Total Synthesis and Stereochemical Assignment of Callyspongiolide

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Supporting Information

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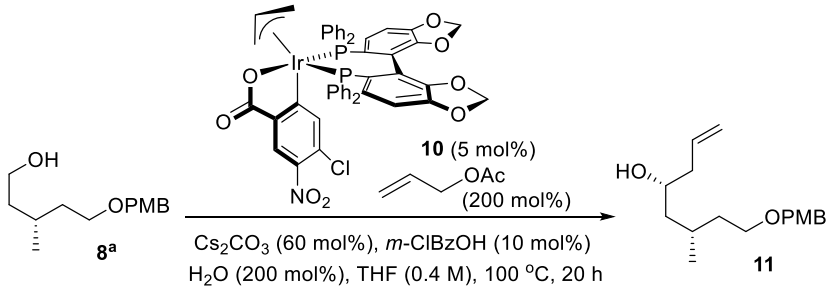
1. General Experimental

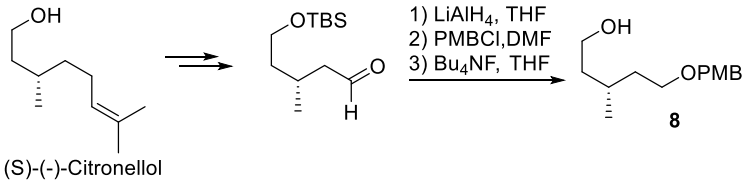
All reactions were conducted in flame-dried or oven-dried glassware under an atmosphere of dry nitrogen or argon. Oxygen and/or moisture sensitive solids and liquids were transferred appropriately. Concentration of solutions in *vacuo* was accomplished using a rotary evaporator fitted with a water aspirator. Residual solvents were removed under high vacuum (0.1-0.2 mm Hg). All reaction solvents were purified before use: Tetrahydrofuran were distilled from sodium benzophenone ketyl. Toluene was distilled over molten sodium metal. Dichloromethane, dimethylformamide, diethylamine, triethylamine and diisoproylethylamine were distilled from CaH_2. Methanol was distilled from Mg/I_2. Flash column chromatography was performed using the indicated solvents on E. Qingdao silica gel 60 (230 – 400 mesh ASTM). TLC was carried out using pre-coated sheets (Qingdao silica gel 60-F250, 0.2 mm). Compounds were visualized with UV light, iodine, *p*-anisaldehyde stain, ceric ammonium molybdate stain, or phosphomolybdic acid in EtOH. ^{1}H NMR spectra were recorded on Bruker DPX 300 MHz, AV 500 MHz or AV 600 MHz spectrometers. Chemical shifts were reported in parts per million (ppm), relative to either a tetramethylsilane (TMS) internal standard or the signals due to the solvent. The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublets; other combinations are derived from those listed above. Coupling constants (J) are reported in Hertz. ^{13}C NMR spectra were completely heterodecoupled and measured at 75, 125, or 150 MHz. High resolution mass spectra were measured on ABI Q-star Elite. Optical rotations were recorded on a Perkin-Elmer 351 polarimeter at 589 nm, 100 mm cell. Data were reported as follow: optical rotation (*c* (g/100 mL), solvent).

2. Experimental procedures

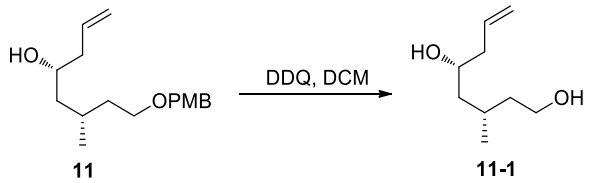


To an oven-dried sealed tube under one atmosphere of nitrogen charged with alcohol **8** (200 mg, 0.84 mmol), catalyst **10** (44 mg, 0.04 mmol), Cs_2CO_3 (85mg, 0.50mmol), *m*-ClBzOH (13 mg, 0.08 mmol), and H_2O (30 mg, 1.68 mmol) was added THF (2.0 mL, 0.4 M) followed by allyl acetate (168 mg, 1.68 mmol). The reaction mixture was allowed to stir at 100 °C for 20 h, at which point the reaction mixture was evaporated. The residue was purified by silica gel flash chromatography to produce **11** (210 mg, 90%) as a colorless oil. R_f = 0.2 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –9.4 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.88 – 5.75 (m, 1H), 5.12 (dd, *J* = 7.7, 6.8 Hz, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.78 – 3.68 (m, 1H), 3.52 – 3.42 (m, 2H), 2.32 – 2.21 (m, 1H), 2.17 – 2.06 (m, 1H), 1.90 (s, 1H), 1.82 – 1.59 (m, 2H), 1.45 – 1.30 (m, 3H), 0.93 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.22, 134.95, 130.67, 129.25, 117.87, 113.82, 72.49, 68.60, 68.31, 55.27, 44.32, 42.19, 36.25, 27.00, 20.68. **HRMS** (*m/z*): calculated for $C_{17}H_{26}O_3Na^+$ $[M + Na]^+$: 301.1774, found 301.1775.

[a] The known alcohol **8** was prepared according to the following scheme.;

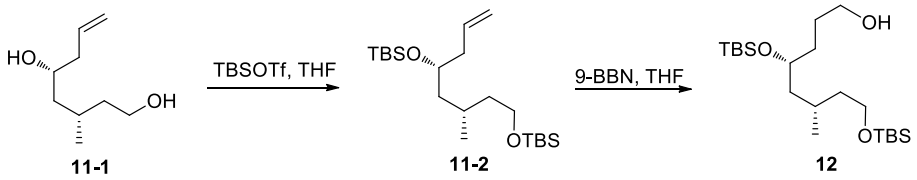


Fujiwara, K.; Naka, J.; Katagiri, T.; Sato, D.; Kawai, H.; Suzuki, T. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 1173.; Lee, E. Lee,Y. R. Moon, Kwon, B. O. Shim, M. S. Yun, J. S. *J. Org. Chem.* **1994**, *59*, 1444.



To a solution of **11** (300 mg, 1.1 mmol) in DCM (10 mL) and phosphate buffer (1 mL, pH 7.0, 100 mM) was added DDQ (500 mg, 2.2 mmol) at room temperature. The reaction mixture was stirred at

room temperature for 2 h., and then washed sequentially with saturated aqueous solution of $Na_2S_2O_3$ (20 mL), $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **11-1** (162 mg, 95%) as a colorless oil. R_f = 0.4 (silica gel, 33% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –22.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.88 – 5.77 (m, 1H), 5.15 – 5.07 (m, 2H), 3.80 – 3.73 (m, 1H), 3.73 – 3.67 (m, 1H), 3.67 – 3.58 (m, 1H), 2.97 (s, 2H), 2.31 – 2.21 (m, 1H), 2.21 – 2.11 (m, 1H), 1.90 – 1.75 (m, 1H), 1.75 – 1.64 (m, 1H), 1.44 – 1.33 (m, 2H), 1.33 – 1.20 (m, 1H), 0.94 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 134.94, 117.73, 68.17, 60.52, 44.21, 42.20, 38.46, 25.82, 20.70. **HRMS** (*m/z*): calculated for $C_9H_{18}O_2Na^+$ $[M + Na]^+$: 181.1199, found 181.1192.

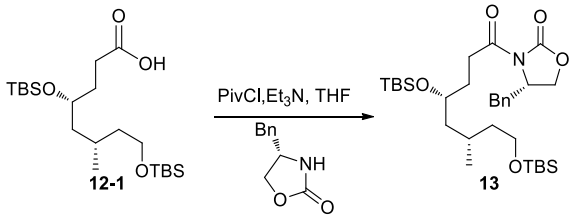


11-1 **11-2** **12**

To a solution of diol **11-1** (272 mg, 1.74 mmol) in DCM (15 mL) was added TBSOTf (1.13 mL, 5.25 mmol) and Et_3N (0.95 mL, 7.00 mmol) at –78 ℃. The reaction mixture was allowed to slowly warm to –30 ℃ and stirred at –30 ℃ for 2 h., and then was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL) at –78 ℃ and allowed to warm to room temperature. The mixture was dissolved in ethyl acetate (50 mL) and the layers were separated. The aqueous phase was extracted with ethyl acetate (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na2SO4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **11-2** (670 mg, 99%) as a colorless oil. R_f = 0.20 (silica gel, hexane);

To a solution of **11-2** (670 mg, 1.76 mmol) in THF (10 mL) was added 9-BBN (12 mL, 0.5 M) at 0 ℃. The mixture was warmed to room temperature and stirred for 2 h., and then slowly quenched by the addition of saturated aqueous solution of $NaHCO_3$ (10 mL) and 30% hydrogen peroxide (10 mL) at 0 ℃. The mixture was allowed to warm to room temperature and stirred for 2 h. Layers were separated and the aqueous phase was extracted with ethyl ether (2 x 30 mL). The organic phase was washed with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated in *vacuo* and purified by silica gel flash chromatography to give **12** as colorless oil (630 mg, 90 %). R_f = 0.4 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 1.8 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.88 – 3.79 (m, 1H), 3.69 – 3.55 (m, 4H), 2.24 (s, 1H), 1.67 – 1.52 (m, 7H), 1.37 – 1.23 (m, 2H), 0.91 – 0.83 (m, 21H), 0.07 (s, 6H), 0.05 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 70.16, 63.24, 61.11, 44.12, 40.48, 33.14, 27.87, 26.29, 25.97, 25.90, 19.94, 18.33, 18.10, -4.43, -4.46, -5.26, -5.29.**HRMS** (*m/z*): calculated for $C_{21}H_{48}O_3Si_2Na^+$ $[M + Na]^+$: 427.3034, found 427.3036.

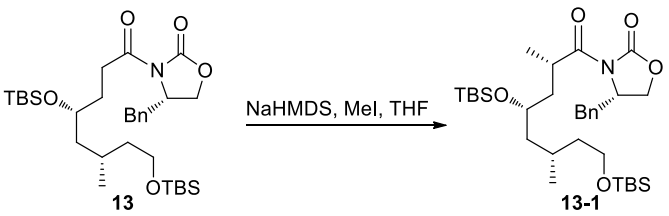
To a solution of compound **12** (630 mg, 1.56 mmol) in CH_3CN (20 mL) and phosphate buffer (20 mL, pH 7.0, 100 mM) were subsequently added $NaClO_2$ (755 mg, 8.39 mmol), NaClO (1.55 mL, 10% chlorine) and TEMPO (15 mg, 0.10 mmol) at room temperature. After being stirred for 2 h, the pH value of the reaction mixture was adjusted to 3 with 1M HCl. Volatiles were removed in *vacuo*, the aqueous residue was extracted with ethyl ether (2 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give **12-1** as a colorless oil (610 mg, 94 %). R_f = 0.4 (silica gel, 10% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 10.1 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.87 – 3.78 (m, 1H), 3.71 – 3.58 (m, 2H), 2.44 (t, *J* = 7.6 Hz, 2H), 1.93 – 1.80 (m, 1H), 1.70 – 1.59 (m, 2H), 1.58 – 1.50 (m, 1H), 1.46 – 1.39 (m, 1H), 1.39 – 1.26 (m, 2H), 0.94 – 0.89 (m, 12H), 0.89 (s, 9H), 0.06 (s, 6H), 0.05 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 180.00, 69.26, 61.10, 44.65, 40.47, 31.15, 29.52, 26.33, 25.95, 25.86, 19.90, 18.30, 18.02, -4.36, -4.56, -5.30, -5.32. **HRMS** (*m/z*): calculated for $C_{21}H_{46}O_4Si_2Na^+$ $[M + Na]^+$: 441.2827, found 441.2825.



To a stirred solution of acid **12-1** (610 mg, 1.46 mmol) in dry THF (10 mL) was sequentially added Et_3N (0.61 mL, 4.38 mmol) and trimethylacetyl chloride (180 uL, 1.61 mmol) at 0 ℃. After being stirred for 20 minutes, the reaction mixture was cooled to -78 ℃.

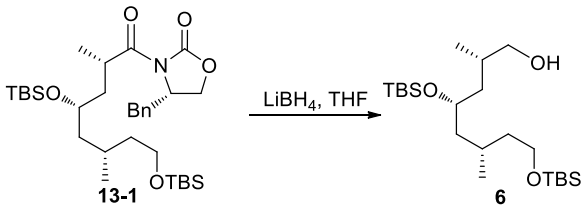
In a separate flask, *n*-butyllithium (1.1 mL, 1.65 mmol, 1.5 M in heptane) was added to a solution of (4*S*)-4-benzyl-1,3-oxazolidin-2-one (550 mg, 3.11 mmol) in THF (5 mL) at -78 ℃. After being stirred for 30 min later, the resulting solution was transferred to the afore-mentioned reaction mixture at -78 ℃. This reaction mixture was stirred for 2 h at -78 ℃ and quenched with saturated aqueous solution of $NaHCO_3$ (10 mL). Volatiles were removed in *vacuo*, the aqueous phase was extracted with ethyl ether (2 x 30 mL). The combined organic phases were washed with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give **13** as a colorless oil (675 mg, 80%). R_f = 0.9 (silica gel, 17% ethyl acetate in

hexane); $[\alpha]_D^{20}$ = 35.4 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H), 7.30 – 7.26 (m, 1H), 7.24 – 7.18 (m, 2H), 4.74 – 4.59 (m, 1H), 4.25 – 4.11 (m, 2H), 3.90 – 3.77 (m, 1H), 3.71 – 3.57 (m, 2H), 3.30 (dd, *J* = 13.4, 3.2 Hz, 1H), 3.15 – 2.89 (m, 2H), 2.82 – 2.70 (m, 1H), 1.98 – 1.85 (m, 1H), 1.76 – 1.62 (m, 2H), 1.62 – 1.54 (m, 1H), 1.51 – 1.42 (m, 1H), 1.39 – 1.28 (m, 2H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 18H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ 173.48, 153.36, 135.36, 129.42, 128.94, 127.32, 69.36, 66.12, 61.27, 55.15, 45.20, 40.50, 37.92, 31.59, 30.92, 26.44, 25.99, 25.91, 20.01, 18.33, 18.05, -4.32, -4.52, -5.25, -5.28. **HRMS** (*m/z*): calculated for $C_{31}H_{55}NO_5Si_2Na^+$ $[M + Na]^+$: 600.3511, found 600.3512.



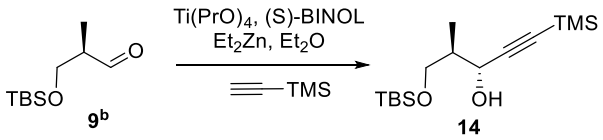
To a solution of **13** (395 mg, 0.68 mmol) in THF (10 mL) was added NaHMDS (0.85 mL, 1.70 mmol, 2.0 M) at –78 ℃. After being stirred for 15 minutes, MeI (131 uL, 2.05 mmol) was added dropwise at –78 ℃. The reaction mixture was stirred overnight at –78 ℃ and then quenched with saturated aqueous NH_4Cl (30 mL). Volatiles were removed in *vacuo*, the aqueous layer was extracted with ethyl ether (2 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give **13-1** (420 mg, 99%) as a colorless oil. R_f = 0.80 (silica gel, 17% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 49.1 (*c* 1.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.2 Hz, 2H), 7.29 – 7.24(m, 1H), 7.24 – 7.17 (m, 2H), 4.74 – 4.63 (m, 1H), 4.21 – 4.09 (m, 2H), 3.88 – 3.80 (m, 1H), 3.80 – 3.72 (m, 1H), 3.71 – 3.59 (m, 2H), 3.24 (dd, *J* = 13.4, 3.2 Hz, 1H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.14 (ddd, *J* = 13.6, 9.6, 3.7 Hz, 1H), 1.73 – 1.64 (m, 1H), 1.60 – 1.51 (m, 1H), 1.51 – 1.43 (m, 1H), 1.40 – 1.33 (m, 2H), 1.25 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.06 (s, 6H), 0.02 (s, 3H) , -0.03 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.82, 152.72, 135.32, 129.48, 128.90, 127.31, 68.73, 65.88, 61.18, 55.18, 45.46, 40.78, 39.80, 37.86, 34.14, 26.42, 25.99, 25.84, 19.85, 19.04, 18.33, 17.98, -4.18, -4.79, -5.26, -5.28. **HRMS** (*m/z*): calculated for $C_{32}H_{57}NO_5Si_2Na^+$ $[M + Na]^+$: 614.3667, found 614.3669.



13-1 6

To a solution of **13-1** (420 mg, 0.71 mmol) in THF (10 mL) was added lithium borohydride (1.2 mL, 2.4 mmol, 2 M) at 0 ℃. After being stirred for 4 h, the reaction mixture was quenched by the addition of MeOH (0.2 mL) at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred for additional 3 h. and then added a saturated aqueous solution of $NaHCO_3$ (10 mL). After the solution was stirred until clear phases were obtained (1.5 h), the aqueous layer was extracted with ethyl ether (2 x 30 mL). The combined organic phases were washed with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give **6** as a colorless oil (260 mg, 88%): R_f = 0.4 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 4.8 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.99 – 3.91 (m, 1H), 3.75 – 3.68 (m, 1H), 3.68 – 3.55 (m, 2H), 3.46 (s, 1H), 3.37 – 3.25 (m, 1H), 1.96 – 1.83 (m, 1H), 1.65 – 1.54 (m, 4H), 1.48 – 1.37 (m, 1H), 1.35 – 1.29 (m, 2H), 0.90 (s, 9H), 0.90 – 0.87 (m, 12H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.10 (s, 3H) , 0.09 (s, 3H), 0.04 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 69.78, 68.78, 60.89, 43.35, 41.97, 40.56, 31.55, 26.19, 25.96, 25.84, 19.63, 18.78, 18.25, 18.07, -4.56, -4.60, -5.28, -5.31. **HRMS** (*m/z*): calculated for $C_{22}H_{50}O_3Si_2Na^+$ $[M + Na]^+$: 441.3191, found 441.3193.

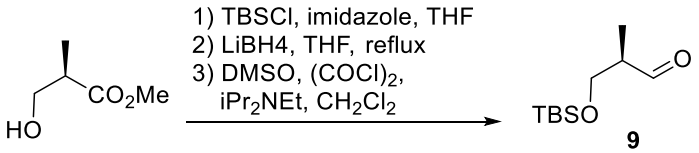


9[b] 14

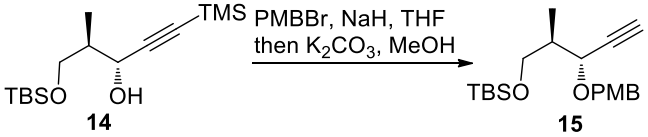
To a solution of Et_2Zn (18.8 mL, 1.0 M, 18.8 mmol) in toluene was carefully added TMS acetylene (2.6 mL, 18.8 mmol). The mixture was heated to reflux for 1 h, cooled to room temperature, followed by addition of (S)-BINOL (0.52 g, 1.88 mmol) in Et_2O (20 mL) and $Ti(OiPr)_4$ (1.39 mL, 4.70 mmol). After being stirred for 1 h later, aldehyde **9** (0.95 g, 4.70 mmol) in Et_2O (10 mL) was added to the reaction solution. The reaction mixture was stirred overnight and quenched with tartaric acid (50 mL, 1.0 M in water). After the solution was stirred until clear phases were obtained, the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give **14** as a colorless oil (1.14 g, 80%): R_f = 0.6 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = -6.2 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.39 (t, *J* = 5.8 Hz, 1H), 3.94 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.57 (dd, *J* = 10.0, 6.6 Hz, 1H), 3.46 (d, *J* = 5.4 Hz, 1H), 1.93 (ddd, *J* = 13.3, 6.7, 4.1 Hz, 1H), 1.60 (s, 1H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.90 (s, 9H), 0.18 (s, 9H), 0.08 (s, 3H) , 0.08 (s,

3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 105.82, 89.87, 67.13, 66.76, 40.62, 25.86, 18.21, 12.91, -0.08, -5.56, -5.61. **HRMS** (*m/z*): calculated for $C_{15}H_{32}O_2Si_2Na^+$ [M + Na]$^+$: 323.1833, found 323.1839.

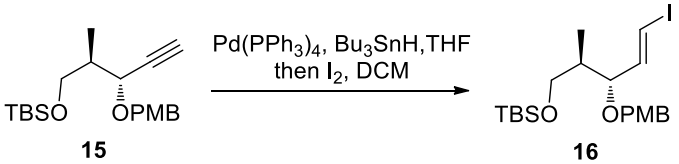
b The known aldehyde **9** was prepared according to the following scheme:



Kirkham, J. E. D.; Lee, V.; Baldwin, J. E. *Chem. Commun.* **2006**, *27*, 2863.

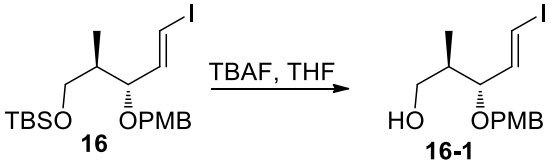


To a solution of **14** (100 mg, 0.33 mmol) in THF (5 mL) was added NaH (27 mg, 0.67 mmol, 60% dispersion in mineral oil) at 0 °C. The resulting solution was stirred for 30 minutes, before 4-methoxybenzyl bromide (59.6 uL, 0.40 mmol) was slowly added at 0 °C. The resulting reaction mixture was stirred overnight at room temperature, and then concentrated in *vacuo*. The residue was dissolved in MeOH (5 mL), and K_2CO_3 (138 mg, 0.99 mmol) was added. The reaction mixture was stirred for 1 h at room temperature and quenched with saturated aqueous solution of NH_4Cl (15 mL). Volatiles were removed in *vacuo*, and the aqueous residue was extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **15** (85 mg, 73%) as a colorless oil. R_f = 0.7 (silica gel, 10% ethyl acetate in hexane); **$[\alpha]_D^{20}$** = 41.4 (*c* 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.74 (d, *J* = 11.4 Hz, 1H), 4.43 (d, *J* = 11.4 Hz, 1H), 4.19 (dd, *J* = 6.0, 2.1 Hz, 1H), 3.80 (s, 3H), 3.62 – 3.45 (m, 2H), 2.45 (d, *J* = 2.1 Hz, 1H), 2.02 (dt, *J* = 12.5, 6.3 Hz, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.85 (s, 9H), 0.01 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.27, 130.15, 129.57, 113.80, 81.50, 74.73, 70.47, 69.79, 64.38, 55.28, 40.46, 25.89, 18.24, 12.21, -5.42, -5.48. **HRMS** (*m/z*): calculated for $C_{20}H_{32}NaO_3SNa^+$ [M + Na]$^+$: 371.2013, found 371.2005.

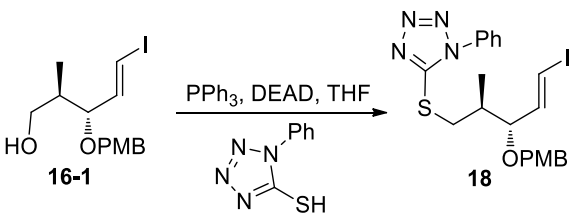


To a stirred solution of **15** (85 mg, 0.24 mmol) and $Pd(PPh_3)_4$ (14 mg, 0.012 mmol) in THF (5 mL) was added *n*-Bu_3SnH (79 uL, 0.29 mmol). After being stirred for 20 minutes, THF was removed under reduced pressure. The residue was purified by silica gel flash chromatography to provide the

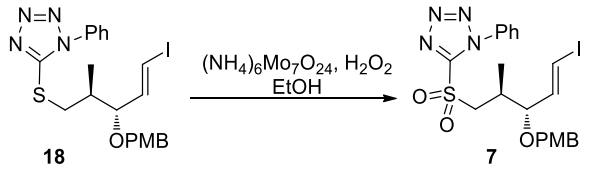
corresponding vinyl tributyltin as a colorless oil. To a solution of the resulting vinyl tributyltin in DCM (5 mL) was added I_2 (1 M in DCM) until the color of the solution persisted. The reaction was quenched with saturated aqueous solution of Na_2SO_3 (30 mL). Layers were separated, the aqueous layer was extracted with DCM (2 x 25 mL). The combined organic layers were dried over $MgSO_4$, and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **16** (90 mg, 77%) as a colorless oil. R_f = 0.80 (silica gel, 5% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 9.7 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.49 (dd, J = 14.5, 8.2 Hz, 1H), 6.27 (d, J = 14.5 Hz, 1H), 4.51 (d, J = 11.3 Hz, 1H), 4.28 (d, J = 11.4 Hz, 1H), 3.82 – 3.77 (m, 4H), 3.64 – 3.50 (m, 2H), 1.87 (dt, J = 12.3, 5.6 Hz, 1H), 0.90 – 0.87 (m, 12H), 0.03 (s, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.12, 145.35, 130.41, 129.26, 113.77, 82.26, 78.41, 70.40, 64.24, 55.27, 39.86, 25.91, 18.25, 12.63, -5.41, -5.45. **HRMS** (*m/z*): calculated for $C_{20}H_{33}IO_3SiNa^+$ [M + Na]$^+$: 499.1136, found 499.1137.



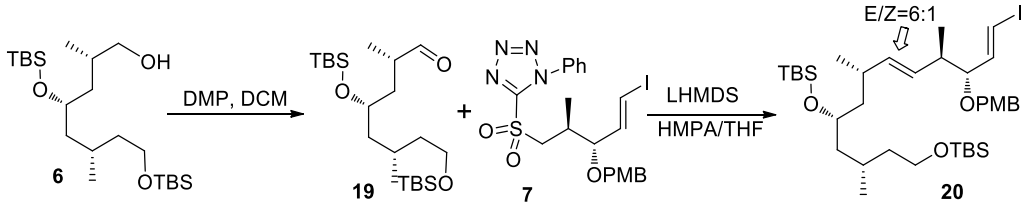
To a solution of **16** (335 mg, 0.70 mmol) in THF (10 mL) was added TBAF (1.5 mL, 1.50 mmol, 1.0 M in THF) at 0 ℃. The reaction mixture was stirred at room temperature for 3h before it was quenched by addition of saturated aqueous solution of NH_4Cl (20 mL), and then extracted with ethyl acetate (3 x 30mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **16-1** (250 mg, 98%) as a colorless oil. R_f = 0.20 (silica gel, 33% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 45.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.48 (dd, *J* = 14.6, 8.3 Hz, 1H), 6.34 (d, *J* = 14.6 Hz, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 4.27 (d, *J* = 11.4 Hz, 1H), 3.81 (s, 3H), 3.72 – 3.57 (m, 2H), 3.58 – 3.47 (m, 1H), 1.87 (ddd, *J* = 14.9, 7.1, 3.7 Hz, 1H), 0.83 (d, *J* = 7.0 Hz, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.36, 145.33, 129.52, 129.48, 113.97, 86.02, 79.54, 70.39, 66.54, 55.25, 39.44, 13.46. **HRMS** (*m/z*): calculated for $C_{14}H_{19}IO_3Na^+$ [M + Na]$^+$: 385.0271, found 385.0276.



To a solution of alcohol **16-1** (250 mg, 0.69 mmol) in THF (20 mL) was sequentially added 1-phenyl-1H-tetrazole-5-thiol (200 mg, 1.12 mmol), Ph_3P (300 mg, 1.12 mmol), and DEAD (170 uL, 1.12 mmol) at 0 ℃. After being stirred at room temperature for 2 h, the reaction mixture was quenched by addition of saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with ethyl acetate (3 x 30mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **18** (328 mg, 91%) as a colorless oil. R_f = 0.40 (silica gel, 33% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 10.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 – 7.50 (m, 5H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.49 (dd, *J* = 14.6, 7.9 Hz, 1H), 6.39 (d, *J* = 14.6 Hz, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 4.27 (d, *J* = 11.4 Hz, 1H), 3.80(s, 3H), 3.71 – 3.56 (m, 2H), 3.47 – 3.36 (m, 1H), 2.22 – 2.17 (m, 1H), 1.03 (d, *J* = 6.9 Hz, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.24, 154.59, 144.47, 133.68, 130.03, 129.74, 129.63, 129.54, 123.81, 113.79, 113.69, 83.63, 79.91, 70.34, 55.22, 37.27, 36.47, 15.41. **HRMS** (*m/z*): calculated for $C_{21}H_{23}IN_4O_2SNa^+$ $[M + Na]^+$: 545.0479, found 545.0477.

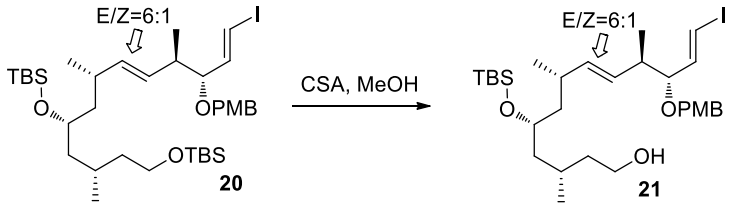


To a solution of **18** (51 mg, 0.10 mmol) in EtOH (10 mL) was added a portion (7 mL) of a stock solution of $(NH_4)_6Mo_7O_{24}$ ·$4H_2O$ (50 mg, 0.04 mmol) and 30% H_2O_2 (2 mL). After being stirred at room temperature for 24 h, the reaction mixture was concentrated in *vacuo* and extracted with ethyl acetate (3 x 30mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **7** (45.3 mg, 84%) as a colorless oil. R_f = 0.39 (silica gel, 33% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 20.4 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 – 7.51 (m, 5H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.50 – 6.36 (m, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 4.26 (d, *J* = 11.4 Hz, 1H), 4.07 (dd, *J* = 14.6, 3.6 Hz, 1H), 3.82 (s, 3H), 3.73 – 3.63 (m, 1H), 3.53 (dd, *J* = 14.6, 8.8 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.39, 153.97, 143.50, 133.00, 131.44, 129.62, 129.52, 129.27, 125.22, 113.93, 83.12, 80.93, 70.52, 58.15, 55.27, 32.73, 16.14. **HRMS** (*m/z*): calculated for $C_{21}H_{23}IN_4O_4SNa^+$ $[M + Na]^+$: 577.0377, found 577.0378.



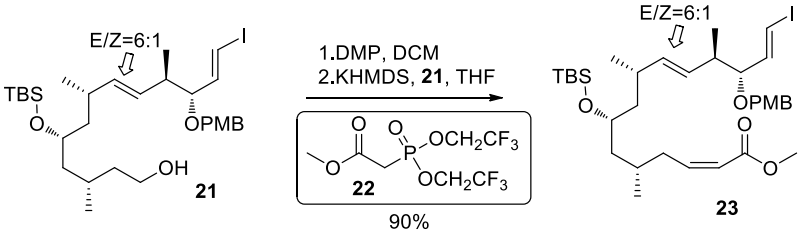
To a solution of **6** (150 mg, 0.36 mmol) in DCM (5 mL), $NaHCO_3$ (50 mg, 0.60 mmol) were added at 0 ℃ followed by addition of Dess-Martin periodinane (250 mg, 0.59 mmol). After being stirred at room temperature for 1 h, the reaction mixture was concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **19** (140 mg, 94%) as a colorless oil, which was used directly in the next step without further purification.

To a cooled solution of sulfone **7** (300 mg, 0.54 mmol) in THF (3 mL,) was added LHMDS (0.56 ml, 1 M) at -78 ℃. After being stirred at -78 ℃ for 30 minutes, aldehyde **19** (140 mg, 0.34 mmol) was added over 30 minutes, and the reaction was allowed to warmed to room temperature and stirred overnight. The reaction mixture was quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **20** (190 mg, 76%, E/Z=6:1) as a colorless oil. R_f = 0.70 (silica gel, 5% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 27.6 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.47 (dd, *J* = 14.5, 7.9 Hz, 1H), 6.24 (d, *J* = 14.5 Hz, 1H), 5.42 – 5.25 (m, 2H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 3.82 (s, 3H), 3.74 – 3.69 (m, 1H), 3.67 – 3.62 (m, 2H), 3.59 – 3.53 (m, 1H), 2.41 – 2.25 (m, 2H), 1.67 – 1.61 (m, 1H), 1.59 – 1.54 (m, 1H), 1.46 – 1.39 (m, 2H), 1.37 – 1.31 (m, 2H), 1.30 – 1.27 (m, 1H), 0.98 (m, 6H), 0.92 – 0.89 (m, 21H), 0.06 (s, 12H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.15, 145.28, 137.01, 130.43, 129.80, 129.17, 113.77, 85.01, 78.22, 70.20, 69.05, 61.24, 55.28, 45.75, 44.83, 40.77, 40.56, 32.99, 26.35, 26.02, 21.88, 20.23, 18.35, 18.10, 15.94, -3.84, -4.04, -5.24, -5.25. **HRMS** (*m/z*): calculated for $C_{36}H_{65}IO_4Si_2Na^+$ $[M + Na]^+$: 767.3358, found 767.3353.



To a solution of **20** (100 mg, 0.13 mmol) in MeOH (5 mL), was added camphorsulfonic acid (10 mg, 0.04 mmol) at 0 ℃. The reaction mixture was stirred at 0 ℃ for 1 h at which point **20** had been consumed as judged by TLC analysis. The reaction was quenched by addition of Et_3N (5 uL, 0.04 mmol) and then concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to

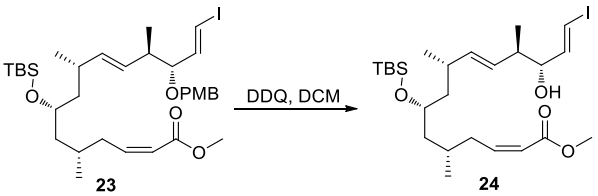
give compound **21** (83 mg, 98%, E/Z=6:1) as a colorless oil. R_f = 0.40 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 32.3 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.52 – 6.39 (m, 1H), 6.24 (d, *J* = 14.5 Hz, 1H), 5.40 – 5.24 (m, 2H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 3.81 (s, 3H), 3.76 – 3.72 (m, 1H), 3.71 – 3.65 (m, 2H), 3.59 – 3.47 (m, 1H), 2.39 – 2.22 (m, 2H), 1.71 – 1.60 (m, 3H), 1.43 – 1.33 (m, 4H), 0.98 (m, 6H), 0.89 (m, 12H), 0.06 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.09, 145.25, 136.90, 130.34, 129.82, 129.18, 113.72, 84.90, 78.32, 70.13, 68.95, 60.92, 55.25, 45.55, 44.68, 40.75, 40.35, 33.02, 25.98, 21.84, 20.17, 18.07, 16.03, -3.89, -4.06. **HRMS** (*m/z*): calculated for $C_{30}H_{51}IO_4SiNa^+$ $[M + Na]^+$: 653.2494, found 653.2490.



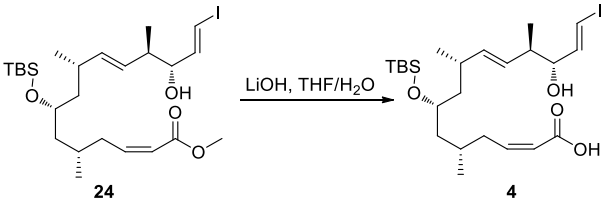
$NaHCO_3$ (69 mg, 0.82 mmol) was added to a solution of **21** (150 mg, 0.24 mmol) in DCM (5 mL) at 0 ℃ followed by addition of Dess-Martin periodinane (150 mg, 0.35 mmol). The reaction was stirred for 1 h at room temperature. The reaction mixture was concentrated in *vacuo*. Followed by filtered through a pad of silica gel, the residue was concentrated in *vacuo* to afford aldehyde (140 mg, 94%) as a colorless oil, which was used directly in the next step without further purification.

