Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

The Stereocontrolled Total Synthesis of Spirastrellolide A Methyl Ester. Fragment Coupling Studies and Completion of the Synthesis

Ian Paterson, Edward A. Anderson, Stephen M. Dalby, Jong Ho Lim and Philip Maltas.*

University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, United Kingdom

Fax: (+44) 1223-336362

E-mail: ip100@cam.ac.uk

Supporting Information available

1) General Experimental Procedures

^{1}H 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 $\delta_{TMS} = 0$), 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 $\delta_{TMS} = 0$.

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 $[M]^+$ or $[M + H]^+$, $[M + NH_4]^+$, $[M + Na]^+$ is quoted.

Optical rotations were measured on a Perkin Elmer 241 polarimeter at the sodium D-line (589 nm) and are reported as follows: $[\alpha]_D^{20}$ 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.

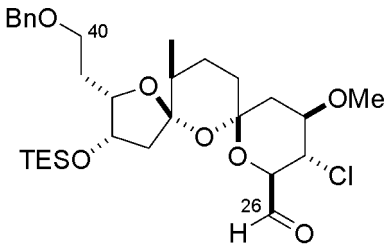
Dichloromethane (CH_2Cl_2; DCM), acetonitrile (MeCN) and methanol (MeOH) were distilled from calcium hydride and stored under an argon atmosphere; tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium or potassium wire / benzophenone ketyl radical under an argon

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 ($NaHCO_3$), ammonium chloride (NH_4Cl), sodium thiosulphate ($Na_2S_2O_3$) 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

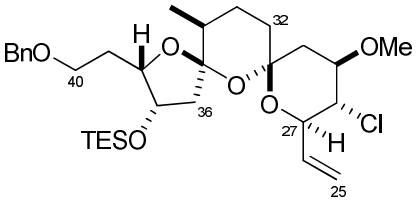
2.1 DEF spiroacetal manipulation

Aldehyde 10



To a solution of alcohol **6** (95.1 mg, 0.162 mmol) in DCM (12 mL) was added dry $NaHCO_3$ (13.6 mg, 0.162 mmol) and Dess-Martin periodinane (207 mg, 0.487 mmol). The reaction mixture was then stirred for 2 h. After addition of $NaHCO_3$ solution (6 mL) and $Na_2S_2O_3$ solution (6 mL), the mixture was stirred for 30 min before phase separation and extraction of the aqueous phase with DCM (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The crude aldehyde (98.9 mg) was used without further purification.

Alkene 11

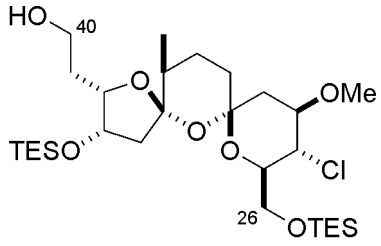


A 0.5M stock solution of methylene Wittig reagent was prepared by dropwise addition of ^{n}BuLi (1.6M in hexane, 700 µL, 1.12 mmol) to a stirred suspension of PPh_3CH_3Br (400 mg, 1.12 mmol) in THF (1.30 mL) at 0 °C. The mixture was stirred at RT for 1 h before use.

To a stirred solution of crude aldehyde **10** (77.0 mg, ≤0.132 mmol) in THF (3 mL) at –78 °C was added methylene Wittig reagent (0.5M in THF, 660 µL, 0.660 mmol). The reaction mixture was allowed to warm to RT and stirred for 30 min before being quenched with NH_4Cl (2 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (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, 1:20) afforded alkene **11** (58.3 mg, 1.01 mmol, 76%) as a colourless oil; $\mathbf{R_f}$ 0.57 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ −6.8 (*c* 0.69, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2954, 2876, 1455, 1379, 1240, 1168, 1079, 1018, 974, 926, 735; ^{1}**H NMR** (500 MHz, C_6D_6) δ 7.35 (2H, d, *J* = 7.6 Hz, ArH), 7.19 (2H, app t, *J* = 7.6 Hz, ArH), 7.08 (1H, app t, *J* = 7.6 Hz, ArH), 6.26 (1H, ddd, *J* = 17.2, 10.8, 4.6 Hz, H26), 5.72 (1H, dd, *J* = 17.2, 1.9 Hz, H25), 5.21

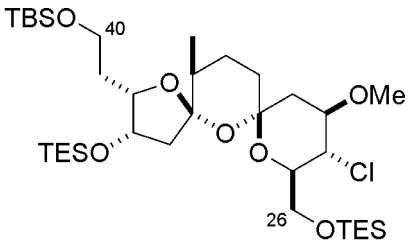
(1H, dd, *J* = 10.8, 1.9 Hz, H25), 4.51 (1H, ddt, *J* = 10.4, 4.6, 1.7 Hz, H27), 4.45 (1H, d, *J* = 12.1 Hz, CH_2Ar), 4.37 (1H, d, *J* = 12.1 Hz, CH_2Ar), 4.26 (1H, dt, *J* = 8.1, 4.3 Hz, H38), 4.07 (1H, ddd, *J* = 6.3, 4.1, 2.5 Hz, H37), 3.91 (1H, ddd, *J* = 11.3, 9.5, 5.0 Hz, H29), 3.63 (1H, app t, *J* = 10.0 Hz, H28), 3.62-3.53 (2H, m, 2 × H40), 3.31 (3H, s, OMe), 2.18 (1H, dd, *J* = 14.2, 6.3 Hz, H36), 2.16 (1H, m, H33), 2.11 (1H, dd, *J* = 12.6, 5.1 Hz, H30), 2.07 (1H, m, H39), 1.98 (1H, m, H39), 1.95 (1H, dd, *J* = 14.2, 2.5 Hz, H36), 1.71 (1H, dt, *J* = 13.1, 3.2 Hz, H32), 1.51 (1H, dqd, *J* = 12.7, 6.5, 3.6 Hz, H34), 1.38-1.30 (2H, m, H32, H30), 1.21 (1H, m, H33), 1.03 (3H, d, *J* = 6.7 Hz, Me34), 0.94 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.51 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ 139.2, 135.4, 116.7, 108.8, 97.6, 81.0, 79.4, 73.3, 72.9, 72.3, 68.1, 64.7, 57.3, 49.1, 43.3, 37.8, 36.1, 29.9, 23.9, 16.5, 6.9, 4.9; **HRMS** (ES^+) calcd for $C_{31}H_{49}ClO_6SiNa$ $[M+Na]^+$ 603.2886, found 603.2890.

Alcohol 54



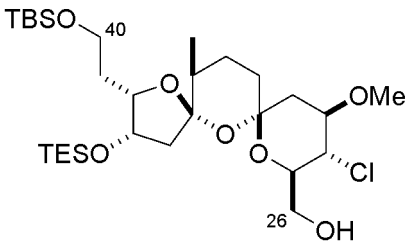
To a stirred solution of benzyl ether **33** (192 mg, 0.275 mmol) in EtOH (10 mL) was added Raney-Ni (ca. 100 mg). The reaction was vacuum-flushed 3 times with hydrogen and stirred under hydrogen (balloon pressure) for 16 h. The mixture was filtered through a pad of Celite and washed with EtOAc (2 × 5 mL). Concentration *in vacuo* afforded alcohol **54** (166 mg, 0.272 mmol, 99 %) as a colourless oil; **R_f** 0.48 (EtOAc / PE 40-60, 1:4); **$[\alpha]_D^{20}$** +2.0 (*c* 1.20, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3534, 2955, 2877, 1459, 1381, 1240, 1132, 1067, 1001, 927, 741; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 4.32 (1H, ddd, *J* = 6.3, 4.0, 2.0 Hz, H37), 4.19 (1H, ddd, *J* = 9.9, 3.9, 3.2 Hz, H38), 4.04 (1H, dd, *J* = 11.4, 2.4 Hz, H26), 3.92 (1H, t, *J* = 9.9 Hz, H28), 3.91 (1H, dd, *J* = 11.4, 1.8 Hz, H26), 3.77 (1H, m, H40), 3.73-3.63 (3H, m, H40, H29, H27), 3.45 (3H, s, OMe), 2.79 (1H, dd, *J* = 8.7, 2.3 Hz, OH), 2.26 (1H, dd, *J* = 14.4, 6.5 Hz, H36), 2.12 (1H, dd, *J* = 12.6, 4.9 Hz, H30), 2.01 (1H, dd, *J* = 14.4, 2.0 Hz, H36), 1.98 (1H, m, H39), 1.86-1.78 (2H, m, H33, H32), 1.70-1.60 (2H, m, H39, H34), 1.54 (1H, td, *J* = 13.9, 3.2 Hz, H32), 1.40 (1H, m, H33), 1.33 (1H, dd, *J* = 11.4, 12.7 Hz, H30), 0.97 (3H, d, *J* = 7.1 Hz, Me34), 0.95 (18H, m, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.60 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 109.2, 97.9, 83.8, 78.9, 74.3, 72.5, 61.7, 61.3, 59.2, 57.3, 49.0, 42.6, 37.6, 35.7, 31.3, 29.7, 23.8, 16.3, 6.8, 4.8, 4.5; **HRMS** (ES^+) calcd for $C_{29}H_{58}ClO_7Si_2$ $[M+H]^+$ 609.3404, found 609.3397.

TBS ether 34



To a stirred solution of alcohol **54** (173 mg, 0.284 mmol) in DCM (2 mL) was added imidazole (38.6 mg, 0.567 mmol) and TBSCl (64.1 mg, 0.425 mmol). The reaction mixture was stirred for 10 min before being diluted with DCM (5 mL) and quenched with NH_4Cl solution (2 mL). The organic phase was separated, the aqueous phase extracted with DCM (2 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 30:1 40-60 petroleum ether / EtOAc) afforded TBS ether **34** (205 mg, 0.283 mmol, 99 %) as a colourless oil; $\mathbf{R_f}$ 0.69 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ = +4.1 (*c* 0.80, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2878, 1461, 1380, 1253, 1134, 1084, 1003, 930, 834, 741; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 4.34 (1H, ddd, *J* = 6.4, 4.4, 3.0 Hz, H37), 4.07 (2H, m, H38, H26), 3.95 (1H, t, *J* = 9.9 Hz, H28), 3.76-3.70 (2H, m, H40, H26), 3.68-3.60 (3H, m, H40, H29, H27), 3.44 (3H, s, OMe), 2.21 (1H, dd, *J* = 14.0, 6.4 Hz, H36), 2.10 (1H, dd, *J* = 12.6, 5.0 Hz, H30), 1.98 (1H, dd, *J* = 14.0, 2.8 Hz, H36), 1.91 (1H, m, H33), 1.82-1.59 (4H, m, 2 × H39, H34, H32), 1.51 (1H, td, *J* = 13.3, 4.1 Hz, H32), 1.38-1.24 (2H, m, H33, H30), 0.98-0.93 (21H, m, 2 × $Si(CH_2C\underline{H}_3)_3$, Me_{34}), 0.90 (9H, s, *t*-BuSi), 0.59 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$), 0.06 (6H, s, 2 × SiMe); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 108.7, 97.7, 80.2, 79.2, 73.9, 72.2, 61.7, 60.8, 58.9, 57.3, 48.5, 42.6, 37.6, 35.7, 33.0, 29.7, 26.0, 23.7, 18.3, 16.4, 6.8, 4.8, 4.6, −5.1, −5.2; **HRMS** (ES^+) calcd for $C_{35}H_{71}ClO_7Si_3Na$ $[M+Na]^+$ 745.4094, found 745.4116.

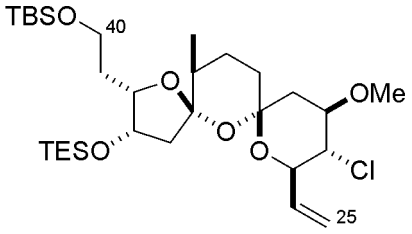
Alcohol 34a



To a stirred solution of *bis*-TES ether **34** (145 mg, 0.200 mmol) in DCM / MeOH (7:1 v/v, 5 mL) at 0 °C was added PPTS (5.0 mg, 0.020 mmol). The reaction mixture was stirred for 1.5 h before

being quenched with $NaHCO_3$ solution (5 mL). The organic phase was separated, the aqueous phase extracted with DCM (2 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. No further purification was required to provide alcohol **34a** (122 mg, 0.199 mmol, 99 %) as a colourless oil; $\mathbf{R_f}$ 0.23 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ –1.2 (*c* 1.70, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3493, 2955, 2931, 2878, 1462, 1380, 1253, 1168, 1095, 986, 835, 776; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 4.35 (1H, dt, *J* = 7.6, 4.9 Hz, H38), 4.25 (1H, m, H37), 4.19 (1H, m, H26), 4.10 (1H, m, H27), 3.92-3.76 (5H, m, 2 × H40, H29, H28, H26), 3.28 (3H, s, OMe), 2.17 (2H, m, H36, OH), 2.09-2.03 (2H, m, H39, H30), 2.00-1.94 (3H, m, H39, H36, H33), 1.58 (1H, dt, *J* = 13.2, 3.2 Hz, H32), 1.47 (1H, m, H34), 1.33-1.25 (2H, m, H32, H30), 1.17 (1H, m, H33), 1.01 (12H, m, Me34, *t*BuSi), 0.96 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.54 (6H, q, $Si(C\underline{H}_2CH_3)_3$), 0.15 (3H, s, SiMe), 0.13 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 108.8, 97.8, 80.8, 79.3, 74.0, 72.0, 62.8, 60.7, 60.4, 57.3, 48.4, 43.1, 37.5, 35.7, 32.8, 26.0, 23.8, 18.3, 16.5, 6.9, 5.1, −5.2, −5.3; **HRMS** (ES^+) calcd for $C_{29}H_{57}ClO_7Si_2Na$ $[M+Na]^+$ 631.3229, found 631.3236.

Alkene 35



To a stirred solution of alcohol **34a** (122 mg, 0.199 mmol) in DCM (25 mL) was added $NaHCO_3$ (16.7 mg, 0.199 mmol) and Dess-Martin periodinane (253 mg, 0.597 mmol). The reaction was stirred for 2 h before being quenched with $NaHCO_3$ solution (5 mL) and $Na_2S_2O_3$ solution (5 mL). The quenching mixture was stirred vigorously for 30 min, then extracted with DCM (3 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The crude mixture (123 mg) was used in the following olefination without further purification.

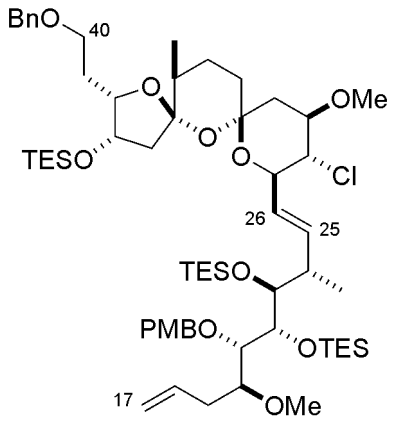
A 0.25 M stock solution of methylene Wittig reagent was prepared by dropwise addition of *n*-BuLi (1.6M in hexane, 313 µL, 0.50 mmol) to a stirred suspension of CH_3PPh_3Br (179 mg, 0.50 mmol) in THF (1.7 mL) at 0 °C. The yellow solution was stirred at 0 °C for 1 h before use.

To a stirred solution of the crude aldehyde (123 mg) in THF (4 mL) at −78 °C was added the freshly prepared methyl Wittig reagent (0.25 M in THF, 2.0 mL, 0.50 mmol). The reaction mixture

was allowed to warm to room temperature and stirred for 30 min before being quenched with NH_4Cl solution (4 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 15:1 40-60 petroleum ether / Et_2O) afforded alkene **35** (84.7 mg, 0.140 mmol, 70 % over 2 steps) as a colourless oil; $\mathbf{R_f}$ 0.61 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ = −4.4 (*c* 0.50, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2878, 1462, 1380, 1254, 1083, 975, 929, 835, 776, 729; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 6.30 (1H, ddd, *J* = 17.1, 10.7, 4.7 Hz, H26), 5.73 (1H, d, *J* = 17.1 Hz, H25), 5.21 (1H, d, *J* = 10.7 Hz, H25), 4.48 (1H, m, H27), 4.23 (1H, m, H38), 4.16 (1H, m, H37), 3.93-3.77 (3H, m, 2 × H40, H29), 3.63 (1H, dd, *J* = 10.1, 9.9 Hz, H28), 3.31 (3H, s, OMe), 2.19 (1H, dd, *J* = 14.1, 2.5 Hz, H36), 2.11 (2H, m, H33eq, H30eq), 2.02 (1H, m, H39), 1.97 (1H, dd, *J* = 14.2, 2.5 Hz, H36), 1.91 (1H, m, H39), 1.71 (1H, dt, *J* = 13.2, 3.1 Hz, H32eq), 1.51 (1H, m, H34), 1.34 (2H, m, H32ax, H30ax), 1.21 (1H, m, H33ax), 1.03 (3H, d, *J* = 6.7 Hz, Me34), 1.01 (9H, s, *t*BuSi), 0.97 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.54 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.13 (3H, s, SiMe), 0.11 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 135.4, 116.7, 108.8, 97.6, 80.7, 79.4, 73.3, 72.4, 64.7, 61.3, 57.3, 49.0, 43.2, 37.8, 36.0, 33.1, 26.0, 23.9, 18.3, 16.5, 6.9, 4.9, −5.2, −5.3; **HRMS** (ES^+) calcd for $C_{30}H_{57}ClO_6Si_2$ $[M+Na]^+$ 627.3280, found 627.3271.

2.2 DEF spiroacetal fragment coupling - Julia

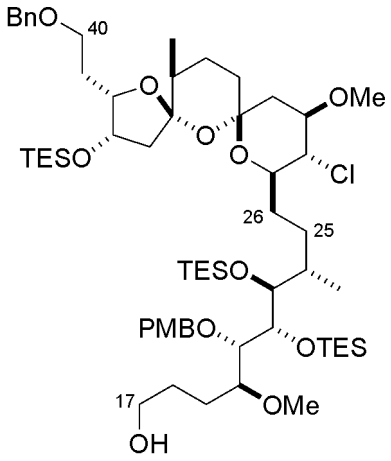
Diene 20



Freshly prepared LiHMDS (0.5 M in THF, 169 μL, 84.6 μmol) was added dropwise to a stirred solution of sulfone **4** (21.1 mg, 28.2 μmol) in THF (1 mL) at –78 °C. The resulting bright yellow solution was stirred for 1 h before the addition of a solution of aldehyde **10** (crude, from 33 mg of alcohol **6**, < 56.4 μmol) in THF (0.5 mL) *via* cannula. The reaction mixture was stirred at –78 °C for 1 h before being allowed to warm to room temperature and stirred for 16 h. The red reaction mixture was quenched with NH_4Cl solution (2 mL) and extracted with Et_2O (3 × 10 mL). The combined organic phases were dried ($MgSO_4$), concentrated *in vacuo* and the residue purified by flash column chromatography (SiO_2, 10:1 40-60 petroleum ether / Et_2O) to afford diene **20** (8.0 mg, 7.1 μmol, 25 % based on sulfone **4**) as a colourless oil; $\mathbf{R_f}$ 0.45 (3:1 40-60 petroleum ether / Et_2O); $\mathbf{[\alpha]_D^{20}}$ –8.1 (c 0.27, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2954, 2877, 1514, 1457, 1380, 1247, 1101, 1006, 977, 739; **^{1}H NMR** (500 MHz, C_6D_6) δ 7.47-7.41 (2H, m, ArH), 7.43 (2H, d, *J* = 8.6 Hz, ArH), 7.25-7.21 (2H, m, ArH), 7.16-7.07 (1H, m, ArH), 6.83 (2H, d, *J* = 8.6 Hz, ArH), 6.26 (1H, ddd, *J* = 15.6, 8.1, 1.2 Hz, H25), 6.20 (1H, dd, *J* = 15.6, 2.9 Hz, H26), 6.20-6.11 (1H, m, H18), 5.22 (1H, dd, *J* = 17.1, 2.0 Hz, H17), 5.11 (1H, dd, *J* = 10.3, 2.0 Hz, H17), 4.93 (1H, d, *J* = 11.2 Hz, $ArCH_2O$), 4.84 (1H, d, *J* = 11.2 Hz, $ArCH_2O$), 4.64-4.59 (2H, m, $ArCH_2O$, H27), 4.50 (1H, d, *J* = 11.9 Hz, $ArCH_2O$), 4.34-4.29 (1H, m, H38), 4.07-4.02 (2H, m, H37, H22), 4.01-3.95 (2H, m, H21, H29), 3.86 (1H, dd, *J* = 7.7, 2.0 Hz, H23), 3.83 (1H, t, *J* = 9.7 Hz, H28), 3.78-3.72 (1H, m, H40), 3.72-3.66 (2H, m, H20, H40), 3.35 (3H, s, OMe), 3.30 (3H, s, MeO), 3.29 (3H, s, MeO), 2.84-2.74 (2H, m, H19, H24), 2.52-2.46 (1H, m, H19), 2.29-2.17 (3H, m, H30, H33, H36), 2.17-2.04 (2H, m, H39), 1.97 (1H, dd, *J* = 14.1, 2.4 Hz, H36), 1.86 (1H, dt, *J* = 13.1, 3.1 Hz, H32), 1.61-1.52 (1H, m, H34), 1.51-1.41 (2H, m, H30, H32), 1.31 (1H, dq, *J* = 13.1, 3.4 Hz, H33), 1.25 (3H, d, *J* = 6.7 Hz, Me24), 1.16 (9H, t, *J* = 7.9 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.09 (9H, t, *J* = 7.9 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.07 (3H, d, *J*

= 6.7 Hz, Me34), 0.95 (9H, t, *J* = 7.9 Hz, Si($CH_2C\underline{H}_3$)$_3$), 0.87 (6H, dq, *J* = 7.9, 5.0 Hz, Si($C\underline{H}_2CH_3$)$_3$), 0.77 (6H, q, *J* = 7.9 Hz, Si($C\underline{H}_2$(CH_3)$_3$), 0.52 (6H, q, *J* = 7.9 Hz, Si($C\underline{H}_2CH_3$)$_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ 159.5, 139.4, 136.4, 135.0, 132.1, 129.3, 128.8, 128.6, 128.5, 127.6, 127.5, 127.4, 127.1, 116.4, 113.9, 108.8, 97.8, 81.9, 81.3, 81.1, 80.0, 79.6, 76.2, 74.1, 73.1, 72.5, 72.5, 68.3, 65.6, 57.5, 57.2, 54.7, 49.5, 43.5, 40.9, 38.1, 36.5, 35.1, 30.0, 24.2, 19.5, 16.6, 7.7, 7.5, 7.1, 5.8, 5.8, 5.1; **HRMS** calc. for $C_{61}H_{103}ClO_{11}Si_3Na$ $[M + Na]^+$ 1153.6394, found 1153.6398.

Alcohol 22



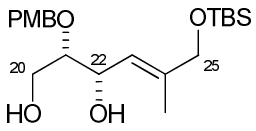
To a stirred solution of diene **20** (1.7 mg, 1.5 μmol) in THF (200 μL) at 0 °C was added $BH_3{\cdot}SMe_2$ (10 M, 1 drop). The reaction mixture was stirred at 0 °C for 1 h before adding 30 % H_2O_2 (0.1 mL) and pH 7 buffer solution (0.1 mL). After stirring for 1 h at room temperature, the mixture was extracted with Et_2O (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Primary alcohol **21** (1.4 mg, 1.2 μmol, 81 %) was submitted for the next reaction without further purification.

A solution of glacial acetic acid (27.0 μL, 0.480 mmol) in MeOH (0.2 mL) was added dropwise to a stirred mixture of **21** (1.4 mg, 1.2 μmol) and freshly prepared dipotassium azodicarboxylate (47 mg, 0.24 mmol) in pyridine (0.1 mL) at room temperature. The reaction mixture was stirred for 5 days before being quenched with NH_4Cl solution (0.5 mL) and diluted with Et_2O (0.5 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 0.5 mL) and the combined organic phases were washed with $CuSO_4$ solution (2 × 0.5 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 6:1 40-60 petroleum ether / EtOAc) afforded alcohol **22** (1.4 mg, 1.2 μmol, 99 %) as a colourless oil; $\mathbf{R_f}$ 0.14 (EtOAc / PE 40-60, 1:4); $\mathbf{[\alpha]}_D^{20}$ +7.9 (*c* 0.62, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3452, 2952, 2876, 1612, 1514, 1457, 1381, 1246, 1170,

1081, 1014, 976, 739; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.45 (2H, d, *J* = 8.6 Hz, ArH), 7.40 (2H, d, *J* = 7.4 Hz, ArH), 7.23 (2H, app t, *J* = 7.7 Hz, ArH), 7.10 (1H, app t, *J* = 7.4, Hz, ArH), 6.84 (2H, d, *J* = 8.6 Hz, ArH), 4.96 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.83 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.55 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.46 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.35 (1H, ddd, *J* = 6.3, 4.4, 0.5 Hz, H38), 4.22 (1H, m, H27), 4.15 (1H, m, H37), 4.03 (1H, dd, *J* = 7.5, 1.2 Hz, H22), 4.01 (1H, dd, *J* = 7.5, 2.0 Hz, H21), 3.93 (1H, m, H28), 3.91 (1H, m, H29), 3.74-3.69 (2H, m, H40, H23), 3.66 (1H, m, H40), 3.59 (1H, m, H20), 3.57-3.49 (2H, m, 2 × H17), 3.34 (3H, s, OMe), 3.31 (3H, s, OMe), 3.30 (3H, s, OMe), 2.33-2.28 (2H, m, 2 × H26), 2.24-2.12 (5H, m, 2 × H39, H36, H33, H30), 2.11-2.00 (3H, m, H25, 2 × H19), 1.97 (1H, dd, *J* = 14.1, 2.9 Hz, H36), 1.89-1.69 (4H, m, H32, H24, 2 × H18), 1.54 (1H, m, H34), 1.46-1.24 (4H, m, H33, H32, H30, H25), 1.17 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.13 (3H, d, *J* = 6.7 Hz, Me_{24}), 1.08 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.06 (3H, d, *J* = 6.4 Hz, Me34), 0.95 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.91 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.90 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.52 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 159.3, 139.0, 132.0, 129.3, 128.4, 113.7, 108.5, 97.5, 82.5, 82.2, 80.8, 80.0, 79.5, 76.1, 74.2, 73.0, 72.1, 67.9, 63.8, 62.5, 57.3, 56.8, 54.5, 48.9, 43.5, 37.8, 36.8, 36.2, 30.2, 30.0, 29.7, 29.6, 26.7, 26.3, 24.0, 17.7, 16.5, 7.5, 7.3, 6.9, 5.9, 5.7, 5.6, 4.9; **HRMS** (ES^+) calcd for $C_{61}H_{107}ClO_{12}Si_3Na$ $[M+Na]^+$ 1173.6694, found 1173.6651.

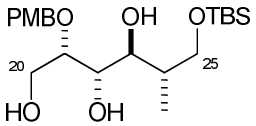
2.3 DEF spiroacetal fragment coupling - Suzuki

Diol 23

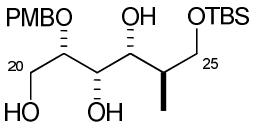


R_f 0.38 (EtOAc / PE 40-60, 1:1); **[α]** $^{20}_{D}$ +13.5 (*c* 0.70, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3428, 2929, 2857, 1613, 1514, 1249, 1111, 1036, 837, 777; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (2H, d, *J* = 8.7 Hz, ArH), 6.89 (2H, d, *J* = 8.7 Hz, ArH), 5.50 (1H, dq, *J* = 9.1, 1.4 Hz, H23), 4.66 (1H, d, *J* = 11.1 Hz, CH_2Ar), 4.62 (1H, d, *J* = 11.1 Hz, CH_2Ar), 4.52 (1H, dd, *J* = 9.1, 6.9 Hz, H22), 4.02 (2H, s, 2 × H25), 3.81 (3H, s, OMe), 3.76 (1H, dd, *J* = 11.9, 4.0 Hz, H20), 3.56 (1H, dd, *J* = 11.9, 4.2 Hz, H20), 3.41 (1H, dt, *J* = 6.9, 4.1 Hz, H21), 2.15 (2H, br s, 2 × OH), 1.68 (3H, d, *J* = 1.4 Hz, Me24), 0.91 (9H, s, *t*-BuSi), 0.02 (6H, s, 2 × SiMe); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.5, 140.3, 130.1, 129.6, 129.1, 121.9, 113.9, 82.6, 72.8, 68.5, 67.5, 61.2, 55.3, 25.9, 18.4, 14.1, −5.3; **HRMS** (ES^+) calcd for $C_{21}H_{37}O_5Si$ $[M+H]^+$ 397.2410, found 397.2415.

Triols 24 & 25



24



25

To a stirred solution of allylic alcohol **23** (11.0 mg, 27.7 μmol) in THF (500 μL) was added $BH_3{\cdot}SMe_2$ (2 M in THF, 41.7 μL, 83.3 μmol). The reaction mixture was stirred for 2 h before being cooled to 0 °C and quenched with MeOH (500 μL), H_2O_2 (30% aq., 500 μL) and NaOH (2.5M, 200 μL). The mixture was stirred for 1 h at RT, then diluted with CH_2Cl_2 (5 mL) and neutralised with NH_4Cl (1 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:1) afforded triols **24** and **25** (inseparable 3:1 mixture, 8.5 mg, 20.5 μmol, 74 %) as a colourless oil.

Major Isomer 24:

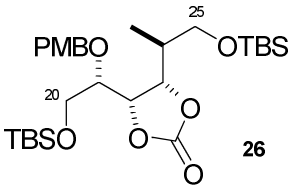
R_f 0.49 (EtOAc / PE 40-60, 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.28 (2H, d, *J* = 8.7 Hz, ArH), 6.89 (2H, d, *J* = 8.7 Hz, ArH), 4.68 (1H, d, *J* = 11.2 Hz, CH_2Ar), 4.57 (1H, d, *J* = 11.2 Hz, CH_2Ar), 3.96 (1H, dd, *J* = 10.2, 2.8 Hz, H21), 3.88-3.74 (7H, m, H25, H23, 2 × H20, ArOMe), 3.72-3.63

(2H, m, H25, OH), 3.61 (1H, m, H22), 3.11 (1H, d, *J* = 5.4 Hz, OH), 2.89 (1H, br m, OH), 2.07 (1H, m, H24), 1.10 (3H, d, *J* = 7.3 Hz, Me24), 0.90 (9H, s, *t*-BuSi), 0.08 (6H, s, 2 × SiMe).

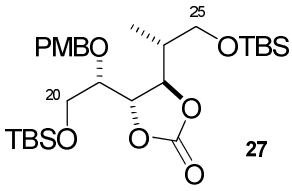
Minor Isomer 25:

R_f 0.49 (EtOAc / PE 40-60, 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.28 (2H, d, *J* = 8.7 Hz, ArH), 6.89 (2H, d, *J* = 8.7 Hz, ArH), 4.66 (1H, d, *J* = 11.4 Hz, CH_2Ar), 4.55 (1H, d, *J* = 11.4 Hz, CH_2Ar), 3.88-3.74 (8H, m, H25, H23, H21, 2 x H20, OMe), 3.72-3.63 (2H, m, H25, OH), 3.58 (1H, m, H22), 3.6 (1H, d, *J* = 6.2 Hz, OH), 2.80 (1H, br m, OH), 1.94 (1H, m, H24), 0.91 (9H, s, *t*-BuSi), 0.87 (3H, d, *J* = 7.3 Hz, Me24), 0.08 (6H, s, 2 × SiMe).

Carbonates 26 & 27



26



27

To a stirred solution of triols **24** and **25** (8.5 mg, 20.5 μmol) in CH_2Cl_2 (500 μL) was added imidazole (2.1 mg, 30.8 μmol) and TBSCl (3.7 mg, 24.6 μmol). The reaction mixture was stirred for 2 h before being diluted with CH_2Cl_2 (3 mL) and quenched with H_2O (500 μL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (500 μL) and cooled to –78 °C. Pyridine (8.3 μL, 0.103 mmol), Et_3N (14.3 μL, 0.103 mmol) and triphosgene (6.1 mg, 20.5 μmol) were added sequentially and the reaction mixture was allowed to warm to 0 °C over 30 min before being quenched with $NaHCO_3$ (500 μL). The mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:7) afforded the carbonates **26** (5.6 mg, 10.1 μmol, 49 %) and **27** (2.0 mg, 3.6 μmol, 18 %) as colourless oils;

Major Isomer 26:

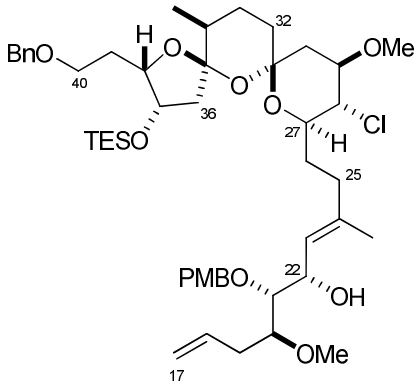
R_f 0.38 (EtOAc / PE 40-60, 1:5); **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.18 (2H, d, *J* = 8.7 Hz, ArH), 6.74 (2H, d, *J* = 8.7 Hz, ArH), 4.54 (1H, d, *J* = 7.0 Hz, H22), 4.42 (1H, d, *J* = 11.7 Hz, CH_2Ar), 4.19 (1H, d, *J* = 11.7 Hz, CH_2Ar), 4.09 (1H, dd, *J* = 11.3, 7.0 Hz, H23), 3.71 (2H, d, *J* = 7.0 Hz, 2 × H20), 3.60 (1H, dd, *J* = 9.8, 5.5 Hz, H25), 3.54 (1H, t, *J* = 7.0 Hz, H21), 3.50 (1H, dd, *J* = 9.7, 2.7 Hz, H25), 3.26 (3H, s, ArOMe), 1.89 (1H, m, H24), 0.93 (9H, s, *t*-BuSi), 0.92 (9H, s, *t*-BuSi), 0.72

(3H, d, *J* = 6.6 Hz, Me24), 0.03 (3H, s, SiMe), 0.02 (3H, s, SiMe), 0.00 (3H, s, SiMe), −0.01 (3H, s, SiMe).

Minor Isomer 27:

R_f 0.32 (EtOAc / PE 40-60, 1:5); **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.15 (2H, obs m, ArH), 6.74 (2H, d, *J* = 8.4 Hz, ArH), 4.62 (1H, dd, *J* = 4.8, 2.8 Hz, H22), 4.51 (1H, d, *J* = 11.9 Hz, CH_2Ar), 4.41 (1H, dd, *J* = 6.7, 4.8 Hz, H23), 4.31 (1H, d, *J* = 11.9 Hz, CH_2Ar), 3.76 (2H, m, 2 × H20), 3.36 (1H, dd, *J* = 6.6, 5.0 Hz, H25), 3.32 (1H, m, H25), 3.28 (1H, m, H21), 3.28 (3H, s, ArOMe), 1.54 (1H, m, H24), 0.93 (9H, s, *t*-BuSi), 0.90 (9H, s, *t*-BuSi), 0.67 (3H, d, *J* = 6.9 Hz, Me24), 0.04 (3H, s, SiMe), 0.02 (3H, s, SiMe), −0.01 (6H, s, 2 × SiMe).

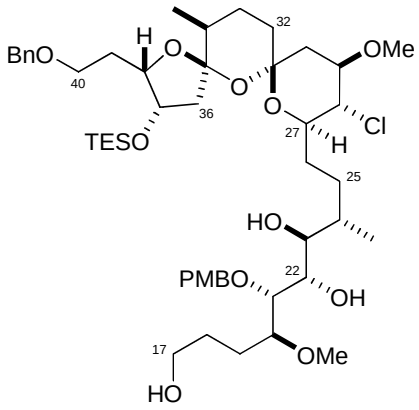
Diene 29



To a stirred solution of olefin **11** (18.0 mg, 31.0 µmol) in THF (750 µL) was added 9-BBN (0.5M in THF, 124 µL, 62.0 µmol). The reaction mixture was stirred for 24 h before being quenched with H_2O (50 µL) and diluted with DMF (2 mL). A solution of vinyl iodide **5** (20.1 mg, 46.5 µmol), Cs_2CO_3 (30.3 mg, 92.9 µmol) and Ph_3As (4.7 mg, 15.5 µmol) was then prepared in degassed DMF (1 mL) and $PdCl_2$(dppf) (4.5 mg, 6.2 µmol) added. The borane solution was then added slowly dropwise and the reaction mixture was stirred for 30 min before being quenched with NH_4Cl (1 mL) and diluted with Et_2O (2 mL). The organic phase was separated and the aqueous phase extracted with Et_2O (3 × 5 mL). The combined organic phases were washed with H_2O (2 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, Et_2O / PE 40-60, 1:2) afforded diene **29** (21.8 mg, 24.6 µmol, 83 %) as a colourless oil; **R_f** 0.44 (EtOAc / PE 40-60, 1:2); **[α]** $^{20}_{D}$ −11.0 (*c* 0.69, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3479, 2934, 2877, 1613, 1514, 1455, 1382, 1248, 1098, 1017, 975, 920, 737; **^{1}H NMR** (500 MHz, C_6D_6) δ 7.41 (2H, d, *J* = 7.5 Hz, ArH), 7.23 (4H, m, ArH), 7.09 (1H, t, *J* = 7.6 Hz, ArH), 6.80 (2H, d, *J* = 8.6 Hz, ArH), 5.97 (1H, ddt, *J* =

17.2, 10.2, 7.0 Hz, H18), 5.57 (1H, dq, *J* = 8.6, 1.1 Hz, H23), 5.10 (1H, dd, *J* = 17.2, 1.5 Hz, H17), 5.05 (1H, dd, *J* = 10.2, 1.5 Hz, H17), 4.66 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.64 (1H, m, H22), 4.52 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.50 (1H, d, *J* = 12.1 Hz, CH_2Ar), 4.40 (1H, d, *J* = 12.1 Hz, CH_2Ar), 4.38 (1H, m, H38), 4.26 (1H, m, H37), 4.12 (1H, m, H27), 3.89 (1H, ddd, *J* = 11.3, 9.7, 4.9 Hz, H29), 3.74 (1H, app t, *J* = 9.8 Hz, H28), 3.64-3.53 (3H, m, 2 × H40, H21), 3.42 (1H, m, H20), 3.33 (3H, s, OMe), 3.30 (3H, s, OMe), 3.15 (3H, s, OMe), 2.73 (1H, d, *J* = 5.5 Hz, OH), 2.60-2.48 (2H, m, H25, H19), 2.45-2.34 (3H, m, H26, H25, H19), 2.18-2.00 (5H, m, 2 × H39, H36, H33, H30), 1.97 (1H, dd, *J* = 13.7, 3.9 Hz, H36), 1.92 (1H, m, H26), 1.72 (1H, m, H32), 1.70 (3H, d, *J* = 1.1 Hz, Me24), 1.54 (1H, m, H34), 1.45-1.19 (3H, m, H33, H32, H30), 1.01 (3H, d, *J* = 6.7 Hz, Me34), 0.96 (9H, t, *J* = 7.8 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.55 (6H, q, *J* = 7.8 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ 159.6, 139.4, 139.1, 129.6, 128.3, 125.5, 116.6, 113.9, 108.3, 97.4, 82.7, 81.7, 80.5, 79.4, 73.7, 73.0, 72.9, 71.8, 71.5, 68.0, 67.6, 64.3, 57.3, 54.6, 48.1, 43.4, 37.6, 36.1, 34.9, 34.7, 31.1, 30.2, 29.8, 27.6, 25.2, 23.9, 22.7, 17.0, 16.6, 6.9, 4.9; **HRMS** (ES^+) calcd for $C_{49}H_{75}ClO_{10}SiNa$ $[M+Na]^+$ 909.4695, found 909.4710.

