Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Total Synthesis of Amphidinins E, F and *epi*-Amphidinin F

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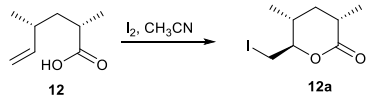
General Experimental

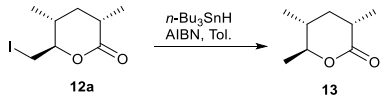
All reactions were conducted in flame-dried or oven-dried glassware under an atmosphere of dry nitrogen or argon. Oxygen and/or moisture sensitive solids and liquids were transferred appropriately. Concentration of solutions in *vacuo* was accomplished using a rotary evaporator fitted with a water aspirator. Residual solvents were removed under high vacuum (0.1-0.2 mm Hg). All reaction solvents were purified before use: Diethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl. Toluene was distilled over molten sodium metal. Dichloromethane and trimethylamine 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 400 MHz or AV 500 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 125, 100, or 75 MHz. Low- and high- resolution EI and ESI mass spectra were obtained using a AB QSTAR Elite mass spectrometer. Optical rotations were recorded on a Rudolph AutoPol I Polarimeter.

Experimental Procedures



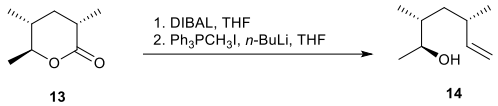
12 **12a**

To a solution of **12** (1.2 g, 8.45 mmol) in acetonitrile (80 mL) at 0 ℃, I_2 (6.44 g, 25.35 mmol) in acetonitrile (30 mL) was added. The reaction mixture was stirred at 0 ℃ for 3.5 h, then poured into a saturated aqueous solution of $Na_2S_2O_3$ (20 mL). Volatiles were removed in *vacuo*. The residue was dissolved in ethyl acetate (100 mL) and washed with brine (30 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated in *vacuo* and the residue was purified by silica gel flash chromatography to afford compound **12a** (1.94 g, 86%) as a colorless oil. **TLC**: R_f = 0.40 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 14.4 (*c* 1.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.64 – 3.50 (m, 2H), 3.38 (dd, *J* = 11.2, 3.3 Hz, 1H), 2.64 – 2.49 (m, 1H), 2.09 – 1.96 (m, 1H), 1.99 – 1.88 (m, 1H), 1.50 (q, *J* = 12.7 Hz, 1H), 1.29 (d, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.60, 83.46, 36.56, 36.40, 34.69, 17.10, 17.00, 9.71. **HRMS** (*m/z*): calculated for $C_8H_{13}IO_2Na^+$ $[M+Na]^+$: 290.9858, found: 290.9854.



12a **13**

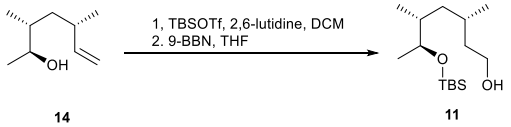
To a solution of **12a** (1.94 g, 7.24 mmol) in toluene (60 mL), *n*-tributyltin hydride (4.01 mL, 14.48 mmol) and AIBN (0.20 g, 1.22 mmol) were subsequently added at room temperature. The resulting mixture was heated at 80 ℃ and stirried for 2 h. After cooled to room temperature, the reaction mixture was concentrated in *vacuo* and purified by silica gel flash chromatography to afford compound **13** (0.92 g, 89%) as a colorless oil. **TLC**: R_f = 0.35 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = –20 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.09 – 3.97 (m, 1H), 2.58 – 2.43 (m, 1H), 1.90 (ddd, *J* = 13.4, 6.3, 3.1 Hz, 1H), 1.76 – 1.63 (m, 1H), 1.35 (d, *J* = 6.3 Hz, 3H), 1.36 – 1.29 (m, 1H), 1.27 (d, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.54, 83.77, 37.80, 36.47, 35.98, 20.32, 17.42, 17.36. **HRMS** (*m/z*): calculated for $C_8H_{14}O_2Na^+$ $[M+Na]^+$: 165.0891, found: 165.0886.



13 **14**

To a solution of ester **13** (0.90 g, 6.34 mmol) in THF (60 mL) at –78 °C, DIBAL-H (7.61 mL, 7.61 mmol, 1 M in toluene) was added. The reaction mixture was stirred at –78 ℃ for 1.5 h before it was quenched by careful addition of MeOH (3 mL) at –78 ℃. After being warmed to room temperature, an aqueous solution of Rochelle's salt (30 mL) was added to the solution, which was then stirred vigorously for 6 h. Volatiles were removed in *vacuo* and the aqueous solution was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the corresponding hemiacetal, which was used in the next step without further purification.

n-Butyllithium (4.5 mL, 11.3 mmol, 2.5 M in hexane) was slowly added to a stirred suspension of methyl triphenylphosphonium iodide (6.40 g, 16.0 mmol) in THF (60 mL) at –78 ℃ and then stirred at –50 ℃ for 2 h. To this solution, a solution of hemiacetal in 5 mL of THF was added at –78 ℃. The reaction mixture was allowed to warm to room temperature, stirred at 60 ℃ for additional 4 h and then quenched with saturated aqueous solution of NH_4Cl (5 mL) and diluted with ethyl acetate (150 mL). The organic phase was washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford alkene **14** (0.77 g, 85% for two steps) as a colorless oil. **TLC**: R_f = 0.4 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 25 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.65 – 5.51 (m, 1H), 5.01 – 4.87 (m, 2H), 3.68 – 3.57 (m, 1H), 2.26 – 2.16 (m, 1H), 1.57 – 1.47 (m, 1H), 1.46 – 1.34 (m, 1H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.10 – 1.00 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.39, 113.27, 72.24, 39.62, 37.65, 35.92, 21.97, 19.52, 14.55. **HRMS** (*m/z*): calculated for $C_9H_{18}ONa^+$ $[M+Na]^+$: 165.1255, found: 165.1258.



14 **11**

To a solution of **14** (0.71 g, 5.00 mmol) and 2, 6-lutidine (1.15 mL, 10.00 mmol) in dry DCM

(30 mL), TBSOTf (1.37 mL, 6.00 mmol) was added at –78 ℃. The reaction mixture was stirred at –78 ℃ for 3 h, then quenched by addition of H_2O (5 mL) and diluted with ethyl acetate (100 mL). Layers were separated and the organic phase was washed sequentially with citric acid (10 mL, 10% in water), saturated aqueous solution of $NaHCO_3$ (10 mL) and brine (10 mL). The organic solution was dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the corresponding alkene, which was used in the next step without further purification.

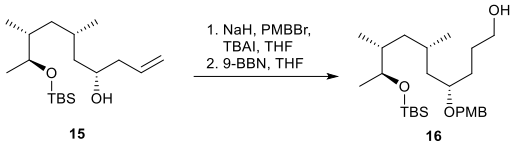
To a solution of the above alkene in THF (30 mL), 9-BBN (15 mL, 7.50 mmol, 0.5 M in THF) was added dropwise at 0 ℃. The reaction was allowed to warm to room temperature and stirred for 8 h. After NaOH (5 mL, 3 M in water) and H_2O_2 (4 mL, 30% in water) were added, and the mixture was refluxed for 1 h. After cooling, the mixture was extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed successively with saturated aqueous NH_4Cl (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford alcohol **11** (1.20 g, 88% for two steps) as a colorless oil. **TLC**: R_f = 0.38 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 11.1 (*c* 0.8, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.76 – 3.58 (m, 3H), 1.69 – 1.50 (m, 4H), 1.36 – 1.24 (m, 2H), 1.01 (d, *J* = 6.2 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 9H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.03 (s, 3H), 0.02 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 71.83, 61.26, 40.84, 39.46, 37.64, 27.29, 26.04, 20.86, 19.20, 18.24, 15.09, -4.25, -4.62. **HRMS** (*m/z*): calculated for $C_{15}H_{34}O_2SiNa^+$ $[M+Na]^+$: 297.2226, found: 297.2225.

11 **15**

To a stirred solution of alcohol **11** (1.00 g, 3.65 mmol) in DCM (30 mL), $NaHCO_3$ (1.23 g, 14.60 mmol) and Dess-Martin periodinane (2.32 g, 5.48 mmol) were subsequently added at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred for additional 1 h and then filtered through a pad of silica gel. The filtrate was concentrated in *vacuo* to afford the corresponding aldehyde as a colorless oil.

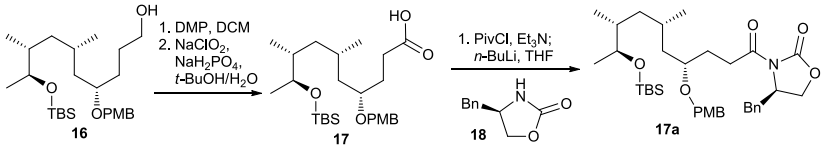
To a stirred solution of (-)-Ipc_2BOMe (1.90 g, 6.00 mmol) in diethyl ether (50 mL), allyl magnesium bromide (6.67 mL, 5.00 mmol, 0.75 M in diethyl ether) was added dropwise at –

78 ℃. The reaction mixture was allowed to warm to room temperature and stirred for 1 h before re-cooled to –78 ℃. To this solution was added a solution of the above fresh prepared aldehyde in diethyl ether (10 mL) via cannula over 30 min. After being stirred at –78 ℃ for 3 h, the reaction mixture was slowly warmed to room temperature. After NaOH (4 mL, 3 M in water) and H_2O_2 (4 mL, 30% in water) were added, the reaction mixture was then refluxed for 1 h. After cooling, the mixture was extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed successively with saturated aqueous NH_4Cl (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to give homoallylic alcohol **15** (1.13 g, 82% for two steps) as a colorless oil. **TLC**: R_f = 0.40 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 12.1 (*c* 1.2, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.90 – 5.75 (m, 1H), 5.18 – 5.08 (m, 2H), 3.80 – 3.71 (m, 1H), 3.68 – 3.61 (m, 1H), 2.30 – 2.21 (m, 1H), 2.19 – 2.10 (m, 1H), 1.77 – 1.64 (m, 1H), 1.60 – 1.53 (m, 2H), 1.51 – 1.46 (m, 1H), 1.33 – 1.24 (m, 1H), 1.11 – 1.04 (m, 1H), 1.02 (d, *J* = 6.2 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88 (s, 9H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.03 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 135.04, 118.26, 71.88, 68.38, 43.87, 43.15, 41.38, 37.55, 26.85, 26.06, 20.59, 19.25, 18.26, 15.08, -4.21, -4.60. **HRMS** (*m/z*): calculated for $C_{18}H_{38}O_2SiNa^+$ $[M+Na]^+$: 337.2539, found: 337.2536.



To a suspension of NaH (153 mg, 3.82 mmol, 60% dispersion in mineral oil) in THF (20 mL) was added a solution of compound **15** (600 mg, 1.91 mmol) in THF (10 mL) at 0 ℃. 20 min later, 4-methoxybenzyl bromide (420 mg, 2.10 mmol) was added dropwise, followed by addition of Bu_4NI (136 mg, 0.37 mmol) at 0 ℃. The resulting reaction mixture was stirred overnight at 60 ℃ and then quenched by addition of saturated aqueous solution of NH_4Cl (10 mL). Volatiles were removed in *vacuo*, the aqueous residue was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with water (10 mL) and brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was used in the next step without further purification.

To a solution of the above alkene in THF (10 mL), 9-BBN (6 mL, 3.00 mmol, 0.5 M in THF) was added dropwise at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred for 8 h. After NaOH (2 mL, 3 M in water) and H_2O_2 (2 mL, 30% in water) were added, the reaction mixture was refluxed for 1 h. After cooling, the mixture was extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed successively with saturated aqueous NH_4Cl (8 mL), brine (8 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford alcohol **16** (621 mg, 75% for two steps) as a colorless oil. **TLC**: R_f = 0.50 (silica gel, 15% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 13.80 (*c* 1.2, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 11.8 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.43 (q, *J* = 7.9 Hz, 2H), 3.80 (s, 3H), 3.68 – 3.59 (m, 3H), 3.55 – 3.47 (m, 1H), 1.89 – 1.83 (m, 1H), 1.71 – 1.60 (m, 6H), 1.30 – 1.24 (m, 1H), 1.10 – 1.04 (m, 1H), 1.00 (d, *J* = 6.2 Hz, 3H), 0.96 – 0.91 (m, 1H), 0.88 (s, 9H), 0.86 (d, *J* = 7.2 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.28, 130.97, 129.51, 113.91, 76.57, 71.71, 70.60, 63.27, 55.43, 41.51, 41.28, 37.57, 31.03, 28.66, 27.04, 26.06, 21.08, 19.10, 18.27, 15.14, -4.23, -4.59. **HRMS** (*m/z*): calculated for $C_{26}H_{48}O_4SiNa^+$ $[M+Na]^+$: 475.3220, found: 475.3213.



To a stirred solution of alcohol **16** (500 mg, 1.11 mmol) in DCM (10 mL), $NaHCO_3$ (373 mg, 4.44 mmol) and Dess-Martin periodinane (706 mg, 1.67 mmol) were subsequently added at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was filtered through a pad of silica gel and the filtrate was concentrated in *vacuo* to afford the corresponding aldehyde as a colorless oil, which was used directly in the next step.

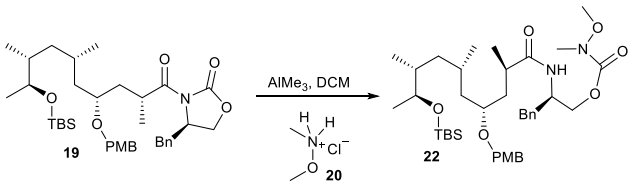
To the above aldehyde in *tert*-butanol (10 mL) and 2,3-dimethyl-but-2-ene (5 mL), a solution of $NaClO_2$ (300 mg, 3.33 mmol) and NaH_2PO_4 (519 mg, 3.33mmol) in water (5 mL) was added at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred for 1 h and then diluted with ethyl acetate-H_2O (40 mL-5 mL). Layers were separated and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The combined organic layers

were dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the corresponding carboxylic acid **17**, which was used in the next step without further purification.

To a stirred solution of the corresponding carboxylic acid **17** (610 mg, 1.46 mmol) in dry THF (10 mL), Et_3N (0.31 mL, 2.22 mmol) and trimethylacetyl chloride (0.16 mL, 1.33 mmol) were sequentially added at 0 ℃. 20 min later, the reaction mixture was cooled to –78 ℃. In a separate flask, *n*-butyllithium (1.11 mL, 1.67 mmol, 1.5M in hexane) was added to a solution of (4R)-4-benzyl-1,3-oxazolidin-2-one (393 mg, 2.22 mmol) in dry THF (15 mL) at –78 ℃. 30 min later, the resulting solution was transferred to the above reaction vessel. This reaction mixture was stirred for 2 h at –78 ℃ and then quenched with saturated aqueous solution of NH_4Cl (5 mL). Volatiles were removed in *vacuo*, and the aqueous phase was extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **17a** (374mg, 83%) as a colorless oil. **TLC**: R_f = 0.50 (silica gel, 10% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{20}}$ = –9.2 (*c* 1.2, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.30 – 7.26 (m, 3H), 7.18 (d, *J* = 6.9 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.57 – 4.49 (m, 1H), 4.45 (s, 2H), 4.11 (d, *J* = 5.2 Hz, 2H), 3.77 (s, 3H), 3.71 – 3.64 (m, 1H), 3.58 – 3.50 (m, 1H), 3.25 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.05 – 2.94 (m, 2H), 2.68 (dd, *J* = 13.4, 9.7 Hz, 1H), 1.99 – 1.86 (m, 2H), 1.74 – 1.65 (m, 2H), 1.63 – 1.58 (m, 1H), 1.34 – 1.26 (m, 2H), 1.15 – 1.06 (m, 1H), 1.02 (d, *J* = 6.2 Hz, 3H), 0.90 – 0.88 (m, 12H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 173.42, 159.24, 153.53, 135.57, 131.23, 129.67, 129.54, 129.07, 127.45, 113.87, 75.70, 71.68, 70.61, 66.26, 55.41, 55.32, 41.83, 41.29, 38.06, 37.59, 31.61, 29.19, 27.14, 26.08, 21.11, 19.03, 18.27, 15.14, -4.23, -4.57. **HRMS** (*m/z*): calculated for $C_{36}H_{55}NO_6SiNa^+$ $[M+Na]^+$: 648.3696, found: 648.3692.