To a solution of 18-crown-6 (100 mg, 0.36 mmol) and $(CF_3CH_2)P(O)CH_2CO_2Me$ (114 mg, 0.36 mmol) in THF(7 mL) was added potassium bis(trimethylsilyl)amide (KHMDS) (714 uL, 0.36 mmol, 0.5 M in toluene) at -78 ℃. After being stirred for 15 minutes, aldehyde (140 mg, 0.22 mmol) in THF (2 mL) was added dropwise. The reaction was stirred overnight at -78 ℃ and quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to provide compound **23** (147 mg, 96%, E/Z=6:1) as a colorless oil. R_f = 0.65 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 26.3 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.46 (dd, *J* = 14.5, 7.9 Hz, 1H), 6.26 – 6.18 (m, 2H), 5.84 (d, *J* = 11.6 Hz, 1H), 5.41 – 5.22 (m, 2H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 3.81 (s, 3H), 3.76 – 3.69 (m, 4H), 3.60 – 3.52 (m, 1H), 2.65 – 2.57 (m, 2H), 2.38 – 2.31 (m, 1H), 2.31 – 2.22 (m, 1H), 1.74 – 1.65 (m, 1H), 1.50 – 1.29 (m, 4H), 1.02 – 0.94 (m, 6H), 0.91 – 0.87 (m, 12H), 0.06 (s, 3H) , 0.05 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.85, 159.16, 149.32, 145.32, 136.96, 130.43, 129.82, 129.18, 120.21, 113.77, 84.99, 78.24, 70.21,

68.90, 55.28, 50.95, 45.04, 44.92, 40.79, 36.25, 32.99, 29.82, 26.00, 21.73, 20.08, 18.09, 15.99, -3.94, -4.02. **HRMS** (*m/z*): calculated for $C_{33}H_{53}IO_5Na^+$ [M + Na]$^+$: 707.2599, found 707.2593.

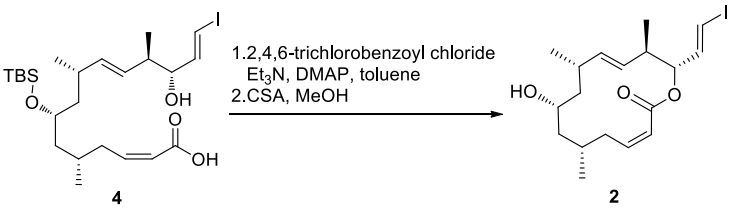


To a solution of **23** (110 mg, 0.17 mmol) in DCM (7 mL) was added phosphate buffer (pH 7.2, 100 mM, 1 mL) and DDQ (120 mg, 0.53 mmol) at room temperature. The reaction mixture was stirred for 3 h at room temperature and then extracted with DCM (3 x 25 mL). The combined organic phases were washed sequentially with saturated aqueous solution of $Na_2S_2O_3$ (20 mL), $NaHCO_3$ (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce 2**4** (74 mg, 82%) as a colorless oil. R_f = 0.40 (silica gel, 5% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 13.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.56 (dd, *J* = 14.4, 6.6 Hz, 1H), 6.36 (d, *J* = 14.5 Hz, 1H), 6.28 – 6.19 (m, 1H), 5.84 (d, *J* = 11.6 Hz, 1H), 5.46 – 5.21 (m, 2H), 3.83 – 3.73 (m, 2H), 3.71 (s, 3H), 2.61 (t, *J* = 6.5 Hz, 2H), 2.37 – 2.30 (m, 1H), 2.25 – 2.14 (m, 1H), 1.71 – 1.58 (m, 2H), 1.46 – 1.34 (m, 4H), 1.01 – 0.96 (m, 6H), 0.91 – 0.87 (m, 12H), 0.06 (s, 3H) , 0.05 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.88, 149.31, 146.70, 139.54, 129.34, 120.24, 77.93, 69.02, 50.99, 44.99, 44.82, 43.19, 36.12, 33.28, 29.86, 29.71, 26.00, 21.85, 20.05, 18.14, 16.33, -3.92, -4.02. **HRMS** (*m/z*): calculated for $C_{25}H_{45}IO_4Na^+$ [M + Na]$^+$: 587.2024, found 587.2023.



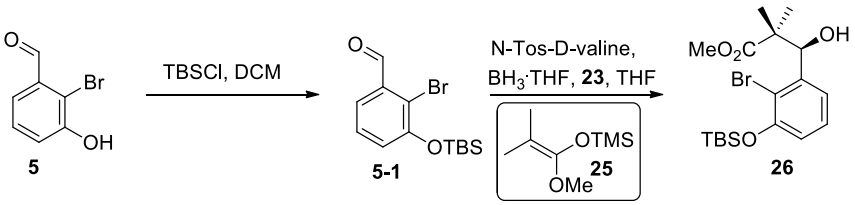
To a solution of **24** (74 mg, 0.13 mmol) in THF (5 mL), MeOH (1 mL) and H_2O (3 mL) was added LiOH (20 mg, 0.49 mmol) at 0 ℃. The reaction mixture was allowed to warm to room temperature, stirred at for 5h, and extracted with DCM (3 x 25 mL). The combined organic phase were dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **4** (62 mg, 86%) as a colorless oil. R_f = 0.50 (silica gel, 25% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 20.6 (*c* 0.35, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.55 (dd, *J* = 14.4, 6.6 Hz, 1H), 6.40 – 6.26 (m, 2H), 5.86 (d, *J* = 11.6 Hz, 1H), 5.50 – 5.17 (m, 2H), 3.86 – 3.71 (m, 2H), 2.70 – 2.53 (m, 2H), 2.38 – 2.25 (m, 1H), 2.25 – 2.13 (m, 1H), 1.78 – 1.65 (m, 1H), 1.49 – 1.32 (m, 4H), 1.02 – 0.94 (m, 6H), 0.94 – 0.87 (m, 12H), 0.06 (s, 3H) , 0.05 (s, 3H). 13C NMR (100 MHz, $CDCl_3$) δ

170.13, 151.53, 146.49, 139.67, 129.29, 119.85, 78.00, 69.01, 44.93, 44.80, 43.19, 36.12, 33.30, 29.93, 29.71, 25.99, 21.93, 20.12, 18.14, 16.46, -3.92, -4.05. **HRMS** (*m/z*): calculated for $C_{24}H_{43}IO_4Na^+$ [M + Na]$^+$: 573.1868, found 573.1868.



To a solution of **4** (15 mg, 0.03 mmol) and triethylamine (18 μL, 0.12 mmol) in dry toluene (20 mL) was added 2,4,6-trichlorobenzoyl chloride (95 μL, 0.09 mmol) at 0 ℃. After being allowed to warm to room temperature and stirred for 1 h, DMAP (18 mg, 0.15 mmol) in toluene (5 mL) was added to the reaction mixture. The mixture was stirred overnight at room temperature and quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was used directly in the next step without further purification.

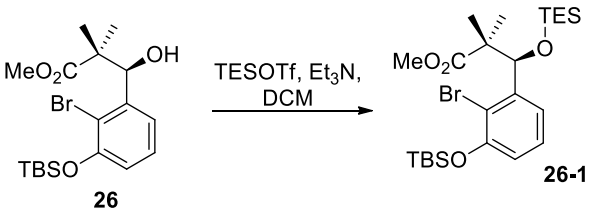
To a solution of the residue in MeOH (5 mL) was added camphorsulfonic acid (2 mg, 0.01 mmol). The reaction mixture was stirred for 1 h at which point **20** had been consumed as judged by TLC analysis, and then quenched by addition of Et_3N (1.2 uL, 0.01 mmol). The solution was concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **2** (7.6 mg, 67%, two steps) as a colorless oil. R_f = 0.40 (silica gel, 10% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 90.0 (*c* 0.2, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.56 – 6.43 (m, 2H), 6.34 – 6.23 (m, 1H), 5.87 (dd, *J* = 11.6, 2.5 Hz, 1H), 5.18 – 5.10 (m, 2H), 5.03 (dd, *J* = 15.0, 9.2 Hz, 1H), 3.81 – 3.70 (m, 1H), 3.37 (t, *J* = 10.7 Hz, 1H), 2.37 – 2.26 (m, 1H), 2.25 – 2.09 (m, 2H), 1.96 (dd, *J* = 14.8, 2.8 Hz, 1H), 1.68 – 1.56 (m, 2H), 1.39 – 1.26 (m, 3H), 1.05 (d, *J* = 7.1 Hz, 3H), 0.98 – 0.93 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.06, 146.49, 143.12, 137.74, 131.55, 121.63, 81.03, 65.94, 45.99, 42.97, 42.67, 34.48, 31.22, 29.70, 27.08, 22.34, 20.03, 17.52. **HRMS** (*m/z*): calculated for $C_{18}H_{27}IO_3Na^+$ [M + Na]$^+$: 441.0897, found 441.0893.



To a solution of compound **5** (500 mg, 2.25 mmol) and imidazole (500 mg, 7.43 mmol) in DCM (20 mL) was added TBSCl (600 mg, 4.03 mmol) at 0 ℃. After being stirred at room temperature for 1 h,

the reaction was quenched by addition of saturated aqueous solution of NH_4Cl (20 mL) and extracted with DCM (3 x 30mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to produce **5-1** (775 mg, 99%) as a colorless oil. R_f = 0.85 (silica gel, 10% ethyl acetate in hexane);

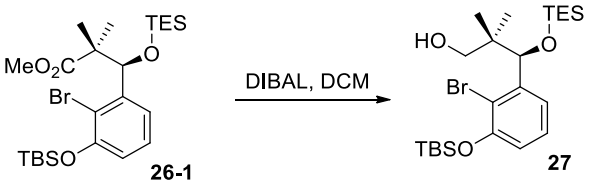
BH_3·THF complex (2.5 mL, 1.0 M solution in THF) was added to a solution of N-Ts-*D*-Val (676 mg, 2.46 mmol) in DCM (7 mL) at 0 ℃ under Ar. The mixture was stirred for 0.5 h and allowed to warm to room temperature for addition 1 h. The resulting mixture was re-cooled to -78 ℃. To this solution, **5-1** (775 mg, 2.46 mmol) in DCM (3 mL) and silyl ketene acetal (0.73 mL, 3.20 mmol) were slowly added. After being stirred at -78 ℃ for 12 h, the reaction mixture was quenched by addition of saturated aqueous solution of NH_4Cl (20 mL) and extracted with DCM (3 x 30mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **26** (1.0 g, 98%) as a colorless oil. R_f = 0.45 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 20.8 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.83 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.56 (d, *J* = 4.6 Hz, 1H), 3.76 (s, 3H), 3.41 (d, *J* = 4.7 Hz, 1H), 1.22 (s, 3H), 1.20 (s, 3H), 1.04 (s, 9H), 0.24 (s, 3H), 0.23 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.41, 152.29, 141.39, 127.22, 121.82, 119.18, 118.09, 52.22, 48.57, 25.80, 23.54, 19.01, 18.41, -4.14, -4.26. **HRMS** (*m/z*): calculated for $C_{18}H_{29}BrO_4SiNa^+$ $[M + Na]^+$: 439.0911, found 439.0910.



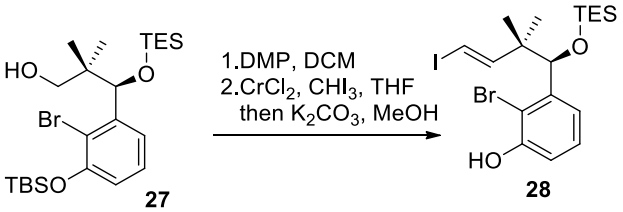
26 **26-1**

To a solution of **26** (680 mg, 1.63 mmol) in DCM (15 mL), was added Et_3N (0.70 mL, 5.03 mmol) and TESOTf (0.60 mL, 2.66 mmol) at –50 ℃. The reaction mixture was allowed to slowly warm to –30 ℃ and stirred at –30 ℃ for 2h before it was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL) at –50 ℃. After the solution was warmed to room temperature and stirred until clear phases were obtained (1.5 h), the aqueous phase was extracted with DCM (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **26-1** (848 mg, 98%) as a colorless oil. R_f = 0.90 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = -10.8 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.17 – 7.08 (m, 2H), 6.82 (dd, *J* = 5.6, 3.9 Hz, 1H), 5.70 (s, 1H), 3.71 (s, 3H), 1.19 (s, 3H), 1.08 (s, 3H), 1.05 (s, 9H), 0.81 (t, *J* = 7.9 Hz, 9H), 0.46 – 0.38 (m, 6H), 0.23 (s, 3H) , 0.23 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.17, 151.96, 142.19, 126.59, 123.62, 119.23, 117.88, 51.78,

50.06, 25.87, 22.90, 18.46, 18.19, 6.62, 4.63, -4.19, -4.28. **HRMS** (*m/z*): calculated for $C_{24}H_{43}BrO_4Si_2Na^+$ $[M + Na]^+$: 553.1775, found 553.1774.



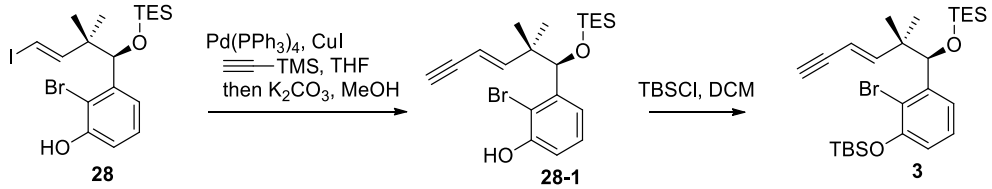
To a solution of ester **26-1** (548 mg, 1.03 mmol) in DCM (15 mL) was added DIBAL-H (2 mL, 1.5 M in toluene) at –78 °C. The reaction mixture was allowed to warm to –40 ℃ and stirred for 1h before it was re-cooled to –78 ℃ and quenched by addition of MeOH (1 mL). Aqueous Rochelle's salt (20 mL) was added, and the solution was stirred for 2 h at room temperature. The aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **27** (485 mg, 95%) as a colorless oil. R_f = 0.20 (silica gel, 3% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 2.6 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 – 7.13 (m, 2H), 6.83 (dd, *J* = 7.6, 1.9 Hz, 1H), 5.23 (s, 1H), 3.75 (dd, *J* = 11.0, 3.5 Hz, 1H), 3.51 (dd, *J* = 6.9, 3.7 Hz, 1H), 3.27 (dd, *J* = 11.0, 6.9 Hz, 1H), 1.15 (s, 3H), 1.05 (s, 9H), 0.84 (t, *J* = 7.9 Hz, 9H), 0.76 (s, 3H), 0.55 – 0.41 (m, 6H), 0.24 (s, 3H) , 0.24 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.09, 142.70, 127.04, 122.80, 119.19, 117.78, 80.76, 70.48, 40.46, 25.87, 23.39, 20.49, 18.46, 6.62, 4.53, -4.17, -4.29. **HRMS** (*m/z*): calculated for $C_{23}H_{43}BrO_3Si_2Na^+$ $[M + Na]^+$: 525.1826, found 525.1827.



To a solution of **27** (210 mg, 0.56 mmol) in DCM (10 mL) was added $NaHCO_3$ (200 mg, 2.38 mmol) and Dess-Martin periodinane (500 mg, 1.2 mmol) at 0 ℃. After being stirred for 1 h at room temperature, the reaction mixture was concentrated in *vacuo* and filtered through a pad of silica gel to afford the corresponding aldehyde as a colorless oil, which was used directly in the next step without further purification.

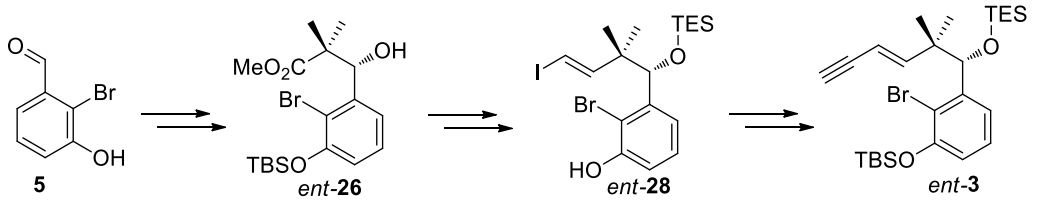
To a solution of anhydrous $CrCl_2$ (510 mg, 4.15 mmol) in THF (5 mL) was added a solution of the aldehyde and iodoform (616 mg, 1.76 mmol,) in THF (5 mL). After being stirred overnight, the reaction mixture was quenched by addition of saturated aqueous solution of NH_4Cl (20 mL) and extracted with DCM (3 x 30mL). The combined organic layers were concentrated in *vacuo* and the residue was dissolved in MeOH (5 mL). To this solution, K_2CO_3 (200 mg, 1.43 mmol) was added and the mixture was stirred at room temperature for 1 h before it was quenched by saturated aqueous

solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **28** (145 mg, 68%, two steps) as a colorless oil. R_f = 0.20 (silica gel, 3% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 52.3 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.18 (t, *J* = 7.9 Hz, 1H), 7.03 – 6.88 (m, 2H), 6.71 (d, *J* = 14.7 Hz, 1H), 5.86 (d, *J* = 14.7 Hz, 1H), 5.63 (s, 1H), 4.87 (s, 1H), 1.06 (s, 3H), 1.00 (s, 3H), 0.84 (t, *J* = 7.9 Hz, 9H), 0.54 – 0.38 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.31, 151.40, 141.84, 127.54, 122.37, 114.74, 112.34, 78.80, 74.92, 47.53, 23.57, 21.95, 6.71, 4.71. **HRMS** (*m/z*): calculated for $C_{18}H_{28}BrIO_2SiNa^+$ [M + $Na]^+$: 532.9979, found 532.9974.

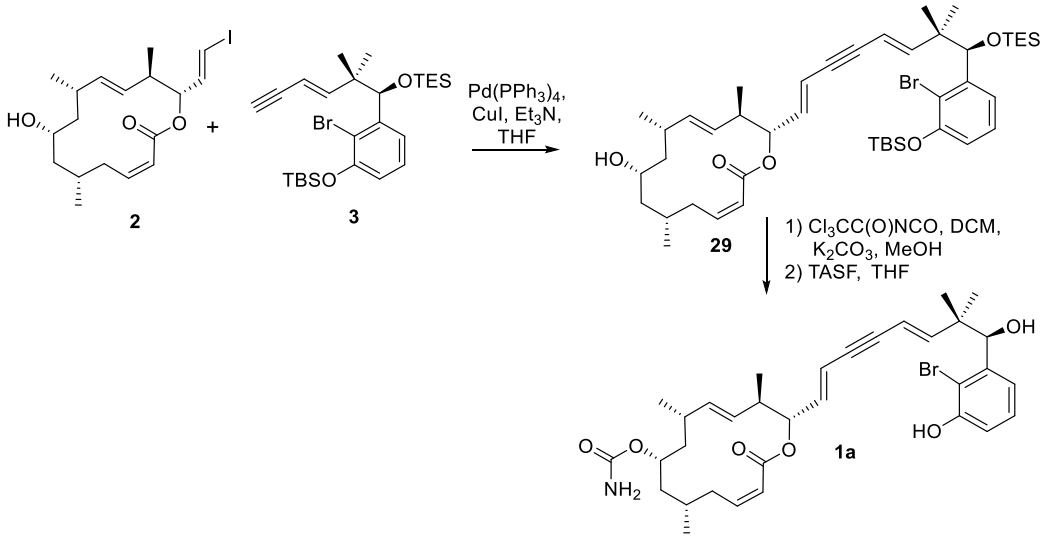


To a solution of **28** (50 mg, 0.10 mmol) and Et_3N (14 uL, 0.10 mmol) in dry THF (2 mL) under argon was added trimethylsilylacetylene (42 uL, 0.30 mmol), Pd (PPh_3)$_4$ (11.5 mg, 0.01 mmol) and CuI (3.8 mg, 0.02 mmol) at room temperature. After being stirred for 2.5 h at room temperature, the reaction mixture was concentrated in *vacuo* and dissolved in MeOH (5 mL). To this solution, K_2CO_3 (40 mg, 0.29 mmol) was added and the mixture was stirred for 1 h at room temperature before it was quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **28-1** (36 mg, 90%) as a colorless oil. R_f = 0.20 (silica gel, 3% ethyl acetate in hexane).

To a solution of compound **28-1** (12 mg, 0.03 mmol) and imidazole (10 mg, 0.15 mmol) in DCM (3 mL) was added TBSCl (25 mg, 0.17 mmol) at 0 ℃. After a catalytic amount of DMAP (one crystal) was added, the reaction mixture was stirred at room temperature for 2 h and then quenched by addition of saturated aqueous solution of NH_4Cl (2 mL) and DCM (10 mL). Layers were separated and the aqueous phase was extracted with DCM (3 x 15 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to produce **3** (15 mg, 98%) as a colorless oil. R_f = 0.80 (silica gel, 3% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 55.8 (*c* 0.5, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.8 Hz, 1H), 7.03 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.79 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.51 (d, *J* = 16.5 Hz, 1H), 5.27 (dd, *J* = 16.5, 2.2 Hz, 1H), 5.06 (s, 1H), 2.80 (d, *J* = 2.0 Hz, 1H), 1.09 (s, 3H), 1.04 (s, 9H), 0.98 (s, 3H), 0.82 (d, *J* = 7.9 Hz, 9H), 0.54 – 0.38 (m, 6H), 0.23 (s, 3H), 0.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.64, 151.81, 143.17, 126.61, 123.13, 119.04, 106.57, 83.12, 78.90, 75.98, 44.00, 29.71, 25.90, 24.33, 22.01, 18.47, 6.72, 4.68, -4.16, -4.27. **HRMS** (*m/z*): calculated for $C_{26}H_{43}BrO_2Si_2Na^+$ $[M + Na]^+$: 545.1877, found 545.1882.



***ent*-3** was synthesized according to the procedures described for **3**. The NMR analytical data of *ent*-**3** were identical to the data of **3**.

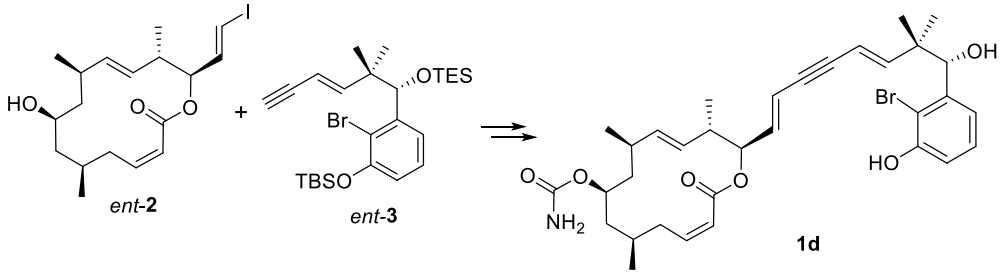


To a solution of **2** (9 mg, 0.02 mmol), **3** (20 uL, 0.04 mmol), and Et_3N (3 uL, 0.02 mmol) in dry THF (2 mL) under argon was added Pd $(PPh_3)_4$ (12 mg, 0.01 mmol) and CuI (8 mg, 0.05 mmol) at room temperature. After being stirred for 3 h at room temperature, the reaction was concentrated in *vacuo* before was quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **29** (13 mg, 74%) as a colorless oil. R_f = 0.60 (silica gel, 25% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 31.0 (*c* 1.0, MeOH); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.8 Hz, 1H), 7.04 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.79 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.42 (d, *J* = 16.4 Hz, 1H), 6.28 (td, *J* = 12.8, 3.4 Hz, 1H), 6.02 (dd, *J* = 15.8, 8.0 Hz, 1H), 5.90 – 5.80 (m, 2H), 5.40 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.24 – 5.11 (m, 2H), 5.09 – 4.98 (m, 2H), 3.77 (td, *J* = 14.2, 4.7 Hz, 1H), 3.42 (t, *J* = 10.6 Hz, 1H), 2.35 – 2.26 (m, 1H), 2.25 – 2.11 (m, 2H), 2.00 – 1.91 (m, 1H), 1.65 – 1.61 (m, 2H), 1.40 – 1.30 (m, 3H), 1.11 (s, 3H), 1.08 – 1.03 (m, 12H), 1.01 – 0.94 (m, 9H), 0.84 (t, *J* = 7.9 Hz, 9H), 0.53 – 0.37 (m, 6H), 0.23 (d, *J* = 4.8 Hz, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 165.21, 151.88, 151.22, 145.98, 143.30, 138.71, 137.48, 132.12, 126.63, 123.17, 121.98, 119.05, 117.67, 114.09, 107.53, 90.50, 86.12, 79.08, 76.12, 66.06, 46.13, 44.12, 43.25, 43.10, 34.52, 31.28, 29.72, 27.17, 25.93, 24.39, 22.37, 20.06, 18.49, 17.66, 6.72, 4.77, -4.15, -4.24. **HRMS** (*m/z*): calculated for $C_{44}H_{69}BrO_5Si_2Na^+$ $[M + Na]^+$: 835.3759, found

835.3762.

To a solution of **29** (13 mg, 0.016 mmol) in DCM (4 mL) was added trichloroacetylisocyanate (2.3 μL, 0.019 mmol) at room temperature. After being stirred for 30 min and concentrated in *vacuo* the mixture was added MeOH (4 mL) and K_2CO_3, and stirred for 1 h. The reaction mixture was quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give the corresponding carbamate (11 mg, 93%) as a colorless oil.

To a solution of carbamate (11 mg, 0.015 mmol) in THF (2 mL) was added a solution of TASF (15 mg, 0.055 mmol) in THF (1 mL) at 0 ℃. After being stirred at 0 ℃ for 36 h, the reaction was quenched with saturated aqueous solution of NH_4Cl (15 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give compound **1a** (7.6 mg, 82%) as a colorless oil. R_f = 0.20 (silica gel, 40% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 66.0 (*c* 0.1, MeOH);

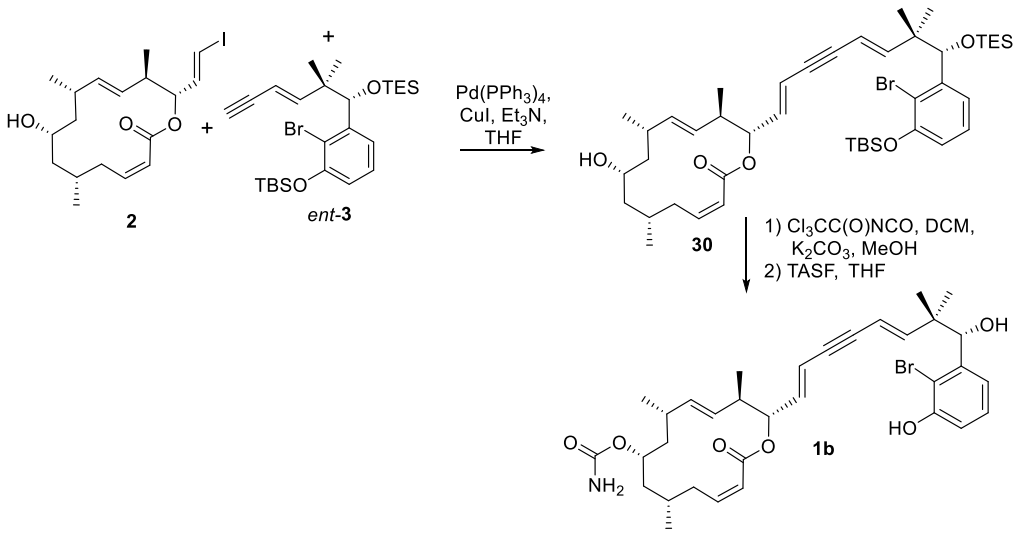


1d was synthesized according to the procedures for the synthesis of **1a**.
Optical rotation for **1d:** $[\alpha]_D^{20}$ = -62.86 (*c* 0.1, MeOH)

NMR analytical data for **1a** and **1d** are identical:

^{1}H NMR (400 MHz, DMSO-*d6*) δ 10.08 (s, 1H), 7.13 (t, *J* = 7.9 Hz, 1H), 6.83 (dd, *J* = 7.8, 2.2 Hz, 2H), 6.36 (d, *J* = 16.4 Hz, 1H), 6.13 (td, *J* = 12.1, 3.1 Hz, 1H), 6.06 (dd, *J* = 15.8, 7.6 Hz, 1H), 5.99 – 5.88 (m, 2H), 5.53 (d, *J* = 4.4 Hz, 1H), 5.45 (dd, *J* = 16.4, 2.0 Hz, 1H), 5.21 (dd, *J* = 15.0, 9.4 Hz, 1H), 5.13 – 4.96 (m, 2H), 4.88 (d, *J* = 4.4 Hz, 1H), 4.53 – 4.41 (m, 1H), 3.47 – 3.36 (m, 1H), 2.29 – 2.17 (m, 1H), 2.05 – 1.93 (m, 1H), 1.89 – 1.81 (m, 1H), 1.80 – 1.68 (m, 1H), 1.44 – 1.32 (m, 2H), 1.09 – 0.99 (m, 5H), 0.99 – 0.91 (m, 6H), 0.91 – 0.84 (m, 6H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 164.08, 156.59, 153.18, 151.55, 143.13, 142.38, 139.55, 136.29, 131.92, 126.79, 122.19, 120.00, 114.25, 113.28, 111.60, 106.71, 90.34, 86.28, 76.45, 75.60, 68.21, 44.04, 42.98, 41.71, 40.98, 33.17, 31.20, 26.76, 24.00, 22.34, 21.92, 19.81, 17.34.

HRMS (*m/z*): calculated for $C_{33}H_{42}BrNO_6Na^+$ [M + Na]$^+$: 650.2088, found 650.2087.



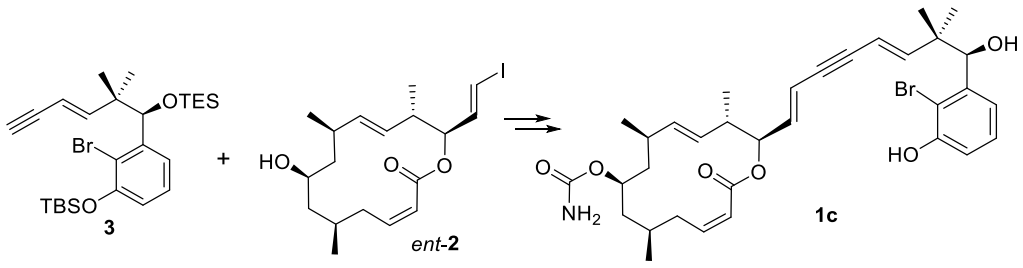
30 and **1b** were synthesized according to the procedures described for the synthesis of **29** and **1a**, respectively.

Analytical data for **30**: (Yield = 68%) R_f = 0.60 (silica gel, 25% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 25.0 (*c* 0.7, CHCl3);

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.9 Hz, 1H), 7.04 (d, *J* = 6.5 Hz, 1H), 6.79 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.42 (d, *J* = 16.4 Hz, 1H), 6.33 – 6.19 (m, 1H), 6.02 (dd, *J* = 15.8, 8.0 Hz, 1H), 5.92 – 5.80 (m, 2H), 5.40 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.26 – 5.11 (m, 2H), 5.09 – 4.99 (m, 2H), 3.86 – 3.68 (m, 1H), 3.42 (t, *J* = 10.9 Hz, 1H), 2.32 – 2.24 (m, 1H), 2.25 – 2.09 (m, 2H), 1.99 – 1.92 (m, 1H), 1.72 – 1.60 (m, 2H), 1.38 – 1.30 (m, 3H), 1.11 (s, 3H), 1.08 – 1.02 (m, 12H), 1.02 – 0.93 (m, 9H), 0.84 (t, *J* = 7.9 Hz, 9H), 0.54 – 0.39 (m, 6H), 0.23 (d, *J* = 4.8 Hz, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 165.21, 151.88, 151.23, 145.98, 143.30, 138.71, 137.48, 132.13, 126.63, 123.17, 121.98, 119.06, 117.67, 114.10, 107.53, 90.51, 86.12, 79.09, 76.13, 66.07, 46.13, 44.12, 43.25, 43.10, 34.53, 31.29, 29.72, 27.18, 25.93, 24.40, 22.37, 20.07, 18.49, 17.67, 6.73, 4.77 , -4.15, -4.24.

HRMS (*m/z*): calculated for $C_{44}H_{69}BrO_5Si_2Na^+$ [M + Na]$^+$: 835.3759, found 835.3757.

1b: (Yield = 65%). R_f = 0.20 (silica gel, 40% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 12.0 (*c* 0.1, MeOH);



1c was synthesized according to the procedures for the synthesis of **1a**. Analytical data for **1c:** $[\alpha]_D^{20}$ = –13.0 (*c* 0.1, MeOH);
NMR and Mass data for **1b** and **1c** are identical:

^{1}H NMR (400 MHz, DMSO-*d6*) δ 10.06 (s, 1H), 7.13 (t, *J* = 7.9 Hz, 1H), 6.83 (dd, *J* = 7.9, 2.9 Hz, 2H), 6.36 (d, *J* = 16.4 Hz, 1H), 6.18 – 6.10 (m, 1H), 6.06 (dd, *J* = 15.8, 7.6 Hz, 1H), 6.00 – 5.90 (m, 2H), 5.52 (d, *J* = 4.4 Hz, 1H), 5.50 – 5.41 (m, 1H), 5.22 (dd, *J* = 15.0, 9.3 Hz, 1H), 5.14 – 5.00 (m, 2H), 4.89 (d, *J* = 4.4 Hz, 1H), 4.51 – 4.41 (m, 1H), 3.48 – 3.35 (m, 1H), 2.28 – 2.18 (m, 1H), 2.05 – 1.92 (m, 1H), 1.90 – 1.80 (m, 1H), 1.80 – 1.68 (m, 1H), 1.45 – 1.32 (m, 2H), 1.11 – 0.99 (m, 5H), 0.99 – 0.91 (m, 6H), 0.91 – 0.84 (m, 6H).**^{13}C NMR** (100 MHz, DMSO-*d6*) δ 164.08, 156.59, 153.18, 151.55, 143.13, 142.38, 139.54, 136.29, 131.91, 126.78, 122.19, 120.00, 114.26, 113.28, 111.61, 106.70, 90.34, 86.28, 76.46, 75.61, 68.24, 44.07, 42.97, 41.70, 40.98, 33.17, 31.21, 26.77, 24.02, 22.33, 21.92, 19.81, 17.34.

HRMS (*m/z*): calculated for $C_{33}H_{42}BrNO_6Na^+$ $[M + Na]^+$: 650.2088, found 650.2100.

Biological Evaluation of Synthetic Compounds

Material and Methods

Compounds: Four synthetic compounds were dissolved in DMSO. The final concentration of DMSO in the assay was below 0.01%.

Cell culture: Breast carcinoma cell line MCF7, neuroblastoma cell line SH-SY5Y, cervical adenocarcinoma cell line HeLa, colon carcinoma cell lines HT-29 and RKO, immortalized human hepatocyte cell line MIHA, lung adenocarcinoma cell line H1299, prostate carcinoma cell line PC-3 and T lymphocyte cell line Jurkat were obtained from American Type Culture Collection (Manassas, VA). These cell lines were cultured in DMEM containing supplements (10%FBS, penicillin/streptomycin and L-glutamine).

The effect of the synthetic compounds on the proliferation of cancer cell lines: Cells were seeded into 96-well plates overnight and cultured with incremental concentrations of the compounds in the medium containing 1% FBS for another 72 h. Cell proliferation was measured using 3-(4, 5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyohenyl)-2-(4-sulfophenyl-2H-tetrazolium) (MTS) assay. (Promega Co., Madison, WI). According to the manufacturer's instruction, 20 μL of CellTiter96 Aqueous solution was added into each well containing 100 μL medium and incubated at 37^{o}C for 4 hours. The absorbance at 490nm was measured using an ELISA plate reader (Bio-Rad microplate reader 680, Bio-Rad Laboratories, California, USA). The IC_{50} values were calculated by Prism 5 (GraphPad Prism software Inc, USA).

