Enantioselective Synthesis of (+)-Hippolide J and Reevaluation of Antifungal Activity

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Supplementary Information – Table of Contents

General.

^{1}H NMR spectra were recorded at room temperature on a Varian I400 (400 MHz), Varian VXR400 (400 MHz), Varian I500 (500 MHz), or a Varian I600 (600 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the residual solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on a Varian I400 (101 MHz) or a Varian I500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). Infrared (IR) spectra were recorded on a Bruker Tensor II FT-IR Spectrometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High Resolution Mass Spectrometry (HRMS) analysis was obtained using Electron Impact Ionization (EI), Chemical Ionization (CI), Atmospheric Pressure Chemical Ionization (APCI) or Electrospray Ionization (ESI) and reported as m/z (relative intensity). ESI was acquired using a Waters/Micromass LCT Classic (ESI-TOF). Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 589 nm wavelength (sodium D-line) using a standard 10 cm cell (1 mL). Specific rotations, $[\alpha]_D^{20}$, are reported in degree mL/(g·dm) at the specific temperature. Concentrations (c) are given in grams per 100 mL of the specific solvent. The diastereomeric and regioisomeric ratios were determined using NMR or GC-MS analysis of unpurified reaction mixtures. Unless otherwise noted, all reactions have been carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (150 °C) and flame-dried glassware with standard vacuum-line techniques. Dichloromethane (DCM), Tetrahydrofuran (THF), Diethyl ether (Et_2O), dioxane and Dimethylformamide (DMF) were purified under a positive pressure of dry argon by passage through two columns of activated alumina. Toluene (PhMe) was purified under a positive pressure of dry argon by passage through columns of activated alumina and Q5 (Grubbs apparatus). Benzene (PhH) and Nitromethane ($MeNO_2$) was distilled over CaH_2. All work-up and purification procedures were carried out with reagent grade solvents in air. Standard flash column chromatography (FCC) techniques using ZEOprep 60/40-63 µm silica gel were used for purification. For difficult separations medium pressure liquid chromatography (MPLC) was performed using a Teledyne ISCO CombiFlash Rf 150 instrument. Chiral HPLC analysis was performed on an Agilent 1220 Infinity LC system using chiral column eluted with a mixture of hexane and isopropyl alcohol.

Reagents and Catalysts:

Bis[2-(2,4-difluorophenyl)-5-trifluoromethylpyridine](2-2'-bipyridyl)iridium hexafluorophosphate {[Ir(dFCF$_3$ppy)bpy]PF$_6$} was purchased from Oakwood and used as received.
2-2'-Bipyridine (bpy) was purchased from Strem and used as received.
Bismuth(III) trifluoromethanesulfonate was purchased from Matrix Scientific and used as received.
1-(3,5-Bis(trifluoromethyl)phenyl)-3-((S)-(6-methoxyquinolin-4-yl)((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)thiourea was synthesized via known literature.[1]
4-Bromofuran-2(5*H*)-one was synthesized via known literature.[2]
Boron trifluoride diethyl etherate (BF$_3$·OEt$_2$) was purchased from Sigma-Aldrich and used as received.
***n*-Butyllithium solution** was purchased from Sigma-Aldrich and titrated before every use.
***tert*-Butyldiphenylchlorosilane (TBDPSCl)** was purchased from TCI and used as received.
Cesium carbonate was purchased from Sigma-Aldrich and used as received.
Cesium hydroxide monohydrate was purchased from Alfa-Aesar and used as received.
Chlorotrimethylsilane (TMSCl) was purchased from Oakwood Chemicals and distilled over calcium hydroxide.
Copper (I) iodide was purchased from Alfa-Aesar and used as received.
Cyclopentyl methyl ether (CPME) was purchased from Sigma-Aldrich and used as received.
Di(1-adamantyl)-*n*-butylphosphine (Ad$_2$P-*n*Bu) was purchased from Sigma-Aldrich and used as received.
1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) was purchased from Alfa Aesar and used as received.
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was purchased from Sigma-Aldrich and used as received.
2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl (RuPhos) was purchased form Sigma-Aldrich and used as received.
Diisopropylamine was purchased from Sigma-Aldrich and distilled over calcium hydroxide.
Diisopropylethlyamine (DIPEA) was purchased from Sigma-Aldrich and distilled over potassium hydroxide.
4,4'-Di-tert-butyl-2,2'-bipyridine (dtbbpy) was purchased from Combi-Blocks and used as received.
Farnesylacetone was purchased from Combi-Blocks and used as received.
L-Selectride (1 M in THF) was purchased from Sigma-Aldrich and used as received.
***N*-Bromosuccinimide (NBS)** was purchased from Oakwood Chemicals and used as received.
***N*-Methylimidazole (NMI)** was purchased from Alfa-Aesar and used as received.
***N,N*-Dimethylacetamide (DMA)** was purchased from Sigma-Aldrich and used as received.
***N*-Phenyl-bis(trifluoromethanesulfonimide)** was purchased from Ark Pharm and used as received.
Nickel chloride ethylene glycol dimethyl ether complex (NiCl$_2$·DME) was purchased from

Strem and used as received.

3-Mesityl-3a,5,6,7,8,8a-hexahydro-4H-cyclohepta[d]thiazol-3-ium perchlorate was synthesized via known literature.[3]

Palladium(II) acetate was purchased from Strem and used as received.

Paraformaldehyde was purchased from Mallinckrodt and used as received.

Potassium carbonate was purchased from VWR and used as received.

Potassium (((4-methoxybenzyl)oxy)methyl)trifluoroborate (PMBOCH$_2$BF$_3$K) was synthesized via known literature.[4]

Potassium phosphate dibasic was purchased from VWR and used as received.

Propargyl alcohol was purchased from Alfa Aesar and used as received.

Sodium borohydride was purchased from Oakwood Chemicals and used as received.

Tetrabutylammoium fluoride 1 M in THF (TBAF) was purchased from Sigma-Aldrich and used as received.

Tetrakis(triphenylphosphine)palladium(0) [Pd(PPh$_3$)$_4$] was purchased from Strem and used as received.

2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) was purchased from Sigma-Aldrich and used as received.

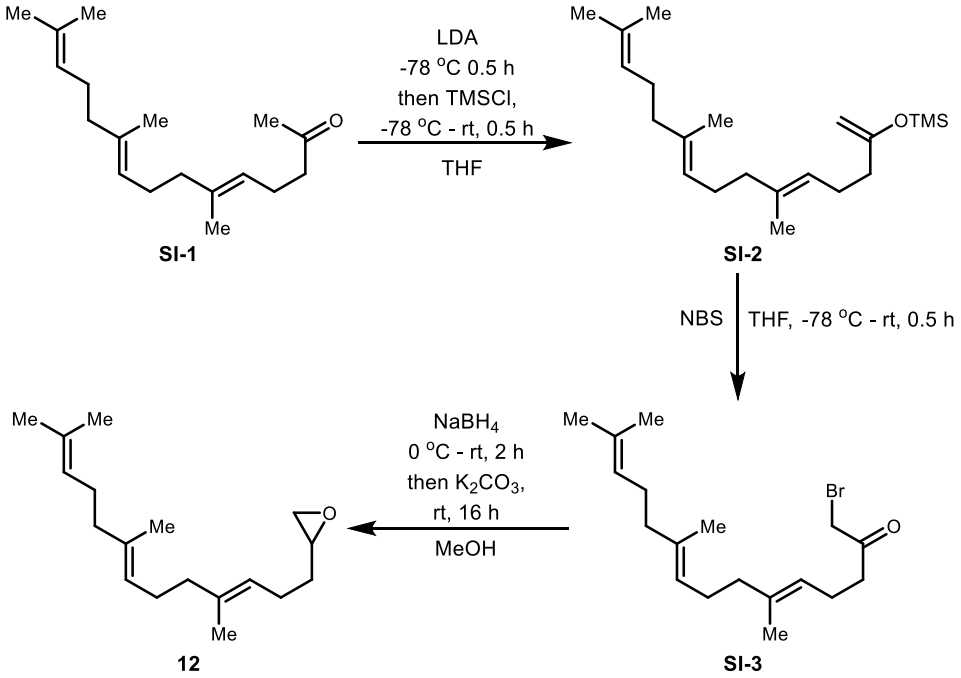
1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one (DMP) was purchased from Chem-Impex and used as received.

Triethylamine was purchased from Sigma-Aldrich and distilled over calcium hydride.

Trimethylsilylacetylene was purchased from Oakwood Chemical and used as received.

(Triphenylphosphoranylidene)ketene (Bestmann ketene) was synthesized via known literature.[5]

Experimental Procedures:



2-((3*E*,7*E*)-4,8,12-Trimethyltrideca-3,7,11-trien-1-yl)oxirane (12): A flame-dried 500 mL round bottom flask equipped with a stir bar was cooled under vacuum. After evacuated/backfilled with N_2 (x 3) and capped with a septum, diisopropylamine (6.2 mL, 44 mmol, 1.2 eq.) and THF (150 mL) were added. To the stirring solution was added *n*-butyllithium (2.48 M in hexanes, 16.4 mL, 40.5 mmol, 1.10 eq.) slowly (~5 min) at 0 °C in an ice/water bath and stirred for 0.5 h. Then the premade LDA solution was cooled to -78 °C in a dry ice/acetone bath and a solution of fanesylacetone **SI-1** (9.66 g, 36.8 mmol, 1.00 eq.) in THF (30 mL) was added slowly to the solution. After stirred for another 0.5 h at the same temperature, TMSCl (7.00 mL, 55.2 mmol, 1.50 eq.) was added. Then the dry ice/acetone bath was removed. The mixture was naturally warmed to room temperature over 0.5 h and quenched with saturated $NaHCO_3$ solution (50 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The crude enolsilylether **SI-2** was directly used to next reaction without further purification.

A flame-dried 500 mL round bottom flask equipped with a stir bar was cooled under vacuum. After evacuated/backfilled with N_2 (x 3) and capped with a septum, above crude enolsilylether **SI-2** (assuming 36.8 mmol, 1.00 eq.) and THF (180 ml) were added. The solution was cooled to -78 °C in a dry ice/acetone bath and NBS (6.55 g, 36.8 mmol, 1.00 eq.) was added. Then the dry ice/acetone bath was removed. The mixture was naturally warmed to room temperature over 0.5 h and quenched with saturated $NaHCO_3$ solution (50 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The crude bromide **SI-3** was directly used to next reaction without further purification.

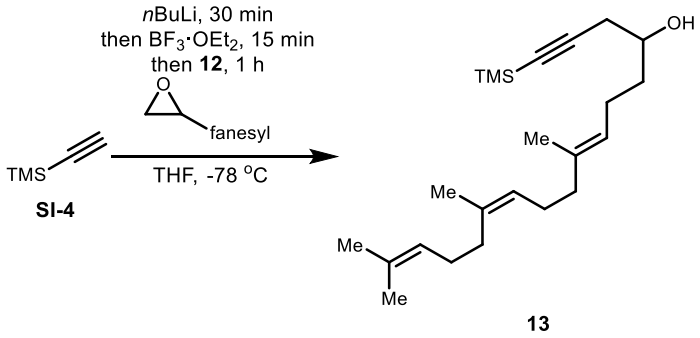
A flame-dried 250 mL round bottom flask equipped with a stir bar was cooled under vacuum. After evacuated/backfilled with N_2 (x 3) and capped with a septum, above crude bromide **SI-3** (assuming 36.8 mmol, 1.00 eq.) and MeOH (90 mL) were added. The solution was cooled to 0 °C in an ice/water bath and sodium borohydride (3 x 0.510 g, 40.5 mmol, 1.10 eq.) was added in three portions every 5 min. The mixture was stirred at the same temperature for 0.5 h and the ice/water bath was removed. Then the reaction was stirred at room temperature for another 1.5 h. After that, potassium carbonate (5.60 g, 40.5 mmol, 1.10 eq.) was added and the mixture was stirred for 16 h at room temperature before quenched with H_2O (50 mL). The aqueous layer was extracted with hexane (3 x 75 mL). The combined organic layer was washed with brine (150 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 49 : 1 to 19 : 1) to afford the epoxide **12** (7.6 g, 79% yield for 3 steps) as colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.15 (tq, *J* = 7.2, 1.4 Hz, 1H), 5.12 – 5.08 (m, 2H), 2.94 – 2.90 (m, 1H), 2.75 (dd, *J* = 5.1, 4.0 Hz, 1H), 2.48 (dd, *J* = 5.1, 2.7 Hz, 1H), 2.16 (q, *J* = 7.4 Hz, 2H), 2.10 – 2.04 (m, 4H), 2.02 – 2.06 (m, 4H), 1.68 (s, 3H), 1.63 (s, 3H), 1.60 (s, 6H), 1.59 – 1.54 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 136.2, 135.2, 131.4, 124.5, 124.2, 123.3, 52.2, 47.4, 39.9, 39.8, 32.9, 26.9, 26.7, 25.8, 24.5, 17.8, 16.1, 16.1.

IR (neat): 3042 (w), 2967 (m), 2920 (s), 2855 (m), 1477 (m), 1382 (m), 832 (m) cm^{-1}.

HRMS (EI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{31}O$ 263.2369. Found 263.2374.



(7*E*,11*Z*)-8,12,16-Trimethyl-1-(trimethylsilyl)heptadeca-7,11,15-trien-1-yn-4-ol (13): A flame-dried 50 mL round bottom flask equipped with a stir bar was cooled under vacuum. After evacuated/backfilled with N_2 (x 3) and capped with a septum, alkyne **SI-4** (0.62 mL, 4.5 mmol, 1.5 eq.) was added followed by THF (9 mL). To the stirring solution was added *n*-butyllithium (2.5 M, 1.8 mL, 4.5 mmol, 1.5 eq.) dropwise at -78 °C in a dry ice/acetone bath and the reaction was stirred for 30 min before boron trifluoride diethyl etherate (0.56 mL, 4.5 mmol, 1.5 eq.) was added. After 15 min, a solution of epoxide **12** (787 mg, 3.00 mmol, 1.00 eq.) in THF (6 mL) was added and the reaction was stirred for another 2 h at the same temperature. Then the reaction was warmed up to room temperature and quenched with saturated NH_4Cl solution (10 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous MgSO4, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 19 : 1 to 4 : 1) to afford alcohol **13** (960 mg, 89%) as pale yellow oil.

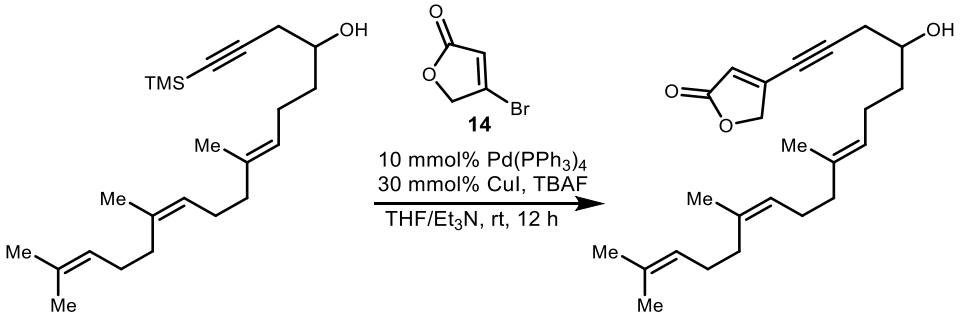
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.15 – 5.09 (m, 3H), 3.74 (q, *J* = 5.0 Hz, 1H), 2.46 (dd, *J* =

16.8, 4.7 Hz, 1H), 2.36 (dd, *J* = 16.8, 6.9 Hz, 1H), 2.15 – 2.02 (m, 8H), 2.00 – 1.97 (m, 2H), 1.95 (d, *J* = 4.5 Hz, 1H), 1.70 – 1.69 (s, 6H), 1.63 – 1.59 (m, 6H), 1.59 – 1.52 (m, 1H), 0.16 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 136.1, 135.3, 131.7, 125.1, 124.5, 123.8, 103.4, 87.7, 69.6, 40.1, 36.3, 32.1, 29.0, 26.8, 26.6, 25.9, 24.2, 23.6, 17.8, 16.2, 0.2.

IR: 3375 (br, s), 3029 (m), 2961 (m), 2175 (m), 1446 (m), 1248 (s) cm^{-1}.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{40}OSiNa$ 383.2741. Found 383.2743.



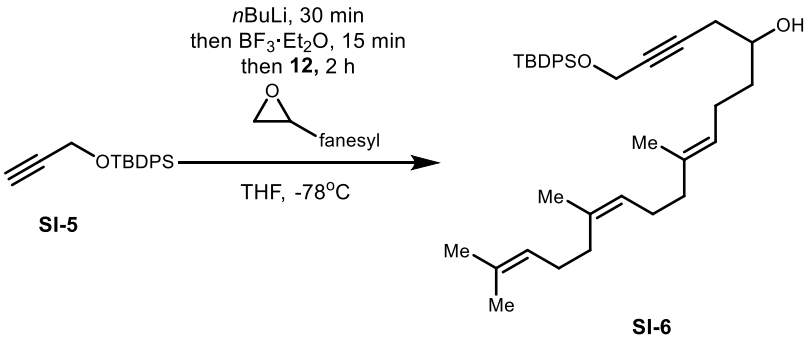
4-((7*E*,11*Z*)-4-Hydroxy-8,12,16-trimethylheptadeca-7,11,15-trien-1-yn-1-yl)furan-2(5*H*)-one (15): A flame-dried 25 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with N_2 and capped with a septum, the flask was transferred into glovebox and charged with $Pd(PPh_3)_4$ (28 mg, 0.025 mml, 0.050 eq.) and CuI (28 mg, 0.15 mmol, 0.30 eq.). Then the flask was moved out and alcohol **13** (180 mg, 0.500 mmol, 1 eq.) was added. 4-Bromofuran-2(5*H*)-one **14** (89 mg, 0.55 mmol, 1.1 eq.), THF (5 mL) and triethylamine (0.21 mL, 1.5 eq. 3.0 eq.) were added sequentially to the flask. To the stirring solution was added TBAF (1.0 M, 0.5 mL, 0.5 mmol, 1.0 eq.) slowly (~5 min) at room temperature. The reaction was stirred at the same temperature for 12 h and filtered through a pad of Celite. The filtrate was concentrated by rotary evaporation and purified by FCC (Hex : EtOAc = 9 : 1 to 4 : 1) to afford alcohol **15** (90 mg, 50%) as yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.14 (s, 1H), 5.16 – 5.12 (m, 3H), 4.78 (s, 2H), 3.87 (q, *J* = 5.7 Hz, 1H), 2.68 (dd, *J* = 17.1, 4.9 Hz, 1H), 2.63 (d, *J* = 6.4 Hz, 1H), 2.20 – 1.93 (m, 10H), 1.86 (d, *J* = 4.2 Hz, 1H), 1.70 (s, 3H), 1.68 (s, 3H), 1.62 (d, *J* = 9.8 Hz, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 147.8, 136.8, 135.6, 131.5, 124.9, 124.4, 124.1, 124.0, 122.2, 104.4, 73.3, 69.6, 39.9, 36.8, 32.1, 28.9, 26.8, 26.6, 25.8, 24.1, 23.6, 17.8, 16.1.

IR: 3457 (br, s), 2963 (m), 2226 (m), 1779 (s), 1610 (m), 1043 (m) cm^{-1}.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{34}O_3Na$ 393.2400. Found 393.2401.



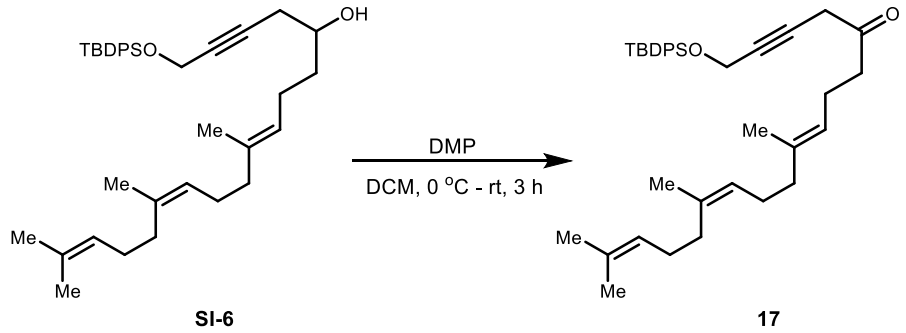
(8*E*,12*E*)-1-((*tert*-Butyldiphenylsilyl)oxy)-9,13,17-trimethyloctadeca-8,12,16-trie-2-yn-5-ol (SI-6): A flame-dried 250 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with N_2 (x 3) and capped with a septum, *tert*-butyldiphenyl(prop-2-yn-1-yloxy)silane **SI-5** (3.24 g, 2.00 eq, 11.0 mmol.) and THF (110 mL) were added. The solution was then cooled to -78 °C in a dry ice/acetone bath and *n*-butyllithium (2.5 M in hexane, 4.4 mL, 11 mmol, 2.0 eq.) was slowly added (~5 min). After stirred for 30 min, boron trifluoride diethyl etherate (1.4 mL, 11 mmol, 2.0 eq.) was added. After 15 min, a solution of epoxide **12** (1.5 g, 5.6 mmol, 1.0 eq.) in THF (20 mL) was added and the reaction was stirred for another 2 h at the same temperature. Then the reaction was then warmed up to room temperature and quenched with saturated NH_4Cl solution (50 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layer was washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 30 : 1 to 9 : 1) to afford the alcohol **SI-6** (2.14 g, 69% yield) as colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (d, *J* = 6.2 Hz, 4H), 7.45 – 7.36 (m, 6H), 5.14 – 5.07 (m, 3H), 4.34 (t, *J* = 2.1 Hz, 2H), 3.67 – 3.60 (m, 1H), 2.38 (ddt, *J* = 16.6, 4.5, 2.1 Hz, 1H), 2.28 (ddt, *J* = 16.6, 6.8, 2.2 Hz, 1H), 2.08 (ddt, *J* = 20.0, 13.6, 7.4 Hz, 6H), 1.98 (dt, *J* = 15.1, 7.7 Hz, 4H), 1.74 (d, *J* = 5.1 Hz, 1H), 1.68 (s, 3H), 1.62 (s, 3H), 1.60 (s, 6H), 1.54 (s, 3H) 1.52 (q, *J* = 7.4 Hz, 3H), 1.06 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 136.1, 135.8, 135.2, 133.4, 131.4, 129.9, 127.8, 124.5, 124.3, 123.8, 82.0, 81.2, 69.8, 53.0, 39.9, 36.3, 27.9, 26.9, 26.9, 26.8, 25.8, 24.3, 19.3, 17.8, 16.2, 16.2.

IR (neat): 3406 (b), 3070 (w), 3049 (m), 2928 (m), 1427 (m), 1065 (m), 700 (s) cm^{-1}.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{37}H_{52}O_2NaSi$ 579.3629. Found 579.3629.



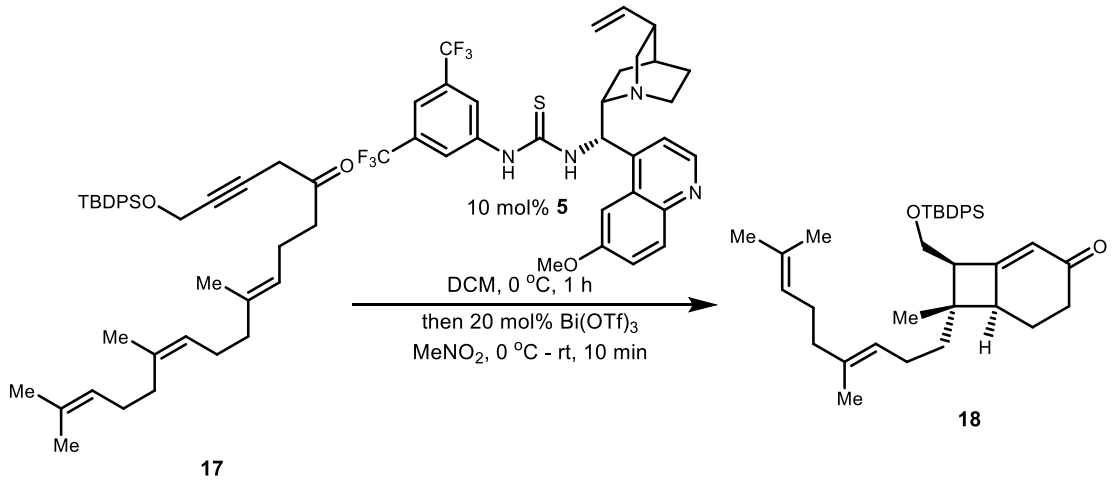
(8*E*,12*E*)-1-((*tert*-Butyldiphenylsilyl)oxy)-9,13,17-trimethyloctadeca-8,12,16-trien-2-yn-5-one (17): A 100 mL round bottom flask equipped with a stir bar was charged with alcohol **SI-6** (1.67 g, 3.00 mmol, 1.00 eq.). After evacuated/backfilled with N_2 (x 3) and capped with a septum, DCM (30 mL) was added. To the stirring solution was added Dess-Martin periodinane (2.54 g, 6.00 mmol, 2.00 eq.) at 0 °C in an ice/water bath. Then ice bath was removed and the reaction was stirred at room temperature for 3 h before quenched with 1 M NaOH solution (20 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation to afford crude ketone **17** (1.62 g, 98% yield), which was used directly into next reaction without further purification.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.72 (d, *J* = 6.3 Hz, 4H), 7.45 – 7.37 (m, 6H), 5.11 – 5.06 (m, 3H), 4.36 (t, *J* = 2.2 Hz, 2H), 3.20 (t, *J* = 2.2 Hz, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 2.27 (q, *J* = 7.2 Hz, 2H) 2.09 – 2.05 (m, 4H), 2.00 – 1.96 (m, 4H), 1.68 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H), 1.59 (s, 3H), 1.07 (s, 9H).