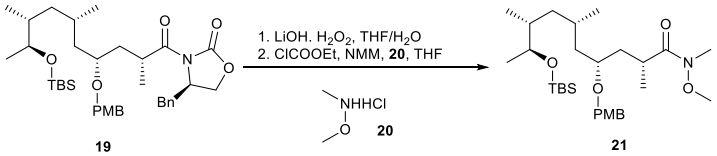
To a solution of **17a** (374 mg, 0.59 mmol) in THF (10 mL), NaHMDS (0.89 mL, 0.89 mmol, 1.0 M) was added at –78 ℃. 30 min later, MeI (73 μL, 1.18 mmol) was added dropwise at –

78 ℃. The reaction mixture was stirred overnight at –78 ℃, before it was quenched with saturated aqueous NH_4Cl (3 mL). Volatiles were removed in *vacuo*, the aqueous layer was extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **19** (301mg, 80%) as a colorless oil. **TLC**: R_f = 0.60 (silica gel, 10% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{20}}$ = –7.30 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.26 – 7.20 (m, 3H), 7.11 (d, *J* = 6.9 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.32 (q, *J* = 7.8 Hz, 2H), 4.17 – 4.09 (m, 1H), 3.99 – 3.88 (m, 2H), 3.71 (s, 3H), 3.71 – 3.68 (m, 1H), 3.51 – 3.46 (m, 1H), 3.15 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.64 (dd, *J* = 13.4, 9.8 Hz, 1H), 2.24 – 2.17 (m, 1H), 1.76 – 1.69 (m, 1H), 1.69 – 1.61 (m, 2H), 1.60 – 1.53 (m, 2H), 1.34 – 1.28 (m, 2H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.11 – 1.06 (m, 1H), 1.03 (d, *J* = 6.2 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.04 (s, 3H), 0.04 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.05, 159.05, 153.16, 135.68, 131.18, 129.50, 129.48, 128.89, 127.25, 113.66, 74.58, 71.56, 70.23, 65.90, 55.30, 41.41, 40.86, 38.42, 37.99, 37.43, 33.33, 27.15, 26.04, 21.28, 19.04, 18.61, 18.23, 15.14, -4.27, -4.62. **HRMS** (*m/z*): calculated for $C_{37}H_{57}NO_6SiNa^+$ $[M+Na]^+$: 662.3853, found: 662.3855.



To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (9 mg, 0.093 mmol) in THF (5 mL), $AlMe_3$ in hexane (0.093 mL, 0.093 mmol, 1.0 M) was added slowly at 0 ℃. After the vigorous gas evolution had ceased, the resulting homogeneous solution was stirred at room temperature for 35 min, then cooled to 0 ℃ again. To this mixture was added dropwise a solution of **19** (20 mg, 0.031 mmol) in THF (4 mL) and rinsing with THF (2 x 3 mL). The reaction mixture was stirred at 0 ℃ for 2.5 h before it was transferred via cannula to an Erlenmeyer flask containing a vigorously stirred mixture of CH_2Cl_2 (20 mL) and 0.5 M aqueous HCl (12 mL) at 0 ℃. The biphasic mixture was stirred for 5 min and then the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), and the combined

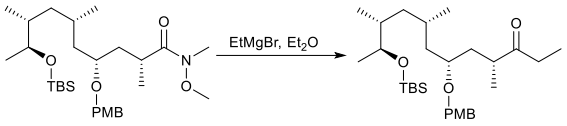
organic phases were dried over Na_2SO_4, concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **22** (19 mg, 90%) as a colorless oil. **TLC**: R_f = 0.60 (silica gel, 50% ethyl acetate in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 5H), 7.17 (d, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.74 (d, *J* = 8.3 Hz, 1H), 4.39 (d, *J* = 11.2 Hz, 2H), 4.32 (d, *J* = 10.9 Hz, 1H), 4.05 (d, *J* = 5.1 Hz, 2H), 3.78 (s, 3H), 3.66 (s, 3H), 3.64 – 3.61 (m, 1H), 3.47 – 3.39 (m, 1H), 3.10 (s, 3H), 2.78 (dd, *J* = 7.2, 3.9 Hz, 2H), 2.39 – 2.28 (m, 1H), 1.82 – 1.73 (m, 1H), 1.69 – 1.44 (m, 6H), 1.24 (s, 4H), 1.01 (dd, *J* = 13.5, 6.5 Hz, 7H), 0.86 (d, *J* = 3.0 Hz, 13H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.02 (d, *J* = 4.0 Hz, 6H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.98, 159.17, 157.07, 137.16, 131.08, 129.28, 129.23, 128.57, 126.70, 113.84, 75.22, 71.59, 70.20, 66.46, 61.64, 55.30, 49.66, 41.62, 41.29, 39.31, 37.85, 37.47, 35.61, 29.70, 26.95, 25.93, 21.08, 18.97, 18.62, 18.12, 14.97, 1.02, -4.35, -4.73 ppm. **HRMS** (m/z): calculated for $C_{39}H_{64}N_2NaO_7Si^+$ $[M+Na]^+$: 723.4380, found: 723.4385.



To a solution of **19** (200 mg, 0.31 mmol) in THF/H_2O (4 mL/4 mL, 1:1), LiOH•H_2O (52 mg, 1.24 mmol) and H_2O_2 (0.14 mL, 1.24 mmol, 30% in water) were sequentially added at 0 ℃. The reaction mixture was stirred at room temperature for 2 h. Volatiles were removed in *vacuo* and diethyl ether (10 mL) was added to the aqueous phase. The reaction mixture was acidified to pH = 3 with dilute HCl (1 N in water) and then extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the corresponding carboxylic acid.

To a solution of the above carboxylic acid in THF (10 mL), NMM (68 μL, 0.62 mmol) and EtOCOCl (44 μL, 0.47 mmol) were sequentially added at 0 ℃. The reaction mixture was stirred at 0 ^oC for 1 h and *N*,O-dimethyl-hydroxyamine (45 mg, 0.47 mmol) was added in one portion. The reaction mixture was stirred at room temperature for further 16 h and quenched by addition of saturated aqueous solution of NH_4Cl (3 mL). Volatiles were removed in *vacuo*. The aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers

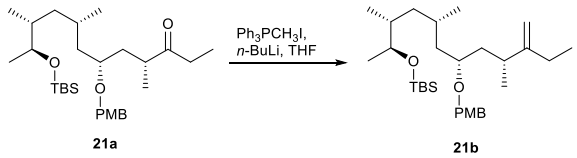
were washed with brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford amide **21** (163 mg, 86% for two steps) as a colorless oil. **TLC**: R_f = 0.50 (silica gel, 10% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{20}}$ = 4.40 (*c* 1.1, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.37 (q, *J* = 2.6 Hz, 2H), 3.80 (s, 3H), 3.69 – 3.64 (m, 1H), 3.63 (s, 3H), 3.51 – 3.40 (m, 1H), 3.14 (s, 3H), 2.06 – 1.95 (m, 1H), 1.73 – 1.62 (m, 3H), 1.61 – 1.51 (m, 2H), 1.35 – 1.26 (m, 2H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.08 – 1.03 (m, 1H), 1.01 (d, *J* = 6.2 Hz, 3H), 0.90 – 0.87 (m, 12H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 177.98, 159.11, 131.26, 129.47, 113.75, 75.30, 71.66, 70.16, 61.45, 55.41, 41.73, 41.38, 38.70, 37.51, 31.58, 29.85, 26.90, 26.05, 21.17, 19.03, 18.58, 18.25, 14.97, -4.24, -4.62. **HRMS** (*m/z*): calculated for $C_{29}H_{53}NO_5SiNa^+$ $[M+Na]^+$: 546.3591, found: 546.3588.



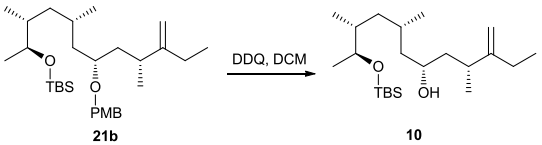
21 **21a**

To a solution of Weinreb amide **21** (100 mg, 0.19 mmol) in diethyl ether (5 mL), EtMgBr (0.39 mL, 0.57 mmol, 2.0 M in diethyl ether) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature and monitored by TLC. Upon the consumption of all starting material, saturated aqueous solution of NH_4Cl (2 mL) was added to the reaction mixture at 0 °C. Layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford ketone **21a** (77 mg, 82%) as a colorless oil. **TLC**: R_f = 0.70 (silica gel, 10% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{20}}$ = 6.50 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.31 (d, *J* = 1.8 Hz, 2H), 3.79 (s, 3H), 3.70 – 3.62 (m, 1H), 3.44 – 3.34 (m, 1H), 2.79 – 2.67 (m, 1H), 2.50 – 2.28 (m, 2H), 2.02 – 1.93 (m, 1H), 1.70 – 1.53 (m, 4H), 1.51 – 1.44 (m, 1H), 1.31 – 1.23 (m, 2H), 1.05 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 6.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.88 (s, 12H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.09, 159.23, 131.02, 129.64, 113.83, 74.84, 71.66, 70.42, 55.41, 41.94, 41.85, 41.30, 38.31, 37.60, 34.93, 27.06,

26.06, 21.21, 19.04, 18.26, 17.90, 15.05, 7.86, -4.23, -4.61. **HRMS** (*m/z*): calculated for $C_{29}H_{52}O_4SiNa^+$ $[M+Na]^+$: 515.3533, found: 515.3534.

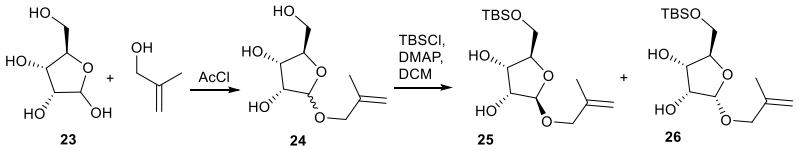


To a solution of methyl triphenylphosphonium iodide (190 mg, 0.45 mmol) in THF (10 mL), *n*-Butyllithium (0.24 mL, 0.36 mmol, 1.5 M in hexane) was added dropwise at –78 ℃ and then stirred for 2 h at –50 ℃. To this mixture, a solution of **21a** (87 mg, 0.18 mmol) in THF (5 mL) was added at –78 ℃. The reaction mixture was allowed to warm to room temperature within 2 h and stirred for additional 6 h. The reaction was quenched with saturated aqueous NH_4Cl (3 mL) and diluted with ethyl acetate (30 mL). The organic phase was washed with water (10 mL) and brine (10 mL), then dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford alkene **21b** (77 mg, 89%) as a colorless oil. **TLC**: R_f = 0.40 (silica gel, 5% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{20}}$ = 7.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.77 – 4.71 (m, 2H), 4.40 (s, 2H), 3.80 (s, 3H), 3.70 – 3.62 (m, 1H), 3.48 – 3.37 (m, 1H), 2.39 – 2.28 (m, 1H), 2.06 – 1.91 (m, 2H), 1.70 – 1.47 (m, 6H), 1.30 – 1.22 (m, 1H), 1.14 – 1.08 (m, 1H), 1.07 – 0.98 (m, 9H), 0.88 (d, *J* = 1.9 Hz, 12H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.20, 156.12, 131.39, 129.49, 113.88, 107.01, 75.54, 71.62, 70.59, 55.44, 42.32, 41.46, 41.43, 37.57, 37.24, 27.04, 26.13, 26.06, 21.25, 20.96, 18.95, 18.26, 15.04, 12.53, -4.24, -4.60. **HRMS** (*m/z*): calculated for $C_{30}H_{54}O_3SiNa^+$ $[M+Na]^+$: 513.3740, found: 513.3738.



To a solution of compound **21b** (50 mg, 0.10 mmol) in dichloromethane (4 mL/0.4 mL), DDQ (28 mg, 0.13 mmol) was added at room temperature. The resulting mixture was stirred vigorously and monitored by TLC analysis. When all the starting material was consumed

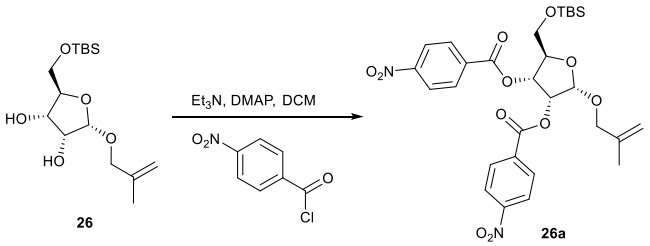
as judged by TLC analysis, the reaction mixture was diluted with DCM (20 mL). The solution was washed with saturated aqueous solution of $Na_2S_2O_3$ (5 mL), $NaHCO_3$ (5 mL) and brine (5 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **10** (32 mg, 86%) as a colorless oil. **TLC**: R_f = 0.45 (silica gel, 15% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{20}}$ = 8.80 (*c* 0.50, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.83 – 4.72 (m, 2H), 3.71 – 3.61 (m, 2H), 2.47 – 2.39 (m, 1H), 2.08 – 1.92 (m, 2H), 1.71 – 1.64 (m, 1H), 1.58 – 1.50 (m, 4H), 1.48 – 1.41 (m, 2H), 1.30 – 1.26 (m, 1H), 1.07 – 1.03 (m, 6H), 1.01 (d, *J* = 6.2 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 9H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.03 (s, 3H), 0.03 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.06, 107.48, 71.90, 67.76, 45.03, 44.24, 41.42, 37.61, 37.48, 29.86, 26.92, 26.07, 21.03, 20.72, 19.21, 18.27, 15.08, 12.58, -4.21, -4.58. **HRMS** (*m/z*): calculated for $C_{22}H_{46}O_2SiNa^+$ $[M+Na]^+$: 393.3165, found: 393.3159.



To a solution of *D*-ribose (3.0 g, 20 mmol) in Methallyl alcohol (25 mL), Acetyl chloride (0.06 mL, 0.85mmol) was added and then stirred overnight. The reaction mixture was quenched by adjusting the pH to neutral by the addition of $NaHCO_3$ (s, 2.0g). The solid was filtered off and the filtrate was then concentrated in *vacuo* to afford **24** as a colorless oil, which was used in the next step without further purification.