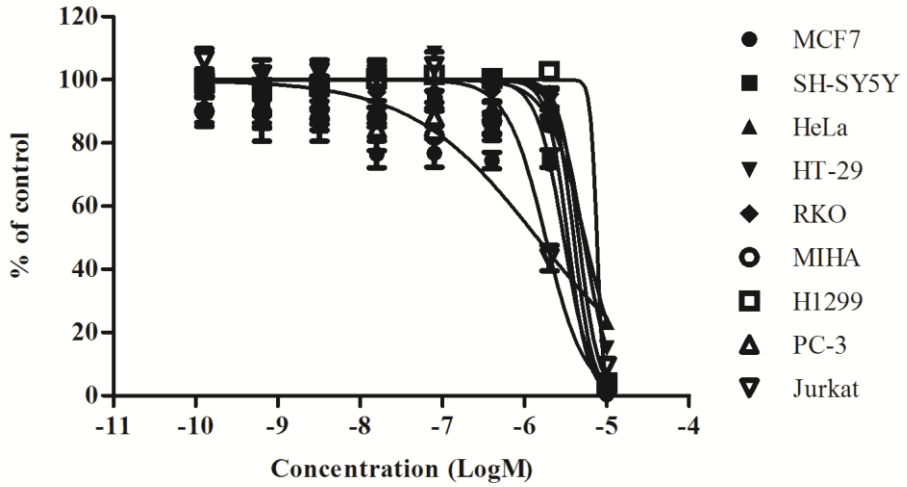


Figure 1. Effect of **1a** on the proliferation of cancer cell lines. Effect of **1a** on proliferation of cancer cell lines was assessed by MTS assay. Cells were incubated for 72 hours in the presence of various concentrations of **1a**. Cell proliferation was measured by MTS assay. Representative data of three experiments were shown, and each concentration was repeated six times in each experiment.

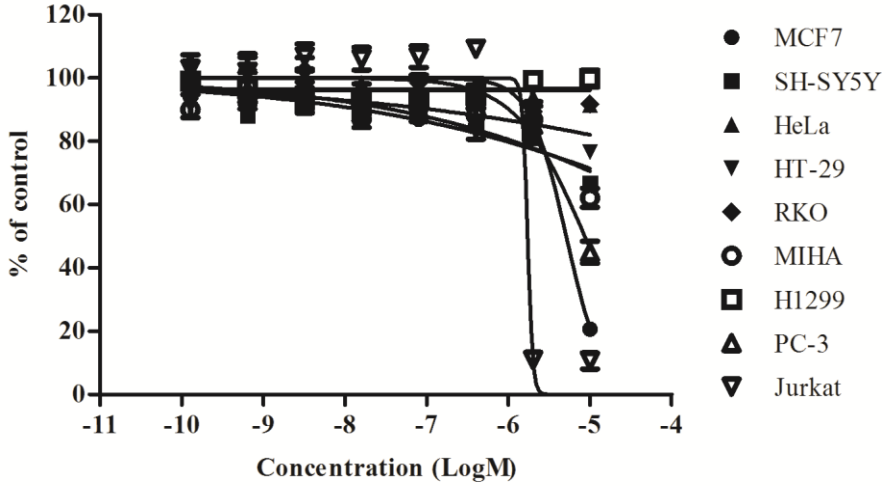


Figure 2. Effect of **1b** on the proliferation of cancer cell lines. Effect of **1b** on proliferation of cancer cell lines was assessed by MTS assay. Cells were incubated for 72 hours in the presence of various concentrations of **1b**. Cell proliferation was measured by MTS assay. Representative data of three experiments were shown, and each concentration was repeated six times in each experiment.

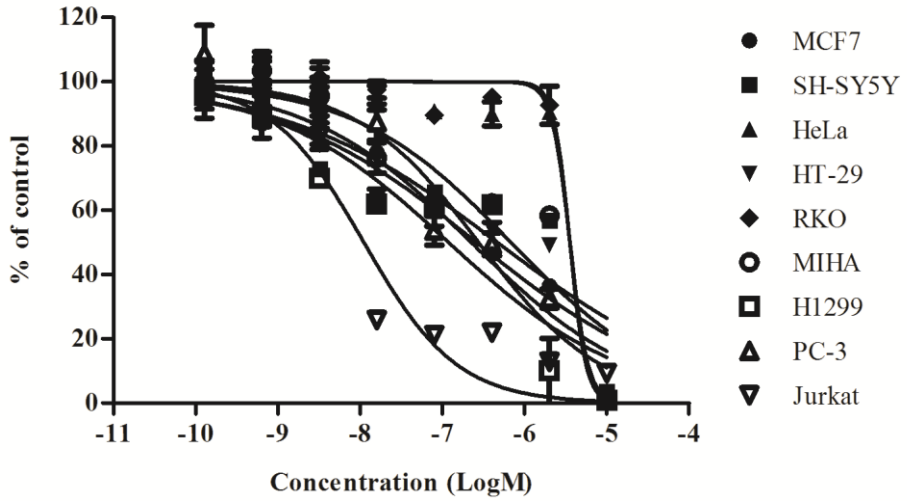


Figure 3. Effect of **1c** on the proliferation of cancer cell lines. Effect of **1c** on proliferation of cancer cell lines was assessed by MTS assay. Cells were incubated for 72 hours in the presence of various concentrations of **1c**. Cell proliferation was measured by MTS assay. Representative data of three experiments were shown, and each concentration was repeated six times in each experiment.

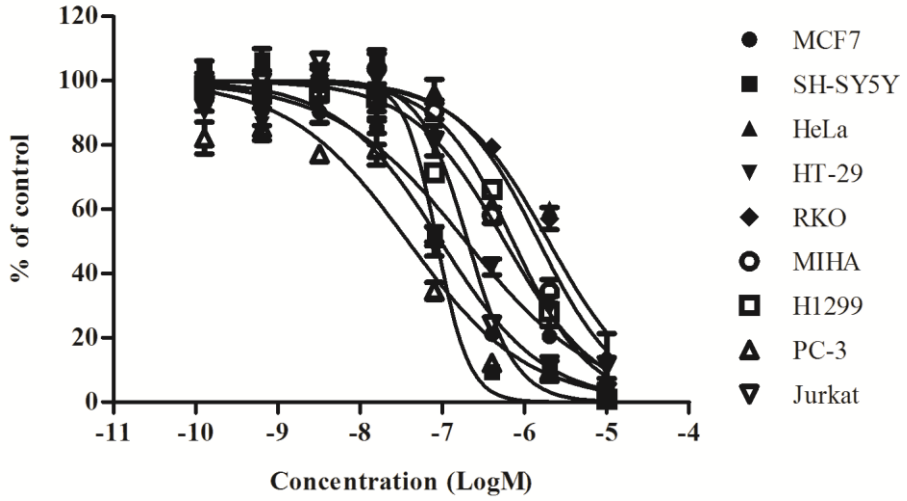
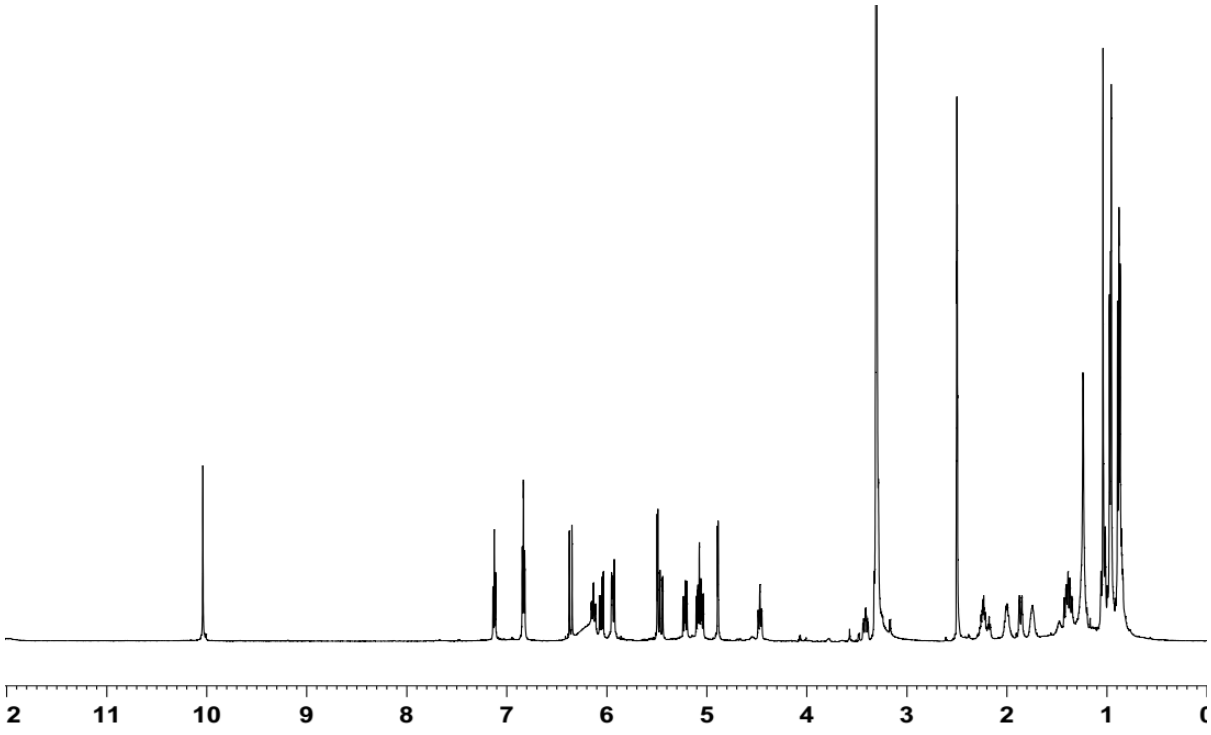


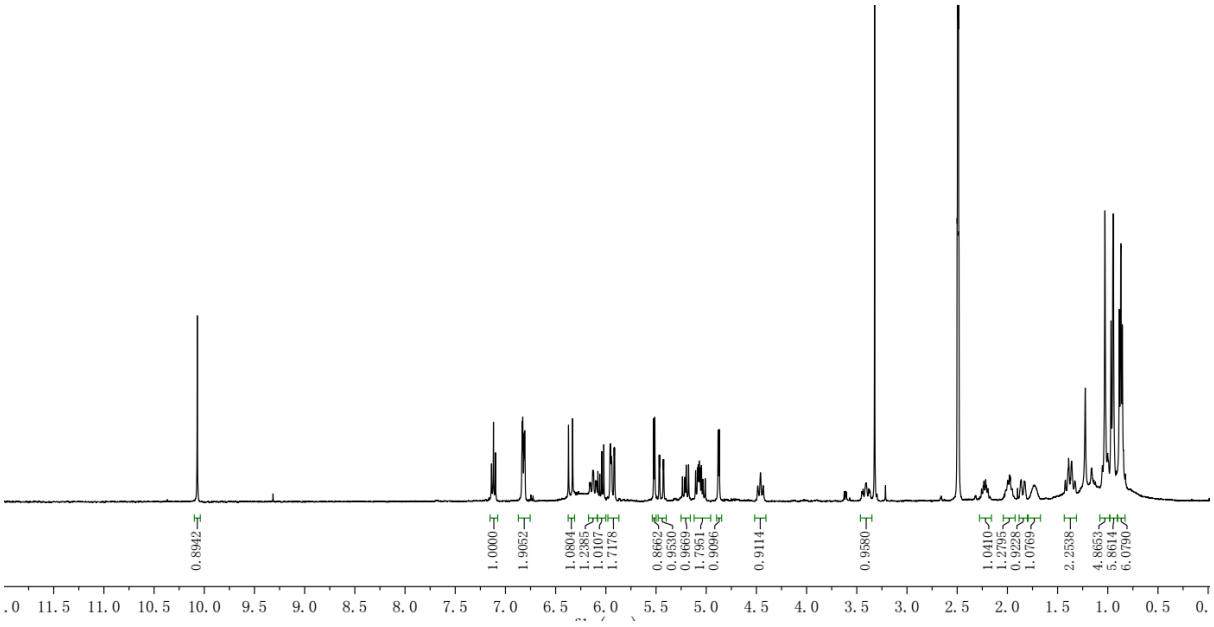
Figure 4. Effect of **1d** on the proliferation of cancer cell lines. Effect of **1d** on proliferation of cancer cell lines was assessed by MTS assay. Cells were incubated for 72 hours in the presence of various concentrations of **1d**. Cell proliferation was measured by MTS assay. Representative data of three experiments were shown, and each concentration was repeated six times in each experiment.

^{1}H NMR Spectra of Natural and Synthetic Callyspongiolide

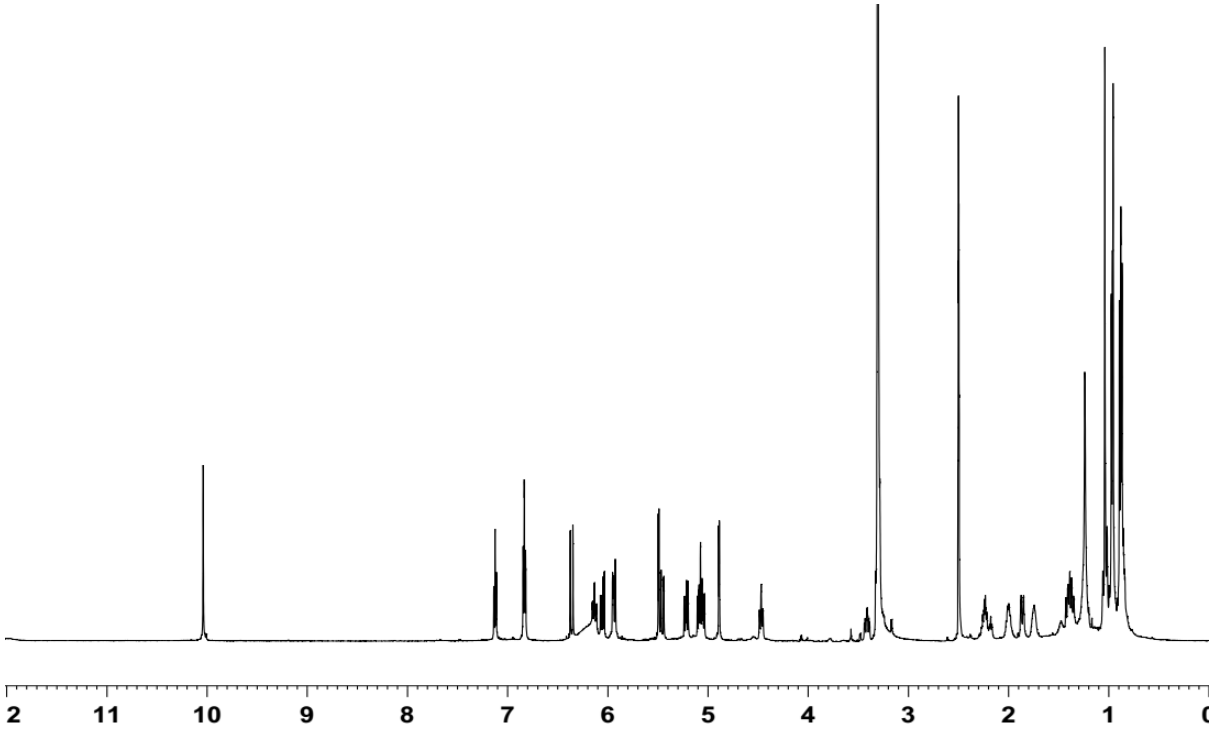
Callyspongiolide (Natural Product, 600 MHz, DMSO-*d6*)



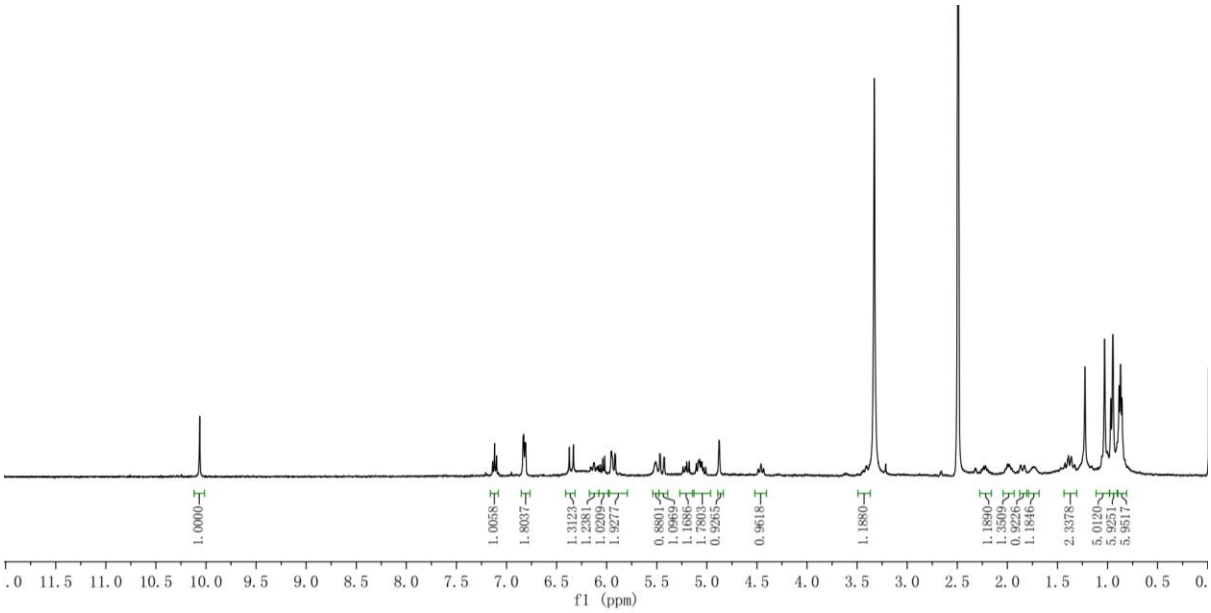
Callyspongiolide **1a** (Synthetic Sample **1a**, 400 MHz, DMSO-*d6*)



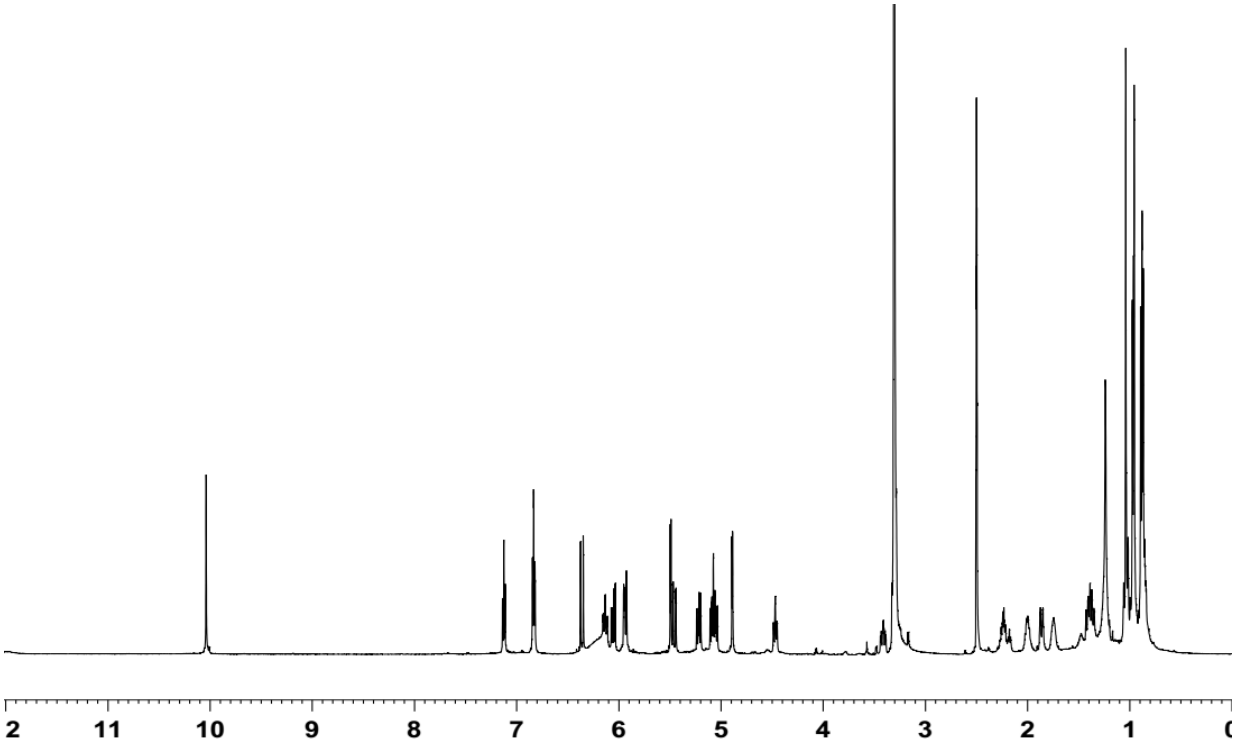
Callyspongiolide (Natural Product, 600 MHz, DMSO-*d6*)



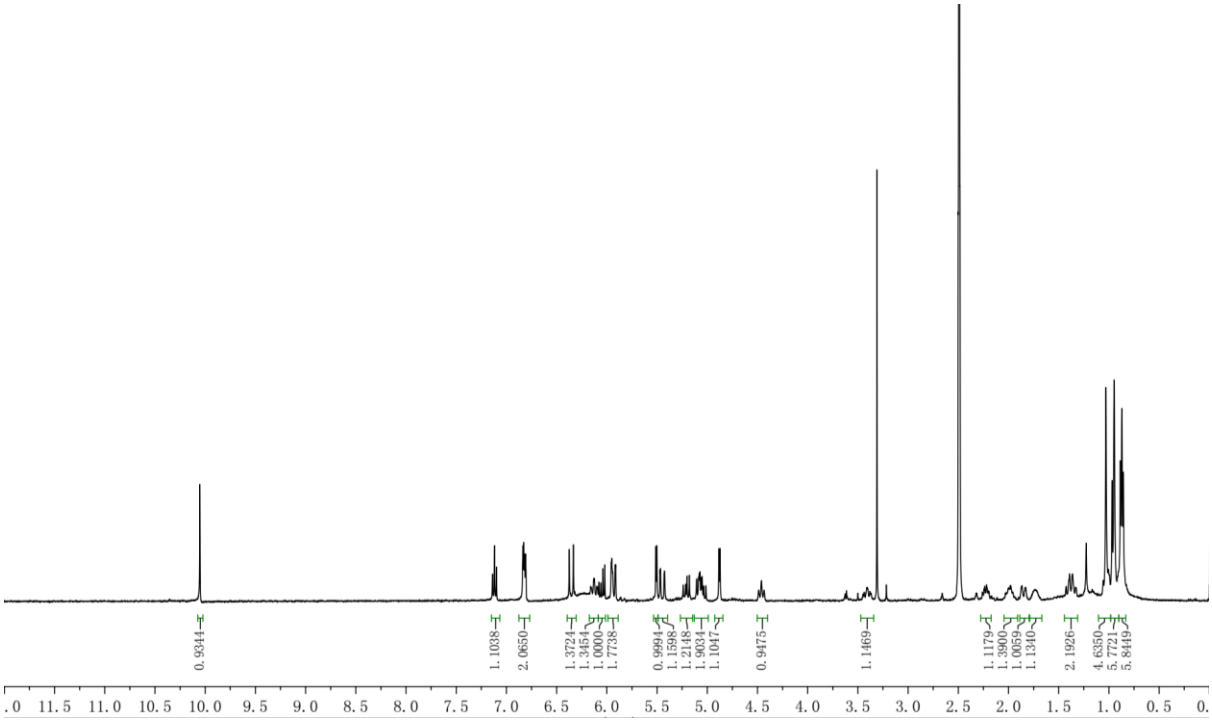
Callyspongiolide **1b** (Synthetic Sample **1b**, 400 MHz, DMSO-*d6*)



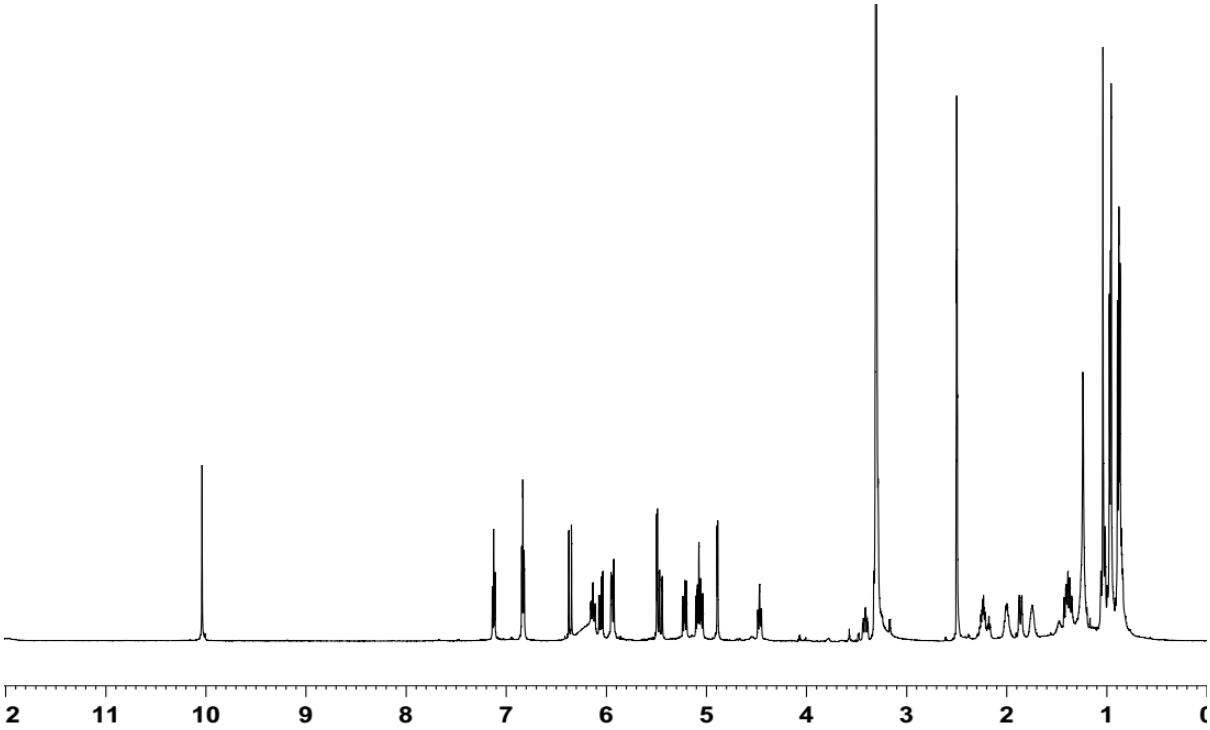
Callyspongiolide (Natural Product, 600 MHz, DMSO-*d6*)



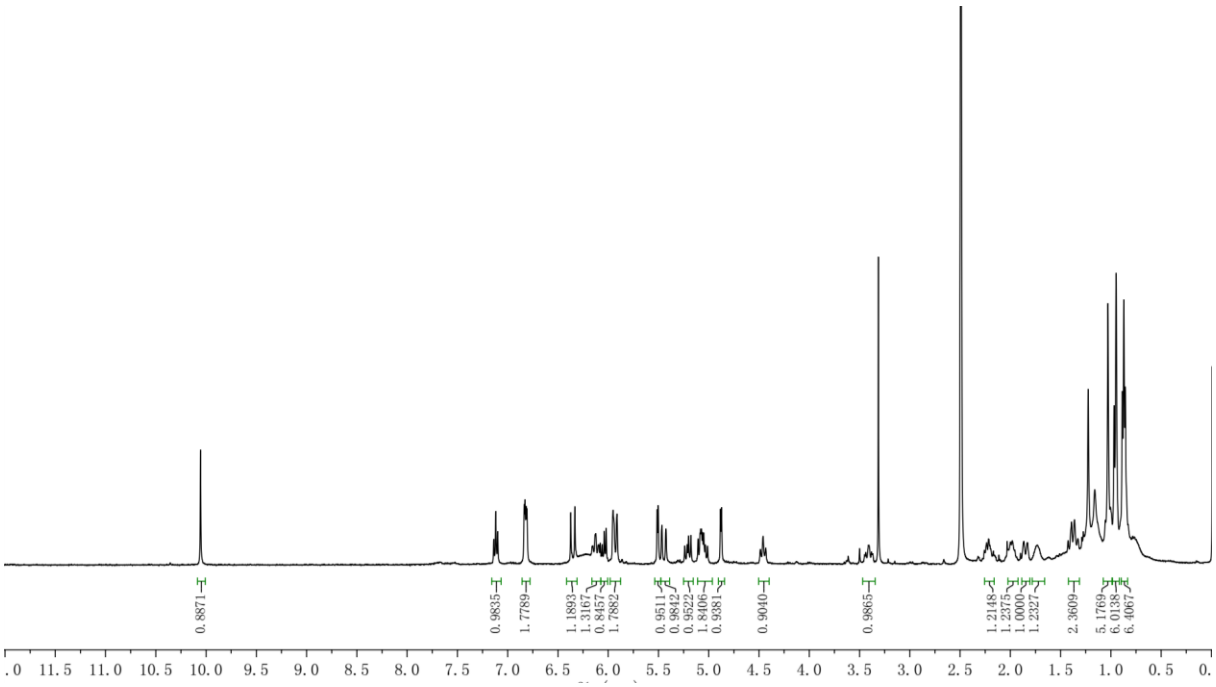
Callyspongiolide **1c** (Synthetic Sample **1c**, 400 MHz, DMSO-*d6*)



Callyspongiolide (Natural Product, 600 MHz, DMSO-*d6*)

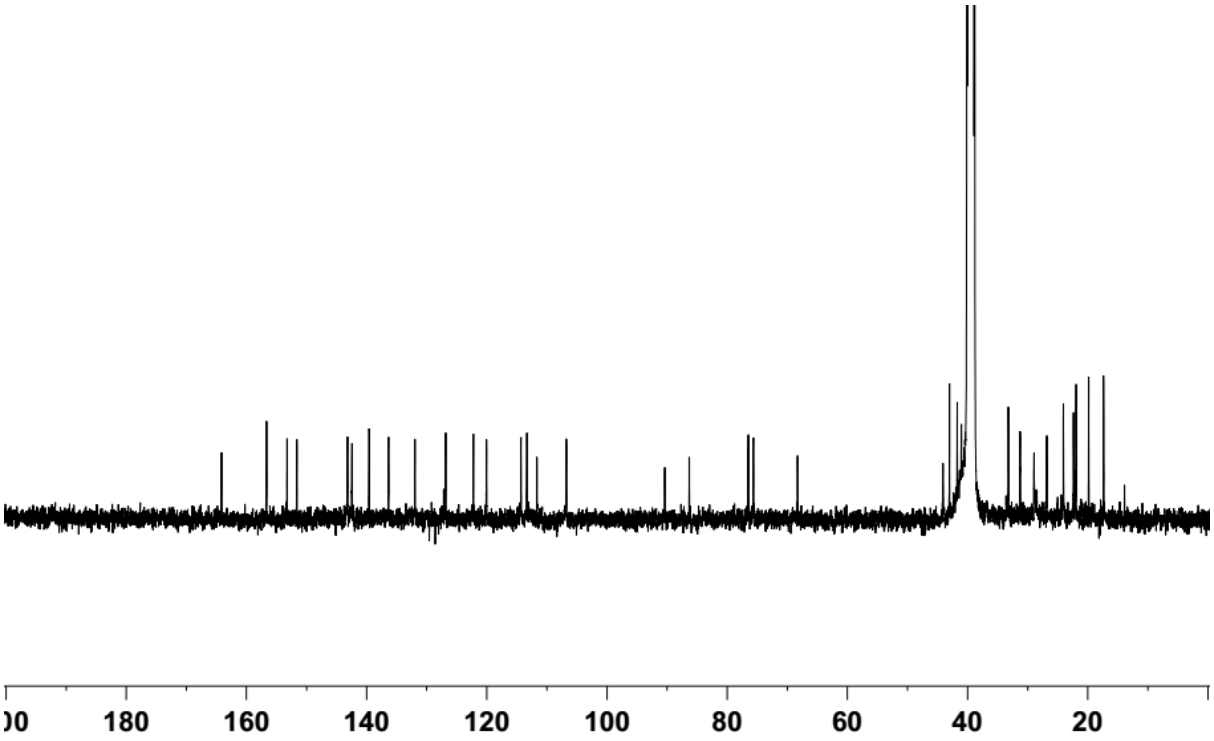


Callyspongiolide **1d** (Synthetic Sample **1d**, 400 MHz, DMSO-*d6*)

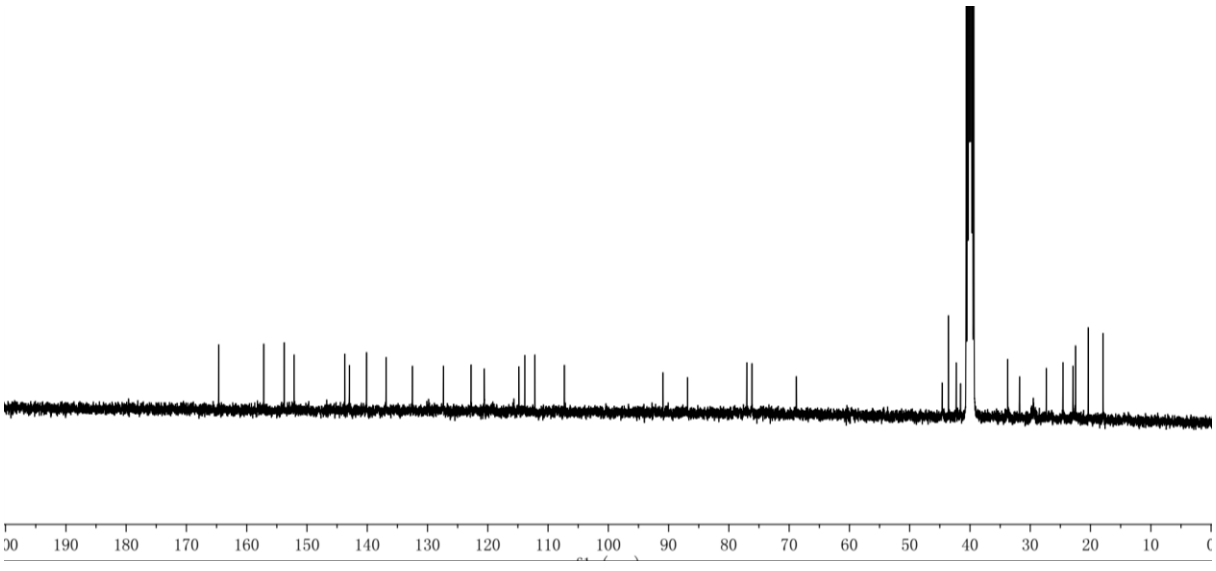


^{13}C NMR Spectra of Natural and Synthetic Callyspongiolides

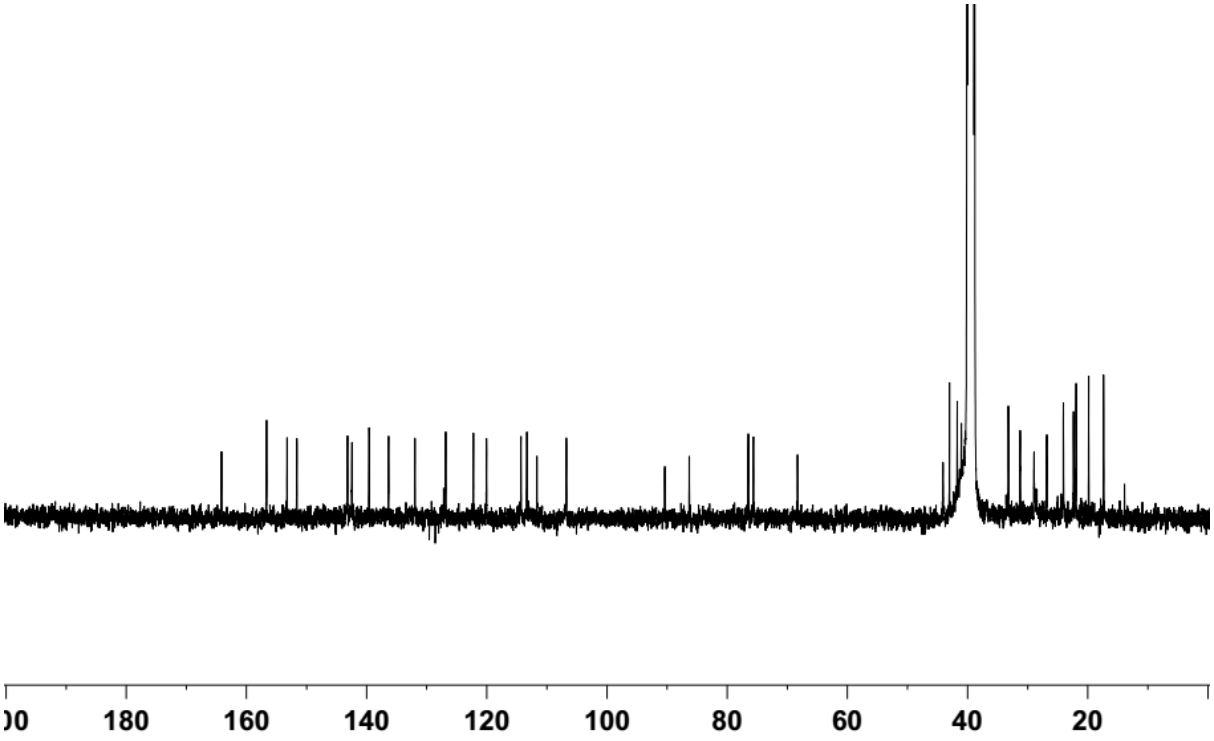
Callyspongiolide (Natural Product, 150 MHz, DMSO-d_6)