^{13}C NMR (151 MHz,$CDCl_3$): δ 204.5, 136.8, 135.7, 134.9, 133.3, 131.4, 129.9, 127.8, 124.5, 124.2, 122.4, 82.9, 78.0, 53.0, 41.5, 39.8, 39.8, 34.4, 26.9, 26.8, 26.7, 25.8, 22.4, 19.3, 17.8, 16.2, 16.1.

IR: 3049 (m), 2959 (m), 2856 (m), 1722 (m), 1427 (m), 1070 (m), 700 (s) cm^{-1}.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{37}H_{50}O_2NaSi$ 577.3472. Found 577.3470.



(6*S*,7*S*,8*R*)-8-(((tert-butyldiphenylsilyl)oxy)methyl)-7-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-7-methylbicyclo[4.2.0]oct-1-en-3-one (18): A flame-dried 25 mL round bottom flask equipped with a stir bar was cooled under vacuum. After evacuated/backfilled with N_2 (x 3)

and capped with a septum, ketone **17** (1.62 g, 2.92 mmol, 1.00 eq.) was added followed by DCM (5.8 mL). To the stirring solution was added thiourea catalyst **5** (174 mg, 0.290 mmol, 0.100 eq.) at 0 ºC in an ice/water bath and the reaction was stirred for 1 h at the same temperature. Then the mixture was diluted with $MeNO_2$ (14.6 mL) and $Bi(OTf)_3$ (380 mg, 0.580 mmol, 0.200 eq.) was added also at 0 ºC. After addition, the ice bath was immediately replaced with a room temperature water bath and the reaction was stirred vigorously for 10 min before it was quenched with saturated NH_4Cl solution (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 15:1 to 9:1) to afford bicyclic enone **18** (1.22 g, 75% yield, >20:1 dr) as pale yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66 (d, *J* = 6.5 Hz, 4H), 7.45 – 7.35 (m, 6H), 5.75 (s, 1H), 5.17 – 5.05 (m, 2H), 3.76 (dd, *J* = 10.6, 6.6 Hz, 1H), 3.66 (dd, *J* = 10.6, 8.0 Hz, 1H), 3.10 (ddd, *J* = 8.4, 6.7, 2.1 Hz, 1H), 2.78 (ddd, *J* = 10.8, 6.4, 2.2 Hz, 1H), 2.41 (ddd, *J* = 16.5, 4.4, 2.4 Hz, 1H), 2.31 (ddd, *J* = 16.5, 14.4, 4.8 Hz, 1H), 2.08 (q, *J* = 7.5 Hz, 2H), 2.04 – 1.99 (m, 3H), 1.95 (dq, *J* = 13.9, 7.0 Hz, 1H), 1.89 (dddd, *J* = 13.3, 6.8, 4.7, 2.1 Hz, 1H), 1.75 (dtt, *J* = 12.3, 10.6, 4.8 Hz, 2H), 1.69 (s, 3H), 1.67 – 1.63 (m, 1H), 1.62 (s, 3H), 1.60 (s, 3H), 1.05 (s, 9H), 0.91 (s, 3H).

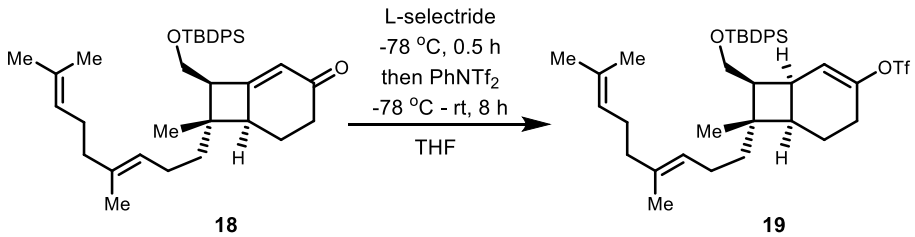
^{13}C NMR (151 MHz, $CDCl_3$): δ 199.5, 171.3, 135.7, 135.7, 135.5, 133.4, 131.5, 129.9, 129.9, 127.9, 127.9, 124.4, 124.1, 118.7, 61.3, 55.6, 49.1, 44.6, 42.6, 39.9, 37.7, 26.9, 26.8, 25.9, 25.1, 23.7, 19.3, 17.8, 16.1, 14.5.

IR: 3071 (w), 2959 (m), 2930 (s), 1673 (s), 1427 (m), 1187 (w), 1111 (s), 702 (m) cm^{-1}.

HRMS (EI) m/z: $[M]^+$ Calcd for $C_{37}H_{50}O_2Si$ 554.3575. Found 554.3563.

Optical rotation: $[\alpha]_D^{20}$: +11.0 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99 : 1 er.

Racemic sample was obtained following the same procedure except for using 0.1 eq. Et_3N instead of thiourea catalyst. The enantiomeric purity was established by HPLC analysis using a chiral column (Chiralpak IA PG024, 22 ºC, 0.5 mL/min, 99 : 1 Hexane:Isopropanol, 254 nm, t_{major} = 11.181 min, t_{minor} = 15.180 min). Absolute stereochemistry was determined according to published literature.[6] Relative stereochemistry was determined by analysis of relevant NOE interactions (see Supporting Information Spectrums).



(1*S*,6*R*,7*S*,8*S*)-8-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-7-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-7-methylbicyclo[4.2.0]oct-2-en-3-yl trifluoromethanesulfonate (19): A flame-dried 250 mL round bottom flask equipped with a stir bar was cooled under vacuum. After evacuated/backfilled with N_2 (x 3) and capped with a septum, enone **18** (4.2 g, 7.6 mmol, 1.0 eq.) and THF (50 mL) were added. Then the solution was cooled -78 ºC in a dry ice/acetone

bath and L-selectride (1 M in THF, 11.4 mL, 1.5 eq.) was added slowly (~5 min) via syringe. The mixture was stirred at the same temperature for 30 min and a solution of N-Phenyl-bis(trifluoromethanesulfonimide) (3.0 g, 8.4 mmol, 1.1 eq.) in THF (24 mL) was added. The reaction was naturally warmed to room temperature and stirred for 8 h before it was quenched with saturated $NaHCO_3$ solution (40 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL). the combined organic layer was sequentially washed with 1 M KOH solution (100 mL), brine (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 99:1 to 49:1) to afford triflate **19** (3.9 g, 75% yield, >20:1 dr) as colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 – 7.57 (m, 4H), 7.47 – 7.30 (m, 6H), 5.90 (d, *J* = 4.0 Hz, 1H), 5.10 (tdd, *J* = 8.4, 4.3, 1.5 Hz, 2H), 3.78 – 3.50 (m, 2H), 3.09 (dddd, *J* = 9.2, 6.7, 4.2, 2.0 Hz, 1H), 2.45 – 2.34 (m, 2H), 2.27 – 2.17 (m, 2H), 2.07 (q, *J* = 7.5 Hz, 2H), 1.98 (dd, *J* = 9.1, 6.4 Hz, 2H), 1.86 (q, *J* = 17.2, 7.0 Hz, 4H), 1.70 (s, 3H), 1.62 (s, 3H), 1.58 (s, 3H), 1.04 (s, 9H), 0.95 (s, 3H).

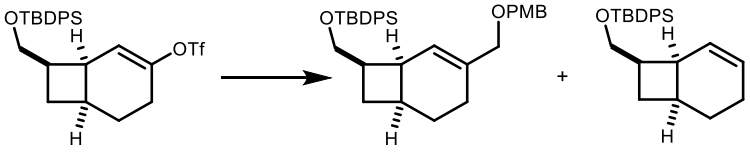
^{13}C NMR (126 MHz, $CDCl_3$): δ 149.8, 135.6, 135.1, 133.9, 133.9, 131.5, 129.8, 127.8, 124.6, 124.5, 119.5, 117.7 (q, *J* = 320.4 Hz), 62.5, 46.4, 46.2, 41.5, 39.9, 37.9, 31.8, 26.9, 26.9, 25.9, 25.8, 23.0, 22.5, 19.3, 17.9, 16.1, 15.7.

IR: 3071 (w), 2959 (m), 2857 (m), 1416 (m), 1245 (m), 1209 (s), 1143 (m), 936 (m), 882 (w), 739 (s), 613 (m) cm^{-1}.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{38}H_{51}O_4F_3SSiNa$ 711.3122. Found 711.3120.

Optical rotaion: $[\alpha]_D^{20}$: +14.8 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99 : 1 er.

[Pd] catalyzed cross coupling with $PMBOCH_2BF_3K$:[4,6,7]



SI-7 **SI-8** **SI-9**

5 mol% $Pd(OAc)_2$, 10 mol% RuPhos $PMBCH_2BF_3K$ (**20**), $CsCO_3$ dioxane/H_2O, 100 °C, 12h	25%	7%
5 mol% $Pd(OAc)_2$, 10 mol% Ad_2P-*n*Bu $PMBCH_2BF_3K$ (**20**), $CsOH{\cdot}H_2O$ CPME/H_2O, 100 °C, 12h	26%	45%

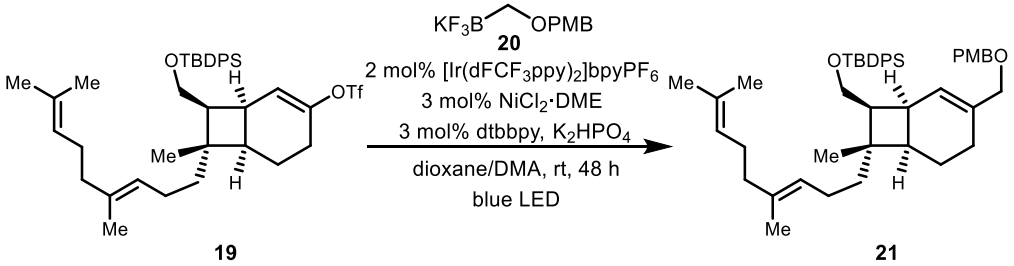
Reactions were run on 0.1 mmol scale and yield was determined using CH_2Br_2 as internal standard.

***tert*-Butyl(((1*S*,6*R*,7*R*)-4-(((4-methoxybenzyl)oxy)methyl)bicyclo[4.2.0]oct-4-en-7-yl)methoxy)diphenylsilane (SI-8, Racemic):**

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.65 (t, *J* = 6.7 Hz, 4H), 7.47 – 7.30 (m, 6H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 5.76 (s, 1H), 4.32 (s, 2H), 3.87 (s, 2H), 3.80 (s, 3H), 3.58 (t, *J* = 9.6 Hz, 1H), 3.47 (dd, *J* = 10.1, 6.1 Hz, 1H), 2.89 (s, 1H), 2.79 (dq, *J* = 17.2, 8.7 Hz, 1H), 2.57 (qt, *J* = 7.9, 3.5 Hz, 1H), 2.09 (dd, *J* = 17.1, 4.9 Hz, 1H), 2.03 – 1.93 (m, 1H), 1.83 (dtd, *J* = 11.1, 8.2, 2.7 Hz, 1H), 1.58 – 1.51 (m, 1H), 1.40 (ddt, *J* = 13.7, 10.9, 5.1 Hz, 1H), 1.31 (q, *J* = 10.1 Hz, 1H), 1.04 (s, 9H).

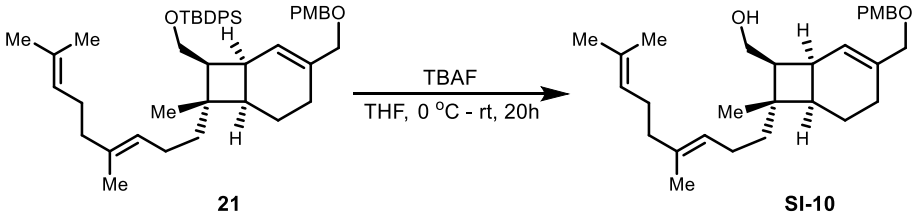
^{13}C NMR (101 MHz, $CDCl_3$): δ 159.2, 136.7, 135.7, 134.3, 130.9, 129.6, 129.5, 127.7, 127.7, 125.6, 113.9, 75.1, 71.1, 65.5, 55.4, 40.5, 35.2, 29.2, 27.0, 24.7, 23.2, 22.2, 19.4.
IR: 3070 (w), 2928 (m), 1612 (m), 1513 (s), 1143 (m), 936 (m), 882 (w) cm^{-1}.
HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{39}H_{42}O_3SiNa$ 549.2795. Found 549.2794.

(((1*S*,6*R*,7*R*)-Bicyclo[4.2.0]oct-4-en-7-yl)methoxy)(*tert*-butyl)diphenylsilane (SI-9, Racemic):
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (t, *J* = 6.9 Hz, 4H), 7.43 – 7.38 (m, 6H), 5.86 (d, *J* = 10.2 Hz, 1H), 5.76 (d, *J* = 10.1 Hz, 1H), 3.62 (t, *J* = 9.5 Hz, 1H), 3.49 (dd, *J* = 10.0, 6.1 Hz, 1H), 2.82 (s, 1H), 2.76 (dq, *J* = 16.5, 8.5 Hz, 1H), 2.56 (dq, *J* = 8.5, 4.8, 4.4 Hz, 1H), 2.05 – 1.92 (m, 1H), 1.81 (q, *J* = 8.7 Hz, 1H), 1.47 – 1.44 (m, 1H), 1.42 – 1.30 (m, 2H), 1.04 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 135.7, 134.5, 129.6, 128.8, 127.7, 127.5, 65.5, 40.5, 34.9, 29.5, 27.0, 24.7, 22.8, 21.2, 19.4.
IR: 3070 (w), 2928 (m), 1589 (M), 1143 (m), 936 (m), 882 (w) cm^{-1}.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{33}OSi$ 377.2295. Found 377.2297.



***tert*-Butyl(((1*R*,6*S*,7*S*,8*S*)-8-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-4-(((4-methoxybenzyl)oxy)methyl)-8-methylbicyclo[4.2.0]oct-4-en-7-yl)methoxy)diphenylsilane (21):**
[Ni pre-catalyst]: A flame-dried 100 mL Schlenk flask equipped with a stir bar was cooled under vacuum. After backfilled with N_2 and capped with a septum, the flask was transferred into glovebox and charged with $NiCl_2$·DME (20.3 mg, 0.0924 mmol, 0.0300 eq.) and dtbbpy (24.8 mg, 0.0924 mmol, 0.0300 eq.). Then the flask was moved out and THF (4.5 mL) was added. The mixture was gently heated by heat gun until all solids dissolved and then concentrated by rotary evaporation to afford the Ni(dtbbpy)Cl_2 pre-catalyst as green solid.
[Photoredox cross coupling]: Then $PMBOCH_2BF_3K$ **20** (956 mg, 3.70 mmol, 1.2 eq.), $[Ir(dFCF_3ppy)_2]bpyPF_6$ (62.0 mg, 0.0616 mmol, 0.0200 eq.) and potassium phosphate dibasic (1.60 g, 9.24 mmol, 3 eq.) were added to the Schlenk flask, evacuated/backfilled with N_2 (x 3). Another Schlenk flask contained a solution of triflate **19** (2.13 g, 3.08 mmol, 1 eq.) in dioxane (50 mL) and DMA (10 mL) was free-pump-thaw (x 3) and then transferred into the flask contained the solids via cannular. The final mixture was irradiated with a 15 W powerPAR™ blue LED bulb[7] (placed 5 cm away from the flask, with a cooling fan to keep room temperature) for 48 h before it was quenched with H_2O (20 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layer was washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 49 : 1 to 19 : 1) to afford the PMB protected alcohol **21** (1.53 g, 72 % yield) as colorless oil.

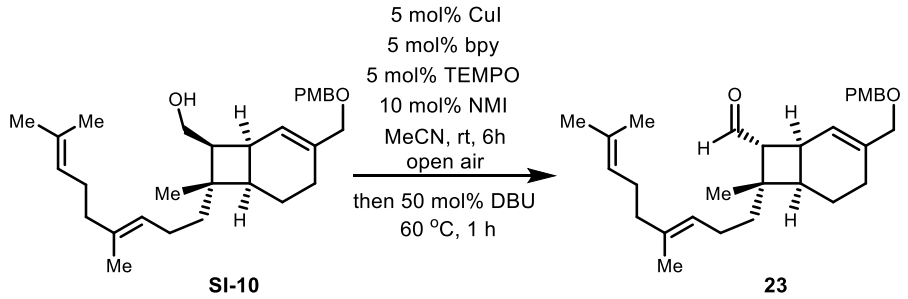
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 – 7.66 (m, 4H), 7.45 – 7.31 (m, 6H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.76 (s, 1H), 5.39 – 4.90 (m, 2H), 4.32 (dd, *J* = 11.4 Hz, 2H), 3.87 (dd, *J* = 11.7 Hz, 1H), 3.81 (s, 3H), 3.75 (ddd, *J* = 31.1, 10.3, 7.9 Hz, 2H), 2.94 (d, *J* = 9.7 Hz, 1H), 2.35 (q, *J* = 8.4 Hz, 1H), 2.17 (q, *J* = 7.6 Hz, 1H), 2.10 (q, *J* = 6.9 Hz, 3H), 2.01 (dd, *J* = 9.2, 6.4 Hz, 2H), 1.94 (dt, *J* = 13.4, 6.5 Hz, 3H), 1.71 (s, 3H), 1.67 (dd, *J* = 19.2, 6.7 Hz, 1H), 1.64 (s, 3H), 1.63 (s, 3H), 1.55 – 1.47 (m, 2H), 1.05 (s, 9H), 0.94 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$): δ 159.2, 136.6, 135.7, 135.7, 134.8, 134.2, 134.2, 131.4, 130.9, 129.6, 129.6, 129.5, 127.7, 127.7, 125.7, 125.1, 124.6, 113.9, 74.9, 71.0, 63.4, 55.4, 47.2, 46.0, 41.2, 39.9, 39.4, 30.9, 27.0, 26.9, 25.9, 23.9, 23.2, 22.2, 19.3, 17.9, 16.1, 16.0.
IR: 3070 (w), 2927 (s), 2855 (m), 1613 (w), 1513 (m), 1247 (s), 1110 (s), 1072 (m), 822 (m), 702 (s) cm^{-1}.
HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{46}H_{62}O_3SiNa$ 713.4360. Found 713.4358.
Optical rotation: $[\alpha]_D^{20}$: +23.7 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99 : 1 er.



21 **SI-10**

((1*R*,6*S*,7*S*,8*S*)-8-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-4-(((4-methoxybenzyl)oxy)methyl)-8-methylbicyclo[4.2.0]oct-4-en-7-yl)methanol (SI-10): A 50 mL flame-dried round bottom flask equipped with a stir bar was charged with protected alcohol **21** (1.46 g, 2.11 mmol, 1.00 eq.). After evacuated/backfilled with N_2 (x 3) and capped with a septum, THF (20 mL) was added followed by TBAF (1.0 M in THF, 3.2 mL, 3.2 mmol, 1.5 eq.) at 0 °C in an ice/water bath. Then ice bath was removed and the mixture was stirred at room temperature for 20 h. The reaction was quenched with saturated NH_4Cl solution (10 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 3 : 1) to afford alcohol **SI-10** (876 mg, 92% yield) as colorless oil.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.77 (s, 1H), 5.12 (dt, *J* = 22.6, 7.0 Hz, 2H), 4.39 (d, *J* = 2.8 Hz, 2H), 4.32 (dd, *J* = 11.4 Hz, 2H), 3.81 (s, 3H) 3.75 (dd, *J* = 10.8, 8.6 Hz, 1H), 3.68 (dd, *J* = 10.9, 6.8 Hz, 1H), 2.96 (m 1H), 2.24 (q, *J* = 7.9 Hz, 1H), 2.17 (q, *J* = 7.9 Hz, 1H), 2.14 – 2.05 (m, 4H), 2.01 – 1.88 (m, 5H), 1.75 – 1.65 (m, 1H), 1.69 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H), 1.53 (t, *J* = 8.3 Hz, 2H), 0.94 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$): δ 159.3, 137.7, 135.0, 131.5, 130.8, 129.5, 124.8, 124.5, 124.5, 113.9, 74.8, 71.4, 62.6, 55.4, 47.7, 45.8, 41.0, 39.9, 39.3, 30.9, 26.9, 25.8, 24.0, 23.2, 22.3, 17.8, 16.1, 15.8.
IR: 3412 (b), 2911 (m), 2844 (m), 1611 (m), 1512 (s), 1246 (s), 1171 (m), 1066 (m), 819 (m), 731 (s) cm^{-1}.
HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{44}O_3Na$ 475.3183. Found 475.3183.
Optical rotation: $[\alpha]_D^{20}$: +12.4 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of

99 : 1 er.



(1*R*,6*S*,7*R*,8*S*)-8-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-4-(((4-methoxybenzyl)oxy)methyl)-8-methylbicyclo[4.2.0]oct-4-ene-7-carbaldehyde (23): To a 50 mL round bottom flask charged with alcohol **SI-10** (800 mg, 1.77 mmol, 1.00 eq.) was added MeCN (8.8 mL). Then copper iodide (16 mg, 0.088 mmol, 0.050 eq.), bpy (13.8 mg, 0.088 mmol, 0.050 eq.), TEMPO (13.8 mg, 0.088 mmol, 0.050 eq.) and NMI (14 ul, 0.18 mmol, 0.10 eq.) were added sequentially to the solution at room temperature. The mixture was stirred at the same temperature under open air for 6 h. Then it was diluted with a solution of DBU (0.13 mL, 0.88 mmol, 0.50 eq) in MeCN (8.8 mL) and warmed to 60 ºC in an oil bath, stirred for another 1 h with a stopper. After cooled down to room temperature, the reaction was quenched with saturated NH_4Cl solution (10 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 19 : 1 to 9 : 1) to afford the aldehyde **23** (693 mg, 87% yield, 10 : 1 dr) as pale yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): (Major dr) δ 9.83 (d, *J* = 1.9 Hz, 1H), 7.25 (d, *J* = 9.3 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.64 (s, 1H), 5.10 – 5.07 (m, 2H), 4.39 (s, 2H), 3.91 – 3.83 (m, 2H), 3.80 (s, 3H), 3.19 (t, *J* = 8.7 Hz, 1H), 2.71 (d, *J* = 9.0 Hz, 1H), 2.14 – 2.02 (m, 4H), 2.02 – 1.84 (m, 5H), 1.81 (ddt, *J* = 13.7, 6.3, 3.8 Hz, 1H), 1.68 (s, 3H), 1.65 – 1.57 (m, 2H), 1.60 (s, 3H), 1.59 (s, 3H), 1.20 (s, 3H).