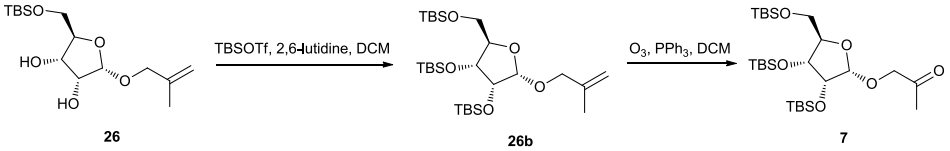
To a solution of **24** in DCM (50 mL), Et_3N (4.17 mL, 30 mmol), TBSCl (3.0 g, 20 mmol) and DMAP (0.05 g) were sequentially added at 0 ℃. The mixture was stirred for 1 h, then quenched by addition of saturated aqueous solution of NH_4Cl (10 mL). Layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed by water (20 mL) and brine (20 mL) and the organic phase was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **26** (1.37 g, 25%) and **25** (2.88 g, 52.5%) as colorless oil. **26**. **TLC**: R_f = 0.55 (silica gel, 20% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 49.14 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.03 (d, *J* = 4.4 Hz, 1H), 4.98 (s, 1H), 4.91 (s, 1H), 4.22 – 4.15 (m, 1H),

4.14 – 4.06 (m, 2H), 4.02 – 3.96 (m, 2H), 3.77 – 3.67 (m, 2H), 2.92 (s, 1H), 2.61 (s, 1H), 1.74 (m, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.21, 112.99, 101.07, 85.99, 72.14, 71.67, 71.51, 63.51, 26.01, 19.70, 18.44, -5.23, -5.37. **HRMS** (*m/z*): calculated for $C_{15}H_{30}O_5SiNa^+$ $[M+Na]^+$: 341.1760, found: 341.1766. **25**. **TLC**: R_f = 0.45 (silica gel, 20% ethyl acetate in hexane); **$[\alpha]_D^{20}$** = –53.66 (*c* 1.5, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.96 (s, 1H), 4.95 (s, 0H), 4.88 (s, 1H), 4.31 – 4.22 (m, 1H), 4.13 – 4.02 (m, 2H), 4.01 – 3.91 (m, 1H), 3.91 – 3.77 (m, 2H), 3.66 (dd, *J* = 10.1, 6.6 Hz, 1H), 2.79 (d, *J* = 3.4 Hz, 1H), 2.51 (d, *J* = 5.0 Hz, 1H), 1.71 (s, 2H), 0.90 (s, 9H), 0.08 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.52, 112.52, 106.31, 82.92, 75.53, 73.64, 71.35, 65.28, 26.05, 19.72, 18.48, -5.27. **HRMS** (*m/z*): calculated for $C_{15}H_{30}O_5SiNa^+$ $[M+Na]^+$: 341.1760, found: 341.1756.



To a solution of **26** in DCM (50 mL), Et_3N (31.8 mg, 0.1 mmol), *p*-nitrobenzoyl chloride (74 mg, 0.4 mmol) and DMAP (0.05 g) were sequentially added at 0 ℃. The mixture was stirred for 3 h and then quenched by addition of saturated aqueous solution of NH_4Cl (5 mL). Layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed by water (10 mL) and brine (10 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 afford **26a** (171 mg, 95%) as colorless oil. **$[\alpha]_D^{20}$** = 59.44 (*c* 1.0, $CHCl_3$); TLC: R_f = 0.4 (silica gel, 20% ethyl acetate in hexane) **^{1}H NMR** (500 MHz, $CDCl_3$) *δ* 8.33 – 8.23 (m, 4H), 8.16 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 5.77 (dd, *J* = 6.3, 2.0 Hz, 1H), 5.49 (d, *J* = 4.6 Hz, 1H), 5.35 (dd, *J* = 6.4, 4.5 Hz, 1H), 4.99 – 4.93 (m, 1H), 4.87 (s, 1H), 4.43 (d, *J* = 2.4 Hz, 1H), 4.25 (d, *J* = 12.7 Hz, 1H), 4.01 – 3.91 (m, 2H), 3.85 (dd, *J* = 11.2, 2.9 Hz, 1H), 1.68 (s, 3H), 0.95 (s, 9H), 0.14 (d, *J* = 3.0 Hz, 6H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 164.17, 163.53, 150.90, 141.56, 135.13, 134.66, 130.91, 130.65, 123.68, 123.57, 111.85, 99.97, 82.92, 72.98,

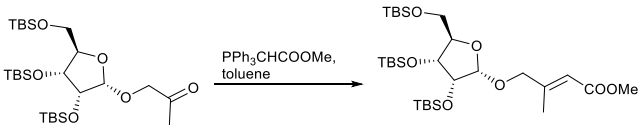
72.41, 71.70, 63.18, 25.89, 19.43, 18.32, -5.31, -5.46 ppm.



To a stirred solution of **26** (1.05 g, 3.30 mmol) and 2,6-lutidine (1.54 mL, 13.20 mmol) in dry DCM (30 mL), TBSOTf (2.13 mL, 9.90 mmol) was added at 0 ℃. The reaction mixture was stirred at 0 ℃ for 1 h, then quenched by addition of H_2O (5 mL) and diluted with ethyl acetate (100 mL). Layers were separated and the organic phase was washed sequentially with citric acid (10 mL, 10% in water), saturated aqueous solution of $NaHCO_3$ (15 mL) and brine (15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **26b** (1.71 g, 95%) as a colorless oil. **TLC**: R_f = 0.55 (silica gel, 10% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 45.50 (*c* 1.2, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.03 (d, *J* = 1.3 Hz, 1H), 4.89 (d, *J* = 4.0 Hz, 1H), 4.82 (d, *J* = 1.2 Hz, 1H), 4.17 – 4.11 (m, 1H), 4.10 – 4.06 (m, 1H), 4.04 – 4.01 (m, 1H), 3.99 – 3.95 (m, 1H), 3.89 – 3.84 (m, 1H), 3.71 – 3.62 (m, 2H), 1.73 (s, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.08 – 0.05 (m, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.51, 111.32, 102.02, 85.42, 74.14, 71.68, 71.43, 63.17, 26.15, 26.07, 26.02, 19.80, 18.59, 18.50, 18.33, -4.23, -4.34, -4.48, -4.74, -5.10, -5.34. **HRMS** (*m/z*): calculated for $C_{27}H_{58}O_5Si_3Na^+$ $[M+Na]^+$: 569.3490, found: 569.3486.

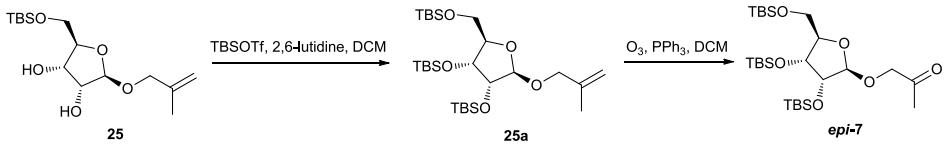
A solution of **26b** (1.71 g, 3.14 mmol) in DCM (25 mL) was cooled to − 78 ℃. O_3 was bubbled through the solution until it turned pale blue in colour (5–10 min). O_2 was then bubbled through the solution to remove the excess O_3, rendering the reaction mixture colourless. Triphenylphosphine (1.62 g, 6.20 mmol) was added and the mixture was allowed to warm to room temperature. The reaction was stirred for 3 h, followed by removal of the solvent in *vacuo*. The residue was purified by silica gel flash chromatography to afford **7** (1.65 g, 89%) as a colorless oil. **TLC**: R_f = 0.65 (silica gel, 10% ethyl acetate in hexane); $\mathbf{[\alpha]_D^{20}}$ = 59.44 (*c* 1.25, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.97 – 4.91 (m, 1H), 4.17 (d, *J* = 16.8 Hz, 1H), 4.09 – 4.00 (m, 4H), 3.66 – 3.60 (m, 2H), 2.22 (s, 3H), 0.92 – 0.87 (m, 27H), 0.09 – 0.02 (m, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 209.24, 102.48, 86.73, 74.05, 72.95,

72.16, 63.63, 27.13, 26.08, 26.03, 25.96, 18.49, 18.46, 18.32, -4.33, -4.50, -4.51, -4.82, -5.20, -5.40. **HRMS** (*m/z*): calculated for $C_{26}H_{56}O_6Si_3Na^+$ $[M+Na]^+$: 571.3282, found: 571.3276.



7 7a

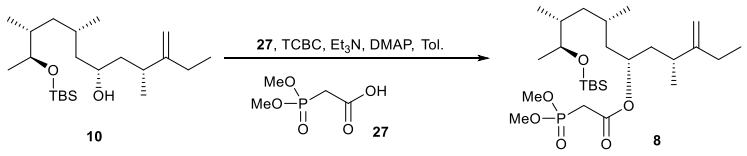
To a solution of **7** (160 mg, 0.28 mmol) in dry toluene (10 mL), $PPh_3CHCOOMe$ (174 mg，0.52 mmol) was added at 0 ℃, then refluxed for overnight. The reaction mixture was diluted with ethyl acetate (40 mL) and the organic phase was washed with saturated aqueous solution of $NaHCO_3$ (15 mL) and brine (15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **7a** (152 g, 89%) as a colorless oil. TLC: R_f = 0.70 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 42.58 (*c* 1.5, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.13 (s, 1H), 4.91 (d, *J* = 4.4 Hz, 1H), 4.25 – 4.17 (m, 1H), 4.08 (dd, *J* = 5.6, 2.1 Hz, 1H), 4.04 – 3.99 (m, 2H), 3.98 – 3.91 (m, 1H), 3.68 (s, 3H), 3.65 (dd, *J* = 3.2, 1.4 Hz, 2H), 2.09 (s, 3H), 0.92 – 0.88 (m, 27H), 0.10 – 0.05 (m, 18H) ppm.**^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.58, 155.35, 114.14, 102.04, 86.33, 73.95, 71.77, 70.93, 50.68, 25.96, 25.90, 25.82, 18.37, 18.33, 18.17, 15.84, -4.51, -4.61, -4.94, -5.32, -5.53 ppm. **HRMS** (*m/z*): calculated for $C_{29}H_{60}NaO_7Si_3^+$ $[M+Na]^+$: 627.3545, found: 627.3539.



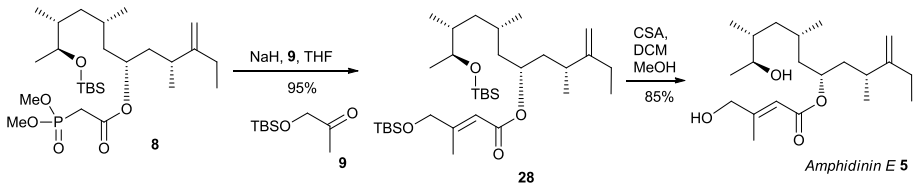
25 25a ***epi*-7**

25a: **TLC**: R_f = 0.50 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –9.58 (*c* 1.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.95 (s, 1H), 4.88 (s, 1H), 4.81 (d, *J* = 1.5 Hz, 1H), 4.18 (dd, *J* = 6.7, 4.2 Hz, 1H), 4.11 – 4.04 (m, 1H), 3.99 – 3.92 (m, 2H), 3.92 – 3.86 (m, 1H), 3.81 – 3.59 (m, 2H), 1.72 (s, 3H), 0.92 – 0.88 (m, 27H), 0.09 – 0.05 (m, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.72, 112.35, 106.05, 83.14, 76.74, 71.73, 71.40, 63.38, 26.18, 26.05, 25.98, 19.74, 18.65, 18.25, 18.22, -4.10, -4.37, -4.45, -4.75, -5.19, -5.25. **HRMS** (*m/z*): calculated for $C_{27}H_{58}O_5Si_3Na^+$ $[M+Na]^+$: 569.3490, found: 569.3487.

***epi*-7**: **TLC**: R_f = 0.55 (silica gel, 10% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –12.64 (*c* 1.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.82 (d, *J* = 1.4 Hz, 1H), 4.27 – 4.17 (m, 2H), 4.11 – 4.04 (m, 1H), 4.04 – 3.94 (m, 2H), 3.81 – 3.56 (m, 2H), 2.12 (s, 3H), 0.90 – 0.86 (m, 28H), 0.10 – 0.04 (m, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.13, 106.76, 83.45, 76.42, 72.49, 71.32, 62.89, 26.62, 26.11, 26.00, 25.92, 18.58, 18.23, 18.19, -4.10, -4.40, -4.45, -4.77, -5.24. **HRMS** (*m/z*): calculated for $C_{26}H_{56}O_6Si_3Na^+$ $[M+Na]^+$: 571.3282, found: 571.3279.

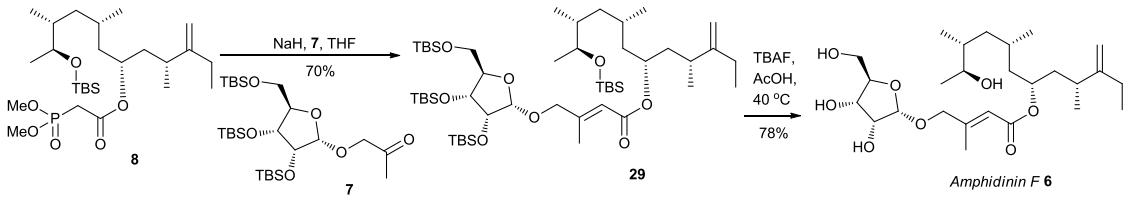


To a solution of dimethylphosphonoacetic acid (9 mg, 0.10 mmol), alcohol **10** (20 mg, 0.05 mmol) and triethylamine (42 μL, 0.30 mmol) in dry toluene (5 mL), 2,4,6-trichlorobenzoyl chloride (23 μL, 0.15 mmol) was added at 0 ℃. The reaction mixture was warmed to room temperature and stirred for 0.5 h. A solution of DMAP (37 mg, 0.30 mmol) in toluene (3 mL) was added to the reaction mixture, which was then stirred for additional 3 h at room temperature. The reaction mixture was quenched by addition of H_2O (2 mL) and diluted with ethyl acetate (20 mL). Layers were separated, the organic phase was washed with saturated aqueous solution of NH_4Cl (10 mL) and brine (10 mL) and then dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford **8** (28 mg, 90%) as a colorless oil. **TLC:** R_f = 0.55 (silica, 50% ethyl acetate in hexane); $[\alpha]_D^{20}$ = 7.80 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.06 – 4.95 (m, 1H), 4.78 – 4.70 (m, 2H), 3.82 (d, *J* = 1.2 Hz, 3H), 3.78 (d, *J* = 1.2 Hz, 3H), 3.65 – 3.54 (m, 1H), 2.99 (d, *J* = 1.0 Hz, 1H), 2.91 (d, *J* = 1.0 Hz, 1H), 2.28 – 2.14 (m, 1H), 2.04 – 1.92 (m, 2H), 1.68 – 1.57 (m, 6H), 1.54 – 1.45 (m, 2H), 1.06 – 0.99 (m, 9H), 0.88 (d, *J* = 3.1 Hz, 12H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.03 (s, 3H), 0.02 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.34, 165.25, 155.06, 107.45, 73.13, 71.98, 53.25, 53.22, 41.47, 41.01, 40.86, 37.61, 36.95, 34.56, 32.77, 29.86, 26.77, 26.04, 20.97, 20.79, 19.44, 18.25, 15.00, 12.47, -4.20, -4.63. **HRMS** (*m/z*): calculated for $C_{26}H_{53}O_6PSiNa^+$ $[M+Na]^+$: 543.3247, found: 543.3242.



To a suspension of NaH (60% in mineral oil, 2.3 mg, 0.058 mmol) in dry THF (3 mL) was added dropwise a solution of **8** (15 mg, 0.028 mol) and **9** (5 mg, 0.028 mmol) in dry THF (1 mL) at 0 ℃. The reaction mixture was stirred at room temperature for 1 h and the THF was removed in *vacuo*. The residue was neutralized with ice-cold dilute HCl (1 N) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the corresponding ester **28**.