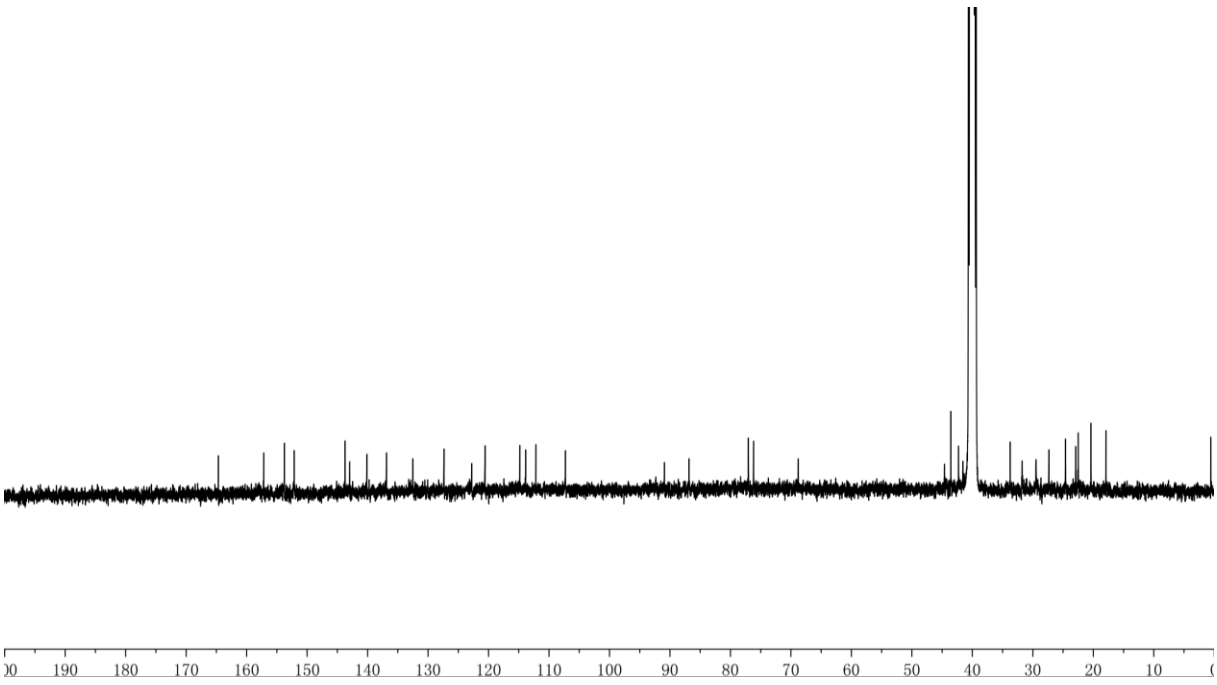
Callyspongiolide **1a** (Synthetic Sample **1a**, 100 MHz, DMSO-d_6)



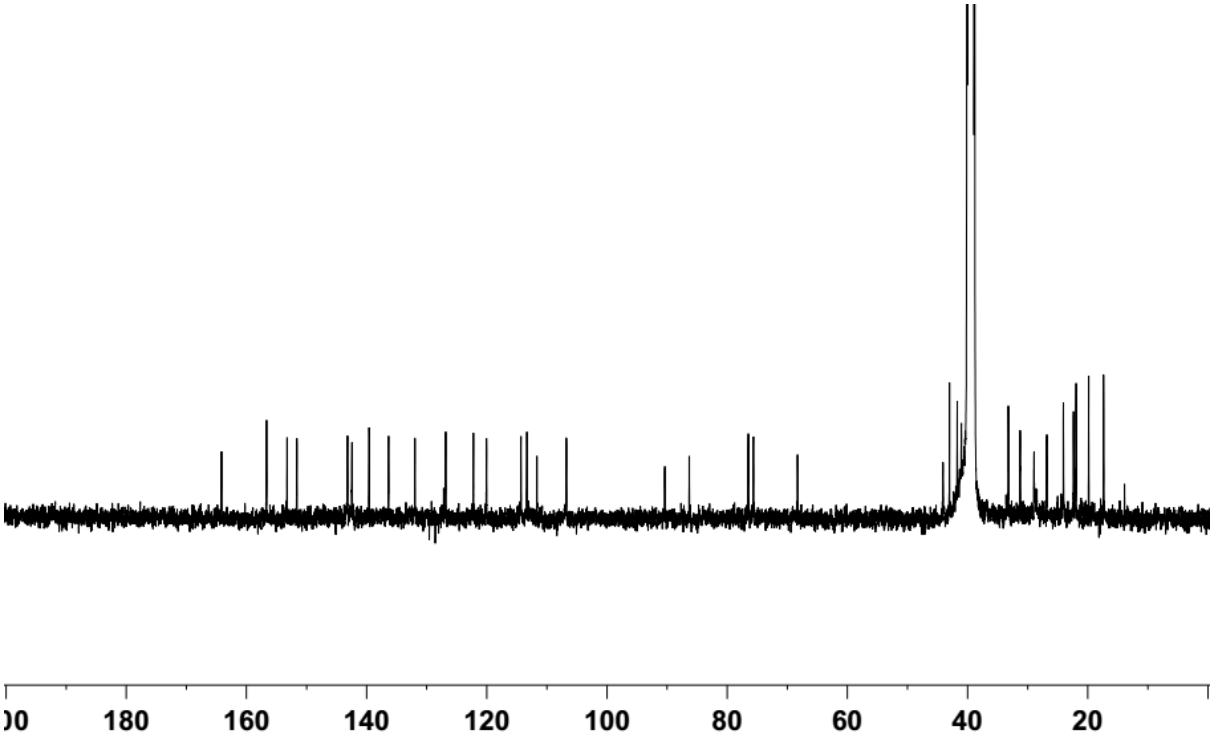
Callyspongiolide (Natural Product, 150 MHz, DMSO-d_6)



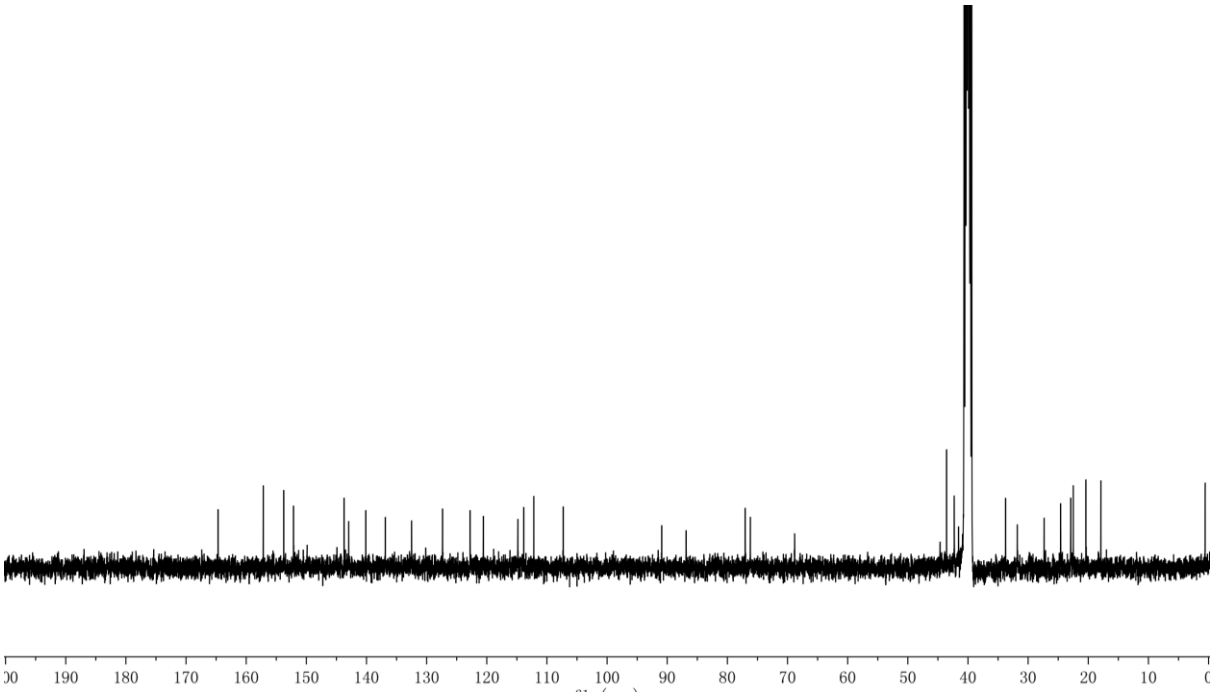
Callyspongiolide **1b** (Synthetic Sample **1b**, 100 MHz, DMSO-d_6)



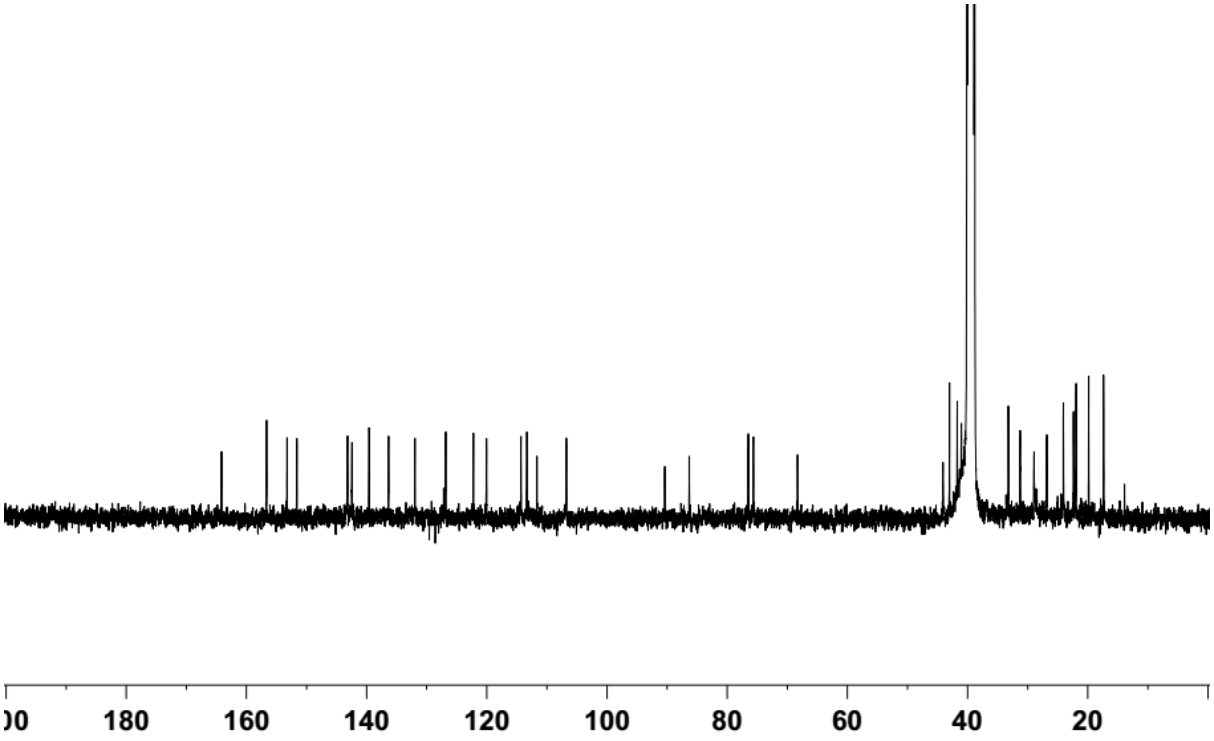
Callyspongiolide (Natural Product, 150 MHz, DMSO-d_6)



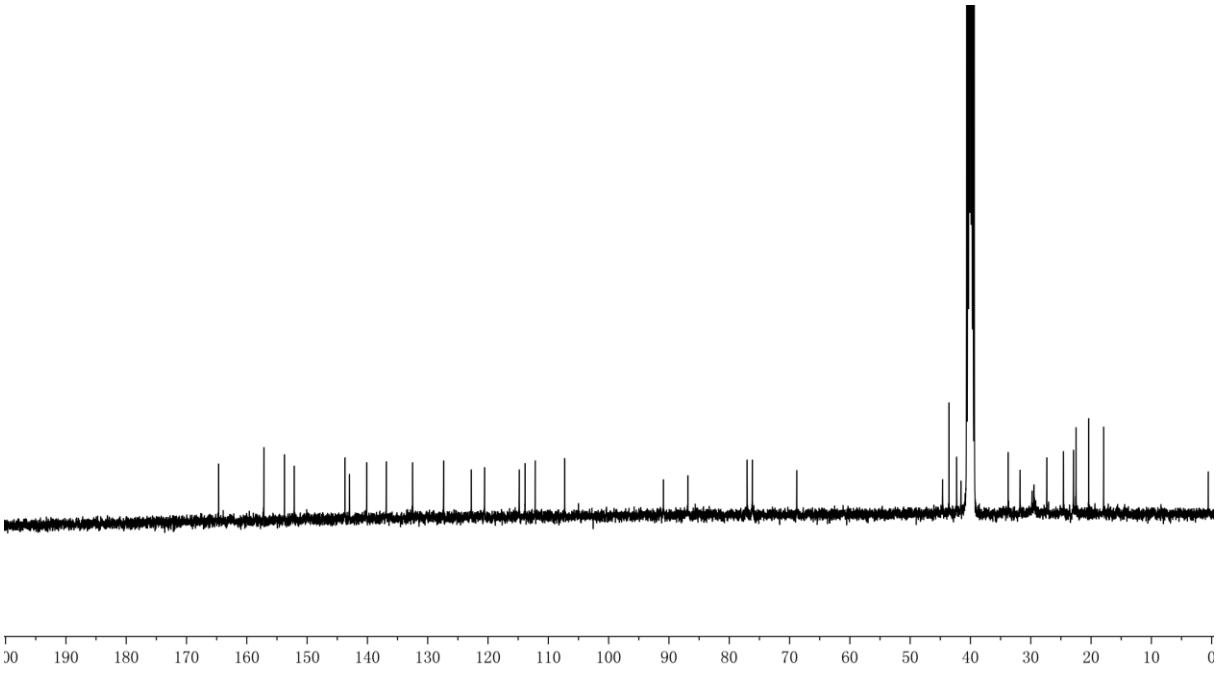
Callyspongiolide **1c** (Synthetic Sample **1c**, 100 MHz, DMSO-d_6)



Callyspongiolide (Natural Product, 150 MHz, DMSO-d_6)



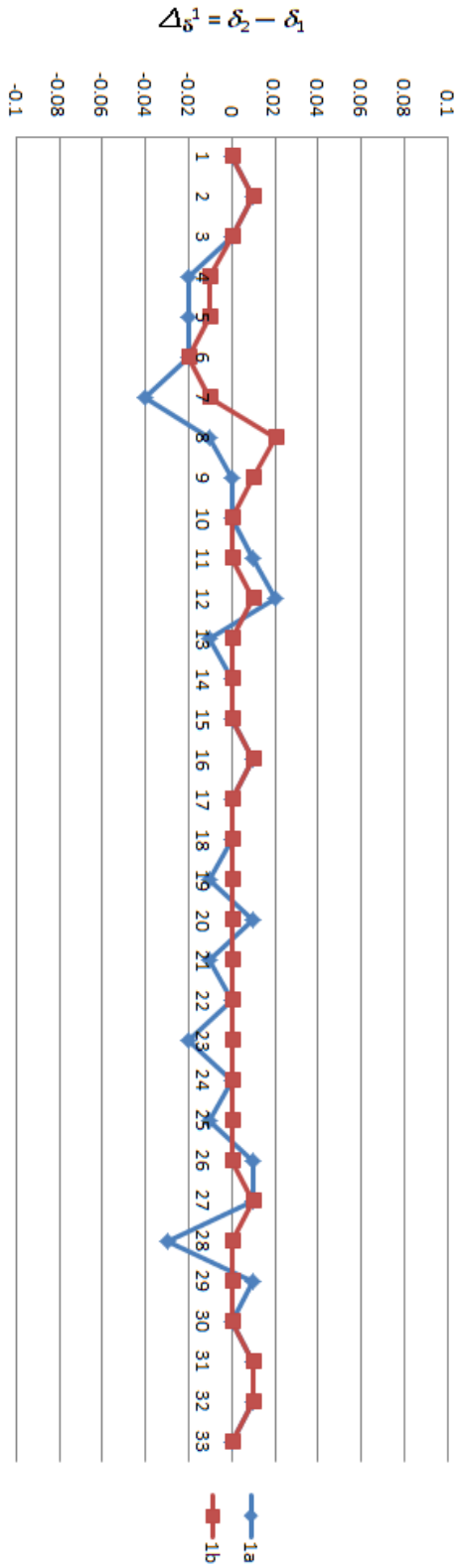
Callyspongiolide **1d** (Synthetic Sample **1d**, 100 MHz, DMSO-d_6)



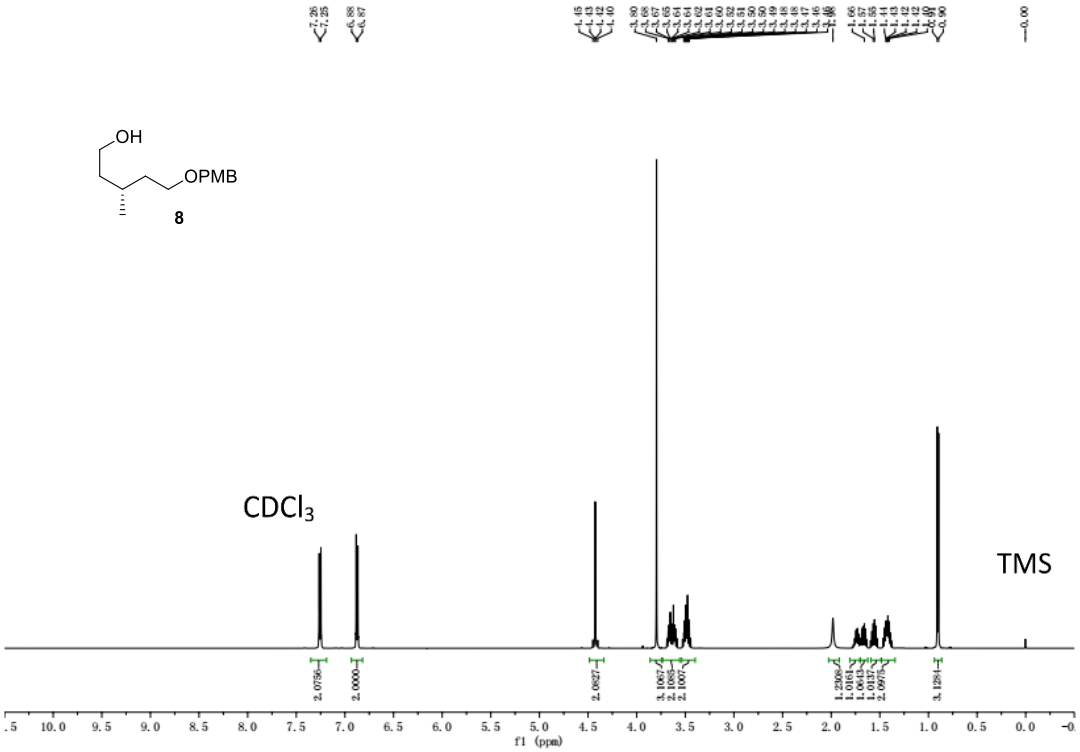
Comparison of ^{13}C NMR Data of Natural, Synthetic Callyspongiolides 1a and 1b

Carbon No.	Callyspongiolide (Natural product) (δ_1)	Callyspongiolide 1a (δ_2= record value + 0.07)	$\Delta_\delta^1 = \delta_2 - \delta_1$	Callyspongiolide 1b (δ_3= record value + 0.07)	$\Delta_\delta^2 = \delta_3 - \delta_1$
1	164.15	164.15	0	164.15	0
2	122.25	122.26	0.01	122.26	0.01
3	142.45	142.45	0	142.45	0
4	31.29	31.27	-0.02	31.28	-0.01
5	26.85	26.83	-0.02	26.84	-0.01
6	41.07	41.05	-0.02	41.05	-0.02
7	68.32	68.28	-0.04	68.31	-0.01
8	44.12	44.11	-0.01	44.14	0.02
9	33.23	33.23	0	33.24	0.01
10	136.36	136.36	0	136.36	0
11	131.98	131.99	0.01	131.98	0
12	41.76	41.78	0.02	41.77	0.01
13	75.68	75.67	-0.01	75.68	0
14	139.61	139.61	0	139.61	0
15	113.35	113.35	0	113.35	0
16	86.34	86.35	0.01	86.35	0.01
17	90.41	90.41	0	90.41	0
18	106.77	106.77	0	106.77	0
19	151.62	151.61	-0.01	151.62	0
20	43.04	43.05	0.01	43.04	0
21	76.53	76.52	-0.01	76.53	0
22	143.2	143.2	0	143.2	0
23	111.68	111.66	-0.02	111.68	0
24	153.25	153.25	0	153.25	0
25	114.33	114.32	-0.01	114.33	0
26	126.85	126.86	0.01	126.85	0
27	120.06	120.07	0.01	120.07	0.01
28	24.09	24.06	-0.03	24.09	0
29	22.4	22.41	0.01	22.4	0
30	19.88	19.88	0	19.88	0
31	21.98	21.99	0.01	21.99	0.01
32	17.4	17.41	0.01	17.41	0.01
33	156.66	156.66	0	156.66	0

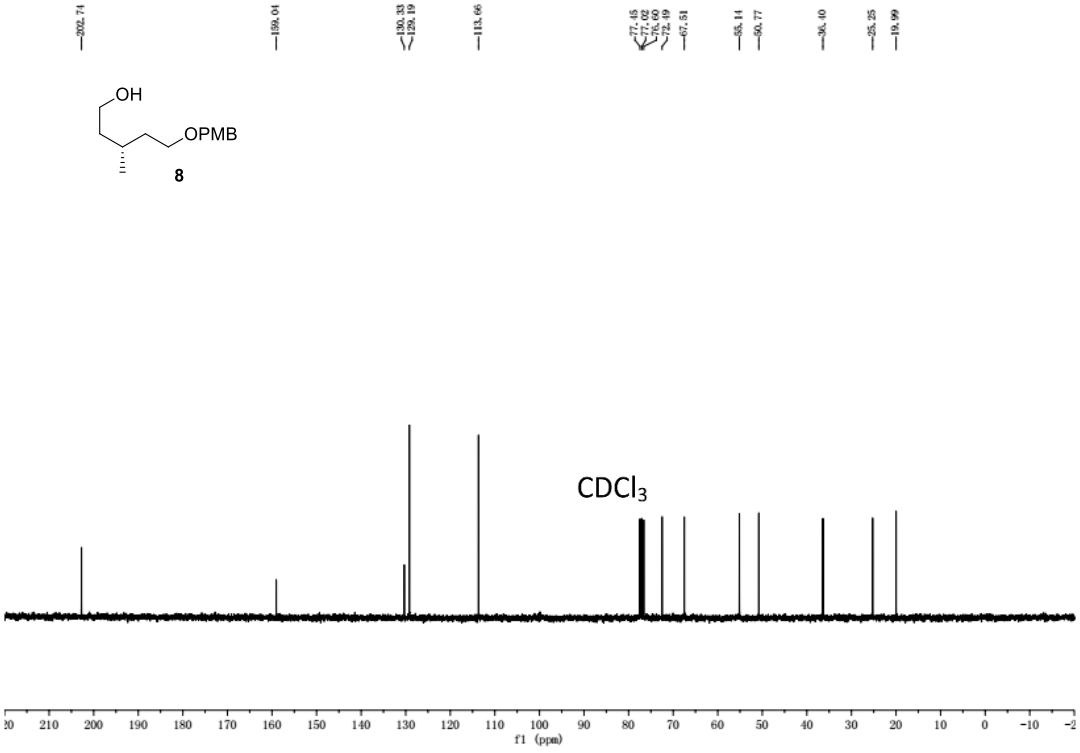
Comparison of ^{13}C NMR Data of Callyspongiolides
(Natural Product and Synthetic Samples 1a and 1b)



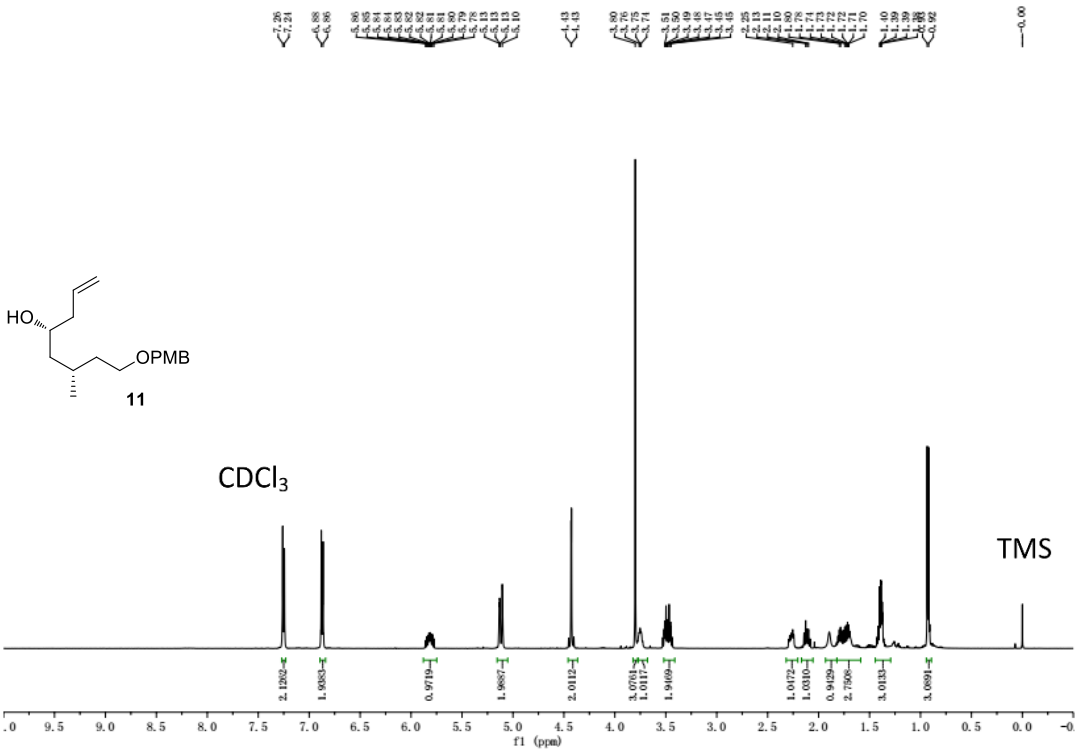
^{1}H NMR ($CDCl_3$, 500 MHz)



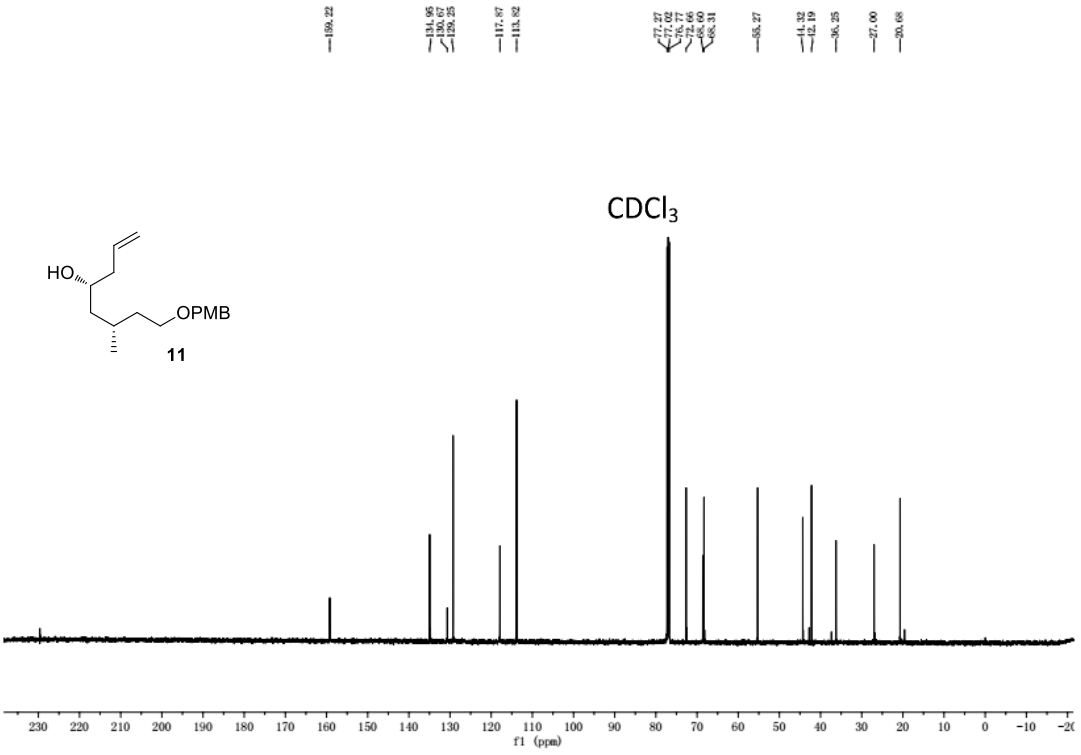
^{13}C NMR ($CDCl_3$, 125 MHz)



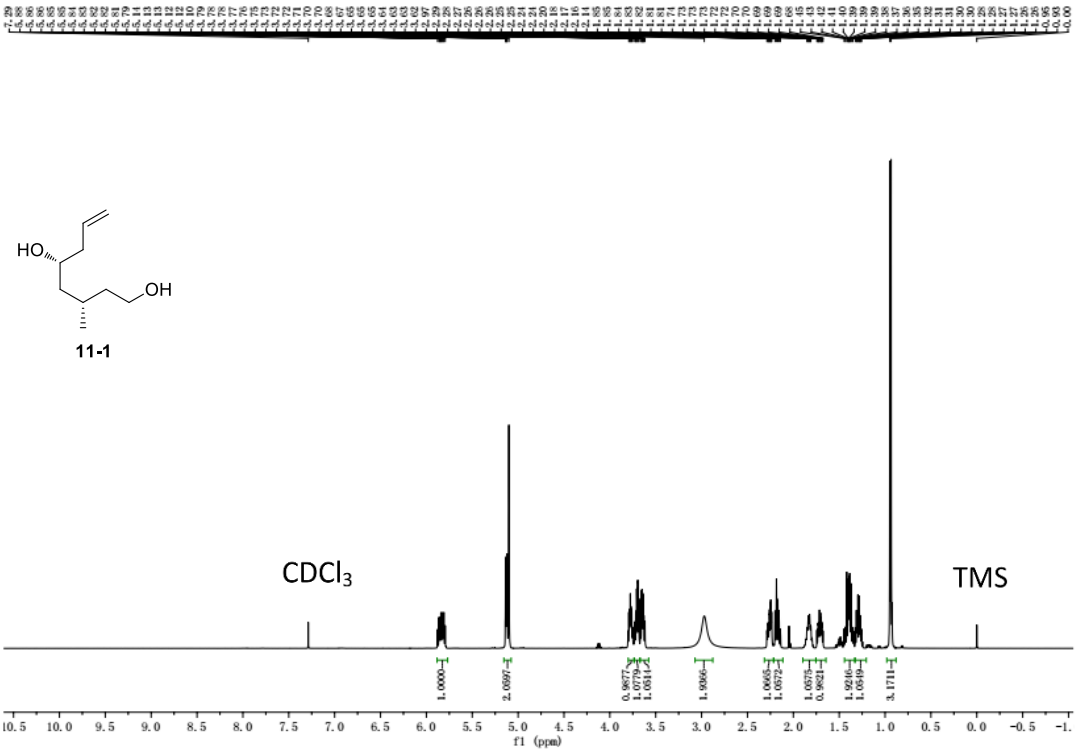
^{1}H NMR ($CDCl_3$, 500 MHz)



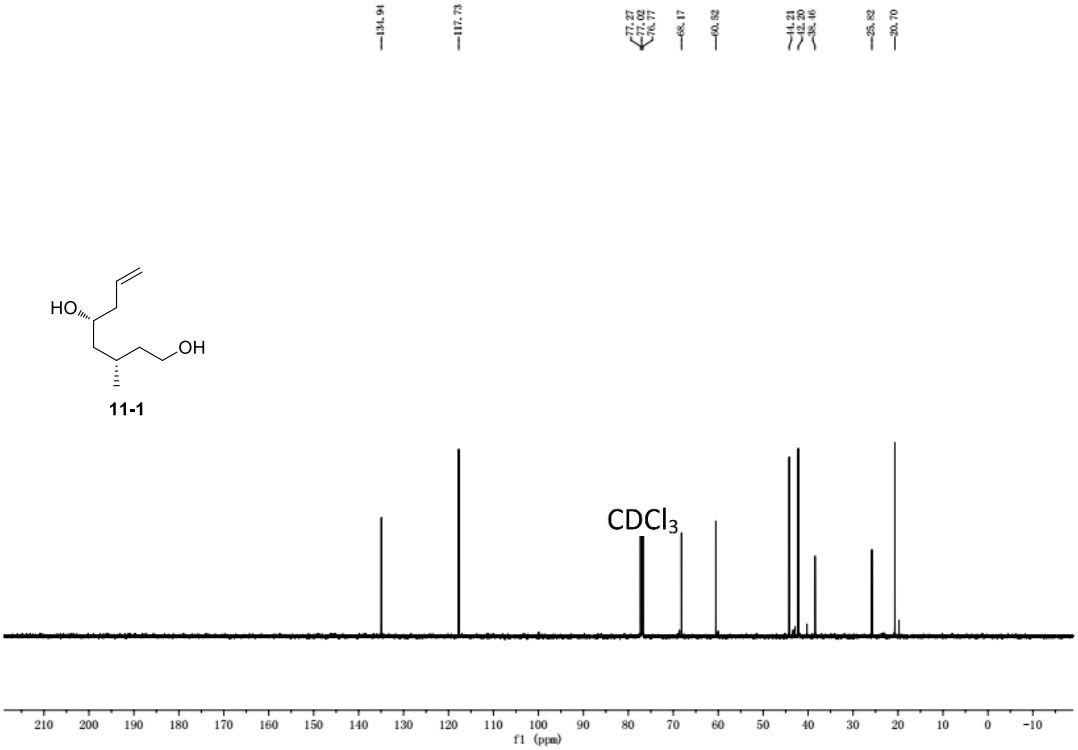
^{13}C NMR ($CDCl_3$, 125 MHz)