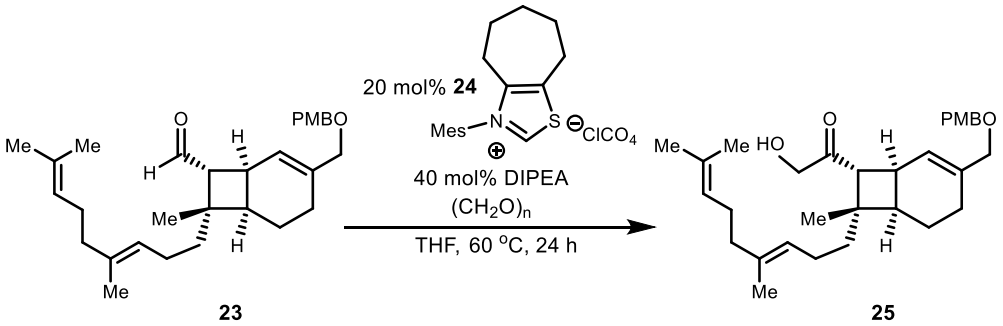
^{13}C NMR (126 MHz, $CDCl_3$): (Major dr) δ 203.5, 159.3, 137.8, 135.4, 131.5, 130.7, 129.4, 125.7, 124.4, 124.1, 113.9, 113.9, 62.2, 55.4, 44.3, 39.8, 38.2, 38.0, 29.0, 26.8, 25.8, 24.1, 23.2, 23.1, 22.0, 17.8, 16.1.

IR: 2926 (s), 2852 (m), 2707 (w), 1709 (s), 1586 (m), 1513 (s), 1247 (s), 1075 (m), 821 (m).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{43}O_3$ 451.3207. Found 451.3207.

Optical rotation: $[\alpha]_D^{20}$: +12.7 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99 : 1 er.

Relative stereochemistry was determined by analysis of relevant NOE interactions (See Supporting Information Spectrums).



1-((1*R*,6*S*,7*R*,8*S*)-8-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-4-(((4-methoxybenzyl)oxy)methyl)-8-methylbicyclo[4.2.0]oct-4-en-7-yl)-2-hydroxyethan-1-one (25): A flame- dried 10 mL vial equipped with a stir bar was cooled under vacuum and charged with NHC catalyst **24** (107 mg, 0.287 mmol, 0.200 eq.) and paraformaldehyde (130 mg, 4.31 mmol, 3.00 eq.). After evacuated/backfilled with N_2 (x 3) and capped with a septum, THF (4 mL) and diisopropylethylamine (0.100 mL, 0.575 mmol, 0.400 eq) were added at room temperature. The mixture was stirred for 5 min at the same temperature and then a solution of the aldehyde **23** (648 mg, 1.45 mmol, 1.00 eq., 10 : 1 dr) in THF (1.8 mL) was added. The septum was then replaced with a screw cap. The reaction was warmed to 60 °C in an oil bath and stirred for 24 h. After cooled back to room temperature, the mixture was concentrated and the residue was purified by FCC (Hex : EtOAc = 9 : 1 to 4 : 1) to afford the α–hydroxylketone **25** (444 mg, 65% yield, >20:1 dr).

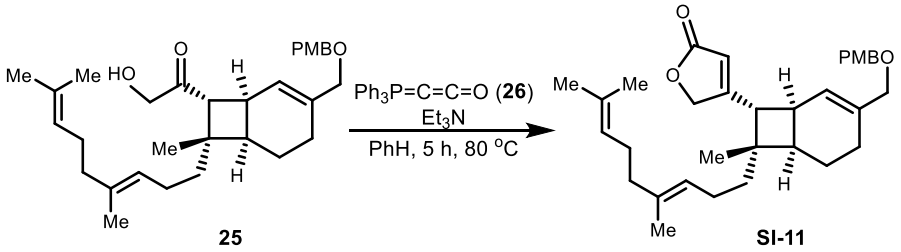
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.60 (s, 1H), 5.11 – 5.01 (m, 2H), 4.40 (s, 2H), 4.11 (qd, *J* = 18.8, 4.7 Hz, 2H), 3.90 – 3.82 (m, 2H), 3.81 (s, 3H), 3.24 (t, *J* = 8.8 Hz, 1H), 3.15 (t, *J* = 4.6 Hz, 1H), 2.76 (d, *J* = 9.7 Hz, 1H), 2.13 – 2.00 (m, 4H), 1.96 (dd, *J* = 9.2, 6.4 Hz, 2H), 1.92 – 1.78 (m, 4H), 1.68 (s, 3H), 1.63 – 1.51 (m, 2H), 1.60 (s, 3H), 1.57 (s, 3H), 1.19 (ddd, *J* = 10.6, 8.3, 5.0 Hz, 1H), 1.16 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 208.3, 159.2, 138.0, 135.3, 131.4, 130.6, 129.4, 125.2, 124.3, 123.9, 113.8, 74.1, 71.8, 68.9, 58.1, 55.3, 43.7, 39.7, 37.5, 36.8, 29.0, 26.7, 25.8, 24.1, 23.1, 22.6, 21.7, 17.8, 16.0.

IR: 3475 (br), 2925 (s), 2852 (m), 1703 (m), 1612 (w), 1513 (s), 1379 (m), 1247 (s), 1073 (s), 821 (m).

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{44}O_4Na$ 503.3132. Found 502.3131.

Optical rotation: $[\alpha]_D^{20}$: +49.1 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99 : 1 er.



4-((1*R*,6*S*,7*R*,8*S*)-8-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-4-(((4-methoxybenzyl)oxy)methyl)-8-methylbicyclo[4.2.0]oct-4-en-7-yl)furan-2(5H)-one (SI-11): A flame-dried 50 mL round bottom flask equipped with a stir bar was cooled under vacuum. After

evacuated/backfilled with N_2 (x 3) and capped with a septum, α–hydroxylketone **25** (436 mg, 0.910 mmol, 1.00 eq.) and PhH (18 mL) were added. Then Bestmann ketene **26** (411 mg, 1.36 mmol, 1.50 eq.) and triethylamine (0.34 mL, 2.7 mmol, 3.0 eq.) were added at room temperature. The septum was quickly replaced with a glass stopper. The mixture was warmed to 80 ºC in an oil bath and stirred for 5 h. After cooled down to room temperature, the solution was concentrated by rotary evaporation and purified by FCC (Hex : EtOAc = 4 : 1) to afford the butenolide **SI-11** (380 mg, 83%) as yellow oil.

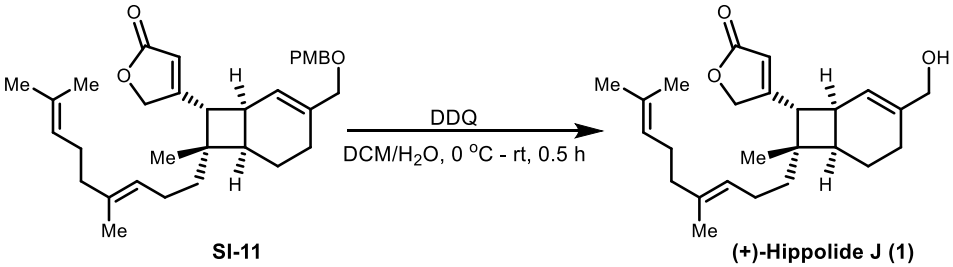
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.85 (q, *J* = 1.8 Hz, 1H), 5.67 (t, *J* = 2.9 Hz, 1H), 5.09 – 5.05 (m, 2H), 4.64 (dd, *J* = 4.5, 1.7 Hz, 2H), 4.41 (s, 2H), 3.94 – 3.84 (m, 2H), 3.81 (s, 3H), 2.86 (t, *J* = 8.5 Hz, 1H), 2.72 (d, *J* = 10.0 Hz, 1H), 2.24 – 2.01 (m, 4H), 1.97 (dd, *J* = 9.2, 6.4 Hz, 2H), 1.91 (q, *J* = 7.3 Hz, 2H), 1.83 (ddt, *J* = 13.2, 6.7, 3.5 Hz, 1H), 1.68 (s, 3H), 1.61 – 1.56 (m, 1H), 1.60 (s, 3H), 1.58 (s, 3H), 1.52 – 1.40 (m, 1H), 1.15 (ddd, *J* = 13.4, 10.5, 7.7 Hz, 1H), 1.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.0, 169.7, 159.3, 138.6, 135.7, 131.6, 130.6, 129.4, 124.3, 124.2, 123.9, 115.5, 115.5, 113.9, 72.0, 55.4, 50.9, 50.9, 43.2, 39.8, 37.7, 37.2, 33.2, 26.8, 25.8, 24.3, 22.9, 22.5, 21.7, 17.8, 16.1.

IR: 3151 (w), 2916 (m), 2850 (m), 1751 (s), 1612 (m), 1512 (m), 1246 (s), 1036 (m), 821 (m) cm^{-1}.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{33}H_{45}O_4$ 505.3312. Found 505.3309.

Optical rotation: $[\alpha]_D^{20}$: +117 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99 : 1 er.



4-((1*R*,6*S*,7*R*,8*S*)-8-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-4-(hydroxymethyl)-8-methylbicyclo[4.2.0]oct-4-en-7-yl)furan-2(5H)-one (1): A 25 mL round bottom flask equipped with a stir bar was charged with alcohol PMB protected alcohol **SI-11** (250 mg, 0.50 mmol, 1.0 eq.). After evacuated/backfilled with N_2 (x 3) and capped with a septum, DCM (5 mL) and H_2O (0.5 mL) were added. The solution was cooled to 0 ºC in an ice/water bath and DDQ (227 mg, 1.00 mmol, 2.00 eq.) was added. Then the ice bath was removed and the reaction was stirred at room temperature for 0.5 h before it was quenched with saturated $NaHCO_3$ solution (5 mL). The aqueous layer was extracted by EtOAc (3 x 5mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by FCC (Hex : EtOAc = 3 : 1 to 1 : 1) to afford (+)-hippolide J (**1**) (135 mg, 70%) as pale yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.86 (d, *J* = 1.7 Hz, 1H), 5.66 (s, 1H), 5.09 – 5.06 (m, 2H), 4.70 – 4.57 (m, 2H), 4.06 – 4.01 (m, 2H), 2.87 (t, *J* = 8.4 Hz, 1H), 2.72 (d, *J* = 10.1 Hz, 1H), 2.16 (ddd, *J* = 12.2, 8.5, 6.4 Hz, 1H), 2.11 – 2.01 (m, 3H), 1.98 – 1.90 (m, 5H), 1.86 (ddt, *J* = 13.2, 6.8, 3.6 Hz, 1H), 1.67 (s, 3H), 1.64 (dd, *J* = 12.4, 4.2 Hz, 1H), 1.60 (s, 3H), 1.58 (s, 3H), 1.51 – 1.46 (m, 1H), 1.18 – 1.12 (m, 1H), 1.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.0, 169.7, 141.0, 135.7, 131.5, 124.3, 123.8, 122.1, 115.4, 73.3, 66.9, 50.9, 43.2, 39.7, 37.7, 37.2, 33.1, 26.7, 25.8, 24.0, 22.9, 22.5, 21.7, 17.8, 16.1.
IR: 3429 (b), 2962 (m), 2920 (m), 1747 (s), 1627 (m), 1447 (m), 1145 (m), 1041 (m), 851 (m) cm^{-1}.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{37}O_3$ 385.2737. Found 385.2737.
Optical rotation: $[\alpha]_D^{20}$: +145 (*c* = 0.05, MeOH) for an enantiomerically enriched sample of 99 : 1 er. {Literature: $[\alpha]_D^{25}$: +141 (c = 0.05, MeOH)}[6]

Comparison of ^{1}H NMR ($CDCl_3$) Spectroscopic Data Natural and Synthetic (+)-Hippolide J:[9]

A: Natural δH [ppm, mult, *J* (Hz)], 600 MHz	B: Our Synthetic δH [ppm, mult, *J* (Hz)], 600 MHz	Error (B – A) $\Delta\delta$/ppm
5.86 (d, *J* = 1.8 Hz, 1H)	5.86 (d, *J* = 1.7 Hz, 1H)	0.00
5.66 (s, 1H)	5.66 (s, 1H)	0.00
5.08 (m, 1H)	5.09 – 5.06 (m, 2H)	-
5.06 (m, 1H)		
4.64 (m, 2H)	4.70 – 4.57 (m, 2H)	-
4.04 (m, 2H)	4.06 – 4.01 (m, 2H),	-
2.87 (t, *J* = 11.4 Hz, 1H),	2.87 (t, *J* = 8.4 Hz, 1H),	0.00
2.72 (d, *J* = 12.0 Hz, 1H)	2.72 (d, *J* = 10.1 Hz, 1H)	0.00
2.13 (m, 1H)	2.16 (ddd, *J* = 12.2, 8.5, 6.4 Hz, 1H)	0.03
2.07 (m, 1H)	2.11 – 2.01 (m, 3H)	-
2.04 (m, 2H)		
1.95 (m, 2H)	1.98 – 1.90 (m, 5H)	-
1.95 (m, 2H)		
1.94 (m, 1H)		
1.86 (m, 1H)	1.86 (ddt, J = 13.2, 6.8, 3.6 Hz, 1H)	0.00
1.67 (s, 3H)	1.67 (s, 3H)	-0.01
1.64 (m, 1H)	1.64 (dd, *J* = 12.4, 4.2 Hz)	0.00
1.60 (s, 3H)	1.60 (s, 3H)	0.00
1.58 (s, 3H)	1.58 (s, 3H)	0.00
1.48 (m, 1H)	1.51 – 1.46 (m, 1H)	-
1.14 (m, 1H)	1.18 – 1.12 (m, 1H)	-
1.08 (s, 3H)	1.08 (s, 3H)	0.00

Comparison of ^{13}C NMR ($CDCl_3$) Spectroscopic Data Natural and Synthetic (+)-Hippolide J:[9]

A: Natural δ (ppm) 150 MHz	B: our Synthetic δ (ppm) 126 MHz	Error (B – A) $\Delta\delta$/ppm
173.9	174.0	0.1
169.6	169.7	0.1
140.8	140.9	0.1
135.6	135.7	0.1
131.5	131.5	0.0
124.2	124.3	0.1
123.7	123.8	0.1
122.1	122.1	0.0
115.3	115.4	0.1
73.2	73.3	0.1
66.9	66.9	0.0
50.7	50.9	0.2
43.0	43.2	0.2
39.6	39.8	0.2
37.5	37.7	0.2
32.9	33.1	0.2
26.6	26.7	0.1
25.7	25.8	0.1
22.8	22.9	0.1
22.4	22.5	0.1
21.6	21.7	0.1
17.7	17.8	0.1
16.0	16.1	0.1

Anitfungal Biological Study:

Species	Strain	Source
Candida albicans	SC5314	Krysan Lab Collection
Candida glabrata	ATCC 2001	Karl Kuchler Lab Collection
Candida glabrata	4720	Clinical isolate from David Andes Collection
Cryptococcus neoformans var. *grubii*	H99	John Perfect Lab Collection
Cryptococcus neoformans var. *grubii*	DUMC 101.24	John Perfect Lab Collection
Aspergillus fumigatus	CEA10	Robert Cramer Lab Collection
Aspergillus fumigatus	AF293	Robert Cramer Lab Collection

Table S1. Fungal strains used for susceptibility testing

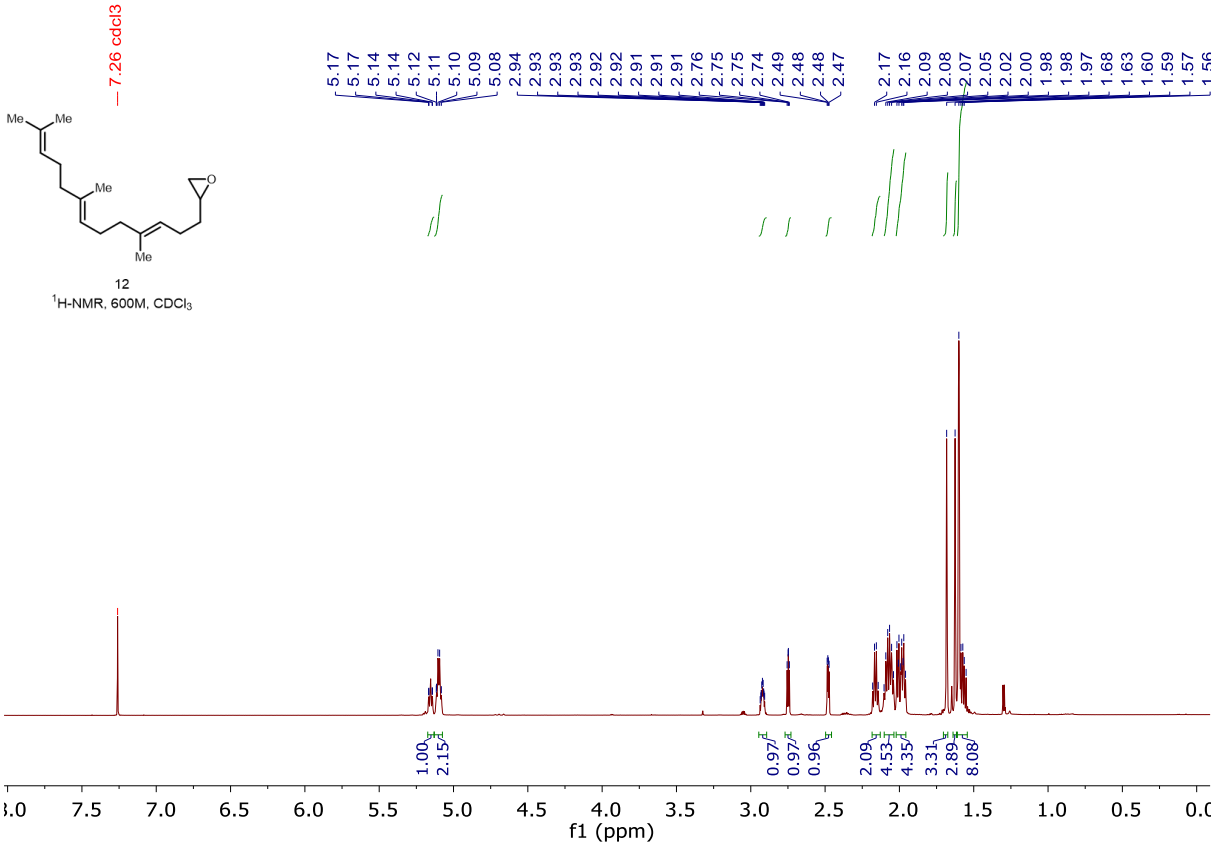
Minimum inhibitory concentration and fractional inhibitory concentration index determination

Minimum inhibitory concentrations were determined using CLSI guidelines.[10] All yeasts were cultured overnight in 3 mL YPD at 30°C, then washed twice in sterile PBS. Two-fold serial dilutions of each drug were prepared in RMPI+MOPS pH 7 (Gibco RPMI 1640 with L-glutamine [11875-093] and 0.165M MOPS), then $1x10^3$ cells were added per well. Plates were incubated at 37°C for 24 (*C. albicans* and *C. glabrata*) or 72 (*C. neoformans*) hours. For *A. fumgiatus*, wells were inoculated with 1.25×10^3 conidia. Plates were incubated at 37°C for 48 hours for *A. fumigatus*. Each assay was done in technical duplicate and at least two independent experiments were performed on different days.

References:

[1]: Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967.
[2]: Jas, G. *Synthesis*, **1991**, *11*, 965.
[3]: Kuhl, N.; Glorius, F.; *Chem. Commun*. **2011**, *47*, 573.
[4]: Molander, G. A.; Wisniewski, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 16856.
[5]: Bestmann, H. J.; Sandmeier, D. *Chem. Ber*. **1980**, *113*, 274.
[6]: Line, N. J.; Witherspoon, B. P.; Hancock, E. N.; Brown, M. K. *J. Am. Chem. Soc.* **2017**, *139*, 14392.
[7]: Molander, G. A.; Canturk, B. *Org. Lett.* **2008**, *10*, 2135.
[8]: For details of spectrums of the light source, see http://www.parsource.com/sites/default/files/downloads/PAR_PPB1001_Lamps_c1060_FINAL.pdf
[9]: Jiao, W.-H.; Hong, L.-L.; Sun, J.-B.; Piao, S.-J.; Chen, G.-D.; Deng, H.; Wang, S.-P.; Yang, F.; Lin, H.-W. *Eur. J. Org. Chem.*, **2017**, 3421.
[10]: a) Clinical and Laboratory Standards Institute. Reference method for broth dilution antifungal susceptibility testing of yeasts; Approved standard, 4th ed, CLSI document M27, Clinical and Laboratory Standards Institute, Wayne, PA 2017. b) CLSI. *Reference Method for Broth Dilution Antifungal Susceptablity Testing of Filamentous Fungi*. *CSLI Standard M38* (Clinical and Labratory Standards Institute, 2017).