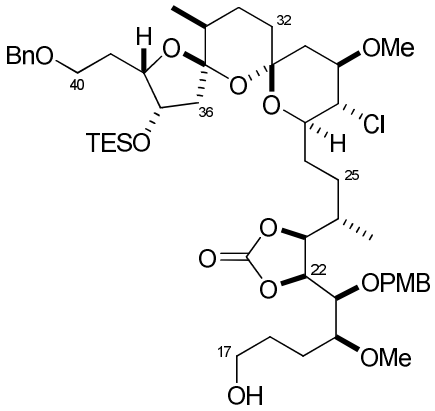
Triol 30



To a stirred solution of diene **29** (25.0 mg, 28.2 μmol) in THF (3 mL) was added $BH_3{\cdot}SMe_2$ (2M in THF, 141 μL, 282 μmol). The reaction mixture was stirred for 2 h before being cooled to 0 °C and quenched cautiously with MeOH (1 mL). H_2O_2 (30% aq., 500 μL) and NaOH (1M, 200 μL) was added, and the mixture was stirred vigorously for 1 h at RT. The organic phase was then separated, the aqueous phase extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was used without further purification. For the purposes of characterisation an additional sample was purified by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:1→3:1) to afford triol **30** as a colourless oil; **R_f** 0.37 (EtOAc / PE 40-60, 2:1); **[α]** $^{20}_{D}$ −4.6 (*c* 0.50, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3465, 2928, 2875, 1613, 1514, 1460,

1380, 1301, 1248, 1172, 1092, 1036, 977, 742; **^{1}H NMR** (500 MHz, C_6D_6) δ 7.41 (2H, m, ArH), 7.27 (2H, d, *J* = 8.7 Hz, ArH), 7.23 (2H, t, *J* = 7.5 Hz, ArH), 7.09 (1H, tt, *J* = 7.5, 1.3 Hz, ArH), 6.80 (2H, d, *J* = 8.6 Hz, ArH), 4.63 (2H, s, CH_2Ar), 4.52 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.45 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.41 (1H, m, H38), 4.35 (1H, ddd, *J* = 9.8, 6.2, 4.6 Hz, H37), 4.06 (1H, m, H27), 4.01 (1H, m, H22), 3.96 (1H, dd, *J* = 5.5, 1.7 Hz, H21), 3.89 (1H, m, H29), 3.74 (1H, app t, *J* = 9.9 Hz, H28), 3.72 (1H, m, H40), 3.69 (1H, m, H23), 3.59 (1H, m, H40), 3.49 (1H, m, H20), 3.47-3.41 (2H, m, 2 × H17), 3.33 (3H, s, OMe), 3.30 (3H, s, OMe), 3.25 (3H, s, OMe), 2.98 (1H, d, *J* = 7.5 Hz, OH22), 2.48-2.40 (2H, m, H26, OH23), 2.34-2.27 (1H, m, H25), 2.21-2.08 (5H, m, H39, H36, H33, H30, H24), 2.02 (1H, m, H39), 1.96 (1H, dd, *J* = 13.6, 4.6 Hz, H36), 1.84-1.62 (5H, m, H32, H26, 2 × H19, H18), 1.61-1.45 (3H, m, H34, H25, H18), 1.40-1.27 (2H, m, H32, H30), 1.26-1.16 (2H, m, H33, OH17), 1.08 (3H, d, *J* = 6.9 Hz, Me24), 1.00 (3H, d, *J* = 6.7 Hz, Me34), 0.96 (9H, t, *J* = 8.0 Hz, Si($CH_2C\underline{H}_3$)$_3$), 0.53 (6H, q, *J* = 8.0 Hz, Si($C\underline{H}_2CH_3$)$_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ 159.7, 142.1, 130.9, 129.9, 128.4, 114.0, 108.1, 97.4, 82.6, 80.0, 79.5, 78.5, 77.0, 73.7, 73.5, 72.6, 71.8, 71.1, 67.2, 65.0, 62.6, 58.1, 57.3, 54.6, 47.5, 43.4, 37.4, 36.1, 35.3, 30.8, 30.0, 29.3, 29.0, 27.3, 24.7, 23.8, 16.7, 16.6, 6.9, 4.9; **HRMS** (ES^+) calcd for $C_{49}H_{79}ClO_{12}SiNa$ $[M+Na]^+$ 945.4952, found 945.4933.

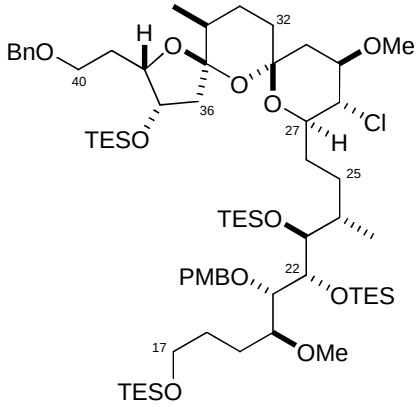
Carbonate 31



To a stirred solution of triol **30** (1.5 mg, 1.6 µmol) in CH_2Cl_2 (300 µL) at –78 °C was added pyridine (1.3 µL, 10.6 µmol), Et_3N (2.3 µL, 10.6 µL) and triphosgene (2.4 mg, 8.1 µmol). The reaction mixture was allowed to warm to RT and stirred for 30 min before being diluted with CH_2Cl_2 (2 mL) and quenched with $NaHCO_3$ (1 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:4) afforded carbonate **31** (0.7 mg, 0.7 µmol, 44%) as a colourless oil; $\mathbf{R_f}$ 0.46 (EtOAc / PE 40-60,

1.2); **^{1}H NMR** (500 MHz, C_6D_6) δ 7.42 (2H, d, *J* = 7.5 Hz, ArH), 7.33 (2H, d, *J* = 8.6 Hz, ArH), 7.22 (2H, app t, *J* = 7.6 Hz, ArH), 7.09 (1H, app t, *J* = 7.5 Hz, ArH), 6.82 (2H, d, *J* = 8.6 Hz, ArH), 4.72 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.70 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.65 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.59 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.41 (1H, m, H38), 4.36 (1H, dt, *J* = 6.4, 4.6 Hz, H37), 4.23 (1H, dd, *J* = 6.7, 2.4 Hz, H22), 4.08 (1H, m, H27), 3.89 (1H, m, H29), 3.85 (1H, dd, *J* = 9.2, 6.7 Hz, H23), 3.80-3.66 (3H, m, 2 × H40, H28), 3.44 (1H, dd, *J* = 6.9, 2.4 Hz, H21), 3.32 (3H, s, OMe), 3.31 (3H, s, OMe), 3.10-3.04 (3H, m, H20, 2 × H17), 2.96 (3H, s, OMe), 2.29-2.21 (4H, m, H39, H36, H26, H18), 2.17-2.09 (5H, m, H39, H30, H32, H25, H18), 1.99 (1H, dd, *J* = 13.6, 4.3 Hz, H36), 1.77 (1H, m, H24), 1.71 (1H, dt, *J* = 13.0, 2.8 Hz, H33), 1.65-1.44 (5H, m, H34, H26, H25, 2 × H19), 1.42-1.14 (3H, m, H33, H32, H30), 1.04 (3H, d, *J* = 6.7 Hz, Me34), 0.97 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.64 (3H, d, *J* = 6.7 Hz, Me24), 0.55 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$).

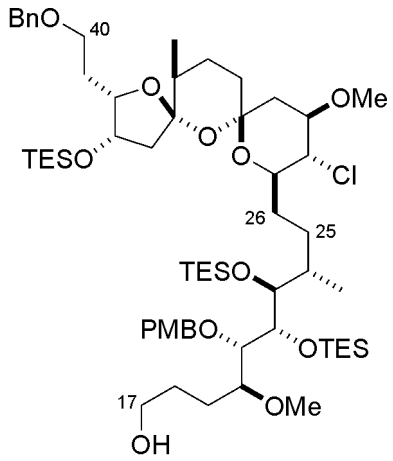
***Tetra*-TES ether 32**



To a stirred solution of crude triol **30** (≤28.2 μmol) in CH_2Cl_2 (2 mL) at 0 °C was added 2,6-lutidine (66.0 μL, 0.567 mmol) and TESOTf (64.1 μL, 0.283 mmol). The reaction was stirred for 30 min before being diluted with CH_2Cl_2 (5 mL) and quenched with $NaHCO_3$ (1 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:20) afforded *tetra*-TES ether **32** (27.5 mg, 21.7 mmol, 77 % from diene **29**) as a colourless oil; $\mathbf{R_f}$ 0.74 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ +10.5 (*c* 0.49, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2953, 2876, 1613, 1514, 1457, 1381, 1246, 1170, 1092, 1009, 976, 739; **^{1}H NMR** (500 MHz, C_6D_6) δ 7.47 (2H, d, *J* = 8.7 Hz, ArH), 7.42 (2H, dd, *J* = 8.1, 1.2 Hz, ArH), 7.24 (2H, app t, *J* = 7.5 Hz, ArH), 7.11 (1H, tt, *J* = 7.5, 1.2 Hz, ArH), 6.85 (2H, d, *J* = 8.7 Hz, ArH), 5.01 (1H, d, *J* = 11.1 Hz, CH_2Ar), 4.86 (1H, d, *J* = 11.1 Hz, CH_2Ar), 4.57 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.48 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.37 (1H, td, *J* = 6.5, 4.4 Hz, H38), 4.20 (1H, m, H37), 4.18 (1H, m, H27), 4.08 (1H, dd, *J* = 7.5, 1.5 Hz, H22), 4.04 (1H, dd, *J* = 7.5, 2.3 Hz, H21), 3.93 (1H, ddd, *J* = 10.6,

9.4, 4.8 Hz, H29), 3.90 (1H, app t, *J* = 9.8 Hz, H28), 3.77 (1H, dd, *J* = 8.0, 1.5 Hz, H23), 3.75-3.63 (4H, m, 2 × H40, 2 × H17), 3.61 (1H, dt, *J* = 9.2, 2.3 Hz, H20), 3.36 (3H, s, OMe), 3.35 (3H, s, OMe), 3.30 (3H, s, OMe), 2.33 (2H, m, 2 × H26), 2.22-2.02 (7H, m, 2 × H39, H36, H33, H30, 2 × H19), 1.98 (1H, dd, *J* = 13.8, 2.9 Hz, H36), 1.96 (1H, m, H25), 1.90-1.78 (4H, m, H32, H24, 2 × H18), 1.54 (1H, m, H34), 1.46-1.25 (4H, m, H33, H32, H30, H25), 1.17 (3H, d, *J* = 6.7 Hz, Me24), 1.07 (3H, d, *J* = 6.6 Hz, Me34), 1.18 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.10 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.04 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.96 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.92 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.80 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.63 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.53 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ 159.2, 139.1, 132.1, 129.1, 113.6, 108.4, 97.5, 82.5, 82.1, 80.8, 79.9, 79.5, 76.1, 74.2, 73.2, 73.0, 72.0, 67.9, 64.0, 63.3, 57.3, 57.0, 54.5, 48.8, 43.5, 37.8, 36.9, 36.2, 30.0, 29.7, 26.9, 26.6, 24.0, 17.8, 16.5, 7.5, 7.3, 7.0, 6.9, 5.9, 5.7, 5.6, 4.9, 4.7; **HRMS** (ES^+) calcd for $C_{67}H_{121}ClO_{12}Si_4Na$ $[M+Na]^+$ 1287.7555, found 1287.7527.

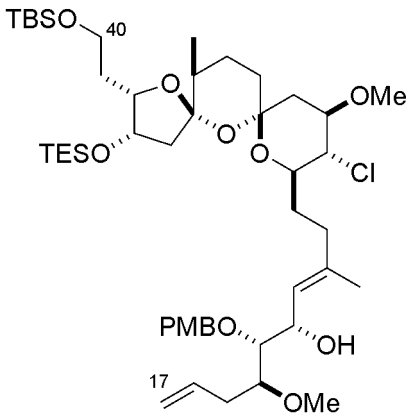
Alcohol 22



To a stirred solution of *tetra*-silyl ether **32** (20.0 mg, 15.5 µmol) in CH_2Cl_2 / MeOH (12:1, 3 mL) at 0 °C was added PPTS (1 crystal). The reaction was stirred for 30 min before being quenched with $NaHCO_3$ (1 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. No further purification was required to afford pure alcohol **22** (17.9 mg, 15.2 µmol, 98 %) as a colourless oil; **R_f** 0.14 (EtOAc / PE 40-60, 1:4); **[α]** $_D^{20}$ +7.9 (*c* 0.62, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3452, 2952, 2876, 1612, 1514, 1457, 1381, 1246, 1170, 1081, 1014, 976, 739; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.45 (2H, d, *J* = 8.6 Hz, ArH), 7.40 (2H, d, *J* = 7.4 Hz, ArH), 7.23 (2H, app t, *J* = 7.7 Hz, ArH), 7.10 (1H, app t, *J* = 7.4, Hz, ArH), 6.84 (2H, d, *J* = 8.6 Hz, ArH), 4.96 (1H, d, *J* = 11.0 Hz, CH_2Ar),

4.83 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.55 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.46 (1H, d, *J* = 12.0 Hz, CH_2Ar), 4.35 (1H, ddd, *J* = 6.3, 4.4, 0.5 Hz, H38), 4.22 (1H, m, H27), 4.15 (1H, m, H37), 4.03 (1H, dd, *J* = 7.5, 1.2 Hz, H22), 4.01 (1H, dd, *J* = 7.5, 2.0 Hz, H21), 3.93 (1H, m, H28), 3.91 (1H, m, H29), 3.74-3.69 (2H, m, H40, H23), 3.66 (1H, m, H40), 3.59 (1H, m, H20), 3.57-3.49 (2H, m, 2 × H17), 3.34 (3H, s, OMe), 3.31 (3H, s, OMe), 3.30 (3H, s, OMe), 2.33-2.28 (2H, m, 2 × H26), 2.24-2.12 (5H, m, 2 × H39, H36, H33, H30), 2.11-2.00 (3H, m, H25, 2 × H19), 1.97 (1H, dd, *J* = 14.1, 2.9 Hz, H36), 1.89-1.69 (4H, m, H32, H24, 2 × H18), 1.54 (1H, m, H34), 1.46-1.24 (4H, m, H33, H32, H30, H25), 1.17 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.13 (3H, d, *J* = 6.7 Hz, Me_{24}), 1.08 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.06 (3H, d, *J* = 6.4 Hz, Me34), 0.95 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.91 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.90 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.52 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 159.3, 139.0, 132.0, 129.3, 128.4, 113.7, 108.5, 97.5, 82.5, 82.2, 80.8, 80.0, 79.5, 76.1, 74.2, 73.0, 72.1, 67.9, 63.8, 62.5, 57.3, 56.8, 54.5, 48.9, 43.5, 37.8, 36.8, 36.2, 30.2, 30.0, 29.7, 29.6, 26.7, 26.3, 24.0, 17.7, 16.5, 7.5, 7.3, 6.9, 5.9, 5.7, 5.6, 4.9; **HRMS** (ES^+) calcd for $C_{61}H_{107}ClO_{12}Si_3Na$ $[M+Na]^+$ 1173.6694, found 1173.6651.

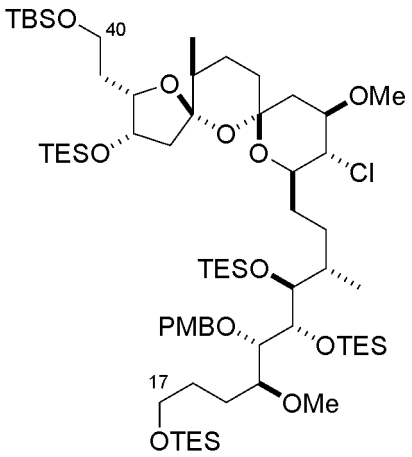
Diene 36



9-BBN (0.5 M in THF, 982 µL, 0.491 mmol) was added to a stirred solution of alkene **35** (198 mg, 0.327 mmol) in THF (1 mL) and the resulting solution was stirred for 4 h before being quenched with H_2O (295 µL) and diluted with DMF (3 mL). Meanwhile, a solution of vinyl iodide **5** (184 mg, 0.426 mmol), Cs_2CO_3 (320 mg, 0.982 mmol), Ph_3As (25 mg, 0.0.082 mol) in THF / DMF (1:1 v/v, 6 mL) was prepared. Both the borane and the vinyl iodide solutions were then carefully degassed before addition of $PdCl_2$(dppf) (24 mg, 0.033 mmol) to the vinyl iodide solution, followed by addition of the borane solution dropwise *via* cannula. The reaction mixture was stirred for 1 h at room temperature before being quenched with NH_4Cl (5 mL) and diluted with DCM (10 mL). After phase separation, the aqueous phase was extracted with DCM (3 × 15 mL) and the combined

organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 3:1 → 2:1 → 1:1 v/v 40-60 petroleum ether / Et_2O) afforded diene **36** (287 mg, 0.315 mmol, 96 %) as a yellow oil; $\mathbf{R_f}$ 0.37 (Et_2O / PE 40-60, 1:1); $[\alpha]_D^{20}$ +6.2 (*c* 0.69, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3503, 2954, 2930, 1613, 1515, 1463, 1382, 1249, 1098, 1039, 834, 776; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.26 (2H, d, *J* = 8.7 Hz, ArH), 6.81 (2H, d, *J* = 8.7 Hz, ArH), 6.01 (1H, ddt, *J* = 17.2, 10.1, 6.9 Hz, H18), 5.56 (1H, dq, *J* = 8.8, 1.3 Hz, H23), 5.13 (1H, dd, *J* = 17.2, 1.7 Hz, H17), 5.07 (1H, dd, *J* = 10.1, 1.7 Hz, H17), 4.71 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.64 (1H, dt, *J* = 8.5, 5.2 Hz, H22), 4.58 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.38 (2H, m, H38, H37), 4.08 (1H, ddd, *J* = 10.2, 7.2, 2.5 Hz, H27), 3.91-3.81 (3H, m, 2 × H40, H29), 3.74 (1H, app t, *J* = 9.9 Hz, H28), 3.58 (1H, app t, *J* = 5.2 Hz, H21), 3.45 (1H, dt, *J* = 6.9, 4.3 Hz, H20), 3.32 (6H, s, OMe, OMe), 3.20 (3H, s, OMe), 2.78 (1H, br d, *J* = 5.4 Hz, OH), 2.58-2.50 (2H, m, H25, H19), 2.46 (1H, m, H19), 2.40-2.31 (2H, m, H26, H25), 2.19 (1H, dd, *J* = 13.9, 6.2 Hz, H36), 2.15-2.01 (4H, m, 2 × H39, H33, H30), 1.99 (1H, dd, *J* = 13.9, 3.4 Hz, H36), 1.95 (1H, m, H26), 1.78 (3H, d, *J* = 1.3 Hz, Me24), 1.72 (1H, dt, *J* = 13.1, 3.2 Hz, H32), 1.50 (1H, m, H34), 1.39-1.30 (2H, m, H32, H30), 1.21 (1H, m, H33), 1.03 (3H, d, *J* = 6.9 Hz, Me34), 1.02 (9H, s, *t*-BuSi), 0.98 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.57 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.15 (3H, s, SiMe), 0.13 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 159.6, 139.2, 135.8, 130.9, 129.6, 125.5, 116.5, 113.9, 108.4, 97.4, 82.8, 81.7, 80.3, 79.4, 73.8, 73.0, 71.9, 68.1, 64.2, 60.7, 57.3, 54.6, 48.2, 43.4, 37.6, 36.1, 34.9, 34.5, 32.9, 30.8, 30.2, 26.1, 23.9, 18.3, 17.1, 16.5, 6.9, 5.0, −5.1, −5.3; **HRMS** (ES^+) calcd for $C_{48}H_{83}ClO_{10}Si_2Na$ $[M+Na]^+$ 933.5111, found 933.5122.

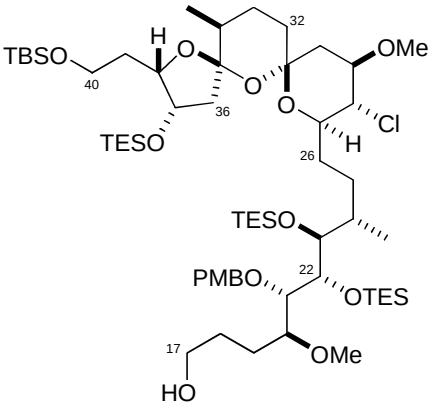
Tetra-TES ether 37



To a stirred solution of BH_3·DMS (10 M, 277 μL, 2.77 mmol) in THF (14 mL) was added a solution of diene **36** (253 mg, 0.277 mmol) in THF (14 mL) *via* syringe pump over 2 h. The

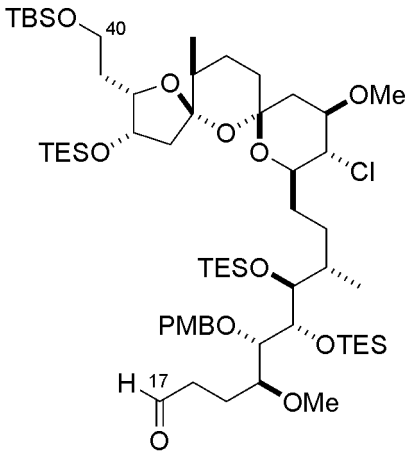
reaction mixture was stirred for an additional 1 h before being cooled to 0 °C and quenched by the sequential addition of MeOH (2.8 mL), 30 % H_2O_2 (2.8 mL), and 10 % NaOH (1.4 mL). The mixture was stirred for 1 h at room temperature before addition of Na^+/K^+ tartrate solution (2.8 mL) and stirring continued for a further 1 h. After removing THF *in vacuo*, the mixture was extracted with DCM (3 × 10 mL), the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The crude triol was redissolved in DCM (5 mL) and cooled to −78 °C. 2,6-lutidine (323 µL, 2.77 mmol) and TESOTf (318 µL, 1.39 mmol) were then added sequentially, and the reaction mixture was stirred for 30 min before being diluted with DCM (10 mL) and quenched with $NaHCO_3$ solution (10 mL). After phase separation, the aqueous phase was extracted with DCM (2 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 10:1 40-60 petroleum ether / Et_2O) afforded tetra-TES ether **37** (273 mg, 0.212 mmol, 77 % over 2 steps, 10:1 dr) as a colourless oil; $\mathbf{R_f}$ 0.62 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ –2.9 (*c* 0.93, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2954, 2877, 1514, 1460, 1415, 1382, 1247, 1094, 1006, 977, 739; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.48 (2H, d, *J* = 8.7 Hz, ArH), 6.86 (2H, d, *J* = 8.7 Hz, ArH), 5.02 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.87 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.37 (1H, ddd, *J* = 7.0, 6.0, 4.5 Hz, H38), 4.29 (1H, ddd, *J* = 7.0, 4.3, 2.9 Hz, H37), 4.18 (1H, ddd, *J* = 10.0, 5.8, 3.1 Hz, H27), 4.10 (1H, dd, *J* = 7.5, 1.6 Hz, H22), 4.05 (1H, dd, *J* = 7.5, 2.5 Hz, H21), 3.96-3.88 (4H, m, 2 × H40, H29, H28), 3.78 (1H, dd, *J* = 7.8, 1.6 Hz, H23), 3.74 (1H, m, H17), 3.68 (1H, m, H17), 3.61 (1H, dt, *J* = 8.9, 1.9 Hz, H20), 3.38 (3H, s, OMe), 3.34 (3H, s, OMe), 3.31 (3H, s, OMe), 2.33 (2H, m, H26, H25), 2.23 (1H, dd, *J* = 13.9, 6.6 Hz, H36), 2.20-2.05 (6H, m, 2 × H39, H33, H30, H19, H18), 2.01 (1H, m, H26), 2.00 (1H, dd, *J* = 13.9, 2.9 Hz, H36), 1.92-1.77 (4H, m, H32, H24, H19, H18), 1.54 (1H, m, H34), 1.46-1.25 (4H, m, H33, H32, H30, H25), 1.23 (3H, d, *J* = 6.9 Hz, Me24), 1.19 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.11 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.07 (3H, d, *J* = 6.9 Hz, Me34), 1.06 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.05 (9H, s, *t*-BuSi), 0.99 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.92 (6H, qd, *J* = 8.0, 2.9 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.80 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.64 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.57 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.20 (3H, s, SiMe), 0.18 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 159.2, 132.1, 129.1, 113.6, 108.5, 97.5, 82.5, 82.1, 80.5, 79.9, 79.5, 76.1, 74.1, 73.1, 72.1, 63.8, 63.3, 60.9, 57.3, 57.0, 54.5, 48.9, 43.5, 37.8, 36.9, 36.2, 33.0, 29.9, 29.8, 27.0, 26.4, 26.0, 24.0, 18.3, 17.9, 16.5, 7.5, 7.3, 7.0, 6.9, 5.7, 5.6, 5.0, 4.7, −5.1, −5.2; **HRMS** (ES^+) calcd for $C_{66}H_{129}ClO_{12}Si_5Na$ $[M+Na]^+$ 1311.7917, found 1311.7924.

Alcohol 37a



To a stirred solution of *tetra*-TES ether **37** (20.0 mg, 15.5 µmol) in CH_2Cl_2 / MeOH (12:1, 3 mL) at 0 °C was added PPTS (1 crystal). The reaction was stirred for 30 min before being quenched with $NaHCO_3$ (1 mL). The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. No further purification was required to afford pure alcohol **37a** (17.9 mg, 15.2 µmol, 98%) as a colourless oil; **R_f** 0.23 (EtOAc / PE 40-60, 1:4); **[α]** $^{20}_{D}$ –2.0 (*c* 0.44, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3500, 2955, 2877, 1615, 1514, 1459, 1382, 1248, 1100, 1009, 977, 932, 835, 738; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.46 (2H, d, *J* = 8.7 Hz, ArH), 6.85 (2H, d, *J* = 8.7 Hz, ArH), 4.97 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.85 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.35 (1H, ddd, *J* = 7.1, 5.8, 4.5 Hz, H38), 4.27 (1H, ddd, *J* = 7.1, 4.3, 2.8 Hz, H37), 4.19 (1H, m, H27), 4.05 (1H, dd, *J* = 7.4, 1.5 Hz, H22), 4.02 (1H, dd, *J* = 7.4, 2.2 Hz, H21), 3.96-3.89 (4H, m, 2 × H40, H29, H28), 3.74 (1H, dd, *J* = 7.8, 1.3 Hz, H23), 3.60 (1H, dt, *J* = 9.4, 2.1 Hz, H20), 3.57 (2H, m, 2 × H17), 3.33 (3H, s, OMe), 3.32 (3H, s, OMe), 3.30 (3H, s, OMe), 2.37-2.26 (2H, m, H26, H25), 2.23 (1H, dd, *J* = 13.9, 6.2 Hz, H36), 2.20-2.02 (7H, m, 2 × H39, H33, H30, H26, H19, OH), 1.99 (1H, dd, *J* = 13.9, 2.8 Hz, H36), 1.92-1.73 (5H, m, H32, H24, H19, 2 × H18), 1.54 (1H, m, H34), 1.47-1.23 (4H, m, H30, H33, H32, H25), 1.19 (3H, d, *J* = 6.6 Hz, Me24), 1.17 (9H, t, *J* = 8.0 Hz, Si($CH_2C\underline{H}_3$)$_3$), 1.10 (9H, t, *J* = 8.0 Hz, Si($CH_2C\underline{H}_3$)$_3$), 1.07 (3H, d, *J* = 6.9 Hz, Me34), 1.04 (9H, s, *t*-BuSi), 0.98 (9H, t, *J* = 8.0 Hz, Si($CH_2C\underline{H}_3$)$_3$), 0.90 (6H, dq, *J* = 8.0, 3.4 Hz, Si($C\underline{H}_2CH_3$)$_3$), 0.79 (6H, q, *J* = 8.0 Hz, Si($C\underline{H}_2CH_3$)$_3$), 0.57 (6H, q, *J* = 8.0 Hz, Si($C\underline{H}_2CH_3$)$_3$), 0.19 (3H, s, SiMe), 0.17 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 159.3, 132.0, 129.3, 127.3, 113.7, 108.5, 97.5, 82.5, 82.2, 80.6, 79.9, 79.5, 76.1, 74.2, 72.9, 72.2, 63.6, 62.6, 60.9, 57.3, 56.8, 54.4, 48.9, 43.5, 37.8, 36.8, 36.2, 33.0, 29.6, 29.5, 26.8, 26.2, 26.0, 24.0, 18.3, 17.8, 16.5, 7.5, 7.3, 6.9, 5.7, 5.6, 5.0, −5.1, −5.2; **HRMS** (ES$^+$) calcd for $C_{60}H_{115}ClO_{12}Si_4Na$ [M+Na]$^+$ 1197.7052, found 1197.7101.

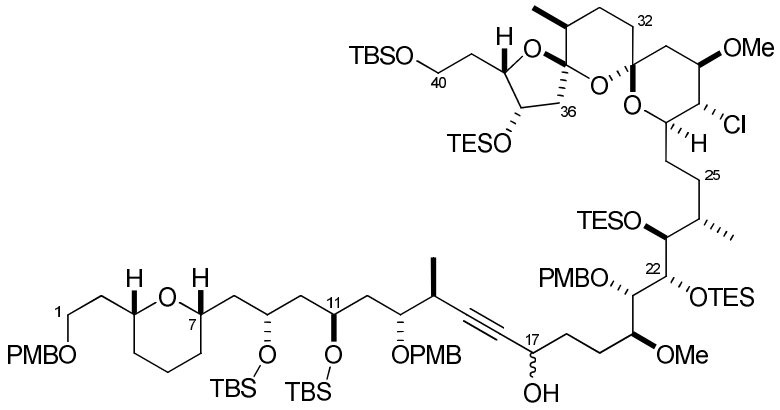
Aldehyde 38



To a stirred solution of alcohol **37a** (23.3 mg, 19.8 µmol) in CH_2Cl_2 (2 mL) was added sequentially $NaHCO_3$ (5.0 mg, 59.4 µmol) and DMP (16.8 mg, 39.7 µmol). The reaction was stirred for 1 h before being quenched with $NaHCO_3$ (1 mL) and $Na_2S_2O_3$ (1 mL) and stirred vigorously for 1 h. The organic phase was separated, the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:8) afforded aldehyde **38** (18.5 mg, 15.8 µmol, 80%) as a colourless oil; $\mathbf{R_f}$ 0.40 (EtOAc / PE 40-60, 1:6); $[\alpha]_D^{20}$ +9.2 (*c* 0.40, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2878, 1727, 1614, 1514, 1460, 1382, 1248, 1100, 1009, 977, 836, 740; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 9.52 (1H, s, H17), 7.43 (2H, d, *J* = 8.6 Hz, ArH), 6.85 (2H, d, *J* = 8.6 Hz, ArH), 4.90 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.82 (1H, d, *J* = 10.9 Hz, CH_2Ar), 4.36 (1H, m, H38), 4.29 (1H, m, H37), 4.19 (1H, m, H27), 4.02 (1H, dd, *J* = 7.3, 1.0 Hz, H22), 3.96-3.89 (5H, m, 2 × H40, H29, H28, H21), 3.73 (1H, dd, *J* = 7.7, 1.0 Hz, H23), 3.52 (1H, m, *J* = 8.9, 2.4 Hz, H20), 3.34 (3H, s, OMe), 3.31 (3H, s, OMe), 3.23 (3H, s, OMe), 2.37-2.13 (8H, m, H39, H36, H33, H30, H26, H25, 2 × H18), 2.12-2.00 (3H, m, H39, H19, H26), 1.99 (1H, dd, *J* = 14.0, 2.7 Hz, H36), 1.93-1.83 (2H, m, H24, H19), 1.80 (1H, dt, *J* = 13.2, 3.2 Hz, H32), 1.54 (1H, m, H34), 1.46-1.23 (4H, m, H33, H32, H30, H25), 1.16 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.19 (3H, d, *J* = 6.9 Hz, Me24), 1.09 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.06 (3H, d, *J* = 7.0 Hz, Me34), 1.05 (9H, s, *t*-BuSi), 0.98 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.89 (6H, qd, *J* = 8.0, 3.2 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.77 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.57 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.19 (3H, s, SiMe), 0.17 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 200.4, 159.4, 131.7, 129.3, 113.7, 108.5, 97.5, 82.0, 81.5, 80.5, 80.0, 79.5, 75.9, 74.3, 72.9, 72.2, 65.7, 63.6, 60.9, 57.3, 56.7, 54.5, 48.9, 43.5, 40.4, 37.8, 36.8, 36.2, 33.1, 29.5, 26.2, 26.0, 24.0, 22.9, 18.3, 17.9, 16.5, 15.3, 7.4, 7.3, 6.9, 5.7, 5.5, 5.0, −5.1, −5.2; **HRMS** (ES^+) calcd for $C_{60}H_{113}ClO_{12}Si_4Na$ $[M+Na]^+$ 1195.6895, found 1195.6924.

2.4 C1-C16 alkyne coupling / macrolactonisation

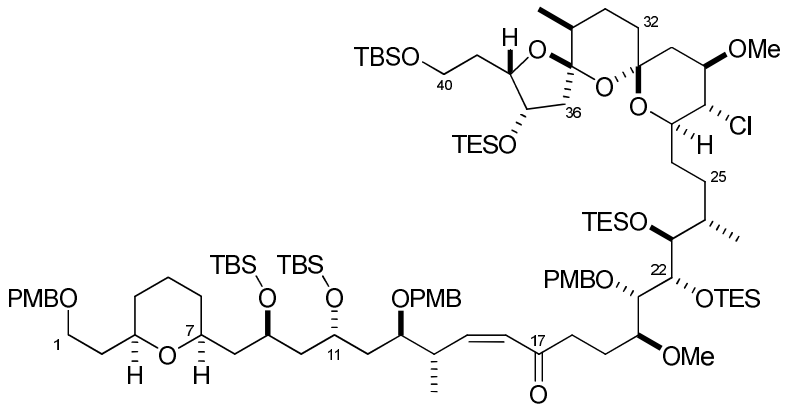
Propargylic Alcohols 39



To a stirred solution of alkyne **3** (237 mg, 0.302 mmol) in THF (2 mL) at −20 °C was added *n*-BuLi (1.6M in hexanes, 185 µL, 0.295 mmol). The mixture was stirred for 30 min before being cooled to −78 °C, and a solution of aldehyde **38** (115 mg, 98.4 µmol) in THF (2 mL) was added dropwise *via* cannula. The reaction mixture was stirred for 30 min at –78 °C, then allowed to warm to –20 °C over 30 min before being quenched with NH_4Cl solution (4 mL) and diluted with Et_2O (10 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 10:1 → 4:1 40-60 petroleum ether / EtOAc) afforded propargylic alcohols **39** (193 mg, 98.4 µmol, 99 % based on aldehyde **38**, 1:1 diastereomeric mixture at C_{17}) as a colourless oil and recovered alkyne **3** (157 mg, 0.200 mmol, 66 %) as a colourless oil. $\mathbf{R_f}$ 0.26 (EtOAc / PE 40-60, 1:4); **IR** (thin film, ν_{max}/cm^{-1}) 3399, 2933, 2878, 1614, 1514, 1463, 1380, 1248, 1079, 1039, 835, 775; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.50-7.46 (2H, m, ArH), 7.37-7.34 (2H, m, ArH), 7.30 (2H, d, *J* = 8.7 Hz, ArH), 6.88 (4H, d, *J* = 8.6 Hz, ArH), 6.83 (2H, d, *J* = 8.7 Hz, ArH), 5.01-4.96 (1H, m, CH_2Ar), 4.88-4.83 (1H, m, CH_2Ar), 4.57-4.38 (5H, m, H17, 2 × CH2Ar), 4.35 (1H, m, H38), 4.30-4.25 (2H, m, H37, H27), 4.21-4.14 (2H, m, H11, H9), 4.09 (1H, m, H22), 4.01 (1H, m, H21), 3.96-3.88 (4H, m, 2 × H40, H29, H28), 3.85 (1H, m, H13), 3.78 (1H, m, H23), 3.72-3.60 (3H, m, H20, 2 × H1), 3.56 (1H, m, H7), 3.48 (1H, m, H3), 3.35-3.32 (15H, m, 5 × OMe), 3.01 (1H, m, H14), 2.46 (0.5H, br s, OH17), 2.37-1.87 (21.5H, m, 2 × H39, 2 × H36, H33, H30, 2 × H26, 2 × H25, H24, 2 × H19, 2 × H18, 2 × H12, 2 × H10, H8, H2, OH17), 1.84-1.73 (2H, m, H32, H2), 1.64-1.51 (3H, m, H34, H30, H6), 1.47-1.25 (14H, m, H33, H32, H8, H6, 2 × H5, 2 × H4, Me24, Me14), 1.24-0.96 (57H, m, Me34, 3 × *t*-BuSi, 3 × $Si(CH_2C\underline{H}_3)_3$), 0.93-0.88 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.84-0.76 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.59-0.54 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.24-0.17 (18H, m, 6 × SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 159.4, 159.3, 132.2, 131.3, 129.3, 129.2, 129.1,

129.0, 113.9, 113.8, 113.7, 108.6, 108.5, 97.5, 86.2, 86.1, 84.5, 84.4, 82.4, 81.8, 81.7, 80.6, 80.5, 79.7, 79.5, 79.3, 78.4, 76.1, 74.5, 74.0, 73.9, 73.6, 73.0, 72.6, 72.3, 72.2, 70.8, 68.3, 67.0, 66.9, 63.7, 63.6, 62.6, 62.4, 60.9, 57.3, 56.8, 54.5, 48.9, 48.0, 45.5, 45.4, 43.5, 39.4, 37.8, 37.2, 36.7, 36.6, 36.2, 35.3, 34.7, 33.2, 33.0, 32.4, 31.9, 30.2, 30.0, 29.5, 29.0, 29.0, 28.9, 18.4, 18.2, 18.1, 17.9, 16.5, 14.9, 7.5, 7.3, 6.9, 5.7, 5.6, 5.0, −3.5, −3.8, −3.9, −4.2, −5.1, −5.2; **HRMS** (ESI^+) calcd for $C_{105}H_{187}ClO_{19}Si_6Na$ $[M+Na]^+$ 1978.1863, found 1978.1920.

