Supporting Information

Synthesis of Proposed Aglycone of Mandelalide A

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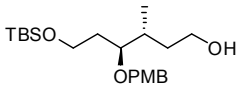
All the air and moisture sensitive reactions were carried out under inert atmosphere (nitrogen or argon). Oven-dried glass apparatus were used to perform all the reactions. Freshly distilled anhydrous solvents were used for air and moisture sensitive reactions. Commercially available reagents were used as such. Purification of compounds was carried out via column chromatography by using silica gel (60-120 or 100-200 mesh) packed in glass columns. ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ solvent on 300 MHz, 400 MHz, 500 MHz, 700 MHz and 75 MHz,100MHz, 125 MHz spectrometer, respectively, using TMS as an internal standard. Chemical shifts are measured as ppm values relative to internal $CHCl_3$ δ 7.26 or TMS δ 0.0 for ^{1}H NMR and $CHCl_3$ δ 77 for ^{13}C NMR. In ^{1}H NMR multiplicity defined as: s = singlet; d = doublet; t = triplet; q = quartet; dd = doublet of doublet; ddd = doublet of double of doublet; dt = doublet of triplet; m = multiplet; brs = broad singlet. Optical rotation values were recorded on Horiba sepa 300 polarimeter using a 2 mL cell with a 10 mm path length. FTIR spectra were recorded on Alpha (Bruker) infrared Spectrophotometer. High resolution mass spectra (HRMS) [ESI^{+}] were obtained using either a TOF or a double focusing spectrometer.

Abbreviations:

KHMDS = Potassium bis(trimethylsilyl)amide; DDQ = 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone; DMPU = 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone; EDCI = 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide; Ipc = Isopinocampheyl; DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene.

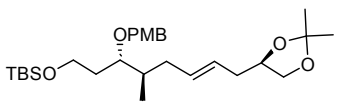
Experimental procedures and analytical data:

(3*R*,4*S*)-6-(*tert*-butyldimethylsilyloxy)-4-(4-methoxybenzyloxy)-3-methylhexan-1-ol (14):



To a stirred solution of **13** (10 g, 27.25 mmol) in dry THF (90 mL) was added $BH_3{\cdot}SMe_2$ (3 mL, 30.0 mmol) at 0 °C under N_2 atmosphere. After stirring 12 h at rt, the reaction mixture was cooled to 0 °C and treated with aqueous NaOH (3 M solution, 50 mL), 30% H_2O_2 (25 mL). After 2 h at room temperature, the mixture was extracted with ethyl acetate (2 x 100 mL). The combined organic extracts were washed sequentially with saturated aqueous $Na_2S_2O_3$ (20 mL), brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave crude residue which was purified by column chromatography (SiO_2, 60-120 mesh, 12% EtOAc/hexane) to afford **14** (8.8 g, 85%) as a colorless oil. R_f = 0.5 (SiO_2, 20% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 10.6 (*c* 0.3, $CHCl_3$); IR (Neat): ν_{max} 3391, 2927, 2855, 1612, 1513, 1462, 1301, 1248, 1173, 1059, 834, 776 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.46 (ABq, *J* = 10.9 Hz, 2H), 3.80 (s, 3H), 3.74-3.68 (m, 3H), 3.61 (m, 1H), 3.47 (m, 1H), 1.97 (m, 1H), 1.73-1.58 (m, 2H), 1.60 (m, 1H), 1.52 (m, 1H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H);^{13}C NMR (75MHz, $CDCl_3$): δ 159.1, 130.8, 129.3(2C), 113.7(2C), 79.4, 71.5, 60.6, 59.8, 55.2, 35.5, 33.6, 32.6, 25.9(3C), 18.3, 15.2, –5.30, –5.32. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{21}H_{38}O_4NaSi$ 405.2431, found 405.2439.

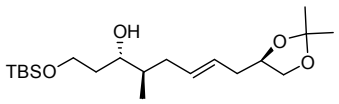
***tert*-Butyl ((3*S*,4*R*,*E*)-8-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxybenzyloxy)-4-methyloct-6-enyloxy)dimethylsilane (16) :**



To a stirred solution of **14** (8 g, 20.94 mmol) in dry CH_2Cl_2 (100 mL) was added $NaHCO_3$ (1.76 g, 20.94 mmol) and Dess-Martin periodinane (13.3 g, 31.41 mmol) at 0 °C under N_2 atmosphere. After 1 h stirring at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (25 mL) and $Na_2S_2O_3$ (40 mL) and extracted with EtOAc (2 x 350 mL). The combined organic extracts were washed with water (20 mL) and brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvent furnished crude aldehyde which was passed through a short pad of silica gel and used as such for the next reaction.

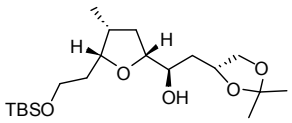
To a stirred solution of sulfone **15** (10.6 g, 31.41 mmol) in THF (60 mL) at –78 °C was added KHMDS (62.8 mL, 0.5 M in toluene, 31.41 mmol) under argon atmosphere. After 30 minutes, the crude aldehyde in THF (15 mL) was added to the reaction mixture at –78 °C via cannula. After 3 h stirring at –78 °C, the reaction was quenched with water (5 mL) and extracted with EtOAc (2 x 250 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 60-120 mesh, 7% EtOAc/hexane) to afford **16** (8.2 g, 80% over two steps) as a colourless oil. R_f = 0.5 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 25.0 (*c* 3, $CHCl_3$); IR (Neat): ν_{max} 2954, 2930, 2856, 1612, 1512, 1462, 1369, 1301, 1246, 1172, 1156,1062, 1037, 831, 774 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 7.25 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.48 (m, 1H), 5.38 (m, 1H), 4.42 (ABq, J = 10.9 Hz, 2H), 4.11 (m, 1H), 4.0 (m, 1H), 3.80 (s, 3H), 3.72-3.65 (m, 2H), 3.56 (m, 1H), 3.41 (q, J = 4.2 Hz, 1H), 2.38 (m, 1H), 2.21 (m, 1H), 2.11 (m, 1H), 1.89-1.79 (m, 2H), 1.69-1.61 (m, 2H), 1.41 (s, 3H), 1.35 (s, 3H), 0.91-0.81 (m, 12H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 132.1, 131.1, 129.2 (2C), 126.2, 113.7(2C), 108.8, 78.8, 75.6, 71.2, 68.8, 59.9, 55.2, 36.8, 36.2, 35.7, 33.2, 26.8, 25.9(3C), 25.6, 18.2, 14.4, –5.28, –5.33. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{28}H_{48}O_5NaSi$ 515.3163, found 515.3165.

(3*S*,4*R*,*E*)-1-(*tert*-butyldimethylsilyloxy)-8-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-methyloct-6-en-3-ol (9) :



To a stirred solution of **16** (7.5 g, 15.24 mmol) in $CHCl_3$: pH = 7 phospahte Buffer (20:1, 55 ml) was added DDQ (6.9 g, 30.4 mmol) at 0 °C. After stirring 2 h at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (50 mL) and extracted with EtOAc (2 x 250 mL). The combined organic extracts were washed with water (15 mL), brine (15 mL), dried over Na_2SO_4 and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to afford **9** (5.37 g, 95%) as a clear oil. R_f = 0.3 (SiO_2, 15% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 2.0 (*c* 0.7, $CHCl_3$); IR (Neat): ν_{max} 3509, 2931, 2858, 1462, 1370, 1253, 1156, 1064, 971, 835, 777 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 5.52 (m, 1H), 5.40 (m, 1H), 4.11 (q, *J* = 6.6 Hz, 1H), 4.0 (m, 1H), 3.92 (m, 1H), 3.80 (m, 1H), 3.63 (m, 1H), 3.57 (m, 1H), 3.44 (brs, OH), 2.38 (m, 1H), 2.27-2.19 (m, 2H), 1.88 (m, 1H), 1.66-1.60 (m, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 0.9 (s, 9H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.08 (s, 6H); ^{13}C NMR (125MHz, $CDCl_3$): δ 132.2, 126.1, 108.8, 75.7, 75.6, 68.8, 63.1, 38.8, 36.8, 35.5, 34.6, 26.8, 25.8(3C), 25.6, 18.0, 15.1, –5.58, –5.56. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{20}H_{40}O_4NaSi$ 395.2588, found 395.2591.

(*R*)-1-((2*R*,4*R*,5*R*)-5-(2-(*tert*-Butyldimethylsilyloxy)ethyl)-4-methyltetrahydrofuran-2-yl)-2-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol (17):

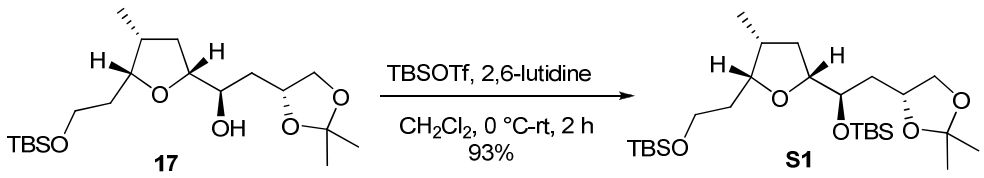


To a stirred solution of **9** (4.5 g, 12.1 mmol) in dry CH_2Cl_2 (40 mL) was added Et_3N (2.6 mL, 18.1 mmol) and MsCl (1.3 mL, 15.73 mmol) drop wise at 0 °C under N_2 atmosphere and stirred at rt for 1.5 h. Then the reaction mixture was quenched with saturated aqueous

$NaHCO_3$ (15 mL) and extracted with EtOAc (2 x 250 mL). The combined organic extracts were washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure afforded the mesylate compound which was used directly without further purification.

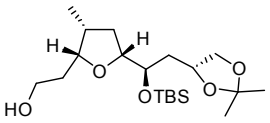
The above mesylate compound was added to a solution of AD-mix-β (33.8 g) and $MeSO_2NH_2$ (2.3 g, 24.2 mmol) in *t*-BuOH:water (1:1, 350 mL) at 0 °C. The mixture was stirred at this temperature for 72 h and then quenched by slow addition of $Na_2S_2O_5$ (34.5 g, 181.5 mmol) and stirred for additional 0.5 h. Then the reaction mixture was diluted with water, and extracted with EtOAc (2 x 250 mL).The combined organic extracts were washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4 and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 13% EtOAc/hexanes) to afford **17** (3.7 g, 79% over two steps) as a clear oil. R_f = 0.3 (SiO_2, 20% EtOAc /hexanes); $[\alpha]_D^{25}$ = + 22.2 (*c* 0.45, $CHCl_3$); IR (Neat): ν_{max} 3463, 2955, 2859, 1461, 1370, 1253, 1095, 1063, 834, 776 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$): δ 4.34 (m, 1H), 4.10 (dd, *J* = 8.0, 5.9 Hz, 1H), 3.99 (m, 1H), 3.79-3.66 (m, 3H), 3.62-3.54 (m, 2H), 2.64 (brs, OH), 2.37 (q, *J* = 7.3 Hz, 1H), 2.06 (dt, *J* = 14.3, 7.2 Hz, 1H), 1.72-1.53 (m, 4H), 1.41 (s, 3H), 1.37 (s, 3H), 1.33 (m, 1H), 0.95 (d, *J* = 7 Hz, 3H), 0.9 (s, 9H), 0.06 (s, 6H);^{13}C NMR (75MHz, $CDCl_3$): δ 108.4, 81.8, 78.7, 73.5, 71.9, 69.8, 60.8, 37.8, 36.2, 35.7, 34.0, 26.9, 25.9(3C), 25.7, 18.4, 14.9, –5.4(2C). HRMS (ESI): $[M + Na]^+$ calcd. for $C_{20}H_{40}O_5NaSi$ 411.2537, found 411.2529.

***tert*-Butyl-(2-((2*R*,3*R*,5*R*)-5-((*R*)-1-*(tert*-butyldimethylsilyloxy)-2-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-3-methyltetrahydrofuran-2-yl)ethoxy)dimethylsilane** (**S1**):



To a stirred solution of **17** (3 g, 7.73 mmol) in dry CH_2Cl_2 (25 mL) was added 2,6-lutidine (2.7 mL, 23.19 mmol) and TBSOTf (2 mL, 8.5 mmol) sequentially at 0 °C under N_2 atmosphere. After 2 h of stirring at rt, the reaction mixture was then quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (2 x 250 ml). The organic extract was washed with saturated aqueous $CuSO_4$ (15 mL), water (10 mL), brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 5% EtOAc/hexanes) to afford **S1** (3.6 g, 93%) as aclear oil. R_f = 0.5 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = +30.3 (*c* 0.6, $CHCl_3$); IR (Neat): ν_{max} 2954, 2931, 2858, 1466, 1374, 1251, 1092, 834, 776, 666 cm^{-1};^{1}H NMR (500MHz, $CDCl_3$): δ 4.26 (m, 1H), 4.04 (dd, *J* = 7.8, 5.9 Hz, 1H), 3.89-3.83 (m, 2H), 3.78 (m, 1H), 3.71-3.64 (m, 2H), 3.48 (t, *J* = 7.7 Hz, 1H), 2.26 (qt, *J* = 7.2 Hz, 1H), 1.97 (dt, *J* = 14.5, 7.2 Hz, 1H), 1.70-1.58 (m, 3H), 1.50 (m, 1H), 1.39 (s, 3H), 1.33 (s, 3H), 1.22 (m, 1H), 0.91 (d, *J* = 7 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.09 (s, 6H), 0.05 (s, 6H); ^{13}C NMR (75MHz, $CDCl_3$): δ 108.5, 81.6, 78.2, 72.5, 71.7, 70.0, 61.2, 37.0, 35.5, 35.3, 34.3, 27.1, 26.0 (6C), 25.8, 18.3, 18.2, 15.6, –4.0, –4.8, –5.3 (2C). HRMS (ESI): $[M + Na]^+$ calcd. for $C_{26}H_{54}O_5NaSi_2$ 525.3402, found 525.3412.

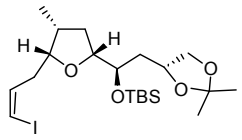
2-((2*R*,3*R*,5*R*)-5-((*R*)-1-(*tert*-butyldimethylsilyloxy)-2-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-3-methyltetrahydrofuran-2-yl)ethanol (18):



To a stirred solution of **S1** (3 g, 5.98 mmol) in dry THF (20 mL) in a polypropylene vial, was added HF-py complex (70 %, 0.8 mL) at 0 °C. The reaction mixture was slowly raised to rt and stirred for 12 h. After completion of the reaction, it was cautiously poured into saturated aqueous $NaHCO_3$ and stirred for 30 min. Then both the layers were separated, aqueous layer was further extracted with EtOAc (2 x 100 ml). The combined organic layers were washed with saturated aqueous $CuSO_4$ (15 mL), water (10 mL), brine (10 mL) and dried over

Na_2SO_4. The solvent was evaporated under *vacuo*. The residue was purified by column chromatography (SiO_2, 25% EtOAc/hexanes) to afford **18** (2.0 g, 86% yield) as a colourless liquid. R_f = 0.2 (SiO_2, 30% EtOAc /hexanes); $[\alpha]_D^{25}$ = + 18.7(*c* 0.65, $CHCl_3$); IR (Neat): ν_{max} 3444, 2955, 2857, 1471, 1370, 1249, 1214, 1058, 836, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.23 (m, 1H), 4.07-3.88 (m, 3H), 3.82-3.72 (m, 3H), 3.48 (t, *J* = 7.5 Hz, 1H), 2.32 (m, 1H), 1.95 (m, 1H), 1.78-1.50 (m, 4H), 1.38 (s, 3H), 1.32 (s, 3H),1.28 (m, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75MHz, $CDCl_3$): δ 108.6, 82.0, 81.2, 72.5, 70.7, 69.9, 61.8, 37.1, 35.6, 34.8, 33.0, 27.0, 25.9 (3C), 25.7, 18.1, 15.2, –4.1, –4.7. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{20}H_{40}O_5NaSi$ 411.2537, found 411.2542.

***tert*-Butyl ((*R*)-2-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-((2*R*,4*R*,5*R*)-5-((*Z*)-3-iodoallyl)-4-methyltetrahydrofuran-2-yl)ethoxy)dimethylsilane(19):**

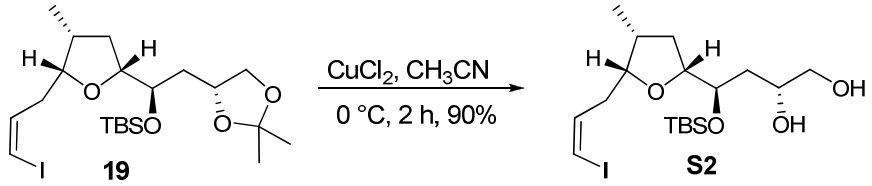


To a stirred solution of **18** (1.8 g, 4.64 mmol) in dry CH_2Cl_2 (20 mL) was added $NaHCO_3$ (0.37 g, 4.64 mmol) and Dess-Martin periodinane (3 g, 6.96 mmol) at 0 °C under N_2 atmosphere. After 2 h stirring at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (15 mL) and saturated aqueous $Na_2S_2O_3$ (15mL) and extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvent furnished crude aldehyde, which was passed through a short pad of silica gel and used as such for the next reaction.

To a suspension of (iodomethyl triphenylphosphonium) iodide (7.36 g, 13.92 mmol) in anhydrous THF (33 mL) was added NaHMDS (13.9 mL, 1.0 M in THF, 13.92 mmol) at 0 °C under argon atmosphere. After 15 min of stirring at 0 °C , the resulting solution was cooled to –78 °C and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) (2.8 mL, 23.2

mmol) was added followed by the addition of above aldehyde in anhydrous THF (10 mL) via cannula. After being stirred at –78 °C for 2 h, the reaction was quenched by addition of saturated aqueous NH_4Cl (5 mL) and stirred at rt for 1 h and extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with water (10 mL), brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 5% EtOAc/hexanes) to afford **19** (1.77 g, 75% over two steps) as a viscous liquid. R_f = 0.6 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = +15.4 (*c* 1.2, $CHCl_3$); IR (Neat): ν_{max} 2954, 2929, 2857, 1463, 1372, 1251, 1062, 1001, 834, 777, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.32 (dt, *J* = 7.4, 6.4 Hz, 1H), 6.26 (dt, *J* = 7.4, 1.4 Hz, 1H), 4.25 (m, 1H), 4.04 (dd, *J* = 7.8, 5.9 Hz, 1H), 3.95-3.87 (m, 2H), 3.72 (dt, *J* = 12.8, 6.4 Hz, 1H), 3.50 (t, *J* = 7.6 Hz, 1H), 2.34 (q, *J* = 7.3 Hz, 1H), 2.25-2.21 (m, 2H), 1.98 (dt, *J* = 14.1, 7.3 Hz, 1H), 1.68 (ddd, *J* = 13.5, 8.8, 2.4 Hz, 1H), 1.52 (ddd, *J* = 13.7, 9.9, 3.8 Hz, 1H), 1.40 (s, 3H), 1.33 (s, 3H), 1.29 (m, 1H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 108.6, 83.3, 81.9, 79.9, 72.5, 71.6, 70.0, 37.0, 36.9, 35.6, 35.3, 27.1, 26.0(3C), 25.8, 18.2, 15.3, –4.0, –4.7. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{21}H_{39}O_4INaSi$ 533.1554, found 533.1563.

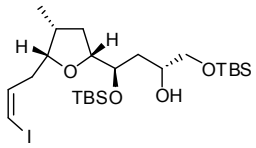
(2*R*,4*R*)-4-(*tert*-butyldimethylsilyloxy)-4-((2*R*,4*R*,5*R*)-5-((*Z*)-3-iodoallyl)-4-methyltetrahydrofuran-2-yl)butane-1,2-diol (S2):



To a stirred solution of **19** (1.4 g, 2.75 mmol) in dry CH_3CN (12 mL) was added $CuCl_2 \cdot H_2O$ (1.4 g, 8.25 mmol) at –5 °C portion wise. After 2 h, the reaction mixture was quenched with H_2O (5 mL) and extracted with EtOAc (3 x 70 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The

residue was purified by column chromatography (SiO_2, 35% EtOAc/hexanes) to afford **S2** (1.16 g, 90%) as a clear oil. R_f = 0.2 (SiO_2, 40% EtOAc /hexanes); $[\alpha]_D^{25}$ = +13.2 (*c* 0.5, $CHCl_3$); IR (Neat): ν_{max} 3733, 3370, 2928, 2856, 2313, 1515, 1463, 1251, 1089, 835, 777 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.32 (dt, *J* = 7.4, 6.4 Hz, 1H), 6.27 (dt, *J* = 7.4, 1.3 Hz, 1H), 3.99-3.94 (m, 2H), 3.93-3.88 (m, 2H), 3.60 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.44 (dd, *J* = 11.1, 6.4 Hz, 1H), 2.37 (q, *J* = 7.3 Hz, 1H), 2.27-2.23 (m, 2H), 2.03 (m, 1H), 1.76 (m, 1H), 1.52 (dq, *J* = 14.6, 2.2 Hz, 1H), 1.27 (m, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.7, 83.6, 81.1, 80.1, 73.6, 69.1, 67.2, 36.9, 36.1, 35.9, 35.6, 25.9(3C), 18.1, 15.4, –4.3, –4.9. HRMS (ESI): $[M + H]^+$ calcd. for $C_{18}H_{36}O_4ISi$ 471.1422, found 471.1416.