Spectrums: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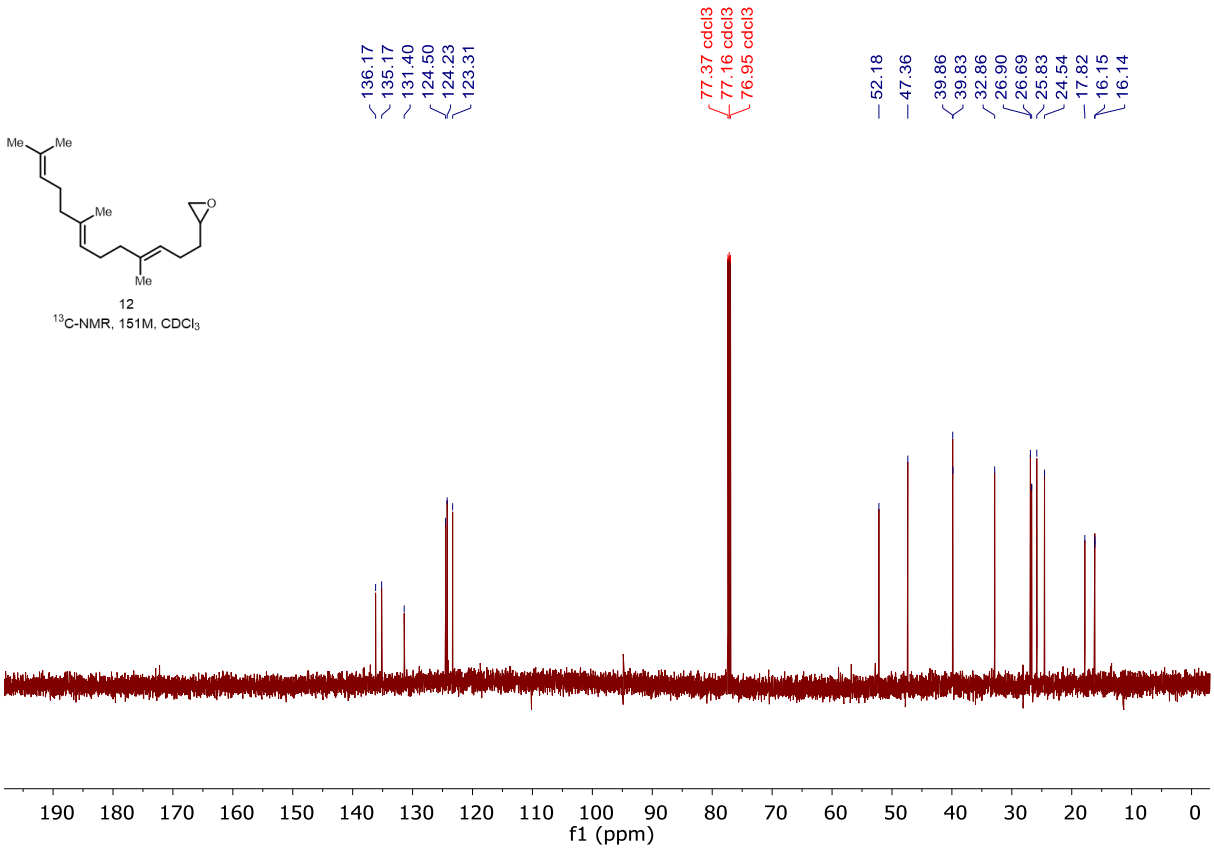
f1 (ppm)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77.16 cdcl3
76.95 cdcl3
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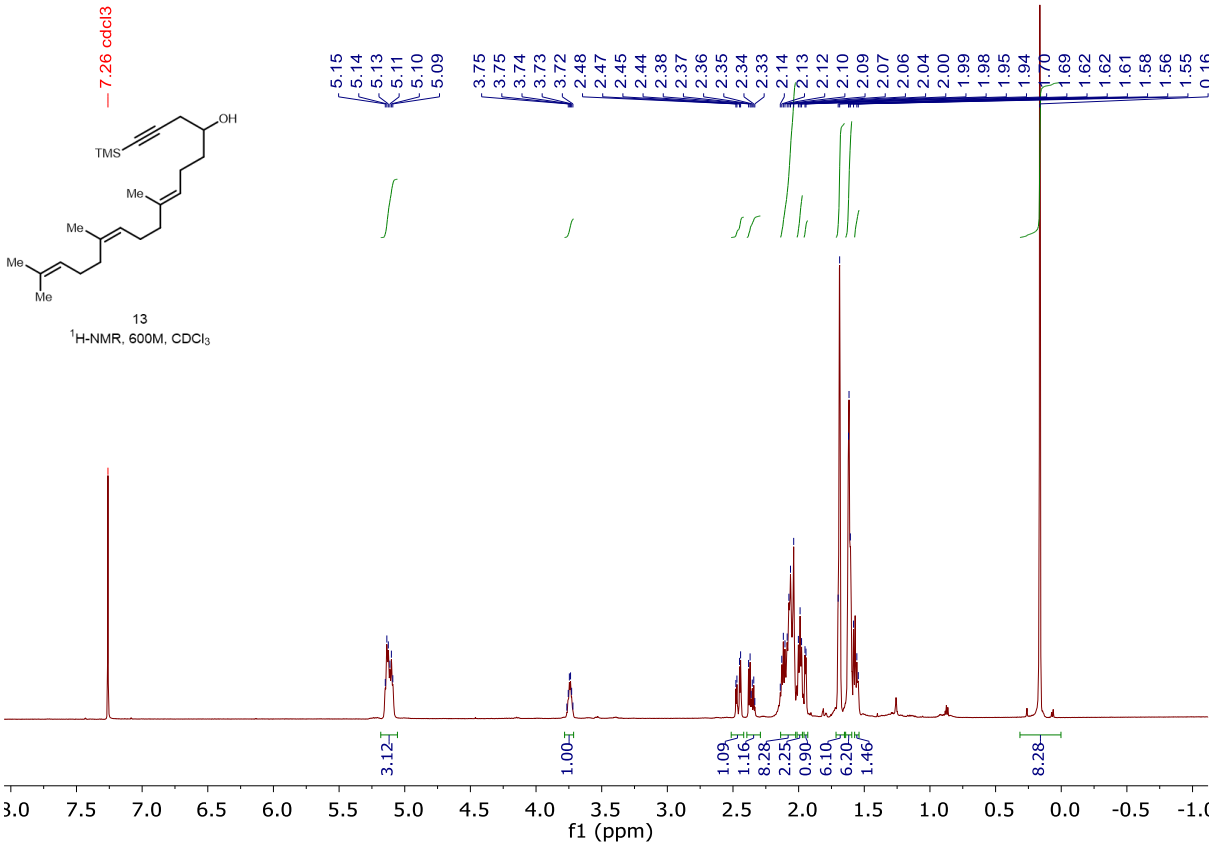
13C-NMR, 151M, CDCl3
f1 (ppm)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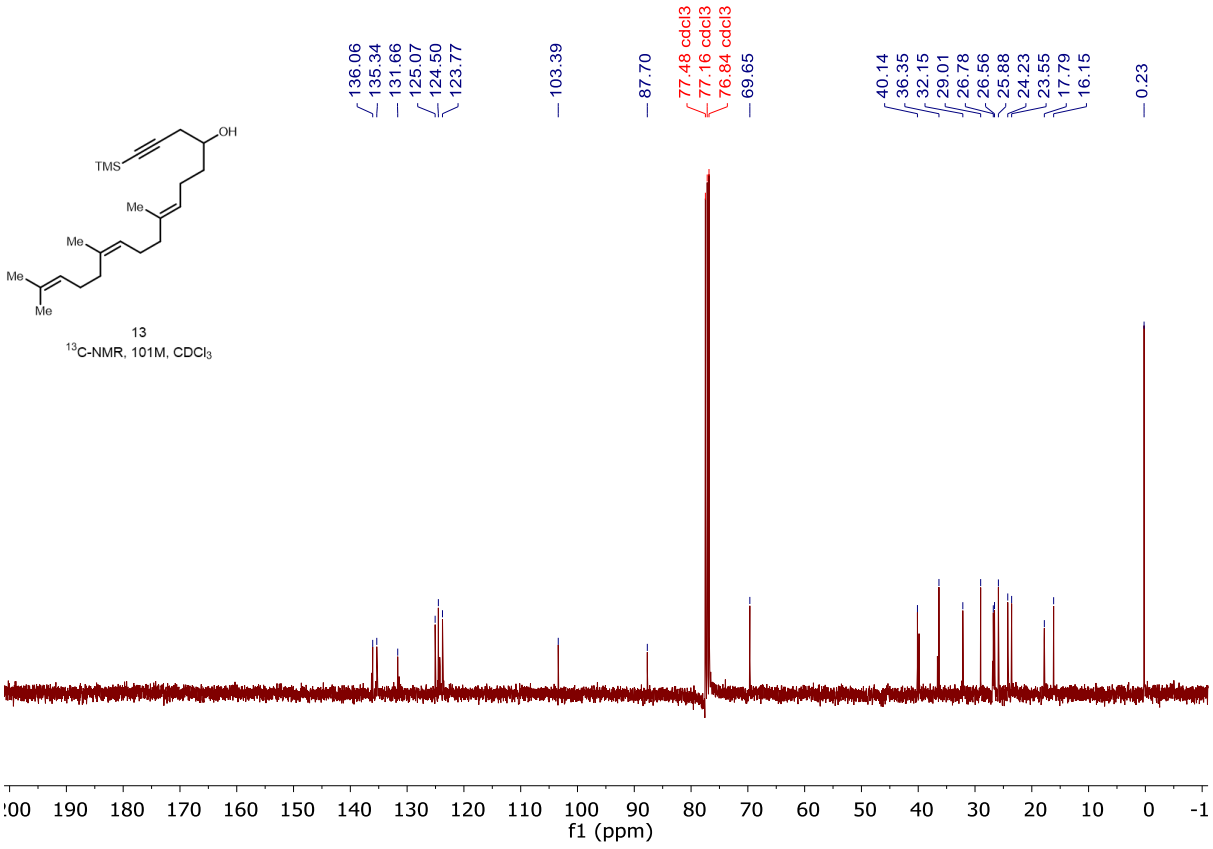
Me
Me
Me
Me
13
1H-NMR, 600M, CDCl3
f1 (ppm)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76.84 cdcl3
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TMS
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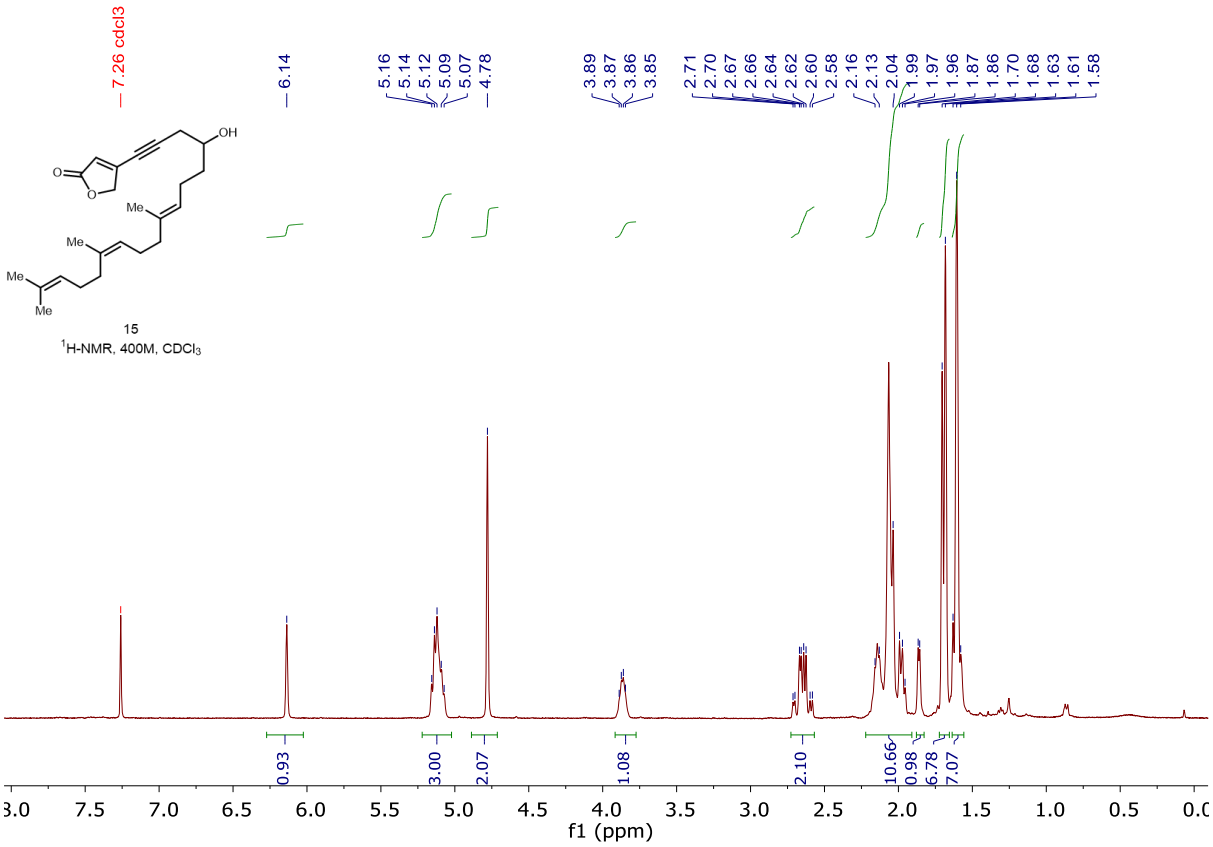
Me
Me
Me
13
13C-NMR, 101M, CDCl3
f1 (ppm)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5.16
5.14
5.12
5.09
5.07
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3.89
3.87
3.86
3.85
2.71
2.70
2.67
2.66
2.64
2.62
2.60
2.58
2.16
2.13
2.04
1.99
1.97
1.96
1.87
1.86
1.70
1.68
1.63
1.61
1.58
OH
O
O
Me
Me
Me
Me
15
1H-NMR, 400M, CDCl3
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2.10
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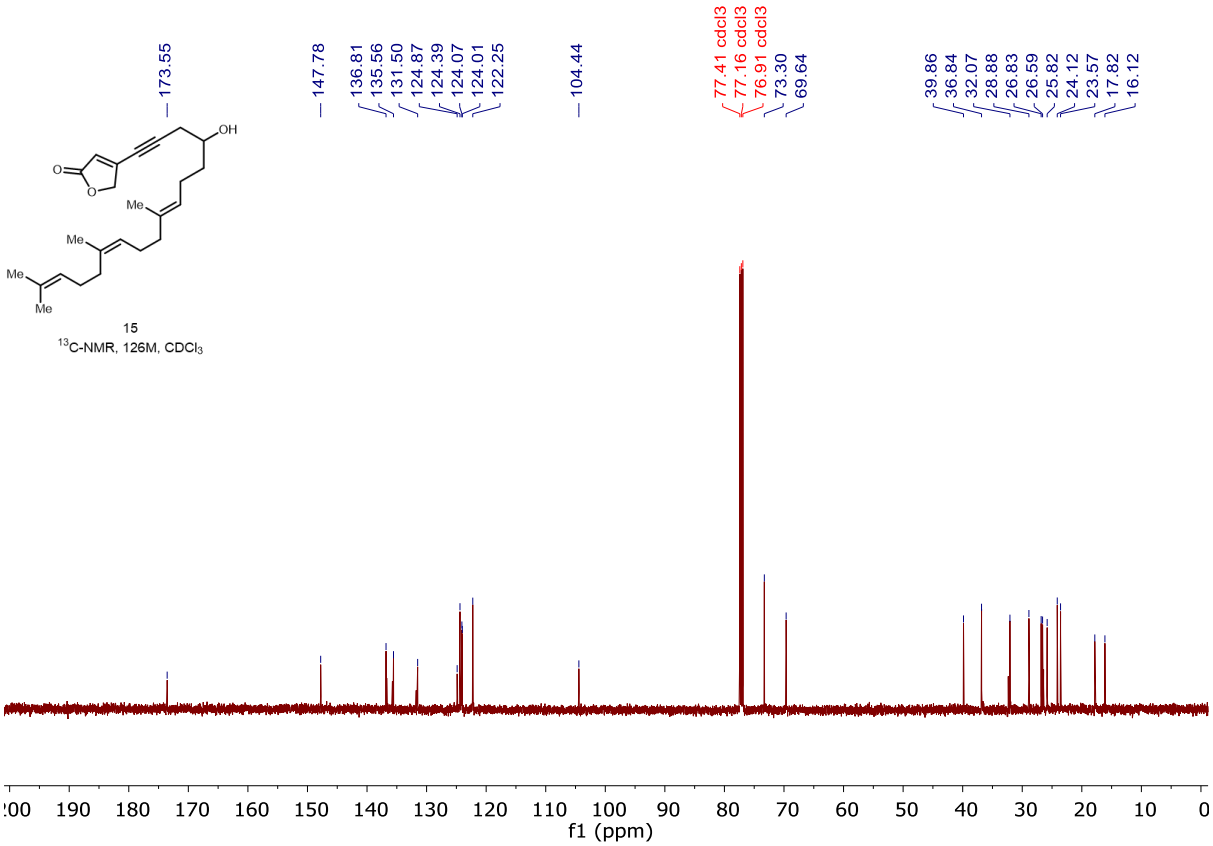
f1 (ppm)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32.07
28.88
26.83
26.59
25.82
24.12
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Me
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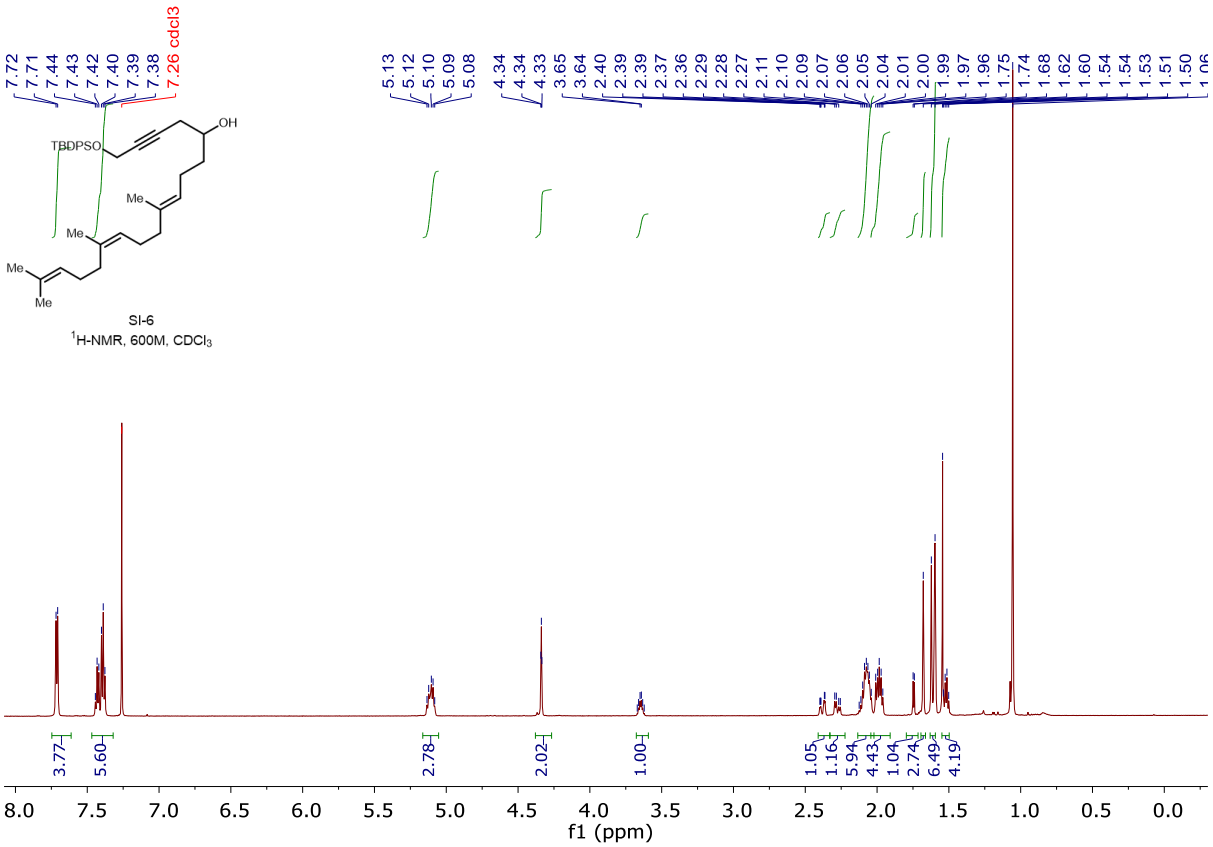
13C-NMR, 126M, CDCl3
f1 (ppm)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7.40
7.39
7.38
7.26 cdcl3
5.13
5.12
5.10
5.09
5.08
4.34
4.34
4.33
3.65
3.64
2.40
2.39
2.39
2.37
2.36
2.29
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1.75
1.74
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1.62
1.60
1.54
1.54
1.53
1.51
1.50
TBDPSO
OH
Me
Me
Me
Me
SI-6
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3.77
5.60
2.78
2.02
1.00
1.05
1.16
5.94
4.43
1.04
2.74
6.49
4.19
8.0
7.5
7.0
6.5
6.0
5.5
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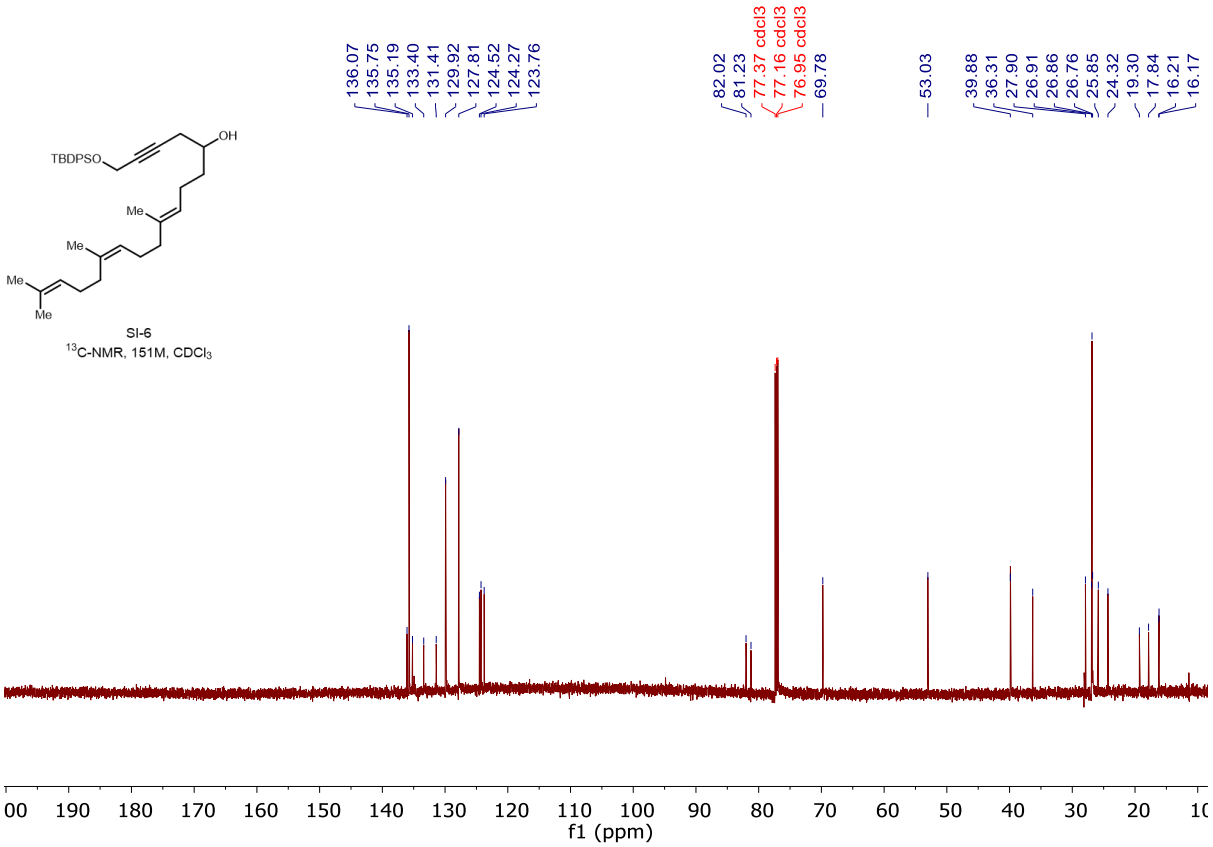
0.0
f1 (ppm)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81.23
77.37 cdcl3
77.16 cdcl3
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69.78
53.03
39.88
36.31
27.90
26.91
26.86
26.76
25.85
24.32
19.30
17.84
16.21
16.17
TBDPSO
OH
Me
Me
Me
Me
SI-6
^{13}C-NMR, 151M, CDCl$_3$
00
190
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140
130
120
110
100
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80
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60
50
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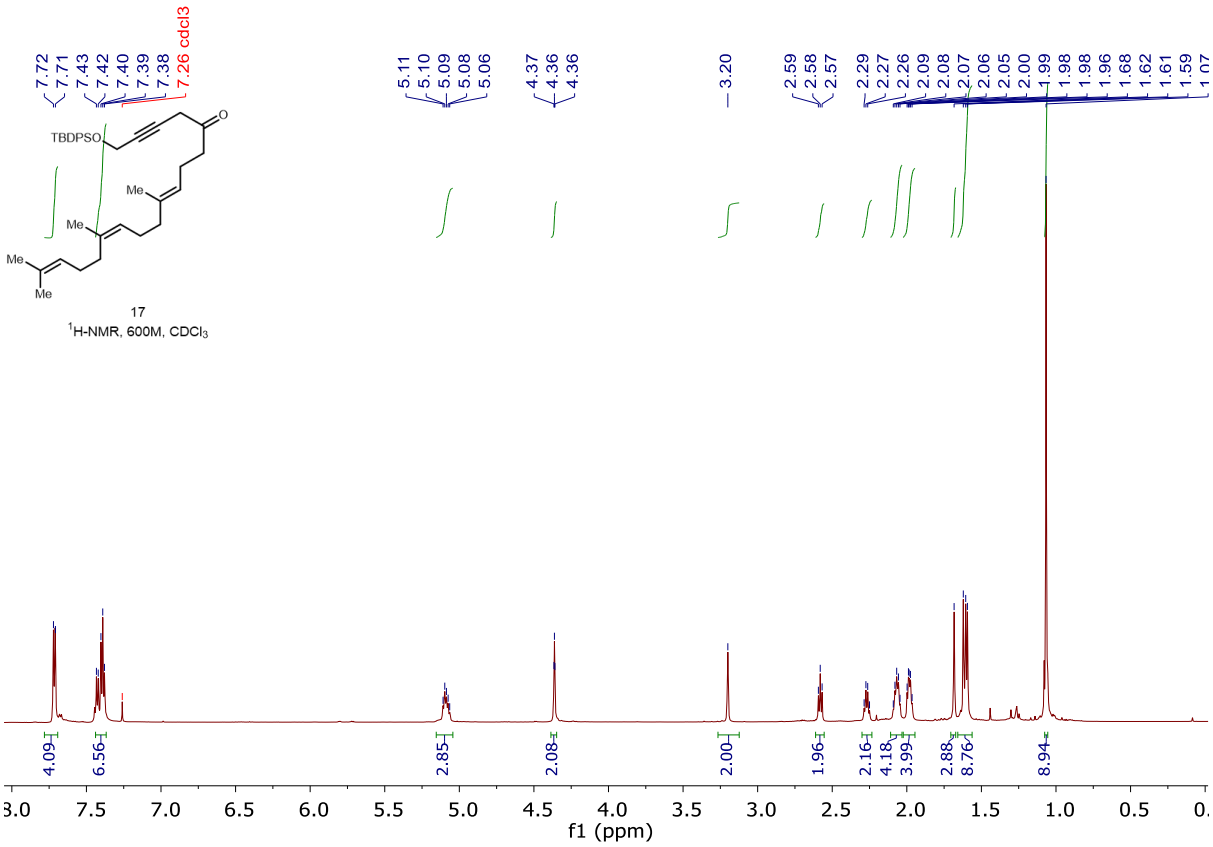
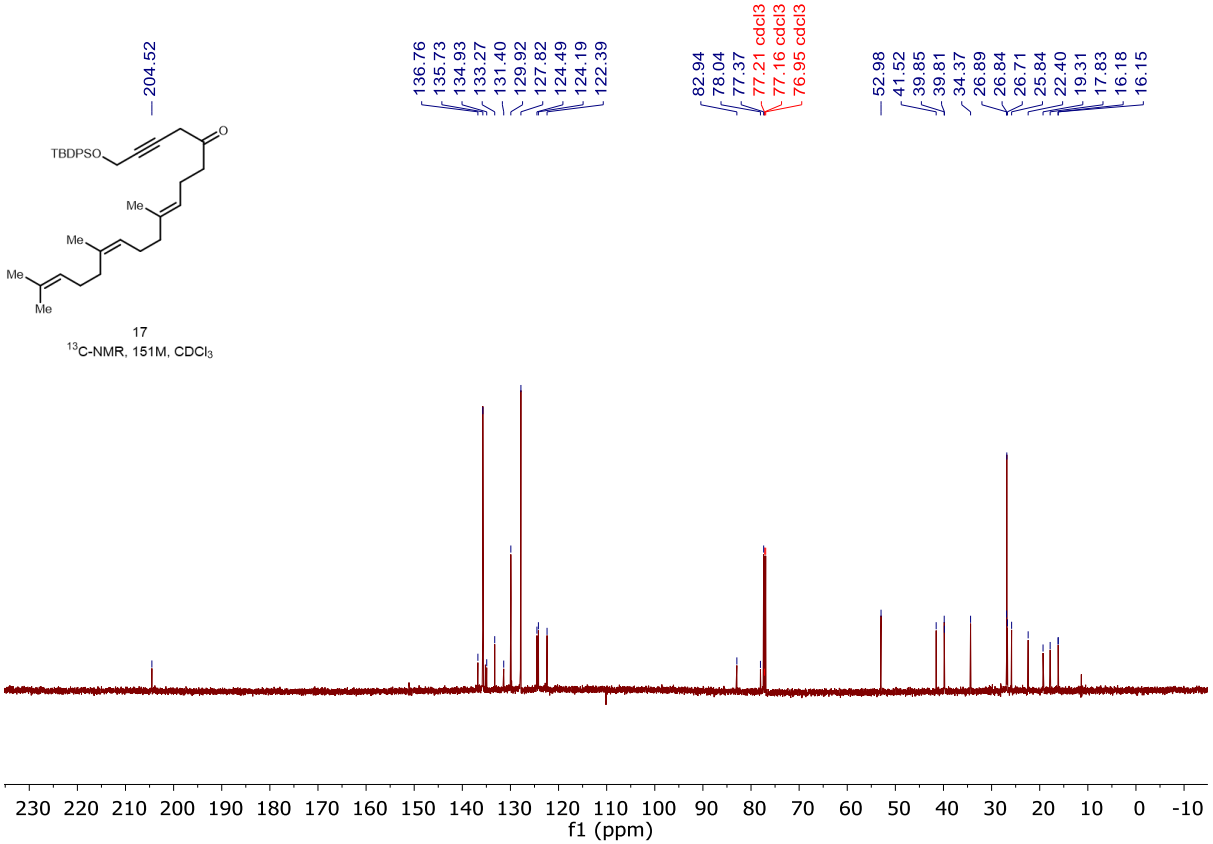
30
20
10
f1 (ppm)