To a solution of compound **28** (15 mg, 0.027 mmol) in MeOH (2 mL)/DCM(2.5 mL), was added a solution of camphorsulfonic acid (7 mg, 0.03 mmol) in MeOH (0.5 mL). The reaction mixture was stirred for 2 h at room temperature then quenched by addition of Et_3N (0.1 mL). The reaction mixture was poured over a saturated aqueous solution of NH_4Cl (5 mL), and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed successively with NH_4Cl (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford amphidinin E (7.9 mg, 80% for two steps) as a colorless oil. **TLC**: R_f = 0.50 (silica gel, 50% ethyl acetate in hexane). $\mathbf{[\alpha]_D^{22}}$ = –8.0 (*c* 0.5, MeOH); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.07 – 4.96 (m, 1H), 4.73 (d, *J* = 1.5 Hz, 1H), 4.73 – 4.70 (m, 1H), 4.15 (s, 2H), 3.69 – 3.59 (m, 1H), 2.25 – 2.16 (m, 1H), 2.09 (s, 3H), 2.03 – 1.93 (m, 2H), 1.75 – 1.68 (m, 1H), 1.65 – 1.60 (m, 3H), 1.55 – 1.49 (m, 1H), 1.36 – 1.31 (m, 1H), 1.21 – 1.14 (m, 1H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.06 – 1.00 (m, 6H), 0.99 – 0.94 (m, 1H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.37, 156.66, 155.25, 114.09, 107.08, 71.78, 70.49, 67.16, 41.60, 41.15, 40.82, 37.24, 36.97, 26.87, 26.12, 21.05, 20.60, 19.08, 15.59, 14.75, 12.33. **HRMS** (*m/z*): calculated for $C_{21}H_{38}O_4Na^+$ $[M+Na]^+$: 377.2668, found: 377.2665.

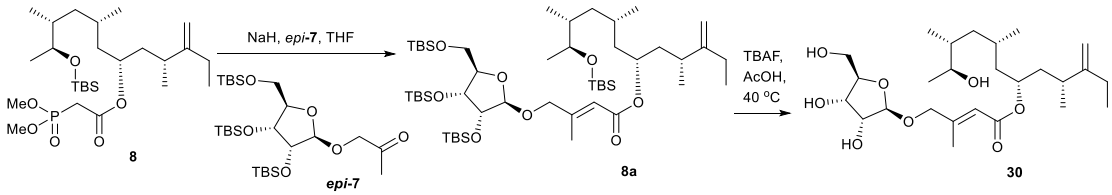


To a suspension of NaH (60% in mineral oil, 2.3 mg, 0.058 mmol) in dry THF (3 mL) was added dropwise a solution of **8** (15 mg, 0.028 mol) and **7** (16 mg, 0.028 mmol) in dry THF (2 mL) at 0 ℃. The reaction mixture was stirred at room temperature for 1 h and the THF was removed in *vacuo*. The residue was neutralized with ice-cold dilute HCl(1 N in water) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with saturated aqueous solution of brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the corresponding ester **29**.

To a solution of **29** (20 mg, 0.021 mmol) in THF (3 mL) was added an equimolar mixture of AcOH/TBAF (1 mL, 0.2 mmol, 0.2 M in THF). The reaction mixture was stirred at room temperature at 40 ^{o}C for 4 days. After cooling, a saturated aqueous solution of $NaHCO_3$ (3 mL) was then added to the mixture, and the two phases were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL), and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography to afford amphidinin F (5.6 mg, 55%) as a colorless oil. **TLC**: R_f = 0.50 (silica gel, ethyl acetate); $\mathbf{[\alpha]_D^{20}}$ = 25.2 (*c* 0.5, MeOH); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.90 (s, 1H), 5.09 (d, *J* = 4.5 Hz, 1H), 5.06 – 4.94 (m, 1H), 4.74 (d, *J* = 1.5 Hz, 1H), 4.72 (s, 1H), 4.29 (d, *J* = 15.4 Hz, 1H), 4.17 – 4.08 (m, 3H), 4.06 – 3.99 (m, 1H), 3.83 (d, *J* = 11.6 Hz, 1H), 3.72 (d, *J* = 12.0 Hz, 1H), 3.68 – 3.58 (m, 1H), 2.99 (d, *J* = 9.1 Hz, 1H), 2.66 (d, *J* = 7.5 Hz, 1H), 2.24 – 2.17 (m, 1H), 2.12 (s, 3H), 2.06 – 1.93 (m, 2H), 1.66 – 1.60 (m, 4H), 1.50 (s, 1H), 1.32 (ddd, *J* = 13.3, 8.3, 4.8 Hz, 1H), 1.18 (ddd, *J* = 13.9, 9.2, 3.3 Hz, 1H), 1.11 (d, *J* = 6.3 Hz, 3H), 1.08 – 1.00 (m, 6H), 1.00 – 0.95 (m, 1H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.04, 155.22, 152.66, 116.28, 107.11, 101.20, 85.13, 71.88, 71.79, 71.63, 70.83, 70.54, 62.62, 41.76, 41.09, 41.00, 37.29, 36.96, 27.06, 26.12, 21.03, 20.55, 18.92, 15.91, 14.74, 12.33. **HRMS** (*m/z*): calculated for $C_{26}H_{46}O_8Na^+$ $[M+Na]^+$: 509.3090, found: 509.3095.

^{1}H NMR (400 MHz, CD_3OD) δ 6.04 (s, 1H), 5.08 – 5.01 (m, 1H), 4.99 (d, J = 4.3 Hz, 1H),

4.76 (s, 1H), 4.73 (s, 1H), 4.26 (d, J = 15.4 Hz, 1H), 4.12 (d, J = 16.6 Hz, 1H), 4.06 – 4.00 (m, 2H), 3.99 – 3.94 (m, 1H), 3.70 – 3.60 (m, 2H), 3.60 – 3.53 (m, 1H), 2.28 – 2.17 (m, 1H), 2.10 (s, 3H), 2.05 – 1.97 (m, 2H), 1.73 – 1.55 (m, 4H), 1.54 – 1.45 (m, 1H), 1.39 – 1.31 (m, 1H), 1.20 – 1.12 (m, 1H), 1.07 (d, J = 6.4 Hz, 3H), 1.06 – 1.01 (m, 6H), 1.00 – 0.95 (m, 1H), 0.94 (d, J = 6.5 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H).

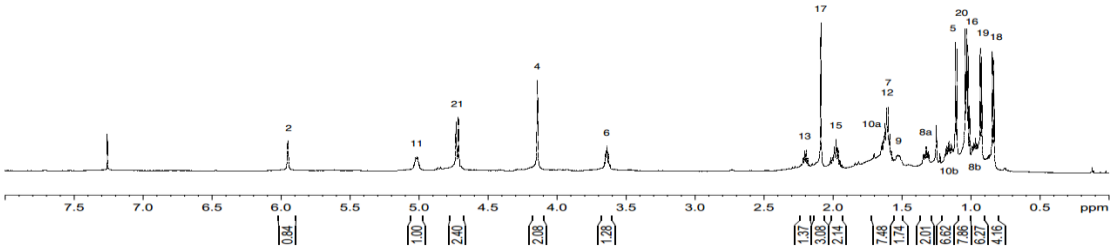


8a: TLC: R_f=0.5 (silica gel, 10% ethyl acetate in hexane). $[\alpha]_D^{20}$ = –30.10 (*c* 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.07 (s, 1H), 5.03 – 4.95 (m, 1H), 4.90 (d, *J* = 4.4 Hz, 1H), 4.72 (d, *J* = 10.5 Hz, 2H), 4.26 – 4.16 (m, 1H), 4.08 (dd, *J* = 5.6, 2.2 Hz, 1H), 4.04 – 3.97 (m, 2H), 3.93 (dd, *J* = 15.6, 1.8 Hz, 1H), 3.65 – 3.59 (m, 3H), 2.24 – 2.16 (m, 1H), 2.07 (s, 3H), 2.00 – 1.93 (m, 2H), 1.64 – 1.52 (m, 5H), 1.51 – 1.43 (m, 1H), 1.28 – 1.21 (m, 1H), 1.15 – 1.07 (m, 1H), 1.03 – 0.99 (m, 9H), 0.89 (t, *J* = 8.6 Hz, 39H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.07 – -0.01 (m, 24H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.84, 155.51, 154.39, 115.22, 107.25, 102.37, 86.48, 77.41, 77.16, 76.91, 74.18, 71.99, 71.94, 71.44, 70.26, 63.60, 42.13, 41.52, 41.08, 37.59, 37.12, 26.97, 26.39, 26.17, 26.10, 21.16, 20.93, 19.18, 18.55, 18.52, 18.36, 18.27, 16.03, 15.03, 12.57, -4.21, -4.27, -4.42, -4.43, -4.57, -4.67, -5.14, -5.34. **HRMS** (*m/z*): calculated for $C_{50}H_{102}O_8Si_4Na^+$ $[M+Na]^+$: 965.6549, found: 965.6548.

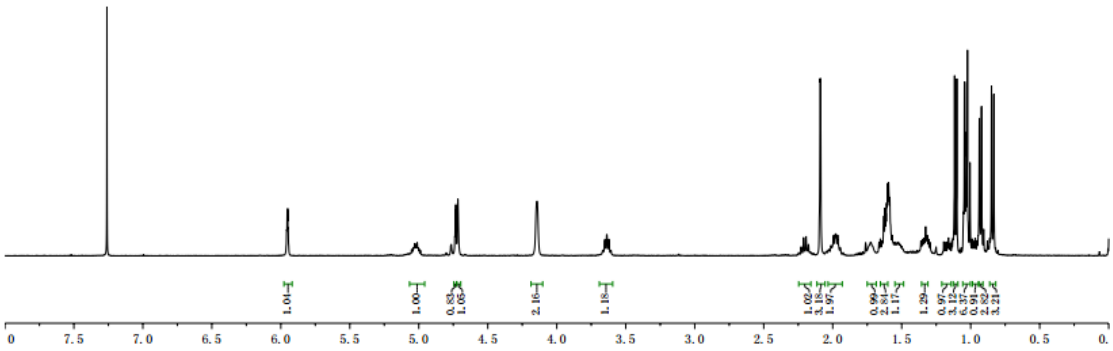
30: TLC: R_f = 0.50 (silica gel, ethyl acetate). $[\alpha]_D^{20}$ = –18.0 (*c* 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.86 (s, 1H), 5.06 – 4.97 (m, 1H), 4.95 (s, 1H), 4.72 (d, *J* = 7.1 Hz, 2H), 4.34 (d, *J* = 6.4 Hz, 1H), 4.19 (d, *J* = 15.3 Hz, 1H), 4.13 – 4.03 (m, 2H), 3.99 (d, *J* = 15.3 Hz, 1H), 3.79 (dd, *J* = 11.9, 3.8 Hz, 1H), 3.73 – 3.59 (m, 3H), 3.49 (s, 1H), 2.64 (s, 1H), 2.22 – 2.15 (m, 1H), 2.07 (s, 3H), 2.01 – 1.95 (m, 2H), 1.67 – 1.55 (m, 4H), 1.53 – 1.42 (m, 1H), 1.30 – 1.23 (m, 2H), 1.22 – 1.15 (m, 1H), 1.09 (d, *J* = 6.3 Hz, 3H), 1.07 – 0.98 (m, 6H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.36, 155.43, 153.09, 115.97, 107.30, 84.44, 75.64, 72.10, 71.88, 71.44, 71.24, 63.40, 42.28, 41.47, 41.38, 37.53, 37.18, 29.84, 27.49, 26.36, 21.22, 20.73, 18.88, 16.04, 14.90, 12.53. **HRMS** (*m/z*): calculated for $C_{26}H_{46}O_8Na^+$ $[M+Na]^+$: 509.3090, found: 509.3088.

^{1}H and ^{13}C NMR Spectra of Natural and Synthetic Amphidinin E

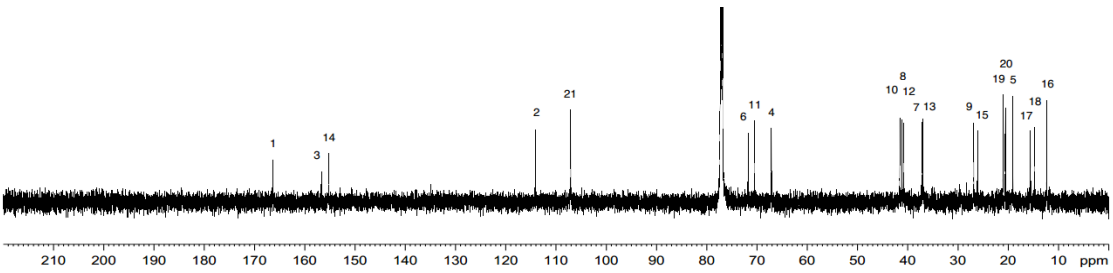
Amphidinin E (Natural Product, 600 MHz, $CDCl_3$)



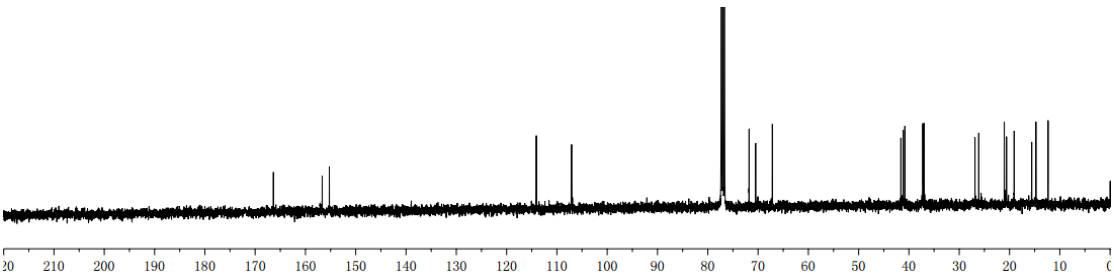
Amphidinin E (Synthetic Sample, 400 MHz, $CDCl_3$)



Amphidinin E (Natural Product, 150 MHz, $CDCl_3$)

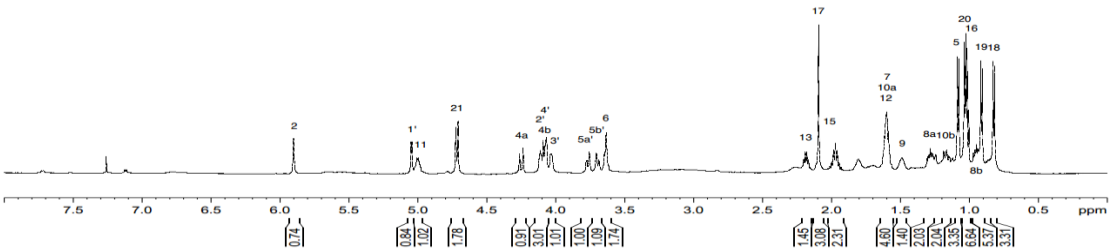


Amphidinin E (Synthetic Sample, 100 MHz, $CDCl_3$)