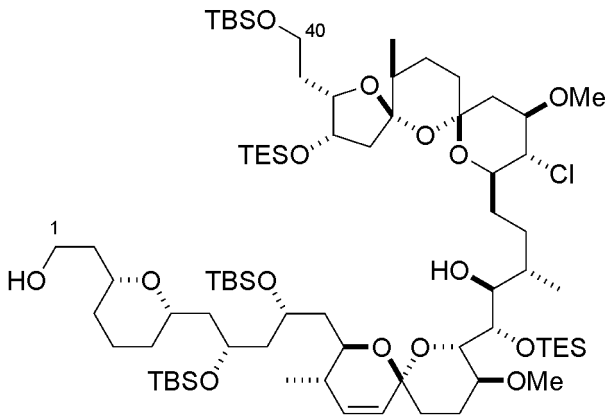
Enone 40



To a stirred solution of propargylic alcohol **39** (164 mg, 0.0837 mmol) in EtOAc (16 mL) was added Lindlar catalyst (Pd 5 wt % on $CaCO_3$ with Pb, 71 mg, 0.034 mmol) and quinoline (132 μL, 1.12 mmol). After vigorous stirring for 10 min, the reaction was vacuum-flushed several times with hydrogen gas and the reaction mixture was stirred for 2 h under a hydrogen balloon before being filtered over a Celite pad. The solid cake was washed with EtOAc (3 × 5 mL) and the filtrate was concentrated *in vacuo*. Conversion was checked by ^{1}H NMR and, in the case of incompleted reaction, the above procedure was repeated. The crude residue was rediluted in DCM (10 mL), $NaHCO_3$ (35.2 mg, 0.419 mmol) and Dess-Martin periodinane (106.5 mg, 0.251 mmol) were added and the reaction mixture was stirred for 30 min before being quenched with $NaHCO_3$ solution (5 mL) and $Na_2S_2O_3$ solution (5 mL). The mixture was vigorously stirred for a further 30 min and extracted with DCM (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 8:1 40-60 petroleum ether / EtOAc) afforded enone **40** (139 mg, 70.8 μmol, 85 % over 2 steps) as a colourless oil: $\mathbf{R_f}$ 0.50 (Et_2O / PE 40-60, 1:4); $\mathbf{[\alpha]_D^{20}}$ −14.6 (*c* 1.63, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2932, 2877, 1692, 1614, 1514, 1462, 1381, 1302, 1248, 1093, 1040, 1006, 835, 775, 741; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.49-7.45 (4H, m, ArH), 7.31 (2H, d, *J* = 8.7 Hz, ArH), 6.90 (2H, d, *J* = 8.7 Hz, ArH), 6.86-6.82 (4H, m, ArH), 6.07 (1H, d, *J* = 11.5 Hz, H16), 5.89 (1H, dd, *J* = 11.5, 9.3 Hz, H15), 4.98 (1H, d, *J* = 11.0 Hz, CH_2Ar), 4.86 (2H, m, CH_2Ar, CH_2Ar), 4.78 (1H, d, *J* = 11.5 Hz, CH_2Ar), 4.49

(1H, d, *J* = 11.5 Hz, CH_2Ar), 4.43 (1H, d, *J* = 11.5 Hz, CH_2Ar), 4.36 (1H, m, H38), 4.31-4.24 (3H, m, H37, H14, H9), 4.19 (1H, m, H27), 4.13 (1H, m, H11), 4.12 (1H, dd, *J* = 7.0, 1.7 Hz, H22), 4.01 (1H, dd, *J* = 7.1, 3.2 Hz, H21), 3.97-3.90 (5H, m, 2 × H40, H29, H28, H13), 3.83 (1H, dd, *J* = 6.9, 2.0 Hz, H23), 3.72 (1H, m, H1), 3.67-3.56 (3H, m, H20, H7, H1), 3.51 (1H, m, H3), 3.36 (3H, s, OMe), 3.35 (3H, s, OMe), 3.34 (3H, s, OMe), 3.32 (3H, s, OMe), 3.31 (3H, s, OMe), 2.80 (1H, ddd, *J* = 17.0, 9.2, 5.3 Hz, H18), 2.64 (1H, ddd, *J* = 17.0, 9.2, 6.0 Hz, H18), 2.46 (1H, m, H19), 2.32 (1H, m, H33), 2.26-2.13 (4H, m, H36, H30, 2 × H26), 2.12-2.02 (3H, m, 2 × H39, H19), 2.01-1.88 (7H, m, H36, H25, H24, 2 × H12, H10, H2), 1.84-1.74 (3H, m, H32, H25, H2), 1.64-1.50 (6H, m, H34, H10, H8, H6, 2 × H5), 1.47-1.27 (5H, m, H33, H32, H30, H8, H4), 1.25 (3H, d, *J* = 6.6 Hz, Me24), 1.19 (1H, m, H6), 1.18 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.16 (3H, obs m, Me14), 1.15 (1H, m, H4), 1.12 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.08 (3H, obs m, Me34), 1.06 (9H, s, *t*-BuSi), 1.05 (9H, s, *t*-BuSi), 1.04 (9H, s, *t*-BuSi), 0.99 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.92 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.82 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.57 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.26 (3H, s, SiMe), 0.24 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.18 (3H, s, SiMe), 0.16 (3H, s, SiMe), 0.12 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 200.1, 159.4, 159.3, 159.2, 149.9, 132.1, 131.9, 131.4, 129.3, 129.1, 126.6, 113.8, 113.7, 108.6, 97.5, 81.4, 81.1, 80.5, 79.5, 79.4, 78.6, 76.3, 74.4, 74.1, 73.5, 73.0, 72.6, 72.2, 70.2, 68.0, 67.1, 66.8, 63.7, 62.5, 60.9, 57.3, 56.9, 54.5, 48.9, 48.2, 45.4, 43.5, 40.4, 40.0, 37.8, 37.3, 36.7, 36.2, 35.2, 33.1, 32.5, 31.9, 30.0, 29.6, 26.1, 26.0, 24.2, 23.9, 18.4, 18.1, 16.5, 14.6, 7.5, 7.4, 6.9, 5.7, 5.6, 5.0, −3.6, −3.8, −4.2, −5.1, −5.2; **HRMS** (ES^+) calcd for $C_{105}H_{187}ClO_{19}Si_6Na$ $[M+Na]^+$ 1978.1869, found 1978.1814.

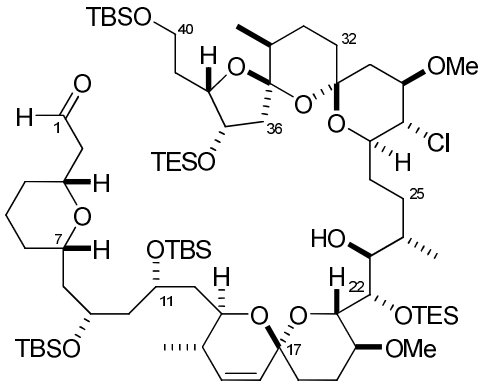
Spiroacetal 41



To a stirred solution of enone **40** (139 mg, 70.8 μmol) in DCM / pH 7 buffer (9:1 v/v, 10 mL) at 0 °C was added DDQ (322 mg, 1.42 mmol). The reaction mixture was stirred for 3 h at 0 °C before being quenched with $NaHCO_3$ (10 mL). The mixture was extracted with DCM (3 × 10 mL) and the

combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 10:1 → 5:1 40-60 petroleum ether / EtOAc) provided diasteromerically pure spiroacetal **41** (64.4 mg, 43.5 mmol, 62 %) as a colourless oil; $\mathbf{R_f}$ 0.35 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ –7.2 (*c* 0.62, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3286, 2928, 1613, 1514, 1457, 1232, 1096, 1021, 977, 737; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 5.45 (1H, dd, *J* = 9.9, 2.0 Hz, H15), 5.42 (1H, dd, *J* = 9.9, 1.1 Hz, H16), 4.54 (1H, dd, *J* = 5.3, 1.3 Hz, H22), 4.43 (1H, m, H11), 4.38-4.31 (2H, m, H38, H37), 4.29 (1H, dd, *J* = 9.3, 1.3 Hz, H21), 4.21 (1H, m, H9), 4.15 (1H, ddd, *J* = 9.9, 5.6, 3.2 Hz, H27), 3.96 (2H, m, 2 × H40), 3.91-3.86 (3H, m, H29, H28, H13), 3.83 (1H, m, H23), 3.78 (2H, m, 2 × H1), 3.59 (1H, d, *J* = 7.2 Hz, OH23), 3.57-3.51 (2H, m, H20, H7), 3.38 (1H, m, H3), 3.30 (3H, s, OMe), 3.22 (3H, s, OMe), 2.46 (1H, m, OH1), 2.41 (1H, dt, *J* = 12.9, 3.7 Hz, H25), 2.35 (1H, dt, *J* = 12.9, 3.7 Hz, H26), 2.30 (1H, m, H14), 2.21 (1H, dd, *J* = 13.8, 6.1 Hz, H36), 2.16-2.07 (5H, m, 2 × H39, H33, H30, H12), 2.06-1.89 (10H, m, H36, H26, H24, 2 × H19, H18, H12, 2 × H10, H8), 1.74-1.66 (4H, m, H32, H25, H4, H2), 1.64-1.55 (2H, m, H18, H8), 1.54-1.46 (2H, m, H34, H2), 1.41 (1H, m, H6), 1.37-1.29 (4H, m, H32, H30, 2 × H5), 1.21 (3H, d, *J* = 6.7 Hz, Me24), 1.20-1.14 (3H, m, H33, H6, H4), 1.17 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.10 (9H, s, *t*-BuSi), 1.06 (9H, s, *t*-BuSi), 1.04 (12H, m, Me34, *t*-BuSi), 0.98 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.91 (3H, d, *J* = 7.1 Hz, Me14), 0.84 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.57 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.39 (3H, s, SiMe), 0.35 (3H, s, SiMe), 0.26 (3H, s, SiMe), 0.23 (3H, s, SiMe), 0.22 (3H, s, SiMe), 0.20 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 134.7, 128.7, 108.4, 97.4, 94.3, 80.6, 80.0, 79.1, 77.5, 74.4, 73.7, 73.5, 73.1, 73.0, 72.2, 69.9, 68.0, 67.8, 63.7, 61.1, 60.9, 57.1, 55.0, 48.7, 45.3, 43.3, 40.9, 39.0, 37.7, 37.1, 36.1, 34.0, 32.8, 32.5, 32.0, 31.7, 30.0, 29.6, 28.6, 26.2, 26.1, 25.5, 23.9, 23.7, 23.6, 20.3, 18.5, 18.4, 18.2, 16.8, 16.6, 16.5, 7.3, 6.9, 6.0, 5.0, −2.9, −3.5, −3.9, −4.1, −5.0, −5.1; **HRMS** (ES^+) calcd for $C_{75}H_{147}ClO_{15}Si_5Na$ $[M+Na]^+$ 1485.9173, found 1485.9487.

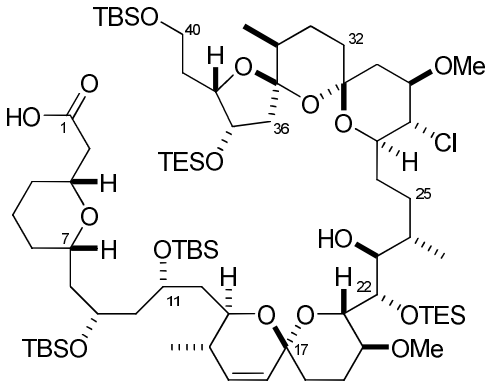
Aldehyde 41a



To a stirred solution of alcohol **41** (9.1 mg, 6.2 µmol) in CH_2Cl_2 / pH 7 buffer (5:1, 1 mL) was added TEMPO / BAIB (100 µL of a stock solution of TEMPO (3.0 mg, 1.9 µmol) and BAIB (50.0

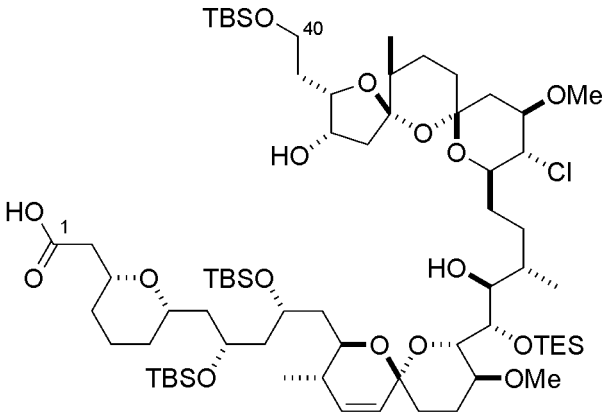
mg, 15.5 μmol) in CH_2Cl_2 / pH 7 buffer (5:1, 500 μL)). The reaction mixture was stirred for 2 h before being quenched with $NaHCO_3$ (500 μL) and $Na_2S_2O_3$ (500 μL). The mixture was stirred vigorously for 30 min before being extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, EtOAc / PE 40-60, 1:10→1:6) afforded aldehyde **41a** (8.3 mg, 5.7 μmol, 91%) as a colourless, waxy oil; $\mathbf{R_f}$ 0.63 (EtOAc / PE 40-60, 1:4); $[\alpha]_D^{20}$ –5.1 (*c* 0.83, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3424, 2955, 2930, 2878, 1730, 1462, 1380, 1254, 1100, 1006, 979, 835, 775; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 9.80 (1H, t, *J* = 2.1 Hz, H1), 5.42 (2H, s, H16, H15), 4.56 (1H, d, *J* = 4.4 Hz, H22), 4.43 (1H, m, H11), 4.39-4.32 (2H, m, H38, H37), 4.28 (1H, d, *J* = 9.4 Hz, H21), 4.20 (1H, m, H9), 4.15 (1H, m, H27), 3.97 (2H, app t, *J* = 6.7 Hz, 2 × H40), 3.93-3.86 (3H, m, H29, H28, H13), 3.80 (1H, td, *J* = 7.5, 4.8 Hz, H23), 3.60 (1H, d, *J* = 7.2 Hz, OH23), 3.59-3.53 (2H, m, H20, H3), 3.49 (1H, m, H7), 3.30 (3H, s, OMe), 3.21 (3H, s, OMe), 2.51 (1H, m, H2), 2.41-2.28 (4H, m, H26, H19, H14, H2), 2.22 (1H, dd, *J* = 13.6, 5.8 Hz, H36), 2.19-1.99 (10H, m, 2 × H39, H36, H33, H30, H26, H25, H19, H18, H12), 1.99-1.84 (5H, m, H24, H12, 2 × H10, H8), 1.69 (1H, dt, *J* = 13.1, 2.9 Hz, H32), 1.66-1.47 (4H, m, H34, H25, H18, H8), 1.41-1.23 (5H, m, H32, H30, H6, 2 × H5), 1.20 (2H, m, H33, H4), 1.19 (3H, d, *J* = 6.7 Hz, Me24), 1.16 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.15 (1H, m, H6), 1.11 (9H, s, *t*-BuSi), 1.07 (9H, s, *t*-BuSi), 1.03 (9H, s, *t*-BuSi), 0.99 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.01-0.98 (4H, m, H4, Me34), 0.91 (3H, d, *J* = 7.2 Hz, Me14), 0.83 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.57 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.40 (3H, s, SiMe), 0.35 (3H, s, SiMe), 0.24 (3H, s, SiMe), 0.23 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.19 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 199.8, 135.0, 132.6, 108.6, 97.6, 94.5, 80.7, 79.8, 79.7, 74.5, 73.8, 73.7, 73.2, 73.0, 72.3, 69.7, 67.9, 67.8, 66.5, 64.3, 61.2, 57.3, 55.3, 50.3, 49.1, 48.9, 45.9, 43.5, 40.9, 37.9, 37.8, 36.3, 34.1, 33.0, 32.4, 32.3, 31.9, 31.5, 30.2, 29.8, 28.7, 26.4, 26.3, 26.2, 26.1, 25.4, 24.1, 23.7, 23.1, 18.5, 18.4, 16.9, 16.7, 16.5, 14.3, 7.5, 7.1, 6.1, 5.2, −2.8, −3.5, −3.6, −3.9, −4.8, −4.9; **HRMS** (ESI^+) calcd for $C_{75}H_{145}ClO_{15}Si_5Na$ $[M+Na]^+$ 1483.9011, found 1483.9020.

Carboxylic Acid 41b



To a stirred solution of aldehyde **41a** (8.3 mg, 5.7 µmol) and 2-methyl-2-butene (100 µL) in *t*-BuOH / H_2O (1:1, 1 mL) was added $NaClO_2$ (3.3 mg, 28.4 µmol) and $NaH_2PO_4{\cdot}H_2O$ (8.9 mg, 56.8 µmol). The reaction mixture was stirred for 2 h before being quenched with brine. The mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. No further purification was required to afford pure carboxylic acid **41b** (8.1 mg, 5.5 µmol, 97%) as a colourless oil; $\mathbf{R_f}$ 0.57 (EtOAc / PE 40-60, 1:2); $[\alpha]_D^{20}$ +4.7 (*c* 0.21, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3300-2600 (br OH), 2929, 1717, 1463, 1382, 1255, 1100, 1017, 979, 835, 775; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 5.46 (2H, s, H16, H15), 4.56 (1H, d, *J* = 5.5 Hz, H22), 4.38 (1H, ddd, *J* = 6.6, 5.6, 4.4 Hz, H38), 4.35-4.26 (3H, m, H37, H21, H11), 4.23 (1H, m, H9), 4.18 (1H, m, H27), 4.03-3.85 (6H, m, 2 × H40, H29, H28, H23, H13), 3.72 (1H, m, H3), 3.61-3.52 (2H, m, H20, H7), 3.31 (3H, s, OMe), 3.22 (3H, s, OMe), 2.46 (1H, dd, *J* = 14.8, 8.8 Hz, H2), 2.40-2.32 (2H, m, H26, H14), 2.29 (1H, dd, *J* = 14.8, 2.9 Hz, H2), 2.25-1.89 (17H, m, 2 × H39, 2 × H36, H33, H30, H26, H25, H24, 2 × H19, H18, 2 × H12, 2 × H10, H8), 1.77 (1H, m, H32), 1.72-1.26 (7H, m, H34, H32, H30, H25, H18, H8, H6), 1.24 (3H, d, *J* = 6.9 Hz, Me24), 1.23-1.18 (3H, m, H33, H5, H4), 1.17 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.16-1.14 (3H, m, H6, H5, H4), 1.07-1.05 (27H, m, 3 × *t*-BuSi), 1.04 (3H, d, *J* = 6.6 Hz, Me34), 0.98 (12H, m, Me14, $Si(CH_2C\underline{H}_3)_3$), 0.84 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.56 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.31 (3H, s, SiMe), 0.30 (3H, s, SiMe), 0.29 (3H, s, SiMe), 0.27 (3H, s, SiMe), 0.22 (3H, s, SiMe), 0.20 (3H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 172.8, 134.9, 128.6, 108.5, 97.5, 94.3, 80.6, 80.0, 78.7, 74.4, 74.3, 74.0, 73.2, 73.1, 73.0, 72.2, 69.9, 68.1, 68.0, 63.5, 61.0, 57.1, 55.1, 48.9, 48.6, 45.1, 43.3, 37.8, 36.6, 36.1, 32.8, 32.7, 31.8, 31.2, 30.0, 29.4, 26.2, 26.1, 23.9, 23.6, 18.4, 18.2, 18.1, 17.0, 16.7, 16.5, 7.3, 6.9, 6.1, 5.0, −3.4, −3.7, −3.8, −4.0, −5.0, −5.2; **HRMS** (ES^+) calcd for $C_{75}H_{146}ClO_{16}Si_5$ $[M+H]^+$ 1477.9146, found 1477.9121.

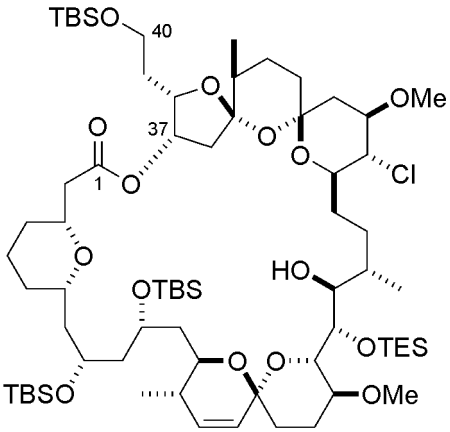
Hydroxy-acid 42



To a stirred solution of carboxylic acid **41b** (16.3 mg, 10.9 μmol) in THF (3 mL) was added TBAF / AcOH (257 μL (0.0437 mmol) of a stock solution of TBAF (1.0 M in THF, 170 μL, 0.170 mmol) and AcOH (30 μL, 0.524 mmol) in THF (0.8 mL)). The reaction mixture was stirred for 45 min before being quenched with brine (3 mL) and diluted with DCM (5 mL). After phase separation, the aqueous phase was extracted with DCM (3 × 3 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 3:1 → 2:1 → 1:1 40-60 petroleum ether / EtOAc) afforded hydroxy-acid **42** (8.5 mg, 6.2 μmol, 57 %) as a colourless oil and unreacted **41b** (5.0 mg, 3.4 μmol, 31 %) as a colourless oil; *Seco*-acid: $\mathbf{R_f}$ 0.46 (EtOAc / PE 40-60, 1:2); $[\alpha]_D^{20}$ = +1.7 (*c* 0.17, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3499, 3300-2600 (br OH), 2953, 2930, 2858, 1714, 1462, 1383, 1255, 1091, 1018, 979, 835, 775; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 5.47 (1H, dd, *J* = 10.0, 1.2 Hz, H15), 5.45 (1H, dd, *J* = 10.0, 2.1 Hz, H16), 4.52 (1H, dd, *J* = 5.4, 1.0 Hz, H22), 4.32-4.25 (4H, m, H38, H37, H21, H11), 4.22 (1H, m, H9), 4.15 (1H, ddd, *J* = 9.9, 7.0, 2.2 Hz, H27), 3.97-3.90 (2H, m, H29, H13), 3.90-3.82 (2H, m, H28, H23), 3.75-3.68 (2H, m, H40, H3), 3.60-3.52 (2H, m, H20, H7), 3.47 (1H, td, *J* = 10.0, 3.2 Hz, H40), 3.28 (3H, s, OMe), 3.23 (3H, s, OMe), 2.49-2.36 (4H, m, H26, H25, H14, H2), 2.32-2.22 (3H, m, 2 × H39, H2), 2.20-2.06 (6H, m, H36, H33, H30, 2 × H12, H10), 2.06-1.89 (7H, m, H36, H24, 2 × H19, H18, H10, H8), 1.82 (1H, m, H26), 1.76 (1H, dt, *J* = 13.0, 3.2 Hz, H32), 1.70-1.50 (5H, m, H34, H25, H18, H8, H5), 1.44-1.21 (5H, m, H33, H32, H30, H6, H4), 1.21 (3H, d, *J* = 6.9 Hz, Me34), 1.19 (3H, d, *J* = 7.0 Hz, Me24), 1.15 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.14 (2H, m, H6, H5), 1.06 (18H, s, 2 × *t*-BuSi), 1.01 (1H, m, H4), 0.99 (3H, d, *J* = 7.0 Hz, Me14), 0.89 (9H, s, *t*-BuSi), 0.81 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.29 (6H, s, 2 × SiMe), 0.28 (3H, s, SiMe), 0.26 (3H, s, SiMe), −0.01 (6H, s, 2 × SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 172.6, 135.0, 128.6, 109.2, 97.6, 94.3, 84.6, 79.4, 78.5, 74.4, 74.1, 74.0, 73.6, 73.2, 71.4, 70.0, 68.0, 64.9, 60.6, 57.1, 55.2, 48.5, 48.2, 45.1, 43.3, 41.5, 40.3, 38.2, 36.6, 36.2, 33.9, 32.5, 31.8, 31.2, 31.1, 30.1, 30.0, 26.9, 26.1, 25.8, 24.1, 23.6, 18.2,

18.1, 18.0, 17.0, 16.6, 16.5, 7.3, 6.0, 1.2, −3.4, −3.7, −3.9, −5.8, −5.9; **HRMS** (ES^+) calcd for $C_{69}H_{132}ClO_{16}Si_4$ $[M+H]^+$ 1363.8281, found 1363.8354.

Macrolactone 43

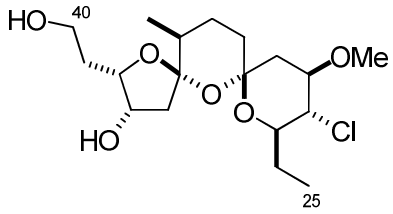


To a stirred solution of *seco*-acid **42** (3.5 mg, 2.5 μmol) in THF (0.5 mL) was added Et_3N (14 μL, 0.10 mmol) and 2,4,6-trichlorobenzoyl chloride (8 μL, 0.05 mmol). The reaction mixture was stirred for 2 h before being diluted with toluene (2 mL). The resulting solution of anhydride was then added over 2 h, *via* syringe pump, to a stirred solution of 4-DMAP (18.6 mg, 0.152 mmol) in toluene (3 mL). The reaction mixture was stirred for a further 30 min before being quenched with $NaHCO_3$ (3 mL). After phase separation, the aqueous phase was extracted with DCM (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 10:1 40-60 petroleum ether / EtOAc) afforded macrolactone **43** (3.5 mg, 2.5 μmol, 99 %) as a colourless oil; $\mathbf{R_f}$ 0.27 (EtOAc / PE 40-60, 1:6); $[\alpha]_D^{20}$ –12.0 (*c* 0.53, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3507, 2953, 2930, 1739, 1462, 1381, 1255, 1101, 1021, 835, 774; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 5.72 (1H, dd, *J* = 6.2, 2.7 Hz, H37), 5.51 (1H, dd, *J* = 9.9, 2.1 Hz, H15), 5.48 (1H, dd, *J* = 9.9, 1.6 Hz, H16), 4.70 (1H, dt, *J* = 10.5, 2.8 Hz, H38), 4.47 (1H, d, *J* = 6.5 Hz, H22), 4.30 (1H, m, H11), 4.24 (1H, d, *J* = 9.4 Hz, H21), 4.02 (2H, m, H27, H9), 3.98-3.93 (3H, m, 2 × H40, H13), 3.85 (2H, m, H29, H23), 3.71 (1H, m, H3), 3.70 (1H, app t, *J* = 9.9 Hz, H28), 3.48 (1H, ddd, *J* = 9.9, 9.7, 5.1 Hz, H20), 3.38 (1H, m, H7), 3.32 (3H, s, OMe), 3.20 (3H, s, OMe), 2.73 (1H, br s, OH23), 2.45-2.28 (5H, m, H39, H36, H26, H14, H2), 2.26-2.06 (6H, m, H39, H33, H30, H25, H12, H2), 2.06-1.89 (8H, m, H36, H26, H24, 2 × H19, 2 × H10, H8), 1.89-1.77 (3H, m, H18, H12, H8), 1.74 (1H, dt, *J* = 13.2, 3.1 Hz, H32), 1.69 (1H, app t, *J* = 7.7 Hz, H25), 1.67-1.48 (3H, m, H18, H12, H5), 1.42-1.22 (6H, m, H33, H32, H30, H6, H5, H4), 1.20 (3H, d, *J* = 6.9 Hz, Me24), 1.18 (1H, m, H6), 1.14 (1H, m, H4), 1.13 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.08

(3H, d, *J* = 6.6 Hz, Me34), 1.07 (3H, d, *J* = 6.9 Hz, Me14), 1.05 (9H, s, *t*-BuSi), 1.04 (9H, s, *t*-BuSi), 0.99 (9H, s, *t*-BuSi), 0.84 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.29 (6H, s, 2 × SiMe), 0.21 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.17 (6H, s, SiMe); **^{13}C NMR** (125 MHz, C_6D_6) δ_C 169.4, 134.6, 129.1, 108.2, 97.7, 94.2, 80.7, 79.3, 77.7, 76.0, 74.5, 73.8, 73.6, 72.6, 72.5, 72.2, 70.5, 68.1, 67.6, 65.9, 64.7, 60.1, 57.6, 55.1, 47.8, 48.4, 45.3, 43.8, 43.6, 42.9, 38.7, 36.6, 35.9, 34.0, 33.7, 31.5, 31.2, 31.1, 30.9, 30.2, 26.4, 26.2, 26.1, 24.3, 23.9, 23.7, 18.6, 18.3, 17.8, 16.9, 7.5, 6.3, −3.1, −3.5, −3.7, −3.8, −5.0, −5.2; **HRMS** (ES^+) calcd for $C_{69}H_{133}ClO_{15}Si_4N$ $[M+NH_4]^+$ 1362.8441, found 1362.8494.

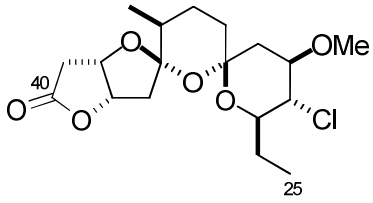
2.5 Side-chain assembly model studies

Diol 11a



$Pd(OH)_2/C$ (20 wt %, 21.2 mg, 19.1 μmol) was added to a solution of olefin **11** (40.5 mg, 69.6 μmol) in EtOH (3 mL) at rt. The system was flushed with H_2 three times and then stirred under an atmosphere of H_2 (balloon pressure) for 30 min. Filtration over celite, concentration *in vacuo* and purification by flash column chromatography (EtOAc / PE (40-60), 1:1) afforded diol **11a** as a white, crystalline solid (25.9 mg, 69.3 μmol, 99 %); $\mathbf{R_f}$ 0.32 (EtOAc / PE (40-60), 1:1); **mp** 129 °C; $\mathbf{[\alpha]}_D^{20}$ + 6.3 (c 2.5, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3381, 2936, 2882, 1462, 1383, 1300; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.39 (1H, ddd, *J* = 7.0, 4.1, 2.2 Hz, H37), 4.21 (1H, ddd, *J* = 8.0, 6.0, 4.1 Hz, H38), 3.88 (1H, ddd, *J* = 10.4, 6.0, 3.6 Hz, H40a), 3.76 (1H, ddd, *J* = 10.4, 8.6, 3.1 Hz, H40b), 3.68 (1H, ddd, *J* = 10.0, 7.2, 2.8 Hz, H27), 3.61 (1H, ddd, *J* = 11.4, 10.0, 4.9 Hz, H29), 3.44 (1H, obs t, *J* = 10.0 Hz, H28), 3.44 (3H, s, OMe), 2.77 (1H, br s, OH40), 2.39 (1H, br s, OH37), 2.32 (1H, dd, *J* = 14.6, 7.0 Hz, H36a), 2.15 (1H, dd, *J* = 12.4, 4.9 Hz, H30a), 2.11 (1H, dd, *J* = 14.6, 2.2 Hz, H36b), 2.02-1.88 (3H, m, H39a, H39b, H26a), 1.89 (1H, dt, 13.1, 3.6 Hz, H32a) 1.77 (1H, dt, *J* = 13.1, 3.3 Hz, H32b), 1.70 (1H, m, H34), 1.62-1.52 (2H, m, H33a, H26b), 1.40 (1H, dq, 12.9, 3.5 Hz, H33b), 1.32 (1H, dd, 12.4, 11.4 Hz, H30b), 1.00 (3H, d, 6.8 Hz, Me34), 0.94 (3H, t, 7.3 Hz, H25); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 101.8, 97.5, 83.3 79.0, 73.3, 71.9, 63.7, 60.2, 57.5, 47.8, 43.2, 37.6, 36.2, 30.7, 24.9, 23.8, 16.6, 8.7; **HRMS** (ES^+) calcd. for $[M+Na]^+$ 401.1701 (^{35}Cl), found 401.1706.

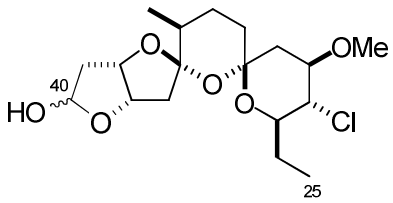
C25-C40 lactone 46



A premixed solution of TEMPO (10 mg, 6.4 mmol) and BAIB (150 mg, 4.6 mmol) in CH_2Cl_2 (1.5 mL) was added to a biphasic mixture of diol **11a** (51.9 mg, 0.138 mmol) in CH_2Cl_2 / pH7 buffer

(5:1, 3 mL). The mixture was stirred for 1 h at rt before quenching with $NaHCO_3$ / $Na_2S_2O_3$ (1:1, 2 mL) and stirred vigorously for 1h. Following phase separation and extraction of the aqueous phase with CH_2Cl_2 (3 × 3 mL) the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield a yellow solid. Purification by flash column chromatography (EtOAc / PE (40-60), 1:10) afforded lactone **46** as a white, crystalline solid (40.7 mg, 0.109 mmol, 79 %); $\mathbf{R_f}$ 0.20 (EtOAc / PE (40-60), 1:4); **mp** 153 °C; $[\alpha]_D^{20}$ + 8.8 (c 0.42, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2932, 1786, 1461, 1383, 1187; **^{1}H NMR** (500 MHz, CDCl3) δ 5.05 (1H, dd, *J* = 6.6, 4.4 Hz, H37), 4.91 (1H, t, *J* = 4.4 Hz, H38), 3.62-3.55 (2H, m, H27, H29), 3.44 (3H, s, OMe), 3.40 (1H, t, *J* = 9.9 Hz, H28), 2.72 (1H, dd, *J* = 18.2, 4.5 Hz, H39a), 2.66 (1H, d, *J* = 18.2 Hz, H39b), 2.51 (1H, d, *J* = 15.7 Hz, H36a), 2.40 (1H, dd, *J* = 15.7, 6.6 Hz, H36b), 2.18 (1H, dd, 12.8, 4.8 Hz, H30a), 2.03 (1H, ddq, *J* = 15.3, 7.5, 2.1 Hz, H26a), 1.89 (1H, dq, *J* = 12.9, 3.6 Hz, H33a), 1.79 (1H, dt, *J* = 13.5, 3.6 Hz, H32a), 1.72 (1H, m, H34), 1.58 (1H, dt, *J* = 13.5, 3.8 Hz, H32b), 1.49-1.40 (2H, m, H33b, H26b), 1.36 (1H, dd, *J* = 12.8, 11.7 Hz, H30b), 0.95 (3H, t, *J* = 7.5 Hz, H25), 0.91 (3H, d, *J* = 7.1 Hz, Me34); **^{13}C NMR** (125MHz, CDCl3) δ 175.1, 111.3, 97.9, 83.5, 79.9, 78.9, 74.0, 64.4, 57.6, 45.3, 42.9, 37.6, 36.1, 36.0, 25.6, 23.6, 16.1, 9.5; **HRMS** (ES^+) calcd. for $[M+Na]^+$ 397.1388 (^{35}Cl), found 397.1382.

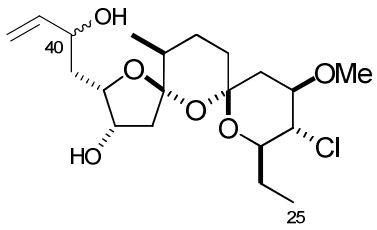
Lactol 46a



Diisobutyl aluminium hydride (1M in CH_2Cl_2, 200 µl, 0.200 mmol) was added to a solution of lactone **46** (38.1 mg, 0.101 mmol) in CH_2Cl_2 (5 mL) at −78 °C. The mixture was stirred for 1 h at this temperature before quenching with Na^+/K^+ tartrate solution (2 mL) and phase separation. The aqueous phase was extracted CH_2Cl_2 (3 × 5 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O / PE (40-60), 1:1) afforded lactol **46a** as a colourless oil (38.0 mg, 0.100 mmol, 99 %, 5:2 ratio of inseparable diastereomers); $\mathbf{R_f}$ 0.47 (EtOAc / PE (40-60), 1:1); **IR** (thin film, ν_{max}/cm^{-1}) 3431, 2932, 1464, 1383; **^{1}H NMR** (500 MHz, $CDCl_3$) major diastereomer δ 5.64 (1H, dt, *J* = 3.2, 5.9 Hz, H40), 4.86 (2H, m, H38, H37), 3.66 (1H, dt, *J* = 2.4, 9.8 Hz, H27), 3.59 (1H, ddd, *J* = 4.9, 9.8, 11.4 Hz, H29), 3.44 (3H, s, OMe), 3.39 (1H, t, *J* = 9.9 Hz, H28), 2.50 (1H, d, *J* = 3.3, OH), 2.33 (1H, dd, *J* = 6.0, 14.0, H36a), 2.28-2.19 (2H, m, H39a, H36b), 2.16 (1H, dd, *J* = 4.7, 12.6 Hz, H30a), 2.08-2.01 (2H, m, H39b, H26a), 1.87 (1H, dq,

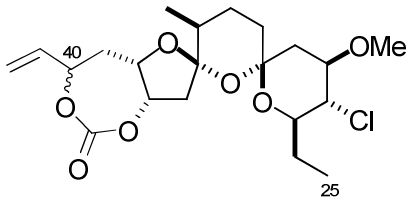
J = 3.3, 12.6 Hz, H33a), 1.76 (1H, dt, *J* = 3.3, 13.3 Hz, H32a), 1.67 (1H, m, H34), 1.57 (1H, m, H33b), 1.47-1.41 (2H, m, H30b, H26b), 1.33 (1H, dd, 11.3, 13.3 Hz, H32b), 0.97 (3H, t, *J* = 8.0 Hz, H25), 0.92 (3H, d, *J* = 6.7 Hz, Me34); **^{13}C NMR** (125MHz, $CDCl_3$) both diastereomers δ 125.6, 111.9, 111.7, 100.6, 100.1, 97.5, 97.4, 84.5, 83.8, 82.2, 78.9, 78.8, 74.1, 73.5, 64.5, 64.3, 57.4, 46.8, 45.6, 43.0, 41.0, 40.0, 37.4, 36.3, 36.1, 30.3, 25.5, 23.7, 23.6, 17.1, 16.0, 9.5, 9.3; **HRMS** (ES^+) calcd. for $[M+Na]^+$ (^{35}Cl) 399.1545, found 399.1546.

