Synthesis of the Monomeric Counterpart of Marinomycin A and B

Frederic Ballaschk,[a] Kathrin Bensberg,[a] Benedikt Crone[b,c], Stefan F. Kirsch[a,e] and Helge Menz[b,d]

[a] Organic Chemistry, University of Wuppertal, Wuppertal, Germany

[b] Department Chemie, Technische Universität München, Garching, Germany

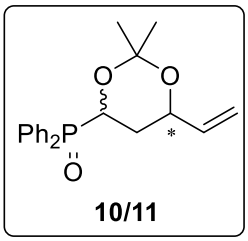
[c] BASF SE, Ludwigshafen am Rhein (Germany)

[d] Pharmpur GmbH, Königsbrunn (Germany)

[e] sfkirsch@uni-wuppertal.de

1. General remarks

The commercially available reagents and solvents were used as purchased. TLC was conducted with precoated aluminum sheets (silica gel 60 F_{254}) and visualized by exposure to UV light (254 nm) or stained with ceric ammonium molybdate (CAM) or basic potassium permanganate ($KMnO_4$), and subsequent heating. Flash column chromatography was performed on silica gel (40-60 µm), the eluent used is reported in the respective experiments. Abbreviations of solvents and chemicals are as followed: CH: cyclohexane, EA: ethyl acetate, THF: tetrahydrofuran, DCM: dichloromethane, MeOH: methanol, DMF: *N*,*N*-dimethylformamide. IR spectra were measured using ATR-technique in the range of 400-4000 cm^{-1}. ^{1}H NMR spectra were recorded with 600 MHz or 400 MHz instruments from *Bruker*, ^{13}C NMR spectra at 151 MHz or 101 MHz, ^{19}F NMR spectra at 376 MHz. Chemical shifts are reported in ppm relative to the solvent signal, coupling constants *J* in Hz. Multiplicities were defined by standard abbreviations. High-resolution mass spectra (HRMS) were obtained using ESI ionization (positive) on a *Bruker* micrOTOF. Optical rotation of unknown chiral substances were measured using a *Krüss* Optronic at 584 nm wavelength. The temperature during measurements was kept at 20 °C with a defined concentration (g/100mL) in the described solvent.



10/11

Both enantiomers of the polyketide building block **10** and **11** used in this work were synthesized analogously to the previously published synthesis by Streiber *et al.*[1] and Kirsch *et al*.[2,3]

2. Experimental procedures

2.1 Condition screening for the acetonide deprotection of 23

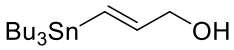
Table 1. Condition screening for the acetonide deprotection of **23**.

entry	acid	solvent	temp.	time	yield
1	Amberlyst 15	MeOH/THF	70 °C	18 h	---[a]
2	BCl_3	DCM	RT	20 min	---[a]
3	$FeCl_3/SiO_2$	$CHCl_3$	RT	1 h	---[b]
4	$CeCl_3 \cdot 7H_2O,(COOH)_2$	MeCN	RT	2 min	48%
5	$CeCl_3 \cdot 7H_2O,(COOH)_2$	MeCN	0 °C	10 min	60%
6	$CeCl_3 \cdot 7H_2O,(COOH)_2$	MeCN	-15 °C	20 min	57%
7	$CeCl_3,(COOH)_2$	THF[c]	-78 °C	16 h	63%

[a] = decomposition; [b] = mixture of compounds; [c] = addition of water (2 equiv.).

2.2 Fragment synthesis

(*E*)-3-(tributylstannyl)prop-2-en-1-ol[4] (**17**)

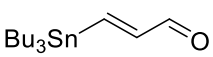


$Pd_2(dba)_3$ (41 mg, 43 µmol, 0.25 mol%) was placed in dry dichloromethane (40 mL, 0.43M) in a flame-dried flask. Tricyclohexylphosphine (0.49 mL, 0.35 mmol, 20 wt% in toluene, 2 mol%) was added and the reaction was stirred at 0 °C for 15 min. Propargyl alcohol (**12**) (1.0 mL, 17 mmol, 1 equiv.) and tributyltin hydride (5.3 mL, 20 mmol, 1.15 equiv.) were then added and the mixture was stirred at 0 °C for an additional three hours. The solvent was removed under reduced pressure and the remaining residue was purified by column chromatography (CH:EA 95:5). The product **17** (3.4 g, 9.9 mmol, 57%) was obtained as a colorless oil.

TLC: R_f = 0.10 (CH:EA 95:5) [$KMnO_4$]; **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 6.24 – 6.12 (m, 2H), 4.17 (t, *J* = 4.5 Hz, 2H), 1.54 – 1.46 (m, 6H), 1.42 – 1.39 (m, 1H), 1.34 – 1.29 (m, 6H), 0.92 – 0.87 (m, 15H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 147.2, 128.5, 66.6, 29.2, 27.4, 13.8, 9.6.

The spectroscopic data were identical to those reported in the literature.[4]

(*E*)-3-(tributylstannyl)acrylaldehyde[5] (**18**)



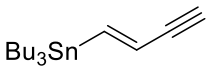
Allyl alcohol **17** (3.40 g, 9.79 mmol, 1 equiv.) was placed in dry acetone (122 mL, 0.08M) and manganese(IV) oxide (18.9 g, 195 mmol, 20 equiv.) was added. The reaction was stirred at room temperature for 18 hours before filtering over Celite®. It was washed with acetone and the filtrate was

concentrated under reduced pressure. Purification of the residue by column chromatography (CH:EA 97:3) afforded the aldehyde **18** (3.27 g, 9.48 mmol, 97%) as a faint yellow oil.

TLC: R_f = 0.50 (CH:EA 95:5) [UV, $KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 9.41 (d, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 19.2 Hz, 1H), 6.63 (dd, *J* = 19.2, 7.5 Hz, 1H), 1.57 – 1.46 (m, 6H), 1.36 – 1.27 (m, 6H), 1.06 – 0.96 (m, 6H), 0.90 (t, *J* = 7.3 Hz, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 193.8, 163.3, 147.8, 29.1, 27.4, 13.8, 10.0.

The spectroscopic data were identical to those reported in the literature.[6]

(*E*)-but-1-en-3-yn-1-yltributylstannane[7] (**19**)

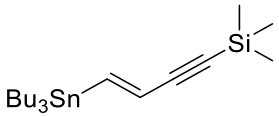


Trimethylsilyldiazomethane (2.67 mL, 5.35 mmol, 2M in diethyl ether, 1.5 equiv.) was placed in dry THF (9.10 mL) and cooled to -78 °C. *n*-Butyllithium (1.93 mL, 4.81 mmol, 2.5M in hexane, 1.35 equiv.) was added and the reaction was stirred at -78 °C for 30 min. Aldehyde **18** (1.23 g, 3.56 mmol, 1 equiv.) dissolved in THF (4.6 mL) was slowly added and then the reaction was stirred for 60 minutes at -78 °C before warming to 0 °C and stirring for another 30 minutes. The reaction was stopped by the addition of sat. NH_4Cl solution$_{(aq)}$ and transferred to a separatory funnel. Extraction of the aqueous phase was carried out with diethyl ether (3x) and the combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. Purification of the residue by column chromatography (PE) afforded the terminal alkyne **19** (715 mg, 2.10 mmol, 59%) as a colorless oil.

TLC: R_f = 0.58 (CH) [UV, $KMnO_4$]; **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 6.99 (d, *J* = 19.9 Hz, 1H), 5.99 – 5.89 (m, 1H), 2.89 (d, *J* = 2.0 Hz, 1H), 1.59 – 1.42 (m, 6H), 1.31 (h, *J* = 7.3 Hz, 6H), 0.99 – 0.83 (m, 15H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 149.6, 124.7, 84.1, 75.6, 29.1, 27.4, 13.8, 9.8.

The spectroscopic data were identical to those reported in the literature.[7]

(*E*)-trimethyl(4-(tributylstannyl)but-3-en-1-yn-1-yl)silane (**6**)

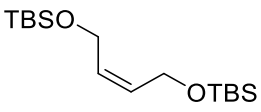


The terminal alkyne **19** (200 mg, 586 µmol, 1 equiv.) was placed in dry THF (5.9 mL, 0.1M) and cooled to -78 °C. To this mixture was added *n*-butyllithium (281 µL, 703 µmol, 2.5M in hexane, 1.2 equiv.) and the reaction was stirred for one hour at -78 °C. TMS chloride (89.9 µL, 703 µmol, 1.2 equiv.) was then added and the reaction was stirred for another hour at -78 °C before warming up to room temperature and stirring for another 16 hours. The reaction was stopped by the addition of sat. NH_4Cl solution$_{(aq)}$ and extracted with ethyl acetate (3x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. Purification of the residue by column chromatography (CH) afforded product **6** (236 mg, 571 µmol, 97%) as a colorless oil.

TLC: R_f = 0.60 (CH) [UV, $KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 6.94 (d, *J* = 19.9 Hz, 1H), 6.00 (d, *J* = 19.9 Hz, 1H), 1.56 – 1.43 (m, 6H), 1.35 – 1.25 (m, 6H), 0.96 – 0.85 (m, 15H), 0.19 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] =148.7, 125.9, 105.5, 92.5, 29.2, 27.4, 13.8, 9.8, 0.1.

The spectroscopic data were identical to those reported in the literature.[8]

(*Z*)-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodec-6-ene[9] (**13a**)

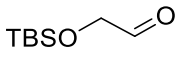


(*Z*)-But-2-ene-1,4-diol (**13**) (4.28 mL, 50 mmol, 1 equiv.) was placed in dry DMF (100 mL, 0.5M). Imidazole (16.3 g, 240 mmol, 4.8 equiv.) was added and the mixture cooled 0 °C before TBS chloride (18.8 g, 125 mmol, 2.5 equiv.) was added and the reaction was stirred for 16 h at room temperature. Sat. $NaHCO_3$ $solution_{(aq)}$ and ethyl acetate were added, the phases were separated, and the aqueous phase was extracted with ethyl acetate (2x). The combined organic phases were washed with sat. NaCl $solution_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. Purification of the residue by column chromatography (CH:EA 99:1) afforded product **13a** (15.8 g, 49.9 mmol, quant.) as a colorless oil.

TLC: R_f = 0.24 (CH:EA 98:2) [$KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.55 (t, *J* = 3.7 Hz, 2H), 4.23 (d, *J* = 3.7 Hz, 4H), 0.90 (s, 18H), 0.07 (s, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 130.4, 59.8, 26.1, 18.5, -5.0.

The spectroscopic data were identical to those reported in the literature.[9]

2-((*tert*-butyldimethylsilyl)oxy)acetaldehyde[10] (**20**)

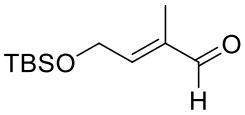


Ozone was passed through a solution of internal alkene **13a** (3.95 g, 12.5 mmol, 1 equiv.) in dichloromethane (74 mL, 0.17M) at -78 °C. After about 20 minutes, a blue coloration of the solution occurred, whereupon oxygen was passed through the reaction mixture until the blue coloration faded. Triphenylphosphine (3.83 g, 14.6 mmol, 1.17 equiv.) was added and the mixture was allowed to warm to room temperature. Stirring was continued at this temperature for 90 minutes before most of the solvent was removed under reduced pressure. The remaining residue was purified by distillation *in vacuo* furnishing aldehyde **20** (3.52 g, 20.2 mmol, 81%) as a colorless liquid.

Bp: 79 °C (40 mbar); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 9.70 (t, *J* = 0.8 Hz, 1H), 4.21 (d, *J* = 0.9 Hz, 2H), 0.93 (s, 9H), 0.11 (s, 6H).

The spectroscopic data were identical to those reported in the literature.[10]

(*E*)-4-((*tert*-butyldimethylsilyl)oxy)-2-methylbut-2-enal[10] (**22**)

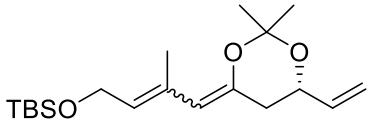


Aldehyde **20** (1.74 g, 10 mmol, 1 equiv.) was dissolved in dry benzene (50 mL, 0.2M) followed by addition of 2-(triphenylphosphoranylidene)propanal (**21**) (3.90 g, 12.0 mmol, 1.2 equiv.). The reaction was stirred at room temperature for 60 h before water was added. The mixture was extracted with diethyl ether (3x) and the combined organic phases were washed with sat. NaCl $solution_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The remaining residue was purified by column chromatography (CH:EA 95:5) to give product **22** (2.01 g, 9.38 mmol, 94%) as a faint yellow oil.

TLC: R_f = 0.41 (CH:EA 90:10) [UV, $KMnO_4$]; **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 9.42 (s, 1H), 6.52 (td, *J* = 5.3, 1.2 Hz, 1H), 4.52 – 4.48 (m, 2H), 1.73 (s, 3H), 0.92 (s, 9H), 0.10 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 194.7, 153.2, 137.9, 60.6, 26.0, 18.4, 9.5, -5.1.

The spectroscopic data were identical to those reported in the literature.[10]

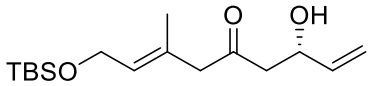
(*S*)-*tert*-butyl((4-(2,2-dimethyl-6-vinyl-1,3-dioxan-4-ylidene)-3-methylbut-2-en-1-yl)oxy)dimethylsilane[2,3] (**23**)



Diisopropylamine (2.22 mL, 15.9 mmol, 1.15 equiv.) was placed in dry THF (53 mL) and cooled to -78 °C. *n*-Butyllithium (6.34 mL, 15.9 mmol, 2.5M in hexane, 1.15 equiv.) was added and cooling was removed for 15 min. Cooling was resumed to -78 °C and the (*S*)-polyketide building block **10** (4.72 g, 13.8 mmol, 1 equiv.), dissolved in dry THF (21 mL), was added. This caused the solution to turn deep red. After one hour, aldehyde **22** (3.84 mg, 17.9 mmol, 1.3 equiv.), dissolved in dry THF (32 mL), was added and warmed to room temperature within 90 minutes. The solution became cloudy and orange in the process. Finally, potassium *tert*-butoxide (1.95 g, 16.5 mmol, 1.2 equiv.) was added and stirred for another 60 minutes at room temperature. The solution turned dark orange to brown. The reaction was stopped by adding sat. NH_4Cl $solution_{(aq)}$ and extracted with dichloromethane (3x). The combined organic phase was washed with sat. NaCl $solution_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. Purification of the crude product by column chromatography (CH:EA 95:5) afforded product **23** (3.88 g, 11.5 mmol, 83%, *E*/*Z* 50:50) as a yellow oil.

TLC: R_f = 0.54 (CH:EA 90:10) [UV, $KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.93 – 5.76 (m, 1H), 5.59 – 5.09 (m, 4H), 4.48 – 4.33 (m, 1H), 4.28 (t, *J* = 5.9 Hz, 2H), 2.85 – 2.07 (m, 2H), 1.91 – 1.73 (m, 3H), 1.55 – 1.47 (m, 6H), 0.92 (d, *J* = 1.8 Hz, 9H), 0.09 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 147.6, 146.3, 138.2, 138.2, 132.6, 131.3, 128.6, 128.4, 116.3, 115.9, 114.0, 101.4, 101.2, 70.7, 69.9, 60.4, 60.3, 35.8, 32.0, 29.2, 29.1, 26.2, 26.1, 22.6, 22.1, 18.5, 17.7, 16.3, -4.9, -4.9; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2991, 2929, 2894, 2856, 1656, 1381, 1255, 1104, 832, 773; **HRMS** (ESI): [m/z] 361.2169 (calc'd for $C_{19}H_{34}NaO_3Si$: 361.2171 $[M+Na]^+$).

(*S*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-7-methylnona-1,7-dien-5-one[11] (**24**)

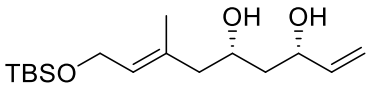


Cerium(III) chloride heptahydrate was dried *in vacuo* at 140 °C for two hours to obtain dry cerium(III) chloride before starting the reaction. Acetonide **23** (674 mg, 1.99 mmol, 1 equiv.) was placed in dry THF (10 mL, 0.2M) and cooled to -78 °C. Cerium(III) chloride (981 mg, 3.98 mmol, 2 equiv.), oxalic acid (45 mg, 0.50 mmol, 25 mol%) and water (71.7 µL, 3.98 mmol, 2 equiv.) were added and the reaction was stirred at 78 °C for 16 hours. Sat. $NaHCO_3$ $solution_{(aq)}$ was added and the mixture was allowed to warm to room temperature. Ethyl acetate was added and the phases were separated. The aqueous

phase was extracted with ethyl acetate (3x). The combined organic phases were dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (CH:EA 80:20) yielding the β-hydroxyketone **24** (375 mg, 1.26 mmol, 63%) as a yellow oil.

TLC: R_f = 0.36 (CH:EA 70:30) [$KMnO_4$]; **[α]$^{20}_D$** = -12.0 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.85 (ddd, *J* = 17.2, 10.5, 5.5 Hz, 1H), 5.48 – 5.42 (m, 1H), 5.29 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.13 (dt, *J* = 10.5, 1.4 Hz, 1H), 4.60 – 4.50 (m, 1H), 4.22 (ddd, *J* = 6.4, 1.6, 0.8 Hz, 2H), 3.11 (s, 2H), 2.69 – 2.65 (m, 2H), 1.65 (d, *J* = 1.2 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 209.4, 139.1, 130.4, 130.0, 115.2, 68.8, 60.2, 54.7, 48.0, 26.1, 18.5, 16.9, -5.0; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3450, 3009, 2954, 2928, 2886, 1710, 1252, 1060, 922, 832, 774; **HRMS** (ESI): [m/z] 321.1858 (calc'd for $C_{16}H_{30}NaO_3Si$: 321.1856 $[M+Na]^+$).

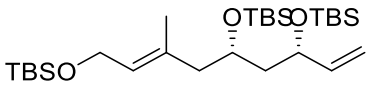
(*3S,5S,E*)-9-((*tert*-butyldimethylsilyl)oxy)-7-methylnona-1,7-diene-3,5-diol (**26**)



β-hydroxyketone **24** (281 mg, 913 µmol, 1 equiv.) was dissolved in dry methanol/THF (9 mL, 0.1M, 1/4) and cooled to 78 °C. Diethylmethoxyborane (273 µL, 1.10 mmol, 4M in THF, 1.2 equiv.) was then added and then the solution was stirred for 20 min at -78 °C. Sodium borohydride (38.0 mg, 1.00 mmol, 1.1 equiv.) was added and the reaction was stirred for an additional two hours at -78 °C. The reaction was stopped by the addition of sodium hydroxide solution$_{(aq)}$ (6 mL, 2M) and hydrogen peroxide solution$_{(aq)}$ (3 mL, 35%) and stirred for 45 minutes at room temperature. After addition of water and ethyl acetate, the phases were separated. The aqueous phase was extracted with ethyl acetate (2x) and the combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 60:40), the residue obtained afforded the *syn*-diol **26** (272 mg, 905 µmol, 99%, *d.r.* >99:1) as a faint yellow oil.

TLC: R_f = 0.36 (CH:EA 50:50) [CAM]; **[α]$^{20}_D$** = +5.1 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 5.87 (ddd, *J* = 17.1, 10.4, 5.9 Hz, 1H), 5.44 – 5.38 (m, 1H), 5.26 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.10 (dt, *J* = 10.4, 1.4 Hz, 1H), 4.42 – 4.33 (m, 1H), 4.23 – 4.18 (m, 2H), 4.02 – 3.96 (m, 1H), 2.92 (s, 2H), 2.20 – 2.14 (m, 2H), 1.70 – 1.56 (m, 5H), 0.90 (s, 9H), 0.07 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 140.8, 133.3, 128.7, 114.5, 73.5, 69.7, 60.1, 48.4, 43.1, 26.1, 18.5, 16.7, -5.0; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3365, 3009, 2952, 2929, 2885, 1252, 1065, 832, 773; **HRMS** (ESI): [m/z] 323.2024 (calc'd for $C_{16}H_{32}NaO_3Si$: 323.2013 $[M+Na]^+$).

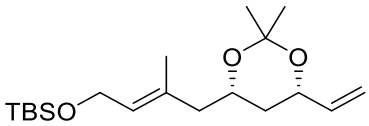
(*9S*,*11S*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,7,13,13,14,14-nonamethyl-11-vinyl-4,12-dioxa-3,13-disilapentadec-6-ene (**27**)



syn-Diol **26** (263 mg, 831 µmol, 1 equiv.) was placed in dry DMF (1.67 mL, 0.5M). Imidazole (271 mg, 3.99 mmol, 4.8 equiv.) was added and the mixture cooled 0 °C before TBS chloride (313 mg, 2.08 mmol, 2.5 equiv.) was added and the reaction was stirred for two hours at room temperature. Sat. $NaHCO_3$ solution$_{(aq)}$ and ethyl acetate were added and the phases were separated. The aqueous phase was extracted with ethyl acetate (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. Purification of the residue by column chromatography (CH:EA 100:0 98:2) afforded product **27** (395 mg, 747 µmol, 90%) as a colorless to light yellow oil.

TLC: R_f = 0.73 (CH:EA 90:10) [$KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.78 (ddd, *J* = 17.0, 10.3, 6.5 Hz, 1H), 5.32 (t, *J* = 5.8 Hz, 1H), 5.14 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.03 (d, *J* = 10.4 Hz, 1H), 4.22 (q, *J* = 6.6 Hz, 1H), 4.17 (d, *J* = 6.2 Hz, 2H), 3.85 (p, *J* = 6.3 Hz, 1H), 2.17 (d, *J* = 6.3 Hz, 2H), 1.70 – 1.57 (m, 5H), 0.90 – 0.87 (m, 27H), 0.07 – 0.02 (m, 18H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 141.7, 133.9, 127.8, 114.2, 71.5, 68.2, 60.3, 48.0, 45.9, 26.2, 26.1 (2C), 18.6, 18.4, 18.2, 17.2, -4.0, -4.1, -4.3, -4.6, -4.9 (2C); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2954, 2922, 2893, 2856, 1471, 1251, 831, 771; **HRMS** (ESI): [m/z] 551.3747 (calc'd for $C_{28}H_{60}NaO_3Si_3$: 551.3742 $[M+Na]^+$).

tert-butyl(((*E*)-4-((*4S*,*6S*)-2,2-dimethyl-6-vinyl-1,3-dioxan-4-yl)-3-methylbut-2-en-1-yl)oxy)dimethylsilane (**28**)

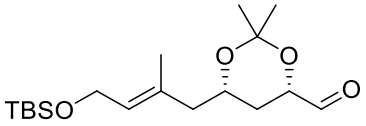


syn-Diol **26** (2.35 g, 7.82 mmol, 1 equiv.) was dissolved in 2,2-dimethoxypropane (24.5 mL, 195 mmol, 25 equiv.) and PPTS (200 mg, 782 µmol, 10 mol%) was added. The reaction mixture was placed on the rotary evaporator at 330 mbar and 45 °C for two hours. The solution was diluted with dichloromethane and washed with sat. $NaHCO_3$ solution$_{(aq)}$. The aqueous phase was extracted with dichloromethane (3x) and the combined organic phases were dried with sodium sulfate, filtered and the solvent was removed under reduced pressure. The product **28** (2.62 g, 7.68 mmol, 98%) was obtained with sufficient purity as a colorless oil after aqueous workup.

TLC: R_f = 0.64 (CH:EA 50:50) [$KMnO_4$]; **$[\alpha]^{20}_D$** = -12.6 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 5.82 (ddd, *J* = 17.3, 10.5, 5.8 Hz, 1H), 5.36 (tq, *J* = 6.3, 1.2 Hz, 1H), 5.24 (dt, *J* = 17.3, 1.4 Hz, 1H), 5.11 (dt, *J* = 10.5, 1.3 Hz, 1H), 4.40 – 4.29 (m, 1H), 4.20 (d, *J* = 6.3 Hz, 2H), 4.08 – 3.96 (m, 1H), 2.27 (dd, *J* = 13.4, 6.6 Hz, 1H), 2.07 (dd, *J* = 13.9, 6.5 Hz, 1H), 1.65 (d, *J* = 0.9 Hz, 3H), 1.56 – 1.52 (m, 1H), 1.47 (s, 3H), 1.43 – 1.41 (m, 3H), 1.29 – 1.20 (m, 1H), 0.90 (s, 9H), 0.07 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 139.0, 133.1, 127.4, 115.4, 98.8, 70.5, 67.6, 60.3, 46.4, 36.7, 30.4, 26.2, 19.9,

18.6, 17.2, -4.9, -4.9; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3081, 2991, 2930, 2857, 1472, 1463, 1442, 1408, 1378, 1253, 1200, 1169, 1142, 1101, 1074, 1004, 987, 970, 919, 832, 813, 773, 664, 633, 587, 520, 453; **HRMS** (ESI): [m/z] 363.2334 (calc'd for $C_{19}H_{36}NaO_3Si$: 363.2326 $[M+Na]^+$).

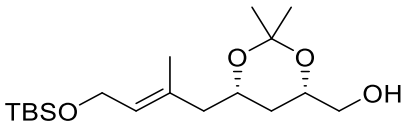
(*4S,6S*)-6-((*E*)-4-((*tert*-butyldimethylsilyl)oxy)-2-methylbut-2-en-1-yl)-2,2-dimethyl-1,3-dioxane-4-carbaldehyde[12] (**30**)



Alkene **28** (2.60 g, 7.63 mmol, 1 equiv.) was placed in dry THF (15.3 mL, 0.5M) and bis(pinacolato)diboron (3.88 g, 15.3 mmol, 2 equiv.), cesium carbonate (746 mg, 2.29 mmol, 30 mol%) and methanol (5.26 mL, 130 mmol, 17 equiv.) were added successively. The reaction vessel was sealed and stirred at 70 °C for 16 hours. The reaction was then cooled to 0 °C and NaOH $solution_{(aq)}$ (15.3 mL, 45.8 mmol, 3M, 6 equiv.) and hydrogen peroxide $solution_{(aq)}$ (15.3 mL, 178 mmol, 35%, 23.4 equiv.) were added dropwise. The reaction was warmed to room temperature and stirred for four hours before being cooled again to 0 °C and very carefully stopped with sat. $Na_2S_2O_3$ $solution_{(aq)}$. It was diluted with water and ethyl acetate and the phases were separated. The aqueous phase was extracted with ethyl acetate (3x) and the combined organic phases were extracted with 40 °C water until no or very little pinacol could be detected via TLC control. The organic phase was then washed with NaCl $solution_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The crude product **29** obtained was dissolved in a THF:water mixture (54 mL, 0.14M, 1:1) and sodium periodate (3.53 g, 16.3 mmol, 2.2 equiv.) was added. The reaction was stirred at room temperature for ten minutes before being stopped by the addition of water and ethyl acetate. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phases were washed with sat. NaCl $solution_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 80:20), the residue obtained afforded the aldehyde **30** (2.23 g, 6.50 mmol, 85% over two steps) as a colorless oil.

TLC: R_f = 0.21 (CH:EA 80:20) [$KMnO_4$]; **$[\alpha]^{20}_D$** = -33.5 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 9.49 (s, 1H), 5.30 (t, *J* = 5.9 Hz, 1H), 4.48 (dd, *J* = 12.1, 2.9 Hz, 1H), 4.21 – 4.07 (m, 3H), 2.15 (dd, *J* = 13.8, 6.9 Hz, 1H), 2.06 (dd, *J* = 13.7, 6.0 Hz, 1H), 1.66 (dt, *J* = 12.9, 2.7 Hz, 1H), 1.62 (s, 3H), 1.44 (s, 3H), 1.34 (s, 3H), 1.20 – 1.06 (m, 1H), 0.86 (s, 9H), 0.03 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 201.3, 132.7, 126.7, 98.5, 73.4, 66.3, 59.4, 45.4, 30.3, 29.6, 25.8, 19.5, 17.9, 16.5, -5.1, -5.1; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2993, 2954, 2929, 2885, 2856, 1738, 1472, 1463, 1442, 1381, 1252, 1201, 1164, 1110, 1076, 1053, 1006, 976, 949, 832, 814, 774, 664, 572, 521, 458; **HRMS** (ESI): [m/z] 365.2123 (calc'd for $C_{18}H_{34}NaO_4Si$: 365.2119 $[M+Na]^+$).

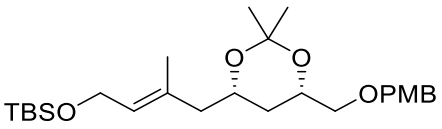
((*4S,6S*)-6-((*E*)-4-((*tert*-butyldimethylsilyl)oxy)-2-methylbut-2-en-1-yl)-2,2-dimethyl-1,3-dioxan-4-yl)methanol (**31**)



Aldehyde **30** (2.23g, 6.50 mmol, 1 equiv.) was dissolved in dry dichloromethane (65 mL, 0.1M) and cooled to -78 °C. To this solution, DIBAL-H (7.05 mL, 8.46 mmol, 1.2M in toluene, 1.3 equiv.) was added over ten minutes and the reaction solution was then stirred at -78 °C for an additional 60 minutes. The reaction was stopped by the addition of total K/Na tartrate solution$_{(aq)}$ (40 mL, 4.5 mL/mmol DIBAL-H) and allowed to warm to room temperature. Glycerol (2 mL, 0.2 mL/mmol DIBAL-H) was added and the emulsion was vigorously stirred for four hours. The phases were separated and the aqueous phase was extracted with dichloromethane (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 70:30), the residue obtained afforded product **31** (2.06 g, 5.98 mmol, 92%) as a colorless oil.

TLC: R_f = 0.25 (CH:EA 80:20) [$KMnO_4$]; **[α]$^{20}_D$** = +1.5 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, d_6-DMSO): δ [ppm] = 5.30 – 5.26 (m, 1H), 4.58 (t, *J* = 5.7 Hz, 1H), 4.14 (dt, *J* = 8.9, 4.8 Hz, 2H), 4.05 – 3.98 (m, 1H), 3.84 (dtd, *J* = 11.5, 5.3, 2.5 Hz, 1H), 3.34 (dt, *J* = 11.1, 5.6 Hz, 1H), 3.24 (dt, *J* = 11.0, 5.4 Hz, 1H), 2.12 (dd, *J* = 13.7, 6.9 Hz, 1H), 2.02 (dd, *J* = 13.7, 5.7 Hz, 1H), 1.61 (s, 3H), 1.46 (dt, *J* = 12.8, 2.5 Hz, 1H), 1.38 (s, 3H), 1.25 (s, 3H), 1.02 – 0.93 (m, 1H), 0.86 (s, 9H), 0.03 (s, 6H); **^{13}C NMR** (151 MHz, d_6-DMSO): δ [ppm] = 133.1, 126.4, 97.8, 69.8, 66.7, 64.8, 59.4, 45.8, 33.1, 30.0, 25.8, 19.7, 17.9, 16.5, -5.1, -5.1; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3410, 2990, 2952, 2929, 2884, 2857, 1463, 1436, 1379, 1253, 1200, 1164, 1076, 1052, 1006, 971, 940, 833, 814, 774, 733, 664, 570, 525; **HRMS** (ESI): [m/z] 367.2261 (calc'd for $C_{18}H_{36}NaO_4Si$: 367.2275 [M+Na]$^+$).

tert-butyl(((*E*)-4-((*4S,6S*)-6-(((4-methoxybenzyl)oxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)-3-methylbut-2-en-1-yl)oxy)dimethylsilane (**32**)

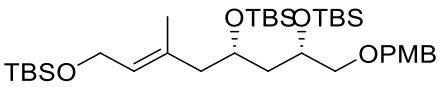


Sodium hydride (287 mg, 7.17 mmol, 60% dispersion in mineral oil, 1.2 equiv.) was placed in dry DMF (12 mL) and cooled to 0°C. Then primary alcohol **31** (2.06 g, 5.98 mmol, 1 equiv.) dissolved in DMF (8.0 mL) was added and the solution was stirred for 30 min at this temperature. PMB chloride (1.00 mL, 7.17 mmol, 1.2 equiv.) and TBAI (441 mg, 1.20 mmol, 20 mol%) were added, stirred for one hour at 0 °C, and the solution was warmed to room temperature and stirred for 18 hours. Sat. NH_4Cl solution$_{(aq)}$ was added and diluted with ethyl acetate. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. The residue

was purified by column chromatography (CH:EA 90:10) and product **32** (2.75 g, 5.86 mmol, 98%) was obtained as a colorless oil.