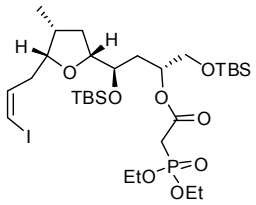
(6*R*,8*R*)-8-((2*R*,4*R*,5*R*)-5-((*Z*)-3-Iodoallyl)-4-methyltetrahydrofuran-2-yl)-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodecan-6-ol (20):



To a stirred solution of **S2** (0.900 g, 1.91 mmol) in dry CH_2Cl_2 (10 mL) was added Imidazole (0.2 g, 2.87 mmol) and TBSCl (0.43 g, 2.87 mmol) sequentially at 0 °C under N_2 atmosphere. After 3 h stirring at rt, the reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 7% EtOAc/hexanes) to afford **20** (1.05 g, 94%) as a oily liquid. R_f = 0.2 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = + 22.0 (*c* 1.4, $CHCl_3$); IR (Neat): ν_{max} 2953, 2928, 2856, 1465, 1367, 1252, 1094, 1002, 837, 776, 672 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.32 (dt, *J* = 7.5, 6.4 Hz, 1H), 6.25 (dt, *J* = 7.5, 1.2 Hz, 1H), 3.96-3.91 (m, 2H), 3.87-3.79 (m, 2H), 3.53 (dd, *J* = 9.7, 4.8 Hz, 1H), 3.47 (dd, *J* = 9.9, 6.7 Hz, 1H), 2.96

(brs, OH), 2.34 (q, J = 7.3, 1H), 2.26-2.21 (m, 2H), 2.01 (m, 1H), 1.53 (m, 1H), 1.30-1.23 (m, 2H), 0.98 (d, J = 7 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.1 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 83.3, 81.7, 80.0, 72.8, 68.6, 67.6, 36.9, 36.5, 35.66, 35.64, 25.9 (3 C), 25.8 (3 C), 18.26, 18.23, 15.4, –4.1, –4.9, –5.4 (2 C). HRMS (ESI): $[M + H]^+$calcd. for $C_{24}H_{50}IO_4Si_2$ 585.2290, found 585.2288.

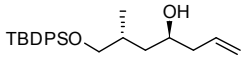
(6*R*,8*R*)-8-((2*R*,4*R*,5*R*)-5-((*Z*)-3-Iodoallyl)-4-methyltetrahydrofuran-2-yl)-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodecan-6-yl 2-(diethoxyphosphoryl) acetate (6):



To a stirred solution of **20** (0.900 g, 1.54 mmol) which was previously azeotroped with benzene, in dry CH_2Cl_2 (10 mL) was added diethyl phosphono acetic acid (0.8 mL, 4.62 mmol) and DMAP (0.038 g, 0.308 mmol) at 0 °C under argon atmosphere. After 10 min stirring at 0 °C, EDCI (0.9 g, 4.62 mmol) was added to it and stirred at rt for another 4 h. Then water was added and extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 30% EtOAc/hexanes) to afford **6** (1.1 g, 94%) as a yellow oil. R_f = 0.2 (SiO_2, 40% EtOAc /hexanes); $[\alpha]_D^{25}$ = + 24.8 (*c* 0.45, $CHCl_3$); IR (Neat): ν_{max} 2927, 2856, 1737, 1465, 1391, 1259, 1102, 1053, 1027, 970, 838, 778, 669 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.31 (dt, J = 7.3, 6.5 Hz, 1H), 6.25 (dt, J = 7.3, 1.2 Hz, 1H), 5.04 (m, 1H), 4.20-4.14 (m, 4H), 3.91 (m, 1H), 3.80-3.71 (m, 2H), 3.65 (qd, J = 10.7, 4.7 Hz, 2H), 2.97 (s, 1H), 2.63 (d, J = 21.5 Hz, 2H), 2.25-2.21 (m, 2H), 2.01 (m, 1H), 1.79 (ddd, J = 14.3, 9.4, 2.6 Hz, 1H), 1.68 (ddd, J = 14.2, 9.2, 2.8 Hz, 1H), 1.34 (td,

J = 7.0, 2.6 Hz, 6H), 1.29 (m, 1H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.86 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H);^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3, 138.9, 83.3, 81.6, 80.0, 73.3, 70.9, 64.3, 62.63, 62.60, 37.0, 35.4, 35.2, 34.9, 34.3, 33.8, 25.9(3C), 25.8(3C), 18.2, 18.17, 16.4, 15.4, –4.0, –4.9, –5.4(2C). HRMS (ESI): $[M + Na]^+$ calcd. for $C_{30}H_{60}INaO_8PSi_2$ 785.2501, found 785.2492.

(4*S*,6*R*)-7-(*tert*-butyldiphenylsilyloxy)-6-Methylhept-1-en-4-ol (21):

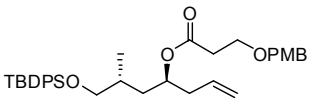


Ozone was bubbled through a stirred solution of **11** (5.7 g, 16.82 mmol) in CH_2Cl_2 (500 mL) at –78 °C until a light blue colour persisted. After 3 h the reaction was complete, Ar was bubbled through the solution until it became colourless. Dimethyl sulfide (12.4 mL, 420.5 mmol) was added via syringe at –78 °C, and the mixture was allowed to slowly warm to room temperature. Solvent was removed under *vacuo* and the residue was purified by flash column chromatography afforded aldehyde which was used directly in the next step.

To a stirred solution of (–)-Ipc_2BOMe (7.98 g, 25.23 mmol) in diethyl ether (60 mL) at –78 °C was added allylmagnesium bromide (1 M in diethyl ether, 23.5 mL, 23.5 mmol).This resultant mixture allowed to room temperature over 1 h before it was cooled back to –78 °C. To this mixture, was added a solution of above aldehyde in diethyl ether (15 mL). The resultant mixture was stirred at –78 °C for 8 h. To this mixture was added a premixed solution of 10% aqueous NaOH (30 mL) and 30% H_2O_2 (60 mL). After being stirred at room temperature overnight, the resultant mixture was diluted with H_2O and extracted with EtOAc (3 x 300 mL). The combined organic extracts were washed with brine (50 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 6% EtOAc/hexanes) to afford **21** (4.5 g, 70% two steps) as a oily liquid. R_f = 0.4 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = + 8.6 (*c* 0.9, $CHCl_3$); IR (Neat): ν_{max} 3396, 2363, 1641, 1107, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69-7.65 (m, 4H),

7.45-7.36 (m, 6H), 5.84 (m, 1H), 5.13 (m, 1H), 5.10 (m, 1H), 3.75 (m, 1H), 3.52-3.49 (m, 2H), 2.45 (brs, OH), 2.29-2.17 (m, 2H), 1.89 (q, J = 6.7 Hz, 1 H), 1.51 (m, 1H), 1.36 (dddd, J = 14.2, 7.6, 3.0 Hz, 1H), 1.06 (s, 9H), 0.89 (d, J = 6.7 Hz, 3H);^{13}C NMR (125 MHz, $CDCl_3$): δ 135.6 (4C), 135.0 (2C), 133.5, 129.6 (2C), 127.6 (4C), 117.6, 69.8, 69.0, 42.6, 41.7, 33.3, 26.8 (3C), 19.2, 17.2. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{24}H_{34}O_2SiNa$ 405.2225, found 405.2228.

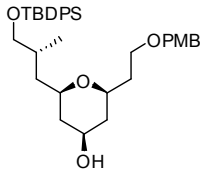
(4*S*,6*R*)-7-(*tert*-butyldiphenylsilyloxy)-6-methylhept-1-en-4-yl 3-(4-methoxybenzyloxy) propanoate (10):



To a stirred solution of alcohol **21** (4 g, 10.47 mmol) and acid **22** (4.1 g, 20.94 mmol) previously azeotroped with dry benzene (3 times), in dry CH_2Cl_2 (40 mL) were added DCC (4.3 g, 20.94 mmol) followed by DMAP (0.3 g, 2.09 mmol) at 0 °C under N_2 atmosphere. After stirring for 12 h at room temperature, then H_2O (10 mL) was added and the solution was kept stirring for another 10 min. Hexanes (200 mL) was added and the white precipitate was filtered off and the precipitate was washed with hexanes/CH_2Cl_2 (2:1, 150 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (15 mL) and dried over anhydrous Na_2SO_4. The residue was purified by column chromatography (SiO_2, 6% EtOAc/hexanes) to afford **10** (5.7 g, 95%) as a colour less oil. R_f = 0.5 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = + 15.6 (c 0.4, $CHCl_3$); IR (Neat): ν_{max} 2957, 2932, 2858, 1732, 1612, 1427, 1247, 1181, 1108, 1036, 822, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68-7.64 (m, 4H), 7.45-7.36 (m, 6H), 7.24 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.74 (m, 1H), 5.11-5.02 (m, 3H), 4.45 (ABq, J = 12.2 Hz, 2H), 3.79 (s, 3H), 3.71 (t, J = 6.5 Hz, 2H), 3.50-3.44 (m, 2H), 2.57 (t, J = 6.5 Hz, 2H), 2.33-2.28 (m, 2H), 1.81-1.70 (m, 2H), 1.27 (m, 1H), 1.06 (s, 9H), 0.92 (d, J = 6.7 Hz, 3H);^{13}C NMR (75 MHz, $CDCl_3$): δ 171.2, 159.2, 135.6

(4C), 133.9, 133.6 (2C), 130.2, 129.5 (2C), 129.2 (2C), 127.6 (4C), 117.6, 113.7 (2C), 72.7, 71.3, 69.2, 65.5, 55.2, 39.5, 37.4, 35.4, 32.2, 26.9 (3C), 19.3, 16.3. HRMS (ESI): $[M + H]^+$calcd. for $C_{35}H_{47}O_5Si$ 575.3187, found 575.3182.

(2*R*,4*S*,6*S*)-2-((*R*)-3-(*tert*-butyldiphenylsilyloxy)-2-methylpropyl)-6-(2-(4-methoxybenzyloxy)ethyl)tetrahydro-2H-pyran-4-ol (23):

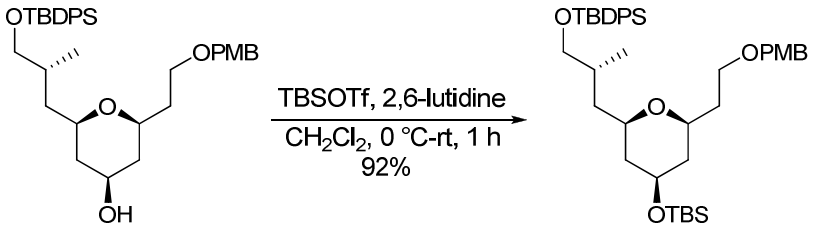


To a stirred solution of ester **10** (5 g, 8.71 mmol) in CH_2Cl_2 (40 mL) was added DIBAL-H (1 M in toluene, 17.5 mL, 17.4 mmol) dropwise via syringe at –78 °C under N_2 atmosphere. After 45 min, the reaction was treated sequentially with pyridine (2.2 mL, 26.1 mmol) dropwise via syringe, a solution of DMAP (2.12 g, 17.42 mmol) in CH_2Cl_2 (7 mL) dropwise via cannula, and acetic anhydride (4.9 mL, 52.2 mmol) dropwise via syringe. The mixture was stirred at –78 °C for 14 h, then warmed to 0 °C and stirred for an additional 30 min and then the reaction was quenched at 0 °C with saturated aqueous NH_4Cl (20 mL) and saturated aqueous sodium potassium tartrate (15 mL). The mixture was warmed to rt and stirred vigorously for 30 min and extracted with EtOAc (2 x 250 mL). The combined organic extracts were washed with ice cooled 1 M sodium bisulfate (2 x 30 mL), saturated aqueous $NaHCO_3$ (2 x 30 mL), and brine (15 mL) and dried over Na_2SO_4 and concentrated under *vacuo* afforded the crude α-acetoxy ether which was used directly in the next reaction.

To a stirred solution of α-acetoxy ether in dry hexanes (80 mL) at 0 °C acetic acid (2.5 mL, 43.5 mmol, 5 equiv) was added followed by dropwise addition of $BF_3{\cdot}OEt_2$ (0.15 mL, 0.871 mmol, 0.1 equiv). After 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc (2 x 200 mL). The combined organic extracts were washed with brine

(10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The crude material was then dissolved in 25 mL methanol and potassium carbonate (2.4 g, 17.4 mmol, 2 eq) was added. The mixture was stirred for 3 h and then concentrated in *vacuo*. Water 5mL was added to the reaction mixture and extracted with EtOAc (2 x 250 mL). The combined organic extracts were washed with brine (20 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 25% EtOAc/hexanes) to afford **23** (2.0 g, 40% over three steps) as a colour less oil. R_f = 0.3 (SiO_2, 30% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 4.5 (*c* 1.1, $CHCl_3$); IR (Neat): ν_{max} 3378, 2930, 2857, 1612, 1510, 1247, 1106, 819, 742, 702, 613 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.68-7.65 (m, 4H), 7.44-7.35 (m, 6H), 7.24 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.39 (s, 2H), 3.78 (s, 3H), 3.75 (m, 1H), 3.58-3.49 (m, 3H), 3.46-3.39 (m, 2H), 3.33 (m, 1H), 1.97-1.84 (m, 3H), 1.75 (m, 1H), 1.66-1.60 (m, 2H), 1.27-1.20 (m, 2H), 1.12 (m, 1H), 1.06 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 135.6 (4C), 134.0, 133.9, 130.6, 129.5 (2C), 129.2 (2C), 127.5 (4C), 113.7 (2C), 73.0, 72.7, 72.3, 69.2, 68.3, 66.5, 55.2, 41.8, 41.3, 39.6, 36.2, 32.1, 26.9(3C), 19.3, 16.6. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{35}H_{48}O_5NaSi$ 599.3163, found 599.3173.

***tert*-Butyl((*R*)-3-((2*R*,4*S*,6*S*)-4-(*tert*-butyldimethylsilyloxy)-6-(2-(4-methoxybenzyloxy)ethyl)tetrahydro-2H-pyran-2-yl)-2-methylpropoxy)diphenylsilane (S3):**

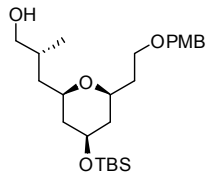


23 **S3**

To a stirred solution of **23** (1.8 g, 3.13 mmol) in dry CH_2Cl_2 (15 mL) was added 2,6-lutidine (1 mL, 9.39 mmol) and TBSOTf (0.8 mL, 3.44 mmol) sequentially at 0 °C under N_2 atmosphere. After 1 h stirring at rt, the reaction mixture was quenched with saturated aqueous

$NaHCO_3$ (5 mL) solution and extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with saturated aqueous $CuSO_4$ (10 mL), water (10 mL), brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 5% EtOAc/hexanes) to afford **S3** (2.0 g, 92%) as a clear oil. R_f = 0.4 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 7.7 (*c* 1.75, $CHCl_3$); IR (Neat): ν_{max} 2931, 2857, 1612, 1512,1366, 1249, 1084, 834, 777, 702, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.69-7.65 (m, 4H), 7.43-7.35 (m, 6H), 7.24 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.39 (s, 2H), 3.79-3.70 (m, 2H), 3.79 (s, 3H), 3.59-3.49 (m, 3H), 3.42 (m, 1H), 3.33 (m, 1H), 1.96 (m, 1H), 1.81-1.69 (m, 3H), 1.66-1.59 (m, 2H), 1.25-1.15 (m, 3H), 1.06 (s, 9H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 135.6 (4C), 134.0, 133.9, 130.6, 129.4 (2C), 129.2 (2C), 127.5 (4C), 113.7 (2C), 73.0, 72.8, 72.2, 69.3, 68.9, 66.6, 55.2, 42.4, 41.9, 39.6, 36.3, 32.1, 26.9 (3C), 25.8 (3C), 19.3, 18.1, 16.5, –4.53, –4.51. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{41}H_{62}O_5NaSi_2$ 713.4028, found 713.4035.

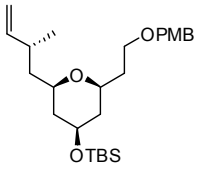
(*R*)-3-((2*R*,4*S*,6*S*)-4-(*tert*-butyldimethylsilyloxy)-6-(2-(4-methoxybenzyloxy)ethyl)tetrahydro-2H-pyran-2-yl)-2-methylpropan-1-ol (24):



To the stirred solution of **S3** (1.8 g, 2.6 mmol) in THF (25 mL) and water (1 mL) was added 18-crown-6 (8.9 g, 33.8 mmol) and KOH (7.4 g, 130 mmol). After 2 h stirring at rt, the reaction mixture was quenched with water (5 mL) and extracted with EtOAc (2 x 100 mL). The combined organic extract were washed with brine (10 mL) and dried over Na_2SO_4 and concentrated under *vacuo.* The residue was purified by column chromatography (SiO_2, 15% EtOAc/hexanes) to afford **24** (0.99 g, 84%) as a yellow liquid. R_f = 0.3 (SiO_2, 20% EtOAc

/hexanes); $[\alpha]_D^{25}$ = +5.6 (*c* 0.9, $CHCl_3$); IR (Neat): ν_{max} 3565, 2922, 2853, 1728, 1512, 1374, 1250, 1074, 837, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.42 (ABq, *J* = 11.6 Hz, 2H), 3.80 (s, 3H), 3.76 (m, 1H), 3.57 (m, 1H), 3.53-3.47 (m, 3H), 3.40-3.34 (m, 2H), 1.84-1.71 (m, 6H), 1.55 (m, 1H), 1.33 (ddd, *J* = 14.6, 5.9, 2.0 Hz, 1H), 1.21 (m, 1H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 130.6, 129.3 (2C), 113.7 (2C), 74.8, 72.8, 72.7, 68.6, 68.3, 66.2, 55.2, 42.5, 41.5, 41.0, 36.1, 34.2, 25.8 (3C), 18.1, 17.9, –4.53, –4.55. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{25}H_{44}O_5NaSi$ 475.2850, found 475.2840.

***tert*-Butyl((2*S*,4*S*,6*R*)-2-(2-(4-methoxybenzyloxy)ethyl)-6-((*R*)-2-methylbut-3-enyl)tetrahydro-2H-pyran-4-yloxy)dimethylsilane (26):**

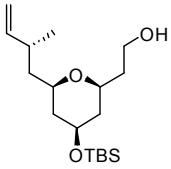


To a stirred solution of **24** (0.800 g, 1.77 mmol) in dry CH_2Cl_2 (10 mL) was added $NaHCO_3$ (0.145 g, 1.77 mmol) and Dess Martin periodinane (1.12 g, 2.65 mmol) at 0 °C under N_2 atmosphere. After 2 h stirring at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$(5 mL) and $Na_2S_2O_3$(10 mL) and extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with water (5 mL) and brine (10 mL) and dried over Na_2SO_4, concentrated under *vacuo* and the residue was purified by flash column chromatography afforded aldehyde which was used directly in the next step.

To a stirred solution of sulfone **25** (1.2 g, 5.31 mmol) in THF (15 mL) at –78 °C was added NaHMDS (3.5 mL, 1M in THF, 3.54 mmol) under argon atmosphere. After 30 minutes the crude aldehyde in THF (10 mL) was added at –78 °C to the reaction mixture via cannula. The reaction mixture was gradually warmed to room temperature and stirred for 12 h. Then the reaction was quenched with water (5 mL) and extracted with EtOAc (2 x 100 mL). The

combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 4% EtOAc/hexanes) to afford **26** (0.64 g, 80% over two steps) as yellow oil. R_f = 0.5 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 11.7 (*c* 0.45, $CHCl_3$); IR (Neat): ν_{max} 2928, 2856, 1513, 1462, 1360, 1248, 1076, 836, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.75 (m, 1H), 4.98-4.88 (m, 2H), 4.42 (s, 2H), 3.80 (s, 3H), 3.75 (m, 1H), 3.59 (m, 1H), 3.53 (m, 1H), 3.43 (m, 1H), 3.29 (m, 1H), 2.35 (q, *J* = 7.0 Hz, 1H), 1.82-1.71 (m, 3H), 1.63 (m, 1H), 1.31-1.14 (m, 4H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 144.6, 130.6, 129.2(2C), 113.7(2C), 112.1, 73.2, 72.7, 72.3, 68.9, 66.5, 55.2, 42.5, 41.88, 41.84, 36.2, 33.8, 25.8 (3C), 19.4, 18.1, –4.5 (2C). HRMS (ESI): $[M + Na]^+$ calcd. for $C_{26}H_{44}O_4NaSi$ 471.2901, found 471.2913.

2-((2*S*,4*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-6-((*R*)-2-methylbut-3-enyl)tetrahydro-2H-pyran-2-yl)ethanol (27):

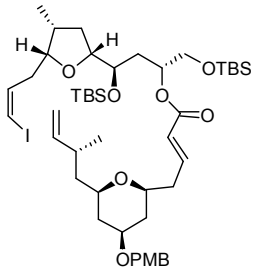


To a stirred solution of **26** (0.600 g, 1.34 mmol) in $CHCl_3$: pH = 7 phospahte buffer (20:1, 8 mL) was added DDQ (0.6 g, 2.68 mmol) at 0 °C. After stirring 2 h at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with water (5 mL), brine (5 mL), dried over Na_2SO_4 and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 7% EtOAc/hexanes) to afford **27** (0.4 g, 91%) as a clear oil.

R_f = 0.3 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 4.3 (*c* 1.6, $CHCl_3$); IR (Neat): ν_{max} 3398, 3077, 2928, 2856, 1464, 1374, 1253, 1075, 911, 839, 775 cm^{-1};^1H NMR (500 MHz, $CDCl_3$): δ 5.70 (ddd, *J* = 17.3, 10.2, 7.6 Hz, 1H), 4.98-4.88 (m, 2H), 3.82-3.71 (m, 3H), 3.53 (m, 1H),

3.35 (m, 1H), 2.76 (brs, OH), 2.28 (q, J = 7.0 Hz, 1H), 1.84-1.60 (m, 5H), 1.35-1.15 (m, 3H), 1.0 (d, J = 6.7 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 112.5, 76.1, 73.9, 68.5, 61.5, 42.5, 41.7, 41.5, 37.7, 34.3, 25.8(3C), 19.9, 18.1, –4.55, –4.57. HRMS (ESI): $[M + H]^+$ calcd. for $C_{18}H_{37}O_3Si$ 329.2506, found 329.2505.`

(*E*)-((6*R*,8*R*)-8-((2*R*,4*R*,5*R*)-5-((*Z*)-3-iodoallyl)-4-methyltetrahydrofuran-2-yl)-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodecan-6-yl) 4-((2*S*,4*R*,6*R*)-4-(4-methoxybenzyloxy)-6-((*R*)-2-methylbut-3-enyl)tetrahydro-2H-pyran-2-yl)but-2-enoate (28):

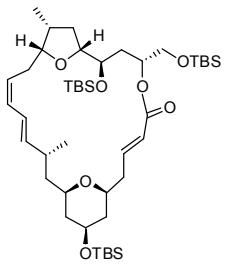


To a stirred solution of **27** (0.200 g, 0.609 mmol) in dry CH_2Cl_2 (6 mL) was added $NaHCO_3$ (0.049 g, 0.609 mmol) and Dess Martin periodinane (0.39 g, 0.913 mmol) at 0 °C under N_2 atmosphere. After 2 h stirring at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and $Na_2S_2O_3$ (5 mL) and extracted with EtOAc (2 x 40 mL). The combined organic extract were washed with water (5 mL), brine (5mL), dried over Na_2SO_4 and concentrated under *vacuo* and the residue was purified by flash column chromatography afforded aldehyde which was used directly in the next step.

