

The Stereocontrolled Total Synthesis of Spirastrellolide A Methyl Ester. Expedient Construction of the Key Fragments[†]

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1) General Experimental Procedures

^1H nuclear magnetic resonance (NMR) spectra were recorded using an internal deuterium lock for the residual protons in CDCl_3 (δ 7.26) and C_6D_6 (δ 7.15) at ambient probe temperatures on the following instruments: Bruker AVANCE BB500 or TCI500 (500 MHz) and AM400 (400 MHz). Data are presented as follows: chemical shift (in ppm on a δ scale relative to $\delta_{\text{TMS}} = 0$), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, br = broad, app = apparent), coupling constant (J / Hz) and assignment. Assignments were determined either on the basis of unambiguous chemical shift or coupling pattern, COSY experiments or by analogy to fully interpreted spectra for related compounds. ^{13}C spectra were recorded by broad band proton spin decoupling, at ambient probe temperatures on the following instruments: Bruker AVANCE BB500 or TCI500 (125 MHz) and AM400 (100 MHz), using an internal deuterium lock for CDCl_3 (δ 77.0) or C_6D_6 (δ 128.0). Chemical shifts are given in ppm on a δ scale relative to $\delta_{\text{TMS}} = 0$.

Infra-red spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer fitted with a universal ATR sampling accessory. Wavelengths of maximum absorbance (ν_{max}) are quoted in cm^{-1} .

High and low resolution mass spectra were recorded by the EPSRC Mass Spectrometry service, Swansea, UK and by the Departmental Mass Spectrometry Service (Cambridge University Chemical Laboratories), using chemical ionization (CI), electron impact (EI) or electron spray ionization (ESI) techniques. The parent ion $[\text{M}]^+$ or $[\text{M} + \text{H}]^+$, $[\text{M} + \text{NH}_4]^+$, $[\text{M} + \text{Na}]^+$ is quoted.

Optical rotations were measured on a Perkin Elmer 241 polarimeter at the sodium D-line (589 nm) and are reported as follows: $[\alpha]_{\text{D}}^{20}$ concentration (c in g/dm^3) and solvent.

Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F254 plates with visualization by ultraviolet light (254 nm) and potassium permanganate or phosphomolybdic acid / cerium sulphate dips. Flash chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) under a positive pressure using distilled solvents; the procedure includes the subsequent evaporation of solvents *in vacuo*. High performance liquid chromatography (HPLC) was carried out using a Waters Spherisorb S5 ODS2 column (4.6×250 mm), equipped with a Gilson UV detector (Model 118) at a wavelength of 200 nm.

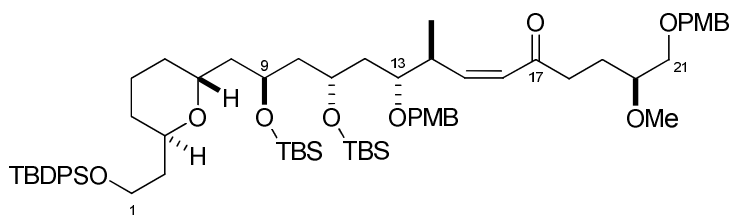
Dichloromethane (CH_2Cl_2 ; DCM), acetonitrile (MeCN) and methanol (MeOH) were distilled from calcium hydride and stored under an argon atmosphere; tetrahydrofuran (THF) and diethyl ether

(Et₂O) were distilled from sodium or potassium wire / benzophenone ketyl radical under an argon atmosphere. Triethylamine, 2,6-lutidine and diisopropylamine were distilled from and stored over calcium hydride. 4Å molecular sieves were activated by heating under high vacuum or in a microwave. Solvents used for all extractions in work-up were distilled. All other chemicals were used as received, except where otherwise noted in the experimental text. All solutions of sodium bicarbonate (NaHCO₃), ammonium chloride (NH₄Cl), sodium thiosulphate (Na₂S₂O₃) and sodium / potassium tartrate (Na⁺/K⁺ tartrate) were aqueous and saturated. The term 'brine' is used to describe a saturated aqueous solution of sodium chloride (NaCl). All experiments were performed under anhydrous conditions under an atmosphere of argon, except where stated, using oven-dried apparatus and employing standard techniques for handling air-sensitive materials.

2) Experimental Data

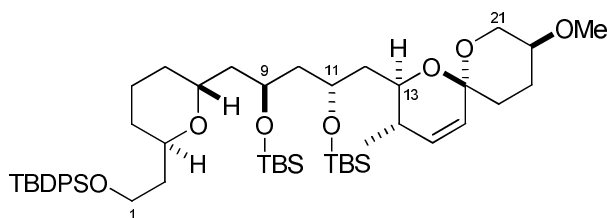
2.1 Synthesis of Spiroacetal **24**

(*Z*)-enone **23**



$R_f = 0.26$ (1:5 EtOAc / PE 40-60); $[\alpha]_D^{20} +35.9$ (c 0.89, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2931, 2857, 1692, 1614, 1514, 1463, 1249, 1111, 835, 775, 703; **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ 7.64-7.68 (m, 4 H), 7.35-7.42 (m, 6 H), 7.27 (d, $J = 8.7$ Hz, 2 H), 7.24 (d, $J = 8.7$ Hz, 2 H), 6.86 (d, $J = 8.7$ Hz, 2 H), 6.85 (d, $J = 8.7$ Hz, 2 H), 6.13 (d, $J = 11.4$ Hz, 1 H), 6.05 (dd, $J = 11.4, 9.7$ Hz, 1 H), 4.54 (d, $J = 11.3$ Hz, 1 H), 4.50 (d, $J = 11.3$ Hz, 1 H), 4.46 (s, 2 H), 3.93 (m, 1 H), 3.88 (m, 1 H), 3.83 (m, 1 H), 3.79 (m, 1 H), 3.67-3.81 (m, 10 H), 3.55 (m, 1 H), 3.37 (s, 3 H), 3.35 (m, 1 H), 2.47 (ddd, $J = 15.1, 8.6, 6.2$ Hz, 1 H), 2.48 (ddd, $J = 15.1, 8.6, 6.5$ Hz, 1 H), 1.93 (m, 1 H), 1.77-1.85 (m, 2 H), 1.51-1.76 (m, 10 H), 1.39-1.48 (m, 2 H), 1.32 (m, 1 H), 1.18 (m, 1 H), 1.04 (s, 9 H), 1.02 (d, $J = 6.9$ Hz, 3 H), 0.87 (s, 9 H), 0.83 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H), 0.01 (s, 3 H), 0.00 (s, 3 H); **$^{13}\text{C NMR}$** (125 MHz, CDCl_3): $\delta = 200.7, 159.2, 159.0, 150.0, 135.6, 134.0, 131.3, 130.4, 129.5, 129.3, 129.1, 127.6, 126.6, 113.8, 113.6, 79.2, 78.8, 73.0, 71.6, 71.1, 68.7, 67.4, 67.3, 61.0, 57.6, 55.3, 46.7, 42.2, 40.5, 40.0, 35.8, 35.5, 30.3, 29.6, 26.9, 26.0, 25.9, 25.7, 19.2, 18.6, 18.0, 16.0, -3.7, -3.8, -4.0, -4.1$; **HRMS** (ES^+) calcd for $\text{C}_{67}\text{H}_{104}\text{O}_{10}\text{Si}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 1175.6830; found 1175.6868.

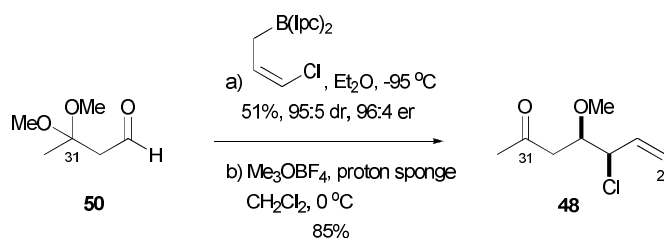
Spiroacetal **24**



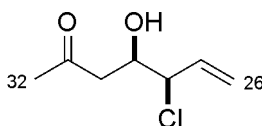
To a stirred solution of enone **23** (17.1 mg, 14.8 μmol) in CH_2Cl_2 (1.5 mL) and pH 7 buffer (150 μL) at 0 $^\circ\text{C}$ was added DDQ (13.2 mg, 59.1 μmol). The reaction mixture was stirred at 0 $^\circ\text{C}$ for 1 h then RT for a further 1 h before being quenched with NaHCO_3 (1 mL). The mixture was extracted with CH_2Cl_2 (3 \times 5 mL), dried (MgSO_4) and concentrated *in vacuo*. Purification by flash chromatography (1:10 EtOAc / PE 40-60) afforded the spiroacetal **24** (8.1 mg, 9.1 μmol , 61%) as a

colourless oil; $R_f = 0.32$ (EtOAc / PE, 1:9); $[\alpha]_D^{20} +34.5$ (c 0.80, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2930, 2857, 1473, 1429, 1388, 1107, 1019, 836, 774, 702; **^1H NMR** (500 MHz, C_6D_6) $\delta = 7.78$ -7.83 (m, 4 H), 7.22-7.29 (m, 6 H), 5.60 (dd, $J = 9.9, 2.4$ Hz, 1 H), 5.51 (dd, $J = 9.9, 1.7$ Hz, 1 H), 4.38 (m, 1 H), 4.22 (m, 1 H), 4.06 (m, 1 H), 4.02 (m, 1 H), 3.94 (m, 1 H), 3.84-3.91 (m, 3 H), 3.80 (m, 1 H), 3.15 (m, 1 H), 3.10 (s, 3 H), 1.90-2.15 (m, 8 H), 1.72-1.87 (m, 3 H), 1.64 (m, 1 H), 1.60 (m, 1 H), 1.45-1.54 (m, 3 H), 1.30-1.40 (m, 2 H), 1.24 (m, 1 H), 1.19 (s, 9 H), 1.05 (s, 9 H), 1.03 (s, 9 H), 0.80 (d, $J = 7.1$ Hz, 3 H), 0.26 (s, 3 H), 0.28 (s, 3 H), 0.24 (s, 3 H), 0.20 (s, 3 H); **^{13}C NMR** (125 MHz, C_6D_6): $\delta = 135.8, 135.7, 134.2, 134.1, 134.0, 129.7, 129.4, 93.0, 74.9, 71.0, 68.4, 68.3, 67.7, 67.6, 63.7, 61.5, 55.7, 46.6, 43.0, 42.5, 36.3, 34.5, 34.3, 30.8, 29.8, 27.0, 26.1, 26.0, 25.3, 19.3, 18.8, 18.2, 18.1, 17.0, -3.5, -3.7, -3.9, -4.0$; **HRMS** (ES^+) calcd for $\text{C}_{51}\text{H}_{87}\text{O}_7\text{Si}_3$ $[\text{M}+\text{H}]^+$ 895.5754; found: 895.5752.

2.2 Synthesis of ketone 48

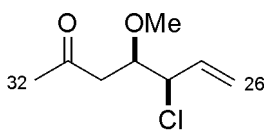


Chlorohydrin **52**



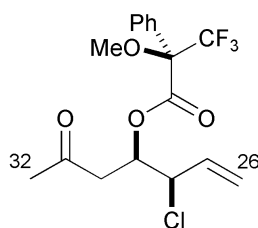
To a stirred solution of *c*-Hex₂NH (1.2 mL, 6.04 mmol) in THF (10 mL) at 0 °C was added *n*-BuLi (1.6 M in hexanes, 3.8 mL, 6.04 mmol) dropwise. Stirring at 0 °C for 30 min produced a solution of *c*-Hex₂NLi in THF. To a stirred solution of (–)-*B*-methoxydiisopinocampheylborane (1.76 g, 5.57 mmol) and allyl chloride (0.5 mL, 6.04 mmol) in Et₂O (15 mL) at –95 °C was added the *c*-Hex₂NLi solution dropwise. The mixture was then stirred at –95 °C for 30 min and at –78 °C for 30 min before being recooled to –95 °C. BF₃·OEt₂ (1.5 mL, 12.1 mmol) was added at –95 °C and the mixture was stirred for 15 min prior to the addition of a solution of aldehyde **50** (609 mg, 4.64 mmol) in Et₂O (5 mL). The reaction mixture was stirred at –95 °C for 3 h and at –78 °C for 16 h. The reaction was quenched with MeOH (10 mL), pH 7 buffer (10 mL) and 30 % H₂O₂ (5 mL), and then stirred for 2 h at room temperature. After phase separation, the aqueous phase was extracted with Et₂O (3 × 15 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO₂, 5:1 → 4:1 → 3:1 → 2:1 40-60 petroleum ether / EtOAc) to afford chlorohydrin **52** (387 mg, 2.38 mol, 51 %) as a pale yellowish oil; ; **R_f** 0.56 (EtOAc/PE (40-60), 1:1); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3415, 2933, 1713, 1645; **[α]_D²⁰** +25 (c 2.8, CHCl₃); **¹H NMR** (500 MHz, CDCl₃) δ 5.97 (1H, ddd, *J* = 17.3, 10.1, 8.0 Hz H27), 5.41 (1H, d, *J* = 17.3 Hz, H26a), 5.29 (1H, d, *J* = 10.1 Hz, H26b), 4.41 (1H, dd, *J* = 5.1, 8.4 Hz, H28), 4.24 (1H, ddd, *J* = 8.4, 5.1, 4.2 Hz, H29), 2.92 (1H, br s, OH), 2.78 (1H, dd, *J* = 17.4, 4.2 Hz, H30a), 2.70 (1H, dd, *J* = 8.4, 17.4 Hz, H30b), 2.21 (3H, s, H32); **¹³C NMR** (125 MHz, CDCl₃) δ 208.1, 134.8, 119.7, 70.7, 66.7, 46.8, 31.2.

Methyl ether **48**



To a stirred solution of chlorohydrin **52** (314 mg, 1.93 mmol) in DCM (10 mL) was added proton sponge[®] (1.24 g, 5.80 mmol) and trimethyloxonium tetrafluoroborate (798 mg, 5.40 mmol). The reaction mixture was stirred for 2 h before being quenched with NH₄Cl solution (10 mL). The mixture was diluted with DCM (10 mL) and the aqueous phase was extracted with DCM (3 × 5 mL). The combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 6:1 40-60 petroleum ether / EtOAc) provided methyl ether **48** (289 mg, 1.63 mol, 85 %) as a pale yellowish oil; **R_f** 0.34 (EtOAc/PE (40-60), 1:4); **[α]_D²⁰** +34 (c 1.6, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 2940, 1719, 1361, 1114; **¹H NMR** (500 MHz, CDCl₃) δ 5.97 (1H, ddd, *J* = 17.1, 10.3, 7.7 Hz H27), 5.41 (1H, d, *J* = 17.1 Hz, H26a), 5.30 (1H, d, *J* = 10.3 Hz, H26b), 4.53 (1H, dd, *J* = 7.7, 4.3 Hz, H28), 3.98 (1H, app dt, *J* = 8.3, 4.4 Hz, H29), 3.47 (1H, s, OMe), 2.77 (1H, dd, *J* = 17.1, 4.4 Hz, H30a), 2.71 (1H, dd, *J* = 17.1, 8.3 Hz, H30b), 2.21 (3H, s, H32); **¹³C NMR** (125 MHz, CDCl₃) δ 206.4, 134.6, 119.2, 79.9, 63.0, 59.2, 44.9, 31.3; **HRMS** (ES⁺) calcd. for [M+H]⁺ 177.0677 (³⁵Cl), found 177.0676.

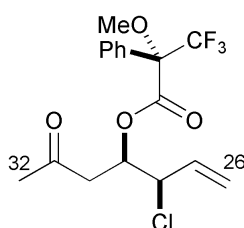
(*R*)-Mosher ester **48a**



(*S*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoyl chloride (26.0 μl, 138 mmol) and DMAP (1 crystal) were added to a solution of alcohol **48** (15.0 mg, 92.1 mmol) in CH₂Cl₂ / pyridine (0.5 ml, 1:1). The mixture was stirred at rt for 1.5 h before quenching with NaHCO₃ (2 ml), separation of the resulting two-phase system and extraction of the aqueous layer with CH₂Cl₂ (3 × 5 ml). Removal of solvents, *in vacuo*, and purification by flash column chromatography (Et₂O / PE (30-40), 1:5) afforded (*R*)-Mosher ester **48a** as a clear, colourless oil (14.1 mg, 37.2 μmol); **R_f** 0.30 (EtOAc / PE

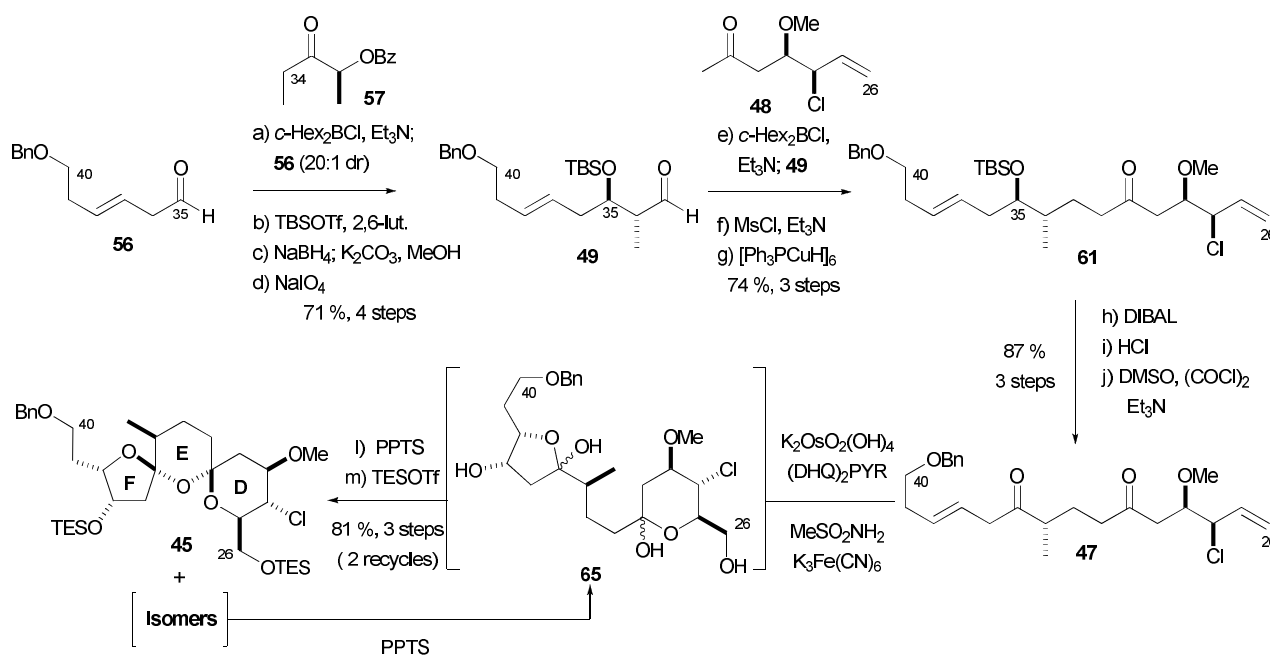
(40-60), 1:4); $[\alpha]_D^{20}$ +79 (c 0.93, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2958, 1756, 1723, 1375, 1248; **¹H NMR** (500 MHz, CDCl₃): δ 7.53 (2H, m, PhH), 7.40 (3H, m, PhH), 5.85 (1H, ddd, $J = 17.0, 10.3, 7.6$ Hz H27), 5.74 (1H, dt, $J = 7.3, 4.7$ Hz, H29), 5.43 (1H, d, $J = 17.0$ Hz, H26a), 5.30 (1H, d, $J = 10.3$ Hz, H26b), 4.67 (1H, dd, $J = 7.5, 4.5$ Hz, H28), 3.55 (3H, s, OMe), 2.91 (1H, dd, $J = 17.9, 4.7$ Hz, H30a), 2.82 (1H, dd, $J = 17.9, 7.3$ Hz, H30b), 2.07 (3H, s, H32); **¹³C NMR** (125MHz, CDCl₃): δ 203.7, 165.6, 133.3, 131.8, 129.7, 128.4, 127.5, 124.3, 122.0, 120.2, 73.4, 61.7, 55.7, 43.7, 30.4.

(S)-Mosher ester **48b**

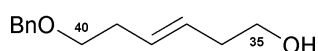


(*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoyl chloride (26.0 μl , 138 μmol) and DMAP (1 crystal) were added to a solution of alcohol **48** (15.0 mg, 92.1 μmol) in CH₂Cl₂ / pyridine (0.5 ml, 1:1). The mixture was stirred at rt for 2 h before quenching with NaHCO₃ (2 ml). The resulting two-phase system was separated and the aqueous layer extracted with CH₂Cl₂ (3 \times 5 ml). Removal of solvents, *in vacuo*, and purification by flash column chromatography (Et₂O / PE (30-40), 1:5) afforded (*S*)-Mosher ester **48b** as a clear, colourless oil (17.1 mg, 45.6 μmol); R_f 0.30 (EtOAc/PE (40-60), 1:4); $[\alpha]_D^{20}$ +29 (c 1.1, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2955, 1753, 1722, 1452, 1360, 1250; **¹H NMR** (500 MHz, CDCl₃) δ 7.52 (2H, m, PhH), 7.40 (3H, m, PhH), 5.69 (1H, m, H27), 5.66 (1H, m, H29), 5.28 (1H, d, $J = 17.0$ Hz, H26a), 5.19 (1H, d, $J = 10.5$ Hz, H26b), 4.65 (1H, dd, $J = 4.2, 7.5$ Hz, H28), 3.51 (3H, s, OMe), 3.01 (1H, dd, $J = 17.9, 4.8$ Hz, H30a), 2.85 (1H, dd, $J = 17.9, 7.5$ Hz, H30b), 2.17 (3H, s, H32); **¹³C NMR** (125MHz, CDCl₃) δ 204.1, 165.7, 132.6, 131.7, 129.7, 128.4, 127.5, 124.3, 122.0, 120.1, 73.3, 60.7, 55.6, 43.7, 30.5; **HRMS** (ES⁺) calcd. for [M+NH₄]⁺ 396.1184, found 396.1188.

2.3 Synthesis of DEF Spiroacetal 45



(*3E*)-6-(Benzyloxy)-hex-3-en-1-ol **55**

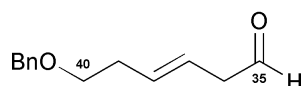


A flask equipped with a Dean-Stark trap was charged with malonic acid (38.0 g, 365 mmol) and piperidine (9.0 μL, 91 μmol) in dry xylene (130 mL) and the system held at reflux (160 °C) for 30 min. 4-Benzyloxy-butyraldehyde **53** (16.3 g, 91.6 mmol) was added and the mixture brought to reflux (155 °C) for a further 3.5 h before cooling to room temperature and diluting with EtOAc (50 mL). The solution was washed with water (2 × 100 mL), dried over MgSO₄ and concentrated *in vacuo* to a yellow oil.

The resulting crude β,γ-unsaturated acid **54** was taken up in THF (150 mL) and added dropwise to a solution of LiAlH₄ (6.94 g, 183 mmol) in THF (400 mL) at 0 °C. After stirring for a further 30 min at 0 °C, then for 1 h at rt, the reaction was cautiously quenched by the sequential, dropwise addition of water (3.29 mL), 10 % aq. NaOH (3.29 mL) and water (9.87 mL) at 0 °C. The resulting solid was removed by filtration and washed with EtOAc (5 × 75 mL), and the combined organic phases were dried over MgSO₄ and concentrated *in vacuo*. Flash column chromatography (Et₂O / PE (30-40), 1:3 → 1:1 → 2:1) afforded alcohol **55** as a clear, colourless oil (12.4 g, 60.2 mmol, 66 %); **R_f** 0.45 (EtOAc / PE (40-60), 1:1); **IR** (thin film, ν_{max}/cm⁻¹) 3395, 2857, 1496, 1454, 1363; **¹H NMR** (500

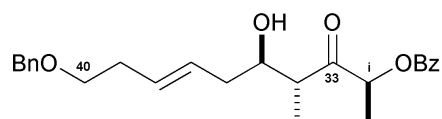
MHz, CDCl₃) δ 7.38-7.28 (5H, m, PhH), 5.58 (1H, dt, *J* = 15.4, 6.4 Hz, H38), 5.49 (1H dt, *J* = 15.4, 6.4 Hz, H37), 4.52 (2H, s, PhCH₂), 3.63 (2H, overlapping dt, *J* = 6.1, 6.1 Hz, H35), 3.52 (2H, t, *J* = 6.5 Hz, H40), 2.36 (2H, overlapping dt, *J* = 6.5, 6.5 Hz, H39), 2.28 (2H, overlapping dt, *J* = 6.1, 6.1 Hz, H36), 1.40 (1H, t, *J* = 6.1 Hz, OH); ¹³C NMR (125 MHz, CDCl₃) δ 138.4, 132.3, 128.4, 128.2, 127.7, 127.6, 72.9, 69.9, 61.9, 36.0, 33.2; HRMS (ES⁺) calcd for [M+NH₄]⁺ 224.1645, found 224.1643.

Aldehyde 56



β,γ-unsaturated alcohol **55** (5.00 g, 24.3 mmol) was added to a stirred solution of Dess-Martin periodinane (11.3 g, 26.7 mmol) and solid NaHCO₃ (6.12 g, 72.9 mmol) in dry CH₂Cl₂ (50 mL) at 0 °C. The reaction was allowed to warm to rt and stirred for 1.5 h before quenching with NaHCO₃ (30 mL) and Na₂S₂O₃ (30 mL). The quenching mixture was stirred for 1 h before separation of the organic phase and extraction of the aqueous phase with Et₂O (3 × 30 mL). The combined organic extracts were washed with water (50 mL) then brine (50 mL) and dried over MgSO₄. After concentration *in vacuo*, aldehyde **56** was isolated as a yellow oil which was used in the subsequent aldol coupling without further purification; R_f 0.67 (EtOAc/PE (40-60), 1:1); IR (thin film, ν_{max}/cm⁻¹) 2860, 1720, 1500, 1450, 1360; ¹H NMR (500 MHz, CDCl₃) δ 9.66 (1H, t, *J* = 2.0 Hz, H35), 7.38-7.28 (5H, m, PhH), 5.67 (1H, overlapping dt, *J* = 20.4, 5.9 Hz, H38), 5.62 (1H, overlapping dt, *J* = 20.4, 6.3 Hz, H37), 4.52 (2H, s, PhCH₂), 3.54 (2H, t, *J* = 6.4 Hz, H40), 3.14 (2H, dd, *J* = 6.3, 2.0 Hz, H36), 2.40 (2H, overlapping dt, *J* = 6.4, 5.9 Hz, H39); ¹³C NMR (125 MHz, CDCl₃) δ 200.0, 138.4, 132.9, 128.4, 127.7, 127.6, 121.4, 72.9, 69.6, 47.3, 33.2; HRMS (ES⁺) calcd for [M+Na]⁺ 227.1048, found 227.1053.

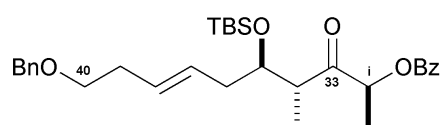
β-hydroxy ketone 58



Ethyl ketone **57** (5.60 g, 27.2 mmol) in dry Et₂O (20 mL) was added to a stirred solution of dicyclohexylboron chloride (6.08 mL, 27.8 mmol) and Et₃N (3.87 mL, 27.8 mmol) in dry Et₂O (40 mL) at -78 °C. The resulting mixture was allowed to warm to 0 °C and stirred for 1 h before re-

cooling to $-78\text{ }^{\circ}\text{C}$. β,γ -unsaturated aldehyde **56** (4.96 g, 24.3 mmol) in dry Et_2O (20 mL) was added to the solution *via* cannula and the mixture allowed to stir at $-78\text{ }^{\circ}\text{C}$ for 3 h before being transferred to a freezer ($-20\text{ }^{\circ}\text{C}$) for 14 h. The reaction was then quenched by the sequential addition of MeOH (35 mL), pH 7 buffer (35 mL) and H_2O_2 (35 mL) and the quenching mixture stirred at rt for 1 h before dilution with H_2O (30 mL). Following separation of the two-phase system and extraction of the aqueous phase with CH_2Cl_2 ($3 \times 30\text{ mL}$), the combined organic extracts were dried over MgSO_4 and concentrated *in vacuo* to give the crude product as a light yellow oil. Purification by flash column chromatography (Et_2O / PE (30-40), 1:4) afforded a material amenable to recrystallisation (Et_2O / PE (30-40), 1:10) giving β -hydroxy ketone **58** as a white solid (8.31 g, 20.3 mmol, 83 % over 2 steps); **mp** $62\text{ }^{\circ}\text{C}$; **R_f** 0.13 (EtOAc / PE (40-60), 1:4); **[α]_D²⁰** $+10$ (c 2.0, CDCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3449 (br), 2930, 2855, 1720, 1600, 1450; **¹H NMR** (500 MHz, CDCl_3) δ 8.10 (2H, d, $J = 7.8\text{ Hz}$, *o*-PhH), 7.60 (1H, t, $J = 7.8\text{ Hz}$, *p*-PhH), 7.48 (2H, t, $J = 7.8\text{ Hz}$, *m*-PhH), 7.38-7.28 (5H, m, PhH), 5.59 (1H, overlapping dt, $J = 15.6, 6.2\text{ Hz}$, H38), 5.53 (1H overlapping dt, $J = 15.6, 6.5\text{ Hz}$, H37), 5.44 (1H, q, $J = 7.0$, Hi), 4.52 (2H, s, PhCH_2), 3.80 (1H, m, H35), 3.51 (2H, t, $J = 6.6\text{ Hz}$, H40), 2.92 (1H, qn, $J = 7.4\text{ Hz}$, H34), 2.45 (1H, d, $J = 5.2$, OH), 2.36 (2H, dt, $J = 6.6, 6.2\text{ Hz}$, H39), 2.36 (1H, obs m, H36a), 2.12 (1H, ddd, $J = 13.1, 6.6, 6.5\text{ Hz}$, H36b), 1.57 (3H, d, $J = 7.0\text{ Hz}$, Me), 1.25 (3H, d, $J = 7.4\text{ Hz}$, Me34); **¹³C NMR** (125 MHz, CDCl_3) δ 211.3, 165.8, 138.4, 133.3, 131.0, 129.8, 129.6, 128.5, 128.4, 127.7, 127.6, 127.4, 74.8, 72.9, 72.7, 69.8, 47.4, 37.9, 33.1, 15.8, 14.1; **HRMS** (ES^+) calcd for $[\text{M}+\text{NH}_4]^+$ 428.2431, found 428.2431.