TLC: R_f = 0.08 (CH:EA 95:5) [$KMnO_4$]; **[α]$^{20}_D$** = -6.0 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, d_6-DMSO): δ [ppm] = 7.23 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.30 – 5.22 (m, 1H), 4.39 (d, *J* = 3.1 Hz, 2H), 4.13 (d, *J* = 6.3 Hz, 2H), 4.08 – 3.99 (m, 2H), 3.74 (s, 3H), 3.35 (dd, *J* = 10.1, 5.8 Hz, 1H), 3.27 (dd, *J* = 10.1, 4.5 Hz, 1H), 2.12 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.01 (dd, *J* = 14.1, 6.2 Hz, 1H), 1.60 (s, 3H), 1.44 (dt, *J* = 12.8, 2.4 Hz, 1H), 1.38 (s, 3H), 1.25 (s, 3H), 1.02 (q, *J* = 11.7 Hz, 1H), 0.85 (s, 9H), 0.02 (s, 6H); **^{13}C NMR** (151 MHz, d_6-DMSO): δ [ppm] = 158.7, 133.0, 130.2, 129.2, 126.5, 113.6, 97.9, 72.8, 71.9, 67.9, 66.5, 59.4, 55.0, 45.7, 33.1, 29.9, 25.8, 19.6, 17.9, 16.5, -5.1, -5.1; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3032, 2992, 2930, 2856, 1613, 1587, 1513, 1463, 1442, 1378, 1362, 1301, 1246, 1199, 1169, 1103, 1036, 1005, 940, 907, 832, 774, 664, 637, 584, 519; **HRMS** (ESI): [m/z] 487.2858 (calc'd for $C_{26}H_{44}NaO_5Si$: 487.2850 $[M+Na]^+$).

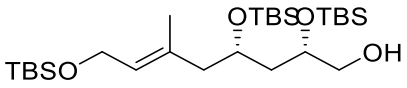
(*9S,11S,E*)-9-((*tert*-butyldimethylsilyl)oxy)-11-(((4-methoxybenzyl)oxy)methyl)-2,2,3,3,7,13,13,14,14-nonamethyl-4,12-dioxa-3,13-disilapentadec-6-ene (**33**)



Acetonide **32** (2.75 g, 5.92 mmol, 1 equiv.) was placed in dry methanol (118 mL, 0.05M) and PPTS (379 mg, 1.48 mmol, 25 mol%) was added at room temperature. The reaction was stirred at room temperature for four hours. Subsequently, the solvent was removed under reduced pressure and the residue obtained was taken up in DMF (59.2 mL, 0.1M). Imidazole (4.03 g, 59.2 mmol, 10 equiv.) and TBS chloride (5.35 g, 35.5 mmol, 6 equiv.) were added to the reaction at 0 °C and the reaction was stirred at room temperature for 16 h before being stopped by the addition of water and ethyl acetate. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 98:2), the residue obtained afforded the triply TBS-protected product **33** (3.42 g, 5.08 mmol, 86% over two steps) as a colorless oil.

TLC: R_f = 0.45 (CH:EA 95:5) [$KMnO_4$]; **[α]$^{20}_D$** = +0.6 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 7.24 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.32 (t, *J* = 5.9 Hz, 1H), 4.48 – 4.39 (m, 2H), 4.20 – 4.15 (m, 2H), 3.96 – 3.88 (m, 2H), 3.80 (s, 3H), 3.36 (d, *J* = 5.0 Hz, 2H), 2.14 (d, *J* = 6.2 Hz, 2H), 1.74 – 1.68 (m, 1H), 1.61 (s, 3H), 1.59 – 1.55 (m, 1H), 0.90 (s, 9H), 0.88 (s, 9H), 0.86 (s, 9H), 0.06 – 0.04 (m, 12H), 0.00 (2x s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.2, 133.9, 130.8, 129.3, 127.8, 113.8, 74.9, 73.1, 69.4, 68.2, 60.3, 55.4, 48.0, 42.7, 26.2, 26.1, 26.1, 18.6, 18.3, 18.2, 17.3, -4.0, -4.2, -4.3, -4.5, -4.9; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2953, 2928, 2887, 2855, 1613, 1513, 1471, 1463, 1442, 1407, 1386, 1361, 1302, 1248, 1173, 1083, 1039, 1005, 938, 831, 808, 772, 664, 574, 513; **HRMS** (ESI): [m/z] 675.4255 (calc'd for $C_{35}H_{68}NaO_5Si_3$: 675.4267 $[M+Na]^+$).

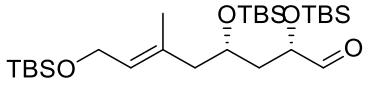
(*2S,4S,E*)-2,4,8-tris((*tert*-butyldimethylsilyl)oxy)-6-methyloct-6-en-1-ol (**34**)



PMB-protected alcohol **33** (400 mg, 612 µmol, 1 equiv.) was placed in a dichloromethane:pH7-phosphate buffer mixture (12 mL, 0.05M, 1:1) and DDQ (208 mg, 919 µmol, 1.5 equiv.) was added at 0 °C. The reaction was stirred at 0 °C for 90 min before being stopped by the addition of sat $NaHCO_3$ $solution_{(aq)}$ and dichloromethane. The phases were separated and the aqueous phase was extracted with dichloromethane (3x). The combined organic phases were washed with water, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 95:5 90:10) to afford the primary alcohol **34** (210 mg, 394 µmol, 64%) as a colorless oil.

TLC: R_f = 0.25 (CH:EA 90:10) [$KMnO_4$]; **[α]$^{20}_D$** = +13.4 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 5.34 (t, *J* = 5.8 Hz, 1H), 4.17 (d, *J* = 6.2 Hz, 2H), 3.94 (dq, *J* = 9.3, 4.7 Hz, 1H), 3.92 – 3.87 (m, 1H), 3.57 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.46 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.25 (dd, *J* = 13.3, 5.7 Hz, 1H), 2.15 (dd, *J* = 13.3, 7.4 Hz, 1H), 1.71 (ddd, *J* = 13.8, 8.6, 4.0 Hz, 1H), 1.65 – 1.60 (m, 4H), 0.90 – 0.88 (m, 27H), 0.09 – 0.05 (m, 18H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 133.4, 128.1, 70.1, 68.4, 66.3, 60.2, 48.0, 41.5, 26.2, 26.0 (2C), 18.6, 18.2, 18.2, 17.0, -4.1, -4.3, -4.4 (2C), -5.0 (2C); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3459, 2953, 2929, 2886, 2857, 1472, 1463, 1387, 1361, 1252, 1076, 1004, 938, 898, 831, 808, 772, 664, 569, 498; **HRMS** (ESI): [m/z] 555.3694 (calc'd for $C_{27}H_{60}NaO_4Si_3$: 555.3692 $[M+Na]^+$).

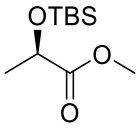
(*2S,4S,E*)-2,4,8-tris((*tert*-butyldimethylsilyl)oxy)-6-methyloct-6-enal (**7**)



Primary alcohol **34** (593 mg, 1.11 mmol, 1 equiv.) was dissolved in DMSO (7.42 mL, 0.15M) and IBX (519 mg, 1.67 mmol, 90% purity, 1.5 equiv.) was added at room temperature. The reaction was stirred at room temperature for 16 hours, the resulting solid was filtered off and washed with plenty of dichloromethane. The filtrate was washed with sat. $NaHCO_3$ $solution_{(aq)}$ and the aqueous phase was extracted with dichloromethane (3x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 95:5) to afford aldehyde **7** (467 mg, 879 µmol, 79%) as a colorless oil.

TLC: R_f = 0.65 (CH:EA 90:10) [$KMnO_4$]; **[α]$^{20}_D$** = +9.7 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 9.60 (d, *J* = 1.4 Hz, 1H), 5.37 – 5.31 (m, 1H), 4.17 (d, *J* = 6.2 Hz, 2H), 4.13 – 4.02 (m, 2H), 2.28 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.11 (dd, *J* = 13.2, 8.1 Hz, 1H), 1.88 (ddd, *J* = 14.1, 7.1, 4.1 Hz, 1H), 1.74 (ddd, *J* = 14.1, 8.0, 4.7 Hz, 1H), 1.64 – 1.60 (m, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.87 (s, 9H), 0.09 – 0.05 (m, 18H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 203.9, 133.5, 128.1, 75.0, 66.6, 60.2, 48.1, 40.6, 26.2, 26.1, 25.9, 18.6, 18.5, 18.1, 16.9, -4.1, -4.2, -4.5, -4.7, -4.9, -5.0; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2953, 2929, 2887, 2857, 1737, 1472, 1463, 1385, 1362, 1253, 1188, 1079, 1005, 937, 832, 807, 773, 666, 572, 509; **HRMS** (ESI): [m/z] 553.3538 (calc'd for $C_{27}H_{58}NaO_4Si_3$: 553.3535 $[M+Na]^+$).

methyl (*R*)-2-((*tert*-butyldimethylsilyl)oxy)propanoate[13] (**35**)

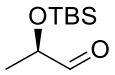


(*R*)-(+)-Methyl lactate (**14**) (2.20 g, 21.1 mmol, 1 equiv.) was dissolved in DMF (16 mL, 1.3M) and imidazole (2.26 g, 31.7 mmol, 1.5 equiv.) and TBS chloride (3.82 g, 25.4 mmol, 1.2 equiv.) were added. The reaction was stirred at room temperature for 30-60 min and then water was added. The mixture was extracted with diethyl ether (3x) and the combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The product **35** (4.80 g, 21.1 mmol, quant.) was obtained without further purification.

^{1}H NMR (600 MHz, $CDCl_3$): δ [ppm] = 4.33 (q, *J* = 6.8 Hz, 1H), 3.72 (s, 3H), 1.39 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 174.7, 68.6, 52.0, 25.9, 21.5, 18.5, -4.8, -5.1.

The spectroscopic data were identical to those reported in the literature.[13]

(*R*)-2-((*tert*-butyldimethylsilyl)oxy)propanal[13] (**36**)

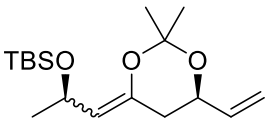


The methyl ester **35** (4.80 g, 21.1 mmol, 1 equiv.) was placed in dry dichloromethane (211 mL, 0.1M) and cooled to -78 °C. Subsequently, DIBAL-H (25.3 mL, 25.3 mmol, 1M in dichloromethane, 1.2 equiv.) was slowly added via syringe pump over 30 min and then stirred at -78 °C for one hour. The reaction was terminated with ethyl acetate (30 mL) and sat. K/Na tartrate solution$_{(aq)}$ (113 mL, 4.5 mL/mmol DIBAL-H) and warmed to room temperature. Glycerol (5 mL, 0.2 mL/mmol DIBAL-H) was subsequently added and the reaction mixture was vigorously stirred for 16 hours. After extraction with dichloromethane (3x), the collected organic phase was washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, and the solvent was removed under reduced pressure. After vacuum distillation, product **35** (3.44 g, 18.3 mmol, 87%) was obtained as a colorless liquid.

[□]$^{20}_D$ = +9.2 (c = 1.0, $CHCl_3$); **Bp** = 81-84°C (27 mmHg); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 9.61 (d, *J* = 1.3 Hz, 1H), 4.09 (qd, *J* = 6.9, 1.3 Hz, 1H), 1.28 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 204.3, 74.0, 25.9, 18.7, 18.3, -4.6, -4.6.

The spectroscopic data were identical to those reported in the literature.[13]

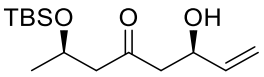
(*R*)-*tert*-butyl((1-(2,2-dimethyl-6-vinyl-1,3-dioxan-4-ylidene)propan-2-yl)oxy)dimethylsilane[2,3] (**37**)



Diisopropylamine (3.28 mL, 23.4 mmol, 2 equiv.) was placed in dry THF (29 mL) and cooled to 78 °C. *n*Butyllithium (9.35 mL, 23.4 mmol, 2.5M in hexane, 2 equiv.) was added and cooling was removed for 15 min. Cooling was resumed to 78 °C and the (*R*)-polyketide building block **11** (4.00 g, 11.7 mmol, 1 equiv.) dissolved in dry THF (11.7 mL) was added. This caused the solution to turn deep red. After one hour, the aldehyde **36** (6.60 g, 35.1 mmol, 3 equiv.), dissolved in dry THF (17.5 mL), was added and allowed to thaw to room temperature within 90 minutes. The solution became cloudy and orange in the process. Finally, potassium *tert*-butoxide (1.45 g, 12.3 mmol, 1.05 equiv.) was added and stirred for another 60 minutes at room temperature. The solution turned dark orange to brown. The reaction was stopped by adding sat. NH_4Cl $solution_{(aq)}$ and extracted with dichloromethane (3x). The combined organic phases were washed with sat. NaCl $solution_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. Purification of the crude product by column chromatography (CH:EA 95:5) afforded product **37** (3.76 g, 11.4 mmol, 98%, *E*/*Z* 50:50) as a yellow oil.

TLC: R_f = 0.60 (CH:EA 80:20) [$KMnO_4$]; **^{1}H NMR** (400 MHz, d_6-DMSO): δ [ppm] = 5.89 – 5.75 (m, 1H), 5.30 – 5.22 (m, 1H), 5.17 – 5.09 (m, 1H), 4.89 – 4.49 (m, 2H), 4.42 – 4.29 (m, 1H), 2.15 (dd, *J* = 13.7, 3.1 Hz, 1H), 2.03 – 1.86 (m, 1H), 1.43 – 1.35 (m, 6H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.86 – 0.83 (m, 9H), 0.07 – 0.05 (m, 3H), 0.02 – -0.02 (m, 3H); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957, 2928, 2897, 1681, 1371, 1255, 1204, 1129, 1071, 1001, 935, 830, 773, 678; **HRMS** (ESI): [m/z] 335.2015 (calc'd for $C_{17}H_{32}NaO_3Si$: 335.2013 $[M+Na]^+$).

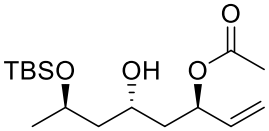
(*2R,6R*)-2-((*tert*-butyldimethylsilyl)oxy)-6-hydroxyoct-7-en-4-one[11] (**38**)



Cerium(III) chloride heptahydrate was dried *in vacuo* at 140 °C for two hours to obtain dry cerium(III) chloride before starting the reaction. Acetonide **36** (2.00 g, 6.40 mmol, 1 equiv.) was placed in dry THF (32 mL, 0.2M) and cooled to -78 °C. Cerium(III) chloride (3.16 g, 12.8 mmol, 2 equiv.), oxalic acid (144 mg, 1.60 mmol, 25 mol%), and water (230 µL, 12.8 mmol, 2 equiv.) were added successively and the reaction was stirred for 16 h at -78 °C. The reaction was stopped by the addition of sat. $NaHCO_3$ solution(aq) at -78 °C and warmed up to room temperature. Extraction was carried out with ethyl acetate (3x) and the combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained, after purification by column chromatography (CH:EA 80:20), afforded the β-hydroxyketone **38** (1.31 g, 4.81 mmol, 75%) as a yellow oil.

TLC: R_f = 0.60 (CH:EA 80:20) [$KMnO_4$]; **$[\alpha]^{20}_D$** = -1.4 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.84 (ddd, *J* = 17.2, 10.5, 5.5 Hz, 1H), 5.27 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.11 (dt, *J* = 10.5, 1.4 Hz, 1H), 4.58 – 4.52 (m, 1H), 4.35 – 4.26 (m, 1H), 2.73 – 2.58 (m, 3H), 2.46 (dd, *J* = 15.1, 5.1 Hz, 1H), 1.17 (d, *J* = 6.1 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 210.2, 139.2, 115.1, 68.7, 65.5, 53.3, 50.5, 25.9, 24.1, 18.1, -4.4, -4.8; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3420, 2954, 2928,2856, 1707, 1374, 1253, 1129, 985, 831, 774; **HRMS** (ESI): [m/z] 295.1696 (calc'd for $C_{14}H_{28}NaO_3Si$: 295.1700 $[M+Na]^+$).

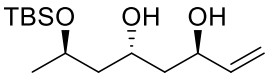
(*3R,5R,7R*)-7-((*tert*-butyldimethylsilyl)oxy)-5-hydroxyoct-1-en-3-yl acetate (**39**)



The reaction was carried out in the absence of light due to the instability of samarium(II) iodide. The β-hydroxyketone **38** (2.20 g, 7.59 mmol, 1 equiv.) was placed in dry THF (15 mL, 0.5M) and cooled to -50 °C. Acetaldehyde (1.50 mL, 26.6 mmol, 3.5 equiv.) and samarium(II) iodide (56.9 mL, 5.69 mmol, 0.1M in THF, 75 mol%) were added. The deep blue solution was stirred at 50 °C for ten minutes and the reaction decolorized. It was then stirred at 20 °C for an additional 16 hours. The reaction was stopped by the addition of sat. $NaHCO_3$ solution$_{(aq)}$ and extracted with ethyl acetate (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 90:10), the residue obtained afforded the reduction product **39** (2.31 g, 7.31 mmol, 96%, *d.r.* >99:1).

TLC: R_f = 0.45 (CH:EA 80:20) [$KMnO_4$]; **[α]$^{25}_D$** = -0.6 (c = 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.84 (ddd, *J* = 17.1, 10.6, 6.0 Hz, 1H), 5.56 – 5.43 (m, 1H), 5.26 (dt, *J* = 17.3, 1.2 Hz, 1H), 5.15 (dt, *J* = 10.6, 1.1 Hz, 1H), 4.22 – 4.11 (m, 1H), 3.91 – 3.78 (m, 1H), 3.31 (d, *J* = 2.8 Hz, 1H), 2.09 (s, 3H), 1.72 – 1.57 (m, 3H), 1.47 – 1.42 (m, 1H), 1.18 (d, *J* = 6.2 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 171.3, 136.8, 116.3, 72.1, 66.4, 64.0, 45.6, 43.2, 26.0, 23.8, 21.3, 18.1, -4.2, -4.9; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3516, 2955, 2929, 2856, 1721, 1372, 1257, 1147, 1080, 1058, 1019, 929, 834, 805, 773; **HRMS** (ESI): [m/z] 339.1963 (calc'd for $C_{16}H_{32}NaO_4Si$: 339.1962 $[M+Na]^+$).

(*3R,5R,7R*)-7-((*tert*-butyldimethylsilyl)oxy)oct-1-ene-3,5-diol (**40**)



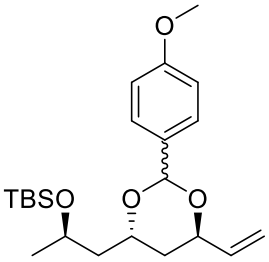
Method A: Tetramethylammonium triacetoxyborohydride (1.07 g, 3.85 mmol, 5 equiv.) was placed in acetonitrile:acetic acid (8 mL, 5:3) and cooled to -25 °C. Subsequently, β-hydroxyketone **38** (210 mg, 770 µmol, 1 equiv.) dissolved in acetonitrile (0.8 mL) was added and the reaction was stirred at -25 °C for 22 hours. Sat. K/Na tartrate solution$_{(aq)}$ was added and the reaction was stirred for an additional 45 minutes at room temperature. The mixture was transferred to a separatory funnel and extracted with dichloromethane (3x). The organic phase was washed with sat. $NaHCO_3$ solution$_{(aq)}$ and the aqueous phase was extracted again with dichloromethane (3x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained, after purification by column chromatography (CH:EA 70:30), gave the product **40** (212 mg, 0.75 mmol, 97%, *d.r.* 77:23) as a colorless oil.

Method B: Acetate **39** (2.31 g, 1.42 mmol, 1 equiv.) was dissolved in methanol:water (22 mL, 0.33M, 3:1) and potassium carbonate (2.02 g, 14.6 mmol, 2 equiv.) was added at 0 °C. The reaction was stirred at room temperature for 60 minutes and then water and ethyl acetate were added. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phases

were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained, after purification by column chromatography (CH:EA 70:30), gave product **39** (1.98 g, 7.22 mmol, 99%) as a colorless oil.

TLC: R_f = 0.44 (CH:EA 50:50) [$KMnO_4$]; **[α]$^{20}_D$** = -16.1 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.93 (ddd, *J* = 17.2, 10.5, 5.4 Hz, 1H), 5.30 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.12 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.50 – 4.43 (m, 1H), 4.40 – 4.32 (m, 1H), 4.29 – 4.18 (m, 1H), 3.93 (s, 1H), 3.06 (s, 1H), 1.81 (ddd, *J* = 14.2, 10.2, 3.9 Hz, 1H), 1.73 (ddd, *J* = 14.3, 8.5, 3.4 Hz, 1H), 1.60 (ddd, *J* = 14.3, 7.8, 3.2 Hz, 1H), 1.46 (ddd, *J* = 14.3, 4.7, 2.1 Hz, 1H), 1.25 (d, *J* = 6.3 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 141.1, 114.2, 70.5, 68.0, 66.1, 43.8, 43.0, 25.9, 22.7, 18.1, -4.4, -4.9; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3374, 2954, 2929, 2856, 1409, 1375, 1253, 1088, 1066, 986, 920, 832, 806, 773; **HRMS** (ESI): [m/z] 297.1847 (calc'd for $C_{14}H_{30}NaO_3Si$: 297.1856 [M+Na]$^+$).

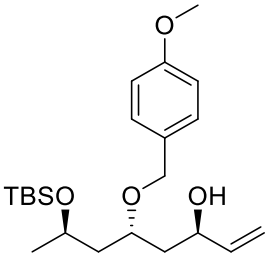
tert-butyl(((*R*)-1-((*4R,6R*)-2-(4-methoxyphenyl)-6-vinyl-1,3-dioxan-4-yl)propan-2-yl)oxy)dimethylsilane (**41**)



To a solution of the *anti*-diol **40** (362 mg, 1.32 mmol, 1 equiv.) in dry dichloromethane (6.6 mL, 0.2M) were added 1-(dimethoxymethyl)-4-methoxybenzene (343 µL, 1.98 mmol, 1.5 equiv.) and PPTS (24 mg, 92 µmol, 7 mol%) and the reaction was stirred for 16 hours at room temperature. The reaction was stopped by the addition of sat. $NaHCO_3$ solution$_{(aq)}$ and extracted with dichloromethane (3x). The combined organic phases were dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. Column chromatographic purification (CH:EA 93:7 → 90:10) gave the protected product **41** (571 mg, 1.18 mmol, 81% purity, 89%, *d.r.* 8:2) as a yellowish oil.

TLC: R_f = 0.49 (CH:EA 80:20) [UV, $KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.42 (dq, *J* = 9.6, 2.4 Hz, 2H), 6.93 – 6.85 (m, 2H), 6.16 – 5.84 (m, 1H), 5.76 (s, 1H), 5.39 (ddd, *J* = 11.0, 2.2, 1.2 Hz, 1H), 5.37 – 5.27 (m, 1H), 4.79 (dt, *J* = 4.4, 2.4 Hz, 1H), 4.24 – 3.95 (m, 2H), 3.80 (s, 3H), 2.13 – 1.99 (m, 1H), 1.73 – 1.58 (m, 2H), 1.48 (ddd, *J* = 14.2, 9.9, 2.3 Hz, 1H), 1.17 (dd, *J* = 32.0, 6.1 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3076, 2953, 2928, 2855, 1615, 1516, 1373, 1246, 1170, 1115, 1034, 922, 823, 773; **HRMS** (ESI): [m/z] 415.2271 (calc'd for $C_{22}H_{36}NaO_4Si$: 415.2275 [M+Na]$^+$).

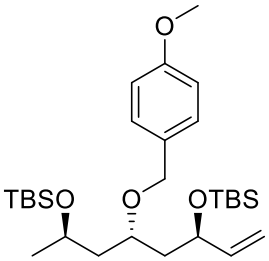
(*3R*,*5R*,*7R*)-7-((*tert*-butyldimethylsilyl)oxy)-5-((4-methoxybenzyl)oxy)oct-1-en-3-ol (**42**)



Acetal **41** (2.51 g, 6.39 mmol, 1 equiv.) was placed in dry dichloromethane (71 mL, 0.09M) and cooled to 0 °C. To this solution was added DIBAL-H (28.5 mL, 28.5 mmol, 1M in DCM, 4.45 equiv.) at 0 °C. The reaction was stirred at 0 °C for ten minutes and then carefully stopped with sat. NH_4Cl solution$_{(aq)}$. Sat. K/Na tartrate solution$_{(aq)}$ (143 mL, 5 mL/mmol DIBAL H) was added and stirred for 30 minutes at room temperature. The resulting phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained, after purification by column chromatography (CH:EA 85:15 → 80:20), gave product **42** (2.35 g, 5.96 mmol, 93%) as a colorless oil.

TLC: R_f = 0.44 (CH:EA 50:50) [UV, $KMnO_4$]; **[α]$^{20}_D$** = -7.9 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.27 (d, *J* = 2.1 Hz, 2H), 6.90 – 6.86 (m, 2H), 5.87 (ddd, *J* = 17.2, 10.5, 5.4 Hz, 1H), 5.27 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.10 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.52 (d, *J* = 10.7 Hz, 1H), 4.45 (d, *J* = 10.7 Hz, 1H), 4.42 – 4.39 (m, 1H), 4.04 – 3.94 (m, 1H), 3.90 – 3.82 (m, 1H), 3.80 (s, 3H), 3.00 (d, *J* = 3.7 Hz, 1H), 1.91 – 1.79 (m, 2H), 1.74 – 1.58 (m, 2H), 1.16 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.5, 141.1, 130.5, 129.6, 114.2, 114.1, 74.8, 71.0, 70.2, 66.1, 55.5, 44.8, 40.4, 26.1, 24.6, 18.2, -3.8, -4.4; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3463, 3076, 3033, 2997, 2953, 2929, 2855, 1612, 1513, 1463, 1246, 1173, 1035, 918, 822, 772; **HRMS** (ESI): [m/z] 417.2431 (calc'd for $C_{22}H_{38}NaO_4Si$: 417.2432 $[M+Na]^+$).

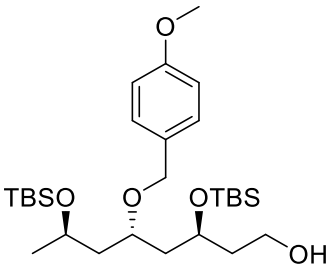
(*5R*,*7S*,*9R*)-7-((4-methoxybenzyl)oxy)-2,2,3,3,5,11,11,12,12-nonamethyl-9-vinyl-4,10-dioxa-3,11-disilatridecane (**43**)



The secondary alcohol **42** (997 mg, 2.48 mmol, 1 equiv.) was dissolved in dry DMF (5 mL, 0.5M) and imidazole (505 mg, 7.43 mmol, 3 equiv.) was added. The reaction was cooled to 0 °C and TBS chloride (560 mg, 3.71 mmol, 1.5 equiv.) was added. The mixture was stirred at room temperature for 16 h and then terminated by the addition of sat. $NaHCO_3$ solution$_{(aq)}$. Extraction was carried out with ethyl acetate (4x) and the combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 95:5), the residue obtained afforded the product **43** (1.20 g, 2.36 mmol, 95%) as a colorless oil.

TLC: R_f = 0.69 (CH:EA 80:20) [UV, $KMnO_4$]; **[α]$^{20}_D$** = -8.9 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.28 – 7.25 (m, 2H), 6.90 – 6.84 (m, 2H), 5.82 (ddd, *J* = 17.1, 10.3, 6.7 Hz, 1H), 5.20 – 5.11 (m, 1H), 5.07 – 5.00 (m, 1H), 4.47 – 4.39 (m, 2H), 4.27 (q, *J* = 6.6 Hz, 1H), 4.06 – 3.96 (m, 1H), 3.80 (s, 3H), 3.70 (p, *J* = 6.8, 6.1 Hz, 1H), 1.83 – 1.57 (m, 4H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 – 0.00 (m, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.2, 142.0, 131.4, 129.2, 114.2, 114.0, 73.3, 71.5, 70.3, 65.9, 55.5, 45.6, 44.0, 26.1 (2C), 24.5, 18.3, 18.2, -3.8, -3.9, -4.4, -4.5; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3075, 2997, 2954, 2928, 2894, 2856, 1513, 1462, 1247, 1064, 1038, 922, 832, 806, 772, **HRMS** (ESI): [m/z] 531.3298 (calc'd for $C_{28}H_{52}NaO_4Si_2$: 531.3296 $[M+Na]^+$).

(*3S*,*5S*,*7R*)-3,7-bis((*tert*-butyldimethylsilyl)oxy)-5-((4-methoxybenzyl)oxy)octan-1-ol (**44**)

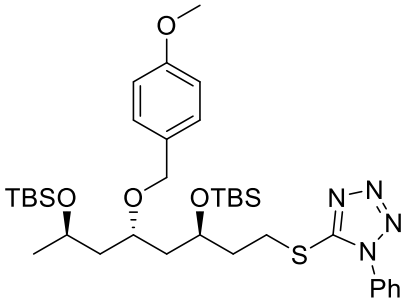


Terminal alkene **43** (1.11 g, 2.18 mmol, 1 equiv.) was placed in dry THF (22 mL, 0.1M) and cooled to 0 °C. 9-BBN (13.1 mL, 6.54 mmol, 0.5M in THF, 3 equiv.) was added and the solution was stirred at 0 °C for 15 minutes before stirring at room temperature for another 15 hours. To stop the reaction, the solution was again cooled to 0 °C and NaOH solution$_{(aq)}$ (2.18 mL, 6.54 mmol, 3M, 3 equiv.) and hydrogen peroxide solution$_{(aq)}$ (2.19 mL, 25.5 mmol, 35%, 11.7 equiv.) were added. The mixture was stirred for 15 minutes at 0 °C and four hours at room temperature. Water was added and the mixture was extracted with diethyl ether (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over

sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue after purification by column chromatography (CH:EA 85:15) afforded the primary alcohol **44** (1.12 g, 2.10 mmol, 97%) as a colorless oil.

TLC: R_f = 0.21 (CH:EA 80:20) [UV, $KMnO_4$]; **[α]$^{20}_D$** = -22.8 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.26 – 7.23 (m, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.46 (d, *J* = 10.8 Hz, 1H), 4.41 (d, *J* = 10.8 Hz, 1H), 4.09 – 3.97 (m, 2H), 3.91 – 3.81 (m, 1H), 3.80 (s, 3H), 3.77 – 3.68 (m, 1H), 3.66 – 3.54 (m, 1H), 2.37 (s, 1H), 1.99 – 1.83 (m, 2H), 1.71 – 1.55 (m, 4H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.3, 131.0, 129.3, 114.0, 73.6, 70.2, 69.5, 65.7, 60.2, 55.5, 45.4, 41.9, 38.3, 26.1, 26.0, 24.6, 18.2, 18.1, -3.8, -4.2, -4.4, -4.5; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3442, 2952, 2928, 2855, 1613, 1513, 1462, 1247, 1108, 1036, 1004, 832, 806, 772; **HRMS** (ESI): [m/z] 549.3402 (calc'd for $C_{28}H_{54}NaO_5Si_2$: 549.3402 $[M+Na]^+$).

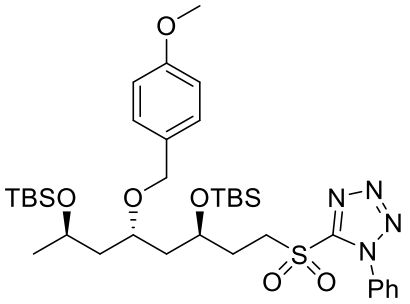
5-(((*3R,5S,7R*)-3,7-bis((*tert*-butyldimethylsilyl)oxy)-5-((4-methoxybenzyl)oxy)octyl)thio)-1-phenyl-*1H*-tetrazole (**45**)



Primary alcohol **44** (1.10 g, 2.07 mmol, 1 equiv.) was placed in dry THF (21 mL, 0.1м) and cooled to 0 °C. To this mixture was added 1-phenyl-*1H*-tetrazole-5-thiol (737 mg, 4.13 mmol, 2 equiv.), triphenylphosphine (813 mg, 3.10 mmol, 1.5 equiv.), and diisopropyl azodicarboxylate (779 µL, 3.72 mmol, 1.8 equiv.) and the reaction was stirred at 0 °C for four hours. The solvent was removed under reduced pressure, and the residue obtained, after purification by column chromatography (CH:EA 95:5 → 90:10), afforded product **45** (1.33 g, 1.94 mmol, 94%) as a colorless oil.