DBU (0.1 mL, 0.609 mmol) was added to a mixture of compound **6** (0.56 g, 0.73 mmol) and LiCl (0.05 g, 1.218 mmol) in MeCN (6 mL) at 0 °C under argon atmosphere. After stirring at room temperature for 15 min, the mixture was again cooled to 0 °C before a solution of aldehyde **7** in MeCN (5 mL) was added dropwise. After stirring at room temperature for 12 h, the reaction mixture was quenched by addition of water and extracted with EtOAc (2 x 40

mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 60-120 mesh, 3% EtOAc/hexane) to afford **28** (0.44 g, 77% two steps) as a colorless oil. R_f = 0.5 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = +17.5 (*c* 0.4, $CHCl_3$); IR (Neat): ν_{max} 2927, 2856, 1722, 1464, 1370, 1254, 1174, 1076, 998, 837, 776, 671 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.96 (dt, *J* = 15.7, 7.2 Hz, 1H), 6.32 (dt, *J* = 7.3, 6.5 Hz, 1H), 6.26 (dt, *J* = 7.3, 1.4 Hz, 1H), 5.87 (dt, *J* = 15.7, 1.0 Hz, 1H), 5.71 (ddd, *J* = 17.5, 10.3, 7.6 Hz, 1H), 5.01 (m, 1H), 4.97-4.88 (m, 2H), 3.92 (m, 1H), 3.79-3.67 (m, 5H), 3.36 (m, 1H), 3.29 (m, 1H), 2.44 (m, 1H), 2.37-2.29 (m, 3H), 2.26-2.22 (m, 2H), 2.01 (m, 1H), 1.88-1.74 (m, 2H), 1.70-1.60 (m, 3H), 1.34-1.13 (m, 4H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.0, 145.3, 144.4, 138.9, 123.3, 112.4, 83.3, 81.7, 80.0, 74.1, 73.5, 71.7, 71.1, 68.7, 64.5, 42.4, 41.4, 41.3, 38.8, 37.0, 35.5, 35.2, 34.3, 34.0, 26.0(3C), 25.8(6C), 19.9, 18.2, 18.1, 18.0, 15.3, –4.0, –4.50, –4.53, –4.9, –5.3(2C). HRMS (ESI): $[M + Na]^+$ calcd. for $C_{44}H_{83}O_7INaSi_3$ 957.4383, found 957.4383.

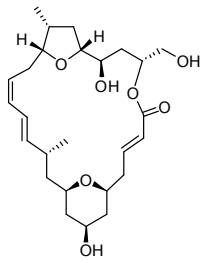
(1*R*,3*R*,4*E*,6*Z*,9*R*,10*R*,12*R*,13*R*,15*R*,18*E*,21*S*,23*R*)-13,23-bis((*tert*-butyldimethylsilyl)oxy)-15-(((*tert*-butyldimethylsilyl)oxy)methyl)-3,10-dimethyl-16,25,26-trioxatricyclo[19.3.1.19,12]hexacosa-4,6,18-trien-17-one (29):



To a stirred solution of vinyl iodide **28** (0.100 g, 0.107 mmol) in DMF (20 mL) was added Cs_2CO_3 (0.06 g, 0.182 mmol), Et_3N (0.03 mL, 0.128 mmol) and $Pd(OAc)_2$ (0.034 g, 0.161

mmol) at rt under argon atmosphere. After stirring 2 days at rt, the reaction mixture was quenched with water and extracted with EtOAc (2 x 30 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, and concentrated under *vacuo*. The residue was purified by column chromatography (SiO_2, 60-120 mesh, 3.5% EtOAc /hexane) to afford **29** (0.05 g, 58%) as a colourless oil. R_f = 0.35 (SiO_2, 10% EtOAc /hexanes); $[\alpha]_D^{25}$ = – 4.5 (*c* 0.5, $CHCl_3$); IR (Neat): ν_{max} 2929, 2857, 1729, 1465, 1370, 1254, 1174, 1090, 838, 776, 621cm^{-1};^{1}H NMR (500 MHz, $CDCl_3$): δ 7.0 (ddd, *J* = 15.7, 8.8, 4.7 Hz 1H), 6.32 (dd, *J* = 15.1, 10.6 Hz, 1H), 6.03 (t, *J* = 10.8 Hz, 1H), 5.93 (d, *J* = 15.7 Hz, 1H), 5.54 (dd, *J* = 15.1, 7.4 Hz, 1H), 5.33 (m, 1H), 4.99 (m, 1H), 3.91 (m, 1H), 3.81-3.66 (m, 5H), 3.42 (m, 1H), 3.32 (m, 1H), 2.52 (m, 1H), 2.44-2.36 (m, 2H), 2.35-2.28 (m, 2H), 2.05-1.93 (m, 2H), 1.85 (m, 1H), 1.78-1.68 (m, 2H), 1.65-1.59 (m, 2H), 1.42-1.28 (m, 3H), 1.18 (m, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.85 (s, 9H), 0.06 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), –0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 144.9, 140.9, 130.4, 127.3, 124.1, 123.3, 82.1, 81.2, 73.2, 72.5, 71.3(2C), 68.8, 64.5, 43.2, 42.1, 40.8, 37.9, 35.9, 35.3, 34.2, 32.5, 30.7, 26.1(3C), 25.8(6C), 19.7, 18.22, 18.2, 18.1, 14.9, –3.9, –4.5(2C), –5.27, –5.3, –5.4. HRMS (ESI): $[M + Na]^+$ calcd. for $C_{44}H_{82}O_7NaSi_3$ 829.5260, found 829.5264.

(1*R*,3*R*,4*E*,6*Z*,9*R*,10*R*,12*R*,13*R*,15*R*,18*E*,21*S*,23*R*)-13,23-dihydroxy-15-(hydroxymethyl)-3,10-dimethyl-16,25,26-trioxatricyclo[19.3.1.19,12]hexacosa-4,6,18-trien-17-one (5):

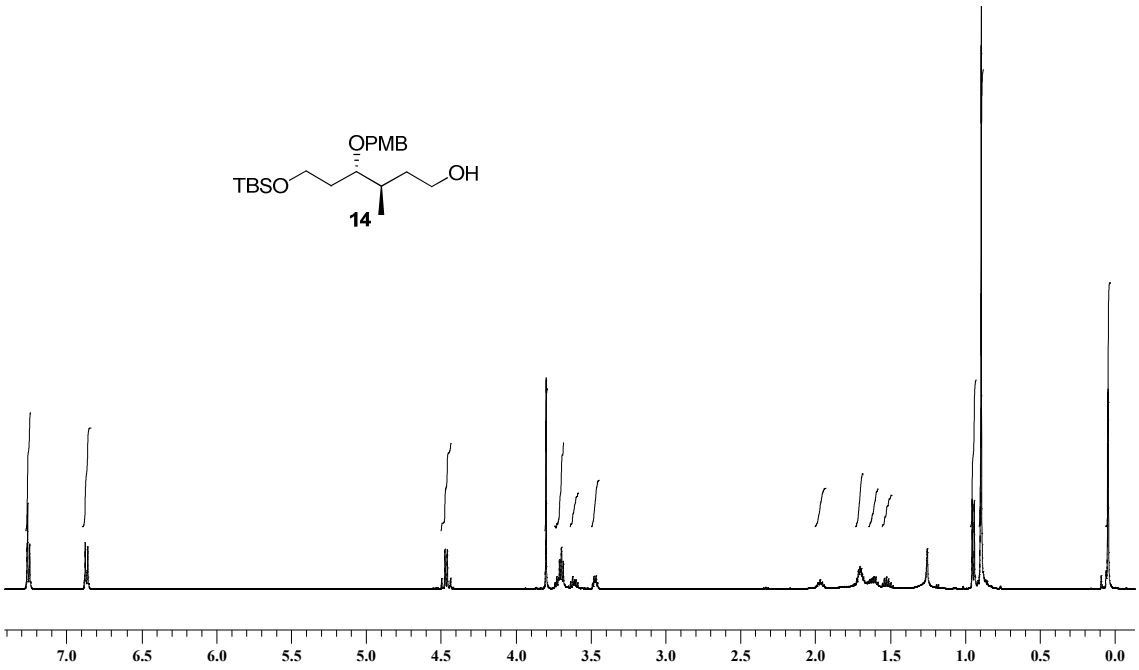


To a stirred solution of **29** (0.03 g, 0.037 mmol) in dry CH_3CN (5 mL) in a polypropylene vial, was added HF-py complex (70%, 0.4 mL) at 0 °C. The reaction mixture was slowly raised to rt and stirred for 36 h. After completion of the reaction, it was cautiously poured into saturated aqueous $NaHCO_3$ (5 mL) and stirred for 30 min. Then both the layers were separated, aqueous layer was further extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated aqueous $CuSO_4$ (5 mL), water (5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was evaporated under *vacuo*. The residue was purified by column chromatography (SiO_2, 6% MeOH/$CHCl_3$) to afford **5** (15 mg, 87% yield) as a colorless semi solid. R_f = 0.3 (SiO_2, 10% MeOH/$CHCl_3$); $[\alpha]_D^{27}$ = – 6.0 (*c* 0.6, EtOAc); IR (Neat): ν_{max} 3441, 3368, 3267, 2923, 2854, 1741, 1711, 1459, 1176, 1048, 953 cm^{-1}; ^1H NMR and ^{13}C NMR data : See table 1. HRMS (ESI): $[M + NH_4]^+$ calcd. for $C_{26}H_{44}O_7N$ 482.3112, found 482.3127.

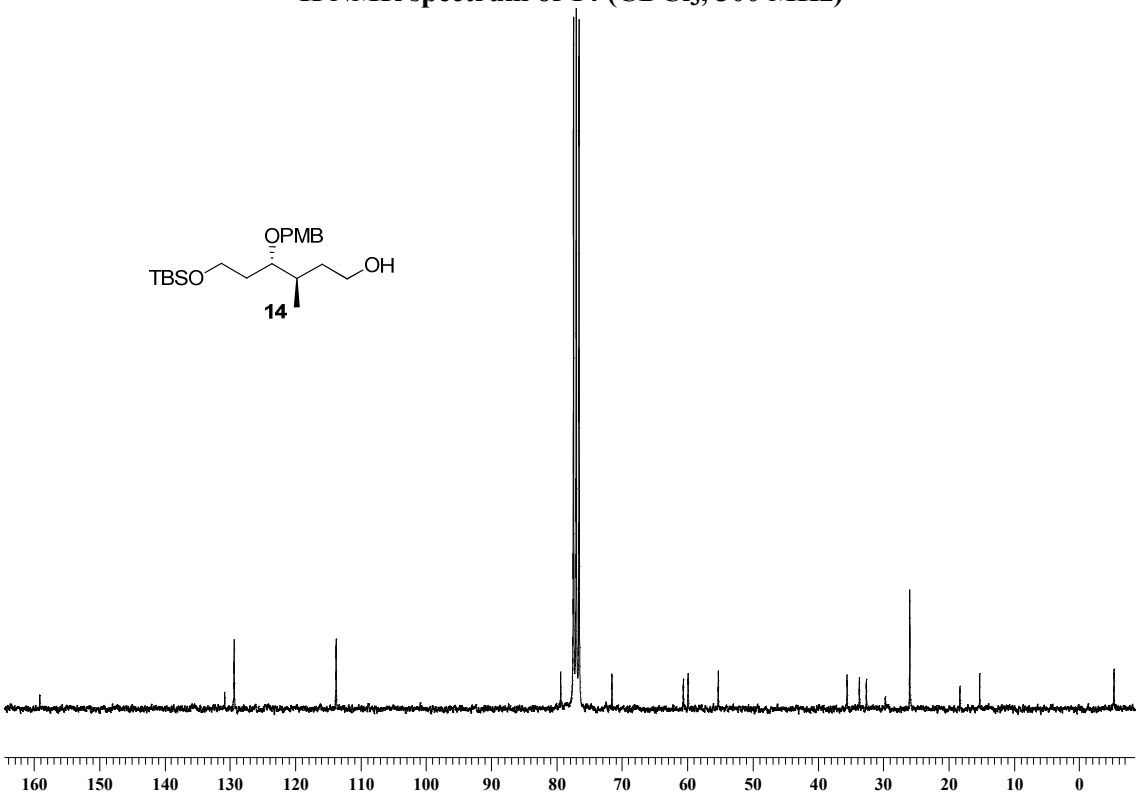
Table 1: Comparison of ^{1}H and ^{13}C chemical shifts of Mandelalide A (Isolation), synthetic Mandelalide A (Fürstner et al) and Compound **5**

Assign ment	Mandelalide A ($CDCl_3$) (Isolation)		Mandelalide A (Fürstner et al)		Compound **5**	
	δ_C in ppm	δ_H in ppm, J in Hz	δ_C in ppm	δ_H in ppm, J in Hz	δ_C in ppm	δ_H in ppm, J in Hz
1	167.4	--	167.3	--	167.1	--
2	123.1	6.01 (dd, 15.5, 1.2)	123.1	5.92 (dt, 15.6, 1.5)	122.5	5.95 (dt, 15.5, 1.4)
3	147.1	6.97 (ddd, 15.2, 10.4, 4.6)	146.3	7.02 (ddd, 15.5, 8.6, 5.5)	146.3	7.07 (ddd, 15.5, 8.5, 5.5)
4a	38.8	2.36 (m)	38.5	2.34 (ddd, 15.2, 6.5, 5.6, 1.8)	37.9	2.38 (dddq, 15.2, 7.0, 5.9, 1.6)
4b	--	2.39 (ddd, 11.4, 10.6, 10.6)	--	2.46 (dddd, 15.2, 8.6, 3.7, 1.2)		2.49 (dddq, 15.2, 8.5, 3.7, 1.0)
5	73.9	3.36 (dddd, 11.4, 11.4, 2.3, 2.3)	73.4	3.42 (m)	73.1	3.45 (m)
6ax	37.6	1.20 (m)	36.7	1.26 (m)	40.2	1.32 (m)
6eq	--	2.02 (dddd, 12.6, 4.4, 2.3, 1.6)	--	1.94 (ddt, 12.0, 4.6, 1.9)		1.92 (ddt, 11.9, 4.5, 1.8)
7	73.1	3.82 (dddd, 11.1, 10.5, 4.4, 4.4)	72.8	3.77 (m)	68.0	3.80(m)
8 ax	39.7	1.22 (m)	39.3	1.22 (m)	41.1	1.13 (dt, 12.2, 11.1)
8 eq	--	1.87 (m)	--	1.84 (dddd, 12.5, 4.2, 1.9, 1.9)		1.88 (ddt, 12.2, 4.3, 1.9)
9	72.5	3.32 (dddd, 11.2, 11.2, 2.2, 2.2)	73.1	3.33 (m)	72.5	3.34 (m)
10a	43.1	1.21 (ddd, 15.2, 9.6, 2.2)	42.9	1.27 (m)	42.4	1.30 (m)
10b	--	1.51 (ddd, 15.2, 11.2, 3.7)	--	1.69 (ddd, 14.1, 9.1, 5.1)		1.72 (ddd, 14.1, 9.1, 5.0)
11	34.2	2.37 (dqd, 9.6, 6.5, 3.7)	32.8	2.44 (m)	32.2	2.47 (m)
12	141.5	5.45 (dd, 14.8, 9.7)	140.9	5.61 (dd, 15.2, 7.6)	140.4	5.64 (dd, 15.3, 7.5)
13	123.9	6.28 (dd, 14.8, 11.0)	123.8	6.22 (ddt, 15.2, 10.8, 1.0)	123.4	6.25 (ddt, 15.3, 10.8, 1.0)
14	131.3	6.05 (dd, 10.9, 10.9)	130.5	6.01 (tt, 10.8, 1.8)	130.1	6.02 (tt, 10.8, 1.5)
15	126.9	5.28 (ddd, 10.8, 10.8, 5.6)	126.5	5.27 (ddd, 10.8, 8.3, 7.5)	126.1	5.29 (m)
16a	31.1	1.88 (m)	31.2	2.14 (dddd, 14.8, 6.8, 5.1, 1.9)	30.7	2.15 (dddd, 14.6, 6.7, 5.2, 1.8)
16b	--	2.28 (ddd, 13.1, 11.4, 11.4)	--	2.29 (dtd, 14.8, 8.5, 1.6)		2.32 (dtd, 14.6, 8.6, 1.6)
17	81.0	3.98 (ddd, 11.1, 8.1, 1.8)	81.3	4.03 (ddd, 8.6, 7.2, 4.9)	80.9	4.05 (ddd, 8.5, 7.4, 5.1)
18	37.3	2.52 (dddq, 12.0, 7.0, 7.0, 7.0)	37.1	2.43 (m)	36.6	2.45 (m)
19a	36.8	1.17 (ddd, 11.9, 11.9, 10.3)	36.0	1.28 (m)	35.5	1.29 (m)
19b	--	2.01 (ddd, 12.2, 7.0, 5.6)	--	2.04 (dt, 12.3, 6.7)		2.06 (dt, 12.3, 6.7)
20	83.2	3.63 (m)	82.7	3.71 (ddd, 8.4, 8.2, 6.7)	82.2	3.73 (ddd, 8.7, 8.2, 6.5)
21	73.0	3.42 (ddd, 11.1, 8.8, 1.8)	73.4	3.45 (m)	72.0	3.46 (m)
22a	34.1	1.46 (ddd, 14.1, 11.1, 1.9)	34.1	1.54 (ddd, 14.4, 10.5, 2.5)	33.6	1.55 (m)
22b	--	1.76 (ddd, 13.9, 11.7, 1.8)	--	1.77 (ddd, 14.4, 10.8, 2.0)		1.80 (ddd, 14.4, 10.7, 2.2)
23	72.3	5.23 (dddd, 11.7, 4.9, 2.9, 1.9)	72.5	5.24 (m)	72.0	5.27 (m)
24a	66.1	3.61 (m)	65.7	3.65 (m)	65.3	3.67 (m)
24b	--	3.81 (dd, 12.2, 2.9)	--	3.78 (dd, 12.1, 3.3)		3.81 (m)
25	18.3	0.85 (d, 6.6)	20.1	1.00 (d, 6.7)	19.6	1.02 (d, 6.7)
26	14.5	1.03 (d, 6.9)	14.7	0.98 (d, 7.0)	14.3	0.99 (d, 7.0)

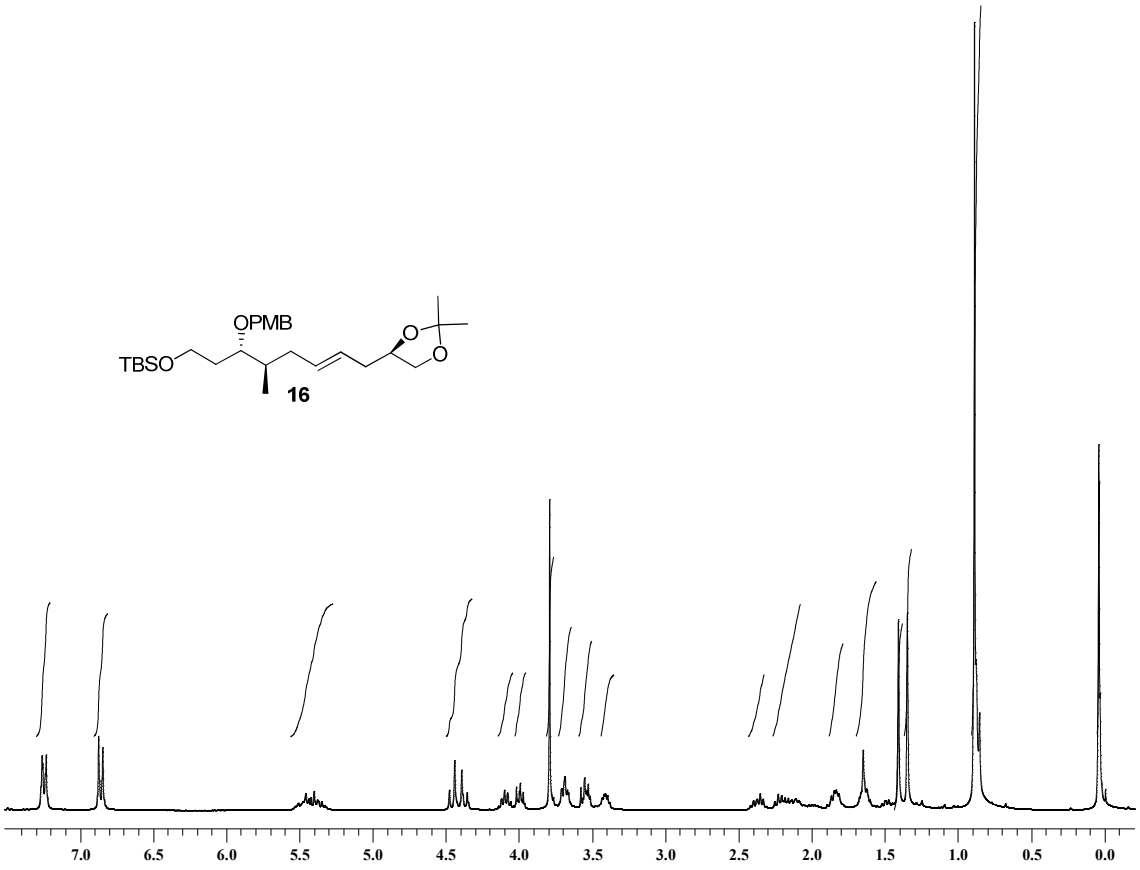
Spectral data:



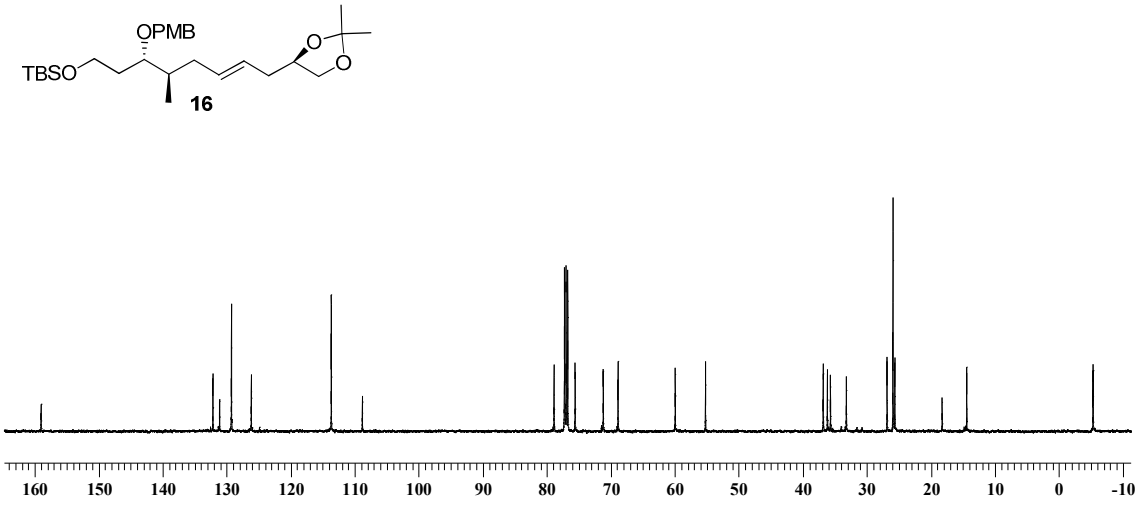
^{1}H NMR spectrum of 14 ($CDCl_3$, 300 MHz)



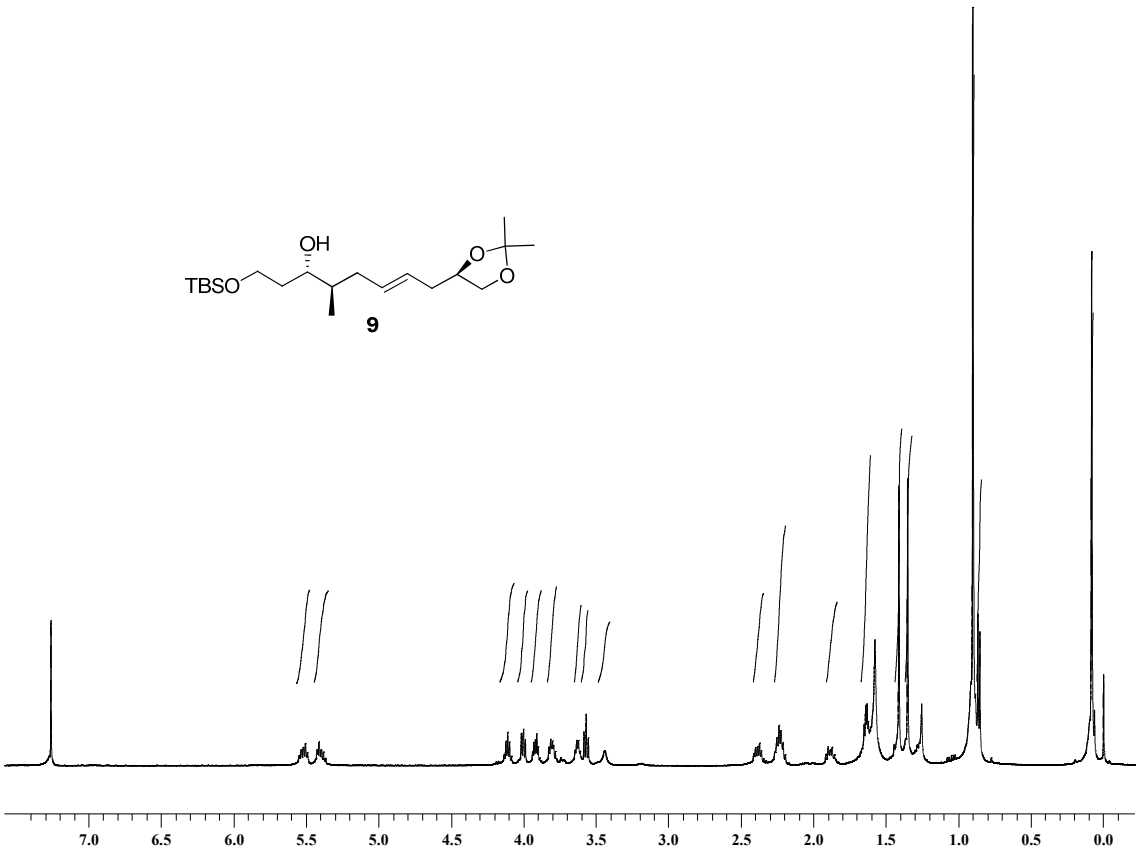
^{13}C NMR spectrum of 14 ($CDCl_3$, 75 MHz)



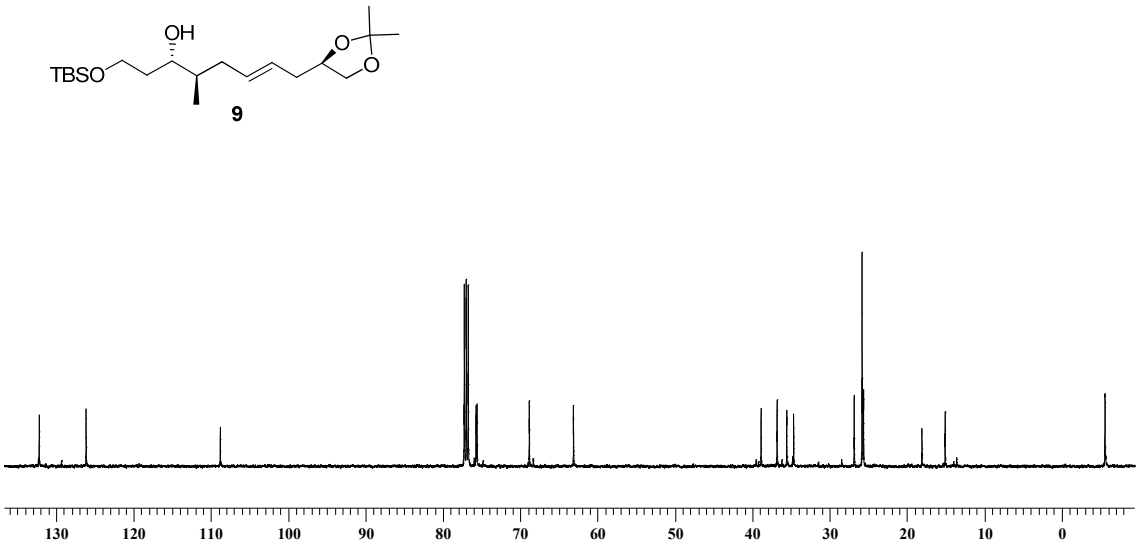
^{1}H NMR spectrum of 16 ($CDCl_3$, 500 MHz)



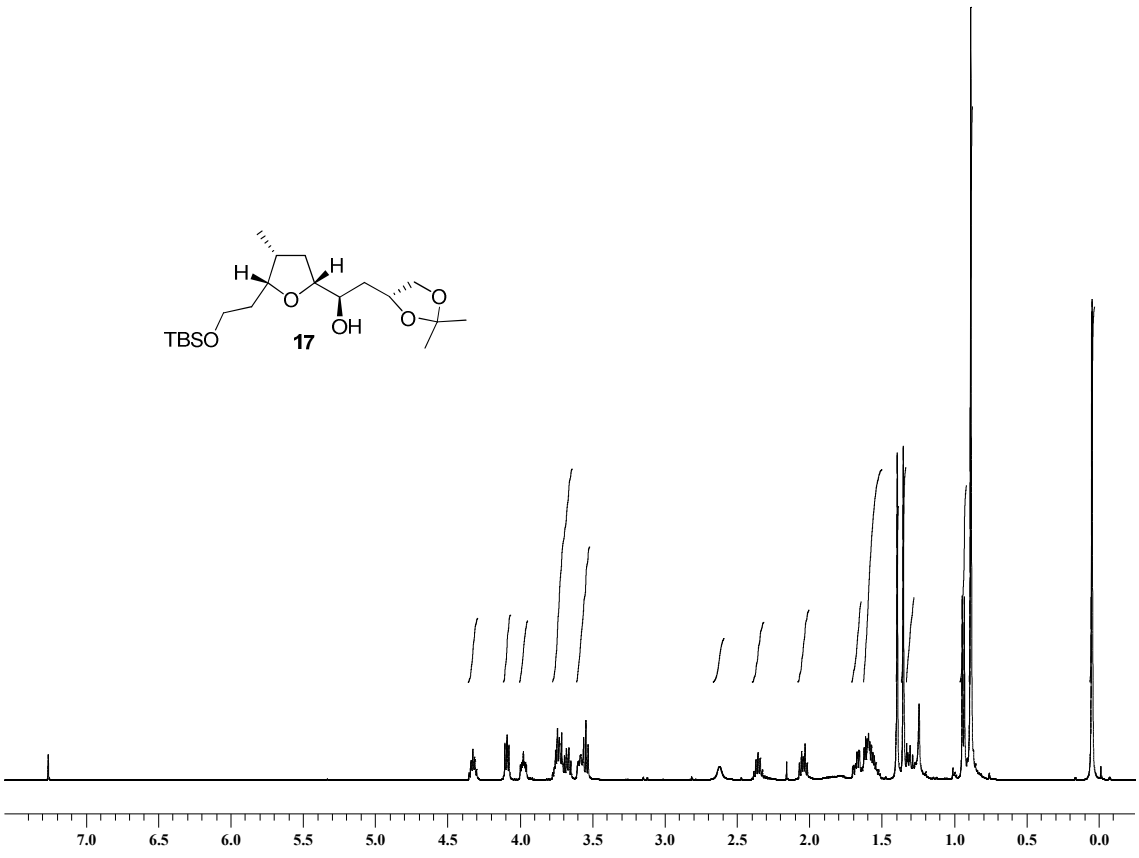
^{13}C NMR spectrum of 16 ($CDCl_3$, 125 MHz)



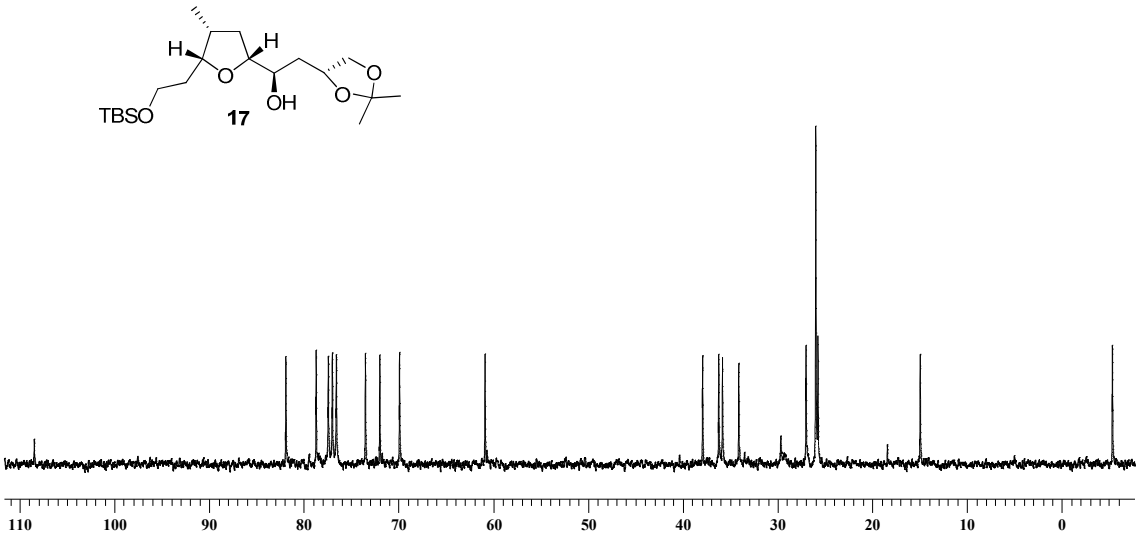
^{1}H NMR spectrum of 9 ($CDCl_3$, 300 MHz)



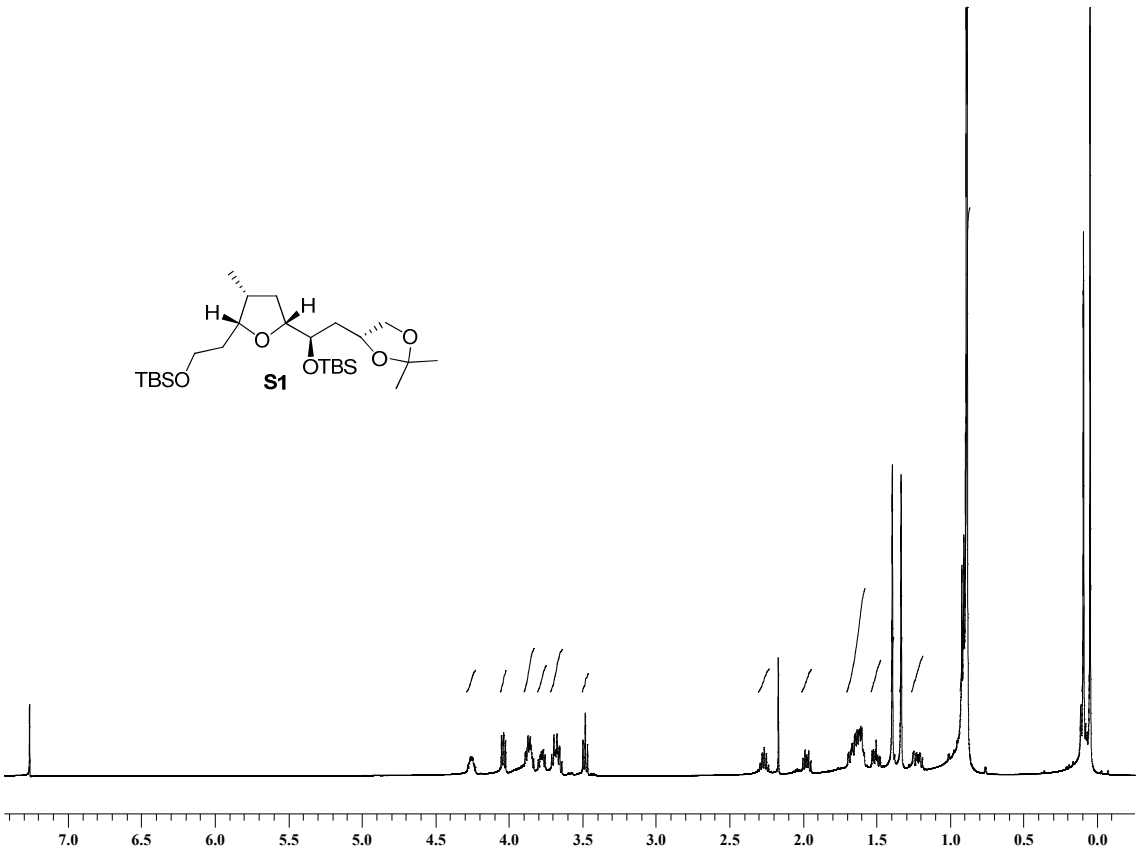
^{13}C NMR spectrum of 9 ($CDCl_3$, 125 MHz)



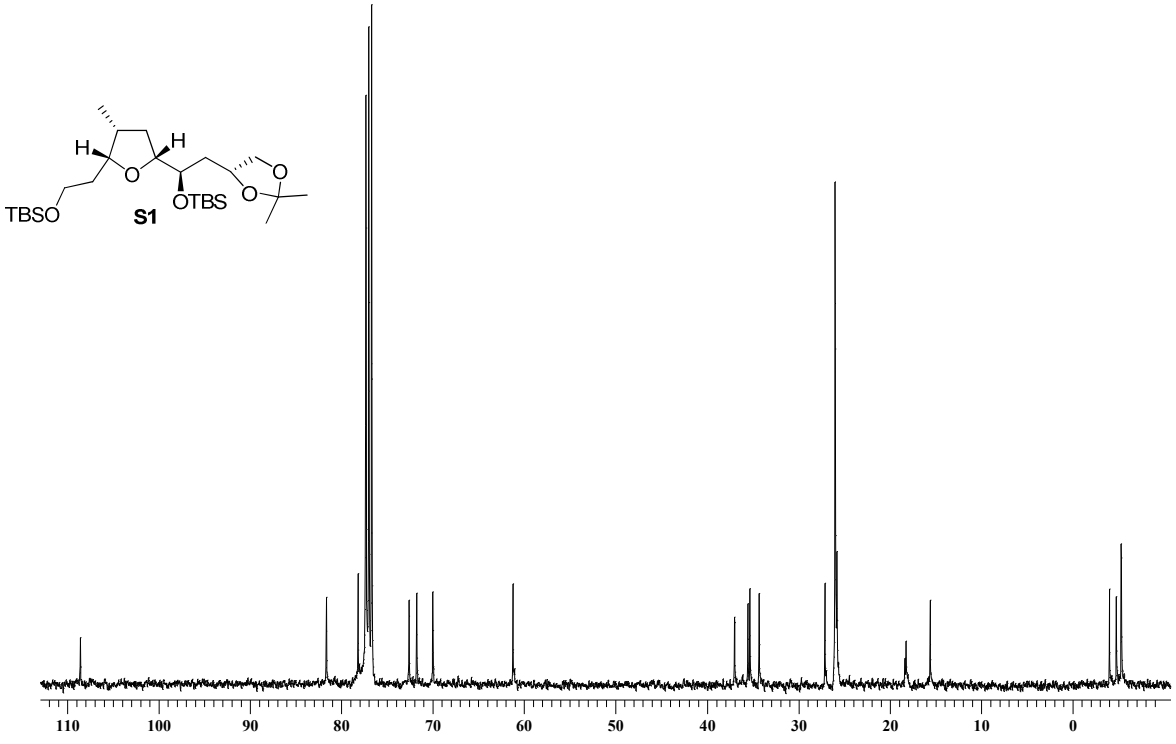
^{1}H NMR spectrum of 17 ($CDCl_3$, 300 MHz)



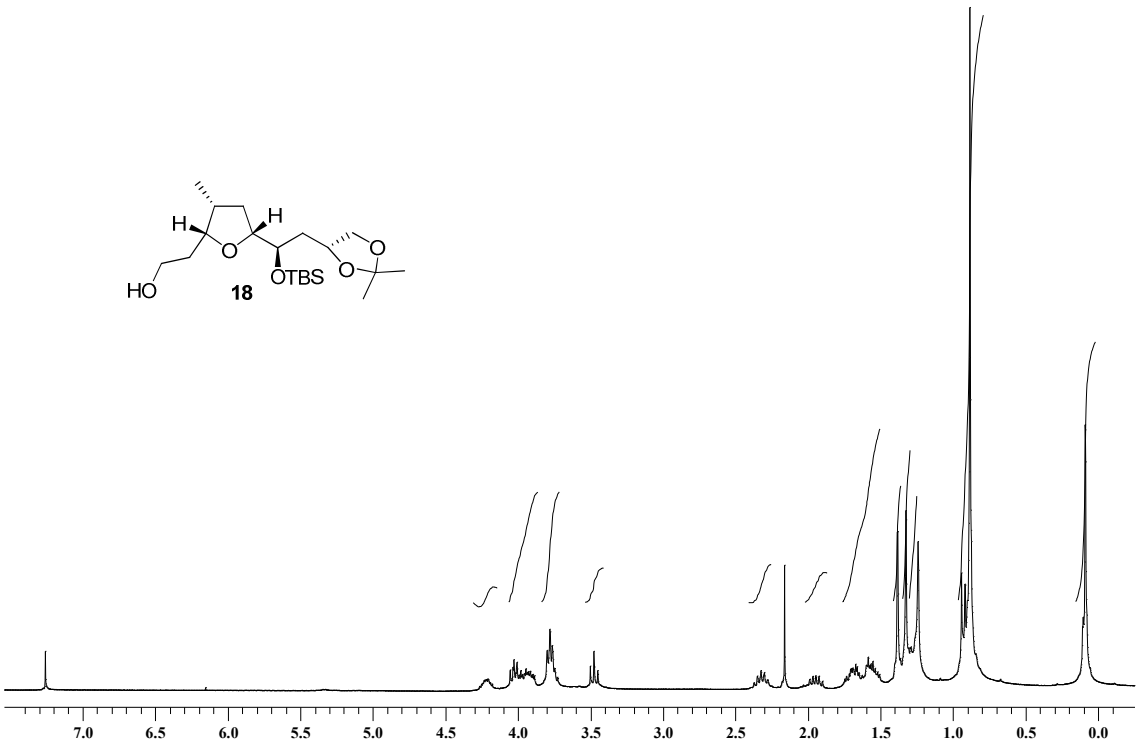
^{13}C NMR spectrum of 17 ($CDCl_3$, 75 MHz)



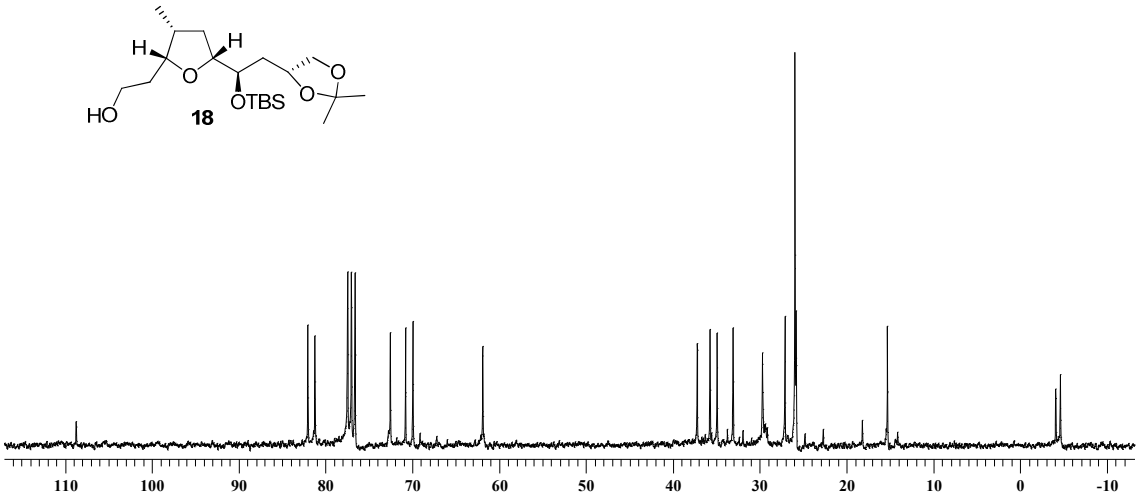
^{1}H NMR spectrum of S1 ($CDCl_3$, 500 MHz)



