Supporting Information

The Total Synthesis of Ircinastatin A (Psymberin)

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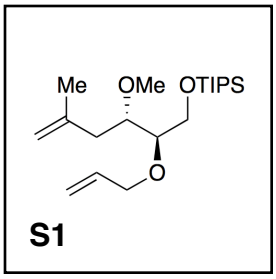
I. Materials and Methods

Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer. Nuclear magnetic resonance (^{1}H, ^{13}C, COSY, NOESY) spectra were recorded on Bruker model Avance 400 (^{1}H at 400 MHz; ^{13}C at 100 MHz) and Bruker model Avance 500 (^{1}H at 500 MHz; ^{13}C at 125 MHz) instruments. Chemical shifts are reported relative to chloroform (δ 7.26), benzene (δ 7.15) or methanol (δ 4.78) for ^{1}H NMR spectra and chloroform (δ 77.23), benzene or (δ 128.0) methanol (δ 49.3), for ^{13}C spectra. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Optical rotations were determined using a Jasco P1010 polarimeter. Mass spectra were obtained using a Bruker BioTOF II mass spectrometer with electrospray ionization (ESI). Thin layer chromatography (TLC) was conducted on silica gel F254 TLC plates purchased from EMD Chemicals Inc. Visualization was accomplished with UV light and/ or aqueous ceric ammonium molybdate solution followed by heating unless otherwise noted. Flash column chromatography was carried out using Ultra Pure Silica Gel Silia-P (40 to 63 μm) purchased from SiliCycle Inc. Dichloromethane (CH_2Cl_2), diethyl ether (Et_2O), tetrahydrofuran (THF), and toluene ($PhCH_3$) were dried by passage through a column of neutral alumina under argon immediately prior to use. All alkylamines, 2,6-

lutidine, benzene, pyridine, and chlorotrimethylsilane (TMSCl) were distilled from calcium hydride immediately prior to use. Boron trifluoride-diethyl etherate was distilled from calcium hydroxide immediately prior to use. Iodomethane was distilled prior to use. Anhydrous N,N-dimethylformamide (DMF) was purchased from Aldrich chemical company in 1L Sure/SealTM bottles. Dess-Martin periodinane was prepared according to literature procedures and stored at -20 ºC. Procedures calling for pH = 4 buffer employed Fisher Scientific Buffer Solution pH 4.00 (0.05 M potassium biphthalate buffer). Sodium hydride, 60% oil dispersion, was washed with pentanes under positive argon pressure prior to use. All other reagents and solvents were used as received from the manufacturer. All air and water sensitive reactions were performed in flasks flame dried under positive flow of argon and conducted under an argon atmosphere. Yield refers to isolated yield of analytically pure material unless otherwise noted.

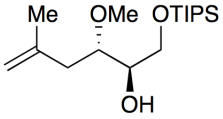
II. Experimental



S1

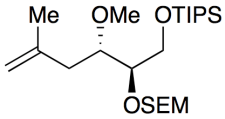
Methyl Ether (-)-S1. To a 0 °C slurry of 60% NaH oil dispersion (128 mg, 3.19 mmol) in THF (10 mL) was added a solution of alcohol **11** (910 mg, 2.66 mmol) in THF (3.5 mL) over 2 min followed by a THF rinse (3.5 mL). The reaction was stirred at 0 °C for 20 min and was then treated with iodomethane (0.25 mL, 3.98 mmol), stirred at 0 °C for 5 min, then the white slurry was warmed to room temperature. After 1 h the transparent reaction was quenched with saturated aqueous NH_4Cl (12 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (5% EtOAc/ Hexanes) gave methyl ether (-)-**S1** (905 mg, 2.53 mmol) as a clear oil in 96% yield. $[\alpha]^{23}_D$ = -4.94 (c = 0.26, CH_2Cl_2); IR (film) 3076, 2942, 2866, 1647, 1382, 1327, 1246, 1107, 1012, 996, 919, 883, 796, 682, 659; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (m, 21 H), 1.79 (s, 3H), 2.30 (m, 2H), 3.40 (s, 3H), 3.55 (m, 2H), 3.79 (m, 2H), 4.17 (m, 2H), 4.80 (m, 2H), 5.14 (dd, *J* = 1.6, 10.2 Hz, 1H), 5.26 (dd, *J* = 1.6, 17.2 Hz, 1H), 5.92 (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9, 18.0, 22.8, 38.5, 57.9, 63.2, 72.0, 80.1, 80.7, 112.24, 116.3, 135.5, 143.2; MS (ESI+) for $C_{20}H_{40}O_3Si$ [M+Na] calc 379.2644 found 379.2639.



12

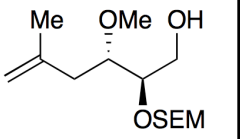
Alcohol (+)-12. To a 0 °C solution of allyl ether (-)-**S1** (905 mg, 2.54 mmol) in ether (25 mL) was added titanium(IV) isopropoxide (0.75 mL, 0.2.53 mmol) to give a yellow solution, which was treated with 2.0 M *n*-BuMgCl in ether (3.17 mL, 6.344 mmol) over 1 h via syringe pump. Immediately following the addition the dark orange solution was quenched with water (3 mL), filtered through celite, and rinsed with EtOAc (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated NH_4Cl, dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (5% EtOAc/Hexanes) afforded alcohol (+)-**12** (690 mg, 2.18 mmol) as yellow oil in 86% yield. $[\alpha]^{25}_D$ = +15.3 (c = 0.25, CH_2Cl_2); IR (film) 3459, 2942, 2867, 1462, 1104, 1066, 883, 800, 682, 660 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (m, 21H), 1.79 (s, 3H), 2.30 (m, 2H), 2.52 (d, *J* = 4.0 Hz, 1H), 3.40 (s, 3H), 3.45 (m, 1H), 3.67 (m, 1H), 3.80 (m, 2H), 4.81 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9, 17.9, 22.9, 38.4, 58.0, 63.8, 72.9, 80.1, 112.6, 142.9; MS (ESI+) for $C_{17}H_{36}O_3Si$ [M+Na] calc 339.2272 found 339.2096.



S2

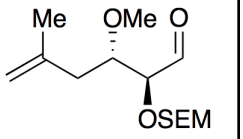
SEM Ether (-)-S2. To a solution of alcohol (+)-**12** (220 mg, 0.690 mmol) in CH_2Cl_2 (2.22 mL) was added *i*-Pr_2NEt (0.97 mL, 5.55 mmol) followed by SEMCl (0.49 mL, 2.78 mmol). The reaction was heated to 30 ˚C and stirred for 1 h giving an orange solution. The reaction was poured into ice cold aqueous $NaHCO_3$, the layers were separated, and the aqueous extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (3% EtOAc/Hexanes) gave SEM ether (-)-**S2** (268 mg, 0.600 mmol) as clear oil in 86% yield. $[\alpha]^{23}_D$ = -14.1 (c = 0.28, CH_2Cl_2); IR (film) 2943, 2867, 1463, 1375, 1248, 1105, 1030, 883, 860, 835, 682 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 9H), 0.93 (t, *J* = 8.5 Hz, 2H), 1.06 (m, 21H), 1.78

(s, 3H), 2.23 (dd, *J* = 4.0, 14.5 Hz, 1H), 2.29 (dd, *J* = 9.5, 14.5 Hz, 1H), 3.39 (s, 3H), 3.60 (m, 2H), 3.66 (m, 1H), 3.73 (dd, *J* = 5.5, 9.5 Hz, 1H), 3.83 (m, 2H), 4.80 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -1.4, 11.9, 18.0, 18.1, 22.7, 38.3, 57.9, 63.07, 65.1, 78.1, 79.9, 95.2, 112.3, 143.1; MS (ESI+) for $C_{23}H_{50}O_4Si_2$ [M+Cs] calc 579.2302 found 579.2332.



13

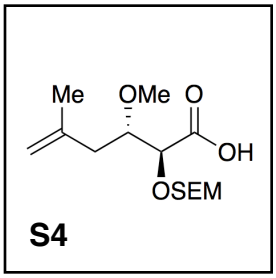
Alcohol (+)-13. To a 0 ˚C solution of TIPS ether (-)-**S2** (500 mg, 1.12 mmol) in THF (3.63 mL) was added 1.0 M TBAF in THF (2.23 mL, 2.23 mmol). The reaction stirred for 15 min at 0 °C and the reaction was poured into saturated aqueous NH_4Cl (3 mL), the layers were separated and the aqueous layer was extracted with EtOAc (3 x 3 mL). The combined organic layers were washed with water (2 mL) and brine (2 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (20% EtOAc/Hexanes) afforded alcohol (+)-**13** (265 mg, 0.91 mmol) as clear oil in 82% yield. $[\alpha]^{20}_D$ = +38.7 (c = 0.25, CH_2Cl_2); IR (film) 3462, 2952, 1647, 1375, 1249, 1107, 1057, 1024, 860, 835, 693 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 9H), 0.96 (t, *J* = 8.8 Hz, 2H), 1.77 (s, 3H), 2.20 (dd, *J* = 5.2, 14.0 Hz, 1H), 2.32 (dd, *J* = 8.0, 14.0 Hz, 1H), 3.25 (dd, 4.4, 8.0 Hz, 1H), 3.39 (s, 3H), 3.49 (m, 1H), 3.59 (m, 2H), 3.69 (m, 3H), 4.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -1.5, 18.1, 22.7, 39.3, 58.3, 62.3, 65.7, 80.8, 82.1, 95.3, 112.8, 142.4; MS (ESI+) for $C_{14}H_{30}O_4Si$ [M+Na] calc 313.1181 found 313.1806.



S3

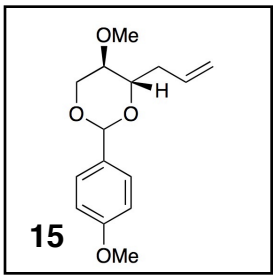
Aldehyde (-)-S3. Aldehyde **(-)-S3** was prepared from **(+)-13** according to literature procedures. Smith, A. B.; Jurica, J. A.; Walsh, S. P., *Org. Lett.* **2008**, *10*, 5625. $[\alpha]^{19}_D$ = -7.6 (c = 0.26, CH_2Cl_2); IR (film) 3078, 2953, 2891, 2826, 2724, 1732, 1644, 1377, 1249, 1109, 1059, 1027, 937, 860, 834 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.09 (s, 9H), 0.81 (m, 2H), 1.61 (s, 3H), 2.20 (dd, *J* = 7.0, 14.0 Hz, 1H), 2.26 (dd, *J* = 6.5, 14.0 Hz, 1H), 3.31 (s, 3H), 2.42 (ddd, *J* = 7.0, 10, 10.0 Hz, 1H), 3.62 (m, 2H), 4.03 (s, 1H), 4.70 (m, 2H), 4.74 (s, 2H), 9.56 (s, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ -1.5, 18.0, 22.5, 38.7, 57.8, 65.8, 81.6, 82.3, 95.3, 114.1, 141.5, 202.0; MS (ESI+) for $C_{14}H_{28}O_4Si$ [M+Na] calc 311.1655 found 311.1622.



S4

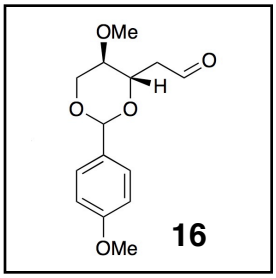
Acid (-)-S4. A solution of aldehyde (-)-**S3** (146 mg, 0.506 mmol) in *t*-BuOH (23 mL) and 2-methyl-2-butene (1.29 mL, 12.15 mmol) was treated with a solution of $NaClO_2$ (687 mg, 6.07 mmol) in 0.05 M potassium biphthalate pH 4 buffer (23 mL) in one portion. The yellow solution was stirred for 1 h, gradually turning clear. The reaction was then poured into brine (50 mL) and EtOAc (50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (4 x 20 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (25% EtOAc/Hexanes to 40% EtOAc/Hexanes) gave acid (-)-**S4** (146 mg, 0.48 mmol) as a clear oil in 95% yield, that was stored frozen in benzene. $[\alpha]^{22}_D$ = -6.2 (c = 0.26, CH_2Cl_2); IR (film) 3076, 2953, 1725, 1443, 1376, 1249, 1190, 1158, 1111, 1061, 891, 860, 835, 758, 693 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ -0.02 (s, 9H), 0.93 (m, 2H), 1.70 (s, 3H), 2.50 (m, 2H), 3.21 (s, 3H), 3.65 (m, 2H), 3.84 (m, 1H), 4.45 (d, *J* = 3.2 Hz, 1H), 4.65 (q, *J* = 8.5, 19.5 Hz, 2H), 4.86 (s, 1H), 4.93 (s, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ -0.4, 19.1, 23.9, 40.2, 58.9, 67.0, 77.7, 82.3, 96.0, 114.5, 143.3, 177.5; MS (ESI+) for $C_{14}H_{28}O_5Si$ [M+Na] calc 327.1604 found 327.1586.



15

Methyl Ether (-)-15. To a 0 °C solution of alcohol (8.80 g, 35.16 mmol) and MeI (4.36 mL, 42.19 mmol) in THF (122 mL) and DMF (12.2 mL) was added NaH 60% oil dispersion (2.02 g, 84.38 mmol). The reaction mixture was stirred for 30 min at 0 °C and 1 h at room temperature then quenched with saturated aqueous NH_4Cl. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by column chromatography (Hexanes to 10% EtOAc/Hexanes) afforded methyl ether (-)-**15** (8.50 g, 32.15 mmol) in 91% yield as clear oil. $[\alpha]^{22}_D$ = -44.03 (c = 0.55, CH_2Cl_2); IR (film) 3074, 2934, 2836, 1615, 1517, 1250, 1102, 1034, 827 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.42 (ddd, *J* = 7.5, 7.5, 14.5

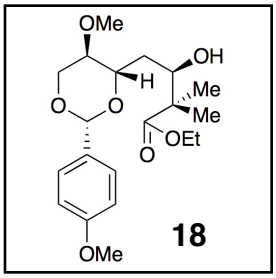
Hz, 1H), 2.65 (m, 1H), 3.24 (ddd, *J* = 5.0, 9.5, 9.5, 1H), 3.43 (s, 3H), 3.56 (t, *J* = 11.0 Hz, 1H), 3.64 (m, 1H), 3.81 (s, 3H) 4.42 (dd, 5.0, 11.0 Hz, 1H), 5.12 (dd, *J* = 2.0, 10.0 Hz, 1H), 5.16 (dd, *J* = 2.0, 17.0 Hz, 1H), 5.43 (s, 1H), 5.99 (dddd, 7.5, 7.5, 10.0, 17.0 Hz, 1H), 6.89 (d, J = 9.0 Hz, 2H), 7.41 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.2, 55.3, 58.1, 69.0, 73.9, 80.1, 100.9, 113.6, 117.2, 127.4, 130.5, 134.4, 160.0; MS (ESI+) for $C_{15}H_{20}O_4$ [M+Cs] calc 397.0416 found 397.0423.



16

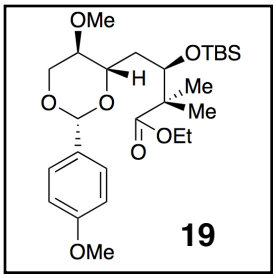
Aldehyde (-)-16 To a solution of alkene (-)-**15** (6.48 g, 24.5 mmol) in THF (48 mL) and water (48 mL) was added NMO (6.12 g, 52.24 mmol) followed by a 20 mg/1.0 mL solution of OsO_4 in water (0.64 mL, 0.05 mmol). The reaction mixture was stirred for 16 h and was quenched with solid $Na_2S_2O_3$ (3.2 g) and stirred for 1 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were concentrated and taken on to the next step without purification.

To a 0 °C biphasic solution of the crude diol (7.36 g, 24.5 mmol) in 0.05 potassium biphthalate pH 4 buffer (66 mL) and CH_2Cl_2 (66 mL), was added $NaIO_4$ (7.82 g, 36.56 mmol). The mixture stirred for 5 min at 0 °C and was then warmed to room temperature for 2 h. The reaction mixture was quenched with aqueous $Na_2S_2O_3$, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to crude oil. Purification by column chromatography (5% EtOAc/Hexanes to 20% EtOAc/ Hexanes) afforded aldehyde (-)-**16**. (6.3 g, 23.7 mmol) in 97% yield over 2 steps. $[\alpha]^{26}_D$ -41.2 (c 0.46, CH_2Cl_2); IR (film) 2935, 2837, 1725, 1615, 1518 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz); δ 2.71 (ddd, *J* = 2.4, 7.6, 16.4 Hz, 1H), 2.83 (ddd, *J* = 2.4, 4.8, 16.4 Hz, 1H), 3.21 (ddd, *J* = 5.2, 9.6, 19.2 Hz, 1H), 3.36 (s, 3H), 3.56 (dd, *J* = 10.4, 10.4 Hz, 1H), 3.76 (s, 3H), 4.12 (ddd, *J* = 4.4, 7.6, 9.2 Hz, 1H), 4.43 (dd, *J* = 5.2, 11.2 Hz, 1H), 5.48 (s, 1H); 6.86 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 9.78 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 46.3, 55.2, 57.7, 68.9, 74.0, 75.5, 101.0, 113.5, 127.3, 129.7, 199.8, 160.0; MS (ESI+) calc for $C_{14}H_{18}O_5$ (M+H) 267.12, found 267.2.



18

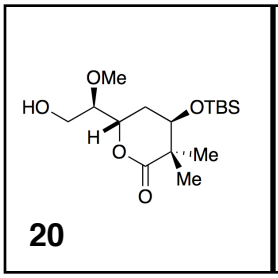
Alcohol (-)-18. To a stirring solution of N-Ts-(L)-valine (2.89 g, 10.6 mmol) in CH_2Cl_2 (100 mL) at 0 ºC was added BH_3·THF (10.6 mL of a 1.0 M solution in THF, 10.6 mmol) in portions over 0.5 h. After the reaction mixture was cooled to -78 ºC neat silyl ketene acetal **17** (3.82 g, 20.2 mmol) was added and stirred for 5 min. Aldehyde (-)-**16** (2.7 g, 10.1 mmol) was added and stirred for 2 h. The reaction mixture was quenched by the addition of a 10% aqueous solution of $NaHCO_3$ (20 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography (10% to 25% EtOAc/Hexanes) gave alcohol (-)-**18 (**3.24 g, 8.47 mmol) in 84% yield as a 9:1 mixture of diastereomers. $[\alpha]^{18}_D$ -39.5 (c = 0.55, CH_2Cl_2); IR (film) 3535, 1726, 1615, 1519 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz); δ 1.17 (s, 3H), 1.14 (s, 3H), 1.22 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.63 (m, 1H), 2.03 (m, 1H), 3.25 – 3.19 (m, 2H), 3.39 (s, 3H), 3.54 (dd, *J* = 10.4, 10.4 Hz, 1H), 3.76 (s, 3H), 3.81 (ddd, *J* = 9.2, 9.2, 2.4 Hz, 1H), 4.16 – 4.05 (m, 3H), 4.41 (dd, *J* = 10.8, 4.8 Hz, 1H), 5.44 (s, 1H), 6.83 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 14.1 20.4, 21.0, 33.8, 47.0, 55.2, 57.9, 60.5, 69.0, 74.5, 75.9, 81.5, 101.0, 113.6, 127.3, 129.6, 160.1, 177.8; MS (ESI+) calc for $C_{20}H_{30}O_7$ (M+H) 383.45, Observed 383.3.



19

Silyl Ether (-)-19. To a solution of alcohol (-)-**18** (3.00 g, 7.83 mmol) in CH_2Cl_2, (50 mL) at 0 ºC was added 2,6-lutidine (2.28 mL, 19.7 mmol) followed by TBSOTf (2.72 g, 10.3 mmol). The reaction stirred for 1 h at 0 °C and warmed to room temperature and stirred for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography (10% EtOAc/Hexanes) gave (3.47 g, 7.00 mmol) of TBS ether (-)-**19** in 89% yield as a clear oil. $[\alpha]^{26}_D$ -36.0 (c = 0.53, CH_2Cl_2); IR (film) 1730, 1616, 1518 cm^{-1};

^{1}H NMR ($CDCl_3$, 400 MHz); δ -0.06 (s, 3H), 0.05 (s, 3H), 0.83 (s, 9H), 1.11 (s, 3H), 1.17 (s, 3H), 1.23 (dd, *J* = 8.0, 8.0 Hz , 3H), 1.64 (ddd, *J* = 13.6, 8.0, 4.0 Hz, 1H), 2.19 (ddd, *J* = 14.8, 5.2, 5.2 Hz, 1H), 3.07 (ddd, *J* = 9.6, 9.6, 4.8 Hz, 1H), 3.55 – 3.46 (m, 2H), 3.39 (s, 3H), 4.05 (dd, *J* = 14.4, 7.2 Hz, 2H), 3.78 (s, 3H), 4.23 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.37 (dd, *J* = 10.8, 4.8 Hz, 1H), 5.35 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm -5.1, -3.9, 14.0, 18.1, 20.3, 21.2, 25.9, 38.2, 48.3, 55.2, 57.9, 60.3, 69.0, 73.2, 76.1, 78.6, 101.1, 113.4, 127.5, 130.3, 159.9, 177.0; MS (ESI+) calc for $C_{26}H_{44}O_7Si$ (M+H) 497.28, found 497.4.



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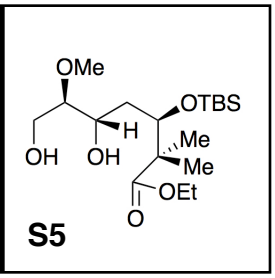
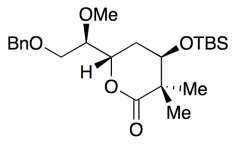


S5

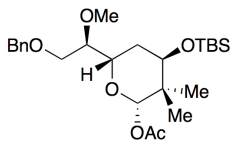
Lactone (-)-20. To a solution of benzylidine acetal (-)-**19** (1.00 g, 2.01 mmol) in methanol (5 mL) at 0 °C was added a 0 °C solution of 0.01 M HCl in methanol (10 mL, 0.10 mmol). The reaction was stirred for 1.25 h at 0 °C and was quenched with saturated aqueous $NaHCO_3$ (16 mL) the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated to oil. Purification by column chromatography (25% EtOAc/CH_2Cl_2) afforded pure lactone (-)-**20** (470 mg, 1.40 mmol) in 70% yield as white solids, as well as diol (-)-**S5** (47 mg, 0.124 mmol) in 7% yield as clear oil. Diol **S5** (47 mg, 0.124 mmol) azeotroped with toluene, was dissolved in CH_2Cl_2 (5 mL), cooled to 0 °C, then treated with TFA (40 µL, 0.536 mmol). The reaction was stirred for 5 min at 0 °C then stirred at room temperature for 5 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (1.5 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated to white solids. Purification by column chromatography (25% EtOAc/CH_2Cl_2) afforded pure lactone (-)-**20** (41 mg, 0.124 mmol) in quantitative yield, for a combined 77% yield. $[\alpha]^{18}_D$ = -36.6 (c = 0.22, CH_2Cl_2); IR (film) 3450, 2930, 1731, 1471, 1391, 1257, 1162, 1131, 1088, 835, 776 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.24 (s, 3H), 1.25 (s, 3H), 1.80 (m, 1H), 2.11 (s, 1H), 2.22 (t, *J* = 12.3 Hz, 1H), 3.50 (s, 3H), 3.52 (m, 1H), 3.70 (m,

1H), 3.65 (m, 1H), 3.79 (s, 1H), 4.76 (dd, *J* = 3.3, 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.6, 18.0, 22.9, 25.7, 26.1, 28.2, 44.2, 59.5, 60.9, 73.1, 76.7, 82.7, 176.8; MS (ESI+) for $C_{16}H_{32}O_5Si$ [M+Cs] calc 465.1073 found 465.1120.



21

Benzyl Ether (-)-21. To a flask containing sodium hydride 60% oil dispersion (220 mg, 5.73 mmol) was added THF (3.5 mL) and cooled to 0 °C. The resulting slurry was treated with an orange room temperature solution of alcohol (-)-**20** (763 mg, 2.29 mmol), tetrabutylammonium iodide (170 mg, 0.45 mmol), and benzyl bromide (0.41 mL, 3.44 mmol) in THF (4.9 mL) over 10 min. The reaction mixture was stirred for 45 min at 0 °C and then was warmed to room temperature and stirred 5 h. The reaction mixture was cooled to 0 °C and quenched with a saturated solution of aqueous NH_4Cl (7 mL) followed by dilution with ethyl acetate (7 mL) and water (2 mL). The layers were separated and the aqueous phase was extracted with ethyl acetate (3 x 7 mL). The organic layers were combined, washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated to orange oil. Purification by column chromatography (5% EtOAc/Hexanes to 25% EtOAc/Hexanes) afforded benzyl ether (-)-**21** (865 mg, 2.04) in 89% yield as clear oil. $[\alpha]^{21}_D$ = -27.3 (c = 0.27, CH_2Cl_2); IR (film) 2929, 2857, 1734, 1462, 1390, 1257, 1164, 1092, 1031, 1016, 835, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.05 (s, 3H), 0.85, (s, 9H) 1.23 (s, 3H), 1.25 (s, 3H), 1.75 (dt, *J* = 4.4, 4.4, 14.0 Hz, 1H), 2.26 (m, 1H), 3.46 (m, 4H), 3.54, (m, 1H), 3.78 (m, 1H), 3.78 (m, 1H), 4.50 (s, 2H), 4.82 (m, 1H), 7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.2, -4.7, 17.8, 22.8, 25.6, 25.7, 27.1, 44.0, 59.3, 68.6, 73.0, 73.4, 76.7, 81.0, 127.5, 127.6, 128.2, 137.7, 176.6; MS (ESI+) for $C_{23}H_{38}O_5Si$ [M+Cs] calc 555.1543 found 555.1550.

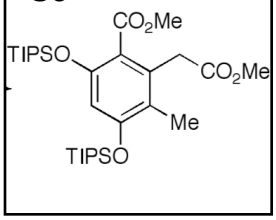


5

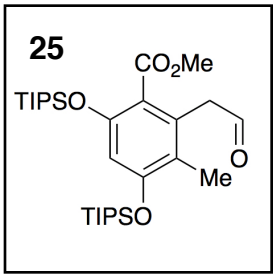
Lactol-Acetate (-)-5. To a -78 °C solution of lactone (546 mg, 1.29 mmol) in CH_2Cl_2 (8.3 mL) was added a 1.0 M solution of DIBAL in hexanes (3.2 mL, 3.23 mmol), dropwise, over 10 min. The solution stirred for 2 h at -78 °C and was treated with pyridine (0.39 mL, 4.85 mmol) over 5 min, a solution of DMAP (395 mg, 3.23 mmol) in

CH_2Cl_2 (1.0 mL) over 5 min, and Ac_2O (1.0 mL, 10.34 mmol) over 5 min, respectively. The yellow solution stirred at -78 °C for 14 h and was warmed to 0 °C over 5 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and stirred for 1 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (10% EtOAc/Hexanes) afforded lactol-acetate (-)-**5** (600 mg, 1.29 mmol) in quantitative yield as pale yellow oil. $[\alpha]^{21}_D$ = -33.4 (c = 0.27, CH_2Cl_2); IR (film) 2929, 2857, 1753, 1473, 1457, 1391, 1364, 1226, 1058, 835, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.88 (s, 3 H), 0.09 (s, 9H), 0.098 (s, 3H), 1.54 (dt, *J* = 2.7, 2.7, 14.0 Hz, 1H), 1.92 (m, 1H), 2.09 (s, 3H), 3.48 (m, 5H), 3.61 (dd, *J* = 3.2, 9.8 Hz, 1H), 3.67 (t, *J* = 2.7 Hz, 1H), 4.10 (ddd , *J* = 2.7, 4.7, 11.7 Hz, 1H), 4.52 (s, 2H), 5.75 (s, 1H), 7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -4.6, 18.0, 18.6, 21.0, 21.6, 25.8, 30.6, 38.6, 58.8, 70.0, 72.1, 73.4, 75.0, 82.0, 96.1, 126.8, 127.4, 128.2, 128.6, 138.3, 169.6; MS (ESI+) for $C_{25}H_{42}O_6Si$ [M+Cs] calc 599.1805 found 599.1801.

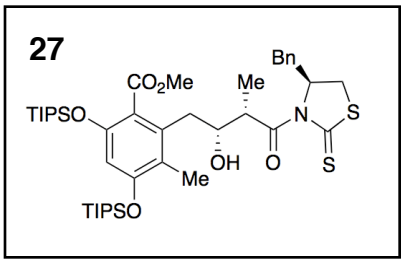
S6



Catechol-S6. To a 0 °C solution of bis-phenol **24** (530 mg, 2.09 mmol) and 2,6-lutidine (1.21 mL, 10.42 mmol) in CH_2Cl_2 (20 mL) was added TIPSOTf (1.40 mL, 5.21 mmol), dropwise, over 2 min. The reaction was stirred for 15 min at 0 °C then warmed to room temperature and was stirred for 16 h. The reaction was quenched with saturated aqueous $NaHCO_3$, the layers separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (Hexanes to 5% Ether/Hexanes) afforded bis-TIPS protected aryl ether **S6** (1.16 g, 2.04 mmol) in 98% yield as pale yellow oil. IR (film) 2946, 2867, 1738, 1592, 1471, 1324, 1262, 1165, 1068, 997, 882, 832, 793, 685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (m, 36H), 1.24 (m, 6H), 2.11 (s, 3H), 3.64 (m, 5H), 3.80 (s, 3H), 6.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 13.0, 13.1, 17.9, 18.0, 36.3, 51.9, 51.9, 108.2, 119.8, 121.1, 132.4, 151.6, 155.7, 169.0, 171.1; MS (ESI+) for $C_{30}H_{54}O_6Si_2$ [M+Cs] calc 699.2513 found 699.2551.



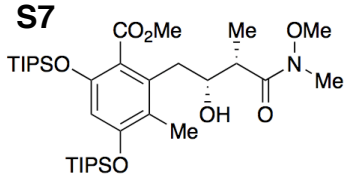
Aldehyde-25. To a -78 °C solution of methyl ester **S6** (1.15 g, 2.03 mmol) in CH_2Cl_2 (26 mL) was added 1.0 M DIBAL in hexanes (2.1 mL, 2.05 mmol) over 5 min. After 2 h at -78 °C the reaction was treated with additional 1.0 M DIBAL in hexanes (1.0 mL, 1.00 mmol) and stirred at -78 °C for 1 h. The reaction was quenched at -78 °C with saturated aqueous Rochelle's salt (10 mL) and warmed to room temperature and stirred for 3 hours. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with Na_2SO_4, filtered, and concentrated to yellow oil. Purification by column chromatography (7% EtOAc/Hexanes) afforded aldehyde **25** (847 mg, 1.58 mmol) in 78% yield as yellow oil. IR (film) 2946, 2867, 2763, 2721, 1726, 1590, 1471, 1345, 1258, 1166, 882, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.09 (m, 36H), 1.26 (m, 6H), 2.07 (s, 3H), 3.60 (d, *J* = 2.0 Hz, 2H), 3.82 (s, 3H), 6.33 (s, 1H), 9.59 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 13.0, 13.2, 17.8, 18.0, 46.1, 51.9, 108.4, 120.0, 121.2, 130.5, 151.9, 156.0, 169.1, 198.76; MS (ESI+) for $C_{29}H_{52}O_5Si_2$ [M+Cs] calc 669.2408 found 669.2411.



Alcohol (+)-27. To a yellow 0 °C solution of N-acylpropionate thiazolidinethione **26** (703 mg, 2.65 mmol) in CH_2Cl_2 (20 mL) was added $TiCl_4$ (0.30 mL, 0.2.78 mmol), dropwise, over 2 min. The resulting orange slurry was stirred for 15 min at 0 °C and was treated with (-)-sparteine (0.67 mL, 2.65 mmol) over 3 min at 0 °C, giving a deep red solution. The reaction mixture stirred at 0 °C for 20 min then cooled to -78 °C and treated with 1-methyl-2-pyrrolidinone (0.085 mL, 0.85 mmol) over 2 min. The reaction mixture stirred at -78 °C for 10 min and was treated with a solution of aldehyde **25** (1.56 g, 2.91 mmol) in CH_2Cl_2 (5 mL) over 10 min followed by a CH_2Cl_2 rinse (5 mL). The reaction mixture stirred at -78 °C for 1 h then warmed to 0 °C and stirred for 1 h. The reaction mixture was quenched with half-saturated aqueous NH_4Cl (5 mL) and diluted with water (3 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 15

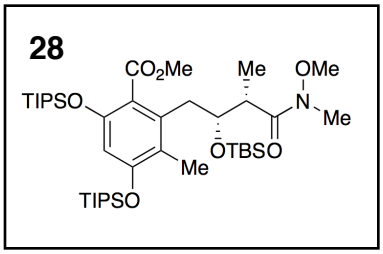
mL), the organics combined, washed with brine (15 mL), dried over Na_2SO_4, filtered, and concentrated to yellow oil. Purification by column chromatography (5% EtOAc/ Hexanes to 10% EtOAc/Hexanes gradient) afforded alcohol (+)-**27** (2.00 g, 2.50 mmol) in 94% yield as bright yellow solids in > 20:1 dr as determined by ^{1}H NMR. $[\alpha]^{19}_D$ = +79.2 (c = 1.0, CH_2Cl_2); IR (film) 3429, 2946, 2868, 1696, 1589, 1469, 1342, 1266, 1166, 1065, 883, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (m, 36H), 1.28 (m, 6H), 1.32 (d, *J* = 6.8 Hz, 3H), 2.16 (s, 3H), 2.63 (dd, *J* = 10.8, 14.0 Hz, 1H), 2.85 (d, *J* = 11.4 Hz, 1H), 2.87 (dd, *J* = 3.2, 14.0 Hz, 1H), 3.06 (dd, *J* = 10.8, 13.0 Hz, 1H), 3.31 (dd, *J* = 3.2, 13.0 Hz, 1H), 3.40 (dd, *J* = 7.2, 11.2 Hz, 1H), 3.87 (s, 3H), 3.90 (d, *J* = 6.8 Hz, 1H), 4.15 (m, 1H), 4.75 (m, 1H), 5.27 (m, 1H), 6.26 (s, 1H), 7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 12.5, 13.1, 13.2, 17.9, 18.0, 32.2, 36.0, 36.7, 45.3, 69.7, 72.0, 107.6, 120.0, 120.7, 127.2, 128.9, 129.5, 136.3, 136.7**,** 151.6, 156.2, 171.4, 176.9, 201.6; MS (ESI+) for $C_{42}H_{67}NO_6S_2Si_2$ [M+K] calc 840.3585 found 840.3582.

S7

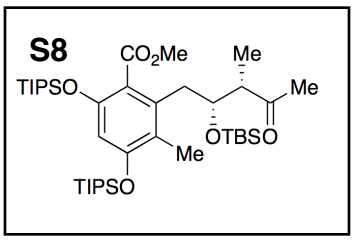


Weinreb Amide (+)-S7. To a bright yellow solution of (+)-**27** (1.07 g, 1.33 mmol) in CH_2Cl_2 (12 mL) was added imidazole (364 mg, 5.34 mmol) and N,O-dimethylhydroxylamine•HCl (261 mg, 2.67 mmol) at room temperature. The reaction mixture was stirred for 16 h at room temperature and was quenched with saturated aqueous NH_4Cl (10 mL), stirred 5 min, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated to yellow oil. Purification by column chromatography (CH_2Cl_2 to 5% EtOAc/CH_2Cl_2 to 20% EtOAc/CH_2Cl_2) gave Weinreb amide (+)-**S7** (835 mg, 1.27 mmol) in 96% yield as clear oil. $[\alpha]^{22}_D$ = +21.1 (c = 0.25, CH_2Cl_2); IR (film) 3457, 2945, 2867, 172, 1589, 1467, 1342, 1266, 1191, 1166, 1066, 996, 882, 686 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (m, 36H), 1.22 (m, 6H), 1.24 (d, *J* = 6.9 Hz, 3H), 2.17 (s, 3H), 2.64 (dd, *J* = 10.0, 14.0 Hz, 1H), 2.84 (dd, *J* = 5.0, 14.0 Hz, 1H), 2.96 (s, 1H), 3.17 (s, 3H), 3.62 (s, 3H), 3.66 (s, 1H), 3.89 (s, 3H), 3.92 (dq, 5.0, 5.0, 5.0, 10.0 Hz, 1H), 6.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 12.2, 13.0, 13.1, 13.2, 17.7, 17.9, 31.9, 35.8, 40.4, 51.9, 61.2, 72.3,

107.2, 120.0, 120.7, 128.2, 136.6, 151.2, 155.8, 170.4; MS (ESI+) for $C_{34}H_{63}NO_7Si_2$ [M +Na] calc 676.4041 found 676.4046.