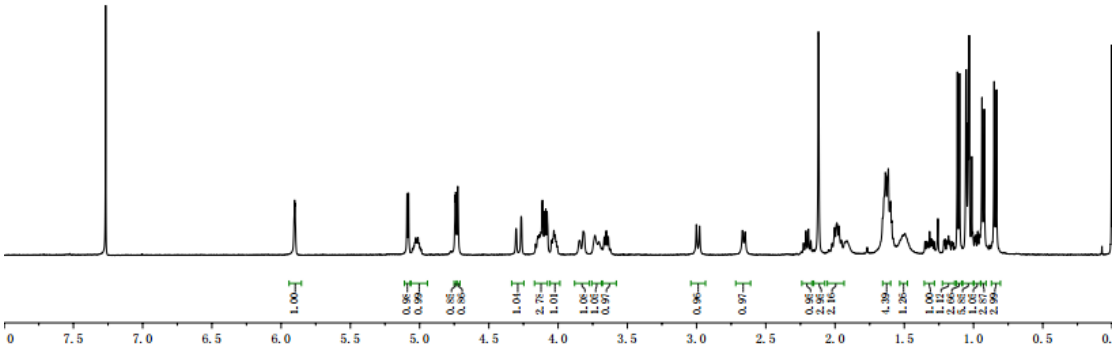


^{1}H and ^{13}C NMR Spectra of Natural and Synthetic Amphidinin F

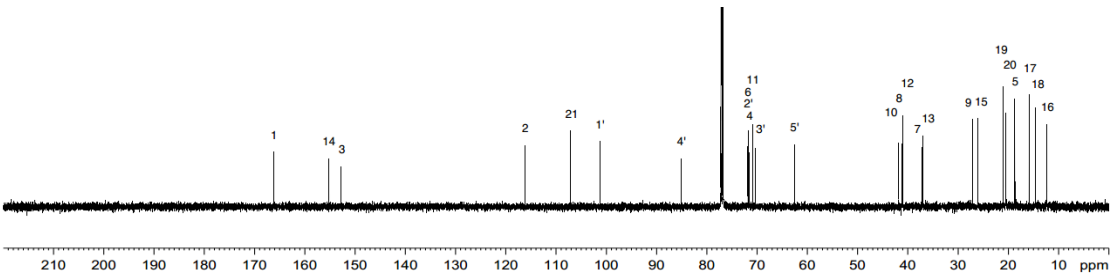
Amphidinin F (Natural Product, 600 MHz, $CDCl_3$)



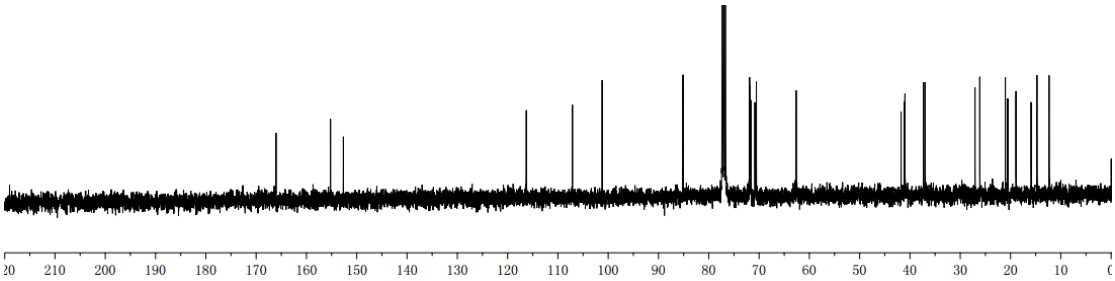
Amphidinin F (Synthetic Sample, 400 MHz, $CDCl_3$)

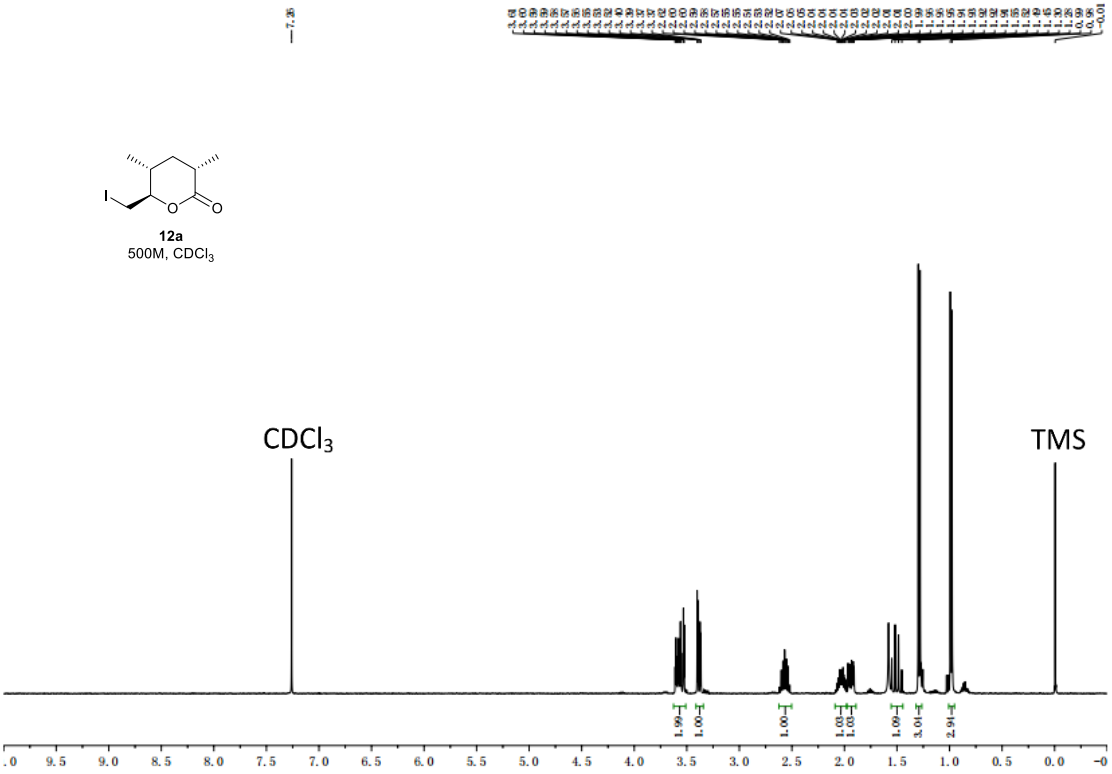


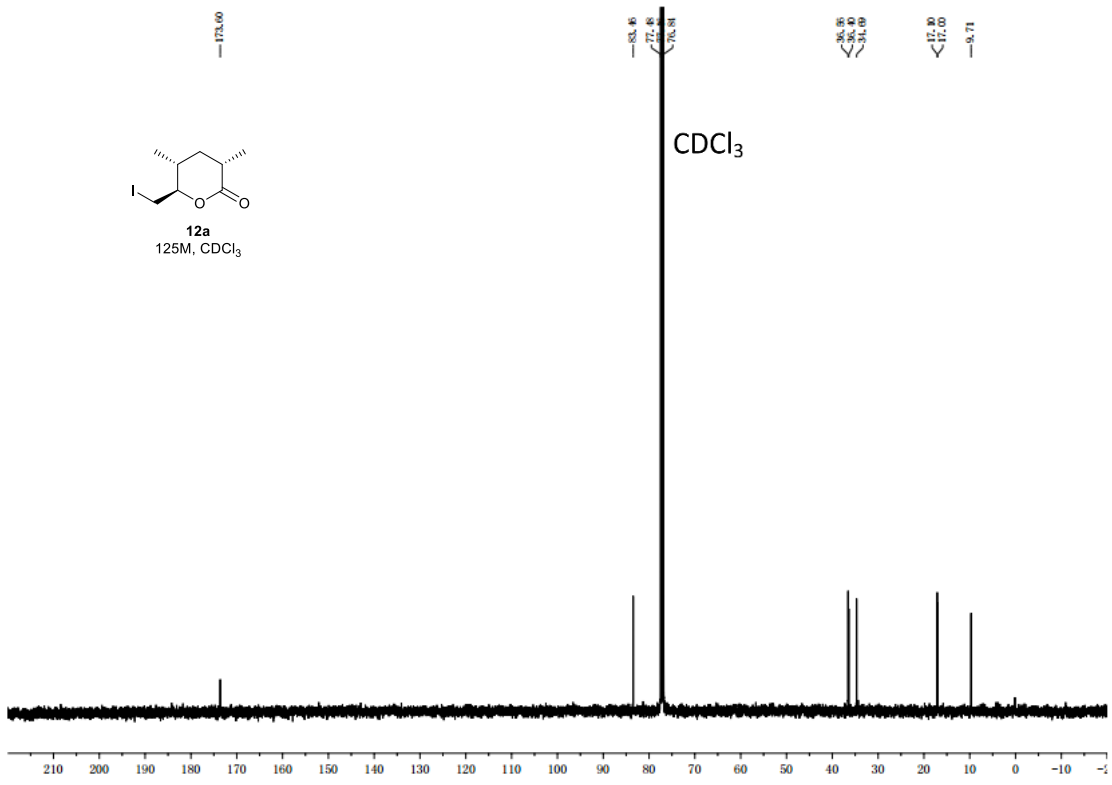
Amphidinin F (Natural Product, 150 MHz, $CDCl_3$)

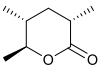


Amphidinin F (Synthetic Sample, 100 MHz, $CDCl_3$)