Allylic alcohol 47



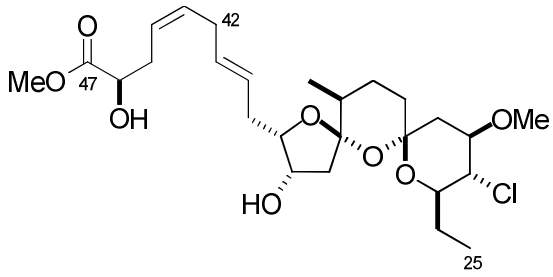
A freshly prepared solution of vinylmagnesium bromide (1 M in THF, 431 μL, 0.431 mmol) was added to lactol **46a** (8.0 mg, 21 μmol) in THF (3 mL) at 0 °C. The reaction was stirred for 1 h at 0 °C before being quenched with NH_4Cl solution (2 mL). The resulting two-phase solution was separated, the aqueous phase extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic phases dried over $MgSO_4$. Concentration *in vacuo* followed by flash column chromatography (Et_2O / PE (40-60), 1:4) afforded allylic alcohol **47** as a colourless oil (8.1 mg, 20 μmol, 95 %, 2:1 dr); **R_f** 0.18 (EtOAc / PE (40-60), 1:4); **IR** (thin film, ν_{max}/cm^{-1}) 3390, 2934, 1463, 1383; **^{1}H NMR** (500 MHz, $CDCl_3$) major diastereomer δ 5.94 (1H, ddd, *J* = 5.6, 10.5, 16.8 Hz, H41), 5.28 (1H, d, *J* = 16.8 Hz, H42a), 5.14 (1H, d, *J* = 10.5 Hz, H42b), 4.44 (1H, m, H37), 4.32 (1H, m, H40), 4.23 (1H, dt, *J* = 4.2, 9.1 Hz, H38), 3.68 (1H, ddd, *J* = 2.9, 7.5, 10.1 Hz, H27), 3.62 (1H, ddd, *J* = 4.6, 9.3, 11.3 Hz, H29), 3.45 (3H, s, OMe), 3.43 (1H, t, *J* = 9.5 Hz, H28), 2.34 (1H, dd, *J* = 6.7, 14.2 Hz, H36a), 2.16 (1H, dd, *J* = 4.6, 12.4 Hz, H30a), 2.12 (1H, dd, *J* = 2.3, 14.2 Hz, H36b), 2.03 (1H, m, H39a), 1.98-1.91 (2H, m, H26a, H39b), 1.87 (1H, m, H33a), 1.77 (1H, dt, *J* = 3.2, 13.3 Hz, H32a), 1.69 (1H, m, H34), 1.56-1.52 (2H, m, H26b, H32b), 1.39 (1H, dq, *J* = 3.5, 12.7 Hz, H33b), 1.32 (1H, dd, *J* = 11.3, 12.4 Hz, H30b), 0.99 (3H, d, *J* = 7.2 Hz, Me34), 0.95 (3H, t, *J* = 7.5 Hz, H25); **^{13}C NMR** (125MHz, $CDCl_3$) both diastereomers δ 140.9, 139.9, 114.9, 114.6, 108.7, 108.6, 97.4, 97.3, 82.6, 82.2, 81.2, 78.9, 78.8, 73.3, 73.2, 71.8, 71.7, 71.0, 70.5, 64.1, 63.3, 57.4, 47.6, 47.5, 43.1, 43.0, 37.6, 37.4, 36.1, 36.0, 35.3, 34.6, 25.2, 24.6, 23.7, 23.7, 16.5, 16.4, 9.0, 8.4; **HRMS** (ES^+) calcd. for $[M+Na]^+$ (^{35}Cl) 427.1858, found 427.1857.

Carbonate 48



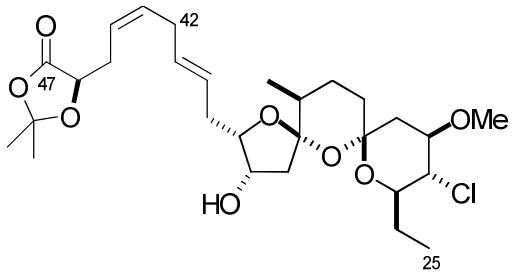
Et_3N (13.0 µl, 94.2 µmol) and pyridine (7.6 µl, 94 µmol) were added to a solution of allylic alcohol **47** (6.3 mg, 16 µmol) in CH_2Cl_2 (0.4 mL) at −78 °C. Triphosgene (9.3 mg, 31 µmol) in CH_2Cl_2 (0.4 mL) was then added and the resulting mixture stirred for 25 min before being quenched with NH_4Cl (2 mL), extracted with CH_2Cl_2 (3 × 5 mL) and dried over $MgSO_4$. Concentration *in vacuo* followed by flash column chromatography (EtOAc / PE (40-60), 1:4) afforded carbonate **48** as a colourless oil (2.7 mg, 6.3 µmol, 39 %, 1:1.6 dr); $\mathbf{R_f}$ 0.23 (EtOAc / PE (40-60), 1:4); **IR** (thin film, ν_{max}/cm^{-1}) 2934, 1768, 1462, 1383; ^{1}**H NMR** (500 MHz, $CDCl_3$) major diastereomer δ 5.93 (1H, ddd, *J* = 5.9, 10.6, 16.1 Hz, H41), 5.52 (1H, dt, *J* = 1.0, 16.9 Hz, H42a), 5.30 (1H, dt, *J* = 1.0, 10.5 Hz, H42b), 4.98 (1H, ddd, *J* = 2.1, 3.8, 6.0 Hz, H37), 4.84 (1H, tq, *J* = 1.0, 5.7 Hz, H40), 4.49 (1H, ddd, *J* = 4.0, 6.0, 10.2 Hz, H38), 3.61-3.53 (2H, m, H27, H29), 3.45 (3H, s, OMe), 3.41 (1H, t, *J* = 10.0 Hz, H28), 2.46-2.40 (2H, m, H36a, H36b), 2.32 (1H, ddt, *J* = 2.3, 6.0, 15.3 Hz, H39a), 2.18 (1H, dd, *J* = 4.8, 12.6 Hz, H30a), 2.06-1.98 (2H, m, H26a, H39b), 1.89 (1H, dq, *J* = 3.5, 13.1 Hz, H33a), 1.79 (1H, dt, *J* = 3.3, 12.9 Hz, H32a), 1.76-1.70 (1H, m, H34), 1.61-1.40 (3H, m, H26b, H32b, H33b), 1.35 (1H, dd, *J* = 11.4, 12.9 Hz, H30b), 0.99 (3H, d, *J* = 6.8 Hz, Me34), 0.95 (3H, t, *J* = 7.3 Hz, H25); ^{13}**C NMR** (125MHz, $CDCl_3$) both diastereomers δ 151.1, 135.3, 134.5, 125.5, 117.9, 117.4, 109.9, 108.5, 97.8, 97.7, 80.9, 79.8, 78.9, 78.7, 78.7, 78.5, 76.0, 73.9, 73.8, 64.2, 63.8, 57.4, 47.3, 45.1, 42.8, 37.5, 36.0, 34.4, 34.2, 33.4, 30.3, 25.4, 23.6, 23.5, 16.3, 16.2, 9.5, 9.1; **HRMS** (ES^+) calcd. for $[M+NH_4]^+$ (^{35}Cl) 448.2097, found 448.2094.

Methyl ester 49



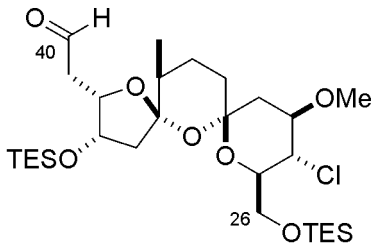
A stock solution of $(MeCN)_2PdCl_2$ (4.0 mg, 0.015 mmol) in degassed DMF / H_2O (4:1, 1 mL) was prepared. A portion of the palladium stock solution (20 µl, 0.3 µmol) was added to a solution of allylic carbonate **48** (1.5 mg, 3.5 µmol) and vinyl stannane **7** (1.5 mg, 5.2 µmol) in degassed DMF / H_2O (4:1, 0.5 mL) and the mixture was stirred at rt for 30 min before quenching with brine (0.5 mL). The resulting two-phase system was separated, the aqueous phase extracted with Et_2O (3 × 5 mL) and the combined organic phases dried over $MgSO_4$. Concentration *in vacuo* followed by flash column chromatography (EtOAc / PE (40-60), 1:4 → 1:0) afforded methyl ester **49** as a colourless oil (1.3 mg, 2.5 µmol, 72 %); $\mathbf{R_f}$ 0.24 (EtOAc / PE (40-60), 1:1); $[\alpha]_D^{20}$ + 2.0 (c 0.10, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.62-5.43 (4H, m, H40, H41, H43, H44), 4.33 (1H, m, H37), 4.27 (1H, q, *J* = 6.4 Hz, H46), 4.09 (1H, ddd, *J* = 3.7, 5.9, 8.2 Hz, H38), 3.79 (3H, s, COOMe), 3.65 (1H, ddd, *J* = 2.7, 7.8, 10.1 Hz, H27), 3.60 (1H, ddd, *J* = 5.0, 10.1, 11.4 Hz, H29), 3.44 (3H, s, OMe), 3.43 (1H, t, *J* = 10.1 Hz, H28), 2.78 (2H, br t, *J* = 5.9 Hz, H42a, H42b), 2.74 (1H, d, *J* = 6.4 Hz, OH46), 2.57 (1H, dt, *J* = 5.9, 14.2 Hz, H45a), 2.48 (1H, dt, *J* = 6.9, 14.2 Hz, H45b), 2.41-2.36 (2H, m, H39a, H39b), 2.30 (1H, dd, *J* = 6.4, 14.6 Hz, H36a), 2.16 (1H, dd, *J* = 5.0, 12.8 Hz, H30a), 2.07 (1H, dd, *J* = 2.3, 14.6 Hz, H36b), 1.97-1.88 (2H, m, H26a, H33a), 1.78 (1H, dt, *J* = 3.2, 13.3 Hz, H32a), 1.69 (1H, m, H34), 1.58-1.51 (2H, m, H26b, H32b), 1.39 (1H, dq, *J* = 3.7, 13.3 Hz, H33b), 1.32 (1H, dd, *J* = 11.4, 12.3 Hz, H30b), 0.99 (3H, d, *J* = 5.9 Hz, Me34), 0.96 (3H, t, *J* = 7.8 Hz, H25); **^{13}C NMR** (125MHz, $CDCl_3$) δ 174.9, 131.1, 130.9, 126.3, 123.9, 108.4, 97.3, 82.3, 78.9, 73.2, 71.6, 70.1, 63.9, 57.4, 52.5, 48.1, 43.0, 37.6, 36.0, 32.1, 31.9, 30.5, 25.1, 23.6, 16.4, 8.8; **HRMS** (ES^+) calcd. for $[M+Na]^+$ (^{35}Cl) 539.2382, found 539.2372.

Acetonide 51



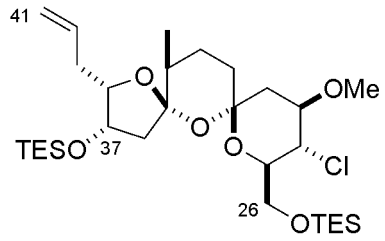
A stock solution was made by dissolving $(MeCN)_2PdCl_2$ (2.0 mg, 7.7 μmol) in degassed DMF / H_2O (1 mL, 4:1). A portion of the above palladium stock solution (100 μL, 0.77 μmol) was added to a solution of allylic carbonate **48** (3.1 mg, 7.2 μmol) and vinyl stannane **50** (6.9 mg, 21.6 μmol) in degassed DMF / H_2O (1 mL, 4:1). The resulting yellow / black solution was stirred at rt for 2 h before quenching with brine and phase separation. The aqueous phase was extracted with Et_2O (3 × 2 mL), dried over $MgSO_4$ and concentrated *in vacuo* giving the crude product, which was purified by flash column chromatography (EtOAc / PE (40-60), 1:4) to afford acetonide **51** as a colourless oil (2.4 mg, 4.4 μmol, 57 %); $\mathbf{R_f}$ 0.09 (EtOAc / PE (40-60), 1:4); $[\alpha]_D^{20}$ + 8.7 (c 0.24, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3427 (br), 2939, 1794, 1464, 1381; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.61 (1H, m, H43), 5.53 (1H, dd, *J* = 6.0, 17.4 Hz, H41), 5.50 (1H, m, H40), 5.46 (1H, m, H44), 4.46 (1H, dd, *J* = 4.8, 6.2 Hz, H46), 4.33 (1H, m, H37), 4.09 (1H, m, H38), 3.65 (1H, m, H27), 3.60 (1H, ddd, *J* = 4.7, 9.7, 11.0 Hz, H29), 3.44 (3H, s, OMe), 3.42 (1H, t, *J* = 9.7 Hz, H28), 2.80 (2H, br t, *J* = 6.0 Hz, H42a, H42b), 2.63 (1H, dt, *J* = 5.7, 15.2 Hz, H45a), 2.54 (1H, dt, *J* = 6.7, 14.7 Hz, H45b), 2.36-2.39 (2H, m, H39a, H39b), 2.29 (1H, dd, *J* = 6.7, 14.7 Hz, H36a), 2.15 (1H, dd, *J* = 5.2, 12.4 Hz, H30a), 2.07 (1H, dd, *J* = 1.9, 14.7 Hz, H36b), 1.88-1.98 (2H, m, H26a, H33a), 1.77 (1H, br d, *J* = 13.3 Hz, H32a), 1.69 (1H, m, H34), 1.61 (3H, s, Me), 1.51-1.59 (3H, m, H26b, H32b, OH), 1.54 (3H, s, Me), 1.38 (1H, m, H33b), 1.32 (1H, t, *J* = 12.4 Hz, H30b), 0.99 (3H, d, *J* = 7.1 Hz, Me34), 0.96 (3H, t, *J* = 7.1 Hz, H25); **^{13}C NMR** (125MHz, $CDCl_3$) δ 172.7, 131.6, 130.7, 126.5, 123.2, 110.7, 108.5, 97.3, 82.4, 78.9, 74.0, 73.3, 71.6, 63.9, 57.4, 48.1, 43.0, 37.6, 36.1, 31.9, 30.6, 29.2, 27.1, 26.0, 25.2, 23.7, 16.5, 8.9; **HRMS** (ES^+) calcd. for $[M+NH_4]^+$ (^{35}Cl) 560.2985, found 560.2981.

Aldehyde 55



To a stirred solution of alcohol **54** (11.0 mg, 18.1 μmol) in DCM (1 mL) was added solid $NaHCO_3$ (4.5 mg, 54.2 μmol) and Dess-Martin periodinane (15.3 mg, 36.1 μmol). The suspension was stirred for 1 h, before being quenched with $NaHCO_3$ solution (1 mL) and $Na_2S_2O_3$ solution (1 mL). The quenching mixture was stirred vigorously for 1 h before extracting the aqueous phase with DCM (3 × 5 mL). The combined organic phases were dried ($MgSO_4$), concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2, 30:1 40-60 petroleum ether / EtOAc) to afford aldehyde **55** (11.0 mg, 18.1 μmol, 99 %) as a colourless oil; $\mathbf{R_f}$ 0.43 (9:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +8.4 (c 1.00, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2954, 2877, 1727, 1459, 1381, 1239, 1132, 1076, 992, 927, 727; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.80 (1H, t, *J* = 2.0 Hz, H40), 4.49-4.44 (2H, m, H37, H38), 4.01 (1H, dd, *J* = 11.2, 2.6 Hz, H26), 3.88 (1H, t, *J* = 10.0 Hz, H28), 3.71 (1H, dd, *J* = 11.2, 1.3 Hz, H26), 3.67-3.61 (2H, m, H27, H29), 3.45 (3H, s, MeO29), 2.61 (2H, dd, *J* = 5.8, 2.0 Hz, H39), 2.26 (1H, dd, *J* = 14.3, 6.1 Hz, H36), 2.12 (1H, dd, *J* = 12.7, 5.0 Hz, H30), 2.02 (1H, dd, *J* = 14.3, 2.6 Hz, H36), 1.90 (1H, dq, *J* = 13.0, 3.5 Hz, H33), 1.79 (1H, td, *J* = 13.2, 3.2 Hz, H32), 1.72-1.63 (1H, m, H34), 1.53 (1H, dt, *J* = 13.2, 4.0 Hz, H32), 1.38 (1H, qd, *J* = 13.0, 3.5 Hz, H33), 1.34 (1H, dd, *J* = 12.5, 11.7 Hz, H30), 0.98-0.92 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.60 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.58 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.9, 195.6, 108.8, 97.8, 79.1, 78.8, 74.3, 72.0, 61.9, 59.1, 57.4, 48.2, 43.6, 42.5, 37.3, 35.6, 23.6, 16.3, 6.8, 6.7, 4.6, 4.5; **HRMS** calc. for $C_{29}H_{59}O_7NClSi_2$ $[M + NH_4]^+$ 624.3513, found 624.3518.

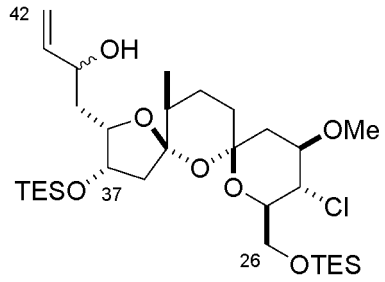
Olefin 57



A 0.25 M stock solution of methylene Wittig reagent was prepared by dropwise addition of *n*-BuLi (1.6 M in hexanes, 310 μL, 0.5 mmol) to a stirred suspension of PPh_3CH_3Br (179 mg, 0.5 mmol) in THF (1.7 mL) at 0°C. The mixture was stirred at 0°C for 1 h before use.

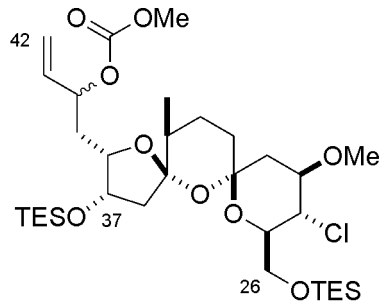
To a stirred solution of aldehyde **55** (26.7 mg, 0.0440 mmol) in THF (1.5 mL) at −78 °C was added the solution of Wittig reagent (0.25 M in THF, 0.60 mL, 0.151 mmol). The reaction mixture was stirred for 1 h at −78 °C and then allowed to warm to room temperature. After 1 h, the reaction was quenched with NH_4Cl solution (2 mL), diluted with Et_2O (2 mL) and the aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude alkene, which was purified by flash column chromatography (SiO_2, 10:1 40-60 petroleum ether / Et_2O) to provide alkene **57** (24.0 mg, 39.6 μmol, 90 %) as a colourless oil; $\mathbf{R_f}$ 0.49 (9:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ −0.8 (c 0.98, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2878, 1459, 1381, 1239, 1134, 1078, 992, 742; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.88-5.78 (1H, m, H40), 5.08 (1H, dd, *J* = 17.3, 1.7 Hz, H41), 5.00 (1H, d, *J* = 10.2 Hz, H41), 4.33-4.30 (1H, m, H37), 3.99 (1H, dd, *J* = 11.4, 2.0 Hz, H26), 3.97-3.91 (2H, m, H38, H28), 3.75 (1H, dd, *J* = 11.4, 1.3 Hz, H26), 3.68-3.60 (2H, m, H27, H29), 3.44 (3H, s, MeO), 2.37-2.28 (1H, m, H39), 2.25-2.17 (2H, m, H36, H39), 2.11 (1H, dd, *J* = 12.6, 5.0 Hz, H30), 2.00 (1H, dd, *J* = 14.3, 2.4 Hz, H36), 1.93 (1H, dq, *J* = 12.9, 3.3 Hz, H33), 1.78 (1H, td, *J* = 13.2, 3.2 Hz, H32), 1.69-1.59 (1H, m, H34), 1.52 (1H, dt, *J* = 13.3, 4.1 Hz, H32), 1.39-1.29 (2H, m, H33, H30), 0.98-0.93 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.60 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.59 (6H, q, *J* = 7.9 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 136.2, 116.1, 108.7, 97.7, 83.5, 79.2, 73.7, 72.0, 62.0, 59.1, 57.3, 48.8, 42.6, 37.6, 35.7, 33.9, 23.8, 16.3, 6.8, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{30}H_{58}O_6ClSi_2$ $[M + H]^+$ 605.3455, found 605.3450.

Allylic alcohols 55a



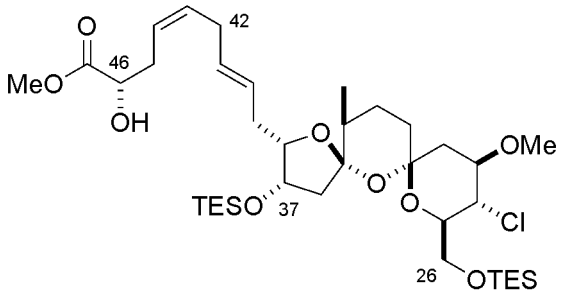
Vinylmagnesium bromide (1.0 M in THF, 65.4 μL, 65.4 mmol) was added dropwise to a stirred solution of aldehyde **55** (30.6 mg, 50.3 μmol) in THF (1 mL) at 0 °C. The reaction mixture was stirred for 1 h and then allowed to warm to room temperature before being quenched with NH_4Cl solution (2 mL) and diluted with Et_2O (5 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 9:1 40-60 petroleum ether / Et_2O) provided allylic alcohol **55a** (15.3 mg, 24.1 μmol, 55 % as a 1:1 diastereomeric mixture of alcohols at C40) as a colourless oil; $\mathbf{R_f}$ 0.30 (9:1 40-60 petroleum ether / EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3519 (br), 2954, 2877, 1459, 1381, 1239, 1167, 1133, 1075, 999, 926, 868, 823, 741; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.95-5.84 (1H, m, H41), 5.31-5.24 (1H, m, H42), 5.10 (1H, dd, *J* = 10.5, 1.2 Hz, H42), 4.39-4.30 (2H, m, H37, H40), 4.24-4.15 (1H, m, H38), 4.07 (0.5H, dd, *J* = 11.7, 2.0 Hz, 0.5 × H26), 4.02-3.97 (1.5H, m, H28, 0.5 × H26), 3.96-3.91 (0.5H, m, 0.5 × H26), 3.87-3.83 (0.5H, m, 0.5 × H26), 3.81-3.76 (0.5H, m, 0.5 × H29), 3.71-3.63 (1.5H, m, H27, 0.5 × H29), 3.45 (1.5H, s, 0.5 × MeO), 3.45 (1.5H, s, 0.5 × MeO), 3.00 (1H, d, *J* = 5.3 Hz, OH40), 2.28-2.21 (1H, m, H36), 2.12 (1H, td, *J* = 12.5, 4.3 Hz, H30), 2.02 (0.5H, dd, *J* = 14.3, 2.2 Hz, 0.5 × H36), 1.92-1.76 (3H, m, H32, H33, H39), 1.72-1.49 (3H, m, H34, H32, H39), 1.45-1.28 (2H, m, H33, H30), 1.00-0.92 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.64-0.56 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 141.7, 140.6, 114.1, 113.5, 109.4, 108.7, 98.1, 97.7, 83.9, 79.9, 79.0, 78.9, 74.4, 73.7, 72.5, 72.4, 71.9, 69.5, 63.1, 61.2, 59.8, 58.9, 57.4, 57.3, 48.5, 42.6, 42.6, 37.5, 37.4, 36.1, 36.0, 35.7, 35.7, 23.8, 23.7, 16.4, 6.8, 6.8, 6.8, 4.8, 4.7, 4.5, 4.5; **HRMS** calc. for $C_{31}H_{60}ClO_7Si_2$ $[M + H]^+$ 635.3561 (^{35}Cl), found 635.3564.

Allylic carbonate 52



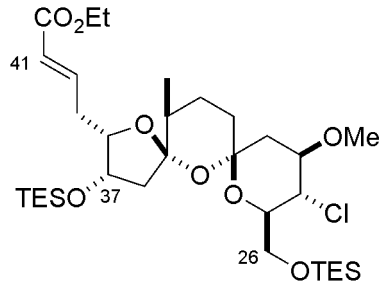
To a stirred solution of allylic alcohols **55a** (14 mg, 0.022 mmol) in DCM (1.5 mL) at 0 °C was added pyridine (36 μL, 0.44 mmol), 4-DMAP (0.2 mg, 0.002 mmol) and methyl chloroformate (17 μL, 0.22 mmol). The white suspension was stirred at 0 °C for 30 min and then allowed to warm to room temperature. After stirring for a further 30 min, the mixture became a clear solution. Additional methyl chloroformate (5 × 17 μL) was added portionwise over 1 h in order to complete the reaction which was then quenched with NH_4Cl solution (2 mL). The aqueous phase was extracted with DCM (3 × 5 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 / EtOAc) to afford allylic carbonate **52** (9.8 mg, 0.014 mmol, 64 % as a diastereomeric mixture) as a colourless oil; **R_f** 0.35 (9:1 40-60 petroleum ether / EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2877, 1751, 1459, 1442, 1380, 1264, 1132, 1071, 990, 925, 727; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.92-5.84 (1H, m, H41), 5.35 (0.5H, td, *J* = 14.4, 1.1 Hz, 0.5 × H42), 5.31 (0.5H, td, *J* = 14.4, 1.1 Hz, 0.5 × H42), 5.24 (0.5H, td, *J* = 10.5, 1.1 Hz, 0.5 × H42), 5.21 (0.5H, td, *J* = 10.5, 1.1 Hz, 0.5 × H42), 5.18 (0.5H, q, *J* = 6.7 Hz, 0.5 × H40), 5.11-5.05 (0.5H, m, 0.5 × H40), 4.55-4.50 (0.5H, m, 0.5 × H37), 4.49-4.44 (0.5H, m, 0.5 × H37), 4.14-4.09 (0.5H, m, 0.5 × H38), 4.09-4.00 (1.5H, m, H26, 0.5 × H38), 3.96 (0.5H, t, *J* = 10.0 Hz, 0.5 × H28), 3.95 (0.5H, t, *J* = 10.0 Hz, 0.5 × H28), 3.77 (1.5H, s, 0.5 × MeO_2CO), 3.77 (1.5H, s, 0.5 × MeO_2CO), 3.73 (1H, ddd, *J* = 16.5, 11.4, 1.5 Hz, H26), 3.68-3.57 (2H, m, H29, H27), 3.45 (3H, s, MeO), 2.15 (1H, ddd, *J* = 13.6, 12.1, 6.5 Hz, H36), 2.10 (1H, dd, *J* = 12.6, 5.0 Hz, H30), 1.98-1.90 (3H, m, H36, H33, H39), 1.90-1.72 (2H, m, H39, H32), 1.71-1.62 (1H, m, H34), 1.56-1.48 (1H, m, H32), 1.40-1.29 (2H, m, H33, H30), 1.00-0.93 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.65-0.58 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.2, 154.9, 136.5, 135.8, 118.2, 117.1, 108.4, 108.3, 97.7, 97.6, 79.3, 79.1, 78.8, 76.4, 74.2, 74.0, 71.8, 71.4, 61.6, 61.5, 58.8, 57.3, 54.6, 54.5, 47.4, 46.7, 42.5, 42.4, 37.1, 36.9, 35.6, 35.5, 34.5, 33.6, 21.5, 16.4, 6.8, 4.7, 4.5; **HRMS** calc. for $C_{33}H_{65}O_9NClSi_2$ $[M + NH_4]^+$ 710.3881, found 710.3890.

Methyl ester 60



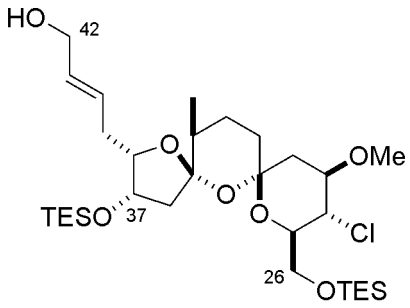
To a stirred solution of allylic carbonate **52** (2.2 mg, 3.2 μmol) and vinyl stannane **8** (1.9 mg, 6.3 μmol) in degassed DMF / H_2O (4:1 v/v, 0.2 mL) was added $(MeCN)_2PdCl_2$ (0.1 mg, 3.2 μmol). The reaction mixture was stirred for 16 h before being quenched with NH_4Cl (0.5 mL) and diluted with Et_2O (2 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 6:1 40-60 petroleum ether / EtOAc) afforded methyl ester **60** (0.8 mg, 1.1 μmol, 33 %) as a colourless oil; $\mathbf{R_f}$ 0.34 (4:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +7.2 (c 0.18, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3457 (br), 2955, 2919, 1740, 1459, 1380, 1260, 1073, 1016, 799, 726; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.62-5.54 (1H, m, H43), 5.50-5.38 (3H, m, H40, H44, H41), 4.32-4.29 (1H, m, H37), 4.29-4.25 (1H, m, H46), 4.01 (1H, dd, *J* = 11.5, 2.1 Hz, H26), 3.94 (1H, t, *J* = 9.9 Hz, H28), 3.93-3.88 (1H, m, H38), 3.79 (3H, s, MeO_2C), 3.74 (1H, dd, *J* = 11.4, 1.5 Hz, H26), 3.68-3.60 (2H, m, H27, H29), 3.44 (3H, s, MeO), 2.78 (2H, br t, *J* = 6.4 Hz, H42), 2.73 (1H, d, *J* = 5.9 Hz, OH46), 2.62-2.54 (1H, m, H45), 2.52-2.44 (1H, m, H45), 2.28-2.16 (3H, m, 2 × H39, H36), 2.11 (1H, dd, *J* = 12.5, 5.0 Hz, H30), 1.98 (1H, dd, *J* = 14.2, 2.6 Hz, H36), 1.91 (1H, dt, *J* = 13.1, 3.1 Hz, H33), 1.77 (1H, td, *J* = 13.1, 3.1 Hz, H32), 1.69-1.59 (1H, m, H34), 1.52 (1H, dt, *J* = 13.2, 4.0 Hz, H32), 1.40-1.28 (2H, m, H33, H30), 0.98-0.92 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.63-0.55 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.0, 131.7, 129.7, 128.0, 123.4, 108.6, 97.7, 83.7, 79.2, 74.0, 71.9, 70.1, 61.8, 59.0, 57.3, 52.5, 48.7, 42.5, 37.6, 35.7, 32.6, 32.1, 30.8, 29.7, 23.7, 16.3, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{37}H_{67}O_9ClSi_2Na$ $[M + Na]^+$ 769.3904, found 769.3931.

Ethyl ester 56



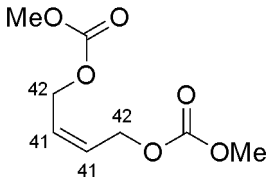
To a stirred solution of triethyl phosphonoacetate (4.8 mg, 0.021 mmol) in THF (200 μL) was added $Ba(OH)_2$ (3.3 mg, 0.019 mmol). The mixture was stirred for 30 min before the addition of a solution of aldehyde **55** (11.7 mg, 19.3 μmol) in wet THF (ca. 5% H_2O, 200 μL). The reaction mixture was stirred for 1 h at room temperature before being quenched with $NaHCO_3$ solution (0.5 mL) and diluted with Et_2O (0.5 mL). The aqueous phase was extracted with Et_2O (2 × 0.5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The product was purified by flash column chromatography (SiO_2, 20:1 40-60 petroleum ether / EtOAc) to afford α,β-unsaturated ester **56** (10.8 mg, 0.0159 mmol, 83 %) as a colourless oil; $\mathbf{R_f}$ 0.43 (9:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +3.9 (c 1.00, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2956, 2878, 1724, 1459, 1381, 1175, 1133, 1076, 997, 743; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.98 (1H, td, *J* = 15.7, 7.2 Hz, H40), 5.90 (1H, d, *J* = 15.7 Hz, H41), 4.46-4.42 (1H, m, H37), 4.21 (2H, dq, *J* = 7.2, 2.0 Hz, $CO_2CH_2CH_3$), 4.10-4.04 (1H, m, H38), 4.01 (1H, dd, *J* = 11.5, 2.1 Hz, H26), 3.95 (1H, t, *J* = 9.9 Hz, H28), 3.73 (1H, dd, *J* = 11.4, 1.1 Hz, H26), 3.70-3.63 (1H, m, H29), 3.59 (1H, d, *J* = 10.3 Hz, H27), 3.45 (3H, s, MeO), 2.49-2.39 (2H, m, H39), 2.23 (1H, dd, *J* = 13.9, 6.6 Hz, H36), 2.13 (1H, dd, *J* = 12.6, 5.0 Hz, H30), 2.03 (1H, dd, *J* = 14.1, 3.4 Hz, H36), 1.94 (1H, dq, *J* = 13.0, 3.2 Hz, H33), 1.80 (1H, td, *J* = 13.3, 3.2 Hz, H32), 1.73-1.64 (1H, m, H34), 1.54 (1H, dt, *J* = 13.3, 3.9 Hz, H32), 1.42-1.27 (2H, m, H33, H30), 1.31 (3H, t, *J* = 7.2 Hz, $CO_2CH_2C\underline{H}_3$), 1.00-0.95 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.62 (12H, dq, *J* = 7.9, 2.7 Hz, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.2, 146.1, 128.3, 127.5, 122.9, 108.8, 108.6, 97.8, 97.7, 81.9, 79.2, 78.8, 74.2, 72.0, 71.9, 61.7, 60.1, 59.1, 58.9, 57.4, 57.3, 48.2, 48.0, 43.6, 42.4, 37.3, 35.6, 32.6, 23.6, 16.3, 14.3, 6.8, 6.8, 5.0, 4.7, 4.6, 4.5, 4.3; **HRMS** calc. for $C_{33}H_{64}ClO_8NSi_2$ $[M + NH_4]^+$ 694.3932 (^{35}Cl), found 694.3930.

Allylic alcohol 56a



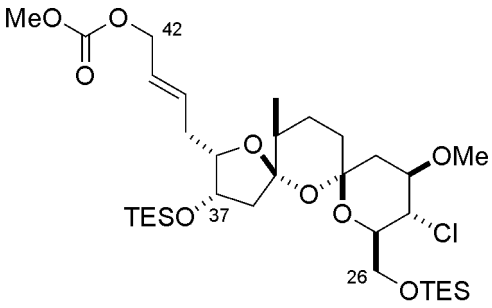
DIBAL-H (1.0 M in DCM, 32.0 μL, 32.0 μmol) was added dropwise to a stirred solution of ester **56** (10.8 mg, 15.9 μmol) in DCM (1 mL) at –78 °C. The mixture was allowed to warm to –40 °C and stirred for 1 h before being quenched with NH_4Cl solution (0.2 mL) and diluted with Na^+/K^+ tartrate solution (0.2 mL). After phase separation, the aqueous phase was extracted with DCM (2 × 0.5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 10:1 40-60 petroleum ether / EtOAc) afforded allylic alcohol **56a** (5.6 mg, 8.8 μmol, 55 %) as a colourless oil; $\mathbf{R_f}$ 0.15 (9:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +1.0 (c 0.31, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3444 (br), 2954, 2876, 1459, 1380, 1239, 1132, 1072, 992, 867, 823, 726; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.73-5.69 (2H, m, H40, H41), 4.35-4.32 (1H, m, H37), 4.13-4.09 (2H, m, H42), 3.99 (1H, dd, *J* = 11.2, 2.3 Hz, H26), 3.96-3.93 (1H, m, H38), 3.92 (1H, t, *J* = 10.0 Hz, H28), 3.72 (1H, dd, *J* = 11.4, 1.5 Hz, H26), 3.68-3.59 (2H, m, H27, H29), 3.44 (3H, s, MeO), 2.33-2.28 (1H, m, H39), 2.27-2.24 (1H, m, H39), 2.21 (1H, dd, *J* = 14.1, 6.4 Hz, H36), 2.11 (1H, dd, *J* = 12.7, 4.9 Hz, H30), 1.99 (1H, dd, *J* = 14.1, 2.7 Hz, H36), 1.92 (1H, dq, *J* = 13.1, 3.4 Hz, H33), 1.78 (1H, td, *J* = 13.2, 3.3 Hz, H32), 1.69-1.61 (1H, m, H34), 1.52 (1H, dt, *J* = 13.2, 4.0 Hz, H32), 1.36 (1H, qd, *J* = 13.1, 3.3 Hz, H33), 1.32 (1H, dd, *J* = 12.5, 11.6 Hz, H30), 0.98-0.93 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.60 (12H, q, *J* = 7.8 Hz, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 130.7, 130.3, 108.6, 97.7, 83.3, 79.1, 74.0, 71.9, 63.8, 61.9, 59.1, 57.3, 48.6, 42.5, 37.5, 35.6, 32.4, 29.7, 23.7, 16.3, 6.8, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{31}H_{63}ClO_7NSi_2$ $[M + NH_4]^+$ 652.3826 (^{35}Cl), found 652.3819.

Carbonic acid (*Z*)-4-methoxycarbonyloxy-but-2-enyl ester methyl ester 58



To a stirred solution of *cis*-2-butene-1,4-diol (1.00 mL, 12.0 mmol) in THF (20 mL) at 0 °C was added pyridine (5.92 mL, 73.4 mmol) and methyl chloroformate (2.82 mL, 36.2 mmol). The reaction mixture was stirred at 0 °C for 1 h before being quenched with NH_4Cl solution (10 mL). After phase separation, the aqueous phase was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 6:1 40-60 petroleum ether / EtOAc) afforded *bis*-allylic carbonate **58** (1.97 g, 9.66 mmol, 80 %) as a colourless oil; $\mathbf{R_f}$ 0.37 (3:1 40-60 petroleum ether / EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 1742, 1443, 1241, 946, 790; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.80 (1H, ddd, *J* = 5.2, 4.0, 1.2 Hz, H41), 4.75 (1H, dd, *J* = 4.0, 1.2 Hz, H42), 3.78 (3H, s, MeO_2CO); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.5, 127.9, 63.1, 54.8; **HRMS** calc. for $C_8H_{16}O_6N$ $[M + NH_4]^+$ 222.0972, found 222.0970.

Allylic carbonate 53



Method 1:

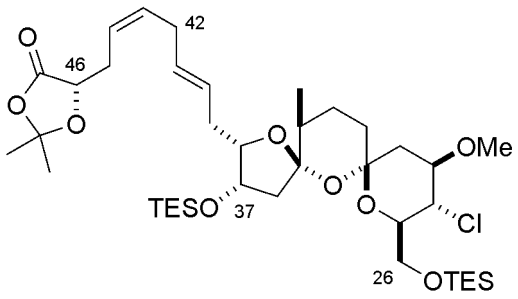
To a stirred solution of allylic alcohol **56a** (2.9 mg, 4.6 μmol) in THF (0.3 mL) at 0 °C was added pyridine (1.0 μL, 0.014 mmol) and methyl chloroformate (0.5 μL, 6.8 μmol). The reaction mixture was stirred at room temperature for 16 h before being quenched with NH_4Cl solution (0.3 mL). The aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 20:1 40-60 petroleum ether / EtOAc) provided allylic carbonate **53** (1.8 mg, 2.6 μmol, 56 %) as a colourless oil.

