-C*H*), 3.51–3.44 (1H, m, 21-C*H*), 3.27 (1H, td, *J* = 9.7, 2.0 Hz, 43-C*H*), 3.23 (3H, s, 21-CHOC*H*$_3$), 3.22 (1H, d, *J* = 8.7 Hz, 39-C*H*), 3.11 (3H, s, OC*H*$_3$ *ketal*), 3.04 (1H, dd, *J* = 10.1, 8.8 Hz, 41-C*H*), 2.99 (1H, dd, *J* = 10.1, 7.1 Hz, 16-C*H*), 2.92 (1H, app t, *J* = 9.0 Hz, 42-C*H*), 2.87 (1H, dd, *J* = 18.0, 3.2 Hz, 18-C*H$_A$*H$_B$), 2.69 (1H, dd, *J* = 18.0, 9.4 Hz, 18-CH$_A$*H$_B$*), 2.59 (1H, br. d, *J* = 13.8 Hz, 44-C*H$_A$*H$_B$), 2.56–2.50 (1H, m, 14-C*H*), 2.51 (1H, dd, *J* = 15.9, 5.3 Hz, 2-C*H$_A$*H$_B$), 2.37–2.26 (3H, m, 2-CH$_A$*H$_B$*, 46-C*H$_A$*H$_B$, 12-C*H$_A$*H$_B$), 2.20–2.06 (5H, m, 12-CH$_A$*H$_B$*, 24-C*H$_A$*H$_B$, 30-C*H*$_2$, 46-CH$_A$*H$_B$*), 2.06–1.98 (2H, m, 20-C*H$_A$*H$_B$, 44-CH$_A$*H$_B$*), 1.96–1.89 (5H, m, 22-C*H$_A$*H$_B$, 36-C*H$_A$*H$_B$, COC*H*$_3$), 1.85 (3H, s, COC*H*$_3$), 1.82–1.79 (1H, m, 4-C*H$_A$*H$_B$), 1.78–1.69 (2H, m, 6-C*H$_A$*H$_B$, 8-C*H$_A$*H$_B$), 1.69–1.63 (1H, m, 40-C*H*), 1.63–1.55 (2H, m, 6-CH$_A$*H$_B$*, 10-C*H$_A$*H$_B$), 1.55–1.50 (1H, m, 26-C*H$_A$*H$_B$), 1.50–1.40 (8H, m, 4-CH$_A$*H$_B$*, 24-CH$_A$*H$_B$*, 26-CH$_A$*H$_B$*, 31-C*H*$_2$, 32-C*H$_A$*H$_B$, 34-C*H*, 36-CH$_A$*H$_B$*), 1.37–1.30 (2H, m, 8-CH$_A$*H$_B$*, 32-CH$_A$*H$_B$*), 1.24–1.20 (1H, m, 10-CH$_A$*H$_B$*), 1.21 (3H, s, 9-CC*H*$_3$), 1.10–1.08 (1H, m, 22-CH$_A$*H$_B$*), 1.08 (3H, d, *J* = 7.0 Hz, 14-CHC*H*$_3$), 1.03 (3H, d, *J* = 7.0 Hz, 16-CHC*H*$_3$), 0.97 (3H, d, *J* = 6.6 Hz, 40-CHC*H*$_3$), 0.94 (9H, t, *J* = 8.0 Hz, 3 × SiCH$_2$C*H*$_3$), 0.89 (9H, s, SiC(C*H*$_3$)$_3$), 0.88 (9H, s, SiC(C*H*$_3$)$_3$), 0.86 (9H, s, SiC(C*H*$_3$)$_3$), 0.82 (3H, d, *J* = 7.2 Hz, 34-CHC*H*$_3$), 0.83–0.79 (1H, m, 20-CH$_A$*H$_B$*), 0.58 (6H, q, *J* = 7.9 Hz, SiC*H*$_2$CH$_3$), 0.06 (3H, s, SiC*H*$_3$), 0.04 (3H, s, SiC*H*$_3$), 0.03 (3H, s, SiC*H*$_3$), 0.02 (3H, s, SiC*H*$_3$), 0.02 (3H, s, SiC*H*$_3$) and 0.01 (3H, s, SiC*H*$_3$); ^{13}C (125 MHz), CD$_3$CN: δ = 211.2 (17-*C*O), 171.4 (*C*OCH$_3$), 170.0 (*C*OCH$_3$), 148.1 (13-*C*), 144.2 (45-*C*), 138.0 (48-*C*H), 137.6 (50-*C*H), 132.0 (28-*C*H), 131.7 (29-*C*H), 130.8 (49-*C*H), 117.3 (51-*C*H$_2$), 115.4 (45-C*C*H$_2$), 114.3 (13-C*C*H$_2$), 101.7 (37-*C*), 99.0 (23-*C*), 98.0 (7-*C*), 78.9 (3C, 39-*C*H, 41-*C*H, 43-*C*H), 78.8 (42-*C*H), 76.0 (15-*C*H), 75.0 (21-*C*H), 74.2 (47-*C*H), 72.7 (9-*C*), 71.5 (35-*C*H), 71.1 (38-C*C*H), 67.8 (5-*C*H), 67.4 (33-*C*H), 67.0 (19-*C*H), 65.4 (25-*C*H), 64.6 (11-*C*H), 62.6 (27-*C*H), 62.0 (3-*C*H), 55.5 (21-CHOC*H*$_3$), 50.8 (18-*C*H$_2$), 48.3 (2C, 8-*C*H$_2$, 16-*C*H), 47.6 (COC*H*$_3$ *ketal*), 46.1 (46-*C*H$_2$), 45.9 (10-*C*H$_2$), 44.5 (22-*C*H$_2$), 43.3 (12-*C*H$_2$), 40.2 (2-*C*H$_2$, weak), 39.7 (3C, 26-*C*H$_2$, 40-*C*H, 44-*C*H$_2$), 39.0 (6-*C*H$_2$), 38.8 (2C, 31-*C*H$_2$, 34-*C*H**),** 38.0 (2C, 14-*C*H, 20-*C*H$_2$), 35.2 (24-*C*H$_2$), 34.5 (4-*C*H$_2$), 31.1 (9-C*C*H$_3$), 30.6 (36-*C*H$_2$), 28.8 (30-*C*H$_2$), 26.8 (32-*C*H$_2$), 26.3 (6C, SiC(*C*H$_3$)$_3$), 26.2 (3C, SiC(*C*H$_3$)$_3$), 21.8 (CO*C*H$_3$), 21.0 (CO*C*H$_3$), 18.8 (Si*C*(CH$_3$)$_3$), 18.7 (Si*C*(CH$_3$)$_3$), 18.6 (Si*C*(CH$_3$)$_3$), 14.0 (16-CH*C*H$_3$), 13.5 (40-CH*C*H$_3$), 12.1 (14-CH*C*H$_3$), 10.4 (34-CH*C*H$_3$), 7.7 (3C, SiCH$_2$*C*H$_3$), 7.4 (3C, Si*C*H$_2$CH$_3$), –4.2 (2C, Si*C*H$_3$), –4.4 (Si*C*H$_3$), –4.6 (Si*C*H$_3$), –4.7 (Si*C*H$_3$) and –4.8 (Si*C*H$_3$)[†]; *m/z* (+ESI) 1699.9982; $C_{88}H_{156}O_{22}Si_4Na$ requires 1700.0058, Δ 4.5 ppm.

[†] The carboxylic acid (C1) carbon was not observed.

Spongistatin 2 (2)



To a solution of **26** (6.7 mg, 3.99 μmol) in toluene (1.5 mL) was added DIPEA (0.4 M solution in toluene, 0.3 mL, 0.12 mmol) followed by freshly distilled 2,4,6-trichlorobenzoyl chloride (0.4 M solution in toluene, 0.2 mL, 80 μmol). The reaction mixture was stirred for 3 h at room temperature after which it was further diluted with toluene (2.4 mL). This solution was then added *via* syringe pump to a solution of DMAP (24.4 mg, 0.20 mmol, 50.0 equiv) in toluene (4.3 mL) at 90 °C dropwise over 24 h. Following addition, the mixed anhydride flask was rinsed with further toluene (1 mL) and the washings added over 7 h. The reaction mixture was maintained 90 °C for a further 7 h before being cooled to room temperature and diluted with Et_2O (4 mL). The mixture was washed with sat. $NaHCO_{3(aq)}$ solution (4 mL), brine (4 mL) and the layers separated. The combined aqueous layers were further extracted with Et_2O (3 × 5 mL), and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product. Flash chromatography using hexane/EtOAc (100:0, 90:10, 80:20, 70:30, 60:40, 50:50, 40:60 then 0:100) afforded the desired macrocycle as well as C37 eliminated material (2.8 mg), which was used directly in the next step of the synthesis.

To the mixture (2.8 mg) dissolved in MeCN (1.8 mL) at –25 °C was added 47–51% $HF_{(aq)}$ (5 M solution in MeCN, 0.64 mL)[†] dropwise *via* syringe pump over 1 h. The reaction was maintained between –20 °C and –25 °C for 5 h, after which Et_3N (4 mL) was added dropwise *via* syringe pump over 1 h to neutralize the reaction. The reaction was warmed to room temperature and quenched by the addition of saturated $NaHCO_{3(aq)}$ (10 mL). The mixture was extracted with EtOAc:CH_2Cl_2 (2:1, 3 × 20 mL) and the combined organics washed with saturated $NaHCO_{3(aq)}$ (30 mL), brine (30 mL), dried ($MgSO_4$) and concentrated *in*

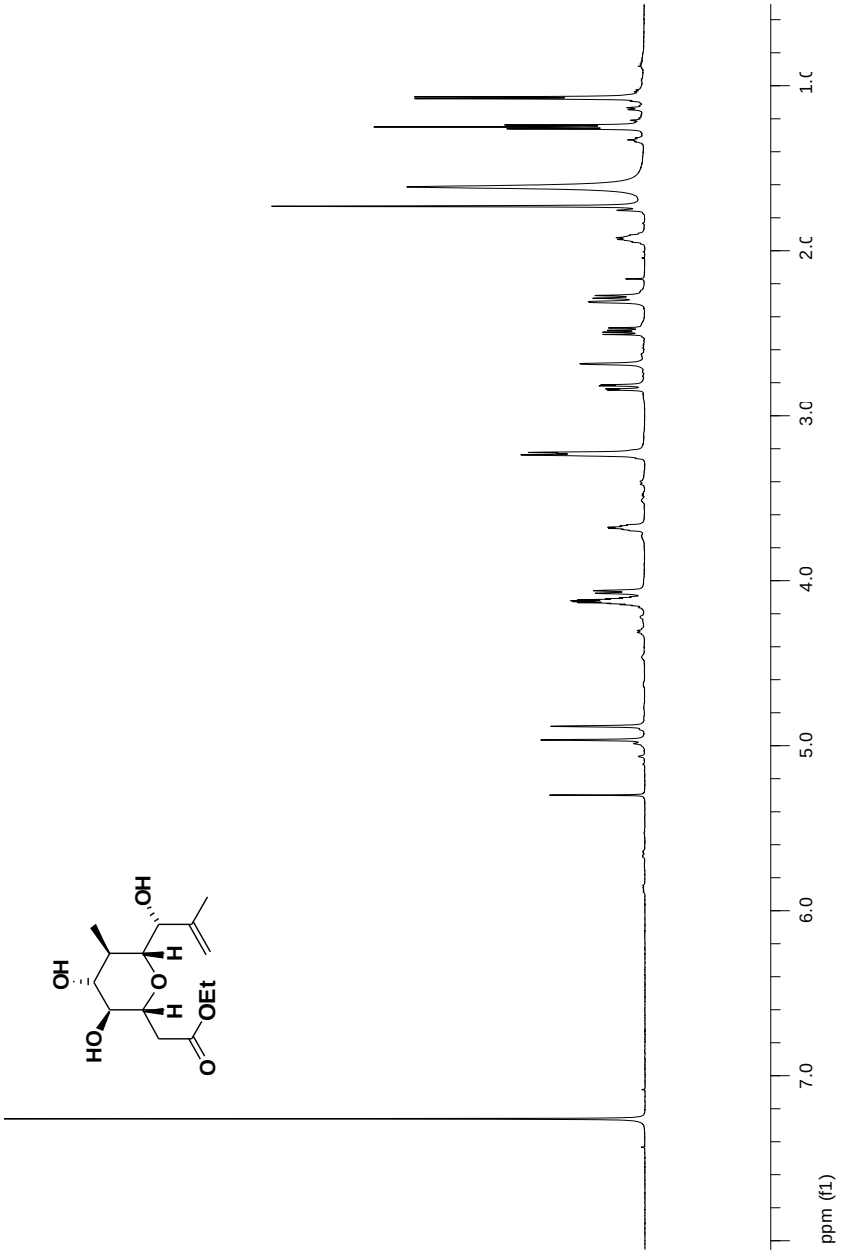
[†] The solution was prepared from 47–51% aqueous HF (2 mL) and MeCN (8 mL).

vacuo to give the crude product. Flash chromatography using hexane (100:0) then CH_2Cl_2/MeCN (70:30, 60:40, 50:50, 40:60, 30:70, 20:80, 10:90 then MeCN) afforded Spongistatin 2 (**2**) as a white foam (1.9 mg, 42% over 2 steps); R_f 0.45 (CH_2Cl_2/CH_3CN, 40:60); $[\alpha]_D^{27.2}$ = +30.0 (*c* 0.016 in MeOH); [lit[9] $[\alpha]_D^{23}$ +29.2 (*c* 1.2, MeOH)]; IR (film) ν_{max}/cm^{-1} 3415, 2965, 2932, 2861, 1734, 1647, 1457, 1434, 1380, 1328, 1259, 1235, 1173, 1085, 1056, 1021, 994, 971, 943, 891, 797; ^{1}H (500 MHz), CD_3CN: δ = 6.36 (1H, m, 50-C*H*), 6.23 (1H, dd, *J* = 15.1, 10.5 Hz, 49-C*H*), 5.72 (1H, dd, *J* = 15.2, 6.4 Hz, 48-C*H*), 5.53–5.47 (1H, m, 29-C*H*), 5.34 (1H, app t, *J* = 10.8, 9.5 Hz, 28-C*H*), 5.20 (1H, dd, *J* = 17.0, 1.7 Hz, 51-CH_AH$_B$), 5.14 (1H, dd, *J* = 10.6, 1.8 Hz, 15-C*H*), 5.07–4.99 (2H, m, 51-CH$_A$$H_B$, 27-C*H*), 4.96–4.92 (1H, m, 5-C*H*), 4.89 (1H, br. s, 45-C=CH_AH$_B$), 4.85 (3H, br. s, 13-C=CH_AH$_B$, 13-C=CH$_A$$H_B$, 45-C=CH$_A$$H_B$), 4.79–4.75 (1H, m, 41-C*H*), 4.74 (1H, s, 37-CO*H*), 4.41 (1H, d, *J* = 6.0 Hz, 25-CHO*H*), 4.39 (1H, s, 42-CHO*H*), 4.35 (1H, s, 9-CO*H*), 4.30–4.23 (3H, m, 3-C*H*, 11-C*H*, 47-C*H*), 4.17–4.13 (1H, m, 33-C*H*), 4.02 (1H, app t, *J* = 11.0 Hz, 19-C*H*), 3.98–3.93 (1H, m, 25-C*H*), 3.85 (1H, d, *J* = 9.4 Hz, 35-CHO*H*), 3.74 (1H, dd, *J* = 10.1, 1.0 Hz, 39-C*H*), 3.70–3.65 (1H, m, 35-C*H*), 3.51–3.44 (2H, m, 21-C*H*, 47-CHO*H*), 3.43–3.37 (1H, m, 43-C*H*), 3.36 (1H, d, *J* = 10.1 Hz, 38-C*H*), 3.26 (3H, s, 21-CHOCH_3), 3.16–3.10 (1H, m, 42-C*H*), 3.10–3.02 (1H, m, 16-C*H*), 2.90 (1H, d, *J* = 10.1 Hz, 38-CHO*H*), 2.86 (1H, d, *J* = 10.1 Hz, 18-CH_AH$_B$), 2.80 (1H, app q, *J* = 5.8 Hz, 14-C*H*), 2.75 (1H, d, *J* = 14.5 Hz, 44-CH_AH$_B$), 2.63 (1H, dd, *J* = 19.2, 1.2 Hz, 18-CH$_A$$H_B$), 2.54 (1H, dd, *J* = 16.1, 1.8 Hz, 2-CH_AH$_B$), 2.47 (1H, dd, *J* = 16.2, 10.6 Hz, 2-CH$_A$$H_B$), 2.34 (1H, dd, *J* = 14.0, 6.6 Hz, 46-CH_AH$_B$), 2.31–2.26 (2H, app br. d, *J* = 14.2 Hz, 12-CH_AH$_B$, 24-CH_AH$_B$), 2.24–2.14 (2H, m, 30-CH_AH$_B$, 46-CH$_A$$H_B$), 2.09–1.98 (5H, m, 12-CH$_A$$H_B$, 20-C$H_AH_B$, 22-C$H_AH_B$, 30-CH$_A$$H_B$, 44-CH$_A$$H_B$), 1.97 (3H, s, COC$H_3$), 1.93–1.86 (2H, m, 36-CH_AH$_B$, 40-C*H*), 1.86 (3H, s, COCH_3), 1.81 (1H, app d, *J* = 15.1 Hz, 6-CH_AH$_B$), 1.73–1.65 (2H, m, 4-CH_AH$_B$, 6-CH$_A$$H_B$), 1.64–1.39 (11H, m, 4-CH$_A$$H_B$, 8-C$H_2$, 10-C$H_AH_B$, 24-CH$_A$$H_B$, 26-C$H_2$, 31-C$H_AH_B$, 32-C$H_AH_B$, 34-C*H*, 36-CH$_A$$H_B$), 1.36–1.22 (3H, 10-CH$_A$$H_B$, 31-CH$_A$$H_B$, 32-CH$_A$$H_B$), 1.17 (3H, d, *J* = 6.9 Hz, 16-CHCH_3), 1.08 (3H, s, 9-CCH_3), 1.13–1.07 (1H, m, 22-CH$_A$$H_B$), 1.06 (3H, d, *J* = 6.8 Hz, 14-CHCH_3), 0.98 (1H, app q, *J* = 11.9 Hz, 20-CH$_A$$H_B$), 0.83 (3H, d, *J* = 7.2 Hz, 34-CHCH_3) and 0.76 (3H, d, *J* = 40-CHCH_3); ^{13}C (125 MHz), CD_3CN: δ = 213.3 (17-*C*O), 172.9 (1-*C*O), 171.5 (*C*OCH$_3$), 170.1 (*C*OCH$_3$), 147.9 (13-*C*), 144.1 (45-*C*), 138.2 (48-*C*H), 137.7 (50-*C*H), 133.4 (29-*C*H), 131.1 (28-*C*H), 130.9 (49-*C*H), 117.3 (51-*C*H$_2$), 116.1 (45-C*C*H$_2$), 114.7 (13-C*C*H$_2$), 99.8 (23-*C*), 99.3 (37-*C*), 99.1 (7-*C*), 81.1 (39-*C*H), 80.5 (41-*C*H), 78.6 (43-*C*H), 75.2 (15-*C*H), 73.8 (21-*C*H), 73.0 (2C, C38-*C*H, 42-*C*H), 71.4 (35-*C*H), 70.7 (47-*C*H), 69.5 (9-*C*), 67.0 (33-*C*H), 66.9 (5-*C*H), 66.0 (19-*C*H), 64.6 (11-*C*H), 64.3 (25-*C*H), 63.4 (3-*C*H), 61.1 (27-*C*H), 55.6 (21-CHO*C*H$_3$), 51.8 (18-*C*H$_2$), 47.5 (16-*C*H), 46.6 (8-*C*H$_2$), 44.8 (10-*C*H$_2$), 44.1 (2C, 12-*C*H$_2$, 22-*C*H$_2$), 43.9 (46-*C*H$_2$), 40.7 (2-*C*H$_2$), 40.0 (44-*C*H$_2$), 39.2 (34-*C*H), 38.9 (26-*C*H$_2$), 38.0 (6-*C*H$_2$), 37.6 (20-*C*H$_2$), 37.1 (40-*C*H), 36.5 (14-*C*H), 34.8 (24-*C*H$_2$), 34.5 (4-*C*H$_2$), 33.6 (36-*C*H$_2$), 32.7 (32-*C*H$_2$), 30.1 (9-C*C*H$_3$), 27.9 (30-*C*H$_2$), 26.9 (31-*C*H$_2$), 21.7 (CO*C*H$_3$), 20.9 (CO*C*H$_3$), 13.6 (16-CH*C*H$_3$), 12.6 (40-

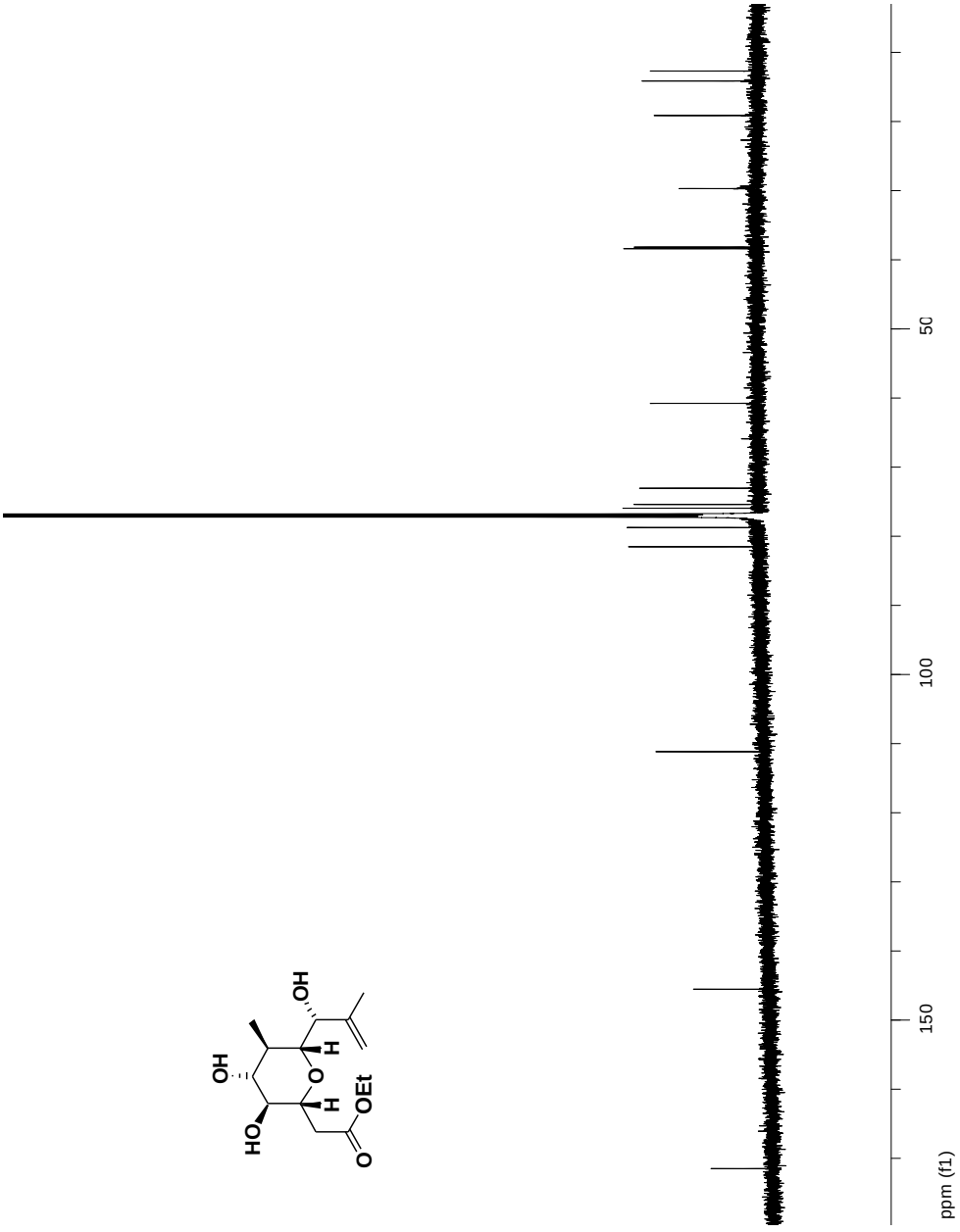
CH*C*H$_3$), 12.0 (14-CH*C*H$_3$), 11.4 (34-CH*C*H$_3$); *m/z* (+ESI) 1211.6329; $C_{63}H_{96}O_{21}Na$ requires 1211.6336, Δ 0.6 ppm.