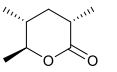



12a
500M, CDCl3
CDCl3
TMS

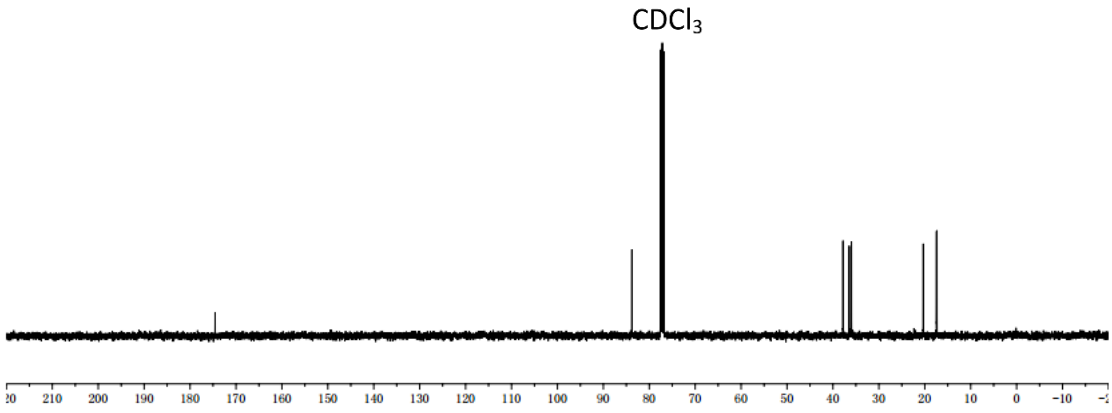

12a
125M, CDCl3
CDCl3

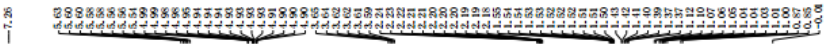


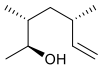
13
400M, $CDCl_3$



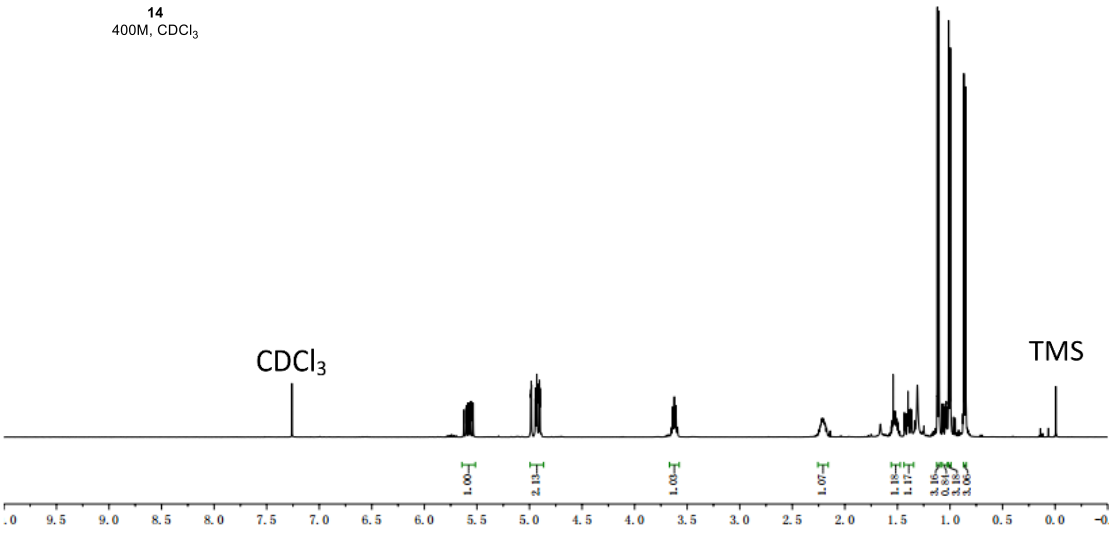
13
100M, $CDCl_3$

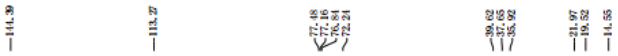


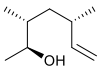




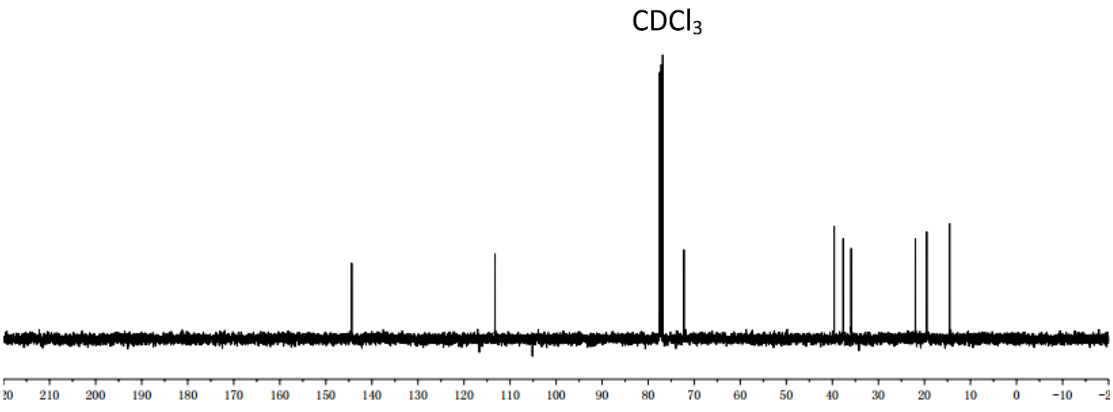
14
400M, $CDCl_3$

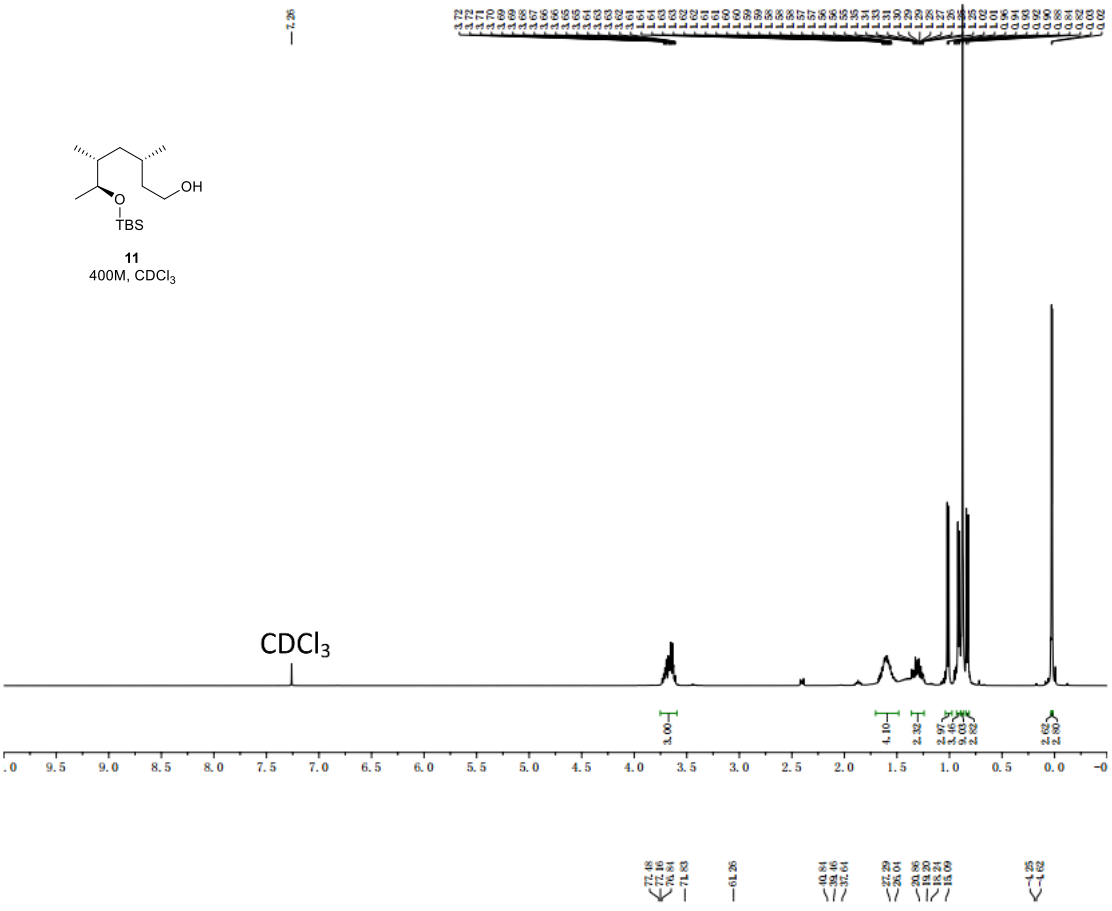




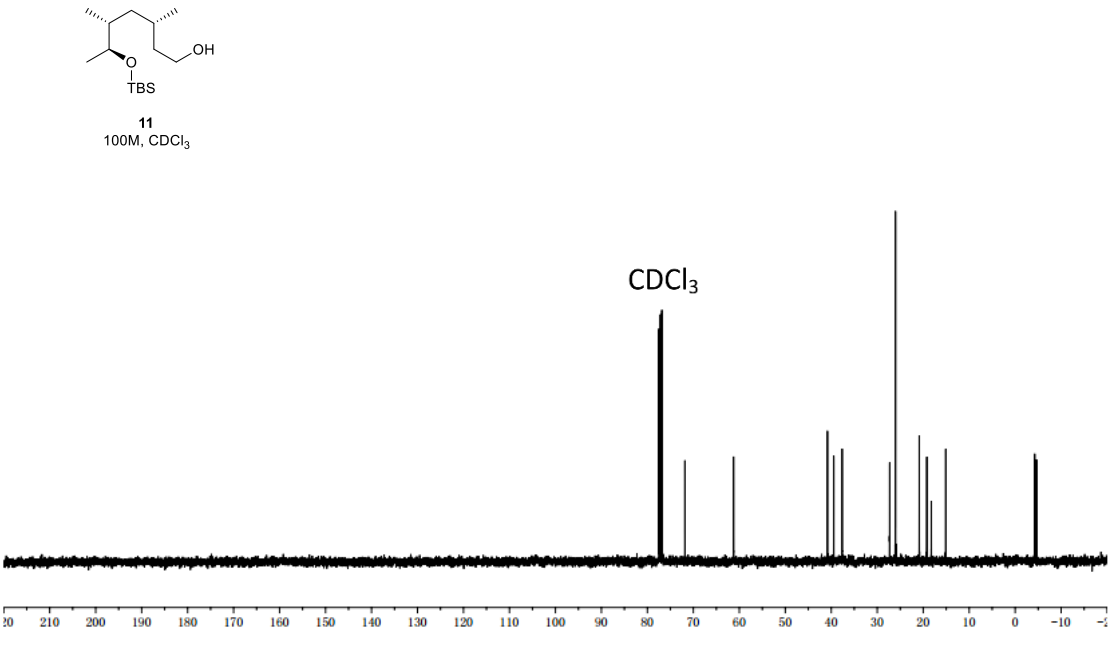