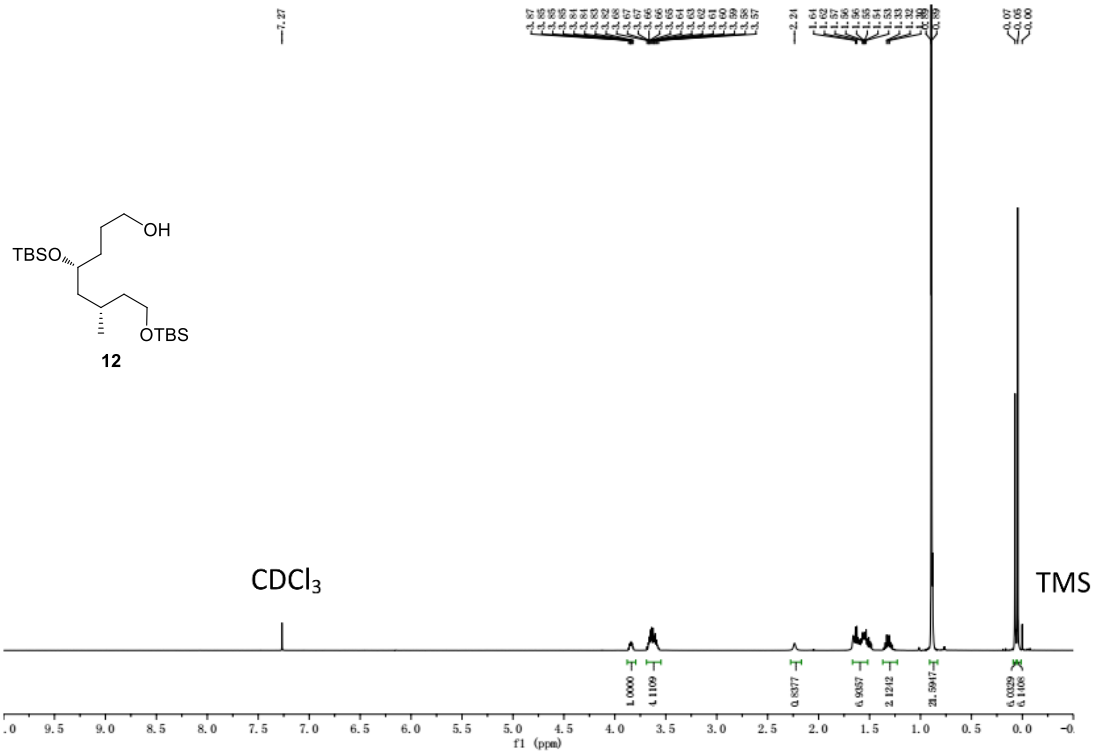
^{1}H NMR ($CDCl_3$, 500 MHz)



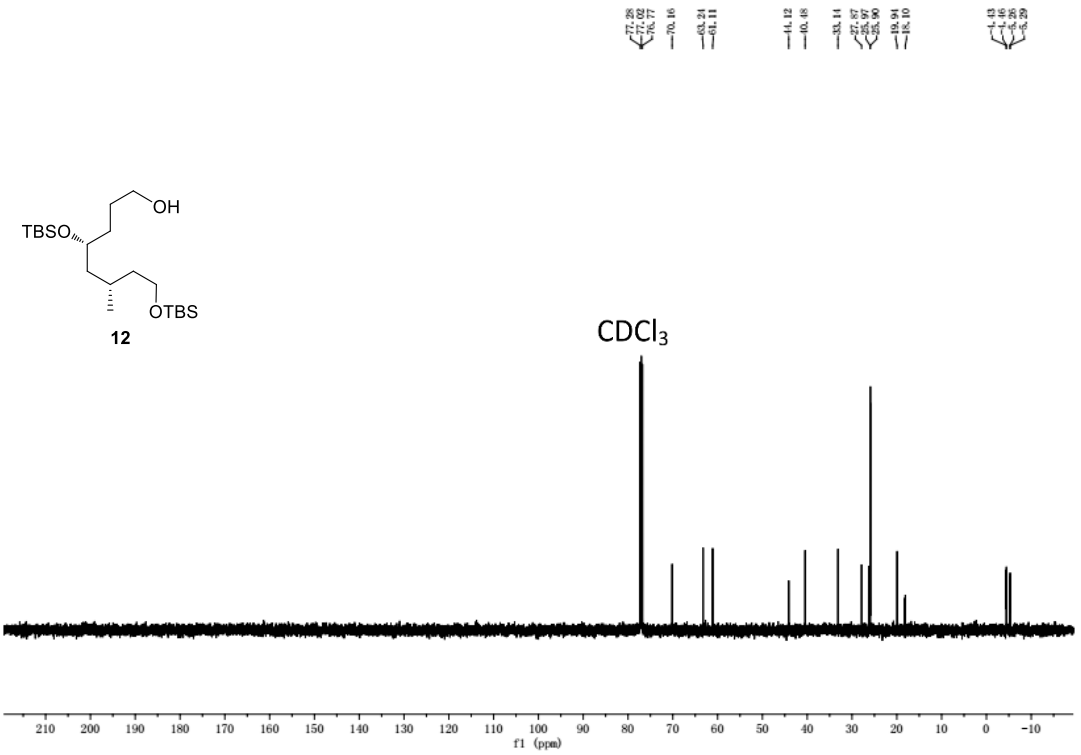
^{13}C NMR ($CDCl_3$, 125 MHz)



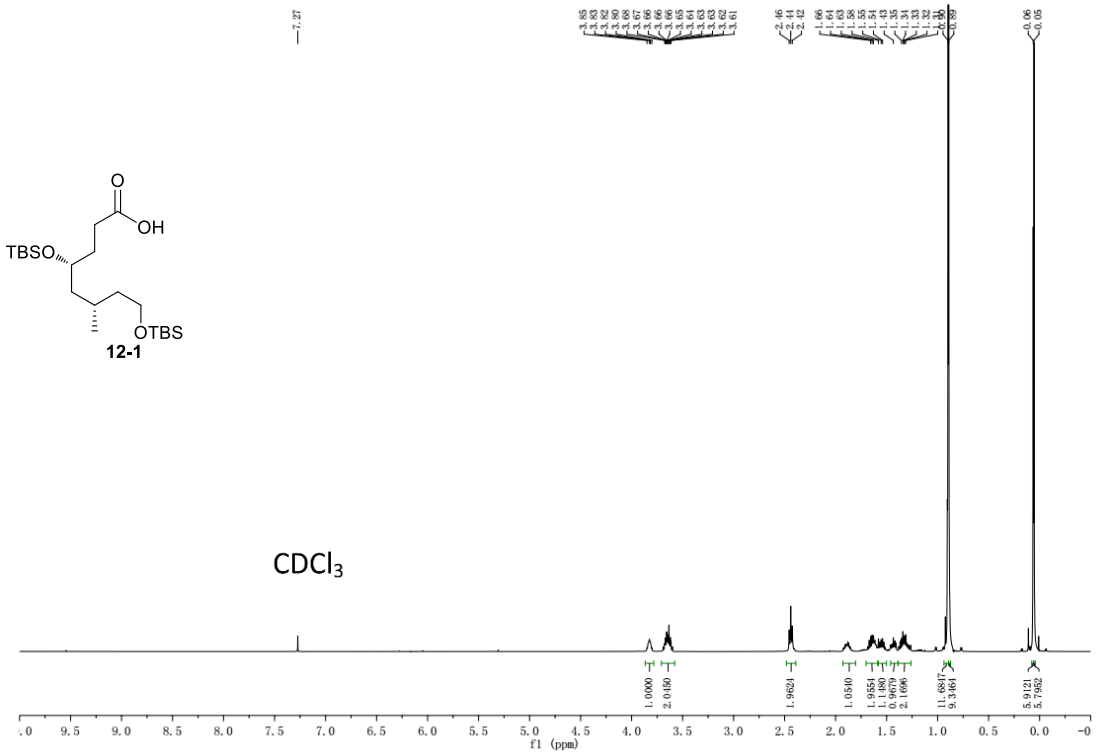
^{1}H NMR ($CDCl_3$, 500 MHz)



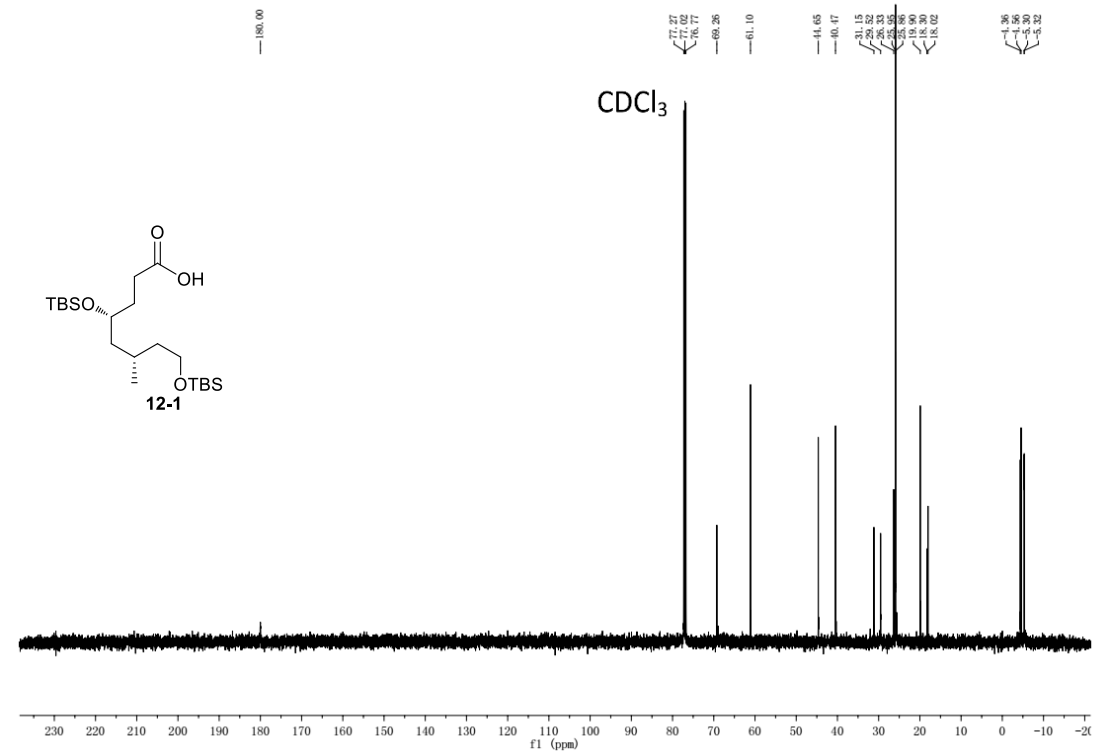
^{13}C NMR ($CDCl_3$, 125 MHz)



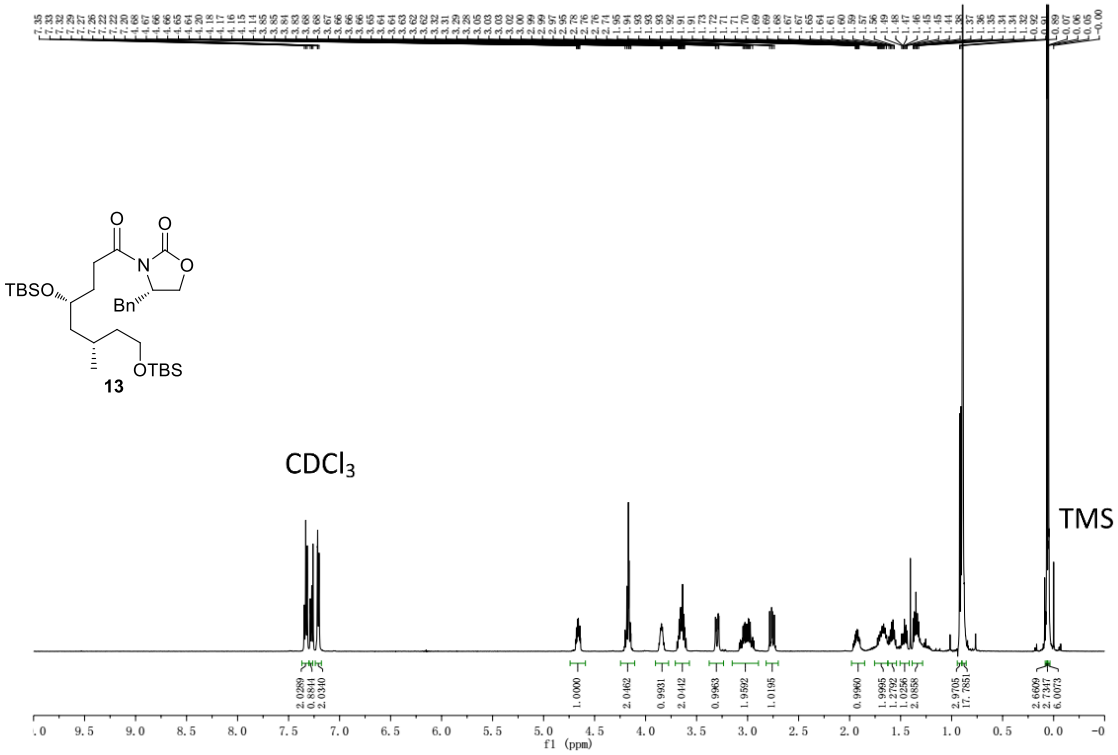
^{1}H NMR ($CDCl_3$, 500 MHz)



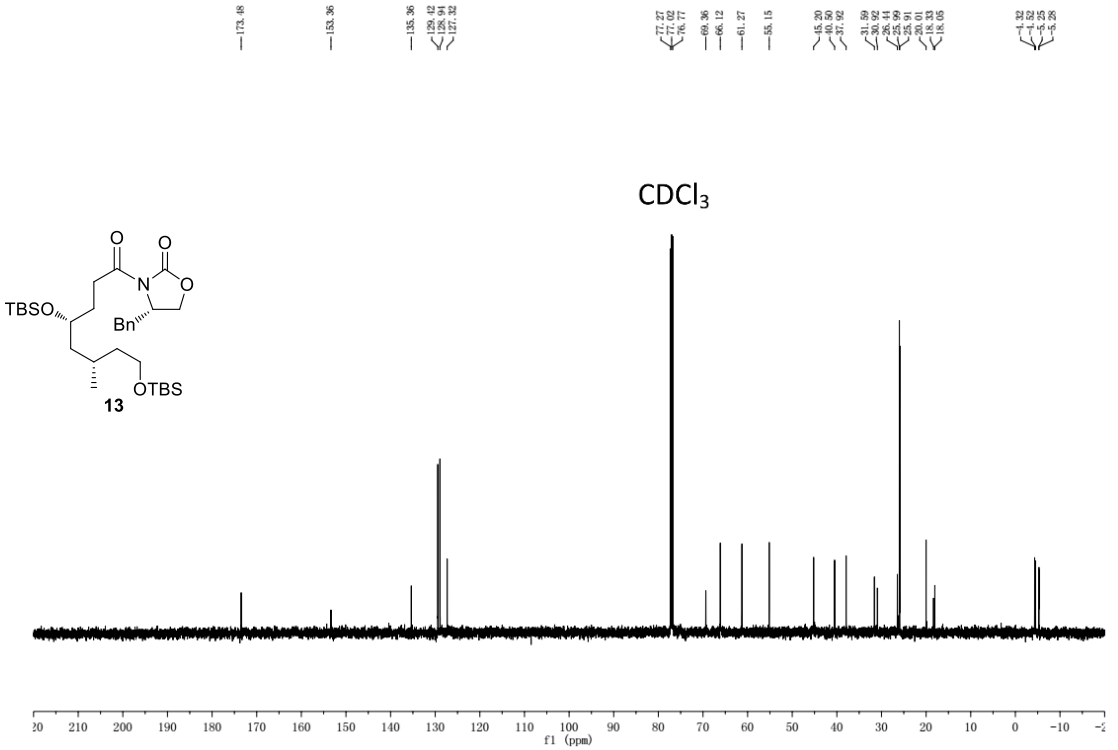
^{13}C NMR ($CDCl_3$, 125 MHz)



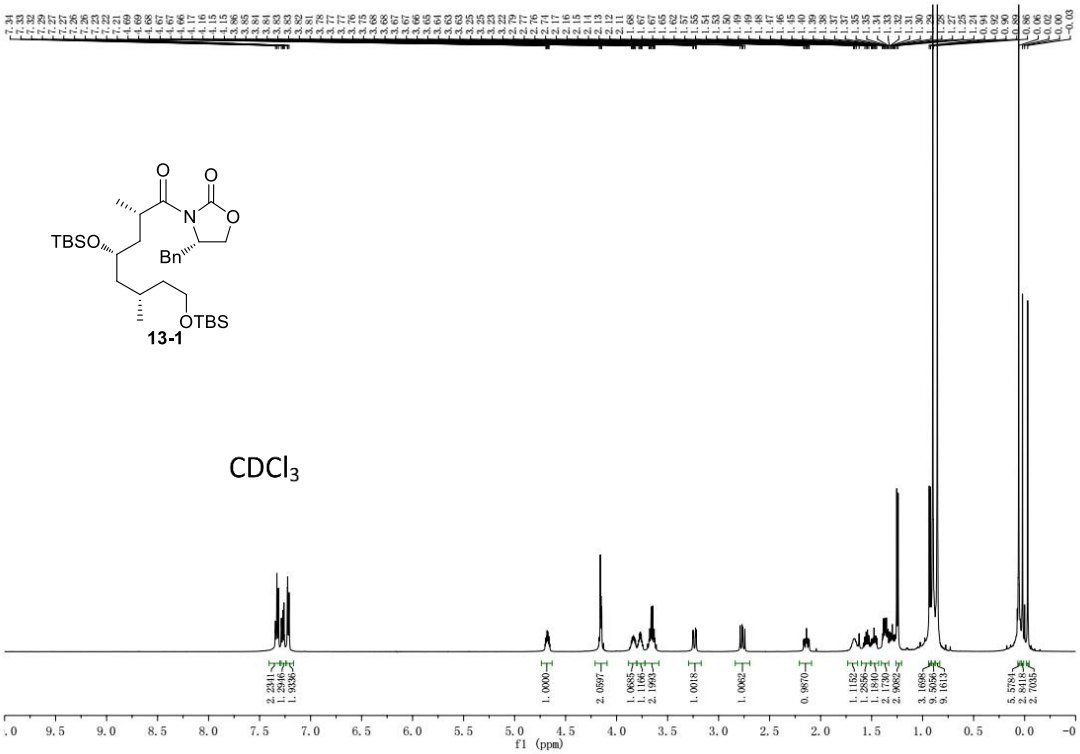
^{1}H NMR ($CDCl_3$, 500 MHz)



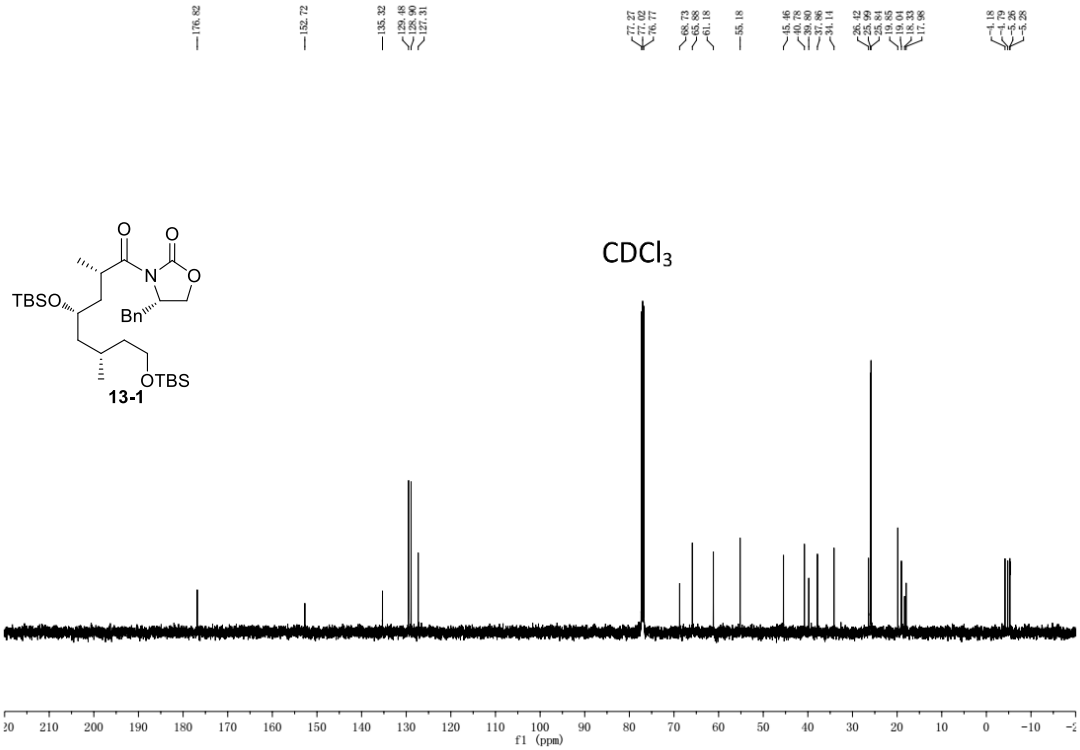
^{13}C NMR ($CDCl_3$, 125 MHz)



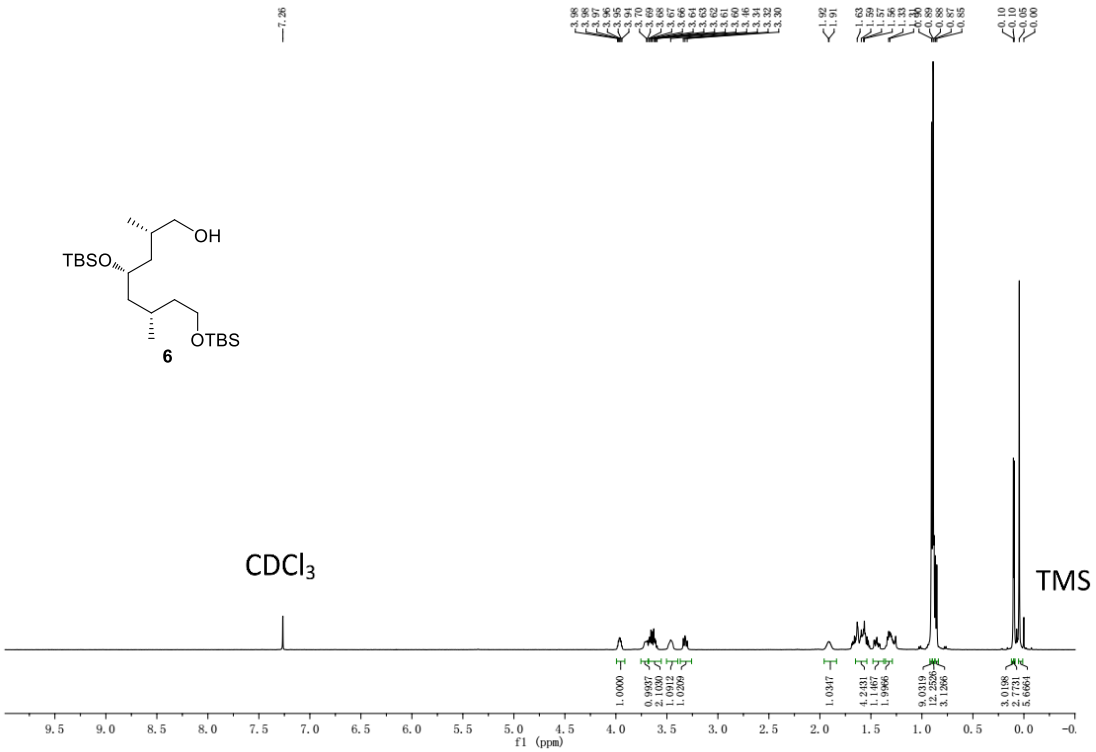
^{1}H NMR ($CDCl_3$, 500 MHz)



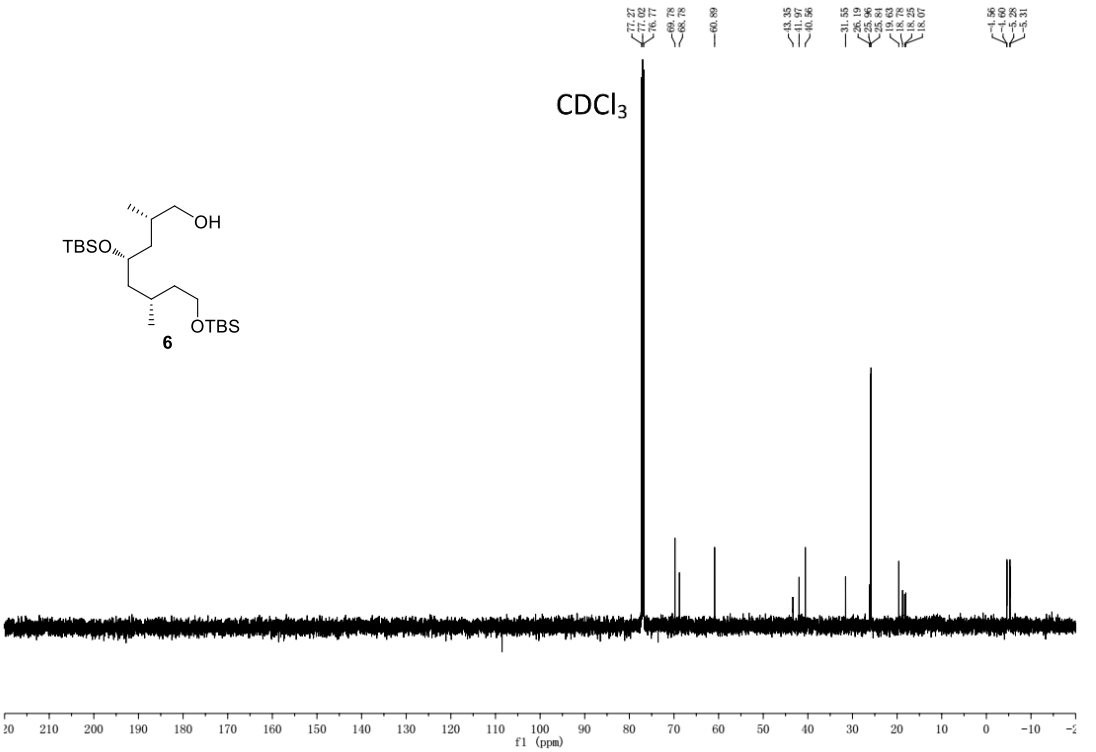
^{13}C NMR ($CDCl_3$, 125 MHz)



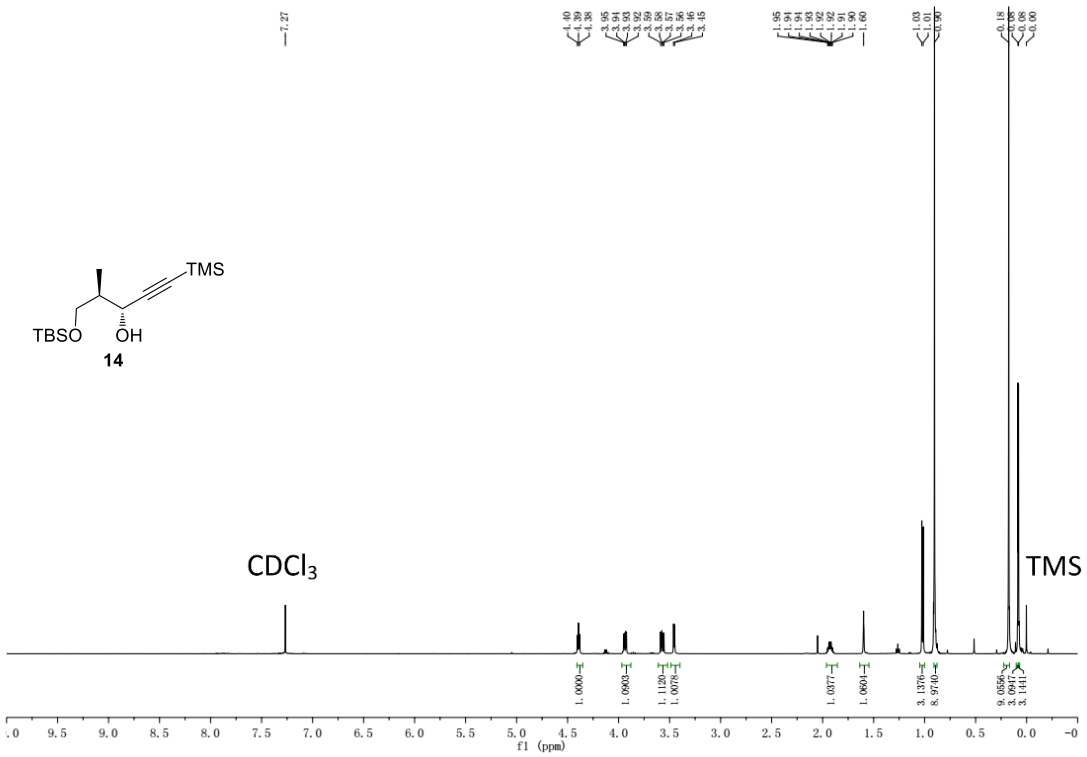
^{1}H NMR ($CDCl_3$, 500 MHz)



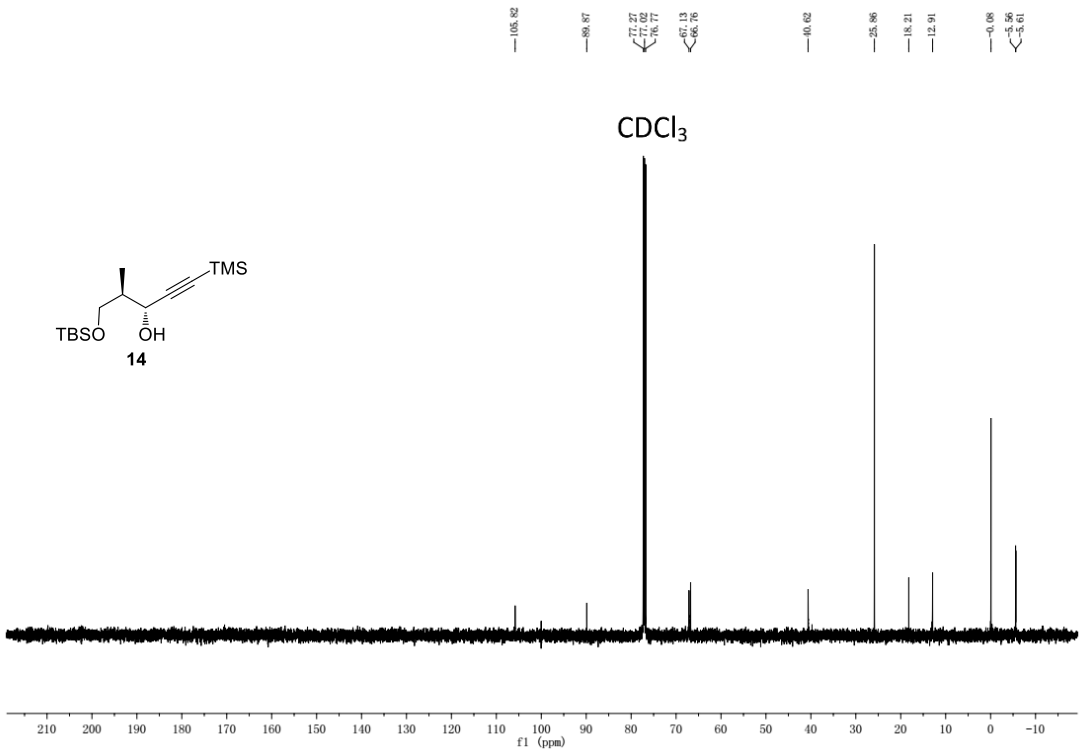
^{13}C NMR ($CDCl_3$, 125 MHz)



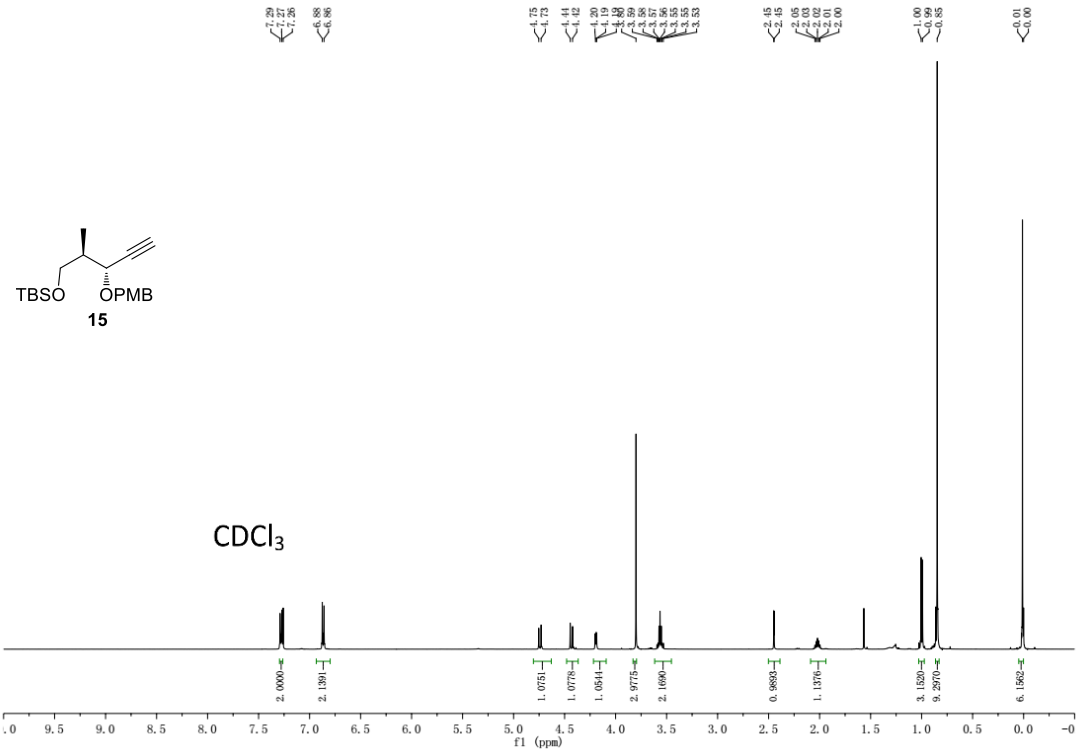
^{1}H NMR ($CDCl_3$, 500 MHz)



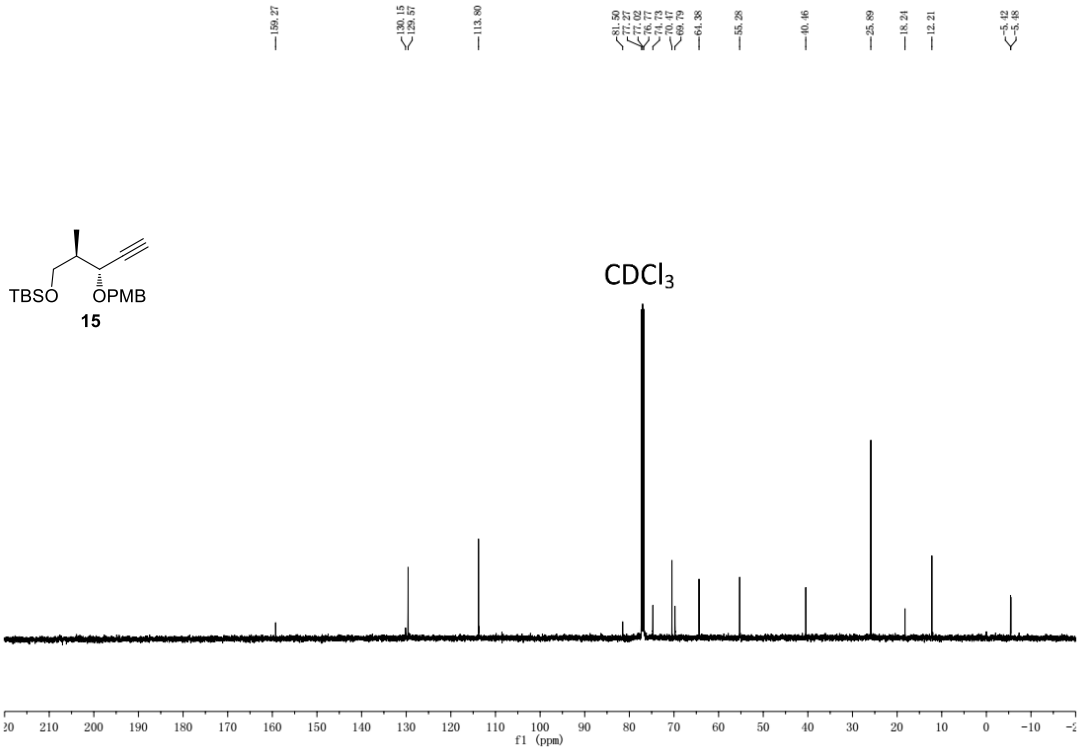
^{13}C NMR ($CDCl_3$, 125 MHz)