Method 2:

To a solution of alkene **57** (18.6 mg, 30.7 μmol) and *bis*-methyl carbonate **58** (12.5 mg, 61.2 μmol) in DCM (1 mL) was added Grubbs 2nd generation catalyst (1.3 mg, 1.6 μmol). The reaction mixture was refluxed at 40 °C for 3 h before allowing to cool to room temperature and concentration *in vacuo*. The crude residue was purified by flash column chromatography (SiO_2, 20:1 40-60 petroleum ether / EtOAc) to afford allylic carbonate **53** (20.5 mg, 29.6 μmol, 95 % as an inseparable mixture of *E* and *Z* isomers, *E*/*Z* = 7:1) as a colourless oil.

53: $\mathbf{R_f}$ 0.38 (9:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +2.4 (c 0.50, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2877, 1751, 1458, 1381, 1263, 1133, 1074, 994, 942, 741; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.87-5.78 (1H, m, H40), 5.66 (1H, td, *J* = 15.4, 6.5 Hz, H41), 4.62-4.54 (2H, m, H42), 4.37-4.33 (1H, m, H37), 4.00 (1H, dd, *J* = 11.4, 2.2 Hz, H26), 3.97-3.93 (1H, m, H38), 3.92 (1H, t, *J* = 9.9 Hz, H28), 3.78 (3H, s, MeO_2CO), 3.70 (1H, dd, *J* = 11.2, 1.3 Hz, H26), 3.67-3.61 (1H, m, H29), 3.59 (1H, d, *J* = 10.3 Hz, H27), 3.44 (3H, s, MeO29), 2.36-2.23 (1H, m, H39), 2.20 (1H, dd, *J* = 14.2, 6.4 Hz, H36), 2.11 (1H, dd, *J* = 12.6, 5.0 Hz, H30), 1.99 (1H, dd, *J* = 14.1, 2.9 Hz, H36), 1.91 (1H, dq, *J* = 13.0, 3.3 Hz, H33), 1.77 (1H, td, *J* = 13.2, 3.2 Hz, H32), 1.69-1.60 (1H, m, H34), 1.52 (1H, dt, *J* = 13.2, 4.0 Hz, H32), 1.36 (1H, qd, *J* = 13.0, 3.4 Hz, H33), 1.32 (1H, dd, *J* = 12.5, 11.5 Hz, H30), 0.98-0.92 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.63-0.55 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.6, 134.1, 125.0, 108.6, 103.8, 102.5, 101.1, 97.7, 82.9, 79.2, 74.0, 71.8, 68.5, 61.8, 59.0, 57.3, 54.7, 48.4, 42.5, 37.4, 35.6, 32.5, 23.7, 16.3, 6.8, 4.8, 4.5; **HRMS** calc. for $C_{33}H_{65}ClO_9NSi_2$ $[M + NH_4]^+$ 710.3881, found 710.3869.

Diene 59



Method 1:

To a stirred solution of allylic carbonate **53** (2.6 mg, 3.7 μmol) and vinyl stannane ***ent*-50** (2.4 mg, 7.5 μmol) in degassed DMF / H_2O (4:1 v/v, 0.2 mL) was added $(MeCN)_2PdCl_2$ (0.1 mg, 3.7 μmol).

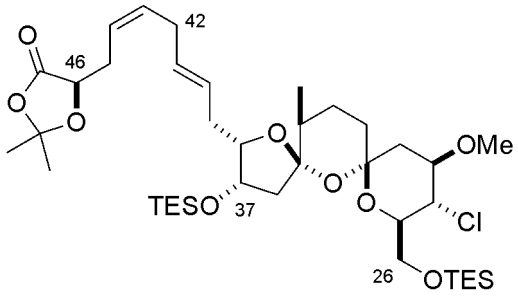
The reaction mixture was stirred for 16 h before being quenched with NH_4Cl (0.2 mL) and diluted with Et_2O (0.5 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 30:1 40-60 petroleum ether / EtOAc) afforded diene **59** (1.7 mg, 2.2 μmol, 59 %) as a colourless oil.

Method 2:

To a stirred solution of allylic carbonate **53** (2.0 mg, 2.9 × 10^{-3} mmol) and vinyl stannane ***ent*-50** (1.8 mg, 5.8 μmol) in degassed DMF / H_2O (4:1 v/v, 0.2 mL) was added $(MeCN)_2PdCl_2$ (0.1 mg, 0.3 μmol). The reaction mixture was stirred for 16 h before being quenched with NH_4Cl (0.5 mL) and diluted with Et_2O (5 mL). After phase separation, the aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 30:1 40-60 petroleum ether / EtOAc) afforded diene **59** (1.8 mg, 2.3 μmol, 80 %) as a colourless oil.

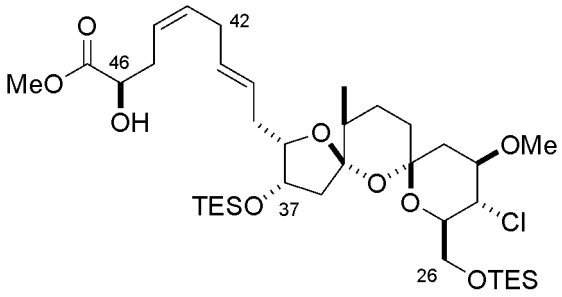
59: $\mathbf{R_f}$ 0.28 (9:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ −1.4 (c 0.66, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 1798, 1458, 1380, 1239, 1131, 992, 933, 745; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.67-5.60 (1H, m, H43), 5.53-5.41 (3H, m, H40, H44, H41), 4.47 (1H, dd, *J* = 6.7, 4.4 Hz, H46), 4.35-4.31 (1H, m, H37), 4.04 (1H, dd, *J* = 11.2, 2.0 Hz, H26), 3.96 (1H, t, *J* = 10.0 Hz, H28), 3.97-3.93 (1H, m, H38), 3.76 (1H, br d, *J* = 11.2 Hz, H26), 3.71-3.63 (2H, m, H27, H29), 3.47 (3H, s, MeO), 2.90-2.76 (2H, m, H42), 2.70-2.61 (1H, m, H45), 2.60-2.52 (1H, m, H45), 2.30-2.18 (3H, m, 2 × H39, H36), 2.14 (1H, dd, *J* = 12.7, 4.9 Hz, H30), 2.01 (1H, dd, *J* = 14.1, 2.3 Hz, H36), 1.94 (1H, dt, *J* = 13.1, 3.1 Hz, H33), 1.80 (1H, td, *J* = 13.1, 3.1 Hz, H32), 1.71-1.63 (1H, m, H34), 1.63 (3H, s, Me), 1.58-1.51 (1H, m, H32), 1.56 (3H, s, Me), 1.42-1.26 (2H, m, H33, H30), 1.01-0.95 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.66-0.58 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.6, 132.1, 129.5, 128.1, 122.9, 110.6, 108.6, 97.7, 83.7, 79.2, 73.9, 71.8, 61.8, 59.0, 57.3, 48.7, 42.5, 37.6, 35.7, 32.6, 30.8, 29.3, 27.1, 25.9, 23.7, 16.3, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{39}H_{73}O_9NClSi_2$ $[M + NH_4]^+$ 790.4507, found 790.4498.

Diene 59a



$(MeCN)_2PdCl_2$ (0.6 mg, 2.2 μmol) was added to a stirred solution of allylic carbonate **53** (15.3 mg, 22.1 μmol) and vinyl stannane **50** (14.1 mg, 44.1 μmol) in degassed DMF / H_2O (4:1 v/v, 1 mL). The reaction mixture was stirred at room temperature for 16 h before being quenched with NH_4Cl (1 mL) and diluted with Et_2O (5 mL). After phase separation, the aqueous phase was extracted with Et_2O (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 30:1 40-60 petroleum ether / EtOAc) afforded diene **59a** (9.5 mg, 12.3 μmol, 56 %; 69 % based on recovered starting material) as a colourless oil; **R_f** 0.27 (9:1 40-60 petroleum ether / EtOAc); **$[\alpha]_D^{20}$** +4.3 (c 0.95, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2954, 2877, 1798, 1459, 1380, 1238, 1129, 1073, 990, 930, 726; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.64-5.57 (1H, m, H43), 5.50-5.39 (3H, m, H40, H44, H41), 4.45 (1H, dd, *J* = 6.6, 4.5 Hz, H46), 4.33-4.29 (1H, m, H37), 4.01 (1H, dd, *J* = 11.4, 2.2 Hz, H26), 3.93 (1H, t, *J* = 10.1 Hz, H28), 3.92-3.88 (1H, m, H38), 3.73 (1H, dd, *J* = 11.2, 1.3 Hz, H26), 3.68-3.60 (2H, m, H27, H29), 3.44 (3H, s, MeO), 2.79 (2H, br t, *J* = 6.1 Hz, H42), 2.67-2.61 (1H, m, H45), 2.56-2.49 (1H, m, H45), 2.25-2.17 (3H, m, 2 × H39, H36), 2.11 (1H, dd, *J* = 12.5, 5.0 Hz, H30), 1.98 (1H, dd, *J* = 14.1, 2.7 Hz, H36), 1.91 (1H, dt, *J* = 13.1, 3.2 Hz, H33), 1.77 (1H, td, *J* = 13.1, 3.1 Hz, H32), 1.68-1.61 (1H, m, H34), 1.60 (3H, s, Me), 1.55-1.48 (1H, m, H32), 1.54 (3H, s, Me), 1.39-1.28 (2H, m, H33, H30), 0.98-0.92 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.63-0.55 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.6, 132.1, 129.5, 128.1, 122.9, 110.5, 108.6, 97.7, 83.7, 79.2, 74.0, 71.8, 61.8, 59.1, 57.3, 48.7, 42.5, 37.6, 35.7, 32.5, 30.8, 29.3, 27.1, 25.9, 23.7, 16.3, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{39}H_{73}O_9NClSi_2$ $[M + NH_4]^+$ 790.4507, found 790.4496.

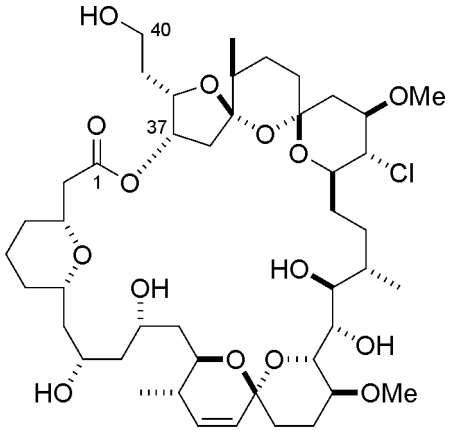
Methyl ester 60a



To a stirred solution of acetonide **59a** (2.3 mg, 3.0 μmol) in MeOH (0.5 mL) was added K_2CO_3 (0.4 mg, 3.0 μmol). The suspension was stirred at room temperature for 30 min before being quenched with pH 7 buffer (0.5 mL) and diluted with DCM (5 mL). After phase separation, the aqueous phase was extracted with DCM (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purificaiton by flash column chromatography (SiO_2, 4:1 40-60 petroleum ether / EtOAc) produced methyl ester **60a** (2.2 mg, 2.9 μmol, 99 %) as a colourless oil; $\mathbf{R_f}$ 0.29 (4:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ –3.6 (c 0.22, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3488 (br), 2954, 2877, 1741, 1459, 1381, 1238, 1132, 1074, 991, 936, 727; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.62-5.55 (1H, m, H43), 5.50-5.38 (3H, m, H40, H44, H41), 4.33-4.29 (1H, m, H37), 4.29-4.25 (1H, m, H46), 4.01 (1H, dd, *J* = 11.2, 2.1 Hz, H26), 3.94 (1H, t, *J* = 10.1 Hz, H28), 3.92-3.88 (1H, m, H38), 3.79 (3H, s, MeO_2C), 3.74 (1H, dd, *J* = 11.2, 1.3 Hz, H26), 3.68-3.61 (2H, m, H27, H29), 3.44 (3H, s, MeO), 2.84-2.71 (2H, m, H42), 2.73 (1H, d, *J* = 6.0 Hz, OH46), 2.62-2.55 (1H, m, H45), 2.52-2.44 (1H, m, H45), 2.27-2.16 (3H, m, 2 × H39, H36), 2.11 (1H, dd, *J* = 12.5, 5.0 Hz, H30), 1.98 (1H, dd, *J* = 14.1, 2.6 Hz, H36), 1.91 (1H, dt, *J* = 13.1, 3.3 Hz, H33), 1.77 (1H, td, *J* = 13.2, 3.3 Hz, H32), 1.69-1.60 (1H, m, H34), 1.52 (1H, dt, *J* = 13.3, 4.0 Hz, H32), 1.36 (1H, qd, *J* = 13.0, 3.4 Hz, H33), 1.32 (1H, dd, *J* = 12.5, 11.5 Hz, H30), 0.98-0.92 (21H, m, Me34, 2 × $Si(CH_2C\underline{H}_3)_3$), 0.63-0.55 (12H, m, 2 × $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.0, 131.7, 129.7, 128.0, 123.4, 108.6, 97.7, 83.7, 79.2, 74.0, 71.9, 70.1, 61.8, 59.1, 57.3, 52.5, 48.7, 42.5, 37.6, 35.7, 32.6, 32.1, 30.8, 29.7, 23.7, 16.3, 6.8, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{37}H_{71}O_9ClSi_2N$ $[M + NH_4]^+$ 764.4350, found 764.4353.

2.6 Side-chain assembly / total synthesis

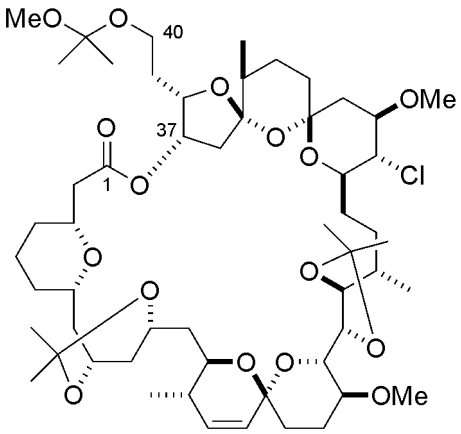
Macrocylic pentaol 44



HF·pyridine complex (HF 70 %, 250 μL) was added dropwise to a stirred solution of pyridine (125 μL) in THF (750 μL) in a Teflon container. The premixed HF·pyridine-pyridine solution (2:1 v/v, 750 μL) was added to a stirred solution of macrolactone **43** (7.6 mg, 5.6×10^{-3} mmol) in THF (750 μL). The reaction mixture was stirred for 5 h at room temperature before being quenched by cautious addition of $NaHCO_3$ solution (1 mL) at 0 °C. The mixture was extracted with DCM (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was diluted with DCM (2 mL) followed by *n*-heptane (2 mL). The clear solution was concentrated slowly to half the total volume and the resulting white solid was filtered, washed with *n*-pentane (2 × 2 mL) and dried *in vacuo*. A second recrystallisation afforded macrocyclic pentaol **44** (4.1 mg, 4.6 μmol, 83 %) as a colourless crystalline solid. Alternatively, this product could also be purified by flash column chromatography (SiO_2, 1:1 → 1:2 40-60 petroleum ether / EtOAc) to obtain **44** in 92 % yield as a white solid; **m.p.** 174 °C; $\mathbf{R_f}$ 0.27 (1:2 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +14.1 (c 0.49, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3481 (br), 2933, 1747, 1380, 1251, 1092, 978; **^{1}H NMR** (500 MHz, C_6D_6) δ 5.64 (1H, dt, *J* = 8.4, 7.3 Hz, H37), 5.57 (1H, dd, *J* = 9.9, 1.3 Hz, H15), 5.53 (1H, dd, *J* = 10.0, 2.3 Hz, H16), 5.11 (1H, br s, OH9), 4.87 (1H, ddd, *J* = 10.8, 6.9, 2.7 Hz, H38), 4.65 (1H, br s, OH40), 4.63 (1H, br t, *J* = 10.6 Hz, H11), 4.49-4.42 (1H, m, H9), 4.31 (1H, d, *J* = 9.8 Hz, H21), 4.22 (1H, br dd, *J* = 17.1, 8.6 Hz, H40), 4.07 (1H, br t, *J* = 10.8 Hz, H22), 3.98-3.87 (4H, m, H7, H40, H27, H13), 3.83 (1H, ddd, *J* = 11.4, 9.7, 5.0 Hz, H29), 3.81-3.74 (2H, m, H3, OH), 3.69 (1H, br d, *J* = 9.7 Hz, H23), 3.60 (1H, br s, OH), 3.54 (1H, t, *J* = 9.9 Hz, H28), 3.36 (1H, ddd, *J* = 11.2, 10.4, 5.0 Hz, H20), 3.31 (3H, s, MeO), 3.10 (3H, s, MeO), 2.42 (1H, br td, *J* = 13.2, 3.2 Hz, H26), 2.35 (1H, dd, *J* = 14.3, 9.9 Hz, H2), 2.19 (1H, dd, *J* = 13.2, 9.2 Hz, H36), 2.16-2.07

(5H, m, H36, H30, H25, H24, H2), 2.00-1.81 (5H, m, 2 × H39, H14, H19, H33), 1.76 (1H, dt, *J* = 13.6, 4.0 Hz, H32), 1.74 (1H, dt, *J* = 13.2, 3.6 Hz, H18), 1.73-1.55 (4H, m, H12, H19, 2 × H8), 1.54-1.15 (14H, m, 2 × H5, H34, 2 × H10, H25, H12, H18, H32, H30, H26, 2 × H6, H33), 1.10-1.02 (2H, m, 2 × H4), 0.99 (3H, d, *J* = 7.0 Hz, Me24), 0.92 (3H, d, *J* = 6.7 Hz, Me34), 0.77 (3H, d, *J* = 7.1 Hz, Me14); **^{13}C NMR** (125 MHz, C_6D_6) δ 170.1 (C1), 135.3 (C15), 128.4 (C16), 107.4 (C35), 97.8 (C31), 93.8 (C17), 79.3 (C29), 77.2 (C38), 76.1 (C23), 75.5 (C27), 74.6 (C7), 74.5 (C20), 74.2 (C3), 73.8 (C37), 71.1 (C21), 70.6 (C13), 69.0 (C22), 66.0 (C28), 63.3 (C11), 62.8 (C9), 60.4 (C40), 57.5 (MeO29), 56.6 (MeO20), 47.2 (C10), 45.1 (C8), 43.6 (C30), 42.8 (C2), 42.8 (C12), 40.4 (C36), 36.0 (C34), 35.7 (C32), 34.9 (C14), 34.5 (C18), 33.9 (C24), 32.2 (C6), 31.9 (C4), 31.5 (C39), 31.0 (C26), 25.5 (C25), 24.2 (C19), 23.9 (C5), 23.8 (C33), 17.9 (Me24), 17.2 (Me34), 16.6 (Me14); **HRMS** calc. for $C_{45}H_{73}O_{15}ClNa$ $[M + Na]^+$ 911.4541, found 911.4512.

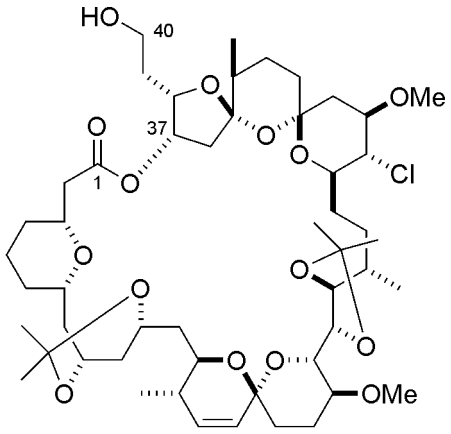
Macrolactone peracetonide 44a



PPTS (10 mg, 0.040 mmol) was added to a stirred solution of macrocyclic pentaol **44** (2.7 mg, 3.0 μmol) in 2,2-dimethoxypropane / DCM (2:1 v/v, 1.5 mL). The reaction mixture was stirred at 35 °C for 16 h before being quenched with $NaHCO_3$ solution (1 mL). The mixture was extracted with DCM (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 2:1 40-60 petroleum ether / EtOAc) to provide peracetonide **44a** (3.0 mg, 2.9 μmol, 95 %) as a colourless oil; **R_f** 0.45 (2:1 40-60 petroleum ether / EtOAc); **$[\alpha]_D^{20}$** +12.5 (c 0.36, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2932, 1736, 1461, 1379, 1216, 1098, 1027, 985, 932; **^{1}H NMR** (500 MHz, C_6D_6) δ 5.69 (1H, dd, *J* = 9.9, 2.3 Hz, H16), 5.59 (1H, dd, *J* = 9.9, 2.8 Hz, H15), 5.47 (1H, dd, *J* = 6.2, 2.6 Hz, H37), 4.68 (1H, d, *J* = 6.0 Hz, H22), 4.56 (1H, dddd, *J* = 13.5, 10.0, 7.2, 2.8 Hz, H11), 4.34 (1H, dt, *J* = 11.3, 2.0 Hz, H38), 4.25 (1H, br ddd, *J* = 12.5, 10.9, 3.7 Hz, H9), 4.15-4.07 (2H, m, H13, H27), 4.00 (1H, dd, *J* = 10.4, 5.9 Hz, H23), 3.89 (1H, d, *J* = 9.3 Hz, H21), 3.82-3.70 (5H, m, H28, H29, 2 × H40, H3), 3.55

(1H, br t, *J* = 9.5 Hz, H7), 3.52-3.45 (1H, m, H20), 3.29 (3H, s, MeO), 3.27 (3H, s, OMe), 3.16 (3H, s, MeO), 2.62-2.53 (1H, m, H26), 2.48-2.39 (3H, m, H39, H25, H2), 2.35 (1H, ddd, *J* = 14.2, 10.5, 3.2 Hz, H12), 2.26 (1H, dd, *J* = 15.3, 6.5 Hz, H36), 2.29-2.22 (1H, m, H24), 2.23-2.12 (3H, m, H39, H2b, H30), 2.07-1.83 (6H, m, H33, H18, 2 × H19, H14, H26), 2.00 (1H, d, *J* = 15.3 Hz, H36), 1.73 (3H, s, Me), 1.72 (3H, s, Me), 1.73-1.62 (2H, m, H10, H32), 1.68 (3H, s, Me), 1.58-1.04 (15H, m, H12, 2 × H6, H34, H18, 2 × H8, H10, 2 × H5, H32, H30, H33, H25, H4), 1.51 (3H, s, Me), 1.40 (3H, s, Me), 1.35 (3H, s, Me), 1.21 (3H, d, *J* = 6.4 Hz, Me24), 1.13 (3H, d, J = 7.2 Hz, Me14), 1.07 (3H, d, *J* = 6.7 Hz, Me34), 0.92-0.83 (1H, m, H4); **^{13}C NMR** (125 MHz, C_6D_6) δ 169.6 (C1), 132.9 (C15), 129.6 (C16), 108.7 (C22/23 acetonide C), 108.0 (C35), 100.8 (C9/11 acetonide C), 100.1 (C40 acetonide C), 98.0 (C31), 92.7 (C17), 82.4 (C23), 80.9 (C38), 79.8 (C29), 76.4 (C22), 75.9 (C7), 75.1 (C20), 73.4 (C37), 73.1 (C3), 72.7 (C27), 72.0 (C21), 69.6 (C13), 64.5 (C9), 62.4 (C28), 62.3 (C11), 58.0 (C40), 57.5 (C40 acetonide OMe), 56.2 (MeO20), 48.7 (MeO29), 47.0 (C36), 44.6 (C12), 44.1 (C2), 43.4 (C30), 42.5 (C8), 39.9 (C10), 38.4 (C34), 36.5 (C32), 36.5 (C14), 34.4 (C18), 34.3 (C24), 32.2 (C6), 32.0 (C4), 28.8 (C39), 28.0 (C26), 28.0 (C9/11 acetonide Me), 27.0 (C22/23 acetonide Me), 26.7 (C22/23 acetonide Me), 25.4 (C9/11 acetonide Me), 24.8 (C40 acetonide Me), 24.8 (C40 acetonide Me), 24.7 (C25), 24.2 (C33), 23.8 (C5), 23.2 (C19), 18.9 (Me24), 18.6 (Me14), 16.5 (Me34); **HRMS** calc. for $C_{55}H_{89}O_{16}ClNa$ $[M + Na]^+$ 1063.5742, found 1063.5703.

Macrolactone *bis*-acetonide 45



PPTS (0.1 mg, 4.2 μmol) was added to a stirred solution of peracetonide **44a** (4.4 mg, 4.2 μmol) in DCM / MeOH (12:1 v/v, 1 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h before being quenched with $NaHCO_3$ solution (1 mL). The aqueous phase was extracted with DCM (3 × 1 mL) and the combined organic phases were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 3:1 → 2:1 40-60 petroleum ether / EtOAc →

EtOAc only) to provide alcohol **45** (2.2 mg, 2.3 μmol, 54 %) as a colourless oil; $\mathbf{R_f}$ 0.45 (1:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +7.5 (c 0.40, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3489 (br), 2935, 1735, 1463, 1379, 1252, 1218, 1097, 1028, 985, 933; **^{1}H NMR** (500 MHz, C_6D_6) δ 5.64 (1H, dd, *J* = 10.0, 2.3 Hz, H16), 5.55 (1H, dd, *J* = 10.0, 2.5 Hz, H15), 5.40-5.36 (1H, m, H37), 4.65 (1H, d, *J* = 6.0 Hz, H22), 4.54-4.48 (1H, m, H11), 4.45-4.41 (1H, m, H38), 4.15 (1H, br t, *J* = 10.0 Hz, H9), 4.12 (1H, dt, *J* = 10.3, 3.2 Hz, H27), 4.07 (1H, dt, *J* = 9.2, 3.3 Hz, H13), 3.98 (1H, dd, *J* = 10.4, 5.9 Hz, H23), 3.95-3.88 (1H, m, H40), 3.88 (1H, d, *J* = 9.5 Hz, H21), 3.87-3.82 (1H, m, H40), 3.80 (1H, td, *J* = 10.5, 4.5 Hz, H29), 3.75 (1H, t, *J* = 9.9 Hz, H28), 3.75-3.70 (1H, m, H3), 3.52-3.44 (2H, m, H7, H20), 3.31 (3H, s, MeO), 3.15 (3H, s, MeO), 2.59-2.51 (1H, m, H26), 2.47-2.40 (1H, m, H25), 2.38 (1H, dd, *J* = 14.6, 10.5 Hz, H2), 2.36-2.30 (1H, m, H39), 2.25-1.80 (13H, m, H2, H12, H14, H18, 2 × H19, H24, H26, H30, H33, 2 × H36, H39), 1.73-1.03 (18H, m, 2 × H4, 2 × H5, 2 × H6, 2 × H8, 2 × H10, H12, H18, H25, H30, 2 × H32, H33, H34), 1.71 (3H, s, Me), 1.66 (3H, s, Me), 1.63 (3H, s, Me), 1.49 (3H, s, Me), 1.17 (3H, d, *J* = 6.4 Hz, Me24), 1.06 (3H, d, *J* = 7.0 Hz, Me14), 1.01 (3H, d, *J* = 6.7 Hz, Me34); **^{13}C NMR** (125 MHz, C_6D_6) δ 170.8, 133.3, 129.5, 108.8, 107.7, 100.8, 98.1, 93.0, 82.3, 80.8, 79.8, 76.3, 76.2, 75.2, 75.1, 73.7, 72.7, 71.9, 70.1, 64.5, 62.4, 62.3, 57.6, 56.2, 45.7, 44.0, 43.8, 43.5, 42.4, 40.5, 38.1, 36.4, 35.9, 34.4, 34.3, 32.1, 32.0, 31.5, 30.2, 28.2, 27.4, 27.0, 26.7, 25.2, 24.9, 24.1, 23.7, 23.3, 18.8, 18.2, 16.5; **HRMS** calc. for $C_{51}H_{81}O_{15}ClNa$ $[M + Na]^+$ 991.5167, found 991.5130.

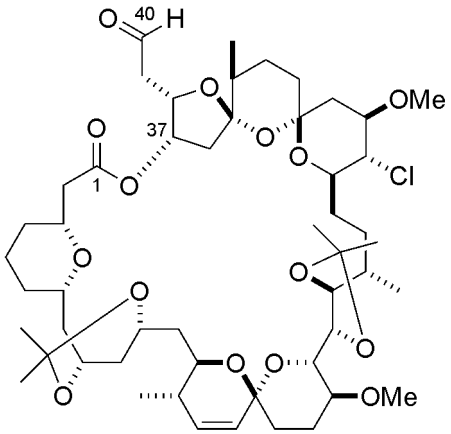
Table 1 – ^{1}H NMR comparisons for pentaol 44 with spirastrellolide A methyl ester (2) and for *bis*-acetonide 45 with *bis*-acetonide 2a of spirastrellolide A methyl ester

Proton number	δ_H (2) [a]	δ_H (44)	$\Delta\delta$	δ_H (2a) [a]	δ_H (45)	$\Delta\delta$
2a	2.48	2.35	-0.03	2.62	2.39	0.23
2b	2.11	2.14	-0.1	2.22	2.13	0.09
3	3.68	3.78	-0.08	3.82	3.74	0.08
4a	1.00	1.08	-0.13	1.06	1.07	-0.01
4b	0.95	1.08	0.26	1.06	0.90	0.16
5a	1.50	1.24	-0.25	1.48	1.45	0.03
5b	1.25	1.50	-0.08	1.27	1.23	0.04
6a	1.17	1.25	-0.19	1.30	1.27	0.03
6b	1.00	1.19	-0.27	1.13	1.07	0.06
7	3.67	3.94	0.44	3.59	3.49	0.1
8a	2.02	1.58	-0.06	1.66	1.70	-0.04
8b	1.52	1.58	-0.17	1.46	1.50	-0.04
9	4.31	4.48	0.45	4.30	4.15	0.15
10a	1.89	1.44	-0.09	1.69	1.70	-0.01
10b	1.28	1.37	0.08	1.34	1.37	-0.03
11	4.70	4.62	0.45	4.55	4.51	0.04
12a	2.09	1.64	-0.02	2.17	2.16	0.01
12b	1.43	1.45	0.03	1.58	1.62	-0.04
13	3.94	3.91	0.02	4.07	4.07	0
14	1.94	1.92	0	1.92	1.88	0.04
15	5.57	5.57	0.01	5.56	5.55	0.01
16	5.54	5.53	0.06	5.66	5.64	0.02
18a	1.80	1.74	0.08	1.95	1.94	0.01
18b	1.45	1.37	0.08	1.49	1.50	-0.01
19a	1.98	1.90	0.18	1.94	1.94	0
19b	1.85	1.67	0.05	1.85	1.85	0
20	3.42	3.37	0.06	3.50	3.47	0.03
21	4.37	4.31	0.09	3.89	3.89	0
22	4.16	4.07	0.12	4.66	4.65	0.01
23	3.80	3.68	0.04	4.00	3.98	0.02
24	2.16	2.12	0.22	2.26	2.20	0.06
25a	2.36	2.14	-0.05	2.44	2.44	0
25b	1.37	1.42	0	1.18	1.15	0.03

Proton number	δ_H (2) [a]	δ_H (44)	$\Delta\delta$	δ_H (2a) [a]	δ_H (45)	$\Delta\delta$
26a	2.42	2.53	-0.11	2.56	2.57	-0.01
26b	1.30	1.38	-0.08	1.90	1.91	-0.01
27	3.96	3.94	0.02	4.12	4.11	0.01
28	3.54	3.57	-0.03	3.75	3.75	0
29	3.83	3.83	0	3.80	3.78	0.02
30a	2.12	2.11	0.01	2.14	2.14	0
30b	1.33	1.36	-0.03	1.34	1.34	0
32a	1.34	1.70	-0.36	1.64	1.63	0.01
32b	1.76	1.34	0.42	1.37	1.37	0
33a	1.17	2.13	-0.96	1.99	2.01	-0.02
33b	1.89	1.22	0.67	1.17	1.18	-0.01
34	1.49	1.49	0	1.51	1.50	0.01
36a	2.19	2.29	-0.1	2.16	2.23	-0.07
36b	2.10	1.98	0.12	1.98	1.95	0.03
37	5.64	5.53	0.11	5.38	5.53	-0.15
38	4.87	4.23	0.64	4.43	4.18	0.25
48 (Me14)	0.77	0.89	-0.12	1.07	1.08	-0.01
49 (MeO20)	3.08	3.27	-0.19	3.15	3.16	-0.01
50 (Me24)	0.99	1.23	-0.24	1.07	1.20	-0.13
51 (MeO29)	3.31	3.35	-0.04	3.31	3.31	0
52 (Me34)	0.92	1.07	-0.15	1.01	1.04	-0.03

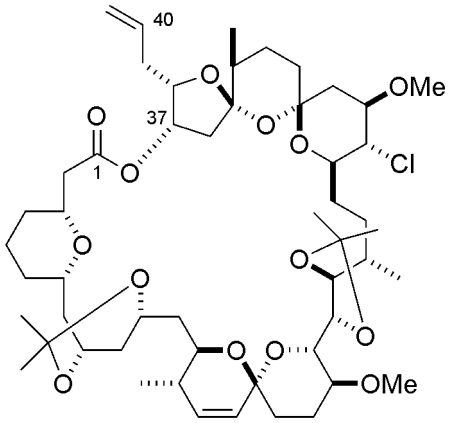
[a] D.E. Williams, M. Roberge, R. Van Soest, R. J. Andersen, *J. Am. Chem. Soc.* **2003**, *125*, 5296.

Macrolactone aldehyde 61



To a stirred solution of alcohol **45** (4.0 mg, 4.1 μmol) in DCM (0.5 mL) was added $NaHCO_3$ (1.7 mg, 21 μmol) and Dess-Martin periodinane (5.3 mg, 12 μmol). The suspension was stirred at room temperature for 1 h before being quenched with $NaHCO_3$ solution (0.5 mL) and $Na_2S_2O_3$ solution (0.5 mL). After vigorous stirring for 30 min, the aqueous phase was extracted with DCM (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 2:1 40-60 petroleum ether / EtOAc) to provide aldehyde **61** (3.2 mg, 3.3 μmol, 80 %) as a colourless oil; $\mathbf{R_f}$ 0.32 (2:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +14.7 (c 0.36, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2931, 1733, 1377, 1217, 1098, 1028, 986, 933; **^{1}H NMR** (500 MHz, C_6D_6) δ 9.93 (1H, br s, H40), 5.61 (1H, dd, *J* = 9.9, 2.3 Hz, H16), 5.50 (1H, dd, *J* = 9.9, 2.7 Hz, H15), 5.21 (1H, dd, *J* = 6.5, 3.2 Hz, H37), 4.80-4.75 (1H, m, H38), 4.64 (1H, d, *J* = 6.0 Hz, H22), 4.54-4.48 (1H, m, H11), 4.25-4.18 (1H, m, H9), 4.08 (1H, td, *J* = 10.3, 3.3 Hz, H27), 4.05-3.99 (1H, m, H23), 3.98 (1H, dd, *J* = 10.5, 6.0 Hz, H13), 3.84 (1H, d, *J* = 9.4 Hz, H21), 3.81-3.69 (3H, m, H3, H28, H29), 3.56-3.45 (2H, m, H7, H20), 3.33 (3H, s, MeO), 3.18-3.06 (2H, m, 2 × H39), 3.15 (3H, s, MeO), 2.65-2.56 (1H, m, H26), 2.48-2.41 (1H, m, H25), 2.37 (1H, dd, *J* = 14.3, 10.8 Hz, H2), 2.26-2.17 (1H, m, H24), 2.16-2.05 (3H, m, H2, H30, H36), 2.05-1.88 (5H, m, H12, H18, H19, H33, H36), 1.88-1.72 (3H, m, H14, H19, H26), 1.72-1.57 (2H, m, H10, H32), 1.69 (3H, s, Me), 1.66 (3H, s, Me), 1.64 (3H, s, Me), 1.57-1.40 (4H, m, H8, H12, H18, H34), 1.49 (3H, s, Me), 1.26-1.10 (8H, m, 2 × H5, H6, H8, H10, H30, H32, H33), 1.15 (3H, d, *J* = 6.4 Hz, Me24), 1.10-0.97 (2H, m, H4, H25), 1.05 (3H, d, *J* = 7.1 Hz, Me14), 0.99 (3H, d, *J* = 6.7 Hz, Me34), 0.95-0.83 (2H, m, H4, H6); **^{13}C NMR** (125 MHz, C_6D_6) δ 198.0, 170.1, 132.8, 129.1, 108.6, 108.0, 100.8, 98.0, 92.5, 82.2, 79.6, 77.5, 76.2, 75.5, 74.9, 73.5, 72.6, 71.9, 69.4, 64.3, 62.1, 61.8, 57.5, 56.0, 45.6, 44.4, 43.8, 43.5, 43.2, 43.0, 42.0, 39.9, 38.0, 36.2, 36.0, 34.1, 32.0, 31.9, 30.0, 29.9, 28.2, 27.8, 26.5, 24.9, 24.6, 23.9, 23.3, 23.0, 18.9, 18.2, 16.2; **HRMS** calc. for $C_{51}H_{79}O_{15}ClNa$ $[M + Na]^+$ 989.5011, found 989.4985.

Macrolactone alkene 62

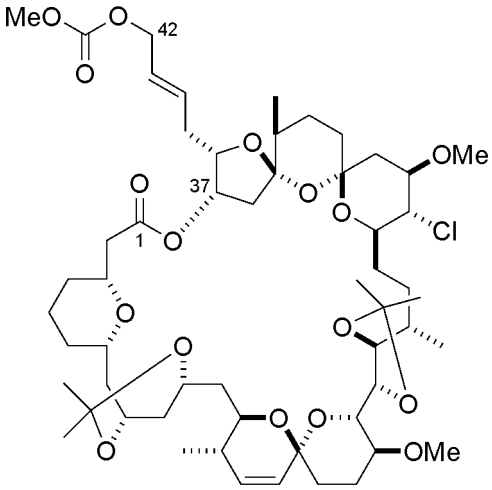


A 0.5 M stock solution of methylene Wittig reagent was prepared by dropwise addition of *n*-BuLi (1.6 M in hexanes, 310 μL, 0.5 mmol) to a stirred suspension of PPh_3CH_3Br (179 mg, 0.5 mmol) in THF (0.7 mL) at 0°C. The mixture was stirred at 0°C for 1 h before use.