14
100M, $CDCl_3$

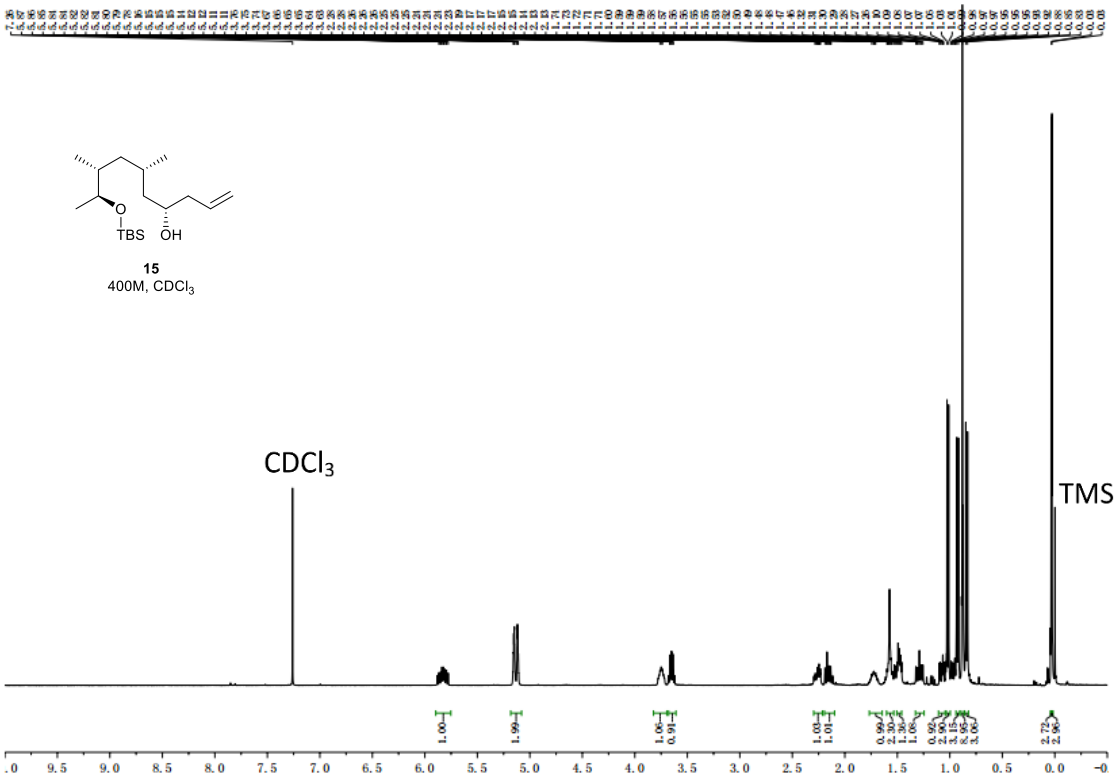




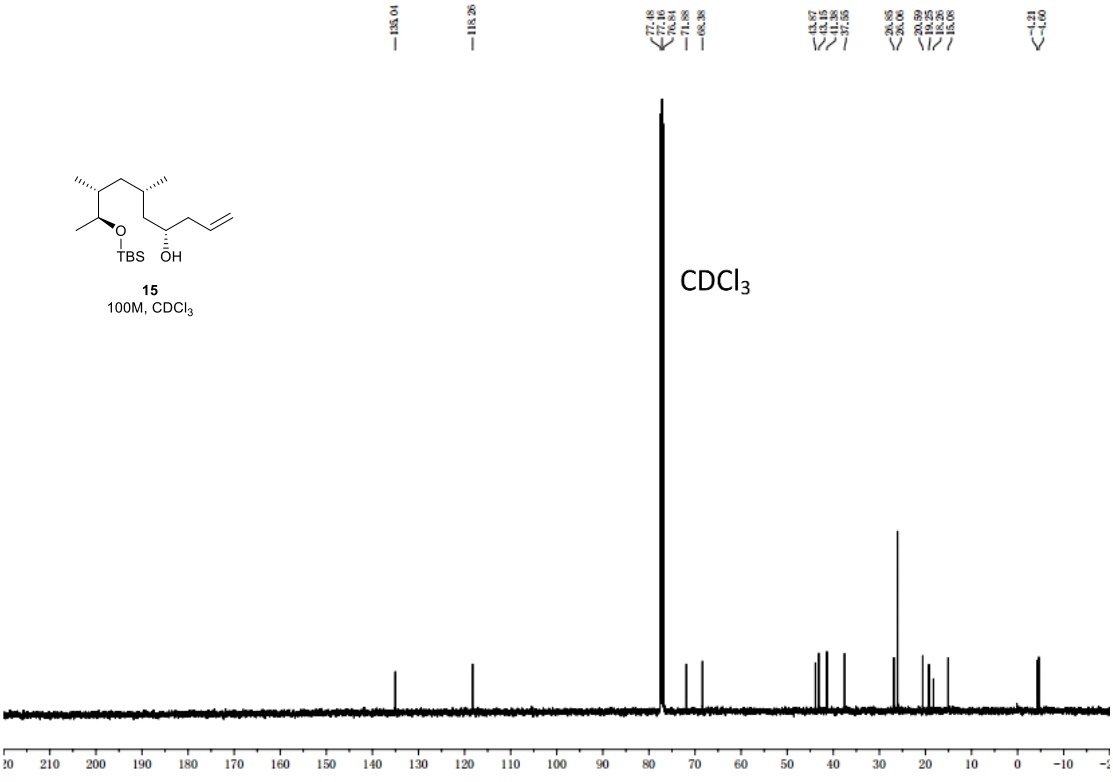
11
400M, $CDCl_3$



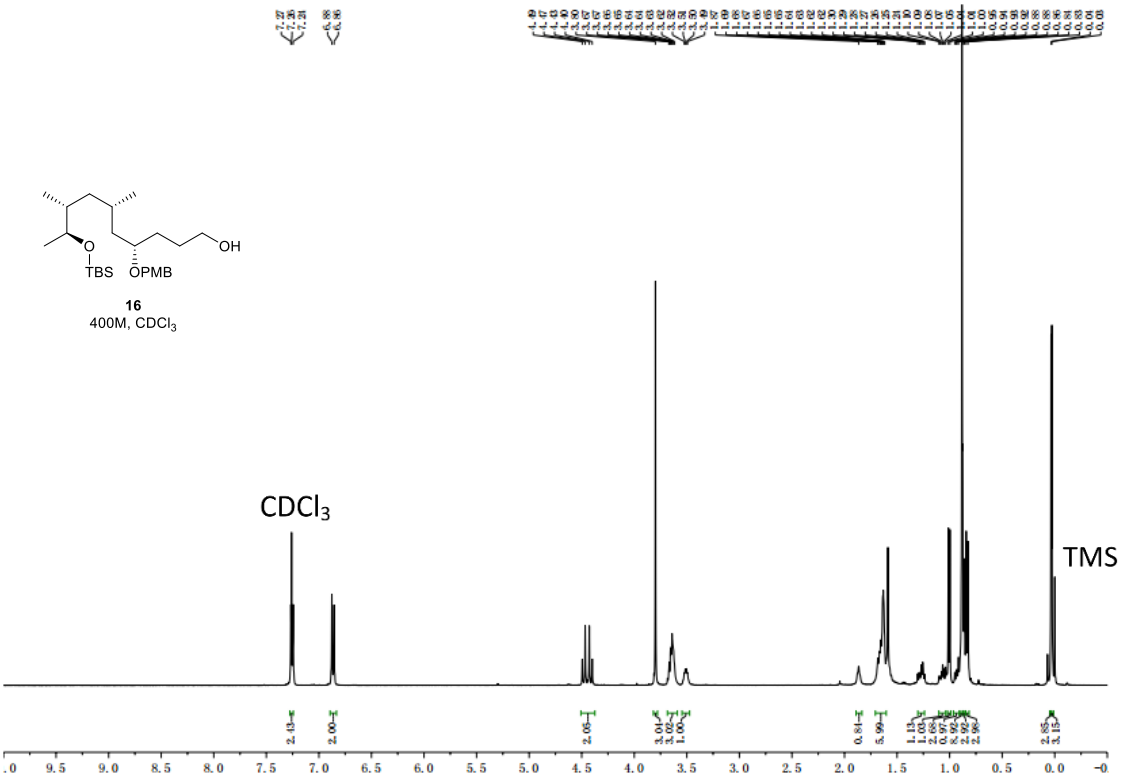
11
100M, $CDCl_3$



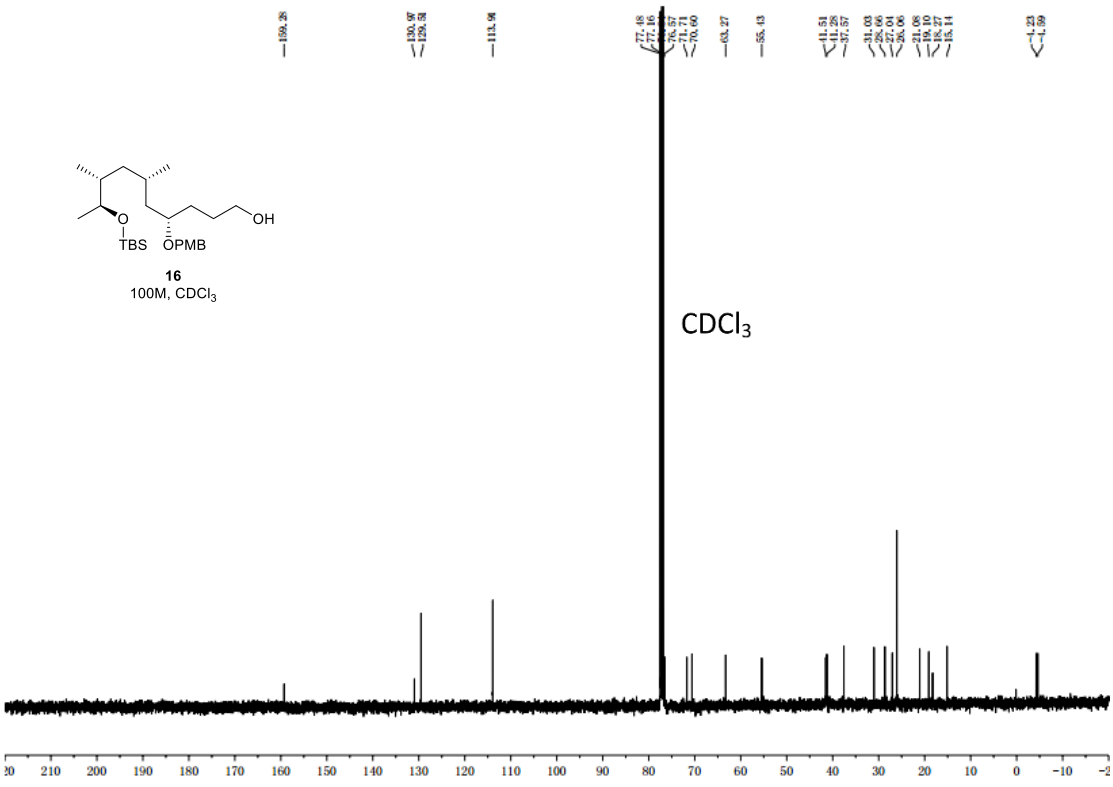
15
400M, $CDCl_3$



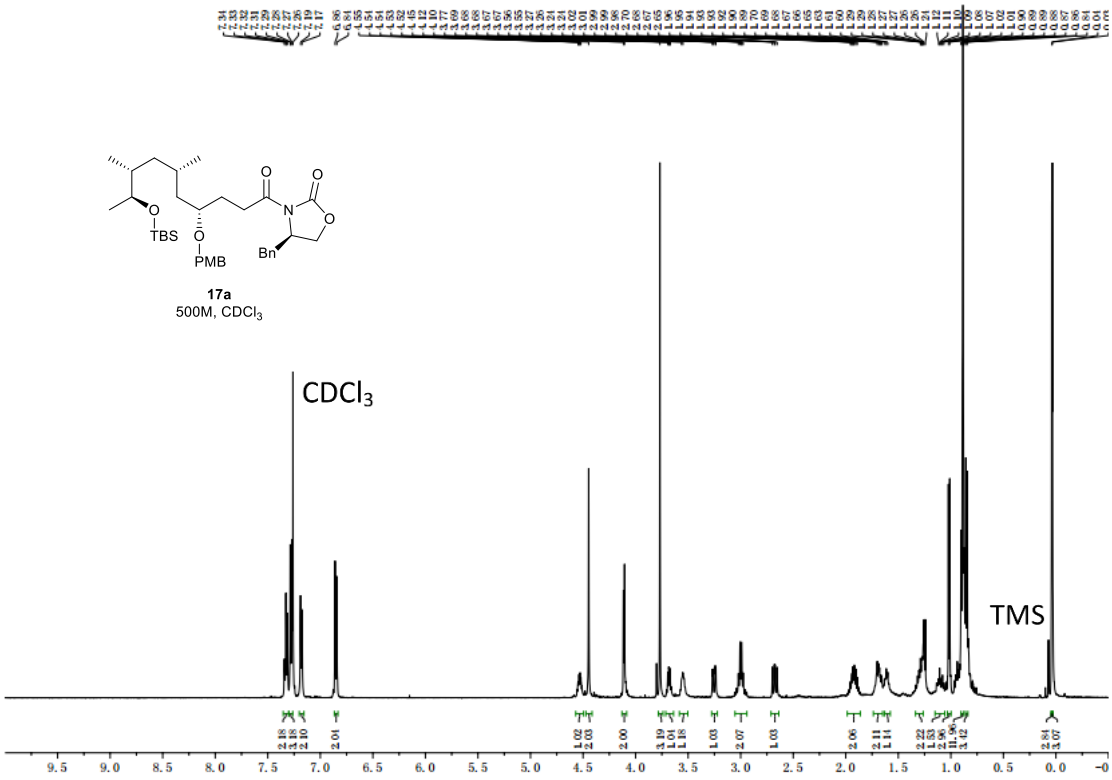
15
100M, $CDCl_3$

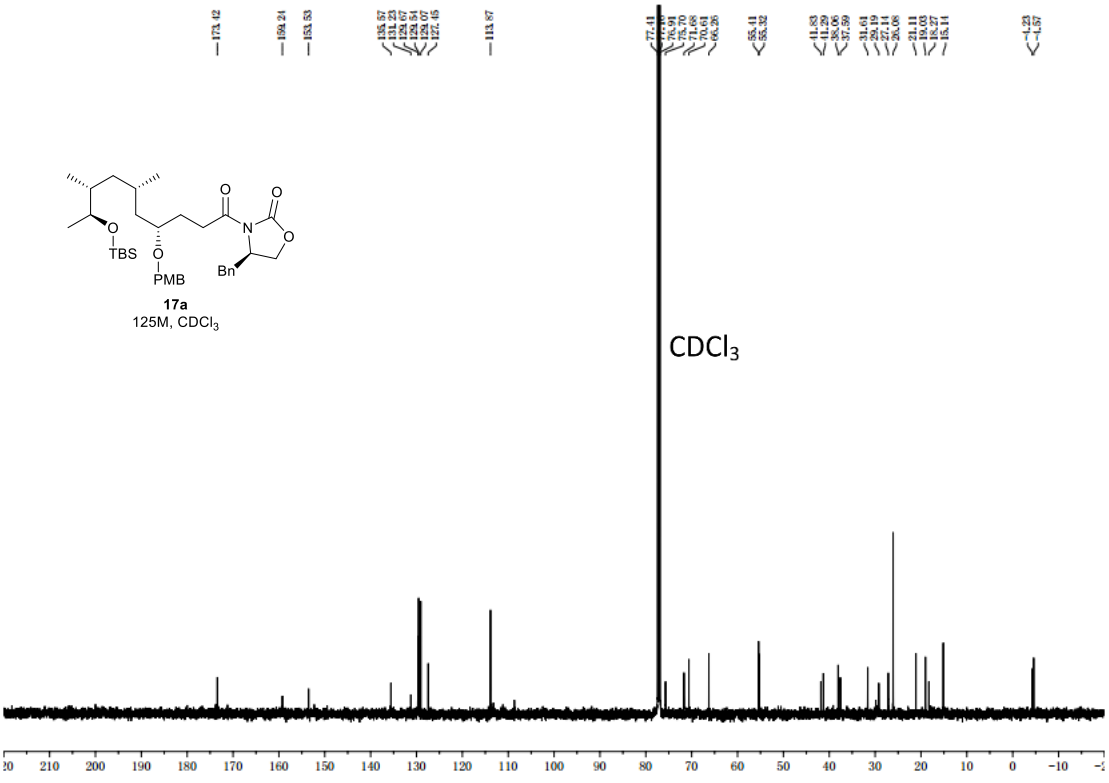


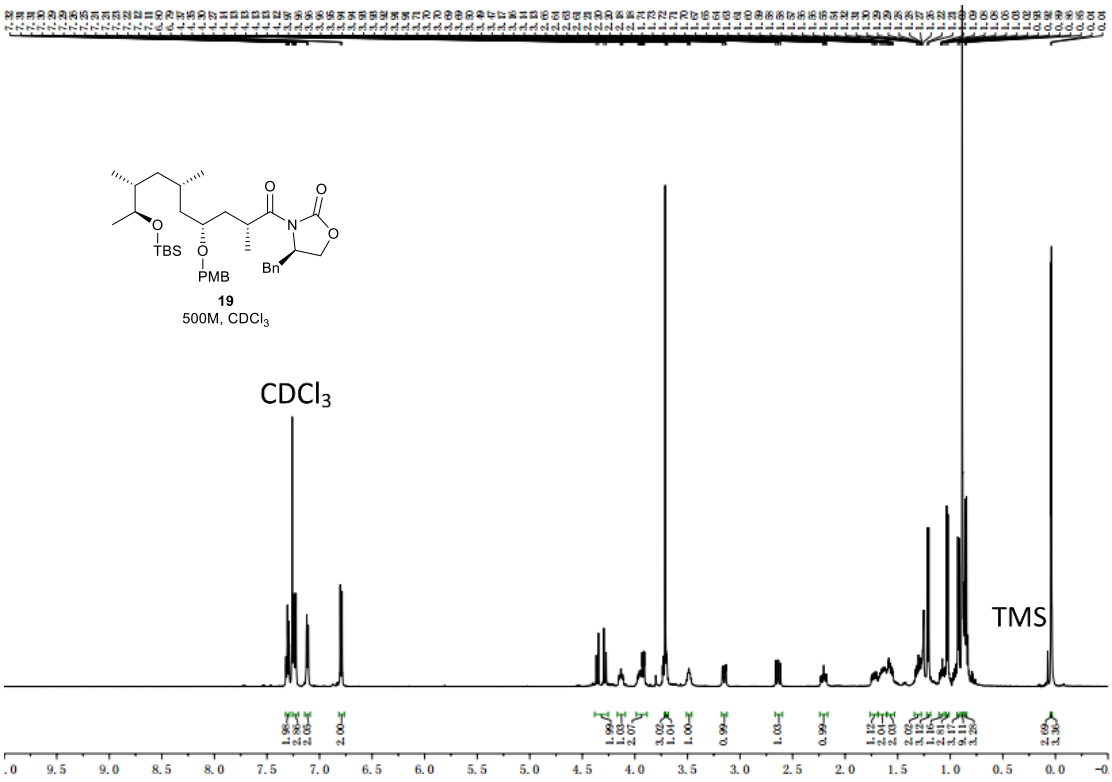
16
400M, $CDCl_3$

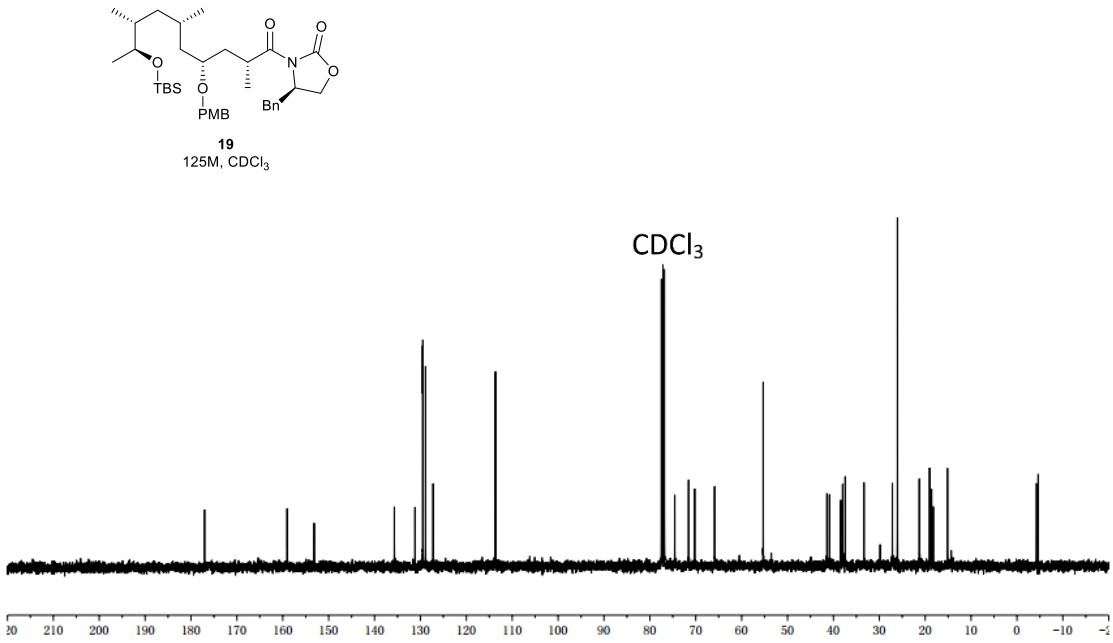


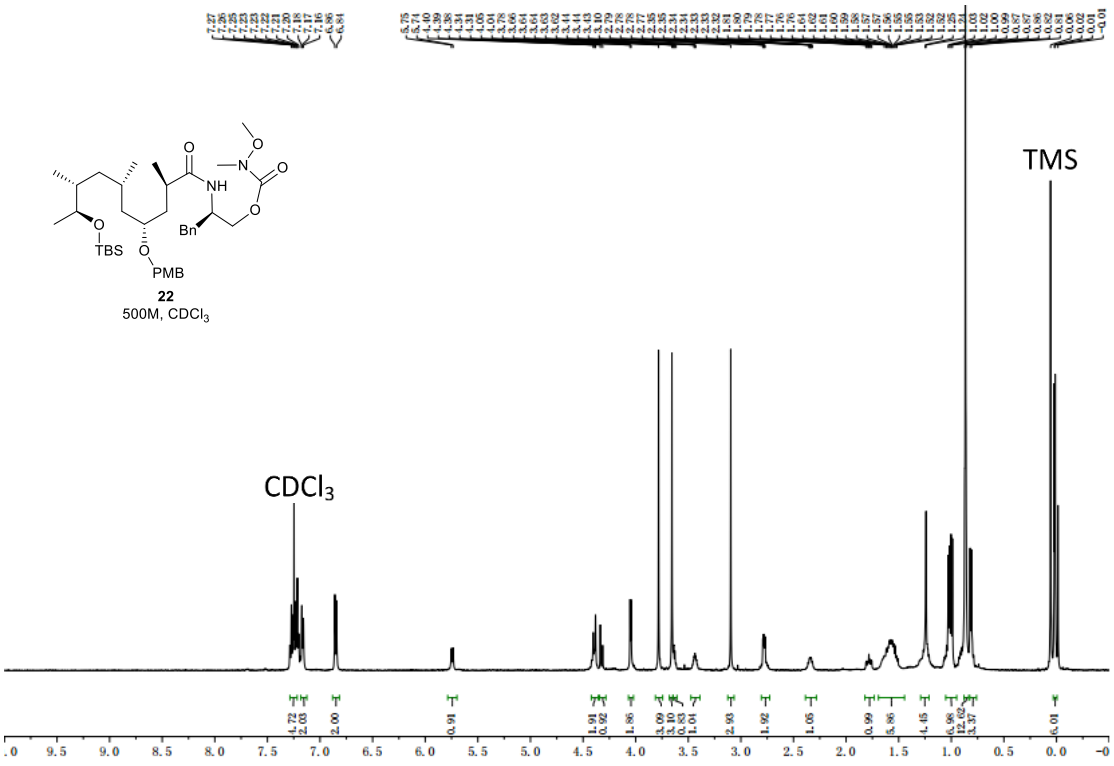
16
100M, $CDCl_3$