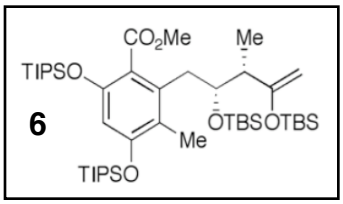


TBS ether (+)-28. To a -78 °C solution of Weinreb amide (+)-**S7** (555 mg, 0.849 mmol) in CH_2Cl_2 (6 mL) was added 2,6-lutidine (0.26 mL, 3.39 mmol) followed by TBSOTf (0.39 mL, 1.70). The reaction was stirred for 60 min at -78 °C and then was quenched with a saturated aqueous solution of $NaHCO_3$ (2 mL), warmed to room temperature and diluted with CH_2Cl_2 (5 mL) and water (1 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (10% EtOAc/Hexanes) afforded TBS ether (+)-**28** (620 mg, 0.807 mmol) as a clear oil in 95% yield. $[\alpha]^{22}_D$ = +19.5 (c = 0.24, CH_2Cl_2); IR (film) 2947, 2868, 1731, 1667, 1589, 1470, 1341, 1257, 1166, 1066, 997, 882, 838, 777, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.43 (s, 3H), -0.05 (s, 3H), 0.82 (s, 9H), 1.07 (m, 39H), 1.25 (m, 6H), 2.17 (s, 3H), 2.74 (dd, *J* = 5.2 Hz, 14.0 Hz, 1H), 2.89 (brs, 1H), 2.92 (dd, *J* = 8.4, 14.0 Hz, 1H), 3.14 (s, 3H), 3.48 (s, 3H), 3.84 (s, 3H), 4.20 (m, 1H), 6.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, 12.2, 12.9, 13.1, 13.2, 26.1, 36.7, 51.8, 60.9, 73.2, 106.3, 120.5, 121.4, 136.4, 151.0, 155.2, 169.6; MS (ESI+) for $C_{40}H_{77}NO_7Si_3$ [M+Cs] calc 900.4062 found 900.4027.

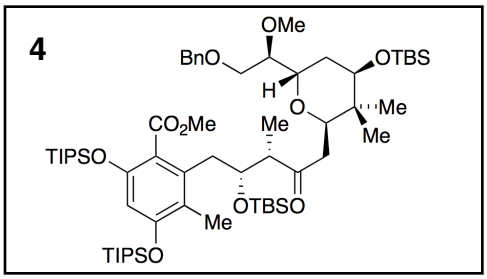


Ketone (+)-S8. To a -78 °C solution of Weinreb amide (+)-**28** (600 mg, 0.781 mmol) in THF (6 mL) was added 3.0 M MeMgBr in Et_2O (0.78 mL, 2.34 mmol). The reaction mixture was stirred for 30 min at -78 °C and then warmed to 0 °C and was stirred for 45 min. The reaction mixture was quenched with a saturated aqueous NH_4Cl (2 mL), warmed to room temperature, and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 4 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by column chromatography (5% EtOAc/Hexanes) provided ketone (+)-**S8** (539 mg, 0.745 mmol) in 95% yield as clear oil. $[\alpha]^{20}_D$ = +53.6 (c = 0.26, CH_2Cl_2); IR (film) 2947, 2868,

1729, 1589, 1345, 1259, 1192, 1167, 1068, 839, 776, 685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.35 (s, 3H), -0.08 (s, 3H), 0.82 (s, 9H), 1.07 (m, 39H), 1.23 (m, 6H), 2.14 (s, 3H), 2.20 (s, 3H), 2.62 (dd, *J* = 4.8, 14.4 Hz, 1H), 2.71 (m, 2H), 3.82 (s, 3H), 4.18 (m, 1H), 6.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.07, 11.789, 12.86, 13.09, 13.27, 17.89, 17.99, 25.98, 30.56, 34.70, 51.73, 52.67, 74.15, 106.67, 120.12, 121.30, 136.10, 151.09, 155.33, 169.52, 210.61; MS (ESI+) for $C_{39}H_{74}O_6Si_3$ [M+Cs] calc 855.3848 found 855.3774.



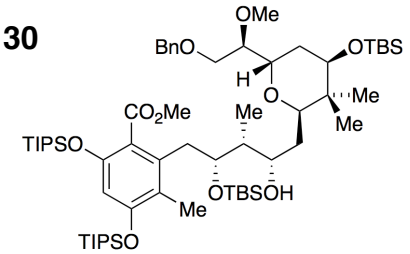
TBS Enolsilane 6. To a 0 °C solution of ketone **S8** (231 mg, 0.319 mmol) in CH_2Cl_2 (2.5 mL) was added *i*-Pr_2NEt (0.33 mL, 1.92 mmol) followed by TBSOTf (0.22 mL, 0.958 mmol). The reaction stirred for 90 min a 0 °C and was quenched with saturated aqueous $NaHCO_3$ (2.5 mL) and warmed to room temperature. The reaction was diluted with water (1 mL) and CH_2Cl_2 (3 mL), the layers separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to minimal volume and filtered through a silica gel plug (3% EtOAc/Hexanes with 1% Et_3N). The filtrate was concentrated to oil, azeotropically dried with toluene, and concentrated for 30 min under high vacuum. The formation of enolsilane **6** was confirmed by ^1H NMR analysis and was then used immediately in the next reaction without further analysis as it showed significant moisture sensitivity. ^1H NMR (400 MHz $CDCl_3$) δ -0.32 (s, 3H), -0.05 (s, 3H), -0.08 (s, 3H), 0.14 (s, 3H), 0.84 (s, 9H), 0.88 (s, 9H), 1.01 (d, *J* = 7.2 Hz, 3H), 1.11 (m, 36H), 1.27 (m, 6H), 2.14 (m, 1H), 2.18 (s, 3H), 2.86 (m, 2H), 3.82 (s, 3H), 4.08 (m, 3H), 6.19 (s, 1H).



Tetrahydropyran (+)-4 A -40 °C solution of lactol-acetate (-)-**5** (103.0 mg, 0.221 mmol; azeotropically dried with toluene and dried further under high vacuum over 1 h immediately prior to use) in CH_2Cl_2 (1 mL) was treated with $BF_3{\cdot}OEt_2$ (56 µL, 0.44 mmol) and stirred at -40 °C for 2 min. The reaction was then treated with a 0.5 M

solution of enolsilane (0.54 mL, 0.27 mmol) in CH_2Cl_2 over 5 min followed by CH_2Cl_2 rinse (0.2 mL). The reaction stirred for 30 min at -40 °C and was then treated with a second portion of $BF_3{\cdot}OEt_2$ (28 µL, 0.22 mmol) and stirred for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (1 mL), warmed to room temperature, then diluted with CH_2Cl_2 (3 mL) and water (1 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by column chromatography (5% EtOAc/Hexanes to 8% EtOAc/Hexanes) afforded tetrahydropyran (+)-**4** (144 mg, 0.13 mmol) in 59% yield as clear oil as well as recovered ketone (+)-**S8** (103 mg, 0.14 mmol) for 85% yield based on recovered ketone. $[\alpha]^{20}_D$ = +49.1 (c = 0.25, CH_2Cl_2); IR (film) 2947, 2864, 1733, 1586, 1471, 1259, 1166, 882, 837 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ -0.19 (s, 3H), 0.04 (s, 3H), 0.08 (s, 3H), 0.10 (s, 3H), 0.97 (m, 21H), 1.14 (m, 39H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.29 (m, 9H), 1.82 (ddd, *J* = 6.7, 11.7, 13.2 Hz, 1H), 2.14 (dd, *J* = 3.6, 13.2 Hz, 1H), 2.36 (s, 3H), 2.68 (d, *J* = 15.0 Hz, 1H) 2.87 (dd, *J* = 3.7, 6.9 Hz, 1H), 2.96 (m, 3H), 3.65 (m, 1H), 3.67 (s, 3H), 3.74 (dd, *J* = 5.8, 10.3 Hz, 1H), 3.79, (m, 1H), 3.96 (dd, *J* = 1.9, 10.3 Hz, 1H), 4.04 (t, *J* = 6.7 Hz, 1H), 4.09 (d, 9.5 Hz, 1H), 4.46 (m, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 6.47 (s, 1H), 7.10 (t, 7.5, 7.5 Hz, 2H), 7.21 (t, *J* = 7.5, 7.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ -4.7, -4.0, 12.5, 13.2, 13.5, 13.6, 13.8, 18.2, 18.2, 18.3, 23.7, 26.1, 26.4, 30.3, 35.4, 39.0, 44.5, 51.5, 54.2, 58.6, 71.2, 72.0, 73.3, 73.8, 75.1, 75.3, 79.0, 107.1, 121.4, 121.8, 127.5, 127.9, 128.2, 137.2, 139.7, 151.6, 155.5, 169.3, 210.4; MS (ESI+) for $C_{62}H_{112}O_{10}Si_4$ [M+Cs] calc 1261.6387 found 1261.638.

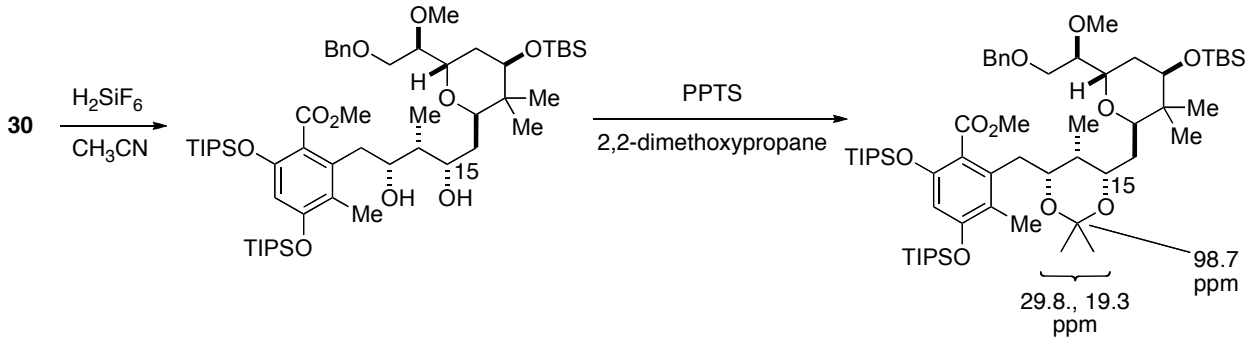
30

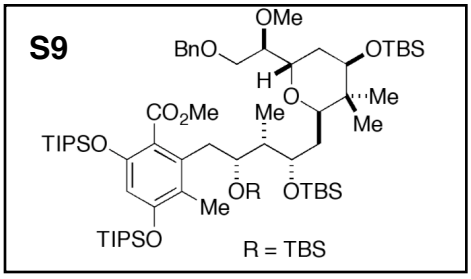


Alcohol (+)-30. A room temperature solution of ketone (+)-**4** (103 mg, 0.091 mmol) in THF (2.2 mL) was treated with (R)-2-methyl-CBS-oxazaborolidine 1 M in toluene (0.18 mL, 0.18 mmol) followed by 1 M $BH_3{\cdot}THF$ in THF (0.18 mL, 0.18 mmol) and stirred for 2 h. The reaction was quenched with saturated aqueous $NaHCO_3$, diluted with CH_2Cl_2 and stirred for 15 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2, dried over Na_2SO_4, filtered, concentrated, and purified by column

chromatography (8% EtOAc/Hexanes) to give alcohol (+)-**30** (84 mg, 0.074 mmol) in 82% yield as clear oil. $[\alpha]^{21}_D$ = +30.6 (c = 0.26, CH_2Cl_2); IR (film) 3508, 2948, 2866, 1729, 1589, 1470, 1344, 1256, 1165, 1070, 881, 836, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ -0.43 (s, 3H), -0.11 (s, 3H), -0.08 (s, 6H), 0.81 (s, 9H), 0.88 (s, 3H), 0.91 (s, 3H), 0.92 (s, 9H), 0.99 (d, *J* = 6.5 Hz, 3H), 1.12 (m, 36H), 1.28 (m, 6H), 1.58 (m, 1H), 1.74 (m, 3H), 1.97 (m, 1H), 2.19 (s, 3H), 2.72 (m, 1H), 2.97 (dd, *J* = 10.5, 13.5 Hz, 1H), 3.50 (s, 3H), 3.53 (m, 1H), 3.61 (m, 3H), 3.81 (m, 4H), 3.92 (m, 1H), 3.98 (m, 1H), 4.05 (m, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 2H), 6.21 (s, 1H), 7.33 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.33, -5.09, -4.99, -4.22, 11.19, 12.95, 12.99, 13.17, 17.87, 17.88, 17.98, 18.01, 23.84, 25.75, 25.93, 29.71, 33.00, 34.88, 39.03, 45.73, 51.63, 58.42, 69.13, 70.69, 71.77, 72.32, 73.36, 77.25, 78.90, 81.92, 106.04, 119.85, 121.43, 127.43, 127.53, 127.58, 128.20, 128.23, 137.80, 138.21, 150.79, 154.95, 169.66; MS (ESI+) for $C_{62}H_{114}O_{10}Si_4$ [M+Cs] calc 1263.654 found 1263.652.

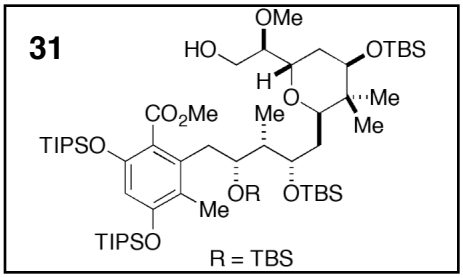
Determination of the C15 Stereochemistry via Rychnovsky Acetonide Method



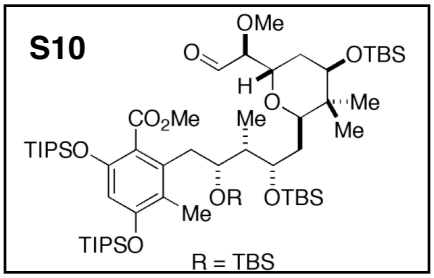


TBS ether (+)-S9. To a 0 °C solution of alcohol (+)-**30** (154 mg, 0.136 mmol) in CH_2Cl_2 (0.7 mL) was added 2,6-lutidine (40 µL, 0.544 mmol) followed by TBSOTf (63 µL, 0.272 mmol). The reaction stirred for 15 min and was warmed to room temperature over 1 h, stirred 15 h at room temperature, and was quenched with $NaHCO_3$ (0.5 mL) and CH_2Cl_2 (0.5 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (4 x 3 mL), the organics combined, dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (Hexanes to 3% EtOAc/Hexanes)

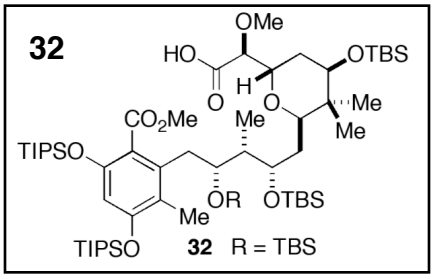
gave TBS ether (+)-**S9** (144 mg, 0.116 mmol) in 85% yield as clear oil. $[\alpha]^{25}_D$ = +25.3 (c = 0.25, CH_2Cl_2); IR (film) 2949, 2866, 1729, 1588, 1256, 1165, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.42 (s, 3H), -0.15 (s, 3H), 0.06 (m, 12H), 0.87 (m, 33H), 1.09 (m, 39H), 1.28 (m, 6H), 1.59 (m, 2H), 1.75 (m, 2H), 1.89 (m, 1H), 2.20, (s, 3H), 2.73 (m, 1H), 2.80 (m 1H), 3.35 (d, *J* = 8.4 Hz, 1H), 3.46 (s, 3H), 3.52 (m, 3H), 3.72 (d, *J* = 8.8 Hz, 2H) 3.81 (s, 3H), 3.98 (brs, 2H), 4.54 (m, 2H), 6.18 (s, 1H), 7.28 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.7, -4.7, -4.2, -3.2, -1.0, 10.6, 13.1, 13.2, 17,9, 18.0, 18.0, 18.1, 18.1, 18.1, 24.6, 25.9, 26.1, 26.3, 29.7, 29.9, 33.9, 35.2, 38.6, 43.2, 51.5, 58.7, 69.5, 71.0, 73.2, 73.4, 79.3, 106.1, 120.5, 121.3, 127.8, 127.4, 128.1, 137.5, 138.8, 150.9, 155.0, 169.5; MS (ESI+) for $C_{68}H_{128}O_{10}Si_5$ [M+Cs] calc 1377.741 found 1377.744



Alcohol (+)-31. A degassed solution of benzyl ether **S9** (106 mg, 0.085 mmol) in THF (0.57 mL) was purged with H_2 and treated with $Pd(OH)_2/C$ (24 mg). The reaction mixture was stirred under H_2 atmosphere for 5 h and was filtered through Celite®, washed with EtOAc (15 mL), and concentrated to clear oil. Purification by plug column chromatography (5% EtOAc/Hexanes) gave **31** (99 mg, 0.085 mmol) in quantitative yield as waxy white solids. $[\alpha]^{22}_D$ = +22.0 (c = 0.25 CH_2Cl_2); IR (film) 3507, 2949, 2866, 1729, 1589, 1471, 1255, 1165, 835, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ -0.31 (s, 3H), -0.12 (s, 3H), 0.32 (s, 6H), 0.07 (m, 6H), 0.80 (s, 3H), 0.82 (s, 9H), 0.88 (s, 3H), 0.88 (m, 21H), 1.09 (m, 36H), 1.21 (m, 6H), 1.56 (m, 2H), 1.72 (m, 1H), 1.80 (m, 2H), 2.19 (s, 3H), 2.45 (brs 1H), 2.77 (m, 2H), 3.31 (m, 2H), 3.41 (s, 3H), 3.46 (m, 1H), 3.67 (m, 2H), 3.72 (s, 1H), 3.81 (s, 3H), 3.97 (m, 2H), 6.17 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.8, -4.4, -4.2, -3.3, 1.0, 10.6, 12.9, 13.3, 13.5, 17.9, 18.0, 18.1, 18.1, 18.2, 24.5, 25.8, 26.0, 26.2, 29.7 30.4, 33.5, 35.7, 38.6, 51.7 58.1 61.5 69.9 73.0, 75.6, 80.54, 106.2, 120.4, 121.2 137.2 150.9 155.1 169.8; MS (ESI+) for $C_{61}H_{122}O_{10}Si_5$ [M +Cs] calc 1287.694 found 1287.694

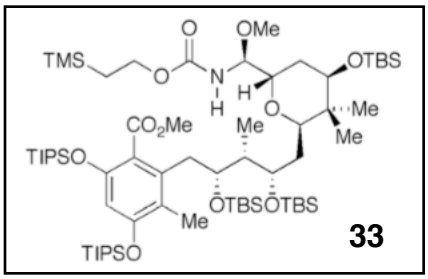


Aldehyde (+)-S10. To a solution of 2.0 M oxalyl chloride in CH_2Cl_2 (85 µL, 0.170 mmol) in CH_2Cl_2 (0.27 mL) at -78 °C was added a solution of DMSO (24 µL, 0.339 mmol) diluted with CH_2Cl_2 (24 µL). The resultant solution stirred at -78 °C for 25 min and was then treated dropwise with a solution of alcohol **31** (98 mg, 0.085 mmol) in CH_2Cl_2 (0.3 mL) at -78 °C, followed by CH_2Cl_2 rinse (2 x 0.1 mL). The resulting cloudy white mixture was stirred at -78 °C for 1 h and was treated with triethylamine (50.0 µL, 0.339 mmol) and stirred for 30 min at -78 °C. The reaction mixture was warmed to 0 °C for 1 h and quenched with saturated $NaHCO_3$. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 4 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by plug column (Hexanes to 4% Ethyl Acetate/Hexanes) afforded aldehyde (+)-**S10** (75.5 mg, 0.065 mmol) in 79% yield. $[\alpha]^{25}_D$ = +26.0 (c = 0.25, CH_2Cl_2); IR (film) 2949, 2866, 2732, 2713, 1731, 1589, 1471, 1256, 1165, 836, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ -0.39 (s, 3H), -0.12 (s, 3H), 0.03 (s, 6H), 0.08 (m, 6H), 0.80 (s, 3H), 0.82 (m, 6H), 0.88 (m, 27H), 1.09 (m, 36H), 1.22 (m, 6H), 1.52 (m, 1H), 1.63 (m, 1H), 1.75 (m, 3H), 2.19 (s, 3H), 2.77 (m, 2H), 3.42 (s, 3H), 3.50 (m, 3H), 3.72 (m, 1H), 3.81 (s, 3H), 3.94 (m, 2H), 6.17 (s, 1H), 9.66 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.2, -5.0, -4.7, -4.6, -4.4, -3.2, -3.1, 1.0, 10.2, 10.4, 12.9, 13.1, 13.2, 17.9, 18.0, 18.1, 18.1, 22.2, 24.7, 25.9, 26.1, 26.2, 26.3, 29.6, 29.7, 30.2, 33.8, 34.4, 38.4, 43.8, 51.6, 58.8, 59.2, 69.1, 72.9, 84.3, 85.7, 106.0, 120.4, 121.4, 137.5, 150.8, 155.0, 169.7, 202.1; MS (ESI+) for $C_{61}H_{120}O_{10}Si_5$ [M+Cs] calc 1285.768 found 1285.675.



Acid (+)-32. To a solution of aldehyde **S10** (75 mg, 0.065 mmol) in *t*-BuOH (3 mL) was added 2-methyl-2-butene (0.17 mL, 1.156 mmol) followed by dropwise addition of a pre-made solution of $NaClO_2$ (71 mg, 0.780 mmol) in 0.05 M potassium biphthalate pH 4 buffer (3 mL). The yellow solution stirred for 1 h, gradually becoming clear and

colorless. The reaction was then diluted with brine (10 mL) and EtOAc (10 mL) and stirred for 5 min. The layers were separated and the aqueous was extracted with EtOAc (4 x 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated, and absorbed on silica gel. Purification by column chromatography (5% EtOAc/Hexanes) afforded acid **32** (67 mg, 0.057 mmol) in 88% yield over two steps. $[\alpha]^{22}_D$ = +25.7 (c = 0.25, CH_2Cl_2); IR (film) 3168, 2949, 2866, 1721, 1589, 1471, 1255, 1166, 1069, 882, 836, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ -0.48 (s, 3H), -0.15, (s, 3H), 0.03 (s, 3H), 0.04 (s, 3H), 0.10 (s, 3H), 0.11 (s, 3H), 0.80 (m, 15H), 0.90 (m, 21H), 1.10 (m, 36H), 1.21 (m, 6H), 1.50 (m, 1H), 1.66 (m, 1H), 1.74 (m, 1H), 1.87 (m, 1H), 1.94 (m, 1H), 2.18 (s, 3H), 2.77 (m, 2H), 3.47 (m, 4H), 3.53 (m, 1H), 3.83 (s, 3H), 3.88 (m, 2H), 4.06 (m, 1H), 4.17 (m, 1H), 6.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.9, -4.7, -4.6, -4.5, -4.4, -4.3, -3.0, 1.0, 10.2, 13.1, 13.2, 17.9, 18.0, 18.1, 18.1, 18.2, 20.2, 22.3, 22.7, 24.5, 25.2, 25.8, 26.0, 26.2, 26.3, 26.5, 29.7, 29.9, 34.0, 34.7, 38.0, 43.5, 51.9, 59.1, 69.3, 72.8, 75.5, 81.4, 105.9, 120.2, 121.3, 137.7, 151.0, 170.1, 172.4; MS (ESI+) for $C_{61}H_{120}O_{11}Si_5$ [M+Cs] calc 1301.673 found 1301.679.

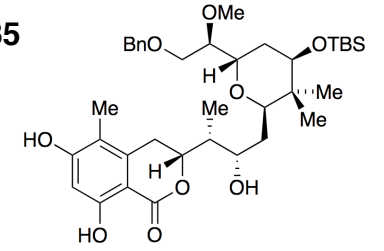


33

Teoc-Protected Hemiaminal (+)-33. A 0 °C solution of carboxylic acid (+)-**32** (11.0 mg, 0.009 mmol) in anhydrous acetone (0.75 mL) was treated with triethylamine (3.1 µL, 0.023 mmol) followed by ethylchloroformate (2.0 µL, 0.021 mmol) and stirred at 0 °C for 30 min. The reaction mixture was then treated with a 0.62 M aqueous solution of NaN_3 (30 µL, 0.019 mmol), stirred at 0 °C for 2 h, poured into ice water (3 mL) and extracted with cold ether (5 x 3 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated at 30 °C. The residue was dissolved in toluene, dried again over Na_2SO_4, filtered, flushed with argon and set into a pre-heated 120 °C sand bath and stirred for 40 min. The reaction mixture was cooled to 50 °C and the solvent removed *in vacuo*. The residue was cooled to room temperature and charged with anhydrous DMF (50 µL). The solution was treated with β-trimethylsilylethanol (47 µL , 0.33 mmol) followed by copper(I) chloride (1.0 mg, 0.009 mmol), giving a pale green mixture. The reaction mixture stirred for 2 h giving a more intense green mixture that

was diluted with water (2 mL) and ether (2 mL). The layers were separated and the aqueous layer was extracted with ether (4 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to clear oil. Purification by column chromatography (3.5% ether/hexanes) afforded hemiaminal (+)-**33** (9.1 mg, 0.007 mmol) in 76% yield as clear oil. $[\alpha]^{25}_D$ = +30.3 (c = 0.25, CH_2Cl_2); IR (film) 3436, 2950, 2866, 1730, 1588, 1471, 1252, 1166, 1067, 836, 773; ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.51 (s, 3H), -0.10 (s, 3H), 0.03 (m, 15H), 0.07 (s, 6H), 0.81 (m, 12H), 0.88 (s, 9H), 0.89 (m, 12H), 1.01 (m, 2H), 1.09 (m, 36H), 1.25 (m, 9H), 1.49 (m, 1H), 1.57 (m, 1H), 1.79 (m, 3H), 2.19 (s, 3H), 2.70 (m, 1H), 2.85 (dd, *J* = 10.5, 14.5 Hz, 1H), 3.32 (s, 3H), 3.41 (m, 1H), 3.52 (m, 1H), 3.84 (s, 3H), 3.86 (m, 1H), 3.95 (m, 2H), 4.12 (m, 1H), 4.22 (m, 1H), 4.90 (m, 1H), 5.30 (brs, 1H), 6.16 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.8, -4.6, -4.4, -4.4, -1.5, 0.7, 1.0, 1.3, 10.4, 13.0, 13.1, 13.2, 13.3, 17.6, 17.8, 17.9, 18.0, 18.1, 22.7, 23.7, 25.8, 25.9, 26.0, 26.1, 26.2, 29.7, 31.0, 33.7, 38.2, 42.6, 51.7, 55.4, 63.1, 69.3, 72.9, 82.3, 105.9, 120.2, 121.5, 137.7, 150.9, 154.9, 157.0, 169.8; MS (ESI+) for $C_{66}H_{133}NO_{11}Si_6$ [M+Cs] calc 1416.7549 found 1416.753.

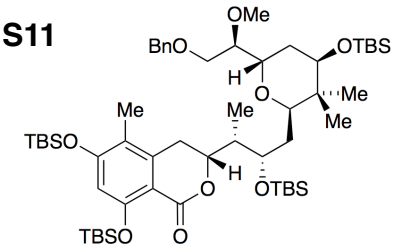
35



Lactone (+)-35. To a 0 °C solution of silyl ether (+)-**30** (70 mg, 0.062 mmol) in DMF (1.0 mL) was added 1.0 M TBAF in THF (0.37 mL, 0.37 mmol) and the reaction stirred for 2 h at 0 °C. The reaction was quenched with saturated aqueous NH_4Cl, the layers were separated, and the aqueous layer was extracted with EtOAc (5 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to orange oil. Purification by column chromatography (25% EtOAc/Hexanes to 40% EtOAc/Hexanes) provided the lactone (+)-**35** (32 mg, 0.048 mmol) in 77% yield as white waxy solid. $[\alpha]^{23}_D$ = +29.1 (c = 0.26, CH_2Cl_2); IR (film) 3378, 2929, 2857, 1661, 1619, 1496, 1470, 1374, 1253, 1172, 1102, 836, 775, 737, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.89 (s, 3H), 0.90 (s, 9H), 0.94 (s, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.50 (d, *J* = 15.3 Hz, 1H), 1.57 (m, 1H), 1.93 (m, 5H), 2.15 (m, 1H), 2.81 (dd, 12.3, 16.5 Hz, 1H), 2.98 (dd, *J* = 3.0, 16.5 Hz, 1H), 3.45 (s, 3H), 3.49 (q, *J* = 5.0, 8.6 Hz, 1H), 3.59 (m, 3H), 3.76 (dd, *J* = 3.5, 10.7 Hz, 1H), 4.04 (d, *J* = 10.0 Hz, 1H), 4.17 (q, *J* = 5.9, 10.7

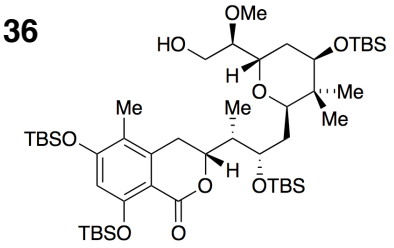
Hz, 1H), 4.25 (brs, 1H), 4.48 (ddd, *J* = 3.0, 6.3, 12.3 Hz, 1H), 4.52 (d, *J* = 11.9 Hz, 1H), 4.58 (d, *J* = 11.9 Hz, 1H), 6.29 (s, 1H), 7.28 (m, 6H), 11.17 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.3, 9.6, 10.5, 18.0, 25.0, 25.8, 28.1, 30.2, 32.3, 38.5, 42.8, 58.4, 69.0, 72.7, 72.7, 73.5, 80.5, 80.6, 82.6, 101.2, 101.4, 113.6, 127.7, 127.7, 128.4, 138.0, 139.8, 161.4, 162.2, 170.8; MS (ESI+) for $C_{37}H_{56}O_9Si$ [M+Cs] calc 805.2748 found 805.2814.

S11



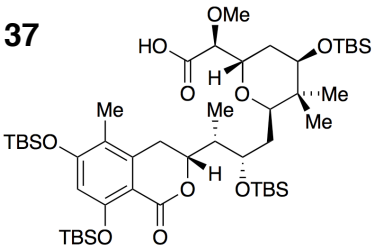
TBS ether (+)-S11. To a 0 °C solution of triol (+)-**35** (31 mg, 0.046 mmol) in THF (0.4 mL) was added 2,6-lutidine (27 µL, 0.37 mmol) followed by TBSOTf (42 µL, 0.18 mmol). The reaction stirred for 2 h at 0 °C and was quenched with $NaHCO_3$ (0.4 mL) and diluted with CH_2Cl_2 (0.4 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 2 mL), the organics combined, dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (Hexanes to 5% EtOAc/ Hexanes) gave TBS ether (+)-**S11** (39 mg, 0.038 mmol) in 83% yield as clear oil. $[\alpha]^{25}_D$ = +46.5 (c = 0.49, CH_2Cl_2); IR (film) 2955, 2930, 2857, 1725, 1592, 1568, 1472, 1360, 1252, 1166, 1069, 1005, 837, 776 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H), 0.10 (s, 3H), 0.25 (s, 3H), 0.27 (m, 9H), 0.84 (s, 9H), 0.09 (s, 3H), 0.93 (s, 9H), 0.96 (s, 3H), 1.05 (s, 9H), 1.05 (s, 9H), 1.10 (d, *J* = 6.7 Hz, 3H), 1.65 (m, 2H), 2.00 (m, 3H), 2.05 (s, 3H), 2.60 (dd, *J* = 12.2, 16.1 Hz, 1H), 2.99 (m, 1H), 3.37 (m, 1H), 3.50 (s, 3H), 3.51 (m, 1H), 3.61 (m, 2H), 3.71 (dd, *J* = 3.6, 10.3 Hz, 1H), 4.01 (q, *J* = 5.5, 10.9 Hz, 1H), 4.13 (m, 1H), 4.26, (m, 1H), 4.56 (s, 2H), 6.34 (s, 1H), 7.28 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.9, -4.8, -4.4, -4.4, -4.3, -4.2, -4.2, -3.4, 9.0, 11.8, 18.0, 18.1, 18.3, 18.6, 25.2, 25.7, 25.8, 25.9, 29.9, 30.0, 33.1, 38.2, 40.1, 58.6, 68.7, 69.3, 69.6, 73.3, 73.5, 76.3, 77.2, 79.0, 80.7, 110.6, 110.7, 118.6, 127.4, 127.5, 128.3, 138.3, 141,2, 156.9, 158.3, 163.4; MS (ESI+) for $C_{55}H_{98}O_9Si_4$ [M+Cs] calc 1147.5342 found 1147.5349.

36



Alcohol (+)-36. A degassed solution of benzyl ether (+)-**S11** (41 mg, 0.040 mmol) in THF was purged with H_2 and treated with $Pd(OH)_2/C$ (11 mg). The reaction mixture stirred under H_2 pressure for 14 h and was filtered through Celite®, washed with EtOAc (15 mL), and concentrated to yellow oil. Purification by plug column (10% EtOAc/Hexanes) gave (+)-**36** (37 mg, 0.040 mmol) in quantitative yield as glassy white solids. $[\alpha]^{25}_D$ = +39.2 (c = 0.24, CH_2Cl_2); IR (film) 3460, 2955, 2930, 2885, 2857, 1708, 1592, 1567, 1472, 1360, 1253, 1166, 1069, 837, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 3H) 0.06 (s, 3H), 0.07 (s, 3H), 0.10 (s, 3H), 0.22 (s, 3H), 0.23 (s, 3H), 0.24 (s, 6H), 0.84 (s, 9H), 0.85 (s, 3H), 0.90 (s, 9H), 0.91 (s, 3H), 1.01 (s, 18H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.70 (m, 2H), 1.91 (m, 2H), 1.99 (m, 1H), 2.07 (s, 3H), 2.74 (dd, *J* = 12.8, 16.4 Hz, 1H), 2.99 (m, 1H), 3.22 (m, 1H), 3.32 (m, 1H), 3.43 (m, 1H), 3.55 (s, 3H), 3.59 (m, 1H), 3.64 (m, 1H), 3.80 (m, 1H), 4.03 (m, 1H), 4.24 (m, 2H), 6.29 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.9, -4.6, -4.3, -4.2, -4.2, -4.1, -3.2, 8.6, 11.7, 18.0, 18.1, 18.3, 18.5, 24.8, 25.7, 25.9, 25.9, 25.9, 29.1, 30.8, 34.4, 38.4, 39.9, 59.2, 62.4, 67.9, 73.1, 76.3, 76.8, 77.2, 79.6, 81.0, 110.1, 110.5, 118.8, 141.7, 157.1, 158.6, 164.3; MS (ESI+) for $C_{48}H_{92}O_9Si$ [M+Cs] calc 1057.4873 found 1057.4695.

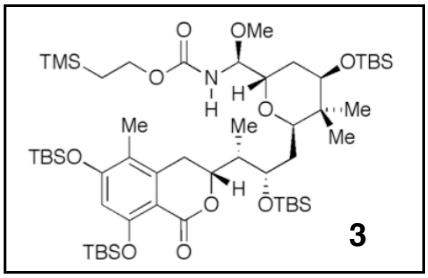
37



Acid (+)-37. To a solution of oxalyl chloride (7.5 µL, 0.086 mmol) in CH_2Cl_2 (0.20 mL) at -78 °C was added DMSO (12.5 µL, 0.173 mmol). The resultant solution stirred at -78 °C for 30 min and was then treated dropwise with a solution of alcohol (+)-**S11** (40 mg, 0.043 mmol) in CH_2Cl_2 (0.2 mL) at -78 °C, followed by CH_2Cl_2 rinse (2 x 0.1 mL). The resulting cloudy white mixture stirred at -78 °C for 1 h and was treated with triethylamine (24.0 µL, 0.173 mmol) and stirred for 30 min at -78 °C. The reaction mixture was warmed to 0 °C for 40 min then warmed to room temperature for 20 min and quenched with saturated $NaHCO_3$. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 3 mL), the combined organic layers were dried over Na_2SO_4, filtered

and concentrated. Filtration through a silica gel plug (Hexanes to 25% Ether/Hexanes) afforded the intermediate aldehyde (40 mg, 0.043 mmol), which was immediately taken on to the next step.