III) Selected NMR Spectra

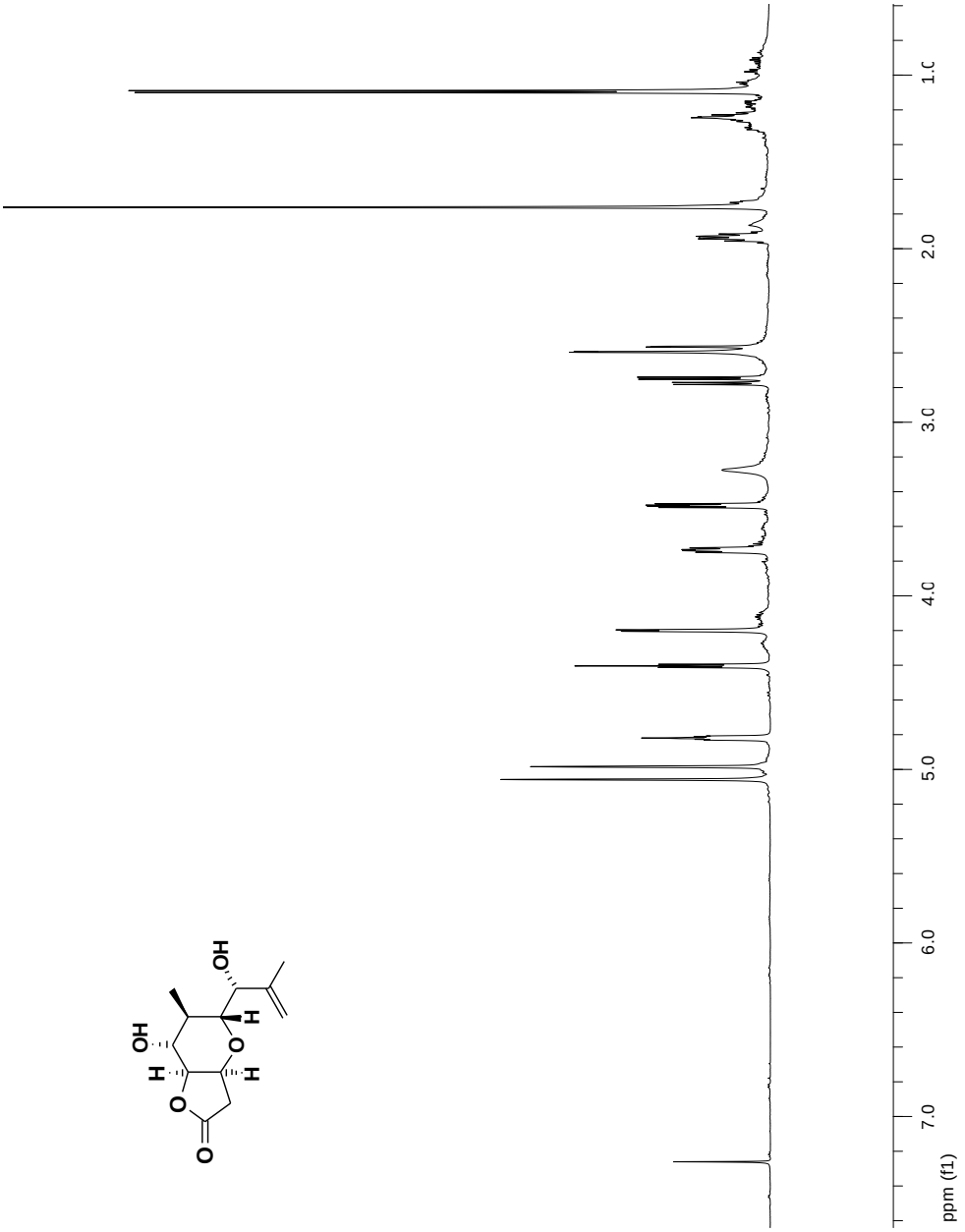
^{1}H NMR: Ethyl 2-((2*R*,3*S*,4*R*,5*R*,6*R*)-3,4-dihydroxy-6-((*S*)-1-hydroxy-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate 16



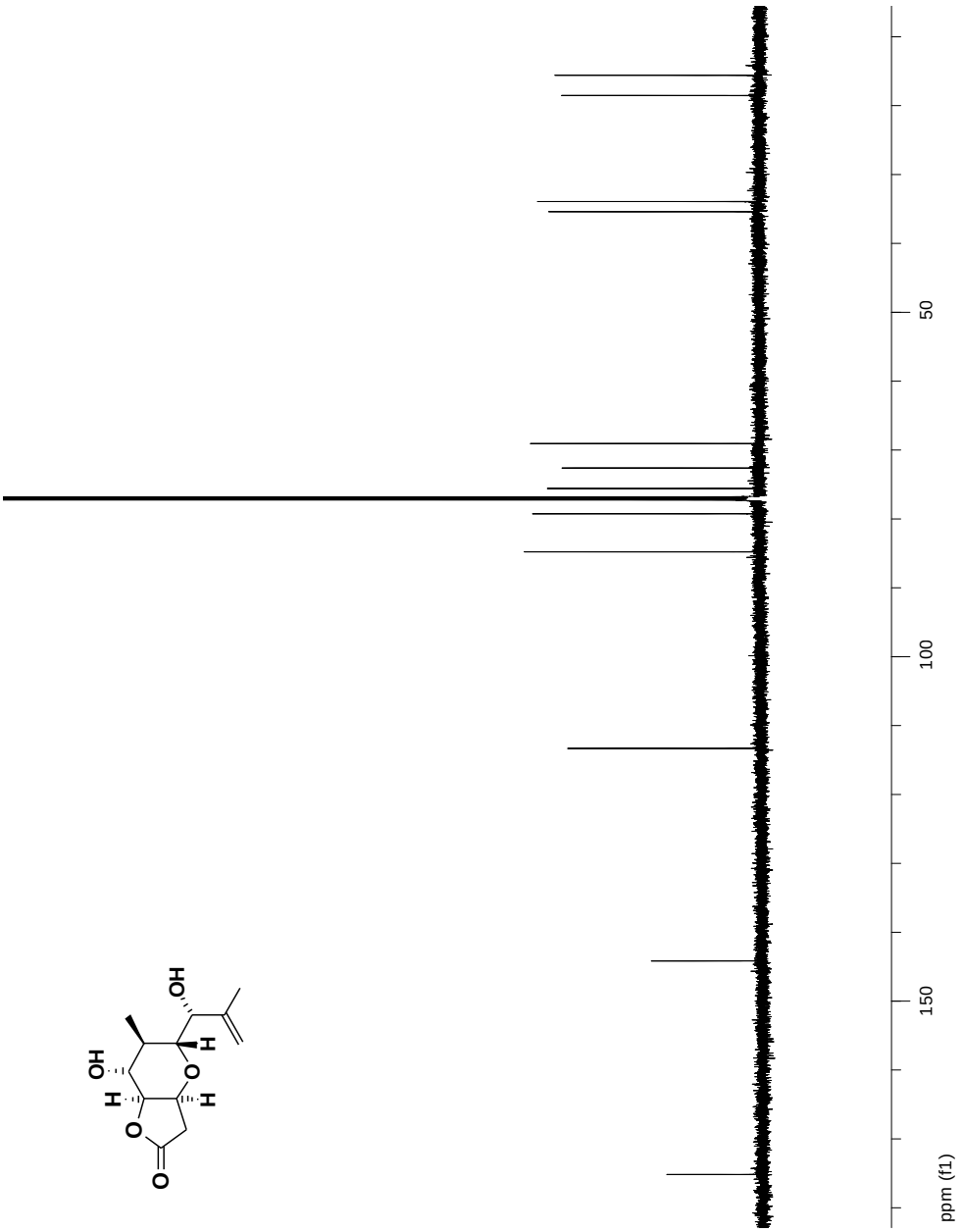
^{13}C NMR: Ethyl 2-((2*R*,3*S*,4*R*,5*R*,6*R*)-3,4-dihydroxy-6-((*S*)-1-hydroxy-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate 16



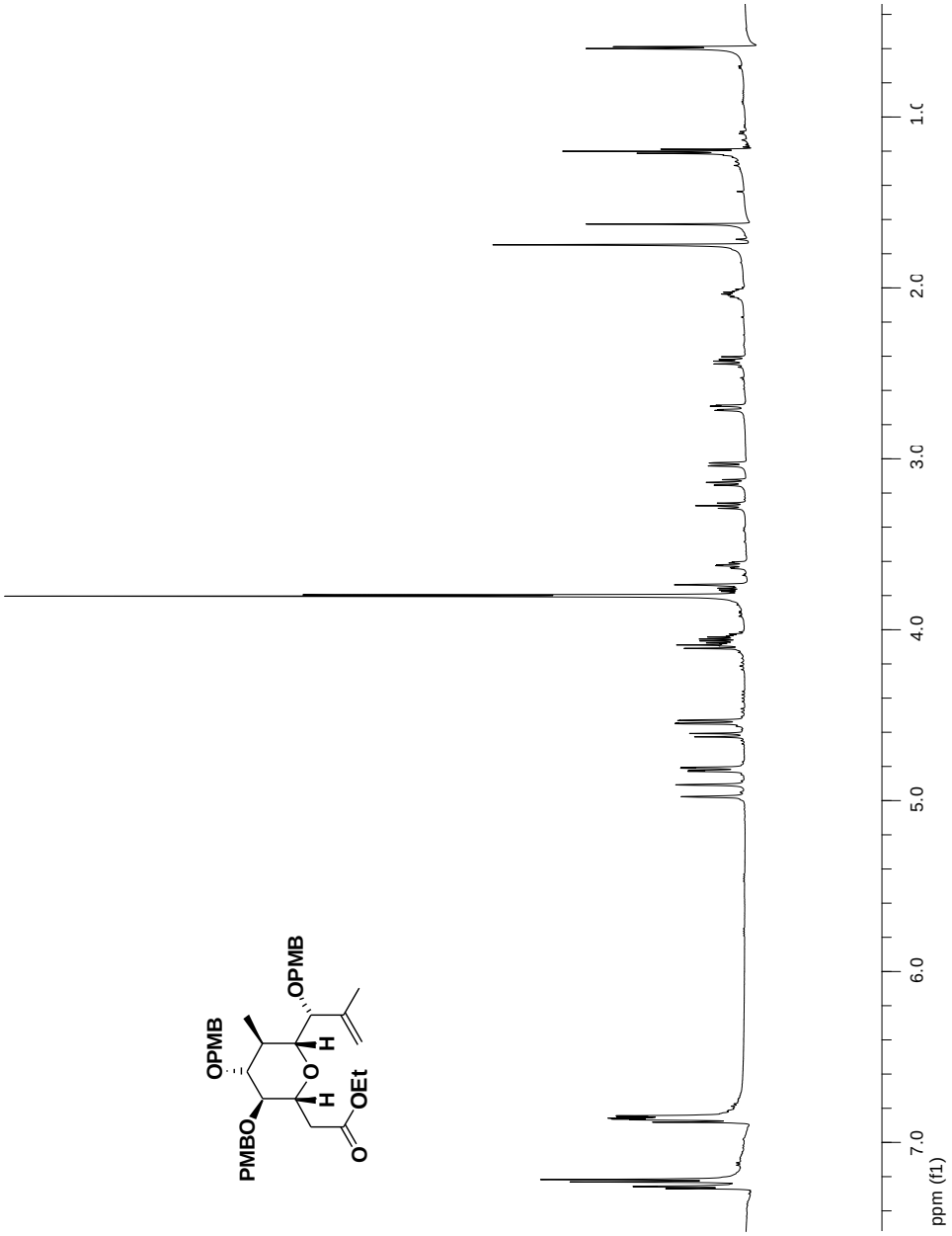
^{1}H NMR (3a*S*,5*R*,6*R*,7*R*,7a*S*)-7-Hydroxy-5-((*S*)-1-hydroxy-2-methylallyl)-6-methylhexahydro-2*H*-furo[3,2-*b*]pyran-2-one 17



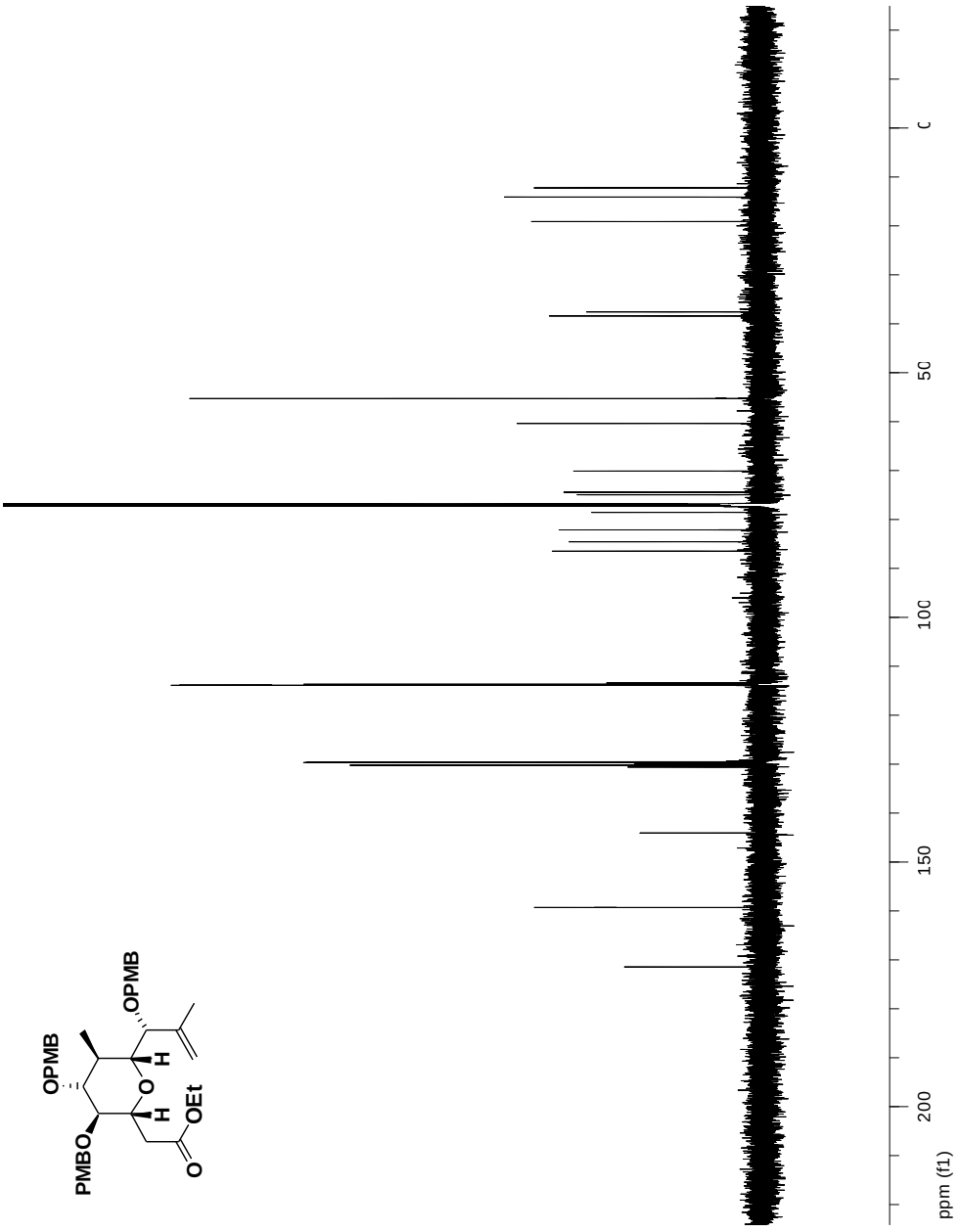
^{13}C NMR (3a*S*,5*R*,6*R*,7*R*,7a*S*)-7-Hydroxy-5-((*S*)-1-hydroxy-2-methylallyl)-6-methylhexahydro-2*H*-furo[3,2-*b*]pyran-2-one 17



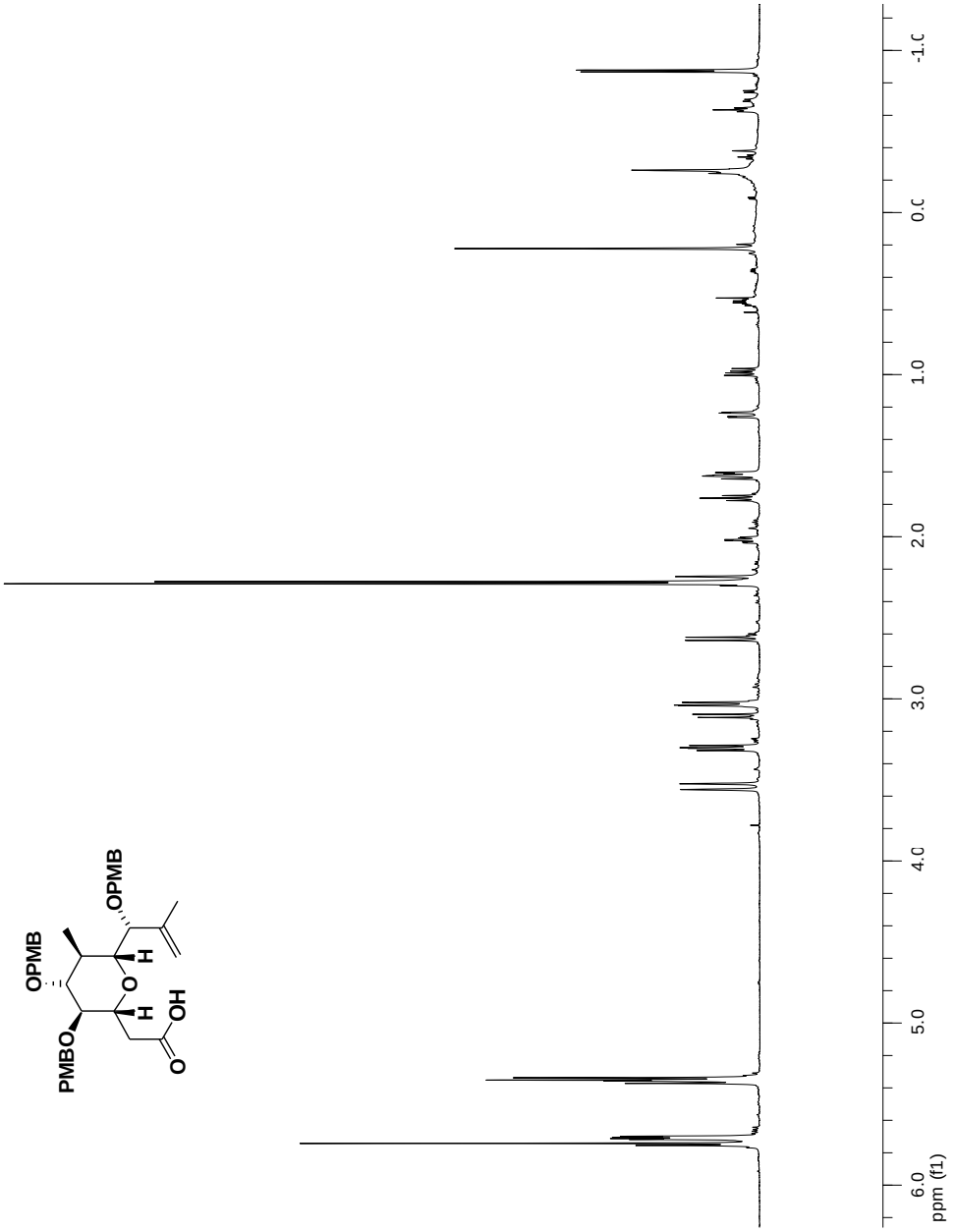
^{1}H NMR: Ethyl 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-bis(4-methoxybenzyloxy)-6-((*S*)-1-(4-methoxy benzyloxy) -2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate 18



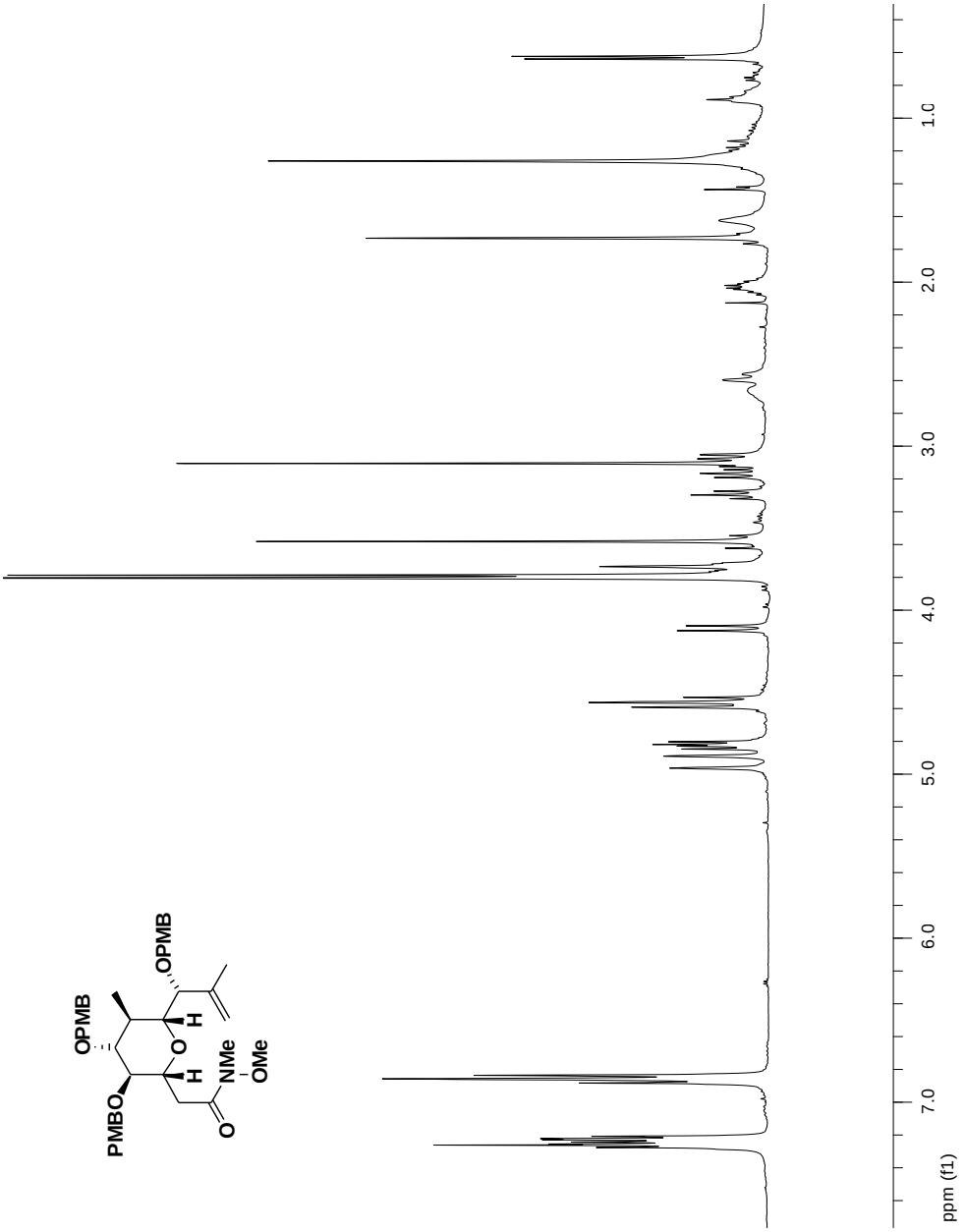
^{13}C NMR: Ethyl 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-bis(4-methoxybenzyloxy)-6-((*S*)-1-(4-methoxy benzyloxy) -2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate 18