TLC: R_f = 0.42 (CH:EA 80:20) [UV, $KMnO_4$]; **[α]$^{20}_D$** = -9.8 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.60 – 7.50 (m, 5H), 7.26 – 7.21 (m, 2H), 6.88 – 6.82 (m, 2H), 4.43 (s, 2H), 4.06 – 3.93 (m, 2H), 3.79 (s, 3H), 3.68 – 3.59 (m, 1H), 3.53 – 3.38 (m, 2H), 2.09 – 1.92 (m, 2H), 1.89 – 1.80 (m, 1H), 1.74 – 1.54 (m, 3H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.08 – 0.04 (m, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.2, 154.5, 134.0, 131.1, 130.2, 129.9, 129.2, 124.0, 114.0, 73.4, 70.2, 68.6, 65.8, 55.4, 45.5, 42.5, 36.8, 29.2, 26.1, 26.1, 24.5, 18.2, 18.2, -3.9, -4.1 (2C), -4.4; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2999, 2952, 2928, 2855, 1610, 1513, 1500, 1385, 1247, 1108, 1071, 1037, 1005, 833, 755, 693; **HRMS** (ESI): [m/z] 709.3612 (calc'd for $C_{35}H_{58}NaO_4SSi_2$: 709.3610 $[M+Na]^+$).

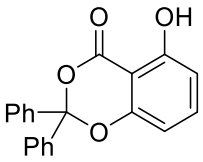
5-(((*3R,5S,7R*)-3,7-bis((*tert*-butyldimethylsilyl)oxy)-5-((4-methoxybenzyl)oxy)octyl)sulfonyl)-1-phenyl-*1H*-tetrazole (**8**)



Sulfide **45** (1.30 g, 1.89 mmol, 1 equiv.) was placed in dry ethanol (9.5 mL, 0.2M) and cooled to 0 °C. To this mixture was added $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (468 mg, 378 µmol, 20 mol%) dissolved in hydrogen peroxide solution$_{(aq)}$ (1.62 mL, 18.9 mmol, 35%, 10 equiv.). The reaction mixture was stirred for three hours at room temperature. Water and dichloromethane were then added to the reaction and the resulting phases were separated. The aqueous phase was extracted with dichloromethane (3x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. Column chromatographic purification (CH:EA 90:10) of the residue afforded sulfone **8** (1.23 g, 1.71 mmol, 90%) as a colorless oil.

TLC: R_f = 0.42 (CH:EA 80:20) [UV, $KMnO_4$]; **$[\alpha]^{20}_D$** = -2.0 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.71 – 7.66 (m, 2H), 7.61 (td, *J* = 5.7, 2.7 Hz, 3H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.47 (d, *J* = 10.8 Hz, 1H), 4.39 (d, *J* = 10.8 Hz, 1H), 4.10 – 3.97 (m, 2H), 3.79 (s, 5H), 3.66 – 3.58 (m, 1H), 2.28 – 2.15 (m, 1H), 2.11 – 2.00 (m, 1H), 1.80 – 1.70 (m, 2H), 1.69 – 1.54 (m, 2H), 1.16 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.07 (m, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.3, 153.7, 133.3, 131.5, 130.9, 129.8, 129.2, 125.2, 114.0, 73.3, 70.2, 67.5, 65.9, 55.4, 52.3, 45.3, 42.6, 29.6, 26.1, 26.0, 24.4, 18.2, 18.1, -3.9, -4.2, -4.3, -4.4; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3069, 2953, 2928, 2896, 1611, 1513, 1462, 1342, 1258, 1072, 1036, 833, 807, 773, 757, 687, 530; **HRMS** (ESI): [m/z] 741.3509 (calc'd for $C_{35}H_{58}N_4NaO_6SSi_2$: 741.3508 $[M+Na]^+$).

5-hydroxy-2,2-diphenyl-*4H*-benzo[*d*][1,3]dioxin-4-one[14] (**16**)



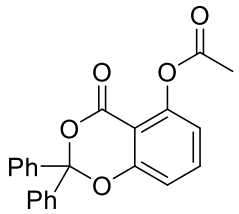
2,6-Dihydroxybenzoic acid (**15**) (3.00 g, 18.9 mmol, 1 equiv.) was placed in dry dimethoxyethane (15.7 mL, 1.2M). Benzophenone (4.47 g, 24.6 mmol, 1.3 equiv.) and DMAP (115 mg, 945 µmol, 5 mol%) were added and the reaction was cooled to 0 °C. Thionyl chloride (1.79 mL, 24.6 mmol, 1.3 equiv.) was added dropwise and the reaction was stirred at 0 °C for an additional 60 min before warming to room temperature and stirring for another 18 hours. The reaction was stopped by adding sat. $NaHCO_3$ solution$_{(aq)}$ and diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether (4x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by column chromatography (CH:EA

95:5). Recrystallization of the combined fractions after removal of the solvent from pentane:diethyl ether (170 mL, 9:1) afforded product **16** (1.83 g, 5.75 mmol, 30%) as a white solid.

TLC: R_f = 0.19 (CH:EA 95:5) [UV]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 10.16 (s, 1H), 7.63 – 7.59 (m, 4H), 7.45 – 7.36 (m, 7H), 6.68 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.59 (dd, *J* = 8.5, 0.9 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 165.7, 161.6, 156.2, 139.3, 138.2, 129.6, 128.8, 126.6, 111.3, 107.7, 107.6, 101.1.

The spectroscopic data were identical to those reported in the literature.[14]

4-oxo-2,2-diphenyl-*4H*-benzo[*d*][1,3]dioxin-5-yl acetate (**9**)

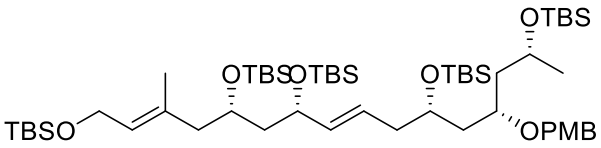


Phenol **16** (5.07 g, 15.9 mmol, 1 equiv.) was dissolved in dry dichloromethane (159 mL, 0.1M). Pyridine (6.44 mL, 79.6 mmol, 5 equiv.) and DMAP (195 mg, 1.59 mmol, 10 mol%) were added and the reaction mixture was cooled to 0 °C. Acetic anhydride (2.71 mL, 28.7 mmol, 1.8 equiv.) was added and the reaction was stirred at 0 °C for 30 min and at room temperature for another 90 min. The reaction was stopped by the addition of sat. $NaHCO_3$ $solution_{(aq)}$ and the two phases were separated. The aqueous phase was extracted with dichloromethane (3x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 8:2) furnishing product **9** (5.10 g, 14.2 mmol, 89%) as a white solid.

TLC: R_f = 0.29 (CH:EA 8:2) [UV, $KMnO_4$]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.58 – 7.53 (m, 4H), 7.50 (t, *J* = 8.2 Hz, 1H), 7.39 – 7.30 (m, 6H), 7.06 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.71 (dd, *J* = 8.1, 1.0 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 169.0, 158.1, 157.5, 151.8, 139.3, 136.3, 129.4, 128.6, 126.7, 118.0, 115.5, 108.9, 107.0, 21.0; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3112, 3094, 3066, 2972, 1737, 1617, 1472, 1449, 1336, 1318, 1269, 1193, 1099, 1059, 960, 907, 877, 820, 758; **HRMS** (ESI): [m/z] 383.0889 (calc'd for $C_{22}H_{16}NaO_5$: 383.0890 $[M+Na]^+$).

2.3 Fragment assembly

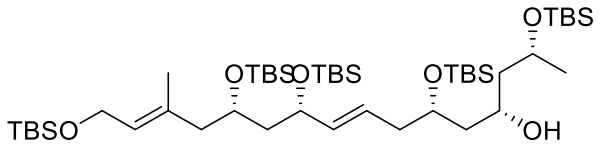
(*6E*,*9S*,*11S*,*12E*,*15S*,*17S*,*19R*)-9,11,15-tris((*tert*-butyldimethylsilyl)oxy)-17-((4-methoxybenzyl)oxy)-2,2,3,3,7,19,21,21,22,22-decamethyl-4,20-dioxa-3,21-disilatricosa-6,12-diene (**46**)



Sulfone **8** (955 mg, 1.12 mmol, 93% purity, 1.15 equiv.) was placed in the reaction vessel before the start of the reaction and dried azeotropically with benzene under reduced pressure. Dry DME (24 mL) was added and the reaction mixture was cooled to -78 °C. To this solution was added KHMDS (2.58 mL, 1.29 mmol, 0.5M in toluene, 1.2 equiv.) and the resulting yellow solution was stirred at -78 °C for 30 min. Aldehyde **7** (570 mg, 1.07 mmol, 1 equiv.) dissolved in DME (10.7 mL) was then added via syringe pump at -78 °C for half an hour. After the addition was completed, the reaction solution was stirred for an additional 2.5 hours at -78 °C before the reaction was warmed to room temperature and stopped by the addition of sat. NH_4Cl solution$_{(aq)}$. Ethyl acetate was added and the phases separated. The aqueous phase was extracted with ethyl acetate (3x) and the combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 97:3), the residue obtained afforded product **46** (961 mg, 910 µmol, 85%, *E*/*Z* >99:1) as a colorless oil.

TLC: R_f = 0.45 (CH:EA 95:5) [$KMnO_4$]; **[α]$^{20}_D$** = -4.6 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 7.24 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.58 (dt, *J* = 15.4, 7.1 Hz, 1H), 5.42 (dd, *J* = 15.4, 7.0 Hz, 1H), 5.36 – 5.30 (m, 1H), 4.42 (s, 2H), 4.20 – 4.14 (m, 3H), 4.03 – 3.98 (m, 1H), 3.95 – 3.91 (m, 1H), 3.85 (p, *J* = 6.1 Hz, 1H), 3.79 (s, 3H), 3.71 – 3.65 (m, 1H), 2.30 – 2.09 (m, 4H), 1.80 – 1.73 (m, 1H), 1.72 – 1.64 (m, 2H), 1.62 – 1.49 (m, 6H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 18H), 0.88 (s, 9H), 0.87 (s, 9H), 0.07 – 0.05 (m, 18H), 0.04 (s, 3H), 0.03 – -0.00 (m, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ [ppm] = 159.0, 136.2, 133.8, 131.3, 128.9, 127.6, 126.2, 113.7, 73.3, 71.0, 69.9, 69.0, 68.1, 65.7, 60.2, 55.3, 47.7, 46.3, 45.3, 42.2, 40.5, 26.0, 26.0 (2C), 26.0, 25.9, 24.3, 18.4, 18.2, 18.1 (2C), 18.0, 17.1, -3.9, -4.0 (2C), -4.2, -4.3, -4.5, -4.5, -4.6, -5.1 (2C); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2953, 2928, 2886, 2856, 1614, 1514, 1472, 1463, 1361, 1301, 1249, 1172, 1068, 1005, 974, 938, 832, 807, 771, 664, 570, 509; **HRMS** (ESI): [m/z] 1045.6988 (calc'd for $C_{55}H_{110}NaO_7Si_5$: 1045.6990 $[M+Na]^+$).

(*5R*,*7S*,*9S*,*11E*,*13S*,*15S*,*17E*)-9,13,15-tris((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,21,21,22,22-decamethyl-4,20-dioxa-3,21-disilatricosa-11,17-dien-7-ol (**47**)

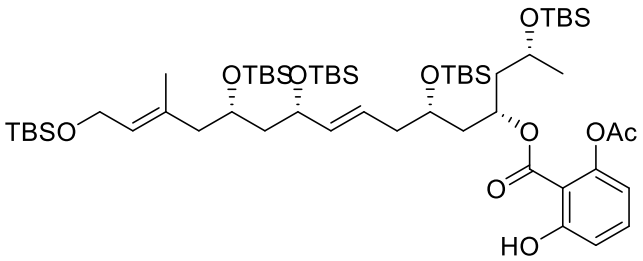


PMB-protected secondary alcohol **46** (50 mg, 47 mmol, 1 equiv.) was placed in a dichloromethane:pH7-phosphate buffer mixture (1.0 mL, 0.05M, 1:1) and cooled to 0 °C. To this solution was added DDQ (16

mg, 71 µmol, 1.5 equiv.) and the reaction was stirred at 0 °C for two hours. Then, sat. $NaHCO_3$ solution$_{(aq)}$ and dichloromethane were added and the phases were separated. The aqueous phase was extracted with dichloromethane (3x) and the combined organic phases were washed with water, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 95:5) to give product **47** (39 mg, 43 µmol, 90%) as a faint yellowish oil.

TLC: R_f = 0.30 (CH:EA 95:5) [$KMnO_4$]; **[α]$^{20}_D$** = -1.2 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 5.52 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.41 (dd, *J* = 15.5, 7.0 Hz, 1H), 5.32 (t, *J* = 6.2 Hz, 1H), 4.21 – 4.11 (m, 5H), 4.06 – 4.01 (m, 1H), 3.84 (p, *J* = 6.2 Hz, 1H), 3.48 (s, 1H), 2.32 – 2.11 (m, 4H), 1.70 – 1.64 (m, 1H), 1.62 – 1.50 (m, 6H), 1.46 – 1.36 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 3H), 0.92 – 0.86 (m, 45H), 0.12 – 0.01 (m, 30H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 136.4, 133.9, 127.8, 126.4, 71.1, 69.8, 68.2, 66.9, 64.4, 60.3, 47.9, 46.4, 46.0, 43.4, 40.4, 26.2, 26.1, 26.1, 26.1, 26.0, 23.5, 18.6, 18.3, 18.2 (2C), 18.1, 17.2, -3.8, -4.0, -4.2, -4.3, -4.3, -4.5, -4.7, -4.8, -4.9 (2C); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3522, 2954, 2929, 2887, 2856, 1472, 1463, 1408, 1379, 1361, 1252, 1068, 1004, 972, 938, 832, 808, 772, 730, 664, 570.; **HRMS** (ESI): [m/z] 925.6414 (calc'd for $C_{47}H_{102}NaO_6Si_5$: 925.6415 $[M+Na]^+$).

(*5R,7S,9S,11E,13S,15S,17E*)-9,13,15-tris((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,21,21,22,22-decamethyl-4,20-dioxa-3,21-disilatricosa-11,17-dien-7-yl 2-acetoxy-6-hydroxybenzoate[14] (**49**)

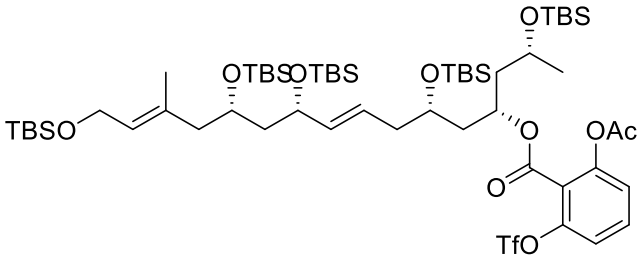


Secondary alcohol **47** (285 mg, 306 µmol, 1 equiv.) and aryl acetate **9** (276 mg, 765 µmol, 2.5 equiv.) were dissolved in dry and degassed dichloromethane (1.53 mL, 0.2M) and distributed to five NMR tubes under argon atmosphere (~0.3 mL solution per tube). The reaction tubes were placed in a UV reactor and irradiated with light (λ_{max} = 310 nm) for five hours. The irradiation was briefly interrupted every 60 minutes and the NMR tubes were shaken for 20 seconds. After the reaction time was completed, the tubes were diluted with dichloromethane and all reaction solutions were worked up together. The organic phase was washed with sat. NaCl solution$_{(aq)}$ and the aqueous phase was extracted with dichloromethane (5x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 97:3). The resulting by-product in the form of benzophenone could not be readily separated and was successfully removed only in the next reaction step. Product **49** (337 mg, 219 µmol, 72%, 70% purity (benzophenone as impurity)) could thus be obtained as a colorless oil.

TLC: R_f = 0.30 (CH:EA 95:5) [$KMnO_4$]; **[α]$^{20}_D$** = -6.1 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 11.48 (s, 1H), 7.40 (t, *J* = 8.2 Hz, 1H), 6.90 (dd, *J* = 8.5, 1.1 Hz, 1H), 6.53 (dd, *J* = 7.9, 1.1 Hz, 1H),

5.57 (dt, *J* = 14.5, 7.0 Hz, 1H), 5.43 (td, *J* = 15.4, 14.6, 7.0 Hz, 2H), 5.32 (t, *J* = 6.2 Hz, 1H), 4.20 – 4.13 (m, 3H), 3.92 – 3.82 (m, 3H), 2.32 – 2.22 (m, 4H), 2.20 – 2.08 (m, 3H), 1.84 – 1.65 (m, 5H), 1.60 (s, 3H), 1.55 – 1.51 (m, 1H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.90 – 0.85 (m, 45H), 0.07 – -0.00 (m, 27H), -0.02 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 169.2, 169.0, 163.6, 150.8, 136.9, 134.9, 133.9, 127.8, 125.6, 116.2, 114.4, 107.6, 72.5, 71.1, 68.7, 68.2, 65.2, 60.3, 47.8, 46.5, 45.8, 42.6, 40.8, 26.2, 26.1, 26.1, 26.1, 24.6, 21.4, 18.6, 18.3, 18.2, 18.2, 18.1, 17.2, -3.8, -3.9, -4.0, -4.1, -4.2, -4.5, -4.6, -4.7, -4.9; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3466, 2954, 2929, 2887, 2856, 1773, 1665, 1617, 1472, 1461, 1362, 1319, 1300, 1250, 1199, 1063, 1032, 1005, 974, 938, 906, 832, 809, 772, 733, 705, 664, 605, 574, 484, 445; **HRMS** (ESI): [m/z] 1098.7128 (calc'd for $C_{56}H_{112}NO_{10}Si_5$: 1098.7127 $[M+NH_4]^+$).

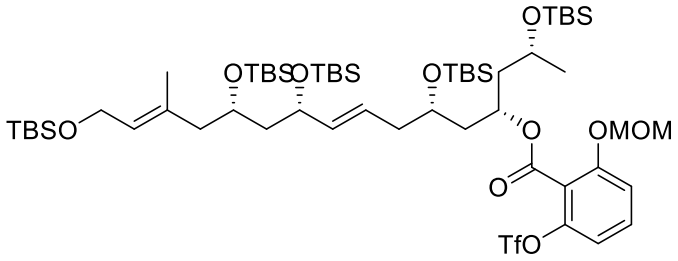
(*5R,7S,9S,11E,13S,15S,17E*)-9,13,15-tris((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,21,21,22,22-decamethyl-4,20-dioxa-3,21-disilatricosa-11,17-dien-7-yl 2-acetoxy-6-(((trifluoromethyl)sulfonyl)oxy)benzoate (**49a**)



Phenol **49** (335 mg, 217 µmol, 70% purity, 1 equiv.) was placed in dry dichloromethane (2.2 mL, 0.1M) and cooled to 0 °C. Pyridine (87.7 µL, 1.08 mmol, 5 equiv.) and trifluoromethanesulfonic anhydride (72.8 µL, 434 µmol, 2 equiv.) were added and the reaction was stirred at 0 °C for 30 minutes before stirring at room temperature for an additional two hours. The reaction was stopped by the addition of sat. $NaHCO_3$ $solution_{(aq)}$ and extracted with dichloromethane (4x). The combined organic phases were dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. The residue obtained, after purification by column chromatography (CH:EA 95:5), afforded product **49a** (239 mg, 197 µmol, 91%) as a colorless oil.

TLC: R_f = 0.12 (CH:EA 95:5) [$KMnO_4$]; **$[\alpha]^{20}_D$** = -3.4 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, $CDCl_3$): δ [ppm] = 7.54 (t, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 8.3, 0.9 Hz, 1H), 5.55 (dt, *J* = 15.4, 7.0 Hz, 1H), 5.42 (dd, *J* = 15.4, 7.0 Hz, 1H), 5.32 (t, *J* = 5.7 Hz, 1H), 5.20 – 5.15 (m, 1H), 4.21 – 4.10 (m, 3H), 3.94 – 3.88 (m, 1H), 3.88 – 3.80 (m, 2H), 2.29 (s, 3H), 2.28 – 2.14 (m, 3H), 2.10 (dd, *J* = 13.3, 7.0 Hz, 1H), 1.94 – 1.86 (m, 2H), 1.83 – 1.72 (m, 2H), 1.71 – 1.63 (m, 1H), 1.60 (s, 3H), 1.57 – 1.48 (m, 1H), 1.16 (d, *J* = 6.1 Hz, 3H), 0.91 – 0.88 (m, 27H), 0.86 (s, 18H), 0.07 – 0.06 (m, 9H), 0.05 (s, 6H), 0.04 (s, 3H), 0.03 – 0.01 (m, 6H), -0.00 (s, 3H), -0.02 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ [ppm] = 168.7, 161.1, 150.8, 147.8, 136.6, 134.0, 132.1, 127.7, 125.8, 124.2, 121.1, 119.78 (q, *J* = 320.6 Hz), 119.5, 74.1, 71.1, 68.8, 68.2, 65.7, 60.3, 47.7, 46.6, 44.9, 41.9, 40.8, 26.2, 26.1, 26.1, 26.1, 26.1, 24.3, 21.0, 18.6, 18.3, 18.2, 18.1, 18.1, 17.2, -3.8, -4.1, -4.2 (2C), -4.2, -4.4, -4.5, -4.6, -4.9 (2C; **^{19}F NMR** (376 MHz, $CDCl_3$): δ [ppm] = -73.2; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2954, 2929, 2887, 2857, 1783, 1731, 1613, 1472, 1461, 1430, 1362, 1252, 1216, 1186, 1141, 1065, 1015, 988, 938, 888, 832, 807, 772, 742, 705, 664, 603, 575, 532, 507; **HRMS** (ESI): [m/z] 1235.6141 (calc'd for $C_{57}H_{107}F_3NaO_{12}SSi_5$: 1235.6174 $[M+Na]^+$).

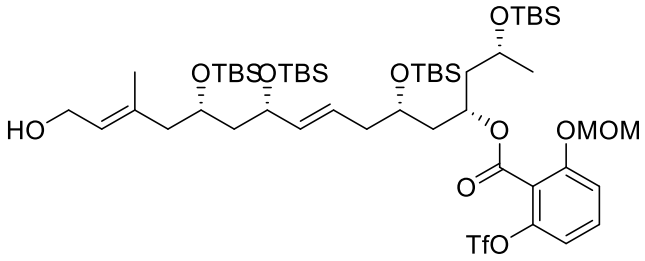
(*5R*,*7S*,*9S*,*11E*,*13S*,*15S*,*17E*)-9,13,15-tris((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,21,21,22,22-decamethyl-4,20-dioxa-3,21-disilatricosa-11,17-dien-7-yl 2-(methoxymethoxy)-6-(((trifluoromethyl)sulfonyl)oxy)benzoate (**50**)



The aryl acetate **49a** (215 mg, 172 µmol, 1 equiv.) was dissolved in a mixture of dry methanol:THF (3.4 mL, 0.05M, 1:1) and potassium carbonate (11.9 mg, 85.9 µmol, 0.5 equiv.) was added at room temperature. The reaction was stirred at room temperature for one hour and then water and dichloromethane were added. The phases were separated and the aqueous phase was extracted with dichloromethane (5x). The combined organic phases were washed with sat. NaCl solution$_{(aq)}$, dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The crude product was dissolved in dry dichloromethane (3.4 mL, 0.05M) and cooled to 0 °C. To this solution was added DIPEA (151 µL, 859 µmol, 5 equiv.) and MOMCl (27.5 µL, 344 µmol, 2 equiv.). The reaction was stirred for 60 min at 0 °C and 16 h at room temperature before being stopped by the addition of water. The phases were separated and the aqueous phase was extracted with dichloromethane (5x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 95:5). Product **50** (208 mg, 163 µmol, 95%) was obtained as a colorless oil.

TLC: R_f = 0.14 (CH:EA 95:5) [$KMnO_4$]; **[α]$^{20}_D$** = +4.3 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, C_6D_6): δ [ppm] = 6.84 – 6.79 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.85 (dt, *J* = 14.6, 7.0 Hz, 1H), 5.69 – 5.56 (m, 3H), 4.78 (q, *J* = 7.0 Hz, 2H), 4.38 (q, *J* = 6.6 Hz, 1H), 4.26 (d, *J* = 6.2 Hz, 2H), 4.19 – 4.12 (m, 2H), 4.08 (p, *J* = 6.1 Hz, 1H), 3.17 (s, 3H), 2.42 (h, *J* = 7.6 Hz, 2H), 2.30 (dd, *J* = 13.3, 5.3 Hz, 1H), 2.26 – 2.16 (m, 2H), 2.12 (ddd, *J* = 14.0, 7.3, 4.2 Hz, 1H), 2.06 – 1.93 (m, 3H), 1.81 (dt, *J* = 13.4, 6.2 Hz, 1H), 1.67 (s, 3H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.07 (d, *J* = 5.6 Hz, 18H), 1.04 – 1.00 (m, 27H), 0.30 (s, 3H), 0.26 (s, 3H), 0.19 (s, 3H), 0.18 – 0.14 (m, 12H), 0.14 – 0.10 (m, 9H); **^{13}C NMR** (151 MHz, C_6D_6): δ [ppm] = 170.0, 162.5, 156.2, 147.3, 137.2, 133.9, 131.4, 126.2, 120.25 (q, *J* = 320.7 Hz), 119.7, 114.8, 114.1, 94.9, 73.4, 71.5, 69.3, 68.7, 66.1, 60.4, 56.2, 48.0, 47.1, 45.7, 42.6, 41.3, 26.3 (2C), 26.3 (2C), 26.2, 24.7, 18.6, 18.4, 18.4 (2C), 18.3, 17.4, -3.5, -3.9 (2C), -4.0, -4.0, -4.1, -4.2, -4.4, -4.9 (2C); **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 2955, 2928, 2856, 1730, 1612, 1581, 1462, 1428, 1254, 1216, 1141, 1121, 1070, 1018, 833, 774; **HRMS** (ESI): [m/z] 1237.6322 (calc'd for $C_{57}H_{109}F_3NaO_{12}SSi_5$: 1237.6330 $[M+Na]^+$).

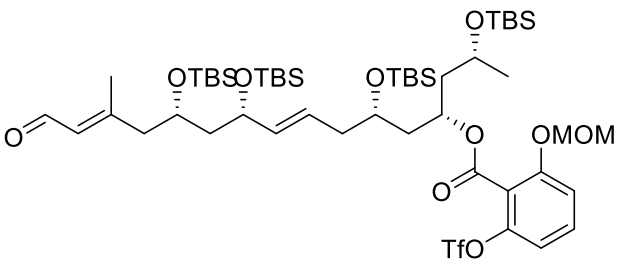
(*5R*,*7S*,*9S*,*13S*,*15S*,*E*)-9,13-bis((*tert*-butyldimethylsilyl)oxy)-15-((*E*)-4-hydroxy-2-methylbut-2-en-1-yl)-2,2,3,3,5,17,17,18,18-nonamethyl-4,16-dioxa-3,17-disilanonadec-11-en-7-yl 2-(methoxymethoxy)-6-(((trifluoromethyl)sulfonyl)oxy)benzoate[15] (**50a**)



TBS-protected primary alcohol **50** (30.0 mg, 23.4 µmol, 1 equiv.) was dissolved in a mixture of THF:water (234 µL, 0.1M, 4:1) and sodium periodate (30.4 mg, 140 µmol, 6 equiv.) was added at room temperature. The reaction was stirred at room temperature for five hours before being stopped by the addition of water and dichloromethane. The phases were separated and the aqueous phase was extracted with dichloromethane (5x). The combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (CH:EA 80:20), the residue obtained afforded product **50a** (10.5 mg, 9.53 µmol, 41% (87% brsm)) and the unreacted starting material **50** (13.0 mg, 10.7 µmol, 46%) as colorless oils.

TLC: R_f = 0.22 (CH:EA 80:20) [$KMnO_4$]; **[α]$^{20}_D$** = -1.4 (c = 1.0, DCM); **^{1}H NMR** (400 MHz, C_6D_6): δ [ppm] = 6.81 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.75 – 6.64 (m, 2H), 5.86 (dt, *J* = 15.4, 7.0 Hz, 1H), 5.71 – 5.56 (m, 2H), 5.50 – 5.43 (m, 1H), 4.83 – 4.73 (m, 2H), 4.38 (q, *J* = 6.6 Hz, 1H), 4.21 – 4.04 (m, 3H), 4.00 (d, *J* = 6.6 Hz, 2H), 3.16 (s, 3H), 2.42 (t, *J* = 6.1 Hz, 2H), 2.33 – 2.16 (m, 3H), 2.14 – 1.92 (m, 4H), 1.85 – 1.76 (m, 1H), 1.62 (s, 3H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.07 – 1.05 (m, 18H), 1.02 – 0.99 (m, 18H), 0.29 (s, 3H), 0.26 (s, 3H), 0.18 – 0.15 (m, 12H), 0.14 (s, 3H), 0.11 (s, 3H); **^{13}C NMR** (151 MHz, C_6D_6): δ [ppm] = 162.6, 156.2, 147.3, 137.2, 135.3, 131.4, 126.2, 119.7, 119.2 (q, *J* = 321.1 Hz), 114.8, 114.1, 95.0, 73.5, 71.5, 69.4, 68.6, 66.0, 59.4, 56.2, 48.0, 47.0, 45.7, 42.6, 41.2, 30.2, 26.3 (2C), 26.2, 26.2, 24.7, 18.4, 18.4, 18.3, 18.3, 17.2, -3.5, -3.9, -4.0, -4.0, -4.0, -4.1, -4.2, -4.4; **^{19}F NMR** (376 MHz, C_6D_6): δ [ppm] = -73.6; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3436, 2954, 2928, 2897, 2856, 1736, 1612, 1582, 1462, 1428, 1253, 1216, 1142, 1088, 1068, 1017, 833, 774, 605; **HRMS** (ESI): [m/z] 1123.5426 (calc'd for $C_{51}H_{95}F_3NaO_{12}SSi_4$: 1123.5466 $[M+Na]^+$).

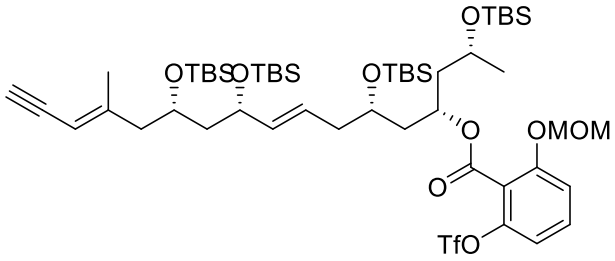
(*5R*,*7S*,*9S*,*13S*,*15S*,*E*)-9,13-bis((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,17,18,18-nonamethyl-15-((*E*)-2-methyl-4-oxobut-2-en-1-yl)-4,16-dioxa-3,17-disilanonadec-11-en-7-yl 2-(methoxymethoxy)-6-(((trifluoromethyl)sulfonyl)oxy)benzoate (**50b**)



Primary alcohol **50a** (68.0 mg, 61.7 µmol, 1 equiv.) was dissolved in dry dichloromethane (1.23 mL, 0.05M) and manganese(IV) oxide (316 mg, 3.09 mmol, 85% strength, 50 equiv.) was added at room temperature. The reaction was stirred for 16 hours and then filtered over Celite®. The filter cake was washed with a large amount of dichloromethane and the filtrate was concentrated under reduced pressure. The obtained aldehyde **50b** (67.9 mg, 61.7 µmol, quant.) was used as crude material for the next reaction without further purification.

TLC: R_f = 0.43 (CH:EA 80:20) [UV, $KMnO_4$]; **^{1}H NMR** (600 MHz, C_6D_6): δ [ppm] = 9.93 (d, *J* = 7.7 Hz, 1H), 6.81 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.73 – 6.65 (m, 2H), 6.01 – 5.97 (m, 1H), 5.86 (dt, *J* = 15.4, 7.0 Hz, 1H), 5.62 (dd, *J* = 15.3, 7.1 Hz, 2H), 4.81 – 4.75 (m, 2H), 4.27 (q, *J* = 7.4 Hz, 1H), 4.20 – 4.05 (m, 3H), 3.16 (s, 3H), 2.43 (t, *J* = 6.1 Hz, 2H), 2.29 – 2.19 (m, 2H), 2.16 – 2.07 (m, 2H), 2.05 – 1.97 (m, 2H), 1.97 – 1.90 (m, 1H), 1.83 (d, *J* = 1.2 Hz, 3H), 1.71 – 1.65 (m, 1H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.09 – 1.05 (m, 18H), 1.00 (s, 9H), 0.96 (s, 9H), 0.29 (s, 3H), 0.27 (s, 3H), 0.18 (s, 3H), 0.16 – 0.14 (m, 6H), 0.13 – 0.11 (m, 6H), 0.03 (s, 3H).