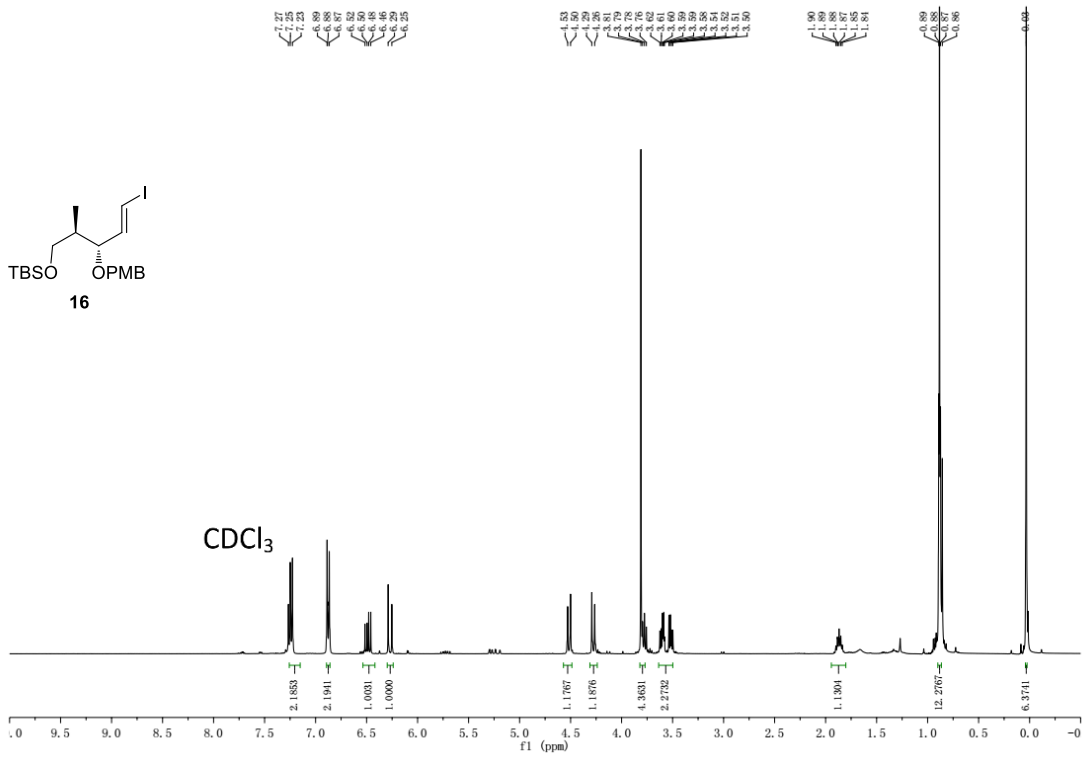
^{1}H NMR ($CDCl_3$, 500 MHz)



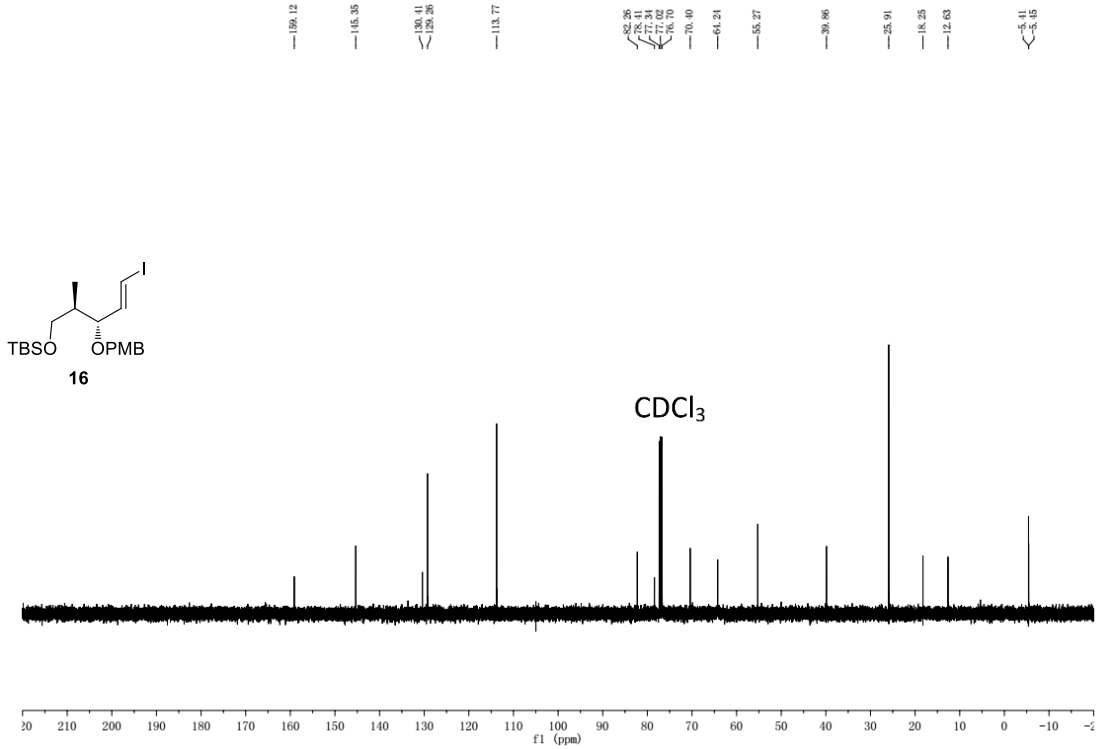
^{13}C NMR ($CDCl_3$, 125 MHz)



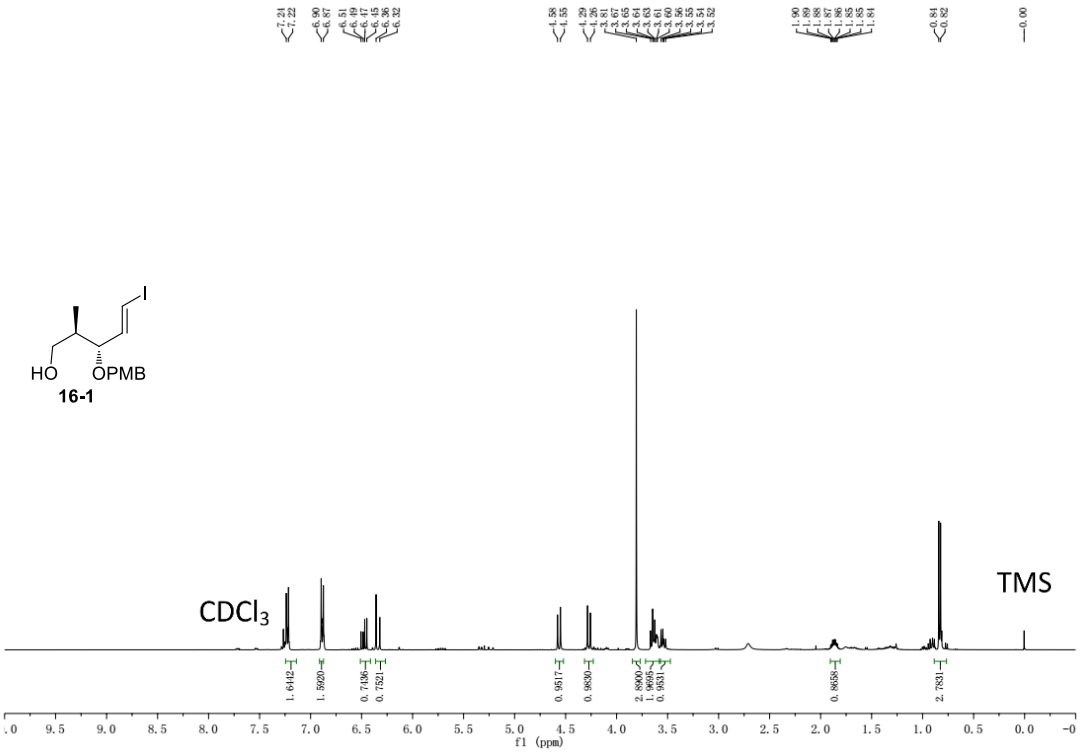
^{1}H NMR ($CDCl_3$, 400 MHz)



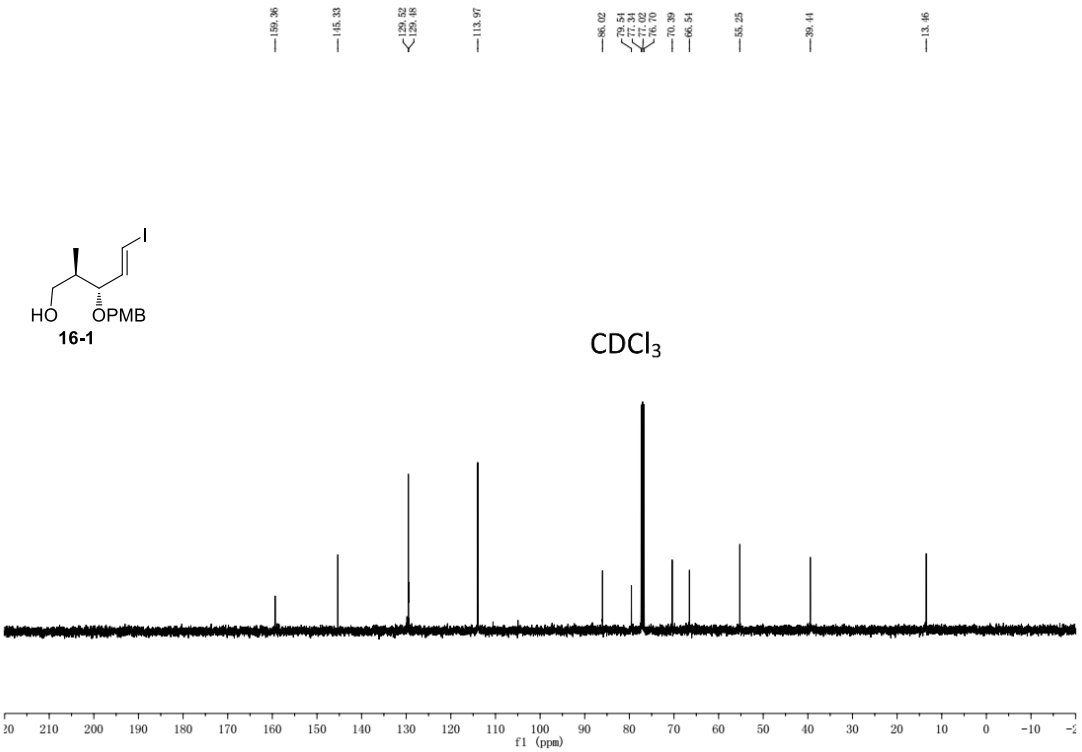
^{13}C NMR ($CDCl_3$, 100 MHz)



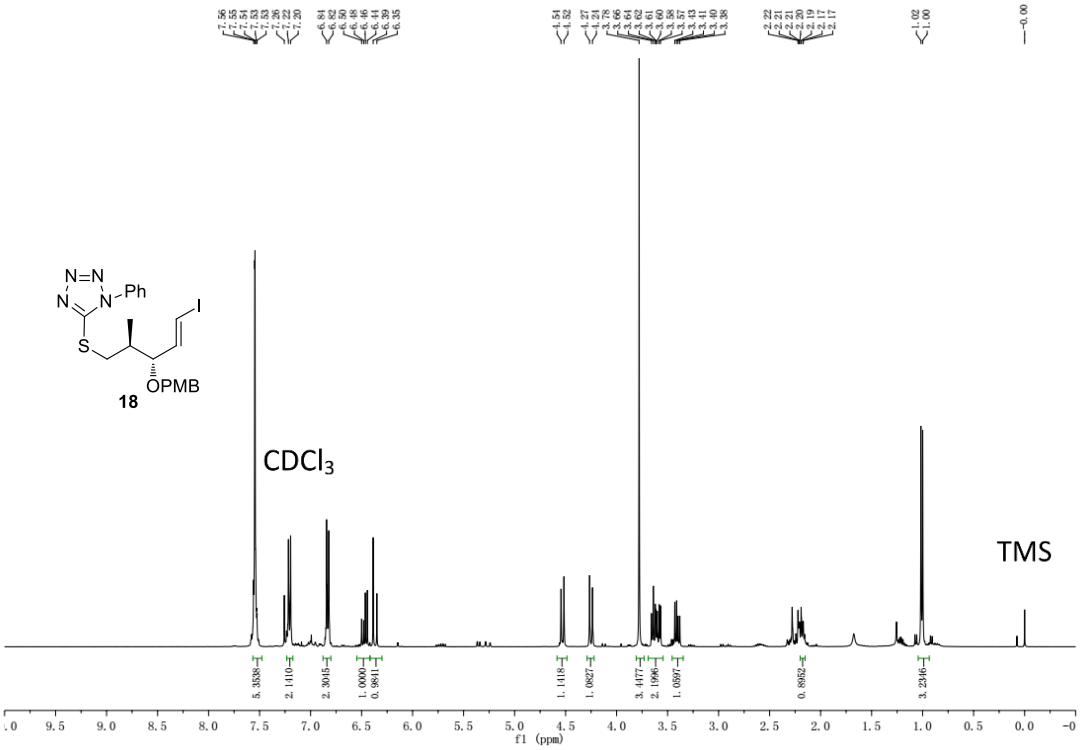
^{1}H NMR ($CDCl_3$, 400 MHz)



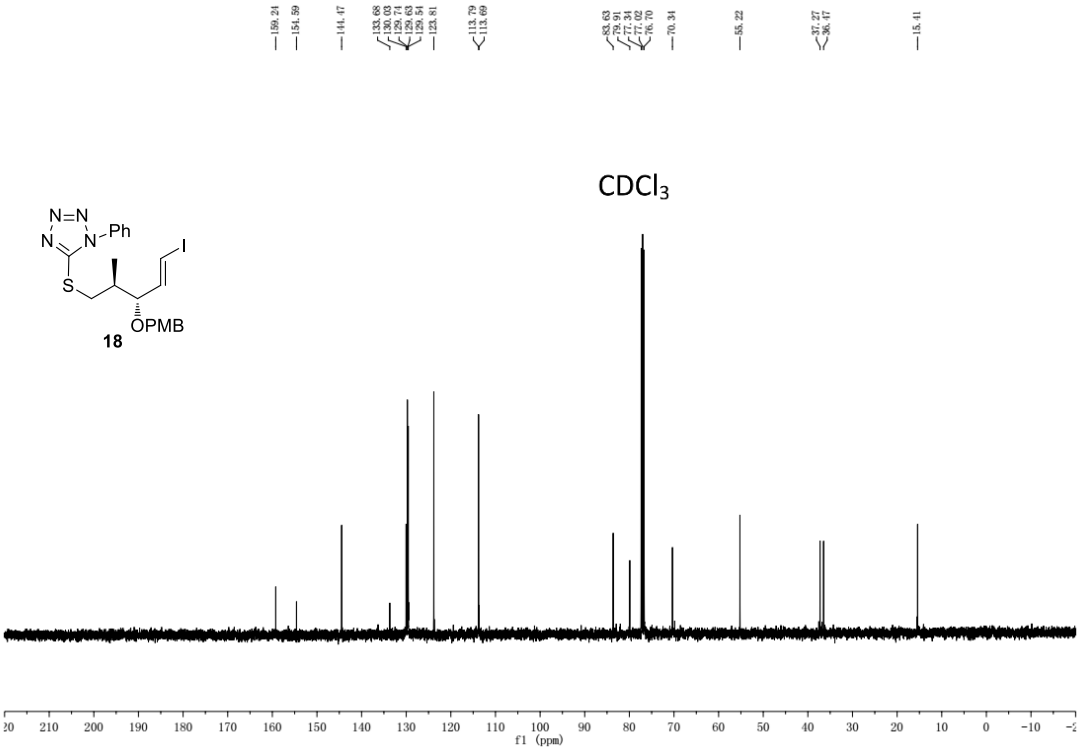
^{13}C NMR ($CDCl_3$, 100 MHz)



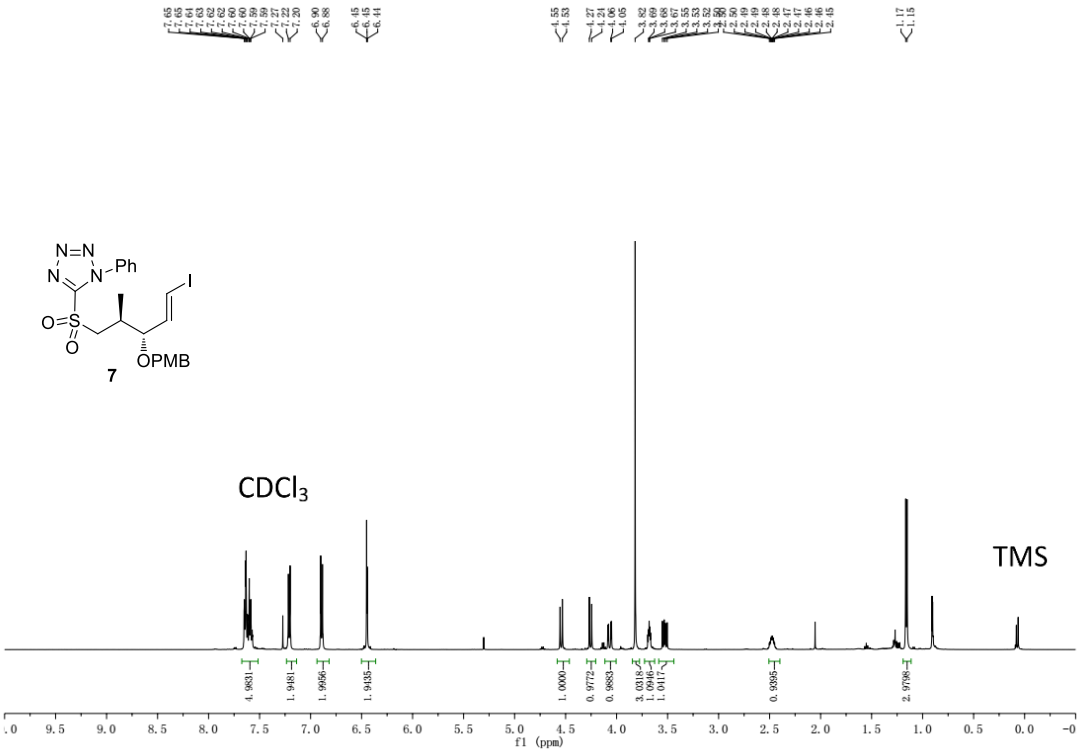
^{1}H NMR ($CDCl_3$, 400 MHz)



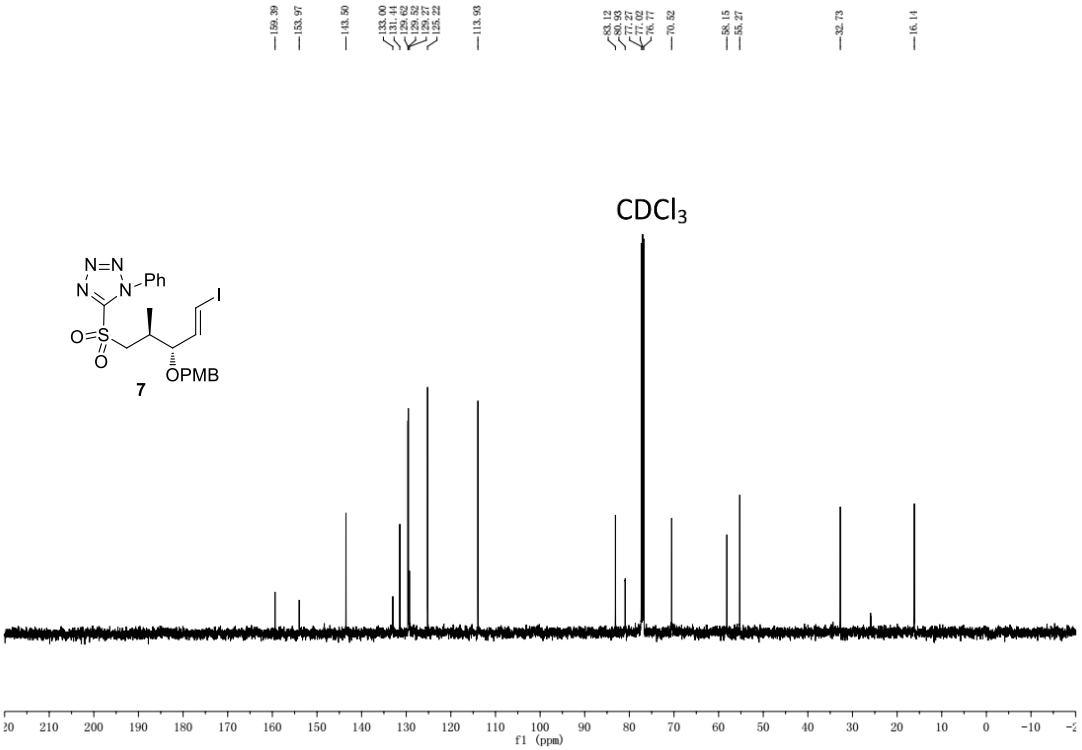
^{13}C NMR ($CDCl_3$, 100 MHz)



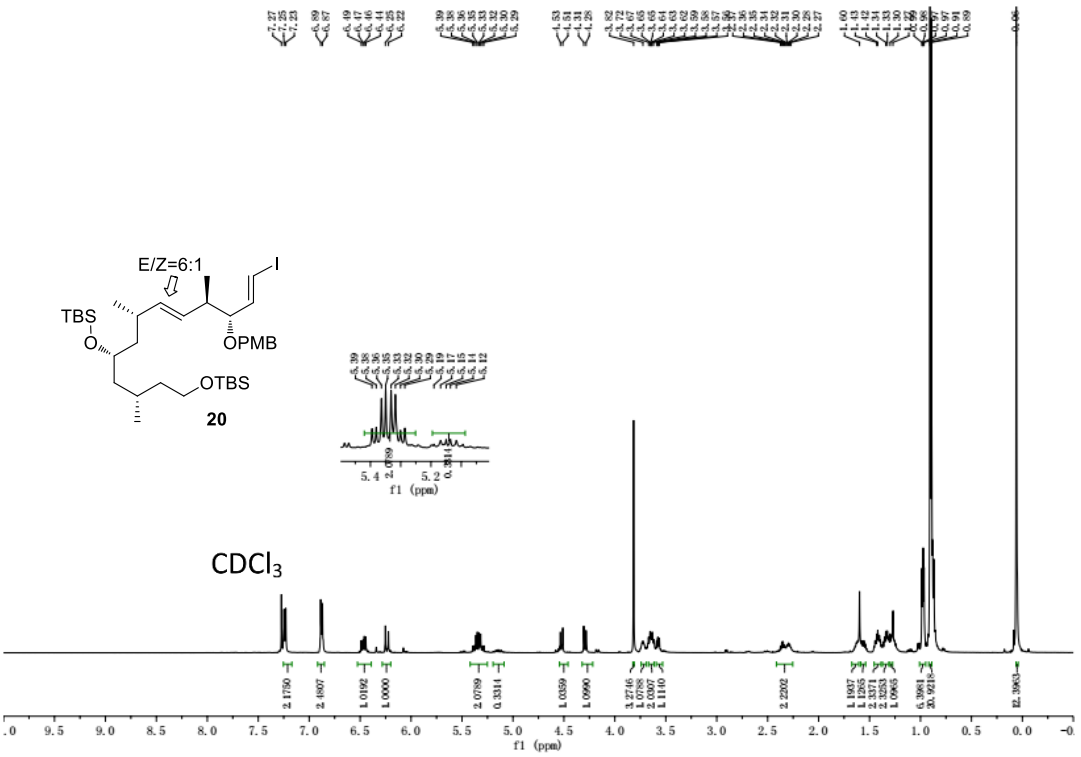
^{1}H NMR ($CDCl_3$, 500 MHz)



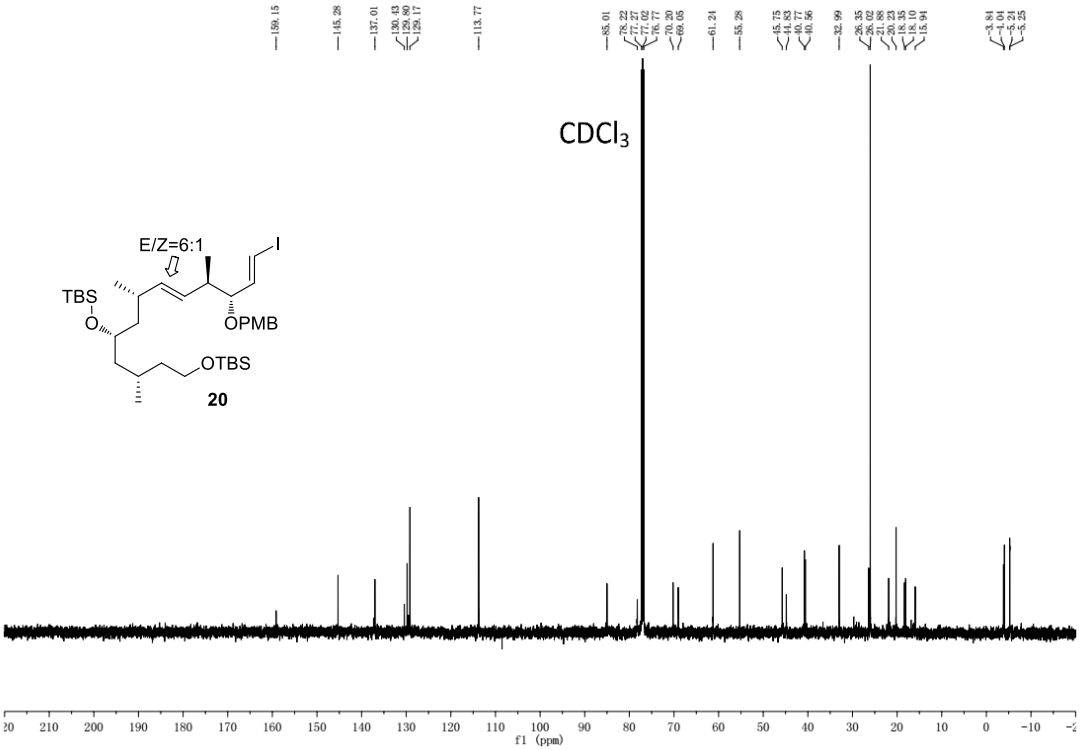
^{13}C NMR ($CDCl_3$, 125 MHz)



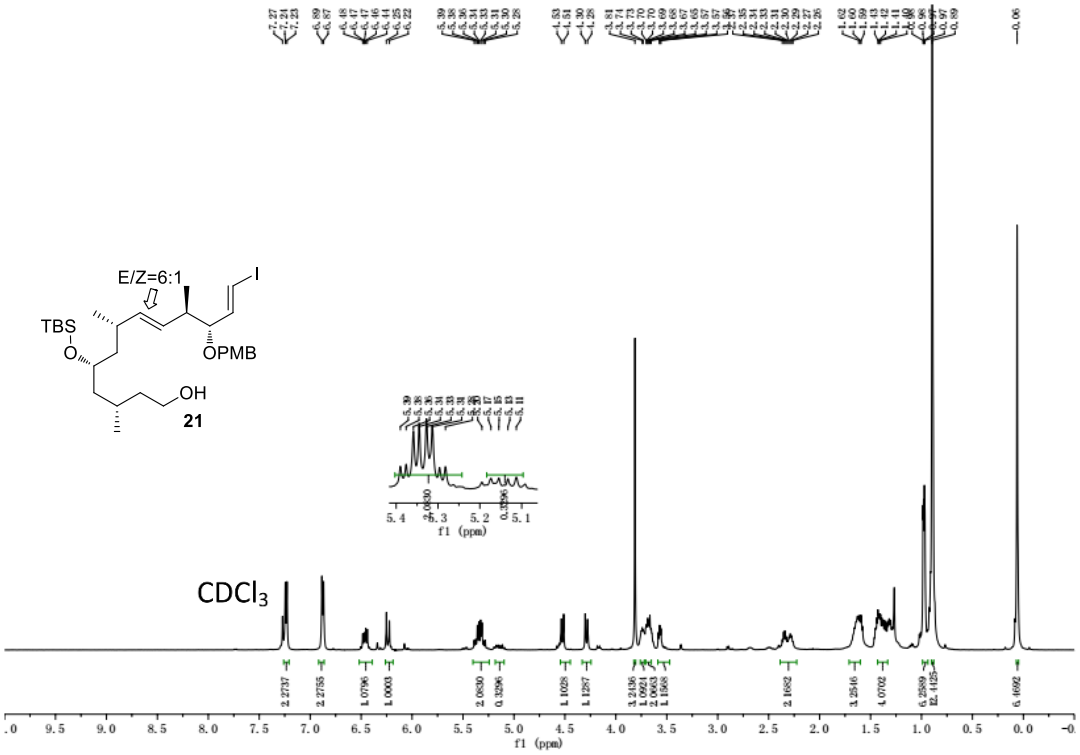
^{1}H NMR ($CDCl_3$, 500 MHz)



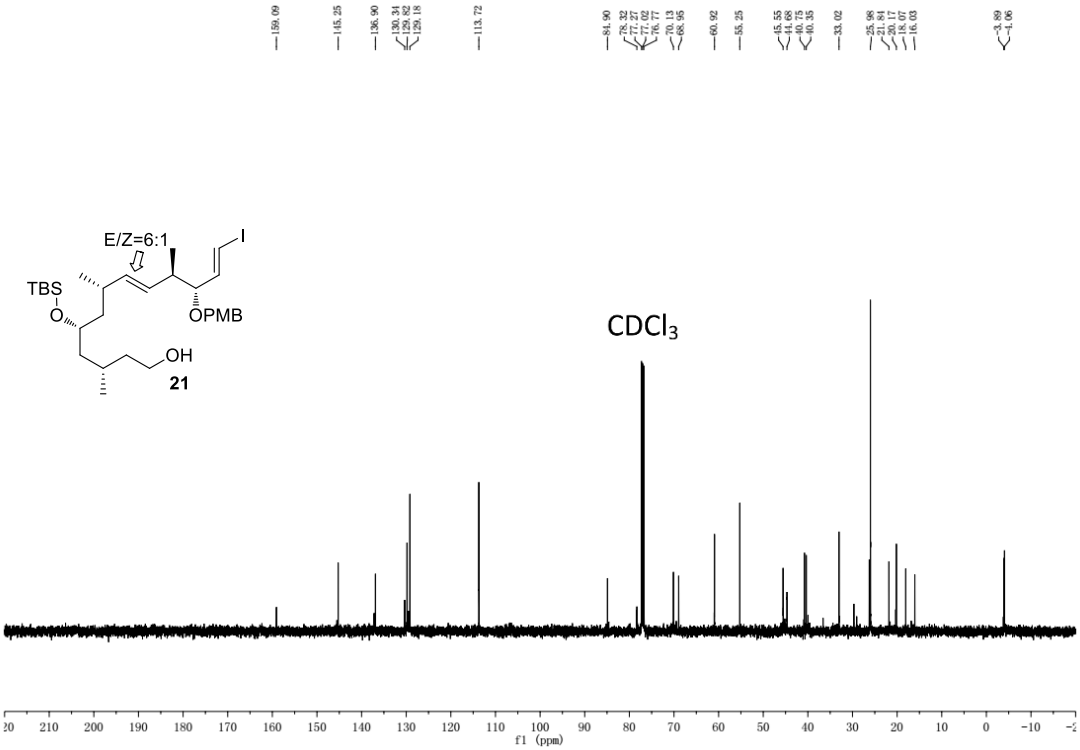
^{13}C NMR ($CDCl_3$, 125 MHz)



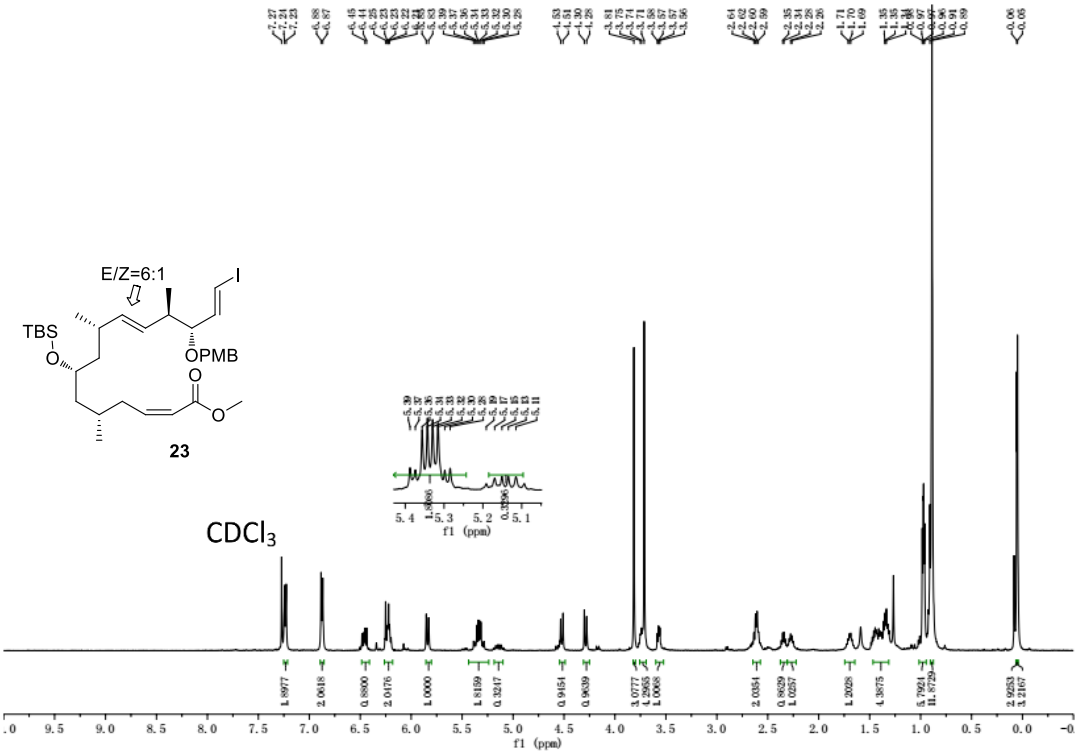
^{1}H NMR ($CDCl_3$, 500 MHz)