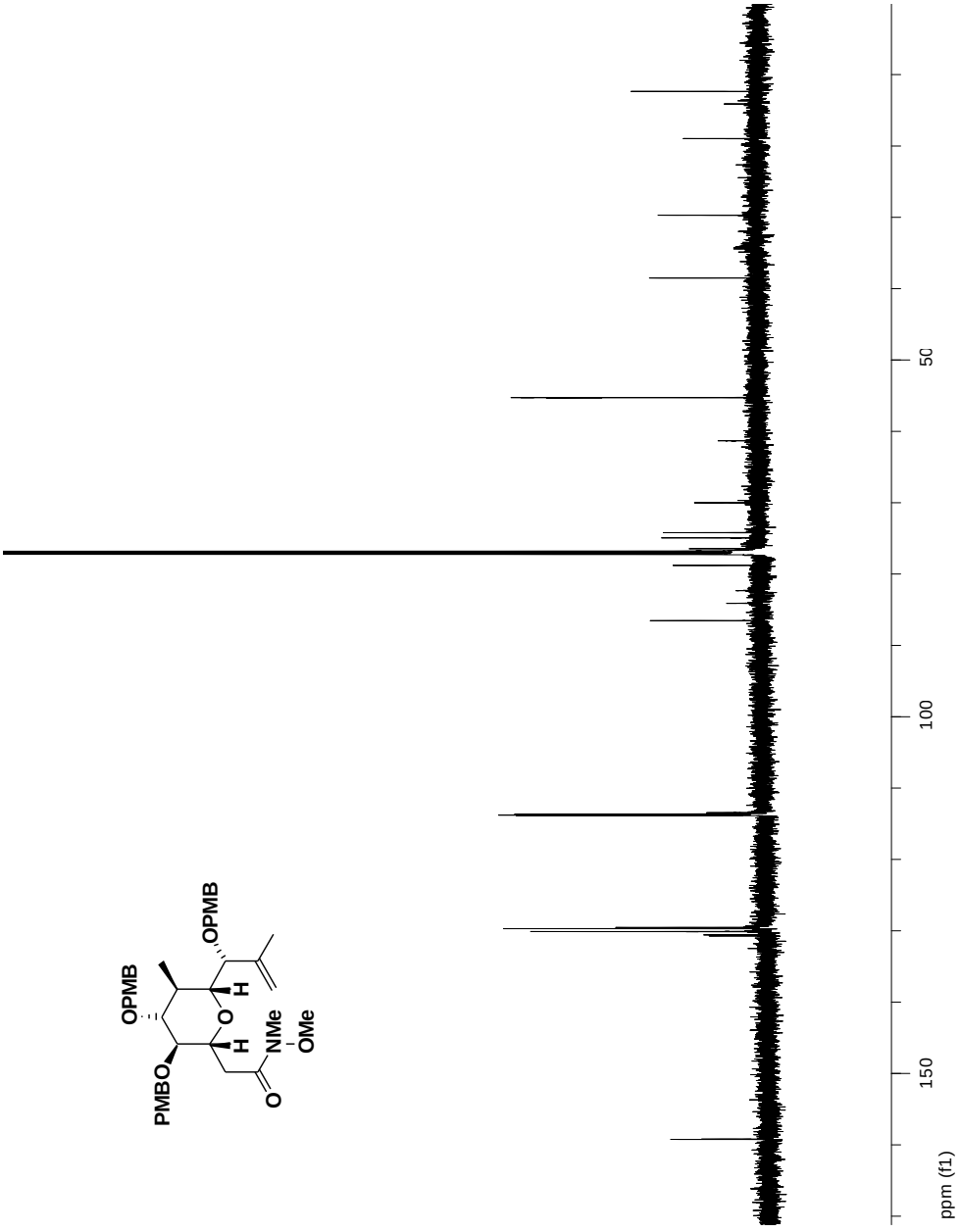
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*R*)-1-(4-methoxy benzyloxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetic acid S7



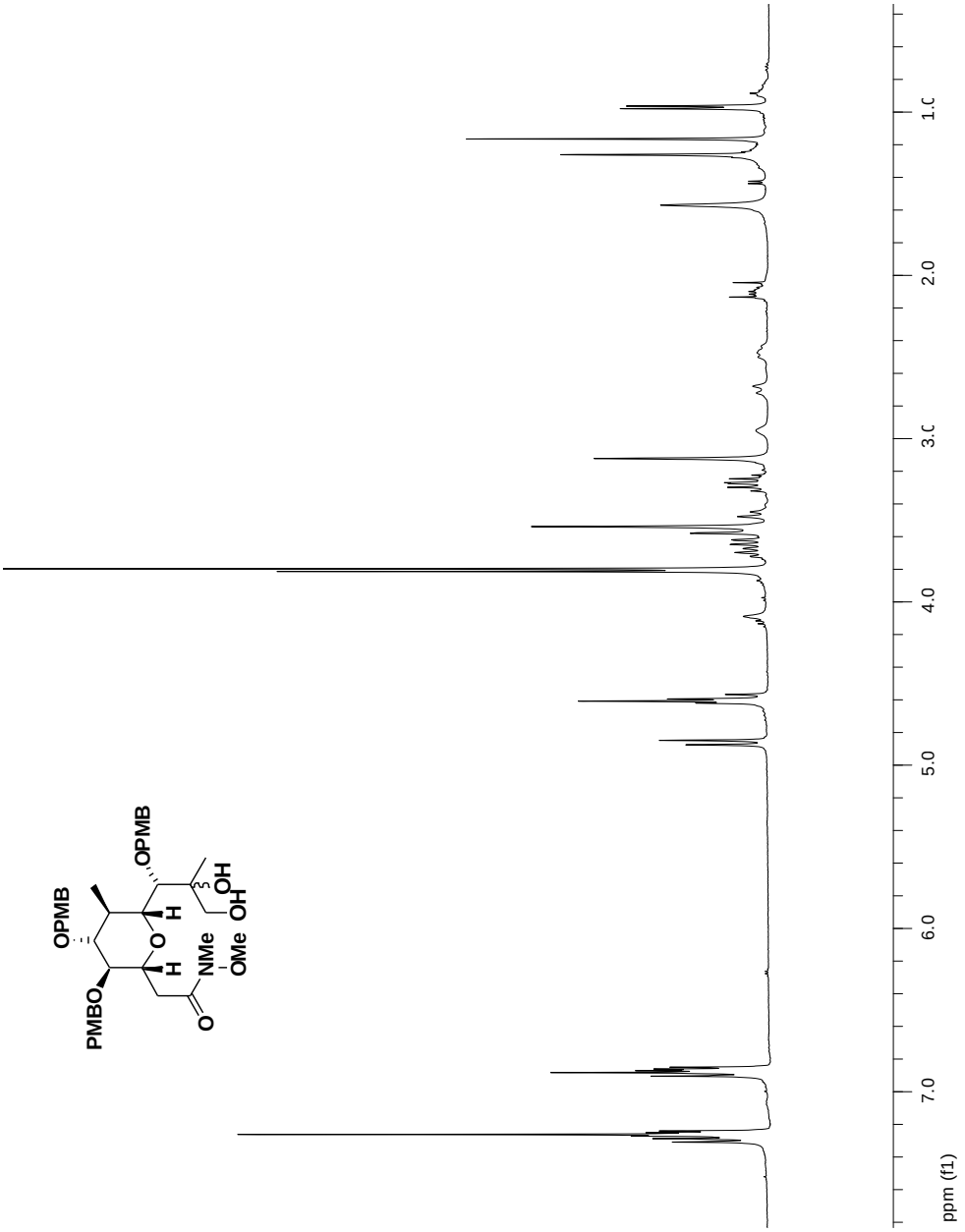
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*R*)-1-(4-methoxy benzyloxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S8



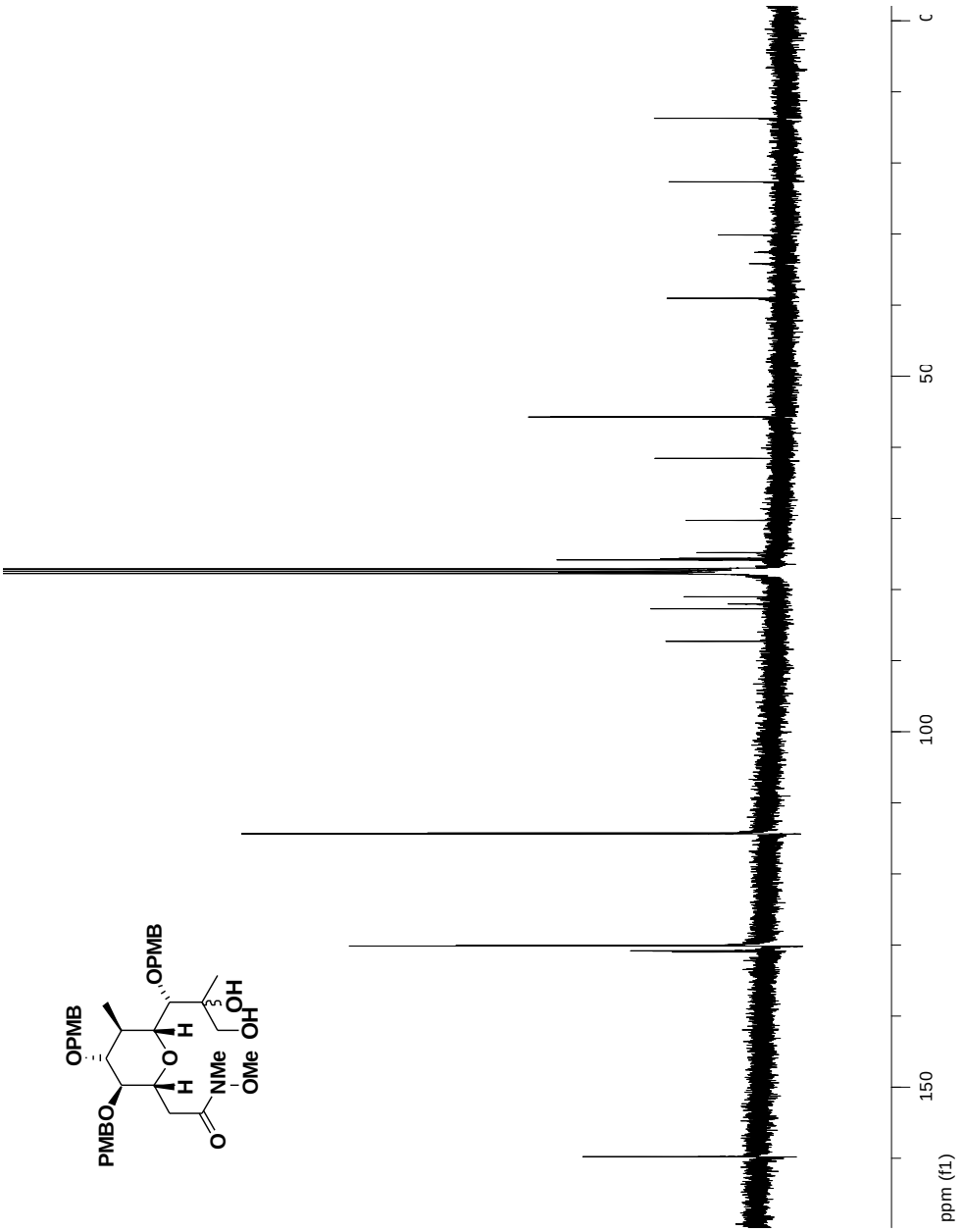
^{13}C NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*R*)-1-(4-methoxy benzyloxy)-2-methylallyl)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S8



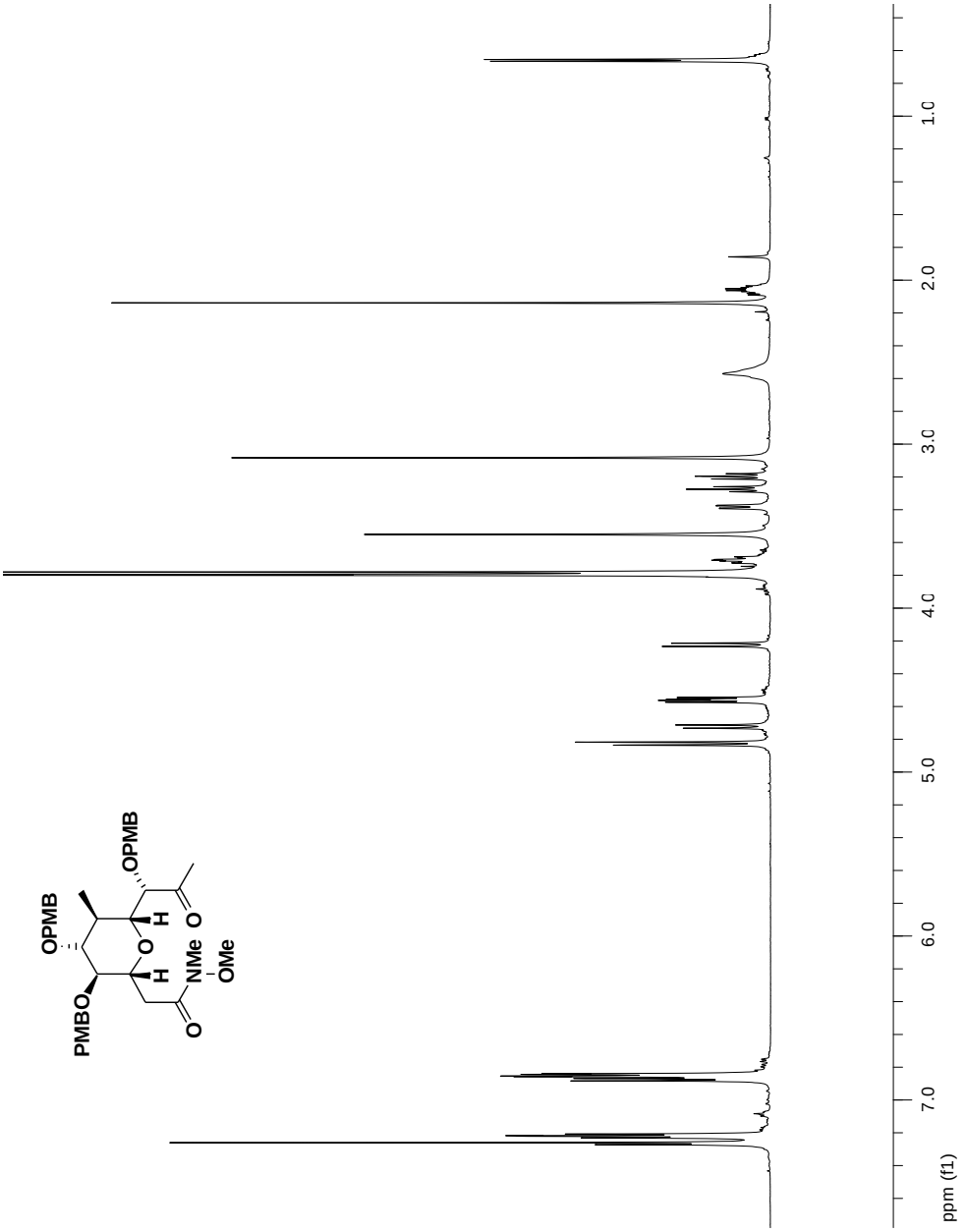
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-2,3-Dihydroxy-1-(4-methoxybenzyloxy)-2-methylpropyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methyacetamdide S9



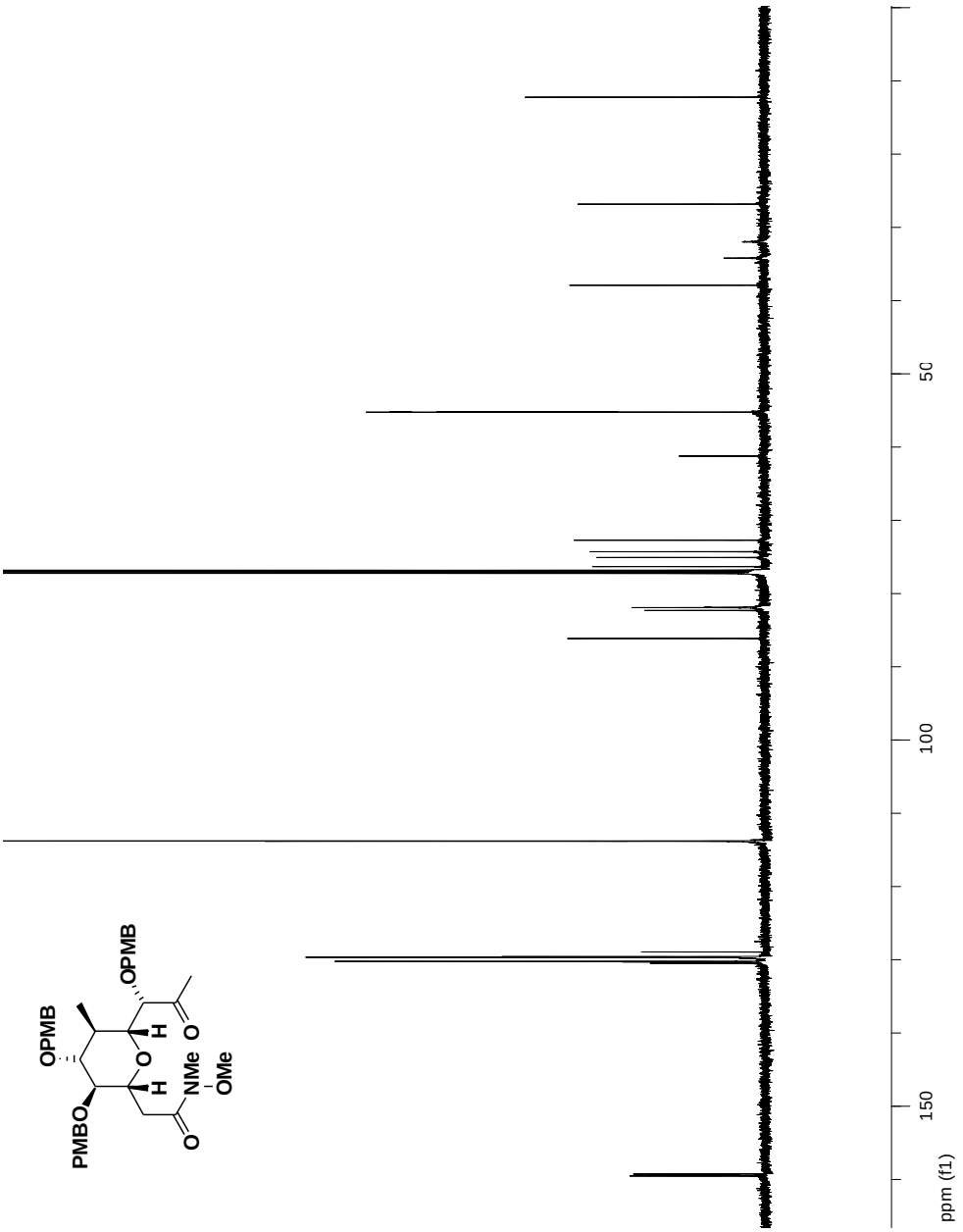
^{13}C NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-2,3-Dihydroxy-1-(4-methoxybenzyloxy)-2-methylpropyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methyacetamdide S9



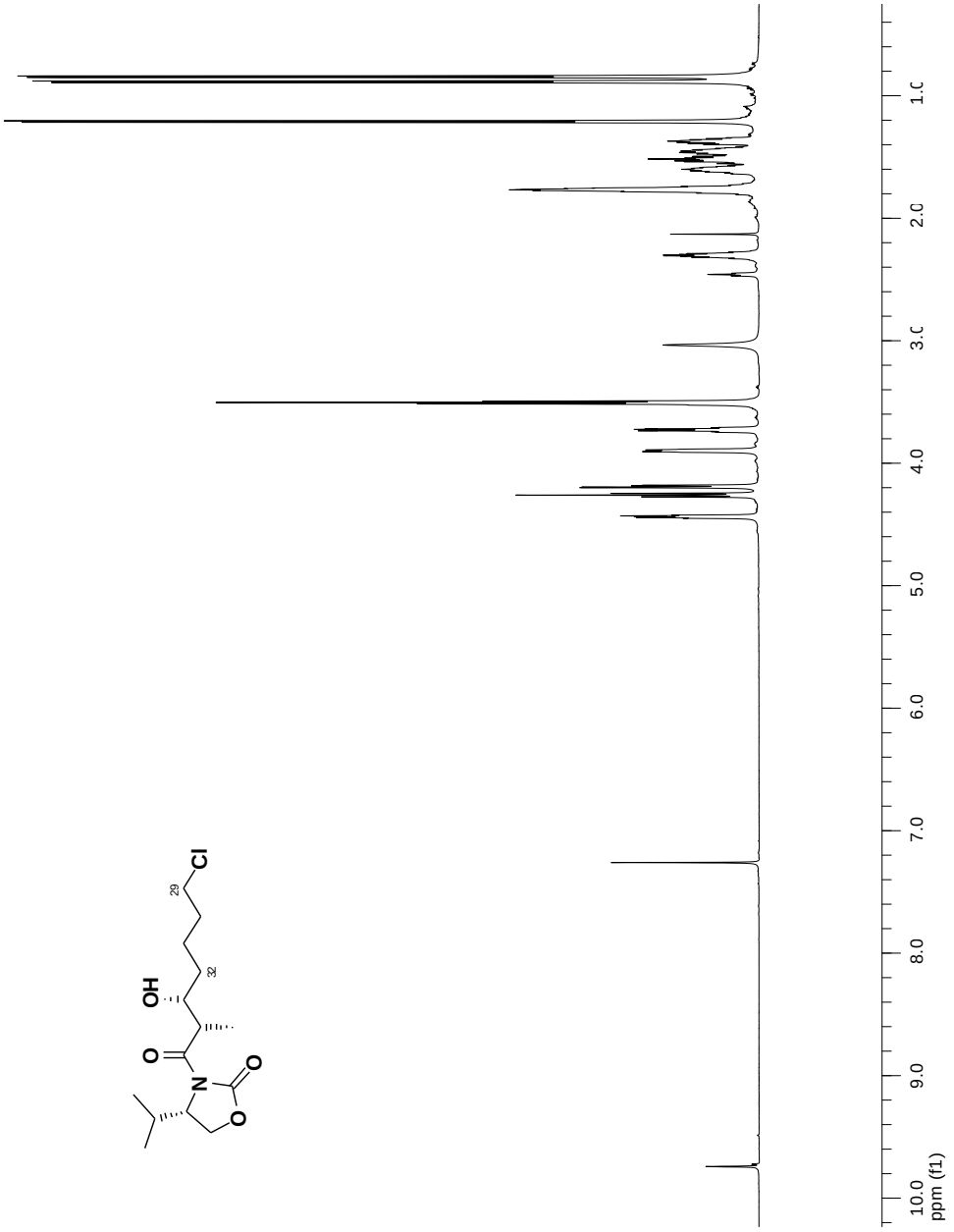
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*S*)-1-(4-methoxy benzyloxy)-2-oxopropyl)-5-methyltetrahydro-2H-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide 5