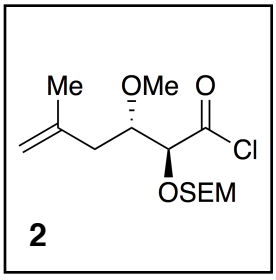
To a solution of the intermediate aldehyde (41 mg, 0.044 mmol) in *t*-BuOH (2.13 mL) was added 2-methyl-2-butene (0.11 mL, 1.065 mmol) followed by dropwise addition of a pre-made solution of $NaClO_2$ (60.2 mg, 0.533 mmol) in 0.05 M potassium biphthalate pH 4 buffer (2.13 mL). The yellow solution stirred for 1 h, gradually becoming clear and colorless. The reaction mixture was then diluted with brine and EtOAc and stirred for 5 min. The layers were separated and the aqueous layer was extracted with EtOAc (4 x 4 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (25% EtOAc/ Hexanes) afforded acid (+)-**37** (38.5 mg, 0.041 mmol) in 93% yield over two steps. $[\alpha]^{25}_D$ = +53.3 (c = 0.26, CH_2Cl_2); IR (film) 3159, 2956, 2930, 2857, 1725, 1592, 1567, 1360, 1255, 1168, 1071, 1005, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.00 (s, 3H), -0.07 (s, 6H), 0.16 (s, 3H), 0.21 (s, 3H), 0.22 (s, 3H), 0.25 (s, 3H), 0.26 (s, 3H), 0.86 (s, 9H), 0.88 (s, 3H), 0.91 (s, 9H), 0.96 (d, *J* = 7.2 Hz, 3H), 0.99 (s, 3H), 1.00 (s, 9H), 1.01 (s, 9H), 1.55 (m, 1H), 1.83 (m, 2H), 2.04 (s, 3H), 2.18 (m, 2H), 2.82 (dd, *J* = 2.4, 16.8 Hz, 1H), 3.01 (dd, *J* = 13.2, 16.8 Hz, 1H), 3.40 (m, 1H), 3.43 (s, 3H), 3.61 (m, 1H), 3.75 (d, *J* = 3.7 Hz, 1H), 4.13 (m, 1H), 4.29 (m, 1H), 4.44 (dd, *J* = 3.6, 10.4 Hz, 1H), 6.28 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.9, -4.4, -4.2, -4.2, -2.8, 8.1, 11.7, 18.0, 18.3, 18.3, 18.5, 25.7, 25.9, 26.0, 26.0, 26.0, 26.2, 28.1, 31.6, 33.1, 37.0, 37.8, 58.4, 66.5, 73.3, 77.2, 77.5, 79.7, 83.2, 109.6, 110.3, 118.9, 142.1, 157.3, 158.9, 166.0, 172.6; MS (ESI+) for $C_{48}H_{90}O_{10}Si_4$ [M+Cs] calc 1071.4665 found 1071.4554.



3

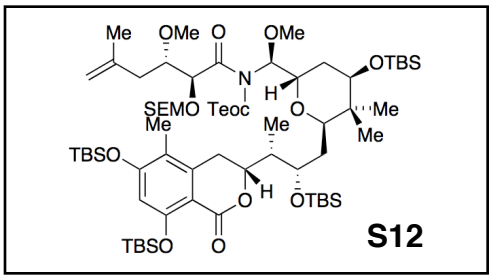
Teoc-Protected Hemiaminal (+)-3. A 0 °C solution of carboxylic acid (+)-**37** (16.0 mg, 0.017 mmol) in anhydrous acetone (1.38 mL) was treated with triethylamine (5.7 µL, 0.041 mmol) followed by ethylchloroformate (3.6 µL, 0.037 mmol) and stirred at 0 °C for 30 min. The reaction mixture was then treated with a 0.62 M aqueous solution of NaN_3 (55 µL, 0.034 mmol), stirred at 0 °C for 2 h, poured into ice water and extracted

with cold ether (5 x 3 mL). The combined extracts were dried over Na_2SO_4, filtered and concentrated at 30 °C. The residue was dissolved in toluene, dried again over Na_2SO_4, filtered, flushed with argon and set into a pre-heated 120 °C sand bath and stirred for 30 min. The reaction mixture was cooled to 50 °C and the solvent removed *in vacuo*. The residue was cooled to room temperature and charged with anhydrous DMF (0.1 mL). The solution was treated with β-trimethylsilylethanol (0.05 mL. 0.34 mmol) followed by copper(I) chloride (1.7 mg, 0.017 mmol), giving a pale green mixture. The reaction mixture stirred for 2 h giving a more intense green mixture that was diluted with water (2 mL) and ether (2 mL). The layers were separated and the aqueous layer was extracted with ether (4 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to clear oil. Purification by column chromatography (10% ether/hexanes) afforded hemiaminal (+)-**3** (13.5 mg, 0.013 mmol) in 76% yield as clear oil. $[\alpha]^{18}_D$ = +27.4 (c = 0.25, CH_2Cl_2); IR (film) 2955, 2857, 1726, 1592, 1568, 1472, 1351, 1250, 1167, 1069, 836, 776; ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.02 (s, 3H), 0.01 (s, 9H), 0.05 (s, 3H), 0.06 (s, 3H), 0.08 (s, 3H), 0.22 (s, 3H), 0.23 (s, 9H), 0.80 (s, 9H), 0.86 (s, 3H), 0.91 (s, 9H), 0.94 (m, 2H), 0.98 (s, 3H), 1.00 (s, 9H), 1.02 (s, 9H), 1.06 (d, *J* = 6.8 Hz, 3H), 1.47 (m, 1H), 1.62 (m, 1H), 1.82 (m, 1H), 1.95 (m, 1H), 2.07 (s, 3H), 2.26 (m, 1H), 2.60 (dd, *J* = 12.4, 16.4 Hz, 1H), 3.03 (m, 1H), 3.36 (s, 3H), 3.38 (m, 1H), 3.59 (m, 1H), 4.00 (m, 1H), 4.12 (m, 4H), 4.81 (m, 1H), 5.45 (m, 1H), 6.30 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.9, -4.5, -4.4, -4.4, -4.3, -4.2, -3.5, -1.5, 8.8, 11.7, 17.5, 18.0, 18.1, 18.3, 18.5, 25.7, 25.8, 25.9, 26.0, 26.5, 29.4, 29.7, 31.4, 32.4, 37.3, 39.5, 55.8, 63.3, 67.4, 68.5, 73.3, 77.4, 79.3, 84.1, 110.6, 110.7, 118.5, 141.3, 156.8, 156.9, 158.2, 163.6; MS (ESI+) for $C_{53}H_{103}NO_{10}Si_5$ [M+Cs] calc 1186.5483 found 1186.5471.



Acid Chloride-2 To a solution of carboxylic acid (-)-**S4** (9.6 mg, 0.032 mmol) in CH_2Cl_2 (0.96 mL) was added 0.62 M pyridine in CH_2Cl_2 (0.20 mL), followed by 0.48 M $SOCl_2$ (0.20 mL). The reaction mixture stirred for 2 hours and the solvent was removed under increased argon pressure, then concentrated further *in vacuo* at 30 °C. The material was suspended in d_6-benzene and analyzed by ^{1}H NMR to confirm the formation of acid chloride **2** then taken on immediately without further

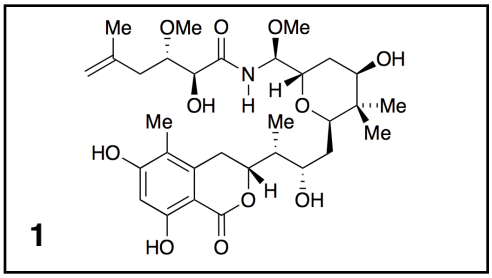
analysis as it showed significant moisture sensitivity. The NMR sample was transferred to an oven dried vial, the tube rinsed with anhydrous toluene, concentrated *in vacuo*, and dissolved in THF (0.32 mL) to make a 0.1 M solution that was used immediately in the next step. ^{1}H NMR δ -0.04 (s, 9H), 0.91 (ddd, m, 2H), 1.64 (s, 3H), 2.30 (dd, *J* = 4.4, 14.4 Hz, 1H), 2.37 (dd, *J* = 7.6, 14.4 Hz, 1H), 3.09 (s, 3H), 3.51 (ddd, *J* = 6.8, 9.6, 9.6 Hz, 1H), 3.76 (m, 2H), 4.36 (d, *J* = 5.6 Hz, 1H), 4.50 (q, *J* = 7.2, 14.8 Hz, 2H), 4.81 (m, 2H).



S12

N-Acyl Hemiaminal (+)-S12. To a -78 °C solution of hemiaminal (+)-**2** (7.5 mg, 0.0071 mmol) in THF (0.28 mL) was added a solution of 2.0 M *i*-PrMgCl in THF (12.5 µL, 0.025 mmol) and stirred for 30 min. The reaction was then treated with a 0.1 M solution of acid chloride (142 µL, 0.0142 mmol), stirred at -78 °C for 30 min, then warmed to -40 °C and stirred for 45 min. The reaction was quenched with saturated aqueous NH_4Cl (0.2 mL), warmed to room temperature and diluted with CH_2Cl_2 (4 mL) and saturated aqueous NH_4Cl (4 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4 x 3 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (5% EtOAc/Hexanes) gave fully protected irciniastatin A (+)-**S12** (8.3 mg, 0.0062 mmol) in 87% yield as well as recovered hemiaminal (+)-**3** (1.0 mg, 0.0009 mmol) in 13% yield. $[\alpha]^{23}_D$ = +42.8 (c = 0.21, CH_2Cl_2); IR (film) cm^{-1}; 3074, 2955, 2931, 2895, 2857, 2740, 2713, 1728, 1592, 1568, 1472, 1411, 1350, 1250, 1168, 1068, 938, 837, 776, 672 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) -0.05 (s, 9H), -0.04 (s, 3H), 0.03 (s, 3H), 0.04 (m, 15H), 0.21 (s, 3H), 0.22 (s, 6H), 0.23 (s, 3H), 0.76 (s, 9H), 0.81 (s, 3H), 0.83 (m, 2H), 0.89 (m, 12H), 1.00 (s, 9H), 1.01 (s, 9H), 1.08 (m, 5H), 1.62 (m, 1H), 1.67 (m, 1H), 1.74 (s, 3H), 1.77 (m, 1H) 1.95 (m, 1H), 2.13 (s, 3H) 2.00 (m, 1H), 2.20 (m, 1H), 2.29 (dd, *J* = 9.5, 14.5 Hz, 1H), 2.86 (dd, *J* = 12.5, 16.0 Hz, 1H), 3.05 (d, *J* = 15.5 Hz, 1H), 3.15 (d, *J* = 10.0 Hz, 1H), 3.27 (s, 3H), 3.34 (s, 3H), 3.54 (m, 3H), 3.62 (m, 2H), 4.09 (m, 1H), 4.18 (m, 1H), 4.29 (m, 2H), 4.64 (m, 2H), 4.76 (d, *J* = 11.5 Hz, 2H), 5.15 (d, *J* = 5.0 Hz, 1H),

5.64, (d, *J* = 5.0 Hz, 1H), 6.29 (s, 1H); δ ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.0, -4.9, -4.4, -4.3, -4.2, -4.2, -4.1, -3.3, -1.6, -1.5, -1.4, 1.0, 8.8, 11.9, 13.5, 13.5, 17.6, 18.0, 18.0, 18.1, 18.3, 18.6, 21.9, 22.8, 24.0, 25.7, 25.8, 25.9, 26.0, 29.7, 29.9, 30.3, 34.9, 38.8, 39.0, 40.4, 56.6, 58.1, 65.9, 66.1, 69.0, 72.7, 74.4, 75.3, 77.3, 79.6, 80.9, 95.8, 110.6, 110.8, 112.7, 119.0, 141.9, 142.6, 154.3, 156.7, 158.19, 163.7, 174.6; MS (ESI+) for $C_{67}H_{129}NO_{14}Si_6$ [M+Na] calc 1362.7926 found 1362.7686.

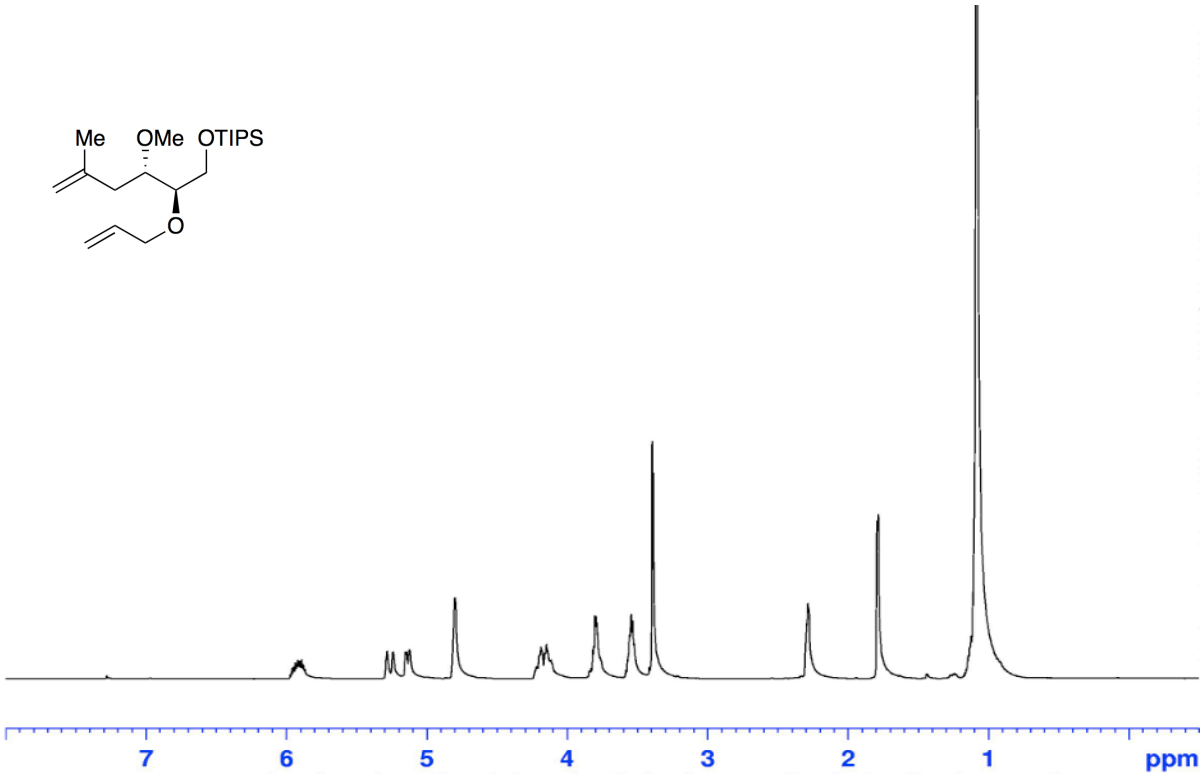


1

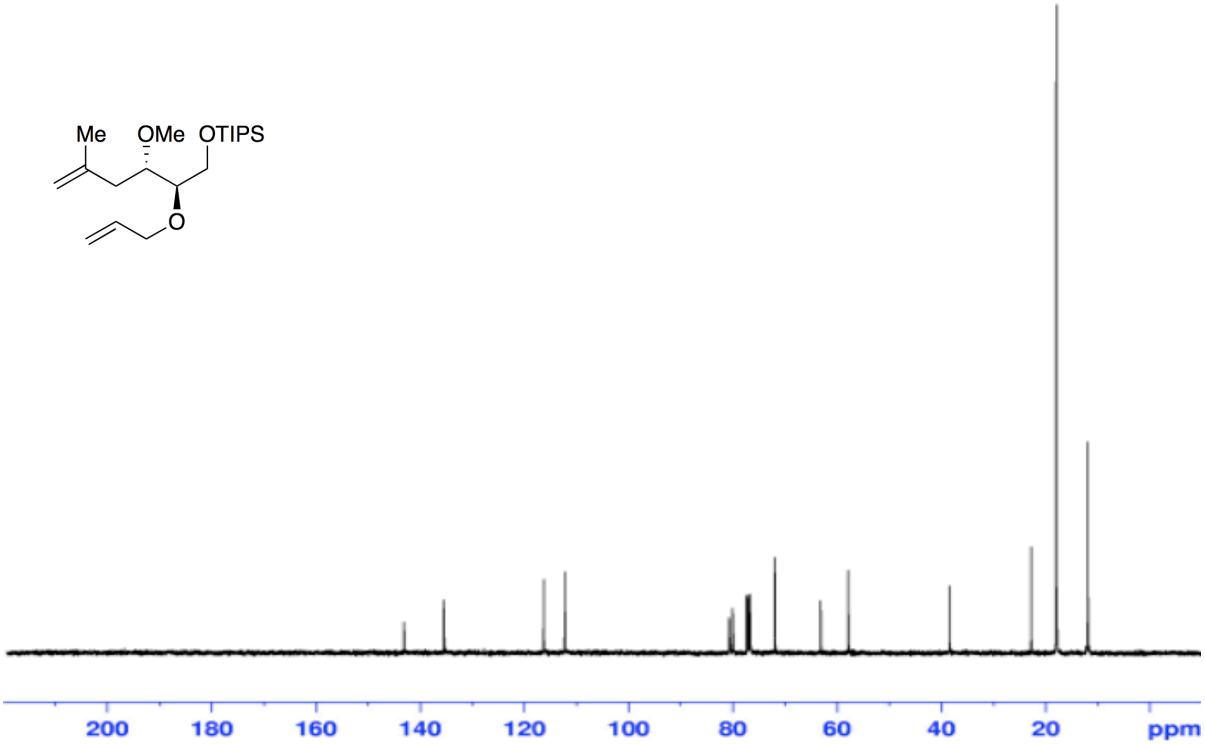
Irciniastatin A (+)-1. To a sample of fully protected irciniastatin A (+)-**S12** (7.5 mg, 0.006 mmol) in a polyethylene vial was added a prepared solution of TASF (23.1 mg, 0.084 mmol) in DMF (0.18 mL). The reaction was set in a 50 °C sand bath and stirred for 36 h. The reaction was quenched with saturated aqueous NH_4Cl (2 mL) and diluted with EtOAc (2 mL). The layers were separated and the aqueous layer was extracted with EtOAc (5 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (CH_2Cl_2 to 5% CH_2Cl_2/MeOH gradient) afforded (+)-irciniastatin A (**1**) (3.2 mg, 0.0052 mmol) 94% yield as white solids. $[\alpha]^{22}_D$ = +27.3 (c = 0.22, MeOH); IR (film) 3370, 2965, 2928, 2853, 1650, 1624, 1558, 1515, 1453, 1387, 1364, 1297, 1252, 1173, 1067, 967 cm^{-1}; ^{1}H NMR (500 MHz, MeOD) δ 0.89 (s, 3H), 0.96 (s, 3H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.72 (m, 6H), 1.89 (m, 1H), 2.00 (m, 1H), 2.06 (m, 4H), 2.34 (dd, *J* = 9.5, 14.5 Hz, 1H), 2.85 (dd, *J* = 12.0, 17.0 Hz, 1H), 3.12 (dd, *J* = 3.0, 17.0 Hz, 1H), 3.19 (s, 3H), 3.34 (s, 3H), 3.49 (m, 1H), 3.58 (dd, *J* = 4.5, 11.0 Hz, 1H), 3.66 (ddd, *J* = 3.0, 3.0, 9.0 Hz, 1H), 3.93 (m, 2H), 4.34 (d, *J* = 2.5 Hz, 1H), 4.48 (ddd, *J* = 3.5, 6.0, 12.5 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 2H), 5.38 (d, *J* = 8.0 Hz, 1H), 6.23 (s, 1H); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (s, 3H), 0.94 (s, 3H), 1.08 (d, *J* = 7.0 Hz, 3H), 1.61 (m, 2H), 1.73 (s, 3H), 1.81 (m, 2H), 1.98 (s, 3H), 2.05 (m, 1H), 2.16 (m, 1H), 2.38 (dd, *J* = 9.0, 14.5 Hz, 1H), 2.78 (m, 2H), 3.36 (s, 6H), 3.52 (m, 1H), 3.66 (m, 1H), 3.74 (m, 1H), 3.88 (m, 1H), 3.92 (m, 1H), 4.43 (m, 1H), 4.51 (m, 1H), 4.78 (s, 2H), 5.43 (t, *J* = 9.5 Hz, 1H), 6.33 (s, 1H), 7.12 (m, 1H), 11.03 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.0, 10.5, 13.7, 22.7, 23.0, 28.5, 29.6, 32.3, 37.6, 38.8, 42.6, 56.3, 57.8, 71.3, 72.9, 74.3, 78.4, 79.6, 80.6, 81.9, 100.8, 101.2, 113.1, 113.7,

139.5, 142.0, 162.0, 162.2, 170.7, 173.9; MS (ESI+) for $C_{31}H_{47}NO_{11}$ [M+Cs] calc 742.2203 found 742.2197.

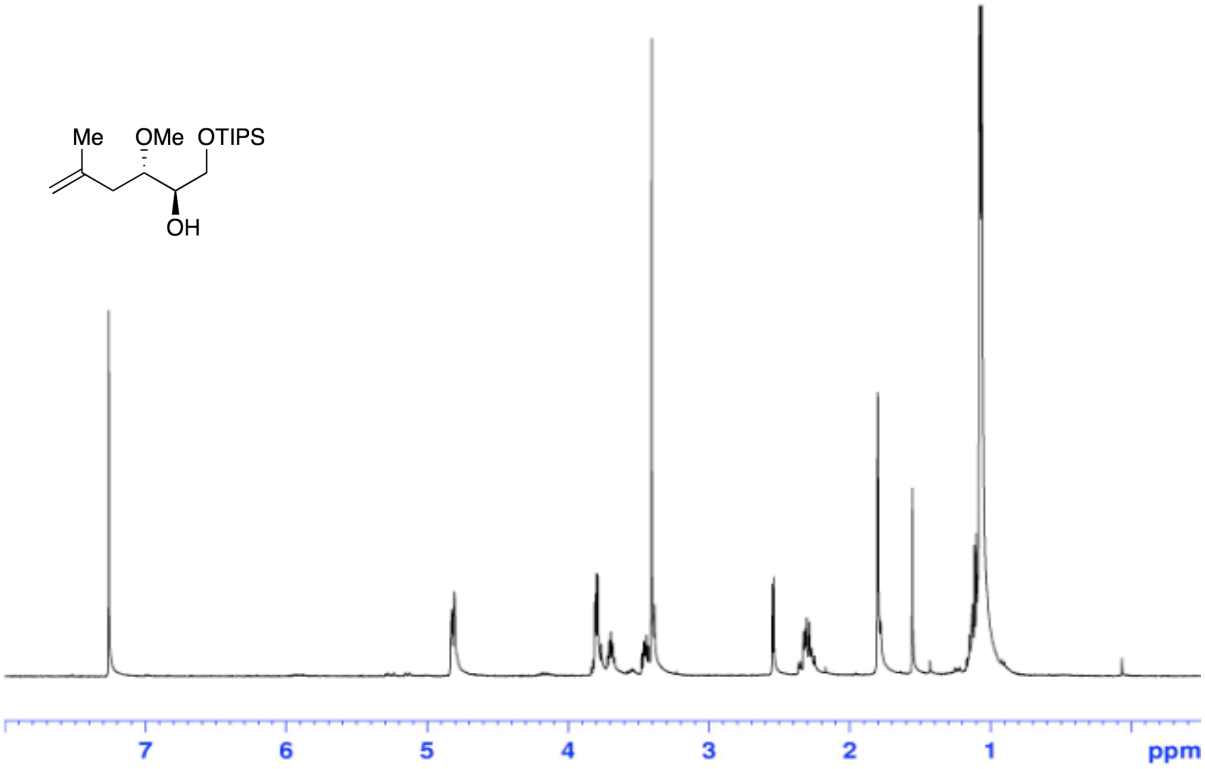
III. NMR Spectra



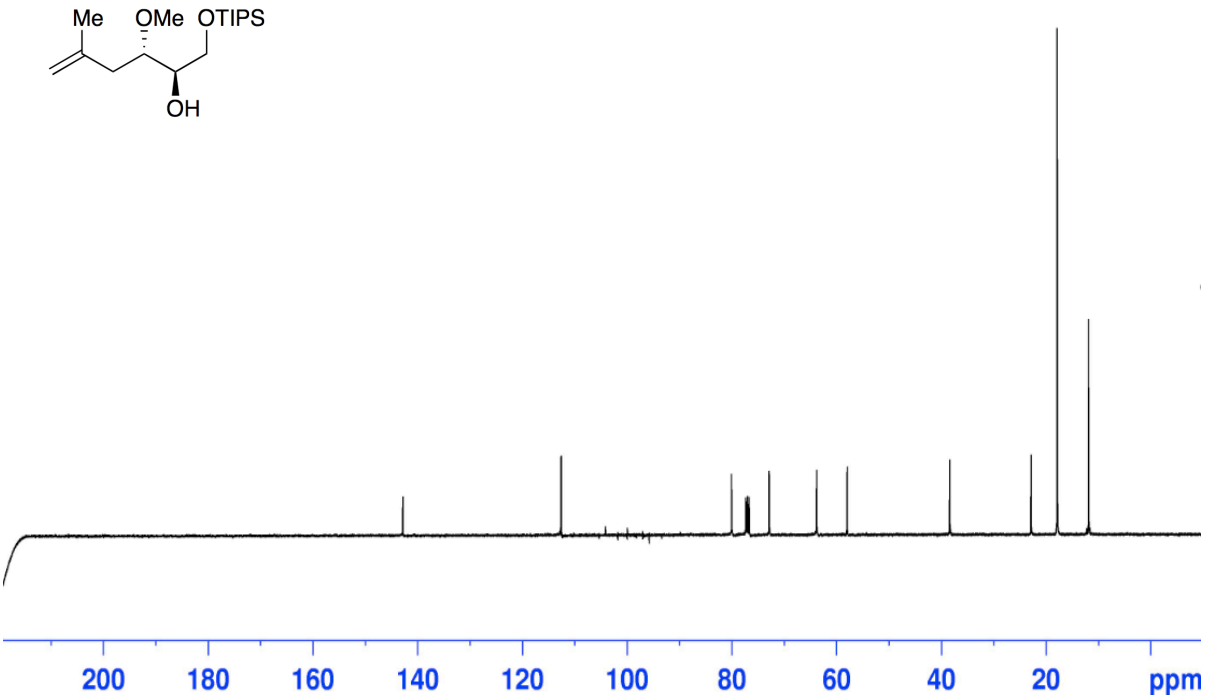
^{1}H NMR Spectra of (-)-S1; 300 MHz ($CDCl_3$)



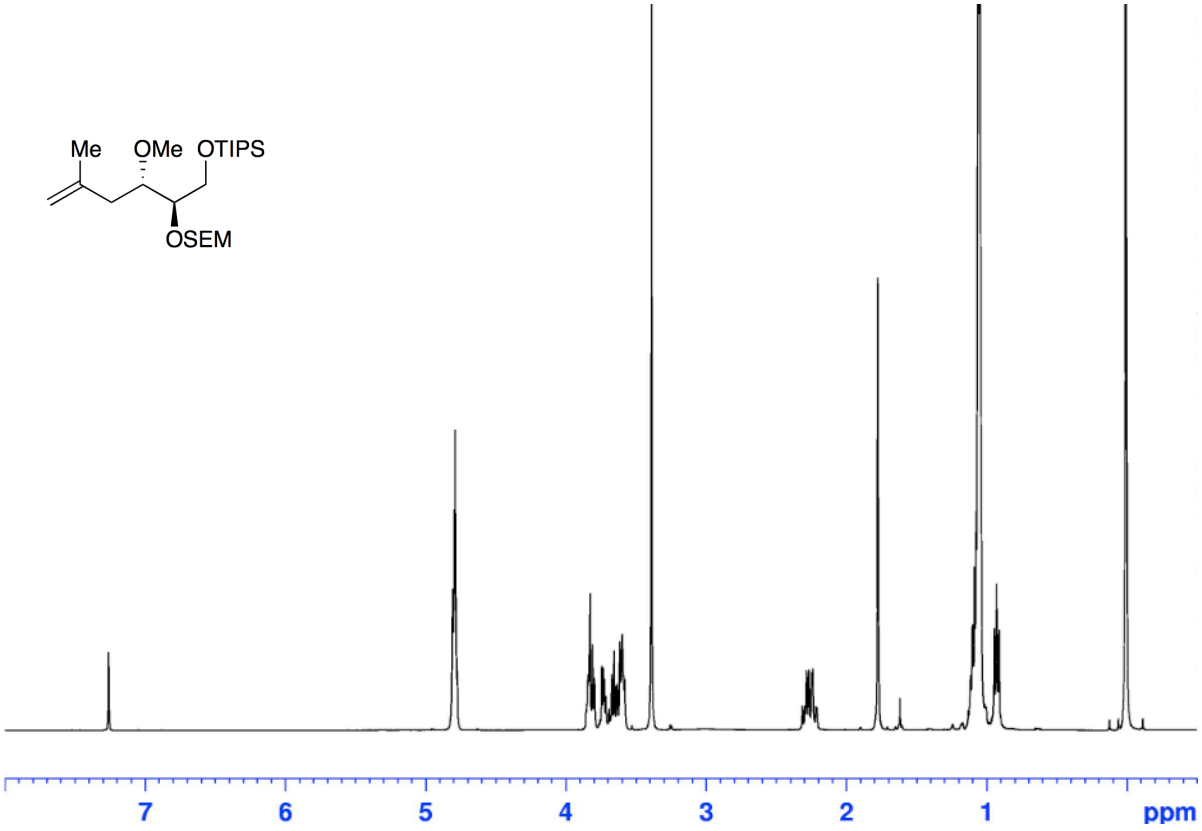
^{13}C NMR Spectrum of (1)-S1; 100 MHz ($CDCl_3$)



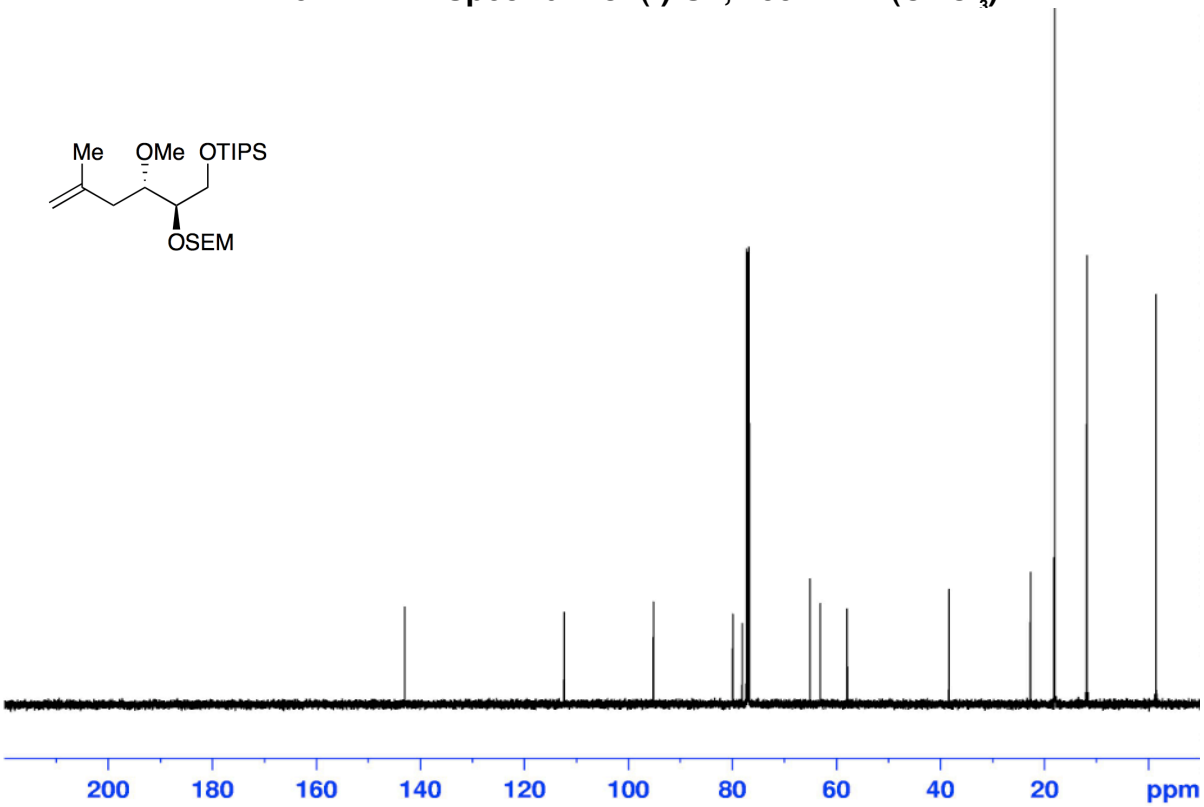
The ^{1}H NMR Spectrum of (+)-12; 400 MHz ($CDCl_3$)



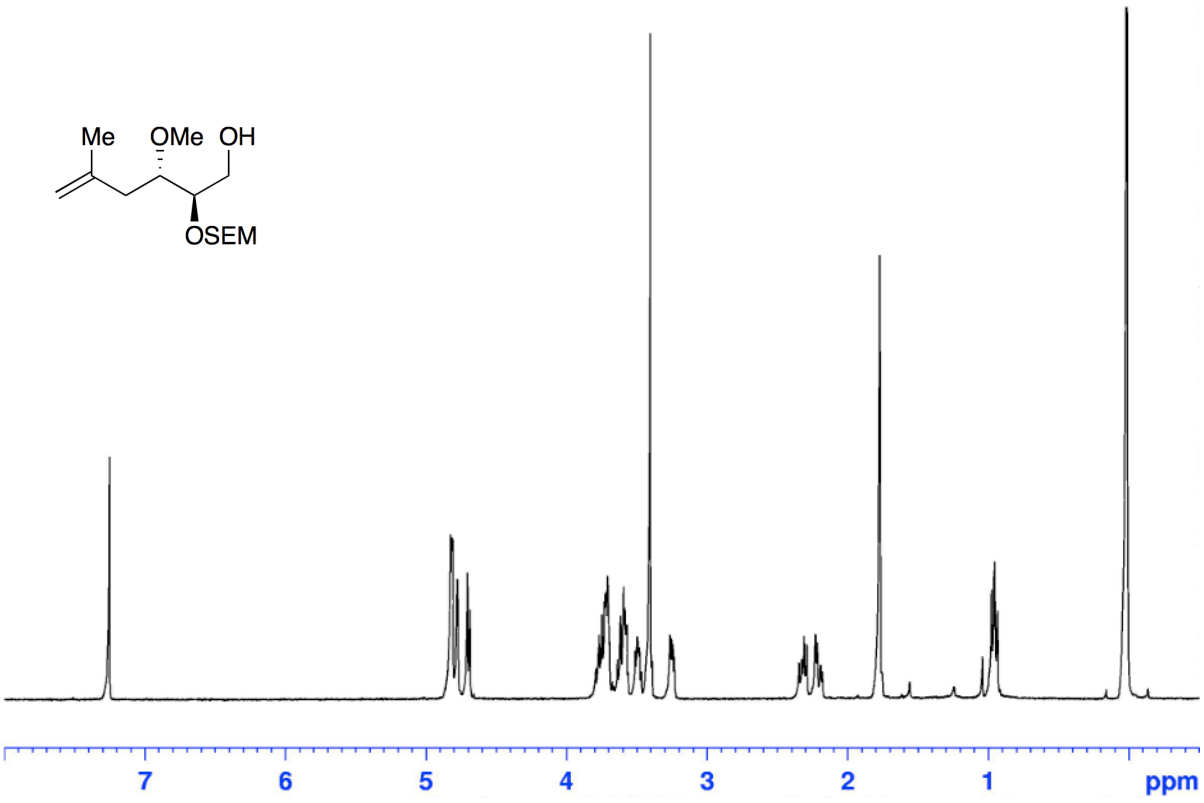
The ^{13}C NMR Spectrum of (+)-12; 100 MHz ($CDCl_3$)