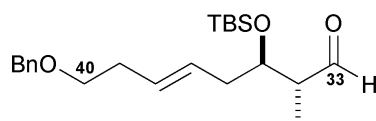
TBS ether **59**



2,6-lutidine (3.30 mL, 28.4 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (3.20 mL, 14.0 mmol) were added to a solution of β -hydroxy ketone **58** (4.67 g, 11.4 mmol) in CH_2Cl_2 (100 mL) at $0\text{ }^{\circ}\text{C}$. The mixture was warmed to rt and stirred for 1 h prior to quenching with NaHCO_3 (50 mL) and extraction with CH_2Cl_2 ($3 \times 40\text{ mL}$). Purification by flash column chromatography (Et_2O / PE (30-40), 1:10 \rightarrow 1:5) afforded TBS ether **59** as a clear, colourless oil (5.92 g, 11.3 mmol, 99 %); **R_f** 0.41 ($\text{Et}_2\text{O}/\text{PE}$ (40-60), 1:4); **[α]_D²⁰** -31 (c 2.4, CDCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2930, 2860, 1720, 1600, 1450; **¹H NMR** (500 MHz, CDCl_3) δ 8.11 (2H, d, $J = 7.8\text{ Hz}$, *o*-PhH), 7.59 (1H, t, $J = 7.5\text{ Hz}$, *m*-PhH), 7.47 (2H, t, $J = 7.8\text{ Hz}$, *p*-PhH), 7.37-7.28 (5H, m, PhH), 5.61 (1H, ddd, $J = 15.5, 8.1, 5.1\text{ Hz}$, H37), 5.55 (1H, dt, $J = 15.5, 6.6\text{ Hz}$, H38), 5.40 (1H, q, $J = 7.0$, Hi), 4.52 (2H, s,

PhCH₂), 4.07 (1H, dt, $J = 8.1, 4.1$ Hz, H35), 3.51 (2H, t, $J = 6.9$ Hz, H40), 3.05 (1H, dt, $J = 15.3, 7.5$ Hz, H34), 2.37 (2H, dt, $J = 6.7, 6.6$ Hz, H39), 2.33 (1H, m, H36a), 2.20 (1H, ddd, $J = 14.7, 8.0, 3.7$ Hz, H36b), 1.52 (3H, d, $J = 7.0$ Hz, Me), 1.12 (3H, d, $J = 7.5$ Hz, Me34), 0.89 (9H, s, *t*-BuSi), 0.08 (3H, s, SiMe), 0.00 (3H, s, SiMe); ¹³C NMR (125 MHz, CDCl₃) δ 209.1, 165.7, 138.6, 133.2, 129.8, 128.4, 128.4, 127.6, 127.5, 126.7, 75.0, 72.9, 72.8, 70.1, 47.0, 36.9, 33.3, 25.9, 18.0, 15.5, 13.2, -4.7, -4.7; HRMS (ES⁺) calcd for [M+H]⁺ 525.3031, found 525.3030.

Aldehyde 49

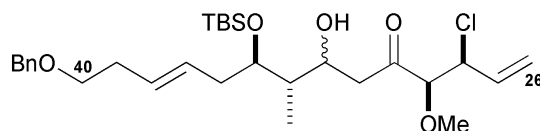


Sodium borohydride (890 mg, 23.5 mmol) was added to a solution of protected β-hydroxy ketone **59** (6.12 g, 11.7 mmol) in MeOH (60 mL) at 0 °C. The mixture was stirred for 0.5 h before the addition of K₂CO₃ (6.79 g, 49.2 mmol), at which point the mixture was allowed to warm to rt and stirred for a further 5 h. After quenching with H₂O (20 mL) and pH7 buffer (20 mL) the resulting two-phase system was separated and the aqueous phase extracted with CH₂Cl₂ (3 × 30 mL). The combined organic extracts were dried over MgSO₄ and concentrated *in vacuo* before removal of methyl benzoate by flash column chromatography (Et₂O/PE (30-40), 1:20 → 1:0) to give the intermediate diol.

Sodium *meta*-periodate (15.0 g, 70.1 mmol) was added to a solution of the intermediate diol in MeOH / pH7 buffer (5:1) (100 mL). The reaction was stirred for 30 min at rt before quenched with H₂O (75 mL), separation of the resulting two-phase system and extraction of the aqueous phase with CH₂Cl₂ (3 × 60 mL). The combined organic extracts were dried over MgSO₄ and concentrated *in vacuo* to give the crude product, which was purified by flash column chromatography (Et₂O / PE (30-40), 1:4) to afford aldehyde **49** as a clear, colourless oil (3.63 g, 10.1 mmol, 86 % over 2 steps); **R_f** 0.55 (EtOAc / PE (40-60), 1:4); [α]_D²⁰ -37 (c 4.1, CDCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 2930, 2860, 1720; ¹H NMR (500 MHz, CDCl₃) δ_H 9.77 (1H, d, $J = 2.2$, H33), 7.36-7.28 (5H, m, PhH), 5.56 (1H, dt, $J = 15.2, 5.9$ Hz, H38), 5.51 (1H, dt, $J = 15.2, 5.9$ Hz, H37), 4.53 (2H, s, PhCH₂), 3.93 (1H, dt, $J = 5.5, 5.4$ Hz, H35), 3.52 (2H, t, $J = 6.8$ Hz, H40), 2.54 (1H, ddq, $J = 7.0, 6.7, 2.2$ Hz, H34), 2.37 (2H, dt, $J = 6.8, 5.9$ Hz, H39), 2.30 (2H, m, H36), 1.08 (3H, d, $J = 7.0$ Hz, Me34), 0.90 (9H, s, *t*-BuSi), 0.09 (3H, s, SiMe), 0.08 (3H, s, SiMe); ¹³C NMR (125 MHz, CDCl₃) δ_C 204.9, 138.5,

130.4, 128.3, 127.6, 127.5, 127.1, 73.8, 72.9, 69.9, 50.7, 38.6, 33.2, 25.8, 18.0, 10.6, -4.2, -4.8;
HRMS (ES⁺) calcd for [M+Na]⁺ 399.2331, found 399.2329.

β -hydroxy ketone **60**



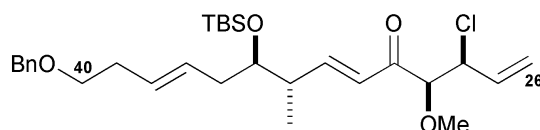
Ketone **48** (1.86 g, 10.5 mmol) in dry Et₂O (10 mL) was added to a solution of *c*-Hex₂BCl (2.73 mL, 12.4 mmol) and Et₃N (2.13 mL, 15.3 mmol) in dry Et₂O (60 mL) at -78 °C. The solution was then warmed to 0 °C and allowed to stir for 1 h during which time a white precipitate was observed to form. After re-cooling to -78 °C, aldehyde **49** (3.60 g, 9.57 mmol) in dry Et₂O (10 mL) was added and the resulting solution stirred for 3 h before standing at -20 °C for 43 h. The reaction was then quenched by the sequential addition of MeOH (20 mL), pH 7 buffer (20 mL) and H₂O₂ (20 mL), and stirred for 1 h at rt. Separation of the organic phase, extraction of the aqueous phase with Et₂O (3 × 50 mL) and drying over MgSO₄ gave, after concentration *in vacuo*, the crude product as a yellow oil which was purified by flash column chromatography (Et₂O / PE (30-40), 1:20 → 1:10 → 1:2) to afford aldol adduct **60** as a clear, colourless oil (4.98 g, 9.33 mmol, 98 %).

Major diastereoisomer: **R_f** 0.31 (EtOAc / PE (40-60), 1:4); [α]_D²⁰ +10.5 (c 6.66, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 3497, 2930, 2857, 1716, 1462, 1362; **¹H NMR** (500 MHz, CDCl₃) δ 7.37-7.28 (5H, m, PhH), 5.95 (1H, ddd, *J* = 16.9, 10.2, 7.7 Hz, H27), 5.53 (1H, dt, *J* = 15.5, 6.4 Hz, H38), 5.51 (1H, dt, *J* = 15.5, 6.8 Hz, H37), 5.38 (1H, d, *J* = 16.9 Hz, H26a), 5.26 (1H, d, *J* = 10.2 Hz, H26b), 4.58 (1H, ddd, *J* = 8.6, 4.0, 1.7 Hz, H33), 4.51 (1H, m, H28), 4.50 (2H, s, PhCH₂), 3.97 (1H, dt, *J* = 8.0, 4.3 Hz, H29), 3.73 (1H, m, H35), 3.49 (2H, t, *J* = 6.8 Hz, 2 × H40), 3.44 (1H, br s, OH), 3.43 (3H, s, OMe), 2.79 (1H, dd, *J* = 17.2, 4.3 Hz, H30a), 2.72 (1H, dd, *J* = 17.2, 7.9 Hz, H30b), 2.72 (1H, dd, *J* = 16.2, 8.7 Hz, H32a), 1.96 (1H, m, H36a), 1.88-1.83 (4H, m, 2 × H39, H36b, H32b), 1.26 (1H, ddq, *J* = 6.8, 3.2, 1.9 Hz, H34), 0.98 (3H, d, *J* = 6.8 Hz, Me34), 0.89 (9H, s, *t*-BuSi), 0.09 (6H, s, 2 × SiMe); **¹³C NMR** (125 MHz, CDCl₃) δ 207.6, 138.5, 134.3, 130.0, 128.4, 127.6, 127.6, 127.5, 118.8, 79.5, 77.9, 72.9, 69.9, 66.2, 62.9, 59.0, 48.8, 44.8, 38.6, 33.2, 26.0, 25.9, 17.9, 11.2, -4.3, -4.8;
HRMS (ES⁺) calcd. for [M+Na]⁺ 575.2930, found 575.2924.

Minor diastereoisomer: **R_f** 0.39 (EtOAc / PE (40-60), 1:4); **¹H NMR** (500 MHz, CDCl₃) δ 7.37-7.28 (5H, m, PhH), 5.98 (1H, ddd, *J* = 16.9, 10.2, 7.7 Hz, H27), 5.52 (2H, m, H38, H39), 5.41 (1H,

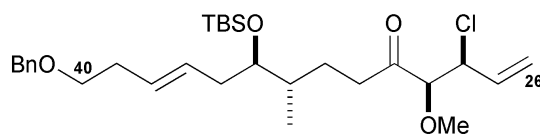
d, $J = 16.9$ Hz, H26a), 5.28 (1H, d, $J = 10.2$ Hz, H26b), 4.51 (1H, m, H28), 4.54 (2H, s, PhCH₂), 4.09 (1H, ddd, $J = 9.6, 8.5, 2.4$ Hz, H33), 4.00 (1H, dt, $J = 7.5, 4.4$ Hz, H29), 3.82 (1H, dd, $J = 11.2, 5.4$ Hz, H35), 3.52 (2H, t, $J = 6.8$ Hz, 2 × H40), 3.45 (3H, s, OMe), 3.43 (1H, br s, OH), 2.80 (1H, dd, $J = 17.2, 4.5$ Hz, H30a), 2.73 (1H, dd, $J = 17.2, 7.7$ Hz, H30b), 2.60 (1H, dd, $J = 16.8, 2.2$ Hz, H32a), 2.54 (1H, dd, $J = 16.8, 9.6$ Hz, H32b), 2.35 (2H, m, 2 × H39), 2.27 (1H, ddd, $J = 13.4, 8.5, 5.7$ Hz, H36a), 2.18 (1H, ddd, $J = 13.9, 8.4, 5.9$ Hz, H36b), 1.80 (1H, m, H34), 0.90 (9H, s, *t*-BuSi), 0.84 (3H, d, $J = 6.8$ Hz, Me34), 0.07 (6H, s, 2 × SiMe).

Enone 60a



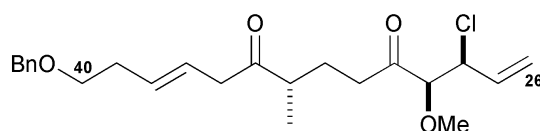
Et₃N (7.25 mL, 52.1 mmol) and methanesulfonyl chloride (1.21 mL, 15.6 mmol) were added to a solution of alcohol **60** (2.88 g, 5.21 mmol) in CH₂Cl₂ (30 mL) at 0 °C. The resulting orange solution was stirred at 0 °C for 1 h then at rt for 3 h before being quenched with NaHCO₃ (30 mL). The organic layer was separated, the aqueous layer extracted with CH₂Cl₂ (3 × 30 mL) and the combined organic phases dried over MgSO₄. Concentration *in vacuo* gave the crude product as a yellow oil, which on purification by flash column chromatography (Et₂O / PE (30-40), 1:10) afforded enone **60a** as a clear, colourless oil (2.26 g, 4.23 mmol, 81 %); **R_f** 0.48 (EtOAc / PE (40-60), 1:4); **[α]_D²⁰** -8.4 (c 2.2, CDCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2929, 2856, 1673, 1628; **¹H NMR** (500 MHz, CDCl₃) δ 7.37-7.29 (5H, m, PhH), 6.89 (1H, dd, $J = 16.2, 8.1$ Hz, H33), 6.09 (1H, d, $J = 16.2$ Hz, H32), 6.01 (1H, ddd, $J = 16.9, 10.2, 7.7$ Hz, H27), 5.49 (1H, m, H38), 5.45 (1H, m, H37), 5.41 (1H, d, $J = 16.9$ Hz, H26a), 5.26 (1H, d, $J = 10.2$ Hz, H26b), 4.54 (1H, m, H28), 4.53 (2H, s, PhCH₂), 4.04 (1H, m, H29), 3.63 (1H, ddd, $J = 6.5, 5.8, 5.0$ Hz, H35), 3.51 (2H, t, $J = 6.8$ Hz, 2 × H40), 3.46 (3H, s, OMe), 2.87 (1H, d, $J = 5.1$ Hz, H30a), 2.86 (1H, d, $J = 6.9$ Hz, H30b), 2.49 (1H, m, H34), 2.35 (2H, dt, $J = 6.8, 5.8$ Hz, 2 × H39), 2.20 (1H, dt, $J = 13.8, 5.8$ Hz, H36a), 2.12 (1H, dt, $J = 13.8, 6.5$ Hz, H36b), 1.08 (3H, d, $J = 6.8$ Hz, Me34), 0.91 (9H, s, *t*-BuSi), 0.06 (6H, s, 2 × SiMe); **¹³C NMR** (125 MHz, CDCl₃) δ 197.9, 150.4, 138.5, 134.6, 130.7, 129.6, 128.3, 127.8, 127.6, 127.5, 118.6, 79.8, 75.5, 72.9, 70.0, 63.3, 58.9, 41.6, 40.9, 38.6, 33.2, 25.9, 18.1, 16.2, -4.2, -4.6; **HRMS** (ES⁺) calcd for [M+Na]⁺ 557.2830, found 557.2808.

Ketone 61



$[(\text{Ph}_3\text{PCuH})_6]$ (0.337 g, 0.172 mmol) and PhSiH_3 (971 μL , 7.90 mmol) were added to a degassed solution of α,β -unsaturated ketone **60a** (2.81 g, 5.27 mmol) in toluene (4 mL, degassed) at 0 °C. The resulting red mixture was warmed to rt and stirred for 30 min before the reaction was quenched by exposure to air and diluted with PE (40-60). Filtration through a plug of silica (Et_2O / PE (30-40) (1:1)) and removal of solvents *in vacuo* afforded the crude product, which was purified by flash column chromatography (Et_2O / PE (30-40), 1:10) giving ketone **61** as a light yellow oil (2.66 g, 4.97 mmol, 94 %); R_f 0.33 (EtOAc / PE (40-60), 1:4); $[\alpha]_D^{20}$ +15.2 (c 1.45, CDCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2930, 2856, 1716, 1462; **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ_{H} 7.36-7.30 (5H, m, PhH), 5.98 (1H, ddd, $J = 17.1, 10.2, 7.7$ Hz, H27), 5.51 (1H, dt, $J = 15.2, 5.7$ Hz, H38), 5.47 (1H, dt, $J = 15.2, 5.3$ Hz, H37), 5.41 (1H, d, $J = 17.1$ Hz, H26a), 5.29 (1H, d, $J = 10.2$ Hz, H26b), 4.53 (2H, s, PhCH_2), 4.52 (1H, m, H28), 3.99 (1H, dt, $J = 7.7, 4.6$ Hz H29), 3.53 (1H, m, H35), 3.51 (2H, t, $J = 6.9$ Hz, 2 \times H40), 3.45 (3H, s, OMe), 2.71 (1H, d, $J = 4.6$ Hz, H30a), 2.70 (1H d, $J = 7.7$ Hz, H30b), 2.50 (1H, ddd, $J = 15.9, 10.1, 5.4$ H32a), 2.38 (1H, obs ddd, $J = 15.9, 10.0, 6.0$ H32b), 2.35 (1H, dd, $J = 6.2, 5.3$ Hz, H36a), 2.34 (1H, dd, $J = 6.2, 5.3$ Hz, H36b), 2.15 (2H, m, 2 \times H39), 1.75 (1H, m, H33a), 1.53 (3H, s, Me34), 1.53 (1H, m, H34), 1.35 (1H, m, H33b), 0.90 (9H, s, *t*-BuSi), 0.87 (3H, d, $J = 6.9$ Hz, Me34), 0.04 (6H, s, 2 \times SiMe); **$^{13}\text{C NMR}$** (125 MHz, CDCl_3) δ_{C} 208.7, 134.3, 133.7, 129.2, 128.5, 128.3, 127.6, 127.5, 118.8, 79.6, 76.1, 72.9, 70.1, 62.8, 58.9, 43.7, 42.1, 37.5, 36.7, 33.2, 25.9, 25.6, 18.1, 15.0, -4.2, -4.6; **HRMS** (ES^+) calcd for $[\text{M}+\text{Na}]^+$ 559.2986, found 559.2966.

Diketone 47



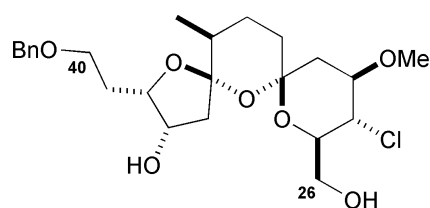
Diisobutylaluminium hydride (1M in CH_2Cl_2 , 18.7 mL, 18.7 mmol) was added dropwise to a stirred solution of ketone **61** (2.50 g, 4.67 mmol) in CH_2Cl_2 (50 mL) at -78 °C. The reaction was stirred for 20 min at -78 °C, cautiously quenched with Na^+ / K^+ tartrate (50 mL) and the resulting two-phase system was separated. The aqueous layer extracted with CH_2Cl_2 (5 \times 20 mL) and the

combined organic phases were dried over MgSO_4 and concentrated *in vacuo* to give a light yellow oil.

The above oil was taken up in MeCN (35.5 mL) and 1 M aq. HCl (6.6 mL) was added. After stirring for 2 h at rt the reaction was quenched with NaHCO_3 (25 mL), the two-phase system was separated and the aqueous phase was extracted with CH_2Cl_2 (3×20 mL). The combined organic phases were then dried over MgSO_4 and concentrated *in vacuo* to give corresponding diols **63** as a light yellow oil.

Diol **63** was taken up in CH_2Cl_2 (5 mL) and added to a solution of DMSO (1.00 mL, 14.0 mmol) and oxalyl chloride (1.20 mL, 14.0 mmol) in CH_2Cl_2 (50 mL) at -78 °C. The mixture was then stirred for 15 min before the addition of Et_3N (3.90 mL, 28.0 mmol). Stirring was continued at -78 °C for 2 h then at 0 °C for 30 min at which point the reaction was quenched by the addition of NaHCO_3 (50 mL). The resulting two-phase system was separated, the aqueous layer extracted with CH_2Cl_2 (5×20 mL) and the combined organic phases were dried over MgSO_4 and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O / PE (30-40), 1:7) afforded diketone **47** as a colourless oil (1.71 g, 4.07 mmol, 87 %); R_f 0.18 (EtOAc/PE (30-40), 1:4); $[\alpha]_D^{20}$ +30.2 (c 2.1, CDCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2933, 1712; **^1H NMR** (500 MHz, CDCl_3) δ 7.36-7.29 (5H, m, PhH), 5.95 (1H, ddd, $J = 16.9, 10.2, 7.6$ Hz, H27), 5.63 (1H, m, H37), 5.59 (1H, m, H38), 5.40 (1H, d, $J = 16.9$ Hz, H26a), 5.23 (1H, d, $J = 10.2$ Hz, H26b), 4.53 (2H, s, PhCH_2), 4.52 (1H, m, H28), 3.96 (1H, dt, $J = 7.3, 4.4$, H29), 3.53 (2H, t, $J = 6.8$ Hz, $2 \times$ H40), 3.44 (3H, s, OMe), 3.19 (1H, d, $J = 6.1$ Hz, H36a), 3.18 (1H, t, $J = 4.7$ Hz, H36b), 2.68 (1H, d, $J = 4.4$ Hz, H30a), 2.66 (1H, d, $J = 7.3$ Hz, H30b), 2.62 (1H, br qn, $J = 6.9$ Hz, H34), 2.49-2.38 (2H, m, $2 \times$ H32), 2.41 (2H, m, $2 \times$ H39), 1.93 (1H, ddt, $J = 14.1, 7.8, 7.7$ Hz, H33a), 1.65 (1H, ddt, $J = 14.1, 8.4, 6.2$ Hz, H33b), 1.10 (3H, d, $J = 7.1$ Hz, Me34); **^{13}C NMR** (125 MHz, CDCl_3) δ 211.9, 207.8, 138.5, 134.2, 131.3, 128.4, 127.6, 127.5, 123.9, 118.9, 79.6, 72.9, 69.8, 62.6, 58.9, 45.0, 44.6, 43.7, 41.0, 33.0, 26.0, 16.4; **HRMS** (ES^+) calcd for $[\text{M}+\text{Na}]^+$ 443.1965, found 443.1963.

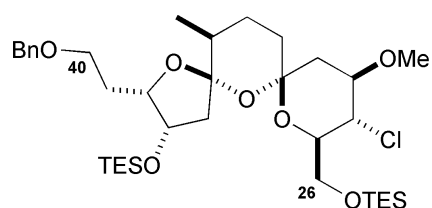
DEF-Spiroacetal **64**



A mixture comprising $\text{K}_2\text{OsO}_2(\text{OH})_4$ (25.0 mg, 67.2 μmol), $(\text{DHQ})_2\text{PYR}$ (0.144 g, 0.163 mmol) and methanesulfonamide (0.129 g, 1.36 mmol) in *t*-BuOH / H_2O (1:1, 4 mL) was stirred at rt for 1.5 h. K_2CO_3 (1.13 g, 8.16 mmol), $\text{K}_3\text{Fe}(\text{CN})_6$ (2.68 g, 8.16 mmol) and H_2O (2 mL) were added and the mixture stirred for a further 1 h before cooling to 0 °C. Diketone **47** (0.570 g, 1.36 mmol) in *t*-BuOH (2 mL) was added and the mixture stirred for 4.5 h at 0 °C and then at rt for 3 h. Once complete, the reaction was quenched by the addition of Na_2SO_3 (10 mL) and the aqueous phase separated and extracted with EtOAc (6 \times 10 mL). The combined organic extracts were dried over MgSO_4 and concentrated to a yellow oil (containing part cyclised hemi-acetals **65**).

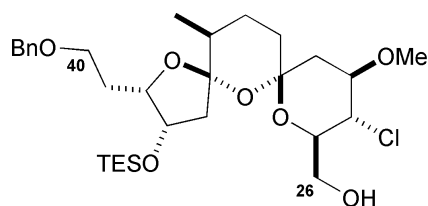
The above oil was taken up in CH_2Cl_2 / MeOH (1:1, 30 mL) and PPTS (ca. 5 crystals) was added. The reaction was stirred at rt for 2 h, before quenching with NaHCO_3 (20 mL), phase separation and extraction of the aqueous layer with CH_2Cl_2 (3 \times 20 mL). The combined organic phases were dried over MgSO_4 and concentration *in vacuo* to give the spirocyclised product **64** as a crude yellow oil, which was used without further purification. For purposes of characterisation a small sample was purified by flash column chromatography (EtOAc / PE (40-60), 1:2)); R_f 0.65 (EtOAc); $[\alpha]_D^{20}$ -17.4 (c 0.80, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3461, 2929; **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ 7.39-7.31 (5H, m, PhH), 4.55 (2H, d, $J = 11.6$ Hz, PhCH_2), 4.52 (2H, d, $J = 11.6$ Hz, PhCH_2), 4.31 (1H, m, H37), 4.17 (1H, dt, $J = 3.7, 8.5$ Hz, H38), 3.99 (1H, ddd, $J = 10.8, 8.4, 2.4$ Hz, H26a), 3.88 (1H, ddd, $J = 10.4, 8.4, 2.4$ Hz, H27), 3.70 (1H, dt, $J = 3.8, 9.9$ Hz, H40a), 3.63-3.55 (3H, m, H26b, H29, H40b), 3.50 (1H, t, $J = 10.4$ Hz, H28), 3.47 (3H, s, OMe), 3.35 (1H, br s, 37-OH), 2.44 (1H, dd, $J = 8.4, 2.4$ Hz, 26-OH), 2.36 (1H, dd, $J = 6.9, 14.8$ Hz, H36a), 2.23 (1H, dd, $J = 12.9, 5.1$ Hz, H30a), 2.17 (1H, t, $J = 14.8$ Hz, H36b), 2.08 (2H, m, 2 \times H39), 1.88 (1H, dq, $J = 3.3, 13.3$ Hz, H33a), 1.80 (1H, dt, $J = 13.3, 3.3$ Hz, H32a), 1.72 (1H, m, H34), 1.63 (1H, dt, $J = 4.1, 13.3$ Hz, H32b), 1.45 (1H, m, H33b), 1.41 (1H dd, $J = 12.9, 11.4$ Hz, H30b), 1.01 (3H, d, $J = 6.7$ Hz, Me34); **$^{13}\text{C NMR}$** (125 MHz, CDCl_3) δ 137.3, 128.6, 128.0, 127.8, 109.5, 97.9, 84.3, 78.9, 73.7, 73.2, 71.2, 67.2, 63.1, 60.3, 57.6, 47.5, 42.9, 37.7, 35.8, 28.3, 23.8, 16.3; **HRMS** (ES^+) calcd for $[\text{M}+\text{Na}]^+$ 493.1969, found 493.1954.