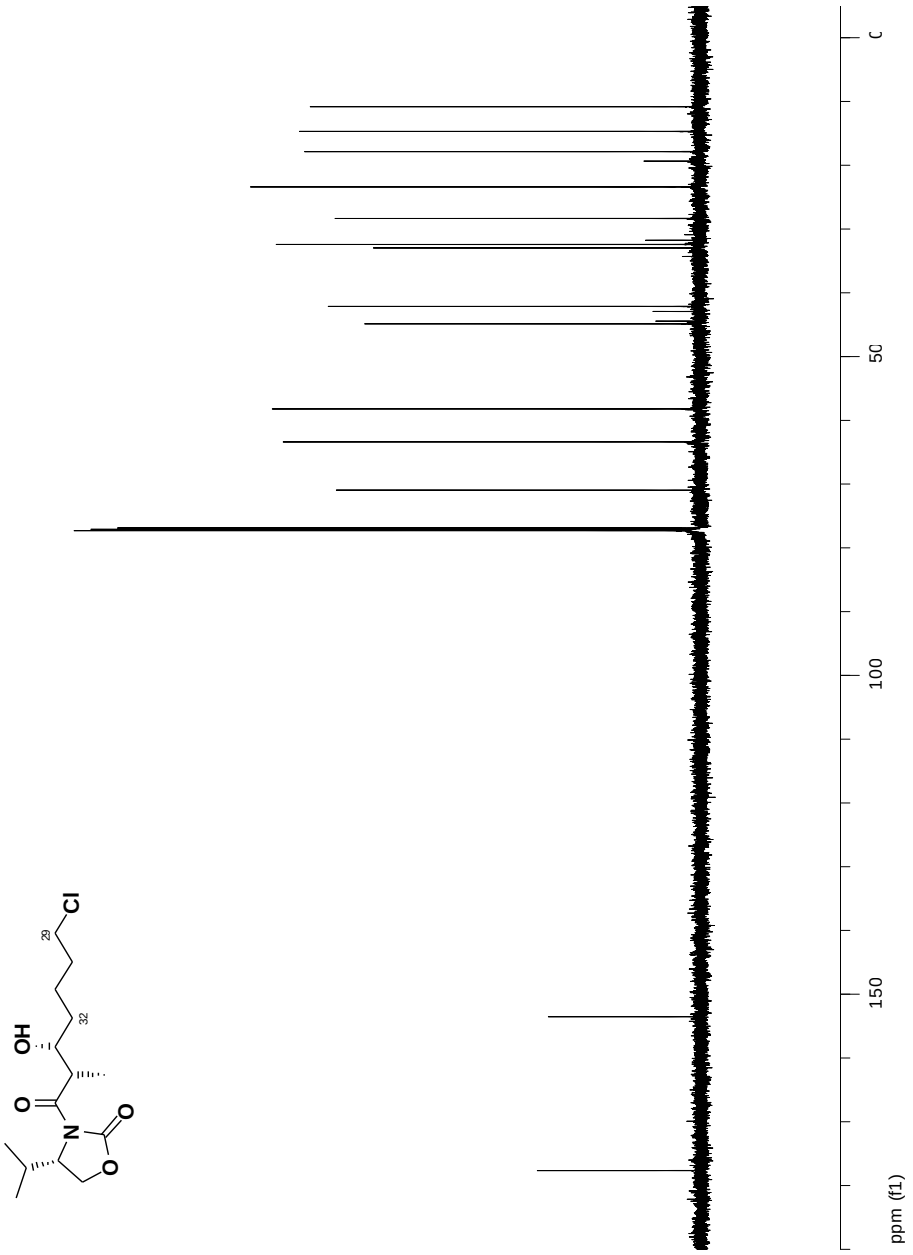
^{13}C NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4-Bis(4-methoxybenzyloxy)-6-((*S*)-1-(4-methoxy benzyloxy)-2-oxopropyl)-5-methyltetrahydro-2H-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide 5



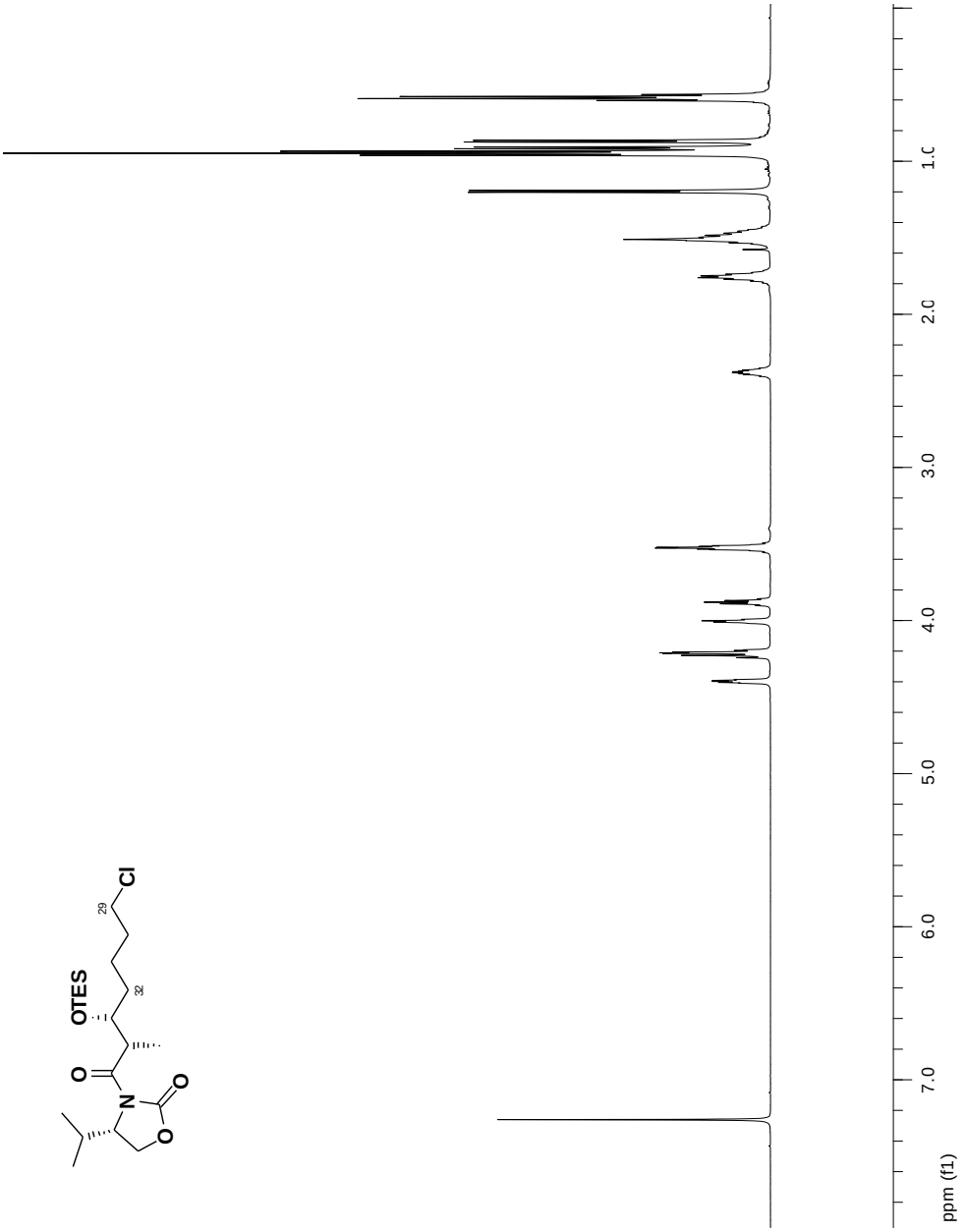
^{1}H NMR: (*S*)-3-((2*S*,3*R*)-7-Chloro-3-hydroxy-2-methylheptanoyl)-4-isopropyloxazolidin-2-one S14



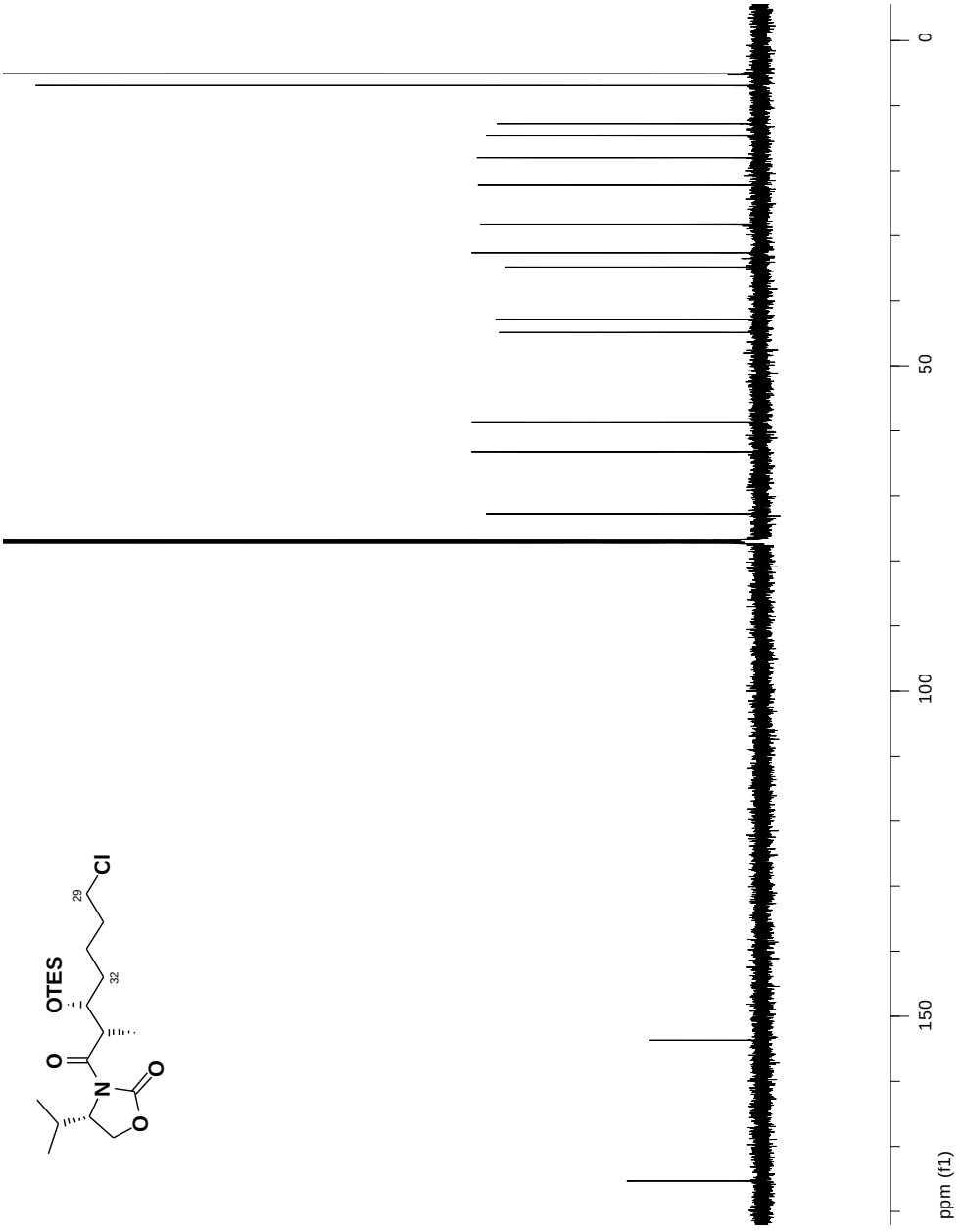
^{13}C NMR: (*S*)-3-((2*S*,3*R*)-7-Chloro-3-hydroxy-2-methylheptanoyl)-4-isopropyloxazolidin-2-one S14



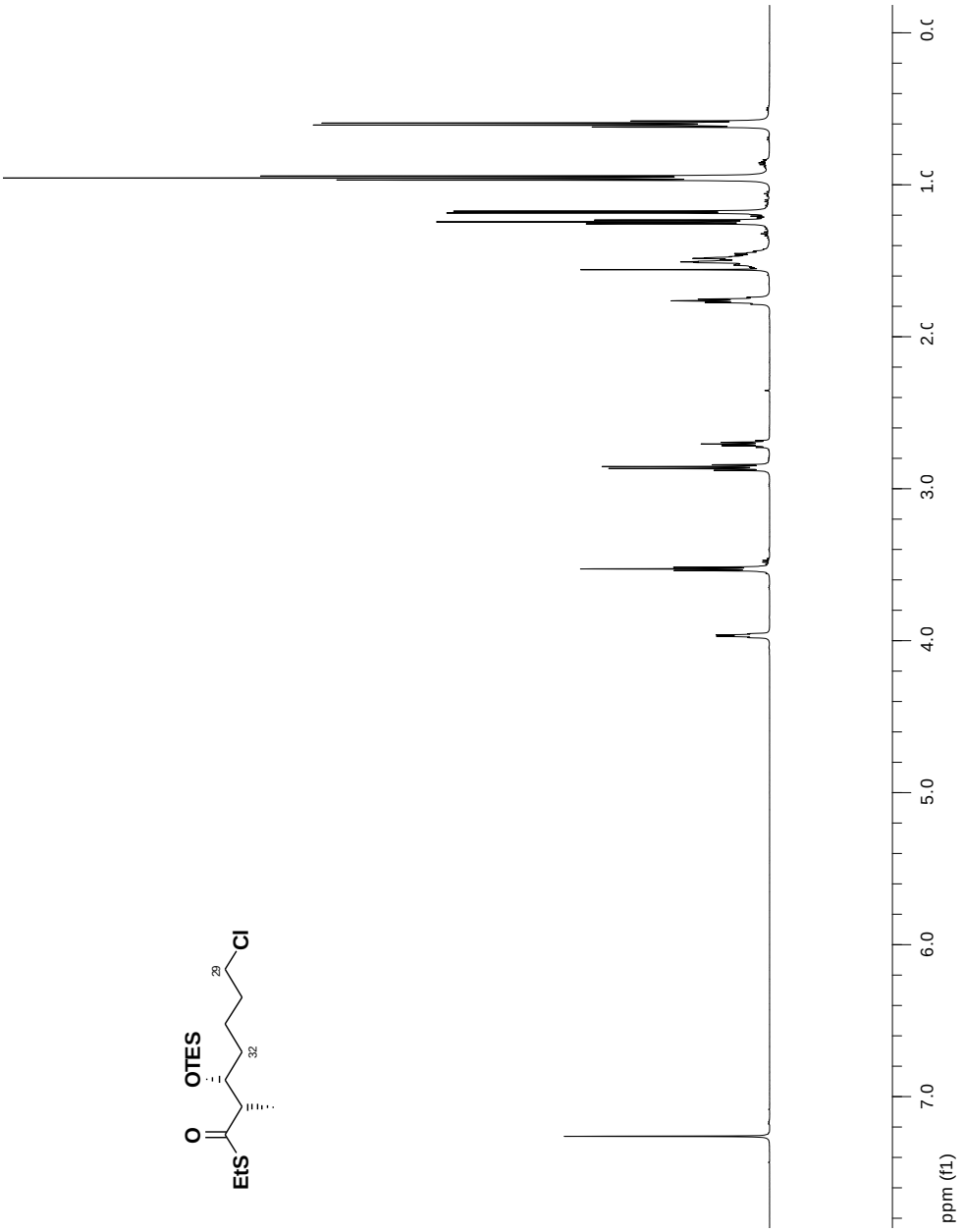
^{1}H NMR: (*S*)-3-((2*S*,3*R*)-7-Chloro-2-methyl-3-(triethylsilyloxy)heptanoyl)-4-isopropyl oxazolidin-2-one S15



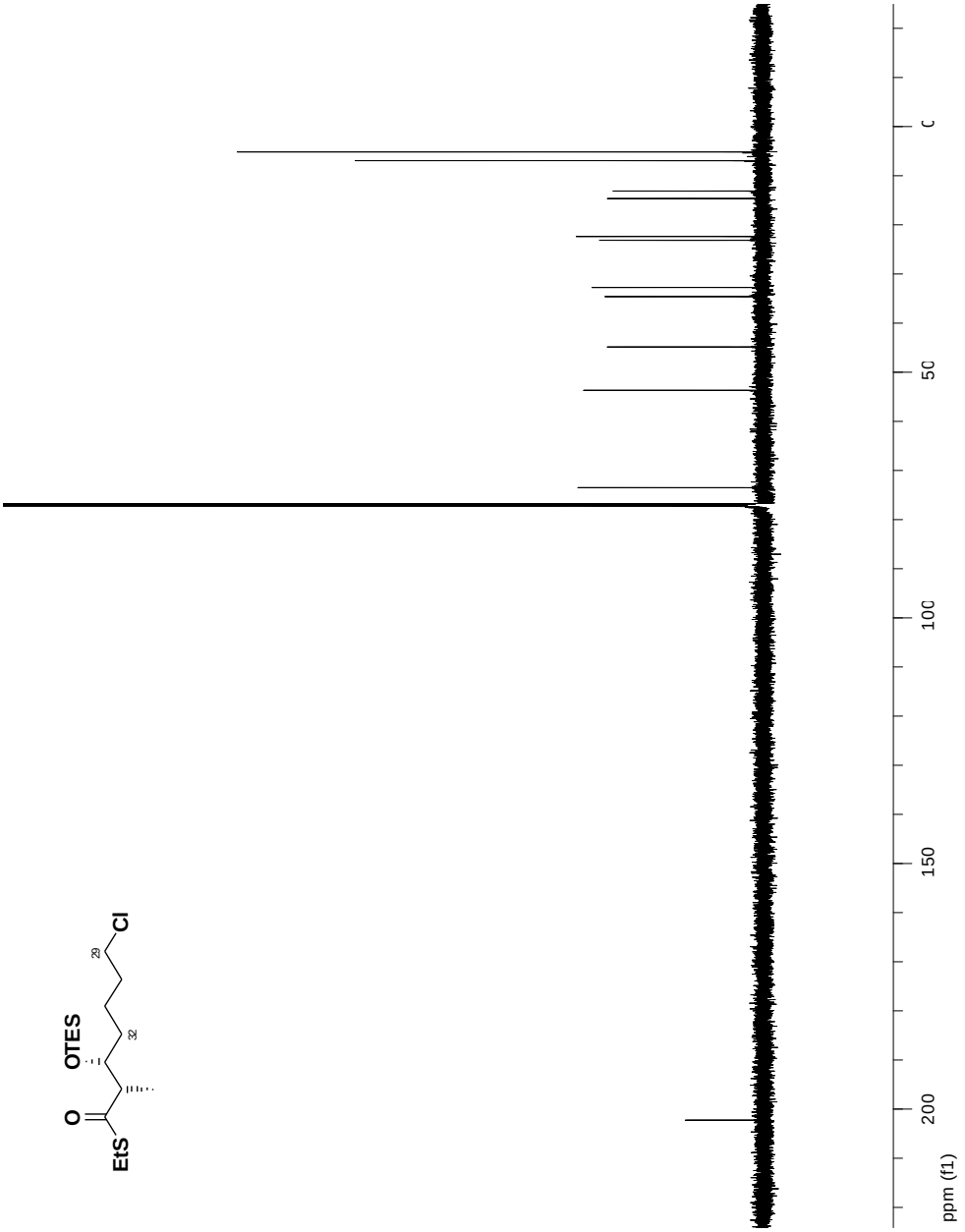
^{13}C NMR: (*S*)-3-((2*S*,3*R*)-7-Chloro-2-methyl-3-(triethylsilyloxy)heptanoyl)-4-isopropyl oxazolidin-2-one S15



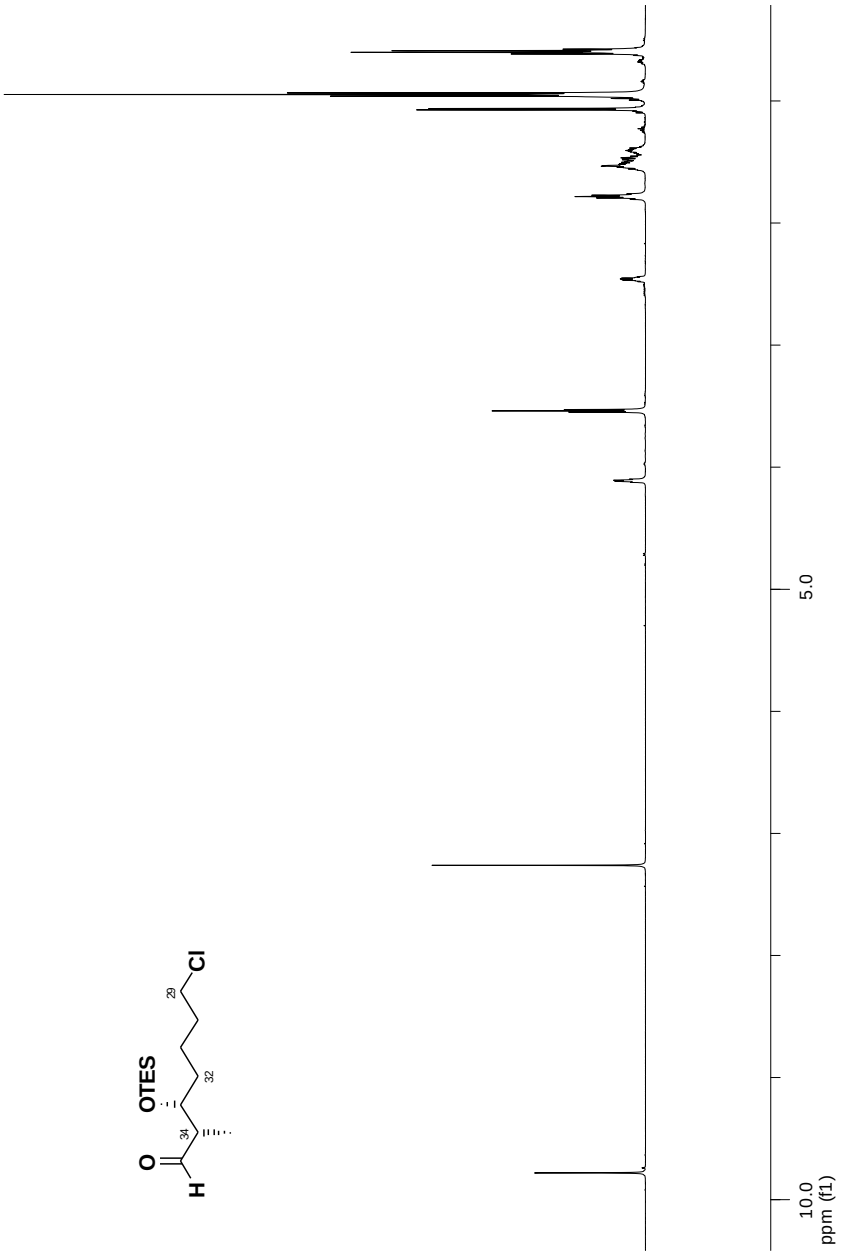
^{1}H NMR: (2*S*,3*R*)-*S*-Ethyl 7-chloro-2-methyl-3-(triethylsilyloxy)heptanethioate S16