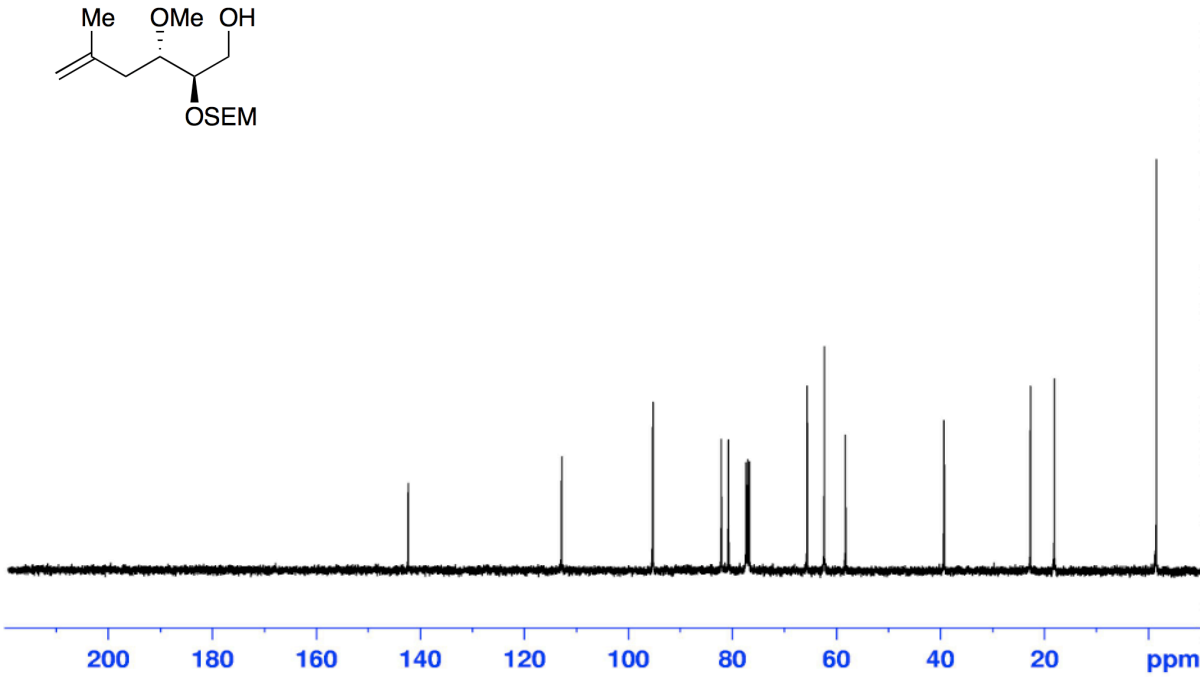
The ^{1}H NMR Spectrum of (-)-S2; 400 MHZ ($CDCl_3$)



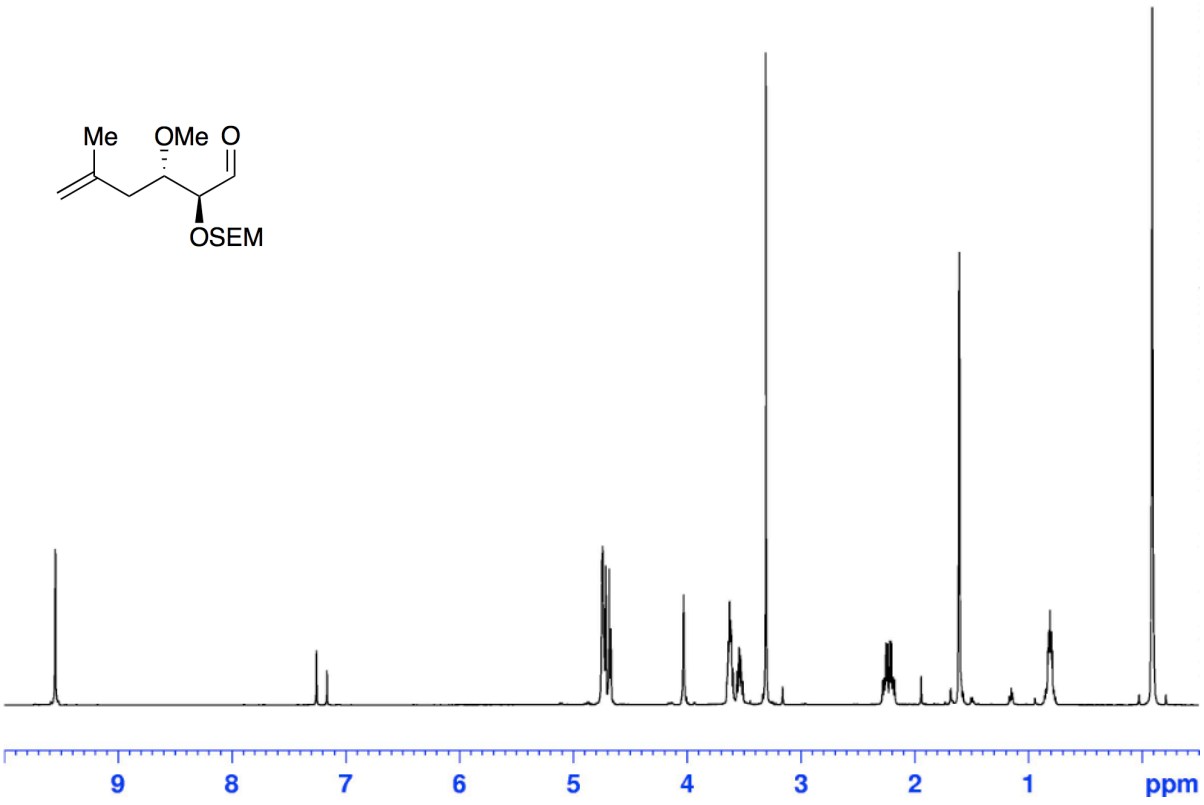
The ^{13}C NMR Spectrum of (-)-S2; 100 MHz ($CDCl_3$)



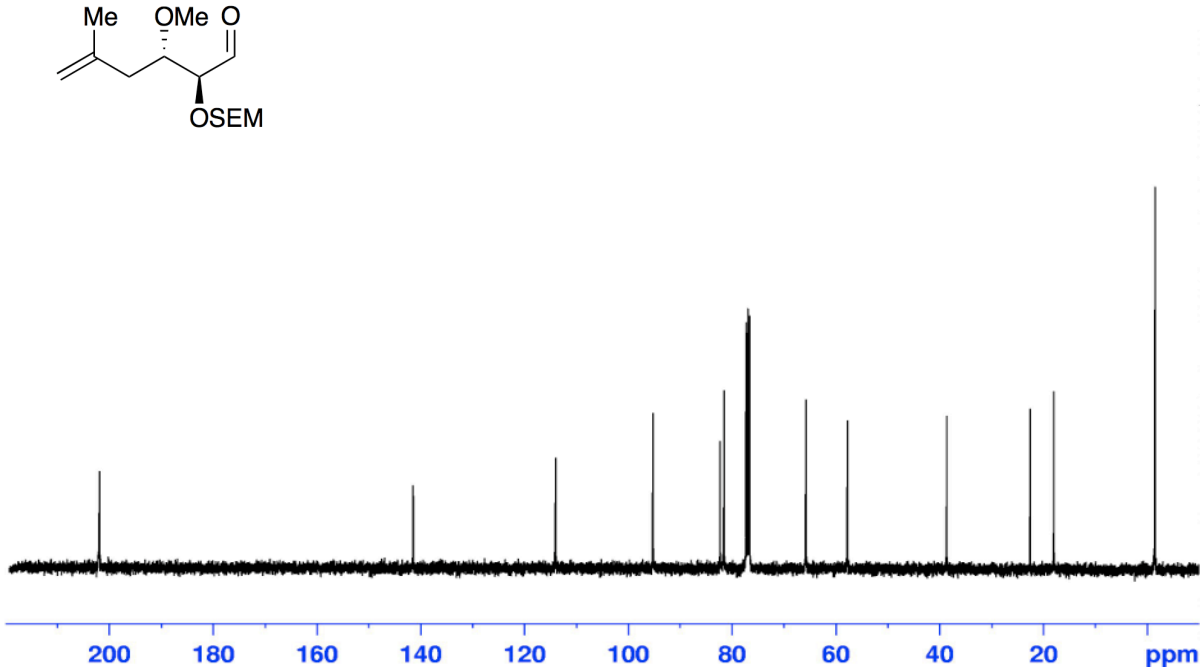
The 1H NMR Spectrum of (+)-13; 400 MHz ($CDCl_3$)



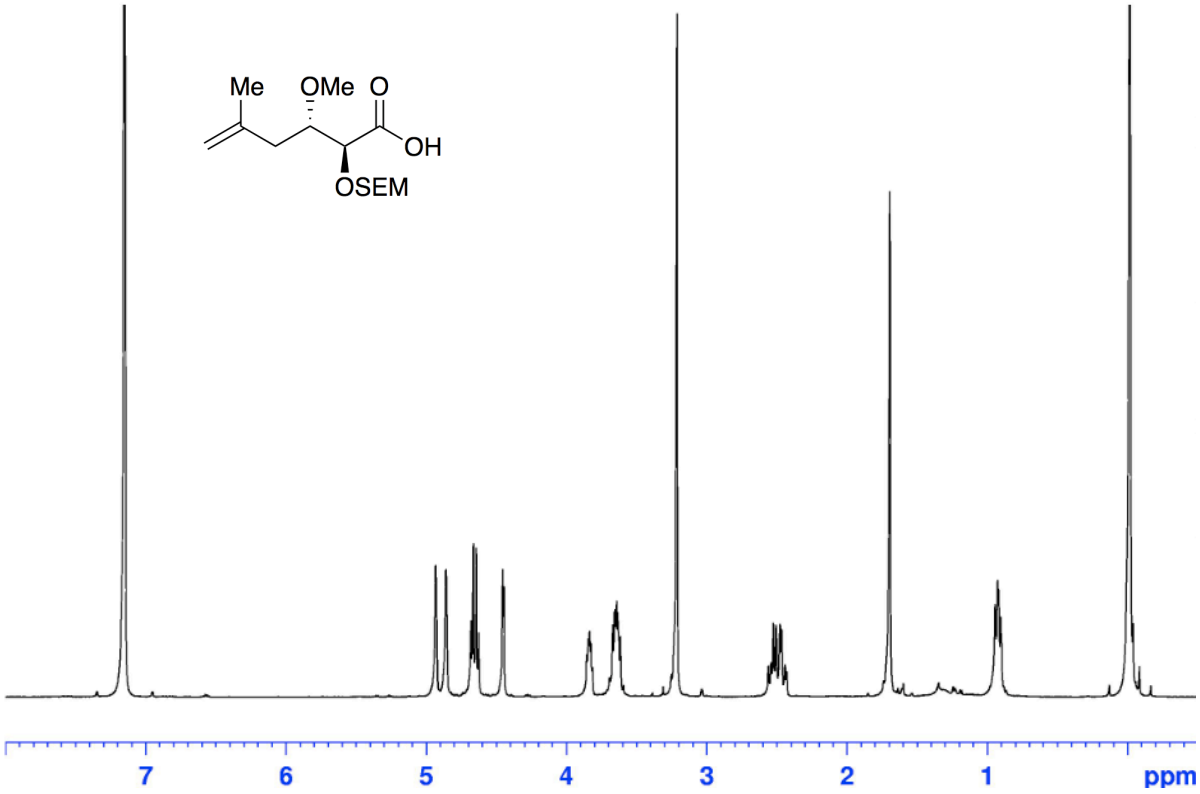
The ^{13}C NMR Spectrum of (+)-13; 100 MHz ($CDCl_3$)



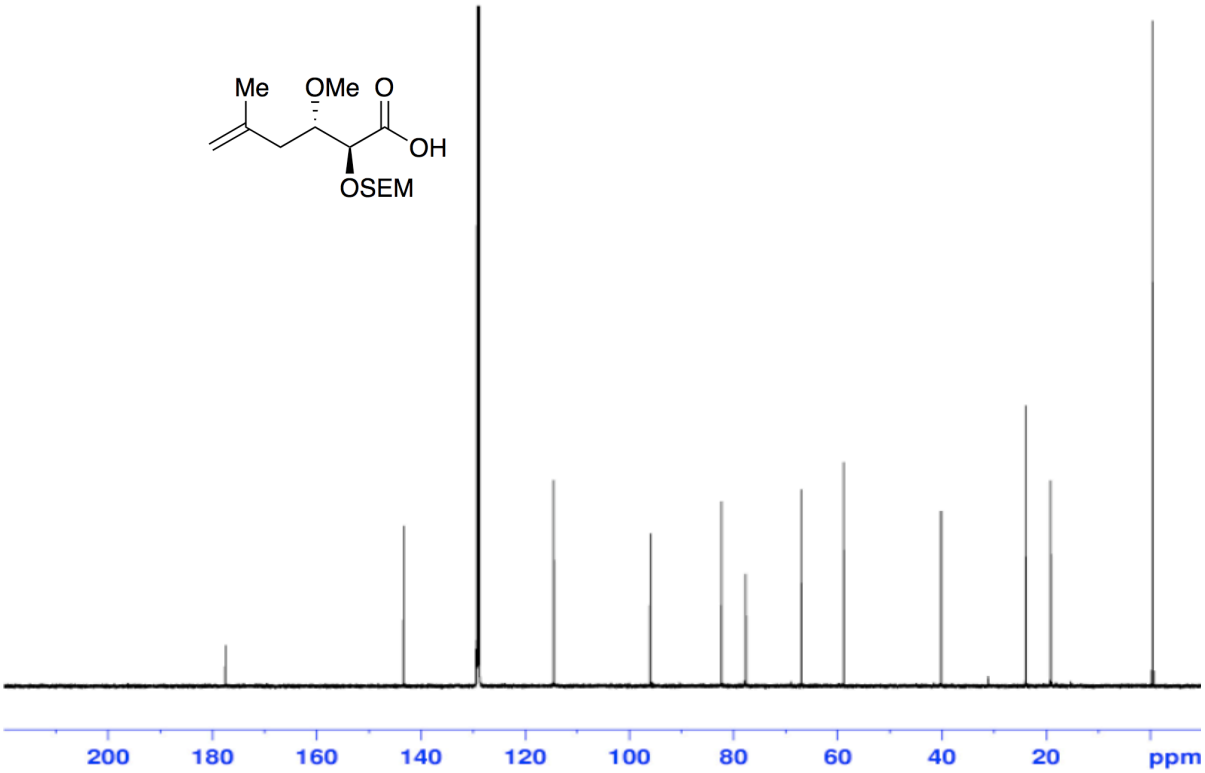
The ^{1}H NMR Spectrum of (-)-S3; 500 MHZ ($CDCl_3$)



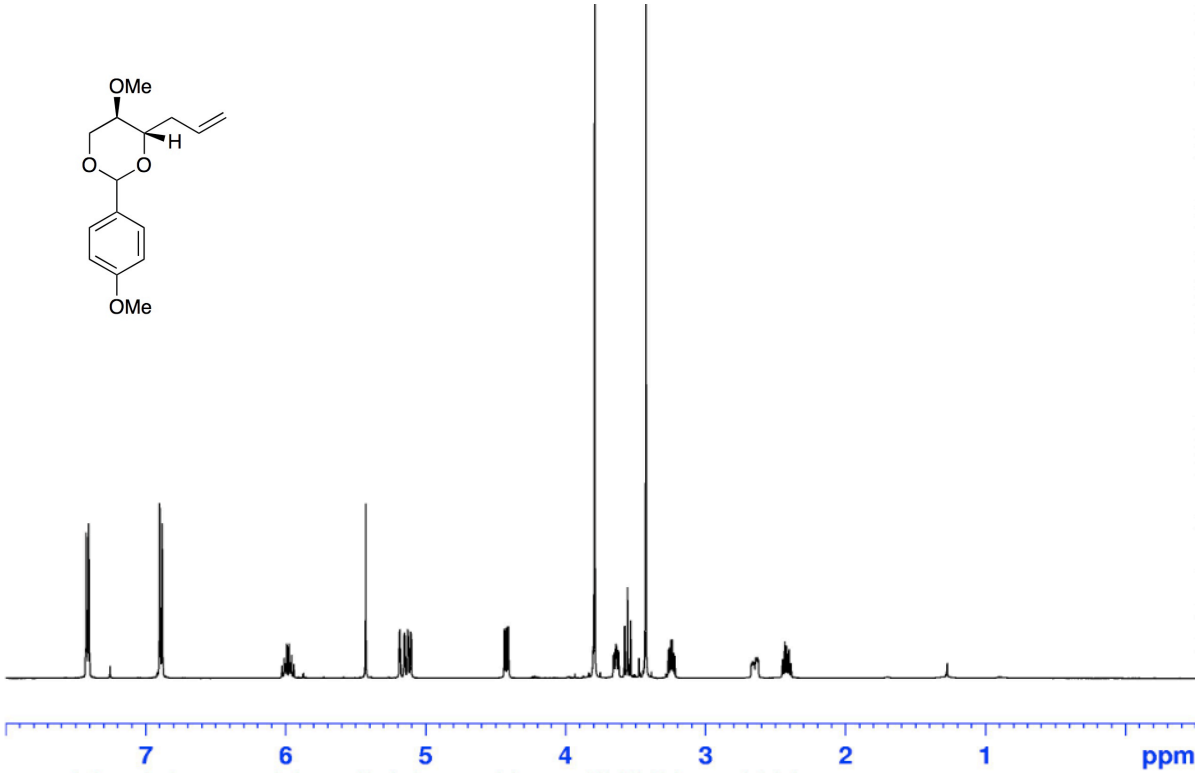
The ^{13}C NMR Spectrum of (-)-S3; 100 MHz ($CDCl_3$)



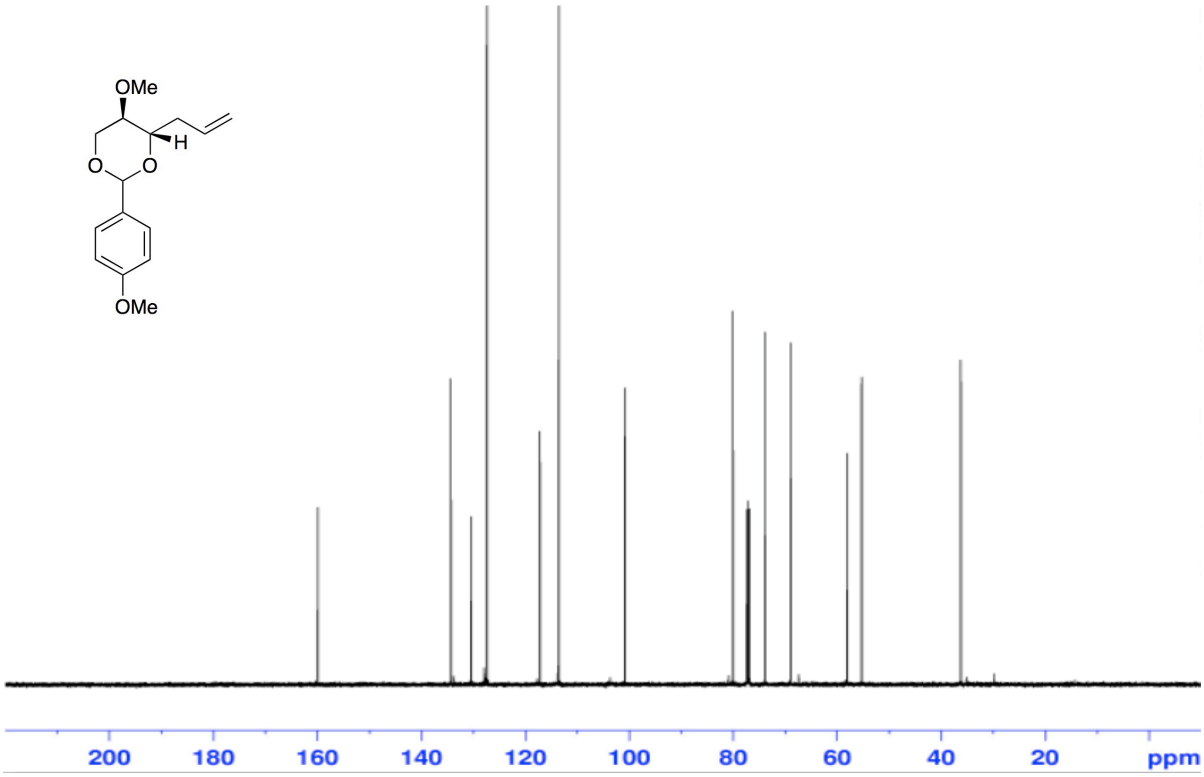
The ^{1}H NMR Spectrum of (-)-S4; 400 MHz (C_6D_6)



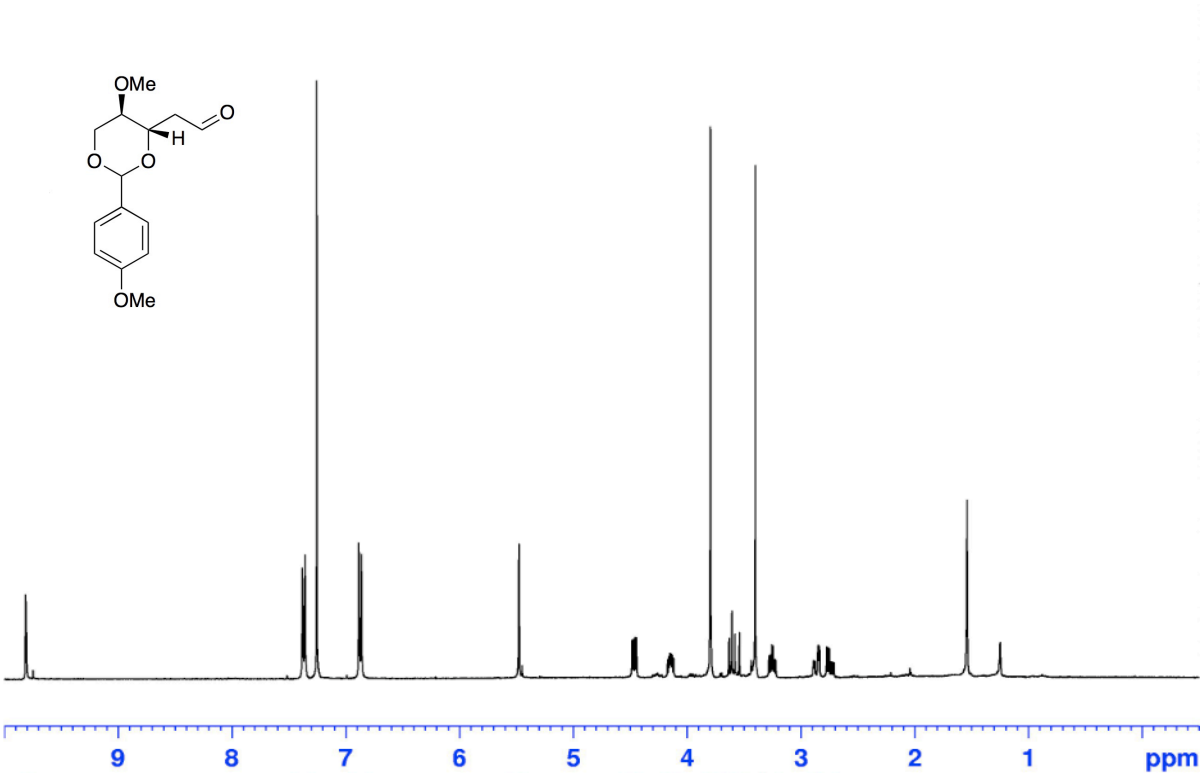
The ^{13}C NMR Spectrum of (-)-S4; 125 MHz C_6D_6



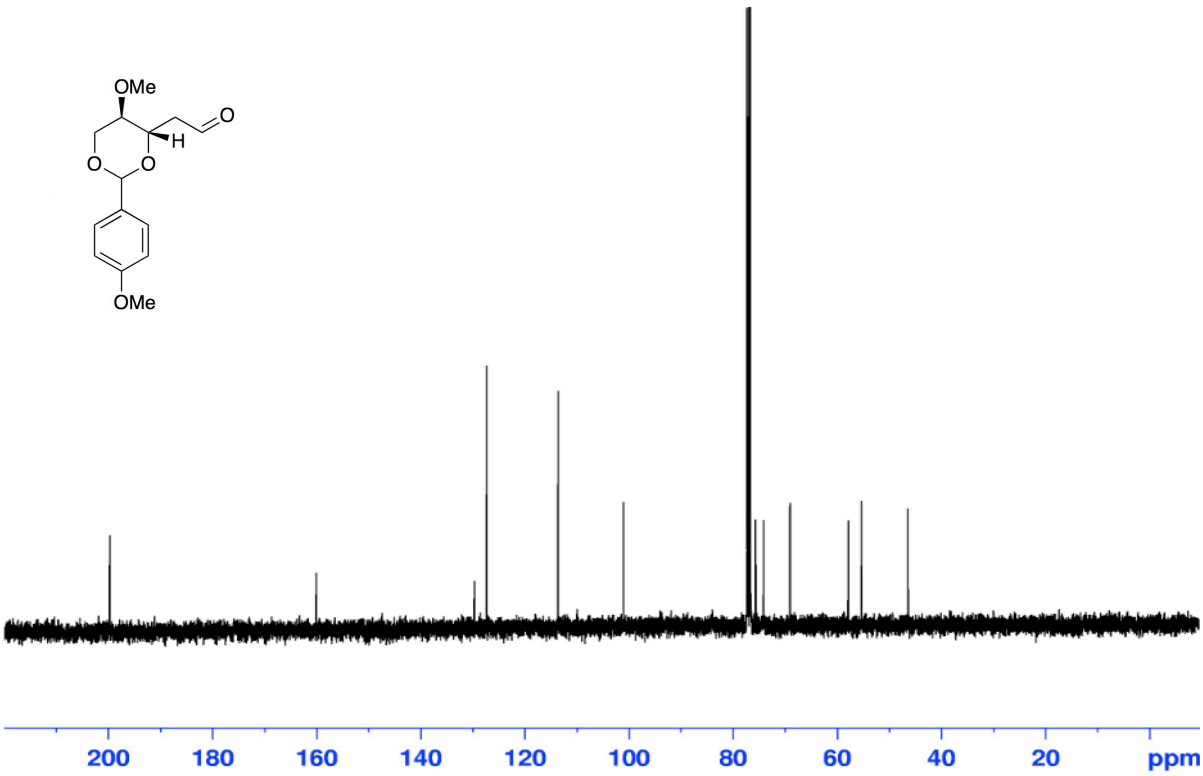
The ^{1}H NMR Spectrum of (-)-15; 500 MHz ($CDCl_3$)



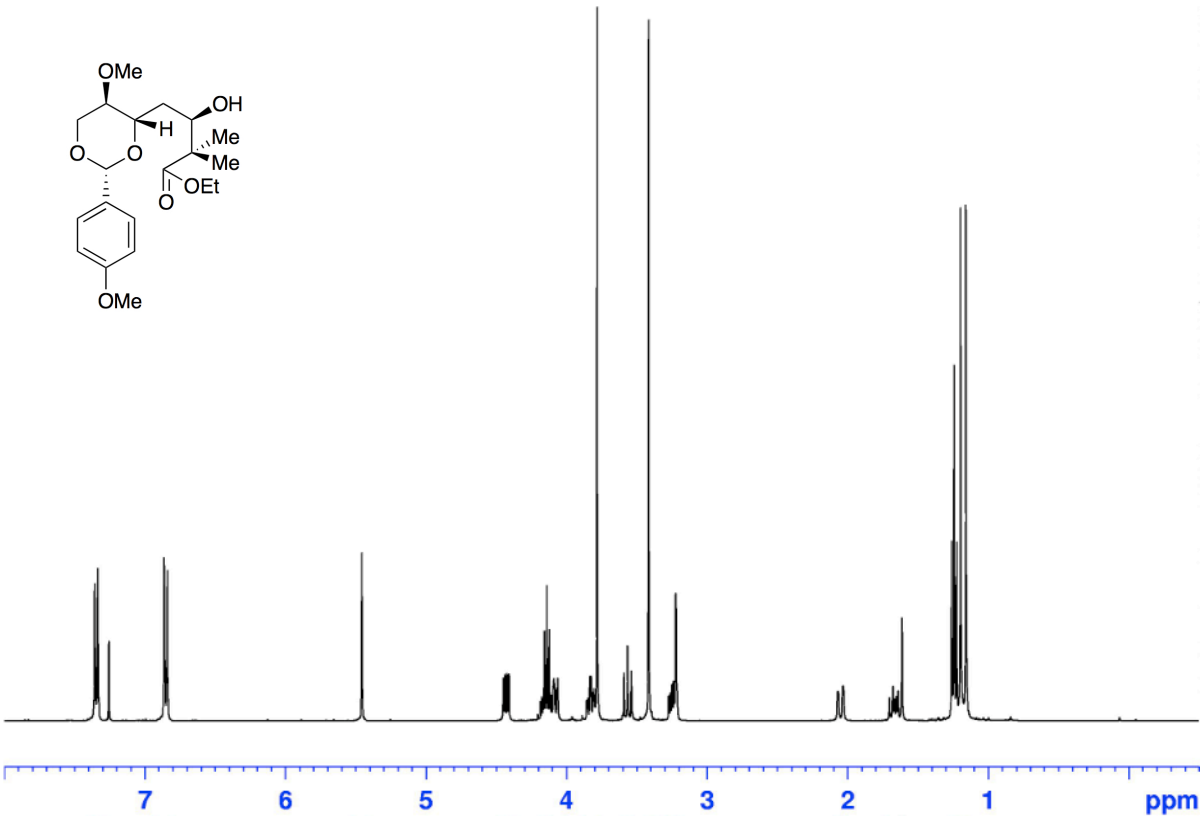
The ^{13}C NMR Spectrum of (-)-15; 125 MHz ($CDCl_3$)



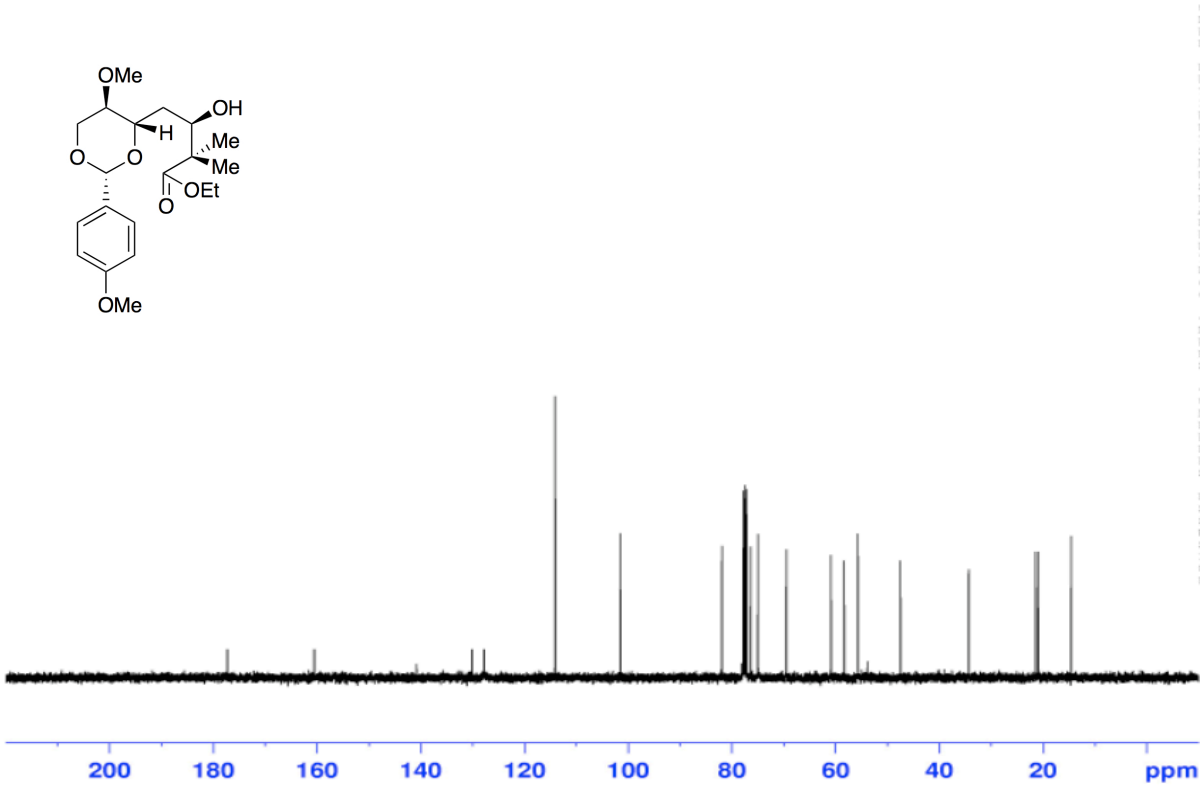
The ^{1}H NMR Spectrum of (-)-16; 400 MHz ($CDCl_3$)



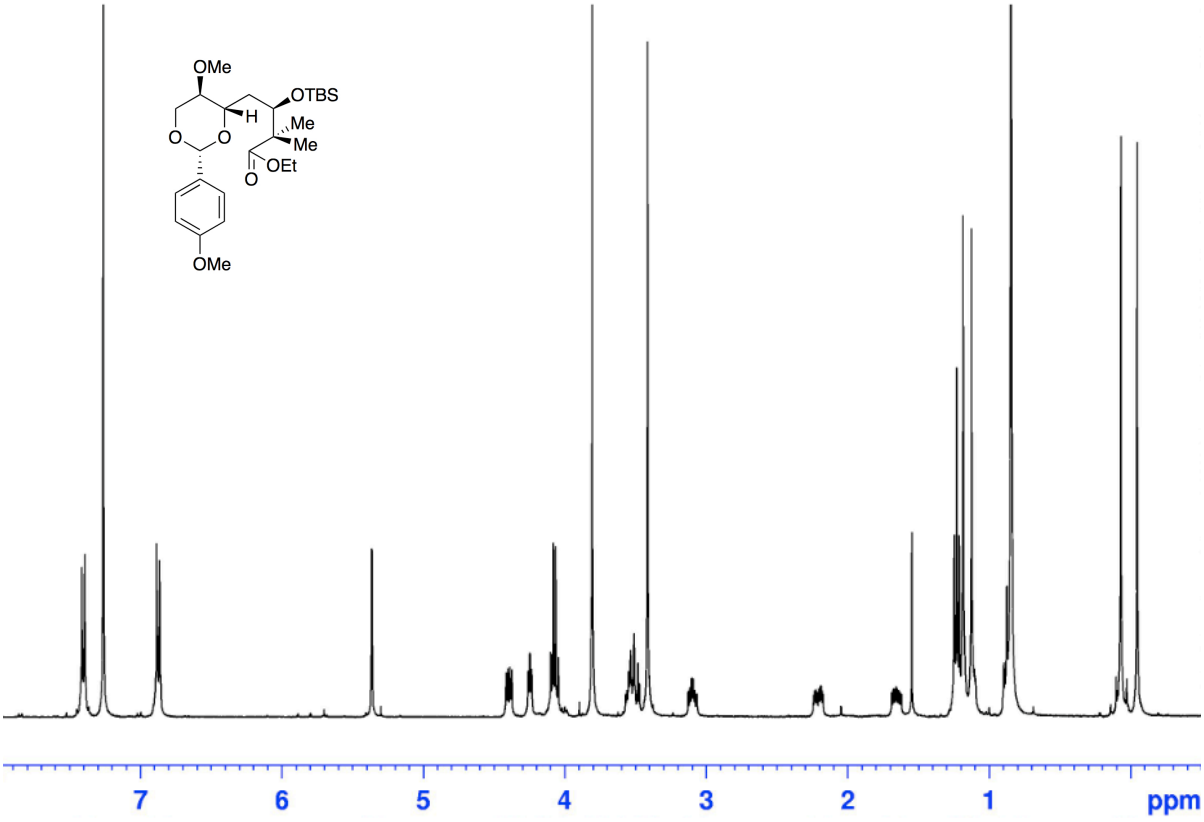
The ^{13}C NMR Spectrum of (-)-16; 100 MHz ($CDCl_3$)



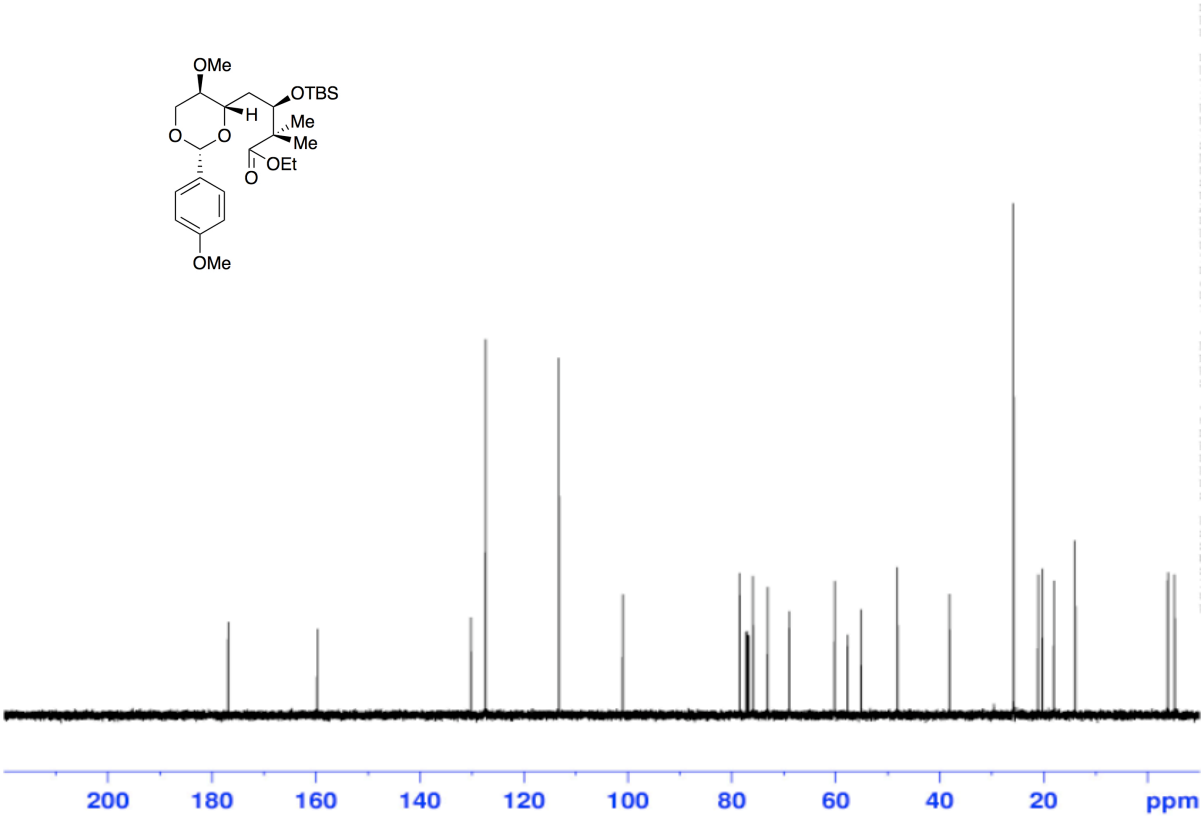
The ^{1}H NMR Spectrum of (-)-18; 400 MHz ($CDCl_3$)