Bis-TES ether **45**



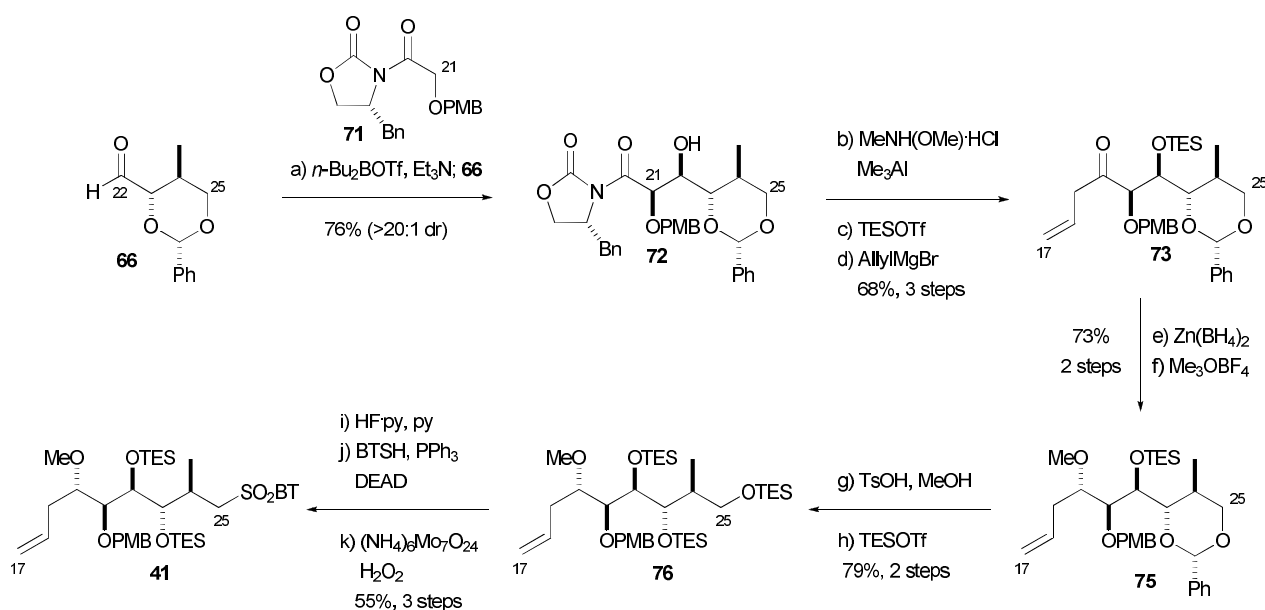
2,6-Lutidine (0.951 mL, 8.16 mmol) and TESOTf (0.924 mL, 4.08 mmol) were added dropwise to a solution of crude diol **64** (< 1.36 mmol) in CH₂Cl₂ (10 mL) at -78 °C. After stirring at -78 °C for 30 min the reaction was quenched with NaHCO₃ (10 mL) and the resulting two-phase system was separated. The aqueous phase was extracted with CH₂Cl₂ (3 × 40 mL), the combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. Flash column chromatography (Et₂O / PE (30-40) 1:20) afforded *bis*-spiroacetal **45** as a clear, colourless oil (0.306 g, 0.438 mmol, 32 % over 2 steps) together with isomer by-products (ca. 0.5 g). These isomers could be resubmitted to PPTS, in MeOH / CH₂Cl₂ then silyl protection to gain additional *bis*-spiroacetal **45**. After recycling isomers twice, **45** could be accessed in a combined 81 % yield (773 mg, 1.10 mmol); **R_f** 0.64 (EtOAc / PE (30-40), 1:4); [α]_D²⁰ +0.80 (c 4.3, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 2955, 2876, 1457, 1380; **¹H NMR** (500 MHz, CDCl₃) δ 7.36-7.25 (5H, m, PhH), 4.56 (1H, d, *J* = 11.7 Hz, PhCH₂), 4.51 (1H, d, *J* = 11.7 Hz, PhCH₂), 4.33 (1H, m, H37), 4.13 (1H, dt, *J* = 8.4, 4.4 Hz, H38), 4.06 (1H, dd, *J* = 11.3, 2.0 Hz, H26a), 3.96 (1H, app t, *J* = 10.0 Hz, H28), 3.76 (1H, dd, *J* = 11.3, 1.2 Hz, H26b), 3.71-3.65 (2H, m, H27, H29), 3.62-3.53 (2H, m, 2 × H40), 3.47 (3H, s, OMe), 2.24 (1H, dd, *J* = 14.1, 6.4 Hz, H36a), 2.13 (1H, dd, *J* = 12.7, 5.0 Hz, H30a), 2.00 (1H, dd, *J* = 14.0, 2.7 Hz, H36b), 1.99-1.77 (4H, m, H32a, H33a, 2 × H39), 1.71-1.62 (1H, m, H34), 1.54 (1H, dt, *J* = 13.4, 4.0 Hz, H32b), 1.41-1.31 (2H, m, H30b, H33b), 1.00-0.93 (21H, m, 2 × Si(CH₂CH₃)₃, Me34), 0.64-0.56 (12H, m, 2 × Si(CH₂CH₃)₃); **¹³C NMR** (125 MHz, CDCl₃) δ 138.6, 128.4, 127.7, 127.5, 108.7, 97.7, 80.4, 79.2, 73.9, 72.9, 72.1, 68.0, 61.8, 59.0, 57.4, 48.7, 42.6, 37.6, 35.7, 29.6, 23.7, 16.4, 7.1, 6.9, 4.8, 4.6; **HRMS** (ES⁺) calcd for [M+NH₄]⁺ 716.4139, found 716.4137.

Alcohol **XX**

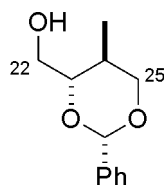


To a stirred solution of *bis*-TES ether **6** (120 mg, 0.172 mmol) in DCM / MeOH (6:1, 4.9 mL) at 0 °C was added PPTS (4.3 mg, 0.017 mmol). The reaction was stirred at 0 °C for 1 h before being quenched with NaHCO₃ solution (5 mL). The aqueous phase was extracted with DCM (3 × 5 mL) and the combined organic phases were dried (MgSO₄). Concentration *in vacuo* afforded alcohol **XX** (95.1 mg, 0.162 mmol, 95 %) as a colourless oil; **R_f** 0.42 (EtOAc/PE (40-60), 1:4); [α]_D²⁰ +4.1 (c 1.3, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 3460, 2957, 2877, 1456, 1381; **¹H NMR** (500 MHz, CDCl₃): δ_{H} 7.32-7.36 (4H, m, ArH), 7.27 (1H, m, ArH), 4.56 (1H, d, *J* = 11.8 Hz, CH₂Ar), 4.47 (1H, d, *J* = 11.8 Hz, CH₂Ar), 4.40 (1H, dt, *J* = 4.2, 6.3 Hz, H37), 4.23 (1H, dt, *J* = 5.3, 6.7 Hz, H38), 3.92 (1H, ddd, *J* = 2.6, 6.5, 11.1 Hz, H26a), 3.83 (1H, ddd, *J* = 2.6, 6.3, 9.5 Hz, H27), 3.65 (1H, dd, *J* = 5.1, 11.1 Hz, H26b), 3.55-3.62 (4H, m, H28, H29, 2 × H40), 3.45 (1H, s, OMe), 2.23 (1H, dd, *J* = 5.1, 6.5 Hz, OH), 2.20 (1H, dd, *J* = 6.3, 13.9 Hz, H36a), 2.17 (1H, dd, *J* = 4.9, 13.7 Hz, H30a), 2.00 (1H, dd, *J* = 3.7, 13.9 Hz, H36b), 1.85-1.89 (3H, m, H33a, 2 × H39), 1.79 (1H, dt, *J* = 3.0, 13.2 Hz, H32a), 1.67 (1H, m, H34), 1.57 (1H, dt, *J* = 4.2, 13.7 Hz, H32b), 1.40 (1H, m, H33b), 1.36 (1H, dd, *J* = 10.9, 13.0 Hz, H33b), 0.95 (9H, t, *J* = 8.1 Hz, Si(CH₂CH₃)₃), 0.94 (1H, d, *J* = 6.5 Hz, Me34), 0.57 (6H, q, *J* = 8.1 Hz, Si(CH₂CH₃)₃); **¹³C NMR** (125MHz, CDCl₃): δ_{C} 138.7, 128.4, 127.8, 127.6, 108.9, 97.8, 80.6, 79.1, 73.4, 72.8, 71.7, 67.7, 62.9, 60.0, 57.7, 47.9, 42.9, 37.3, 35.8, 29.2, 23.7, 16.5, 7.0, 4.9; **HRMS** (ES⁺) calcd. for [M+NH₄]⁺ 602.3274, found 602.3266.

2.4 Synthesis of Sulfone 41



Alcohol 70

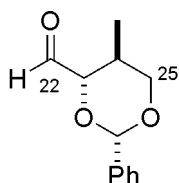


To a suspension of LiAlH_4 (1.80 g, 47.1 mmol) in THF (100 mL) was added a solution of (2*S*,3*R*)-dimethyl 2-hydroxy-3-methylsuccinate^[1] (**68**, 3.77 g, 21.4 mmol) in THF (50 mL) dropwise. The mixture was stirred for 2 h before being quenched by slow addition of acetic acid (3.80 mL, 66.3 mmol) at 0 °C. Without purification of the triol, pyridine (93.2 mL, 1.16 mol) and acetic anhydride (46.4 mL, 0.492 mol) were added and the mixture was heated to reflux for 16 h before cooling to 0 °C. The resulting solution was diluted with 1 N HCl (100 mL), extracted with Et_2O (2×100 mL) and the combined organic phases were washed with NaHCO_3 solution (2×50 mL), dried (MgSO_4) and concentrated *in vacuo*.

To a stirred solution of the crude peracetate in MeOH (150 mL) was added NaOMe (231 mg, 4.28 mmol). The reaction mixture was heated to reflux for 16 h before being quenched by addition of *p*-TsOH· H_2O (1.02 g, 5.35 mmol). The mixture was concentrated *in vacuo*, then diluted with DCM (40 mL). Benzaldehyde dimethyl acetal (3.91 mL, 25.7 mmol) was added and the reaction mixture was stirred for 16 h, before being quenched by the addition of Et_3N (1.0 mL). After washing with

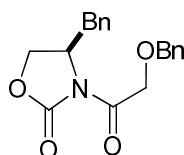
NaHCO₃ solution (50 mL), the organic phase was dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 2:1 40-60 petroleum ether / EtOAc) provided acetal **70** (3.43 g, 16.5 mmol, 77 %) as a white solid; ¹H NMR (500 MHz, CDCl₃) δ 7.52-7.48 (2H, m, ArH), 7.40-7.33 (3H, m, ArH), 5.54 (1H, s, ArCHO₂), 4.15 (1H, dd, *J* = 11.4, 5.0 Hz, H25), 3.86 (1H, br d, *J* = 11.4 Hz, H22), 3.74-3.68 (1H, m, H22), 3.61 (1H, ddd, *J* = 10.0, 6.3, 2.6 Hz, H23), 3.53 (1H, t, *J* = 11.3 Hz, H25), 2.12-2.02 (1H, m, H24), 0.83 (3H, d, *J* = 6.7 Hz, Me24). The data was consistent with that reported in the literature.^[2]

Aldehyde **66**



To a stirred solution of alcohol **70** (596 mg, 2.86 mmol) in DCM (20 mL) was added pyridine (0.5 mL, 5.72 mmol) and Dess-Martin periodinane (2.42 g, 5.72 mmol). After stirring for 3 h, the reaction mixture was poured into K₂CO₃ solution (10 mL). Na₂S₂O₃ solution (10 mL) was added and the biphasic mixture was stirred vigorously for 10 min. After phase separation, the aqueous phase was extracted with DCM (2 × 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 3:1 40-60 petroleum ether / EtOAc) provided aldehyde **66** (412 mg, 2.00 mmol, 70 %) as a white solid; ¹H NMR (500 MHz, CDCl₃) δ 9.69 (1H, d, *J* = 1.9 Hz, H22), 7.58-7.47 (2H, m, ArH), 7.43-7.33 (3H, m, ArH), 5.57 (1H, s, ArCHO₂), 4.22 (1H, dd, *J* = 11.4, 5.0 Hz, H25), 3.91 (1H, dd, *J* = 10.7, 1.8 Hz, H23), 3.58 (1H, t, *J* = 11.3 Hz, H25), 2.22-2.11 (1H, m, H24), 0.94 (3H, d, *J* = 6.7 Hz, Me24). The data was consistent with that reported in the literature.^[3]

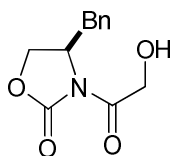
(*R*)-4-benzyl-3-(2-(benzyloxy)acetyl)oxazolidin-2-one (**71a**)



To a stirred solution of (*R*)-4-benzyloxazolidin-2-one (4.30 g, 24.3 mmol) in THF (30 mL) at -78 °C was added *n*-BuLi (1.6M in hexane, 16.7 mL, 26.7 mmol). The mixture was stirred for 30 min

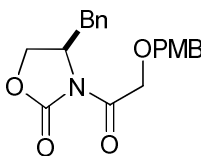
before addition of benzyloxyacetyl chloride (4.60 mL, 29.2 mmol). The reaction mixture was allowed to warm to 0 °C over 30 min, before being quenched with NH₄Cl (5 mL). The organic phase was separated, the aqueous phase extracted with Et₂O (2 × 20 mL) and the combined organic extracts were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, EtOAc / PE 40-60, 1:3) afforded imide **71a** (7.66 g, 23.6 mmol, 97%) as a colourless oil; ¹H NMR (500 MHz, CDCl₃) δ_H 7.49-7.13 (10H, m, ArH), 4.75-4.57 (5H, m, OCH₂Ar, CH₂OBn, CHN), 4.27 (1H, dd, *J* = 9.1, 3.0 Hz, OCH₂CHBn), 4.23 (1H, dd, *J* = 16.9, 9.1 Hz, OCH₂CHBn), 3.34 (1H, dd, *J* = 13.4, 3.1 Hz, PhCH₂), 2.82 (1H, dd, *J* = 13.4, 9.5 Hz, PhCH₂). The data was consistent with that reported in the literature.^[4]

Alcohol **71b**



To a stirred solution of benzyl ether **71a** (8.15 g, 25.1 mmol) in EtOAc (90 mL) was added Pd(OH)₂ (20% wt. on C, 878 mg, 1.25 mmol). The mixture was exposed to an atmosphere of H₂ (balloon) and stirred vigorously for 2 h. The reaction was then filtered (Celite™) and concentrated *in vacuo*. No further purification was required to afford alcohol **71b** (5.78 g, 24.6 mmol, 98%) as a colourless oil; ¹H NMR (500 MHz, CDCl₃) δ_H 7.38-7.33 (2H, m, ArH), 7.31 (1H, m, ArH), 7.21 (2H, d, *J* = 7.1 Hz, ArH), 4.75-4.70 (3H, m, CH₂OH, CHN), 4.33 (1H, dd, *J* = 9.1, 7.9 Hz, OCH₂CHBn), 4.27 (1H, dd, *J* = 9.1, 3.0 Hz, OCH₂CHBn), 3.34 (1H, dd, *J* = 13.5, 3.2 Hz, PhCH₂), 3.07 (1H, app t, *J* = 5.4 Hz, OH), 2.86 (1H, dd, *J* = 13.5, 9.5 Hz, PhCH₂).

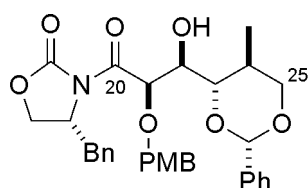
PMB ether **71**



To a stirred solution of alcohol **71b** (6.57 g, 27.9 mmol) and PMBTCA (11.9 g, 42.0 mmol) in THF (70 mL) at 0 °C was added Ph₃CBF₄ (92.0 mg, 0.280 mmol). The reaction mixture was stirred for 30 min before being quenched with NaHCO₃ (10 mL). The organic phase was separated, the

aqueous phase extracted with Et₂O (2 × 30 mL) and the combined organic extracts were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, EtOAc / PE 40-60, 1:3) afforded PMB ether **71** (9.43 g, 26.6 mmol, 95%) as a white foam; ¹H NMR (500 MHz, CDCl₃) δ_H 7.36-7.31 (4H, m, ArH), 7.29 (1H, m, ArH), 7.20 (2H, m, ArH), 6.90 (2H, d, *J* = 8.7 Hz, ArH), 4.71-4.60 (5H, m, OCH₂Ar, CH₂OPMB, CHN), 4.27 (1H, dd, *J* = 9.1, 8.8 Hz, OCH₂CHBn), 4.22 (1H, dd, *J* = 9.1, 3.0 Hz, OCH₂CHBn), 3.81 (3H, s, OMe), 3.33 (1H, dd, *J* = 13.4, 3.2 Hz, PhCH₂), 2.82 (1H, dd, *J* = 13.4, 9.4 Hz, PhCH₂).

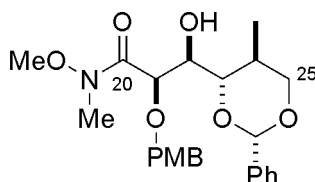
Imide **72**



Et₃N (403 μL, 2.87 mmol) and dibutylboron triflate (669 mg, 2.44 mmol) were added dropwise to a stirred solution of imide **71** (787 mg, 2.21 mmol) in dry toluene (10 mL) at -50 °C and the mixture was stirred at -50 °C for 1.5 h. A solution of aldehyde **66** (502 mg, 2.44 mmol) in dry toluene (10 mL) was added dropwise and the reaction mixture was then allowed to warm to -30 °C and stirred for 21 h. The yellow solution was allowed to warm to 0 °C, before being quenched with MeOH (8 mL), pH 7 buffer solution (4 mL) and 30 % H₂O₂ (4 mL), and the quenching mixture was stirred at room temperature for 1 h. After phase separation, the aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 3:1 → 1:1 40-60 petroleum ether / EtOAc) afforded aldol adduct **72** (938 mg, 1.67 mmol, 76 %) as a white solid; **m.p.** 54 °C; **R_f** 0.40 (1:1 40-60 petroleum ether / EtOAc); **[α]_D²⁰** -9.0 (c 1.55, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 3488 (br), 2928, 1778, 1705, 1612, 1514, 1391, 1248, 1212, 1112, 1029, 759, 700; ¹H NMR (500 MHz, CDCl₃) δ 7.45 (2H, d, *J* = 6.9 Hz, ArH), 7.34-7.23 (8H, m, ArH), 7.10 (2H, d, *J* = 6.9 Hz, ArH), 6.81 (2H, d, *J* = 8.9 Hz, ArH), 5.54 (1H, d, *J* = 5.7 Hz, H21), 5.36 (1H, s, acetal CH), 4.57 (2H, abq, *J* = 11.3, 9.4 Hz, ArCH₂O), 4.17-4.10 (2H, m, H22, NCHCH₂Ph), 4.04 (1H, dd, *J* = 11.3, 4.7 Hz, H25), 3.79-3.74 (1H, m, oxazolidinone CH₂O), 3.74 (3H, s, ArOMe), 3.64 (1H, dd, *J* = 10.1, 7.8 Hz, H23), 3.49 (1H, t, *J* = 11.3 Hz, H25), 3.19-3.13 (2H, m, oxazolidinone CH₂O, NCHCH₂Ph), 2.82 (1H, br d, *J* = 3.9 Hz, OH), 2.39 (1H, dd, *J* = 13.7, 10.6 Hz, NCHCH₂Ph), 2.11-2.01 (1H, m, H24), 0.98 (3H, d, *J* = 6.7 Hz, Me24); ¹³C NMR (125 MHz, CDCl₃) δ 171.0, 159.6, 153.2, 138.3, 135.3, 130.1, 129.3,

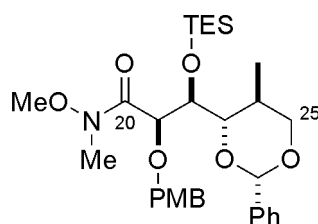
129.2, 129.0, 128.9, 128.2, 127.2, 126.6, 113.9, 101.4, 83.2, 74.8, 73.2, 73.0, 66.1, 55.2, 55.1, 37.8, 34.0, 12.9; **HRMS** calc. for C₃₂H₃₅O₈NNa [M + Na]⁺ 584.2255, found 584.2252.

Weinreb amide **72a**



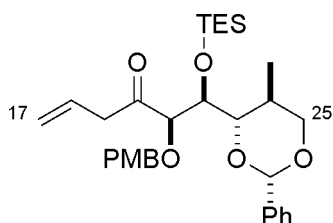
To a stirred suspension of *N,O*-dimethylhydroxylamine hydrochloride (93.6 mg, 0.96 mmol) in THF (2.5 mL) at 0 °C was added trimethylaluminum (2.0 M in hexanes, 0.492 mL, 0.984 mmol). The resulting solution was stirred at room temperature for 30 min and then cooled to -20 °C. A solution of aldol adduct **72** (179 mg, 0.319 mmol) in THF (2.5 mL) was slowly added at -20 °C and the solution was stirred at 0 °C for 1 h and at room temperature for an additional 1 h. The reaction was quenched with Na⁺/K⁺ tartrate solution (5 mL) and extracted with DCM (3 × 5 mL). The combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 1:1 40-60 petroleum ether / EtOAc) afforded Weinreb amide **72a** (115 mg, 0.258 mmol, 81 %) as a colourless oil; **R_f** 0.16 (1:1 40-60 petroleum ether / EtOAc); [**α**]_D²⁰ +66.0 (c 1.06, CHCl₃); **IR** (thin film, ν_{\max} /cm⁻¹) 3471 (br), 2937, 1669, 1612, 1513, 1389, 1249, 1120, 1073, 1030, 700; **¹H NMR** (500 MHz, CDCl₃) δ 7.32-7.27 (5H, m, ArH), 7.22 (2H, d, *J* = 8.6 Hz, ArH), 6.74 (2H, d, *J* = 8.6 Hz, ArH), 5.35 (1H, s, acetal CH), 4.74-4.71 (1H, m, H21), 4.73 (1H, d, *J* = 11.7 Hz, ArCH_aH_bO), 4.37 (1H, d, *J* = 11.7 Hz, ArCH_aH_bO), 4.07 (1H, dd, *J* = 11.4, 4.9 Hz, H25), 3.99 (1H, dt, *J* = 8.0, 2.1 Hz, H22), 3.67 (3H, s, ArOMe), 3.58 (1H, dd, *J* = 9.9, 7.8 Hz, H23), 3.49 (1H, t, *J* = 11.3 Hz, H25), 3.42 (3H, br s, MeON), 3.16 (3H, s, MeN), 2.87 (1H, d, *J* = 8.0 Hz, OH), 2.03-1.93 (1H, m, H24), 0.98 (3H, d, *J* = 6.6 Hz, Me24); **¹³C NMR** (125 MHz, CDCl₃) δ 159.4, 138.5, 129.9, 129.8, 129.3, 128.6, 127.9, 125.9, 113.7, 100.4, 81.6, 74.7, 73.2, 72.1, 71.3, 61.1, 55.1, 33.6, 32.4, 13.2; **HRMS** calc. for C₂₄H₃₂O₇N [M + H]⁺ 446.2173, found 446.2179.

TES ether 72b



To a stirred solution of alcohol **72a** (115 mg, 0.258 mmol) in DCM (1 mL) was added 2,6-lutidine (0.178 mL, 1.55 mmol) and TESOTf (0.182 mL, 0.774 mmol). The reaction mixture was stirred for 30 min, before being quenched with NaHCO₃ solution (2 mL). The aqueous phase was extracted with DCM (2 × 2 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 1:1 40-60 petroleum ether / Et₂O) gave silyl ether **72b** (128 mg, 0.228 mmol, 89 %) as a colourless oil; *R_f* 0.64 (1:1 40-60 petroleum ether / EtOAc); [α]_D²⁰ +9.5 (c 1.04, CHCl₃); IR (thin film, ν_{max}/cm⁻¹) 2953, 2875, 1663, 1513, 1457, 1247, 1073, 1027, 726, 699; ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.40 (2H, m, ArH), 7.35-7.29 (3H, m, ArH), 7.26 (2H, d, *J* = 8.6 Hz, ArH), 6.82 (2H, d, *J* = 8.6 Hz, ArH), 5.36 (1H, s, acetal CH), 4.61 (1H, br d, *J* = 11.9 Hz, ArCH_aH_bO), 4.52 (1H, d, *J* = 11.9 Hz, ArCH_aH_bO), 4.48-4.35 (2H, m, H21, H22), 4.06 (1H, dd, *J* = 11.4, 4.8 Hz, H25), 3.77 (3H, s, ArOMe), 3.56 (1H, br d, *J* = 9.9 Hz, H23), 3.47-3.39 (4H, m, H25, MeON), 3.08 (3H, s, MeN), 2.07-1.96 (1H, m, H24), 0.97 (9H, t, *J* = 8.0 Hz, 3 × SiCH₂CH₃), 0.86 (3H, d, *J* = 6.5 Hz, Me24), 0.66 (6H, q, *J* = 8.0 Hz, 3 × SiCH₂CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 159.2, 138.6, 129.6, 128.5, 127.9, 126.3, 113.5, 101.3, 85.1, 74.8, 73.3, 72.1, 55.2, 30.6, 12.8, 6.9, 5.1; HRMS calc. for C₃₀H₄₉O₇N₂Si [M + NH₄]⁺ 577.3304, found 577.3310.

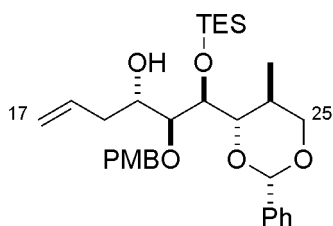
Ketone 73



To a stirred solution of Weinreb amide **72b** (499 mg, 0.891 mmol) in THF (10 mL) at -20 °C was added allylmagnesium bromide (1.0 M in Et₂O, 1.78 mL, 1.78 mmol). The reaction mixture was stirred at -20 °C for 1 h, before being quenched with NH₄Cl solution (5 mL). The aqueous phase was extracted with Et₂O (3 × 5 mL) and the combined organic phases were dried (MgSO₄) and

concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 3:1 40-60 petroleum ether / Et₂O) afforded ketone **73** (459 mg, 0.849 mmol, 95 %) as a colourless oil; **R_f** 0.62 (3:1 40-60 petroleum ether / EtOAc); [α]_D²⁰ +14.5 (c 1.49, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2955, 2876, 1719, 1612, 1513, 1457, 1248, 1098, 1028, 820, 742, 698; **¹H NMR** (500 MHz, CDCl₃) δ 7.45-7.40 (2H, m, ArH), 7.37-7.29 (3H, m, ArH), 7.23 (2H, d, J = 8.6 Hz, ArH), 6.85 (2H, d, J = 8.6 Hz, ArH), 5.72-5.62 (1H, m, H18), 5.32 (1H, s, acetal CH), 5.02 (1H, dd, J = 10.2, 1.4 Hz, H17), 4.91 (1H, dd, J = 17.3, 1.5 Hz, H17), 4.59 (1H, d, J = 11.6 Hz, ArCH_aH_bO), 4.39 (1H, d, J = 11.6 Hz, ArCH_aH_bO), 4.18 (1H, dd, J = 5.4, 2.7 Hz, H22), 4.06 (1H, dd, J = 11.4, 4.7 Hz, H25), 3.92 (1H, d, J = 5.4 Hz, H21), 3.80 (3H, s, ArOMe), 3.51 (1H, dd, J = 10.4, 2.7 Hz, H23), 3.40 (1H, t, J = 11.3 Hz, H25), 3.24 (2H, abx, J = 19.8, 17.4, 6.6 Hz, H19), 2.30-2.19 (1H, m, H24), 0.94 (9H, t, J = 8.0 Hz, 3 \times SiCH₂CH₃), 0.83 (3H, d, J = 6.5 Hz, Me24), 0.61 (6H, q, J = 8.0 Hz, 3 \times SiCH₂CH₃); **¹³C NMR** (125 MHz, CDCl₃) δ 207.9, 159.3, 138.4, 131.0, 129.8, 129.6, 128.7, 128.1, 126.4, 118.2, 113.7, 101.8, 85.2, 85.1, 74.3, 73.1, 72.5, 55.2, 45.2, 29.9, 12.8, 6.8, 4.9; **HRMS** calc. for C₃₁H₄₈O₆NSi [M + NH₄]⁺ 558.3245, found 558.3247.

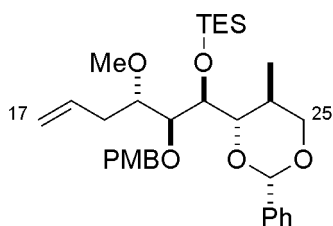
Homoallylic alcohol **74**



To a stirred solution of ketone **73** (78.2 mg, 0.153 mmol) in Et₂O (5 mL) at -78 °C was added zinc borohydride (0.15 M in Et₂O, 2.00 mL, 0.300 mmol). The reaction mixture was stirred at -78 °C for 30 min and then allowed to warm to -10 °C. The reaction was quenched with Na⁺/K⁺ tartrate solution (5 mL) and the aqueous phase was extracted with Et₂O (3 \times 5 mL). The combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 3:1 40-60 petroleum ether / Et₂O) provided alcohol **74** (62.7 mg, 0.112 mmol, 78 %) as a colourless oil; **R_f** 0.52 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ -7.8 (c 1.02, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3552 (br), 2954, 2876, 1612, 1514, 1457, 1248, 1030, 744; **¹H NMR** (500 MHz, CDCl₃) δ 7.51-7.46 (2H, m, ArH), 7.39-7.30 (3H, m, ArH), 7.22 (2H, d, J = 8.8 Hz, ArH), 6.84 (2H, d, J = 8.6 Hz, ArH), 5.99-5.90 (1H, m, H18), 5.43 (1H, s, acetal CH), 5.13-5.08 (2H, m, H17), 4.61 (1H, d, J = 10.8 Hz, ArCH_aH_bO), 4.50 (1H, d, J = 10.8 Hz, ArCH_aH_bO), 4.25 (1H, dd, J = 4.3, 2.8 Hz, H22), 4.19-4.14 (1H, m, H20), 4.10 (1H, dd, J = 10.6, 2.5 Hz, H25), 3.80

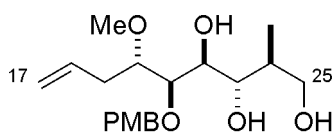
(3H, s, ArOMe), 3.76 (1H, dd, $J = 10.6, 2.4$ Hz, H23), 3.50-3.39 (2H, m, H21, H25), 2.57-2.50 (1H, m, H19), 2.45-2.35 (1H, m, H24), 2.28-2.20 (1H, m, H19), 0.98 (9H, t, $J = 7.9$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.84 (3H, d, $J = 6.4$ Hz, Me24), 0.65 (6H, q, $J = 7.9$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$); ^{13}C NMR (125 MHz, CDCl_3) δ 159.3, 138.3, 135.6, 130.1, 129.5, 128.7, 128.2, 126.1, 116.7, 113.8, 101.8, 85.9, 82.3, 73.4, 73.2, 72.9, 71.5, 55.2, 38.0, 29.8, 12.9, 6.8, 4.8; HRMS calc. for $\text{C}_{31}\text{H}_{50}\text{O}_6\text{NSi}$ $[\text{M} + \text{NH}_4]^+$ 560.3402, found 560.3406.