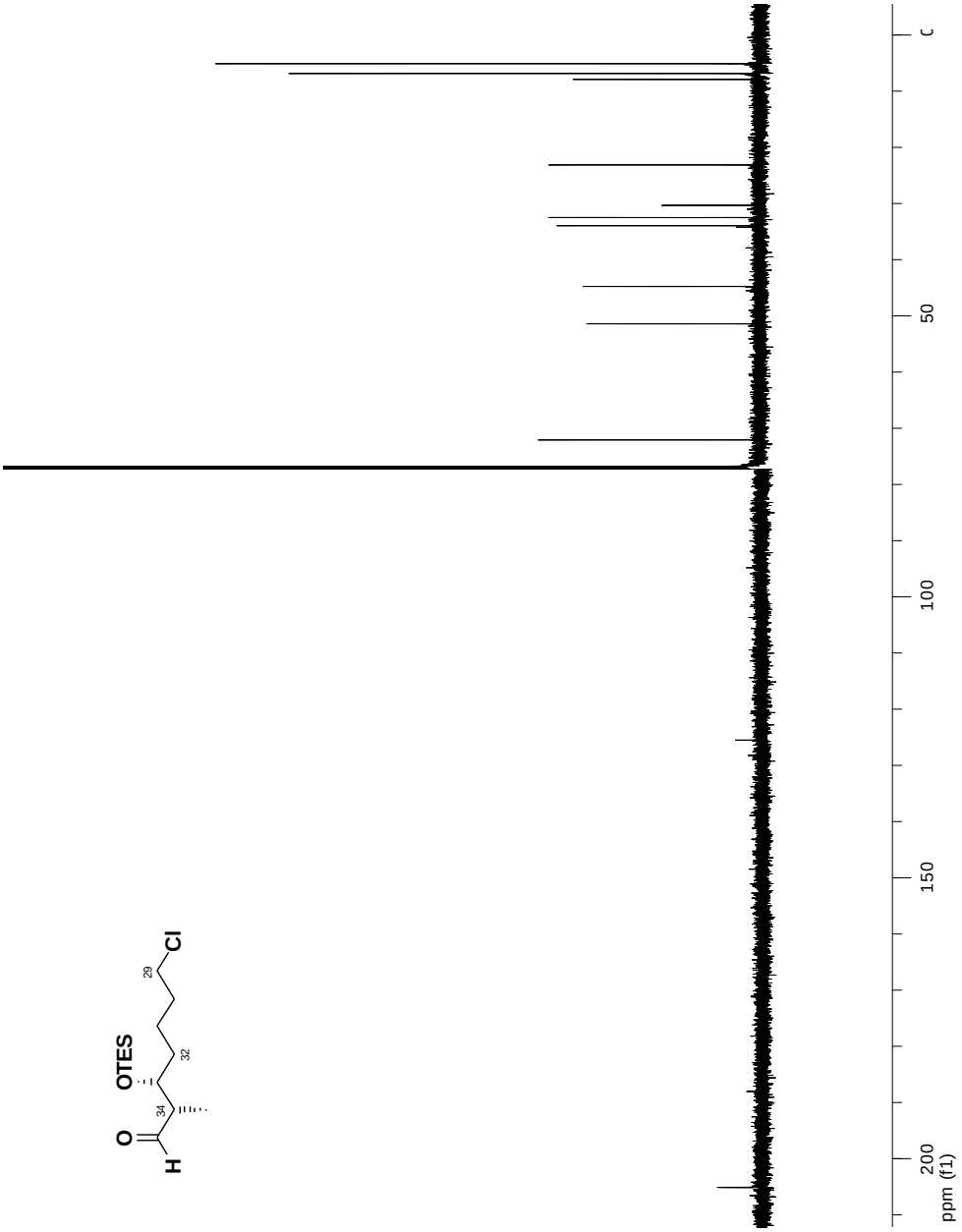
^{13}C NMR: (2*S*,3*R*)-*S*-Ethyl 7-chloro-2-methyl-3-(triethylsilyloxy)heptanethioate S16



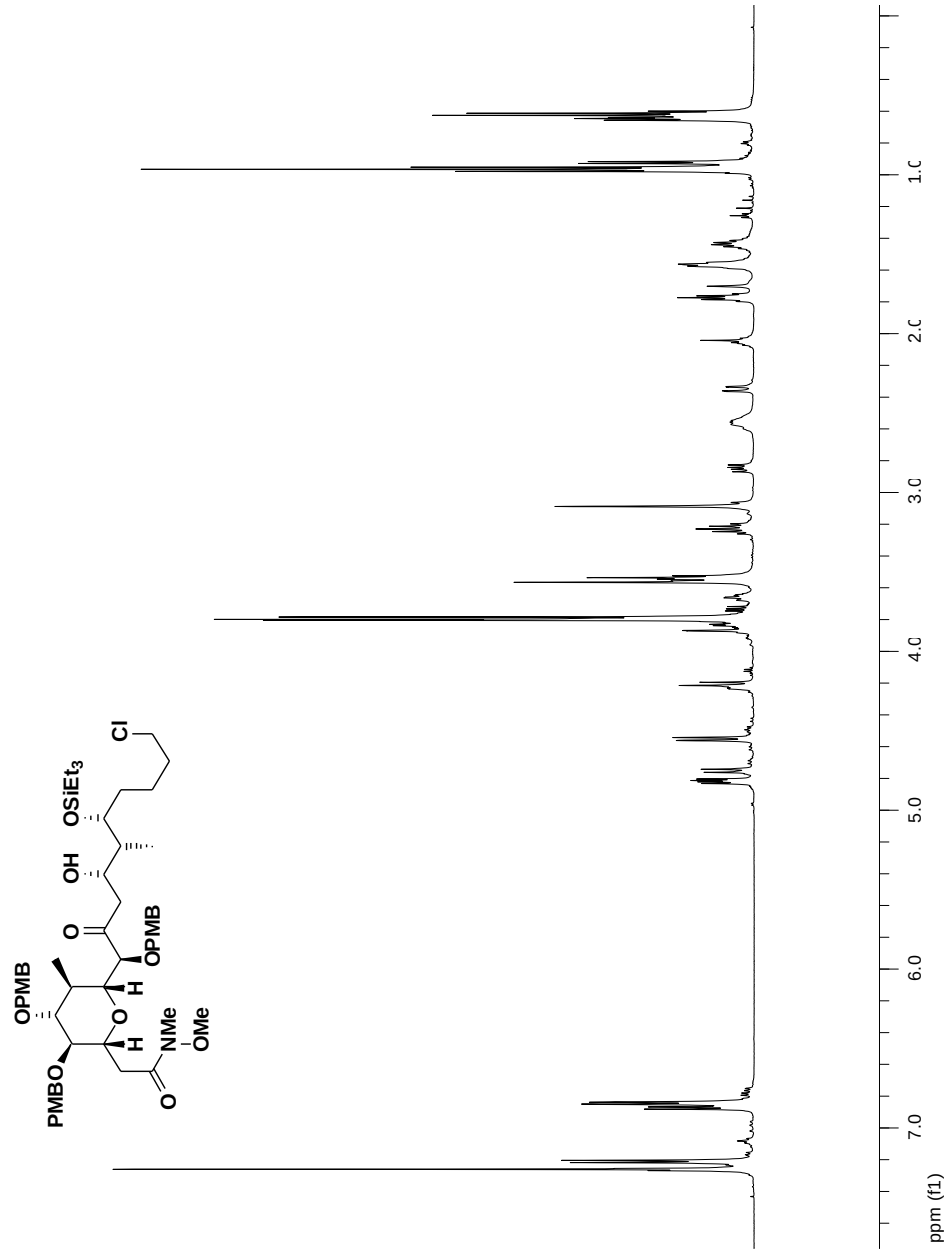
^{1}H NMR: (2*S*,3*R*)-7-Chloro-2-methyl-3-(triethylsilyloxy)heptanal 19



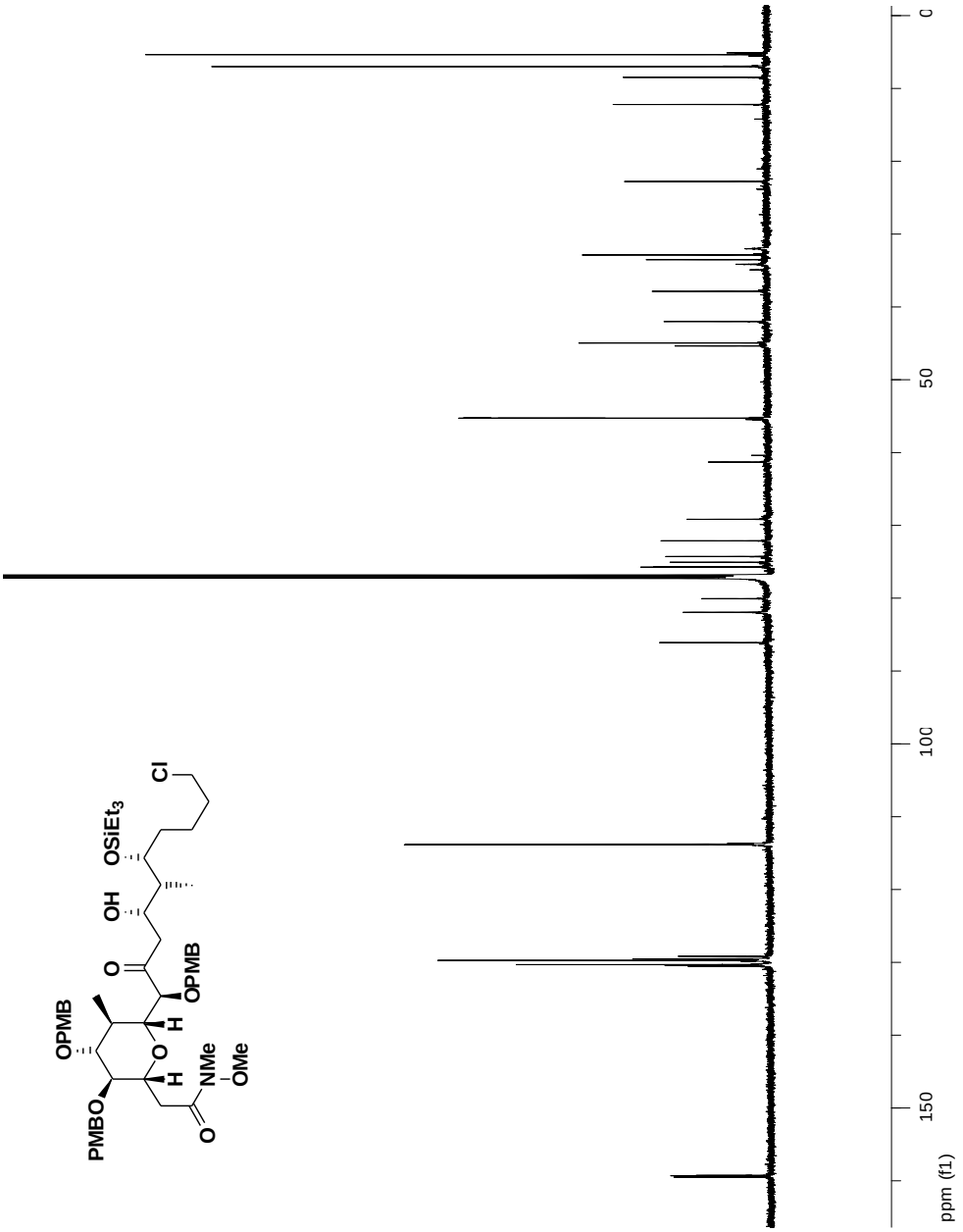
^{13}C NMR: (2*S*,3*R*)-7-Chloro-2-methyl-3-(triethylsilyloxy)heptanal 19



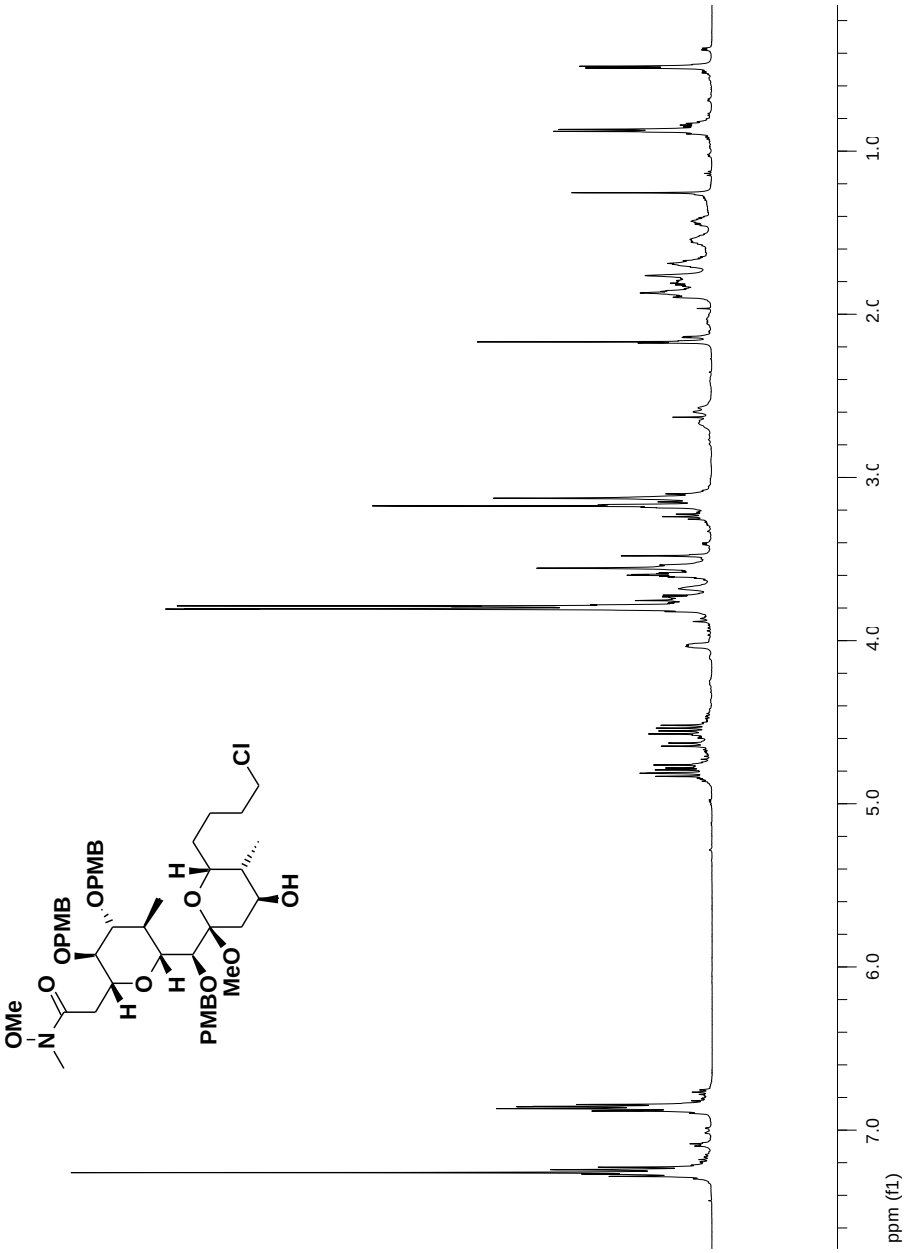
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((1*S*,4*S*,5*R*,6*R*)-10-Chloro-4-hydroxy-1-(4-methoxybenzyloxy)-5-methyl-2-oxo-6-(triethylsilyloxy)decyl)-3,4-bis(4-methoxybenzyl oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide 20



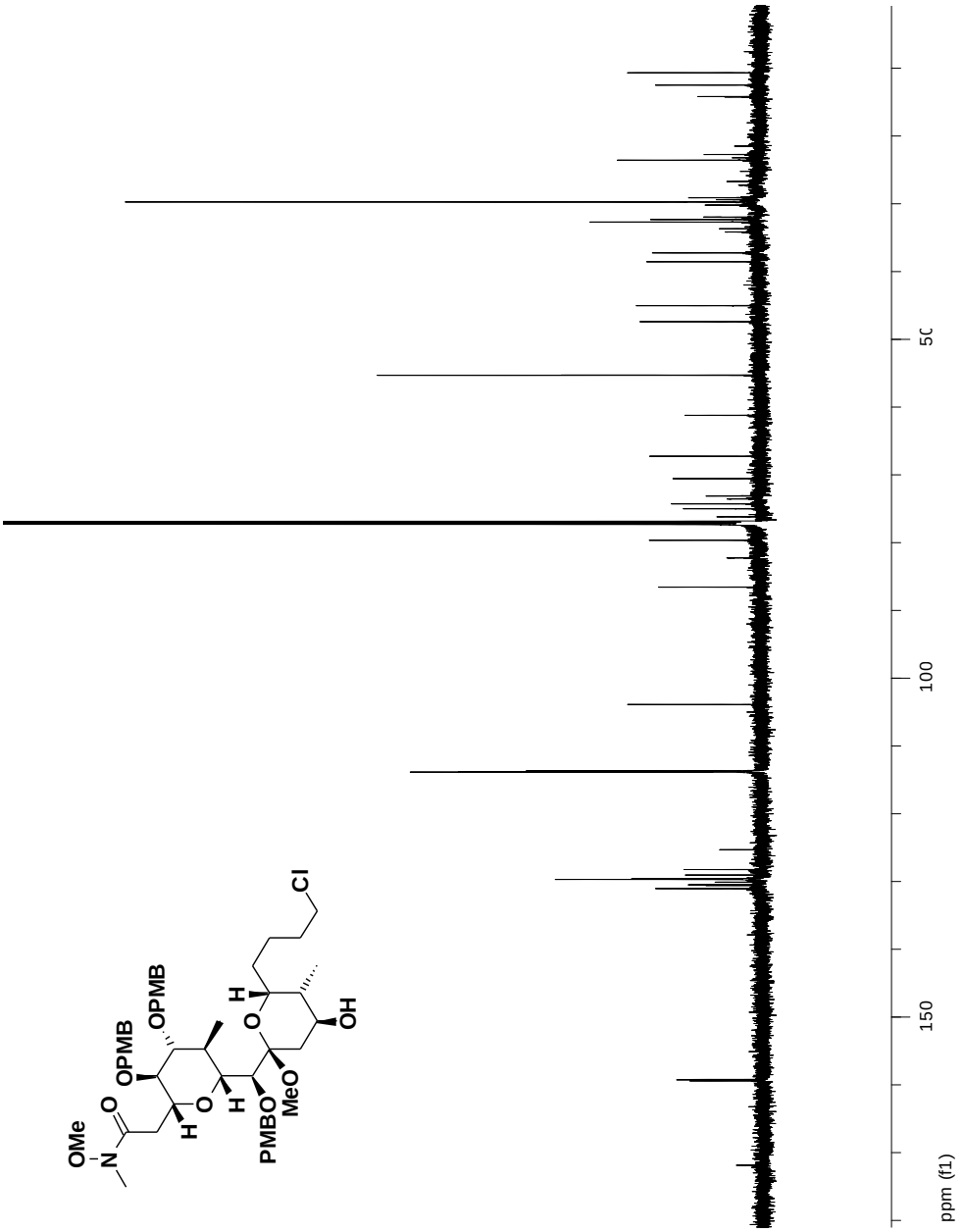
^{13}C NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((1*S*,4*S*,5*R*,6*R*)-10-Chloro-4-hydroxy-1-(4-methoxybenzyloxy)-5-methyl-2-oxo-6-(triethylsilyloxy)decyl)-3,4-bis(4-methoxybenzyl oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide 20



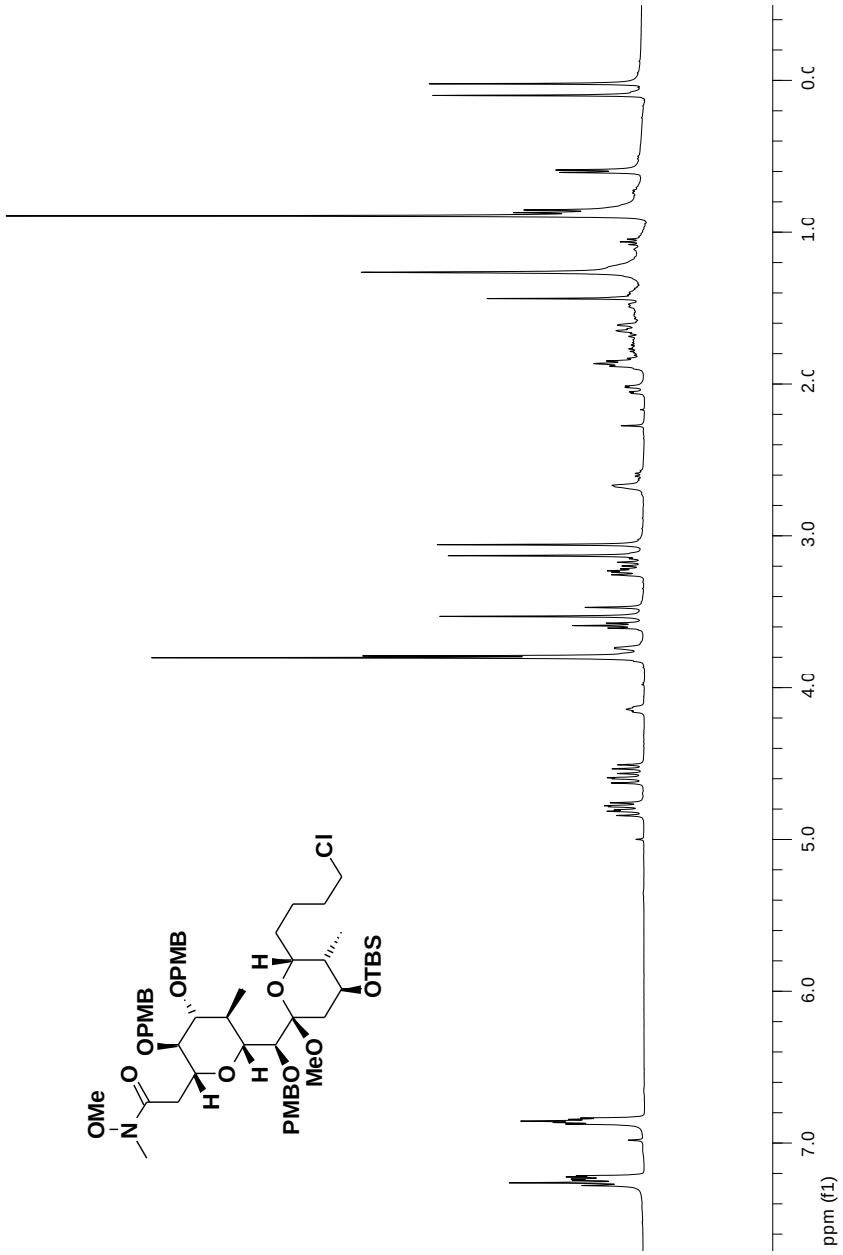
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*R*,6*R*)-6-(4-Chlorobutyl)-4-hydroxy-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S17



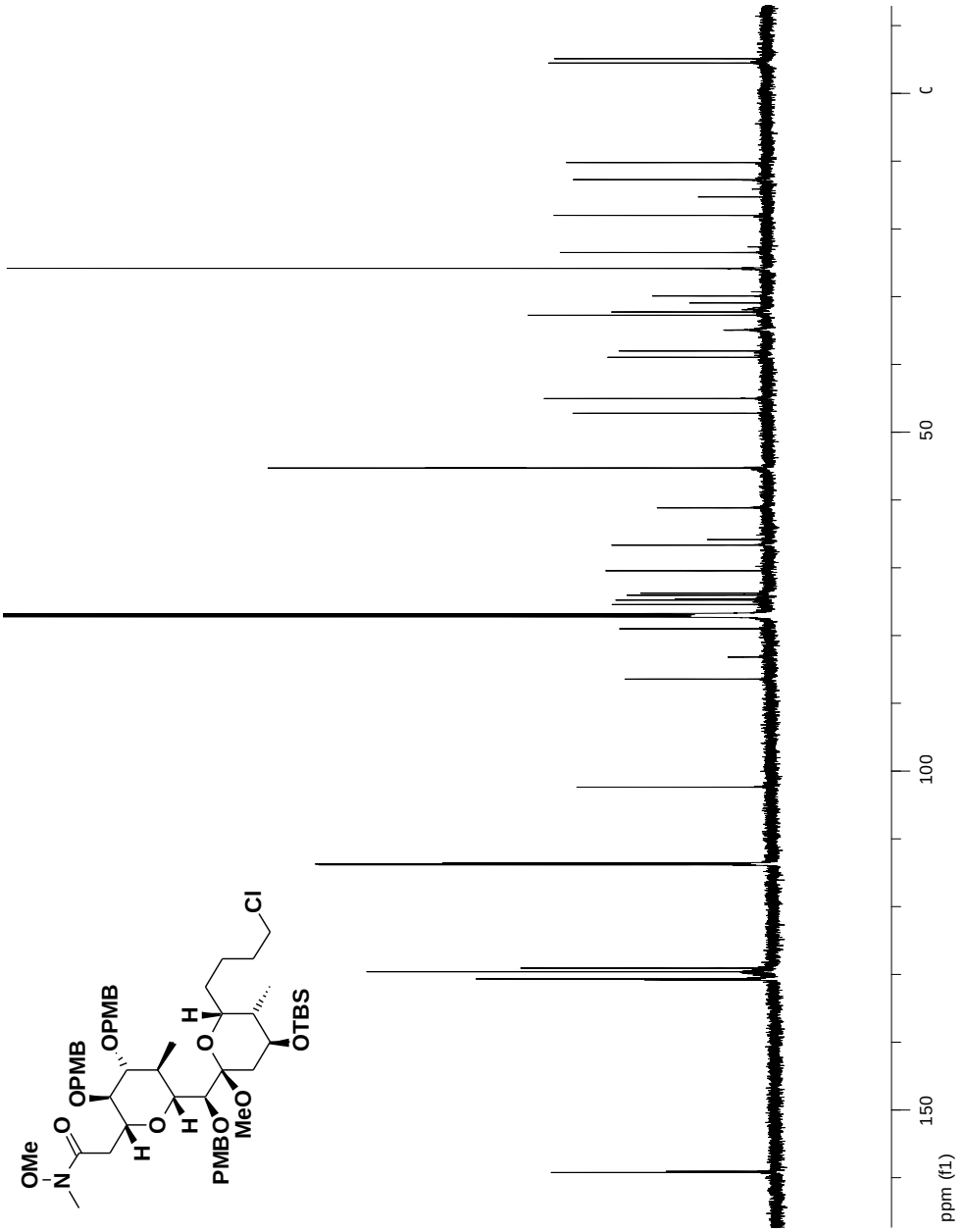
^{13}C NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*R*,6*R*)-6-(4-Chlorobutyl)-4-hydroxy-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S17