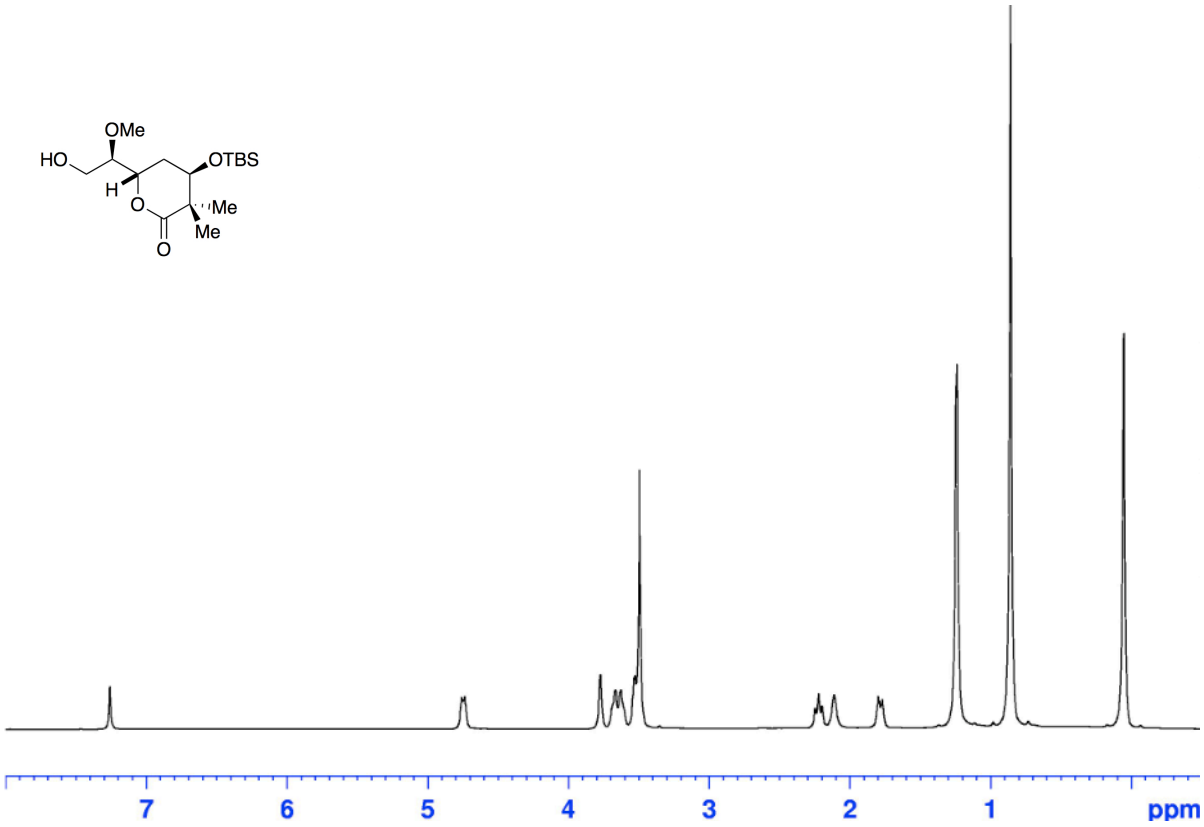
The ^{13}C NMR Spectrum of (-)-18; 100 MHz ($CDCl_3$)



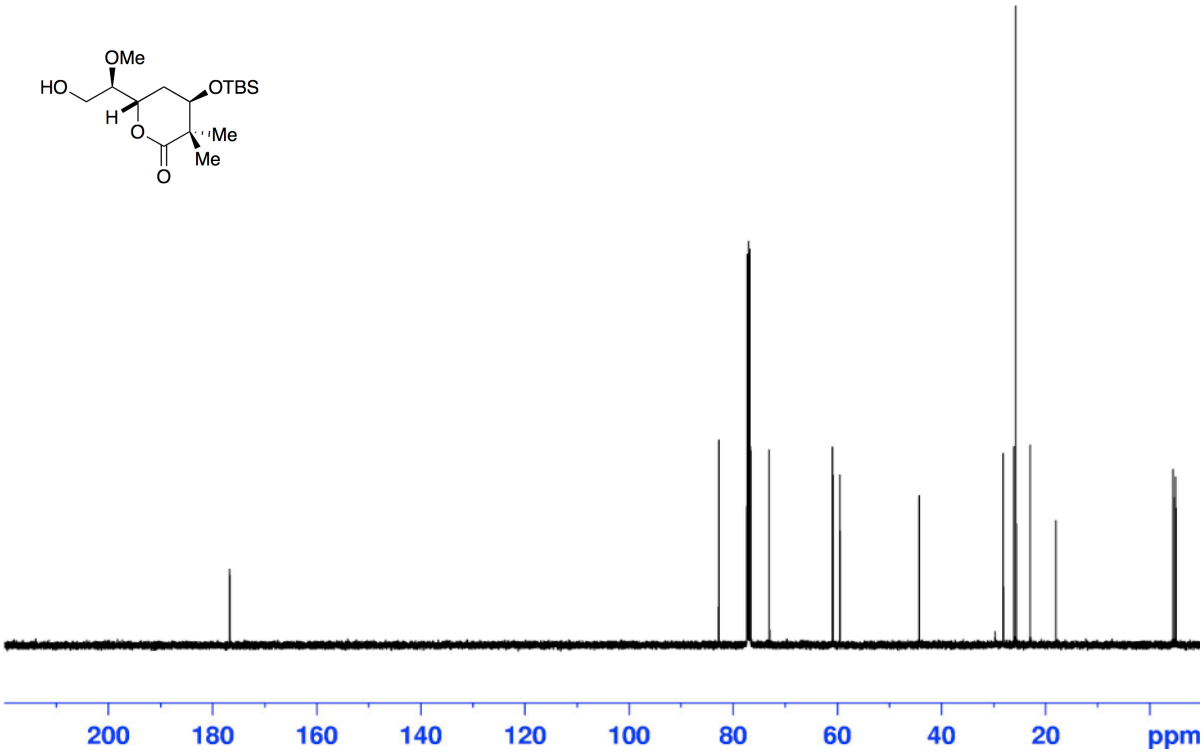
The ^{1}H NMR Spectrum of (-)-19; 400 MHz ($CDCl_3$)



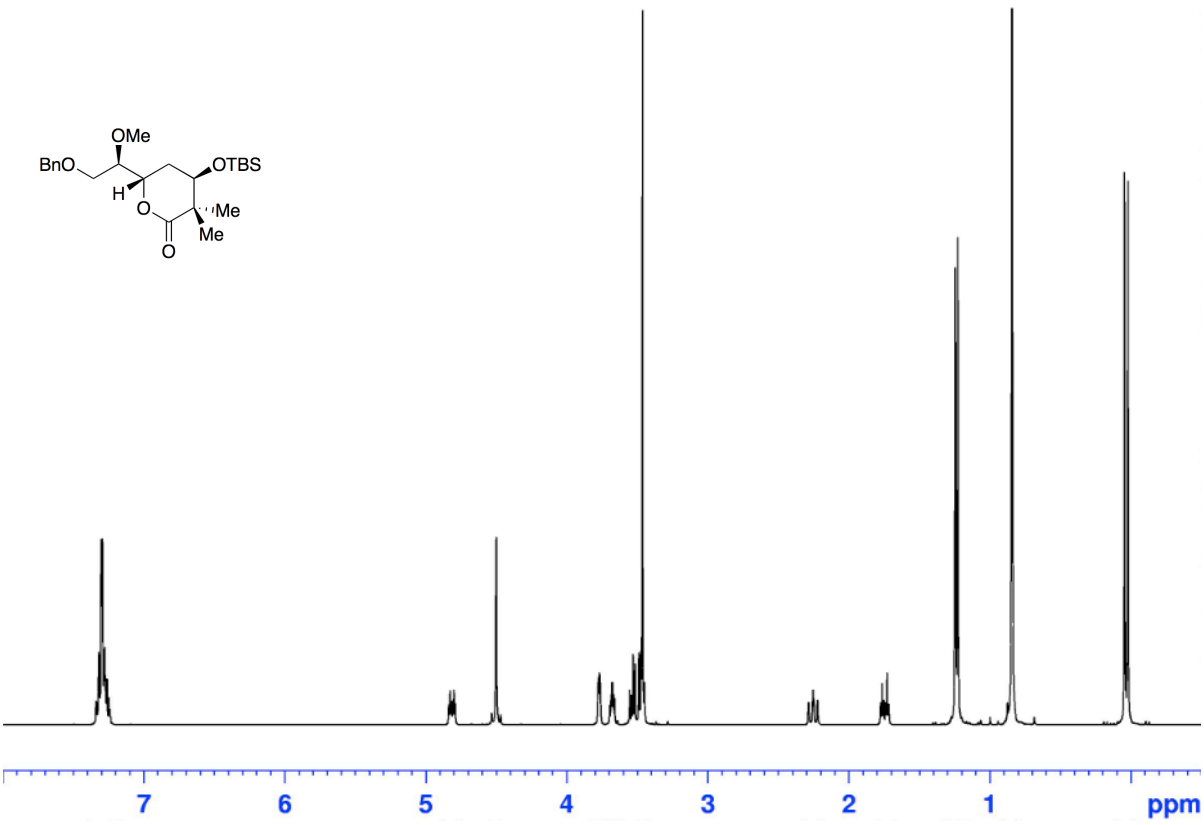
The ^{13}C NMR Spectrum of (-)-19; 125 MHz ($CDCl_3$)



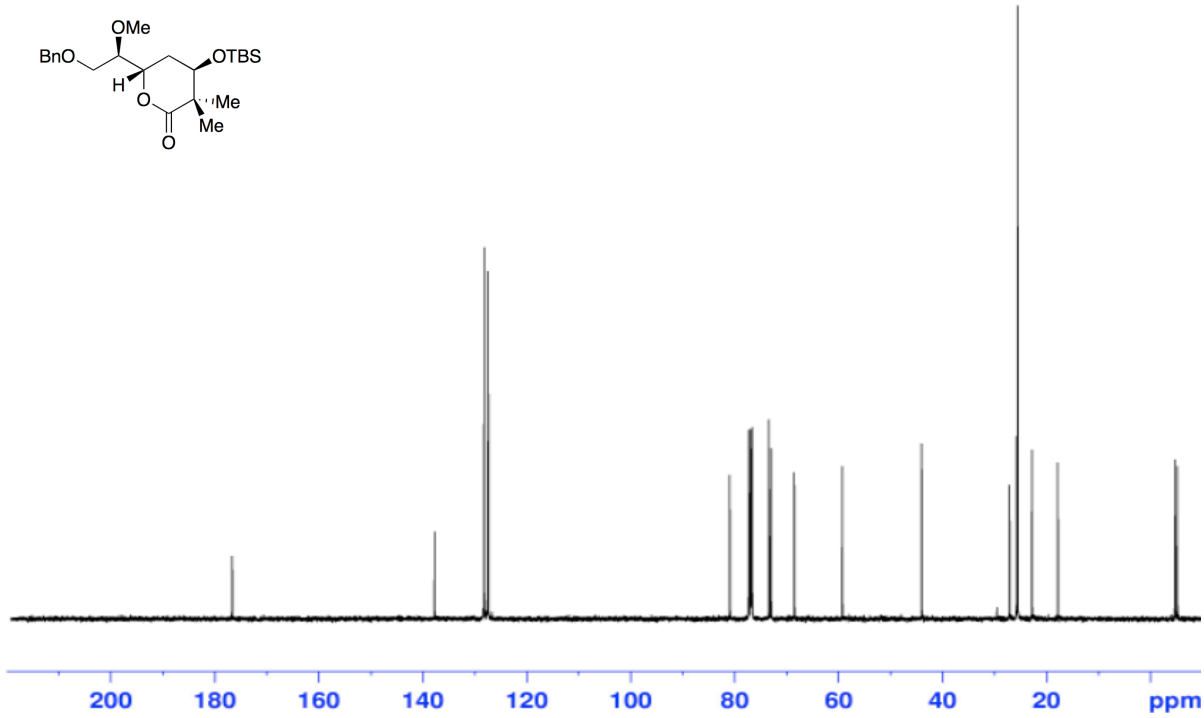
The ^{1}H NMR Spectrum of (-)-20; 500 MHz ($CDCl_3$)



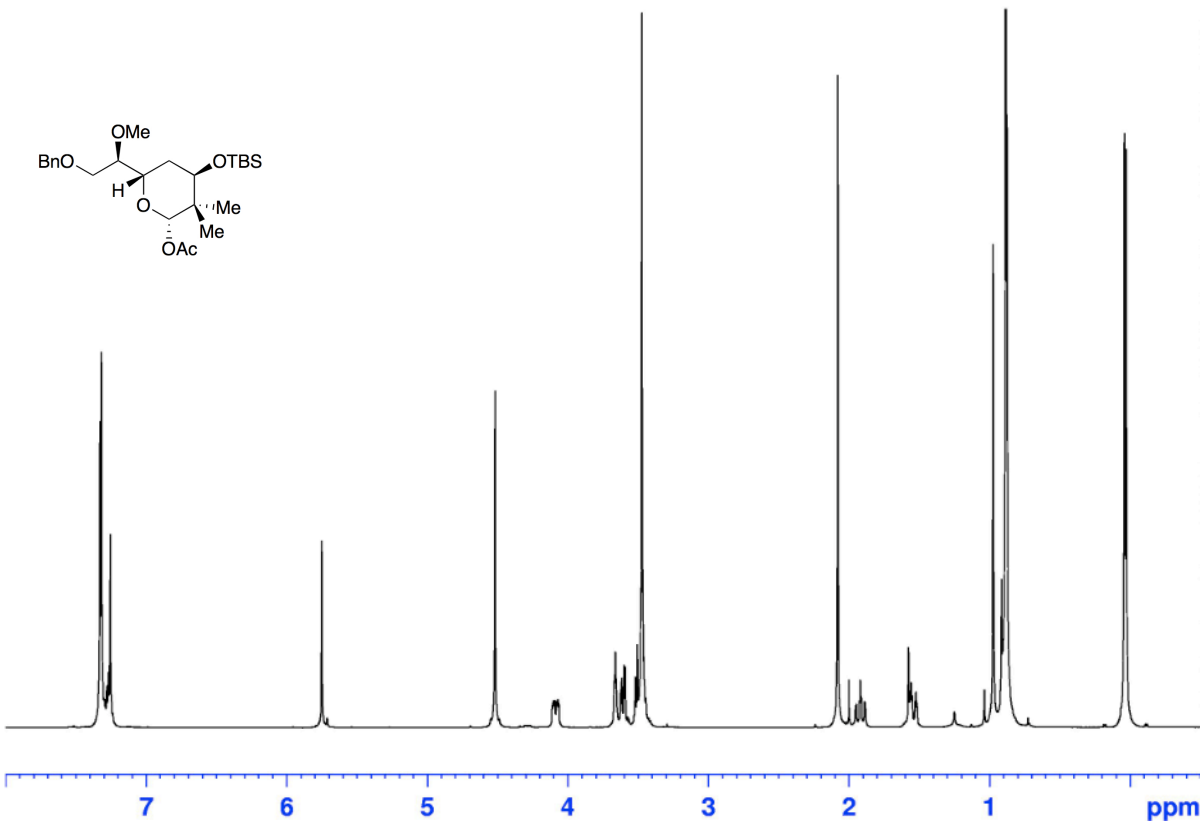
The ^{13}C NMR Spectrum of (-)-20; 125 MHz ($CDCl_3$)



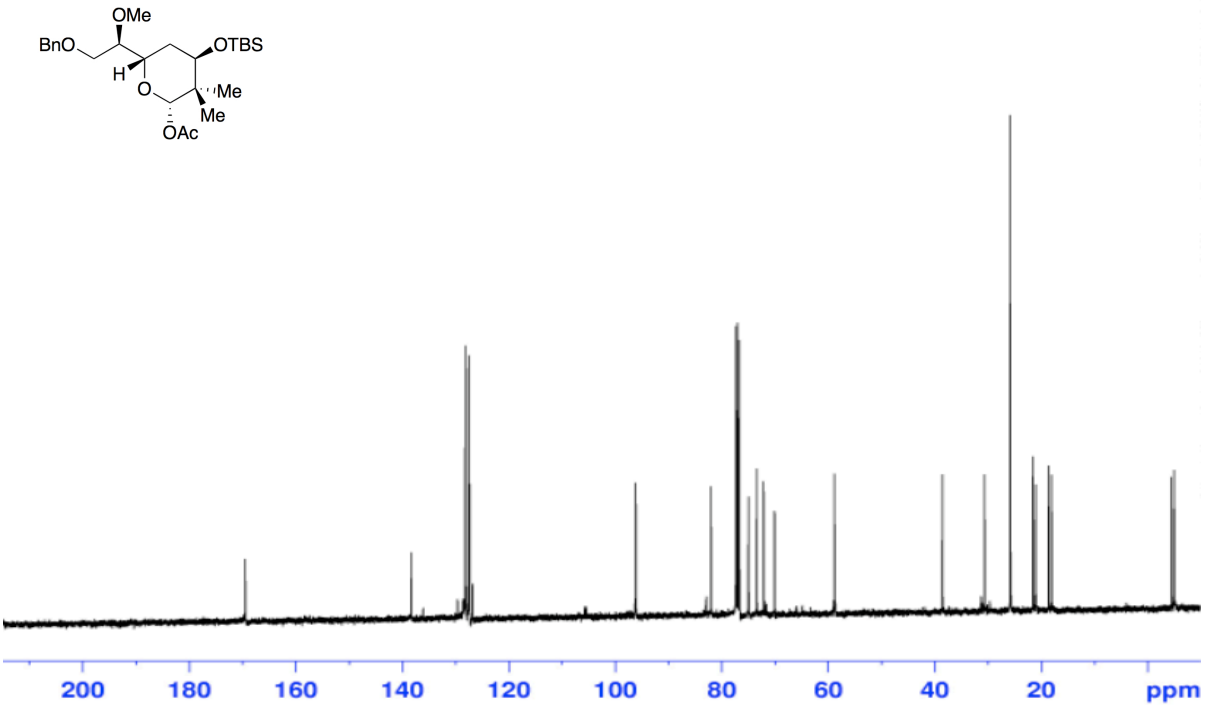
The ^{1}H NMR Spectrum of (-)-21; 400 MHz ($CDCl_3$)



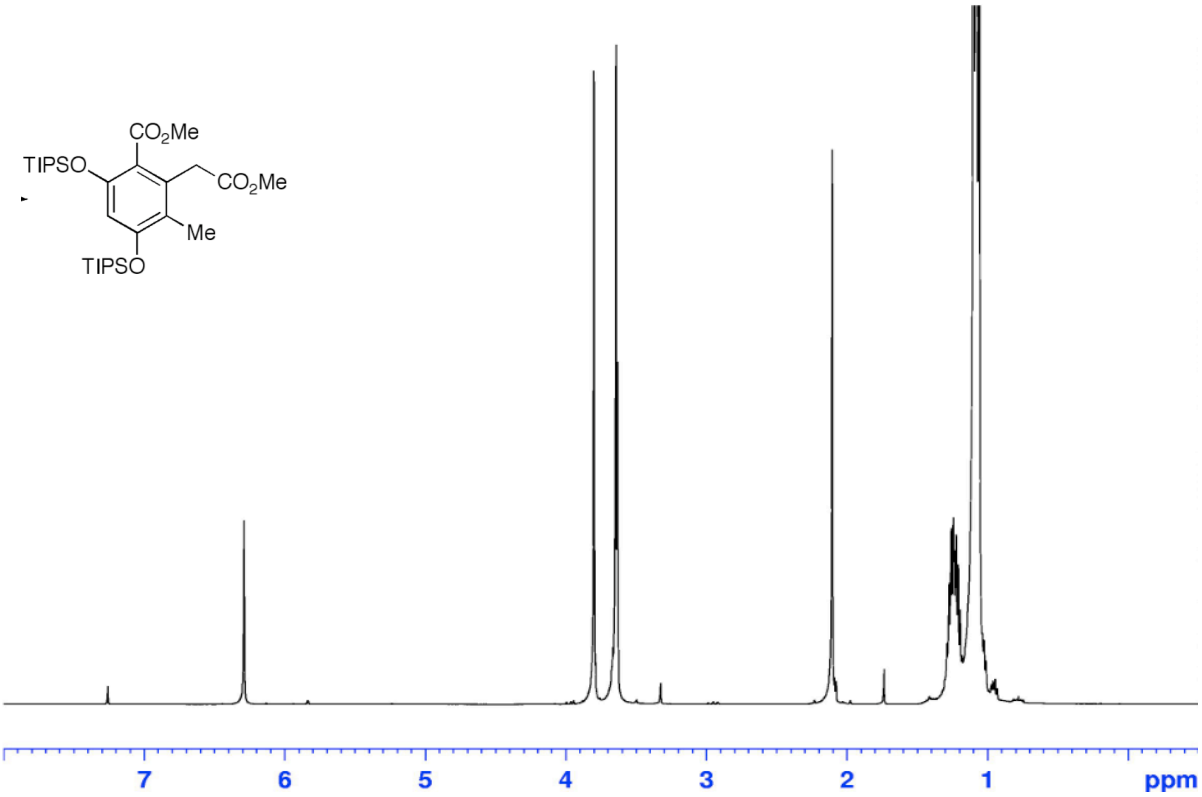
The ^{13}C NMR Spectrum of (-)-21; 100 MHz ($CDCl_3$)



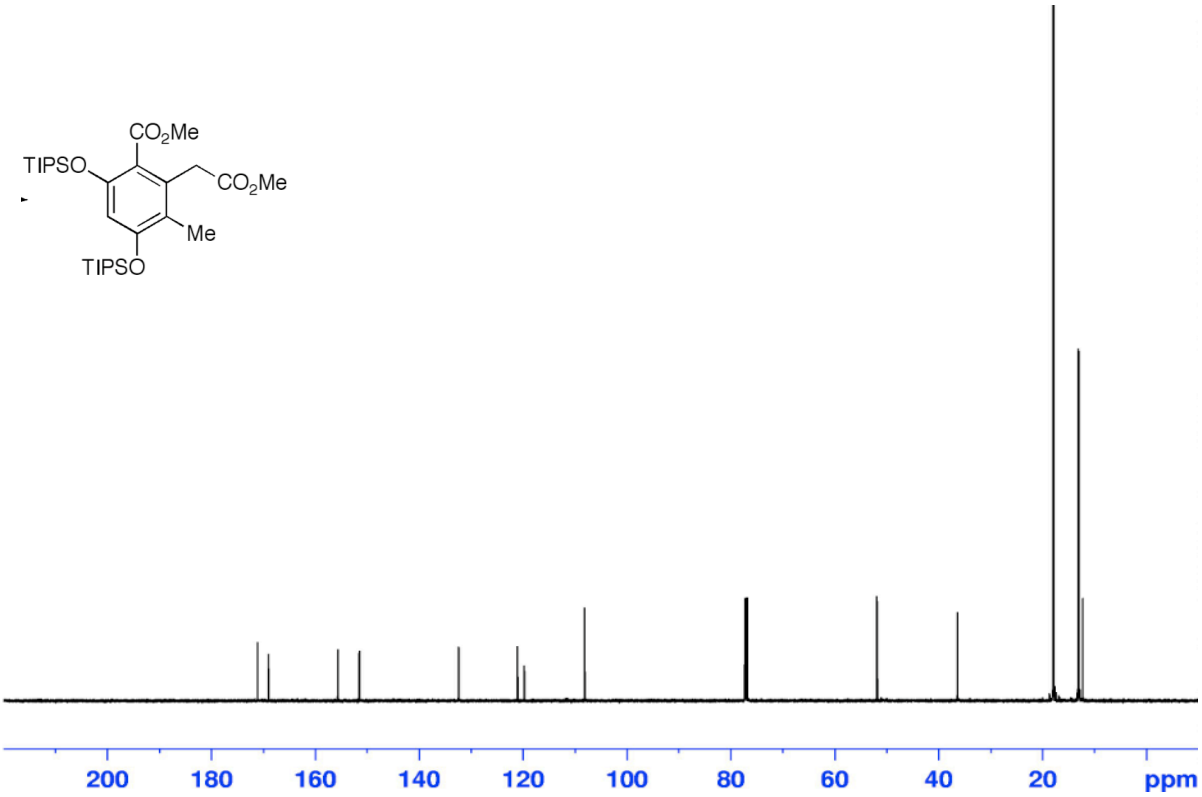
The ^{1}H NMR Spectrum of (-)-5; 400 MHz ($CDCl_3$)



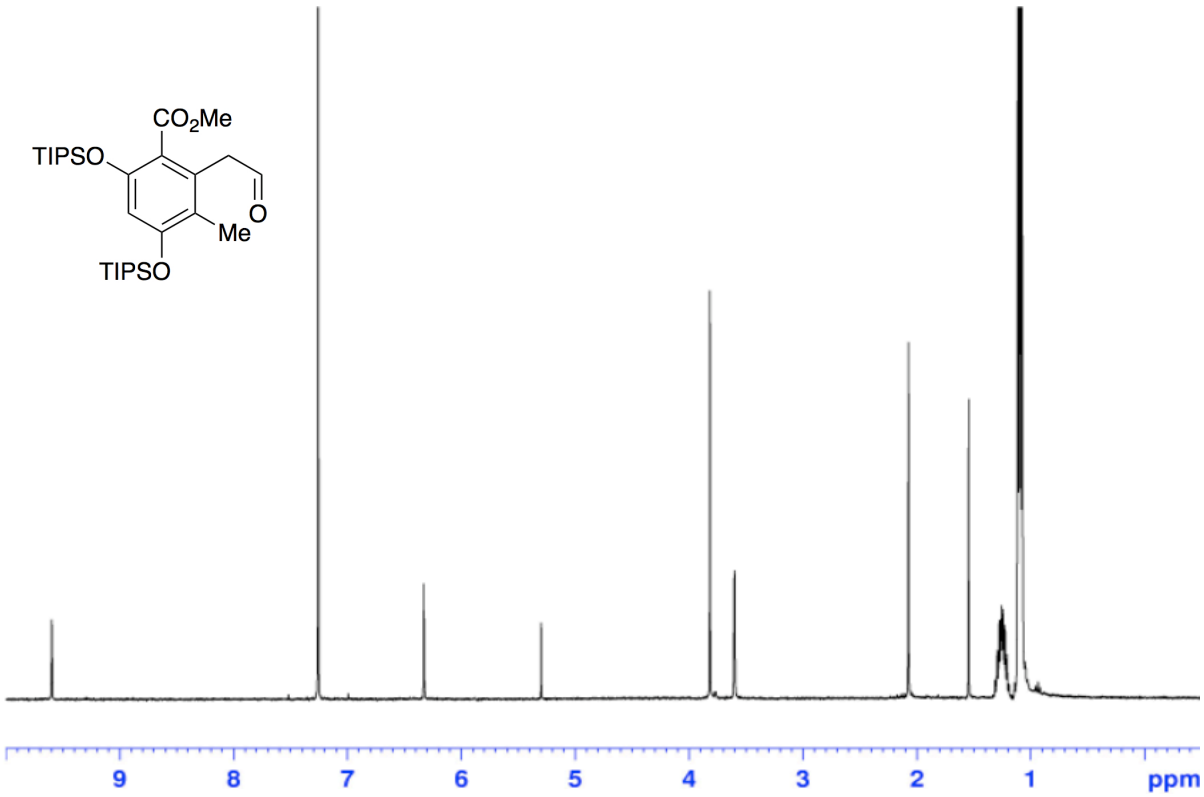
The ^{13}C NMR Spectrum of (-)-5; 125 MHz ($CDCl_3$)



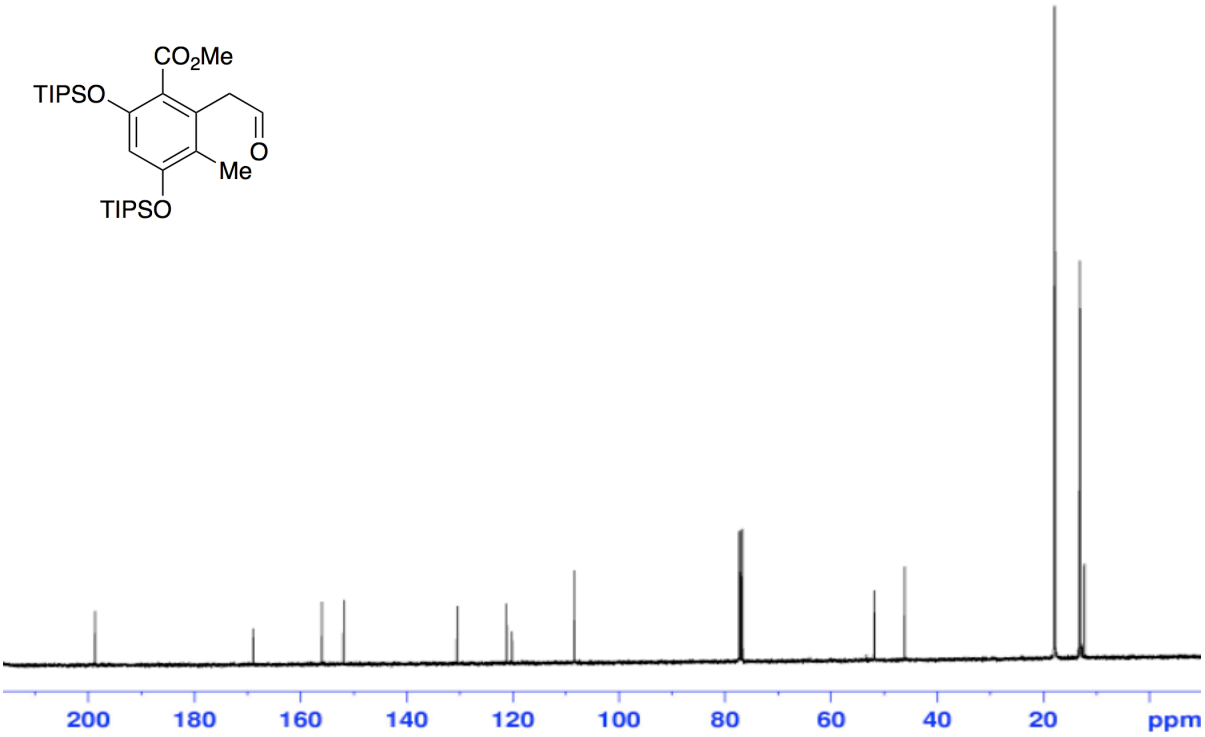
The ^{1}H NMR Spectrum of S6; 500 MHz ($CDCl_3$)



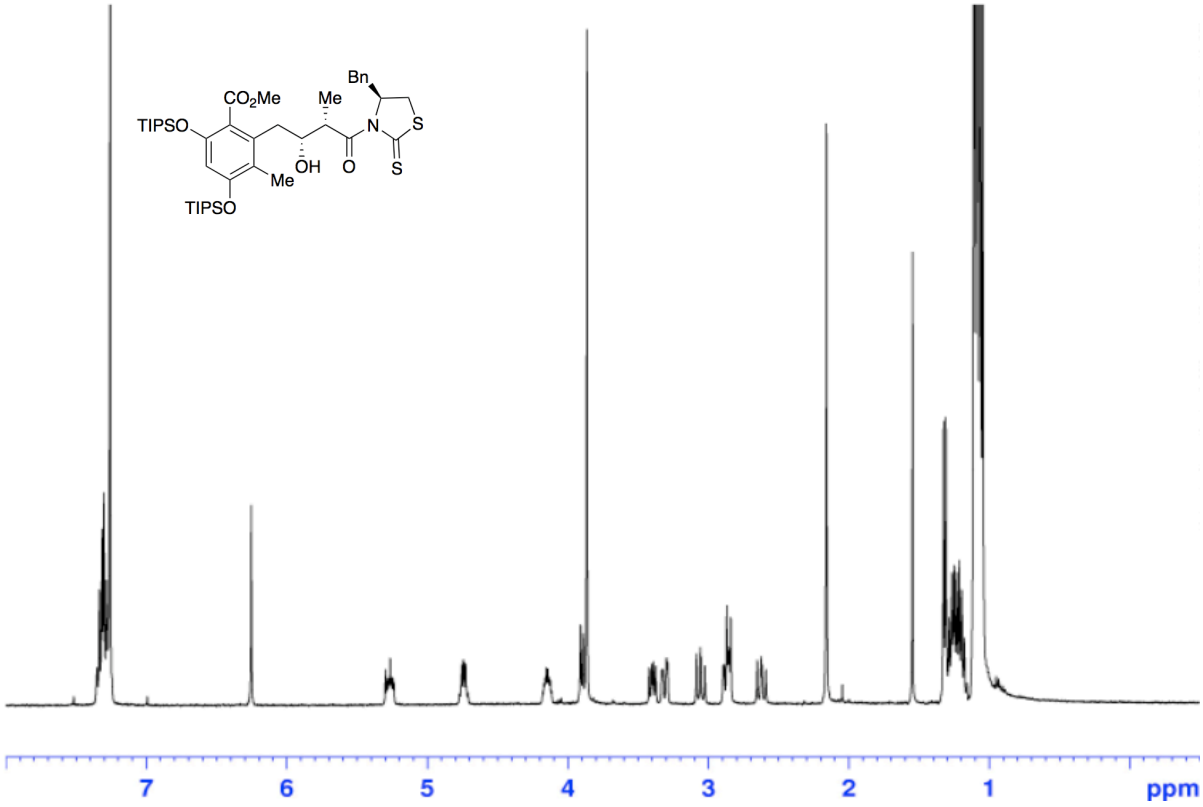
The ^{1}H NMR Spectrum of S6; 125 MHz ($CDCl_3$)



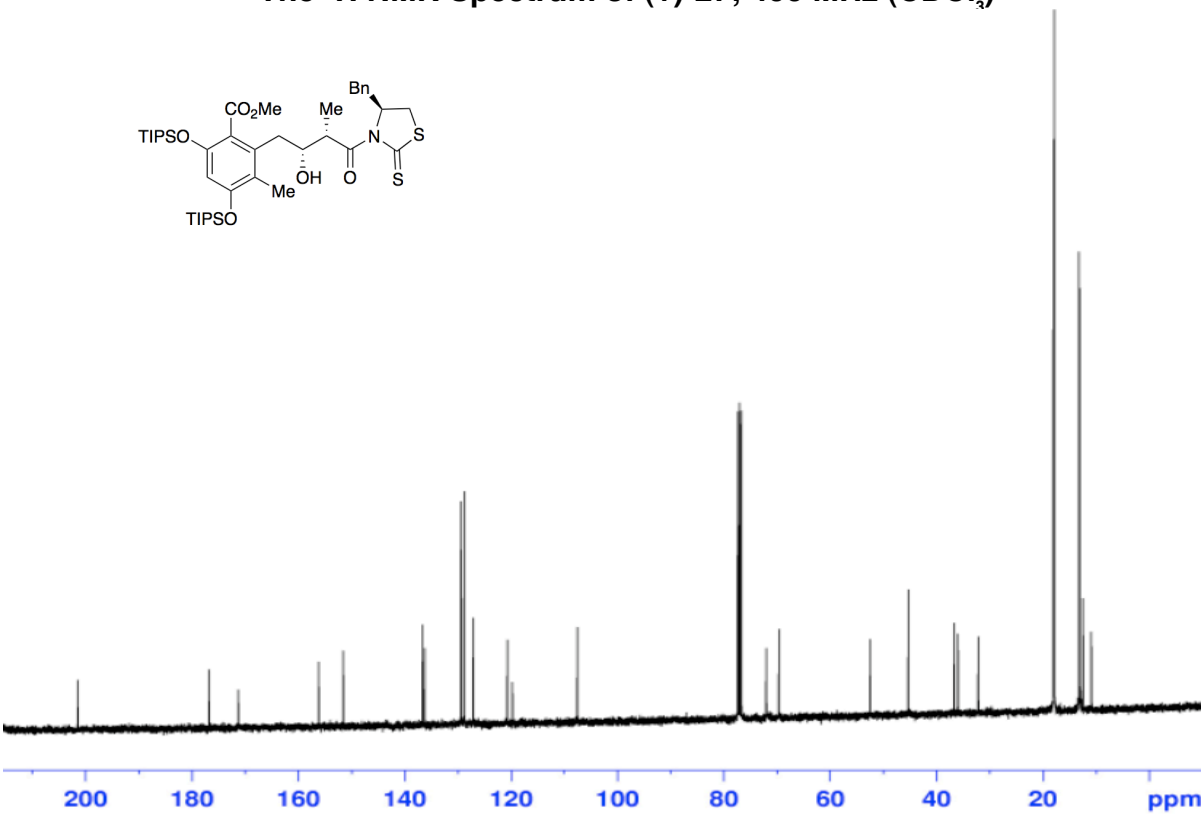
The ^{1}H NMR Spectrum of 25; 400 MHz ($CDCl_3$)