Methyl ether 75



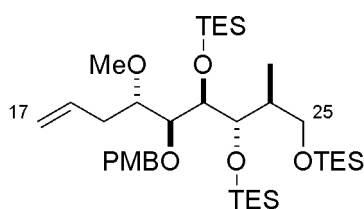
To a stirred solution of alcohol **74** (55.4 mg, 0.107 mmol) in DCM (1 mL) at room temperature was added proton sponge[®] (64.2 mg, 0.303 mmol) and trimethyloxonium tetrafluoroborate (44.1 mg, 0.306 mmol). The reaction mixture was stirred for 1 h before quenching with NH_4Cl solution (1 mL) and extraction with DCM (3×1 mL). The combined organic phases were dried (MgSO_4) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2 , 3:1 40-60 petroleum ether / Et_2O) gave methyl ether **75** (52.9 mg, 94.3 μmol , 94 %) as a colourless oil; R_f 0.72 (1:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20} +1.1$ (c 1.23, CHCl_3); IR (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2954, 2876, 1613, 1513, 1461, 1247, 1103, 1031, 741, 698; ^1H NMR (500 MHz, CDCl_3) δ 7.50-7.44 (2H, m, ArH), 7.35-7.29 (3H, m, ArH), 7.22 (2H, d, $J = 8.4$ Hz, ArH), 6.81 (2H, d, $J = 8.6$ Hz, ArH), 5.89-5.80 (1H, m, H18), 5.43 (1H, s, acetal CH), 5.07-4.99 (2H, m, H17), 4.72 (1H, d, $J = 11.2$ Hz, $\text{ArCH}_a\text{H}_b\text{O}$), 4.58 (1H, d, $J = 11.2$ Hz, $\text{ArCH}_a\text{H}_b\text{O}$), 4.12 (1H, dd, $J = 11.2, 5.0$ Hz, H25), 4.02 (1H, dd, $J = 6.3, 1.7$ Hz, H22), 3.79 (3H, s, ArOMe), 3.69 (1H, dd, $J = 6.2, 4.7$ Hz, H21), 3.61 (1H, dd, $J = 10.2, 1.5$ Hz, H23), 3.52-3.44 (2H, m, H20, H25), 3.32 (3H, s, MeO20), 2.44 (2H, br t, $J = 6.5$ Hz, H19), 2.26-2.16 (1H, m, H24), 0.96 (9H, t, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.87 (3H, d, $J = 6.6$ Hz, Me24), 0.65 (6H, q, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$); ^{13}C NMR (125 MHz, CDCl_3) δ 158.8, 138.6, 135.7, 131.5, 129.1, 128.6, 128.0, 126.2, 116.4, 113.4, 101.6, 86.4, 81.7, 79.1, 74.1, 73.6, 73.3, 57.2, 55.2, 34.3, 30.3, 12.9, 7.0, 5.2; HRMS calc. for $\text{C}_{32}\text{H}_{52}\text{O}_6\text{NSi}$ $[\text{M} + \text{NH}_4]^+$ 574.3558, found 574.3555.

Triol **75a**



To a stirred solution of acetal **75** (188 mg, 0.337 mmol) in MeOH (20 mL) at room temperature was added *p*-TsOH·H₂O (6.4 mg, 0.034 mmol). The reaction mixture was stirred for 1 h before being quenched with a few drops of Et₃N and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO₂, 1:1 40-60 petroleum ether / EtOAc) to afford triol **75a** (94.0 mg, 0.265 mmol, 79 %) as a colourless oil; **R_f** 0.22 (1:1 40-60 petroleum ether / EtOAc); [α]_D²⁰ +21.9 (c 1.80, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 3395 (br), 2933, 1612, 1514, 1247, 1094, 1032, 822; **¹H NMR** (500 MHz, CDCl₃) δ 7.27 (2H, d, *J* = 8.6 Hz, ArH), 6.89 (2H, d, *J* = 8.6 Hz, ArH), 5.88-5.79 (1H, m, H18), 5.16-5.10 (2H, m, H17), 4.65 (1H, d, *J* = 11.0 Hz, ArCH₂H_bO), 4.56 (1H, d, *J* = 11.0 Hz, ArCH₂H_bO), 3.87-3.82 (2H, m, H22, H23), 3.80 (3H, s, ArOMe), 3.75 (1H, dd, *J* = 5.0, 1.5 Hz, H21), 3.68-3.62 (2H, m, H25), 3.59 (1H, q, *J* = 5.6 Hz, H20), 3.53 (1H, br s, OH), 3.45 (3H, s, MeO20), 2.91 (2H, br s, OH), 2.43 (2H, t, *J* = 6.5 Hz, H19), 2.05-1.97 (1H, m, H24), 1.04 (3H, d, *J* = 7.1 Hz, Me24); **¹³C NMR** (125 MHz, CDCl₃) δ 159.6, 134.1, 129.9, 129.7, 117.7, 114.0, 82.0, 72.7, 70.6, 65.7, 58.6, 55.3, 36.1, 34.9, 13.9; **HRMS** calc. for C₁₉H₃₁O₆ [M + H]⁺ 355.2115, found 355.2116.

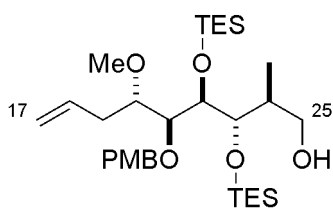
Tris-TES ether **76**



To a stirred solution of triol **75a** (64.7 mg, 0.180 mmol) in DCM (2 mL) at 0 °C was added 2,6-lutidine (418 μ L, 3.60 mmol) and TESOTf (406 μ L, 1.80 mmol) sequentially. The reaction mixture was stirred at 0 °C before being quenched with NaHCO₃ solution (1 mL). The aqueous phase was extracted with DCM (2 \times 5 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO₂, 20:1 40-60 petroleum ether / Et₂O) to afford TES ether **76** (125 mg, 0.180 mmol, 99 %) as a colourless

oil; R_f 0.50 (9:1 40-60 petroleum ether / Et₂O); $[\alpha]_D^{20}$ -20.7 (c 1.50, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2954, 2877, 1514, 1247, 1092, 1007, 809, 740; **¹H NMR** (500 MHz, CDCl₃) δ 7.29 (2H, d, $J = 8.5$ Hz, ArH), 6.85 (2H, d, $J = 8.5$ Hz, ArH), 5.96-5.87 (1H, m, H18), 5.08 (1H, dd, $J = 17.2, 1.3$ Hz, H17), 5.03 (1H, d, $J = 10.2$ Hz, H17), 4.70 (1H, d, $J = 11.1$ Hz, ArCH_aH_bO), 4.63 (1H, d, $J = 11.1$ Hz, ArCH_aH_bO), 3.88 (1H, dd, $J = 9.6, 3.5$ Hz, H23), 3.80 (3H, s, ArOMe), 3.78-3.72 (2H, m, H21, H22), 3.62 (1H, d, $J = 7.8$ Hz, H25), 3.46-3.41 (2H, m, H20, H25), 3.33 (3H, s, MeO20), 2.54-2.45 (1H, m, H19), 2.21 (1H, dd, $J = 15.0, 6.8$ Hz, H19), 1.86-1.77 (1H, m, H24), 1.02-0.91 (30H, m, Me24, 9 × SiCH₂CH₃), 0.67 (6H, q, $J = 8.0$ Hz, 3 × SiCH₂CH₃), 0.60 (6H, q, $J = 8.0$ Hz, 3 × SiCH₂CH₃), 0.59 (6H, q, $J = 8.0$ Hz, 3 × SiCH₂CH₃); **¹³C NMR** (125 MHz, CDCl₃) δ 158.7, 136.1, 131.7, 129.0, 116.0, 113.4, 81.9, 79.9, 78.6, 75.9, 73.9, 64.9, 57.2, 55.3, 38.6, 34.6, 15.5, 7.1, 7.0, 6.8, 5.2, 5.2, 4.5; **HRMS** calc. for C₃₇H₇₃O₆Si₃ [M + H]⁺ 697.4709, found 697.4714.

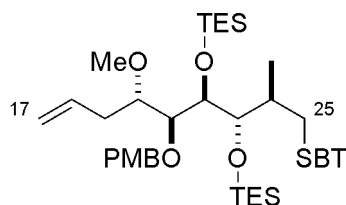
Alcohol 76a



To a stirred solution of pyridine (750 μL) in THF (4 mL) in a Teflon container was added HF·pyridine complex (HF 70 %, 250 μL) dropwise. The premixed HF·pyridine-pyridine solution (HF 1.9 M, 150 μL , 0.285 mmol) was then added to a stirred solution of TES ether **76** (66.3 mg, 95.1 μmol) in THF (1 mL) at 0 °C. The reaction mixture was stirred at room temperature for 30 min before being cooled to 0 °C, quenched with pH 7 buffer solution (1 mL) and diluted with Et₂O (2 mL). The aqueous phase was extracted with Et₂O (2 × 1 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO₂, 1:1 40-60 petroleum ether / Et₂O) to provide alcohol **76a** (44.1 mg, 75.6 μmol , 80 %) as a colourless oil; R_f 0.39 (1:1 40-60 petroleum ether / Et₂O); $[\alpha]_D^{20}$ -16.1 (c 1.68, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3434 (br), 2954, 2877, 1614, 1514, 1459, 1248, 1094, 1006, 823, 740; **¹H NMR** (500 MHz, CDCl₃) δ 7.29 (2H, d, $J = 8.6$ Hz, ArH), 6.88 (2H, d, $J = 8.6$ Hz, ArH), 5.96-5.86 (1H, m, H18), 5.14-5.06 (2H, m, H17), 4.75 (1H, d, $J = 11.0$ Hz, ArCH_aH_bO), 4.60 (1H, d, $J = 11.0$ Hz, ArCH_aH_bO), 4.08 (1H, br s, OH), 3.84-3.75 (2H, m, H22, H25), 3.82 (3H, s, ArOMe), 3.71-3.65 (2H, m, H21, H23), 3.40-3.35 (1H, m, H25), 3.37 (3H, s, MeO20), 3.31-3.27 (1H, m, H20), 2.55-2.48 (1H, m, H19), 2.26-2.18 (1H, m, H19), 1.98-1.90 (1H, m, H24), 1.04-0.93 (21H, m,

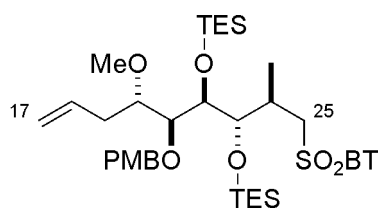
Me24, $6 \times \text{SiCH}_2\text{CH}_3$), 0.73-0.62 (12H, m, $6 \times \text{SiCH}_2\text{CH}_3$); ^{13}C NMR (125 MHz, CDCl_3) δ 135.5, 131.2, 128.9, 116.6, 113.5, 82.4, 79.6, 77.9, 77.4, 73.8, 63.5, 57.5, 55.2, 37.6, 34.6, 17.5, 7.1, 6.9, 5.2, 5.2; HRMS calc. for $\text{C}_{31}\text{H}_{59}\text{O}_6\text{Si}_2$ $[\text{M} + \text{H}]^+$ 583.3845, found 583.3842.

Sulfide 77



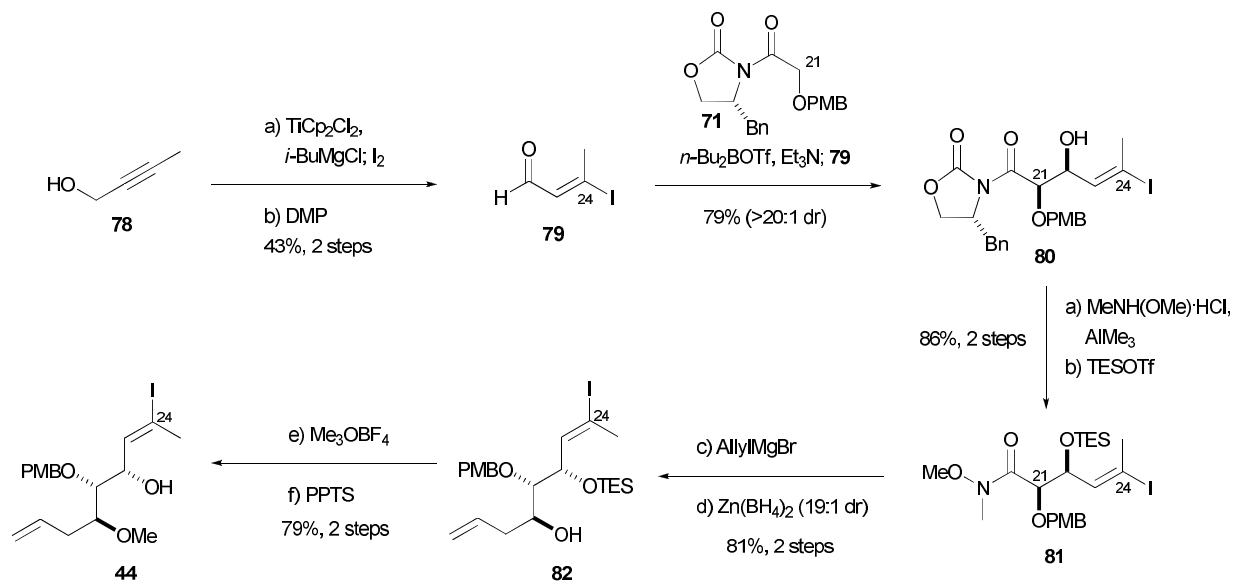
To a stirred solution of alcohol **76a** (44.1 mg, 75.6 μmol) in THF (4.5 mL) was added 2-mercaptobenzothiazole (19.0 mg, 0.113 mmol), triphenylphosphine (39.7 mg, 0.151 mmol) and diethyl azodicarboxylate (26.3 mg, 0.151 mmol). The reaction mixture was stirred at room temperature for 30 min before concentration *in vacuo*. The crude residue was purified by flash column chromatography (SiO_2 , 20:1 40-60 petroleum ether / Et_2O) affording sulfide **77** (54.5 mg, 74.4 μmol , 99 %) as a colourless oil; R_f 0.65 (3:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20}$ -31.2 (c 1.00, CHCl_3); IR (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2954, 2876, 1613, 1514, 1460, 1428, 1247, 1094, 1002, 726; ^1H NMR (500 MHz, CDCl_3) δ 7.84 (1H, d, $J = 8.3$ Hz, ArH), 7.74 (1H, d, $J = 7.9$ Hz, ArH), 7.40 (1H, t, $J = 7.9$ Hz, ArH), 7.30-7.25 (3H, m, ArH), 6.85 (2H, d, $J = 8.6$ Hz, ArH), 5.85-5.75 (1H, m, H18), 5.01 (1H, dd, $J = 17.0, 1.3$ Hz, H17), 4.93 (1H, d, $J = 10.0$ Hz, H17), 4.67 (2H, abq, $J = 20.6, 11.1$ Hz, ArCH_2O), 4.01 (1H, dd, $J = 12.8, 3.4$ Hz, H25), 3.83 (1H, dd, $J = 7.3, 1.3$ Hz, H22), 3.80 (3H, s, ArOMe), 3.70-3.65 (2H, m, H21, H23), 3.41 (1H, td, $J = 8.6, 3.0$ Hz, H20), 3.33 (3H, s, MeO20), 3.07 (1H, dd, $J = 12.8, 9.9$ Hz, H25), 2.49-2.41 (1H, m, H19), 2.28-2.18 (2H, m, H19, H24), 1.15 (3H, d, $J = 6.8$ Hz, Me24), 1.02 (9H, t, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.94 (9H, t, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.72 (6H, q, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.62 (6H, q, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$); ^{13}C NMR (125 MHz, CDCl_3) δ 167.9, 158.8, 153.5, 135.6, 135.3, 131.4, 129.0, 125.9, 124.0, 121.5, 120.8, 116.3, 113.5, 81.7, 79.6, 78.9, 73.6, 57.2, 55.2, 37.3, 35.6, 34.5, 18.0, 7.2, 7.1, 5.3, 5.2; HRMS calc. for $\text{C}_{38}\text{H}_{62}\text{O}_5\text{NS}_2\text{Si}_2$ $[\text{M} + \text{H}]^+$ 732.3602, found 732.3606.

Sulfone 41

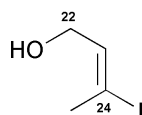


To a stirred solution of sulfide **77** (19.0 mg, 25.9 μmol) in EtOH (1 mL) was added a catalytic amount of $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$ (6.5 mg, 5.0 μmol) and 30 % H_2O_2 (30 μL , 0.26 mmol). The reaction mixture was stirred for 16 h before quenching with NH_4Cl solution (1 mL) and removal of EtOH *in vacuo*. The mixture was extracted with DCM (3×1 mL), and the combined organic phases were dried (MgSO_4) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO_2 , 3:1 40-60 petroleum ether / Et_2O) to provide sulfone **41** (13.8 mg, 18.1 μmol , 70 %) as a colourless oil; R_f 0.30 (3:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20}$ -18.8 (c 1.25, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2955, 2877, 1614, 1514, 1459, 1318, 1247, 1147, 1092, 729; **^1H NMR** (500 MHz, CDCl_3) δ 8.20 (1H, d, $J = 7.7$ Hz, ArH), 8.01 (1H, d, $J = 7.8$ Hz, ArH), 7.60 (2H, dt, $J = 21.4, 7.1, 7.1$ Hz, ArH), 7.20 (2H, d, $J = 8.6$ Hz, ArH), 6.84 (2H, d, $J = 8.6$ Hz, ArH), 5.80 (1H, dd, $J = 17.1, 10.2$ Hz, H18), 5.04 (1H, d, $J = 5.0$ Hz, H17), 5.02 (1H, s, H17), 4.54 (1H, d, $J = 15.6$ Hz, H25), 4.52 (1H, d, $J = 11.3$ Hz, $\text{ArCH}_a\text{H}_b\text{O}$), 4.41 (1H, d, $J = 11.3$ Hz, $\text{ArCH}_a\text{H}_b\text{O}$), 3.80 (3H, s, ArOMe), 3.76 (1H, dd, $J = 7.5, 1.8$ Hz, H22), 3.60 (1H, m, H23), 3.36 (1H, dd, $J = 7.5, 3.5$ Hz, H21), 3.31 (1H, dd, $J = 10.9, 1.6$ Hz, H25), 3.29 (3H, s, MeO20), 3.24-3.20 (1H, m, H20), 2.71-2.63 (1H, m, H24), 2.42-2.34 (1H, m, H19), 2.23-2.16 (1H, m, H19), 1.29 (3H, d, $J = 6.8$ Hz, Me24), 0.96 (9H, t, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.84 (9H, t, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.63 (6H, q, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$), 0.53 (6H, q, $J = 8.0$ Hz, $3 \times \text{SiCH}_2\text{CH}_3$); **^{13}C NMR** (125 MHz, CDCl_3) δ 167.2, 158.8, 152.8, 136.9, 135.1, 131.0, 129.0, 127.8, 127.4, 125.4, 122.3, 116.8, 113.5, 82.0, 79.3, 78.7, 73.4, 57.7, 57.3, 55.2, 34.4, 30.0, 19.6, 7.0, 7.0, 5.1, 5.1; **HRMS** calc. for $\text{C}_{38}\text{H}_{65}\text{O}_7\text{N}_2\text{S}_2\text{Si}_2$ $[\text{M} + \text{NH}_4]^+$ 781.3766, found 781.3759.

2.5 Synthesis of vinyl iodide 44

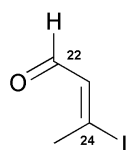


(2E)-3-iodobut-2-en-1-ol (78a)



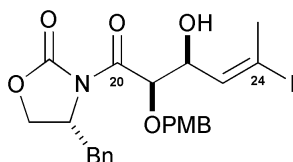
Bis-(cyclopentadienyl)titanium(IV) dichloride (0.572 g, 2.30 mmol) was added portionwise to a solution of *i*-BuMgCl (2 M in Et₂O, 53.0 mL, 106 mmol) in Et₂O (60 mL) at 0 °C. The mixture was stirred at 0 °C for 10 min before the dropwise addition (30 min) of 2-butyn-1-ol **78** (3.00 mL, 40.1 mmol) in Et₂O (12 mL). The solution was raised to rt and stirred for 4 h until complete reaction was observed by TLC (**R_f** 0.27 (EtOAc/PhMe, 1:2)). The reaction mixture was then cooled to -78 °C and stirred vigorously while I₂ (35.1 g, 138 mmol) was added portionwise. The resulting mixture was warmed to 0 °C and stirred for 1 h prior to quenching with NH₄Cl (30 mL) and dilution with Et₂O (60 mL) and water (20 mL). The organic layer was separated and the aqueous layer extracted with Et₂O (3 × 100 mL). The combined organic phases were washed with Na₂S₂O₃ (3 × 300 mL) dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified using flash column chromatography (Et₂O / PE (30-40), 1:7 → 1:4 → 1:2) affording alcohol **78a** as a light yellow oil (3.88 g, 20.0 mmol, 49 %); **R_f** 0.18 (Et₂O / PE (30-40), 1:3); ¹H NMR (500 MHz, CDCl₃) δ_H 6.41 (1H, t, *J* = 6.3 Hz, H₂₃), 4.10 (2H, t, *J* = 6.3 Hz, H₂₂), 2.46 (3H, s, Me₂₄), 1.36 (1H, br s, OH). The data was consistent with that reported in the literature.^[243]

Aldehyde **79**



Dess-Martin periodinane (3.49 g, 8.23 mmol) was added to a solution of alcohol **78a** (1.48 g, 7.47 mmol) in CH₂Cl₂ (20 mL) at 0 °C. The reaction was warmed to rt and stirred for 1 h before being cooled to 0 °C and quenched with NaHCO₃ (30 mL) and Na₂S₂O₃ (30 mL). After vigorous stirring for 1h at rt the organic layer was separated and the aqueous phase extracted with Et₂O (3 × 20 mL). The combined organic phases were dried over MgSO₄, concentrated *in vacuo* and the resulting crude oil purified by flash column chromatography (Et₂O / PE (30–40), 1:9) to afford aldehyde **79** as a yellow oil (1.28 g, 6.53 mmol, 87 %); **R_f** 0.62 (EtOAc / PE 40-60, 1:2); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2853, 1672, 1615, 1423, 1374, 1122; **¹H NMR** (500 MHz, CDCl₃) δ 9.78 (1H, d, $J = 7.0$ Hz, H22), 6.85 (1H, dq, $J = 7.1, 1.4$ Hz, H23), 2.99 (3H, d, $J = 1.4$ Hz, Me24); **¹³C NMR** (125 MHz, CDCl₃) δ 185.9, 141.9, 125.9, 29.9; **HRMS** (EI⁺) calcd for C₄H₅OI [M]⁺ 195.9380, found 195.9384.

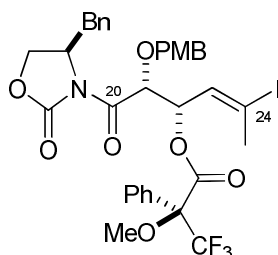
Imide **80**



Et₃N (1.09 mL, 7.84 mmol) was added to a solution of imide **71** (2.14 g, 6.03 mmol) in PhMe (8 mL) and cooled to –50 °C prior to the careful addition of Bu₂BOTf (1.82 mL, 6.63 mmol) *via* cannula. The resulting yellow solution was stirred at –50 °C for 1.5 h, during which time a light precipitate formed. Aldehyde **79** (2.17 g, 11.1 mmol) in PhMe (8 mL) was added to the mixture *via* cannula and the system allowed to warm to –30 °C and stirred for a further 1.5 h. The subsequent orange solution was quenched by the addition of MeOH (5 mL), pH7 buffer (5 mL) and H₂O₂ (5 mL) and stirred vigorously for 1 h at rt before separation of the organic phase and extraction of the aqueous layer (3 × 15 mL Et₂O). The combined organic phases were dried over MgSO₄, concentrated *in vacuo* and purified by flash column chromatography (EtOAc/PE (40-60), 1:5) to reveal imide **80** as a light yellow oil (2.55 g, 4.63 mmol, 77 %); **R_f** 0.19 (EtOAc / PE 40-60, 1:2);

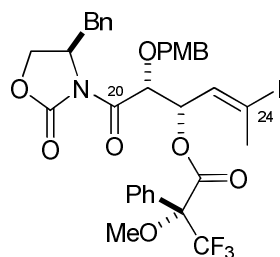
$[\alpha]_D^{20}$ -46.6 (c 1.08, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3479, 2917, 1776, 1705, 1612, 1513, 1390, 1249, 1211, 1112, 1033, 701; **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ 7.36-7.30 (4H, m, ArH), 7.29 (1H, m, ArH), 7.19 (2H, d, $J = 6.9$ Hz, ArH), 6.91 (2H, d, $J = 8.7$ Hz, ArH), 6.31 (1H, dq, $J = 8.9, 1.5$ Hz, H_{23}), 5.19 (1H, d, $J = 4.3$ Hz, H_{21}), 4.64 (1H, d, $J = 11.4$ Hz, CH_2Ar), 4.61-4.55 (2H, m, H_{22} , CHN), 4.55 (1H, d, $J = 11.4$ Hz, CH_2Ar), 4.27 (1H, dd, $J = 9.1, 7.6$ Hz, OCH_2CHBn), 4.19 (1H, dd, $J = 9.1, 2.3$ Hz, OCH_2CHBn), 3.78 (3H, s, OMe), 3.17 (1H, dd, $J = 13.6, 3.4$ Hz, PhCH_2), 2.66 (1H, dd, $J = 13.6, 9.8$ Hz, PhCH_2), 2.61 (1H, br s, OH), 2.42 (3H, d, $J = 1.5$ Hz, Me24); **$^{13}\text{C NMR}$** (125 MHz, CDCl_3) δ 169.9, 159.8, 153.3, 138.3, 135.0, 130.4, 129.3, 129.1, 128.7, 127.5, 114.0, 100.1, 78.9, 73.2, 70.4, 67.0, 55.7, 55.3, 37.8, 28.7; **HRMS** (ES^+) calcd for $\text{C}_{24}\text{H}_{26}\text{INO}_6$ $[\text{M}+\text{Na}]^+$ 574.0697, found 574.0700.

(S)-Mosher ester 80a



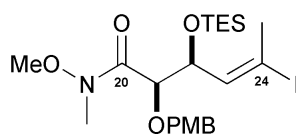
To a stirred solution of alcohol **80** (5.0 mg, 9.1 μmol) and DMAP (1 crystal) in CH_2Cl_2 / pyridine (1:1, 500 μL) was added (*R*)-(-)- α -Methoxy- α -(trifluoromethyl)-phenylacetyl chloride (8.0 μL , 45.4 μmol). The reaction mixture was stirred for 30 min before being concentrated. Purification by flash column chromatography (SiO_2 , EtOAc / PE 40-60, 1:4) afforded ester **80a** (4.7 mg, 6.1 μmol , 67%) as a colourless oil; R_f 0.56 (EtOAc / PE 40-60, 1:2); **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ 7.50 (2H, d, $J = 7.1$ Hz, ArH), 7.41-7.32 (4H, m, ArH), 7.31 (2H, d, $J = 7.5$ Hz, ArH), 7.28 (2H, d, $J = 8.7$ Hz, ArH), 7.17 (2H, d, $J = 7.1$ Hz, ArH), 6.87 (2H, d, $J = 8.8$ Hz, ArH), 6.19 (1H, dq, $J = 9.5, 1.5$ Hz, H_{23}), 5.93 (1H, dd, $J = 9.5, 5.4$ Hz, H_{22}), 5.42 (1H, d, $J = 5.4$ Hz, H_{21}), 4.58 (1H, d, $J = 11.4$ Hz, OCH_2Ar), 4.54 (1H, d, $J = 11.4$ Hz, OCH_2Ar), 4.45 (1H, m, CHN), 4.27 (1H, app t, $J = 8.0$ Hz, CH_2Ar), 4.16 (1H, dd, $J = 9.0, 2.4$ Hz, CH_2Ar), 3.78 (3H, s, ArOMe), 3.59 (3H, s, OMe), 3.13 (1H, dd, $J = 13.6, 3.3$ Hz, OCH_2CHBn), 2.59 (1H, dd, $J = 13.6, 9.9$ Hz, OCH_2CHBn), 2.46 (3H, d, $J = 1.5$ Hz, Me24).