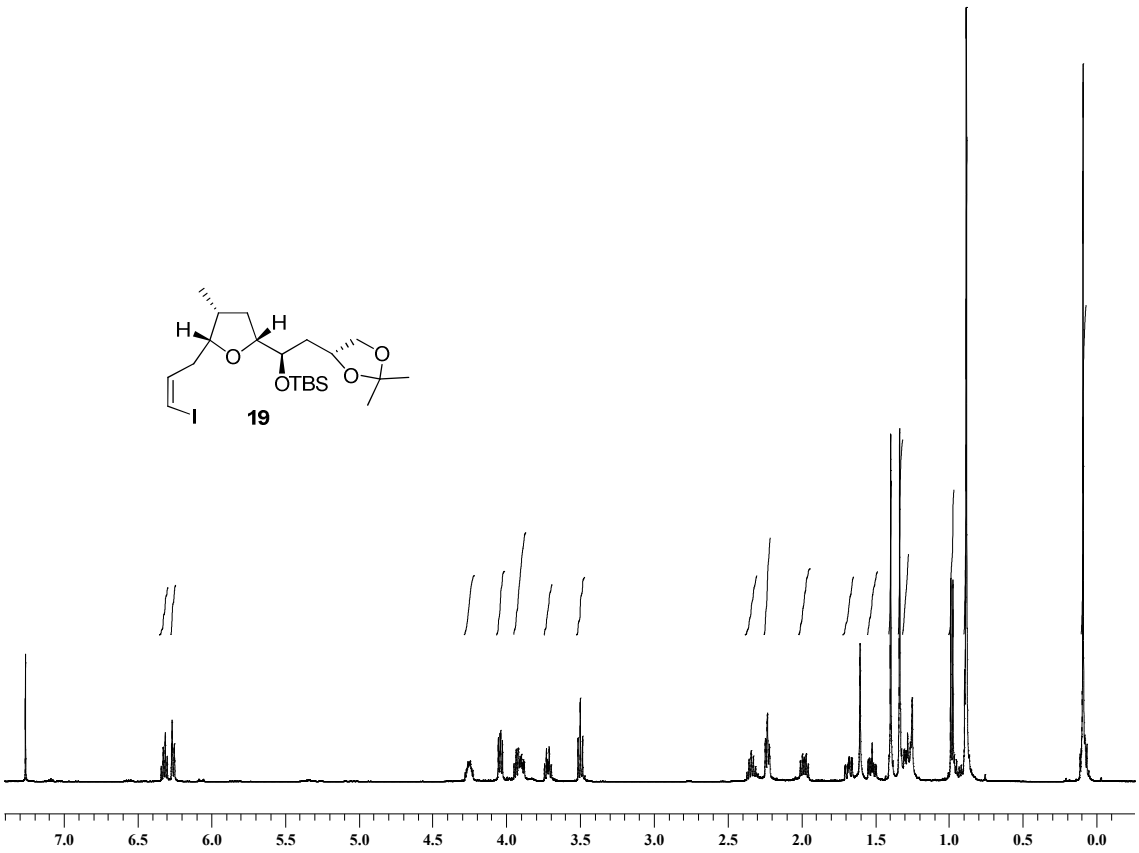
^{13}C NMR spectrum of S1 ($CDCl_3$, 100 MHz)



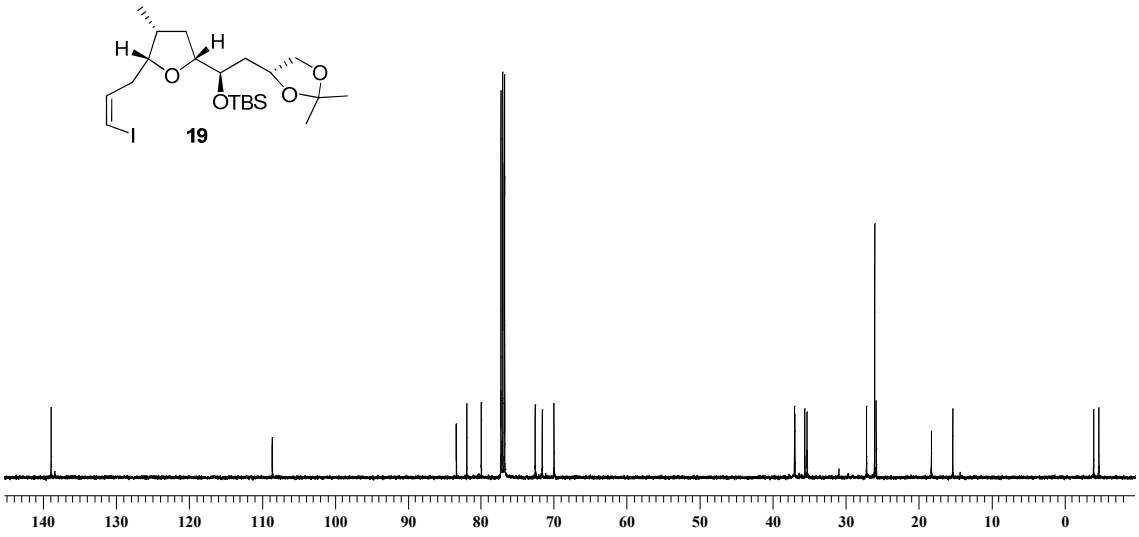
^{1}H NMR spectrum of 18 ($CDCl_3$, 300 MHz)



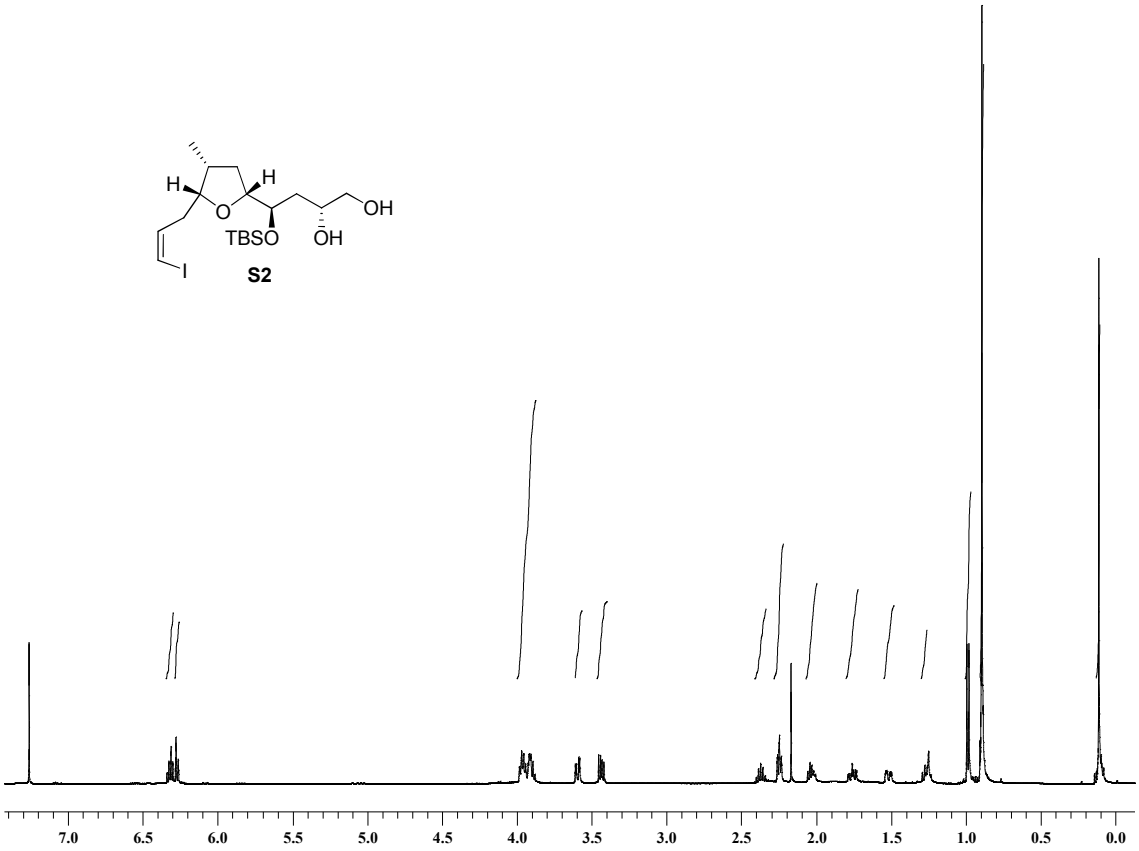
^{13}C NMR spectrum of 18 ($CDCl_3$, 75 MHz)



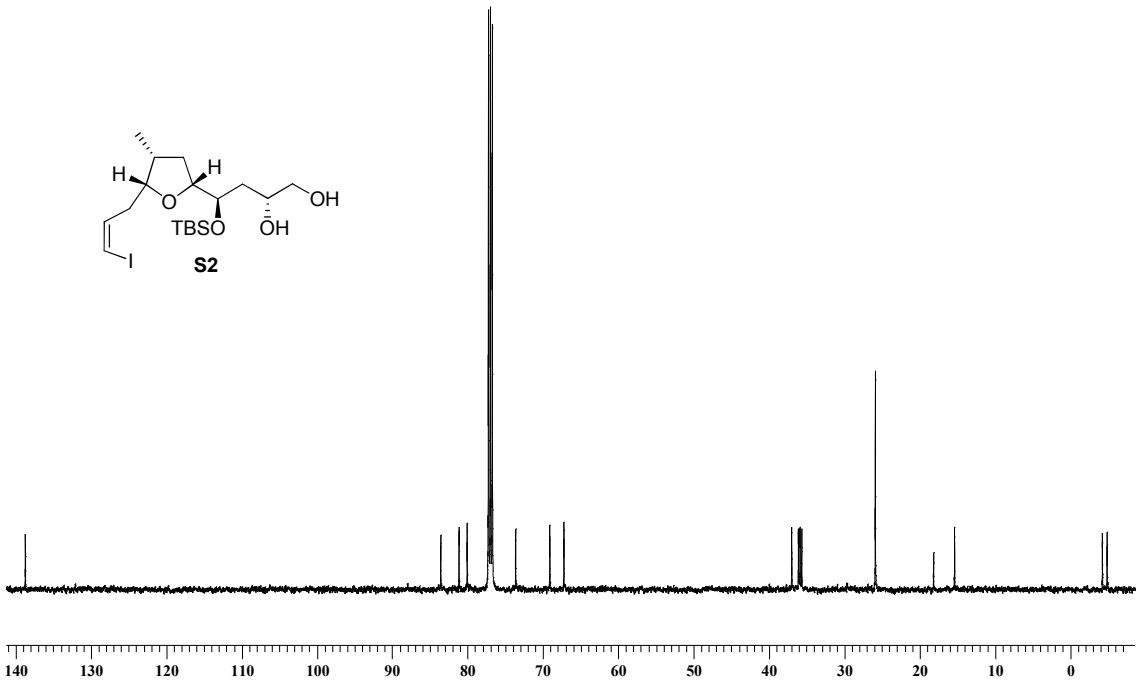
^{1}H NMR spectrum of 19 ($CDCl_3$, 500 MHz)



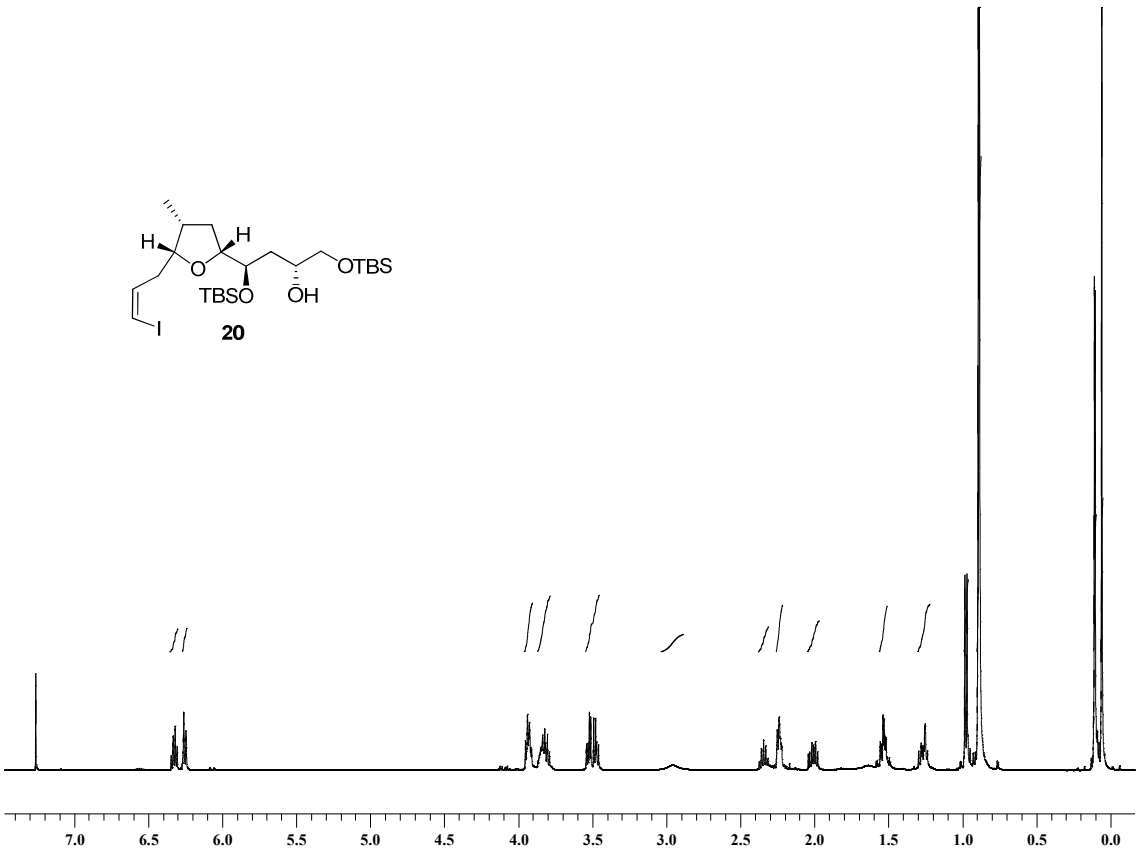
^{13}C NMR spectrum of 19 ($CDCl_3$, 125 MHz)



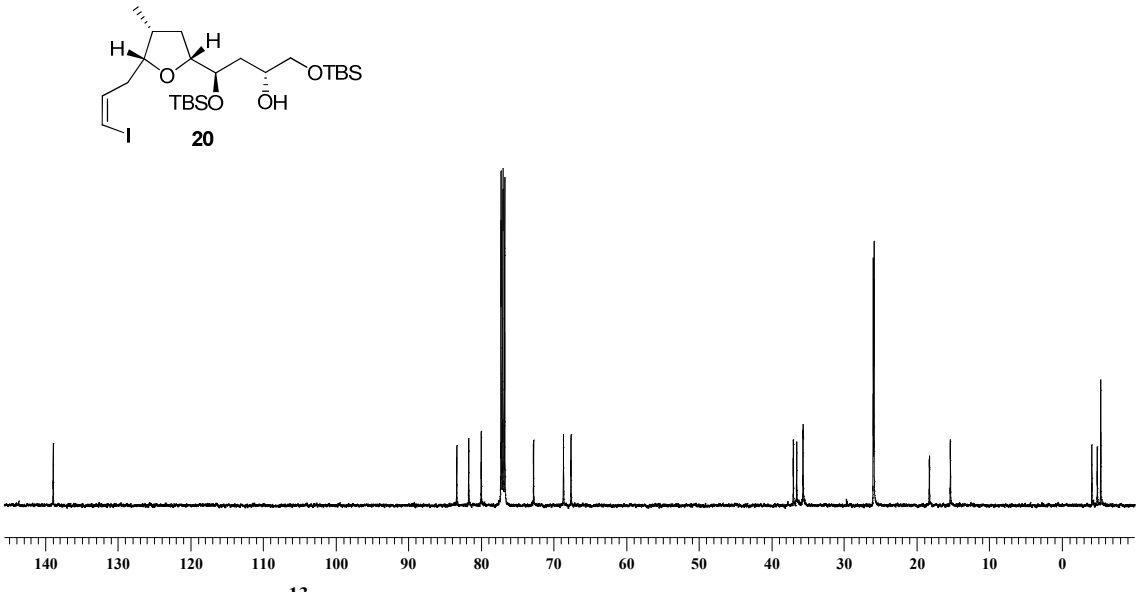
^{1}H NMR spectrum of S2 ($CDCl_3$, 500 MHz)



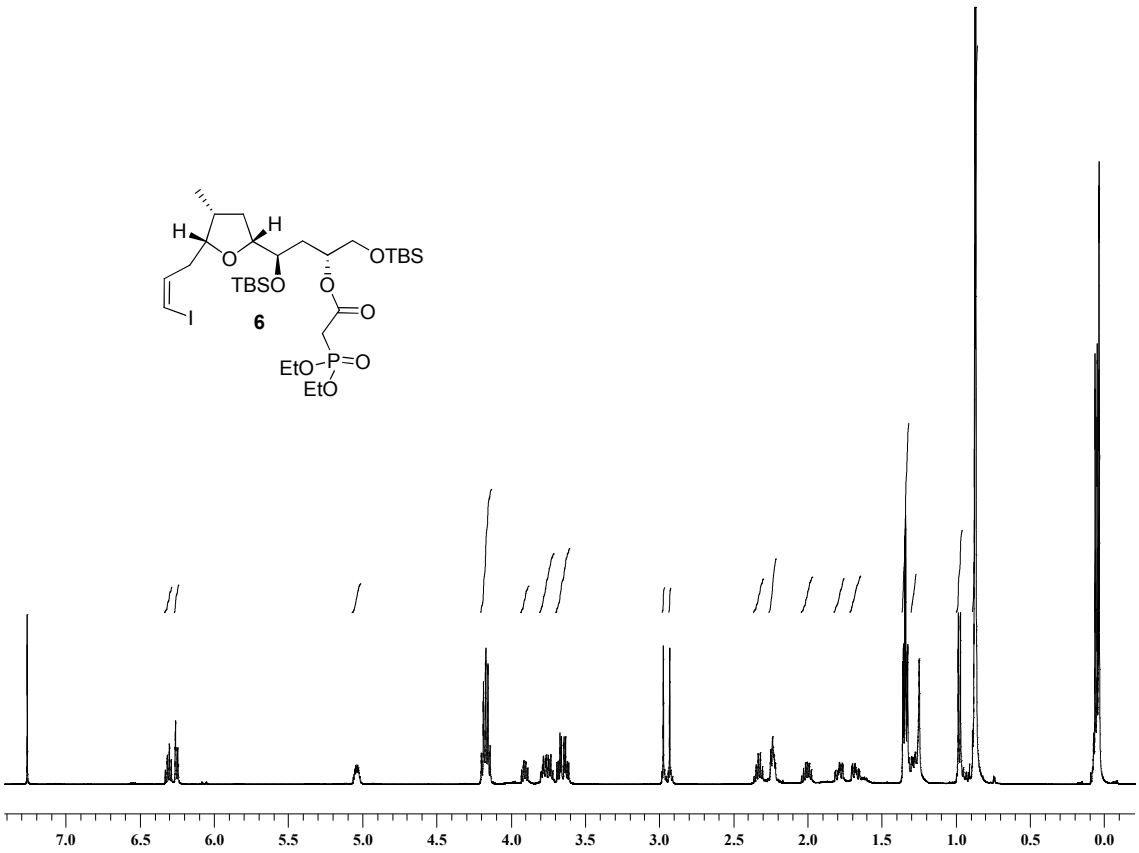
^{13}C NMR spectrum of S2 ($CDCl_3$, 125 MHz)



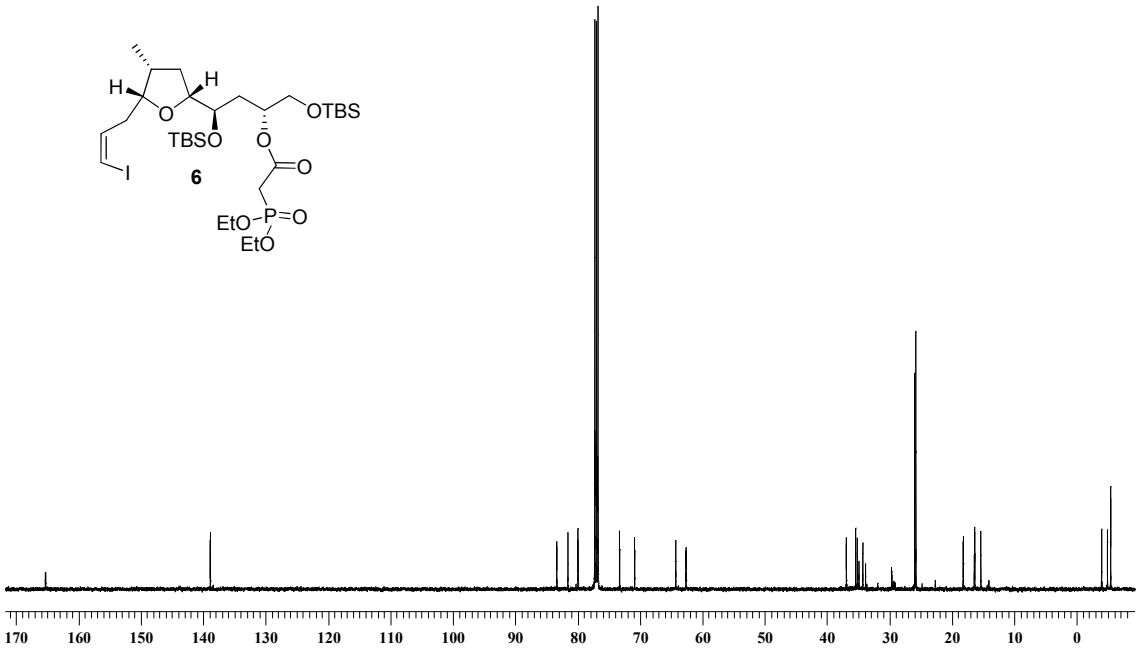
^{1}H NMR spectrum of 20 ($CDCl_3$, 500 MHz)