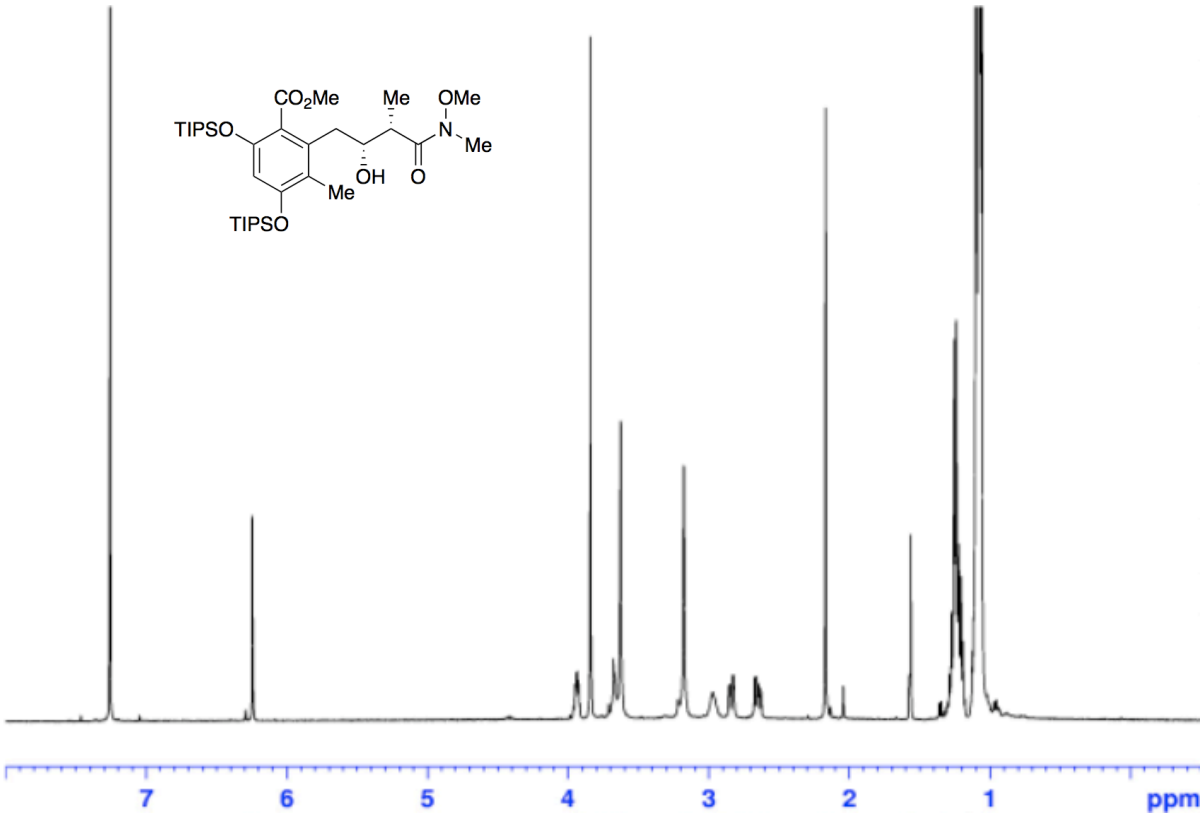
The ^{13}C NMR Spectrum of 25; 100 MHz ($CDCl_3$)



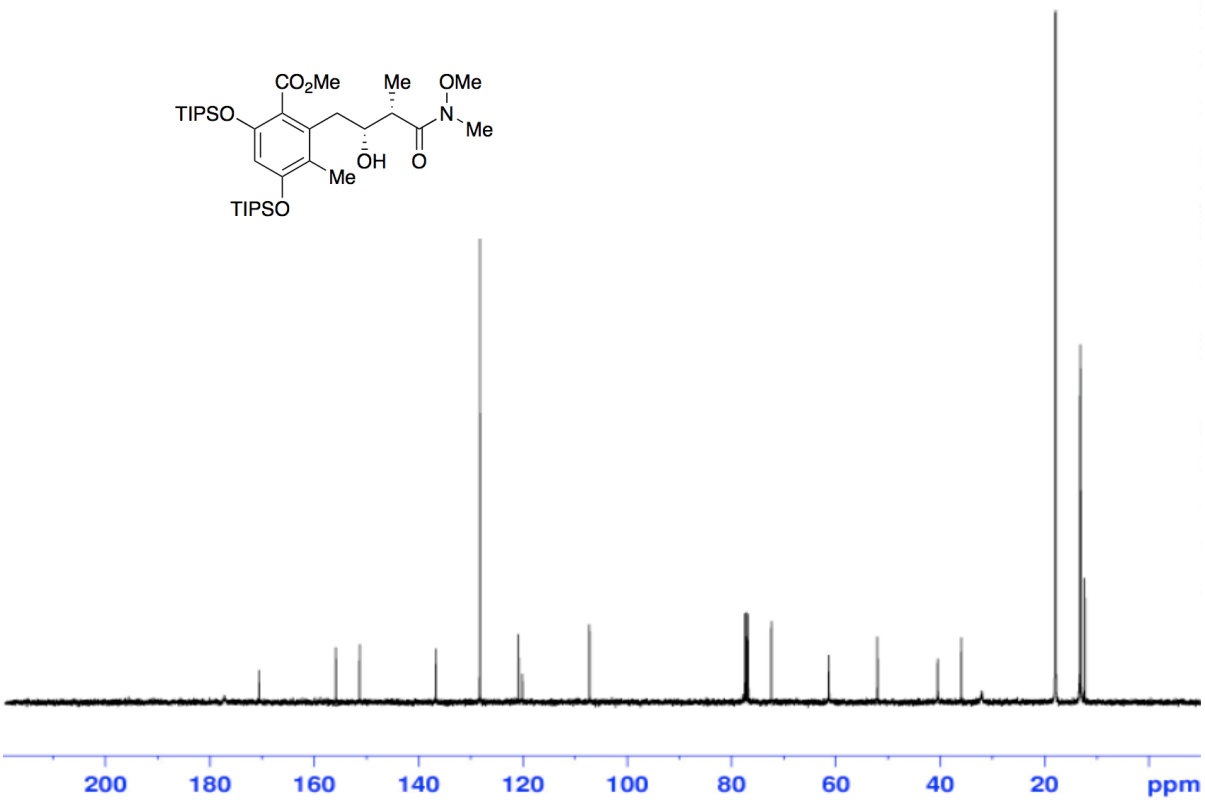
The ^{1}H NMR Spectrum of (+)-27; 400 MHz ($CDCl_3$)



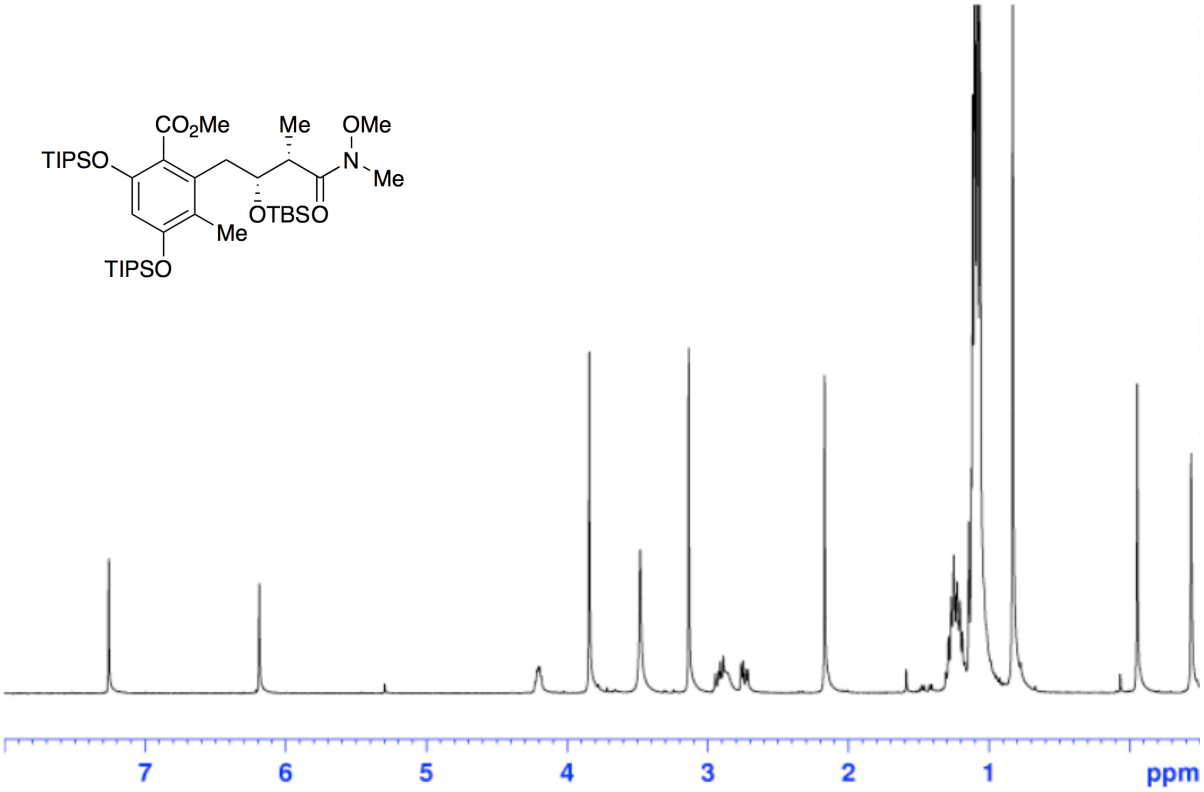
The ^{13}C NMR Spectrum of (+)-27; 100 MHz ($CDCl_3$)



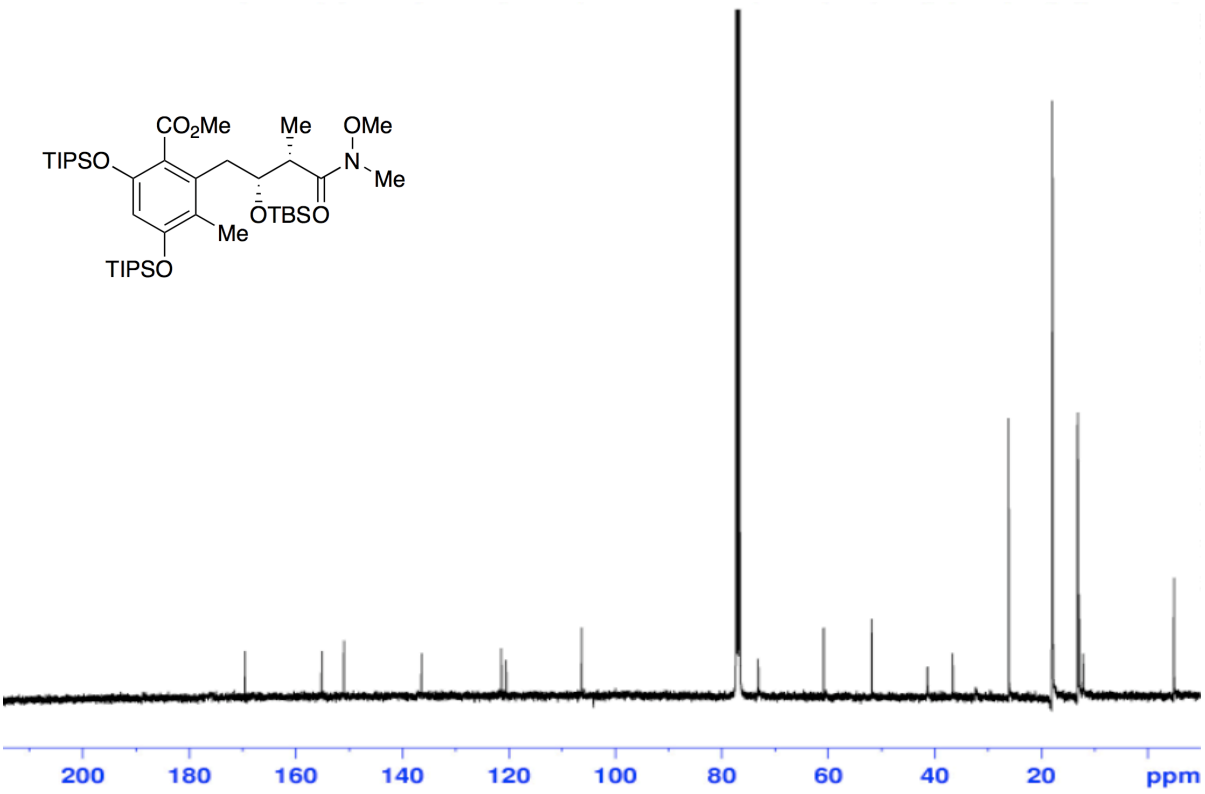
The ^{1}H NMR Spectrum of (+)-S7; 500 MHz ($CDCl_3$)



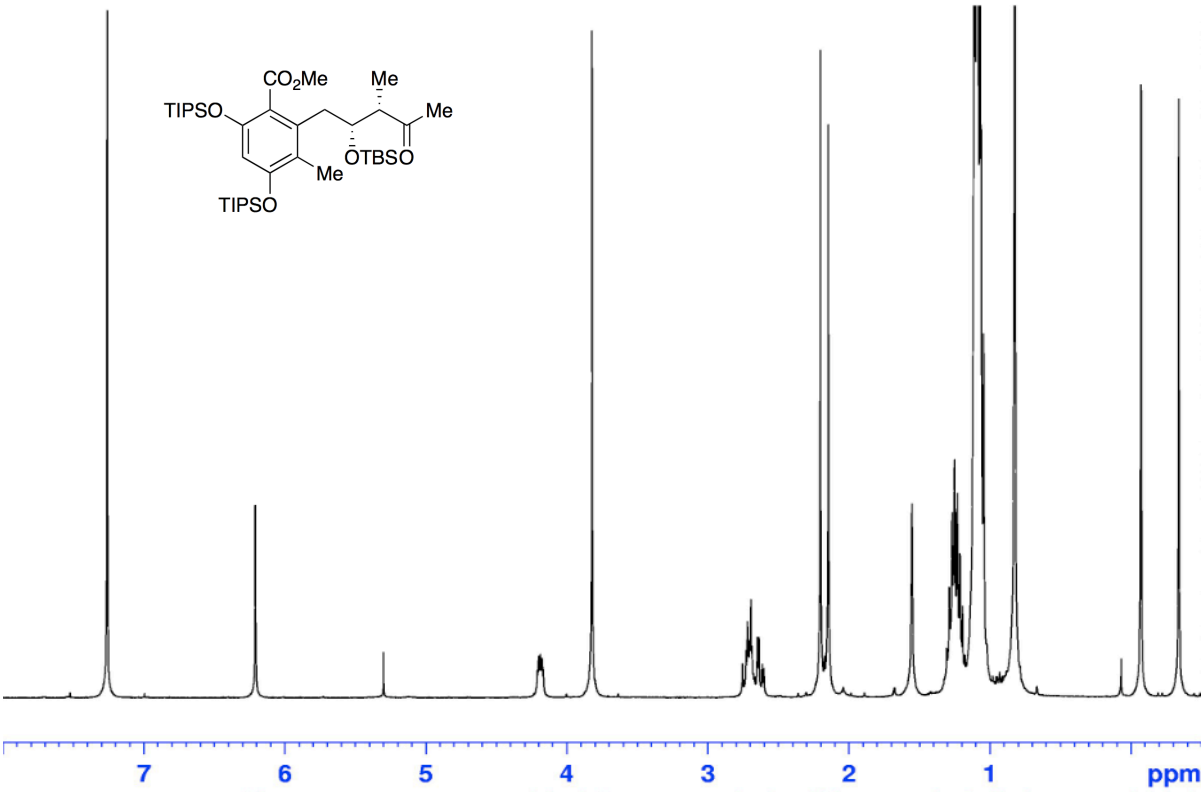
The ^{13}C NMR Spectrum of (+)-S7; 100 MHz ($CDCl_3$)



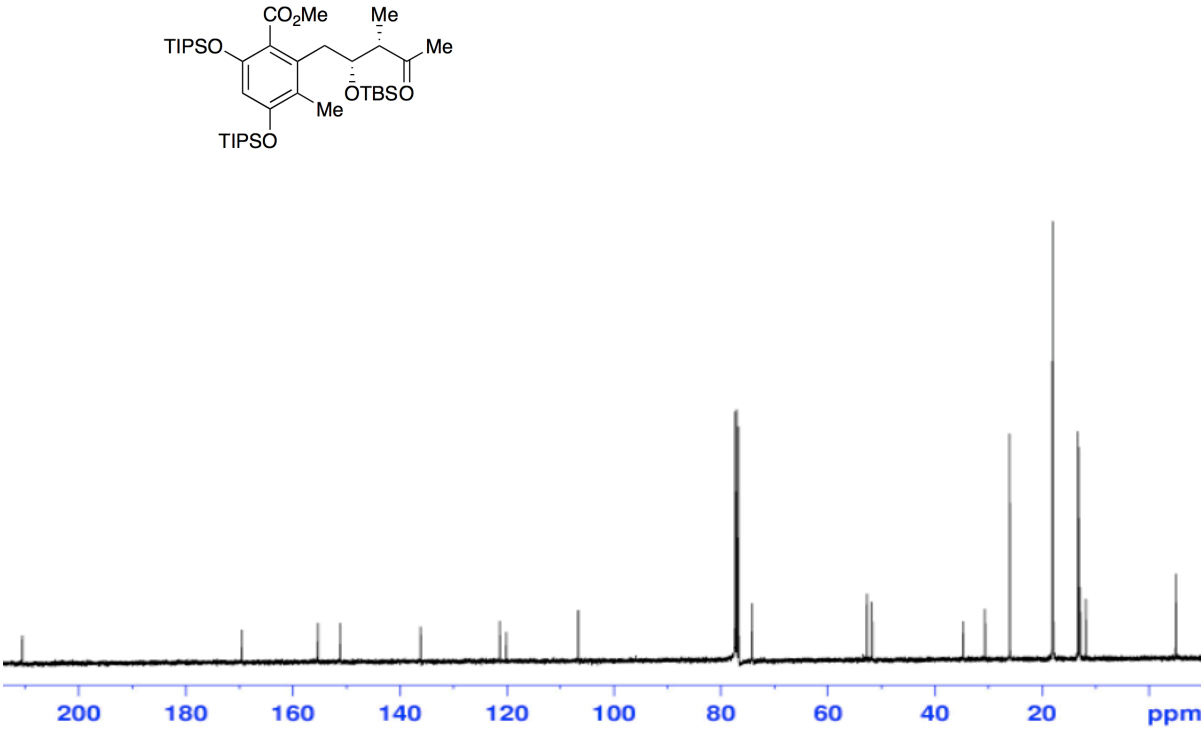
The ^{1}H NMR Spectrum of (+)-28; 400 MHz ($CDCl_3$)



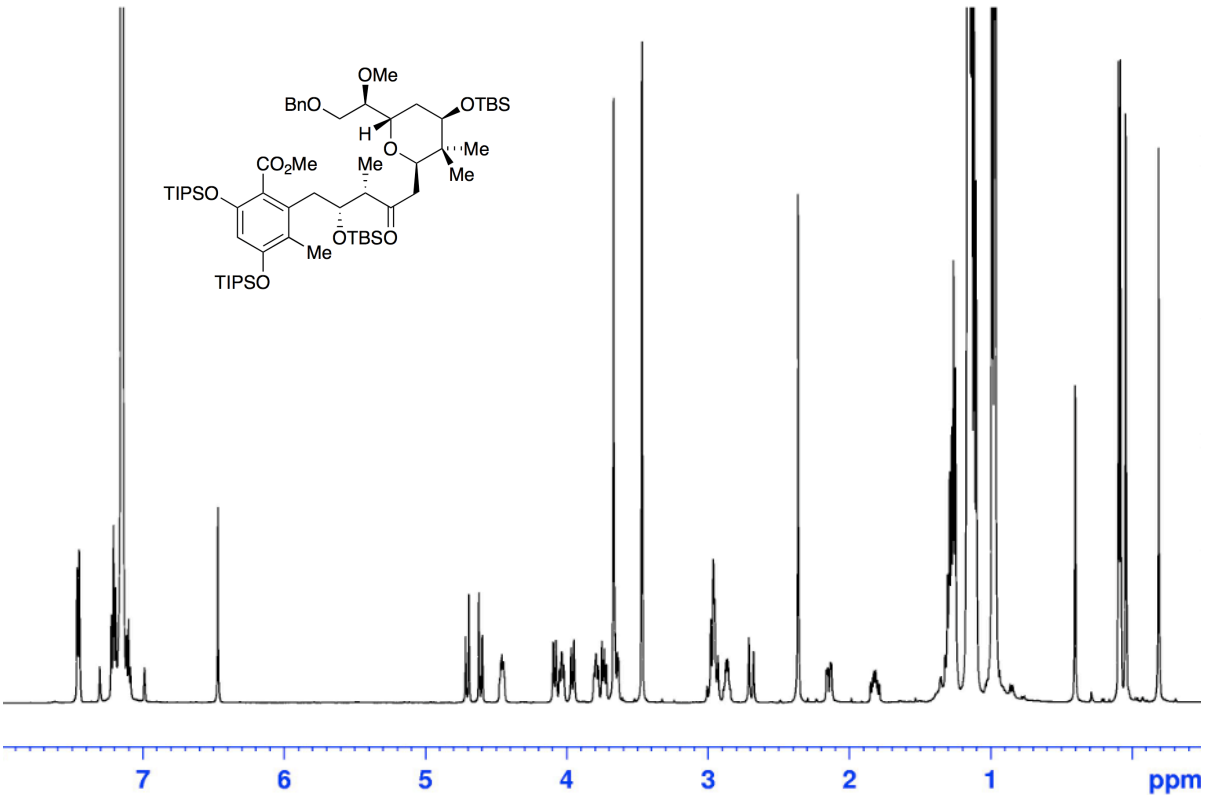
The ^{13}C NMR Spectrum of (+)-28; 100 MHz ($CDCl_3$)



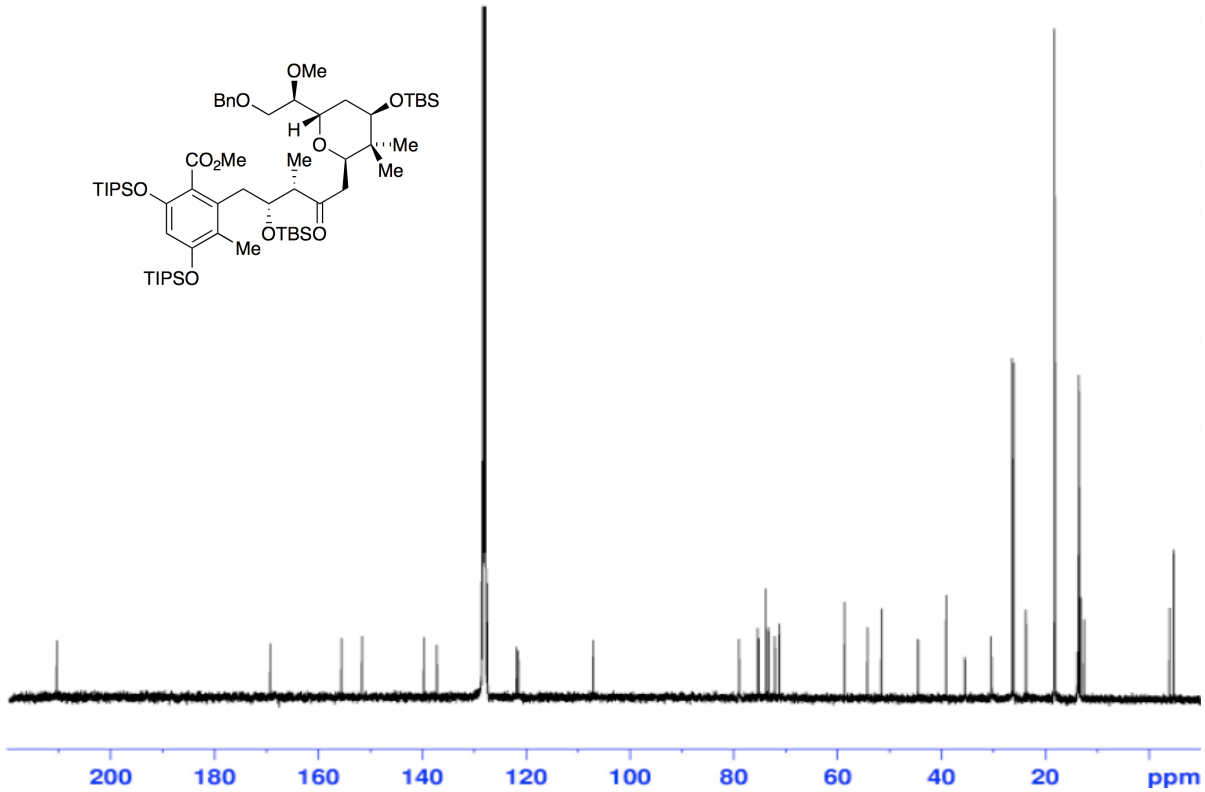
The ^{1}H NMR Spectrum of (+)-S8; 400 MHz ($CDCl_3$)



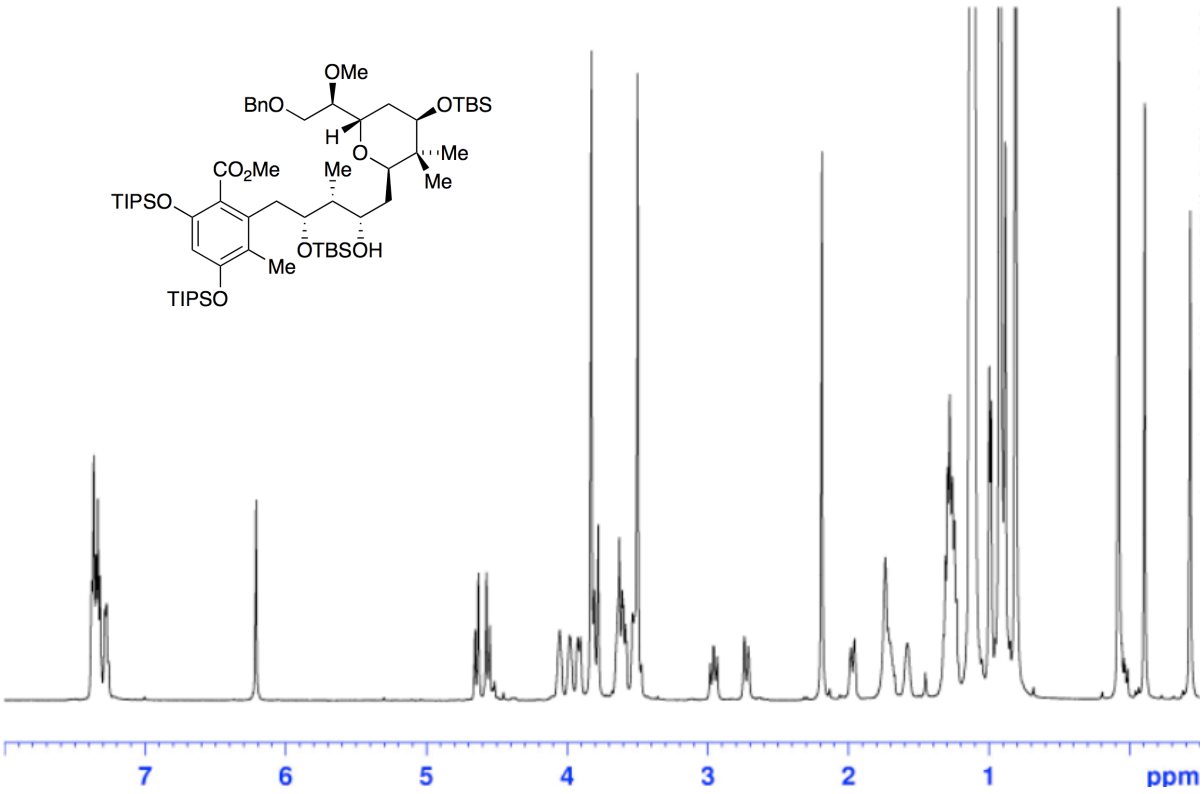
The ^{13}C NMR Spectrum of (+)-S8; 100 MHz ($CDCl_3$)



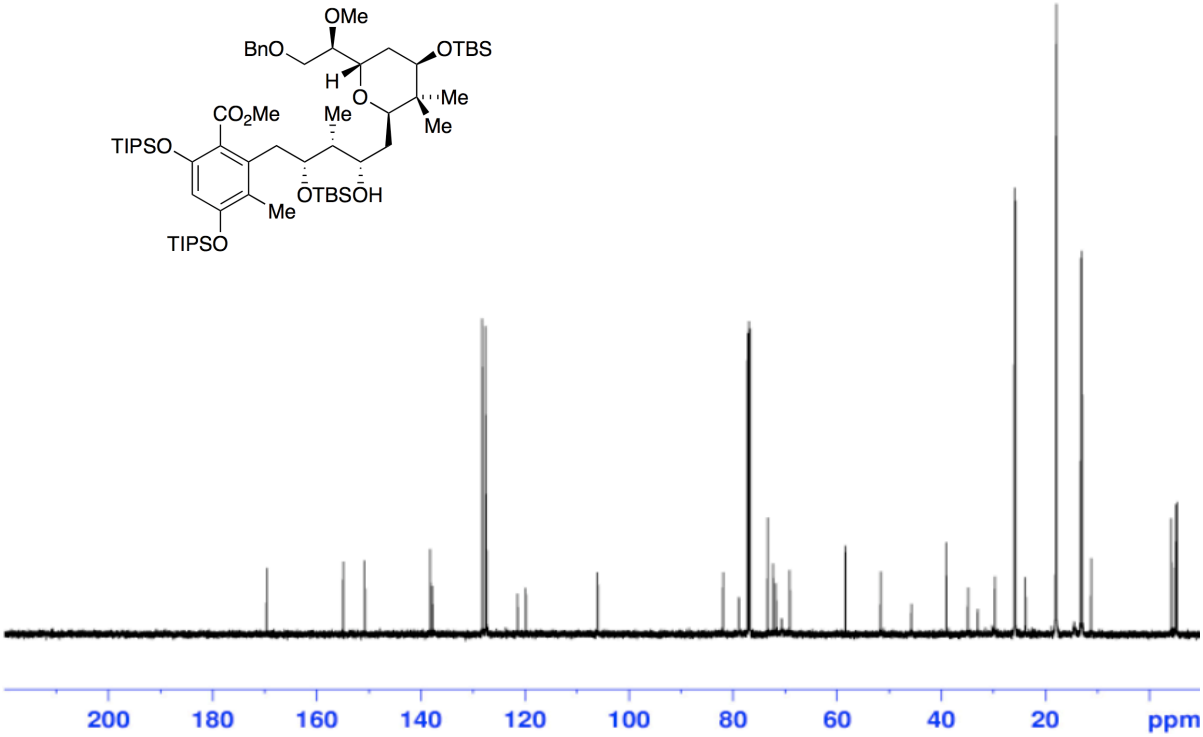
The ^{1}H NMR Spectrum of (+)-4; 500 MHz (C_6D_6)



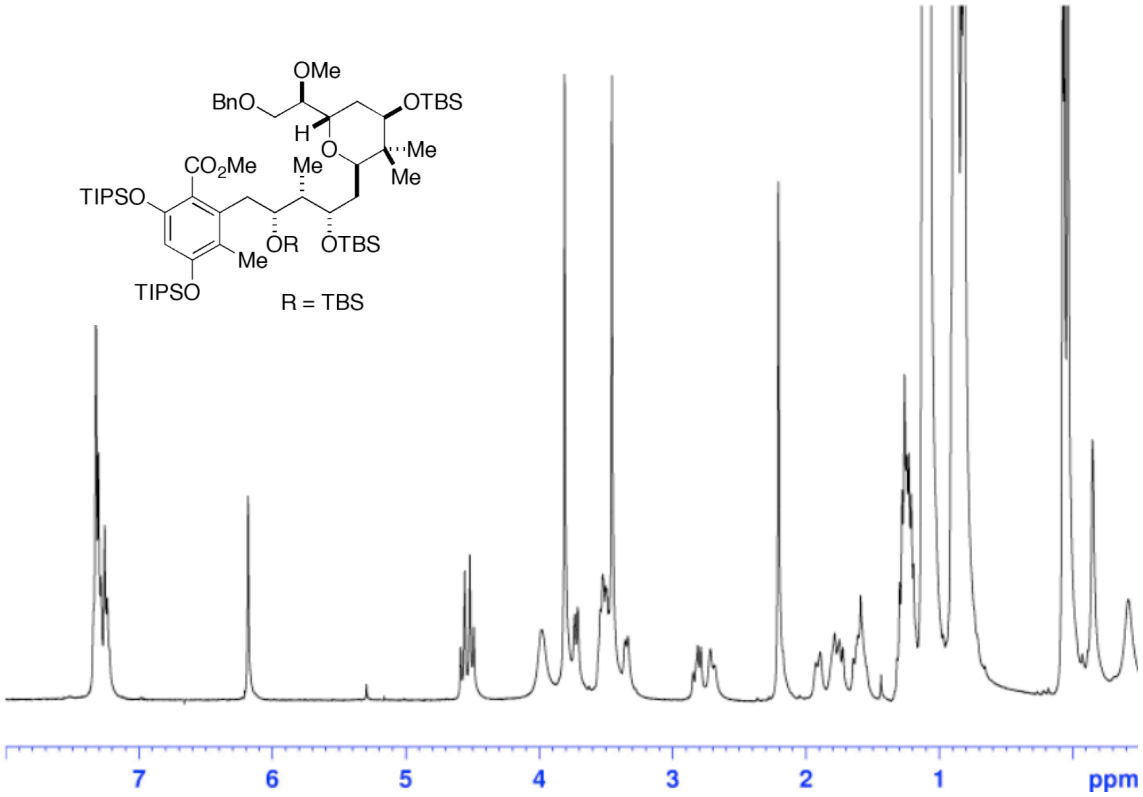
The ^{13}C NMR Spectrum of (+)-4; 100 MHz (C_6D_6)