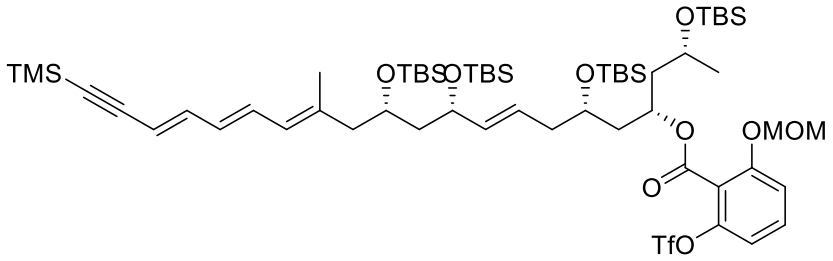
(*5R*,*7S*,*9S*,*13S*,*15S*,*E*)-9,13-bis((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,17,18,18-nonamethyl-15-((*E*)-2-methylpent-2-en-4-yn-1-yl)-4,16-dioxa-3,17-disilanonadec-11-en-7-yl 2-(methoxymethoxy)-6-(((trifluoromethyl)sulfonyl)oxy)benzoate (**51**)



Trimethylsilyldiazomethane (66.3 µL, 133 µmol, 2M in diethyl ether, 1.8 equiv.) was placed in dry THF (736 µL) and cooled to -78 °C. To this solution was added *n*-butyllithium (44.2 µL, 110 µmol, 2.5M in hexane, 1.5 equiv.) and the reaction was stirred at 78 °C for 30 min. Aldehyde **50b** (81.0 mg, 73.7 µmol, 1 equiv.) dissolved in dry THF (736 µL) was then added to this solution. After completed addition, the reaction was stirred at -78 °C for 30 minutes, then at 0 °C for two hours, and finally at room temperature for 60 minutes before the reaction was stopped by the addition of total NH_4Cl $solution_{(aq)}$. Extraction was carried out with dichloromethane (5x) and the combined organic phases were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 95:5 → 90:10). The terminal alkyne **51** (54.2 mg, 49.5 µmol, 67%) was obtained as a colorless oil.

TLC: R_f = 0.22 (CH:EA 80:20) [$KMnO_4$]; **[α]$^{20}_D$** = -4.0 (c = 1.0, DCM); **^{1}H NMR** (600 MHz, C_6D_6): δ [ppm] = 6.81 (dd, *J* = 8.4, 0.7 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.67 (t, *J* = 8.4 Hz, 1H), 5.84 (dt, *J* = 15.4, 7.1 Hz, 1H), 5.65 – 5.57 (m, 2H), 5.46 – 5.43 (m, 1H), 4.80 – 4.75 (m, 2H), 4.30 (q, *J* = 7.1 Hz, 1H), 4.20 – 4.10 (m, 2H), 4.10 – 4.03 (m, 1H), 3.16 (s, 3H), 2.83 (d, *J* = 2.1 Hz, 1H), 2.46 – 2.37 (m, *J* = 6.2, 5.1 Hz, 2H), 2.27 (dd, *J* = 13.3, 4.6 Hz, 1H), 2.23 – 2.14 (m, 2H), 2.14 – 2.07 (m, 1H), 2.05 – 1.92 (m, 6H), 1.75 – 1.69 (m, 1H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.08 – 1.06 (m, 18H), 1.01 – 0.99 (m, 18H), 0.30 (s, 3H), 0.27 (s, 3H), 0.19 (s, 3H), 0.16 – 0.12 (m, 15H); **^{13}C NMR** (151 MHz, C_6D_6): δ [ppm] = 162.5, 156.2, 150.8, 147.3, 137.1, 131.4, 126.3, 119.7, 119.2 (q, *J* = 320.5 Hz), 114.8, 114.1, 107.8, 94.9, 81.9, 80.7, 73.4, 71.4, 69.3, 68.3, 66.0, 56.2, 47.2, 46.7, 45.7, 42.6, 41.1, 26.3, 26.3, 26.2, 26.2, 24.7, 20.3, 18.4, 18.4, 18.3, 18.3, -3.5, -3.9, -4.0, -4.1, -4.1, -4.2, -4.2, -4.4; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3314, 2954, 2929, 2896, 2857, 2099, 1736, 1612, 1582, 1472, 1462, 1428, 1387, 1361, 1253, 1217, 1157, 1142, 1087, 1070, 1019, 976, 938, 889, 834, 774, 725, 664, 604, 509; **HRMS** (ESI): [m/z] 1117.5350 (calc'd for $C_{52}H_{93}F_3NaO_{11}SSi_4$: 1117.5360 $[M+Na]^+$).

(*5R*,*7S*,*9S*,*13S*,*15S*,*E*)-9,13-bis((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,5,17,17,18,18-nonamethyl-15-((*2E*,*4E*,*6E*)-2-methyl-9-(trimethylsilyl)nona-2,4,6-trien-8-yn-1-yl)-4,16-dioxa-3,17-disilanonadec-11-en-7-yl 2-(methoxymethoxy)-6-(((trifluoromethyl)sulfonyl)oxy)benzoate[16,17] (**5**)



Under argon atmosphere and light exclusion, zirconocene dichloride (44.8 mg, 153 µmol, 4 equiv.) was dissolved in dry THF (383 µL). Super-Hydride® solution (153 µL, 153 µmol, 1M in THF, 4 equiv.) was slowly added. The reaction was stirred at room temperature for one hour before adding a solution of alkyne **51** (42 mg, 38 µmol, 1 equiv.) dissolved in dry THF (164 µL). The mixture was stirred for an additional hour at room temperature and then *N*-iodosuccinimide (43.1 mg, 192 µmol, 5 equiv.) was added in one portion. After 15 minutes of reaction time, sat. $Na_2S_2O_3$ solution$_{(aq)}$ was added until complete decolorization. The mixture was transferred to a separatory funnel and extracted with dichloromethane (5x). The combined organic phases were dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure. The residue obtained was purified by column chromatography (CH:EA 95:5). The unstable dienyl iodide **52** (22 mg, 18 µmol, 47%) was obtained as an intermediate.

TLC: R_f = 0.17 (CH:EA 95:5) [$KMnO_4$]; **^{1}H NMR** (600 MHz, C_6D_6): δ [ppm] = 7.27 (dd, *J* = 14.2, 11.2 Hz, 1H), 6.81 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.68 (t, *J* = 8.4 Hz, 1H), 5.97 (d, *J* = 14.2 Hz, 1H), 5.89 – 5.81 (m, 1H), 5.71 (d, *J* = 11.1 Hz, 1H), 5.66 – 5.59 (m, 2H), 4.81 – 4.74 (m, 2H), 4.35 (q, *J* = 6.7 Hz, 1H), 4.20 – 4.10 (m, 2H), 4.02 (p, *J* = 6.2 Hz, 1H), 3.16 (s, 3H), 2.47 – 2.38 (m, 2H), 2.23 – 2.17 (m, 2H), 2.17 – 2.07 (m, 2H), 2.05 – 1.92 (m, 3H), 1.80 – 1.71 (m, 1H), 1.55 – 1.52 (m, 3H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.08 – 1.05 (m, 18H), 1.01 (s, 9H), 0.99 (s, 9H), 0.30 (s, 3H), 0.27 (s, 3H), 0.20 – 0.13 (m, 15H), 0.06 (s, 3H).

Intermediate **52** was immediately further reacted. Lithium chloride (11.4 mg, 270 µmol, 15 equiv.), Ph_3As (4.4 mg, 14 µmol, 80 mol%), and $Pd_2(dba)_3$ (1.7 mg, 1.8 µmol, 10 mol%) were placed in a heated 4-mL vial and dry DMF (180 µL) was added. The reaction mixture was stirred at room temperature for five minutes before a solution of the intermediate **52** (22 mg, 18 µmol, 1 equiv.) and stannane **6** (8.2 mg, 20 µmol, 1.1 equiv.) in dry DMF (540 µL) was added. The reaction mixture was stirred for two hours at room temperature and then stirred further at 40 °C for two hours. After purification by column chromatography (CH:EA 95:5), the reaction mixture afforded the protected monomer **5** (8.0 mg, 6.6 µmol, 36% (17% over two steps)) as an orange oil.

TLC: R_f = 0.17 (CH:EA 95:5) [$KMnO_4$]; **$[\alpha]^{20}_D$** = -7.3 (c = 0.7, DCM); **^{1}H NMR** (600 MHz, C_6D_6): δ [ppm] = 6.81 (d, *J* = 7.9 Hz, 1H), 6.78 – 6.70 (m, 2H), 6.67 (dd, *J* = 9.8, 7.0 Hz, 1H), 6.38 (dd, *J* = 14.6, 11.4 Hz,

1H), 6.01 (dd, *J* = 14.6, 11.2 Hz, 1H), 5.95 (d, *J* = 11.2 Hz, 1H), 5.91 – 5.80 (m, 1H), 5.70 – 5.61 (m, 2H), 5.60 (d, *J* = 15.5 Hz, 1H), 4.78 (q, *J* = 7.0 Hz, 2H), 4.38 (q, *J* = 6.6 Hz, 1H), 4.20 – 4.13 (m, 2H), 4.09 (p, *J* = 6.1 Hz, 1H), 3.16 (s, 3H), 2.47 – 2.38 (m, 2H), 2.35 (dd, *J* = 13.2, 5.1 Hz, 1H), 2.31 – 2.25 (m, 1H), 2.24 – 2.17 (m, 1H), 2.15 – 2.08 (m, 1H), 2.06 – 1.96 (m, 3H), 1.83 – 1.69 (m, 4H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.08 – 1.06 (m, 18H), 1.03 – 1.01 (m, 18H), 0.30 (s, 3H), 0.27 (s, 3H), 0.23 (s, 9H), 0.19 – 0.16 (m, 12H), 0.15 (s, 3H), 0.10 (s, 3H); **^{13}C NMR** (101 MHz, C_6D_6): δ [ppm] = 162.5, 156.2, 147.3, 143.9, 139.1, 137.1, 134.2, 132.3, 131.4, 130.5, 126.3, 119.7, 119.2 (q, *J* = 320.7 Hz), 114.9, 114.1, 110.4, 106.2, 97.6, 95.0, 73.4, 71.5, 69.4, 68.7, 66.0, 56.2, 48.7, 47.3, 45.7, 42.6, 41.2, 26.3 (2C), 26.2, 26.2, 24.7, 18.4, 18.4, 18.3, 18.3, 17.9, 0.2, -3.5, -3.9, -4.0, -4.0, -4.1, -4.1, -4.2, -4.4; **^{19}F NMR** (376 MHz, C_6D_6): δ [ppm] = -73.5; **IR** (ATR): $\tilde{\nu}$ [cm^{-1}] = 3025, 2955, 2929, 2897, 2856, 2164, 2117, 1737, 1611, 1582, 1472, 1462, 1429, 1375, 1361, 1252, 1217, 1156, 1142, 1070, 1020, 981, 938, 835, 775, 726, 664, 605, 509; **HRMS** (ESI): [m/z] 1241.6089 (calc'd for $C_{59}H_{105}F_3NaO_{11}SSi_5$: 1241.6068 $[M+Na]^+$).

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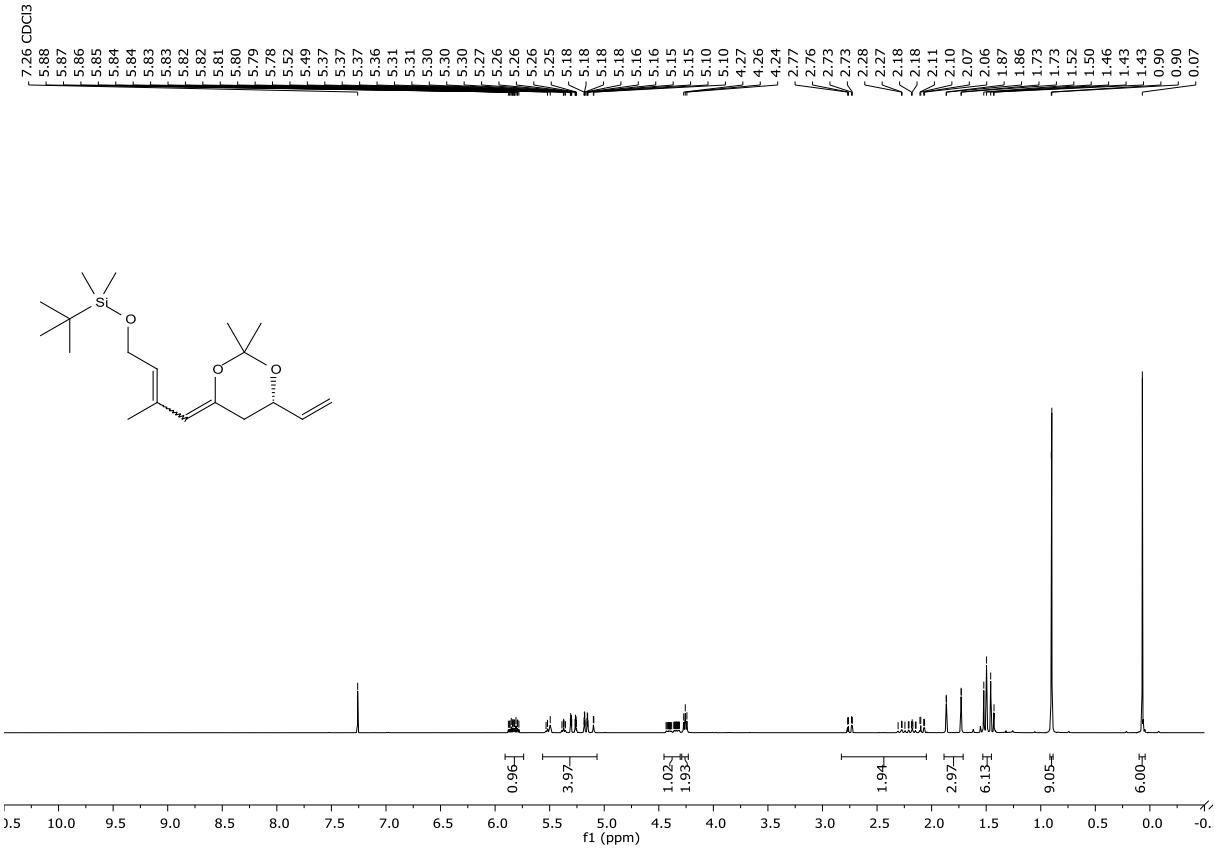
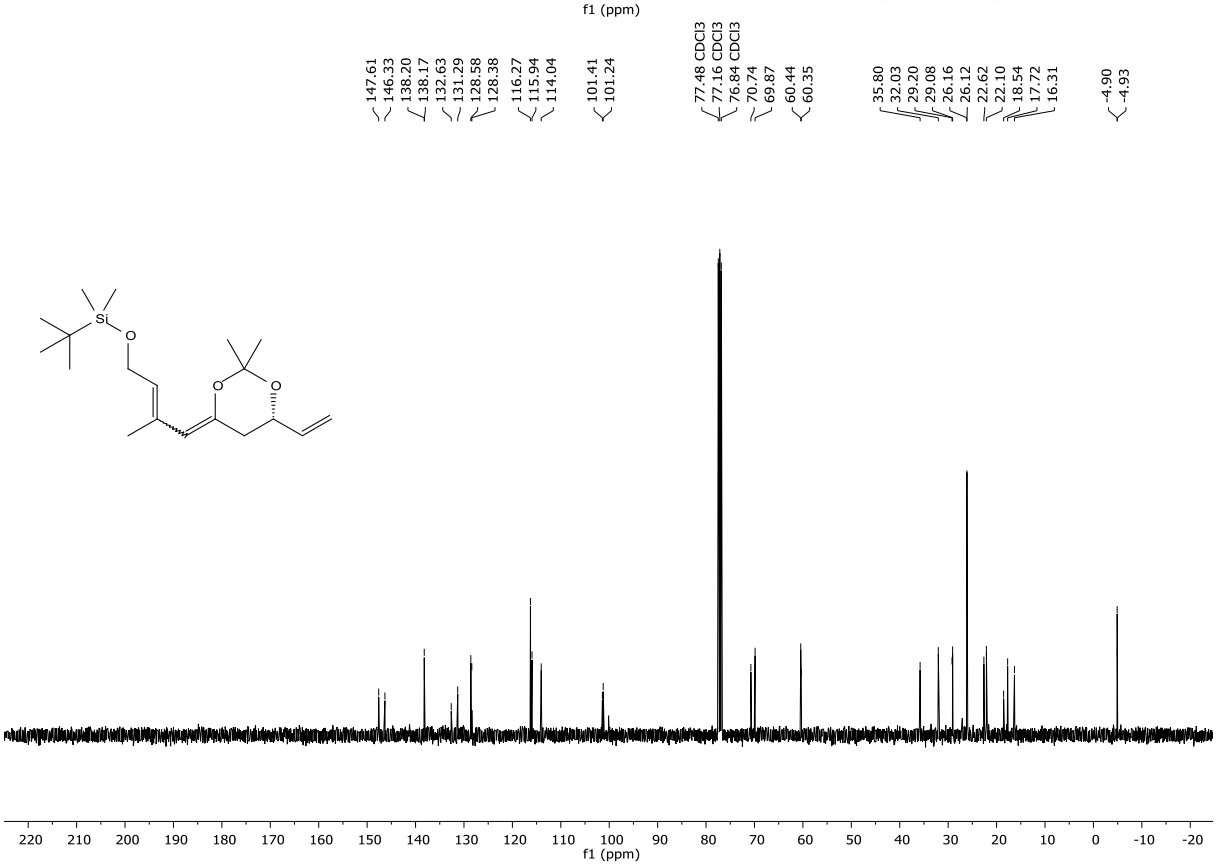
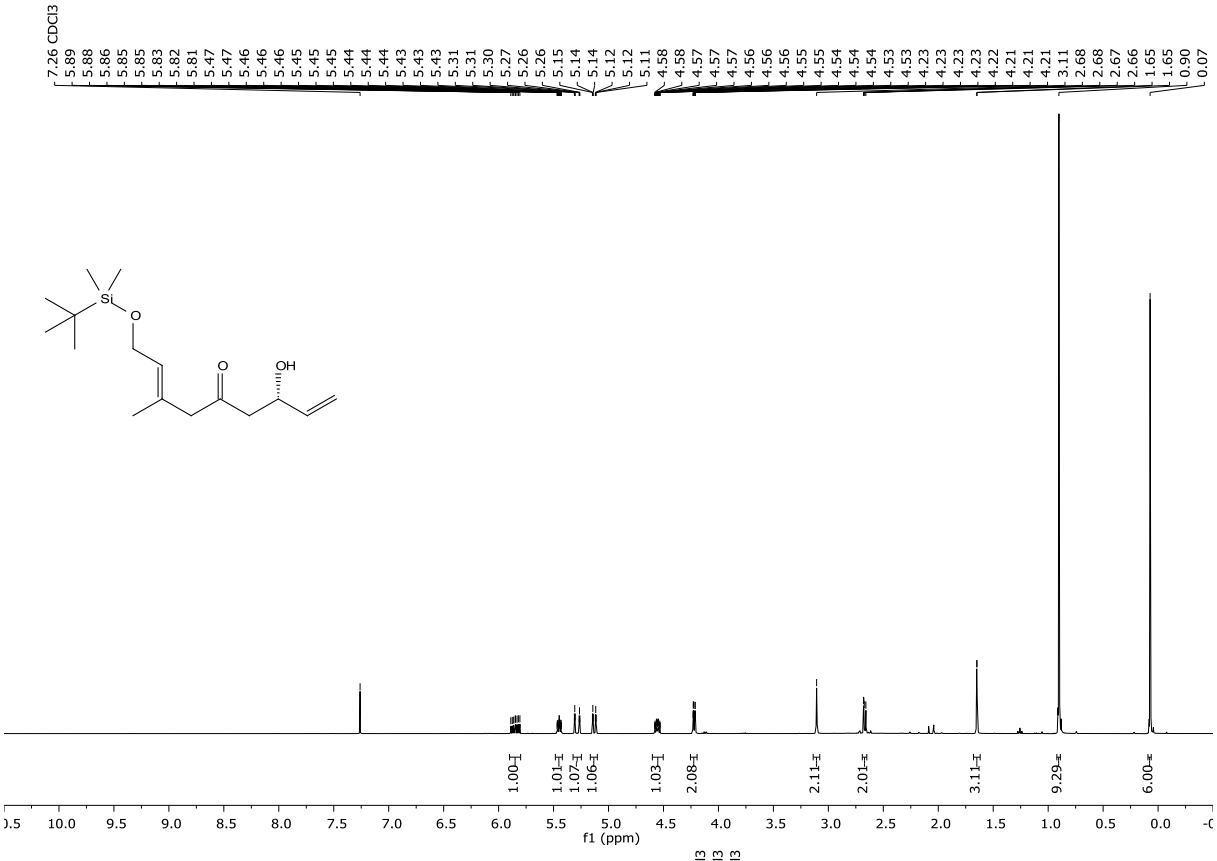
4. Spectra