To a stirred solution of aldehyde **61** (3.2 mg, 3.3 μmol) in THF (1 mL) at −78 °C was added methyl Wittig reagent (0.5 M in THF, 33 μL, 17 μmol). The reaction mixture was allowed to warm to room temperature and stirred for 30 min before being quenched with NH_4Cl solution (1 mL). The organic phase was separated, the aqueous phase extracted with DCM (3 × 5 mL), and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 3:1 40-60 petroleum ether / EtOAc) afforded alkene **62** (2.4 mg, 2.5 μmol, 75 %) as a colourless oil; $\mathbf{R_f}$ 0.48 (2:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +11.7 (c 0.24, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2932, 1740, 1379, 1218, 1097, 985, 935; **^{1}H NMR** (500 MHz, C_6D_6) δ 6.12-6.02 (1H, m, H40), 5.65 (1H, dd, *J* = 9.9, 2.3 Hz, H16), 5.54 (1H, dd, *J* = 9.9, 2.6 Hz, H15), 5.48 (1H, dd, *J* = 5.8, 3.2 Hz, H37), 5.37 (1H, d, *J* = 17.1 Hz, H41), 5.19 (1H, d, *J* = 10.5 Hz, H41), 4.66 (1H, d, *J* = 6.0 Hz, H22), 4.54-4.47 (1H, m, H11), 4.27-4.20 (1H, br t, *J* = 10.0 Hz, H9), 4.09 (1H, dt, *J* = 10.0, 3.2 Hz, H27), 4.05 (1H, dd, *J* = 9.3, 3.3 Hz, H13), 3.99 (1H, dd, *J* = 10.4, 5.9 Hz, H23), 3.89 (1H, br d, *J* = 9.3 Hz, H21), 3.84-3.72 (3H, m, H29, H28, H3), 3.53 (1H, br t, *J* = 9.8 Hz, H7), 3.47 (1H, br ddd, *J* = 10.6, 9.9, 4.9 Hz, H20), 3.31 (3H, s, MeO), 3.15 (3H, s, MeO), 2.82-2.81 (1H, m, H39), 2.75 (1H, dt, *J* = 13.8, 8.9 Hz, H39), 2.61-2.52 (1H, m, H26), 2.49 (1H, dd, *J* = 15.5, 10.3 Hz, H2), 2.43 (1H, br dt, *J* = 11.0, 9.7 Hz, H25), 2.25-2.20 (1H, m, H24), 2.20-2.10 (4H, m, H2, H12, H30, H36), 2.05-1.99 (1H, m, H33), 1.98-1.80 (6H, m, H14, H18, 2 × H19, H26, H36), 1.71 (3H, s, Me), 1.70 (3H, s, Me), 1.65 (3H, s, Me), 1.50 (3H, s, Me), 1.73-0.90 (18H, m, 2 × H4, 2 × H5, 2 × H6, 2 × H8, 2 × H10, H12, H18, H25, H30, H32, H32, H33, H34), 1.18 (3H, d, *J* = 6.4 Hz, Me24), 1.04 (6H, d, *J* = 7.0 Hz, Me14, Me34); **^{13}C NMR** (125 MHz, C_6D_6) δ 169.4, 135.0, 133.1, 129.6,

118.7, 108.8, 108.2, 100.8, 98.1, 93.0, 83.4, 82.4, 79.8, 76.3, 76.0, 75.1, 73.3, 73.2, 72.7, 71.9, 69.9, 64.7, 62.4, 62.4, 57.6, 56.2, 46.3, 44.0, 43.9, 43.5, 42.5, 40.2, 38.2, 36.4, 36.2, 34.4, 34.3, 33.5, 32.3, 32.1, 28.3, 27.6, 27.1, 26.7, 25.4, 25.0, 24.2, 23.8, 23.2, 18.9, 18.3, 16.5; **HRMS** calc. for $C_{52}H_{81}O_{14}ClNa$ $[M + Na]^+$ 987.5207, found 987.5186.

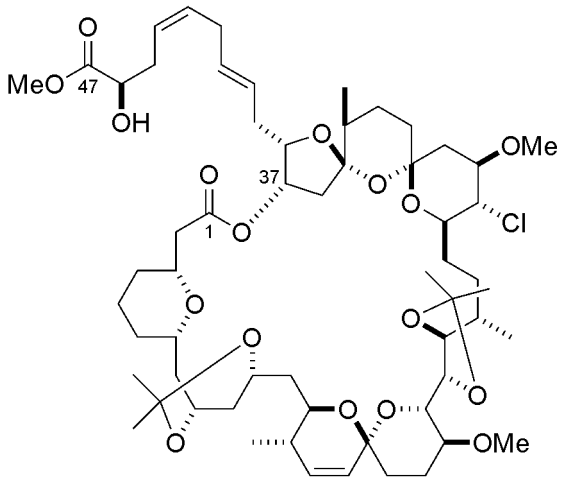
Macrolactone carbonate 63



Grubbs 2nd generation catalyst (0.1 mg, 0.12 μmol) was added in one portion to a stirred solution of alkene **62** (0.8 mg, 0.8 μmol) and (*Z*)-but-2-ene-1,4-diyl dimethyl dicarbonate (**58**, 2.5 mg, 12 μmol) in degassed benzene (200 μL) and the mixture was heated to 80 °C for 14 h. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO_2, 4:1 → 3:1 → 2:1 40-60 petroleum ether / EtOAc) to provide carbonate **63** (0.5 mg, 0.5 μmol, 57 %) as a colourless oil; $\mathbf{R_f}$ 0.28 (2:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +1.7 (c 0.06, $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2924, 2854, 1751, 1660, 1633, 1467, 1378, 1262, 1097, 793; **^{1}H NMR** (500 MHz, C_6D_6) δ 6.00-5.93 (1H, m, H41), 5.82-5.75 (1H, m, H40), 5.65 (1H, dd, *J* = 9.9, 2.3 Hz, H16), 5.57 (1H, dd, *J* = 9.9, 2.6 Hz, H15), 5.37 (1H, dd, *J* = 6.2, 2.8 Hz, H37), 4.65 (1H, d, *J* = 5.9 Hz, H22), 4.62-4.49 (3H, m, H11, 2 × H42), 4.30-4.23 (1H, m, H9), 4.12-4.03 (3H, m, H38, H13, H27), 4.00 (1H, dd, *J* = 10.5, 5.9 Hz, H23), 3.89 (1H, d, *J* = 9.4 Hz, H21), 3.82-3.71 (3H, m, H3, H28, H29), 3.57 (1H, br t, *J* = 9.7 Hz, H7), 3.53-3.46 (1H, m, H20), 3.33 (3H, s, MeO), 3.32 (3H, s, MeO_2CO), 3.15 (3H, s, MeO), 2.94-2.87 (1H, m, H39), 2.85-2.76 (1H, m, H39), 2.61-2.52 (1H, m, H26), 2.50 (1H, dd, *J* = 15.9, 10.0 Hz, H2), 2.48-2.40 (1H, m, H25), 2.31-2.21 (2H, m, H24, H36), 2.21-2.02 (4H, m, H2, H12, H30, H36), 2.02-1.89 (4H, m, H14, H18, H19, H33), 1.89-1.81 (2H, m, H19, H26), 1.73-1.53 (5H, m, H6, H8, H10, H12, H32), 1.71 (3H, s, Me), 1.69 (3H, s, Me), 1.65 (3H, s, Me), 1.53-1.41 (4H, m, H5, H8, H18, H34), 1.50 (3H, s, Me), 1.41-1.12 (8H, m, H4, H5, H10, 2 × H25, H30, H32, H33), 1.19 (3H, d, *J* = 6.4 Hz, Me24), 1.10 (3H, d, *J* = 7.0 Hz, Me14), 1.08-1.05

(1H, m, H6), 1.02 (3H, d, *J* = 6.7 Hz, Me34), 0.98-0.88 (1H, m, H4); **^{13}C NMR** (125 MHz, C_6D_6) δ 169.3, 156.0, 133.0, 131.5, 128.7, 108.7, 108.4, 100.8, 98.1, 92.8, 82.9, 82.3, 79.9, 76.4, 75.9, 75.0, 73.2, 72.8, 72.6, 72.1, 69.7, 68.0, 64.4, 62.4, 62.3, 57.6, 56.1, 54.1, 46.8, 44.4, 43.9, 43.4, 42.2, 39.6, 38.3, 36.4, 36.2, 34.2, 32.3, 32.2, 32.2, 32.1, 28.0, 27.9, 27.1, 26.6, 25.5, 24.8, 24.3, 23.8, 23.2, 23.1, 18.8, 18.4, 16.5; **HRMS** calc. for $C_{55}H_{85}O_{17}ClNa$ $[M + Na]^+$ 1075.5368, found 1075.5332.

Spirastrellolide A methyl ester *bis*-acetonide 64



(MeCN)$PdCl_2$ (0.05 mg, 0.2 μmol) was added to a stirred solution of carbonate **63** (0.5 mg, 0.5 μmol) in degassed DMF / H_2O (4:1 v/v, 50 μL) at 35 °C. A solution of vinyl stannane **7** (1.4 mg, 4.7 mmol) in degassed DMF / water (4:1 v/v, 50 μL) was added portionwise over 3 h and the reaction mixture stirred for an additional 1 hr before being quenched with NH_4Cl solution (0.5 mL). The aqueous phase was extracted with DCM (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 2:1 40-60 petroleum ether / EtOAc) afforded the *bis*-acetonide of spirastrellolide A methyl ester (**64**, 0.5 mg, 0.5 μmol, 96 %) as a colourless oil; $\mathbf{R_f}$ 0.38 (1:1 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +7.7 (c 0.08, CH_2Cl_2); **IR** (thin film, ν_{max}/cm^{-1}) 2924, 2854, 1736, 1669, 1633, 1465, 1378, 1260, 1217, 1096, 1022, 799; **^{1}H NMR** (500 MHz, C_6D_6) δ 5.77 (1H, dt, *J* = 15.0, 6.5 Hz, H41), 5.73-5.64 (1H, m, H43), 5.65 (1H, dd, *J* = 9.9, 2.6 Hz, H16), 5.56 (1H, dd, *J* = 9.9, 2.6 Hz, H15), 5.56-5.47 (3H, m, H37, H40, H44), 4.65 (1H, d, *J* = 6.2 Hz, H22), 4.59-4.53 (1H, m, H11), 4.30 (1H, br t, *J* = 10.0 Hz, H9), 4.18 (1H, dt, *J* = 11.0, 3.1 Hz, H38), 4.15-4.04 (2H, m, H27, H46), 4.07 (1H, td, *J* = 9.5, 3.0 Hz, H13), 4.01 (1H, dd, *J* = 10.2, 5.9 Hz, H23), 3.89 (1H, d, *J* = 9.4 Hz, H21), 3.87-3.72 (2H, m, H3, H29), 3.75 (1H, t, *J* = 10.1 Hz, H28), 3.59 (1H, br t, *J* = 9.4 Hz, H7), 3.51 (1H, td, *J* = 10.9, 4.2 Hz, H20), 3.31 (3H, s, MeO), 3.27 (3H, s, MeO_2C), 3.16 (3H, s, MeO), 3.04 (1H, d, *J* = 6.7 Hz,

OH), 2.93-2.74 (4H, m, 2 × H39, 2 × H42), 2.63 (1H, dd, *J* = 16.4, 10.3 Hz, H2), 2.61-2.49 (2H, m, H26, H45), 2.49-2.37 (2H, m, H25, H45), 2.31-2.21 (1H, m, H24), 2.22 (1H, dd, *J* = 15.6, 6.5 Hz, H36), 2.21 (1H, dd, *J* = 16.2, 1.5 Hz, H2), 2.18-2.11 (1H, m, H12), 2.14 (1H, dd, *J* = 12.9, 4.8 Hz, H30), 2.06-1.99 (1H, m, H33), 1.98-1.88 (4H, m, H18, H19, H14, H26), 1.95 (1H, d, *J* = 15.7 Hz, H36), 1.87-1.81 (1H, m, H19), 1.75-1.54 (4H, m, H8, H10, H32, H12), 1.71 (6H, br s, 2 × Me), 1.65 (3H, s, Me), 1.54-1.43 (4H, m, H5, H8, H18, H34), 1.50 (3H, s, Me), 1.42-1.23 (5H, m, H5, H6, H10, H30, H32), 1.22-1.12 (3H, m, H6, H25, H33), 1.19 (3H, d, *J* = 6.2 Hz, Me24), 1.10-1.04 (2H, m, 2 × H4), 1.07 (3H, d, *J* = 7.1 Hz, Me14), 1.04 (3H, d, *J* = 7.0 Hz, Me34); **^{13}C NMR** (125 MHz, C_6D_6) δ 175.0 (C47), 169.4 (C1), 133.1 (C41), 132.9 (C15), 131.4 (C43), 129.5 (C16), 126.0 (C40), 124.4 (C44), 108.7 (C22/C23 acetonide C), 108.5 (C35), 100.8 (C9/C11 acetonide C), 98.1 (C31), 92.8 (C17), 83.4 (C38), 82.3 (C23), 79.9 (C29), 76.4 (C22), 76.2 (C7), 75.0 (C20), 73.3 (C3), 72.9 (C37), 72.6 (C27), 72.1 (C21), 70.3 (C46), 69.6 (C13), 64.5 (C9), 62.4 (C11), 62.4 (C28), 57.6 (MeO29), 56.2 (MeO20), 51.8 (MeO47), 46.9 (C36), 44.5 (C12), 43.9 (C2), 43.5 (C30), 42.2 (C8), 39.6 (C10), 38.3 (C34), 36.4 (C32), 36.3 (C14), 34.3 (C18), 32.5 (C45), 32.4 (C39), 32.3 (C24), 32.2(C6), 32.0 (C4), 31.2 (C42), 28.0 (C26), 27.9 (C9/C11 acetonide Me), 27.1 (C22/23 acetonide Me), 26.6 (C22/23 acetonide Me), 25.6 (C9/C11 acetonide Me), 24.8 (C25), 24.2 (C5), 23.9 (C33), 23.2 (C19), 18.8 (Me24), 18.3 (Me14), 16.5 (Me34); **HRMS** calc. for $C_{59}H_{91}O_{17}ClNa$ $[M + Na]^+$ 1129.5837, found 1129.5880.

Table 2 – ^{1}H and ^{13}C NMR comparison for *bis*-acetonide 60 and spirastrellolide A methyl ester *bis*-acetonide (2a)

Proton #	δ_H (2a) (800 MHz, C_6D_6) [a]	δ_H (64) (500 MHz, C_6D_6)	Carbon #	δ_C (2a) (200 MHz, C_6D_6) [a]	δ_C (64) (125 MHz, C_6D_6)
			1	169.4	169.4
2a	2.48	2.39	2	43.9	43.9
2b	2.11	2.13			
3	3.68	3.74	3	73.3	73.3
4a	1.00	1.07	4	32.1	32.0
4b	0.95	0.90			
5a	1.50	1.45	5	24.2	24.2
5b	1.25	1.23			
6a	1.17	1.27	6	32.2	32.2
6b	1.00	1.07			
7	3.67	3.49	7	76.2	76.2
8a	2.02	1.70	8	42.2	42.2
8b	1.52	1.50			
9	4.31	4.15	9	64.5	64.5
10a	1.89	1.70	10	39.7	39.6
10b	1.28	1.37			
11	4.70	4.51	11	62.4	62.4
12a	2.09	2.16	12	44.4	44.5
12b	1.43	1.62			
13	3.94	4.07	13	69.6	69.6
14	1.94	1.88	14	36.3	36.3
15	5.57	5.55	15	132.9	132.9
16	5.54	5.64	16	129.6	129.5
			17	92.8	92.8
18a	1.80	1.94	18	34.3	34.3
18b	1.45	1.50			
19a	1.98	1.94	19	23.2	23.2
19b	1.85	1.85			
20	3.42	3.47	20	75.1	75.0
21	4.37	3.89	21	72.1	72.1
22	4.16	4.65	22	76.4	76.4
23	3.80	3.98	23	82.3	82.3
24	2.16	2.20	24	34.2	34.2

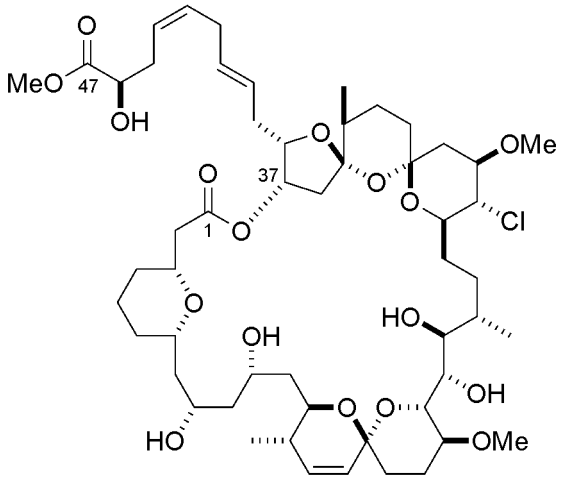
Proton #	δ_H (2a) (800 MHz, C_6D_6) [a]	δ_H (64) (500 MHz, C_6D_6)
25a	2.36	2.44
25b	1.37	1.15
26a	2.53	2.56
26b	1.38	1.90
27	3.94	4.12
28	3.57	3.75
29	3.83	3.80
30a	2.11	2.14
30b	1.36	1.34
31		
32a	1.70	1.64
32b	1.34	1.37
33a	2.13	1.99
33b	1.22	1.17
34	1.50	1.50
36a	2.21	2.22
36b	1.95	1.95
37	5.52	5.52
38	4.18	4.18
39a	2.88	2.88
39b	2.78	2.78
40	5.52	5.52
41	5.77	5.77
42a	2.82	2.82
42b	2.82	2.82
43	5.69	5.69
44	5.51	5.51
45a	2.50	2.50
45b	2.41	2.41
46	4.12	4.12
48 (Me14)	1.07	1.07

Carbon #	δ_C (2a) (200 MHz, C_6D_6) [a]	δ_C (64) (125 MHz, C_6D_6)
25	24.8	24.8
26	28.0	28.0
27	72.6	72.6
28	62.4	62.4
29	79.9	79.9
30	43.5	43.5
31	98.1	98.1
32	36.5	36.4
33	23.9	23.9
34	38.3	38.3
35	108.5	108.5
36	46.9	46.9
37	72.9	72.9
38	83.4	83.4
39	32.4	32.4
40	126.0	126.0
41	133.1	133.1
42	31.2	31.2
43	131.3	131.4
44	124.4	124.4
45	32.6	32.5
46	70.4	70.3
47	175.0	175.0
48	18.3	18.3

Proton #	δ_H (2a) (800 MHz, C_6D_6) [a]	δ_H (64) (500 MHz, C_6D_6)	Carbon #	δ_C (2a) (200 MHz, C_6D_6) [a]	δ_C (64) (125 MHz, C_6D_6)
49 (MeO20)	3.16	3.16	49	56.2	56.2
50 (Me24)	1.19	1.19	50	18.8	18.8
51 (MeO29)	3.31	3.31	51	57.6	57.6
52 (Me34)	1.04	1.04	52	16.5	16.5
53 (MeO47)	3.27	3.27	53	51.8	51.8
C9/11 acetonide Me	1.71, 1.65	1.71, 1.65	C9/11 acetonide Me	27.9, 25.6	27.9, 25.6
			C9/11 acetonide C	100.8	100.8
C22/23 acetonide Me	1.71, 1.50	1.71, 1.50	C22/23 acetonide Me	27.1, 26.6	27.1, 26.6
			C22/23 acetonide C	108.7	108.7

[a] D. E. Williams, M. Lapawa, X. Feng, T. Tarling, M. Roberge and R. J. Andersen, *Org. Lett.,* **2004**, *6*, 2607.

Spirastrellolide A methyl ester (2)



PPTS (ca. 0.5 mg) was added to a stirred solution of *bis*-acetonide **64** (0.4 mg, 0.4 μmol) in MeOH (0.4 mL) at 35 °C. The reaction mixture was stirred for 20 h at 35 °C before being concentrated *in vacuo*, quenched with $NaHCO_3$ solution (1 mL) and extracted with DCM (3 × 5 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by HPLC (25 % water in MeOH, 1.0 mL/min) 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 to afford spirastrellolide A methyl ester **2** (retention time = 29 min, 0.2 mg, 0.2 μmol, 54 %) as a colourless oil; $\mathbf{R_f}$ 0.10 (1:2 40-60 petroleum ether / EtOAc); $\mathbf{[\alpha]_D^{20}}$ +28.6 (c 0.007, CH_2Cl_2); **IR** (thin film, ν_{max}/cm^{-1}) 3352 (br), 2923, 2853, 1740, 1556, 1464, 1261, 1096, 804; ^{1}**H NMR** (500 MHz, C_6D_6) δ 5.89 (1H, dt, *J* = 15.4, 6.8 Hz, H41), 5.71-5.63 (1H, m, H43), 5.58 (1H, dd, *J* = 9.9, 1.4 Hz, H15), 5.58-5.51 (3H, m, H16, H40, H37), 5.49-5.42 (1H, m, H44), 4.67 (1H, br t, *J* = 10.4 Hz, H11), 4.64 (1H, d, *J* = 6.9 Hz, OH), 4.61 (1H, d, *J* = 3.8 Hz, OH), 4.39 (1H, d, *J* = 9.4 Hz, H21), 4.36-4.29 (1H, m, H9), 4.24 (1H, td, *J* = 11.0, 3.3 Hz, H38), 4.22-4.14 (2H, m, H46, H22), 4.04 (1H, d, *J* = 7.6 Hz, OH), 3.94 (2H, t, *J* = 10.3 Hz, H13, H27), 3.83 (1H, ddd, *J* = 11.3, 9.8, 5.1 Hz, H29), 3.79 (1H, dd, *J* = 9.5, 7.1 Hz, H23), 3.73-3.66 (2H, m, H3, H7), 3.56 (1H, t, *J* = 10.2 Hz, H28), 3.41 (1H, ddd, *J* = 10.8, 9.7, 4.4 Hz, H20), 3.35 (3H, s, MeO), 3.32 (3H, s, MeO_2C), 3.22 (3H, s, MeO), 3.21-3.14 (1H, m, H39), 2.79-2.71 (1H, m, H42), 2.69-2.61 (1H, m, H42), 2.59-2.48 (4H, m, H45, H2, H26, H39), 2.40-2.29 (2H, m, H45, H25), 2.28 (1H, dd, *J* = 15.5, 7.0 Hz, H36), 2.20-2.07 (4H, m, H24, H33, H2, H30), 2.04 (1H, br dd, *J* = 14.4, 9.2 Hz, H12), 2.03-1.93 (3H, m, H8, H19, H14), 1.97 (1H, d, *J* = 15.3 Hz, H36), 1.90-1.77 (3H, m, H19, H10, H18), 1.73-1.67 (1H, m, H32), 1.67 (1H, d, *J* = 12.1 Hz, OH), 1.54-1.32 (9H, m, H8, H5, H34, H12, H18, H25, H26, H30, H32), 1.30-1.15 (4H, m, H5, H33, H10, H6), 1.23 (3H, d, *J* = 6.8 Hz, Me24), 1.08 (3H, d, *J* =

6.8 Hz, Me34), 1.05-0.98 (3H, m, 2 × H4, H6), 0.88 (3H, d, *J* = 7.2 Hz, Me14); **HRMS** calc. for $C_{53}H_{83}O_{17}ClNa$ $[M + Na]^+$ 1049.5211, found 1049.5234.

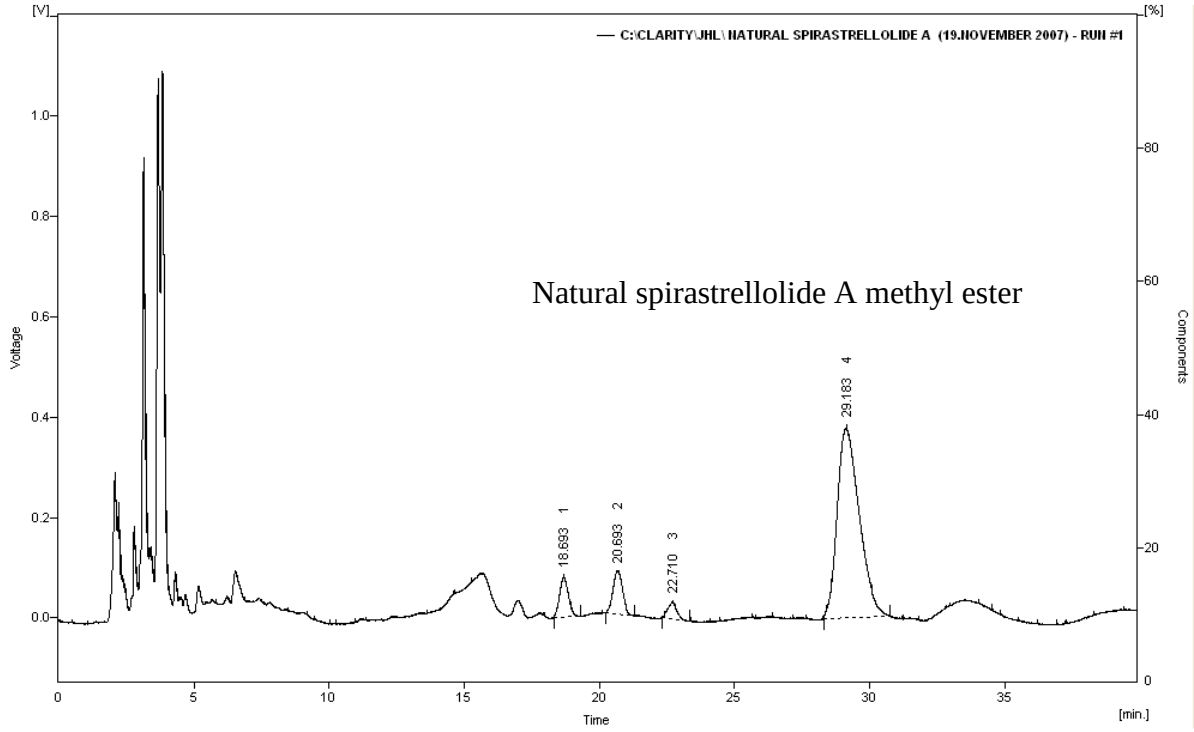
Table 3 – ^{1}H NMR comparison for natural and synthetic spirastrellolide A methyl ester (2)

Proton number	δ_H (800 MHz, C_6D_6), natural product literature data[a]	δ_H (500 MHz, C_6D_6), natural product sample[b]	δ_H (500 MHz, C_6D_6), synthetic sample
2a	2.48	2.50	2.50
2b	2.11	2.11	2.11
3	3.68	3.68	3.68
4a	1.00	1.00	1.00
4b	0.95	0.95	0.95
5a	1.50	1.50	1.50
5b	1.25	1.24	1.24
6a	1.17	1.17	1.17
6b	1.00	1.00	1.00
7	3.67	3.67	3.67
8a	2.02	2.00	2.00
8b	1.52	1.52	1.52
9	4.31	4.33	4.33
10a	1.89	1.89	1.89
10b	1.28	1.25	1.25
11	4.70	4.67	4.67
12a	2.09	2.09	2.09
12b	1.43	1.43	1.43
13	3.94	3.94	3.94
14	1.94	1.94	1.94
15	5.57	5.58	5.58
16	5.54	5.54	5.54
18a	1.80	1.80	1.80
18b	1.45	1.45	1.45
19a	1.98	1.98	1.98
19b	1.85	1.85	1.85
20	3.42	3.41	3.41
21	4.37	4.39	4.39
22	4.16	4.17	4.17
23	3.80	3.79	3.79
24	2.16	2.16	2.16
25a	2.36	2.35	2.35
25b	1.37	1.36	1.36
26a	2.53	2.53	2.53
26b	1.38	1.34	1.34

Proton number	δ_H (800 MHz, C_6D_6), natural product literature data[a]	δ_H (500 MHz, C_6D_6), natural product sample[b]	δ_H (500 MHz, C_6D_6), synthetic sample
27	3.94	3.94	3.94
28	3.57	3.56	3.56
29	3.83	3.83	3.83
30a	2.11	2.10	2.10
30b	1.36	1.36	1.36
32a	1.70	1.70	1.70
32b	1.34	1.34	1.34
33a	2.13	2.14	2.14
33b	1.22	1.23	1.23
34	1.49	1.50	1.50
36a	2.29	2.28	2.28
36b	1.98	1.97	1.97
37	5.53	5.54	5.54
38	4.23	4.24	4.24
39a	3.21	3.19	3.19
39b	2.52	2.51	2.51
40	5.56	5.56	5.56
41	5.90	5.89	5.89
42a	2.75	2.75	2.75
42b	2.65	2.65	2.65
43	5.68	5.67	5.67
44	5.45	5.45	5.45
45a	2.53	2.54	2.54
45b	2.37	2.37	2.37
46	4.19	4.19	4.19
48 (Me14)	0.89	0.88	0.88
49 (MeO20)	3.27	3.22	3.22
50 (Me24)	1.23	1.22	1.22
51 (MeO29)	3.35	3.35	3.35
52 (Me34)	1.07	1.08	1.08
53 (MeO47)	3.32	3.32	3.32
OH	4.57, 4.46, 4.17, 1.67	4.64, 4.61, 4.04, 1.67	4.64, 4.61, 4.04, 1.67

[a] D.E. Williams, M. Roberge, R. Van Soest, R. J. Andersen, *J. Am. Chem. Soc.* **2003**, *125*, 5296. [b] A sample of methyl ester of natural spirastrellolide A was kindly provided by Professor R. J. Andersen.

Figure 1 – HPLC Chromatograms of natural and synthetic spirastrellolide A methyl ester



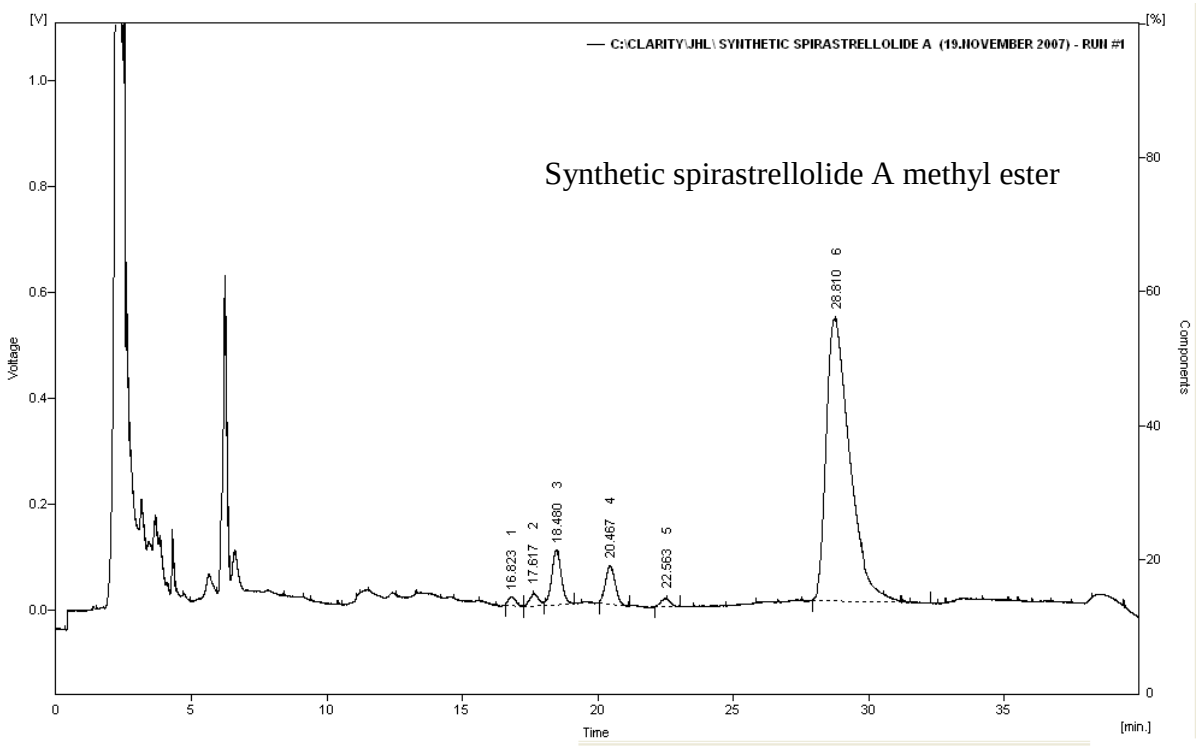
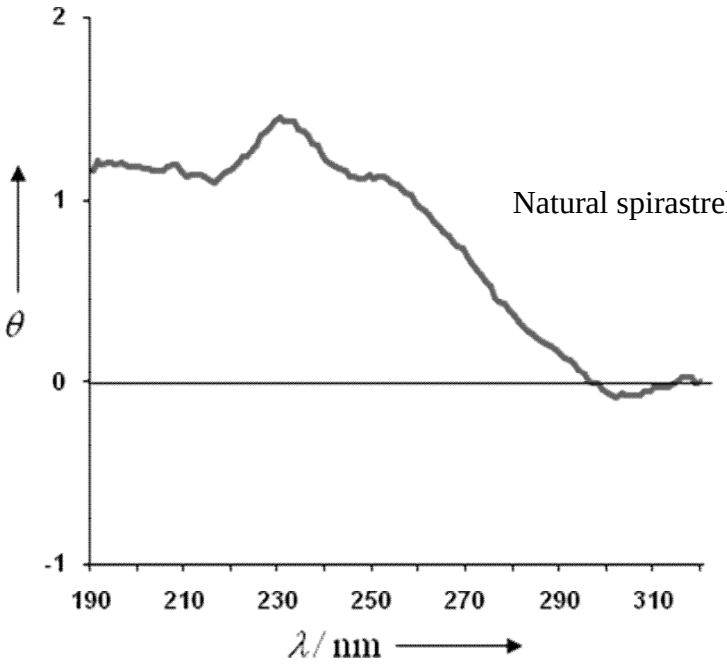
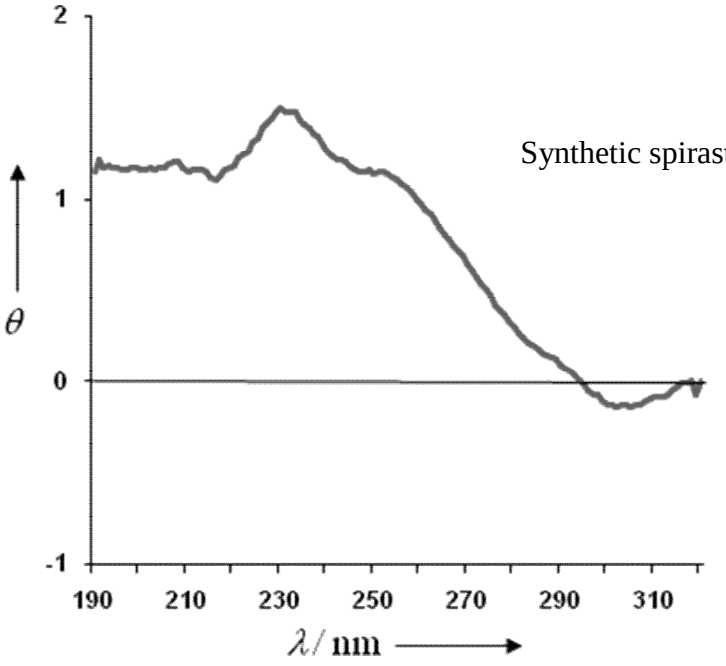