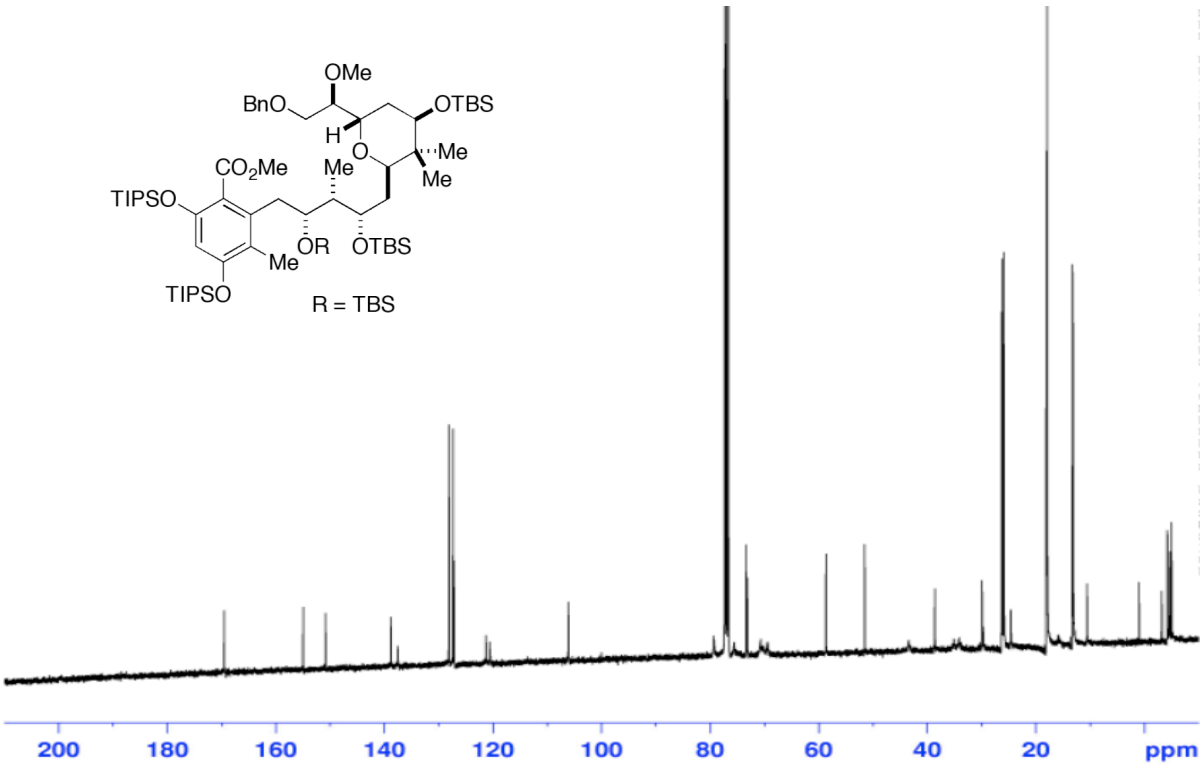
The ^{1}H NMR Spectrum of (+)-30; 500 MHz ($CDCl_3$)



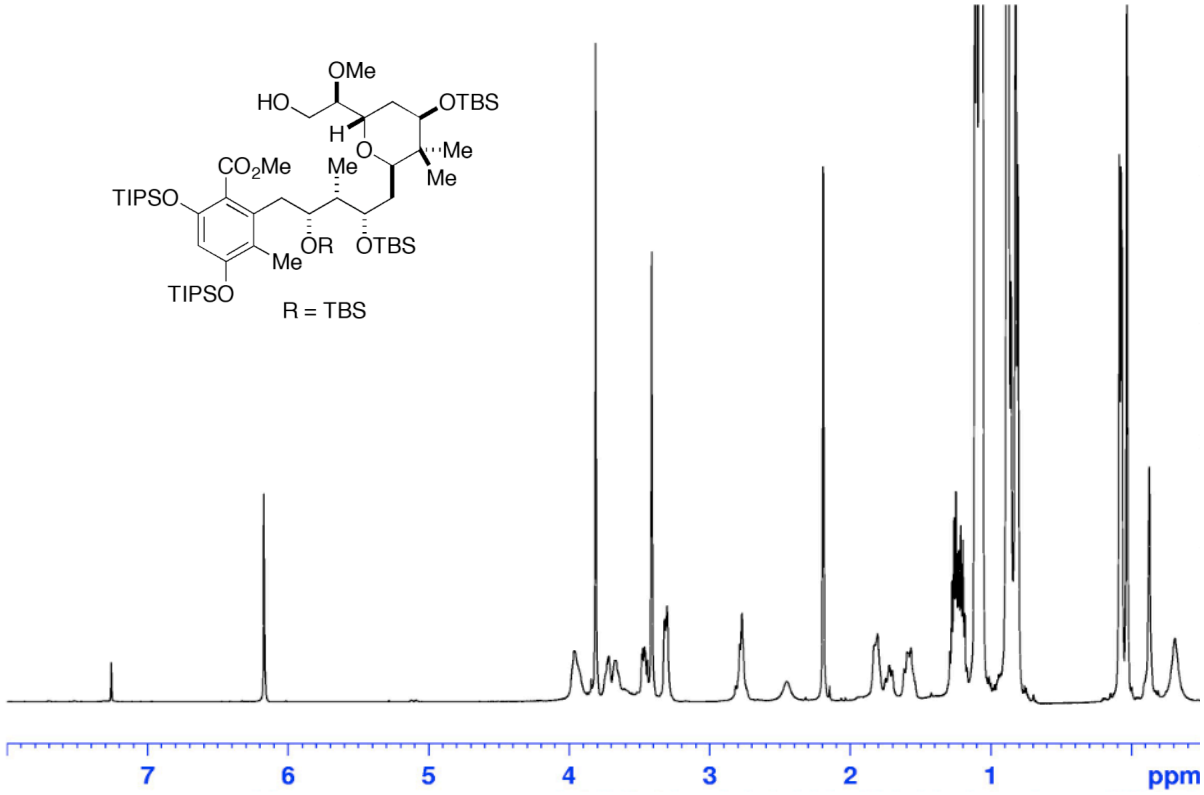
The ^{13}C NMR Spectrum of (+)-30; 100 MHz ($CDCl_3$)



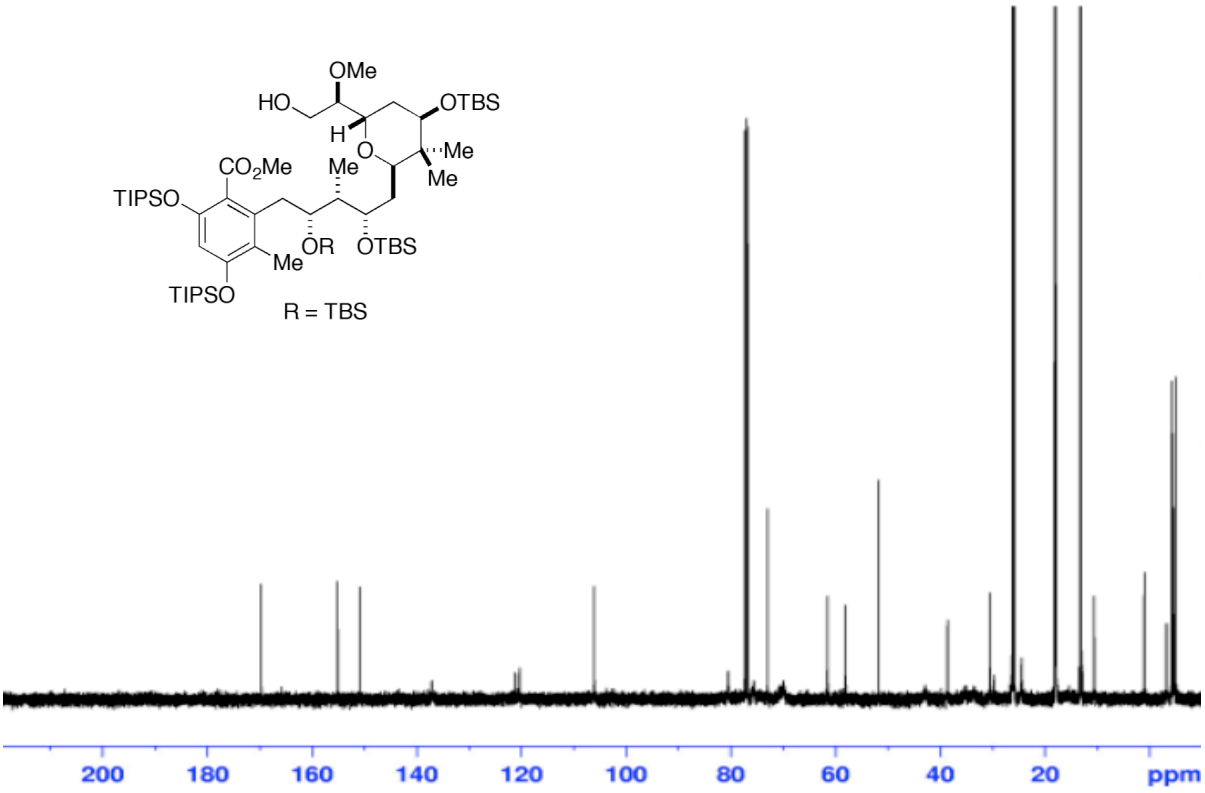
The ^{1}H NMR Spectrum of (+)-9; 500 MHz ($CDCl_3$)



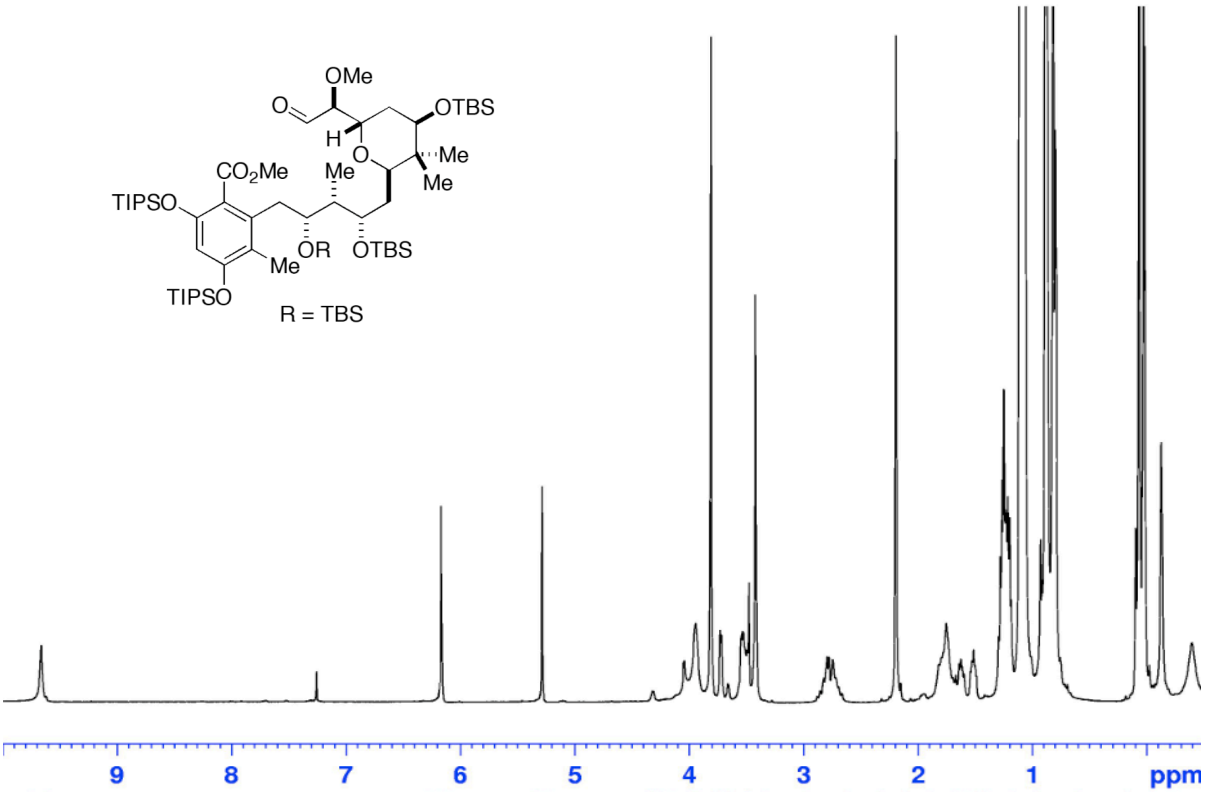
The ^{13}C NMR Spectrum of (+)-S9; 125 MHz ($CDCl_3$)



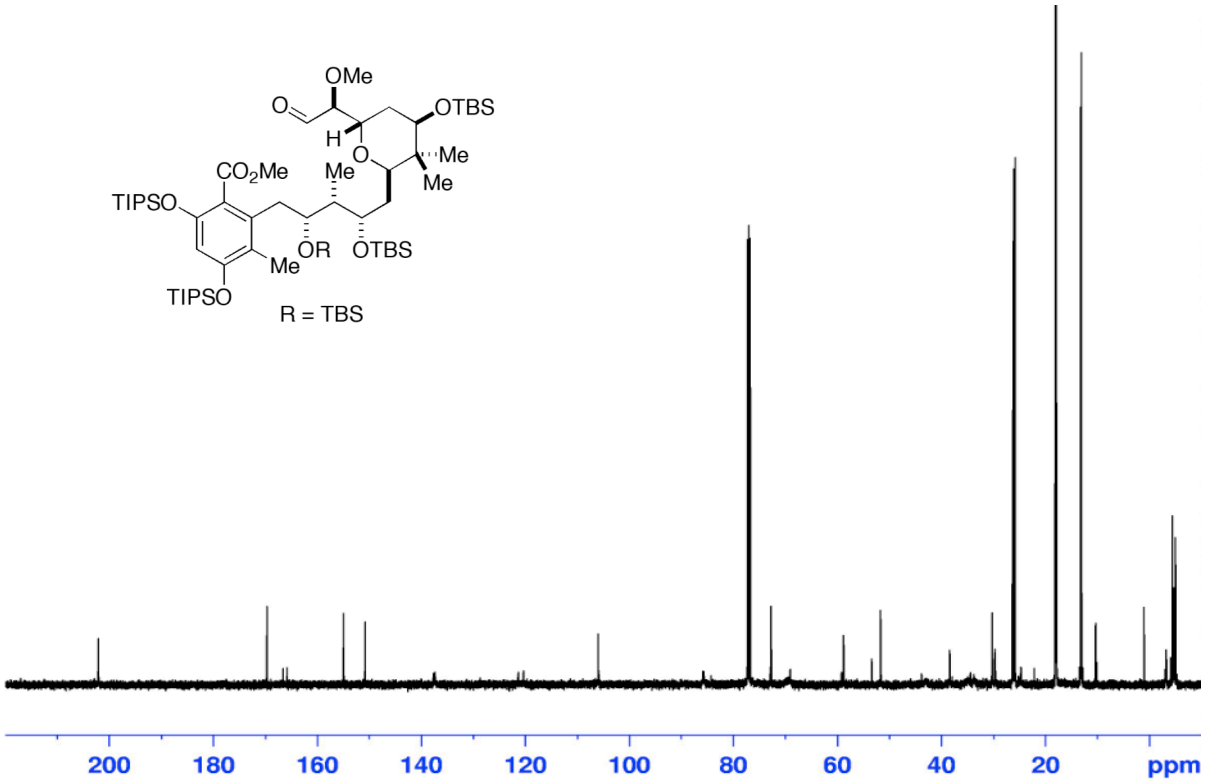
The ^{1}H NMR Spectrum of (+)-31; 500 MHz ($CDCl_3$)



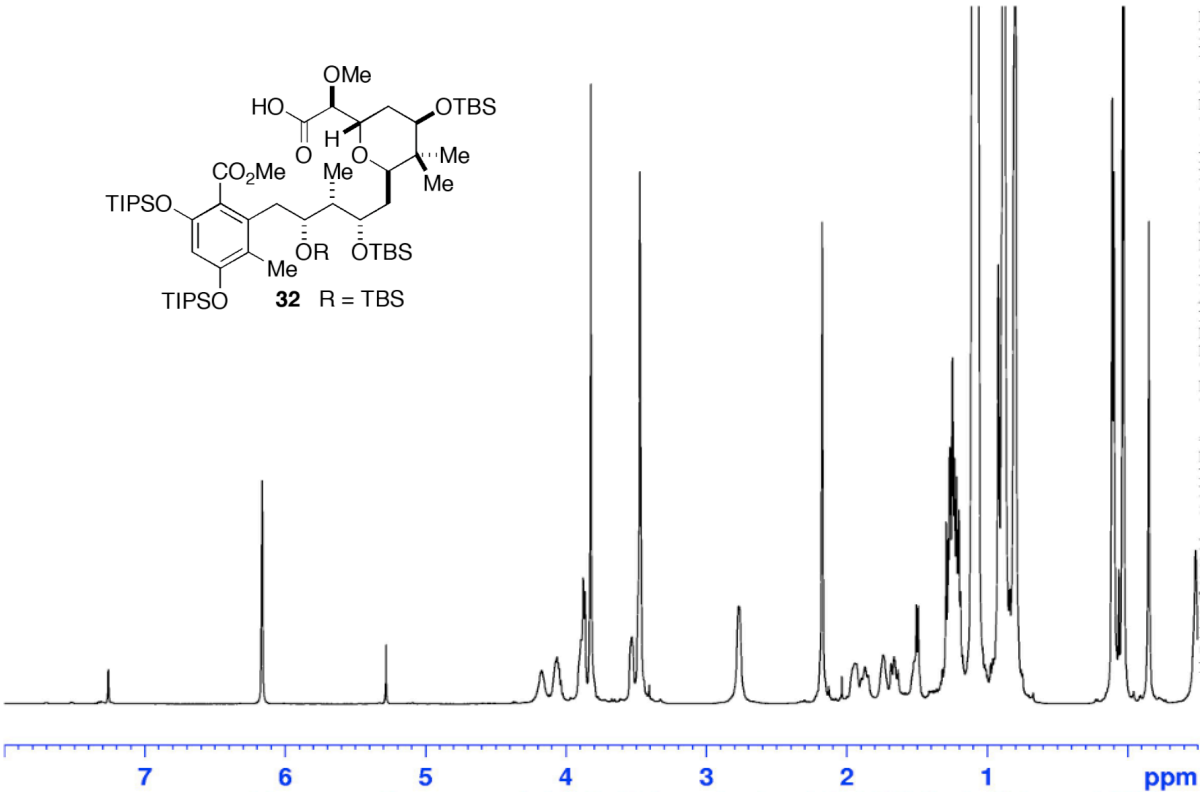
The ^{13}C NMR Spectrum of (+)-31; 125 MHz ($CDCl_3$)



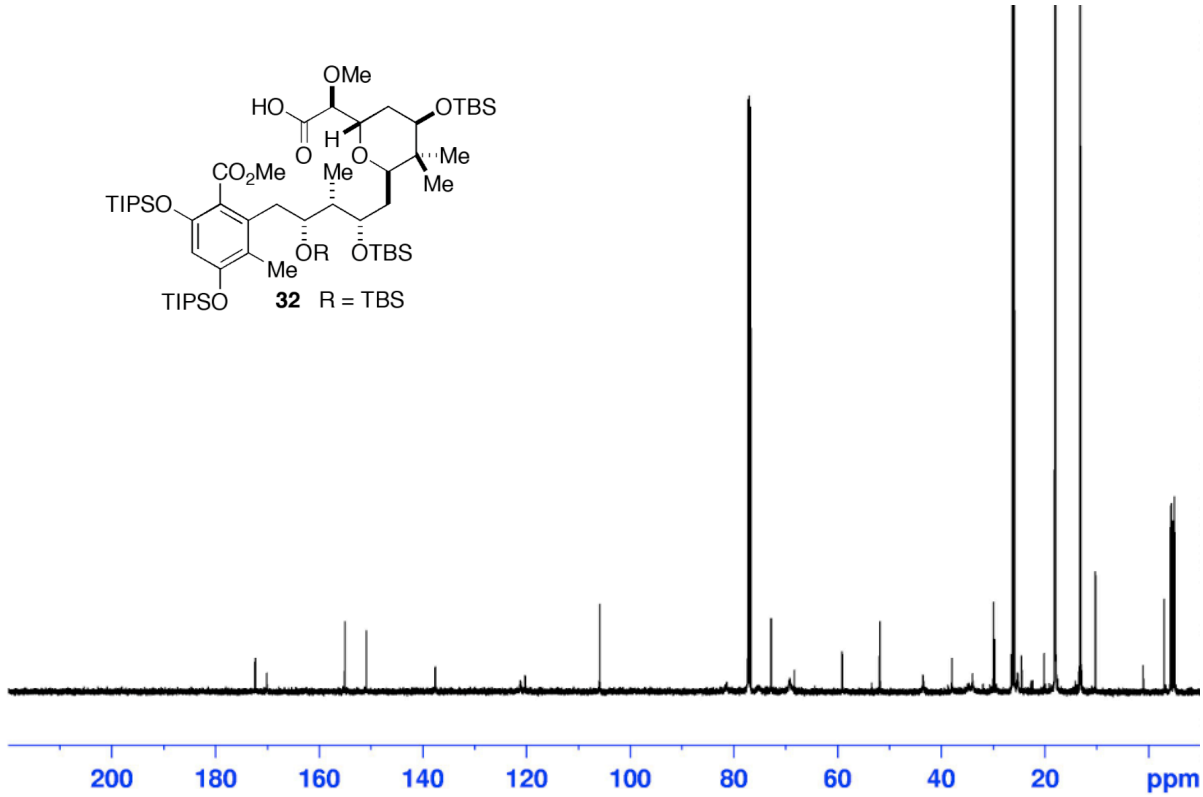
The ^{1}H NMR Spectrum of (+)-S10; 500 MHz ($CDCl_3$)



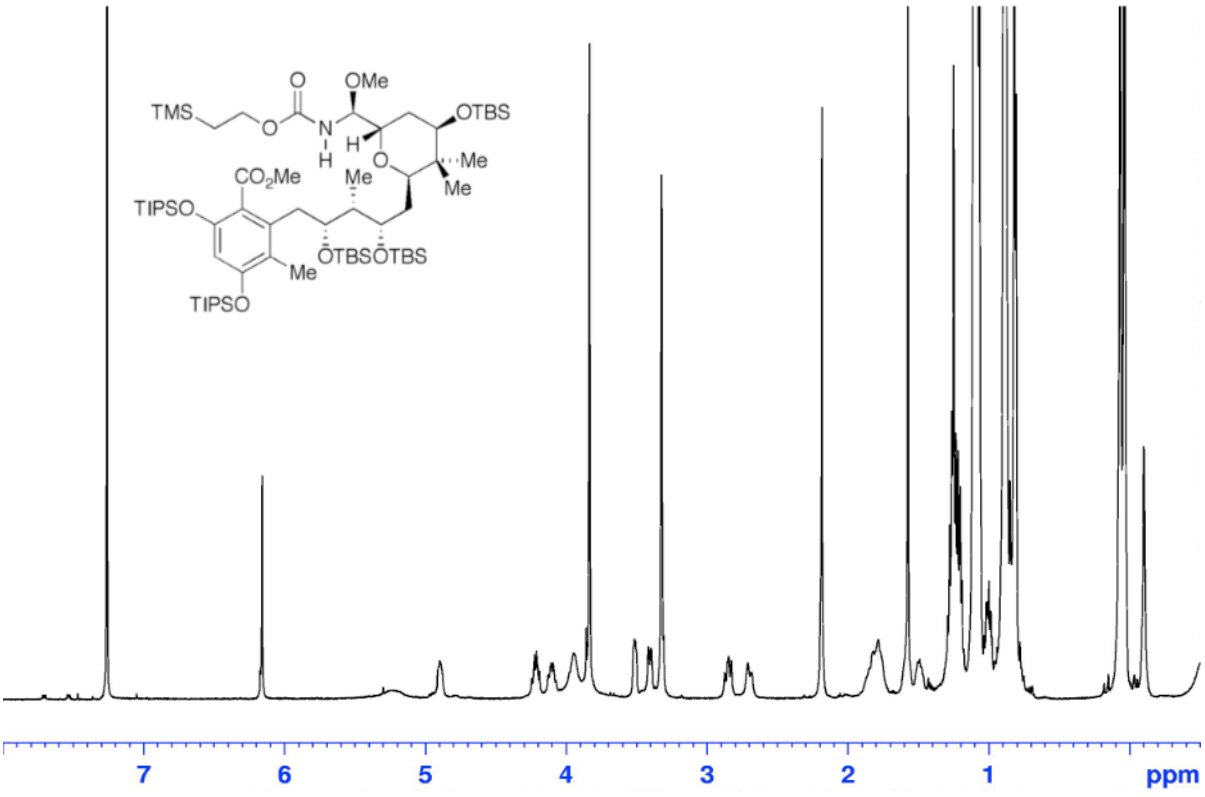
The ^{13}C NMR Spectrum of (+)-S10; 125 MHz ($CDCl_3$)



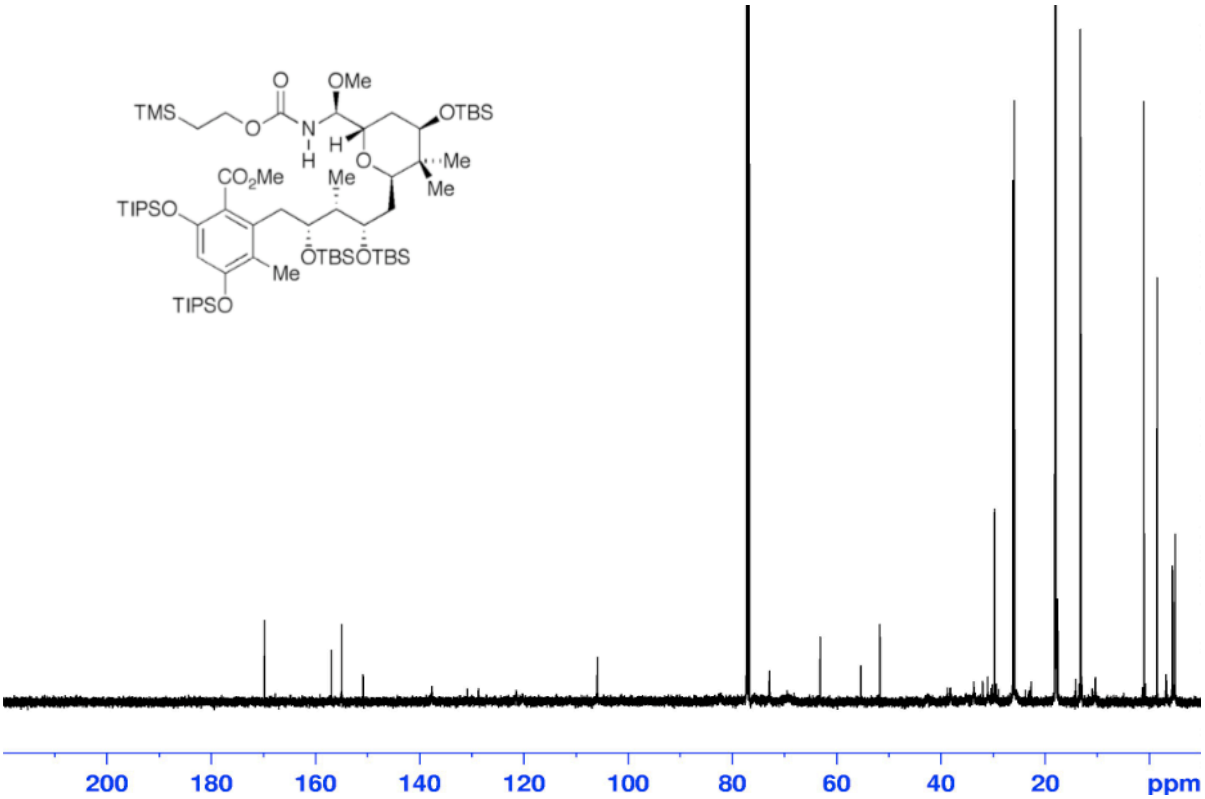
The ^{1}H NMR Spectrum of (+)-32; 500 MHz ($CDCl_3$)



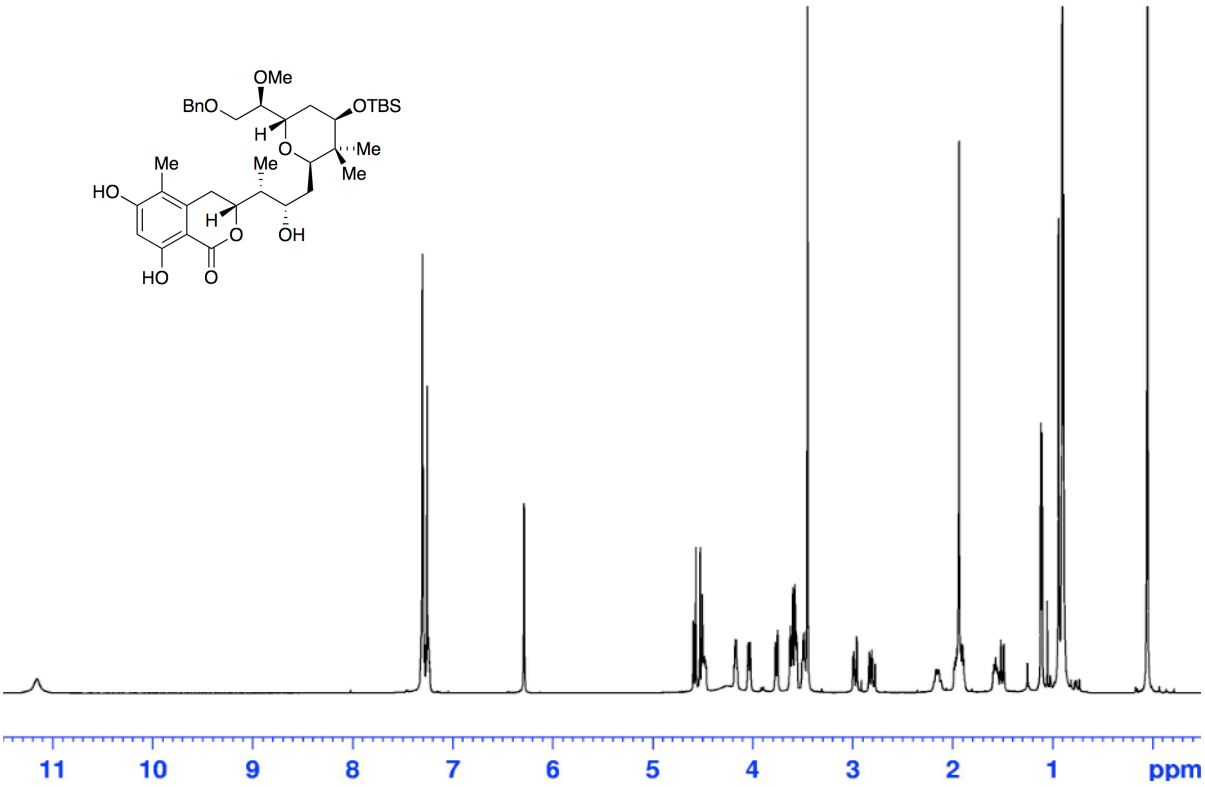
The ^{13}C NMR Spectrum of (+)-32; 125 MHz ($CDCl_3$)



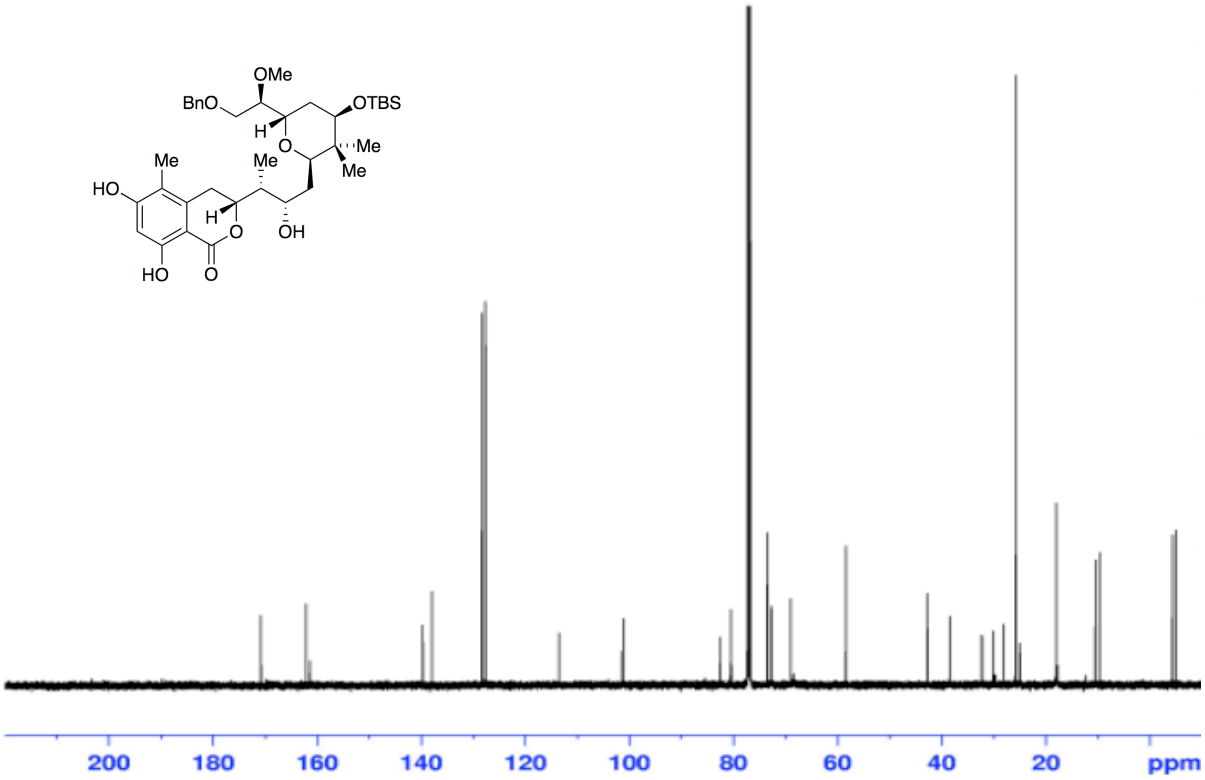
The ^{1}H NMR Spectrum of (+)-33; 500 MHz ($CDCl_3$)



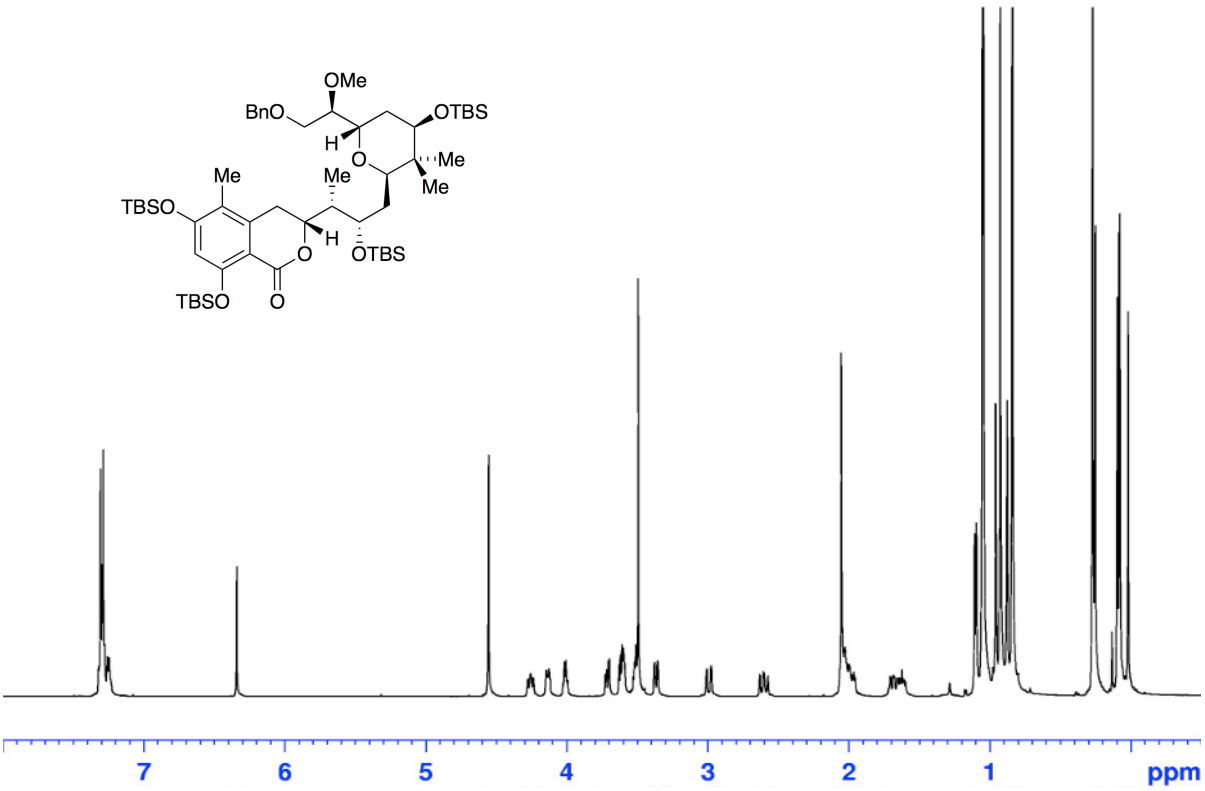
The ^{13}C NMR Spectrum of (+)-33; 125 MHz ($CDCl_3$)