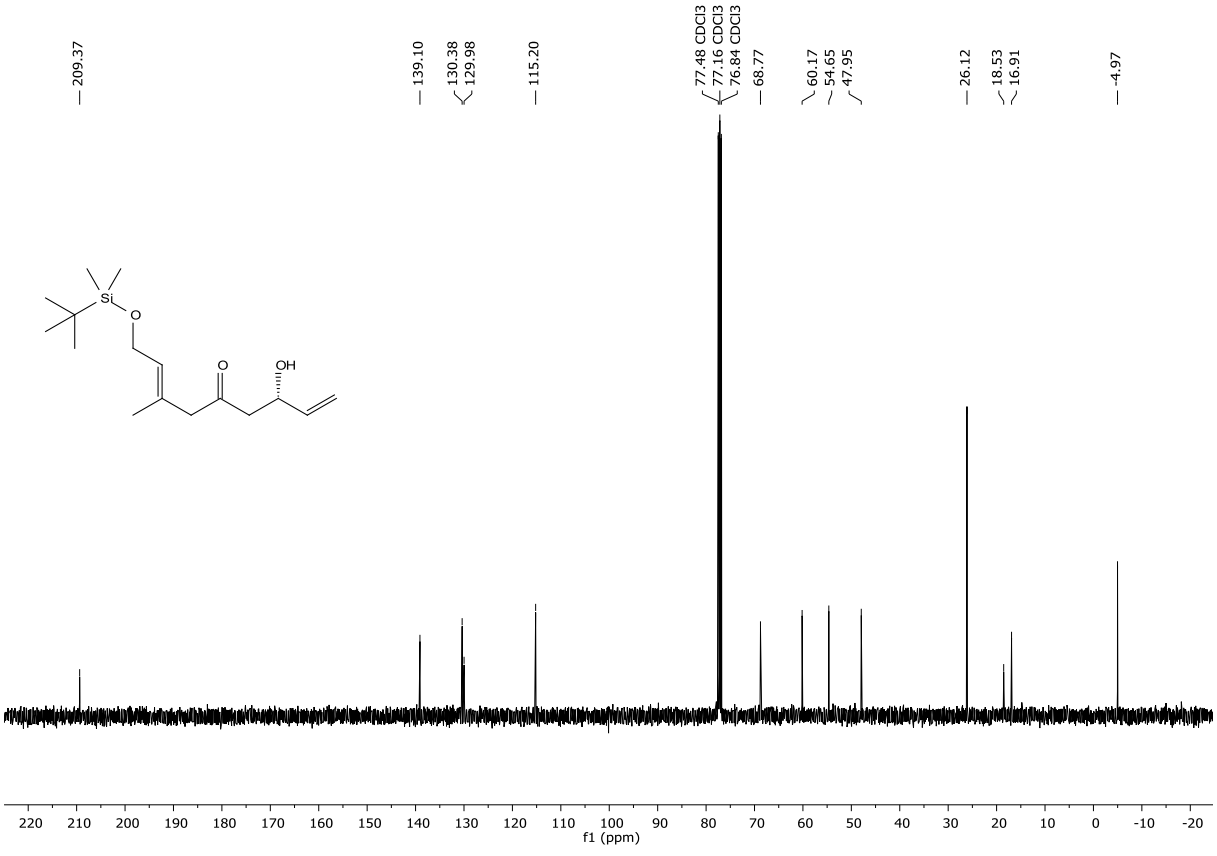
^{1}H and ^{13}C spectra of compound 23



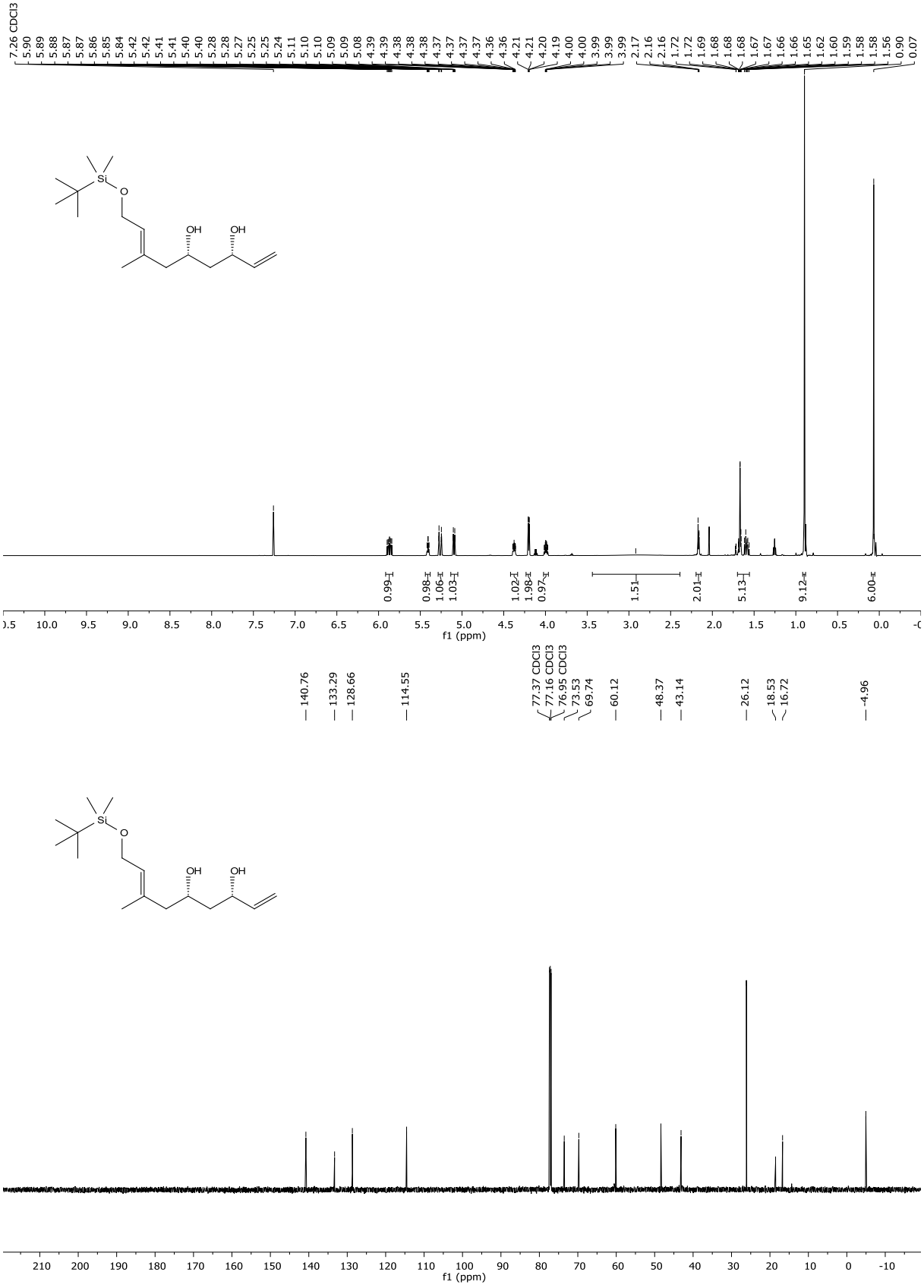


^{1}H and ^{13}C spectra of compound 24

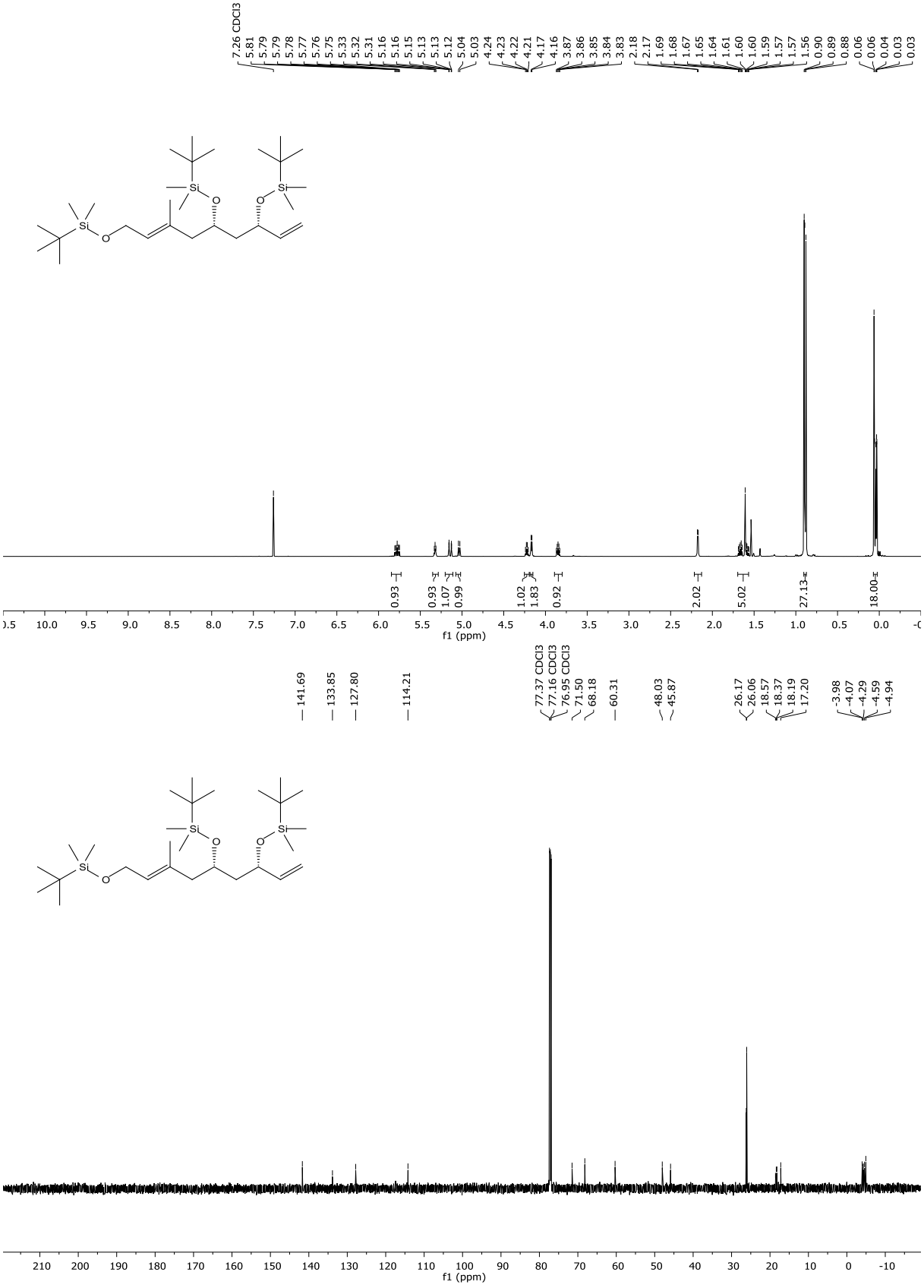




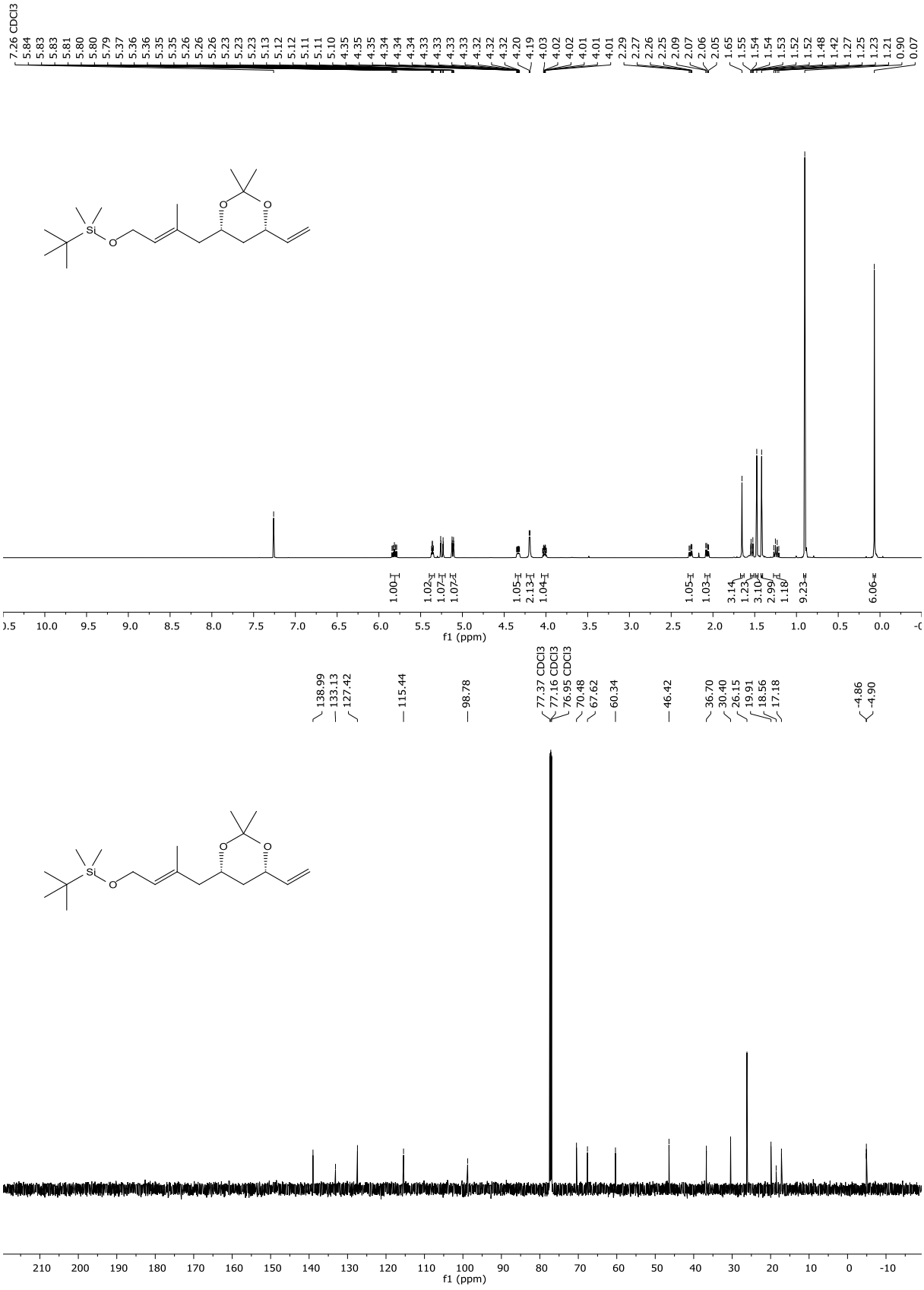
^{1}H and ^{13}C spectra of compound 26



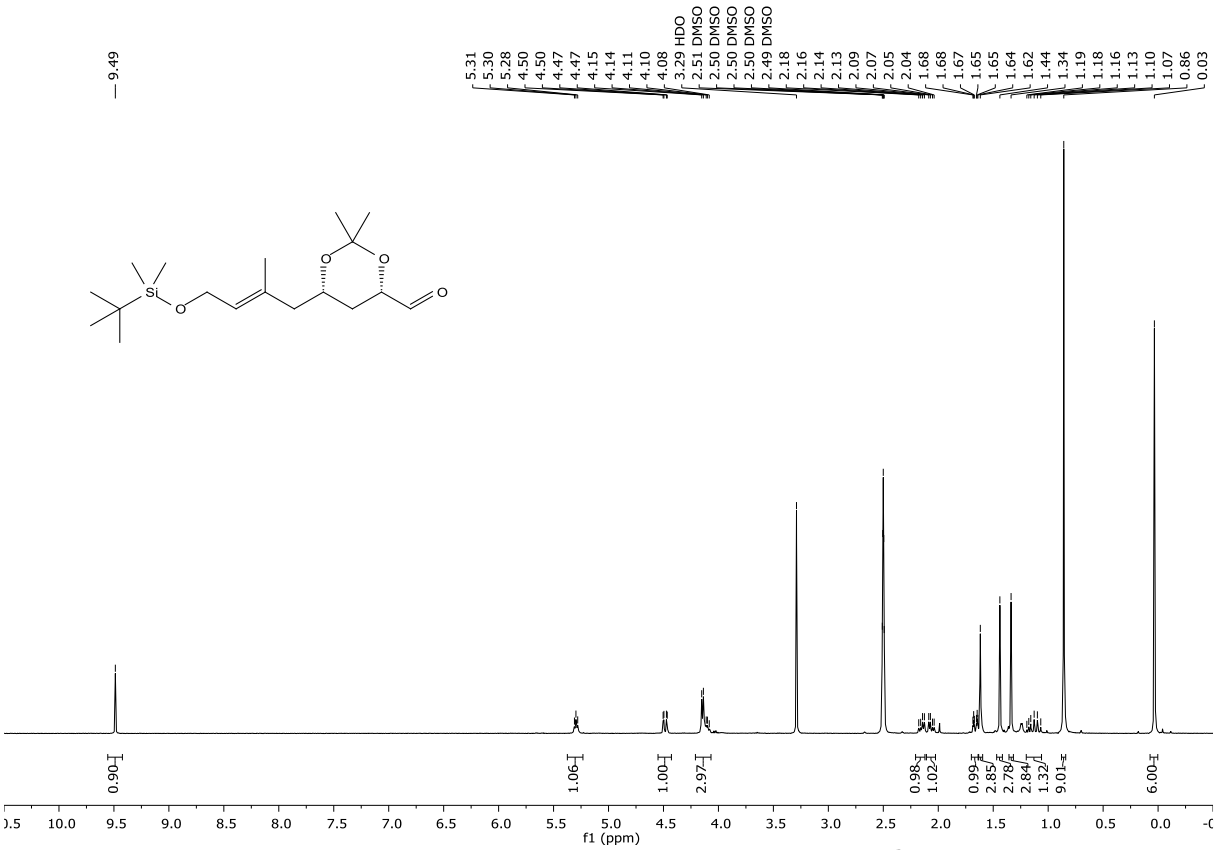
^{1}H and ^{13}C spectra of compound 27

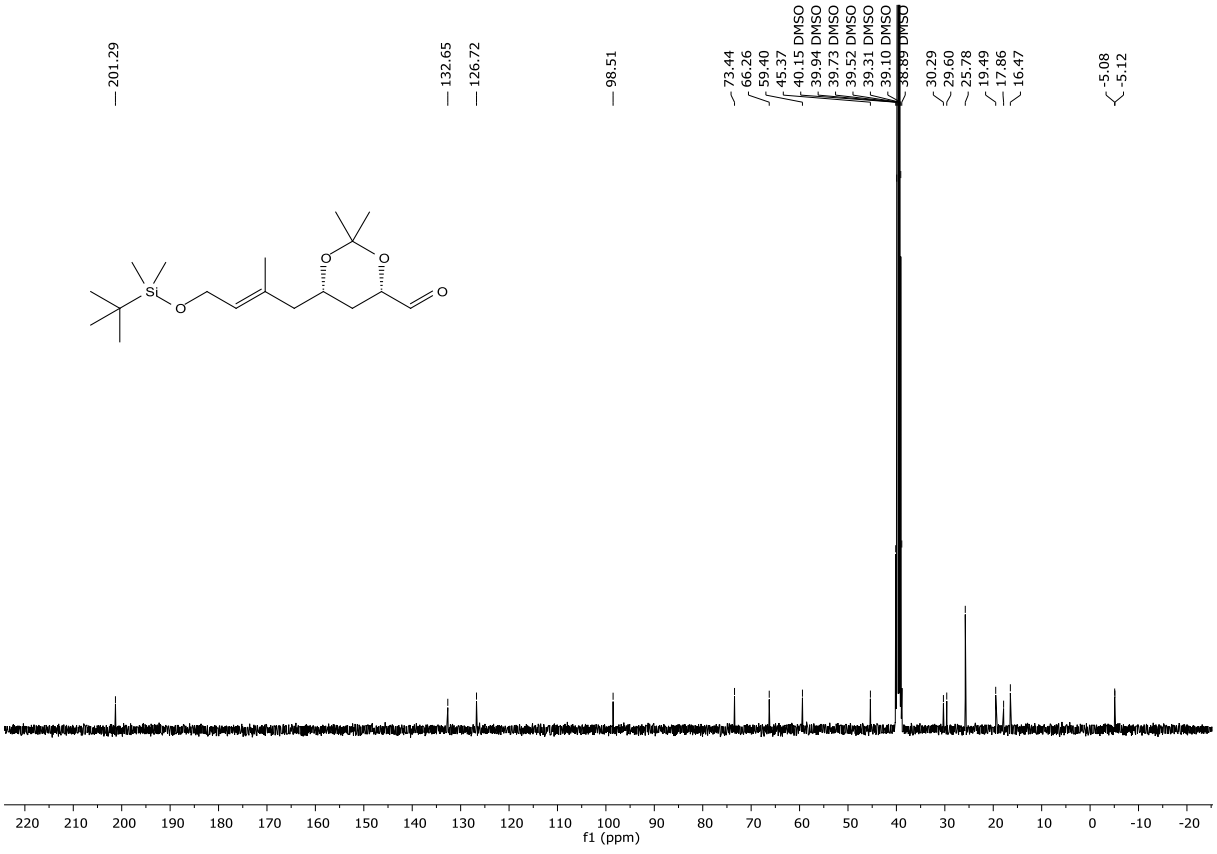


^{1}H and ^{13}C spectra of compound 28

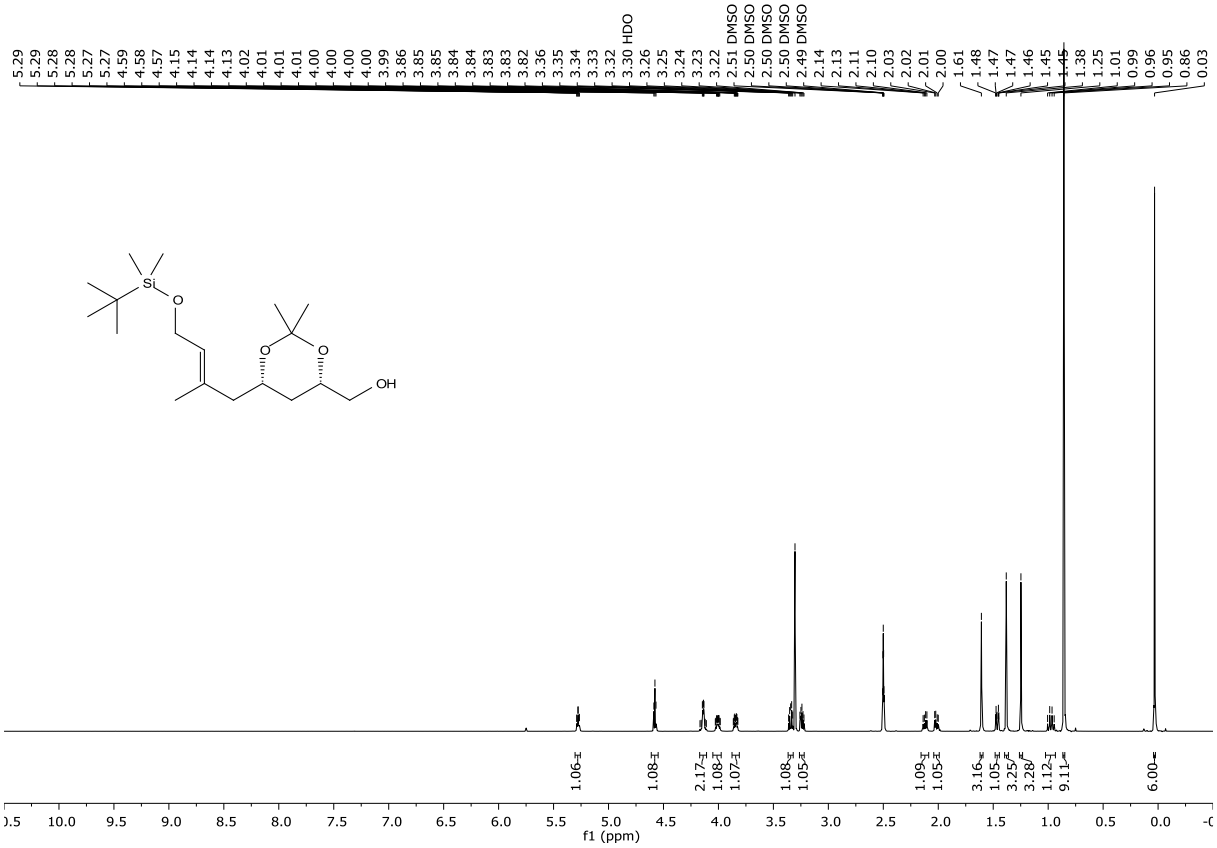


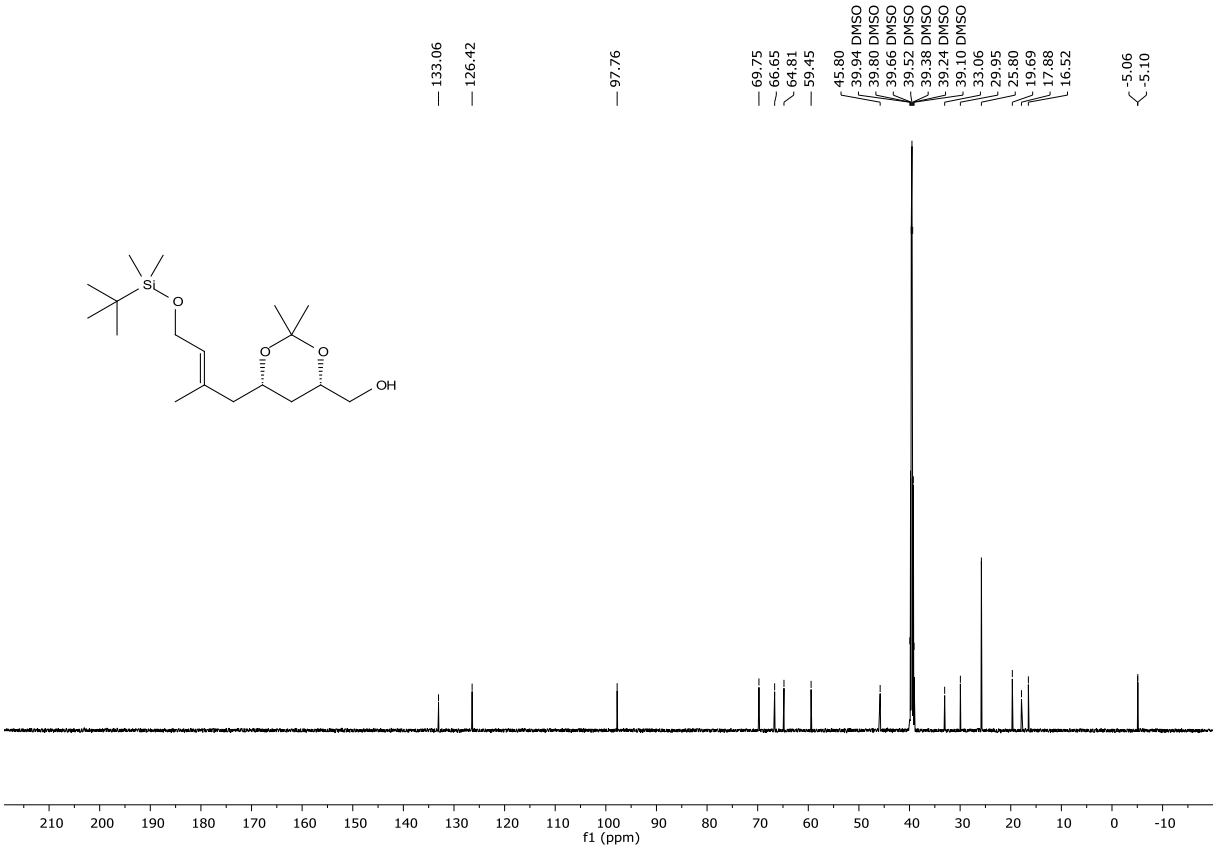
^{1}H and ^{13}C spectra of compound 30



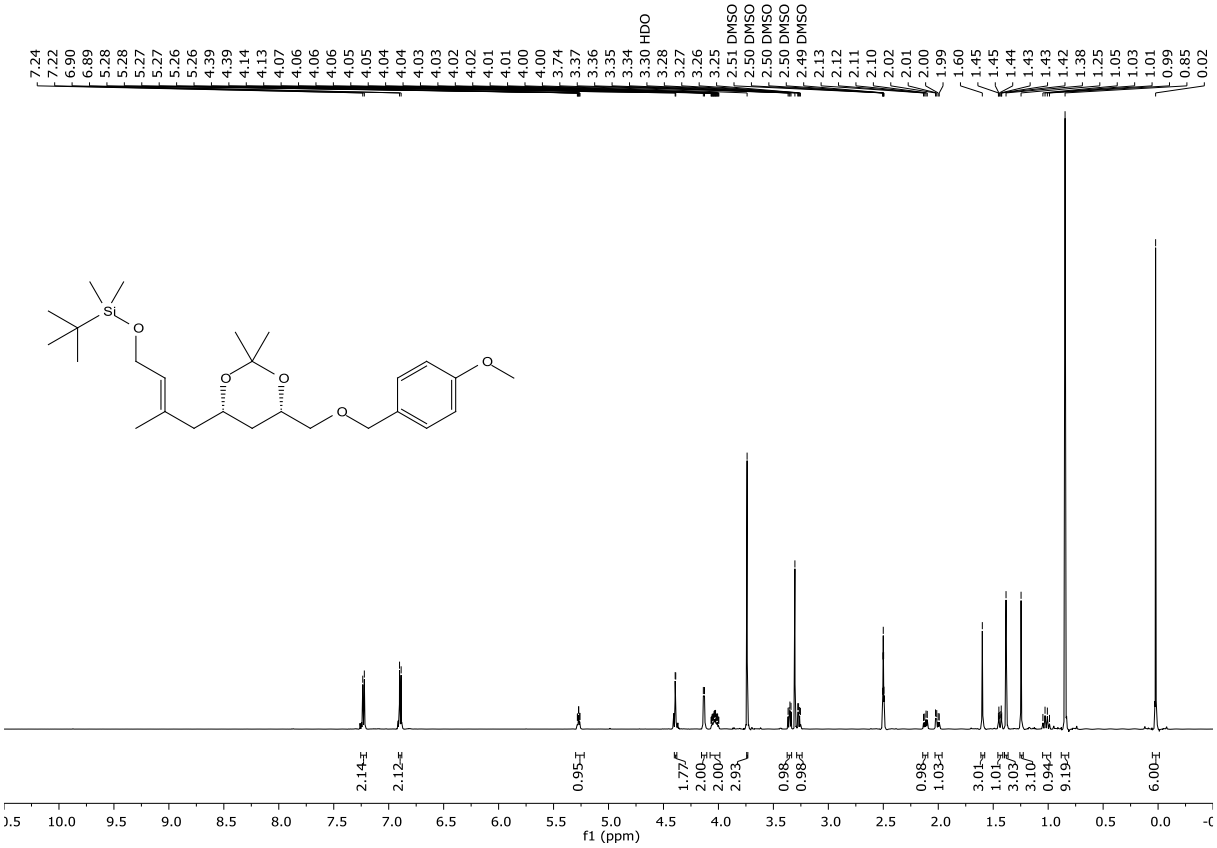


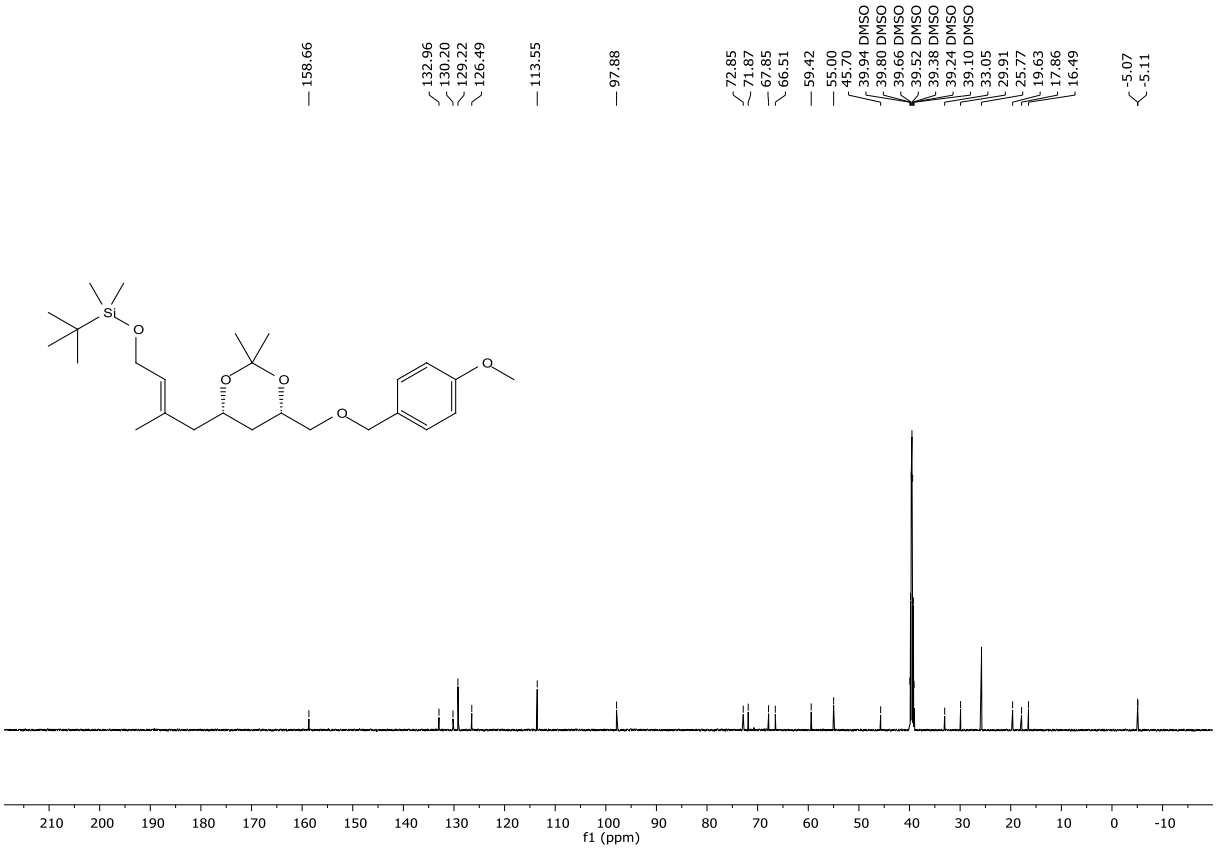
^{1}H and ^{13}C spectra of compound 31





^{1}H and ^{13}C spectra of compound 32





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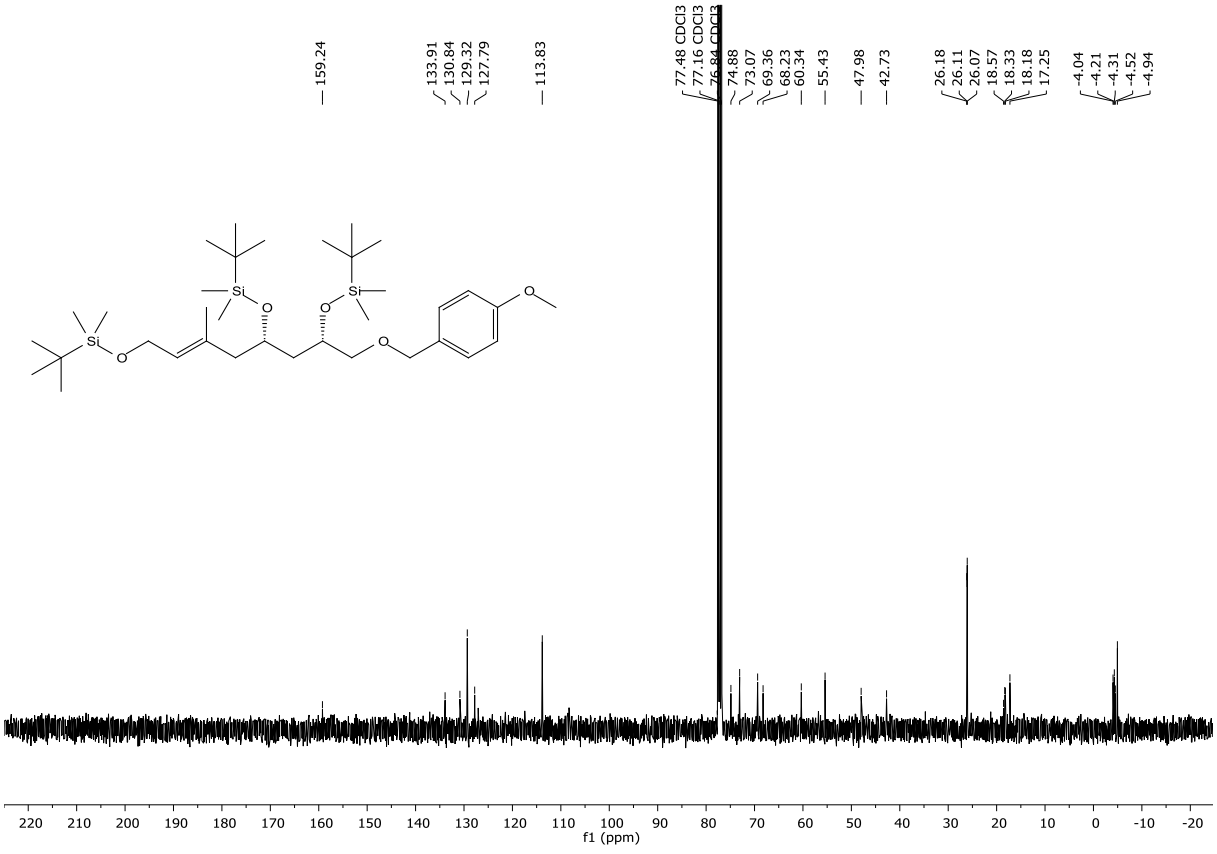
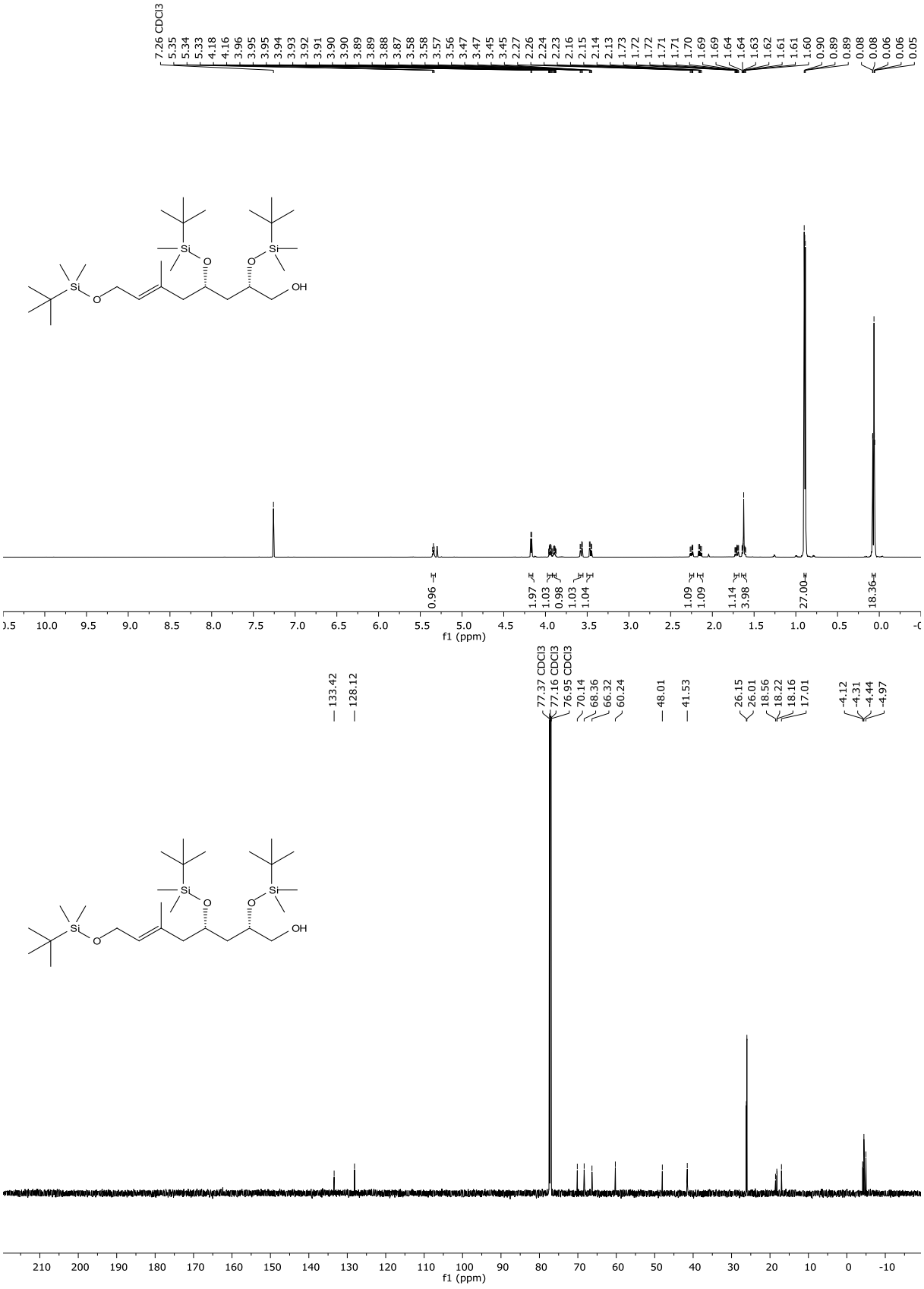
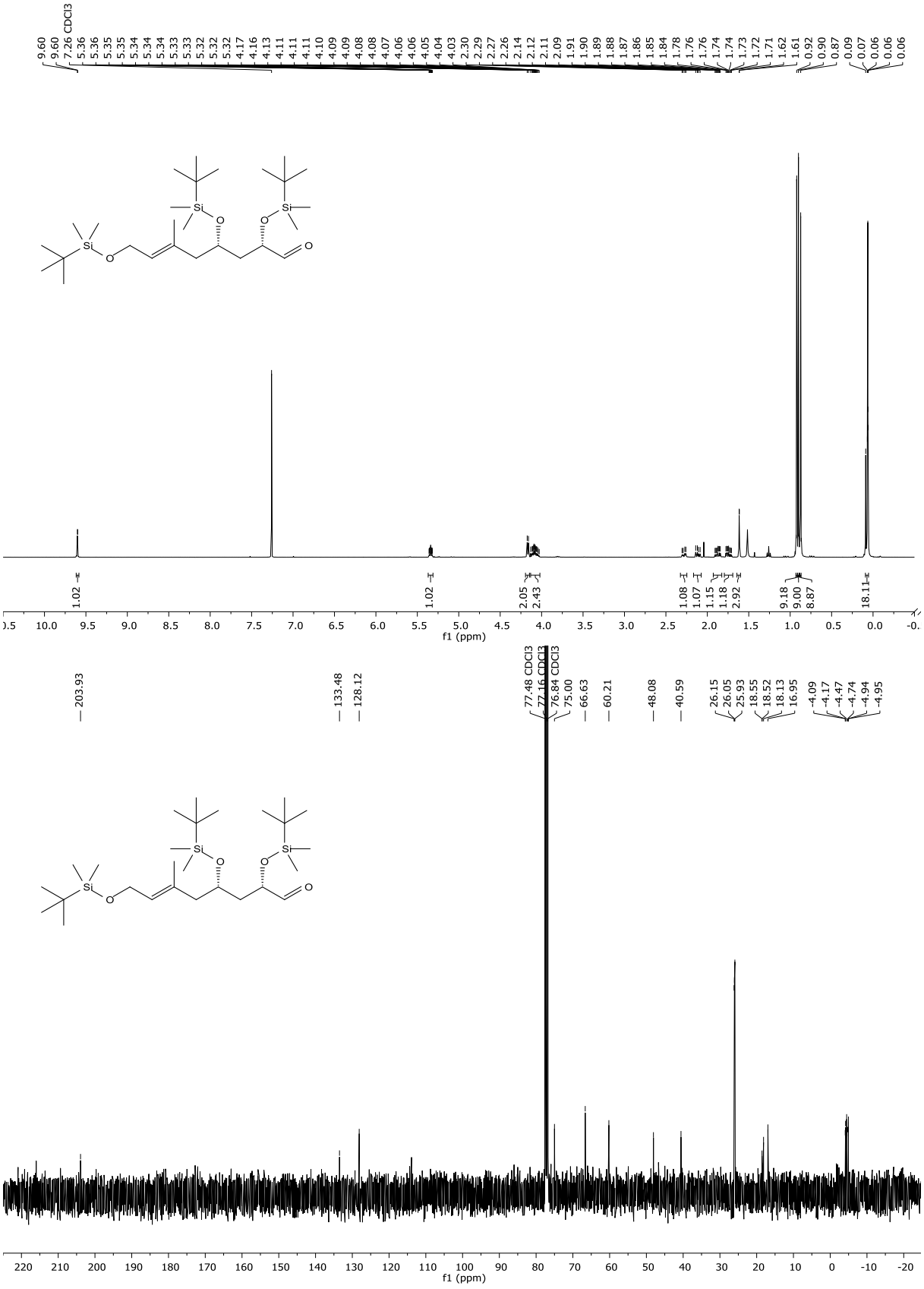