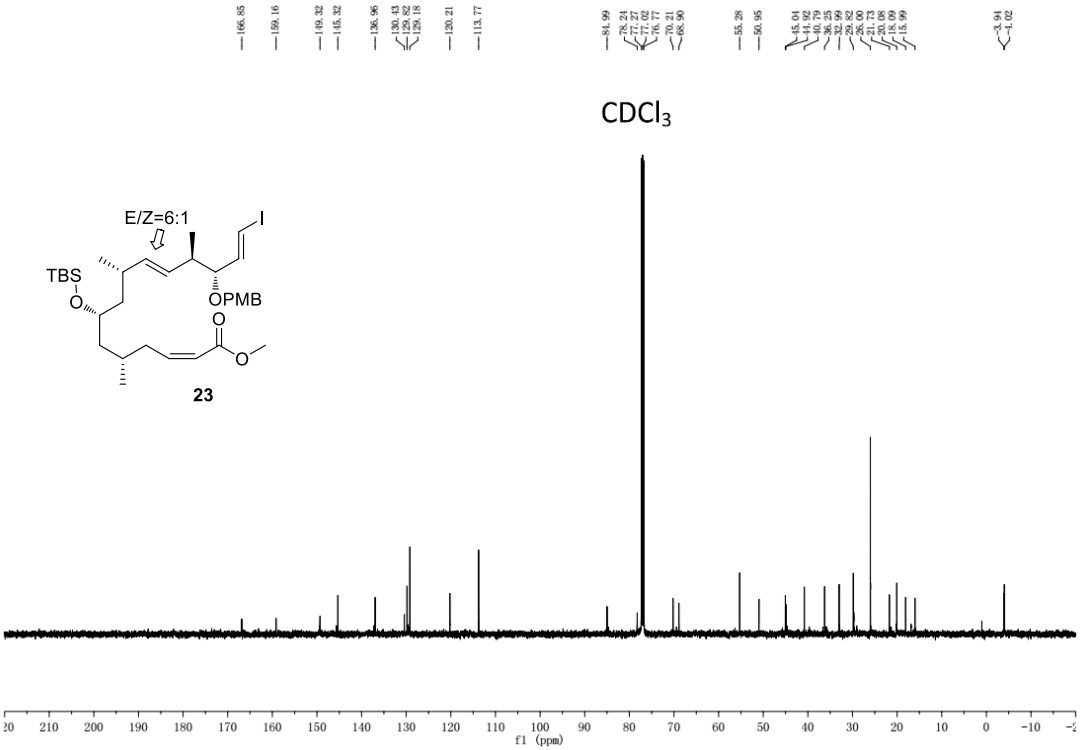
^{13}C NMR ($CDCl_3$, 125 MHz)



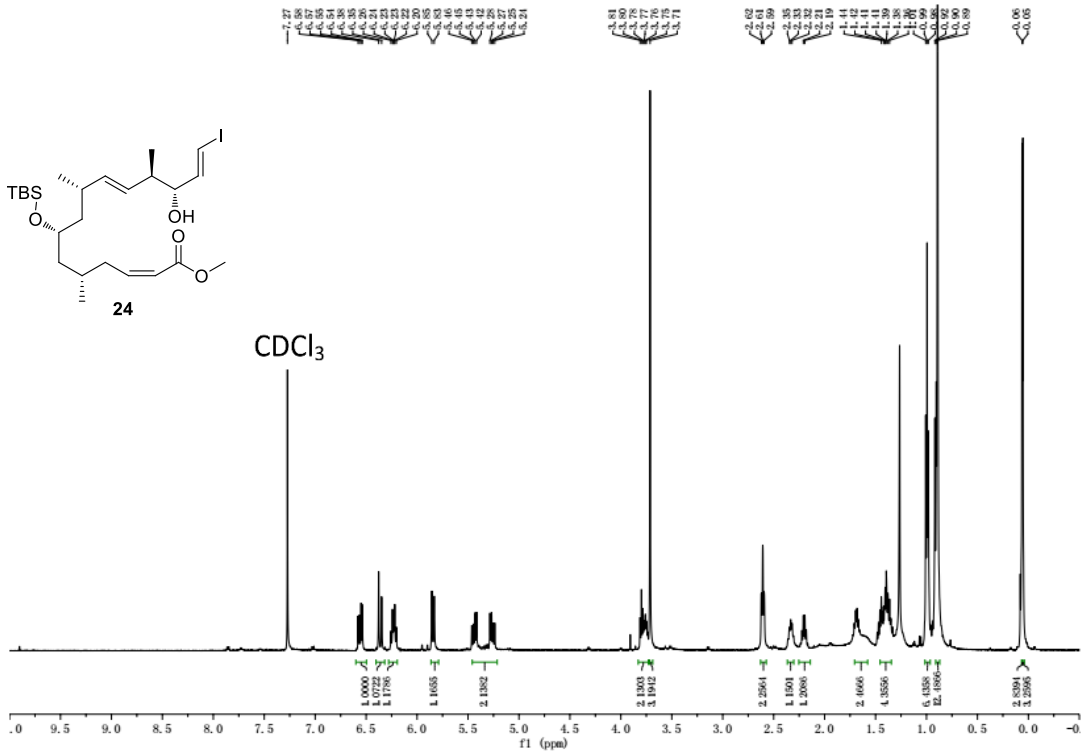
^{1}H NMR ($CDCl_3$, 500 MHz)



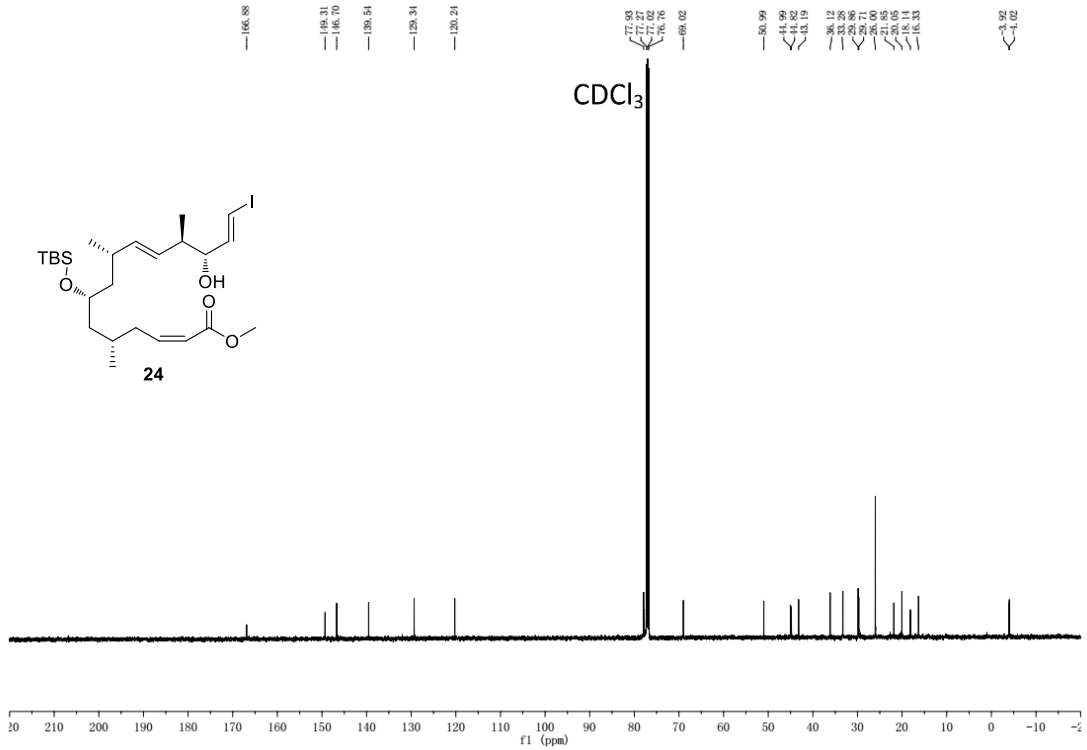
^{13}C NMR ($CDCl_3$, 125 MHz)



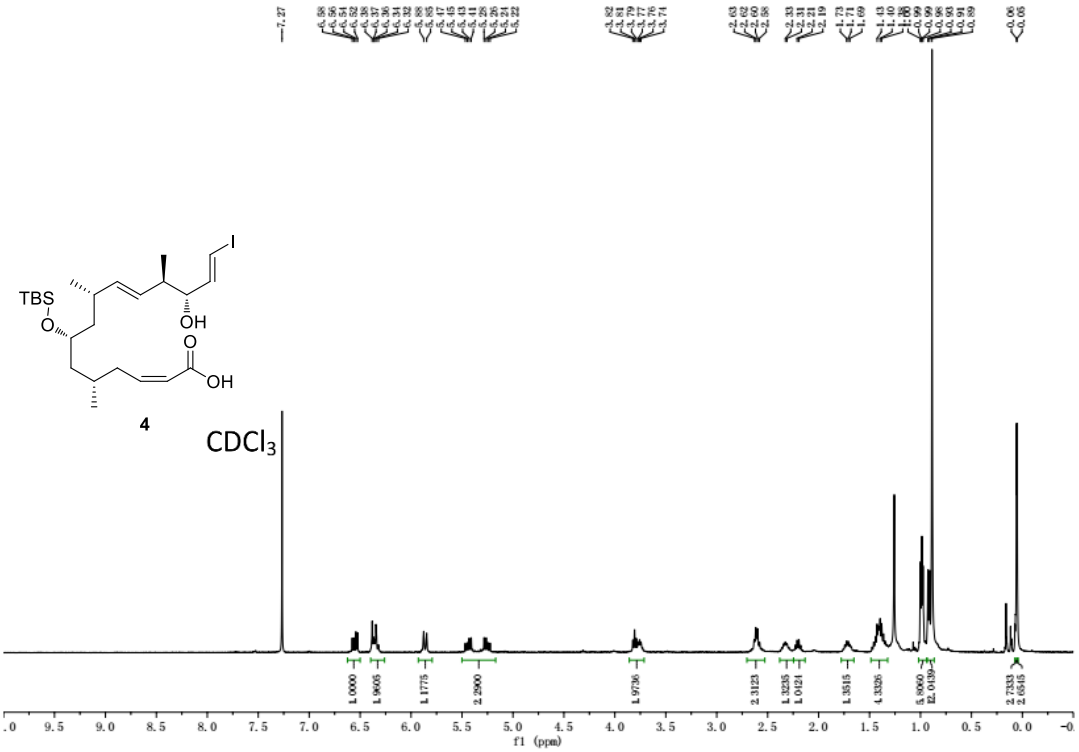
^{1}H NMR ($CDCl_3$, 500 MHz)



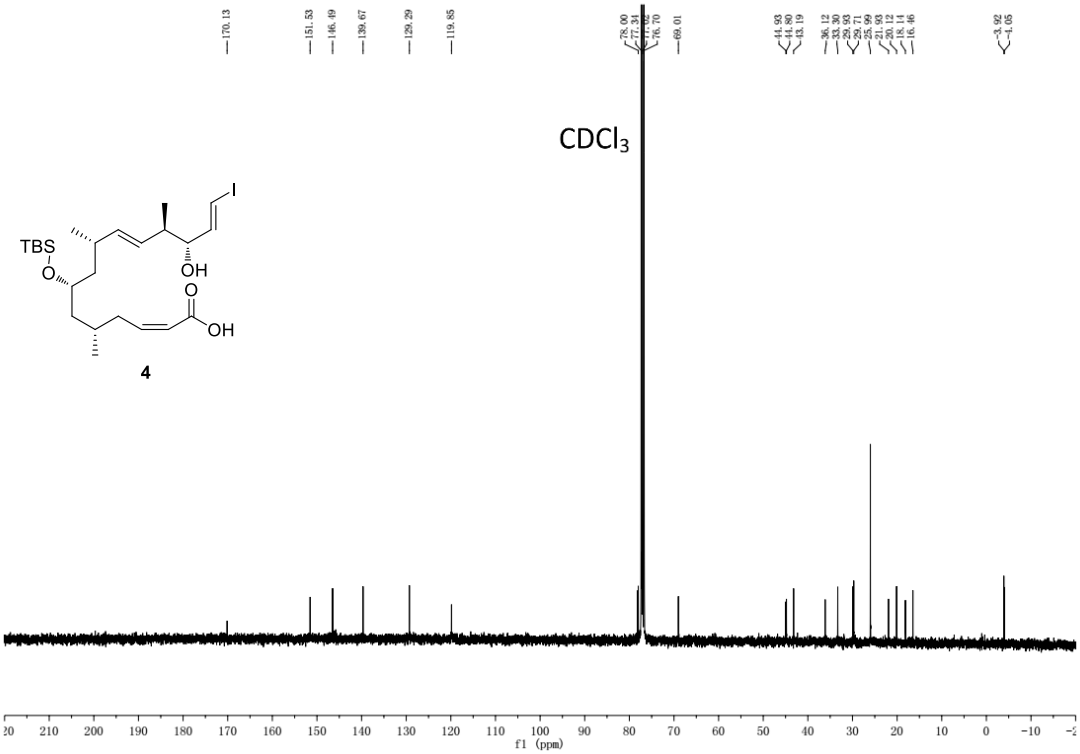
^{13}C NMR ($CDCl_3$, 125 MHz)



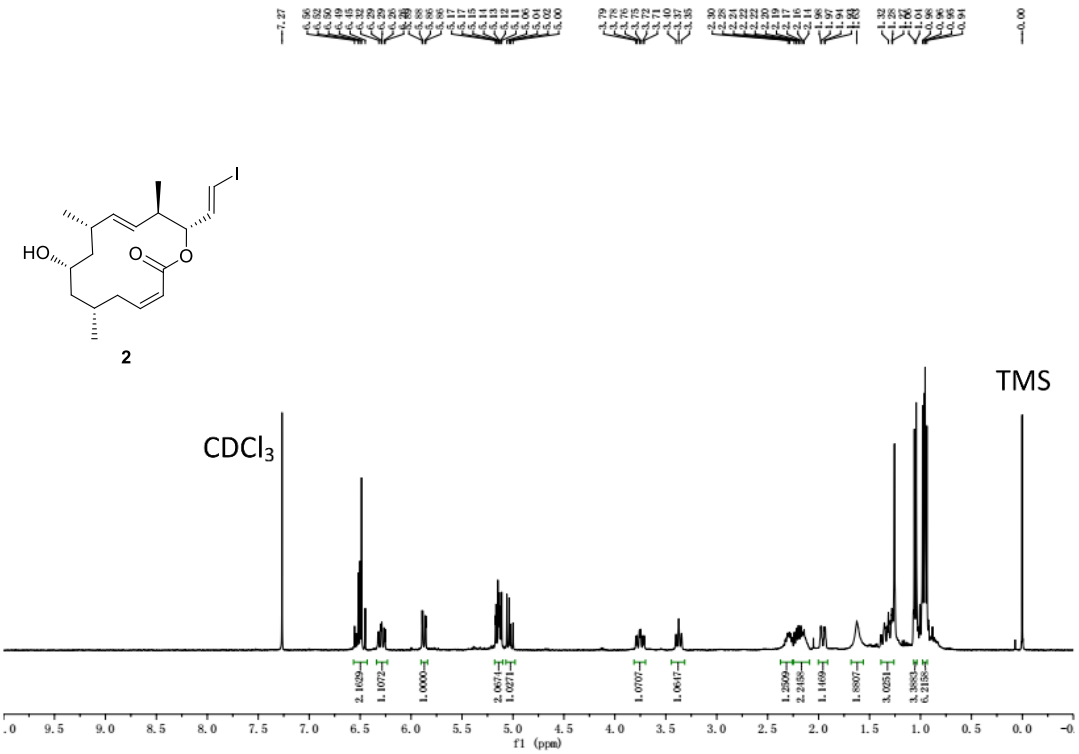
^{1}H NMR ($CDCl_3$, 400 MHz)



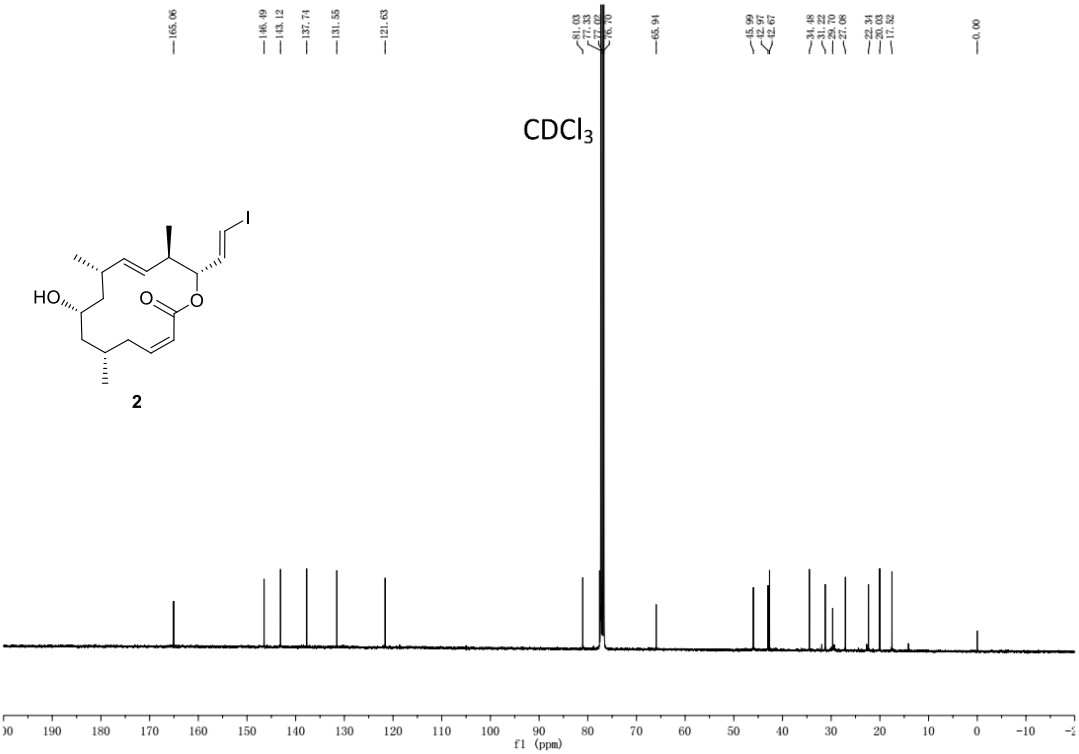
^{13}C NMR ($CDCl_3$, 100 MHz)



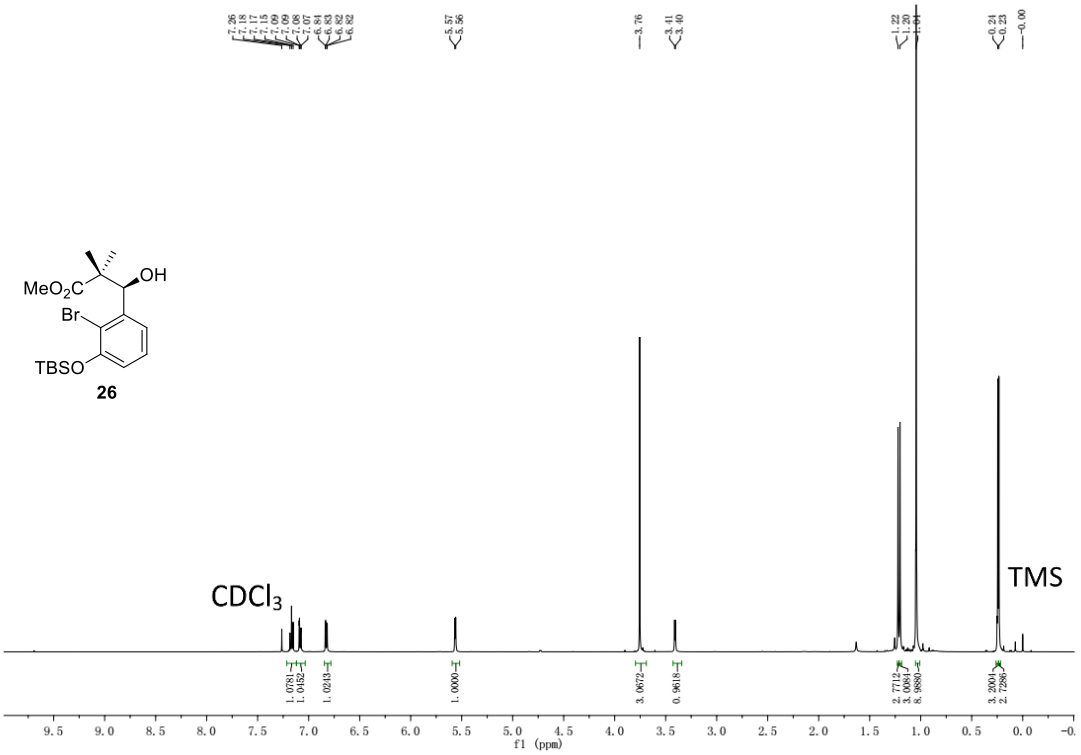
^{1}H NMR ($CDCl_3$, 400 MHz)



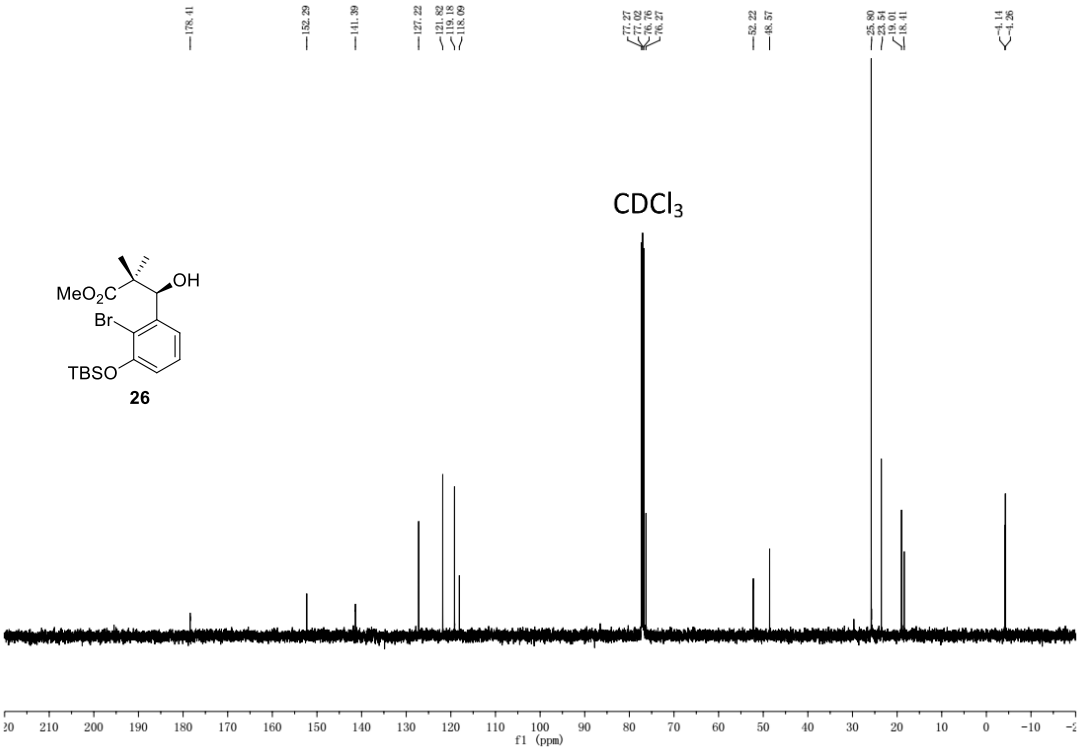
^{13}C NMR ($CDCl_3$, 100 MHz)



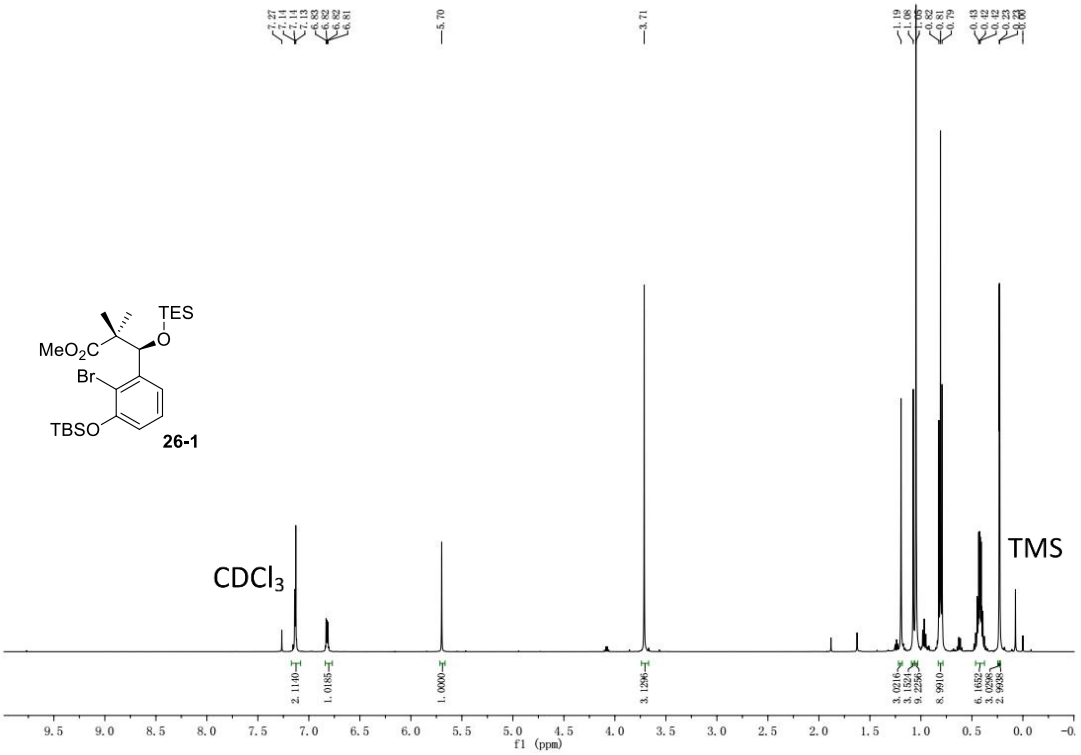
^{1}H NMR ($CDCl_3$, 500 MHz)



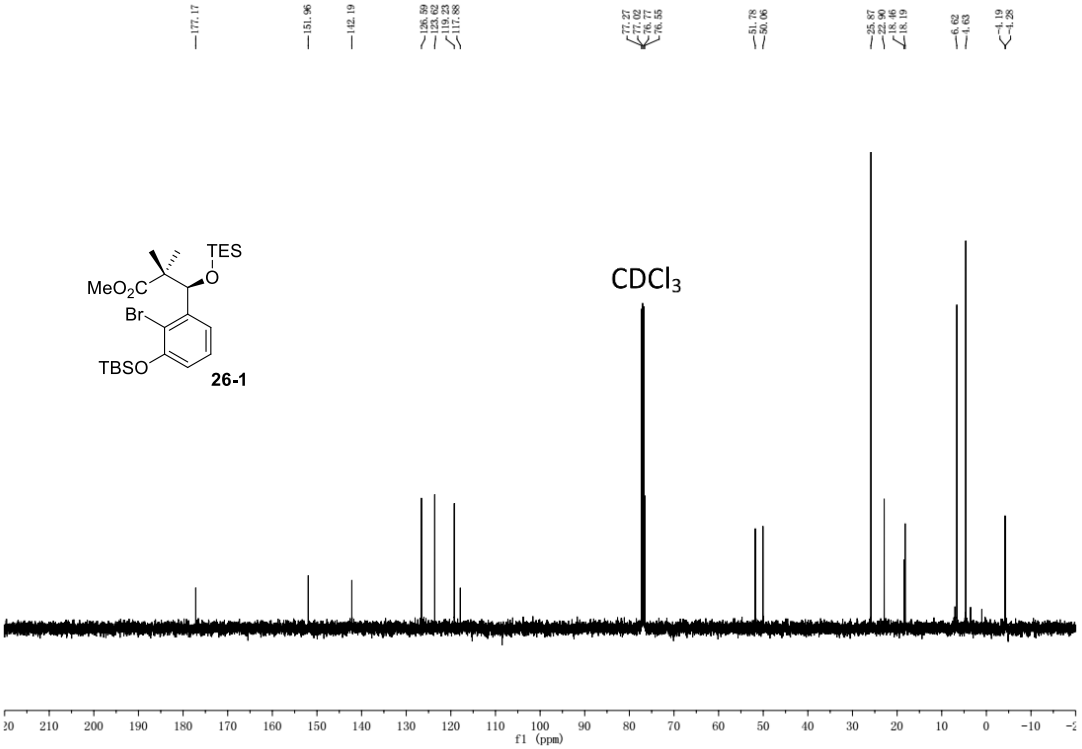
^{13}C NMR ($CDCl_3$, 125 MHz)



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



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



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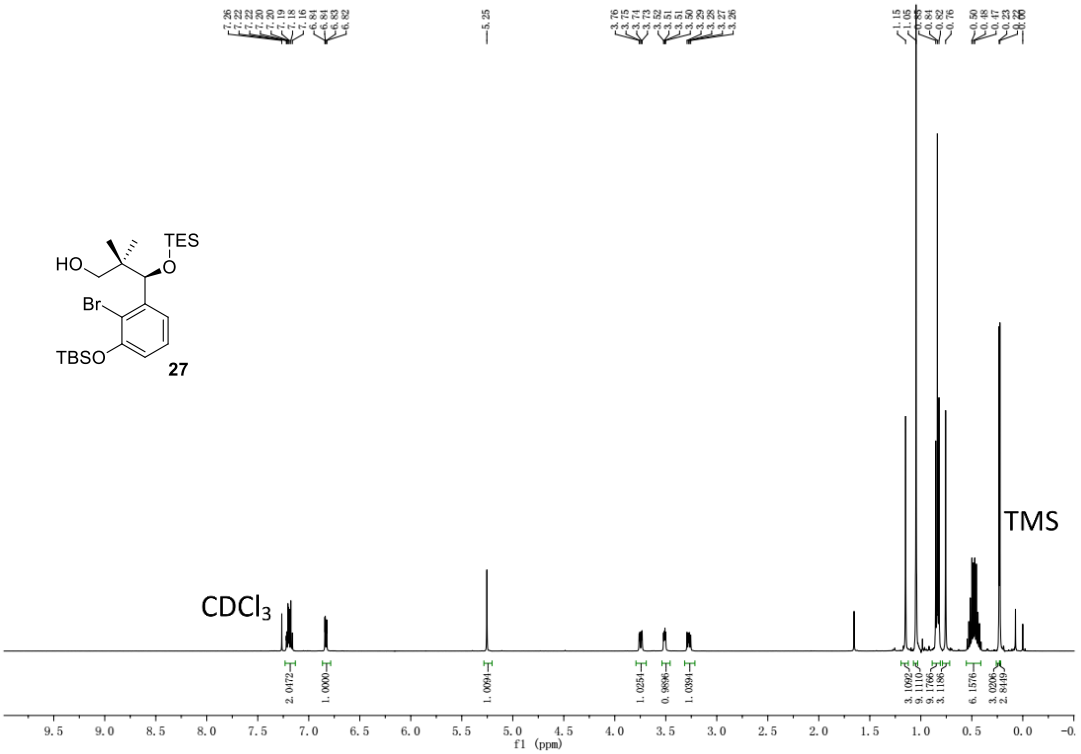
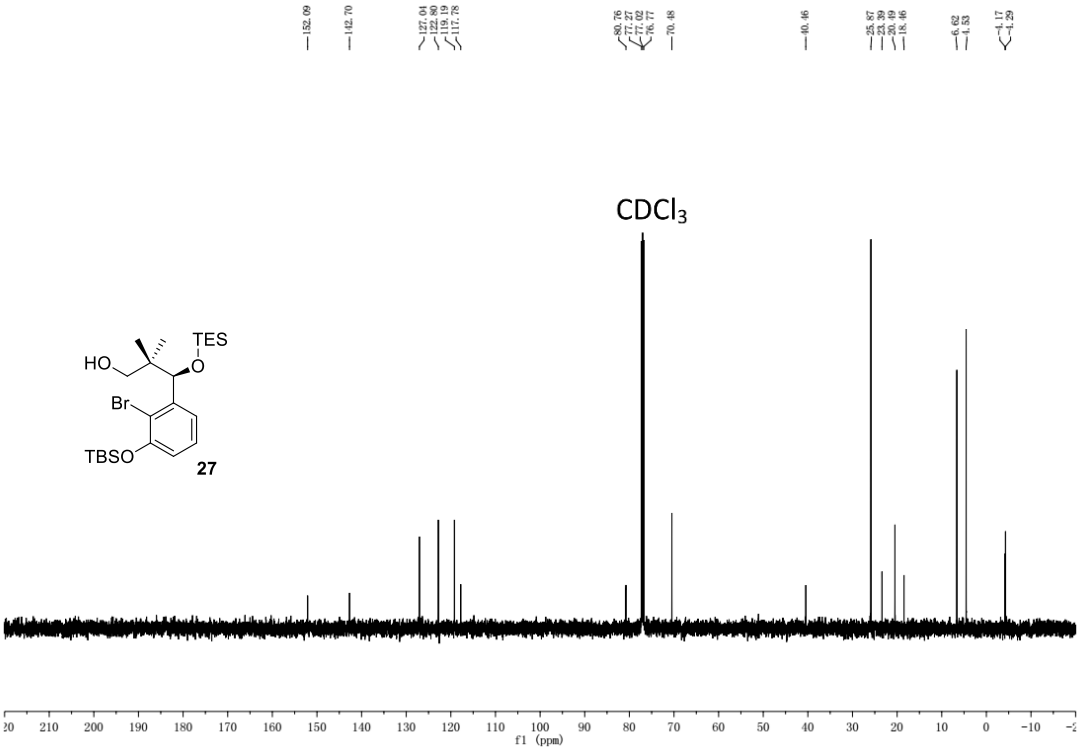
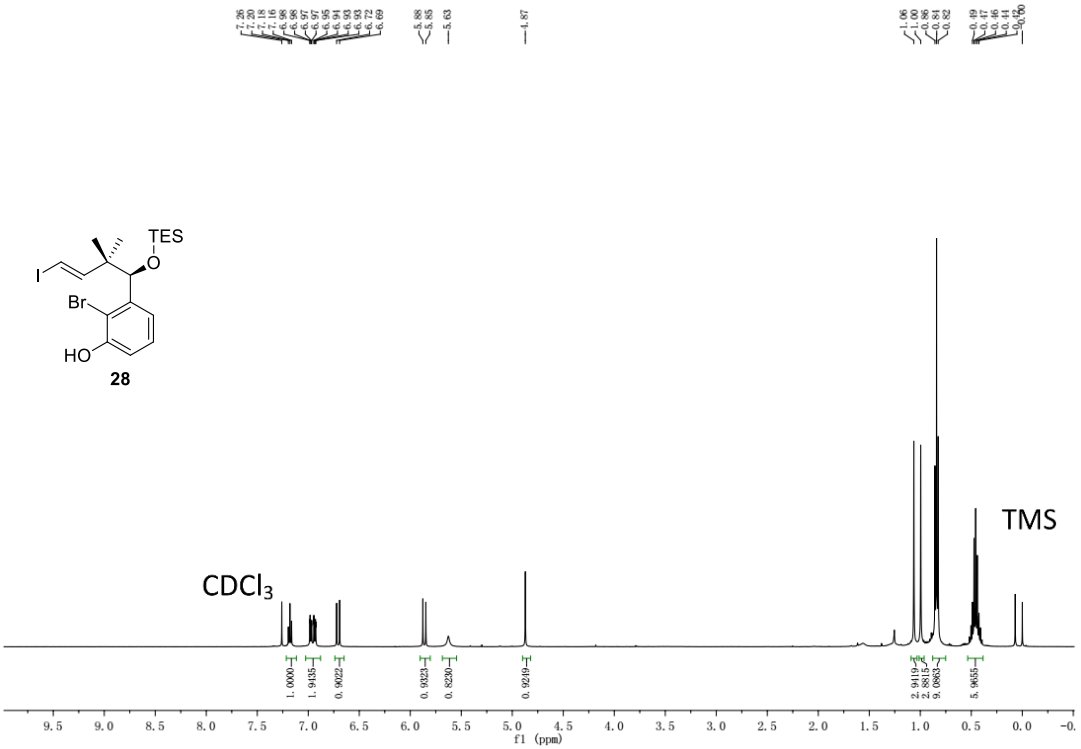