Figure 2 – CD Spectra for natural and synthetic spirastrellolide A methyl ester



Natural spirastrellolide A methyl ester

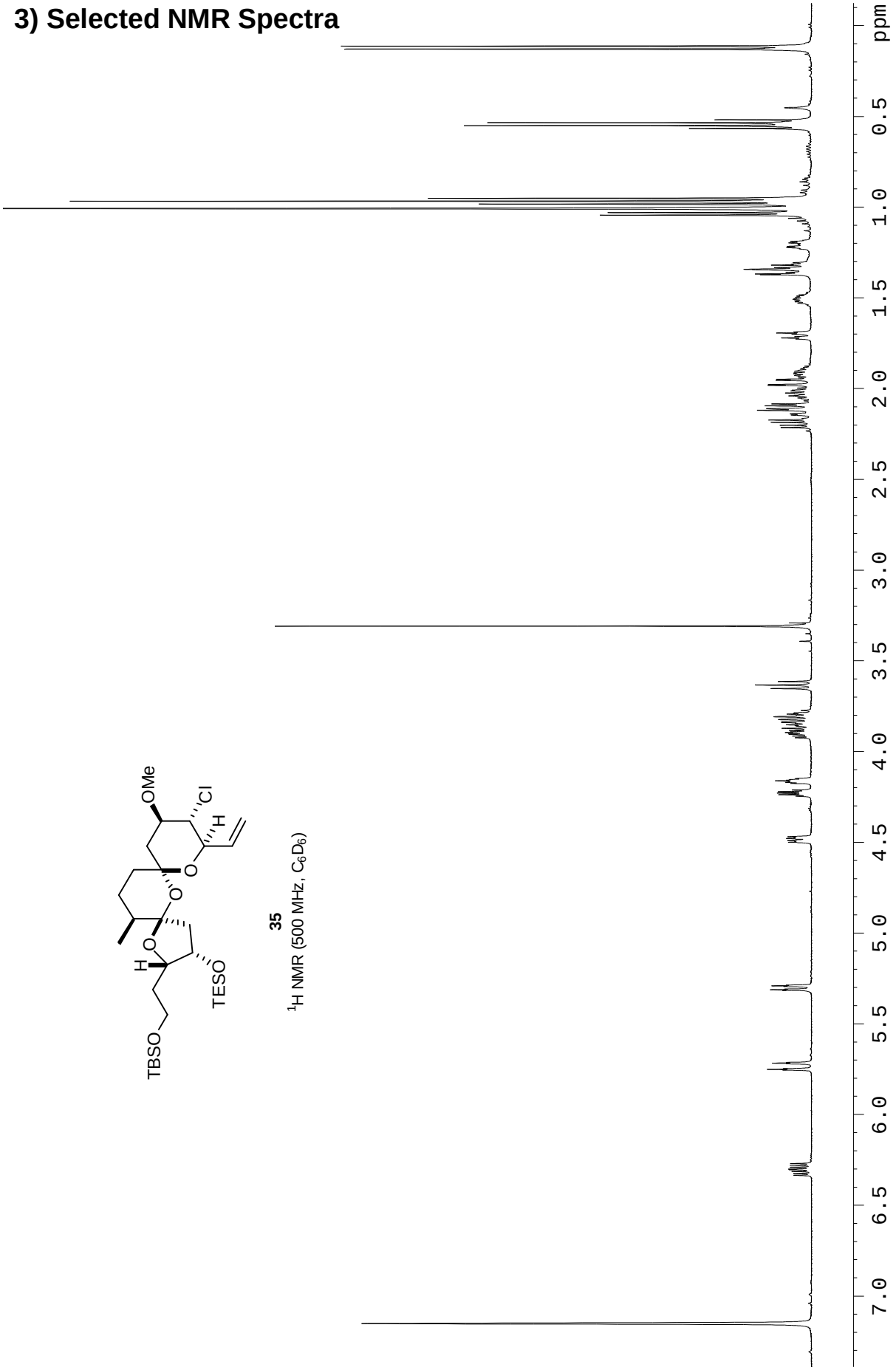
c = 0.000126 M in DCM



Synthetic spirastrellolide A methyl ester

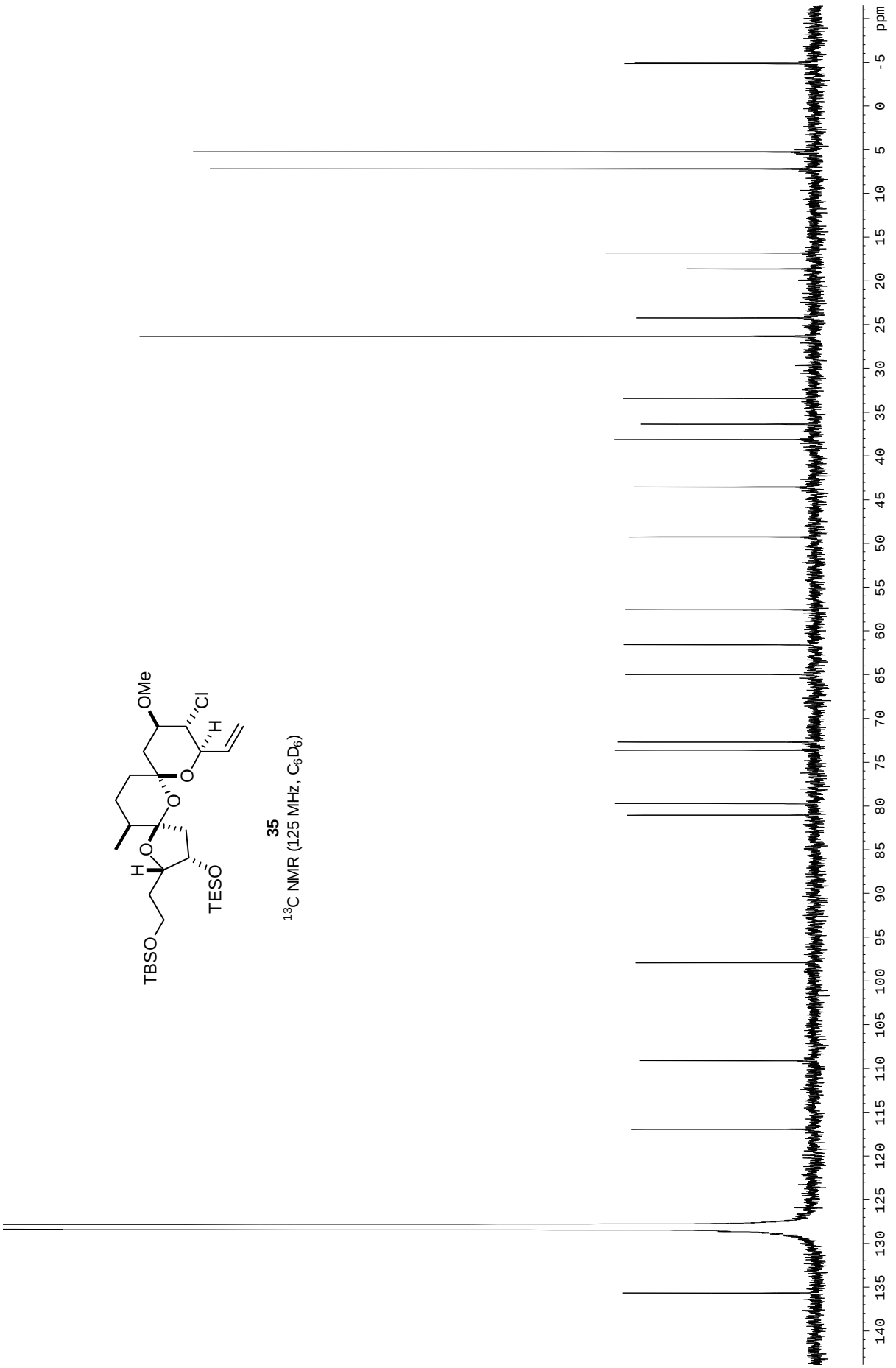
c = 0.000214 M in DCM

3) Selected NMR Spectra



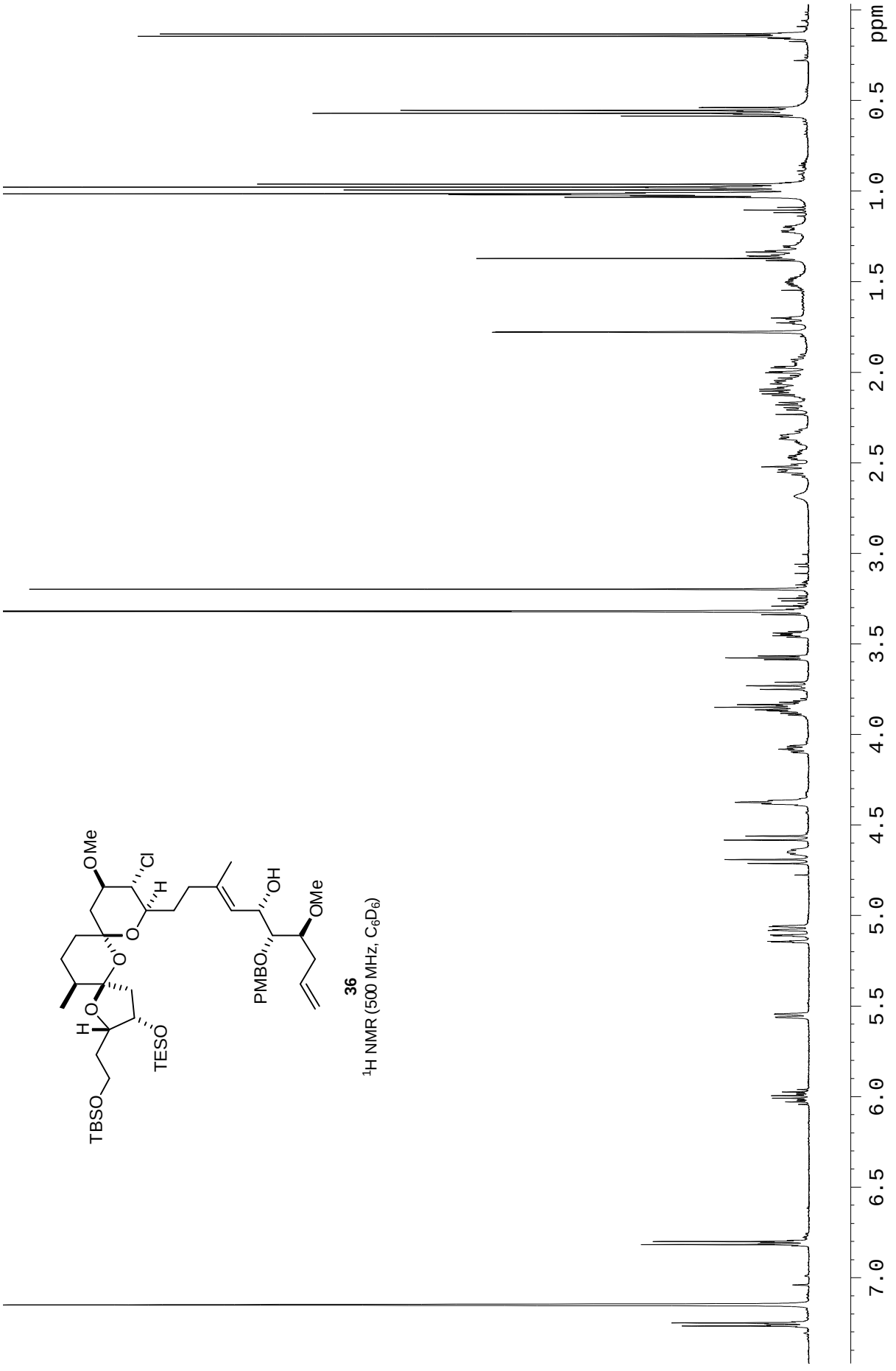
35

^{1}H NMR (500 MHz, C_6D_6)

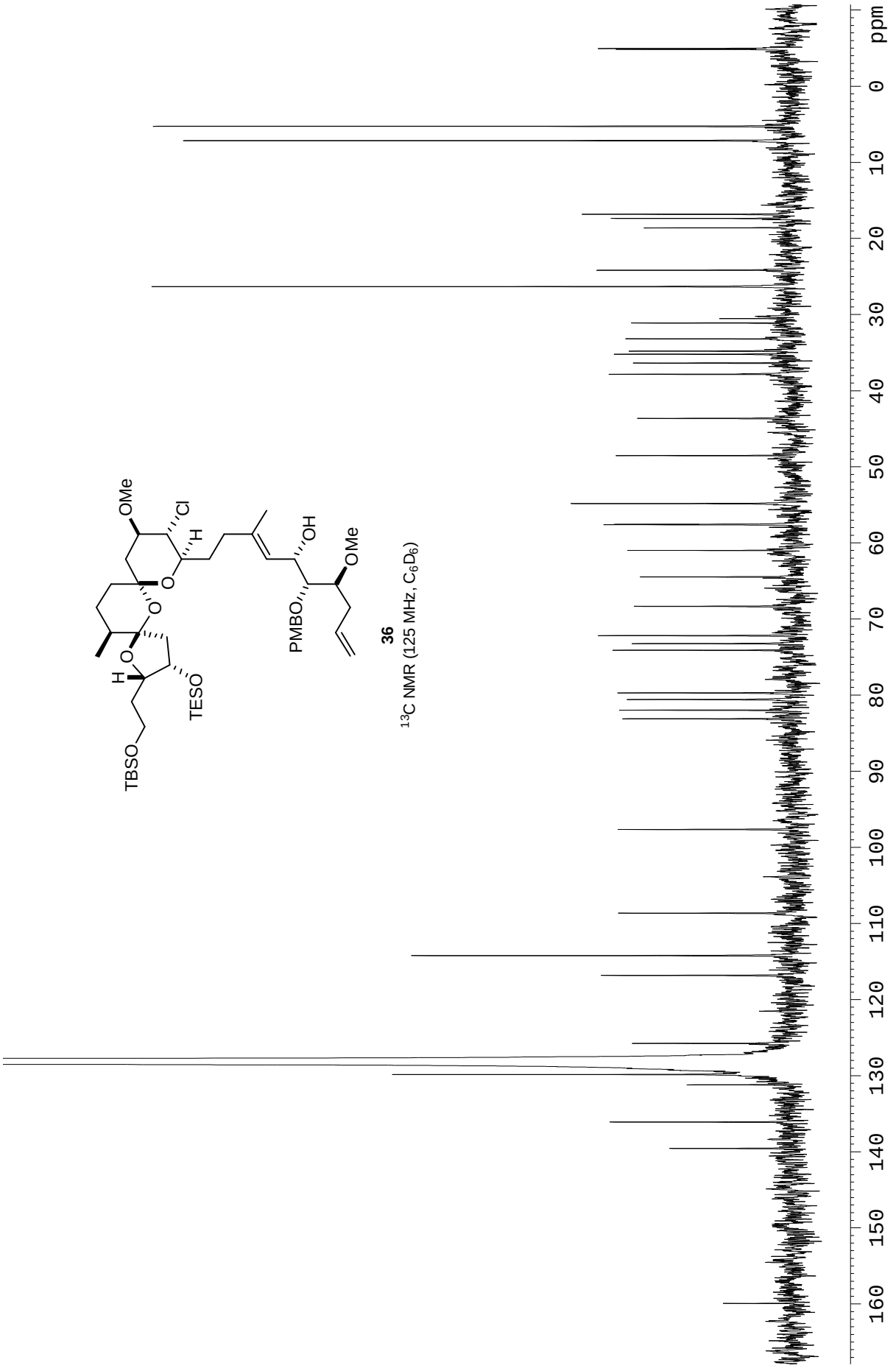


35

^{13}C NMR (125 MHz, C_6D_6)

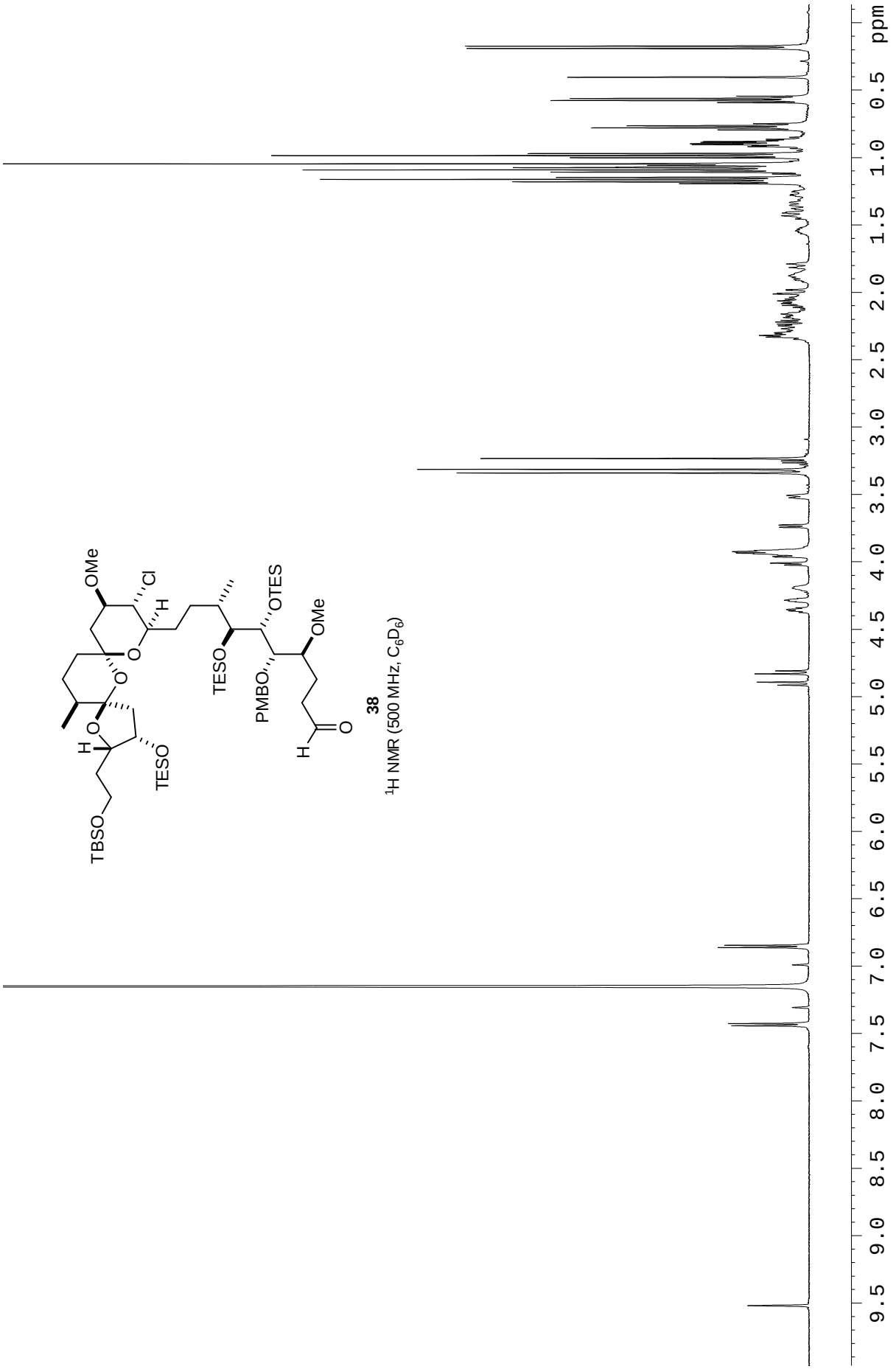


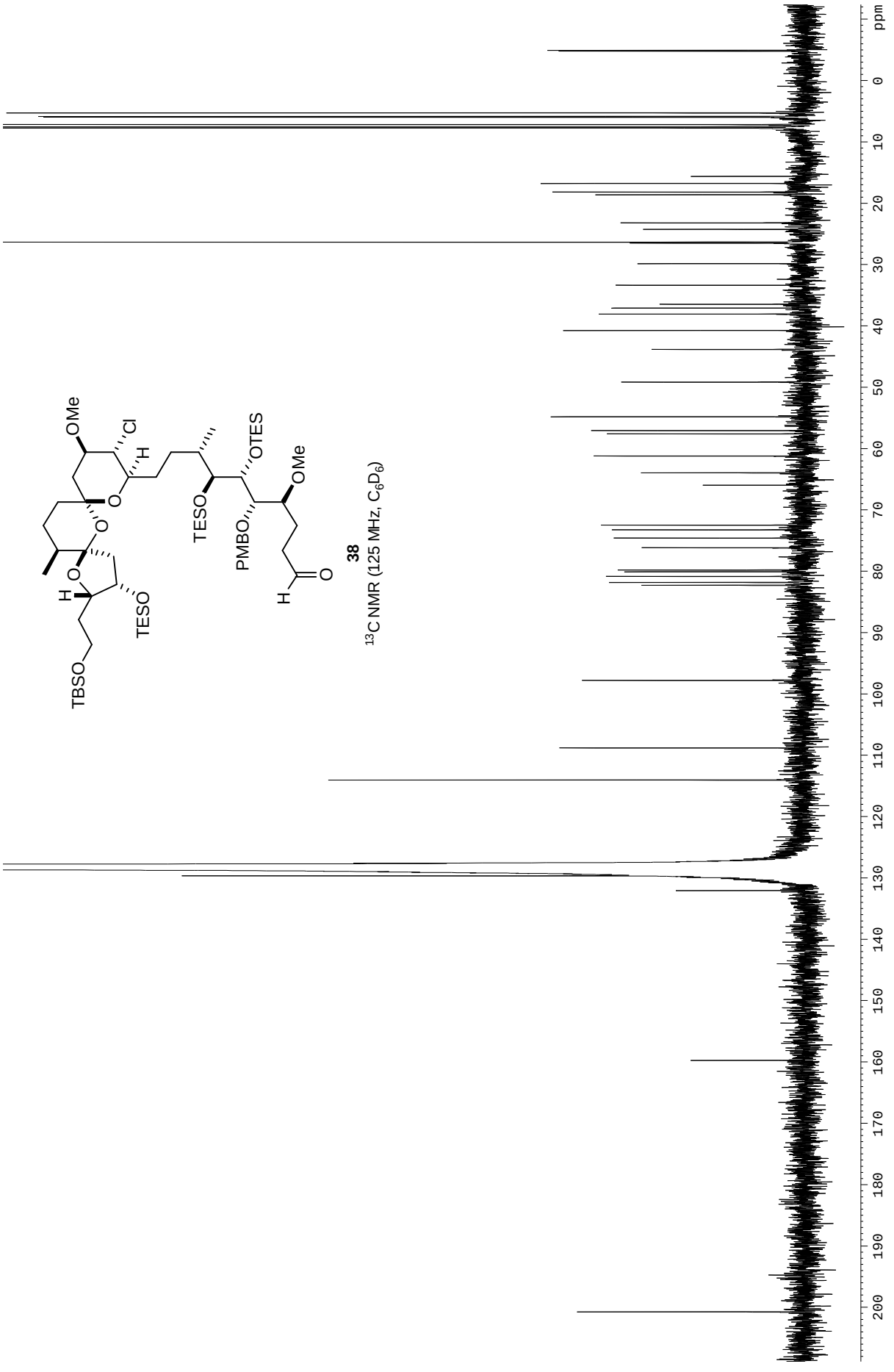
36
^{1}H NMR (500 MHz, C_6D_6)



36

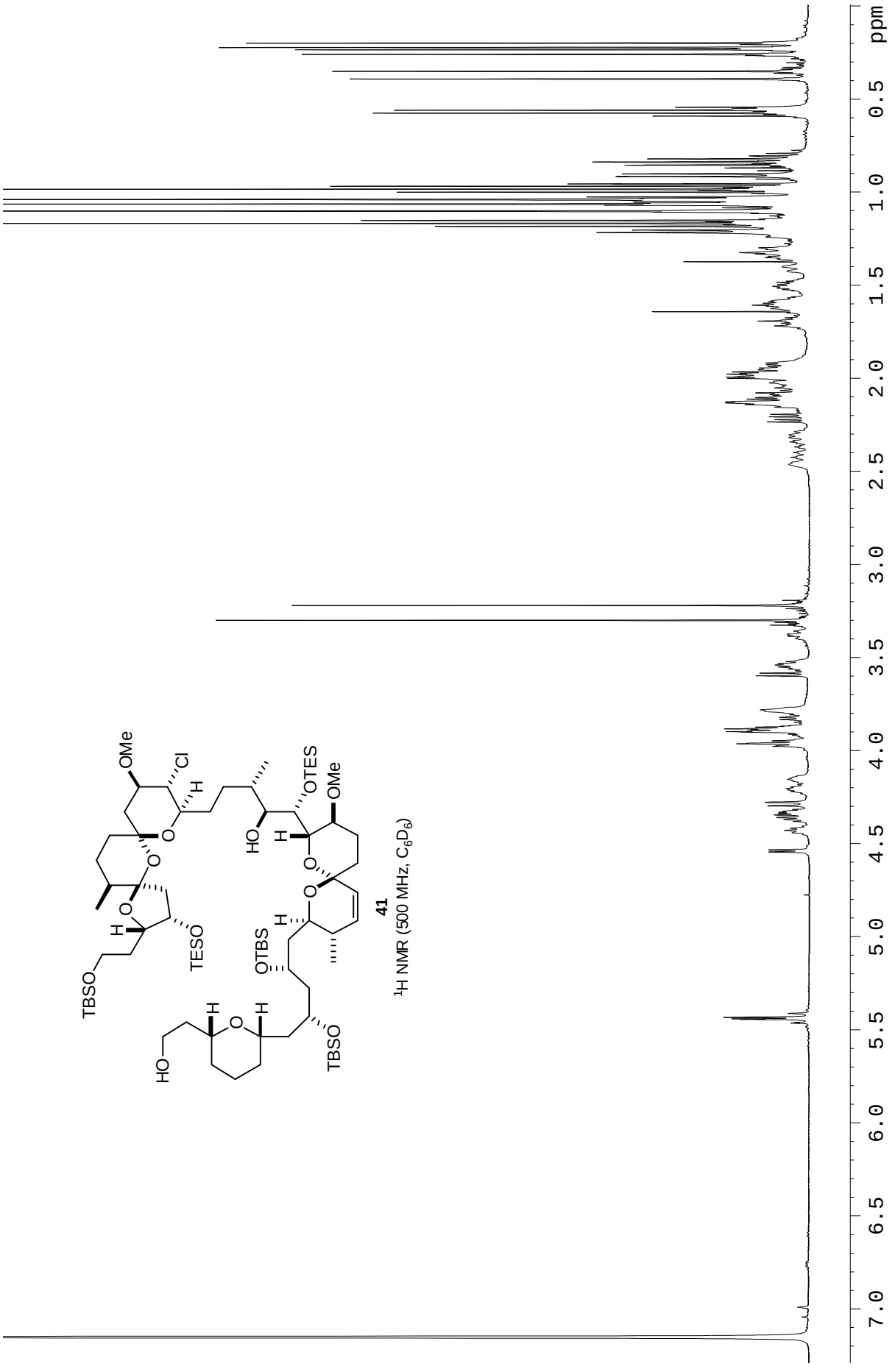
^{13}C NMR (125 MHz, C_6D_6)





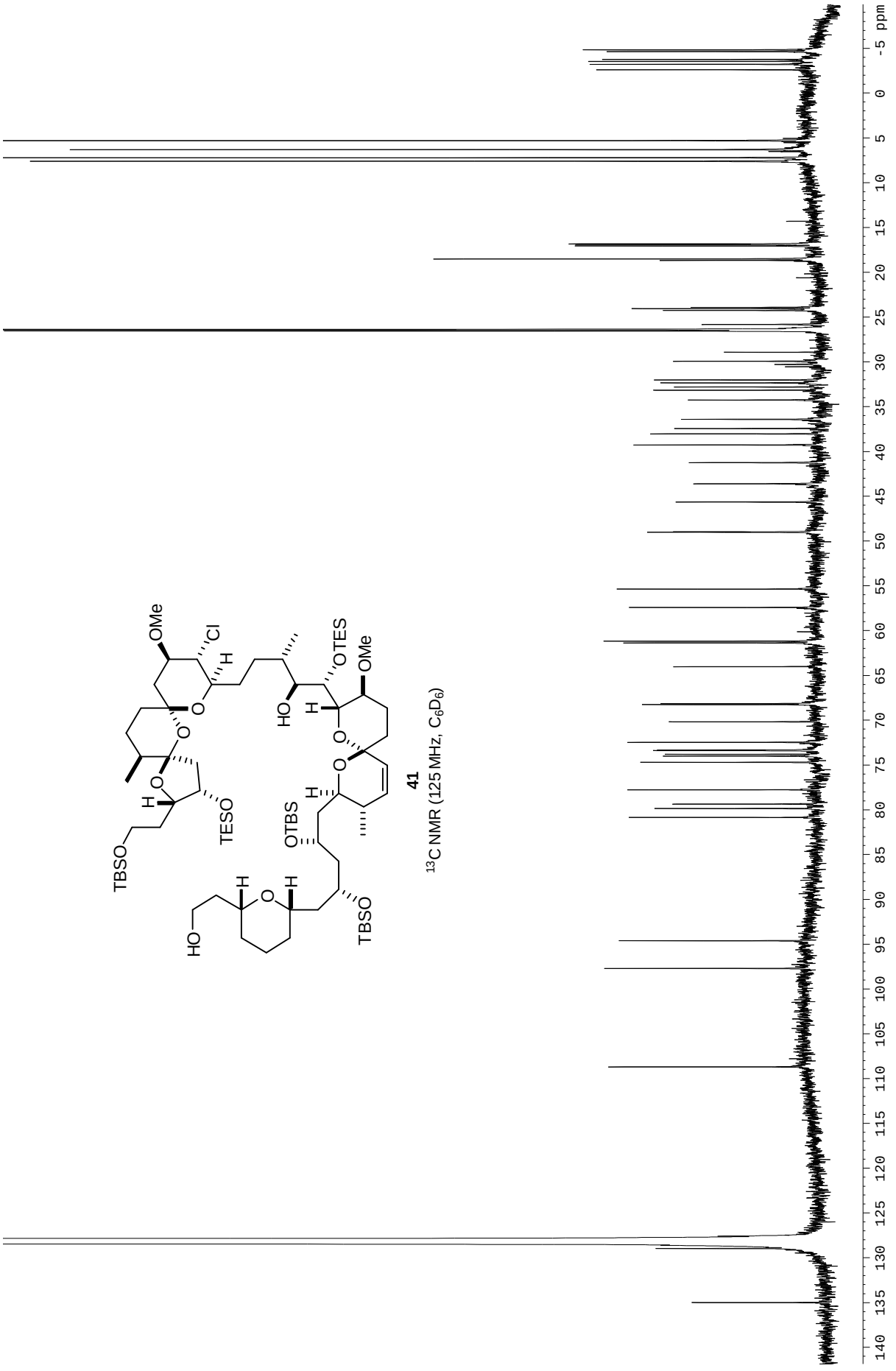
38

^{13}C NMR (125 MHz, C_6D_6)



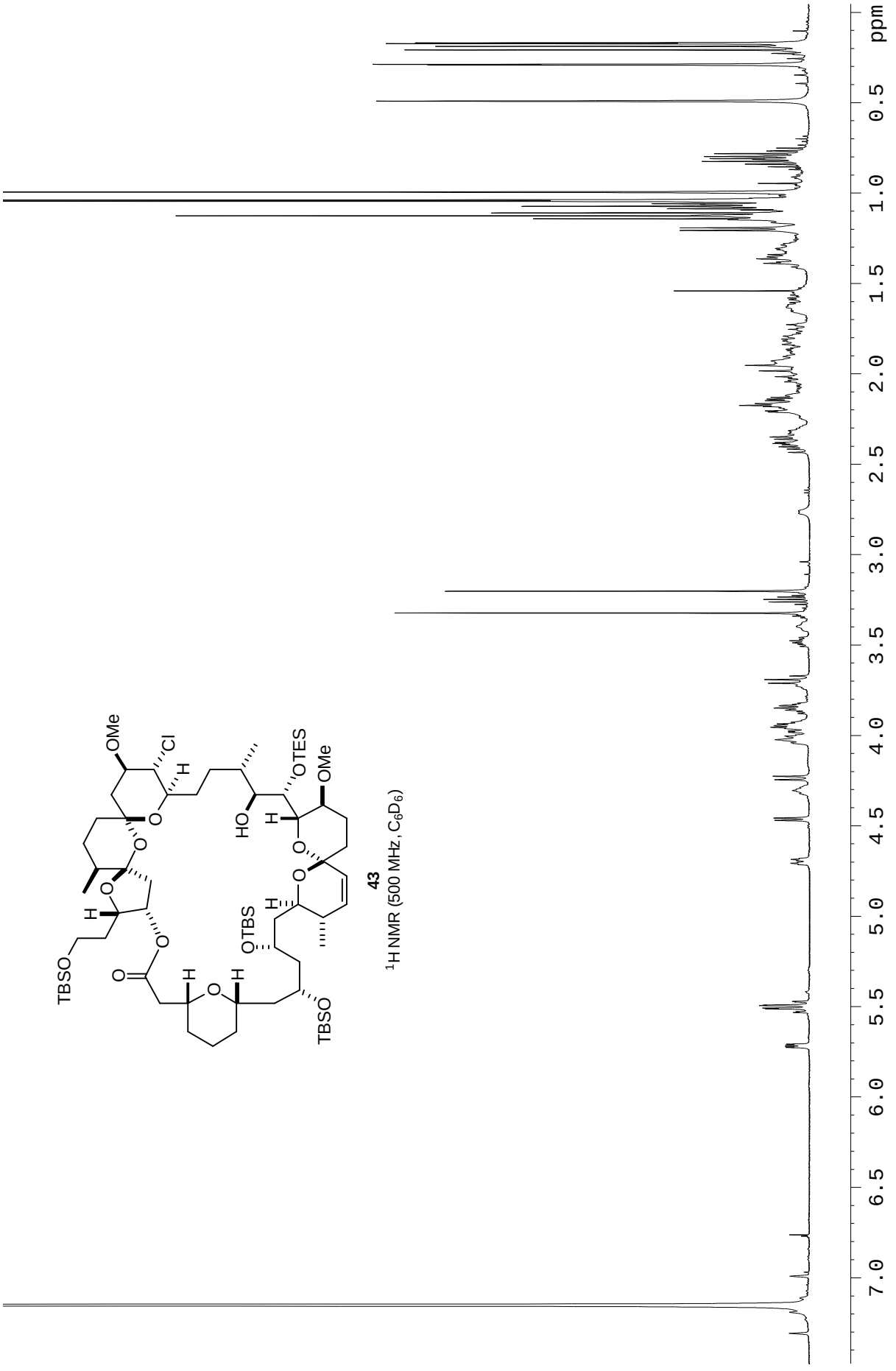
41

^{1}H NMR (500 MHz, C_6D_6)



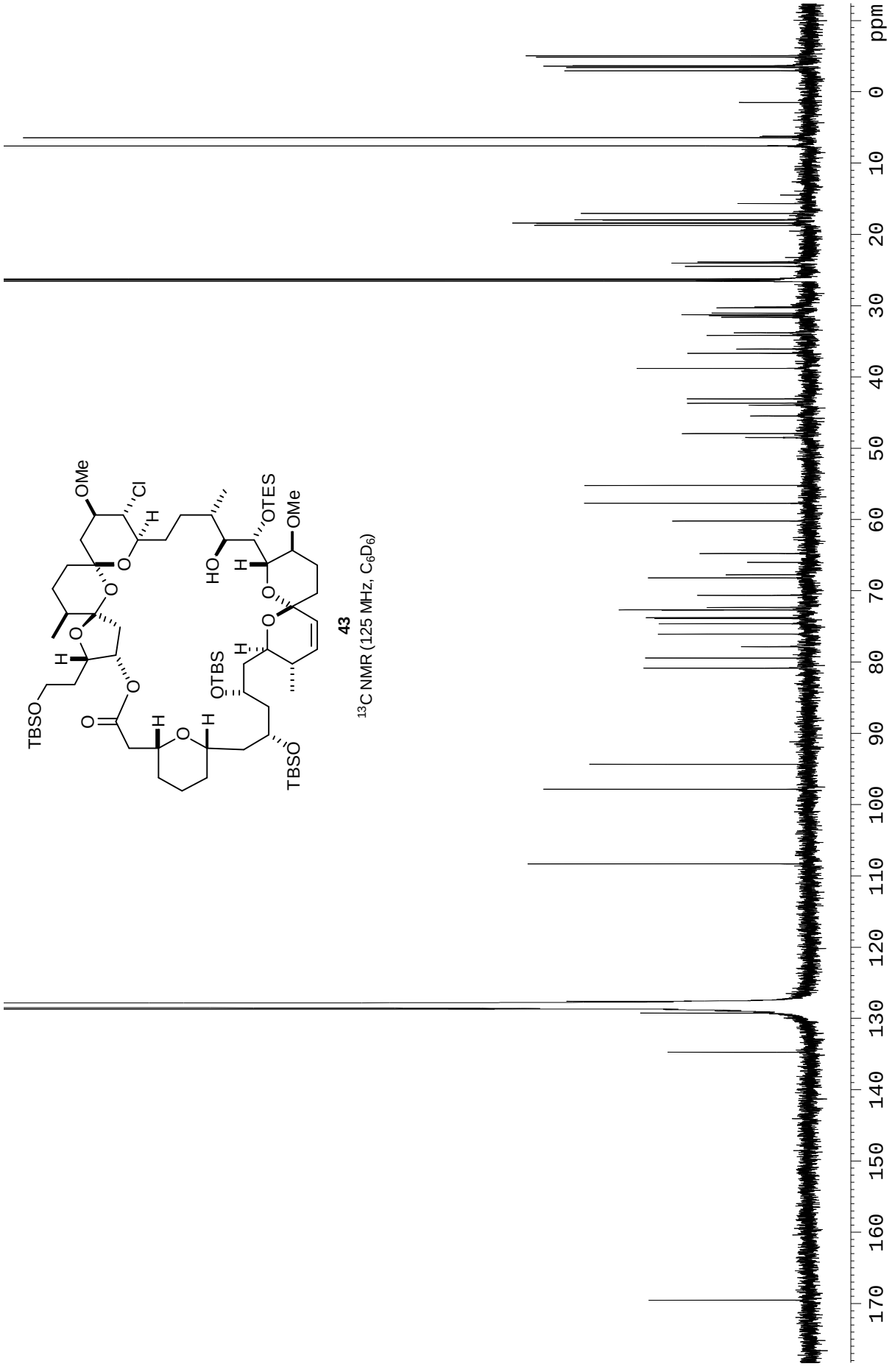
41

^{13}C NMR (125 MHz, C_6D_6)



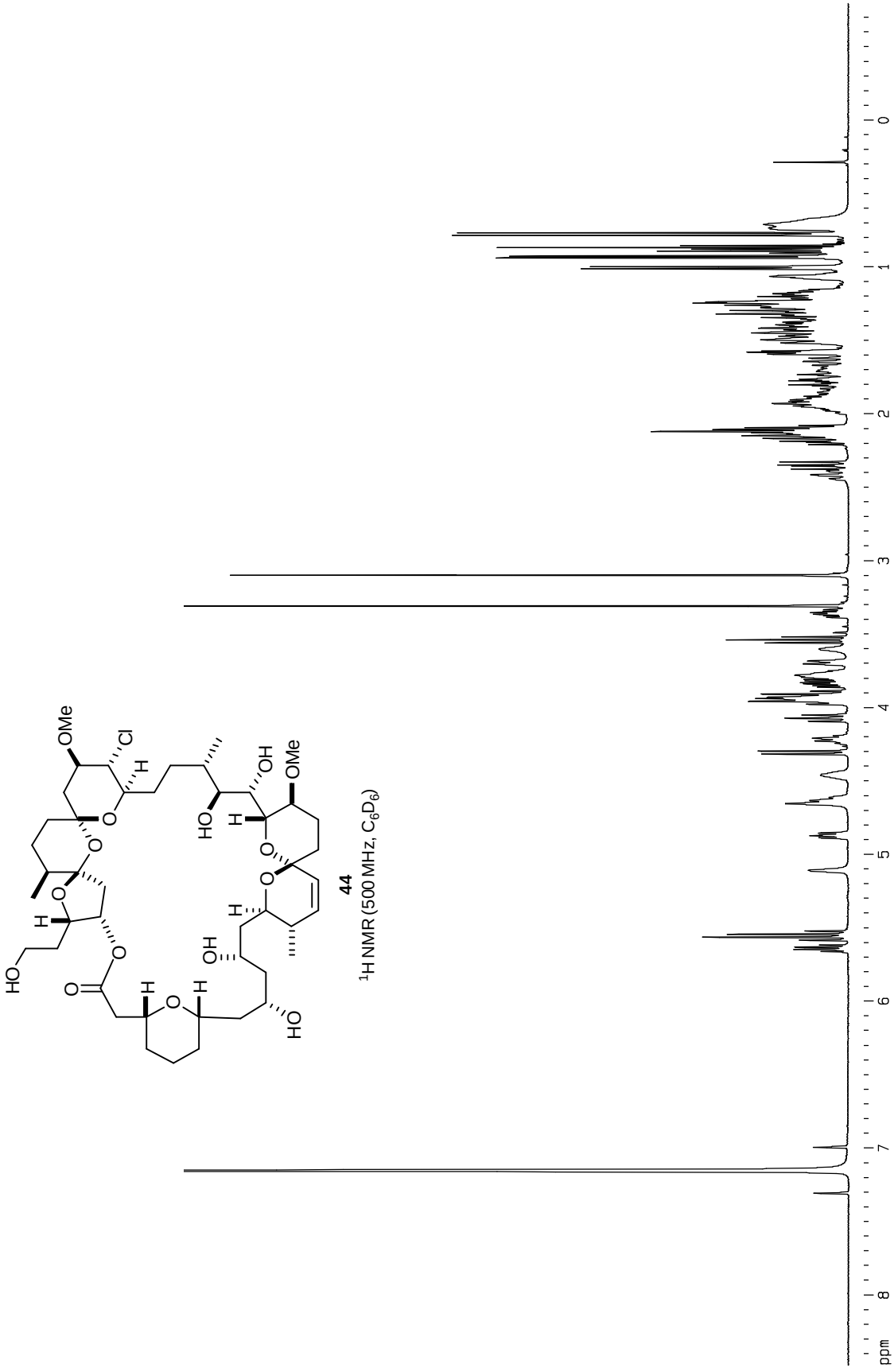
43

^{1}H NMR (500 MHz, C_6D_6)