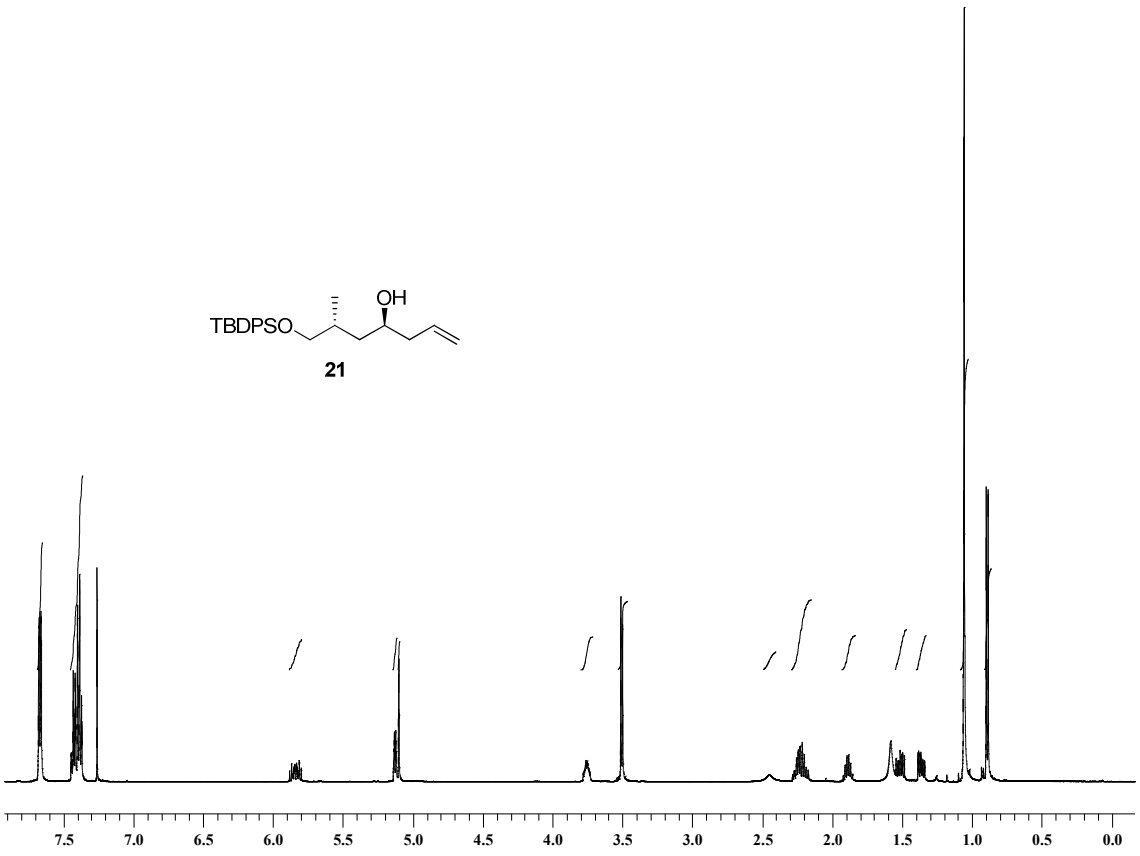
^{13}C NMR spectrum of 20 ($CDCl_3$, 125MHz)



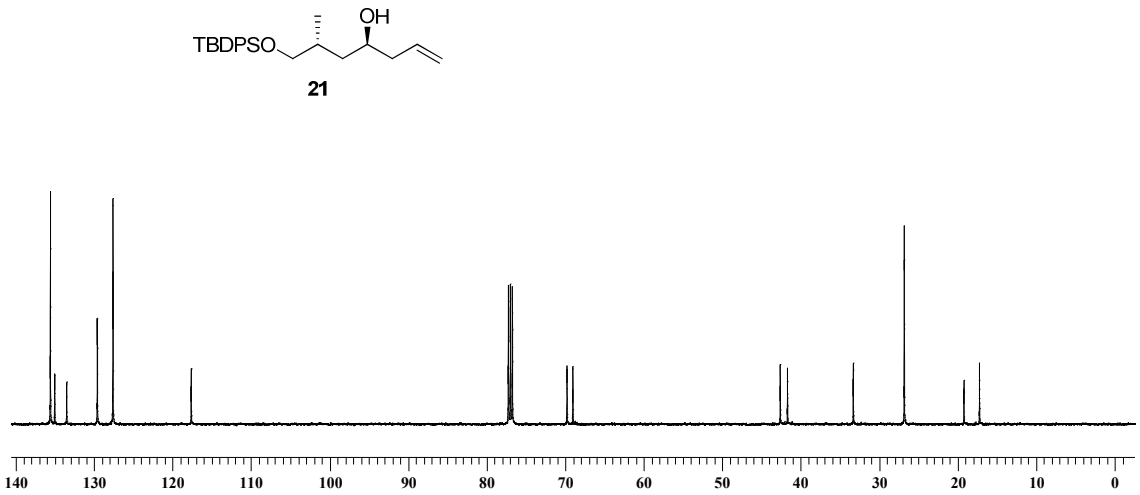
^{1}H NMR spectrum of 6 ($CDCl_3$, 500 MHz)



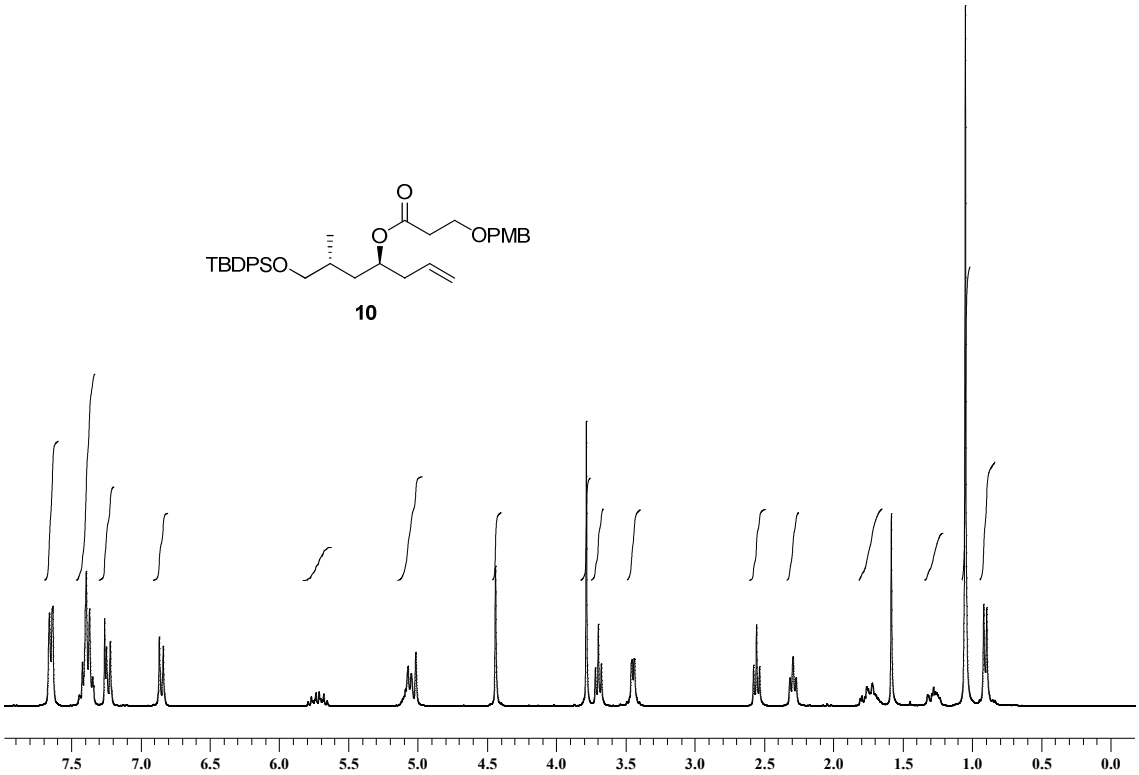
^{13}C NMR spectrum of 6 ($CDCl_3$, 125 MHz)



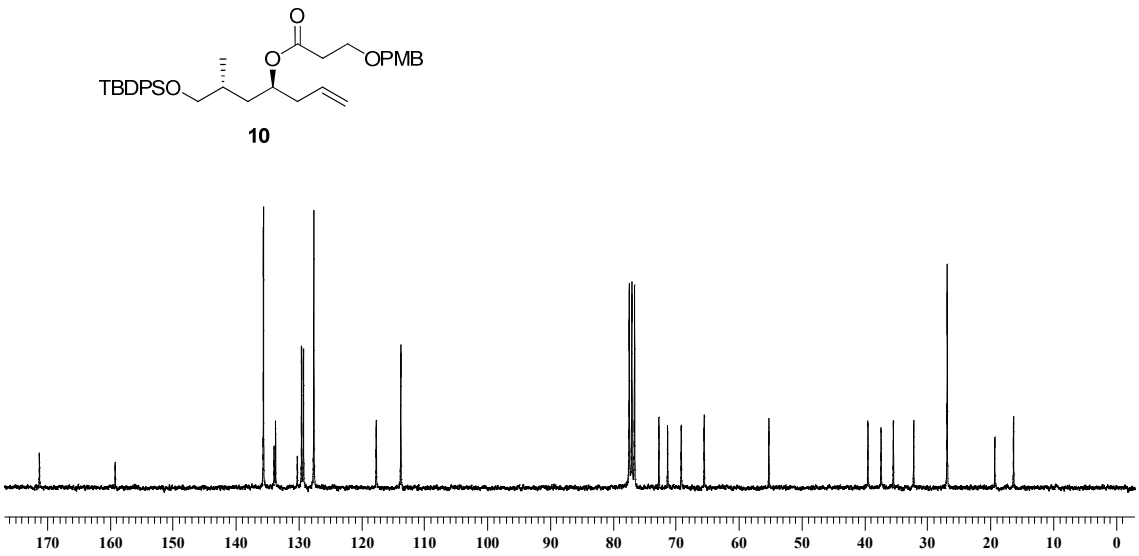
^{1}H NMR spectrum of 21 ($CDCl_3$, 500 MHz)



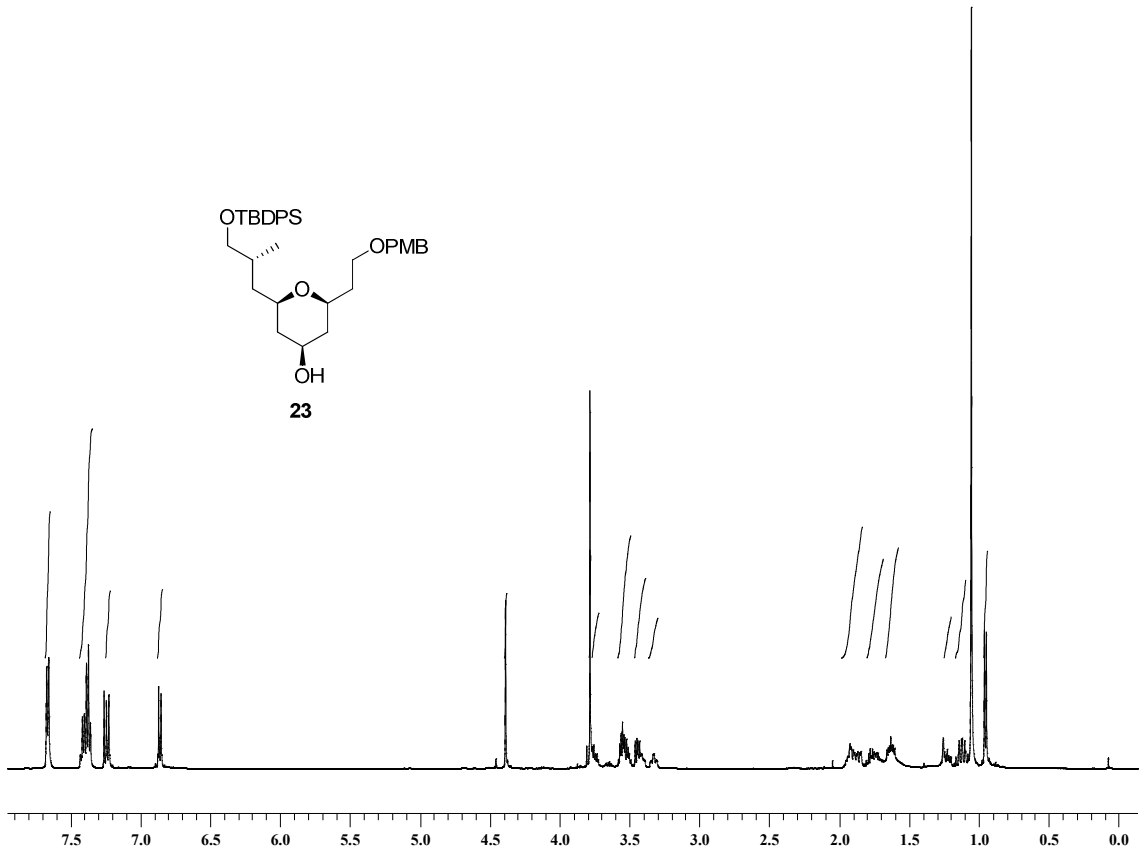
^{13}C NMR spectrum of 21 ($CDCl_3$, 125 MHz)



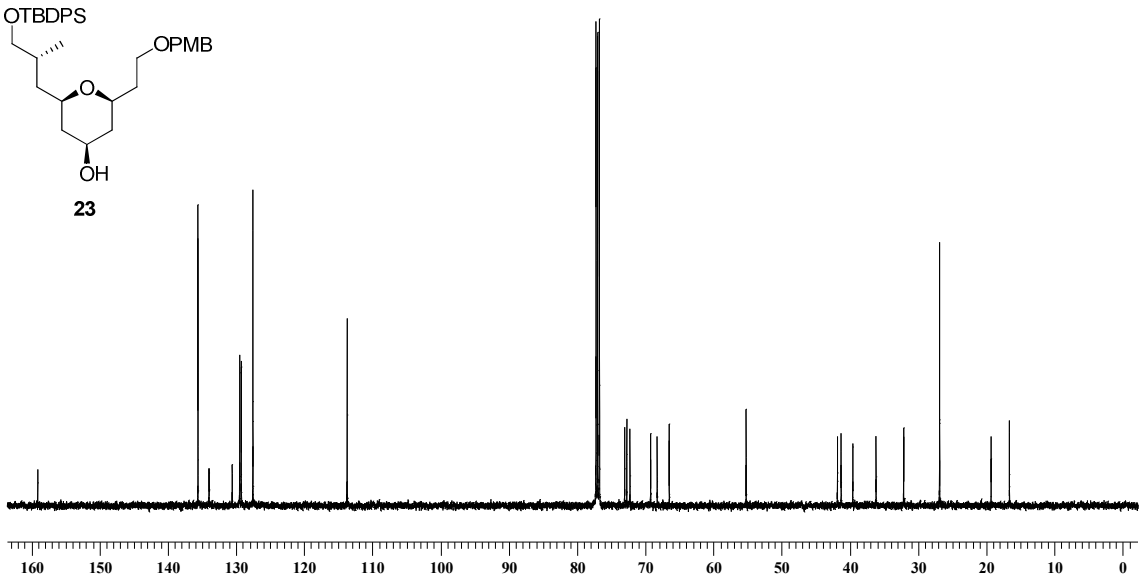
^{1}H NMR spectrum of 10 ($CDCl_3$, 500 MHz)



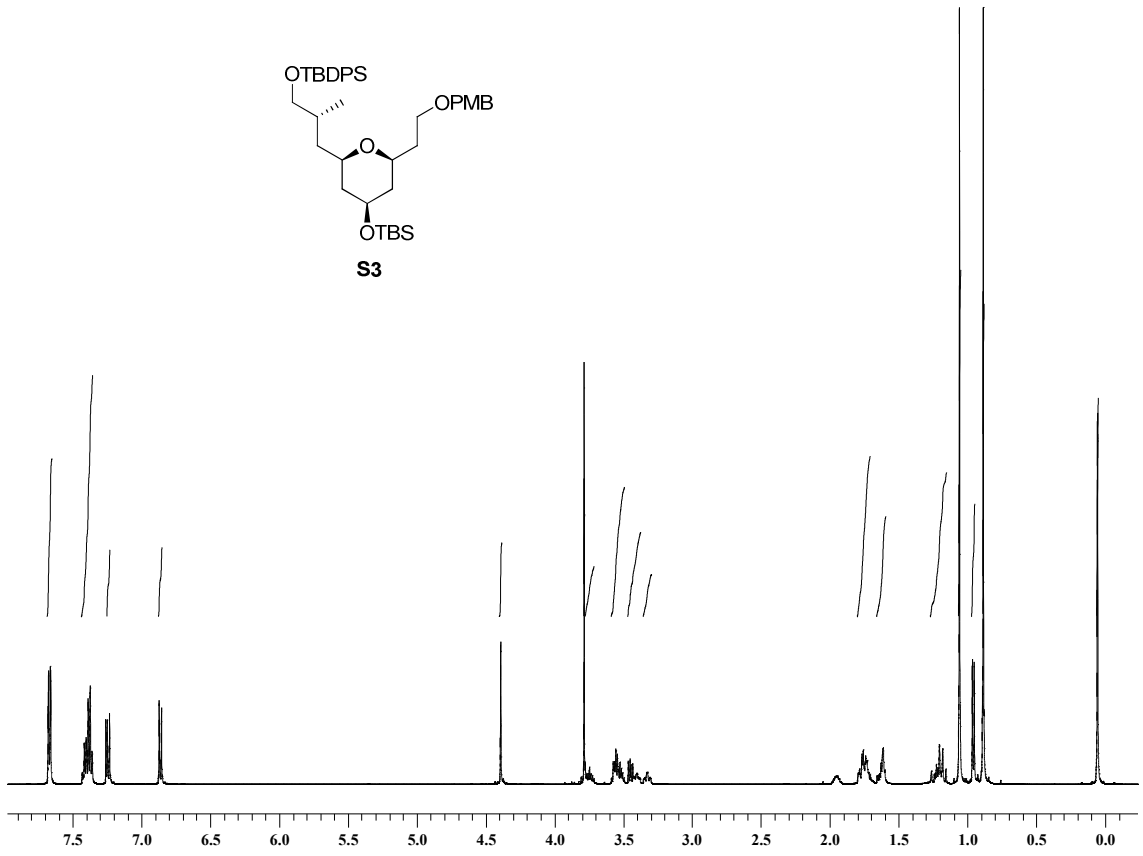
^{13}C NMR spectrum of 10 ($CDCl_3$, 500 MHz)



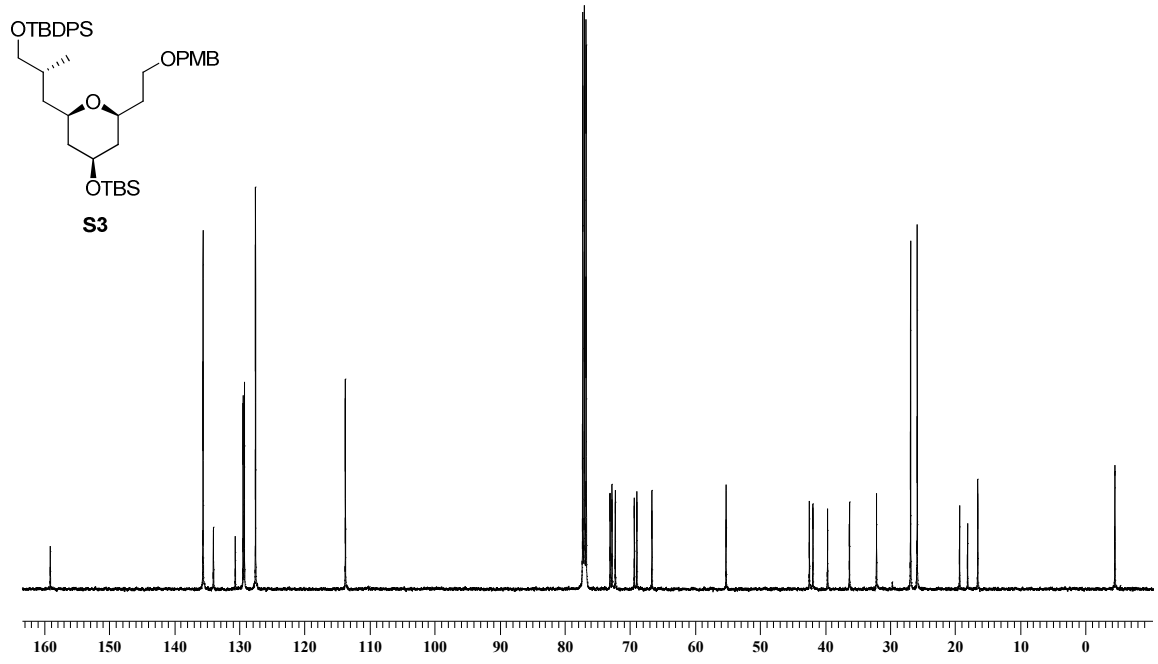
^{1}H NMR spectrum of 23 ($CDCl_3$, 500 MHz)