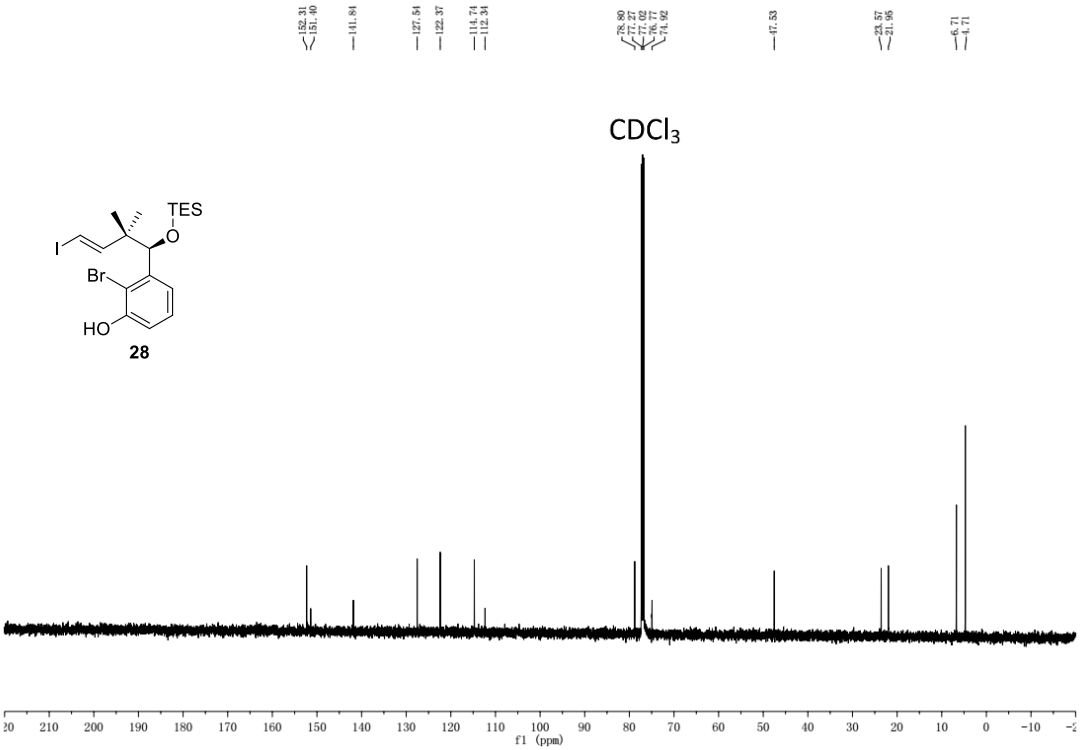
^{13}C NMR ($CDCl_3$, 125 MHz)



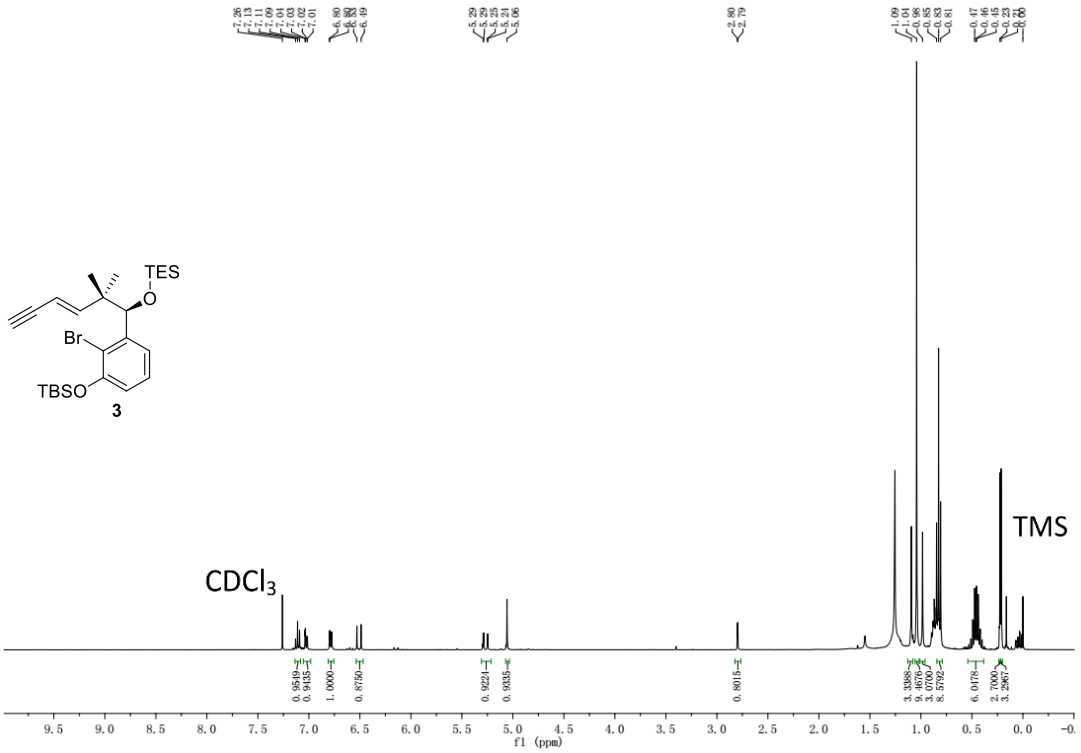
^{1}H NMR ($CDCl_3$, 500 MHz)



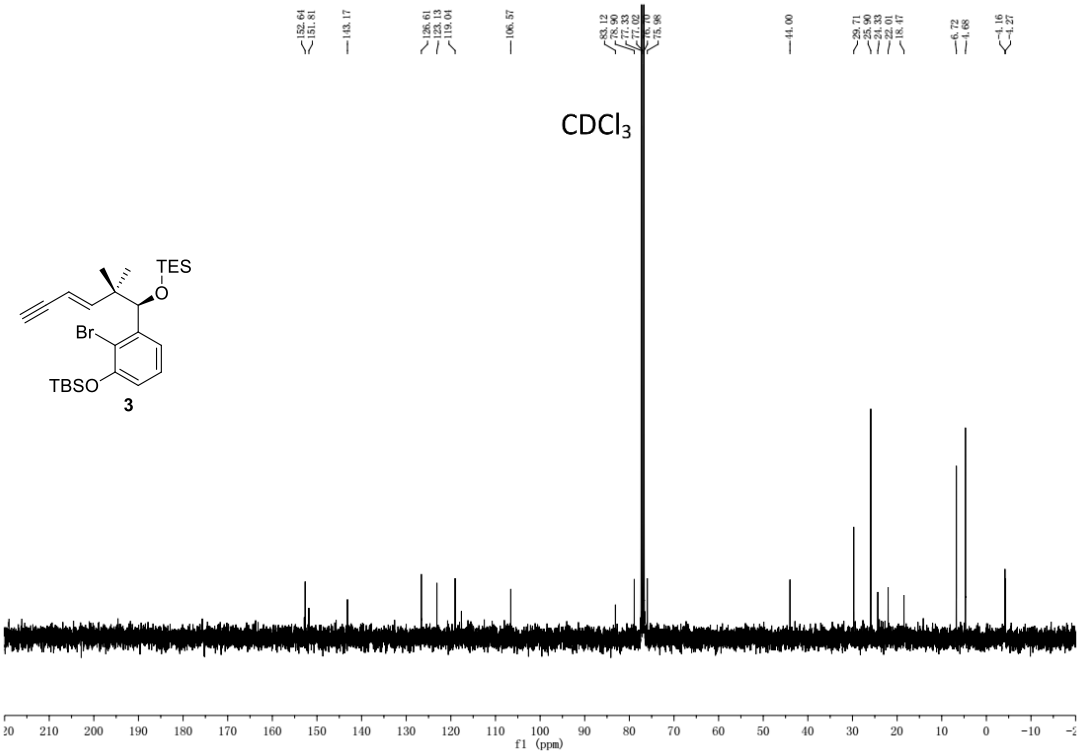
^{13}C NMR ($CDCl_3$, 125 MHz)



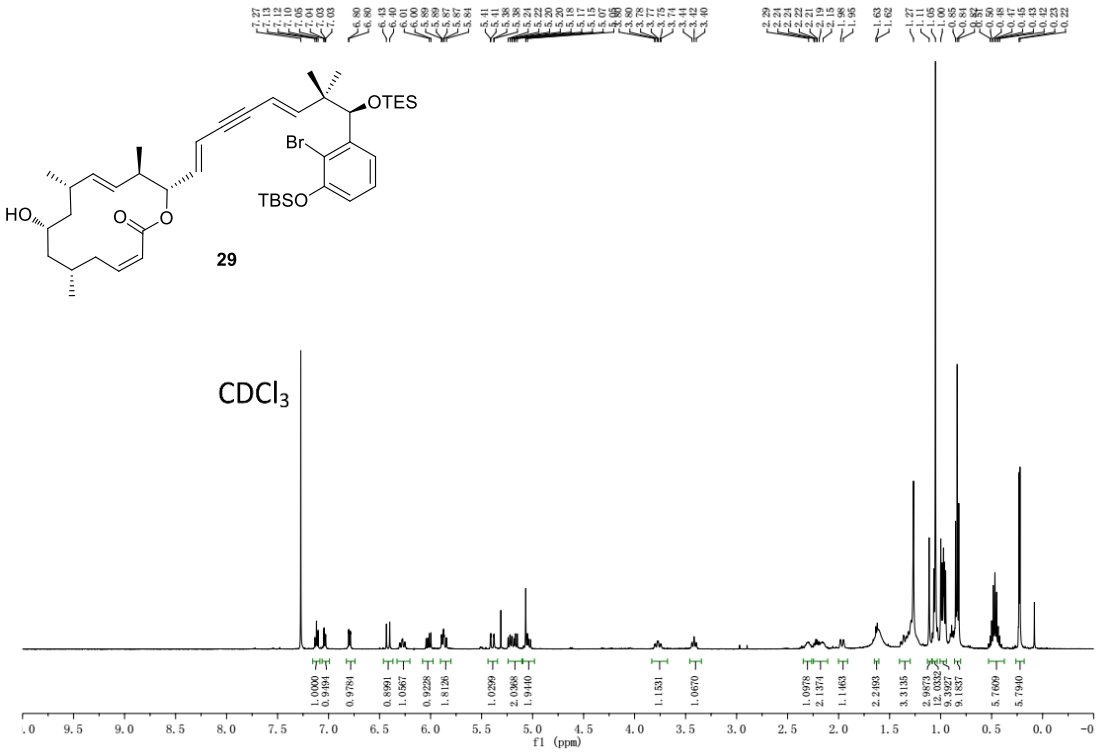
^{1}H NMR ($CDCl_3$, 400 MHz)



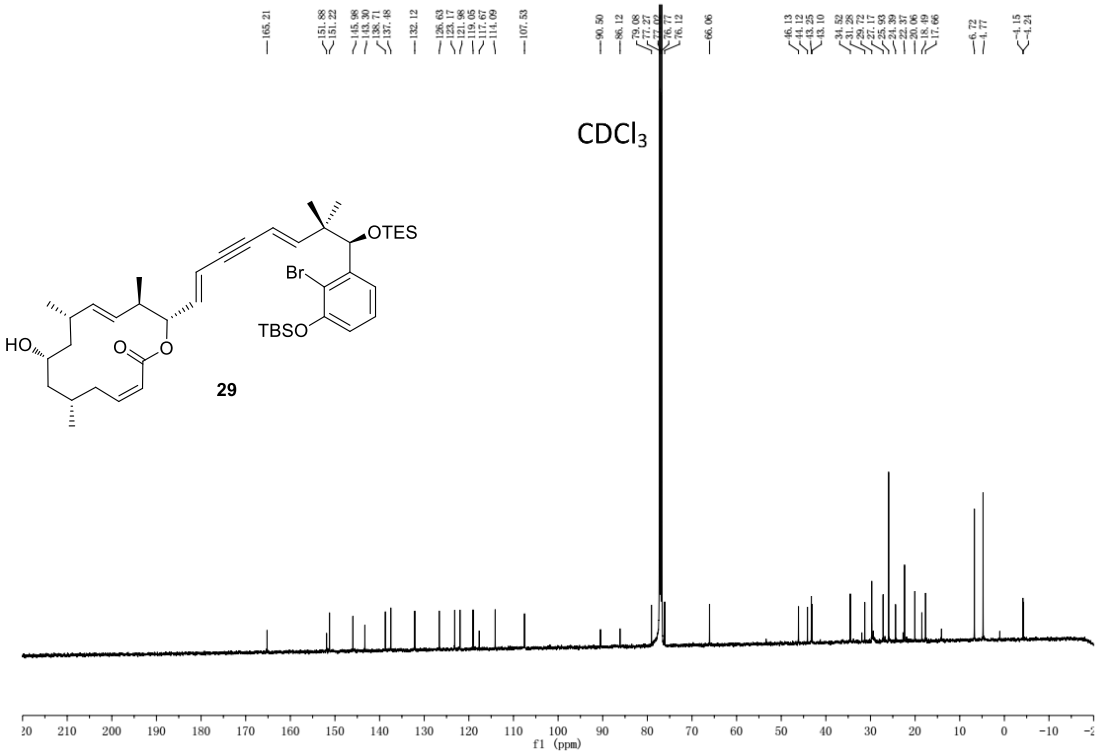
^{13}C NMR ($CDCl_3$, 100 MHz)



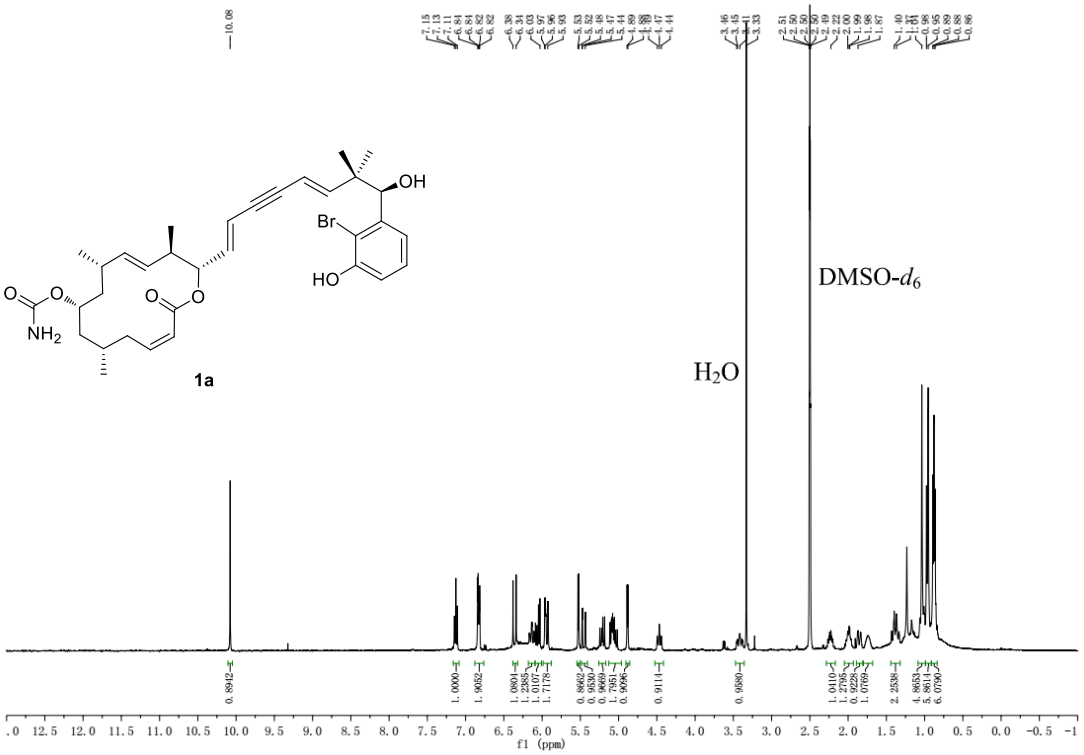
^{1}H NMR ($CDCl_3$, 500 MHz)



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



^{1}H NMR (DMSO-*d6*, 400 MHz)



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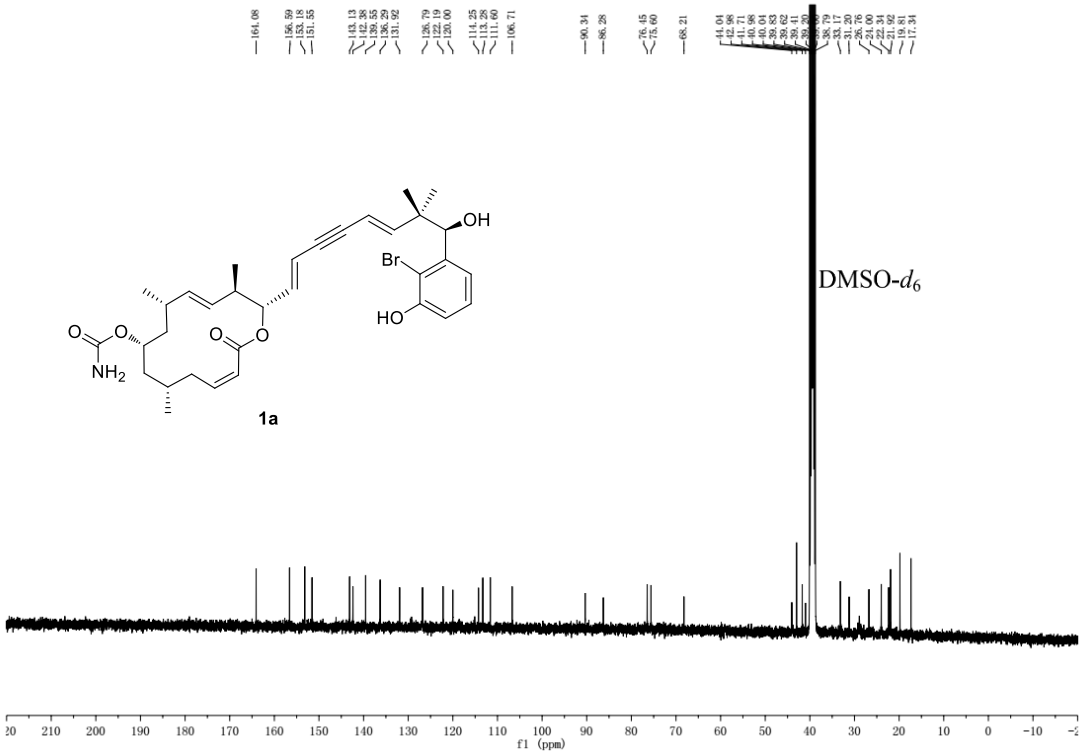
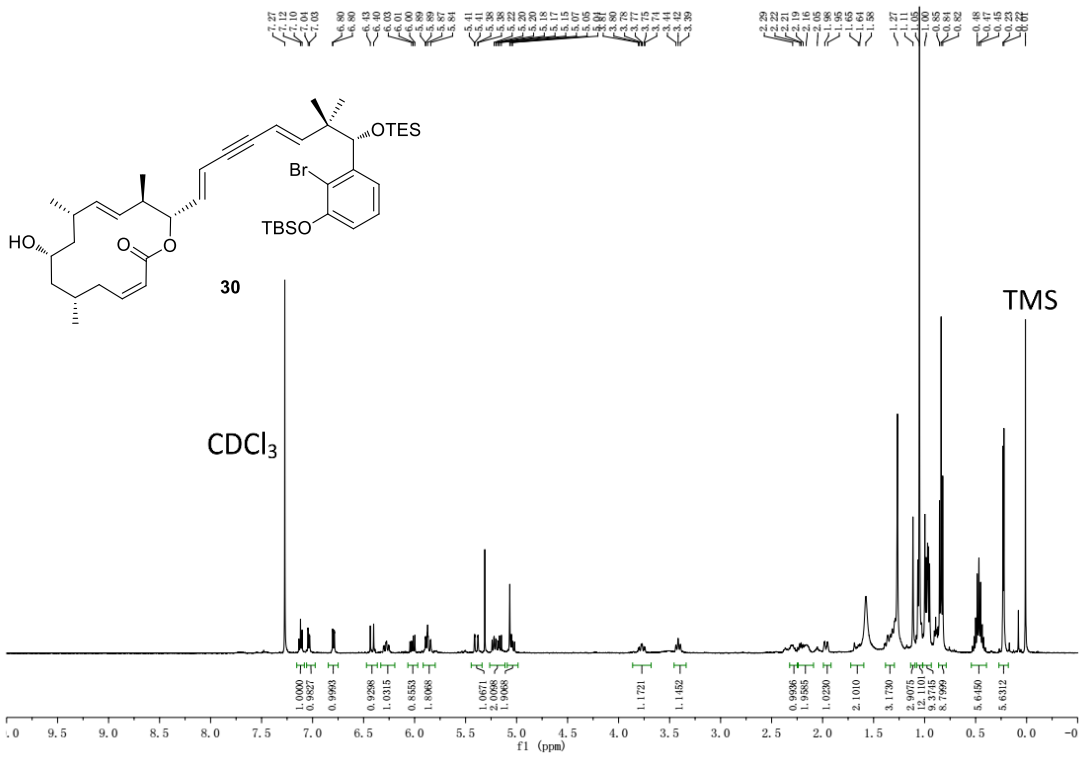
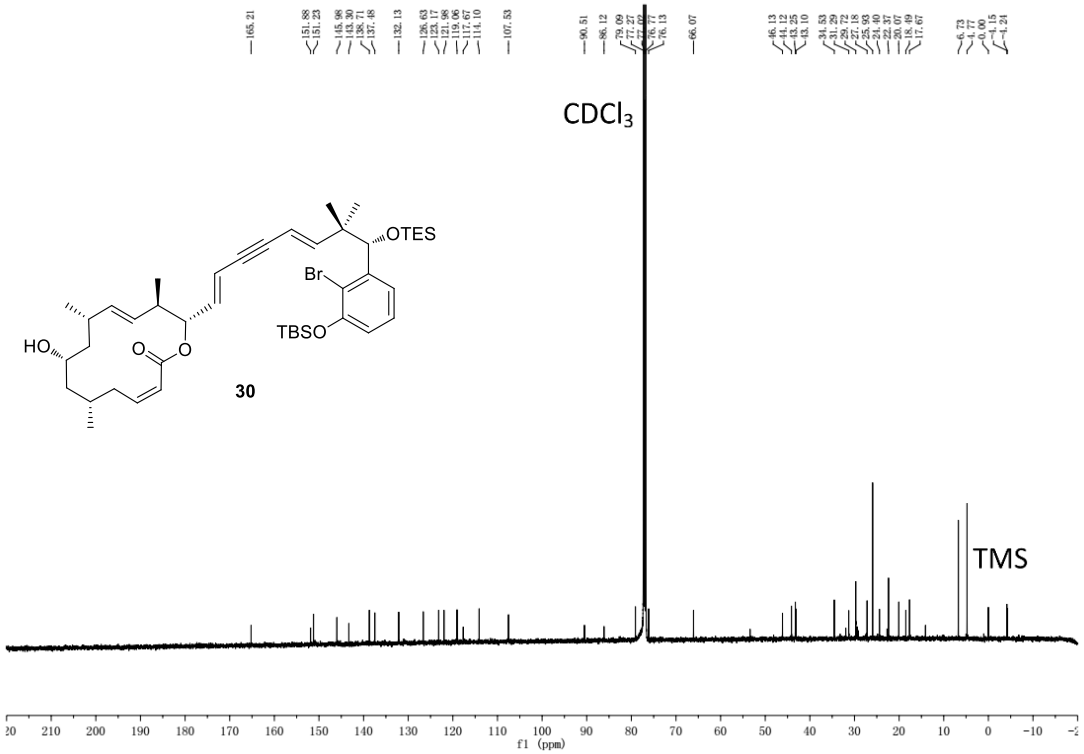


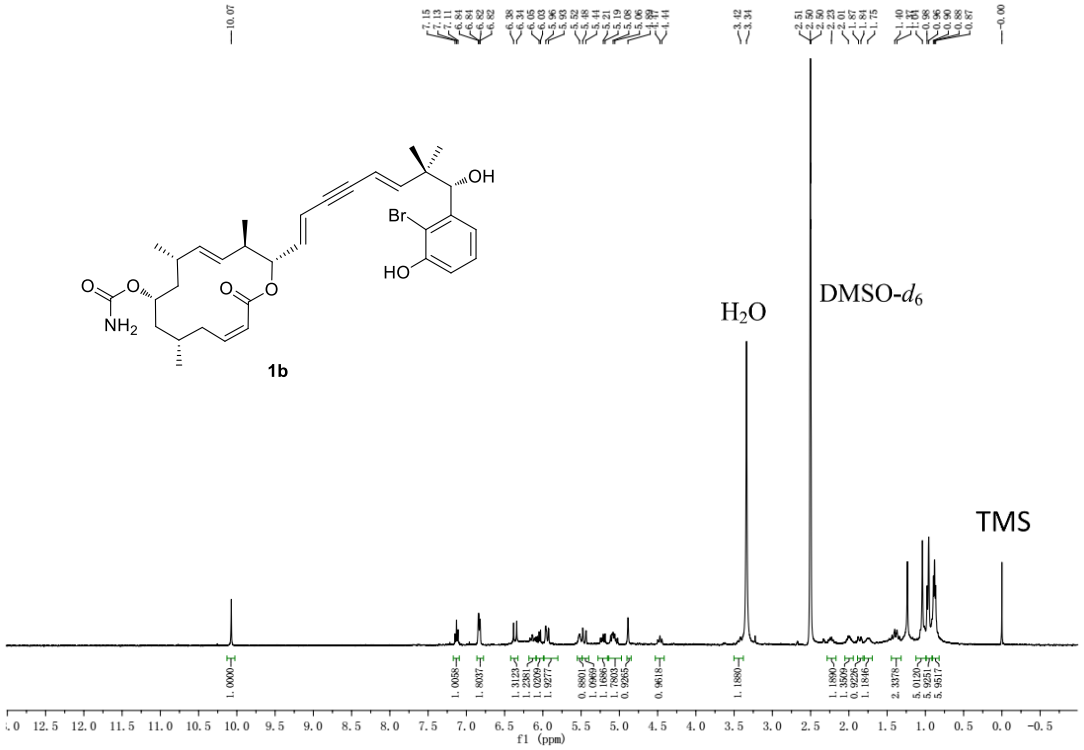
^{1}H NMR ($CDCl_3$, 500 MHz)



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



^{1}H NMR (DMSO-*d6*, 400 MHz)



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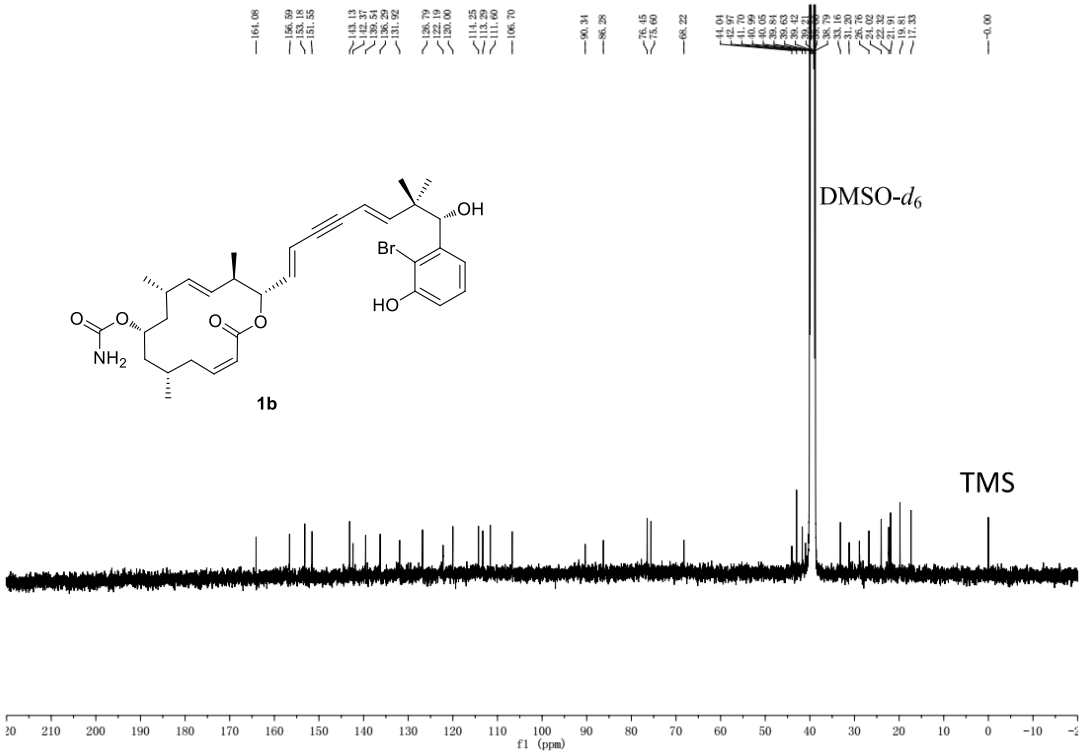
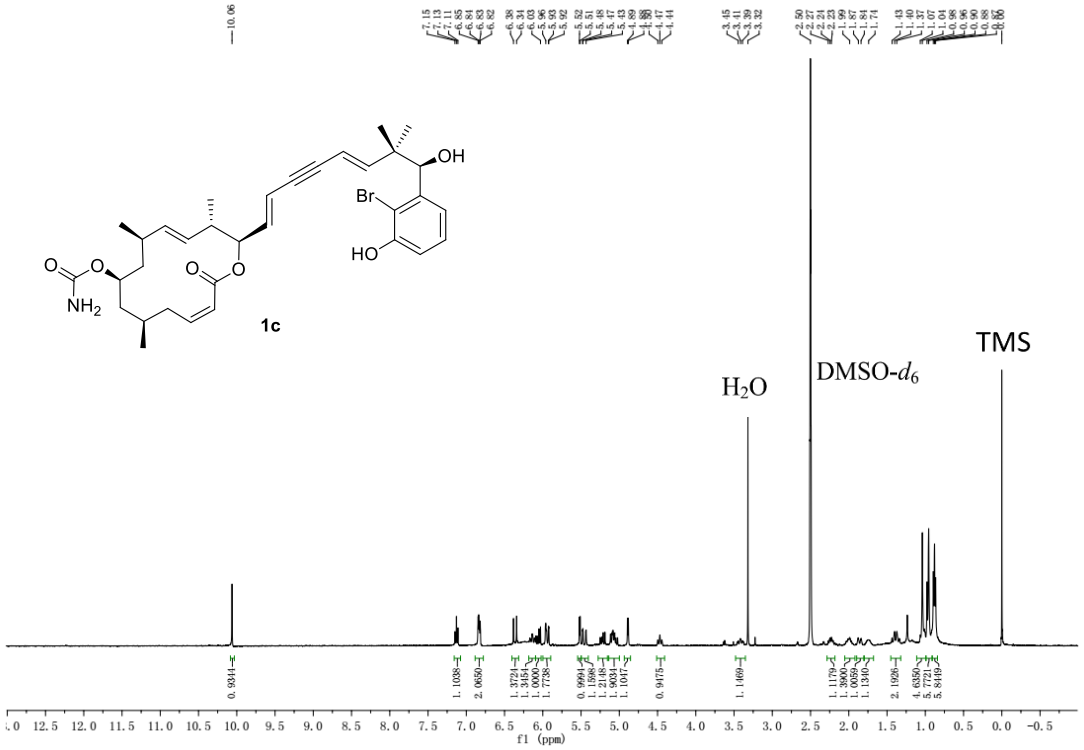


^{1}H NMR (DMSO-*d6*, 400 MHz)



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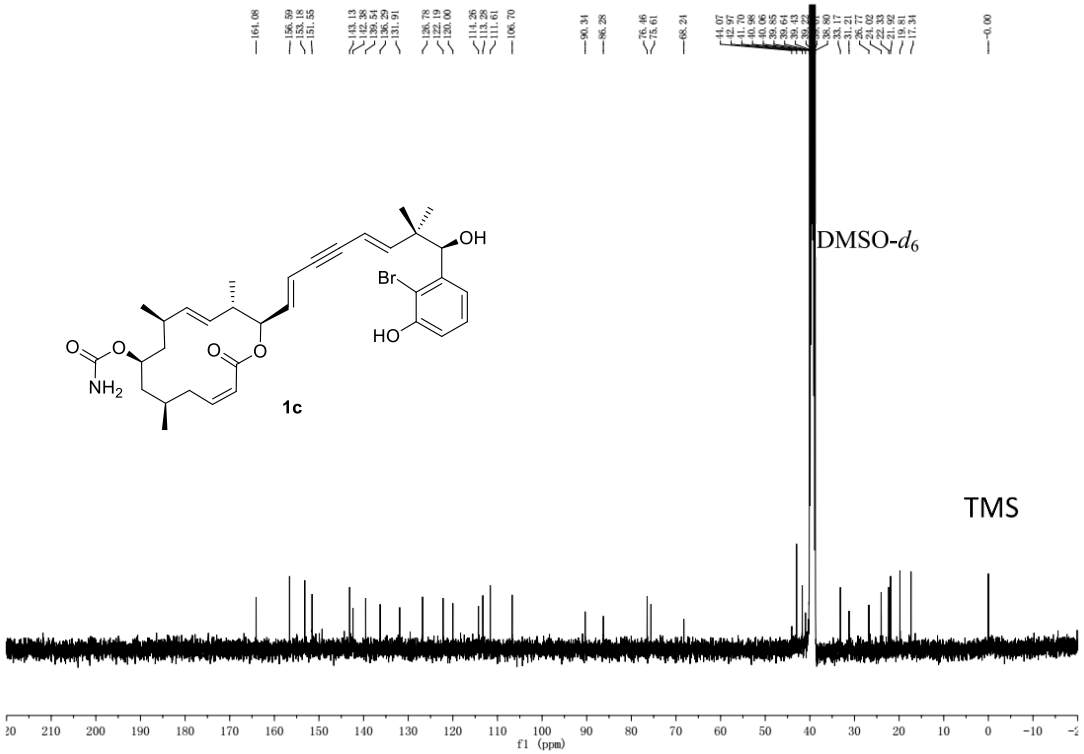

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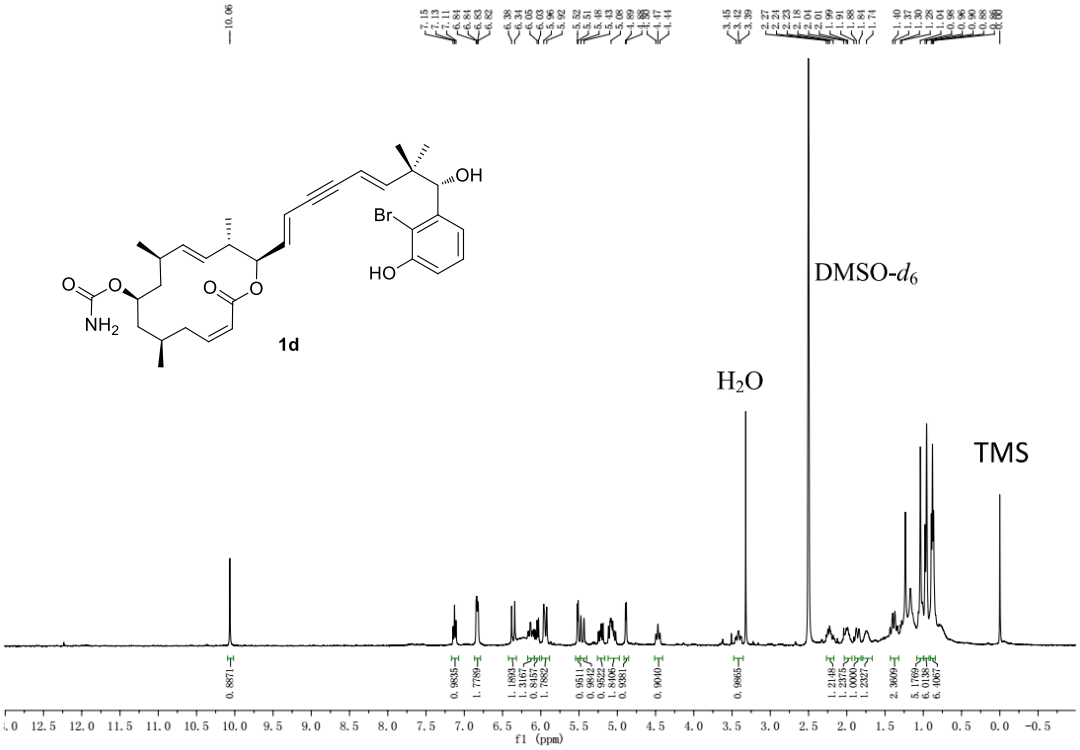

^{13}C NMR (DMSO-*d6*, 100 MHz)