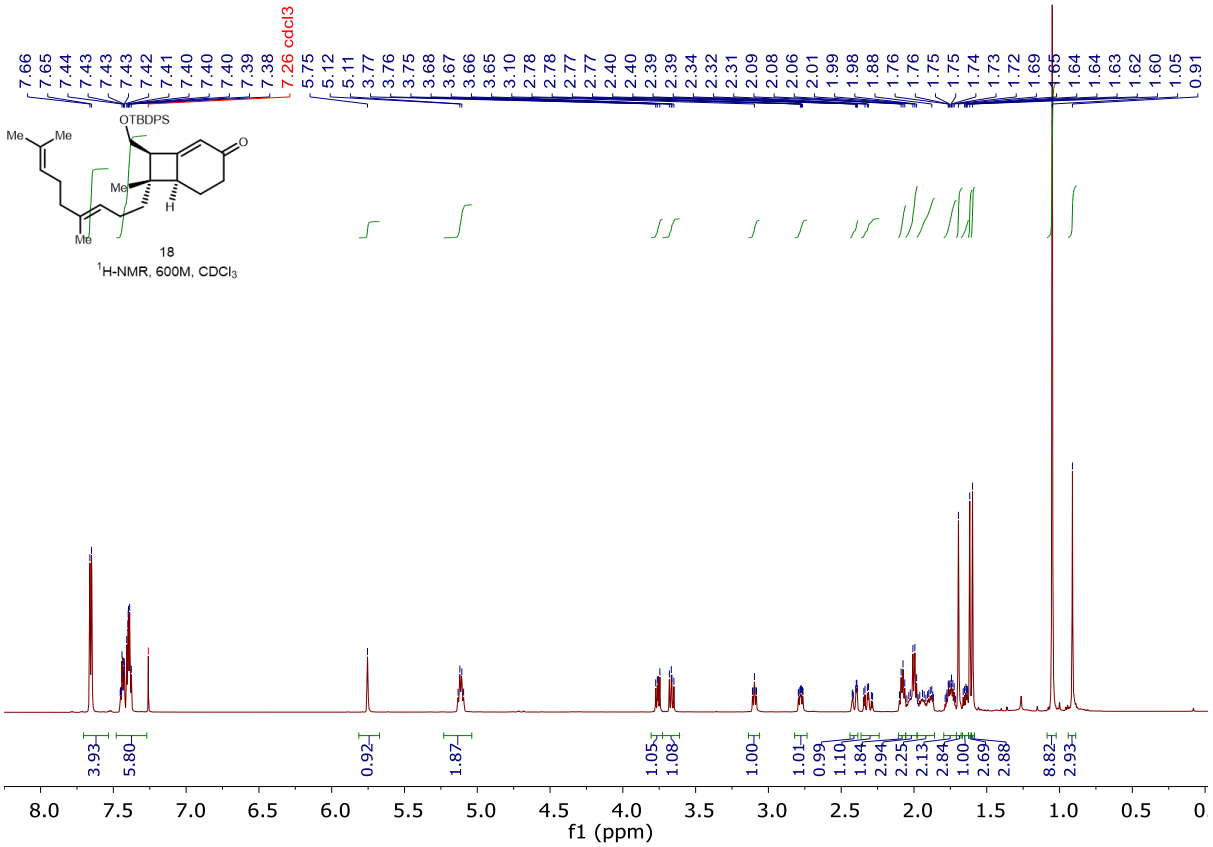
17

^{1}H-NMR, 600M, $CDCl_3$



17

^{13}C-NMR, 151M, $CDCl_3$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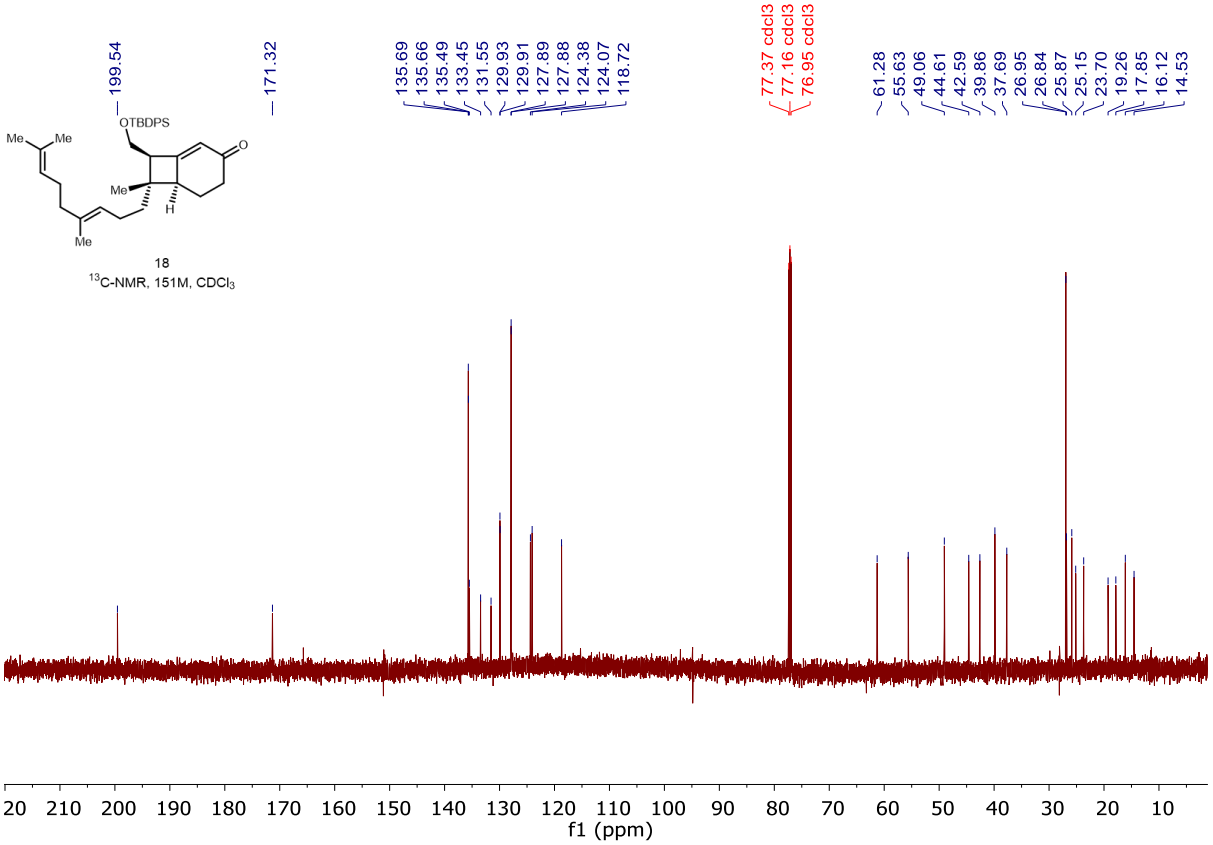
OTBDPS
Me
Me
Me
H
O
Me
18
1H-NMR, 600M, CDCl3
3.93 5.80 0.92 1.87 1.05 1.08 1.00 1.01 0.99 1.10 1.84 2.94 2.25 2.13 2.84 1.00 2.69 2.88 8.82 2.93
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)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171.32
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76.95 cdcl3
61.28 55.63 49.06 44.61 42.59 39.86 37.69 26.95 26.84 25.87 25.15 23.70 19.26 17.85 16.12 14.53
OTBDPS
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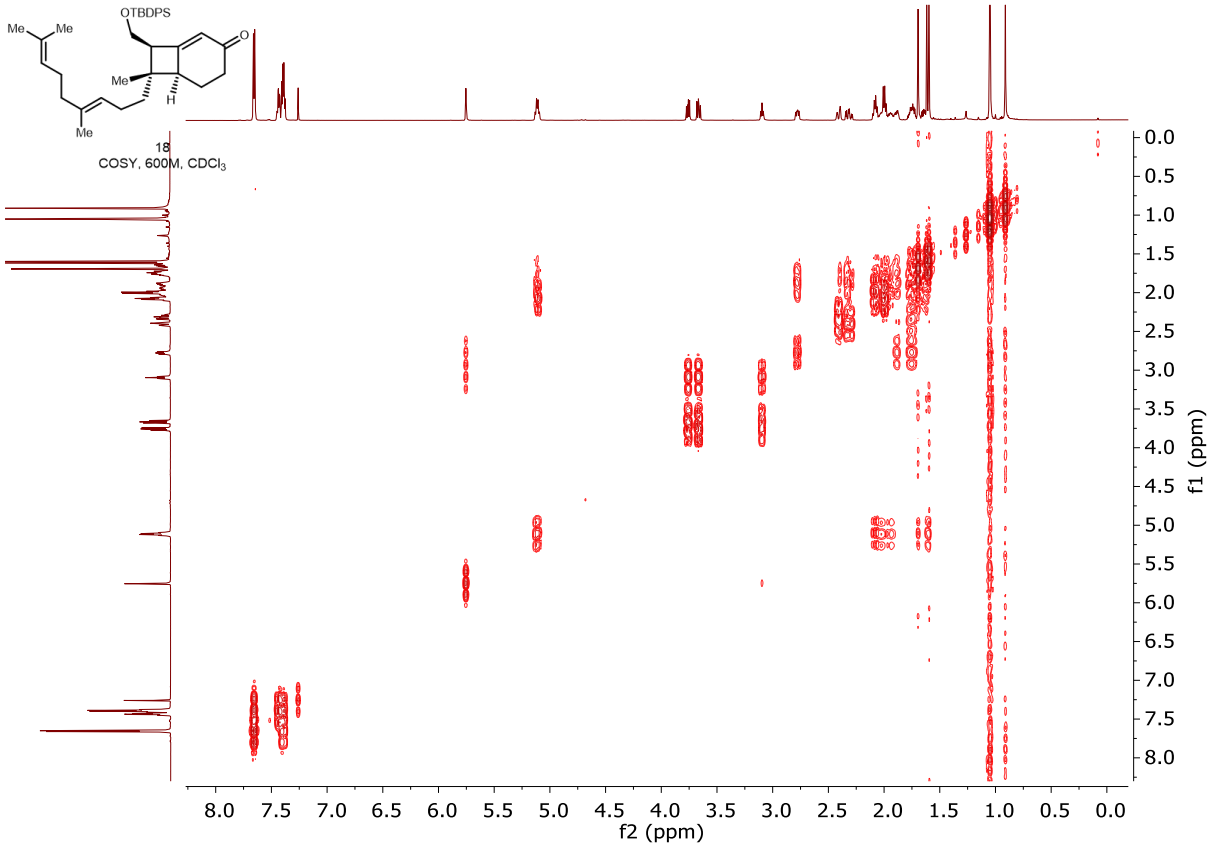
f1 (ppm)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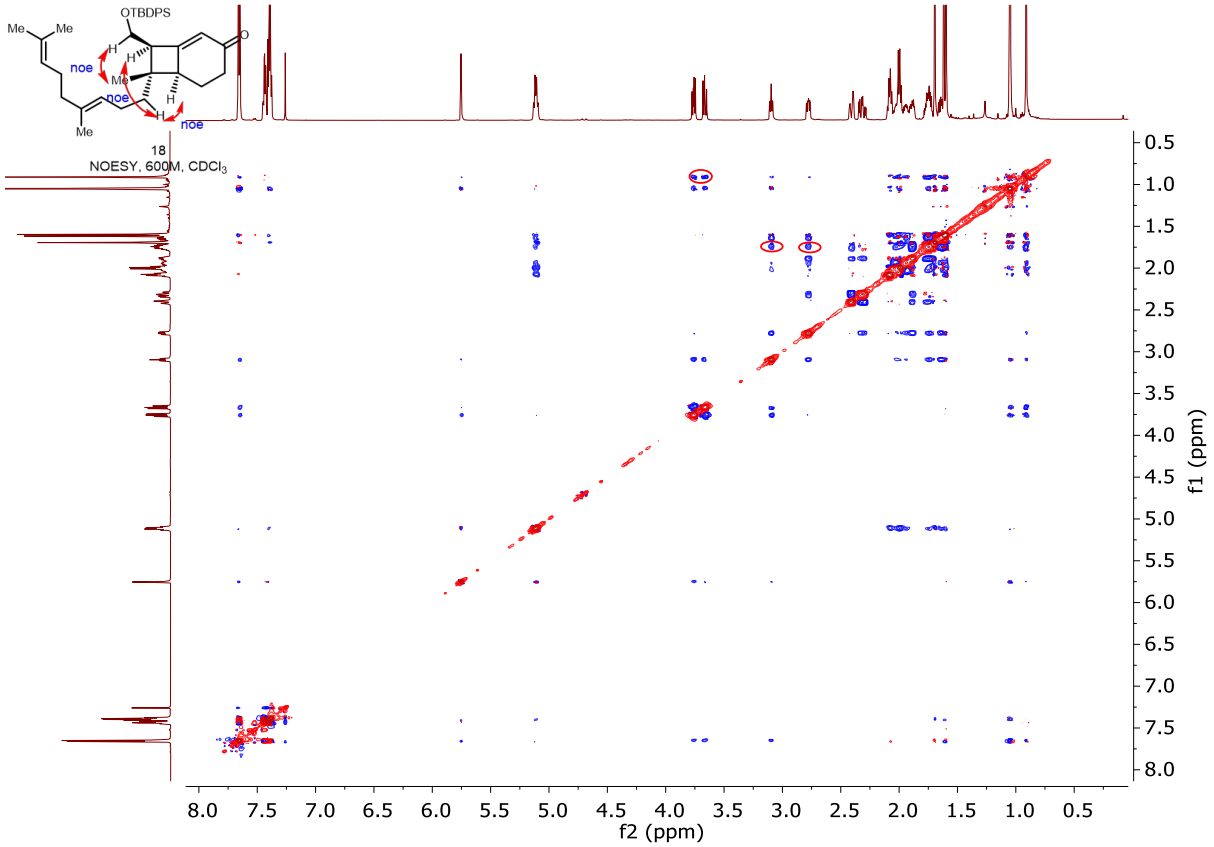
COSY, 600M, CDCl3
f2 (ppm)
f1 (ppm)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Me
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noe
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H
H
Me
Me
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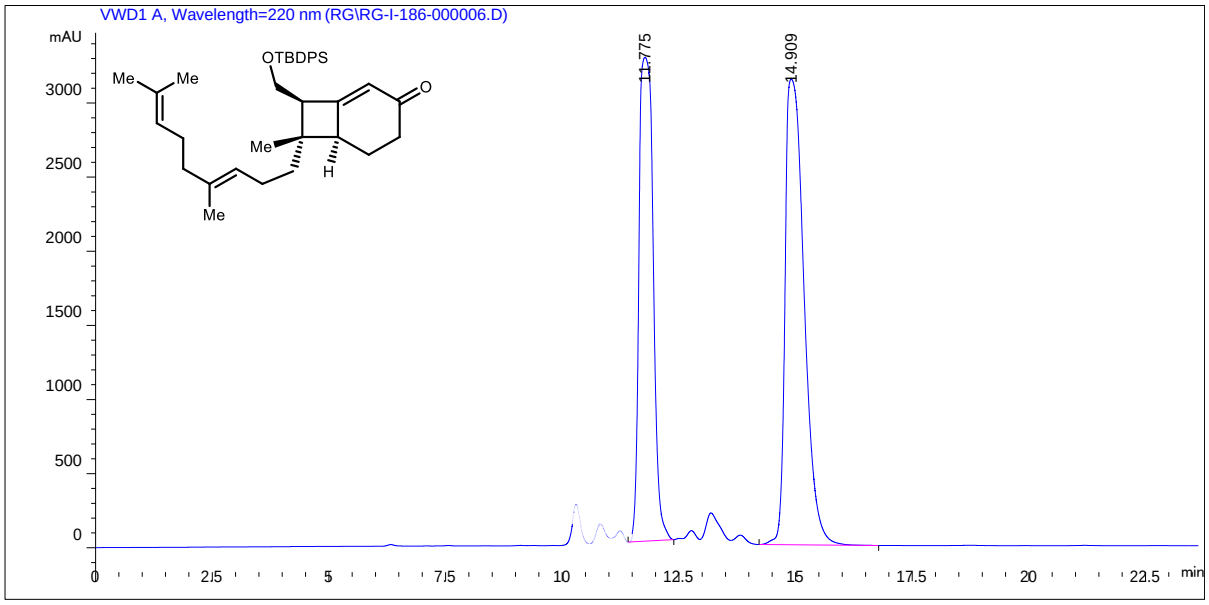
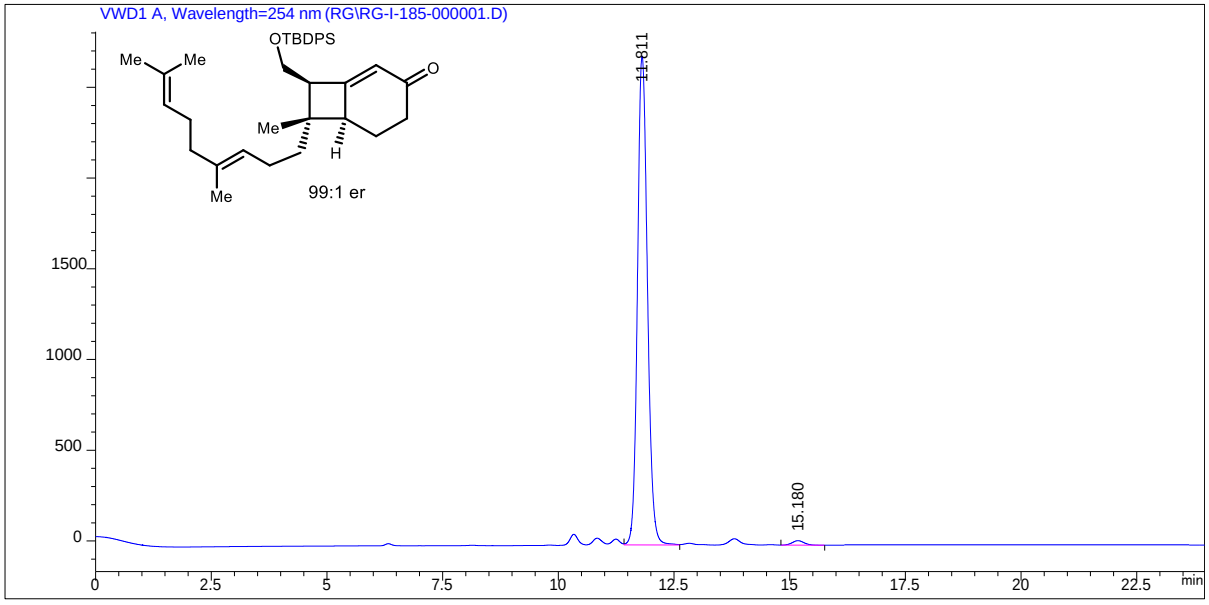
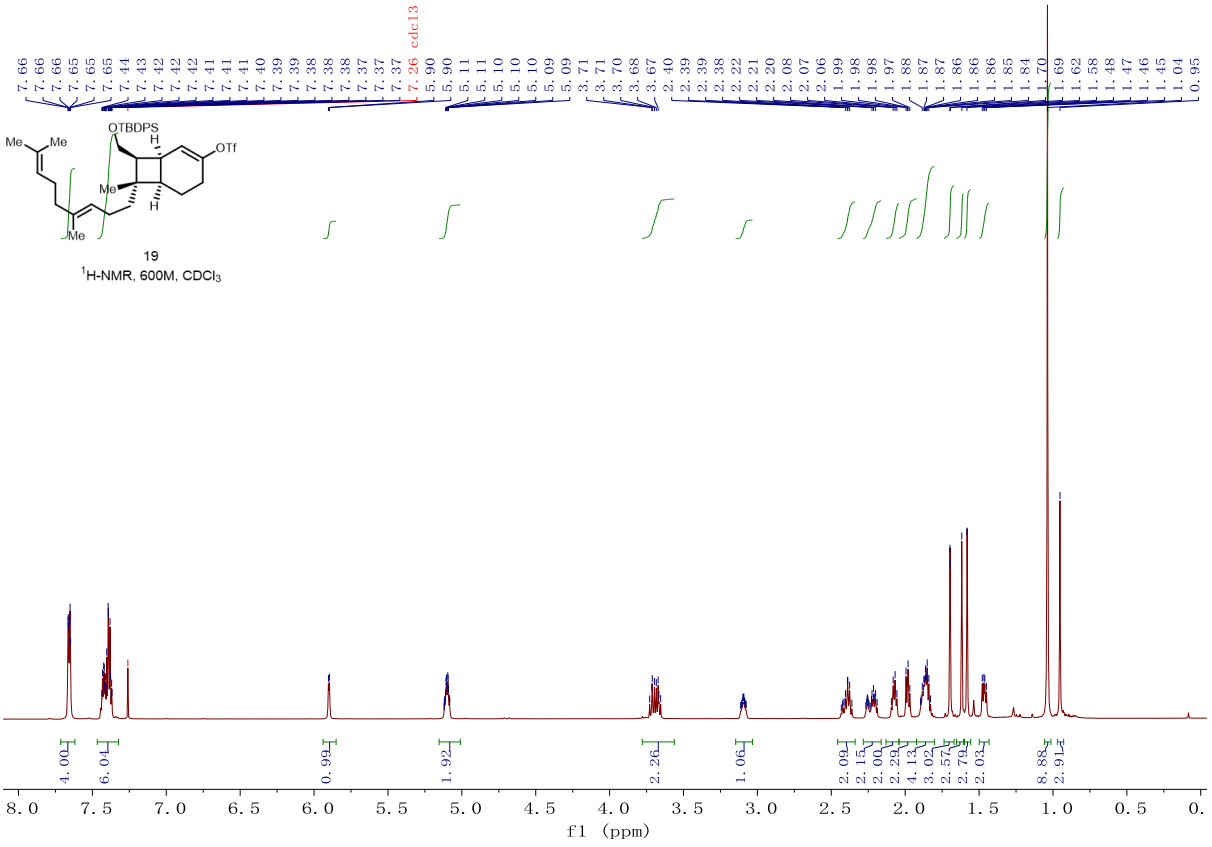
18
NOESY, 600M, CDCl3
f2 (ppm)
f1 (ppm)