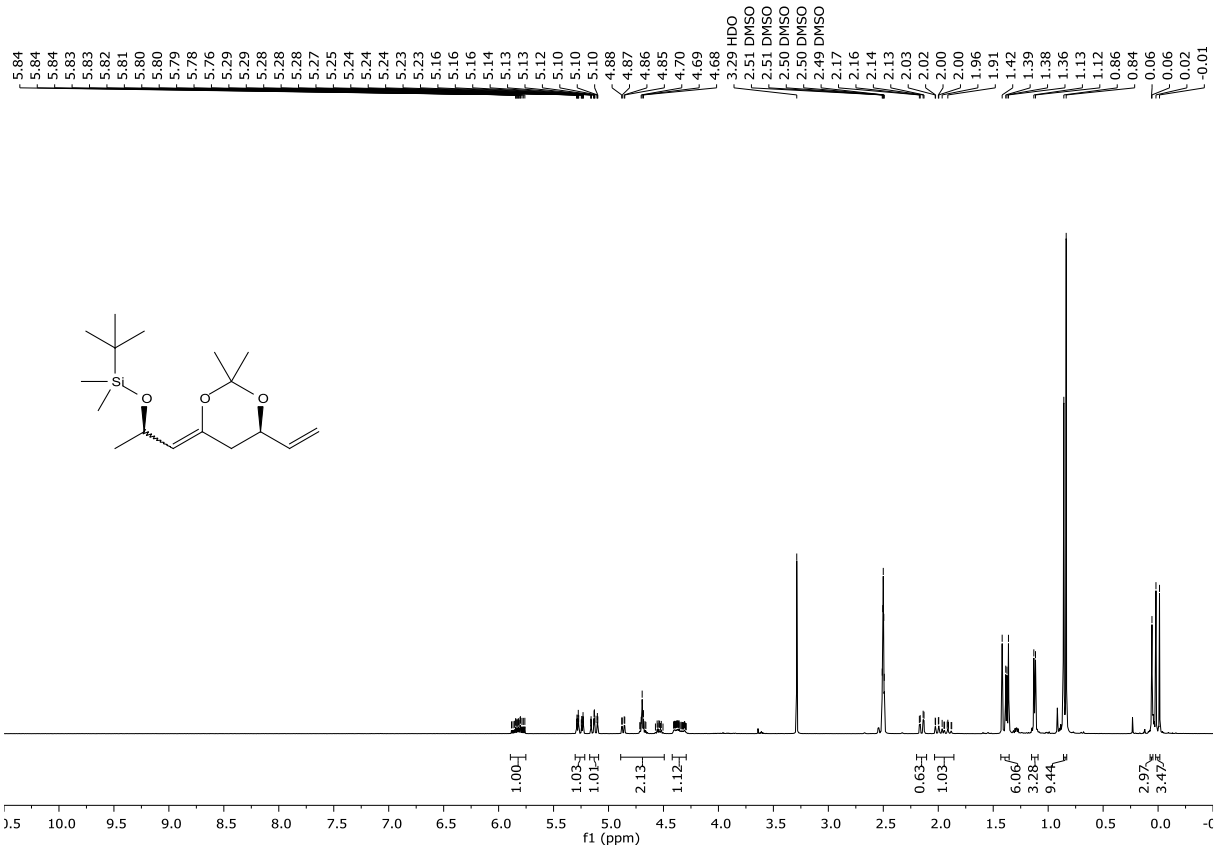
^{1}H and ^{13}C spectra of compound 34



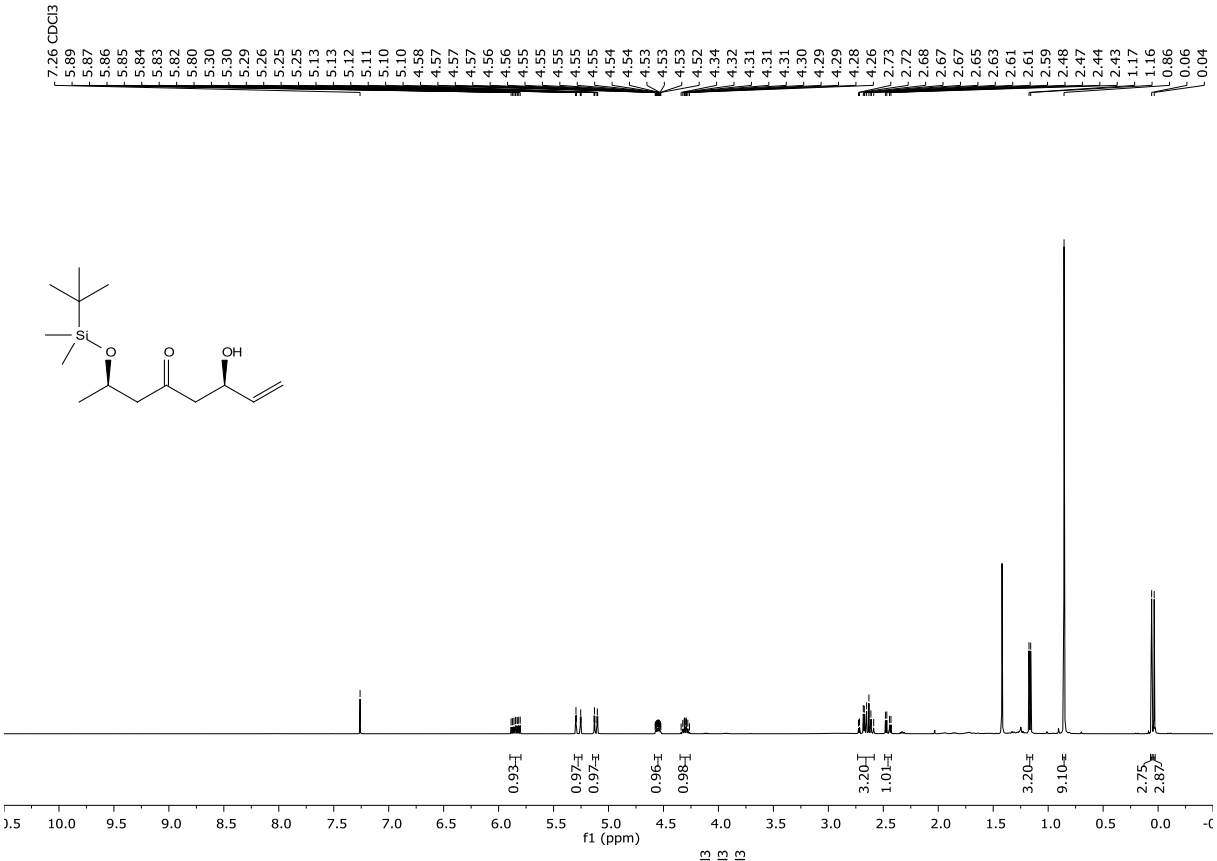
^{1}H and ^{13}C spectra of compound 7

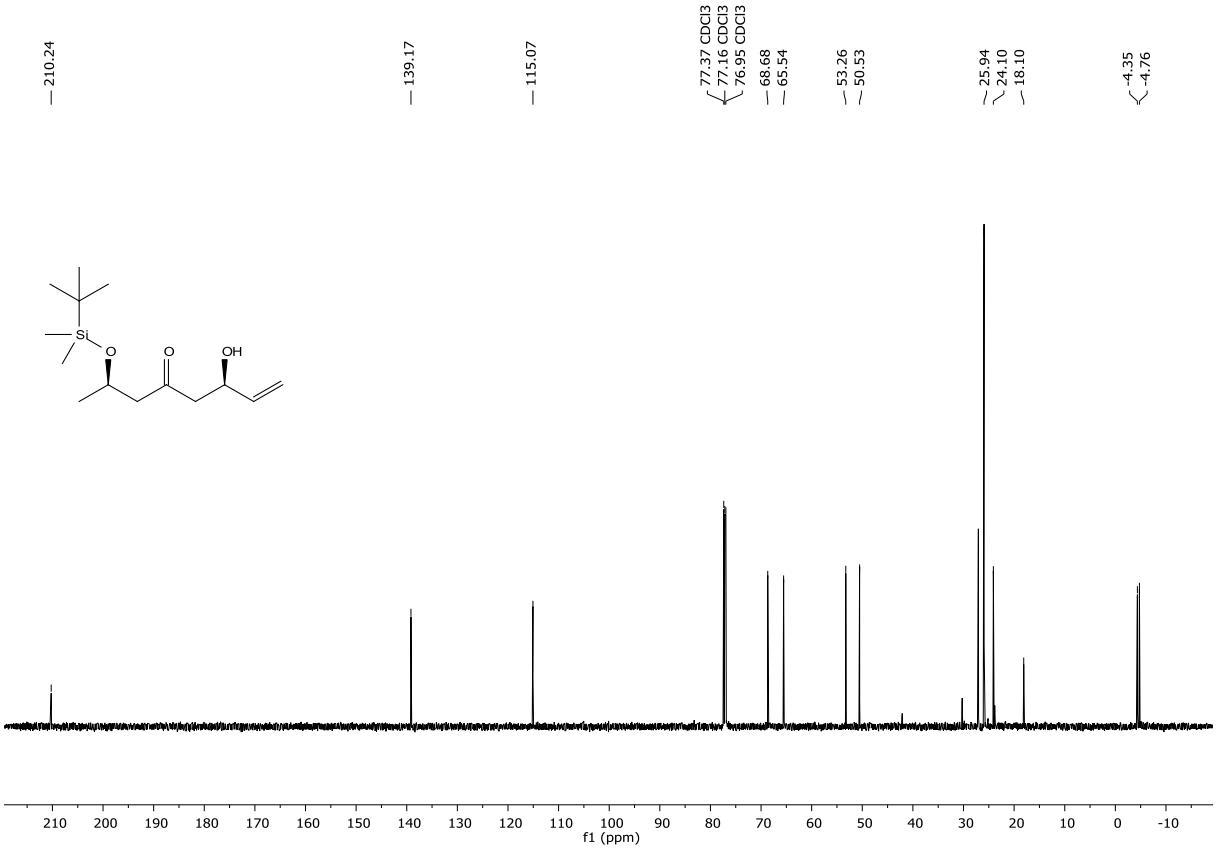


^{1}H spectrum of compound 37

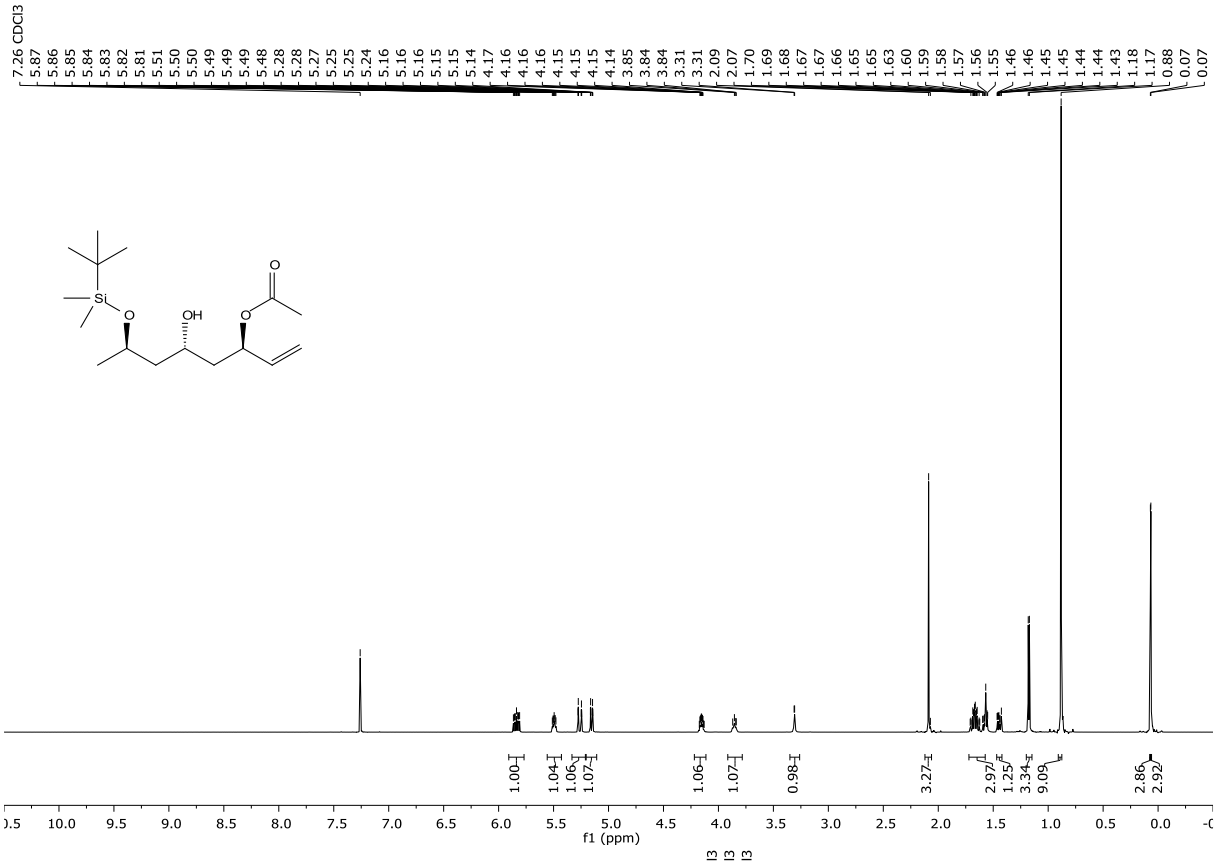


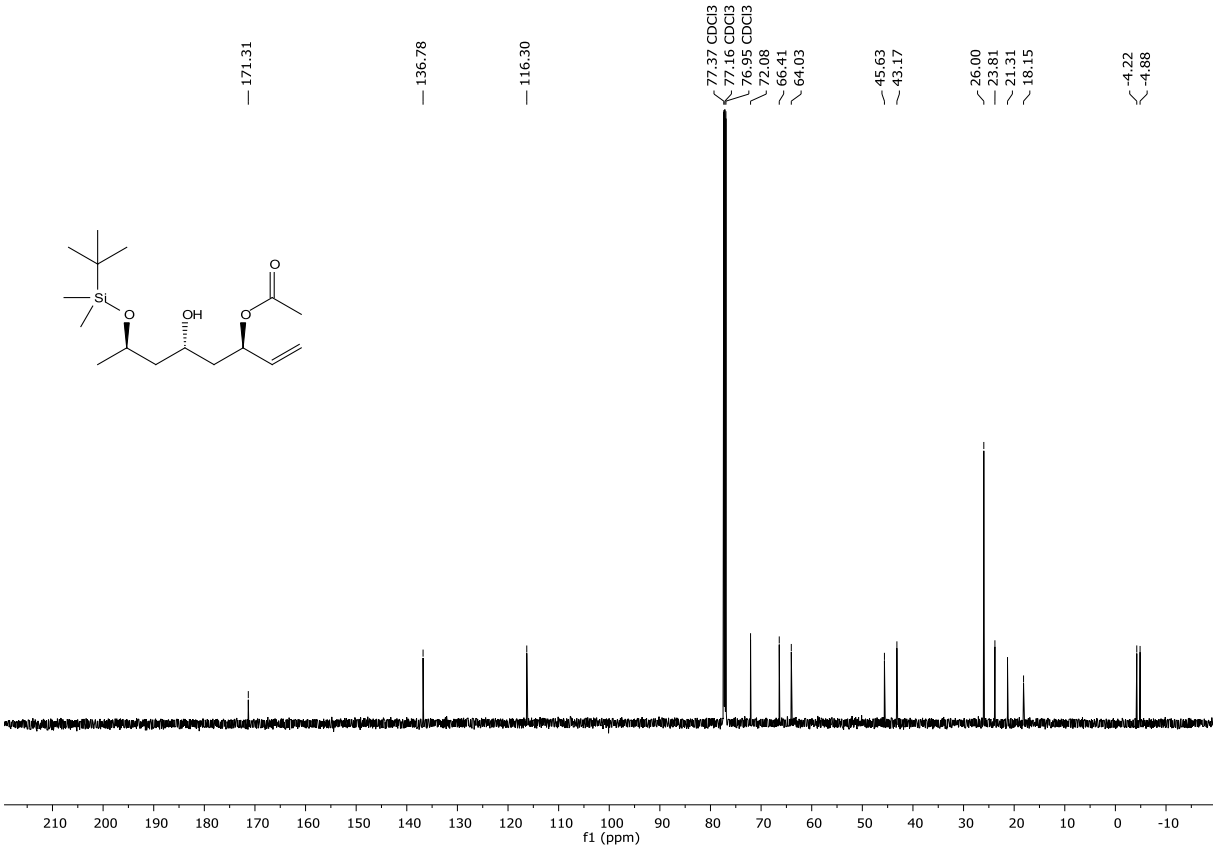
^{1}H and ^{13}C spectra of compound 38



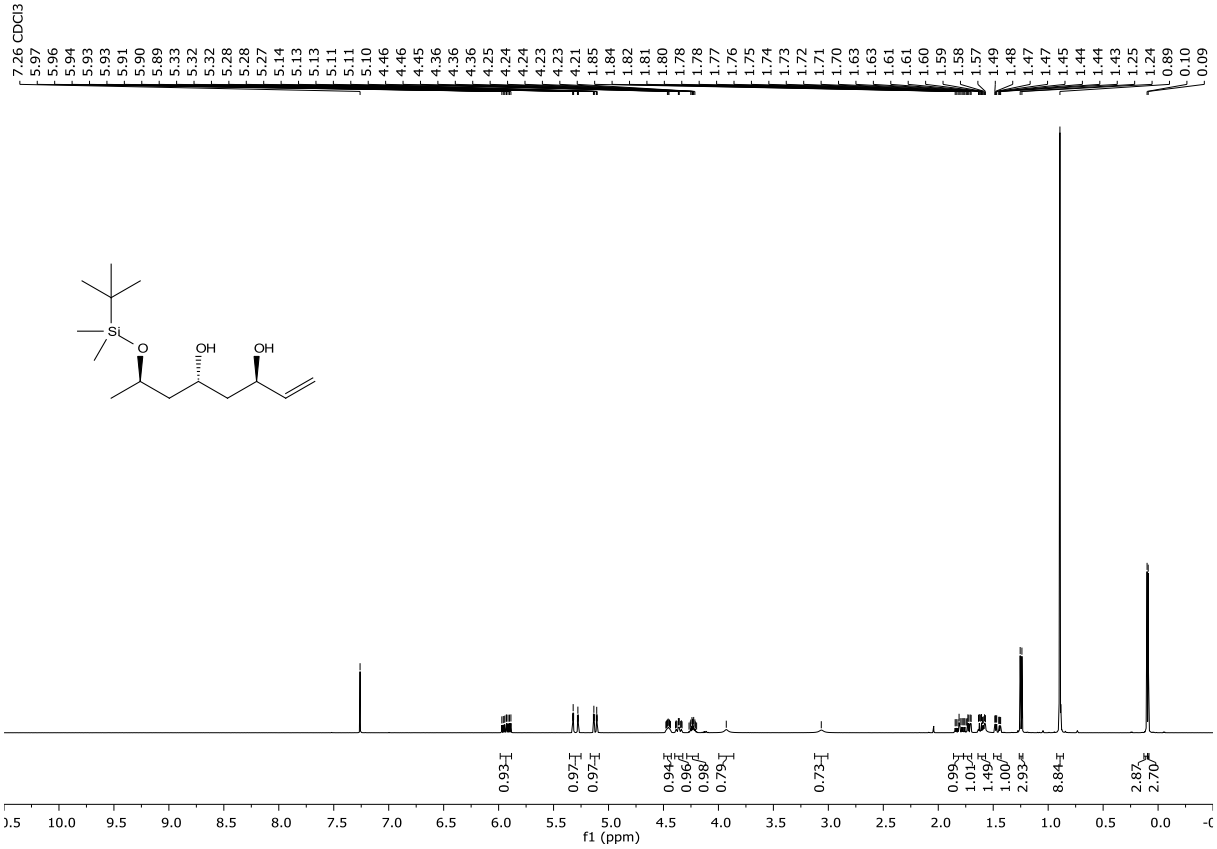


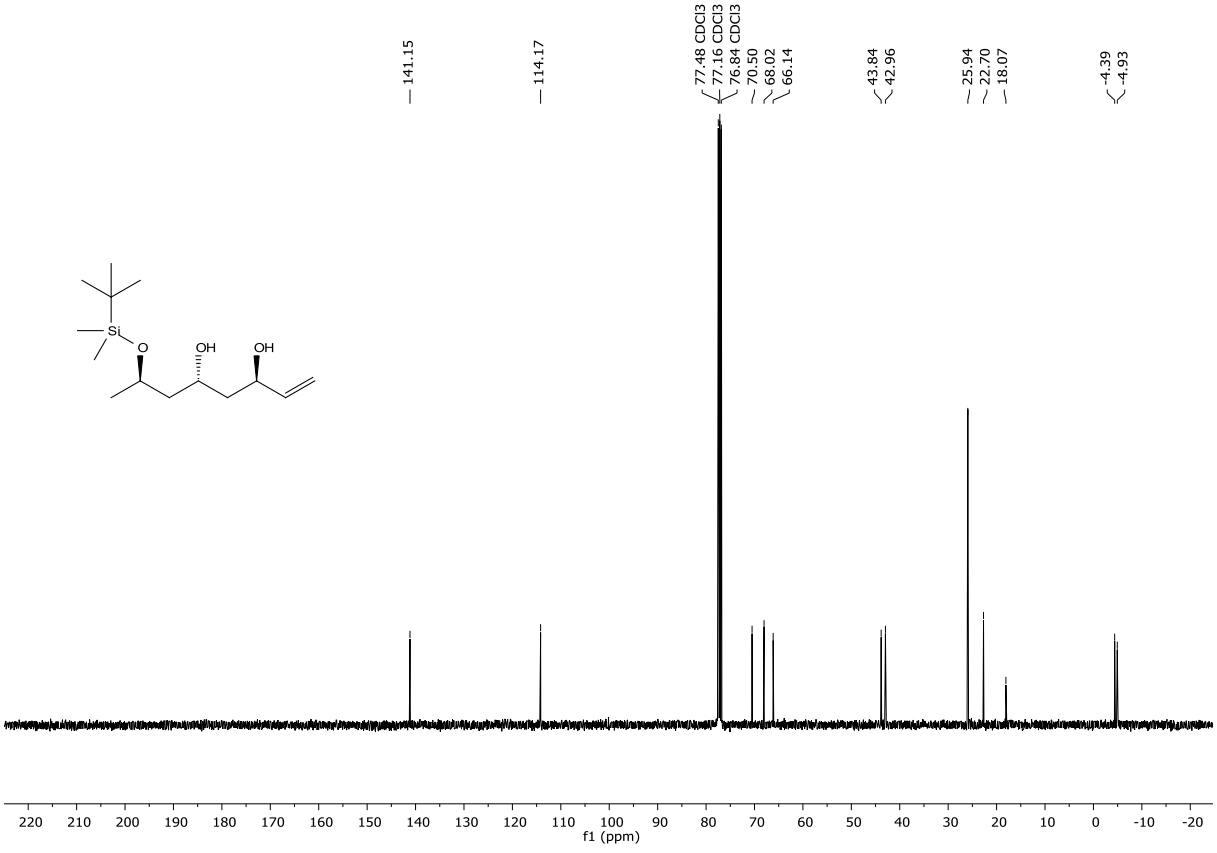
^{1}H and ^{13}C spectra of compound 39



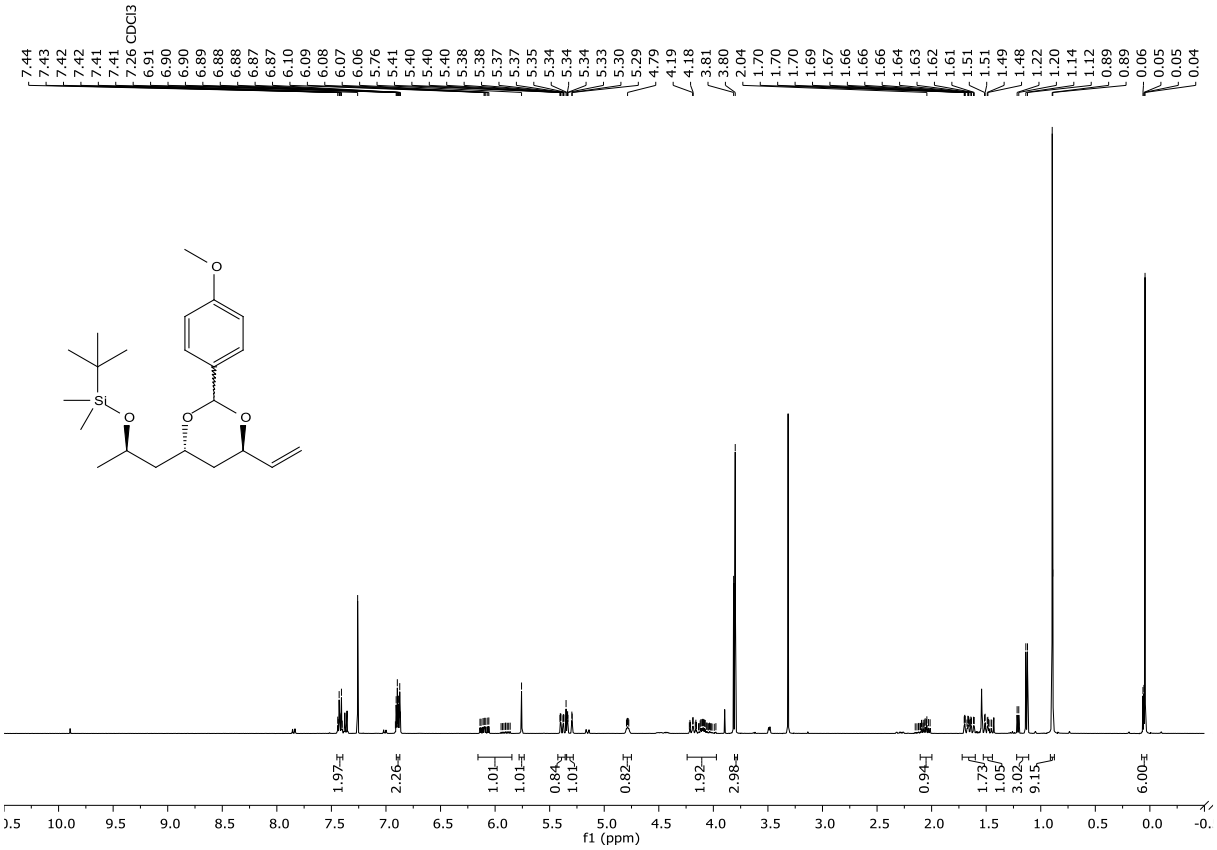


^{1}H and ^{13}C spectra of compound 40

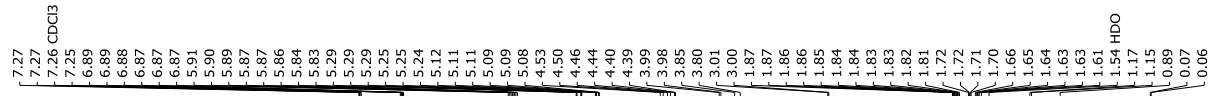


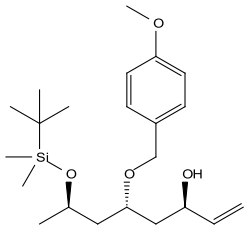


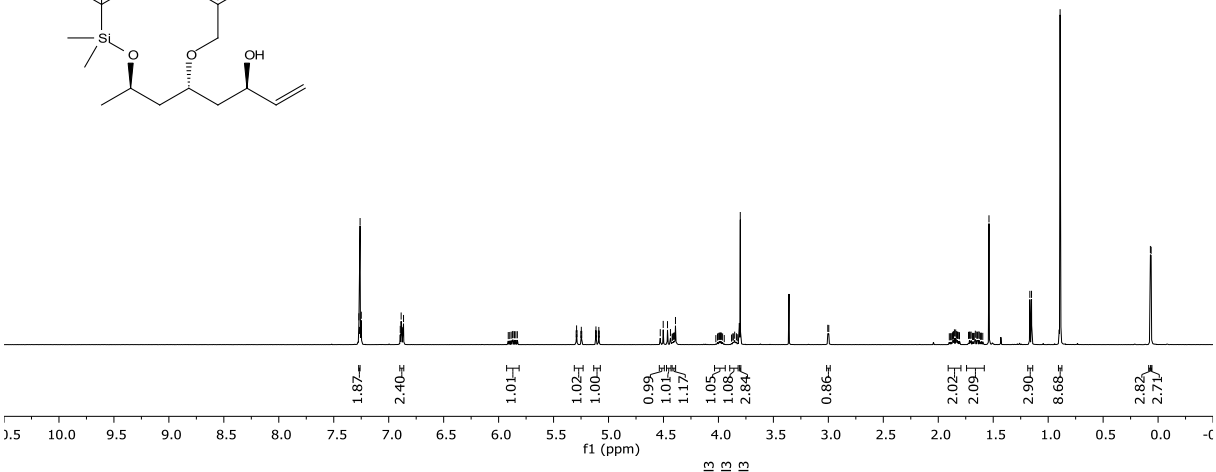
^{1}H spectrum of compound 41

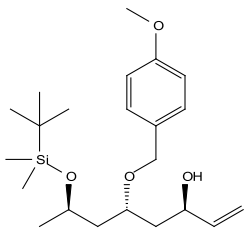