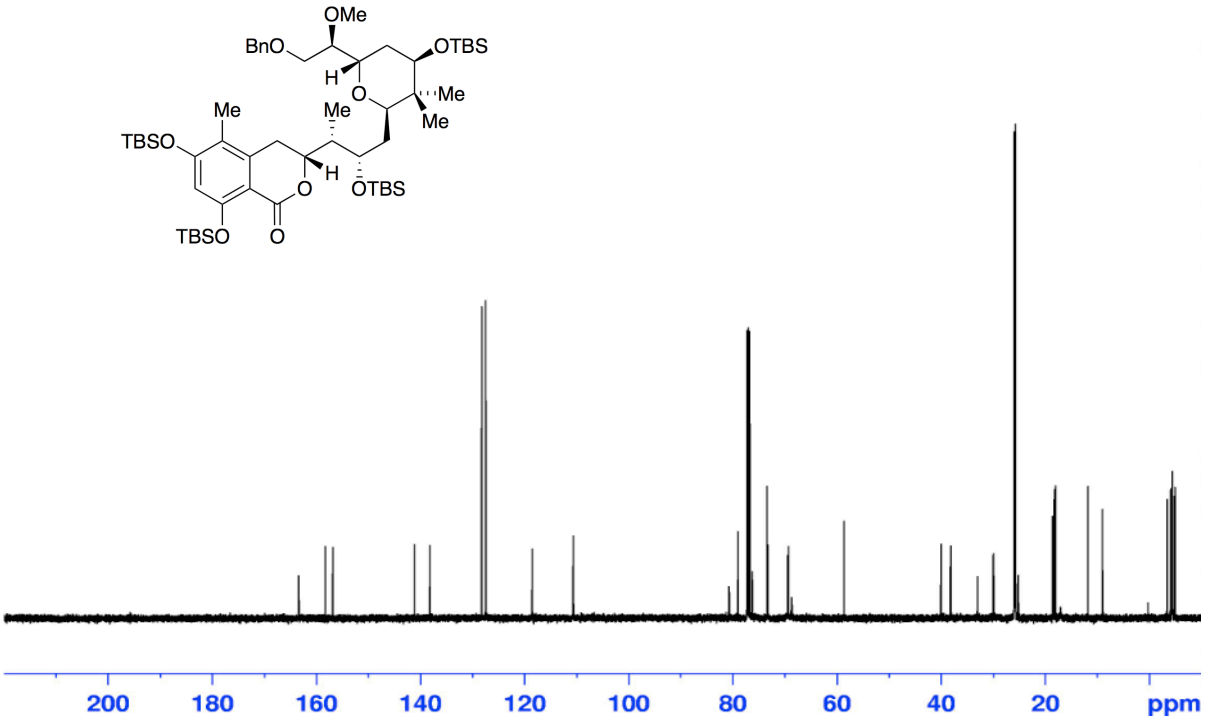
The ^{1}H NMR Spectrum of (+)-35; 500 MHz ($CDCl_3$)



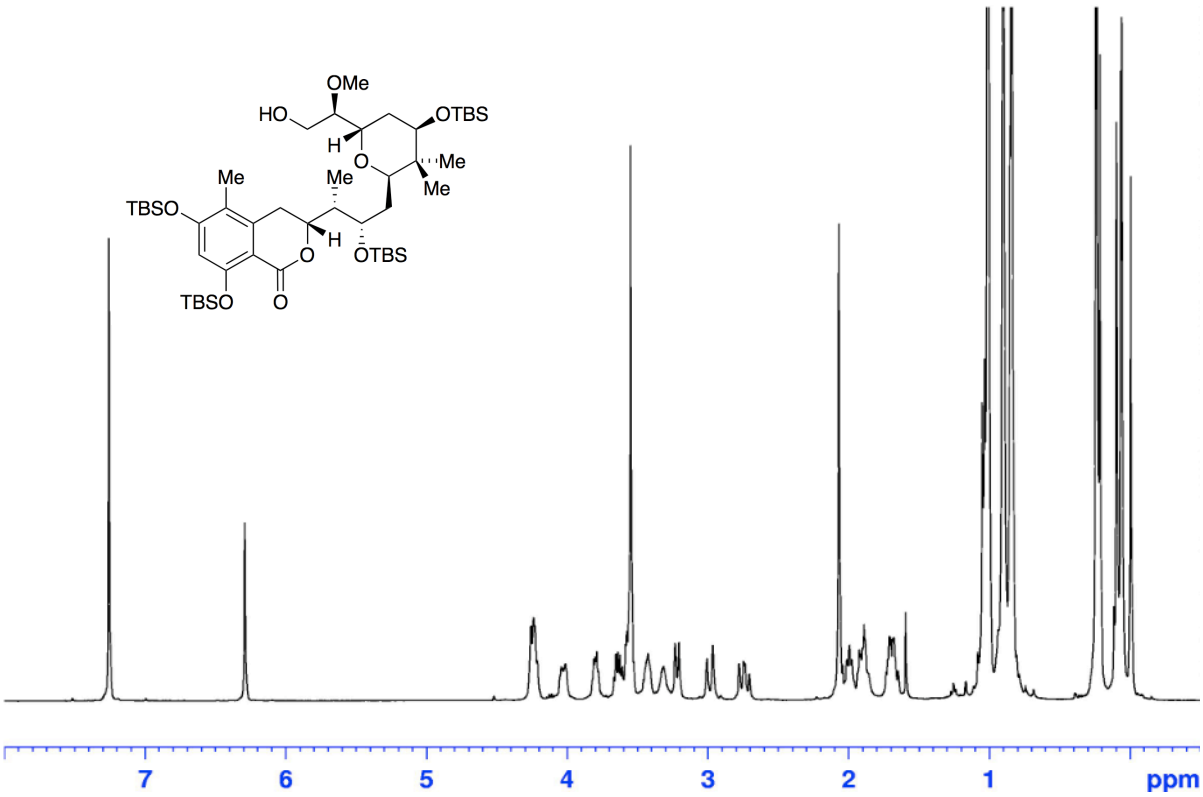
The ^{13}C NMR Spectrum of 35; (+)-125 MHz ($CDCl_3$)



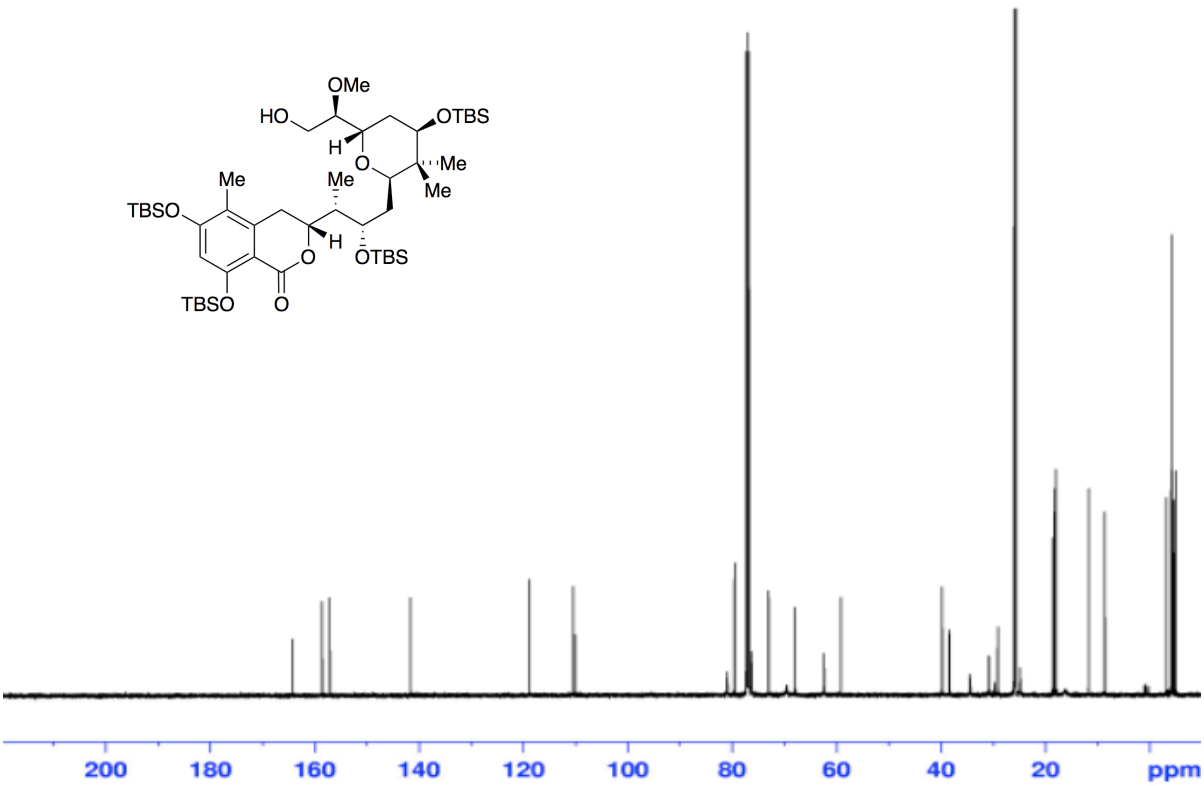
The ^{1}H NMR Spectrum of (+)-S11; 500 MHz ($CDCl_3$)



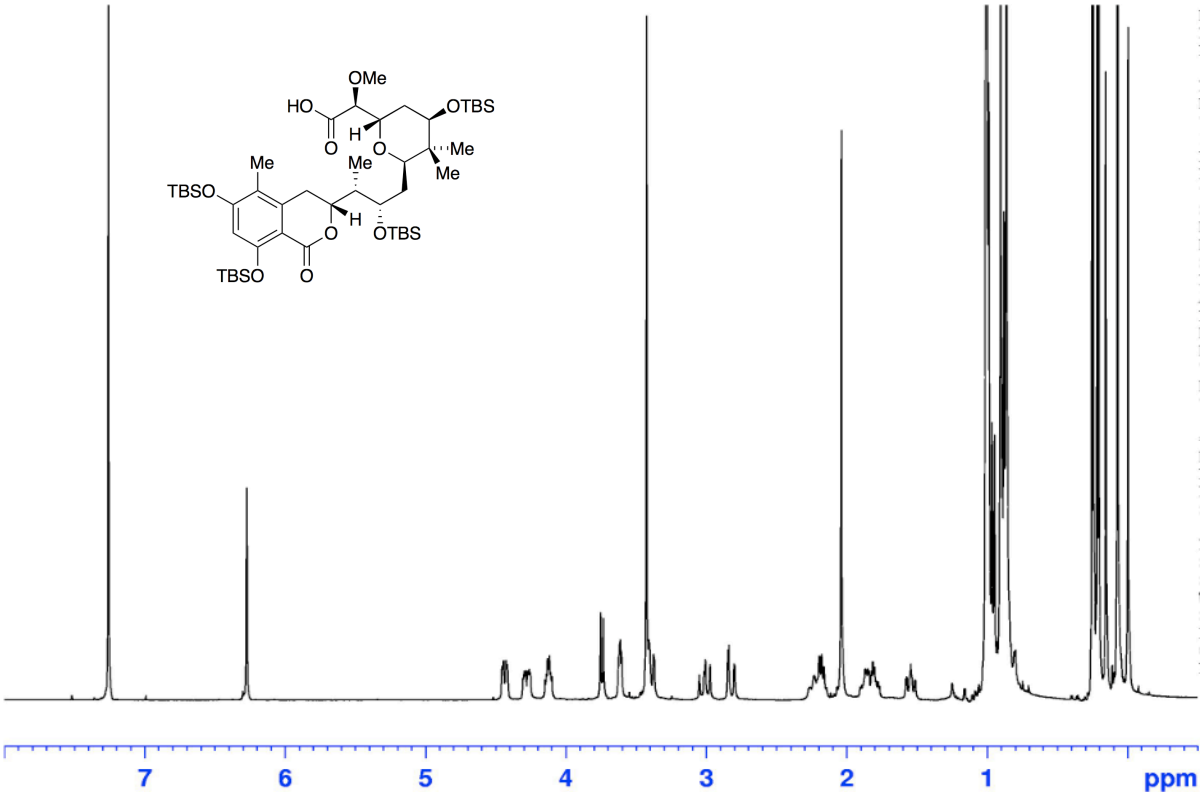
The ^{13}C NMR Spectrum of (+)-S11; 125 MHz ($CDCl_3$)



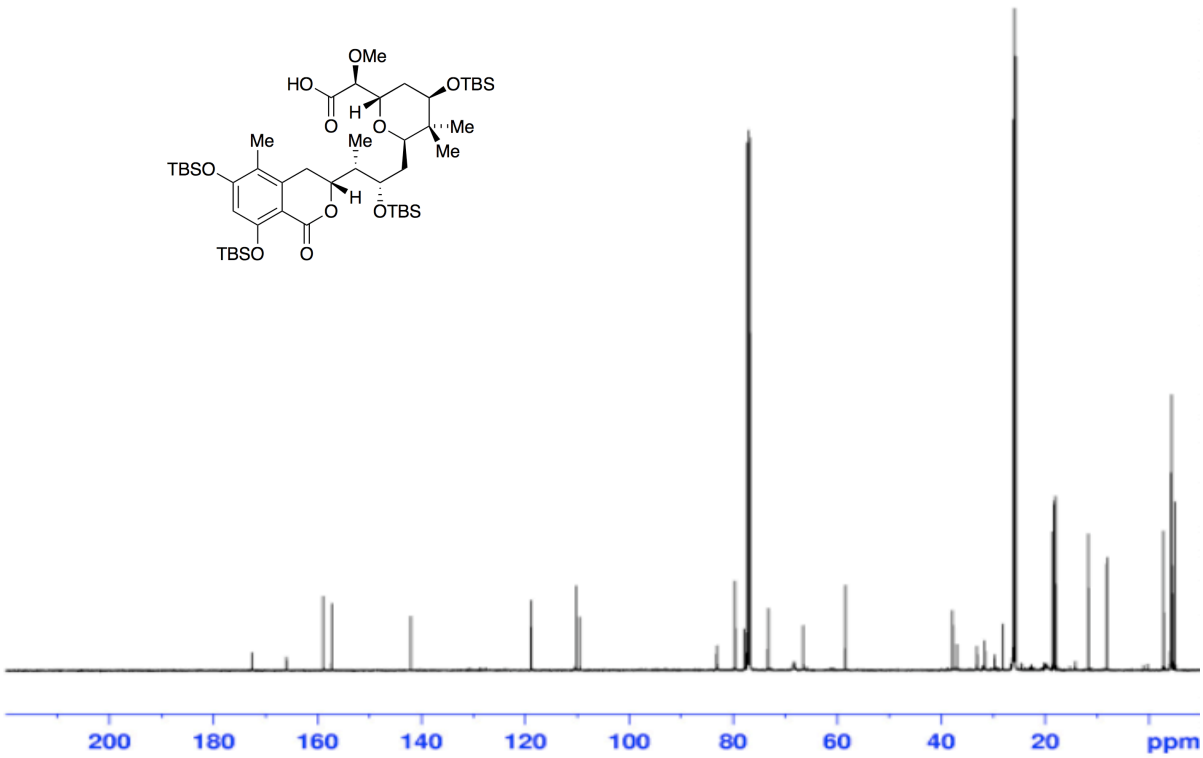
The ^{1}H NMR Spectrum of (+)-36; 400 MHz ($CDCl_3$)



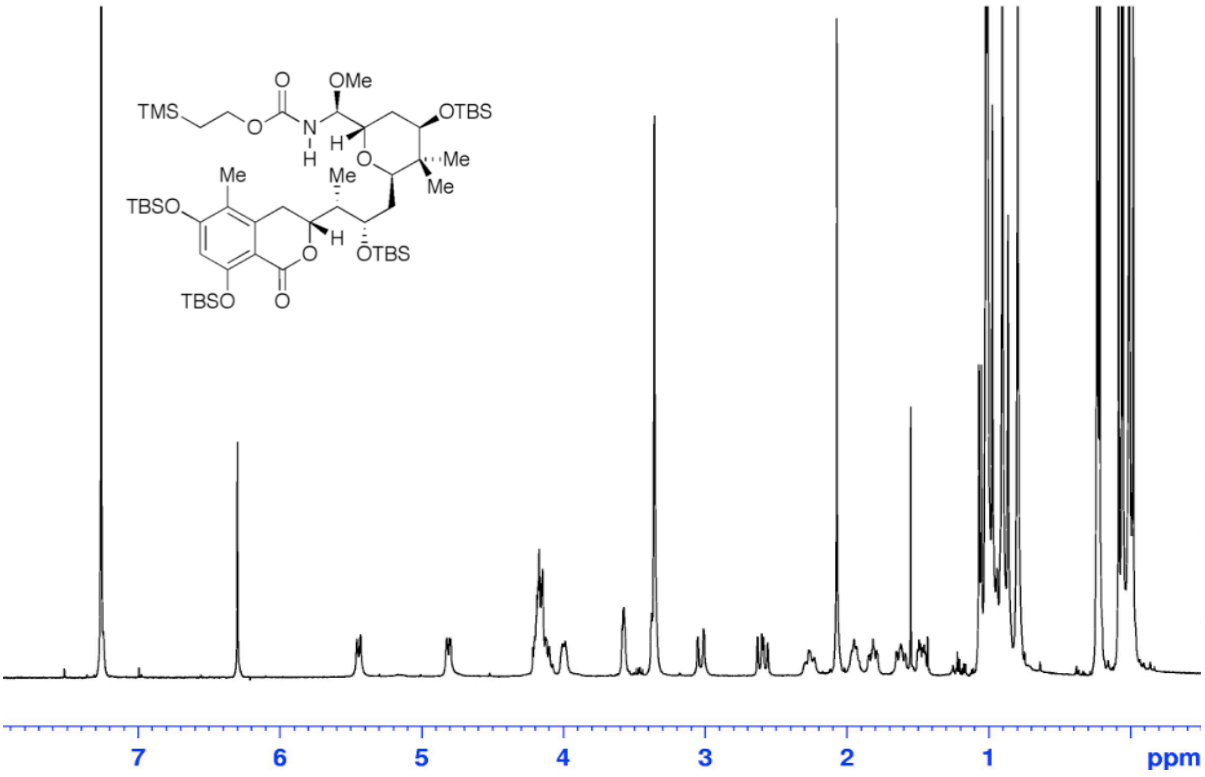
The ^{13}C NMR Spectrum of (+)-36; 125 MHz ($CDCl_3$)



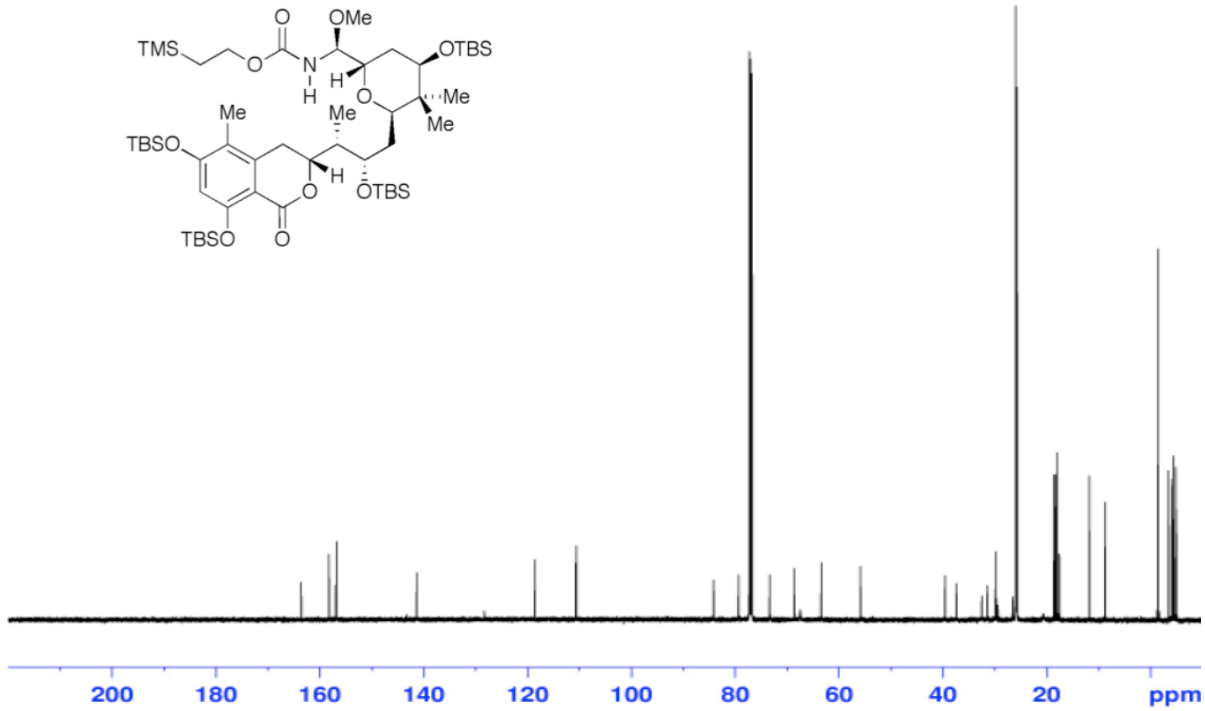
The ^{1}H NMR Spectrum of (+)-37; 400 MHz ($CDCl_3$)



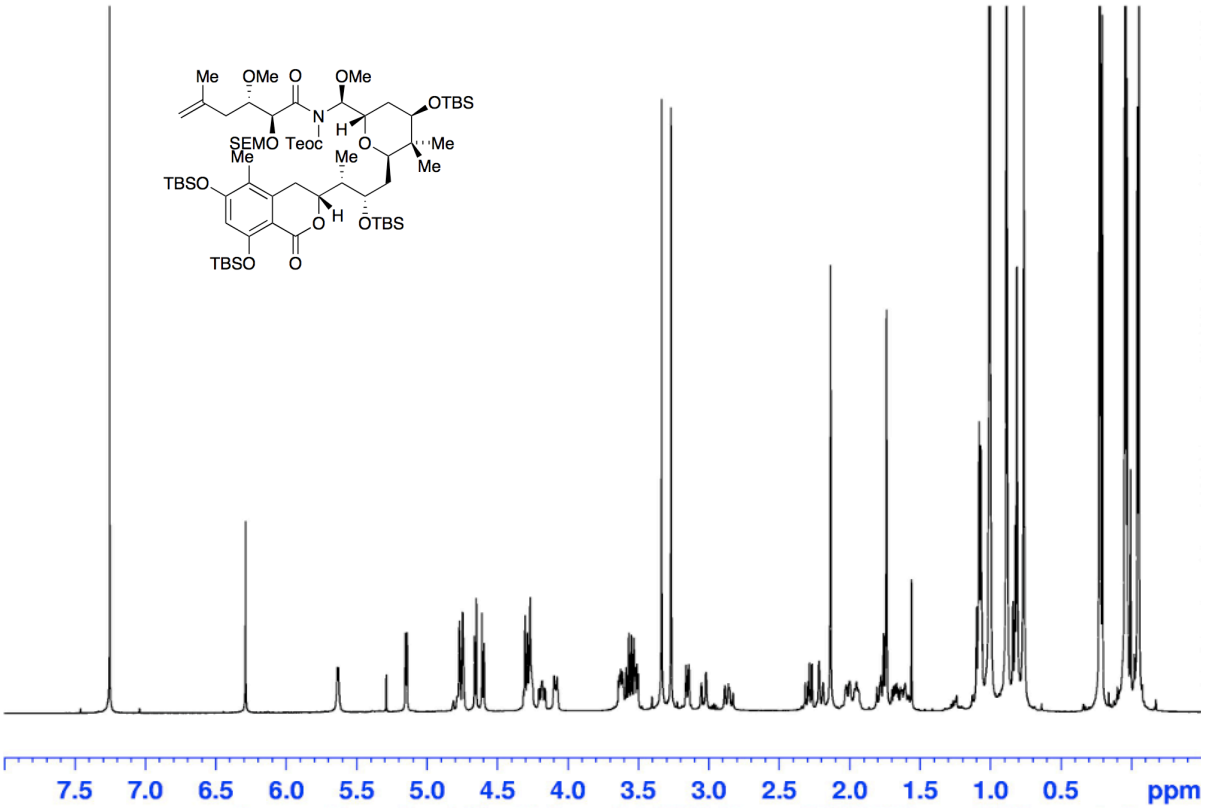
The ^{13}C NMR Spectrum of 37; (+)-125 MHz ($CDCl_3$)



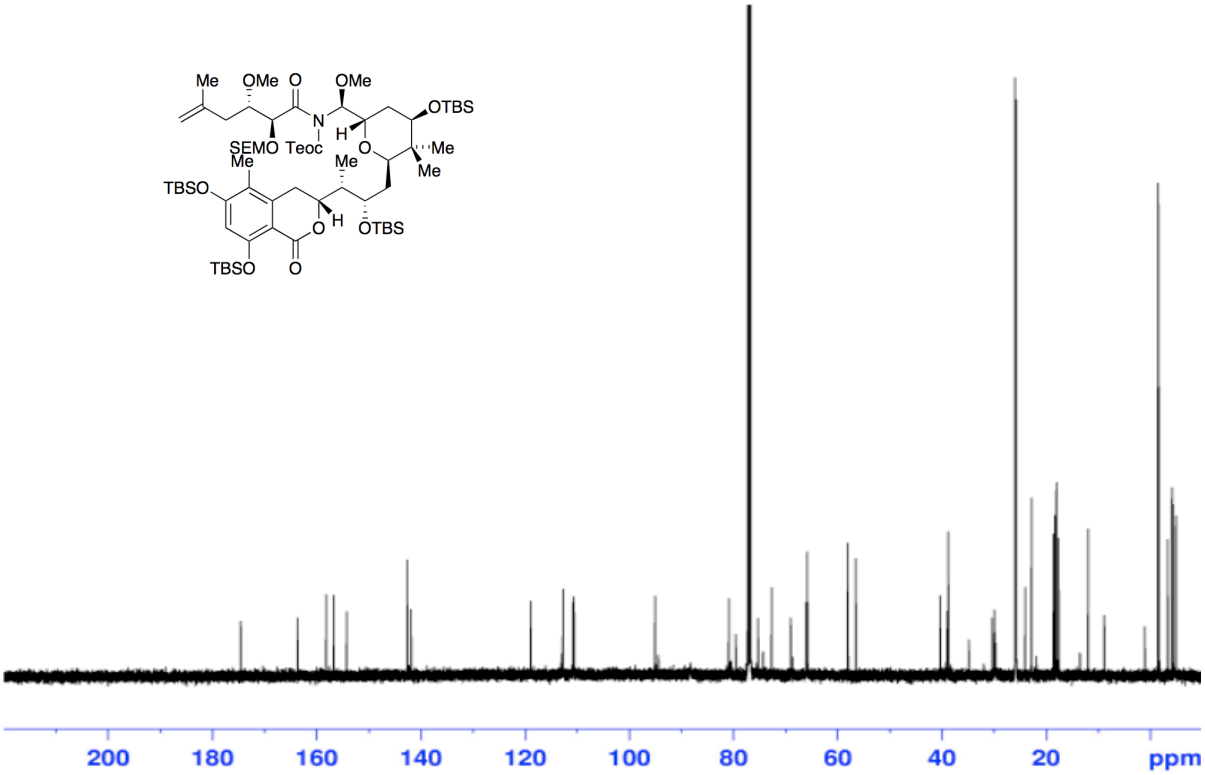
The ^{1}H NMR Spectrum of (+)-3; 400 MHz ($CDCl_3$)



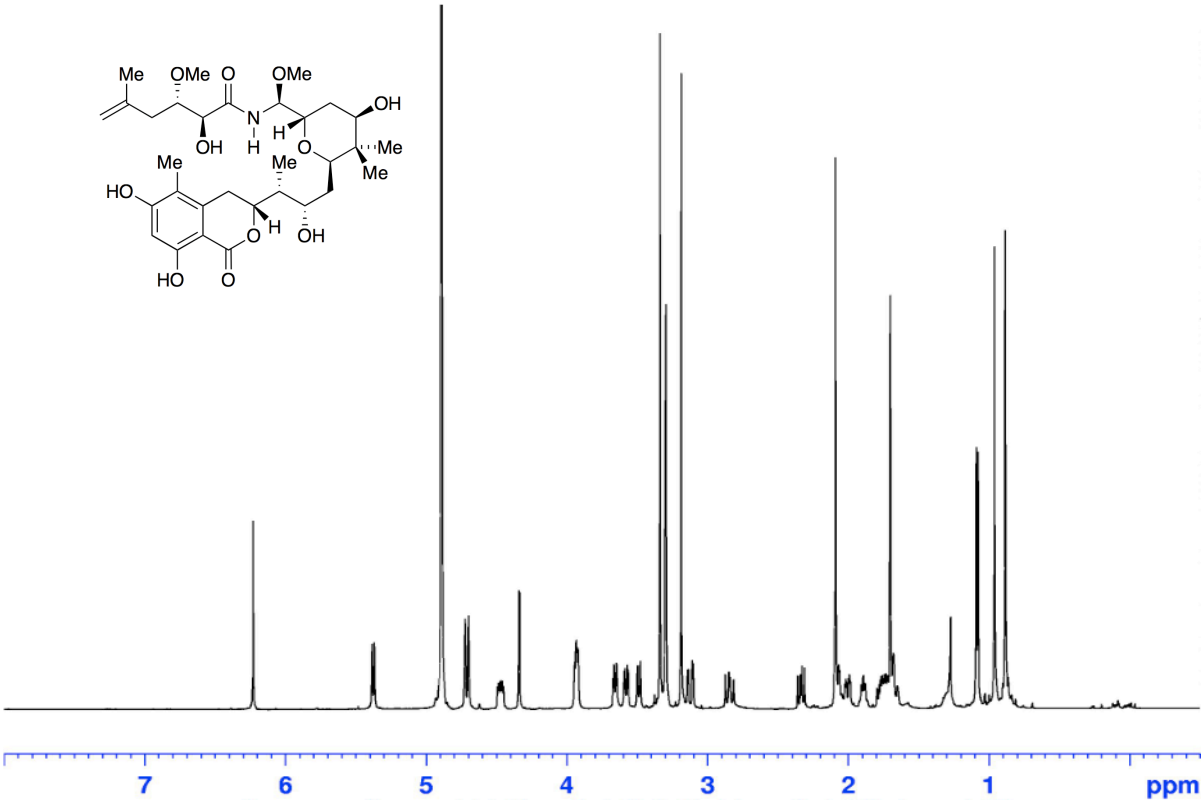
The ^{13}C NMR Spectrum of (+)-3; 125 MHz ($CDCl_3$)



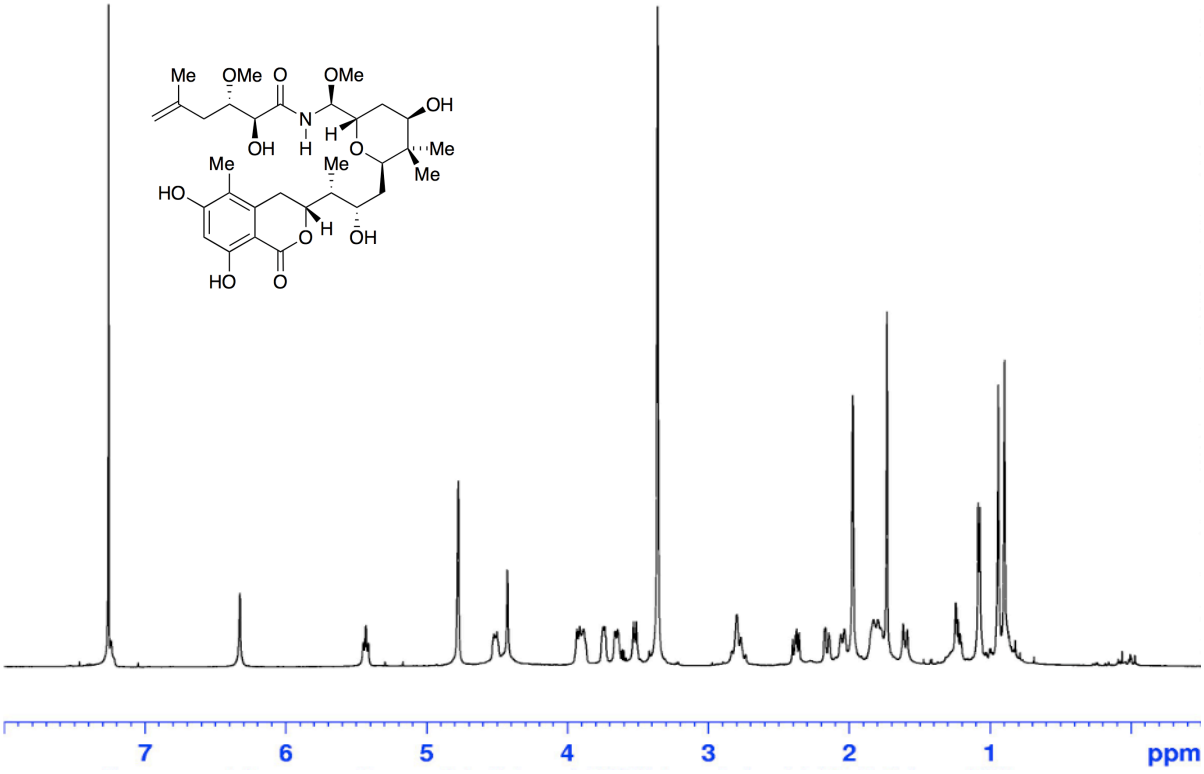
The ^{1}H NMR Spectrum of (+)-S12; 500 MHz ($CDCl_3$)



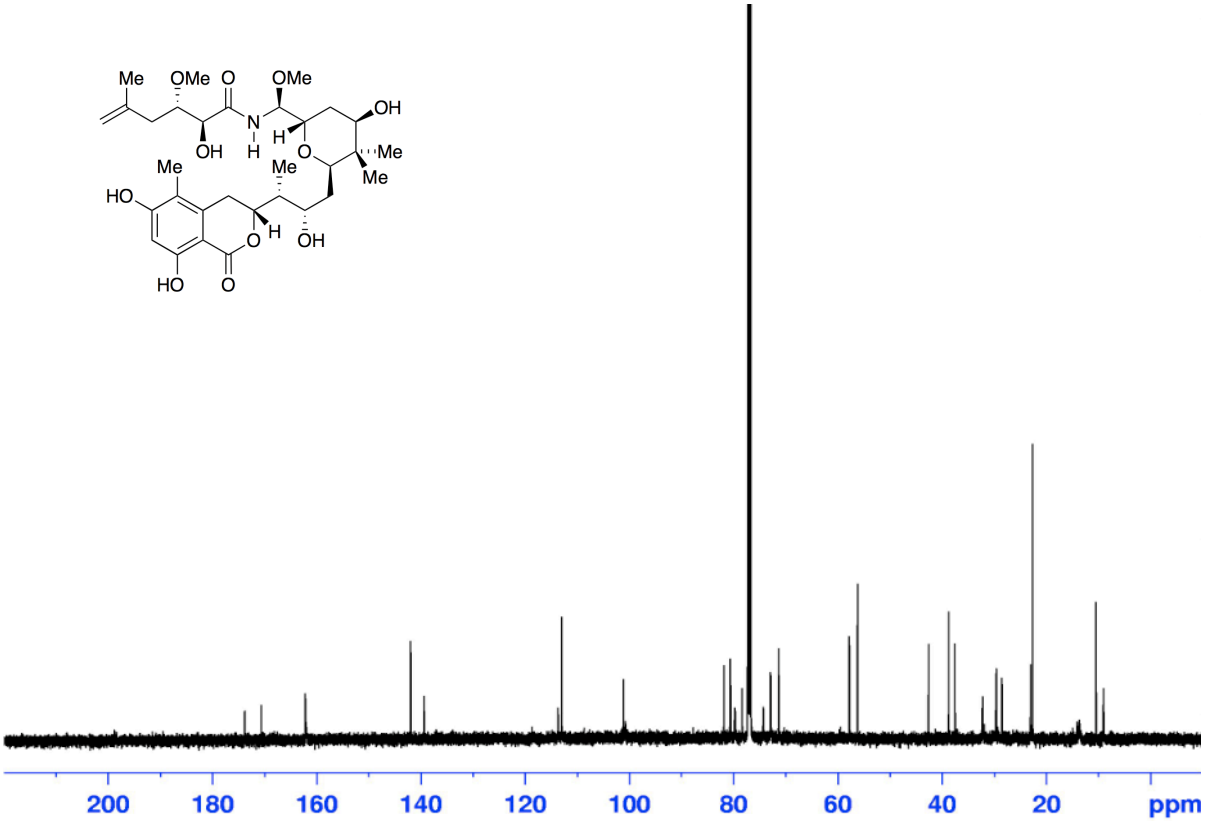
The ^{13}C NMR Spectrum of (+)-S12; 125 MHz ($CDCl_3$)



The ^{1}H NMR Spectrum of (+)-Irciniastatin A (1); 500 MHz (MeOD)



The ^{1}H NMR Spectrum of (+)-Irciniastatin A (1); 500 MHz ($CDCl_3$)



The ^{13}C NMR Spectrum of (+)-Irciniastatin A (1); 125 MHz ($CDCl_3$)