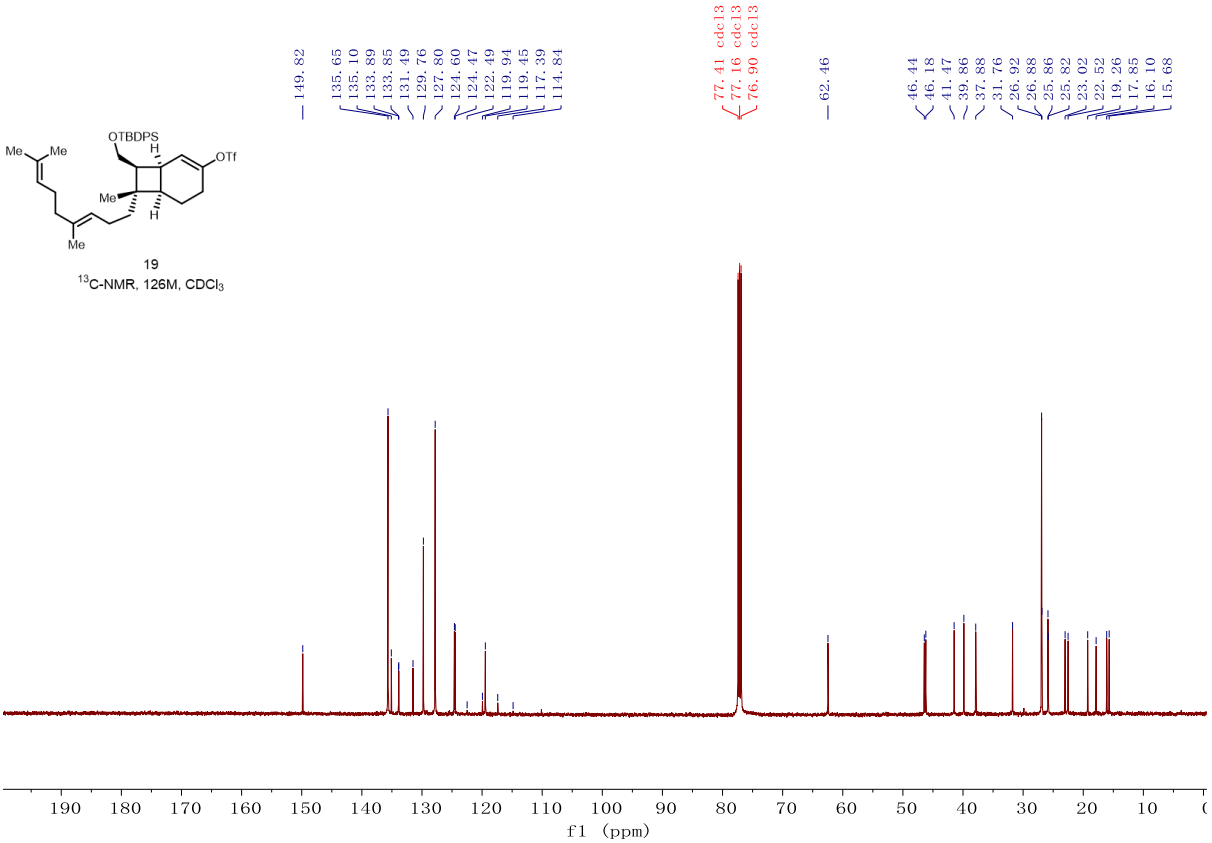


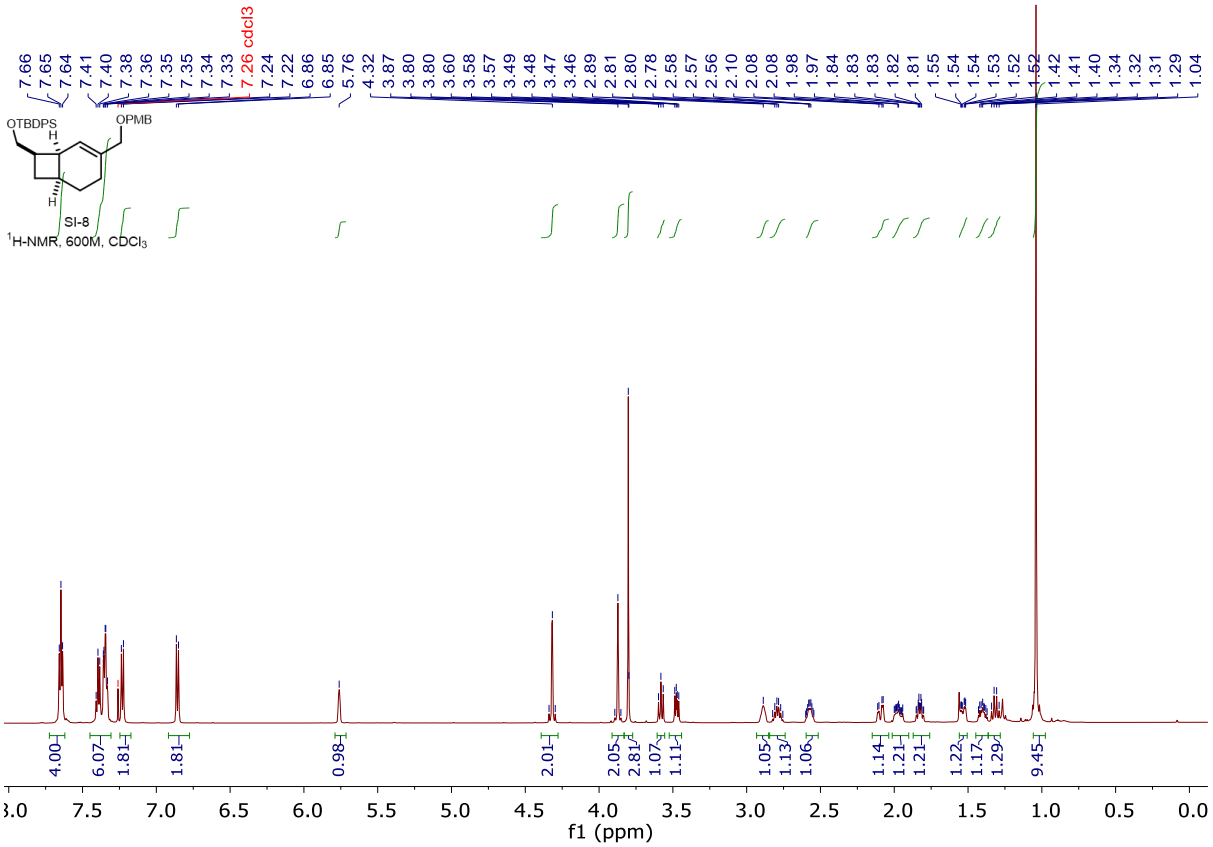
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.775	BB	0.3339	6.87981e4	3263.72900	43.6924
2	14.909	BB	0.4372	8.86620e4	3142.24463	56.3076

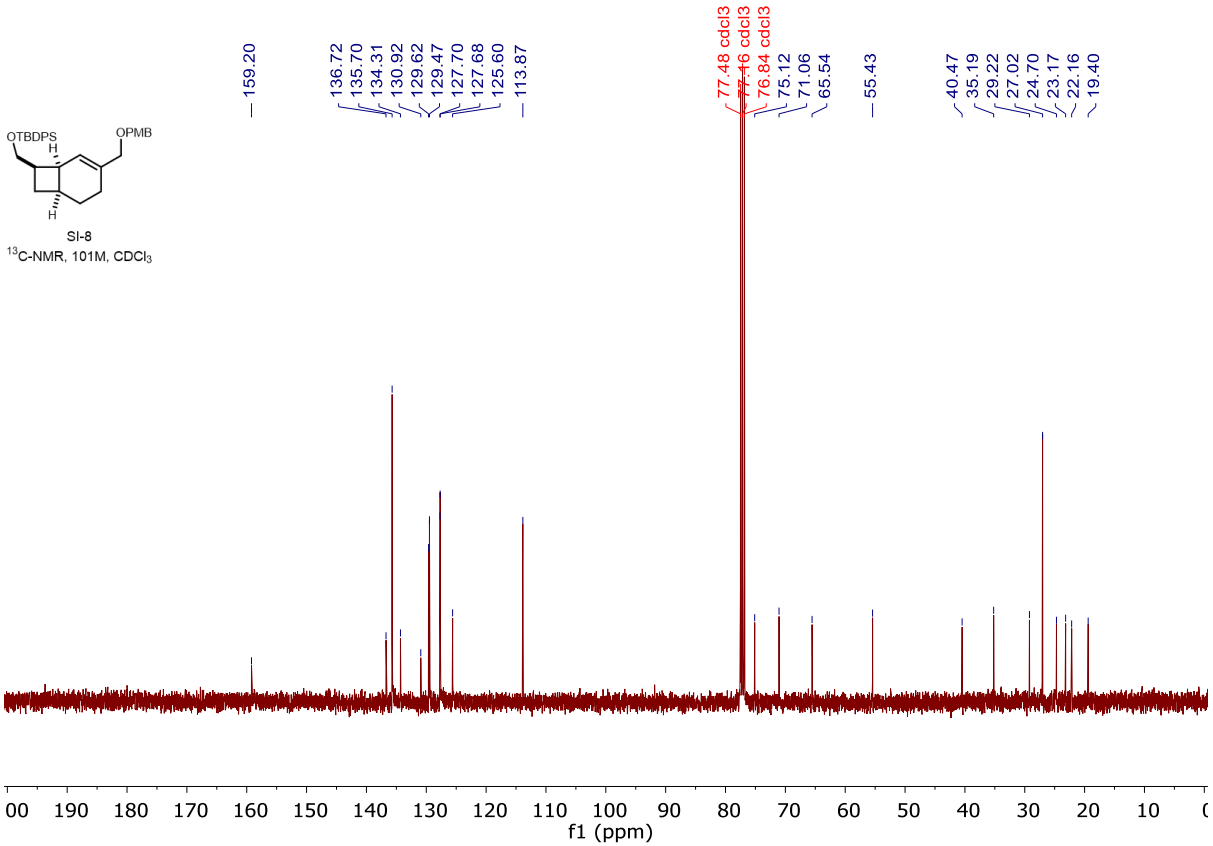


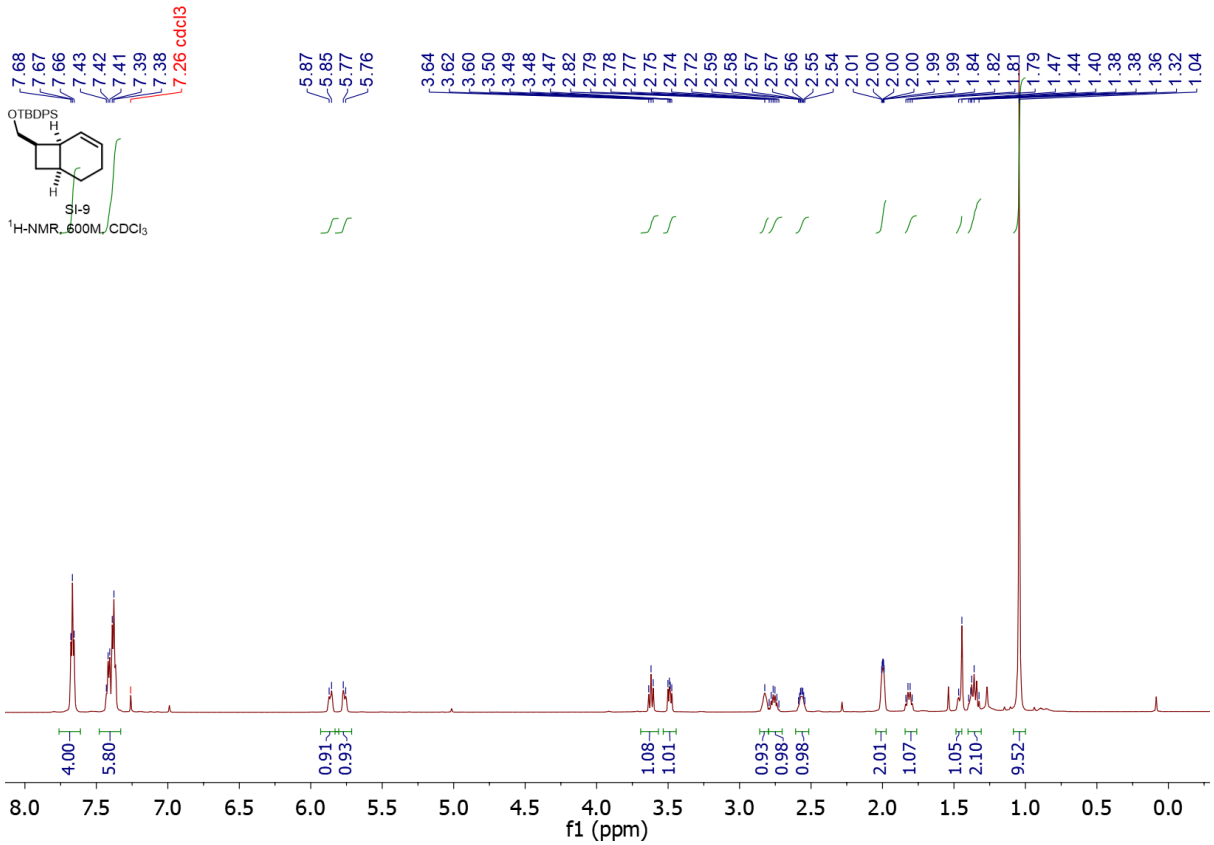
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.811	VV	0.2304	4.02702e4	2693.27271	98.9124
2	15.180	BB	0.2776	442.77759	24.64094	1.0876

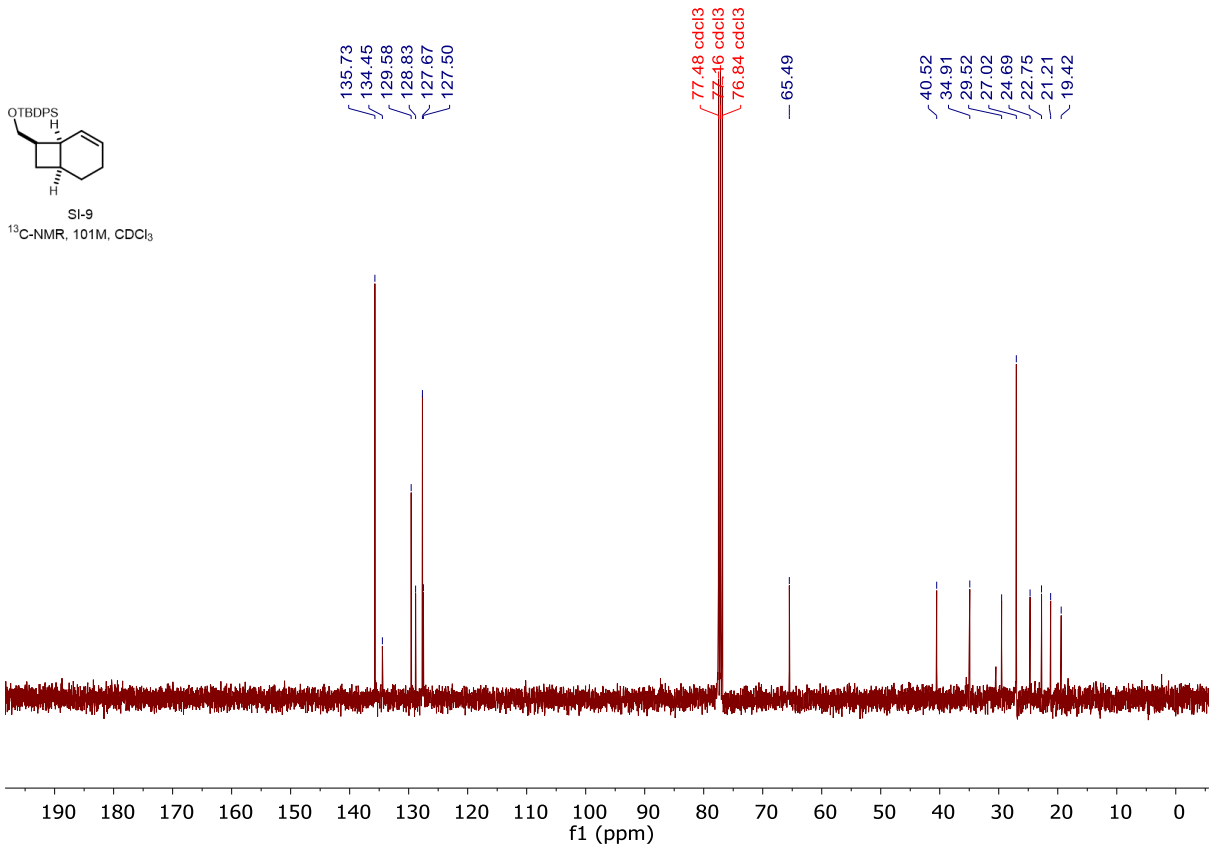

OTBDPS
OTf
Me
H
19
1H-NMR, 600M, CDCl3
f1 (ppm)

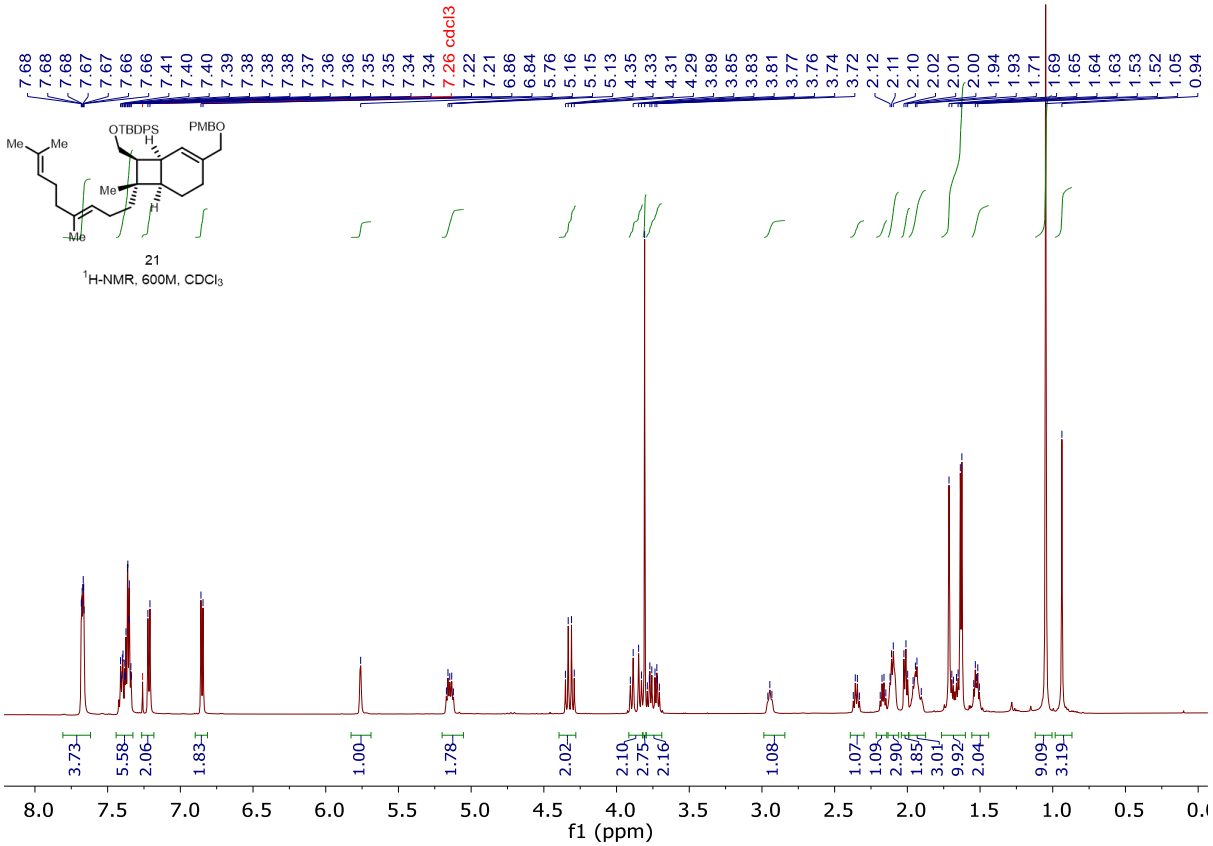

OTBDPS
OTf
Me
H
19
13C-NMR, 126M, CDCl3
f1 (ppm)

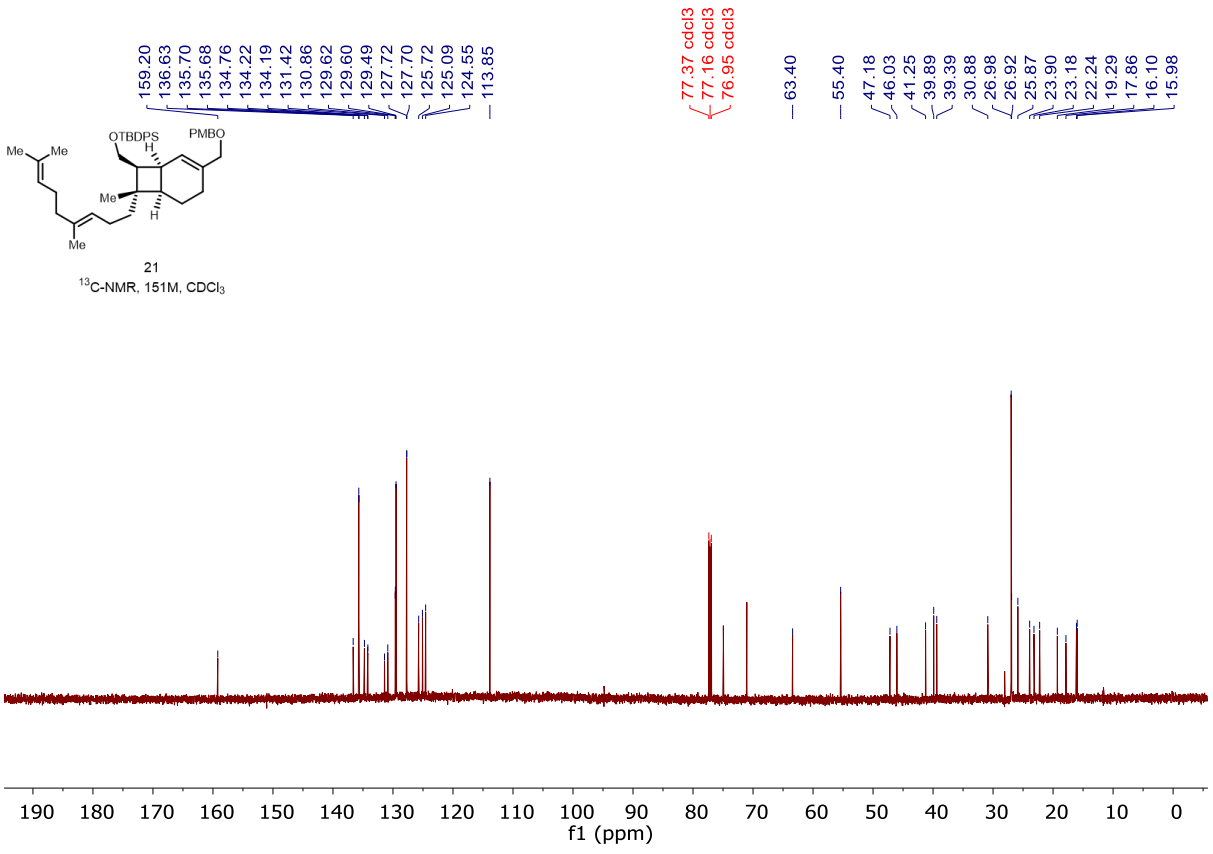

OTBDPS
OPMB
H
H
SI-8
^{1}H-NMR, 600M, CDCl$_3$
f1 (ppm)