^{1}H and ^{13}C spectra of compound 42

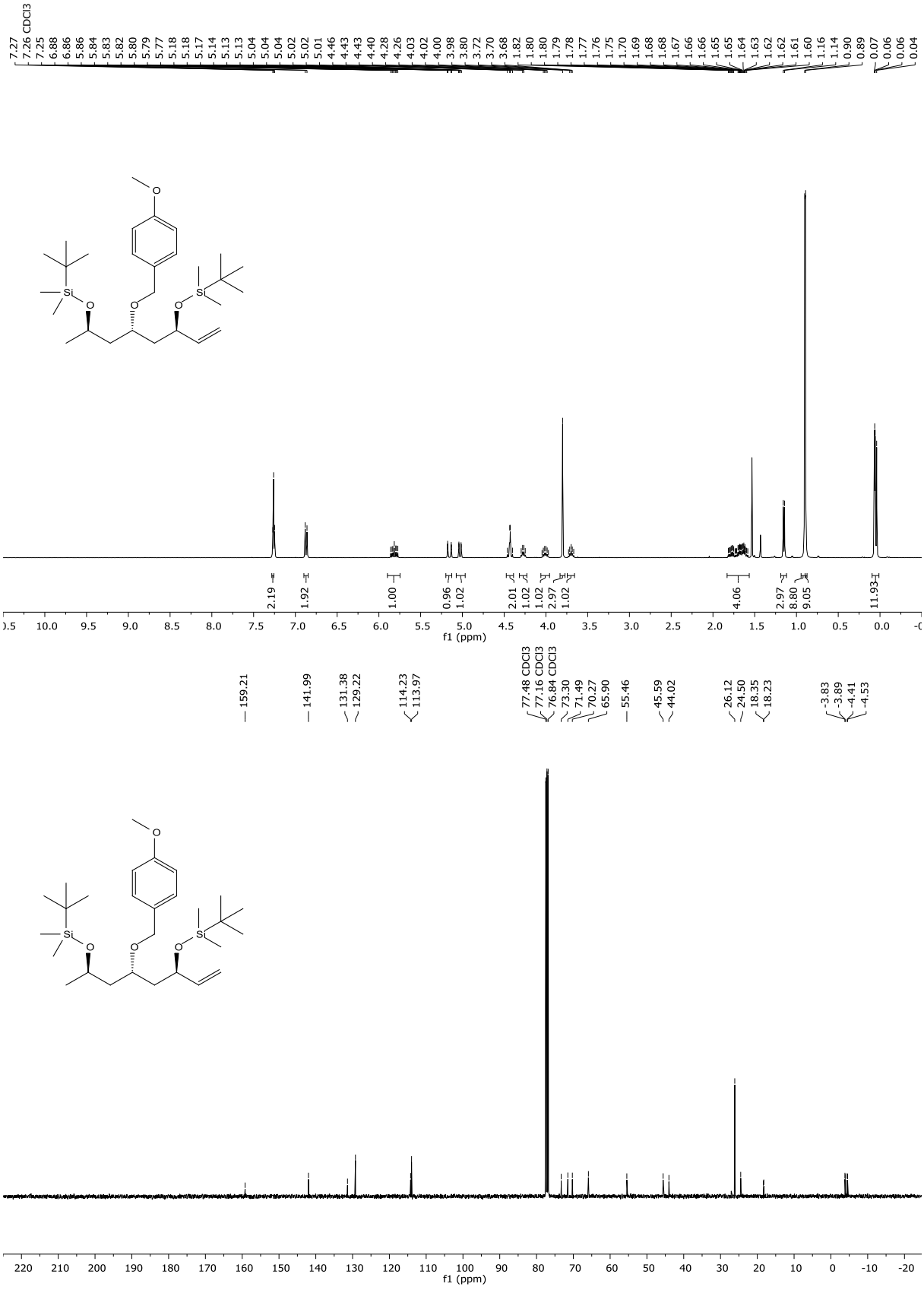




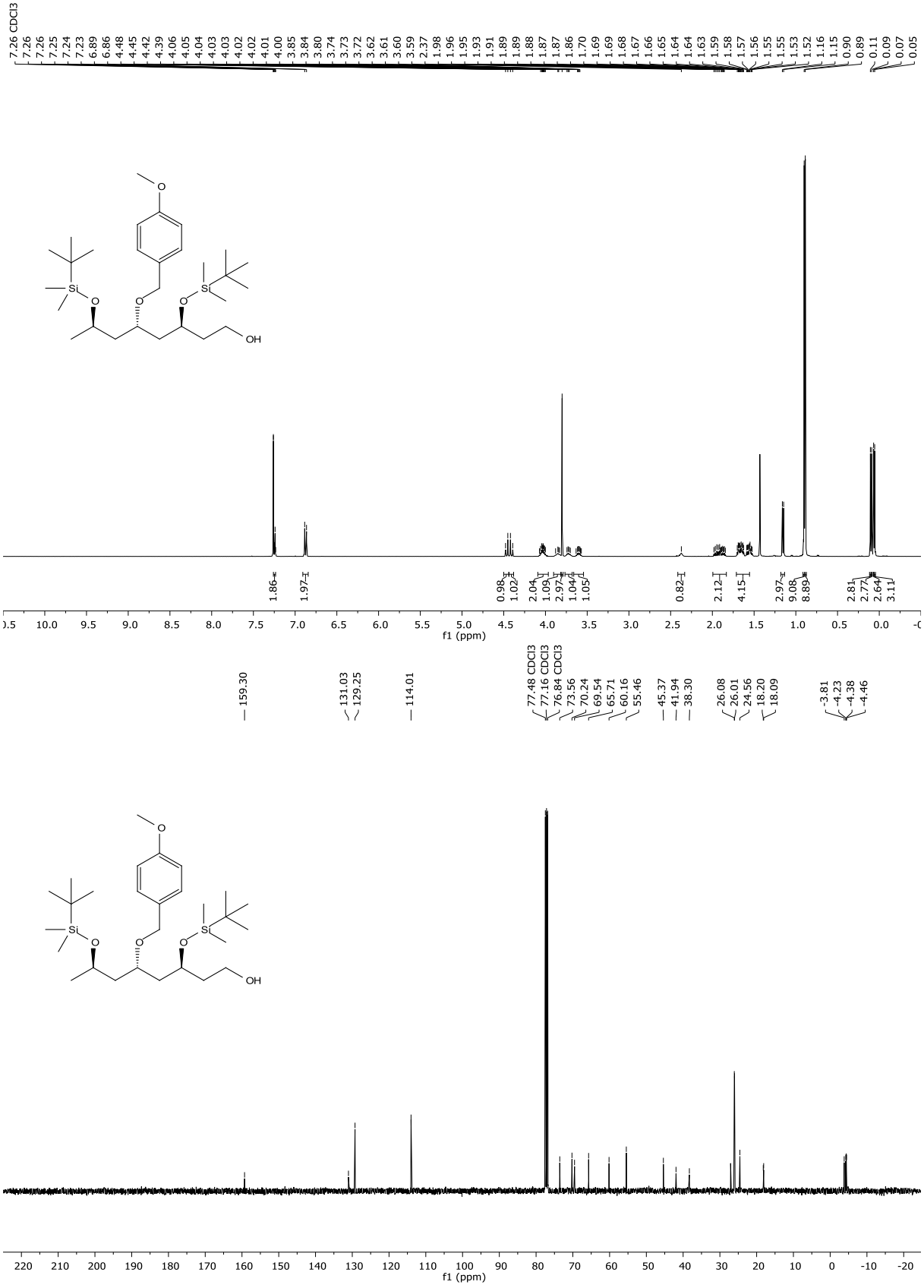




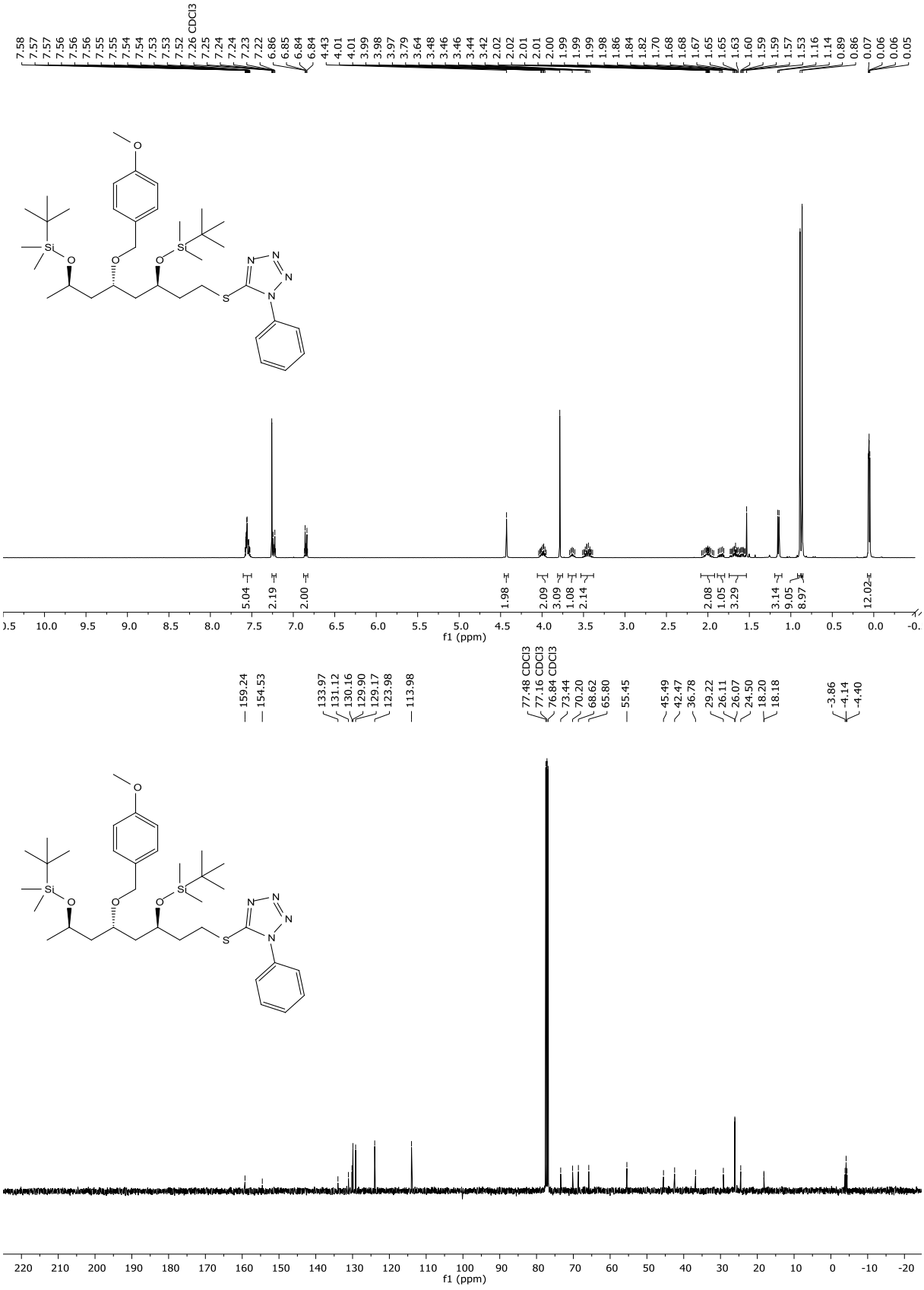
^{1}H and ^{13}C spectra of compound 43



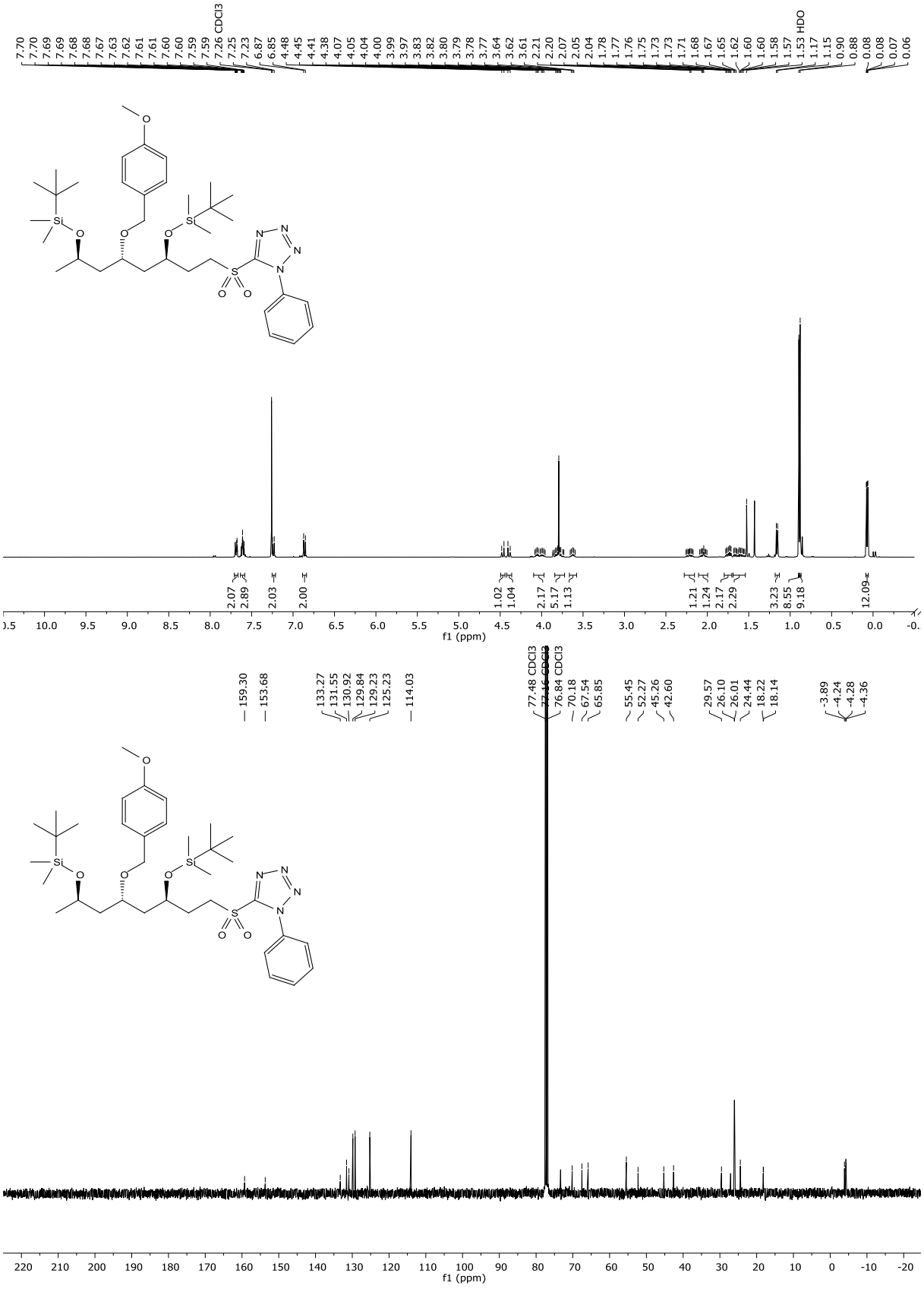
^{1}H and ^{13}C spectra of compound 44



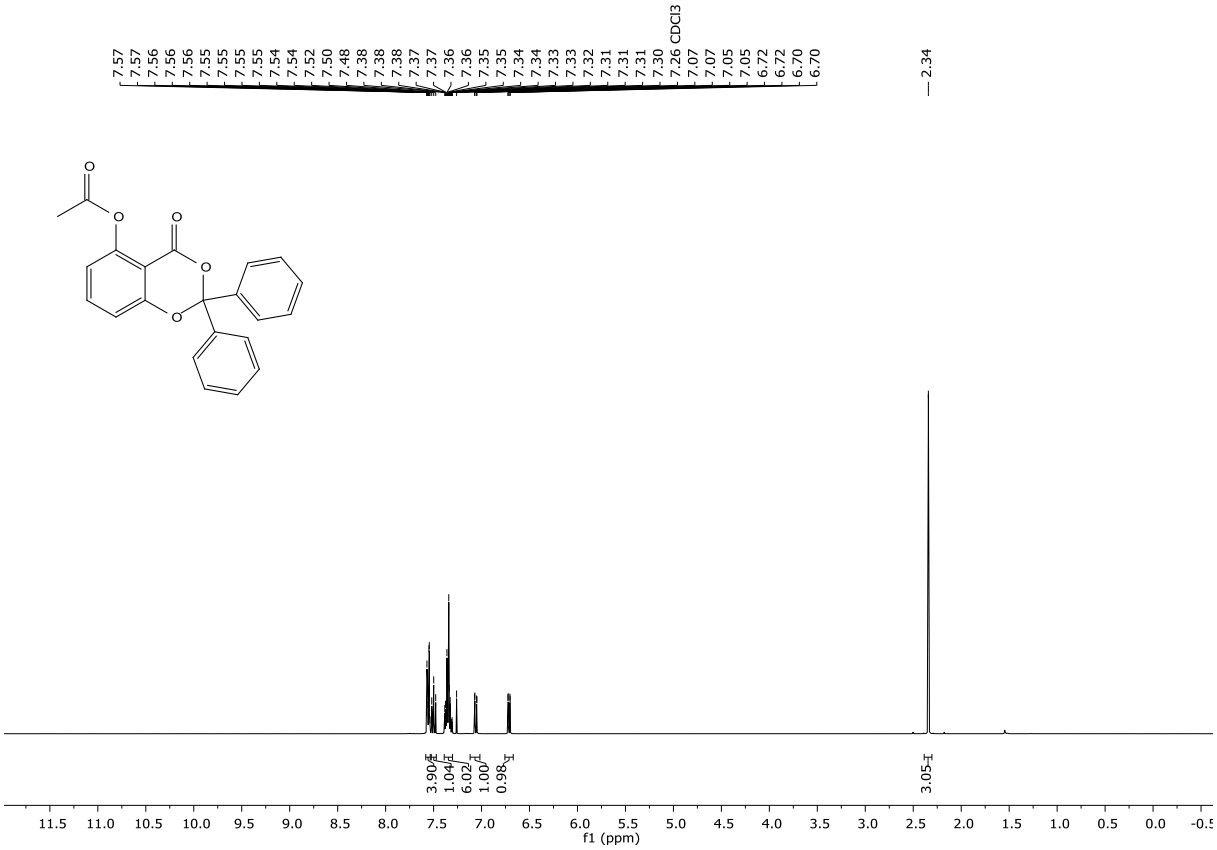
^{1}H and ^{13}C spectra of compound 45

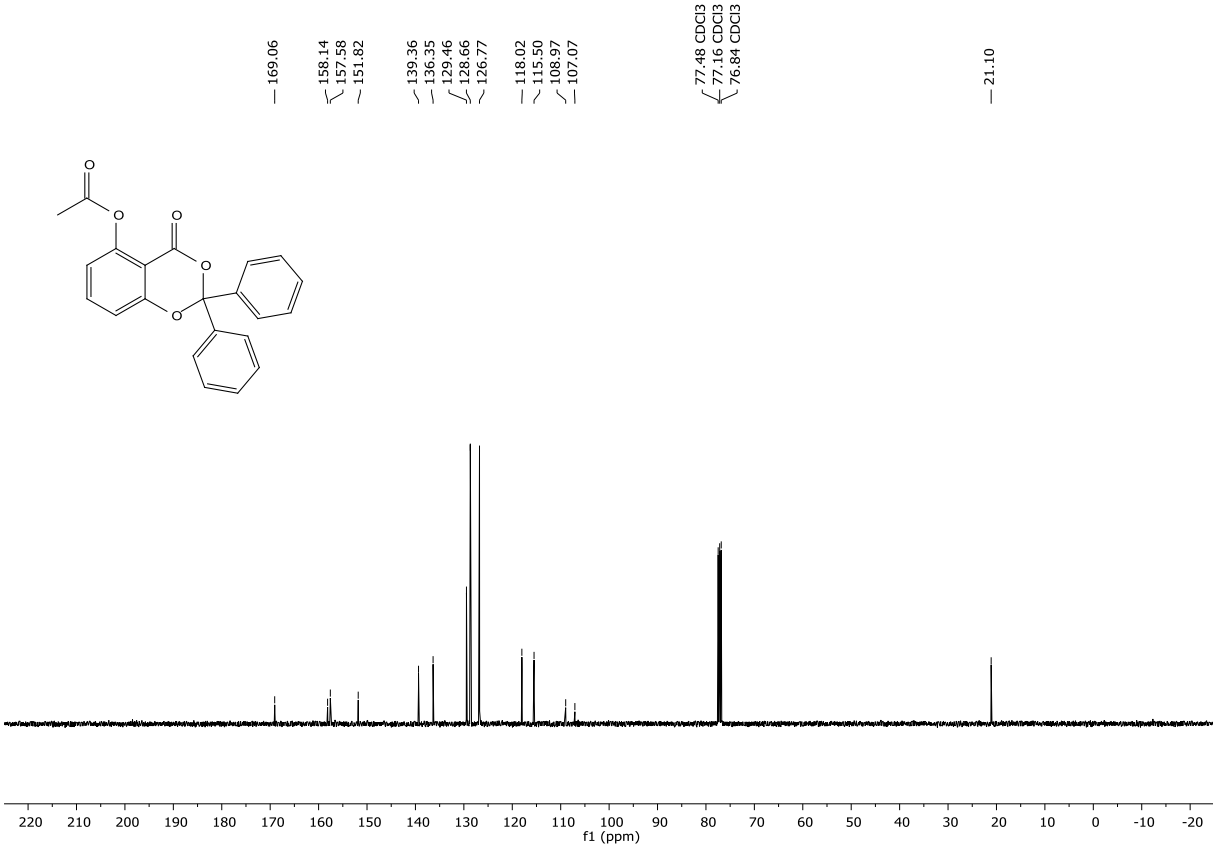


^{1}H and ^{13}C spectra of compound 8

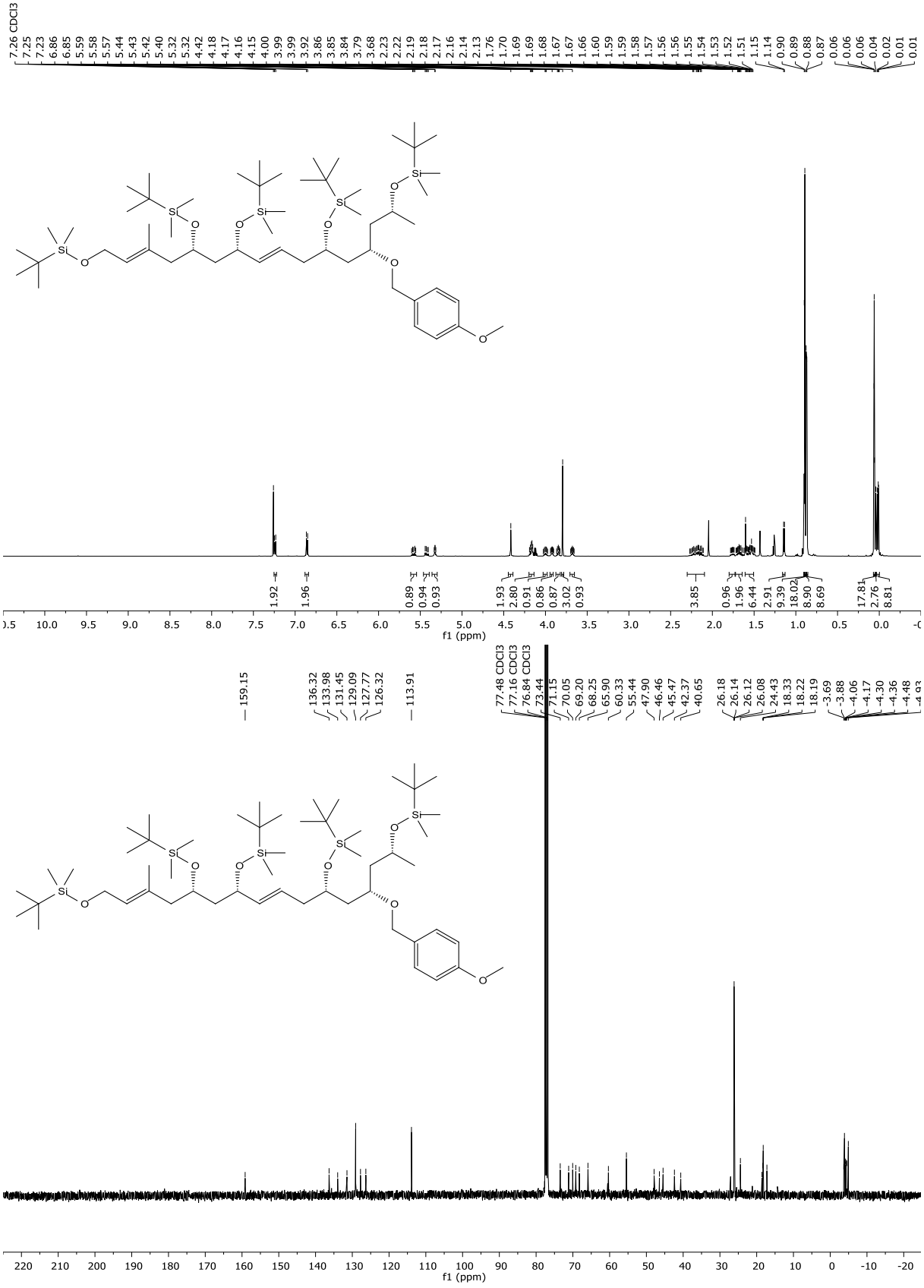


^{1}H and ^{13}C spectra of compound 9

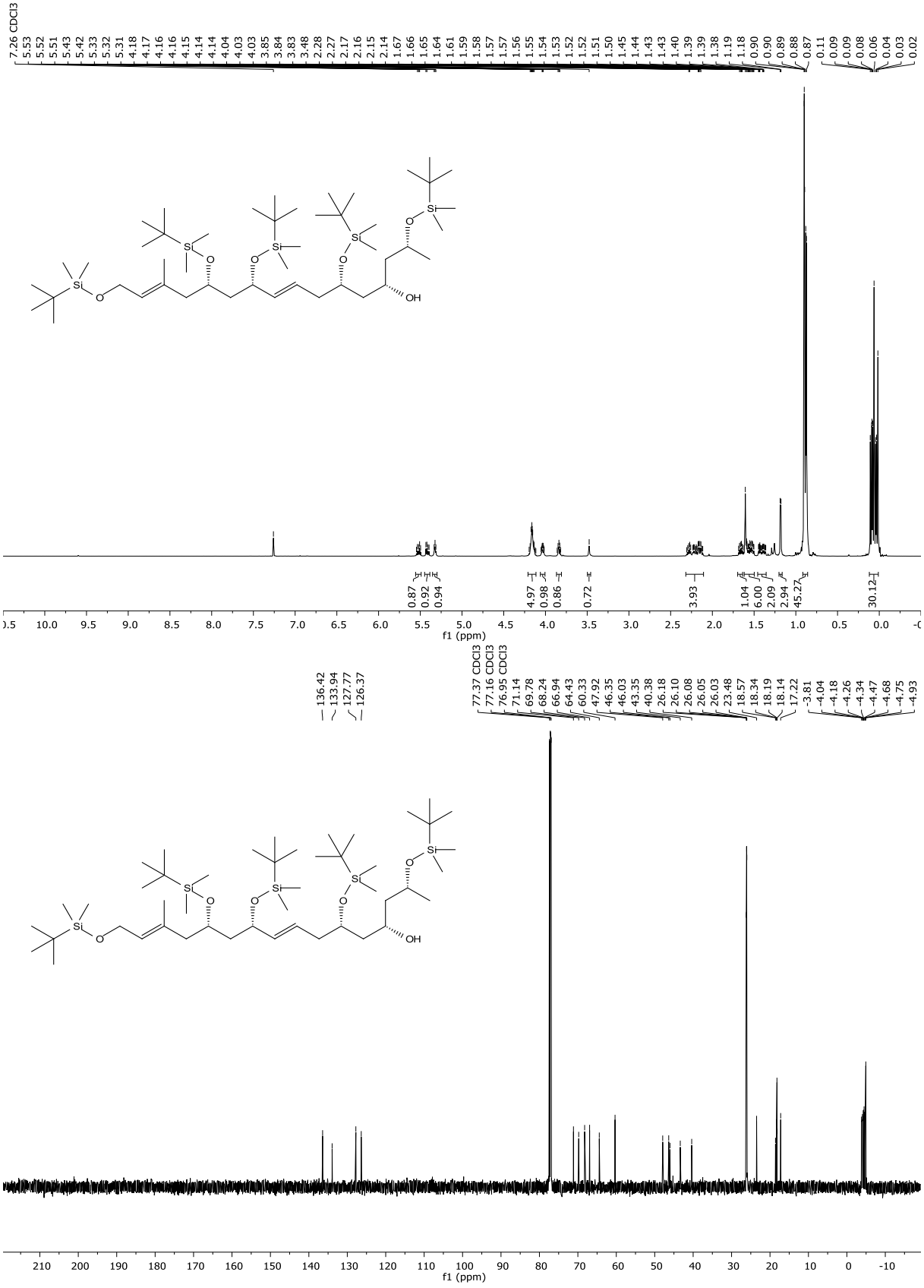




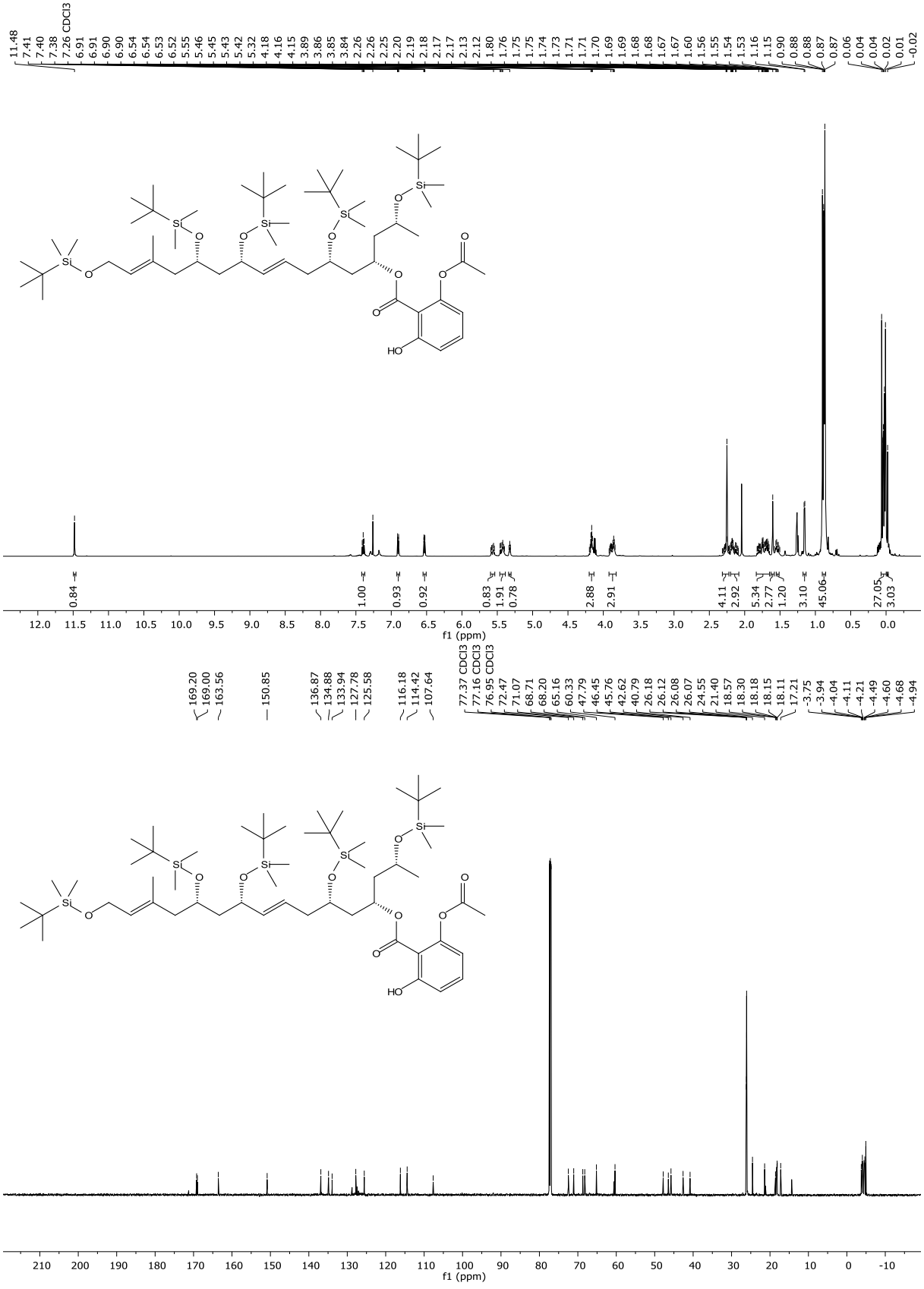
^{1}H and ^{13}C spectra of compound 46



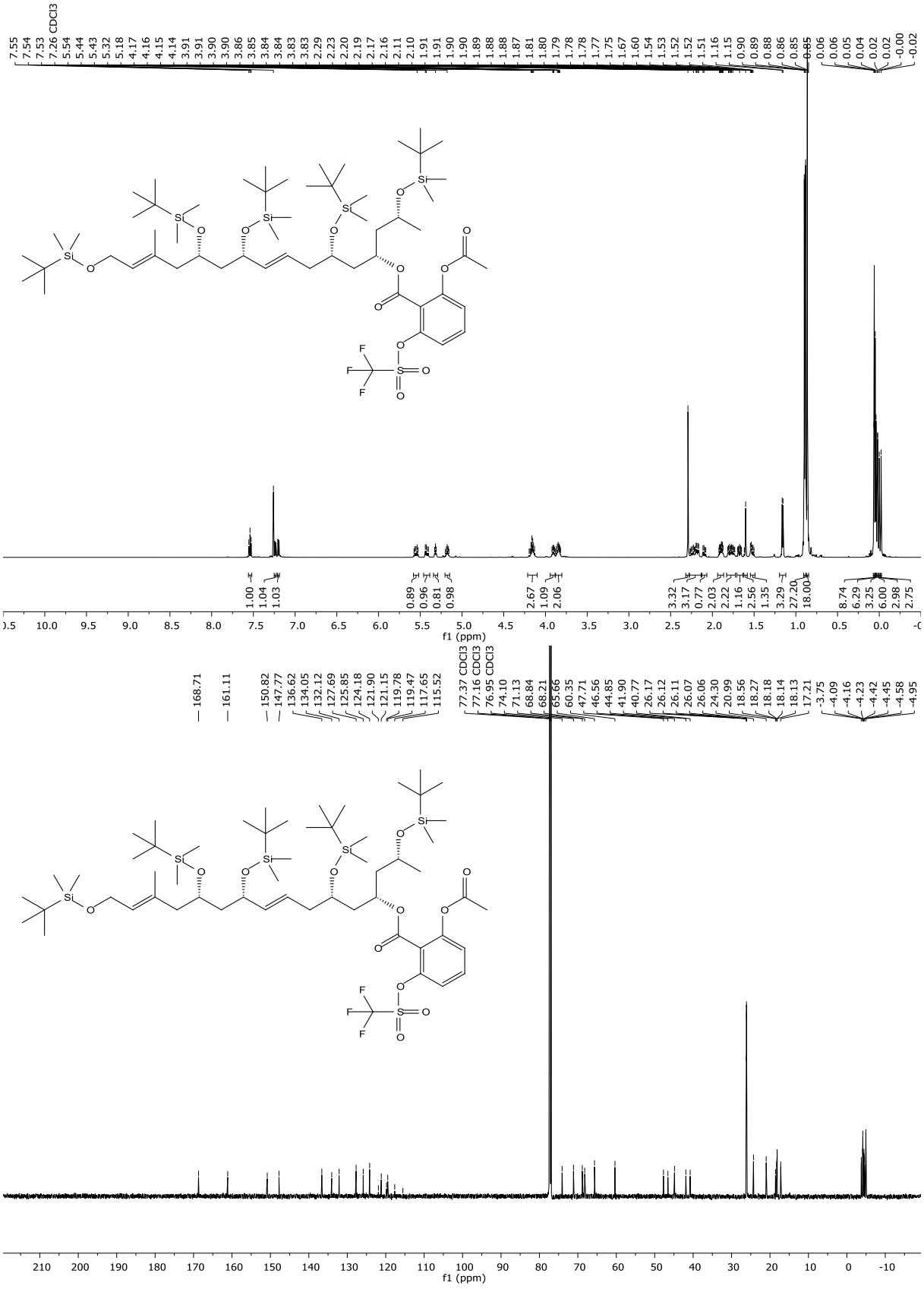