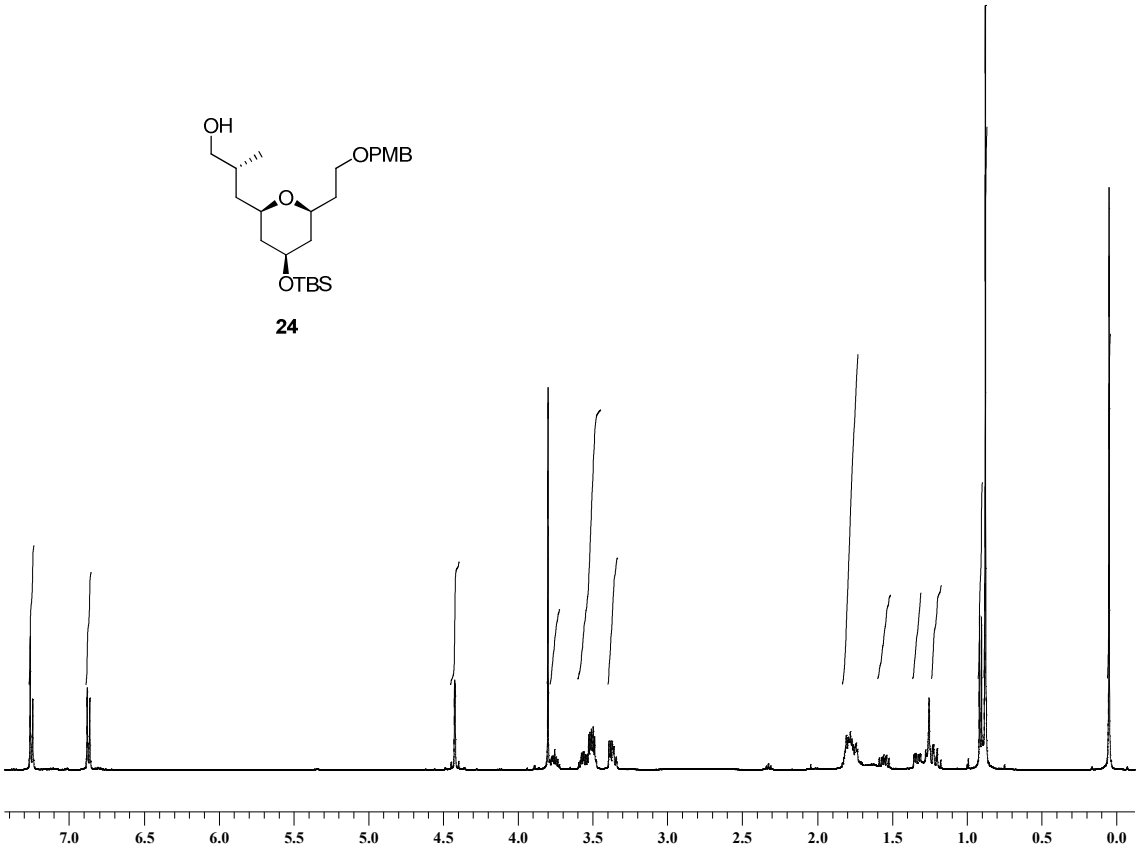
^{13}C NMR spectrum of 23 ($CDCl_3$, 125 MHz)



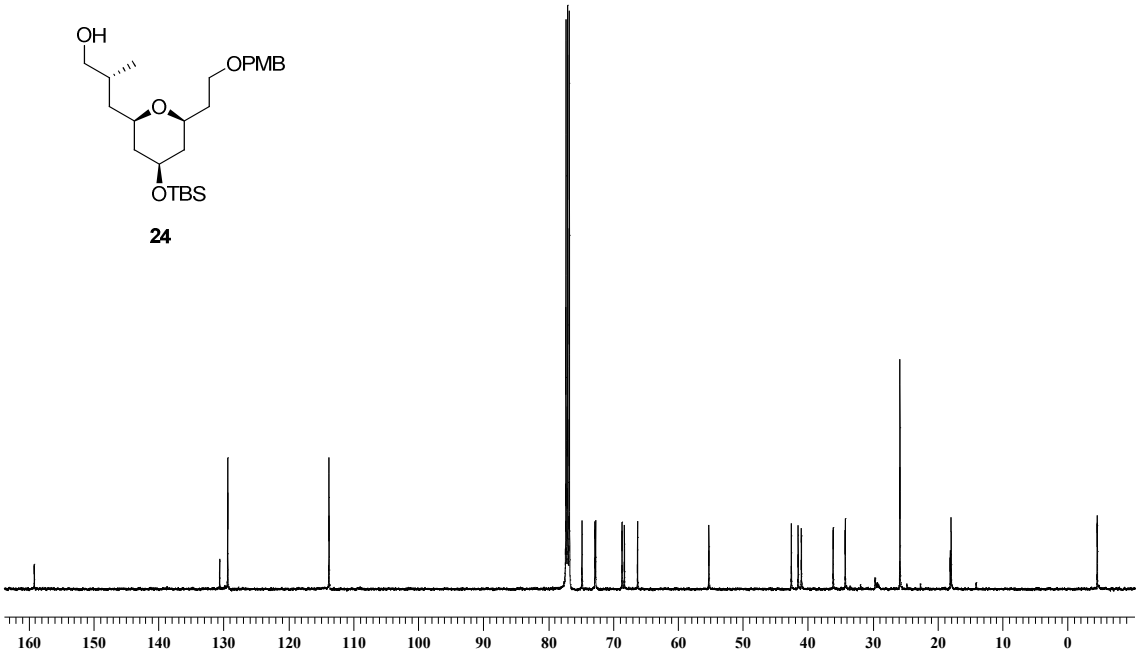
^{1}H NMR spectrum of S3 ($CDCl_3$, 500 MHz)



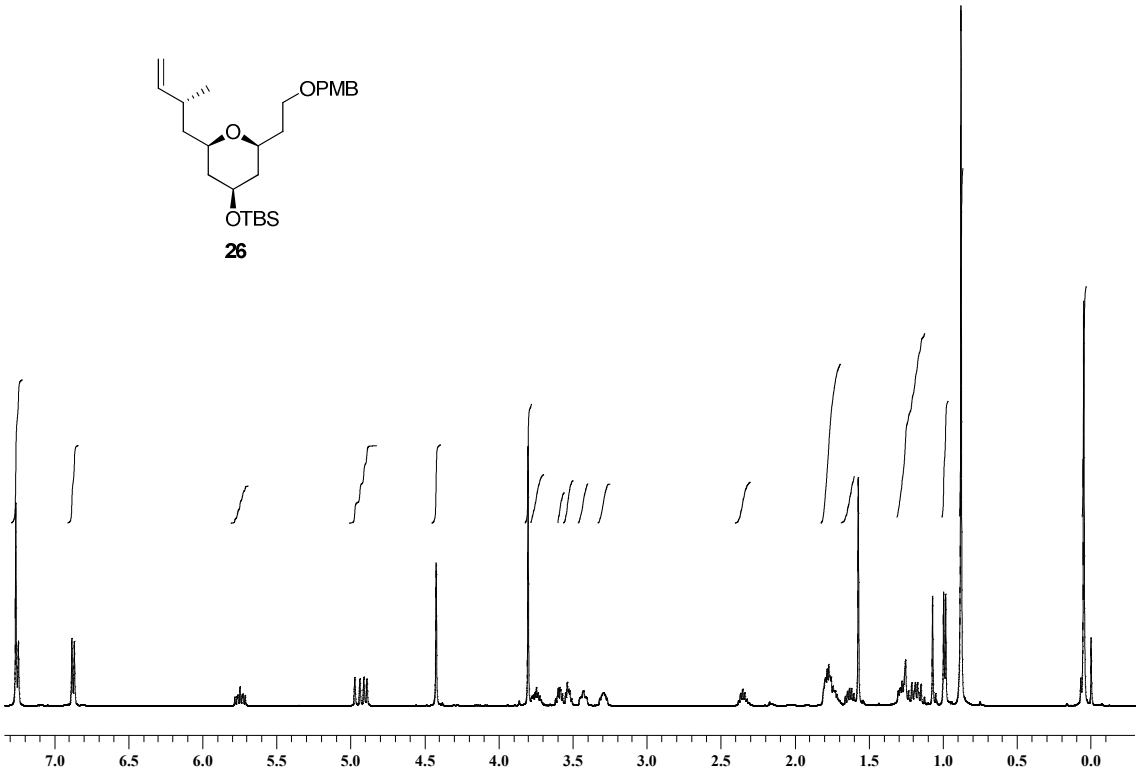
^{13}C NMR spectrum of S3 ($CDCl_3$, 125 MHz)



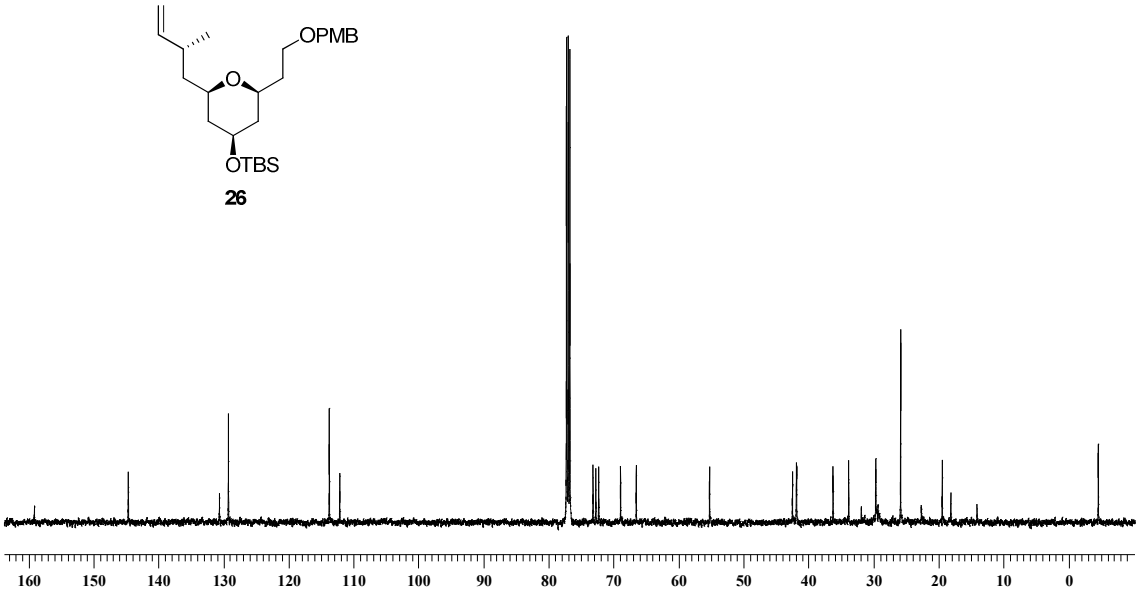
^{1}H NMR spectrum of 24 ($CDCl_3$, 500 MHz)



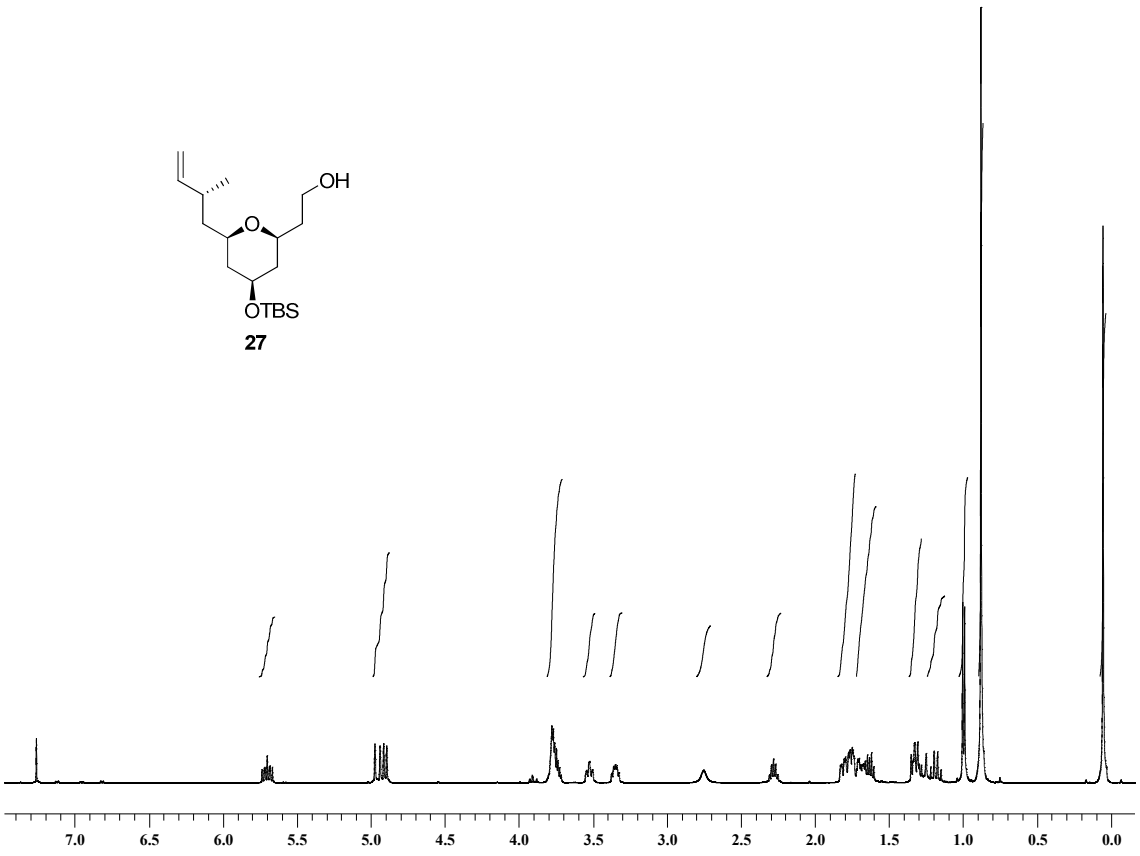
^{13}C NMR spectrum of 24 ($CDCl_3$, 125 MHz)



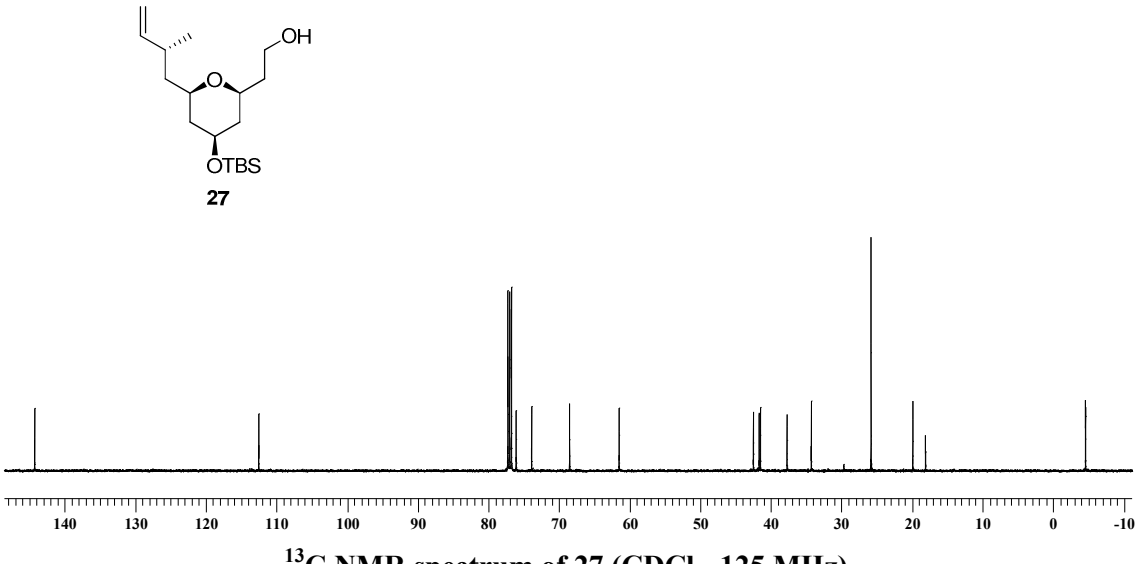
^{1}H NMR spectrum of 26 ($CDCl_3$, 500 MHz)



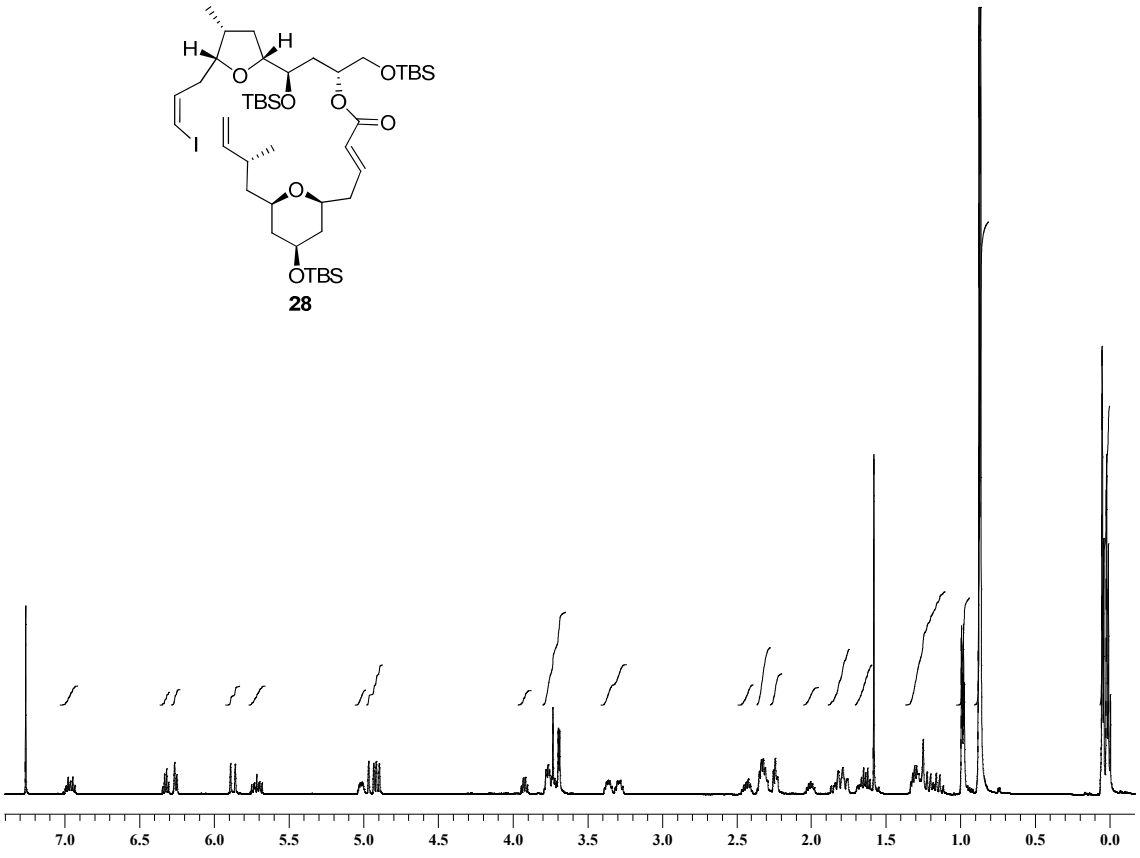
^{13}C NMR spectrum of 26 ($CDCl_3$, 125 MHz)



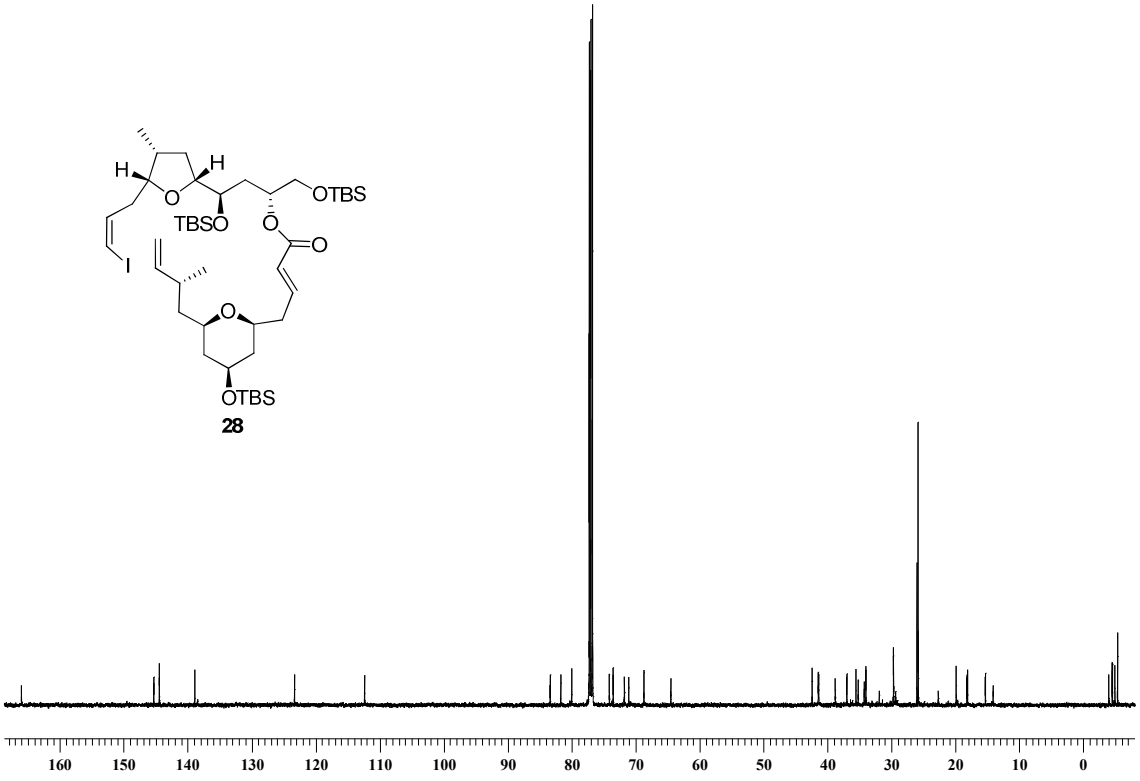
^{1}H NMR spectrum of 27 ($CDCl_3$, 500 MHz)