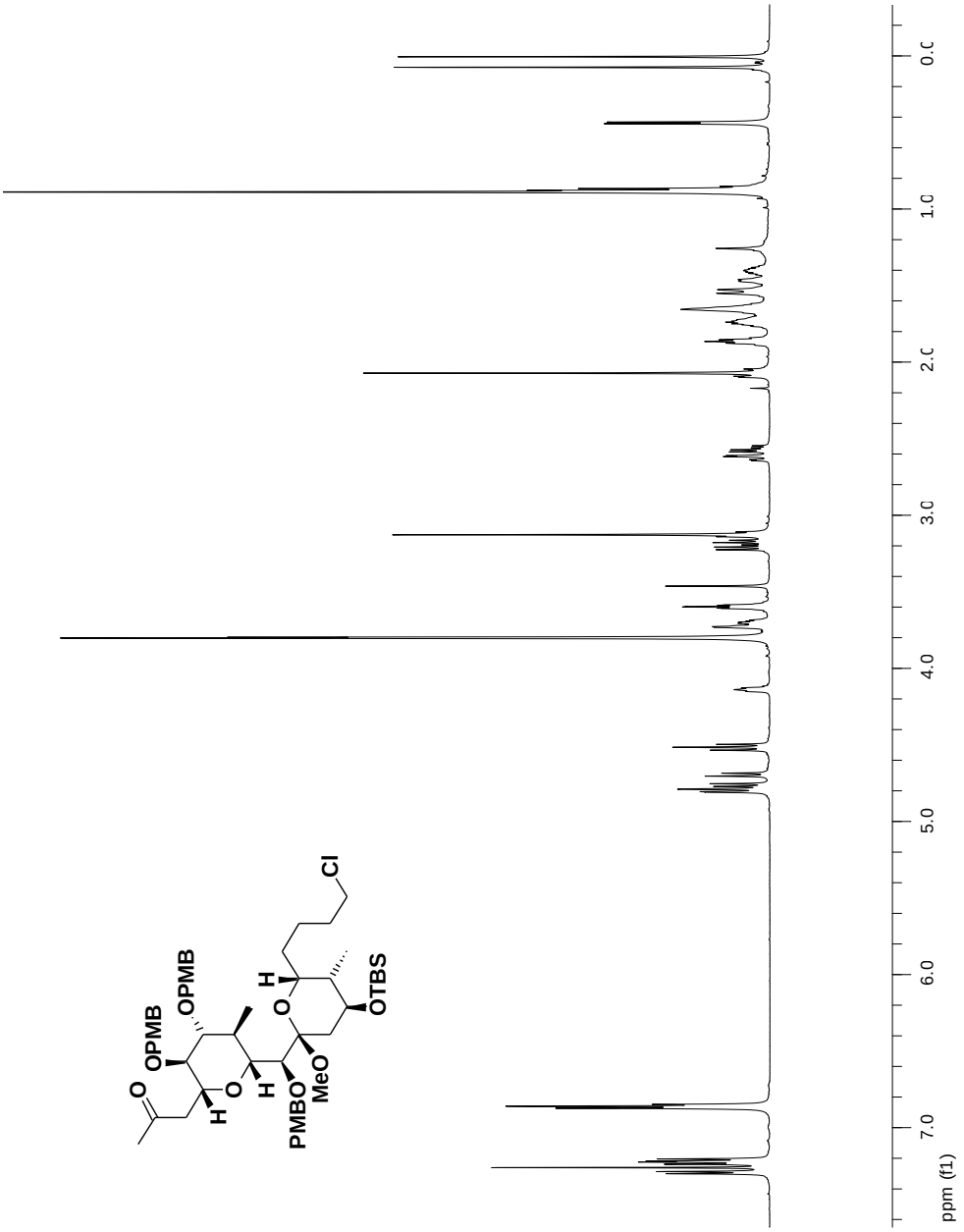
^{1}H NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S18



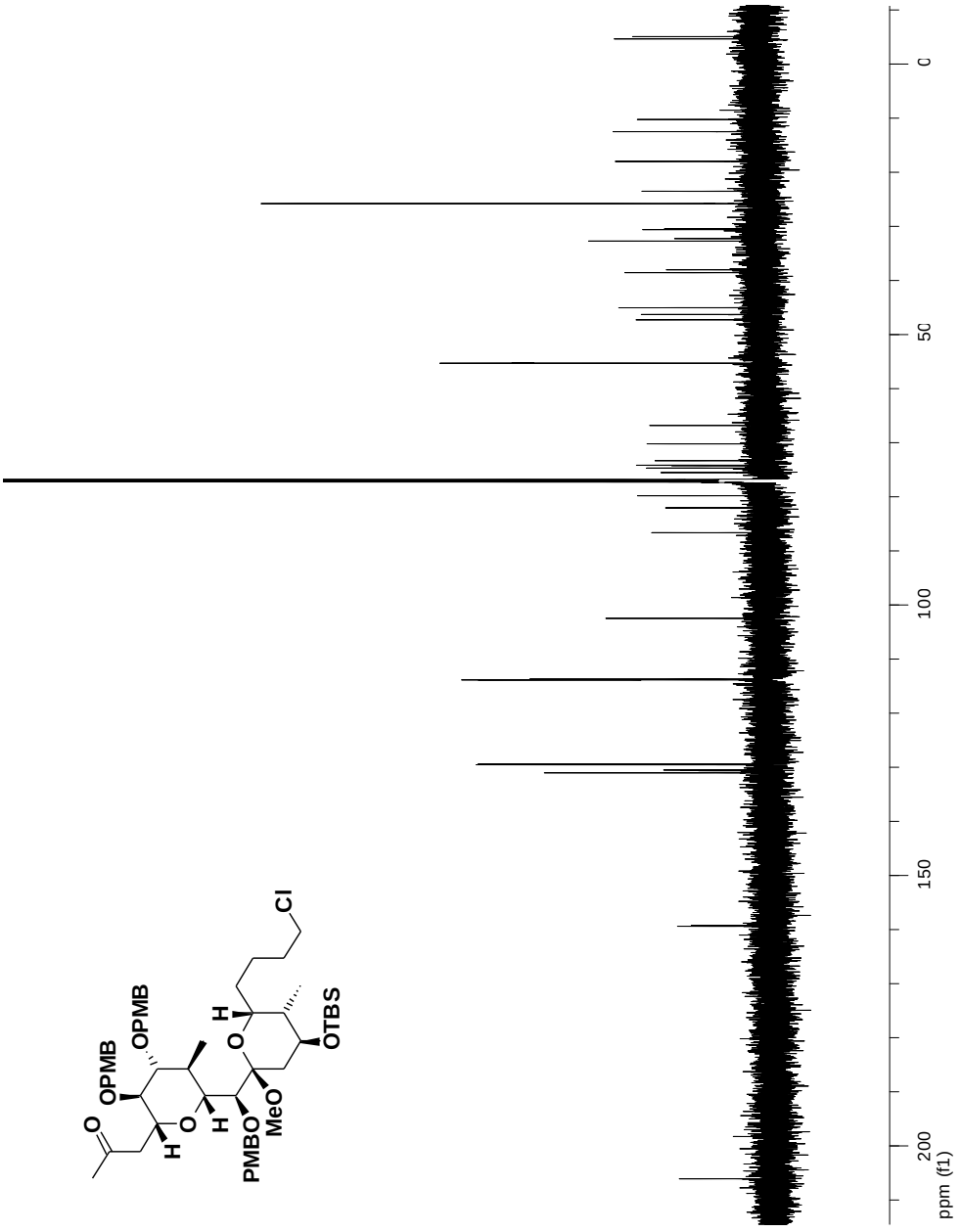
^{13}C NMR: 2-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-*N*-methoxy-*N*-methylacetamide S18



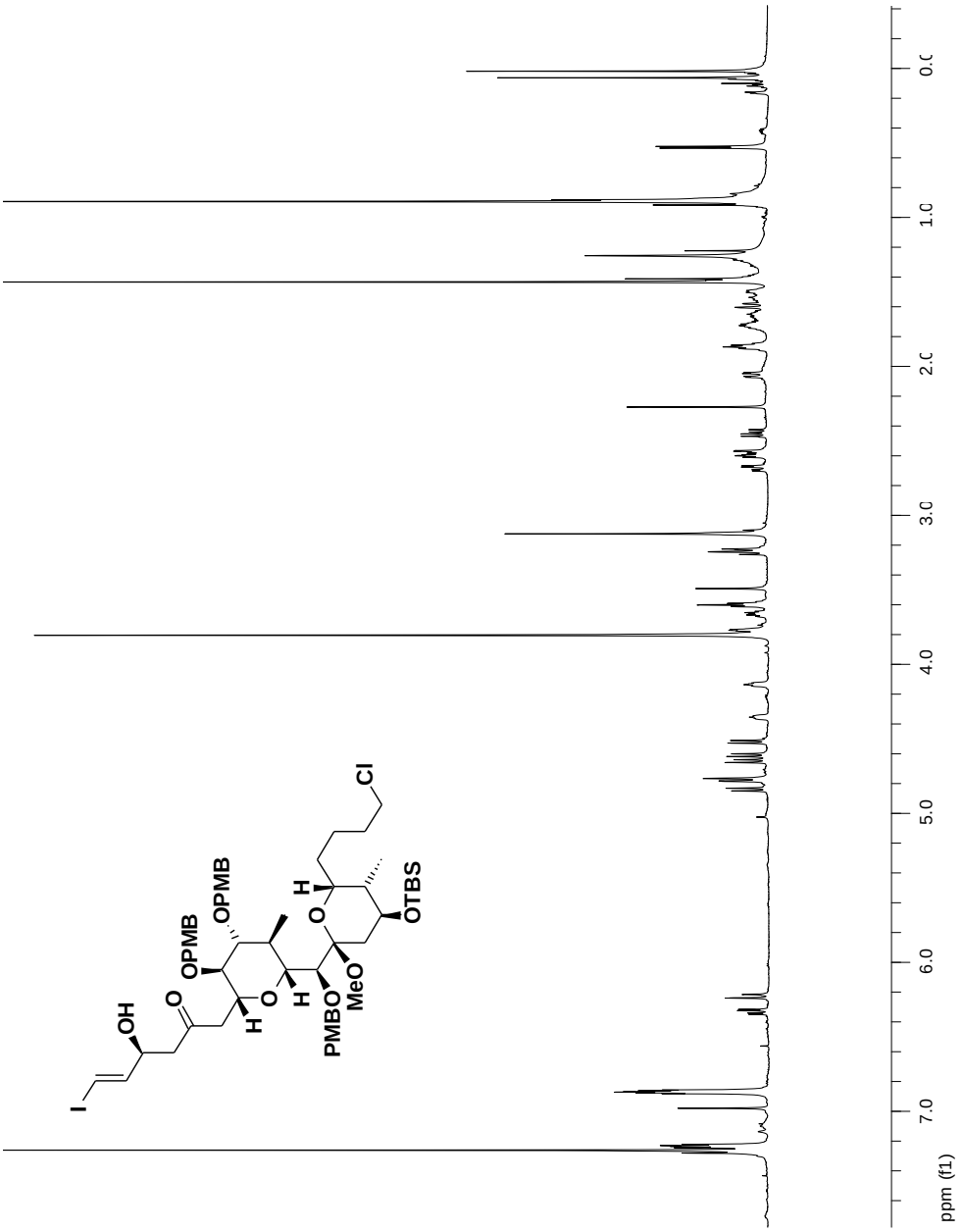
^{1}H NMR: 1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)propan-2-one 21



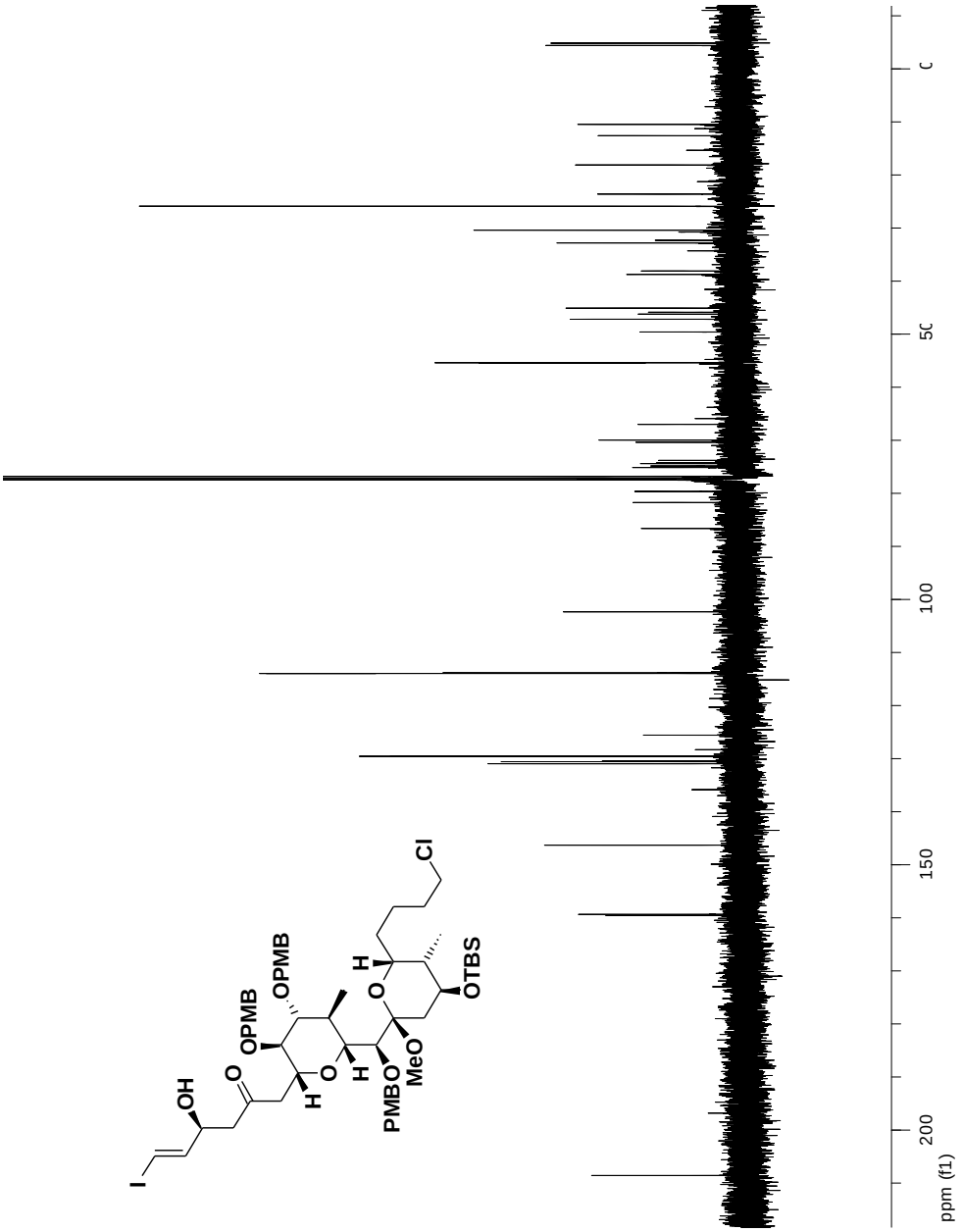
^{13}C NMR: 1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)(4-methoxybenzyloxy)methyl)-3,4-bis(4-methoxybenzyloxy)-5-methyltetrahydro-2*H*-pyran-2-yl)propan-2-one 21



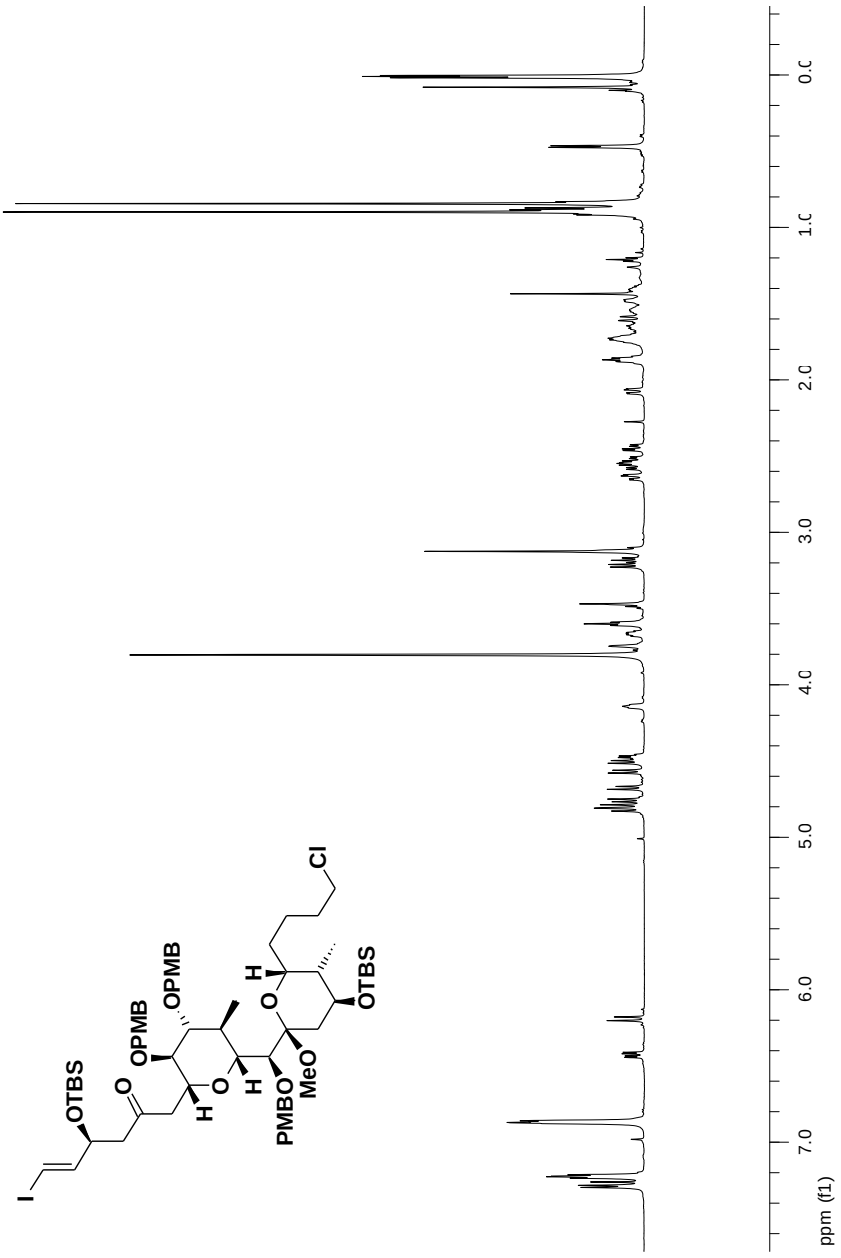
^{1}H NMR: (4*S*,5*E*)-1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-4-hydroxy-6-iodohex-5-en-2-one 23



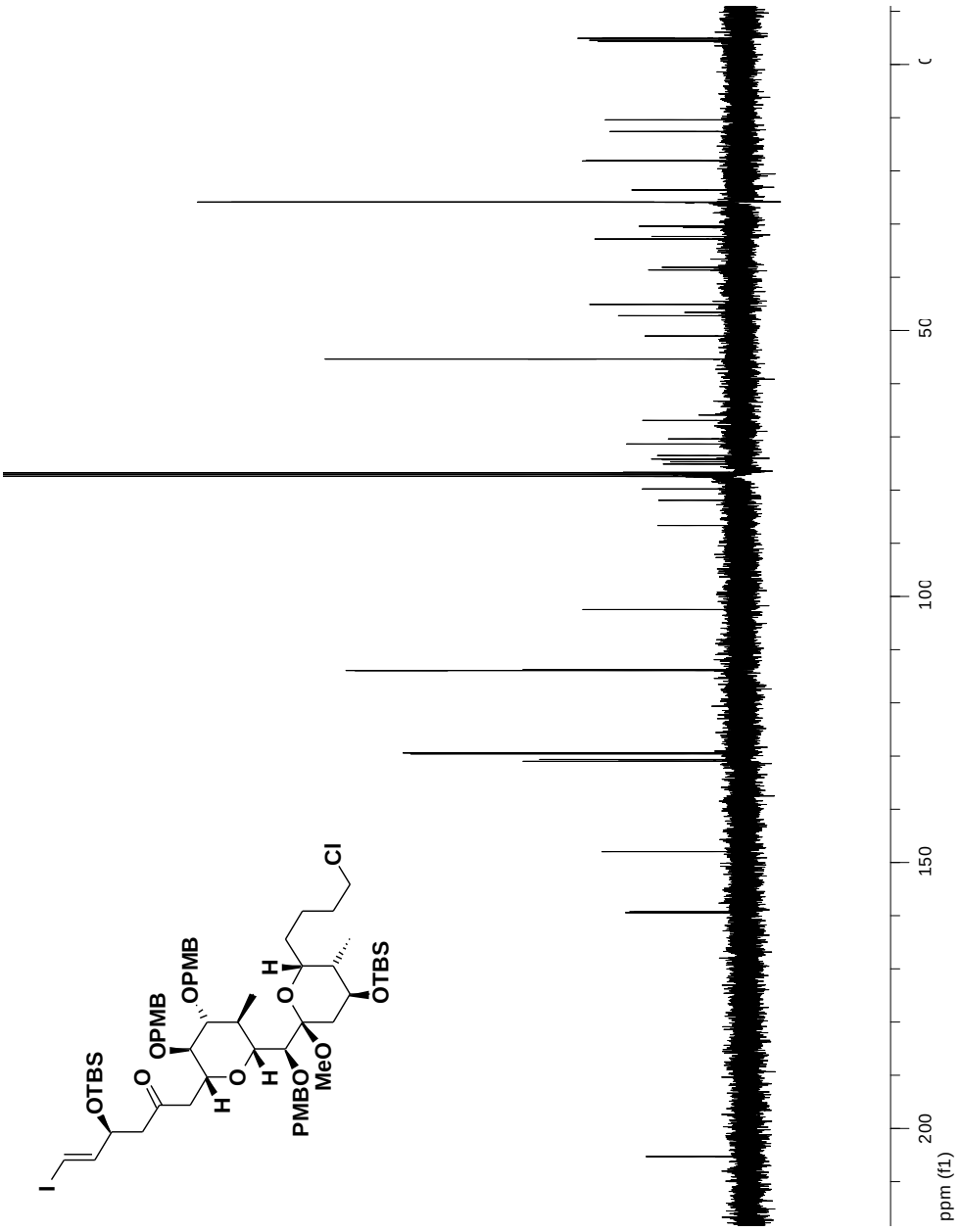
^{13}C NMR: (4*S*,5*E*)-1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-4-hydroxy-6-iodohex-5-en-2-one 23