(R)-Mosher ester **80b**



To a stirred solution of alcohol **80** (5.0 mg, 9.1 μmol) and DMAP (1 crystal) in CH_2Cl_2 / pyridine (1:1, 500 μL) was added (*S*)-(+)- α -Methoxy- α -(trifluoromethyl)-phenylacetyl chloride (8.0 μL , 45.4 μmol). The reaction mixture was stirred for 30 min before being concentrated. Purification by flash column chromatography (SiO_2 , EtOAc / PE 40-60, 1:4) afforded ester **80b** (3.2 mg, 4.2 μmol , 46%) as a colourless oil; R_f 0.51 (EtOAc / PE 40-60, 1:2); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.54 (2H, m, ArH), 7.41-7.37 (3H, m, ArH), 7.34-7.27 (3H, m, ArH), 7.19 (2H, d, $J = 8.6$ Hz, ArH), 7.15 (2H, d, $J = 7.2$ Hz, ArH), 6.84 (2H, d, $J = 8.6$ Hz, ArH), 6.30 (1H, dq, $J = 9.7, 1.5$ Hz, H23), 5.92 (1H, dd, $J = 9.7, 6.2$ Hz, H22), 5.41 (1H, d, $J = 6.2$ Hz, H21), 4.43 (1H, d, $J = 11.7$ Hz, OCH_2Ar), 4.38 (1H, m, CHN), 4.37 (1H, d, $J = 11.7$ Hz, OCH_2Ar), 4.22 (1H, app t, $J = 8.3$ Hz, CH_2Ar), 4.13 (1H, dd, $J = 9.0, 2.4$ Hz, CH_2Ar), 3.76 (3H, s, ArOMe), 3.53 (3H, s, OMe), 3.04 (1H, dd, $J = 13.4, 3.2$ Hz, OCH_2CHBn), 2.51 (3H, d, $J = 1.5$ Hz, Me24), 2.48 (1H, dd, $J = 13.4, 10.0$ Hz, OCH_2CHBn).

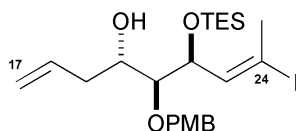
Weinreb amide **81**



To a stirred slurry of *N,O*-dimethylhydroxylamine hydrochloride (1.63 g, 16.7 mmol) in THF (15 mL) at 0 $^\circ\text{C}$ was added AlMe_3 (2M in hexane, 8.35 mL, 16.7 mmol) dropwise. The mixture was allowed to warm to RT and was stirred for 30 min before being recooled to -20 $^\circ\text{C}$. A solution of β -hydroxyketone **80** (3.06 g, 5.55 mmol) in THF (15 mL) was then added *via* cannula and the reaction mixture allowed to warm to 0 $^\circ\text{C}$ and stirred for 1 h before being cautiously quenched with Na^+ / K^+ tartrate (10 mL). This mixture was stirred vigorously for 1 h at RT, then diluted with Et_2O (10 mL) and H_2O (5 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 \times 20 mL) and the combined organic extracts were dried (MgSO_4) and concentrated *in vacuo*.

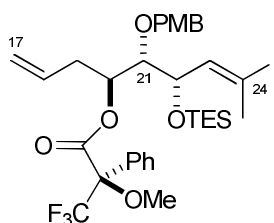
(6H, q, $J = 8.0$ Hz, $3 \times \text{Si}(\text{CH}_2\text{CH}_3)$); ^{13}C NMR (125 MHz, CDCl_3) δ 209.9, 159.6, 140.8, 130.2, 130.0, 129.0, 118.7, 114.0, 96.8, 86.1, 73.5, 71.7, 55.3, 45.4, 28.4, 6.7, 4.7; HRMS (ES^+) calcd for $\text{C}_{23}\text{H}_{35}\text{IO}_4\text{SiNa}$ $[\text{M}+\text{Na}]^+$ 553.1247, found 553.1246.

Homoallylic alcohol **82**



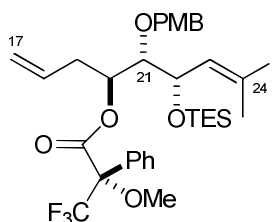
Zinc borohydride (0.15 M, 11.0 mL, 1.65 mmol) was added to a solution of ketone **81a** (0.810 g, 1.53 mmol) in Et_2O (10 mL) at -50 °C. The reaction was stirred at this temperature for 30 min, during which time a white precipitate evolved, before being quenched with Na^+ / K^+ tartrate (10 mL). The quenching mixture was stirred for 1 h at rt prior to separation of the organic layer and extraction of the aqueous phase with Et_2O (3×10 mL). The combined organic phases were dried over MgSO_4 , concentrated *in vacuo* and purified using flash column chromatography ($\text{Et}_2\text{O} / \text{PE}$ (30-40), 1:4) to give alcohol **82** as a clear, colourless oil (0.735 g, 1.38 mmol, 90 %); R_f 0.41 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ -35.0 (c 0.70, CHCl_3); IR (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3492, 2955, 1612, 1514, 1463, 1248, 1077, 1038, 1004, 811, 745; ^1H NMR (500 MHz, CDCl_3) δ 7.24 (2H, d, $J = 8.8$ Hz, ArH), 6.89 (2H, d, $J = 8.8$ Hz, ArH), 6.33 (1H, dq, $J = 9.1, 1.5$ Hz, H23), 5.89 (1H, dddd, $J = 17.1, 10.3, 7.7, 6.2$ Hz, H18), 5.17-5.11 (2H, m, H17), 4.56 (1H, dd, $J = 9.2, 4.2$ Hz, H22), 4.56 (1H, d, $J = 11.2$ Hz, CH_2Ar), 4.53 (1H, d, $J = 11.2$ Hz, CH_2Ar), 3.83 (1H, m, H20), 3.81 (3H, s, ArOMe), 3.29 (1H, dd, $J = 7.5, 4.2$ Hz, H21), 3.24 (1H, d, $J = 3.2$ Hz, OH), 2.45 (1H, m, H19), 2.40 (3H, d, $J = 1.5$ Hz, Me24), 2.20 (1H, m, H19), 0.95 (9H, t, $J = 7.9$ Hz, $3 \times \text{Si}(\text{CH}_2\text{CH}_3)$), 0.58 (6H, q, $J = 7.9$ Hz, $3 \times \text{Si}(\text{CH}_2\text{CH}_3)$); ^{13}C NMR (125 MHz, CDCl_3) δ 159.5, 140.6, 135.1, 129.9, 129.8, 117.3, 113.9, 97.3, 82.0, 73.5, 70.9, 55.3, 38.2, 28.7, 6.7, 4.7; HRMS (ES^+) calcd for $\text{C}_{23}\text{H}_{37}\text{IO}_4\text{SiNa}$ $[\text{M}+\text{Na}]^+$ 555.1404, found 555.1389.

(R)-Mosher ester **82a**



To a mixture of alcohol **82** (7.0 mg, 13.2 μmol), DMAP (1 crystal) and (*R*)-(+)- α -Methoxy- α -trifluoromethylphenylacetic acid (9.2 mg, 39.5 μmol) in CH_2Cl_2 (200 μL) was added DCC (1M in CH_2Cl_2 , 132 μL , 132 μmol). The reaction mixture was stirred for 30 min before being concentrated. Purification by flash column chromatography (SiO_2 , Et_2O / PE 40-60, 1:20) afforded ester **82a** (6.5 mg, 8.7 μmol , 66%) as a colourless oil; R_f 0.55 (Et_2O / PE 40-60, 1:8); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.55 (2H, d, $J = 7.2$ Hz, ArH), 7.38-7.35 (3H, m, ArH), 7.10 (2H, d, $J = 8.8$ Hz, ArH), 6.81 (2H, d, $J = 8.8$ Hz, ArH), 6.20 (1H, dq, $J = 9.3, 1.5$ Hz, H23), 5.76 (1H, dddd, $J = 17.1, 10.3, 7.5, 6.4$ Hz, H18), 5.39 (1H, ddd, $J = 8.7, 4.1, 2.1$ Hz, H20), 5.16-5.08 (2H, m, $2 \times$ H17), 4.33 (2H, s, CH_2Ar), 4.32 (1H, dd, $J = 9.3, 5.7$ Hz, H22), 3.81 (3H, s, ArOMe), 3.58 (3H, s, OMe), 3.41 (1H, dd, $J = 5.7, 2.1$ Hz, H21), 2.59-2.48 (2H, m, $2 \times$ H19), 2.37 (3H, d, $J = 1.5$ Hz, Me24), 0.94 (9H, t, $J = 8.0$ Hz, $3 \times$ Si(CH_2CH_3)), 0.55 (6H, q, $J = 8.0$ Hz, $3 \times$ Si(CH_2CH_3)).

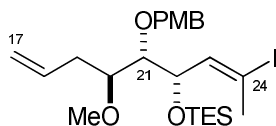
(S)-Mosher ester **82b**



To a mixture of alcohol **82** (7.0 mg, 13.2 μmol), DMAP (1 crystal) and (*S*)-(-)- α -Methoxy- α -trifluoromethylphenylacetic acid (9.2 mg, 39.5 μmol) in CH_2Cl_2 (200 μL) was added DCC (1M in CH_2Cl_2 , 132 μL , 132 μmol). The reaction mixture was stirred for 30 min before being concentrated. The residue was purified by flash column chromatography (SiO_2 , Et_2O / PE 40-60, 1:20) afforded ester **82b** (4.3 mg, 5.7 μmol , 44%) as a colourless oil; R_f 0.52 (Et_2O / PE 40-60, 1:8); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.53 (2H, d, $J = 7.5$ Hz, ArH), 7.40-7.31 (3H, m, ArH), 7.20 (2H, d, $J = 8.6$ Hz, ArH), 6.85 (2H, d, $J = 8.6$ Hz, ArH), 6.20 (1H, dq, $J = 9.3, 1.5$ Hz, H23), 5.68 (1H, ddt, $J = 17.1, 10.1, 7.0$ Hz, H18), 5.38 (1H, ddd, $J = 8.7, 4.5, 2.2$ Hz, H20), 5.08-5.01 (2H, m, $2 \times$ H17), 4.54 (1H,

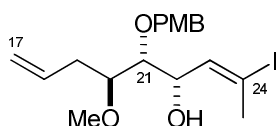
d, $J = 11.1$ Hz, CH₂Ar), 4.51 (1H, d, $J = 11.1$ Hz, CH₂Ar), 4.40 (1H, dd, $J = 9.3, 6.0$ Hz, H22), 3.81 (3H, s, ArOMe), 3.50 (1H, m, H21), 3.48 (3H, s, OMe), 2.53-2.40 (2H, m, 2 × H19), 2.32 (3H, d, $J = 1.5$ Hz, Me24), 0.92 (9H, t, $J = 8.0$ Hz, 3 × Si(CH₂CH₃)), 0.55 (6H, q, $J = 8.0$ Hz, 3 × Si(CH₂CH₃)).

Methyl ether **82c**



To a stirred solution of alcohol **82** (460 mg, 0.86 mmol) in CH₂Cl₂ (5 mL) was added Proton Sponge™ (557 mg, 2.59 mmol) and Me₃OBF₄ (384 mg, 2.59 mmol). The reaction mixture was stirred for 1 h before being quenched with brine (3 mL) and the organic phase separated. The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, EtOAc / PE 40-60, 1:15) afforded methyl ether **82c** (437 mg, 0.800 mmol, 93 %) as a clear, colourless oil; **R_f** 0.66 (EtOAc / PE 40-60, 1:8); $[\alpha]_D^{20} +8.0$ (c 0.75, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2954, 1613, 1514, 1463, 1248, 1103, 1040, 820, 744; **¹H NMR** (500 MHz, CDCl₃) δ 7.27 (2H, d, $J = 8.8$ Hz, ArH), 6.87 (2H, d, $J = 8.8$ Hz, ArH), 6.24 (1H, dq, $J = 9.2, 1.5$ Hz, H23), 5.86 (1H, ddt, $J = 17.2, 10.3, 7.0$ Hz, H18), 5.11 (1H, dd, $J = 17.2, 2.2$ Hz, H17), 5.06 (1H, dd, $J = 10.3, 2.2$ Hz, H17), 4.60 (2H, s, CH₂Ar), 4.48 (1H, dd, $J = 9.2, 4.6$ Hz, H21), 3.81 (3H, s, ArOMe), 3.40 (1H, app t, $J = 4.6$ Hz, H22), 3.38 (1H, ddd, $J = 9.6, 5.8, 4.6$ Hz, H20), 3.32 (3H, s, OMe), 2.43 (3H, d, $J = 1.5$ Hz, Me24), 2.38 (2H, m, 2 × H19), 0.95 (9H, t, $J = 8.0$ Hz, 3 × Si(CH₂CH₃)), 0.58 (6H, q, $J = 8.0$ Hz, 3 × Si(CH₂CH₃)); **¹³C NMR** (125 MHz, CDCl₃) δ 159.2, 142.5, 135.5, 130.7, 129.5, 116.7, 113.7, 96.1, 82.0, 80.6, 74.0, 70.7, 57.3, 55.3, 34.6, 28.6, 6.8, 5.0; **HRMS** (ES⁺) calcd for C₂₄H₃₉IO₄SiNa [M+Na]⁺ 569.1560, found 569.1573.

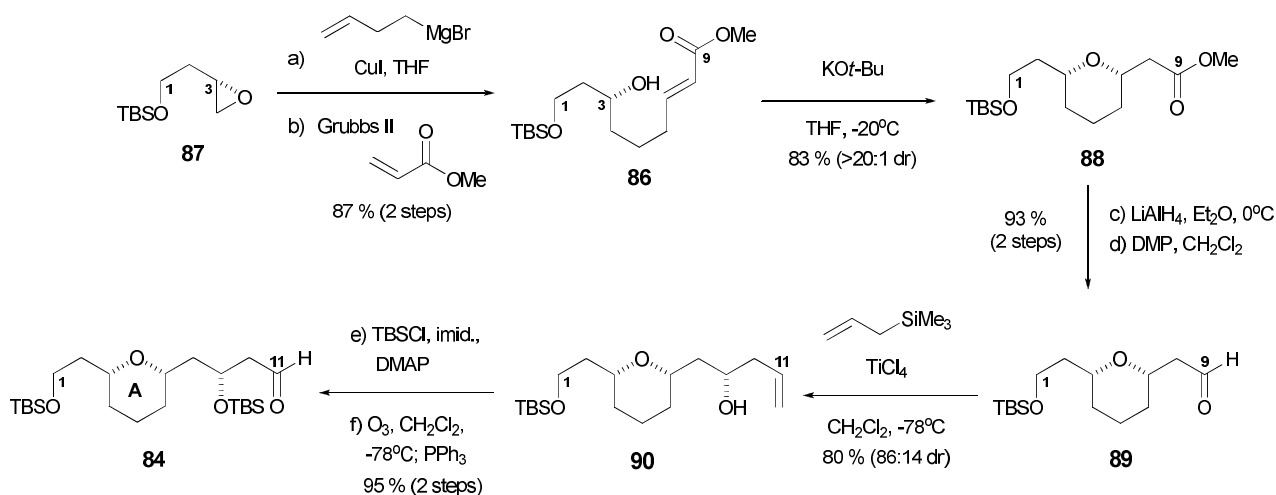
Alcohol **44**



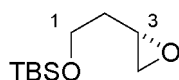
To a stirred solution of silyl ether **82c** (430 mg, 0.788 mmol) in MeOH (5 mL) was added PPTS (10.0 mg, 39.2 μmol). The reaction mixture was stirred for 30 min before being quenched with water (2 mL). The organic phase was separated, the aqueous phase extracted with CH₂Cl₂ (3 × 5

mL) and the combined organic phases dried (MgSO_4) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2 , EtOAc / PE 40-60, 1:7) afforded vinyl iodide **44** (338 mg, 99%) as a colourless oil; R_f 0.14 (EtOAc / PE 40-60, 1:8); $[\alpha]_D^{20}$ -6.7 (c 1.15, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3478, 2932, 1638, 1612, 1514, 1463, 1248, 1174, 1098, 1034, 822; **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ 7.25 (2H, d, $J = 8.8$ Hz, ArH), 6.90 (2H, d, $J = 8.8$ Hz, ArH), 6.23 (1H, dq, $J = 8.6$, 1.5 Hz, H23), 5.82 (1H, ddt, $J = 17.1$, 10.4, 7.2 Hz, H18), 5.13-5.08 (2H, m, $2 \times$ H17), 4.62 (1H, d, $J = 11.0$ Hz, CH_2Ar), 4.52 (1H, d, $J = 11.0$ Hz, CH_2Ar), 4.45 (1H, m, H21), 3.82 (3H, s, ArOMe), 3.43-3.38 (2H, m, H20, H22), 3.42 (3H, s, OMe), 3.04 (1H, d, $J = 6.2$ Hz, OH), 2.47-2.34 (2H, m, $2 \times$ H19), 2.44 (3H, d, $J = 1.5$ Hz, Me24); **$^{13}\text{C NMR}$** (125 MHz, CDCl_3) δ_C 159.5, 141.0, 134.2, 129.8, 129.7, 117.6, 114.0, 98.5, 81.0, 80.7, 73.5, 68.8, 57.9, 55.3, 34.4, 28.6; **HRMS** (ES^+) calcd for $\text{C}_{18}\text{H}_{25}\text{IO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 455.0695, found 455.0709.

2.6 Synthesis of Aldehyde 84



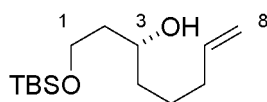
Epoxide 87



To a mixture of (*S,S*)-(+)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane-diamino-cobalt (II) (665 mg, 1.10 mmol), racemic *tert*-Butyl-dimethyl-(2-oxiranyl-ethoxy)-silane (44.6 g, 220 mmol), acetic acid (252 μL , 4.40 mmol) and THF (2.2 mL) at 0°C was added water (2.18 mL, 121 mmol) in one portion. The reaction was allowed to warm to room temperature and stirred for 24 h. The reaction mixture was purified by flash column chromatography (SiO_2 , 9:1 40-60 petroleum ether / Et_2O) to provide chiral epoxide **87** (20.5 g, 101 mmol, 46 %) as a yellowish oil together with 4-(*tert*-Butyl-dimethyl-silanyloxy)-butane-1,2-diol (25.2 g, 114 mmol, 52 %) as a dark greenish oil. The absolute configuration and enantiopurity of epoxide **87** was determined as >95:5 er based upon ^1H NMR analysis of the corresponding Mosher ester derivative **87b**. Epoxide **87**; R_f 0.53 (3:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20}$ -11.2 (c 2.26, CHCl_3), lit. $[\alpha]_D^{26}$ -12.8 (c 2.11, CHCl_3);^[5] ^1H NMR (500 MHz, CDCl_3) δ 3.79-3.76 (2H, m, H1), 3.08-3.02 (1H, m, H3), 2.78 (1H, t, $J = 4.5$ Hz, H4), 2.52 (1H, dd, $J = 5.1, 2.7$ Hz, H4), 1.80-1.66 (2H, m, H2), 0.90 (9H, s, *t*-BuSi), 0.07 (6H, s, $2 \times \text{MeSi}$).

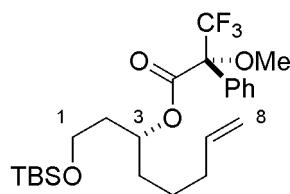
The data was consistent with that reported in the literature.^[5]

Alcohol **87a**



To a stirred suspension of magnesium turnings (1.08 g, 44.5 mmol) in THF (50 mL) was added 4-bromobut-1-ene (4.50 mL, 44.5 mmol) and 1,2-dibromoethane (one drop). The reaction mixture was stirred at room temperature until the magnesium had completely dissolved. A suspension of copper iodide (570 mg, 3.00 mmol) and chiral epoxide **87** (3.00 g, 14.8 mmol) in THF (50 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ before addition of the Grignard reagent. The reaction mixture was allowed to warm to room temperature and stirred for 1 h at this temperature before being quenched with NH_4Cl solution (50 mL). The mixture was extracted with Et_2O ($3 \times 50\text{ mL}$), and then the combined organic phases were dried (MgSO_4) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2 , 4:1 40-60 petroleum ether / Et_2O) provided alcohol **87a** (3.66 g, 14.2 mmol, 96 %) as a yellowish oil; R_f 0.31 (3:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20} +9.7$ (c 1.14, CHCl_3); IR (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3450, 2930, 2860, 1640, 1460, 1250, 1090, 835, 776; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.85-5.77 (1H, m, H7), 5.02-4.98 (1H, d, $J = 17.1\text{ Hz}$, H8_{trans}), 4.95-4.93 (1H, d, $J = 10.2\text{ Hz}$, H8_{cis}), 3.92-3.88 (1H, m, H3), 3.83-3.79 (2H, m, H1), 3.35 (1H, d, $J = 2.3\text{ Hz}$, OH), 2.10-2.06 (2H, m, H6), 1.66-1.63 (2H, m, H2), 1.55-1.49 (2H, m, H4), 1.46-1.42 (2H, m, H5), 0.90 (9H, s, *t*-BuSi), 0.08 (6H, s, $2 \times \text{MeSi}$); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 138.8, 114.4, 72.1, 62.9, 38.3, 37.0, 33.8, 25.9, 24.8, 18.1, -5.6 ; HRMS calc. for $\text{C}_{14}\text{H}_{31}\text{O}_2\text{Si}$ $[\text{M} + \text{H}]^+$ 259.2088, found 259.2091.

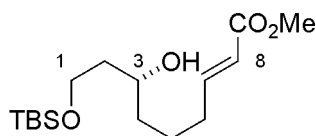
Mosher ester **87b**



To a stirred solution of alcohol **87a** (11.5 mg, 44.5 μmol) and a catalytic amount of 4-DMAP in DCM / pyridine (1:1, 0.40 mL) at room temperature was added (*S*)-(+)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride (12.1 mg, 48.6 μmol). The mixture was stirred for 1.5 h at room temperature, then diluted with DCM (10 mL) and washed sequentially with NH_4Cl solution (5 mL), 1 N HCl ($2 \times 5\text{ mL}$) and NaHCO_3 solution (5 mL), dried (MgSO_4) and concentrated *in vacuo*.

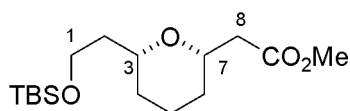
The residue was purified by flash column chromatography (SiO₂, 9:1 40-60 petroleum ether / Et₂O) to provide (*R*)-Mosher ester **87b** (15.6 mg, 32.9 μmol, 75 %) as a colourless oil; **R_f** 0.45 (9:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +15.0 (c 0.98, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2952, 2930, 2858, 1744, 1642, 1473, 1463, 1452, 1256, 1169, 1101, 1019, 836, 776, 715; **¹H NMR** (500 MHz, CDCl₃) δ 7.55-7.53 (2H, m, Ph), 7.40-7.37 (3H, m, Ph), 5.75-5.66 (1H, m, H7), 5.28-5.23 (1H, m, H3), 4.98-4.93 (2H, m, H8), 3.67-3.60 (2H, m, H1), 3.55 (3H, s, MeO), 2.02-1.97 (2H, m, H6), 1.89-1.81 (2H, m, H4), 1.67-1.61 (2H, m, H2), 1.35-1.26 (2H, m, H5), 0.89 (9H, s, *t*-BuSi), 0.03 (6H, s, 2 × MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 166.1, 138.1, 132.5, 129.5, 128.3, 127.4, 114.9, 74.7, 59.2, 55.3, 36.8, 33.3, 33.2, 25.9, 24.0, 18.2, -5.4; **HRMS** calc. for C₂₄H₃₈F₃O₄Si [M + H]⁺ 475.2486, found 475.2489.

Enoate **86**



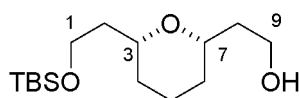
To a stirred solution of alkene **87a** (28.7 g, 111 mmol) and methyl acrylate (20.0 mL, 222 mmol) in DCM (300 mL) was added Grubbs 2nd generation catalyst (471 mg, 0.555 mmol, 0.5 mol %) in one portion. The reaction was heated to reflux for 21.5 h before being concentrated *in vacuo* and direct purification on a silica gel column, eluting with 40-60 petroleum ether / Et₂O (1:1), to provide ester **86** (32.1 g, 101 mmol, 91 %) as a pale brown oil; **R_f** 0.33 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +7.9 (c 1.32, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3510, 2930, 2858, 1726, 1657, 1472, 1463, 1436, 1255, 1084, 835, 775; **¹H NMR** (500 MHz, CDCl₃) δ 6.96 (1H, dt, *J* = 15.6, 6.9 Hz, H7), 5.82 (1H, *J* = 15.7 Hz, H8), 3.92-3.88 (1H, m, H3), 3.83-3.78 (2H, m, H1), 3.71 (3H, s, OMe), 3.44 (1H, br s, OH), 2.25-2.21 (2H, m, H6), 1.69-1.61 (3H, m, 2 × H2, H4), 1.57-1.38 (3H, m, H4, 2 × H5), 0.89 (9H, s, *t*-BuSi), 0.07 (6H, s, 2 × MeSi); **¹³C NMR** (100 MHz, CDCl₃) δ 167.1, 149.4, 121.1, 71.9, 62.9, 51.3, 38.2, 36.9, 32.1, 25.8, 24.0, 18.1, -5.6; **HRMS** calc. for C₁₆H₃₃O₄Si [M + H]⁺ 317.2143, found 317.2140.

Tetrahydropyran **88**



To a stirred solution of alcohol **86** (1.49 g, 7.02 mmol) in THF (100 mL) at -78 °C was added potassium *tert*-butoxide (470 mg, 4.20 mmol) in one portion. The reaction was allowed to warm to -30 °C over 1 h, before being quenched with NH_4Cl solution (20 mL). The product was extracted with Et_2O (3×50 mL) and the combined organic phases were washed with brine (20 mL), dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2 , 9:1 40-60 petroleum ether / Et_2O) to provide tetrahydropyran **88** (1.24 g, 5.84 mmol, 83 %) as a colourless oil; R_f 0.48 (3:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20}$ -10.6 (c 1.25, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2930, 2858, 1744, 1472, 1437, 1253, 1196, 1084, 835, 776; **$^1\text{H NMR}$** (500 MHz, CDCl_3) δ 3.67 (3H, s, OMe), 3.77-3.70 (1H, m, H7), 3.70-3.63 (2H, m, H1), 3.48-3.40 (1H, m, H3), 2.53 (1H, dd, $J = 14.8, 7.6$ Hz, H8), 2.38 (1H, dd, $J = 14.8, 5.9$ Hz, H8), 1.88-1.79 (1H, m, H5eq), 1.71-1.50 (5H, m, $2 \times \text{H2, H4eq, H5ax, H6ax}$), 1.25-1.15 (2H, m, H4ax, H6ax), 0.88 (9H, s, *t*-BuSi), 0.04 (3H, s, MeSi), 0.03 (3H, s, MeSi); **$^{13}\text{C NMR}$** (125 MHz, CDCl_3) δ 171.9, 74.7, 74.3, 59.6, 51.5, 41.6, 39.6, 31.4, 31.3, 26.0, 23.5, 18.3, -5.4 ; **HRMS** calc. for $\text{C}_{16}\text{H}_{33}\text{O}_4\text{Si}$ $[\text{M} + \text{H}]^+$ 317.2143, found 317.2143.

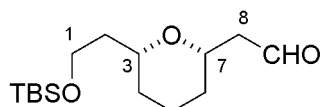
Alcohol **88a**



To a stirred suspension of lithium aluminum hydride (700 mg, 18.4 mmol) in Et_2O (80 mL) at -78 °C was added a solution of ester **88** (2.92 g, 9.23 mmol) in Et_2O (10 mL + 10 mL rinse) *via* syringe. The mixture was allowed to warm to 0 °C and stirred for 1 h at this temperature. The reaction was quenched *via* the sequential dropwise addition of water (0.7 mL), 20 % aqueous NaOH solution (0.7 mL) and further water (2.1 mL). After stirring for 1 h, the resulting white granular suspension was filtered, and the filtrate was dried (MgSO_4) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2 , 1:1 40-60 petroleum ether / Et_2O) afforded alcohol **88a** (2.62 g, 9.08 mmol, 98 %) as a colourless oil; R_f 0.35 (1:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20}$ -14.3 (c 1.01, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 3408, 2930, 1472, 1389, 1255, 1084, 1047, 835, 776; **$^1\text{H NMR}$** (500 MHz,

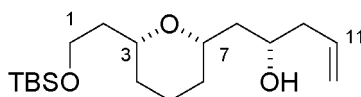
CDCl₃) δ 3.78 (2H, t, *J* = 5.4 Hz, H₉), 3.75-3.64 (2H, m, H₁), 3.60-3.52 (1H, m, H₃), 3.52-3.44 (1H, m, H₇), 1.89-1.79 (1H, m, H_{5eq}), 1.77-1.44 (7H, m, 2 × H₂, H_{4eq}, H_{5ax}, H_{6eq}, 2 × H₈), 1.38-1.27 (1H, m, H_{4ax}), 1.27-1.17 (1H, m, H_{6ax}), 0.89 (9H, s, *t*-BuSi), 0.06 (3H, s, MeSi), 0.05 (3H, s, MeSi); ¹³C NMR (125 MHz, CDCl₃) δ 78.6, 74.8, 61.7, 59.5, 39.5, 38.0, 31.5, 31.5, 26.0, 23.5, 18.3, -5.3, -5.4; HRMS calc. for C₁₅H₃₃O₃Si [M+H]⁺ 289.2193, found 289.2192.