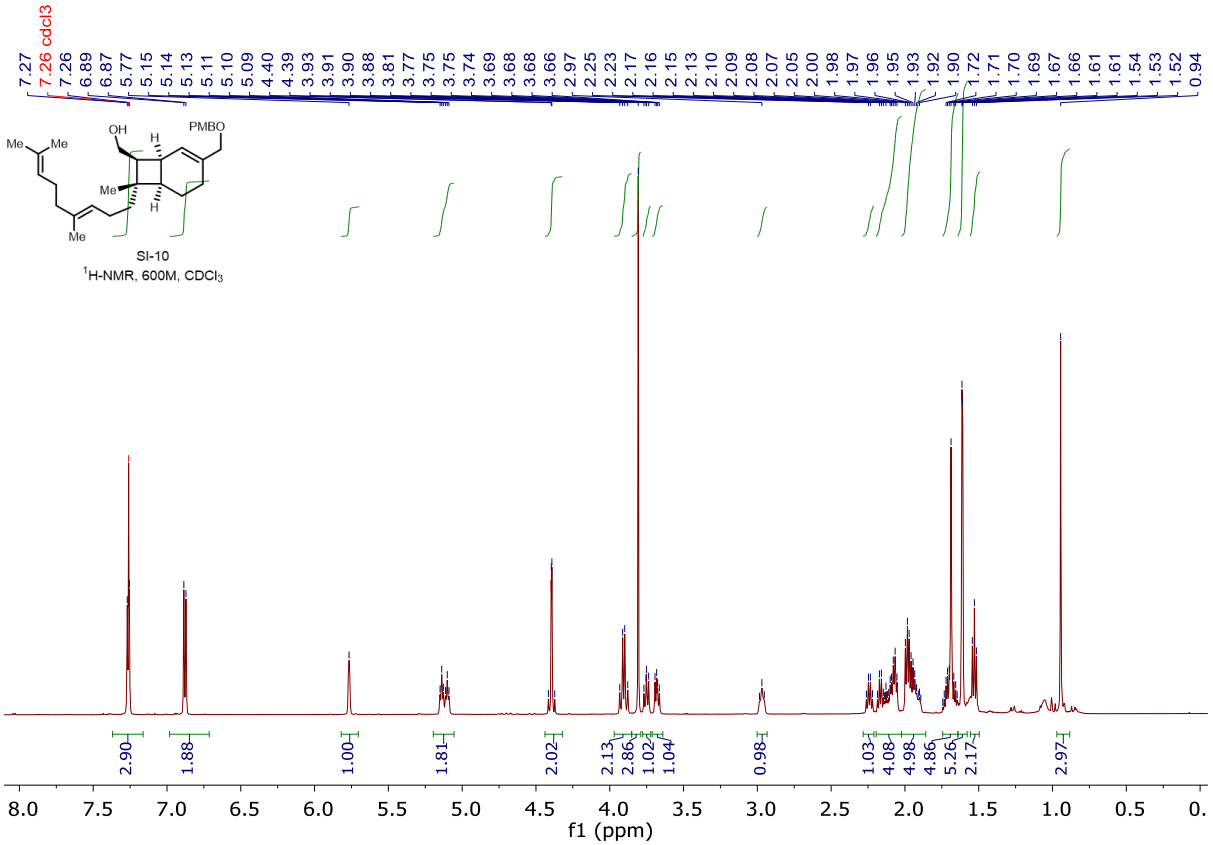

OTBDPS
OPMB
H
H
SI-8
^{13}C-NMR, 101M, CDCl$_3$
f1 (ppm)

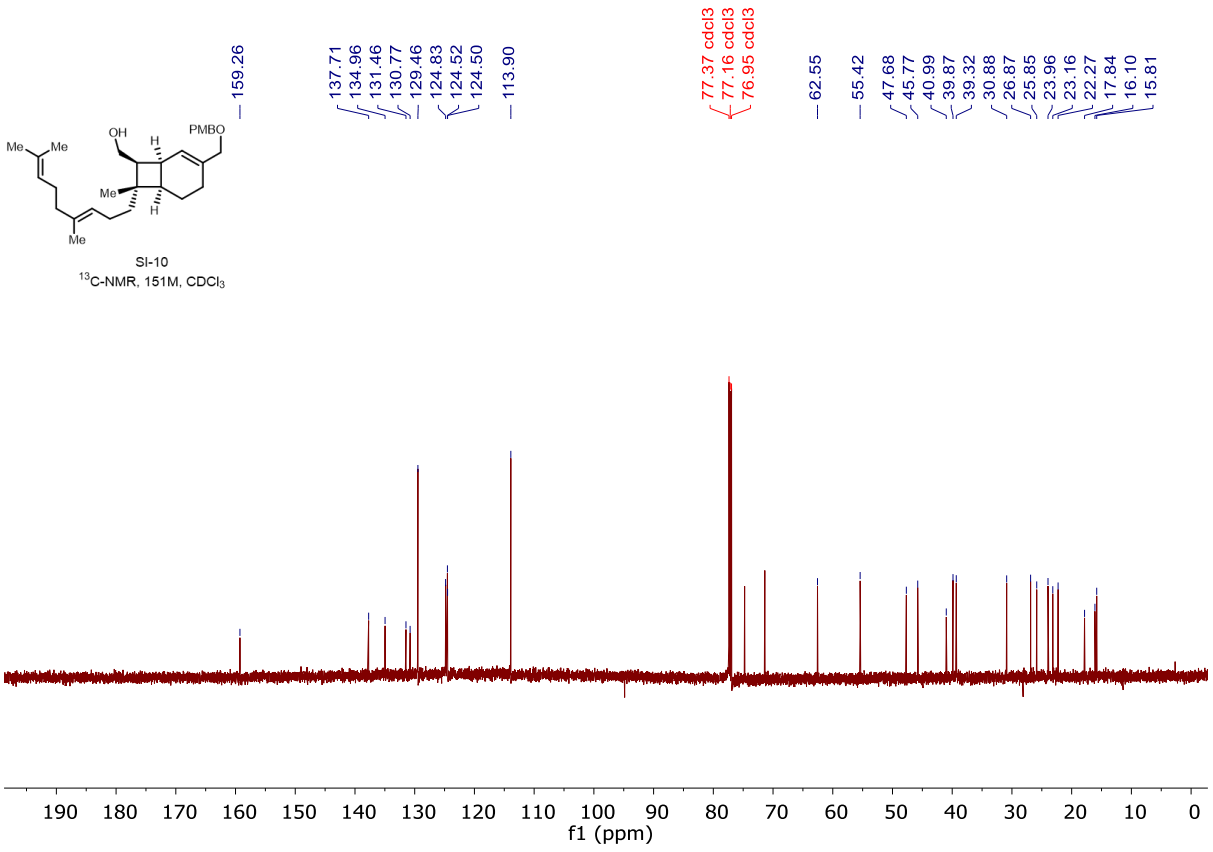

7.68
7.67
7.66
7.43
7.42
7.41
7.39
7.38
7.26 cdcl3
5.87
5.85
5.77
5.76
3.64
3.62
3.60
3.50
3.49
3.48
3.47
2.82
2.79
2.78
2.77
2.75
2.74
2.72
2.59
2.58
2.57
2.57
2.56
2.55
2.54
2.01
2.00
2.00
2.00
1.99
1.99
1.84
1.82
1.81
1.79
1.47
1.44
1.40
1.38
1.38
1.36
1.32
1.04
OTBDPS
SI-9
1H-NMR, 600M, CDCl3
4.00
5.80
0.91
0.93
1.08
1.01
0.93
0.98
0.98
2.01
1.07
1.05
2.10
9.52
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

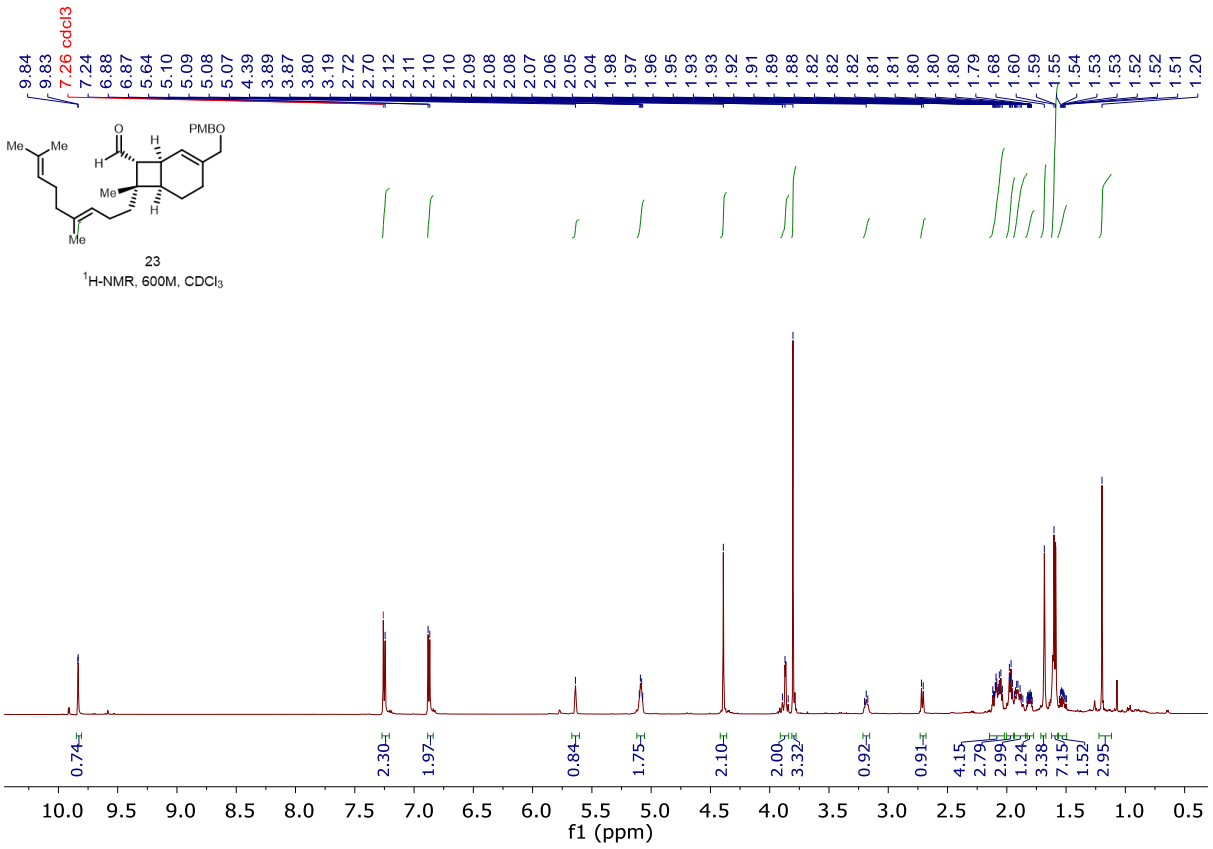

135.73
134.45
129.58
128.83
127.67
127.50
77.48 cdcl3
77.16 cdcl3
76.84 cdcl3
65.49
40.52
34.91
29.52
27.02
24.69
22.75
21.21
19.42
OTBDPS
SI-9
13C-NMR, 101M, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

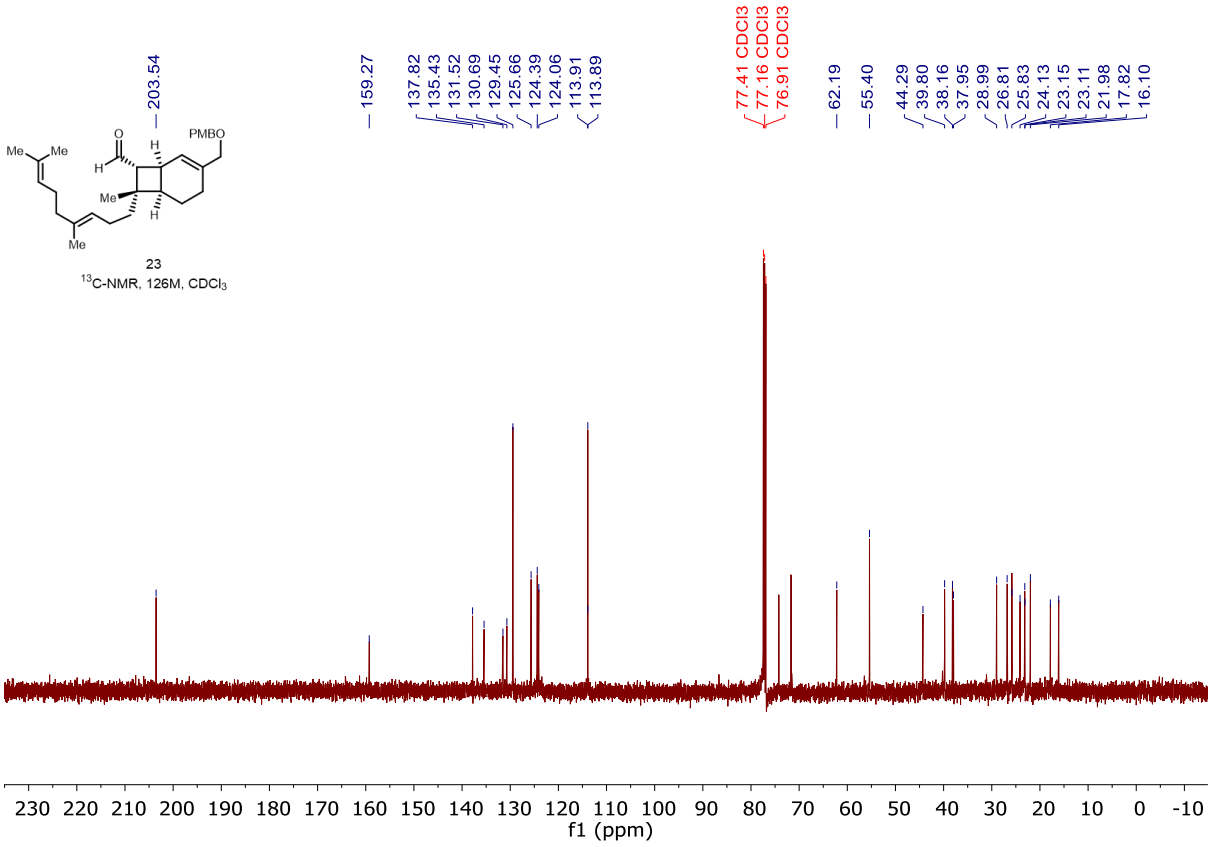

7.68 7.68 7.68 7.67 7.67 7.66 7.66 7.41 7.40 7.40 7.39 7.38 7.38 7.38 7.37 7.36 7.36 7.35 7.35 7.34 7.34 7.26 cdcl3 7.22 7.21 6.86 6.84 5.76 5.16 5.15 5.13 4.35 4.33 4.31 4.29 3.89 3.85 3.83 3.81 3.77 3.76 3.74 3.72 2.12 2.11 2.10 2.02 2.01 2.00 1.94 1.93 1.71 1.69 1.65 1.64 1.63 1.53 1.52 1.05 0.94
OTBDPS
PMBO
Me
Me
Me
H
H
Me
21
1H-NMR, 600M, CDCl3
3.73 5.58 2.06 1.83 1.00 1.78 2.02 2.10 2.75 2.16 1.08 1.07 1.09 2.90 1.85 3.01 9.92 2.04 9.09 3.19
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

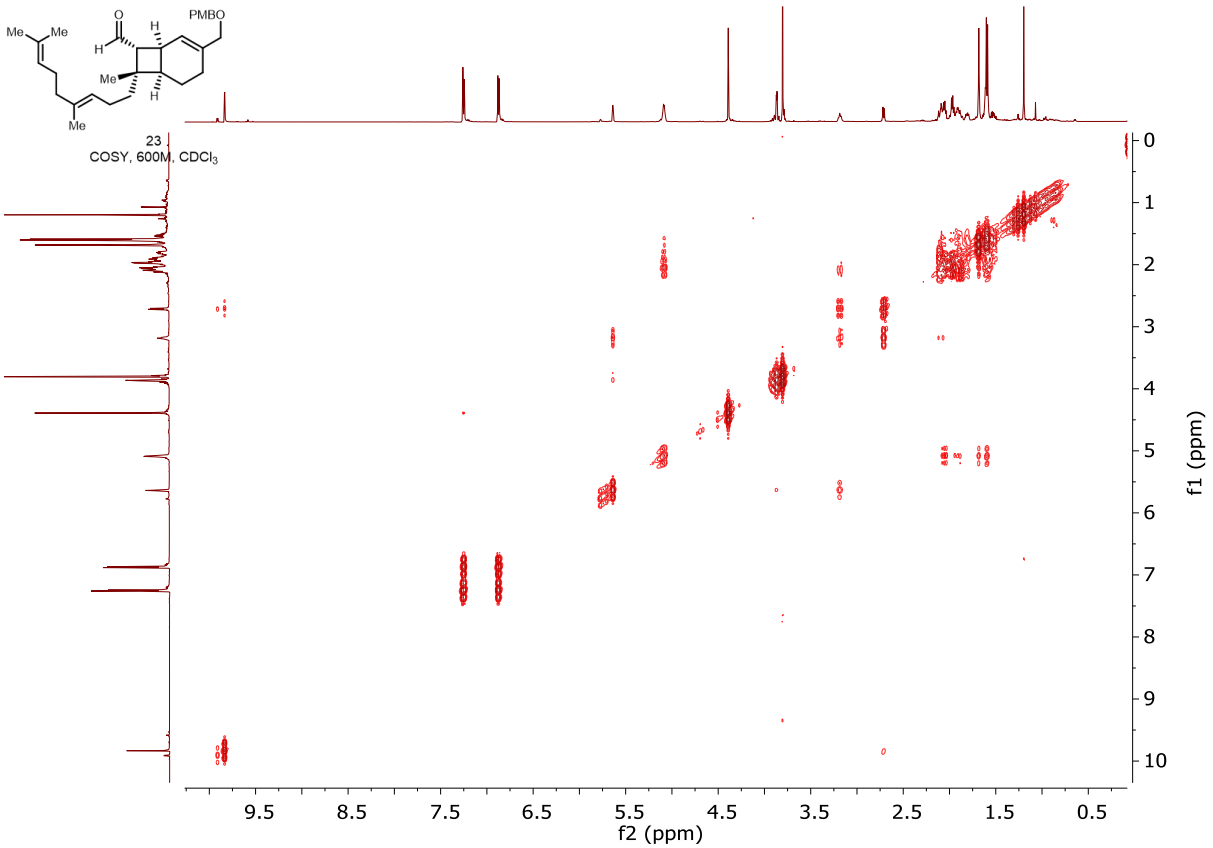

159.20 136.63 135.70 135.68 134.76 134.22 134.19 131.42 130.86 129.62 129.60 129.49 127.72 127.70 125.72 125.09 124.55 113.85
77.37 cdcl3 77.16 cdcl3 76.95 cdcl3
63.40
55.40
47.18 46.03 41.25 39.89 39.39 30.88 26.98 26.92 25.87 23.90 23.18 22.24 19.29 17.86 16.10 15.98
OTBDPS
PMBO
Me
Me
Me
H
H
Me
21
13C-NMR, 151M, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

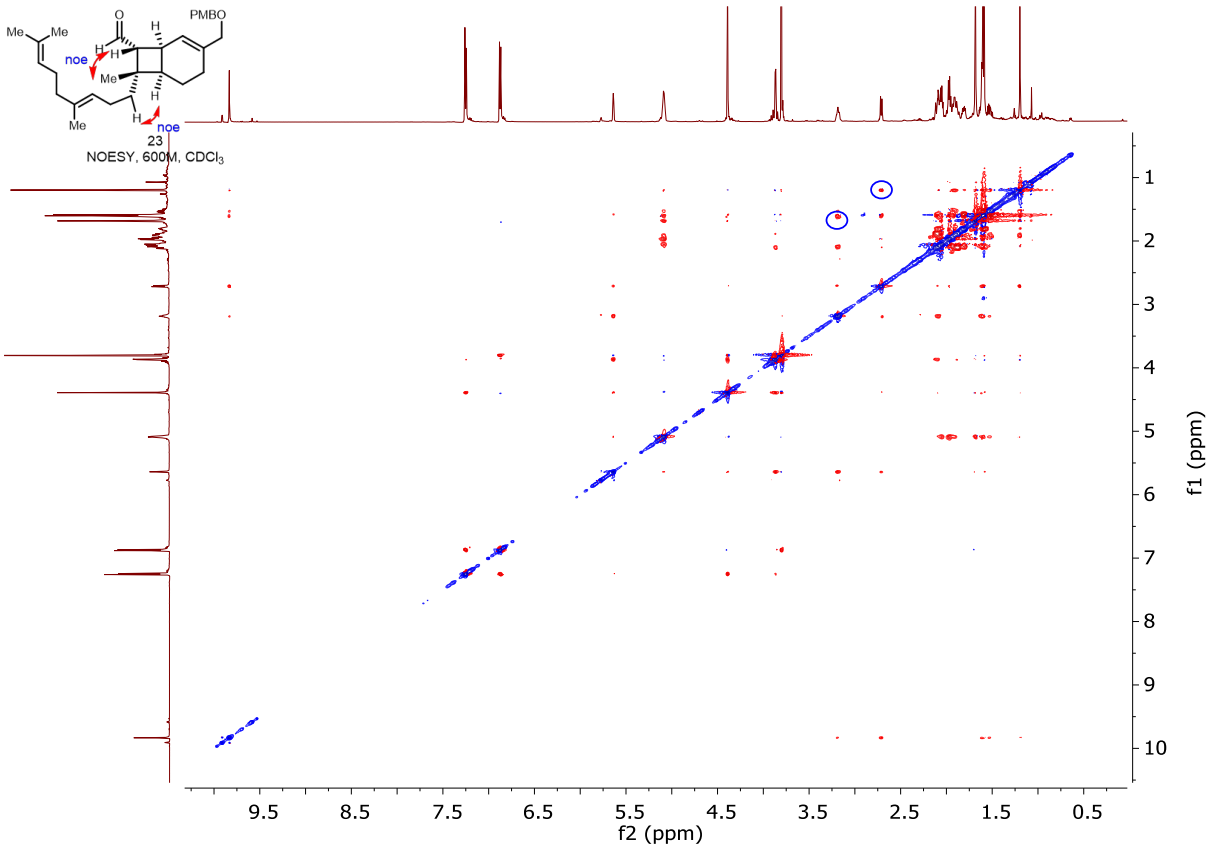

7.27
7.26 cdcl3
7.26
6.89
6.87
5.77
5.15
5.14
5.13
5.11
5.10
5.09
4.40
4.39
3.93
3.91
3.90
3.88
3.81
3.77
3.75
3.75
3.74
3.69
3.68
3.68
3.66
2.97
2.25
2.23
2.17
2.16
2.15
2.13
2.10
2.09
2.08
2.07
2.05
2.00
1.98
1.97
1.96
1.95
1.93
1.92
1.90
1.72
1.71
1.70
1.69
1.67
1.66
1.61
1.61
1.54
1.53
1.52
0.94
Me
Me
OH
H
PMBO
Me
H
Me
SI-10
1H-NMR, 600M, CDCl3
2.90
1.88
1.00
1.81
2.02
2.13
2.86
1.02
1.04
0.98
1.03
4.08
4.98
4.86
5.26
2.17
2.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