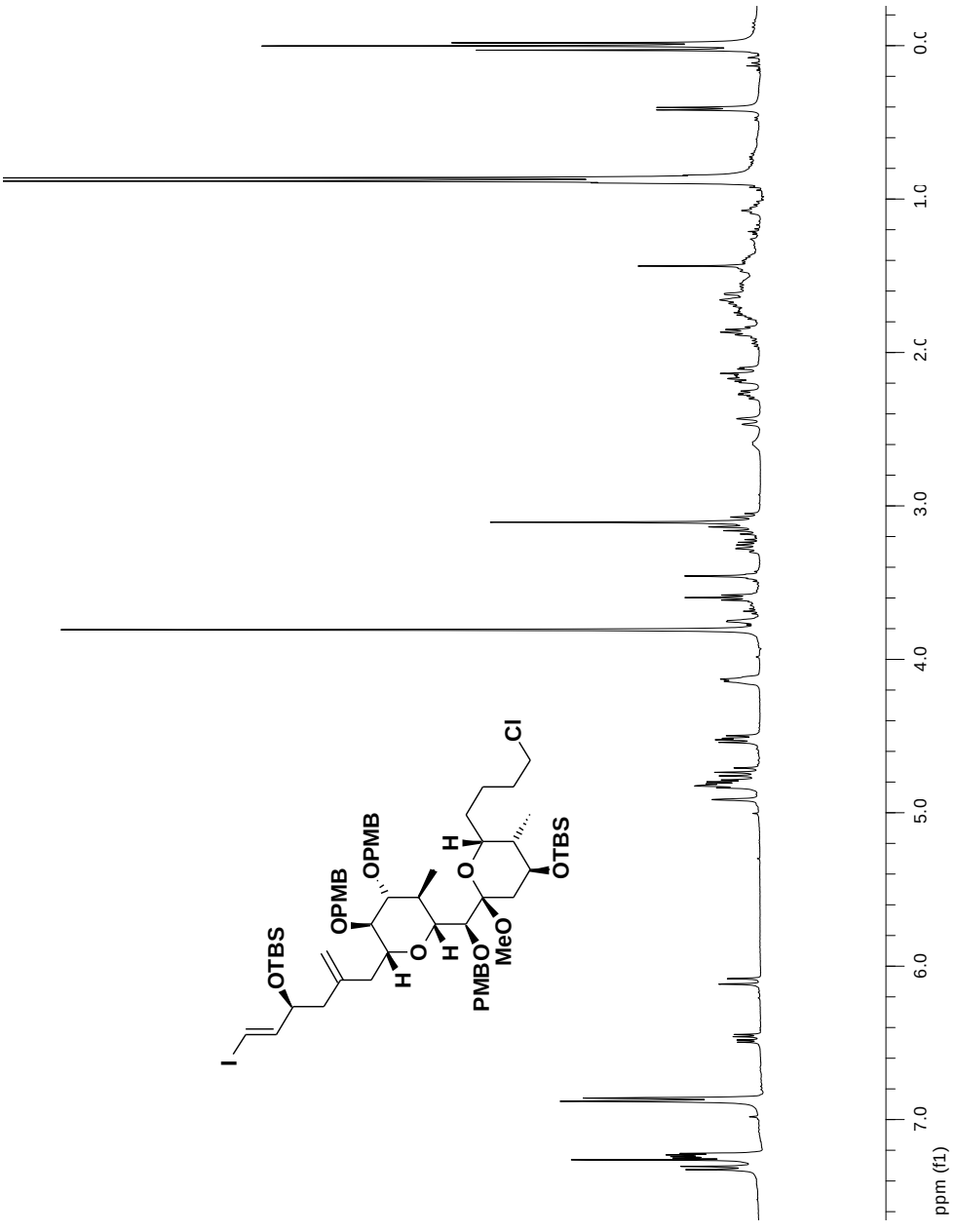
^{1}H NMR: (4*S*,5*E*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-6-iodohex-5-en-2-one S22



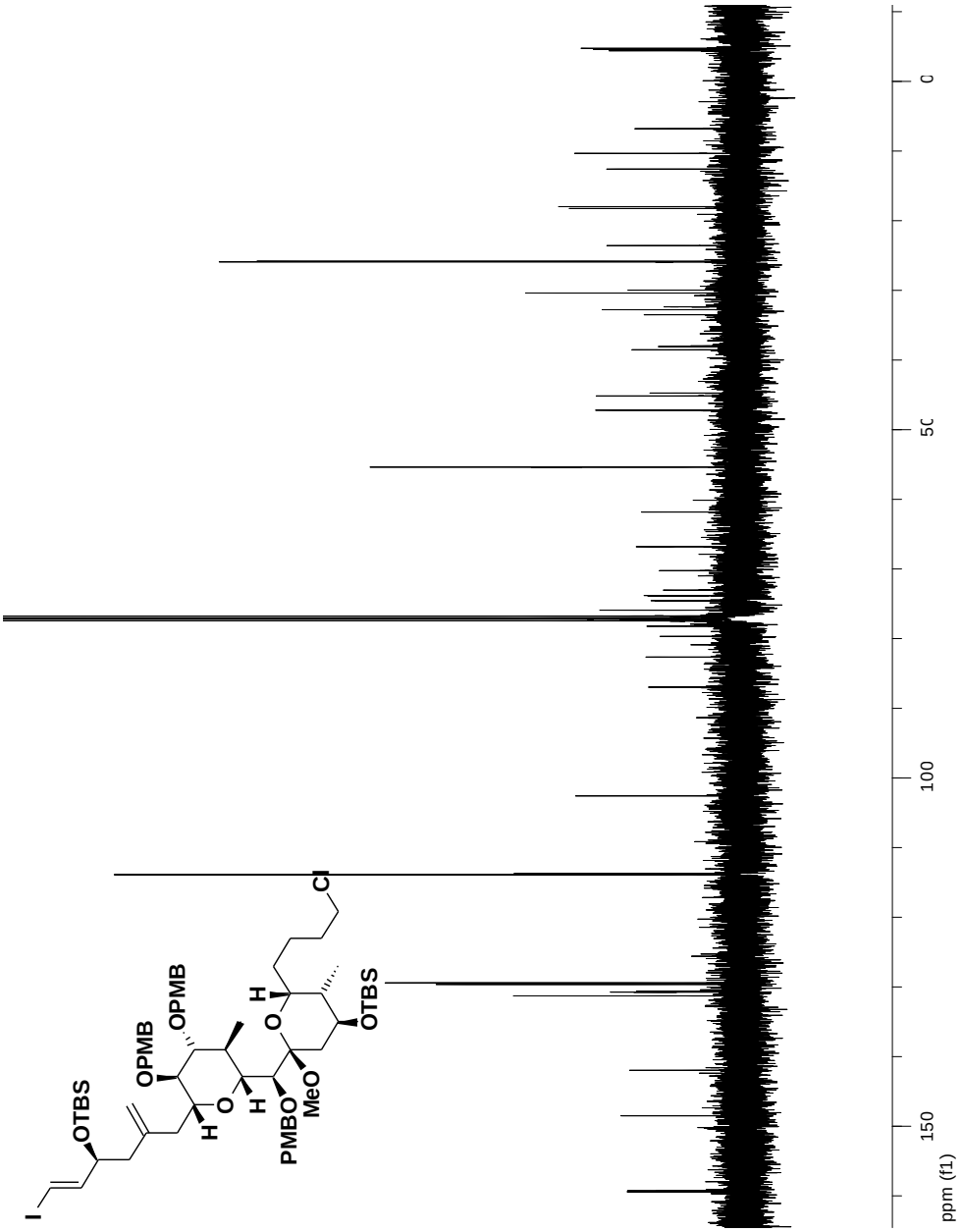
^{13}C NMR: (4*S*,5*E*)-4-((*tert*-Butyl(dimethyl)silyl)oxy)-1-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)-6-iodohex-5-en-2-one S22



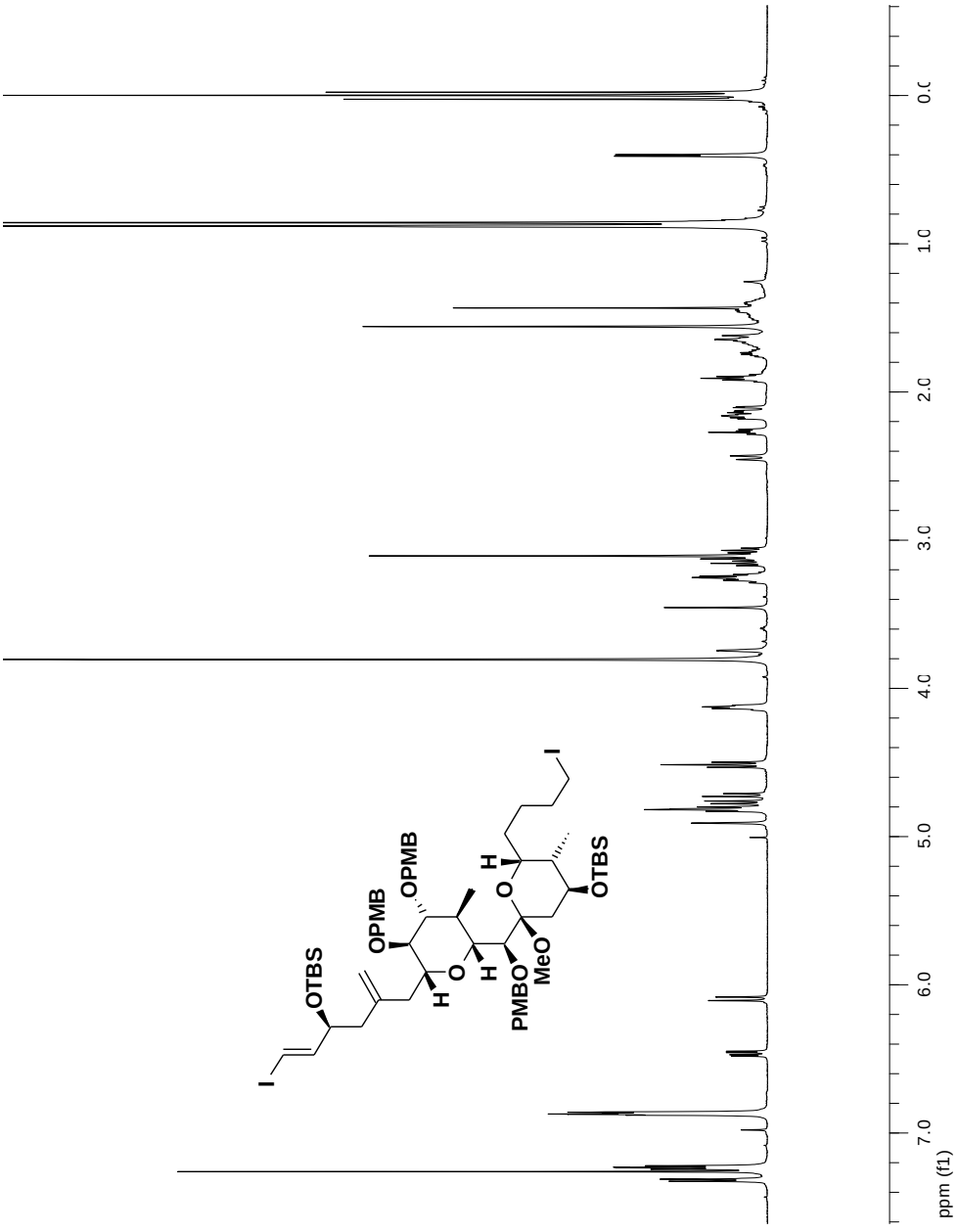
^{1}H NMR: *tert*-Butyl(((1*E*,3*S*)-5-(((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)methyl)-1-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane S23



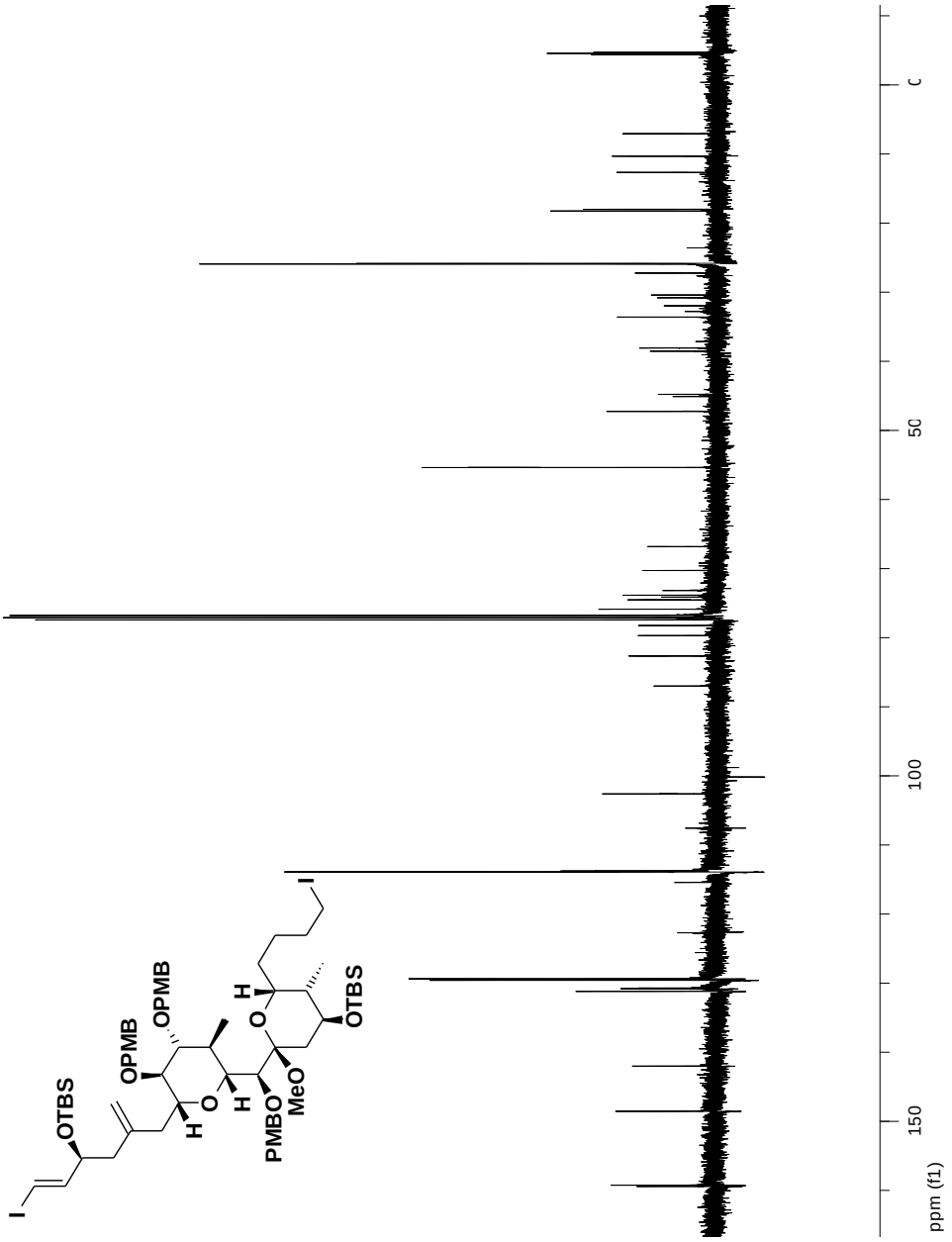
^{13}C NMR: *tert*-Butyl(((1*E*,3*S*)-5-(((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-chlorobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)methyl)-1-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane S23



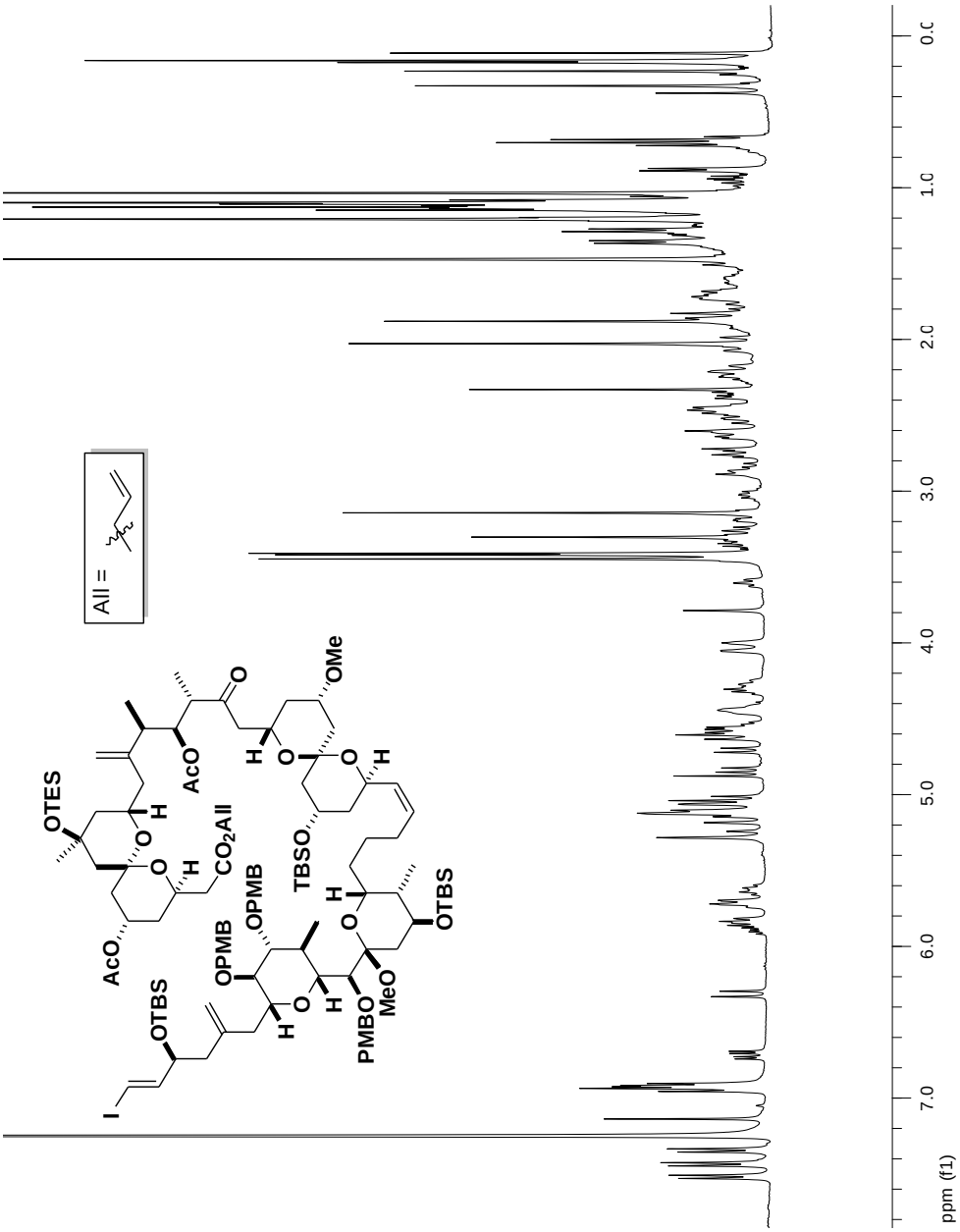
^{1}H NMR: *tert*-Butyl(((1*E*,3*S*)-5-(((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-iodobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)methyl)-1-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane S24



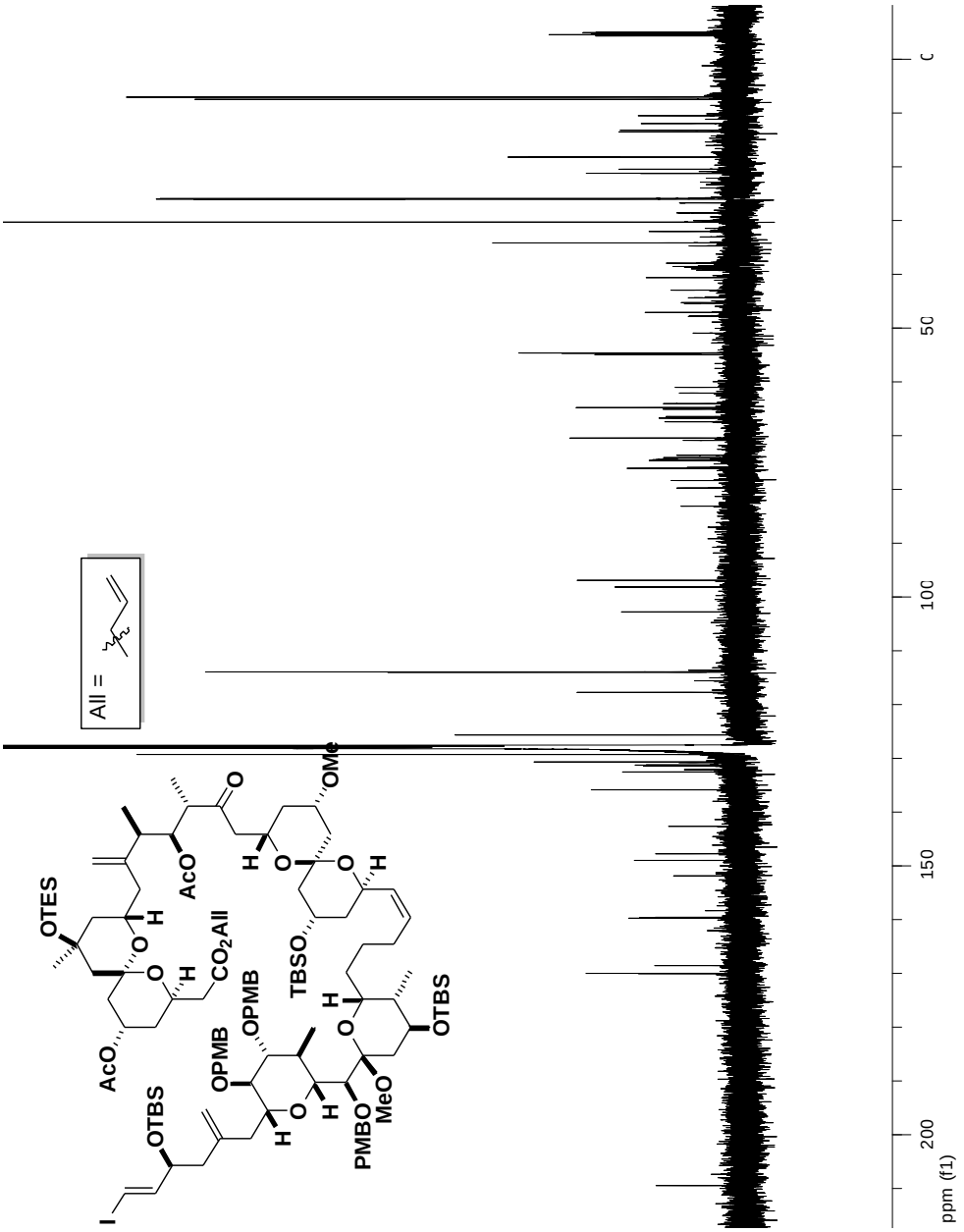
^{13}C NMR: *tert*-Butyl(((1*E*,3*S*)-5-(((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((*S*)-((2*R*,4*S*,5*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-(4-iodobutyl)-2-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-3,4-bis((4-methoxybenzyl)oxy)-5-methyltetrahydro-2*H*-pyran-2-yl)methyl)-1-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane S24