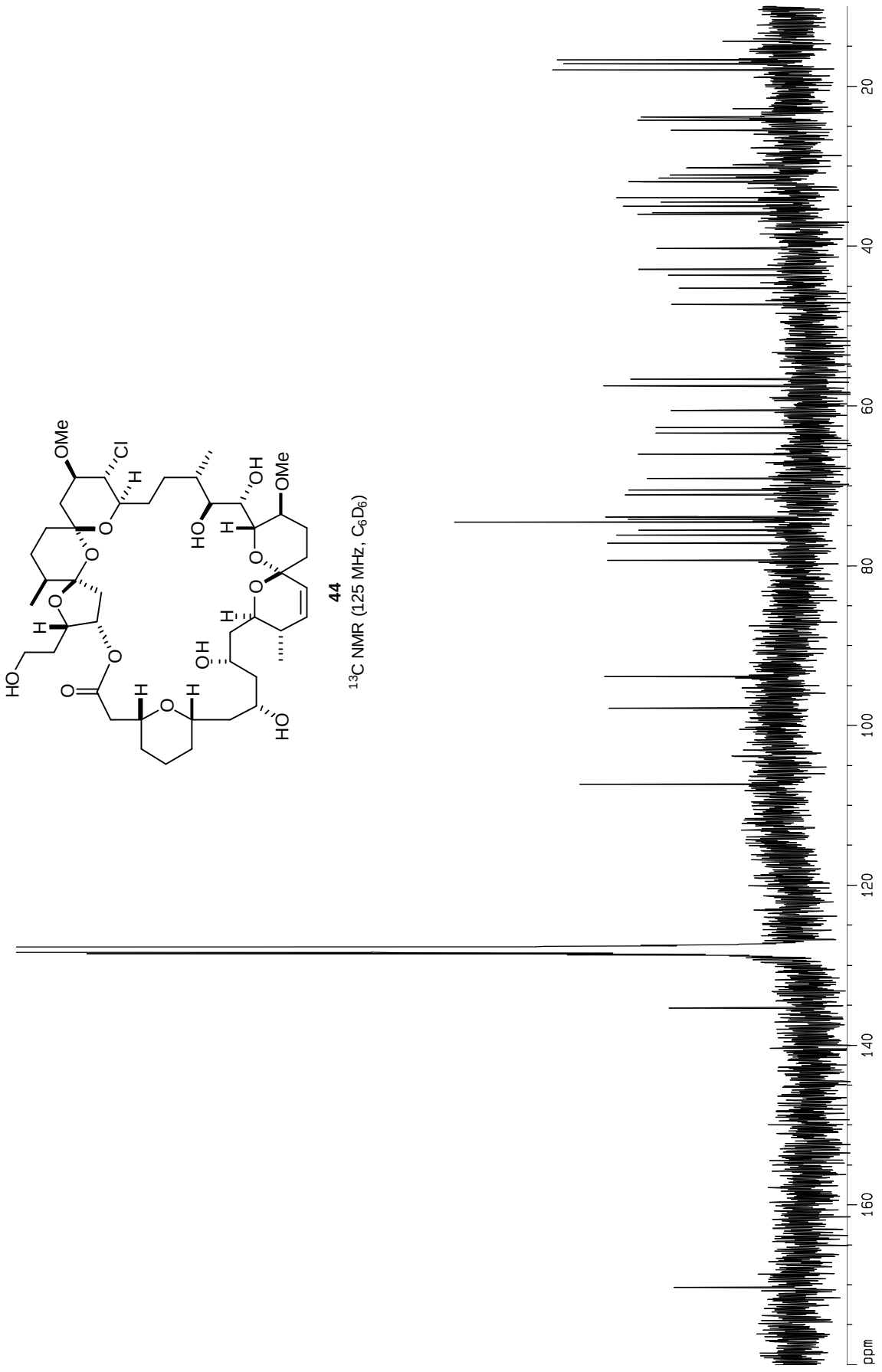


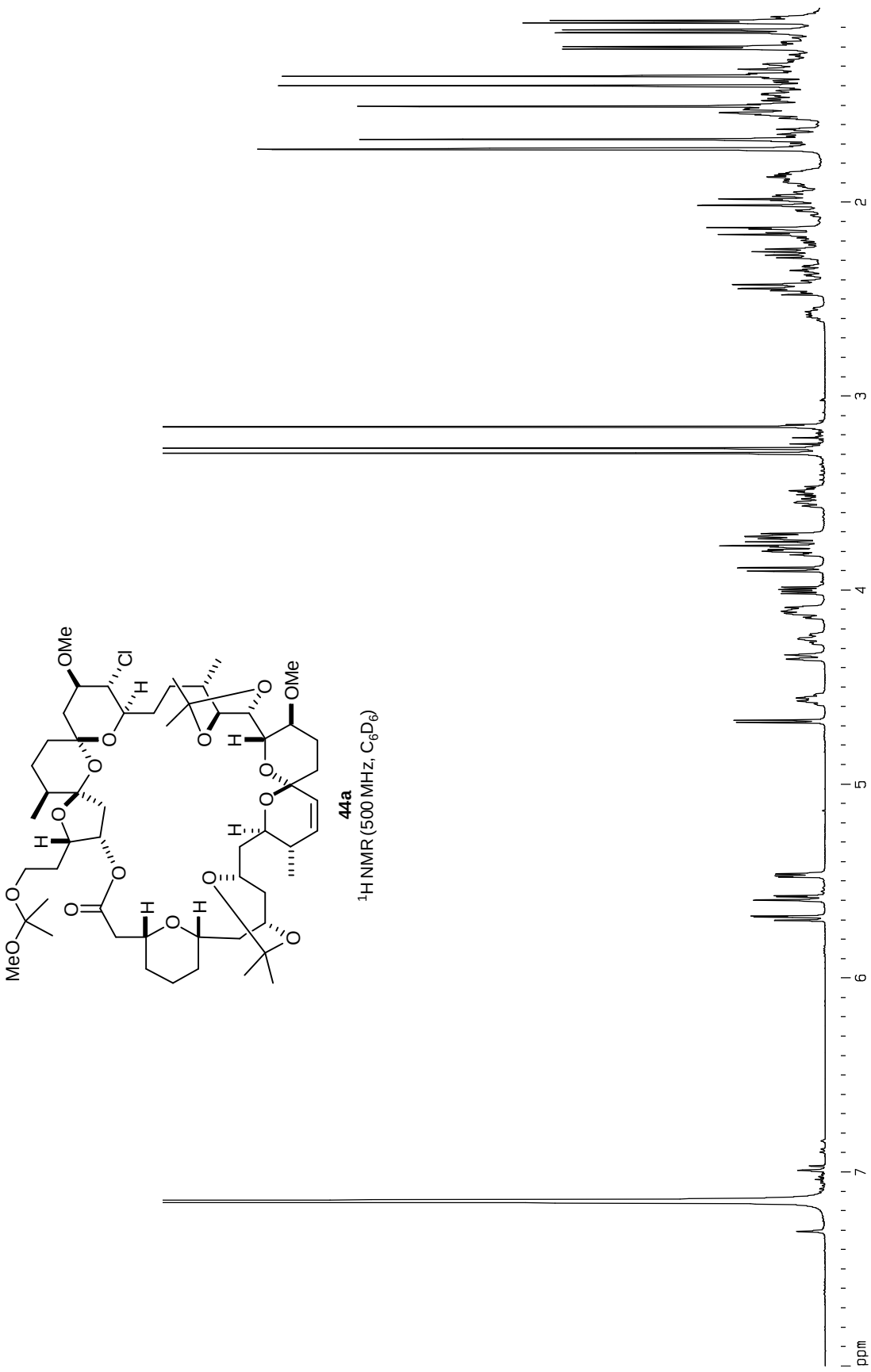
43

^{13}C NMR (125 MHz, C_6D_6)



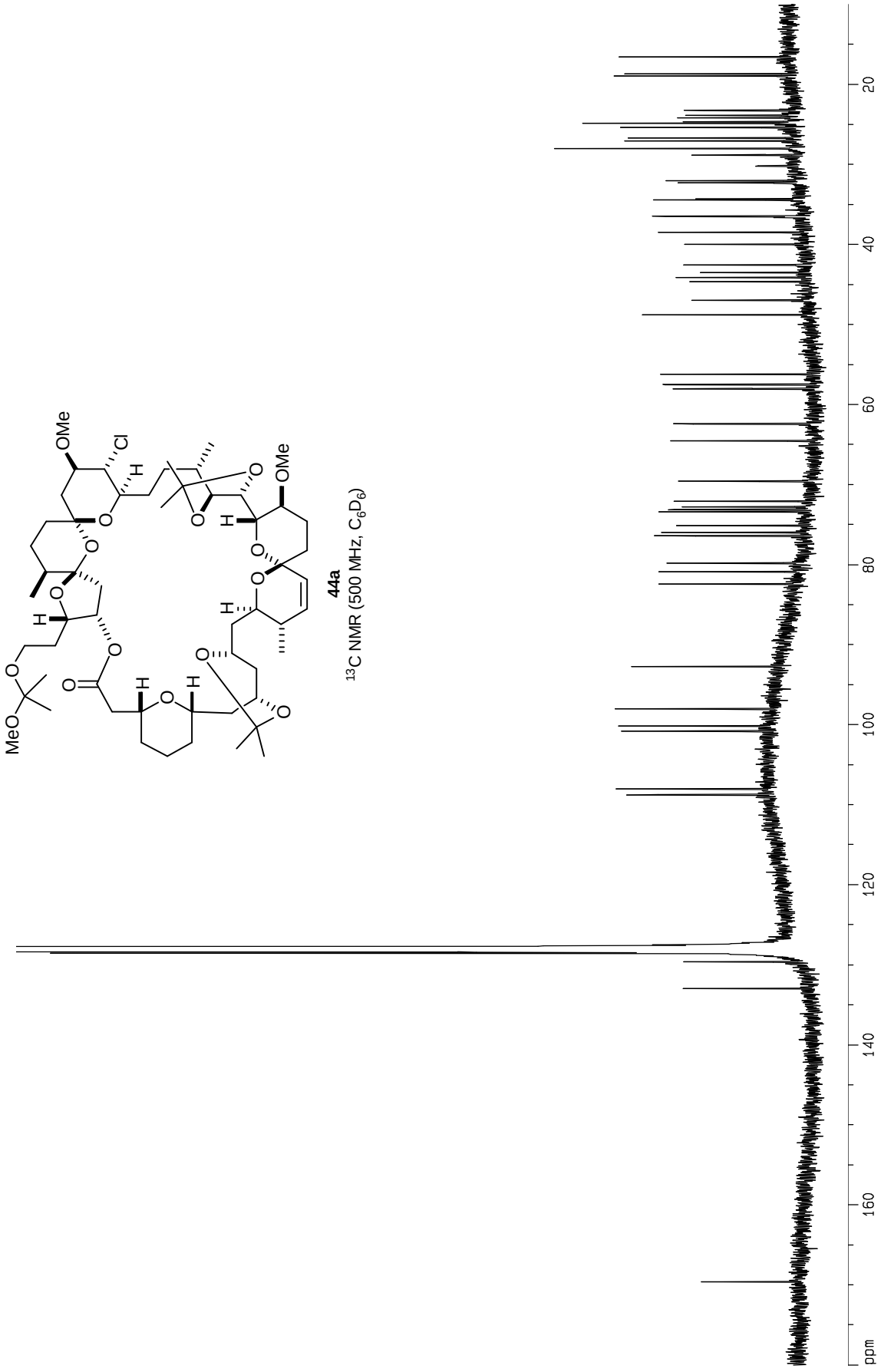
44
^{1}H NMR (500 MHz, C_6D_6)





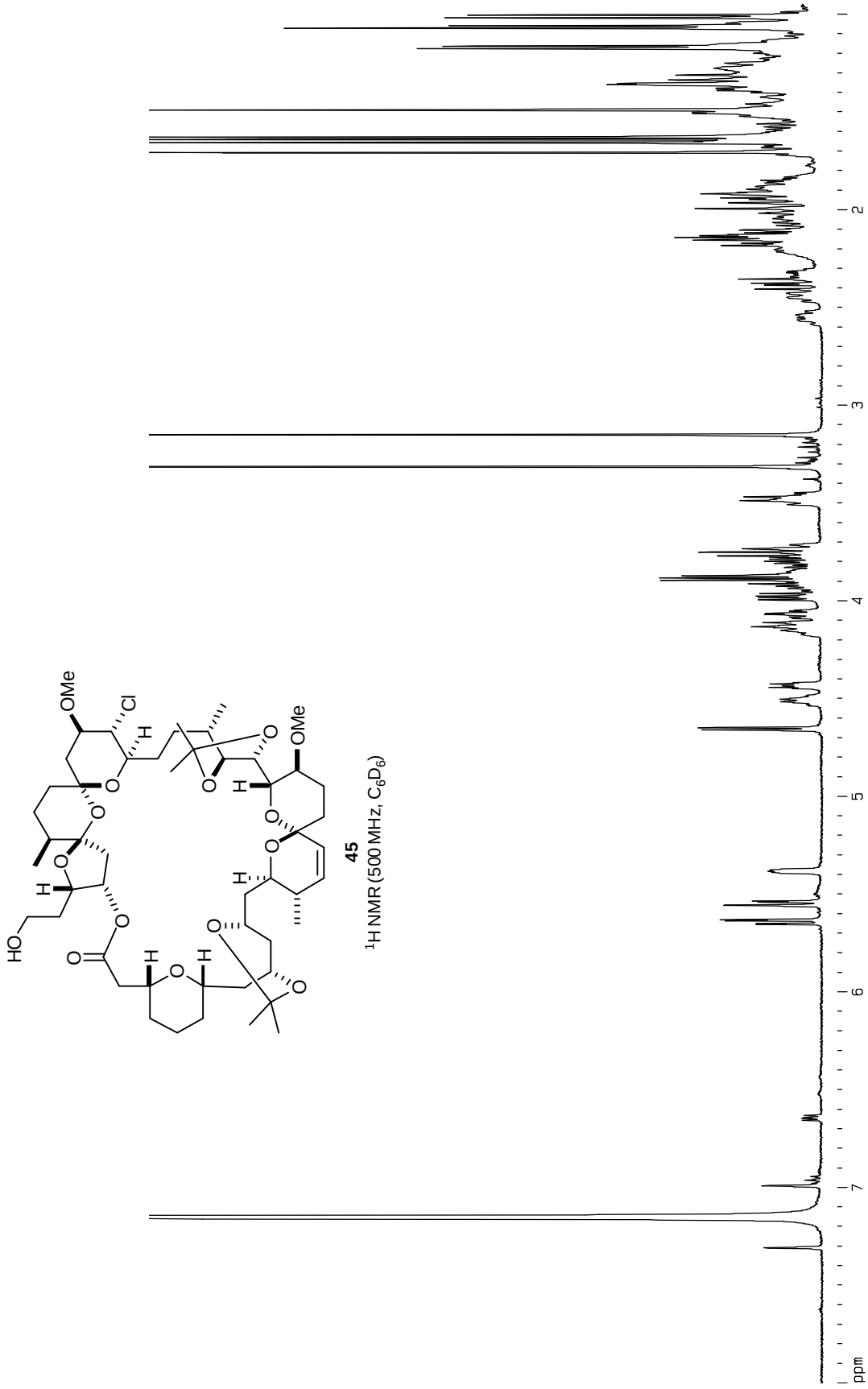
44a

^{1}H NMR (500 MHz, C_6D_6)



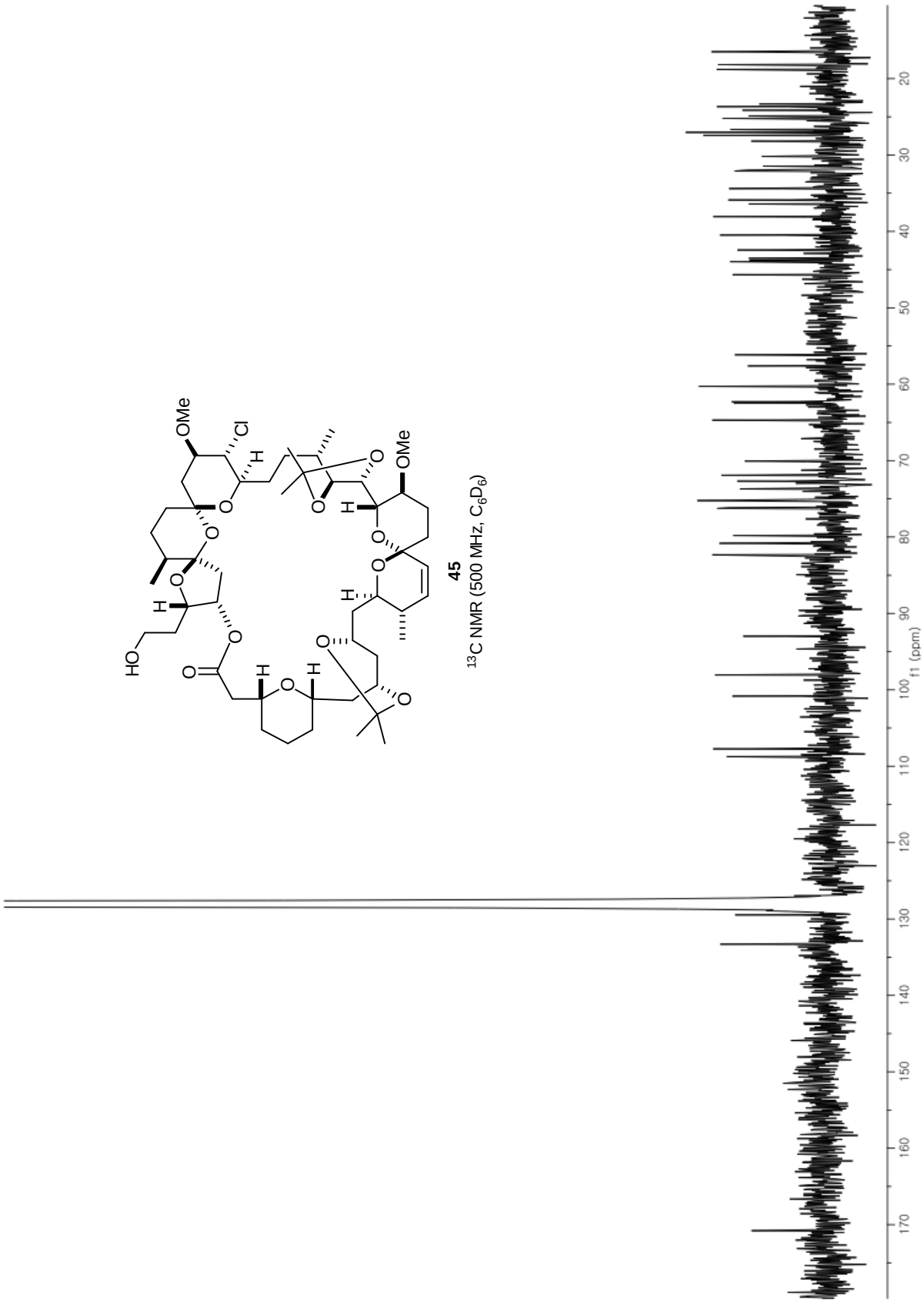
44a

^{13}C NMR (500 MHz, C_6D_6)



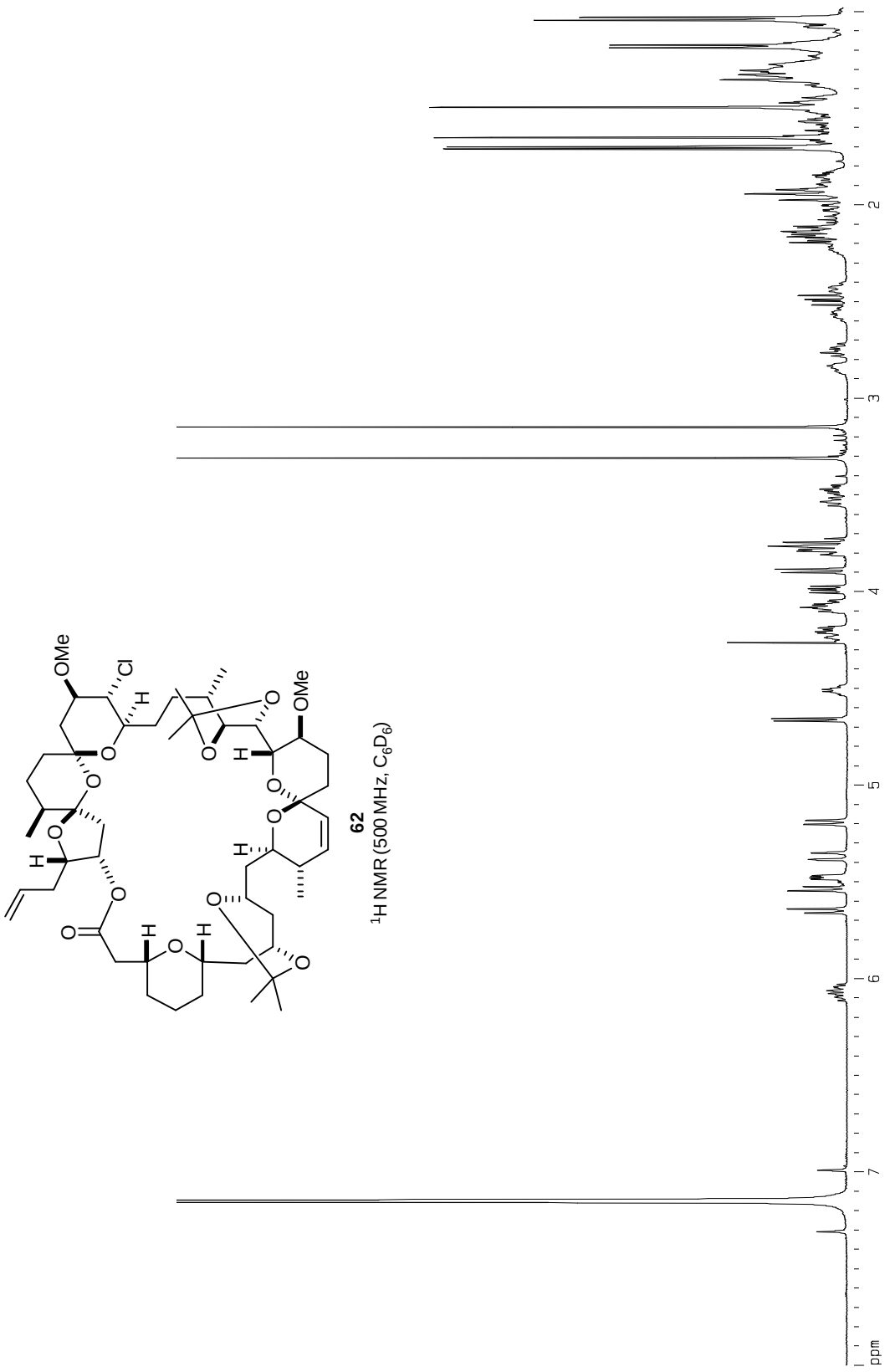
45

^{1}H NMR (500 MHz, C_6D_6)



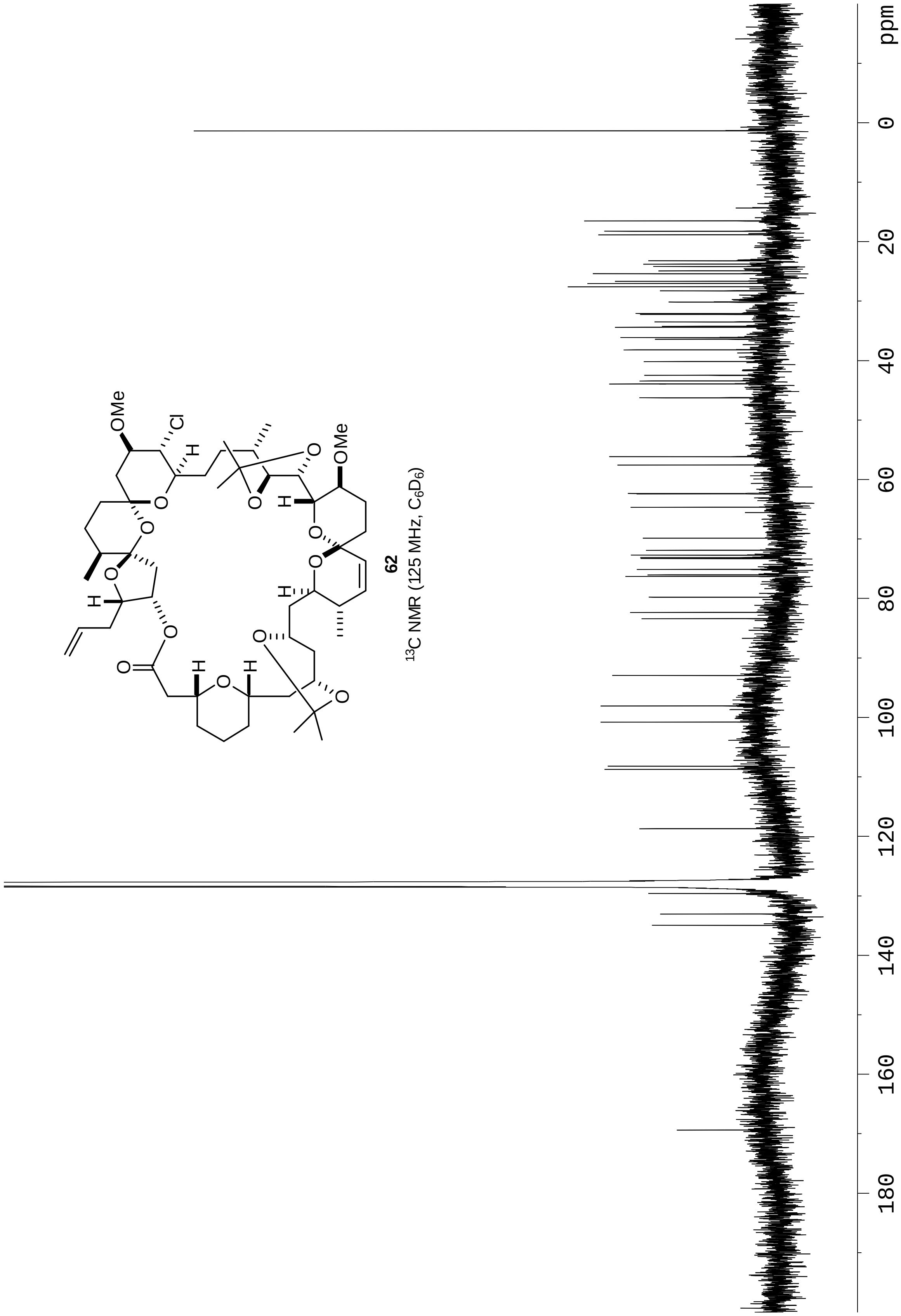
45

^{13}C NMR (500 MHz, C_6D_6)



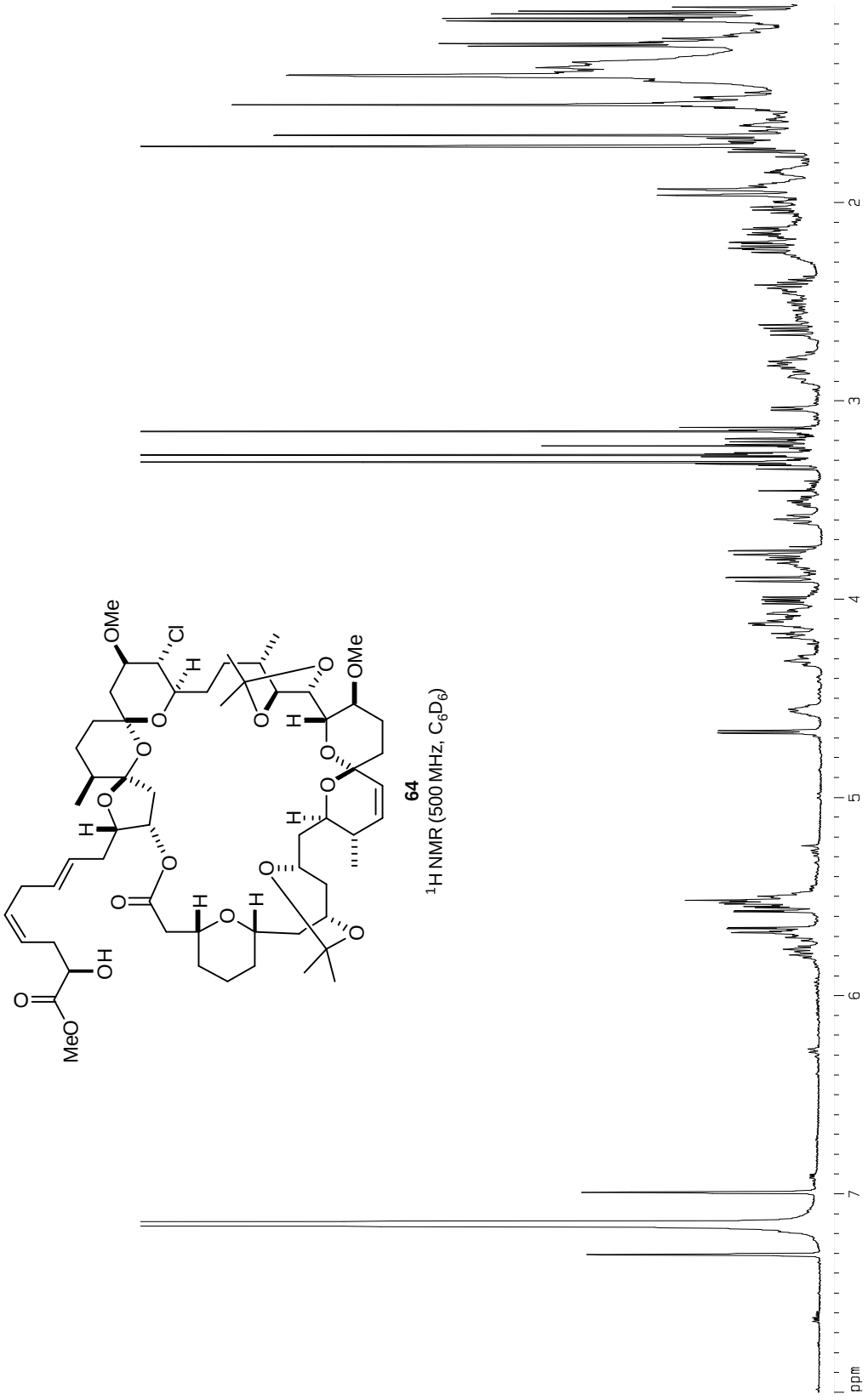
62

^{1}H NMR (500 MHz, C_6D_6)



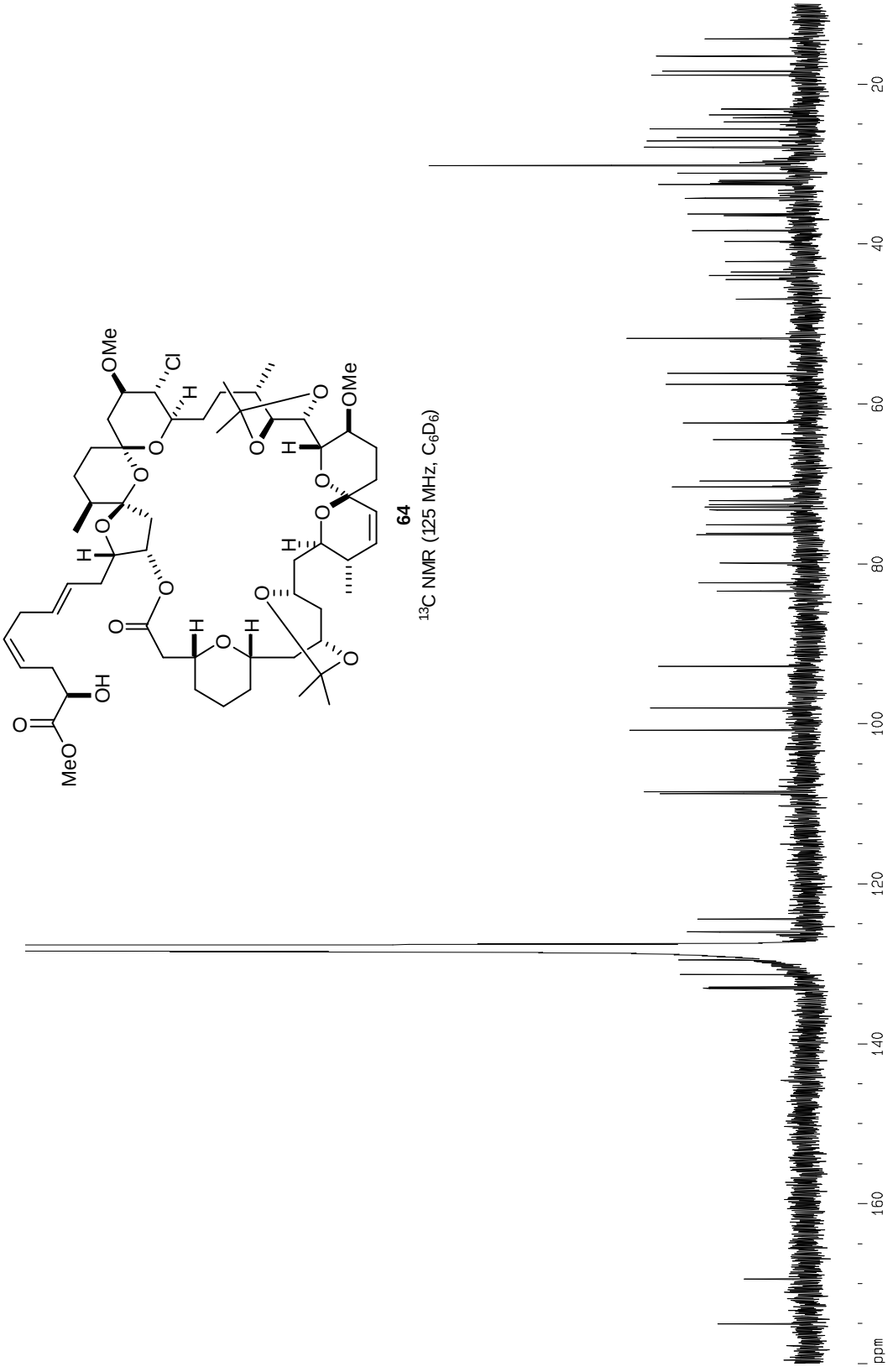
62

^{13}C NMR (125 MHz, C_6D_6)



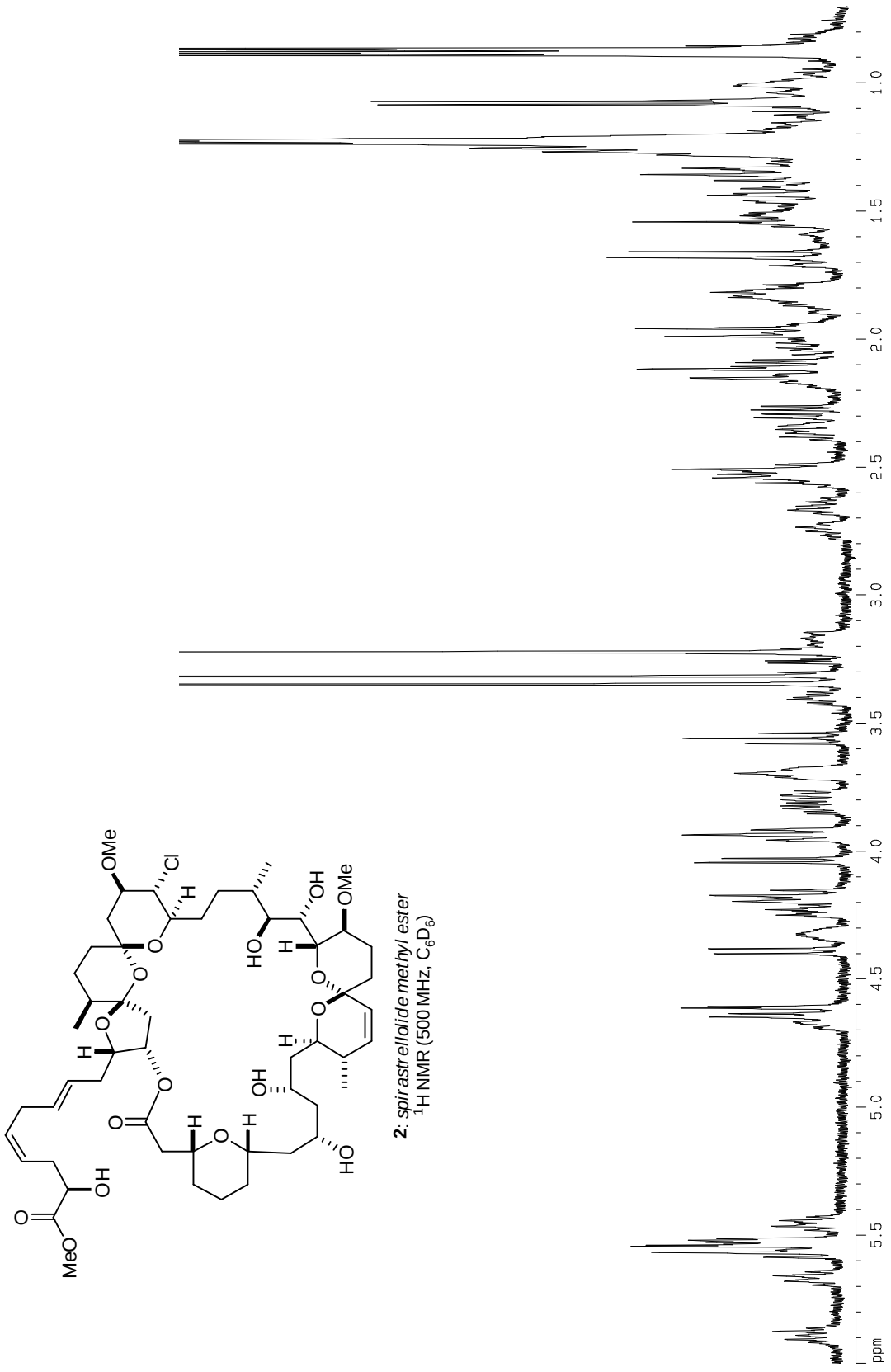
64

^{1}H NMR (500 MHz, C_6D_6)



64

^{13}C NMR (125 MHz, C_6D_6)



2: *spirastrelladide methyl ester*
^{1}H NMR (500 MHz, C_6D_6)