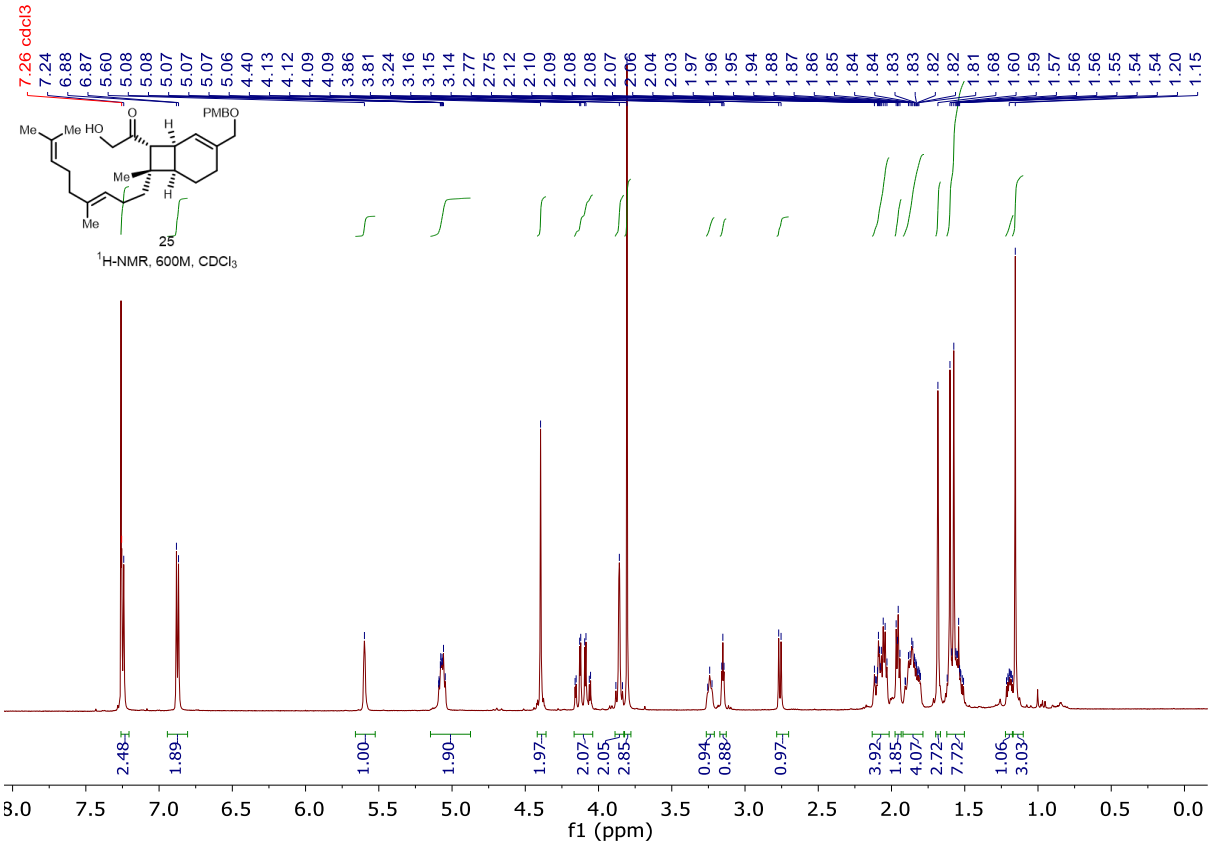

159.26
137.71
134.96
131.46
130.77
129.46
124.83
124.52
124.50
113.90
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
62.55
55.42
47.68
45.77
40.99
39.87
39.32
30.88
26.87
25.85
23.96
23.16
22.27
17.84
16.10
15.81
Me
Me
OH
H
PMBO
Me
H
Me
SI-10
13C-NMR, 151M, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

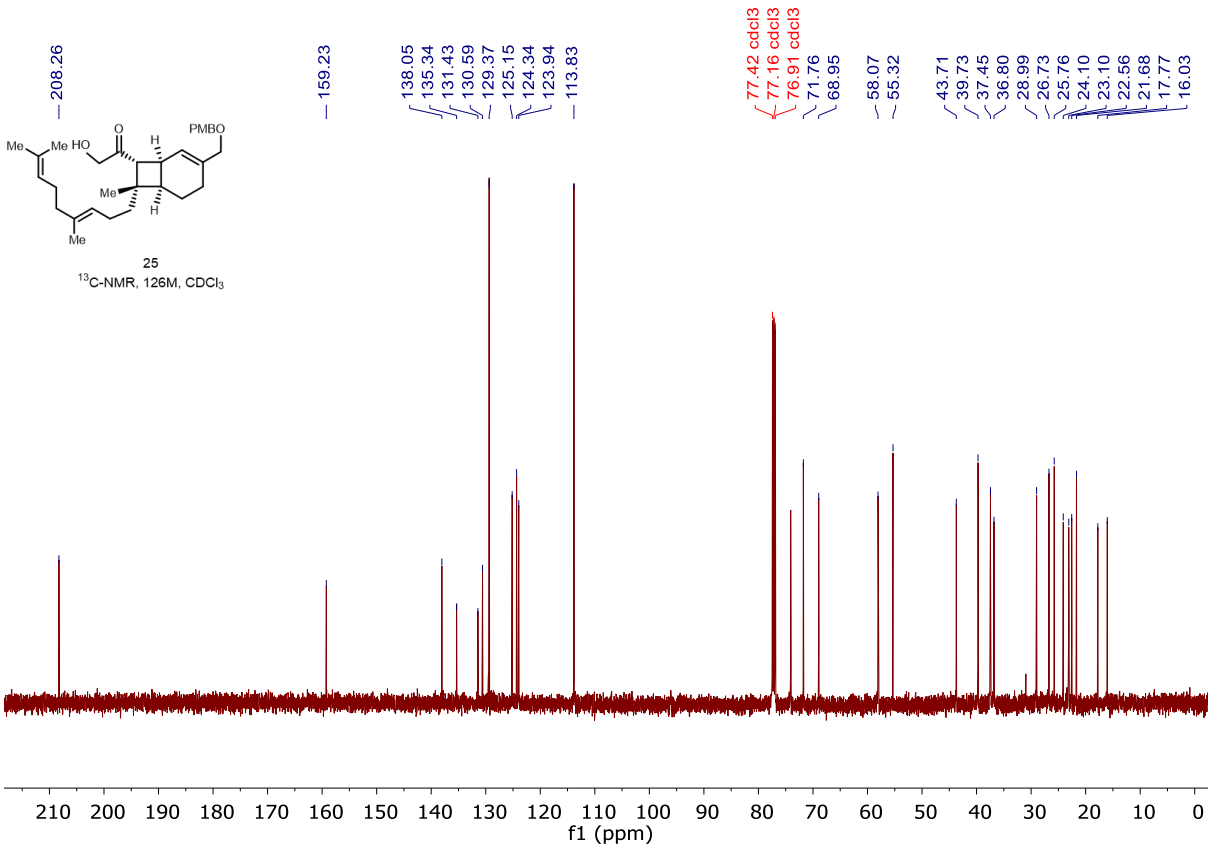

9.84 9.83 7.26 cdcl3 7.24 6.88 6.87 5.64 5.10 5.09 5.08 5.07 4.39 3.89 3.87 3.80 3.19 2.72 2.70 2.12 2.11 2.10 2.10 2.09 2.08 2.08 2.07 2.06 2.05 2.04 1.98 1.97 1.96 1.95 1.93 1.93 1.92 1.91 1.89 1.88 1.82 1.82 1.82 1.81 1.81 1.80 1.80 1.80 1.79 1.68 1.60 1.59 1.55 1.54 1.53 1.53 1.52 1.52 1.51 1.20
PMBO
Me
Me
Me
Me
H
H
H
O
23
^{1}H-NMR, 600M, CDCl$_3$
0.74 2.30 1.97 0.84 1.75 2.10 2.00 3.32 0.92 0.91 4.15 2.79 2.99 1.24 3.38 7.15 1.52 2.95
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

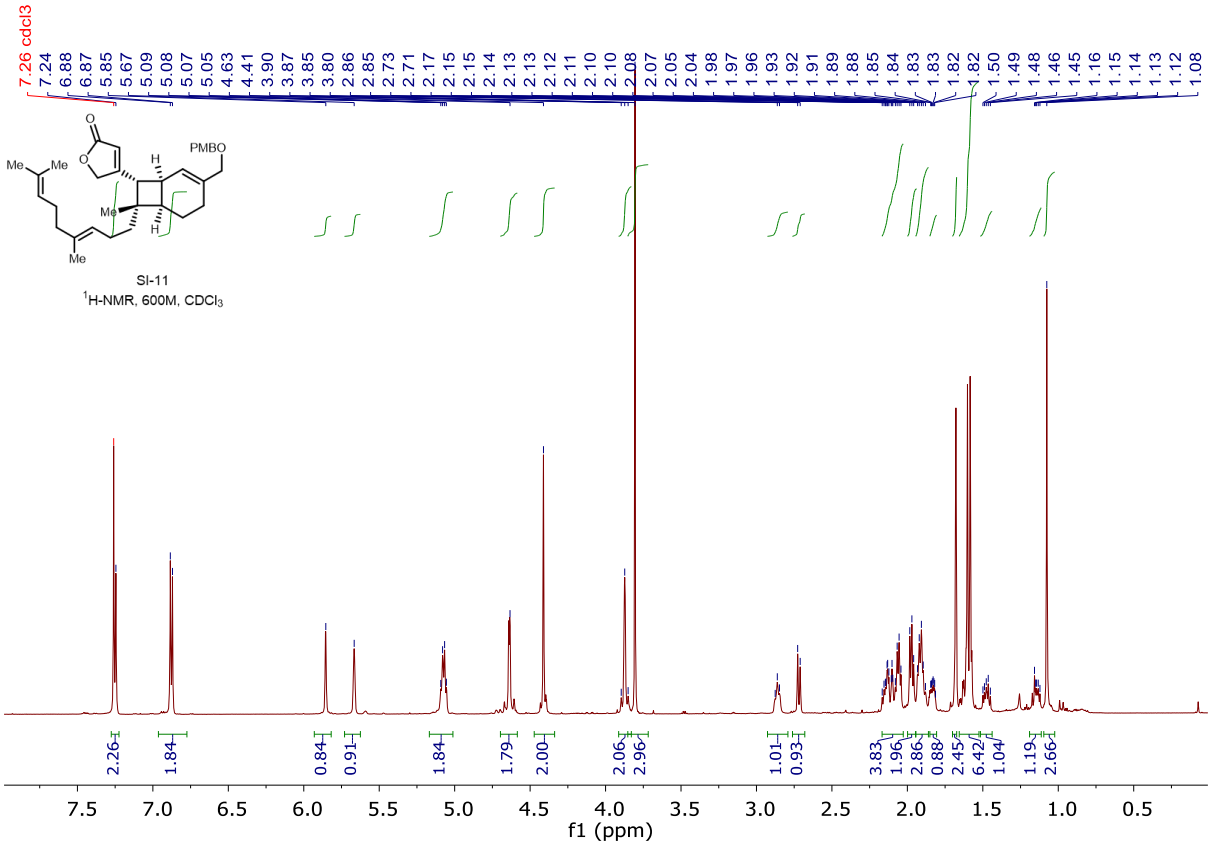

203.54
159.27
137.82 135.43 131.52 130.69 129.45 125.66 124.39 124.06 113.91 113.89
77.41 CDCl3 77.16 CDCl3 76.91 CDCl3
62.19
55.40
44.29 39.80 38.16 37.95 28.99 26.81 25.83 24.13 23.15 23.11 21.98 17.82 16.10
PMBO
Me
Me
Me
Me
H
H
H
O
23
^{13}C-NMR, 126M, CDCl$_3$
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

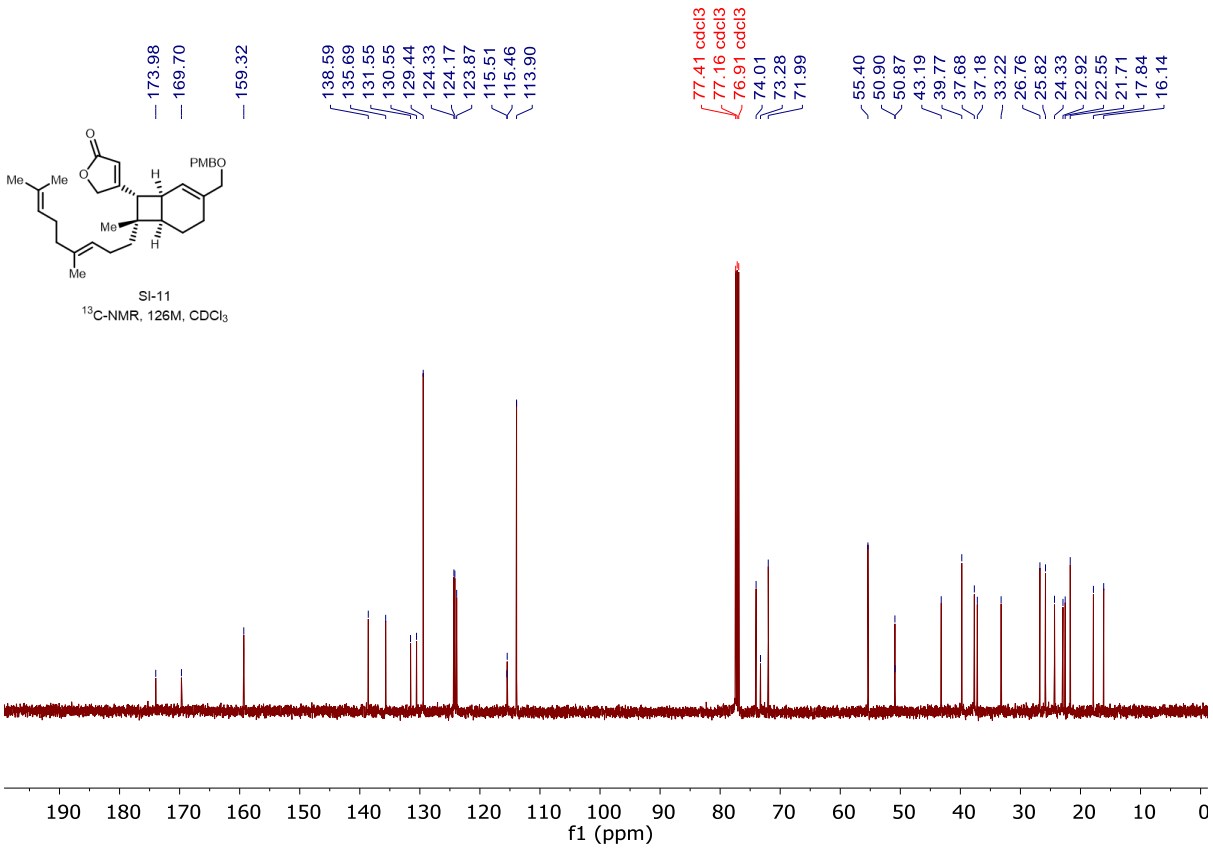

PMBO
Me
Me
Me
O
H
H
H
23
COSY, 600M, CDCl3
f1 (ppm)
f2 (ppm)
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
0
1
2
3
4
5
6
7
8
9
10

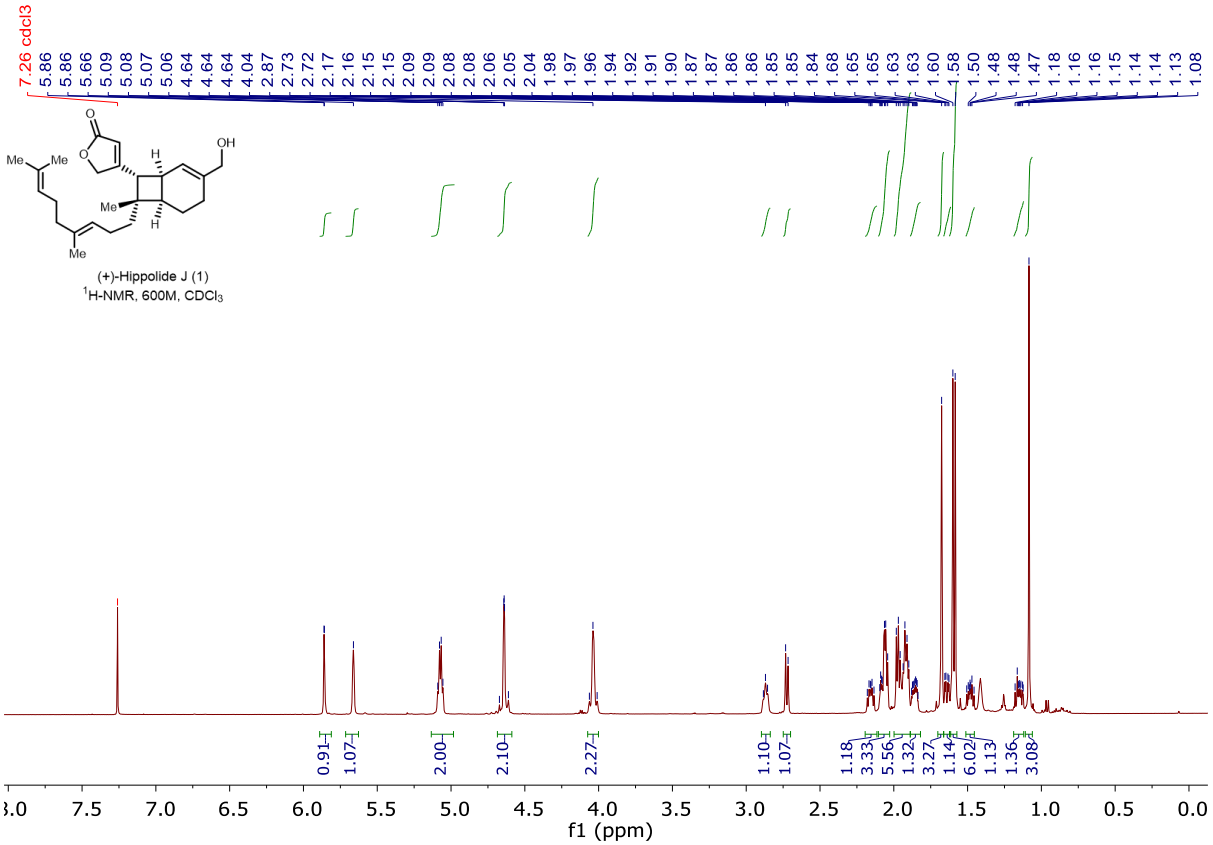

PMBO
Me
Me
Me
noe
noe
O
H
H
H
23
NOESY, 600M, CDCl3
f1 (ppm)
f2 (ppm)
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
1
2
3
4
5
6
7
8
9
10

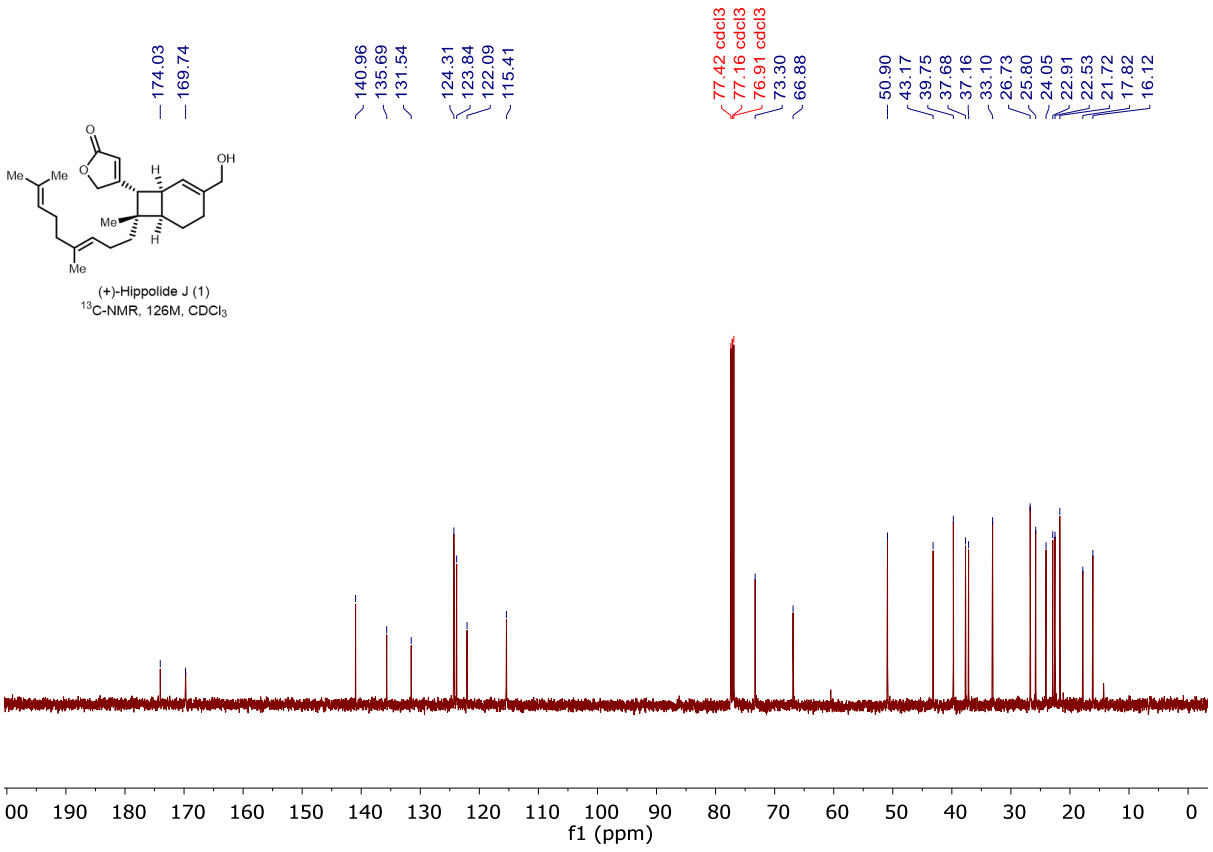

7.26 cdcl3
7.24 6.88 6.87 5.60 5.08 5.08 5.07 5.07 5.07 5.06 4.40 4.13 4.12 4.09 4.09 3.86 3.81 3.24 3.16 3.15 3.14 2.77 2.75 2.12 2.10 2.09 2.08 2.08 2.07 2.06 2.04 2.03 1.97 1.96 1.95 1.94 1.88 1.87 1.86 1.85 1.84 1.84 1.83 1.83 1.82 1.82 1.81 1.68 1.60 1.59 1.57 1.56 1.56 1.55 1.54 1.54 1.20 1.15
Me
Me HO
O
H
PMBO
Me
H
Me
25
1H-NMR, 600M, CDCl3
2.48 1.89 1.00 1.90 1.97 2.07 2.05 2.85 0.94 0.88 0.97 3.92 1.85 4.07 2.72 7.72 1.06 3.03
f1 (ppm)


208.26
159.23
138.05 135.34 131.43 130.59 129.37 125.15 124.34 123.94
113.83
77.42 cdcl3
77.16 cdcl3
76.91 cdcl3
71.76 68.95 58.07 55.32 43.71 39.73 37.45 36.80 28.99 26.73 25.76 24.10 23.10 22.56 21.68 17.77 16.03
Me
Me HO
O
H
PMBO
Me
H
Me
25
13C-NMR, 126M, CDCl3
f1 (ppm)


7.26 cdcl3
7.24
6.88
6.87
6.85
5.67
5.09
5.08
5.07
5.05
4.63
4.41
3.90
3.87
3.85
3.80
2.86
2.85
2.73
2.71
2.17
2.15
2.15
2.14
2.13
2.13
2.12
2.11
2.10
2.10
2.08
2.07
2.05
2.04
1.98
1.97
1.96
1.93
1.92
1.91
1.89
1.88
1.85
1.84
1.83
1.83
1.82
1.82
1.50
1.49
1.48
1.46
1.45
1.16
1.15
1.14
1.13
1.12
1.08
PMBO
Me
Me
Me
Me
H
H
O
O
SI-11
1H-NMR, 600M, CDCl3
2.26
1.84
0.84
0.91
1.84
1.79
2.00
2.06
2.96
1.01
0.93
3.83
1.96
2.86
0.88
2.45
6.42
1.04
1.19
2.66
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


173.98
169.70
159.32
138.59
135.69
131.55
130.55
129.44
124.33
124.17
123.87
115.51
115.46
113.90
77.41 cdcl3
77.16 cdcl3
76.91 cdcl3
74.01
73.28
71.99
55.40
50.90
50.87
43.19
39.77
37.68
37.18
33.22
26.76
25.82
24.33
22.92
22.55
21.71
17.84
16.14
PMBO
Me
Me
Me
Me
H
H
O
O
SI-11
13C-NMR, 126M, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


(+)-Hippolide J (1)
^{1}H-NMR, 600M, CDCl$_3$
f1 (ppm)


(+)-Hippolide J (1)
^{13}C-NMR, 126M, CDCl$_3$
f1 (ppm)