Aldehyde **89**



To a stirred solution of alcohol **88a** (10.0 g, 34.7 mmol) in DCM was added Dess-Martin periodinane (22.1 g, 52.1 mmol) at room temperature. The reaction mixture was stirred for 2 h and then concentrated *in vacuo*. The product was purified by flash column chromatography (SiO₂, 3:1 40-60 petroleum ether / Et₂O) to afford aldehyde **89** (9.48 g, 33.1 mmol, 95 %) as a colourless oil; **R_f** 0.58 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ -19.7 (c 1.56, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 2930, 1729, 1472, 1389, 1255, 1091, 1051, 834, 776; ¹H NMR (500 MHz, CDCl₃) δ 9.79 (1H, t, *J* = 2.4 Hz, H₉), 3.86-3.79 (1H, m, H₇), 3.75-3.62 (2H, m, H₁), 3.53-3.45 (1H, m, H₃), 2.54 (1H, ddd, *J* = 16.0, 8.0, 2.7 Hz, H₈), 2.46 (1H, ddd, *J* = 16.0, 4.7, 2.2 Hz, H₈), 1.89-1.82 (1H, m, H_{5eq}), 1.72-1.51 (5H, m, 2 × H₂, H_{4eq}, H_{5ax}, H_{6eq}), 1.34-1.16 (2H, m, H_{4ax}, H_{6ax}), 0.89 (9H, s, *t*-BuSi), 0.04 (3H, s, MeSi), 0.03 (3H, s, MeSi); ¹³C NMR (125 MHz, CDCl₃) δ 201.7, 74.6, 73.0, 59.4, 39.5, 31.5, 31.3, 26.0, 23.5, 18.3, -5.3, -5.4; HRMS calc. for C₁₅H₃₁O₃Si [M+H]⁺ 287.2037, found 287.2033.

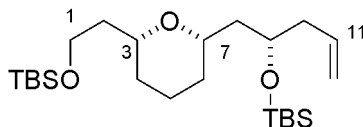
Homoallylic alcohol **90**



To a stirred solution of aldehyde **89** (1.20 g, 4.19 mmol) in DCM (40 mL) at -78 °C under argon atmosphere was added freshly distilled TiCl₄ (0.46 mL, 4.2 mmol) dropwise *via* syringe. After stirring for 5 min, allyltrimethylsilane (1.00 mL, 6.28 mmol) was added at -78 °C and the mixture was stirred for 1 h. The reaction was quenched by cannulation into a cooled (0 °C) NaHCO₃

solution (30 mL). The mixture was extracted with DCM (3 × 20 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO₂, 4:1 40-60 petroleum ether / Et₂O) to provide allylic alcohol **90** (1.11 g, 3.37 mmol, 80 %) as a colourless oil. The diastereomeric ratio was determined by ¹H NMR of the crude mixture (86:14) and the stereochemistry of major diastereomer was confirmed as 9-(*S*) by comparison of ¹H NMR data for *bis*-TBS-protected product **90a** with that reported in the literature.^[6] Major diastereomer; **R_f** 0.23 (3:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ -7.6 (c 1.62, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 3479, 2930, 2857, 1641, 1463, 1472, 1254, 1085, 835, 775; **¹H NMR** (500 MHz, CDCl₃) δ 5.91-5.79 (1H, m, H11), 5.14-5.03 (2H, m, H12), 4.00-3.91 (1H, m, H9), 3.79-3.60 (3H, m, 2 × H1, H3), 3.53-3.42 (1H, m, H7), 3.05 (1H, br s, OH), 2.35-2.21 (2H, m, H10), 1.94-1.78 (1H, m, H5eq), 1.73-1.42 (7H, m, 2 × H2, H4eq, H5ax, H6eq, 2 × H8), 1.42-1.31 (1H, m, H4ax), 1.30-1.14 (1H, m, H6ax), 0.89 (9H, s, *t*-BuSi), 0.05 (3H, s, MeSi), 0.04 (3H, s, MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 135.3, 117.1, 75.7, 74.7, 68.2, 59.4, 41.9, 41.5, 39.6, 32.1, 31.6, 31.1, 26.0, 25.6, 23.6, 18.3, -5.3, -5.4; **HRMS** calc. for C₁₈H₃₇O₃Si [M + H]⁺ 329.2506, found 329.2504.

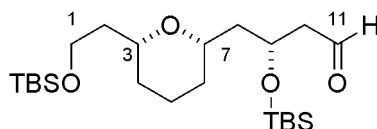
TBS ether **90a**



To a stirred solution of alcohol **90** (3.00 g, 9.13 mmol) in *N,N*-dimethylformamide (10 mL) at 0 °C was added sequentially TBSCl (2.06 g, 13.7 mmol), imidazole (1.24 g, 18.3 mmol) and 4-DMAP (56.2 mg, 0.460 mmol). The reaction was allowed to warm to room temperature and was stirred for 2 h before quenching with water (25 mL). The mixture was extracted with DCM (3 × 30 mL), and the combined organic phases washed with water (25 mL), dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 20:1 40-60 petroleum ether / Et₂O) provided *bis*-silyl ether **90a** (4.04 g, 9.13 mmol, 99 %) as a colourless oil; **R_f** 0.21 (20:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +21.2 (c 1.07, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 2931, 1473, 1255, 1085, 835, 774; **¹H NMR** (500 MHz, CDCl₃) δ 5.86-5.77 (1H, m, H11), 5.05-5.00 (2H, m, H12), 4.01-3.95 (1H, m, H9), 3.76-3.65 (2H, m, H1), 3.42-3.33 (2H, m, H3, H7), 2.28-2.15 (2H, m, H10), 1.83-1.71 (2H, m, H2, H5eq), 1.65-1.38 (6H, m, H2, H4eq, H5ax, H6eq, 2 × H8), 1.22-1.12 (2H, m, H4ax, H6ax), 0.89 (18H, s, 2 × *t*-BuSi), 0.07 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.04 (6H, s, 2 × MeSi);

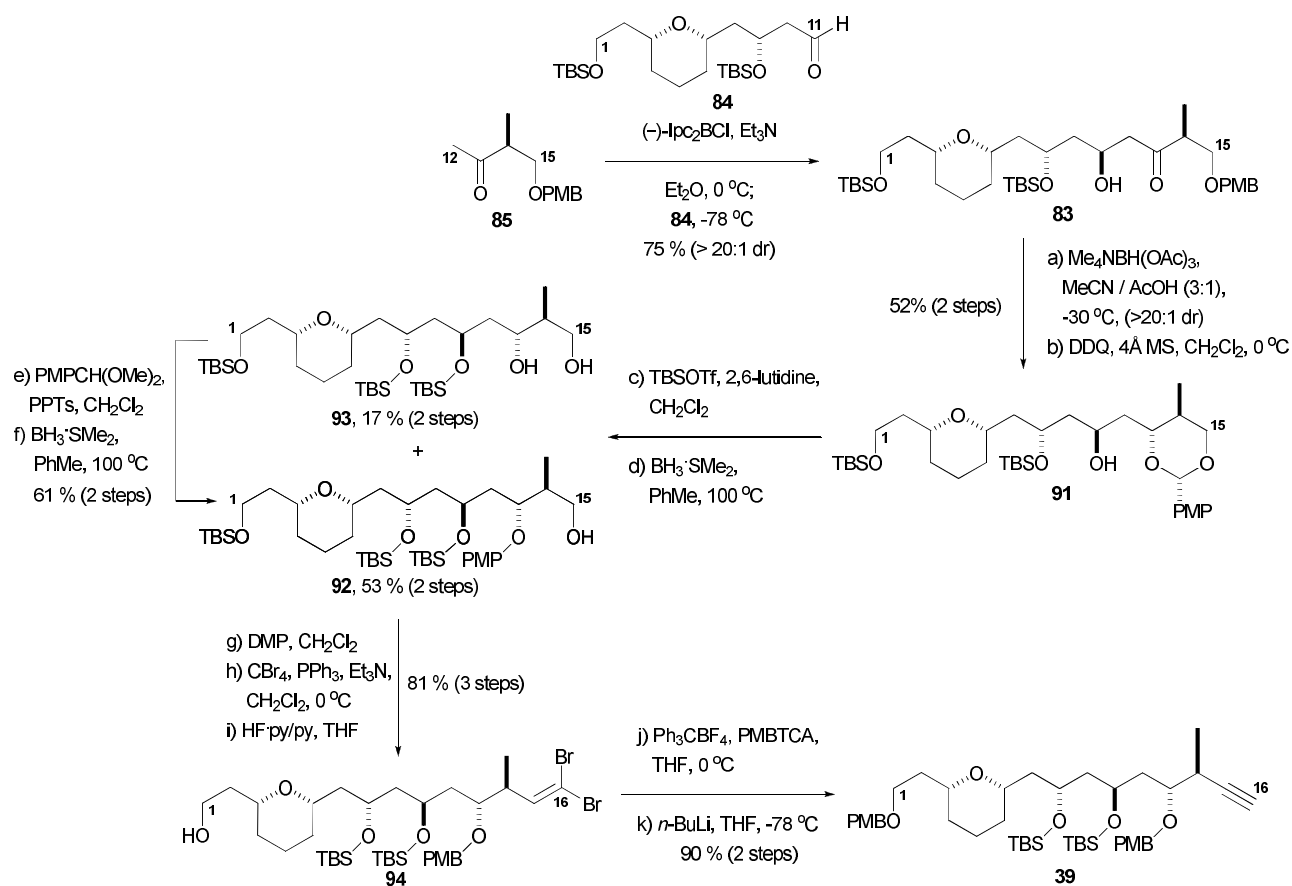
^{13}C NMR (125 MHz, CDCl_3) δ 135.0, 116.8, 74.6, 73.8, 68.2, 60.2, 44.0, 42.9, 39.9, 32.3, 31.7, 26.0, 26.0, 23.8, 18.3, 18.1, -4.3, -4.6, -5.3, -5.3; HRMS calc. for $\text{C}_{24}\text{H}_{51}\text{O}_3\text{Si}_2$ $[\text{M}+\text{H}]^+$ 443.3371, found 443.3368.

Aldehyde **84**

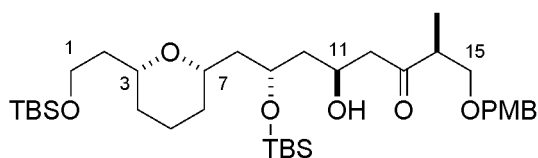


A solution of alkene **90a** (6.43 g, 14.5 mmol) in DCM (150 mL) was cooled to $-78\text{ }^\circ\text{C}$. Ozone was passed through the solution *via* a frit-tipped entry tube until the solution became a persistent blue colour. Excess ozone was purged with a stream of oxygen until the blue colour faded, then the oxygen supply was removed and triphenylphosphine (4.60 g, 17.4 mmol) was added in one portion. The reaction was allowed to warm to room temperature, and stirred for 4 h. The mixture was concentrated, then resuspended in 2:1 40-60 petroleum ether / Et_2O (100 mL) and stirred for 30 min. The solution was filtered and concentrated *in vacuo*, and the residue was purified by flash column chromatography (SiO_2 , 10:1 40-60 petroleum ether / Et_2O) to provide aldehyde **84** (6.19 g, 13.9 mmol, 95 %) as a colourless oil; R_f 0.30 (5:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20}$ +13.7 (c 1.03, CHCl_3); IR (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2930, 1728, 1473, 1255, 1090, 835, 775; ^1H NMR (500 MHz, CDCl_3) δ 9.82 (1H, br t, $J = 2.7$ Hz, H11), 4.42-4.36 (1H, m, H9), 3.74-3.65 (2H, m, H1), 3.42-3.36 (2H, m, H3, H7), 2.60 (1H, ddd, $J = 15.7, 5.3, 2.4$ Hz, H10), 2.48 (1H, ddd, $J = 15.7, 5.3, 3.0$ Hz, H10), 1.84-1.78 (1H, m, H5eq), 1.78-1.70 (1H, m, H2), 1.65-1.44 (6H, m, H2, H4eq, H5ax, H6eq, $2 \times$ H8), 1.25-1.12 (2H, m, H4ax, H6ax), 0.89 (9H, s, *t*-BuSi), 0.88 (9H, s, *t*-BuSi), 0.86 (3H, s, MeSi), 0.71 (3H, s, MeSi), 0.04 (6H, s, $2 \times$ MeSi); ^{13}C NMR (125 MHz, CDCl_3) δ 202.3, 74.6, 73.7, 65.4, 60.0, 51.9, 45.0, 39.8, 32.2, 31.5, 26.0, 25.8, 23.7, 18.3, 18.0, -4.5, -4.6, -5.3; HRMS calc. for $\text{C}_{23}\text{H}_{49}\text{O}_4\text{Si}_2$ $[\text{M}+\text{H}]^+$ 445.3164, found 445.3163.

2.7 Synthesis of Alkyne 39



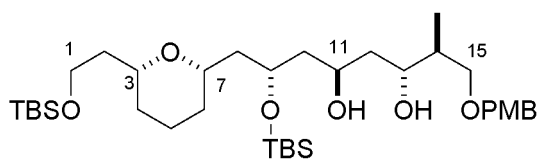
β -hydroxy ketone **83**



To a stirred solution of $(-)$ -diisopinocampheylboron chloride (795 mg, 2.48 mmol) in Et_2O (20 mL) at $0\text{ }^\circ\text{C}$ was added Et_3N (368 μL , 2.64 mmol) followed by a solution of methyl ketone **85** (551 mg, 2.48 mmol) in Et_2O (4 mL + 1 mL rinse). The solution was stirred for 1 h then cooled to $-78\text{ }^\circ\text{C}$, and a solution of aldehyde **84** (735 mg, 1.65 mmol) in Et_2O (4 mL + 1 mL rinse) was added *via* cannula. The mixture was stirred for 3 h at $-78\text{ }^\circ\text{C}$, and then allowed to stand at $-20\text{ }^\circ\text{C}$ for 14 h. Subsequently, the reaction was warmed to $0\text{ }^\circ\text{C}$ and quenched by the consecutive addition of MeOH (6 mL), pH 7 buffer (6 mL) and 30 % H_2O_2 (3 mL). The mixture was stirred vigorously for 2 h at room temperature, then the organic phase was separated and the aqueous phase extracted with Et_2O ($2 \times 10\text{ mL}$). The combined organic phases were dried (MgSO_4) and concentrated *in vacuo*. The

residue was purified by flash column chromatography (9:1 40-60 petroleum ether / Et₂O → 3:1 40-60 petroleum ether / EtOAc) to provide β-hydroxy ketone **83** (825 mg, 1.24 mmol, 75 %) as a colourless oil; **R_f** 0.33 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +7.0 (c 1.13, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3484, 2931, 2857, 1709, 1613, 1514, 1463, 1250, 1088, 835, 776; **¹H NMR** (500 MHz, CDCl₃) δ 7.21 (2H, d, $J = 8.5$ Hz, ArH), 6.86 (2H, d, $J = 8.5$ Hz, ArH), 4.45-4.34 (3H, m, H11, ArCH₂O), 4.24-4.13 (1H, m, H9), 3.80 (3H, s, MeO), 3.78-3.69 (2H, m, H1), 3.63-3.59 (1H, m, H15), 3.43-3.40 (1H, dd, $J = 9.0, 5.3$ Hz, H15), 3.40-3.33 (2H, m, H3, H7), 2.93-2.82 (1H, m, H14), 2.67 (1H, dd, $J = 16.8, 7.7$ Hz, H12), 2.56 (1H, dd, $J = 16.8, 4.5$ Hz, H12), 1.85-1.76 (1H, m, H5eq), 1.76-1.70 (1H, m, H2), 1.70-1.45 (8H, m, H2, H4eq, H5ax, H6eq, 2 × H8, 2 × H10), 1.24-1.11 (2H, m, H4ax, H6ax), 1.06 (3H, d, $J = 7.0$ Hz, Me14), 0.89 (18H, s, 2 × *t*-BuSi), 0.11 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.04 (6H, s, 2 × MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 212.9, 159.2, 130.1, 129.2, 113.8, 74.6, 73.9, 72.9, 71.9, 67.6, 64.6, 60.0, 55.2, 49.9, 46.8, 44.1, 43.2, 39.8, 32.2, 31.6, 26.0, 25.9, 23.7, 18.3, 18.0, 13.2, -4.5, -4.7, -5.3; **HRMS** calc. for C₃₆H₆₇O₇Si₂ [M + H]⁺ 667.4420, found 667.4422.

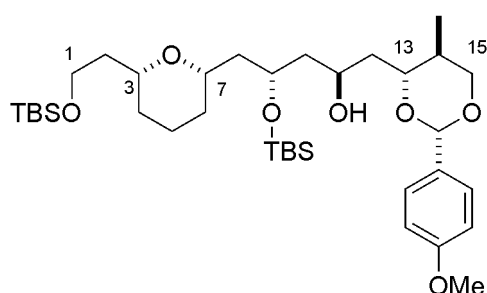
Diol **83a**



To a stirred suspension of tetramethylammonium triacetoxyborohydride (6.59 g, 25.0 mmol) in acetonitrile (30 mL) was added acetic acid (15 mL), and the solution was stirred for 30 min at room temperature. The solution was cooled to -30 °C and a solution of hydroxyketone **83** (1.67 g, 2.50 mmol) in acetonitrile (15 mL) was added *via* cannula. The reaction was stirred for 5 h at -30 °C and allowed to stand at -20 °C for 16 h before being cannulated cautiously into a vigorously stirred mixture of NaHCO₃ solution (150 mL) and Na⁺/K⁺ tartrate solution (75 mL) cooled to 0 °C. The mixture was stirred for 3 h, then the product was extracted with Et₂O (3 × 250 mL), the combined organic phases were washed with brine (250 mL), dried (MgSO₄) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (SiO₂, 2:1 → 1:1 40-60 petroleum ether / Et₂O) afforded diol **83a** (1.23g, 1.84 mmol, 74 %) as a colourless oil; **R_f** 0.18 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +4.0 (c 0.75, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3460, 2930, 2860, 1610, 1510, 1470, 1460, 1250, 1080, 835, 775; **¹H NMR** (500 MHz, CDCl₃) δ 7.24 (2H, d, $J = 8.5$ Hz, ArH), 6.73 (2H, d, $J = 8.5$ Hz, ArH), 4.44 (2H, s, ArCH₂O), 4.39-4.30 (1H, m, H11), 4.28-4.19

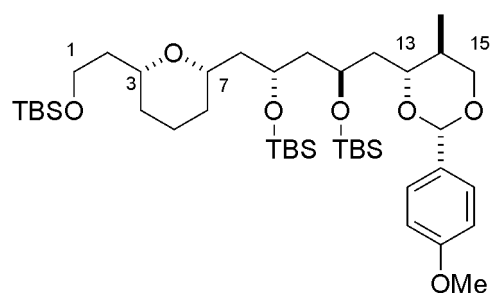
(1H, m, H9), 3.90-3.76 (1H, m, H13), 3.80 (3H, s, MeO), 3.76-3.67 (2H, m, H1), 3.60-3.49 (2H, m, H15), 3.42-3.30 (2H, m, H3, H7), 1.95-1.86 (1H, m, H14), 1.86-1.76 (2H, m, H5eq, H10), 1.76-1.69 (2H, m, H2, H8), 1.67-1.43 (8H, m, H2, H4eq, H5ax, H6eq, H8, H10, 2 × H12), 1.25-1.11 (2H, m, H4ax, H6ax), 0.93-0.86 (21H, m, Me14, 2 × *t*-BuSi), 0.12 (3H, s, MeSi), 0.10 (3H, s, MeSi), 0.04 (6H, s, 2 × MeSi); ¹³C NMR (125 MHz, CDCl₃) δ 159.2, 130.2, 129.3, 113.8, 74.7, 74.6, 73.9, 73.1, 72.8, 68.4, 65.8, 60.0, 55.3, 43.6, 43.2, 41.2, 39.8, 38.7, 32.2, 31.5, 26.0, 25.9, 23.7, 18.3, 17.9, 13.8, -4.4, -4.9, -5.3, -5.3; HRMS calc. for C₃₆H₆₉O₇Si₂ [M + H]⁺ 669.4576, found 669.4571.

PMP acetal 91



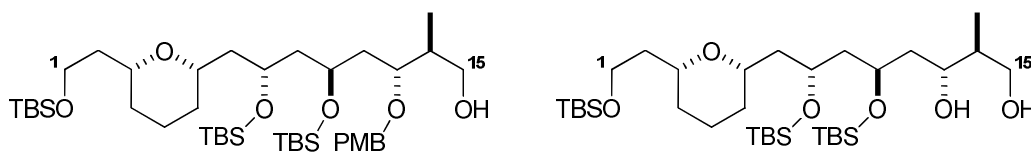
To a stirred suspension of diol **83a** (2.28 g, 3.41 mmol) and powdered 4Å molecular sieves (40 g) in DCM (100 mL) was added DDQ (1.20 g, 5.12 mmol) in one portion at 0 °C. The resultant mixture was stirred for 1 h before being filtered through Celite™ (DCM wash, 2 × 50 mL). The filtrate was washed with NaHCO₃ solution (100 mL) and the aqueous phase was extracted with DCM (2 × 50 mL). The combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The product was purified by flash column chromatography (2:1 40-60 petroleum ether / Et₂O) to provide cyclic acetal **91** (1.59 g, 2.39 mmol, 70 %) as a colourless oil; **R**_f 0.35 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +20.0 (c 1.37, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 3480, 2930, 2860, 1620, 1520, 1460, 1250, 1080, 835, 775; ¹H NMR (500 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.7 Hz, ArH), 6.87 (2H, d, *J* = 8.7 Hz, ArH), 5.49 (1H, s, CHAr), 4.34-4.26 (1H, app. t, *J* = 9.7 Hz, H11), 4.25-4.18 (1H, m, H9), 4.13-4.06 (1H, dd, *J* = 11.3 Hz, 4.7 Hz, H15eq), 3.80 (3H, s, MeO), 3.77-3.70 (1H, t, *J* = 9.7 Hz, H13), 3.70-3.65 (2H, t, *J* = 6.8 Hz, H1), 3.51 (1H, t, *J* = 11.2 Hz, H15ax), 3.40-3.30 (2H, m, H3, H7), 1.90-1.77 (3H, m, H5eq, H10, H14), 1.77-1.66 (3H, m, H2, H8, H10), 1.66-1.39 (7H, m, H2, H4eq, H5ax, H6eq, H8, 2 × H12), 1.22-1.10 (2H, m, H4ax, H6ax), 0.90 (9H, s, *t*-BuSi), 0.89 (9H, s, *t*-BuSi), 0.80 (3H, d, *J* = 6.7 Hz, Me14), 0.12 (3H, s, MeSi), 0.09 (3H, s, MeSi), 0.04 (6H, s, 2 × MeSi); ¹³C NMR (125 MHz, CDCl₃) δ 159.8, 131.4, 127.3, 113.5, 100.9, 79.9, 74.6, 73.9, 73.1, 68.3, 64.5, 60.0, 55.3, 43.9, 43.8, 40.9, 39.8, 34.0, 32.2, 31.6, 26.0, 25.9, 23.7, 18.3, 18.0, 12.4, -4.4, -4.7, -5.3, -5.3; HRMS calc. for C₃₆H₆₇O₇Si₂ [M + H]⁺ 667.4420, found 667.4418.

TBS ether **91a**



To a stirred solution of alcohol **91** (1.59 g, 2.38 mmol) in DCM (16 mL) at 0 °C was added 2,6-lutidine (1.67 mL, 14.3 mmol) and TBSOTf (1.64 mL, 7.15 mmol) sequentially. The reaction was allowed to warm to room temperature, and was stirred for 30 min before being quenched with water (50 mL). The mixture was extracted with DCM (3 × 50 mL), and the combined organic phases were washed with water (50 mL), dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 10:1 40-60 petroleum ether / Et₂O) provided *tris*-silyl ether **91a** (1.60 g, 2.04 mmol, 86 %) as a colourless oil; **R_f** 0.47 (3:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +25.2 (c 1.24, CHCl₃); **IR** (thin film, ν_{\max} /cm⁻¹) 2950, 2930, 2860, 1620, 1520, 1460, 1390, 1250, 1080, 835, 775; **¹H NMR** (500 MHz, CDCl₃) δ 7.41 (2H, d, J = 8.6 Hz, ArH), 6.87 (2H, d, J = 8.7 Hz, ArH), 5.39 (1H, s, CHAr), 4.14-4.05 (1H, dd, J = 11.2, 4.7 Hz, H15eq), 4.05-3.96 (1H, m, H11), 3.96-3.88 (1H, m, H9), 3.80 (3H, s, MeO), 3.75-3.63 (2H, m, H1), 3.61-3.53 (1H, m, H13), 3.47 (1H, t, J = 11.4 Hz, H15ax), 3.43-3.31 (2H, m, H3, H7), 1.88-1.77 (2H, m, H2, H14), 1.77-1.34 (11H, m, H2, H4eq, 2 × H5, H6eq, 2 × H8, 2 × H10, 2 × H12), 1.29-1.11 (2H, m, H4ax, H6ax), 0.89 (18H, s, 2 × *t*-BuSi), 0.87 (9H, s, *t*-BuSi), 0.77 (3H, d, J = 6.7 Hz, Me14), 0.05 (6H, s, 2 × MeSi), 0.04 (6H, s, 2 × MeSi), 0.04 (3H, s, MeSi), 0.02 (3H, s, MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 159.7, 131.6, 127.5, 113.5, 113.4, 100.8, 79.2, 74.5, 73.7, 73.1, 66.7, 65.9, 60.2, 55.3, 47.6, 44.6, 40.9, 39.9, 34.1, 32.3, 31.7, 26.0, 26.0, 23.8, 18.3, 18.1, 12.5, -3.9, -4.0, -4.3, -4.5, -5.3; **HRMS** calc. for C₄₂H₈₁O₇Si₃ [M + H]⁺ 781.5285, found 781.5294.

PMB ether **92** & Diol **93**



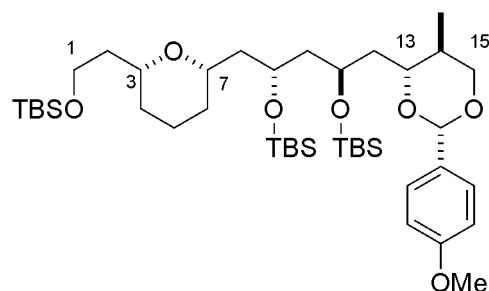
To a stirred solution of cyclic acetal **91a** (446 mg, 0.570 mmol) in toluene (20 mL) at 100 °C was added borane-dimethylsulfide complex (10 M, 86.0 μ L, 0.860 mmol). The reaction mixture was

stirred for 3 h at this temperature before being cooled to 0 °C and then quenched with MeOH (4 mL) and NaHCO₃ solution (4 mL). The aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic phases were washed with brine (4 mL), dried (MgSO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO₂, 3:1 40-60 petroleum ether / EtOAc) to provide alcohol **92** (275.0 mg, 0.35 mmol, 62 %) and diol **93** (76.1 mg, 0.12 mmol, 20 %) as colourless oils;

Alcohol **92**: **R_f** 0.39 (1:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +6.1 (c 1.00, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3490, 2930, 2857, 1613, 1514, 1472, 1463, 1250, 1084, 835, 774; **¹H NMR** (500 MHz, CDCl₃) δ 7.27 (2H, d, *J* = 9.5 Hz, ArH), 6.87 (2H, d, *J* = 8.6 Hz, ArH), 4.52 (1H, d, *J* = 11.1 Hz, ArCH_aH_bO), 4.43 (1H, d, *J* = 11.1 Hz, ArCH_aH_bO), 4.00-3.91 (1H, m, H9), 3.88-3.79 (1H, m, H11), 3.80 (3H, s, MeO), 3.79-3.73 (1H, m, H15), 3.73-3.65 (2H, m, H1), 3.62-3.50 (2H, m, H13, H15), 3.44-3.33 (2H, m, H3, H7), 2.52 (1H, t, *J* = 5.7 Hz, OH), 1.94-1.85 (1H, m, H14), 1.85-1.75 (2H, m, H2, H12), 1.74-1.66 (1H, m, H5eq), 1.66-1.35 (9H, m, H2, H4eq, H5ax, H6eq, 2 × H8, 2 × H10, H12), 1.22-1.11 (2H, m, H4ax, H6ax), 0.98 (3H, d, *J* = 7.0 Hz, Me14), 0.88 (18H, s, 2 × *t*-BuSi), 0.87 (9H, s, *t*-BuSi), 0.07 (6H, s, 2 × MeSi), 0.05 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.02 (3H, s, MeSi), 0.01 (3H, s, MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 159.1, 130.7, 120.1, 113.8, 80.3, 74.4, 73.6, 71.0, 68.2, 56.4, 55.3, 47.4, 44.8, 40.1, 39.0, 32.3, 31.7, 26.0, 25.9, 23.8, 18.3, 18.1, 18.0, 18.0, 13.8, -3.7, -4.0, -4.1, -4.3, -5.3, -5.3; **HRMS** calc. for C₄₂H₈₃O₇Si₃ [M + H]⁺ 783.5441, found 783.5446.