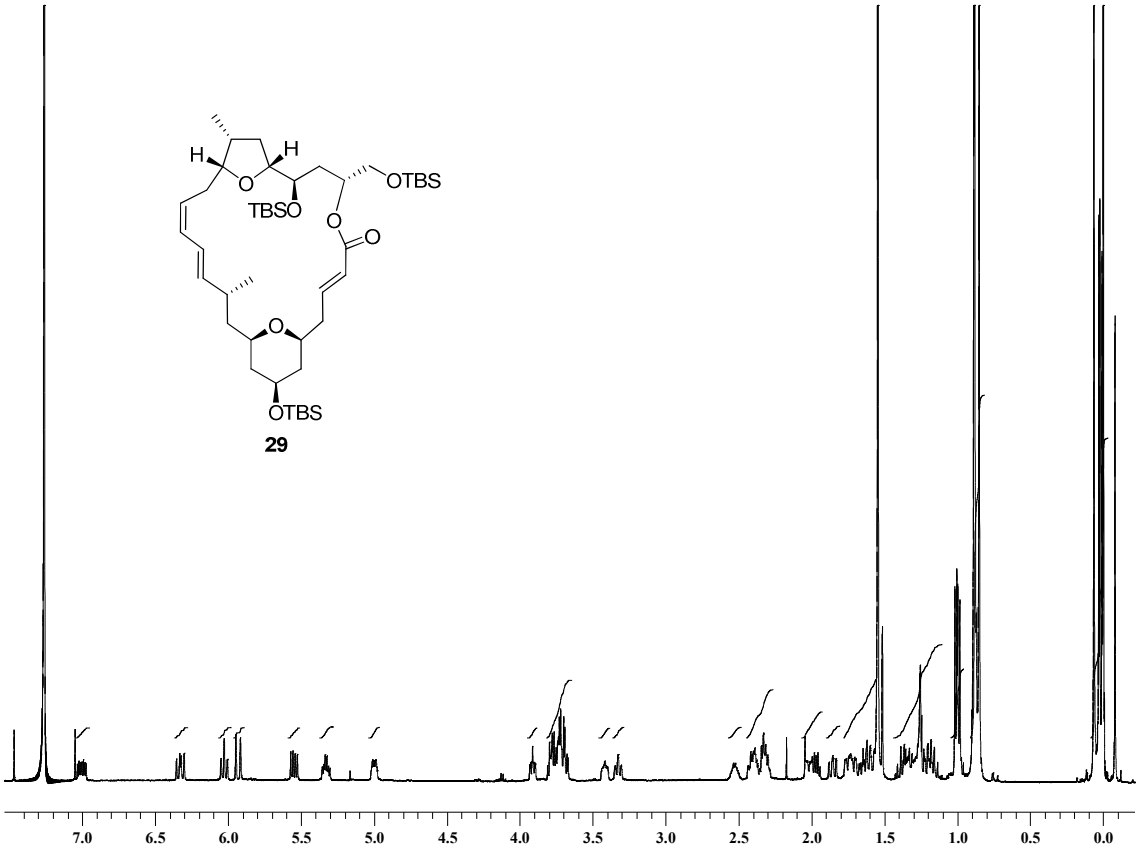
^{13}C NMR spectrum of 27 ($CDCl_3$, 125 MHz)



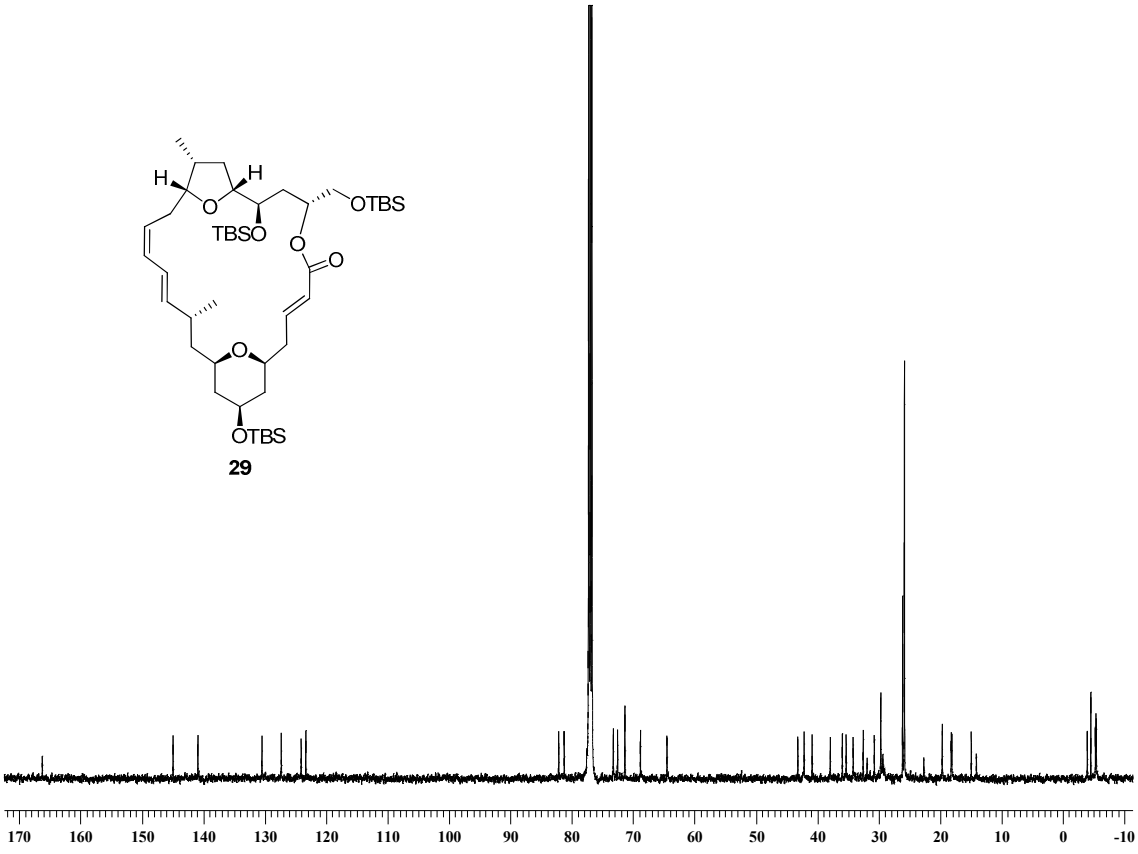
^{1}H NMR spectrum of 28 ($CDCl_3$, 500 MHz)



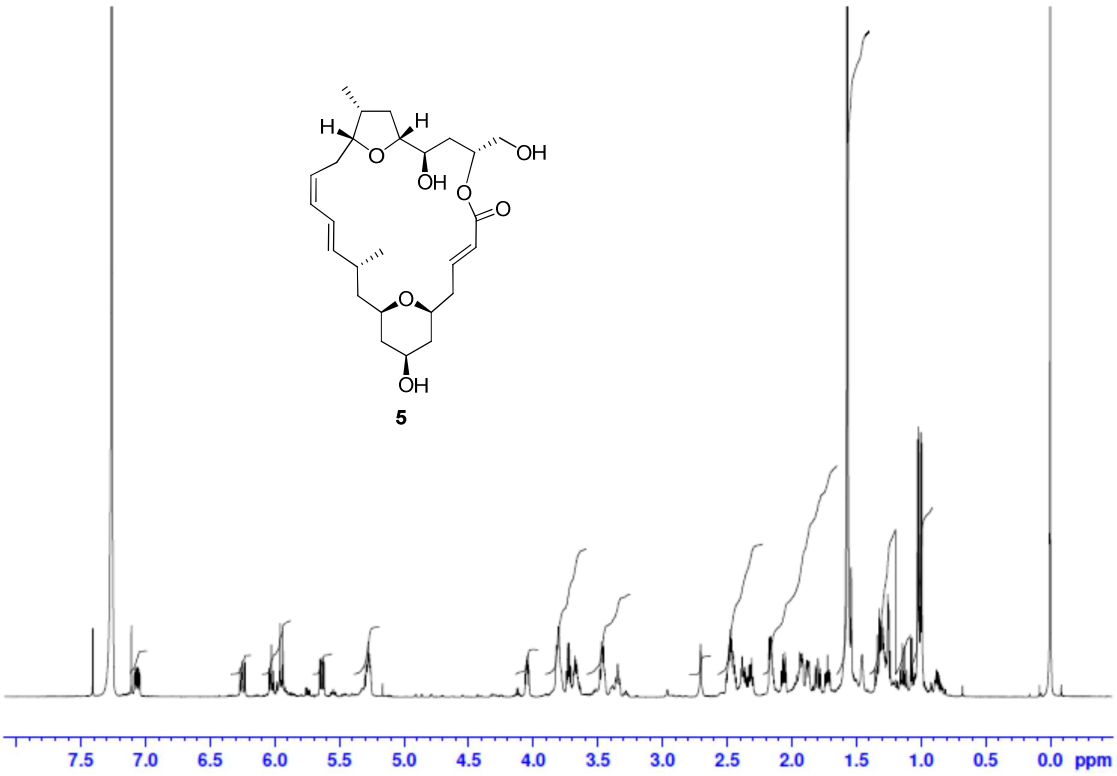
^{13}C NMR spectrum of 28 ($CDCl_3$, 125 MHz)



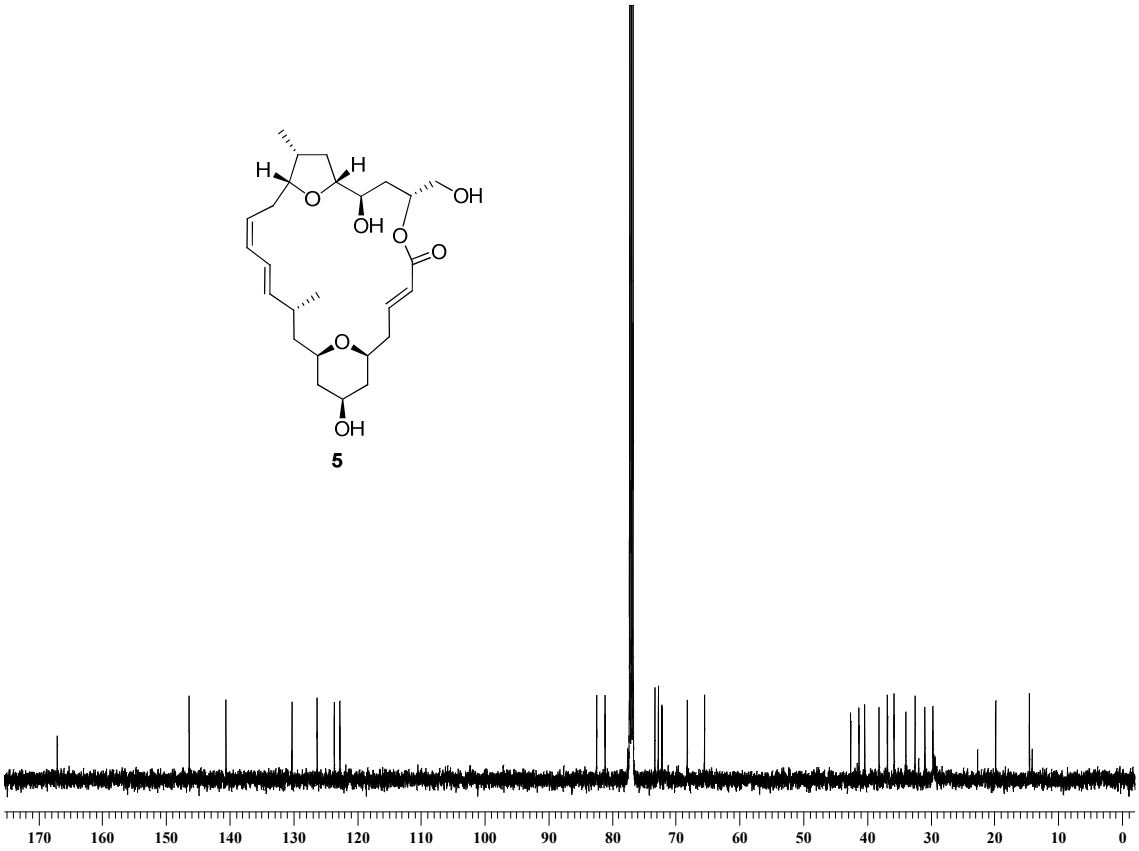
^{1}H NMR spectrum of 29 ($CDCl_3$, 500 MHz)



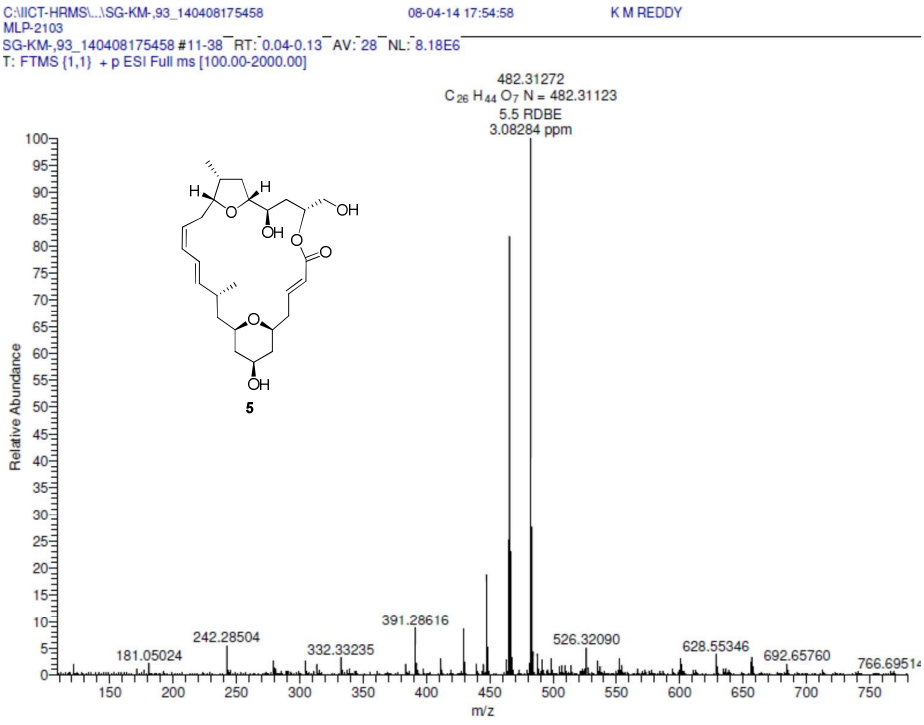
^{13}C NMR spectrum of 29 ($CDCl_3$, 125 MHz)

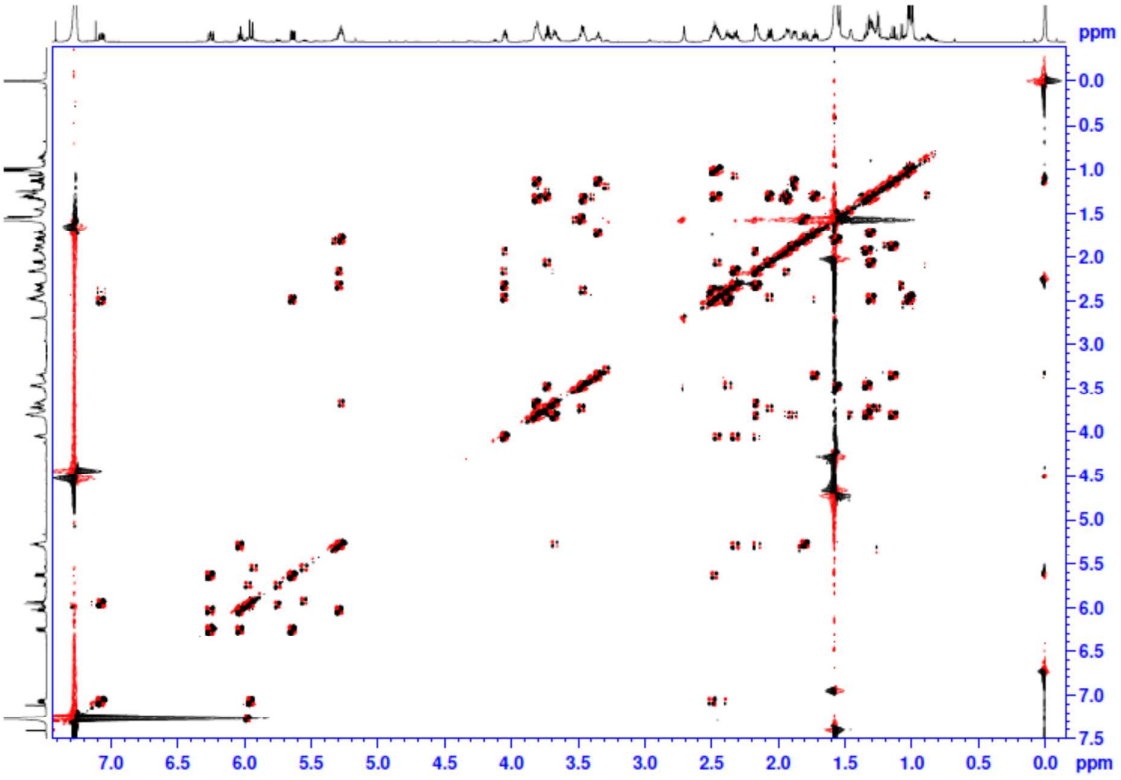


^{1}H NMR spectrum of 5 ($CDCl_3$, 700 MHz)

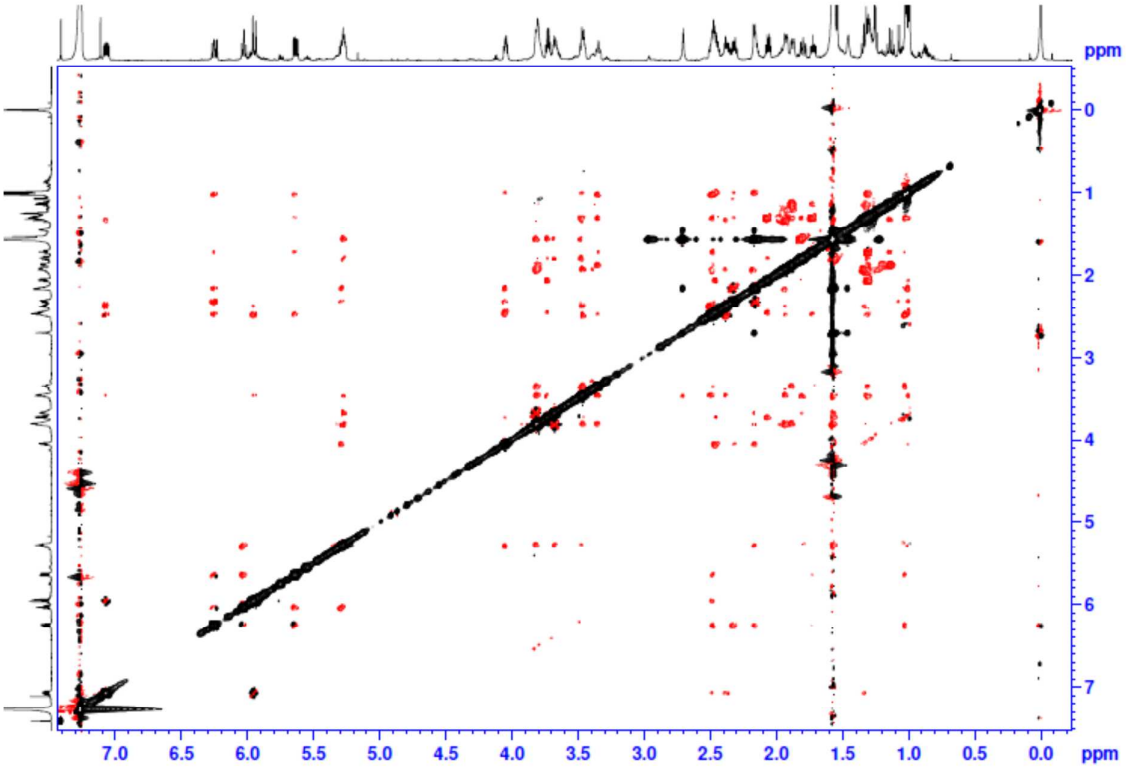


^{13}C NMR spectrum of 5 ($CDCl_3$, 125 MHz)

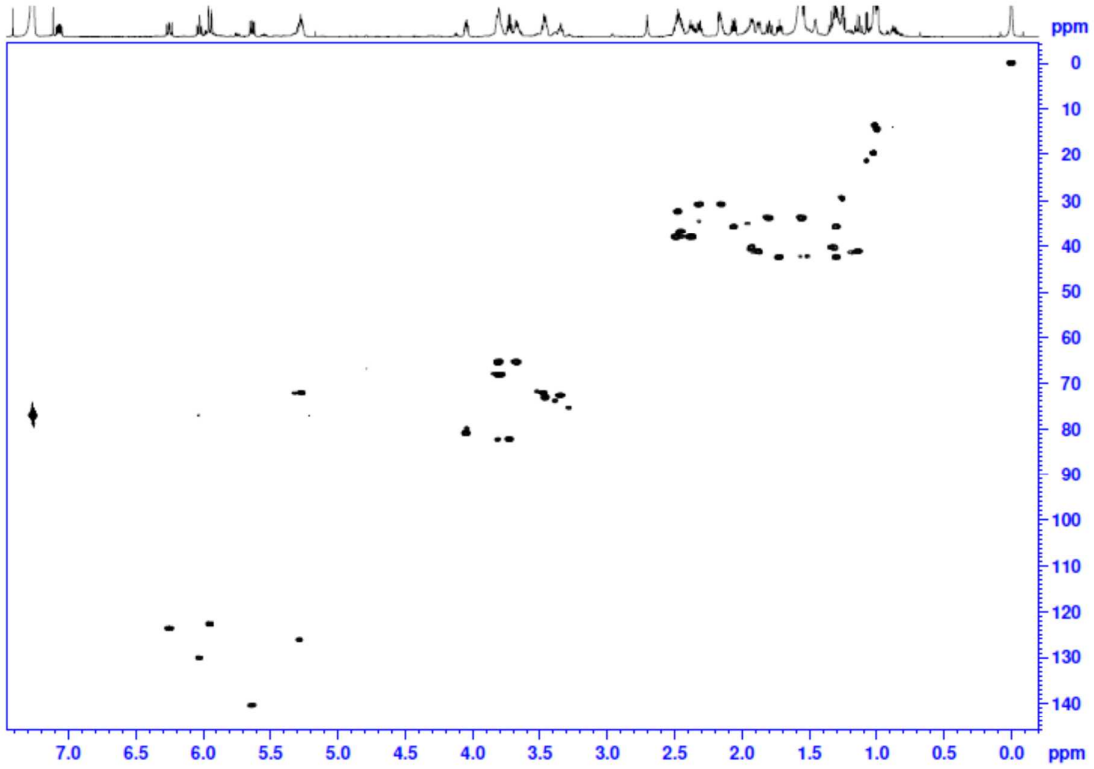




2D DQCOSY (Double Quantum Coherence Spectroscopy) spectrum of compound 5 recorded on 700 MHz at 25 ^{o}C in $CDCl_3$.



2D NOESY (Nuclear Overhauser Effect Spectroscopy) spectrum of compound 5 recorded on 700 MHz at 25 °C in $CDCl_3$.



2D ^{1}H-^{13}C HSQC (Heteronuclear Single Quantum Coherence Spectroscopy) spectrum of compound 5 recorded on 700 MHz at 25 ^{o}C in $CDCl_3$.