^{1}H and ^{13}C spectra of compound 47



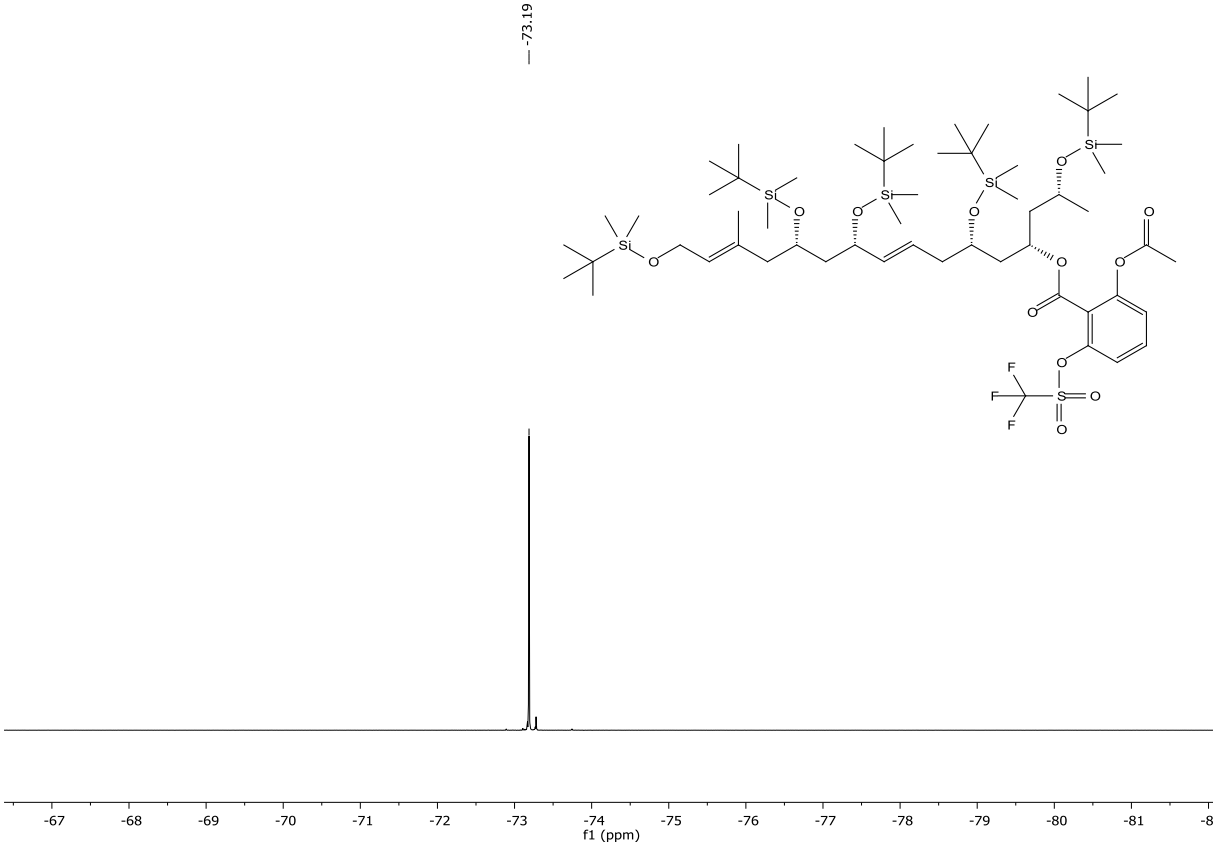
^{1}H and ^{13}C spectra of compound 49



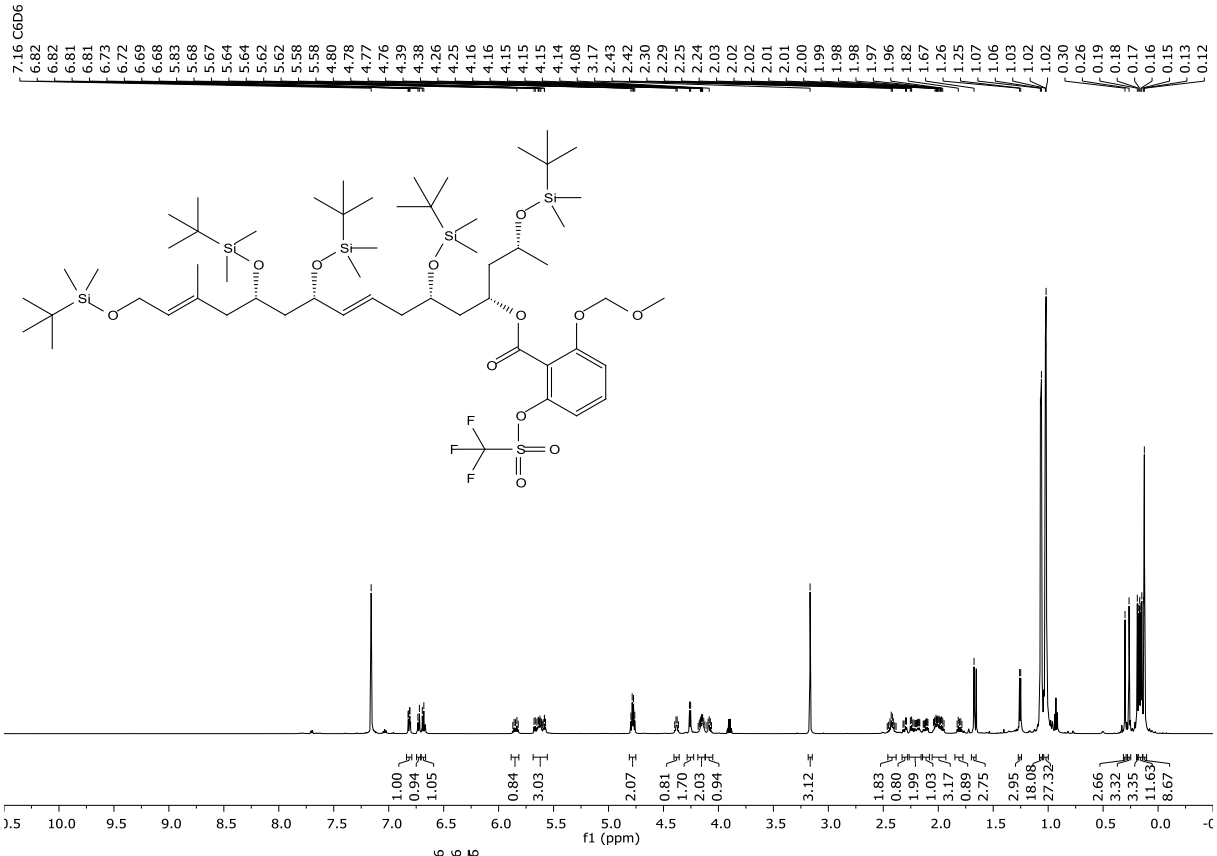
^{1}H and ^{13}C spectra of compound 49a

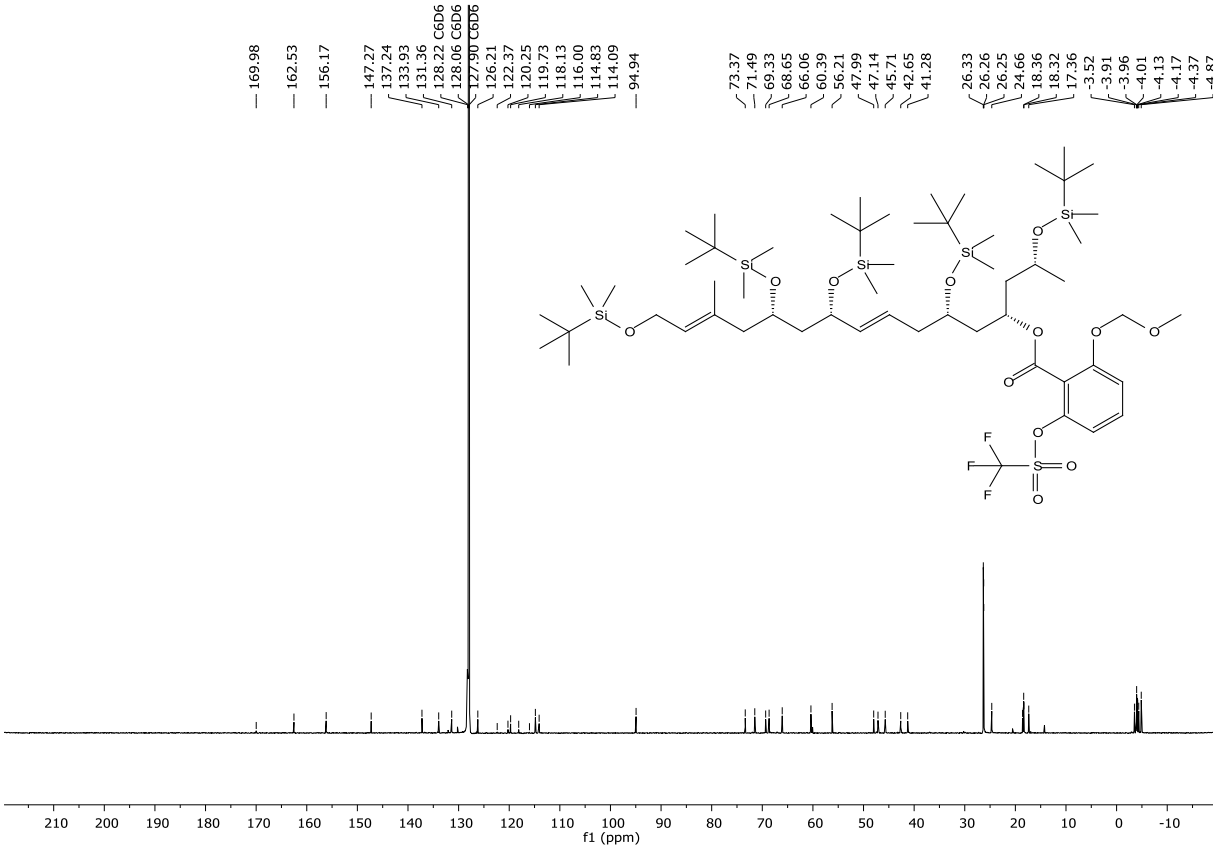


^{19}F spectrum of compound 49a

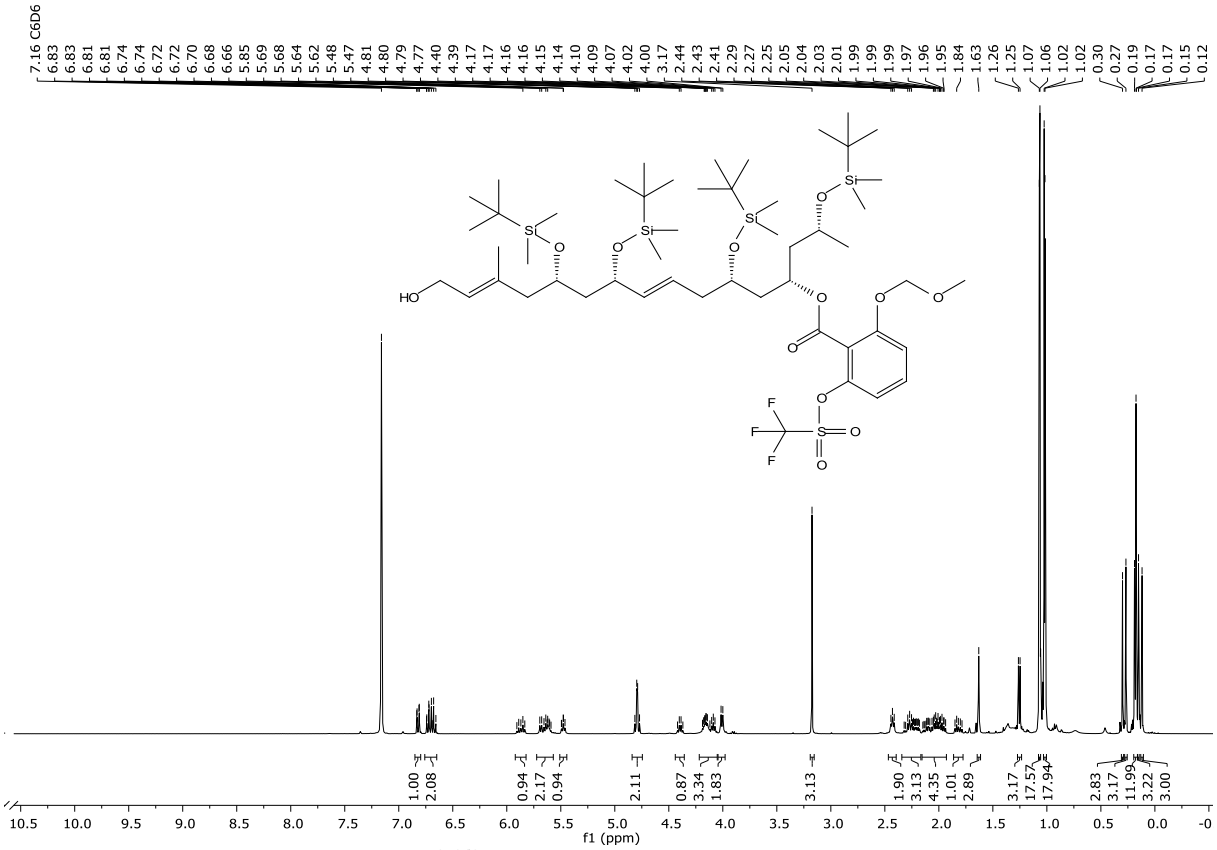


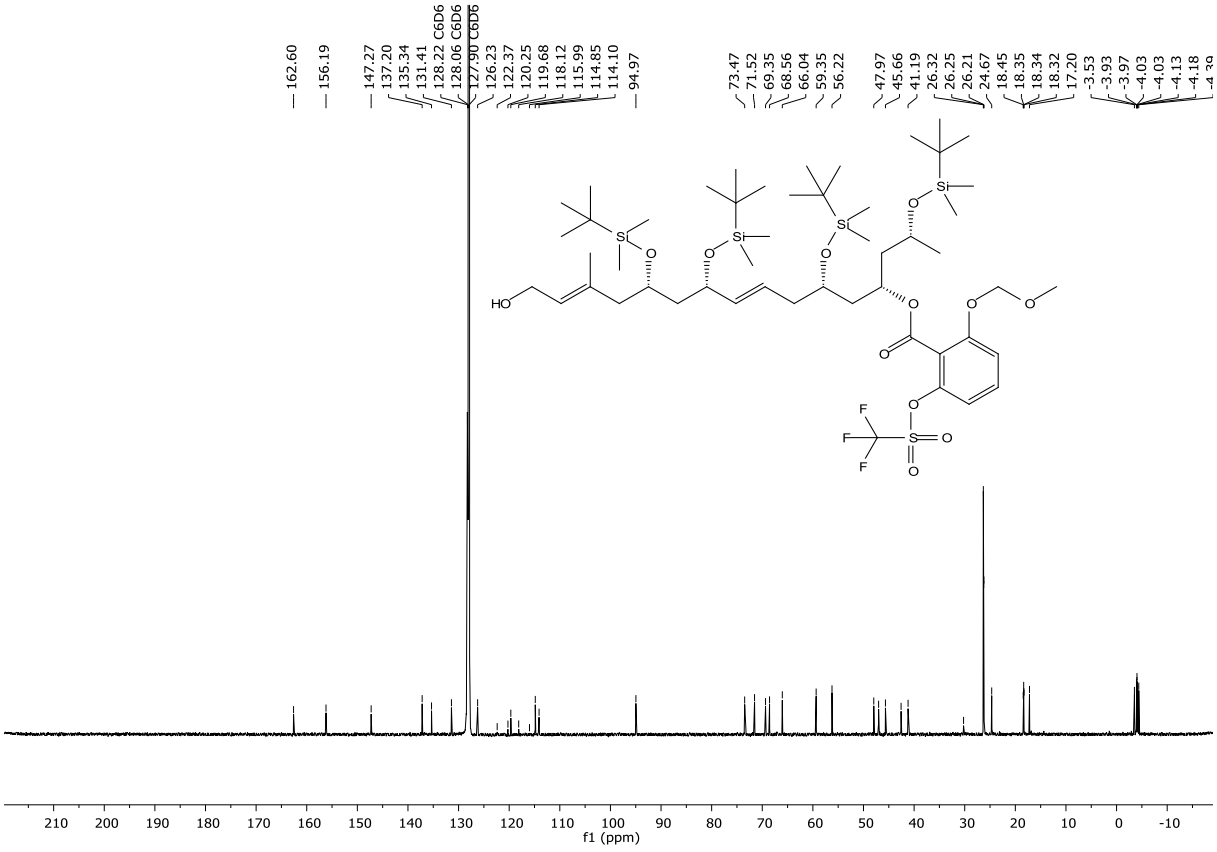
^{1}H and ^{13}C spectra of compound 50



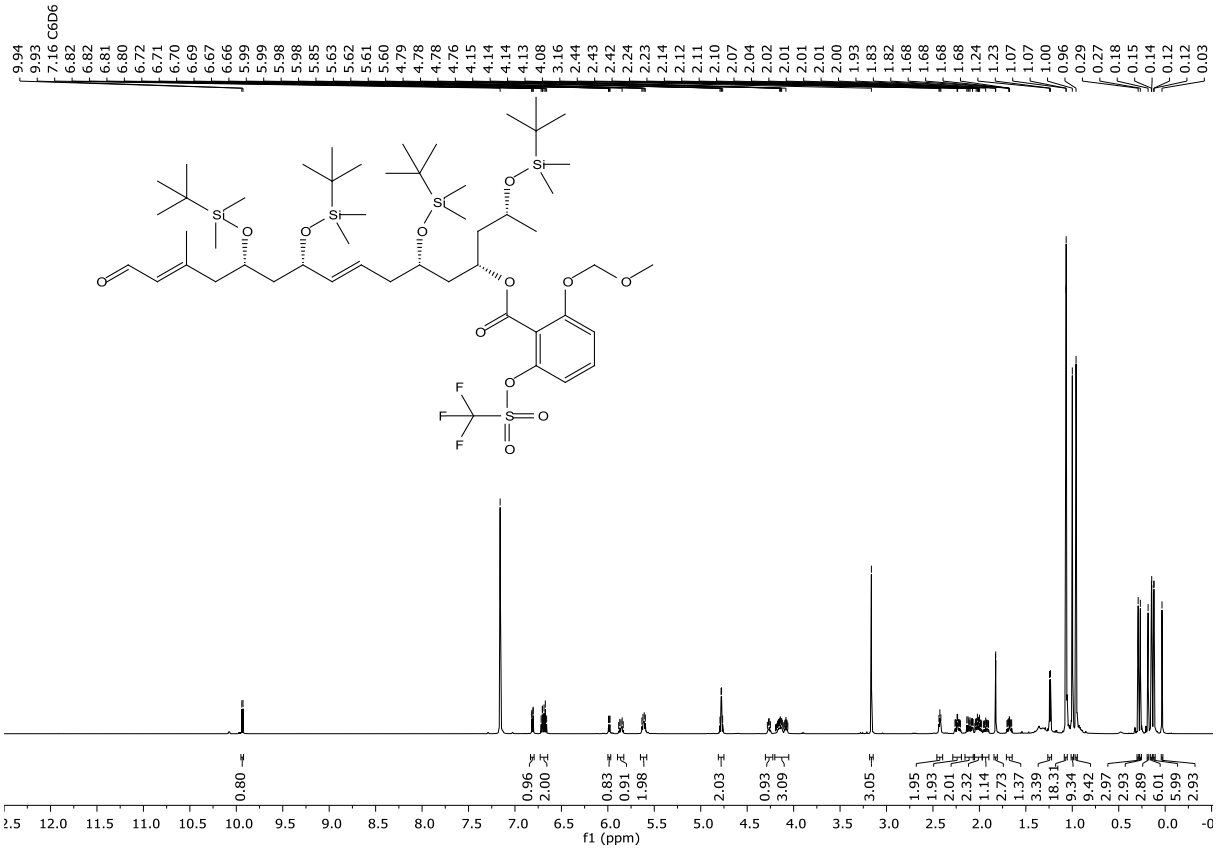


^{1}H and ^{13}C spectra of compound 50a

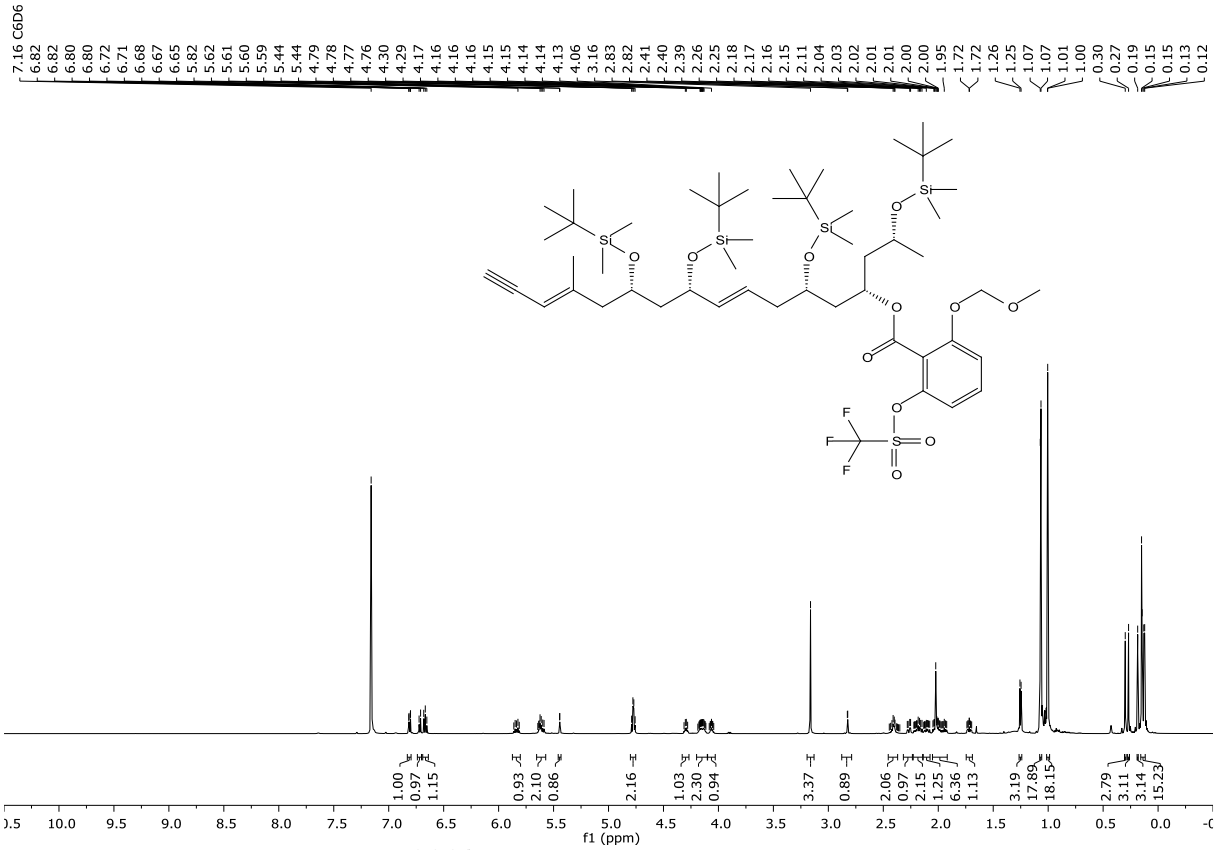


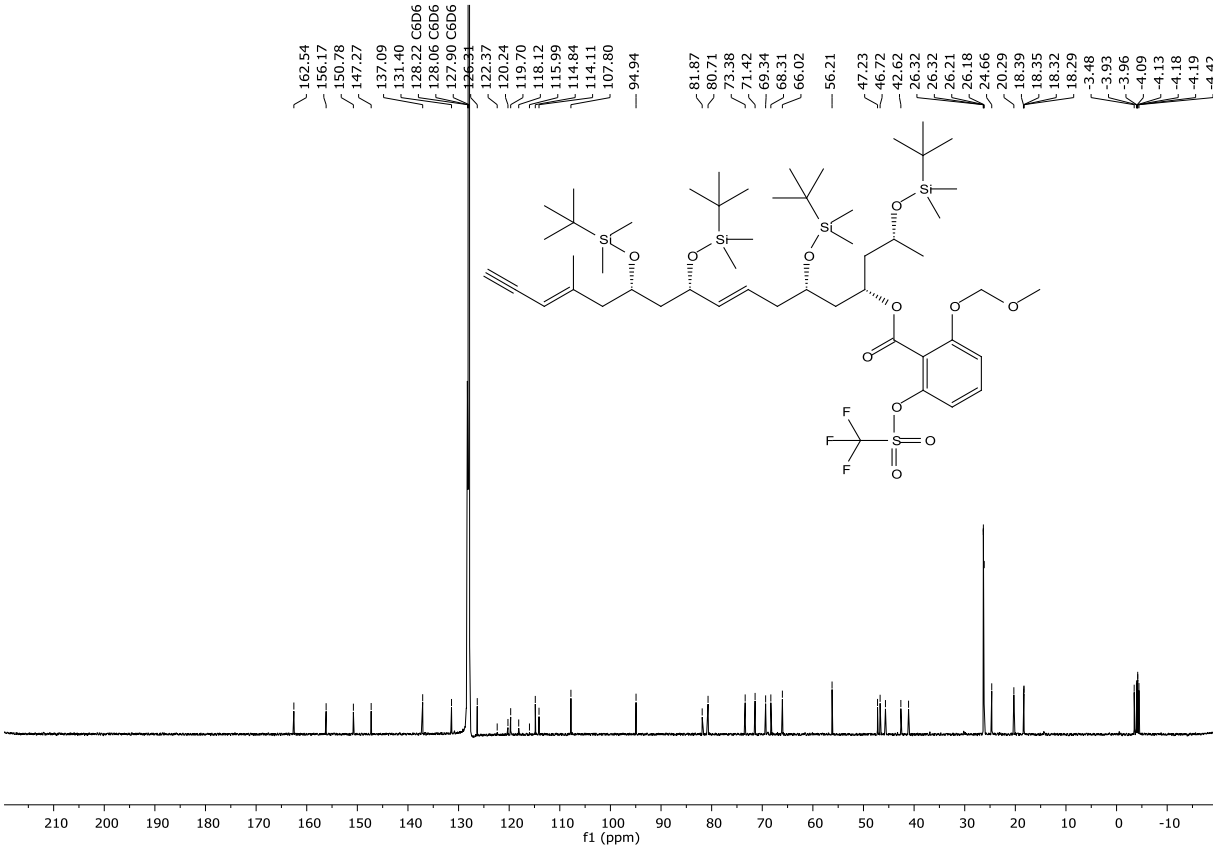


^{1}H spectrum of compound 50b

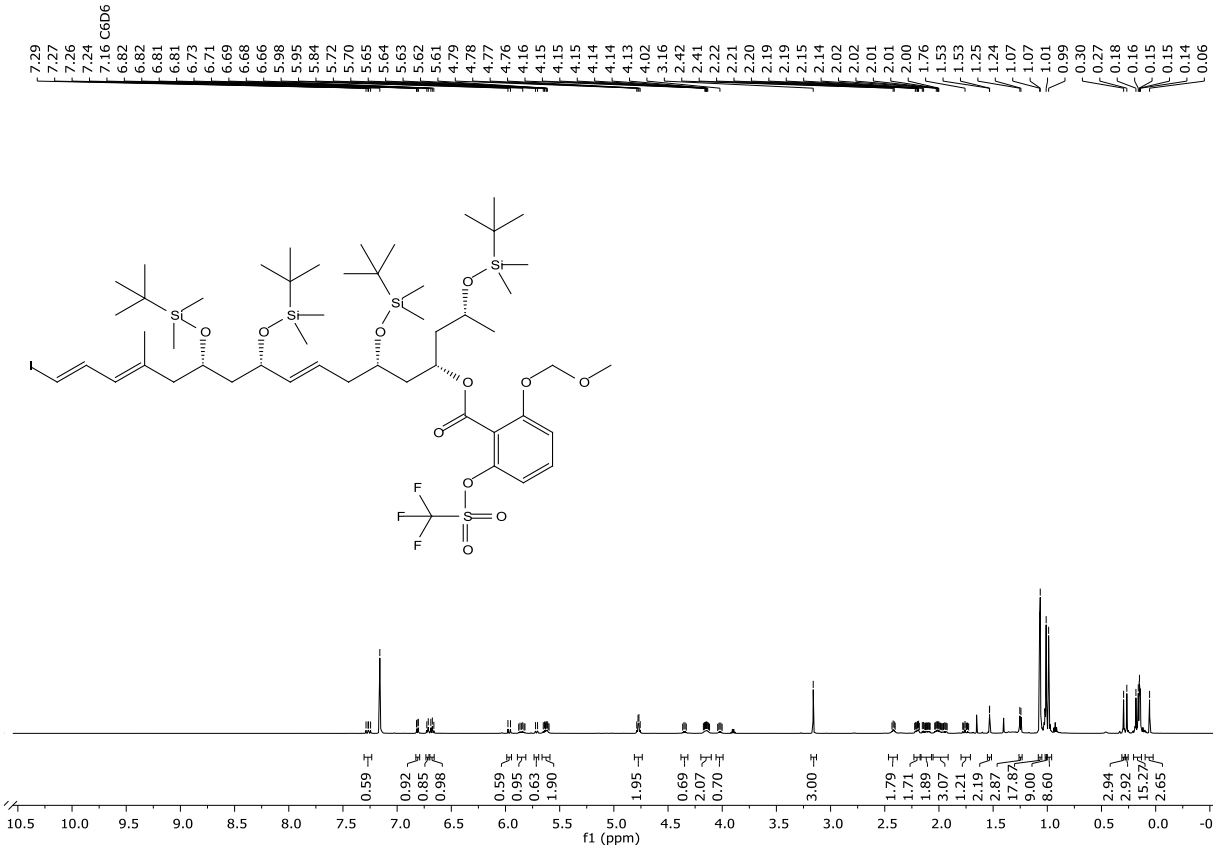


^{1}H and ^{13}C spectra of compound 51





^{1}H spectrum of compound 52



^{1}H and ^{13}C spectra of compound 5