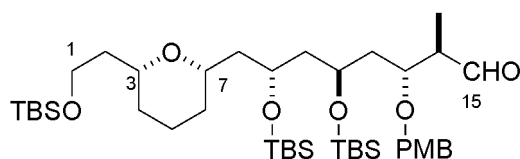
Diol **93**: **R_f** 0.17 (2:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +21.2 (c 1.24, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3418 (br), 2930, 2857, 1472, 1254, 1081, 835, 774; **¹H NMR** (500 MHz, CDCl₃) δ 4.38 (1H, br d, *J* = 0.9 Hz, OH13), 4.12-4.07 (1H, m, H11), 3.94 (1H, br t, *J* = 9.1 Hz, H13), 3.86-3.79 (1H, m, H9), 3.71-3.62 (4H, m, H15, 2 × H1, OH15), 3.51 (1H, dd, *J* = 7.0, 4.2 Hz, H15), 3.44-3.33 (2H, m, H7, H3), 1.91 (1H, ddd, *J* = 13.4, 9.6, 4.7 Hz, H10), 1.83-1.76 (1H, m, H5eq), 1.76-1.64 (5H, m, H14, H10, H2, 2 × H12), 1.62-1.43 (5H, m, H2, H5ax, H4eq, H6eq, H8), 1.35 (1H, ddd, *J* = 13.8, 9.4, 2.4 Hz, H8), 1.21-1.11 (2H, m, H4ax, H6ax), 0.90-0.85 (30H, m, Me14, 3 × *t*-BuSi), 0.11 (3H, s, MeSi), 0.10 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.03 (6H, s, 2 × MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 74.8, 74.6, 73.4, 70.0, 67.8, 66.0, 60.0, 44.2, 40.7, 39.9, 38.5, 32.3, 31.5, 25.9, 25.8, 23.7, 18.3, 18.0, 17.9, 14.0, -4.0, -4.4, -4.5, -4.8, -5.3, -5.3; **HRMS** calc. for C₃₄H₇₅O₆Si₃ [M + H]⁺ 663.4866, found 663.4859.

PMP acetal **91a**



To a stirred solution of diol **93** (323 mg, 0.492 mmol) in DCM (10 mL) was added *para*-anisaldehyde dimethyl acetal (107 mg, 0.592 mmol) and PPTS (12.0 mg, 0.049.1 μ mol). The reaction mixture was stirred at room temperature for 1 h. After concentration *in vacuo*, the crude residue was purified by flash column chromatography (SiO₂, 15:1 40-60 petroleum ether / Et₂O) to afford cyclic acetal **91a** (377 mg, 0.481 mmol, 99 %), identical in all respects to that synthesised previously.

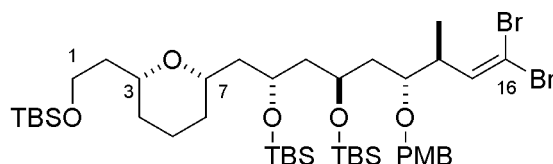
Aldehyde **92a**



To a stirred solution of alcohol **92** (233 mg, 0.298 mmol) in DCM (10 mL) was added Dess-Martin periodinane (189 mg, 0.447 mmol) at room temperature. After stirring for 2 h, the mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography (SiO₂, 5:1 40-60 petroleum ether / Et₂O) to afford aldehyde **92a** (230 mg, 0.294 mmol, 99 %) as a colourless oil; **R_f** 0.24 (9:1 40-60 petroleum ether / Et₂O); **[α]_D²⁰** -1.8 (c 1.18, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2929, 2856, 1727, 1614, 1514, 1472, 1463, 1248, 1079, 835, 773; **¹H NMR** (500 MHz, CDCl₃) δ 9.73 (1H, d, J = 1.7 Hz, H15), 7.25 (2H, d, J = 6.7 Hz, ArH), 6.86 (2H, d, J = 11.3 Hz, ArH), 4.46 (2H, s, ArCH₂O), 4.00-3.85 (3H, m, H9, H11, H13), 3.80 (3H, s, MeO), 3.75-3.61 (2H, m, H1), 3.47-3.32 (2H, m, H3, H7), 2.81-2.70 (1H, m, H14), 1.90-1.79 (2H, m, H12), 1.78-1.36 (10H, m, 2 \times H2, H4eq, 2 \times H5, H6eq, 2 \times H8, 2 \times H10), 1.22-1.11 (2H, m, H4ax, H6ax), 1.09 (3H, d, J = 7.0 Hz, Me14), 0.88 (18H, s, 2 \times *t*-BuSi), 0.87 (9H, s, *t*-BuSi), 0.06 (6H, s, 2 \times MeSi), 0.05 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.02 (3H, s, MeSi), 0.01 (3H, s, MeSi); **¹³C NMR** (100 MHz, CDCl₃) δ 204.0, 159.1, 130.5, 129.0, 113.7, 76.1, 74.4, 73.5, 70.5, 67.6, 66.4, 60.1, 55.3, 49.8, 47.4, 44.8,

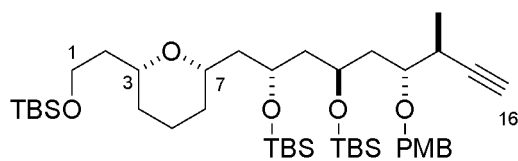
40.0, 39.3, 32.3, 31.7, 26.0, 23.8, 18.3, 18.0, 18.0, 15.3, 9.4, -3.6, -4.1, -4.2, -4.3, -5.3, -5.3;
HRMS calc. for C₄₂H₈₁O₇Si₃ [M + H]⁺ 781.5285, found 781.5281.

Vinyl dibromide **92b**



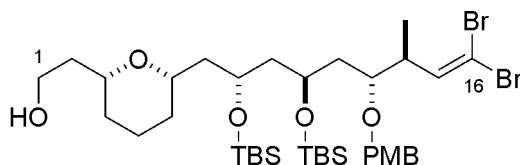
To a stirred solution of carbon tetrabromide (195 mg, 0.588 mmol) in DCM (3 mL) was added a solution of triphenylphosphine (308 mg, 1.18 mmol) in DCM (3 mL) dropwise at 0°C. The resulting mixture was stirred for 10 min at 0°C before addition to a stirred solution of aldehyde **92a** (230 mg, 0.294 mmol) and Et₃N (410 μL, 2.94 mmol) in DCM (4 mL) 0°C. The reaction was stirred for a further 20 min before being quenched with NH₄Cl solution (10 mL). The organic phase was separated and the aqueous phase was extracted with DCM (2 × 5 mL). The combined organic phases were washed with brine (5 mL), dried (MgSO₄) and concentrated *in vacuo*. Flash column chromatography (SiO₂, 20:1 40-60 petroleum ether / Et₂O) gave vinyl dibromide **92b** (264 mg, 0.281 mmol, 96 %) as a colourless oil; **R_f** 0.38 (9:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +11.4 (c 1.38, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 2929, 2856, 1613, 1513, 1471, 1462, 1248, 1076, 835, 772; **¹H NMR** (500 MHz, CDCl₃) δ 7.27 (2H, d, *J* = 8.6 Hz, ArH), 6.87 (2H, d, *J* = 8.6 Hz, ArH), 6.40 (1H, d, *J* = 9.3 Hz, H15), 4.47 (2H, s, ArCH₂O), 4.00-3.92 (1H, m, H9), 3.85-3.78 (1H, m, H11), 3.81 (3H, s, MeO), 3.72-3.65 (2H, m, H1), 3.54-3.46 (1H, m, H14), 3.41-3.32 (2H, m, H3, H7), 2.82-2.71 (1H, m, H14), 1.86-1.77 (1H, m, H5eq), 1.77-1.69 (2H, m, H2, H12), 1.69-1.48 (7H, m, H2, H4eq, H5ax, H6eq, 2 × H8, H10), 1.48-1.36 (2H, m, H10, H12), 1.22-1.11 (2H, m, H4ax, H6ax), 1.04 (3H, d, *J* = 6.9 Hz, Me14), 0.88 (27H, s, 3 × *t*-BuSi), 0.07 (6H, s, 2 × MeSi), 0.05 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.01 (3H, s, MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 159.0, 140.5, 131.0, 129.0, 113.7, 88.8, 78.0, 74.5, 73.6, 70.8, 67.9, 66.6, 60.1, 55.3, 47.5, 45.1, 41.6, 40.2, 40.0, 32.3, 31.7, 26.0, 23.8, 18.3, 18.1, 18.0, 14.6, -3.7, -4.0, -4.3, -5.3; **HRMS** calc. for C₄₃H₈₄O₆NBr₂Si₃ [M + NH₄]⁺ 952.3968, found 952.3971.

Alkyne 92c



To a stirred solution of vinyl dibromide **92b** (573 mg, 0.612 mmol) in THF (20 mL) at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (1.6 M in hexanes, 1.15 mL, 1.84 mmol) dropwise. The mixture was allowed to warm to $-20\text{ }^{\circ}\text{C}$ and stirred for 1 h before being quenched with NH_4Cl solution (20 mL) and diluted with Et_2O (20 mL). The aqueous phase was extracted with Et_2O ($2 \times 20\text{ mL}$) and the combined organic phases were dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2 , 20:1 40-60 petroleum ether / Et_2O) to provide alkyne **92c** (436 mg, 0.561 mmol, 92 %) as a colourless oil; R_f 0.38 (9:1 40-60 petroleum ether / Et_2O); $[\alpha]_D^{20} +4.9$ (c 0.79, CHCl_3); IR (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2929, 2857, 1614, 1514, 1472, 1463, 1249, 1079, 835, 773; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.28 (2H, d, $J = 8.6\text{ Hz}$, ArH), 6.86 (2H, d, $J = 8.6\text{ Hz}$, ArH), 4.47 (2H, q, $J = 8.4\text{ Hz}$, ArCH_2O), 4.00-3.90 (1H, m, H9), 3.90-3.83 (1H, m, H11), 3.80 (3H, s, MeO), 3.69 (2H, t, $J = 6.9\text{ Hz}$, H1), 3.59-3.51 (1H, m, H13), 3.44-3.32 (2H, m, H3, H7), 2.90-2.76 (1H, m, H14), 2.08 (1H, d, $J = 2.5\text{ Hz}$, H16), 1.88-1.67 (4H, m, H2, H5eq, $2 \times$ H12), 1.67-1.33 (8H, m, H2, H4eq, H5ax, H6eq, $2 \times$ H8, $2 \times$ H10), 1.22-1.11 (2H, m, H4ax, H6ax), 1.15 (3H, d, $J = 7.0\text{ Hz}$, Me14), 0.87 (27H, s, $3 \times t\text{-BuSi}$), 0.07 (6H, s, $2 \times$ MeSi), 0.06 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.02 (3H, s, MeSi); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 159.0, 130.9, 129.1, 113.7, 86.2, 77.8, 74.4, 73.7, 70.7, 69.8, 68.0, 66.7, 60.1, 55.3, 47.3, 45.0, 39.9, 39.1, 32.2, 31.7, 28.9, 25.9, 23.8, 18.3, 18.1, 15.2, -3.7 , -4.0 , -4.0 , -4.3 , -5.3 ; HRMS calc. for $\text{C}_{43}\text{H}_{81}\text{O}_6\text{Si}_3$ $[\text{M} + \text{H}]^+$ 777.5335, found 777.5335.

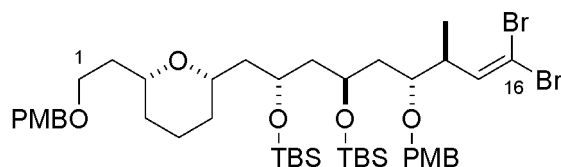
Alcohol 94



HF·pyridine complex (HF 70 %, 250 μL) was added dropwise to a stirred solution of pyridine (750 μL) in THF (4 mL) in a Teflon container. The premixed HF·pyridine-pyridine solution (HF 1.9 M solution in THF, 5 mL) was added to a stirred solution of *tris*-TBS ether **92b** (264 mg, 0.281 mmol) in THF (10 mL) at room temperature and the mixture was stirred for 7 h. The reaction was then

cooled to 0 °C, quenched with NaHCO₃ solution (10 mL) and diluted with Et₂O (20 mL). The aqueous phase was extracted with Et₂O (2 × 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO₂, 1:1 40-60 petroleum ether / Et₂O) to provide alcohol **94** (196 mg, 0.238 mmol, 85 %) as a colourless oil; **R_f** 0.26 (4:1 40-60 petroleum ether / EtOAc); [α]_D²⁰ +15.7 (c 1.09, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 3510 (br), 2929, 2856, 1614, 1514, 1472, 1463, 1386, 1249, 1062, 835; **¹H NMR** (500 MHz, CDCl₃) δ 7.28 (2H, d, *J* = 8.6 Hz, ArH), 6.88 (2H, d, *J* = 8.6 Hz, ArH), 6.39 (1H, d, *J* = 9.2 Hz, H15), 4.51 (1H, d, *J* = 11.2 Hz, ArCH₂O), 4.45 (1H, d, *J* = 11.2 Hz, ArCH₂O), 3.90-3.84 (1H, m, H9), 3.83-3.77 (1H, m, H11), 3.81 (3H, s, OMe), 3.75 (2H, q, *J* = 5.5 Hz, H1), 3.53-3.43 (3h, m, H13, H3, H7), 2.83-2.74 (1H, m, H14), 2.50 (1H, t, *J* = 5.5 Hz, OH), 1.85-1.78 (1H, m, H5eq), 1.72-1.61 (6H, m, 2 × H2, 2 × H8, H10, H12), 1.56-1.48 (3H, m, H5ax, H4eq, H6eq), 1.45-1.36 (2H, m, H10, H12), 1.33-1.23 (1H, m, H4ax), 1.23-1.12 (1H, m, H6ax), 1.05 (3H, d, *J* = 6.9 Hz, Me14), 0.89 (9H, s, *t*-BuSi), 0.88 (9H, s, *t*-BuSi), 0.09 (3H, s, MeSi), 0.09 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.02 (3H, s, MeSi); **¹³C NMR** (125 MHz, CDCl₃) δ 140.5, 131.0, 129.1, 113.7, 88.8, 78.0, 77.6, 74.1, 70.9, 67.6, 66.6, 61.2, 55.3, 47.2, 44.6, 41.3, 39.9, 38.4, 32.0, 31.6, 26.0, 23.5, 18.0, 18.0, 14.3, -3.7, -4.0, -4.1, -4.4; **HRMS** calc. for C₃₇H₆₇O₆Br₂Si₂ [M + H]⁺ 821.2837 (⁷⁹Br), found 821.2830.

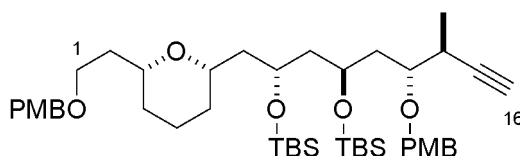
PMB ether **94a**



Triphenylcarbenium tetrafluoroborate (1.5 mg, 4.6 μmol) was added to a stirred solution of alcohol **94** (189 mg, 0.230 mmol) and PMBTCA (97.3 mg, 0.344 mmol) in THF (5 mL) at 0 °C. The reaction was stirred at 0 °C for 1 h, before being quenched with NaHCO₃ solution (5 mL). The resulting mixture was extracted with Et₂O (3 × 5 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO₂, 6:1 40-60 petroleum ether / Et₂O) to afford PMB ether **94a** (196 mg, 0.208 mmol, 90 %) as a colourless oil; **R_f** 0.57 (4:1 40-60 petroleum ether / EtOAc); [α]_D²⁰ +10.1 (c 1.02, CHCl₃); **IR** (thin film, $\nu_{\max}/\text{cm}^{-1}$) 2930, 2857, 1614, 1514, 1463, 1248, 1074, 835, 775; **¹H NMR** (500 MHz, CDCl₃) δ 7.28 (2H, d, *J* = 8.6 Hz, ArH), 7.24 (2H, d, *J* = 8.6 Hz, ArH), 6.87 (2H, d, *J* = 8.6 Hz, ArH), 6.86 (2H, d, *J* = 8.6 Hz, ArH), 6.40 (1H, d, *J* = 9.4 Hz, H15), 4.48 (2H, s, ArCH₂O), 4.42 (1H, d, *J* = 11.4

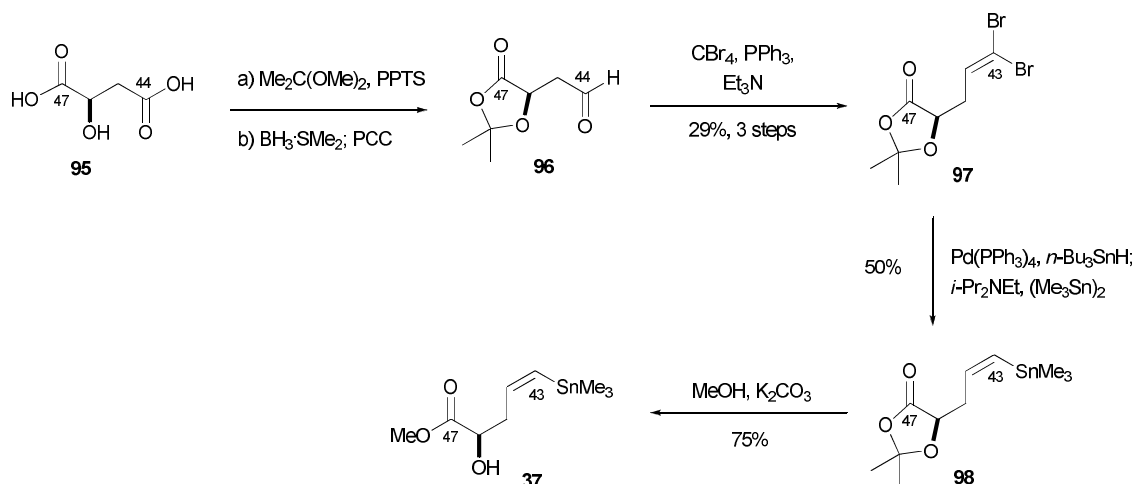
Hz, ArCH₂O), 4.37 (1H, d, $J = 11.4$ Hz, ArCH₂O), 3.98-3.91 (1H, m, H₉), 3.84-3.77 (1H, m, H₁₁), 3.80 (3H, s, OMe), 3.58-3.53 (2H, m, H₁), 3.53-3.48 (1H, m, H₁₃), 3.44-3.37 (2H, m, H₃, H₇), 2.81-2.73 (1H, m, H₁₄), 1.77-1.61 (7H, m, H_{5eq}, 2 × H₂, H₁₂, 2 × H₁₀, H₈), 1.58-1.46 (3H, m, H_{5ax}, H_{4eq}, H_{6eq}), 1.46-1.38 (2H, m, H₈, H₁₂), 1.22-1.11 (2H, m, H_{4ax}, H_{6ax}), 1.04 (3H, d, $J = 6.9$ Hz, Me₁₄), 0.89 (9H, s, *t*-BuSi), 0.88 (9H, s, *t*-BuSi), 0.08 (3H, s, MeSi), 0.07 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.01 (3H, s, MeSi); ¹³C NMR (125 MHz, CDCl₃) δ 159.0, 159.0, 140.4, 130.9, 130.8, 129.2, 129.0, 113.7, 88.8, 78.0, 74.4, 73.5, 72.6, 70.8, 67.8, 67.1, 66.6, 55.3, 47.4, 45.1, 41.6, 40.2, 36.8, 32.3, 31.8, 26.0, 23.7, 18.1, 18.0, 14.6, -3.7, -4.0, -4.1, -4.3; HRMS calc. for C₄₅H₇₈O₇NBr₂Si₂ [M + NH₄]⁺ 958.3678 (⁷⁹Br), found 958.3688.

Alkyne 39

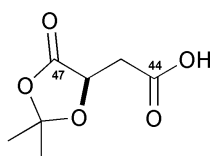


To a solution of vinyl dibromide **94a** (188 mg, 0.199 mmol) in THF (5 mL) at -78 °C was added *n*-BuLi (1.6 M in hexanes, 373 μL, 0.597 mmol). The reaction mixture was allowed to warm to -20 °C and stirred for 1 h before being diluted with Et₂O (10 mL) and quenched with NH₄Cl solution (5 mL). After phase separation, the aqueous phase was extracted with Et₂O (2 × 5 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 20:1 → 15:1 40-60 petroleum ether / EtOAc) afforded alkyne **39** (156 mg, 0.199 mmol, 99 %) as a colourless oil; R_f 0.43 (EtOAc / PE 40-60, 1:6); $[\alpha]_D^{20} +2.6$ (c 0.69, CHCl₃); IR (thin film, ν_{max}/cm^{-1}) 2929, 2856, 1614, 1514, 1463, 1248, 1078, 1038, 835, 774; ¹H NMR (500 MHz, CDCl₃) δ 7.28 (2H, d, $J = 8.6$ Hz, ArH), 7.24 (2H, d, $J = 8.6$ Hz, ArH), 6.86 (4H, m, ArH), 4.50 (1H, d, $J = 11.5$ Hz, CH₂Ar), 4.45 (1H, d, $J = 11.5$ Hz, CH₂Ar), 4.41 (1H, d, $J = 11.5$ Hz, CH₂Ar), 4.36 (1H, d, $J = 11.5$ Hz, CH₂Ar), 3.94 (1H, m, H₉), 3.85 (1H, m, H₁₁), 3.80 (3H, s, OMe), 3.79 (3H, s, OMe), 3.59-3.52 (3H, m, H₁₃, 2 × H₁), 3.42-3.36 (2H, m, H₇, H₃), 2.83 (1H, m, H₁₄), 2.08 (1H, d, $J = 2.5$ Hz, H₁₆), 1.82-1.71 (4H, m, H₁₂, H₁₀, H_{6eq}, H₂), 1.70-1.60 (4H, m, H₁₂, H₁₀, H₈, H₂), 1.58-1.45 (3H, m, 2 × H₅, H_{4eq}), 1.42 (1H, m, H₈), 1.22-1.16 (2H, m, H_{6ax}, H_{4ax}), 1.15 (3H, d, $J = 7.1$ Hz, Me₁₄), 0.88 (18H, s, 2 × *t*-BuSi), 0.07 (3H, s, SiMe), 0.06 (6H, s, 2 × SiMe), 0.02 (3H, s, SiMe); ¹³C NMR (125 MHz, CDCl₃) δ 159.1, 159.0, 130.9, 129.4, 129.2, 129.1, 113.8, 113.7, 86.2, 77.8, 74.5, 73.7, 72.6, 70.7, 69.9, 67.9, 67.1, 66.6, 55.3, 47.3, 45.0, 39.1, 36.8, 32.2, 31.8, 30.3, 29.7, 28.9, 26.0, 23.7, 18.1, 15.2, -3.6, -4.0, -4.2; HRMS (ES⁺) calcd for C₄₅H₇₄O₇Si₂Na [M+Na]⁺ 805.4871, found 805.4860.

2.8 Synthesis of vinyl stannane **37**



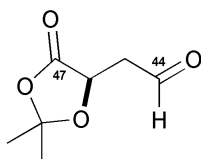
(5R)-(2,2-Dimethyl-5-oxo-[1,3]dioxolan-4-yl)-acetic acid (**95a**)



PPTS (0.357 g, 1.42 mmol) was added to a solution of D-Malic acid **95** (2.02 g, 15.1 mmol) in dimethoxypropane (20 mL). The reaction was stirred at rt for 20 h before concentration *in vacuo*. Purification by flash column chromatography (EtOAc / PE (30-40), 2:1) afforded carboxylic acid **95a** as a white, crystalline solid (2.04 g, 11.7 mmol, 78 %); R_f 0.13-0.38 (EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ_{H} 4.71 (1H, dd, $J = 3.9, 6.3$ Hz, H46), 2.98 (1H, dd, $J = 3.9, 17.1$ Hz, H45a), 2.85 (1H, dd, $J = 6.3, 17.1$ Hz, H45b), 1.62 (3H, s, Me), 1.57 (3H, s, Me).

The data was consistent with that reported in the literature.^[7]

Aldehyde **96**

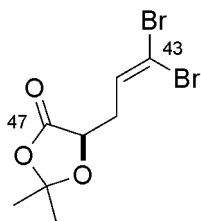


$\text{BH}_3\cdot\text{SMe}_2$ (10 M, 375 μL , 3.75 mmol) was added dropwise to a stirred solution of carboxylic acid **95a** (502 mg, 2.88 mmol) in THF (1.5 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h

and then at room temperature for 16 h. After being cooled to 0 °C, MeOH (1.5 mL) was added dropwise and the mixture was stirred for 5 min. After concentration *in vacuo*, additional MeOH (3 mL) was added and the resulting solution was concentrated *in vacuo*. The product was diluted with EtOAc (3.0 mL) and a final concentration *in vacuo* afforded the crude alcohol; **R_f** 0.31 (1:1 40-60 petroleum ether / EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 4.57 (1H, dd, *J* = 7.1, 4.9 Hz, H₄₆), 3.93-3.74 (2H, m, H₄₄), 2.20-2.10 (1H, m, H₄₅), 2.06-1.96 (1H, m, H₄₅), 1.63 (3H, s, Me), 1.56 (3H, s, Me). The data was consistent with that reported in the literature.^[7]

To a stirred solution of the crude alcohol in DCM (20 mL) at 0 °C was added pyridinium chlorochromate (3.16 g, 14.4 mmol). The reaction mixture was stirred for 4 h before being poured into Et₂O (50 mL) and filtered over Celite. The filtrate was treated with activated carbon powder and stirred for 20 min before being filtered over Celite again. Concentration *in vacuo* gave crude aldehyde **96**; **R_f** 0.38 (1:1 40-60 petroleum ether / EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 9.78 (1H, br t, *J* = 0.7 Hz, H₄₄), 4.79 (1H, dd, *J* = 7.0, 3.5 Hz, H₄₆), 3.10 (1H, ddd, *J* = 18.5, 3.5, 0.7 Hz, H₄₅), 2.93 (1H, ddd, *J* = 18.3, 7.0, 0.7 Hz, H₄₅), 1.63 (3H, s, Me), 1.58 (3H, s, Me). The data was consistent with that reported in the literature.^[7]

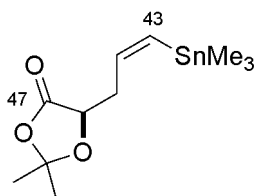
Vinyl dibromide **97**



A solution of PPh₃ (3.00 g, 11.5 mmol) in DCM (10 mL) was added dropwise to a stirred solution of CBr₄ (1.92 g, 5.76 mmol) in DCM (10 mL) at 0 °C and the mixture was stirred for 10 min. Et₃N (4.00 mL, 28.8 mmol) and premixed ylid solution were added sequentially to a solution of crude aldehyde **96** in DCM (30 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h before being quenched with pH 7 buffer (30 mL). The aqueous phase was extracted with DCM (2 × 25 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 4:1 40-60 petroleum ether / EtOAc) afforded vinyl dibromide **97** (336 mg, 1.07 mmol, 37 % over 3 steps) as a yellowish oil; **R_f** 0.29 (4:1 40-60 petroleum ether / Et₂O); [α]_D²⁰ +12.1 (c 1.24, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 2993, 1793, 1388, 1270, 1239, 1127; ¹H NMR (400 MHz, CDCl₃) δ 6.48 (1H, t, *J* = 7.1 Hz, H₄₄), 4.48 (1H, dd, *J* = 7.0, 4.7 Hz, H₄₆),

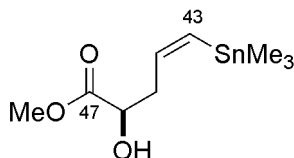
2.71 (1H, ddd, $J = 15.5, 7.5, 4.7$ Hz, H45), 2.56 (1H, td, $J = 15.5, 7.0$ Hz, H45), 1.63 (3H, s, Me), 1.56 (3H, s, Me); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 171.8, 131.8, 111.1, 92.9, 72.2, 35.1, 27.2, 25.9; **HRMS** calc. for $\text{C}_8\text{H}_{14}\text{O}_3\text{NBr}_2$ $[\text{M} + \text{NH}_4]^+$ 329.9335 (^{79}Br), found 329.9337.

(Z)-Vinyl stannane **98**



To a stirred solution of vinyl dibromide **97** (487 mg, 1.55 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (90.0 mg, 78.2 μmol) in degassed benzene (10 mL) was added $n\text{-Bu}_3\text{SnH}$ (459 μL , 1.71 mmol). The reaction mixture was stirred at 40 °C for 16 h with conversion being confirmed by crude $^1\text{H NMR}$ analysis. Once the starting material had been consumed, $i\text{-Pr}_2\text{NEt}$ (135 μL , 0.78 mmol) and hexamethylditin (762 mg, 2.33 mmol) were added and the reaction mixture was heated to 80 °C and stirred for 2 h. After cooling to room temperature, solvent was removed *in vacuo* and the crude residue was purified by flash column chromatography (SiO_2 , 9:1 40-60 petroleum ether / EtOAc) to afford vinyl stannane **98** (246 mg, 0.77 mmol, 50 %) as a pale yellowish oil; R_f 0.38 (9:1 40-60 petroleum ether / EtOAc); $[\alpha]_D^{20}$ -3.2 (c 1.22, CHCl_3); **IR** (thin film, $\nu_{\text{max}}/\text{cm}^{-1}$) 2976, 1796, 1387, 1278, 1237, 1120, 771; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.47 (1H, ddd, $J = 13.9, 7.1, 6.8$ Hz, H44), 6.10 (1H, td, $J = 12.7, 1.2$ Hz, H43), 4.46 (1H, dd, $J = 7.3, 4.2$ Hz, H46), 2.68 (1H, dddd, $J = 14.6, 6.6, 4.0, 1.2$ Hz, H45), 2.46 (1H, dtd, $J = 14.6, 7.3, 1.0$ Hz, H45), 1.61 (3H, s, Me), 1.54 (3H, s, Me), 0.20 (9H, s, $3 \times \text{MeSn}$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 172.4, 141.5, 134.7, 110.7, 73.8, 37.9, 27.2, 25.8, -8.6 ; **HRMS** calc. for $\text{C}_{11}\text{H}_{20}\text{O}_3\text{SnNa}$ $[\text{M} + \text{Na}]^+$ 343.0327, found 343.0314.