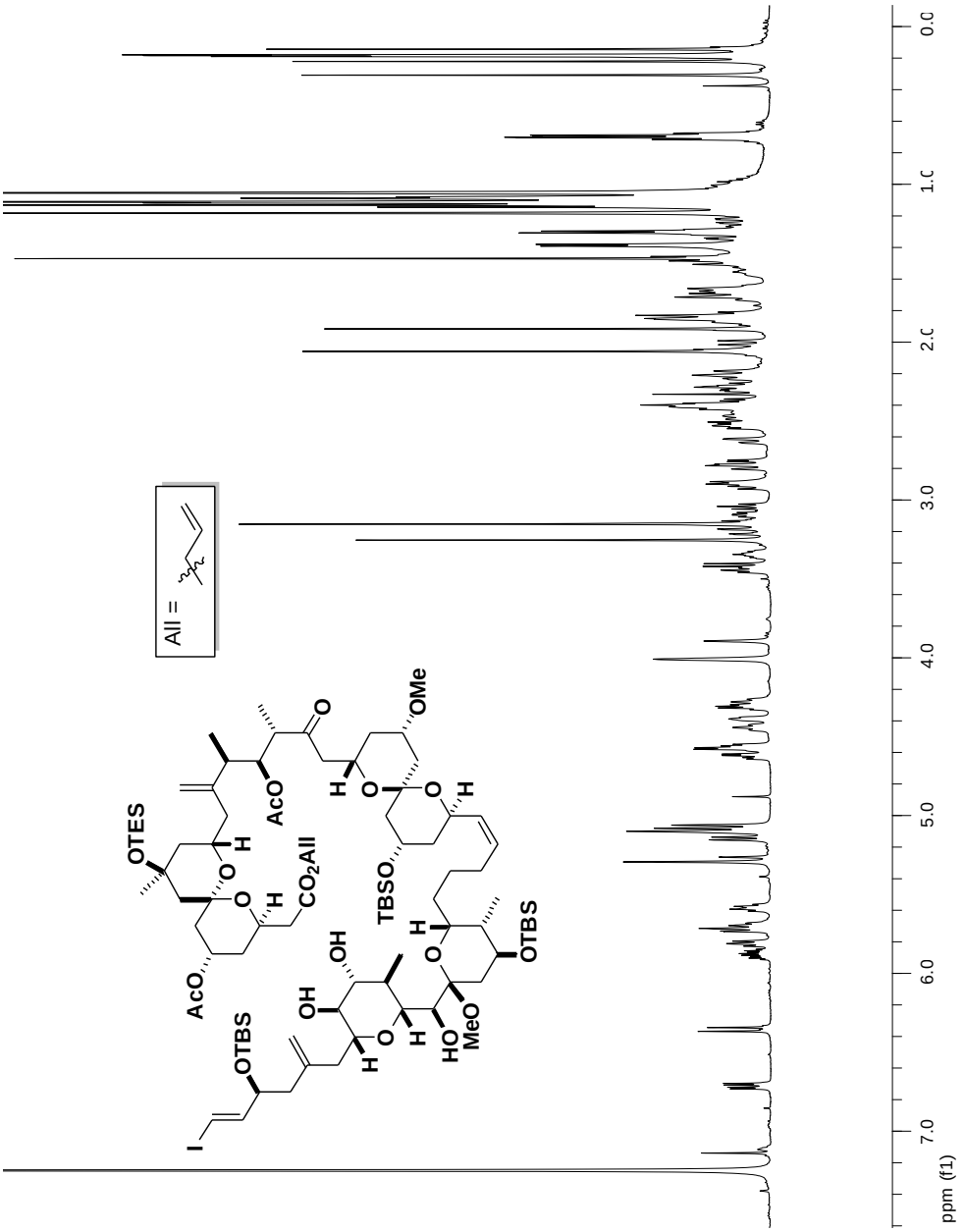
^{1}H NMR: Prop-2-en-1-yl ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-bis((4-methoxybenzyl)oxy)-3-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetate 25



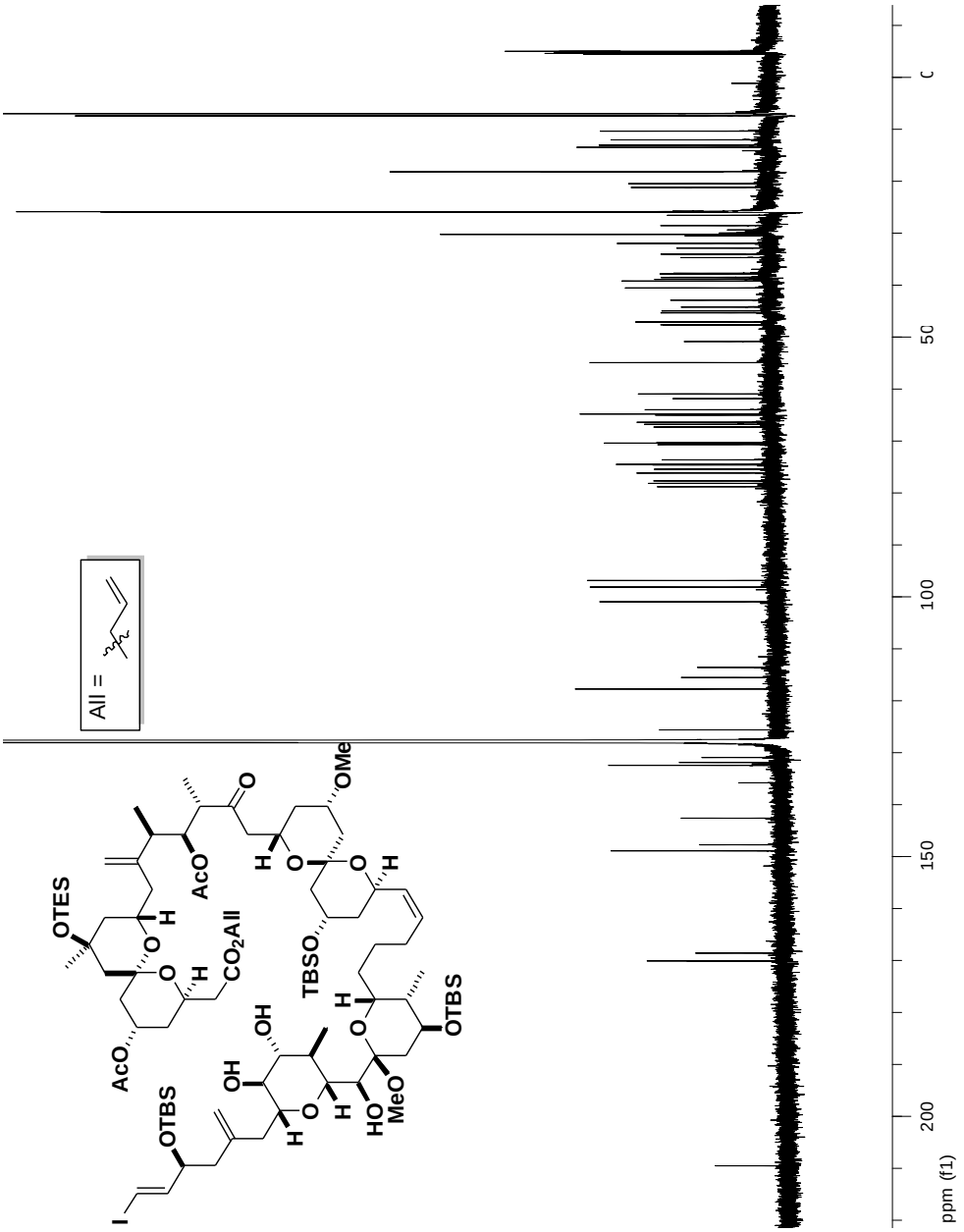
^{13}C NMR: Prop-2-en-1-yl ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-bis((4-methoxybenzyl)oxy)-3-methyltetrahydro-2*H*-pyran-2-yl)((4-methoxybenzyl)oxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetate 25



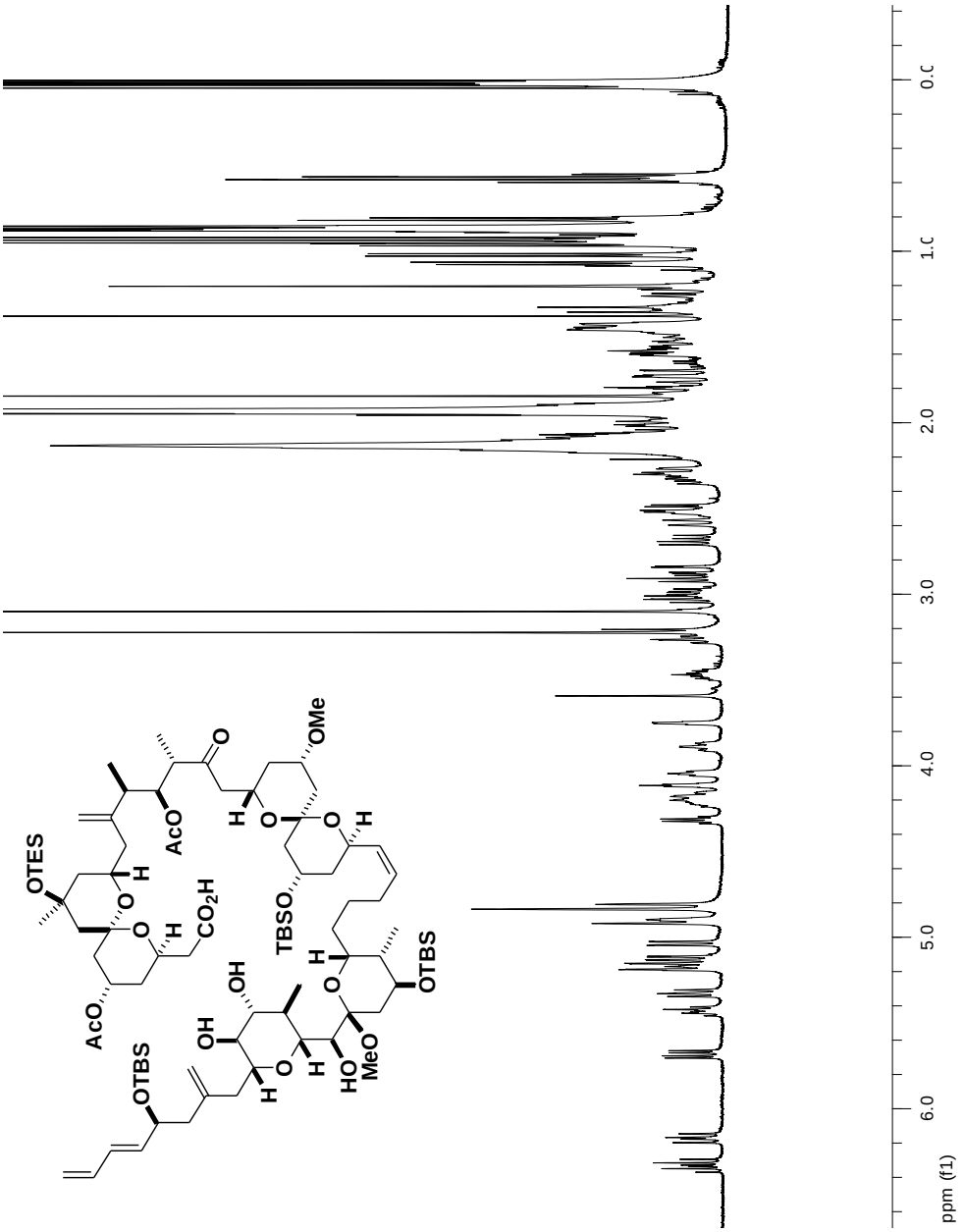
^{1}H NMR: Prop-2-en-1-yl ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*S*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-dihydroxy-3-methyltetrahydro-2*H*-pyran-2-yl)(hydroxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetate S25



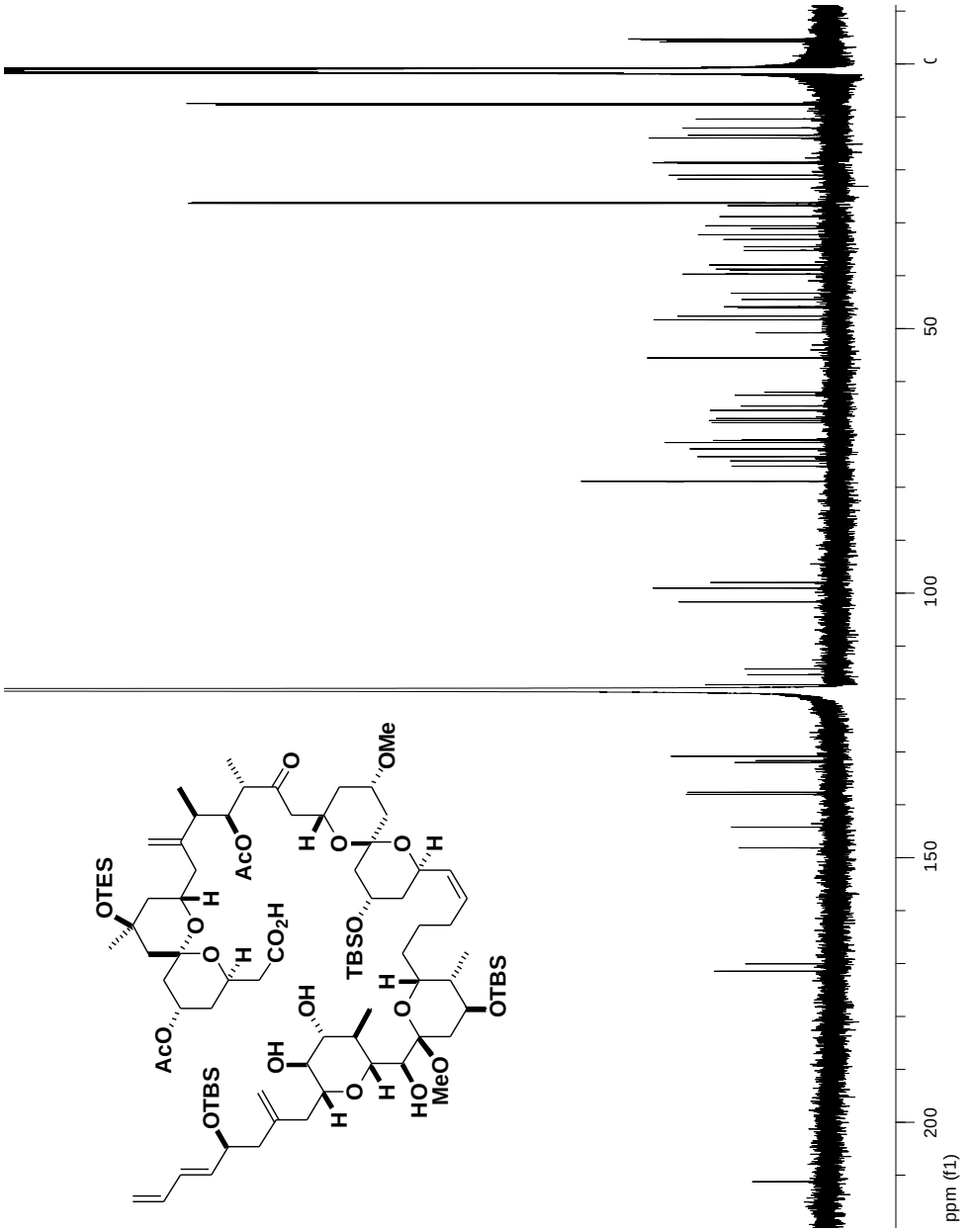
^{13}C NMR: Prop-2-en-1-yl ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*S*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-iodo-2-methylidenehex-5-en-1-yl)-4,5-dihydroxy-3-methyltetrahydro-2*H*-pyran-2-yl)(hydroxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetate S25



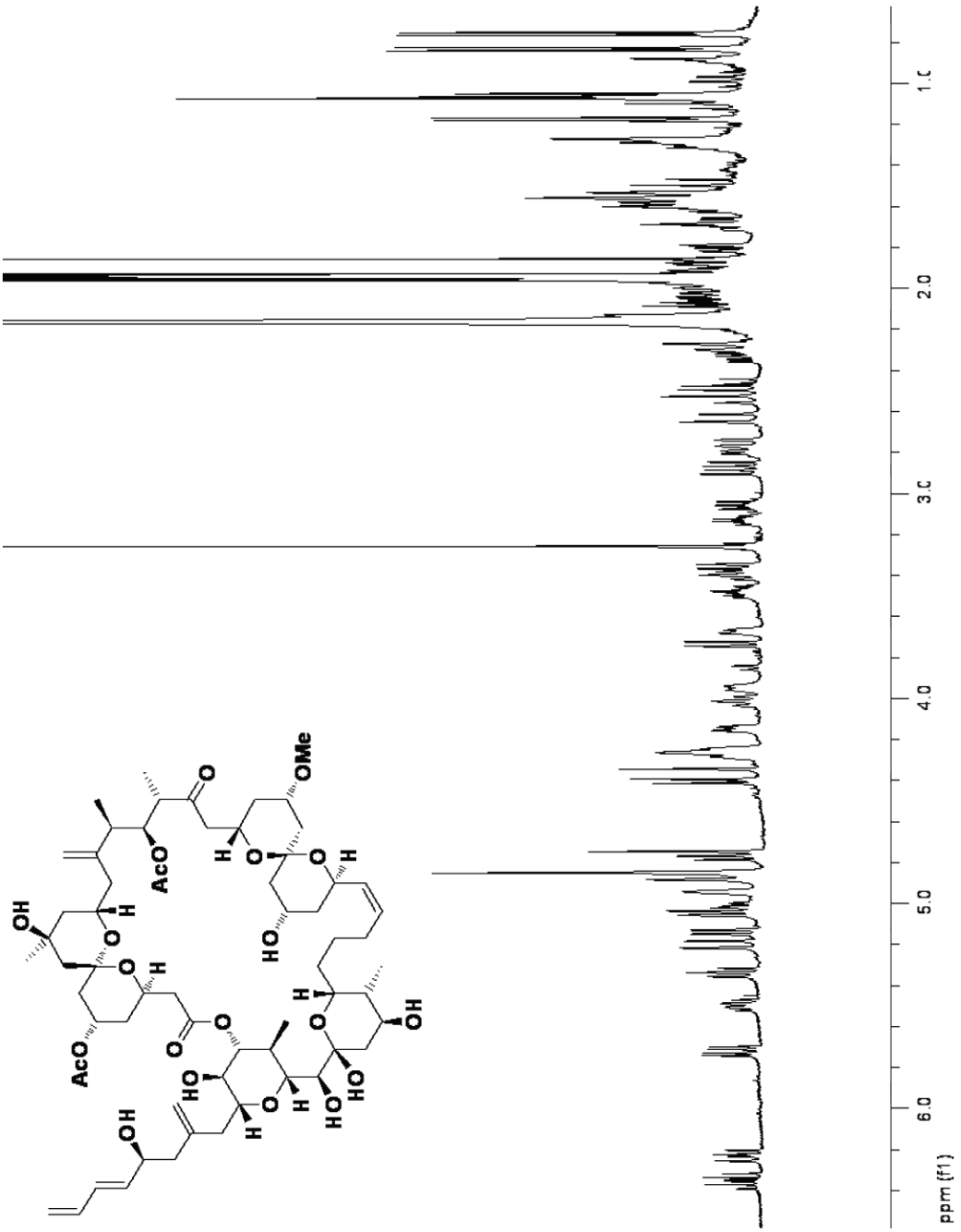
^{1}H NMR: ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(Acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*S*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-2-methylideneocta-5,7-dien-1-yl)-4,5-dihydroxy-3-methyltetrahydro-2*H*-pyran-2-yl)(hydroxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetic acid 26



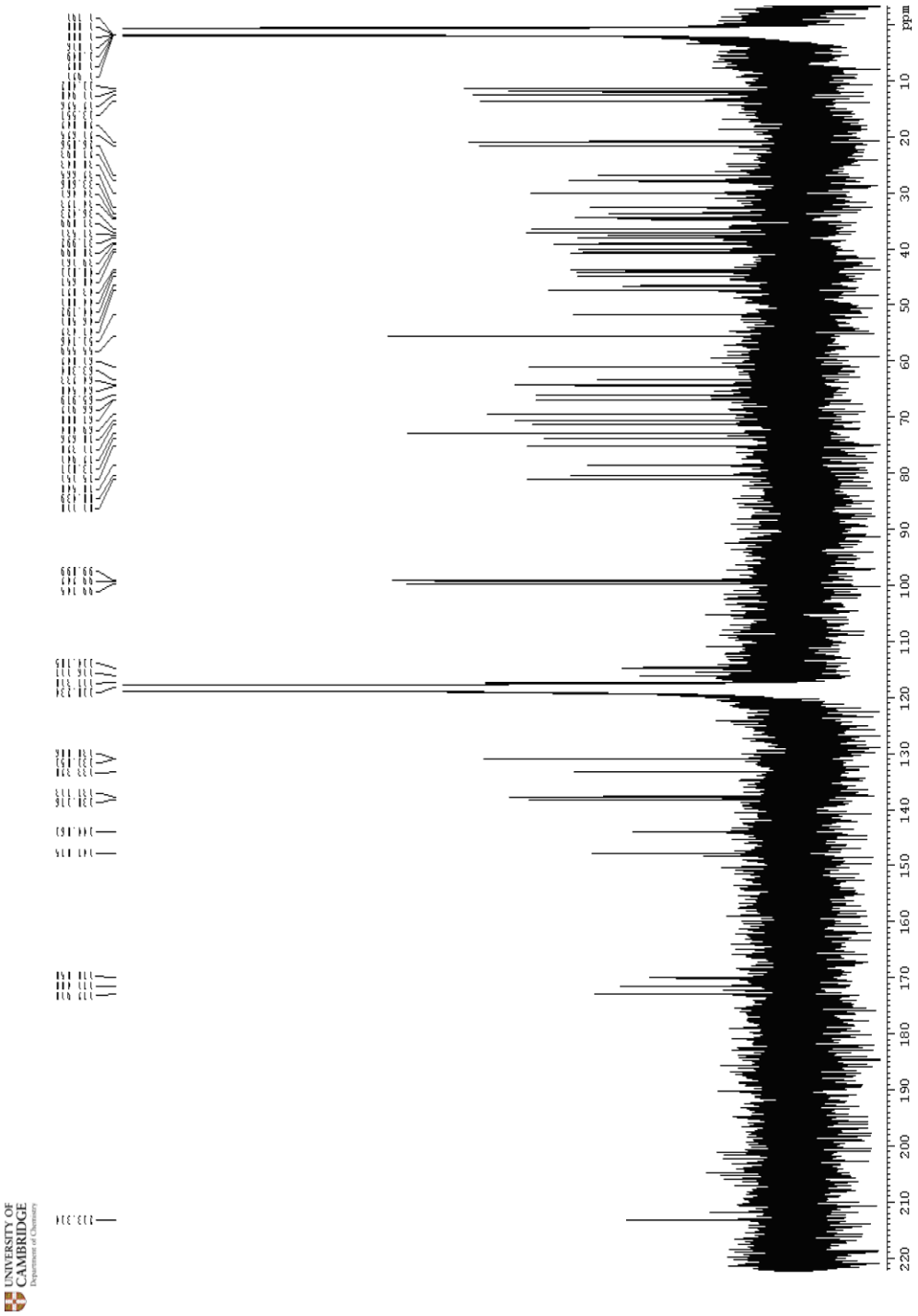
^{13}C NMR: ((2*R*,4*S*,6*S*,8*S*,10*S*)-4-(Acetyloxy)-8-((3*R*,4*S*,5*S*)-4-(acetyloxy)-7-((2*S*,4*S*,6*S*,8*R*,10*S*)-10-((*tert*-butyl(dimethyl)silyl)oxy)-8-((1*Z*)-5-((2*R*,3*S*,4*S*,6*R*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-6-((*S*)-((2*R*,3*R*,4*R*,5*S*,6*R*)-6-((4*S*,5*E*)-4-((*tert*-butyl(dimethyl)silyl)oxy)-2-methylideneocta-5,7-dien-1-yl)-4,5-dihydroxy-3-methyltetrahydro-2*H*-pyran-2-yl)(hydroxy)methyl)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)pent-1-en-1-yl)-4-methoxy-1,7-dioxaspiro[5.5]undec-2-yl)-3,5-dimethyl-2-methylidene-6-oxoheptyl)-10-methyl-10-((triethylsilyl)oxy)-1,7-dioxaspiro[5.5]undec-2-yl)acetic acid 26



^{1}H NMR: synthetic spongistatin 2 (2)



^{13}C NMR: synthetic spongistatin 2 (2)



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