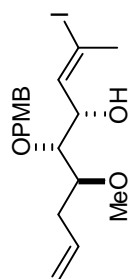
Methyl ester **37**



To a stirred solution of acetone **98** (32.1 mg, 0.101 mmol) in MeOH (1 mL) was added K_2CO_3 (13.9 mg, 0.101 mmol). The suspension was stirred for 30 min before being quenched with pH 7

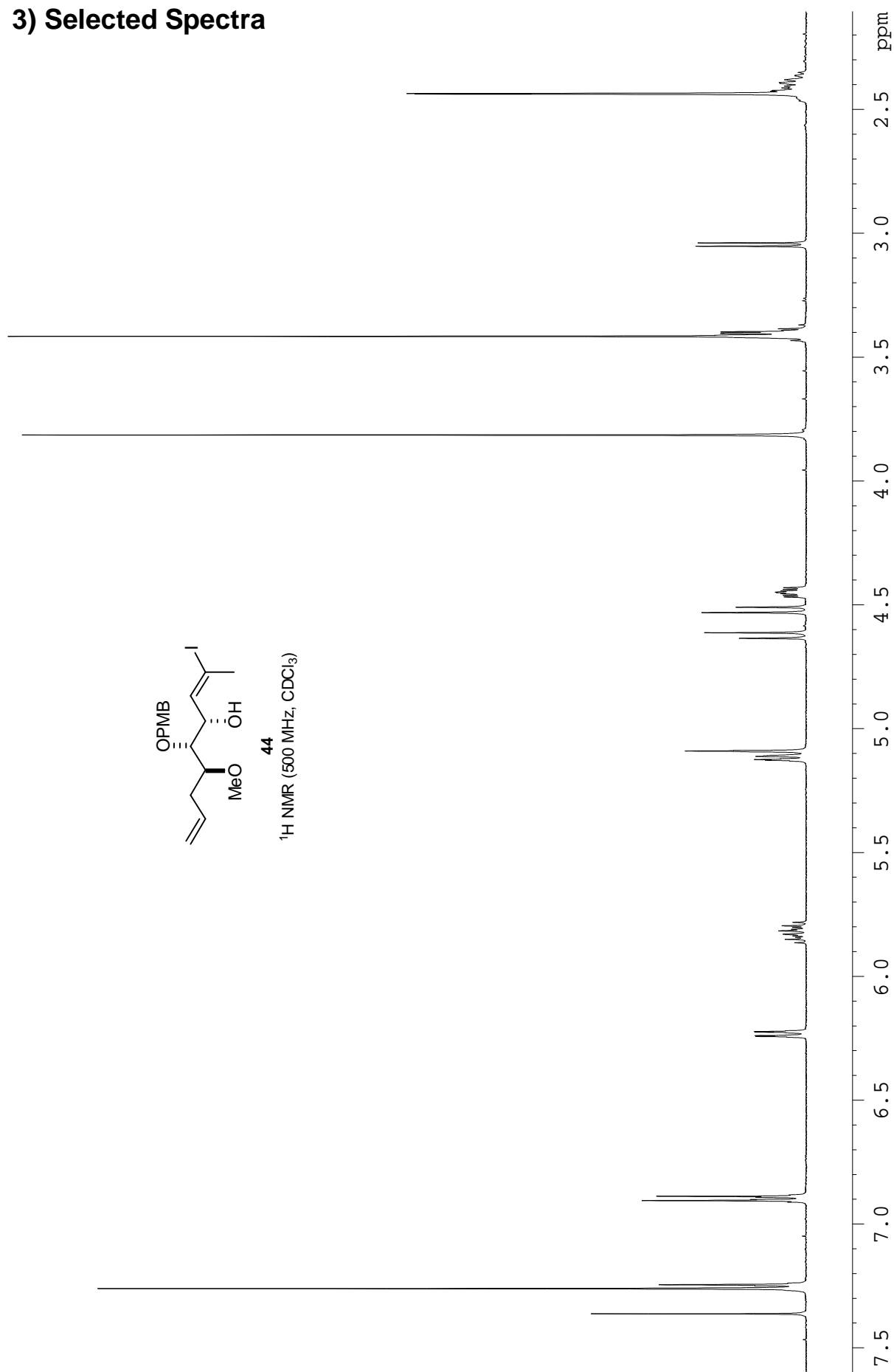
buffer (1 mL) and diluted with DCM (2 mL). After phase separation, the aqueous phase was extracted with DCM (3 × 5 mL) and the combined organic phases were dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography (SiO₂, 10:1 40-60 petroleum ether / EtOAc) produced methyl ester **37** (22.1 mg, 75.4 μmol, 75 %) as a colourless oil; **R_f** 0.23 (9:1 40-60 petroleum ether / EtOAc); [α]_D²⁰ -8.0 (c 1.51, CHCl₃); **IR** (thin film, ν_{max} /cm⁻¹) 3489 (br), 2972, 2918, 1737, 1599, 1439, 1212, 1094, 767, 720; **¹H NMR** (500 MHz, CDCl₃) δ 6.45 (1H, dt, J = 12.6, 7.1 Hz, H44), 6.05 (1H, d, J = 12.6 Hz, H43), 4.27 (1H, dd, J = 6.6, 4.6 Hz, H46), 3.79 (3H, s, MeO₂C), 2.73 (1H, br s, OH), 2.57 (1H, dddd, J = 14.2, 7.0, 4.6, 1.2 Hz, H45), 2.45 (1H, m, H45), 0.18 (9H, s, 3 × MeSn); **¹³C NMR** (125 MHz, CDCl₃) δ 174.9, 142.0, 134.3, 70.1, 52.5, 40.6, -8.6; **HRMS** calc. for C₉H₁₉O₃Sn [M + H]⁺ 295.0351, found 295.0349.

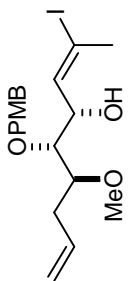
3) Selected Spectra



44

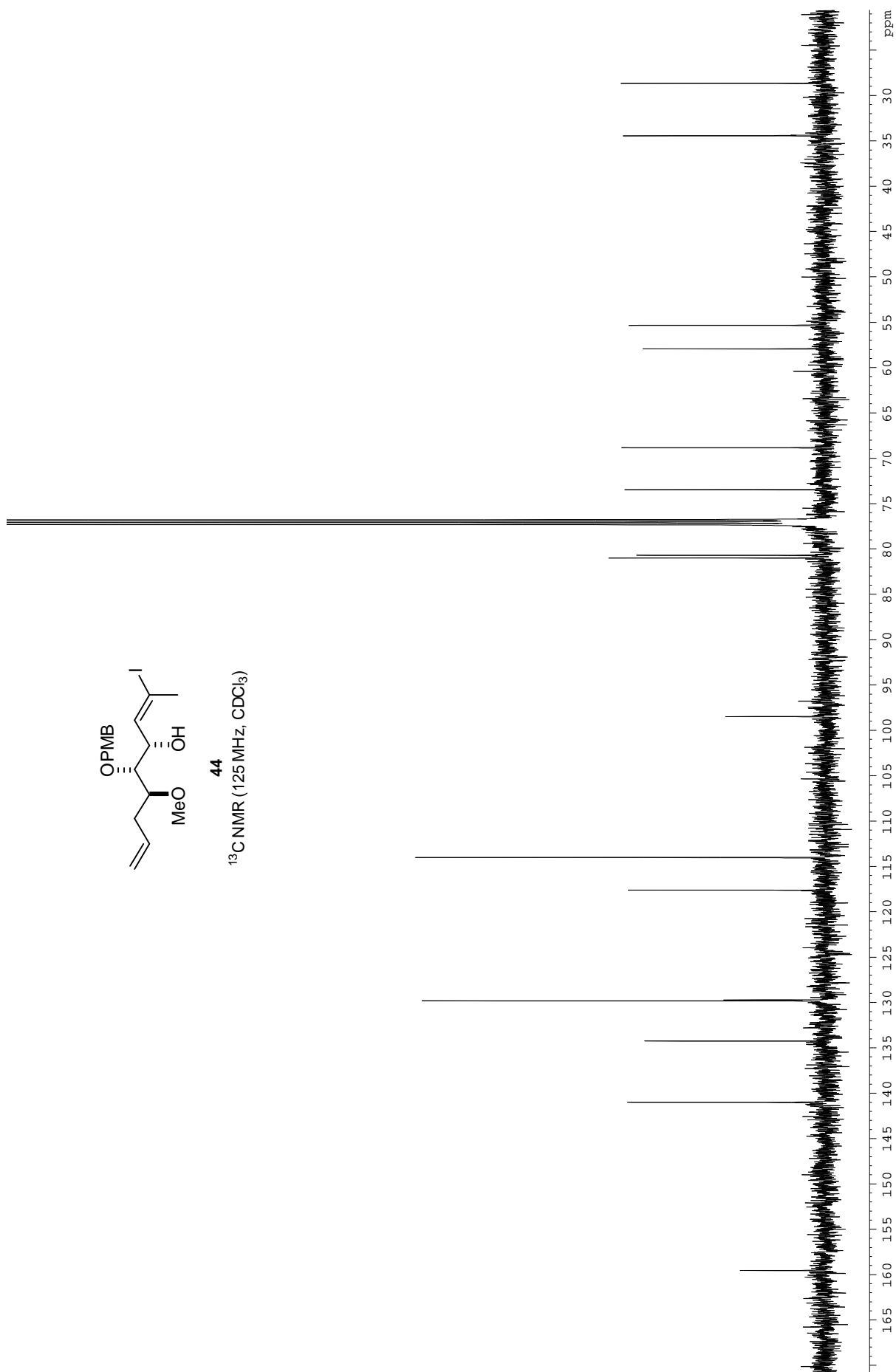
¹H NMR (500 MHz, CDCl₃)

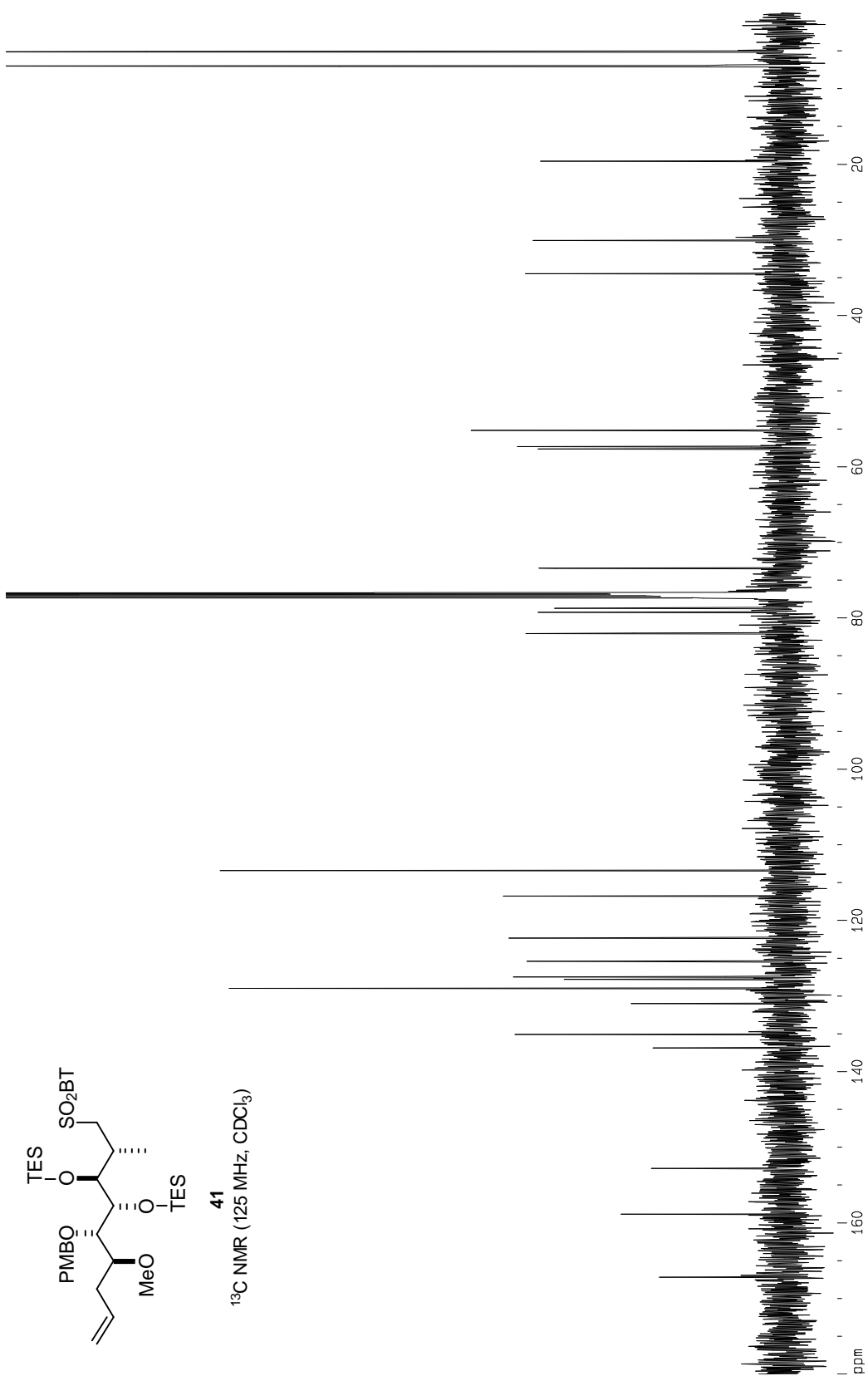


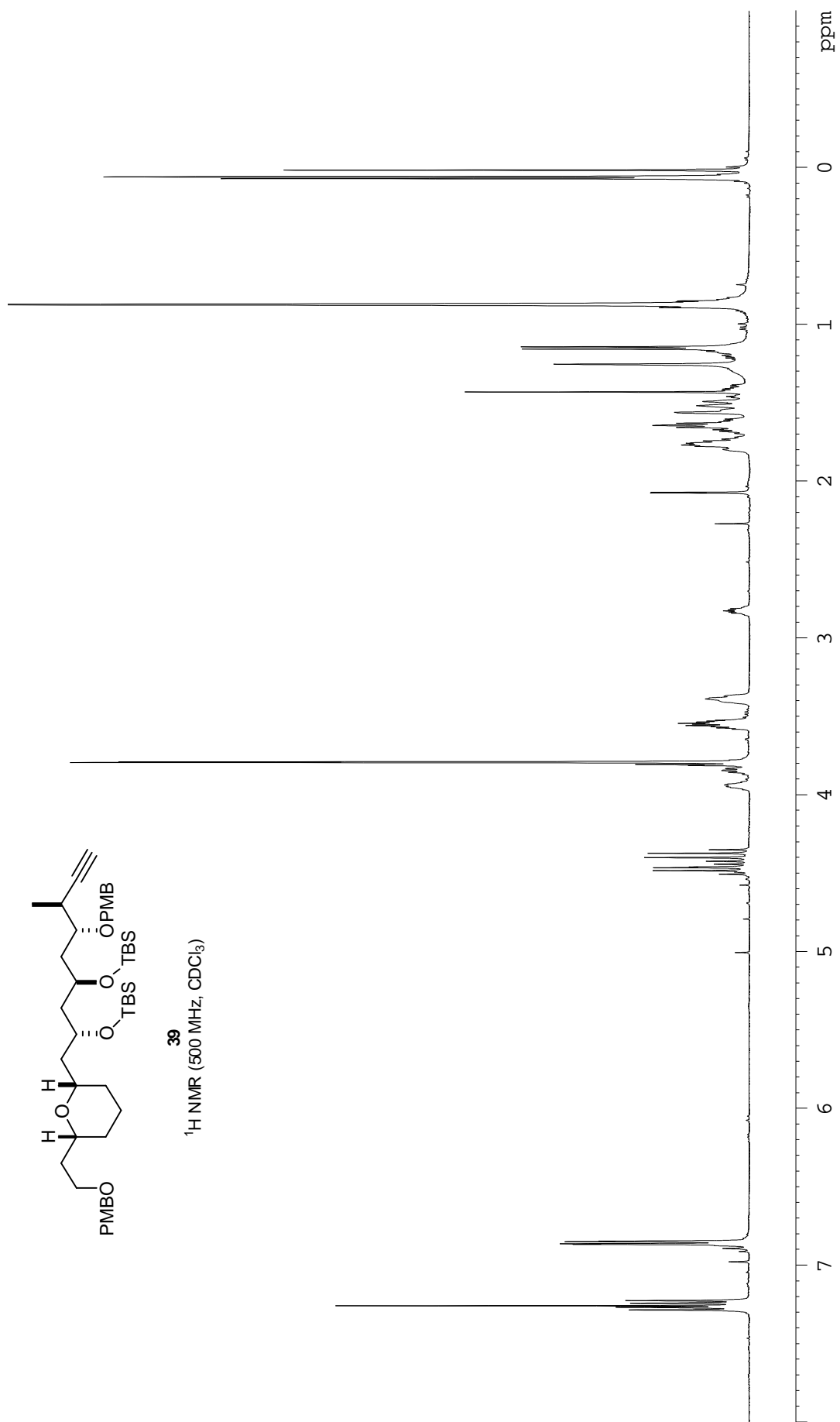


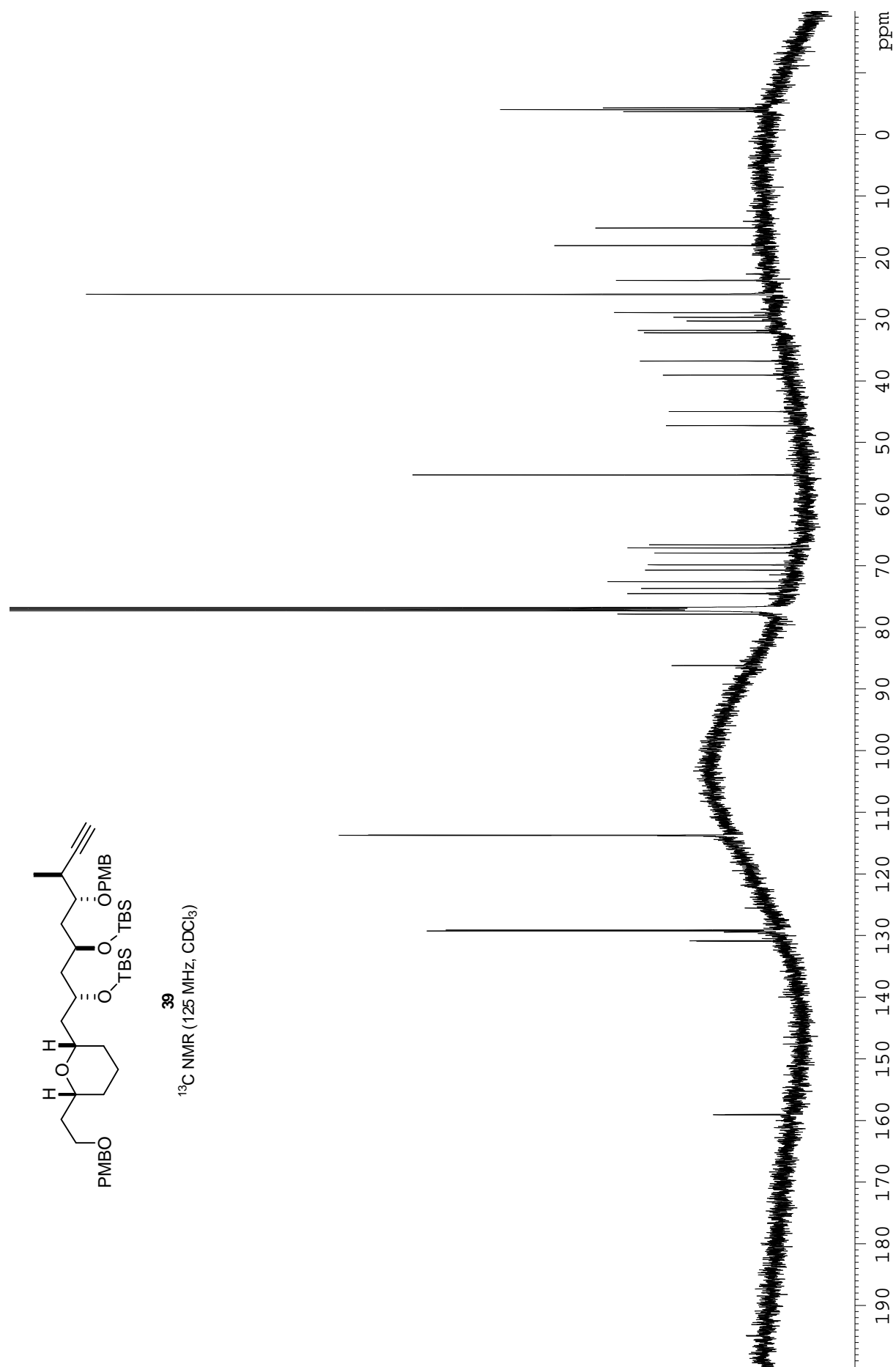
44

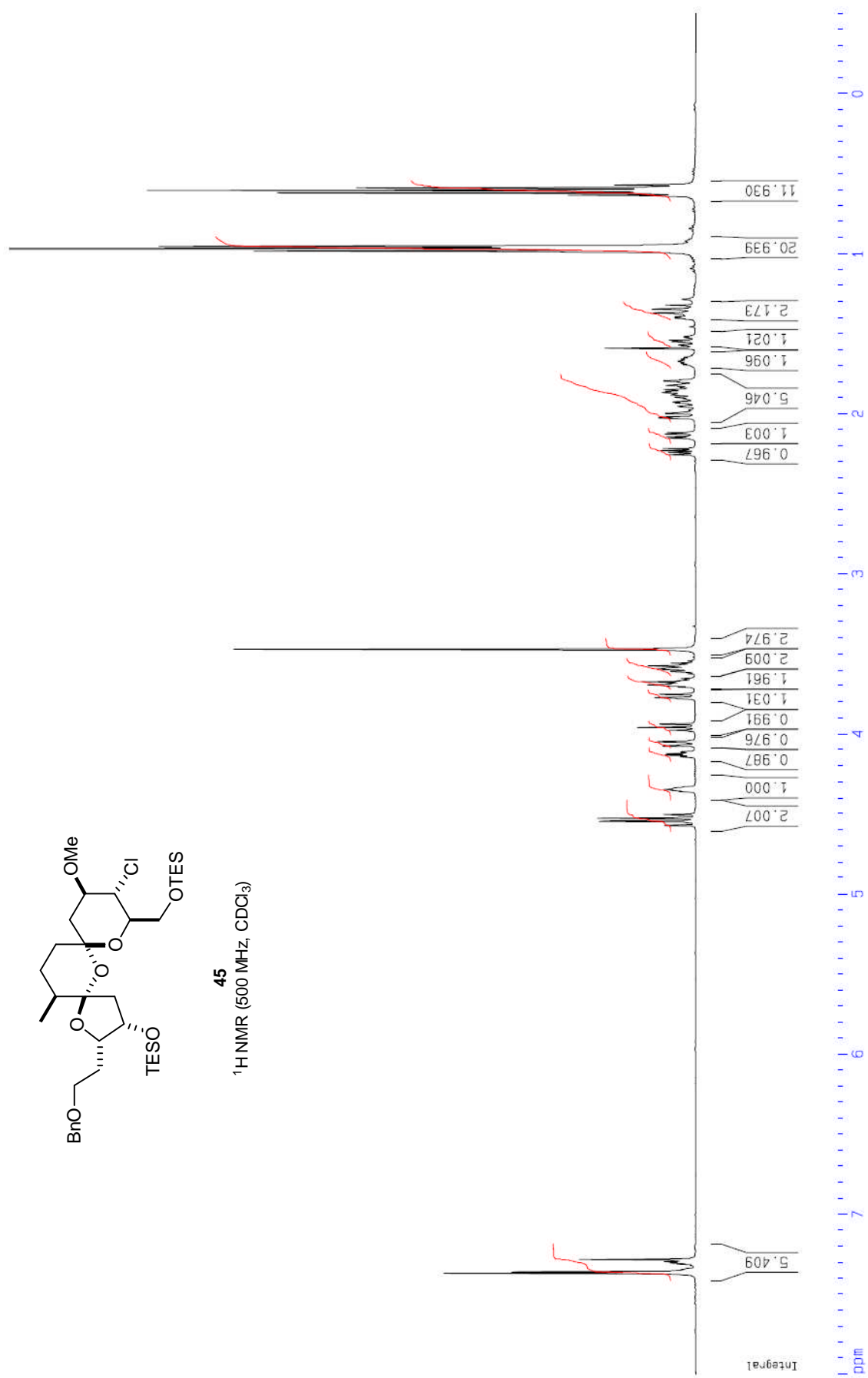
¹³C NMR (125 MHz, CDCl₃)

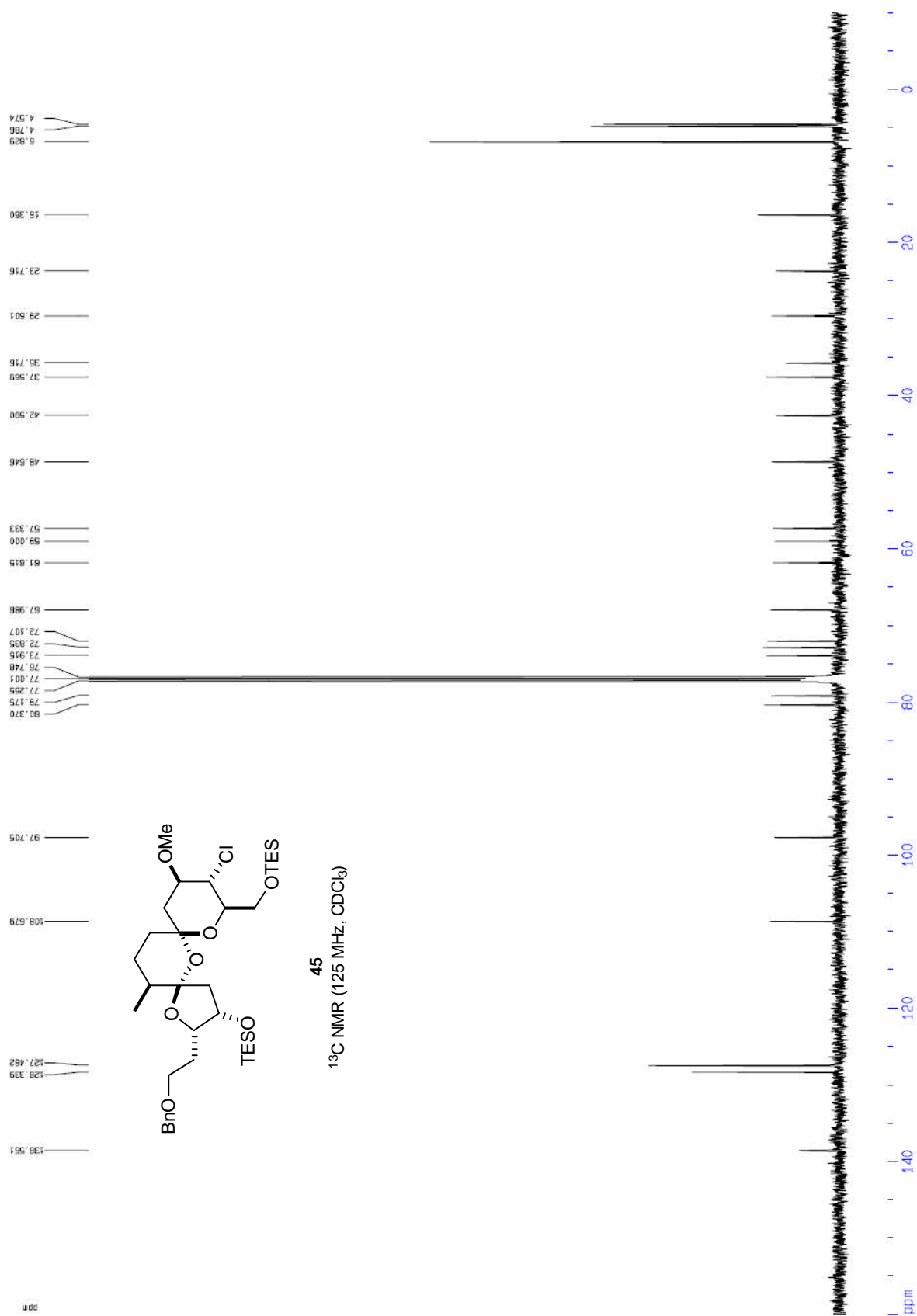












4) References

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