TBS
PMB
Bn
17a
500M, CDCl3
CDCl3
TMS

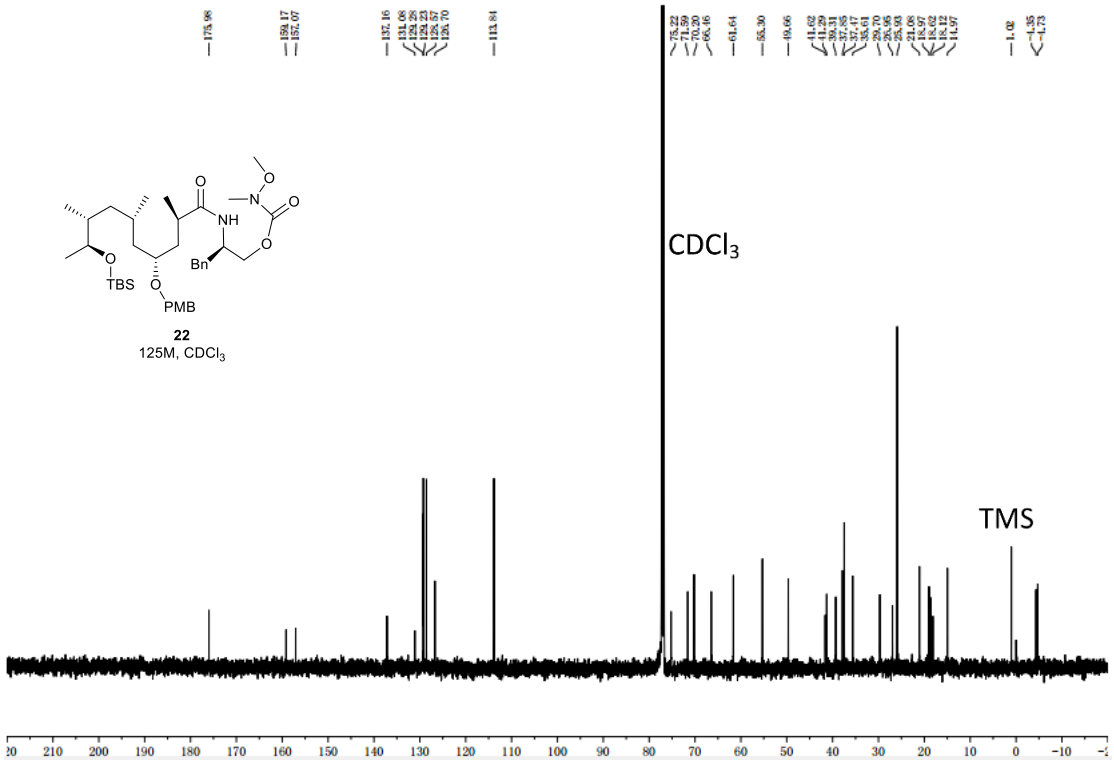

TBS
PMB
Bn
17a
125M, CDCl3
CDCl3


TBS
O
PMB
O
N
O
O
Bn
19
500M, CDCl3
CDCl3
TMS

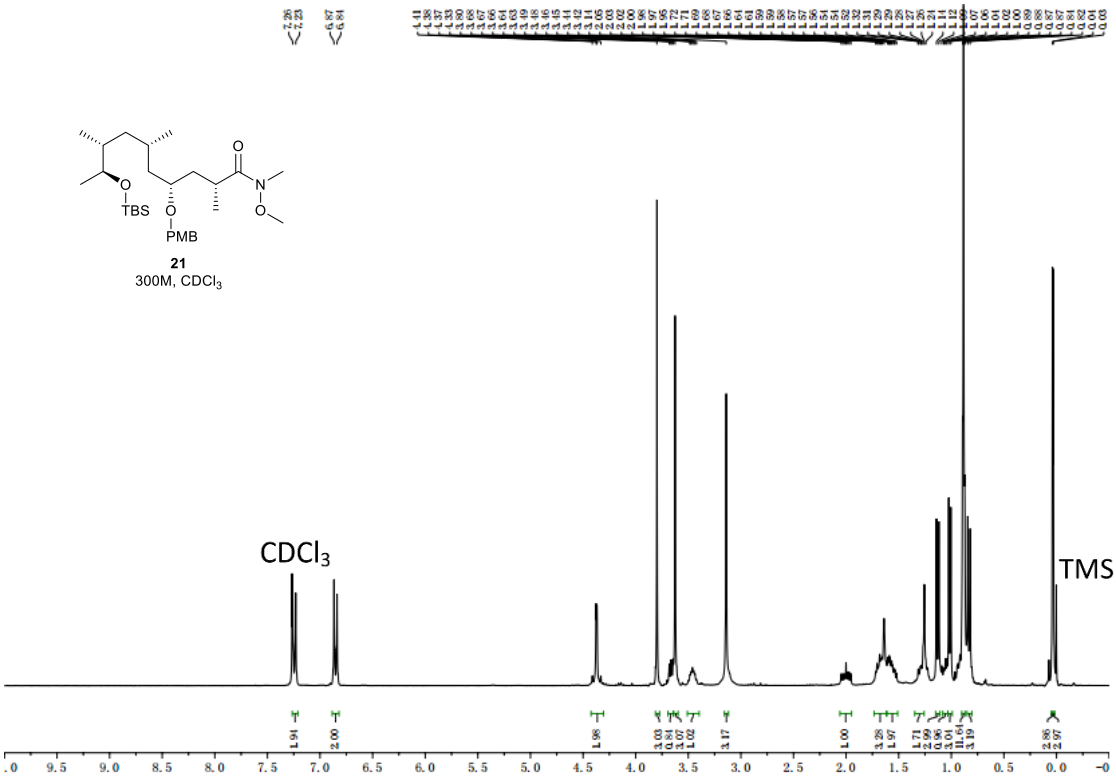

TBS
O
PMB
O
N
O
O
Bn
19
125M, CDCl3
CDCl3

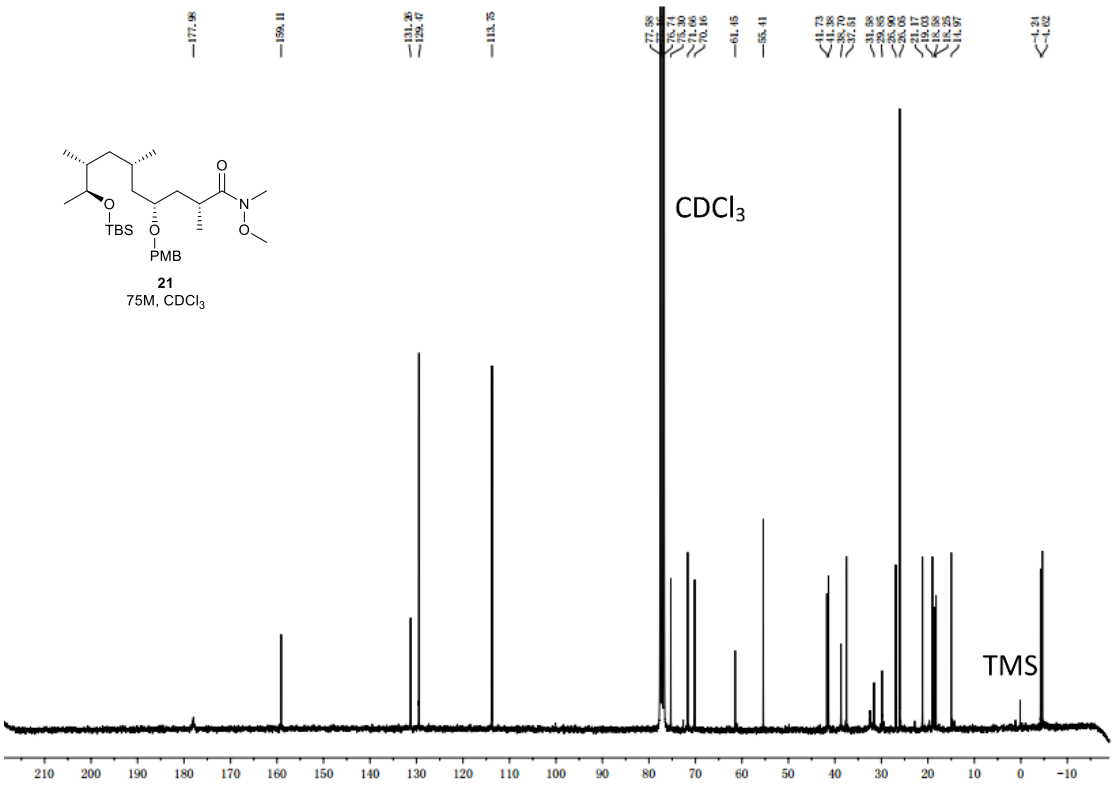


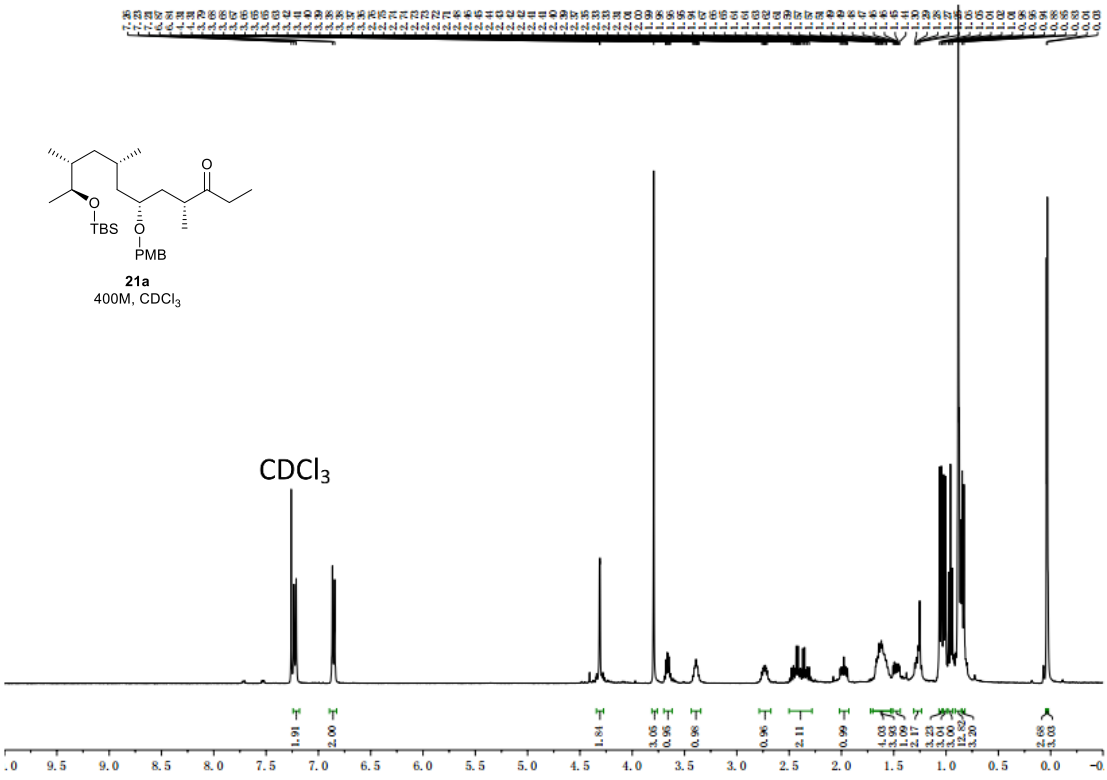
22
500M, $CDCl_3$



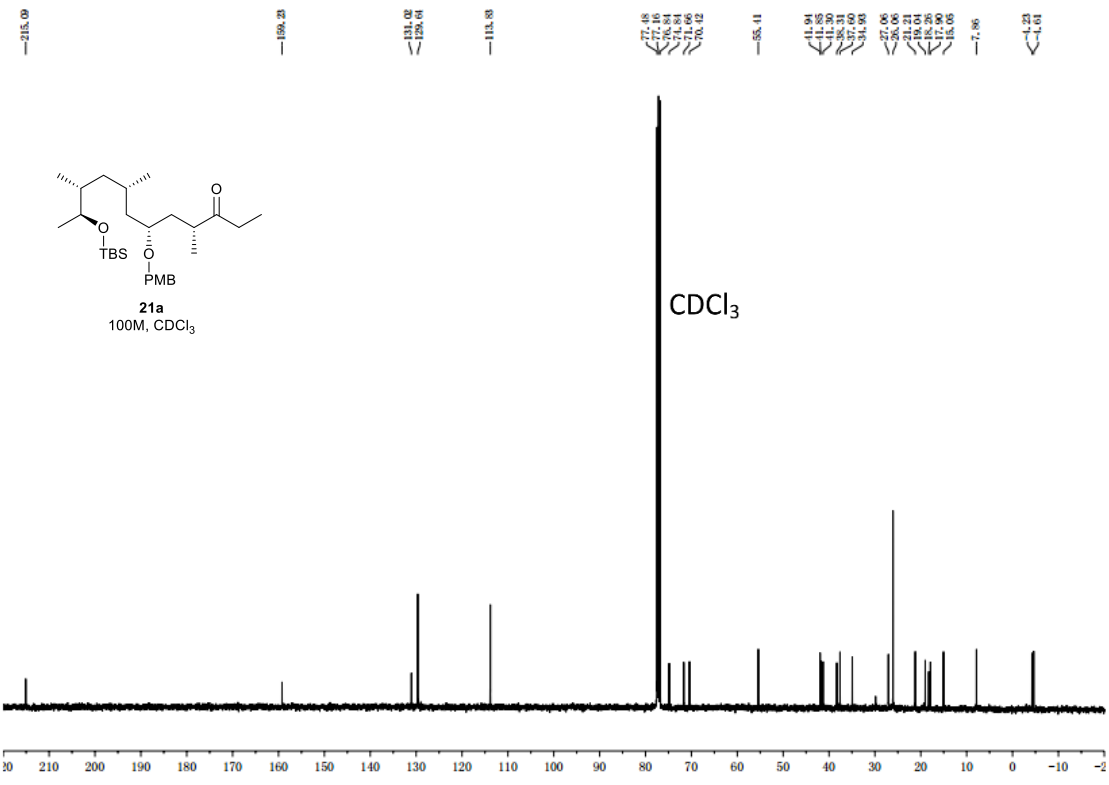
22
125M, $CDCl_3$


TBS
PMB
21
300M, CDCl3
CDCl3
TMS

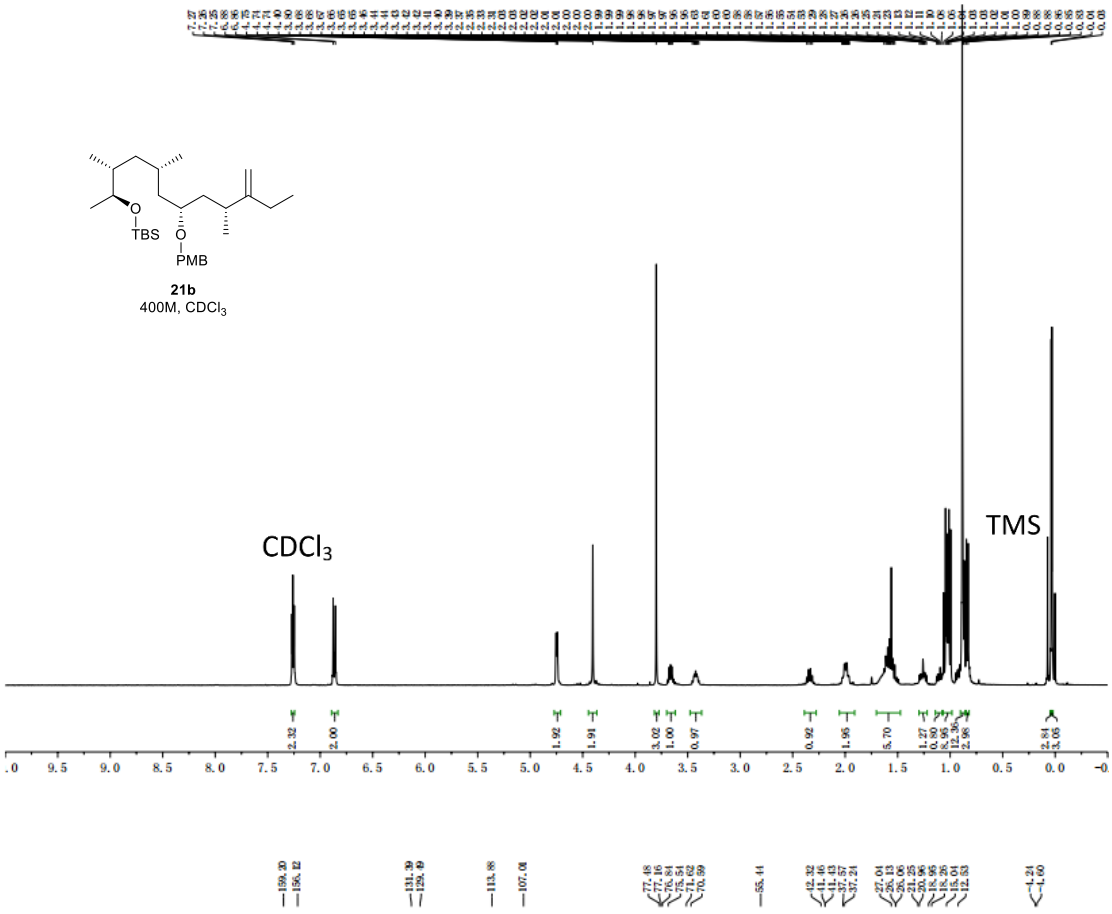

TBS
PMB
21
75M, CDCl3
CDCl3
TMS

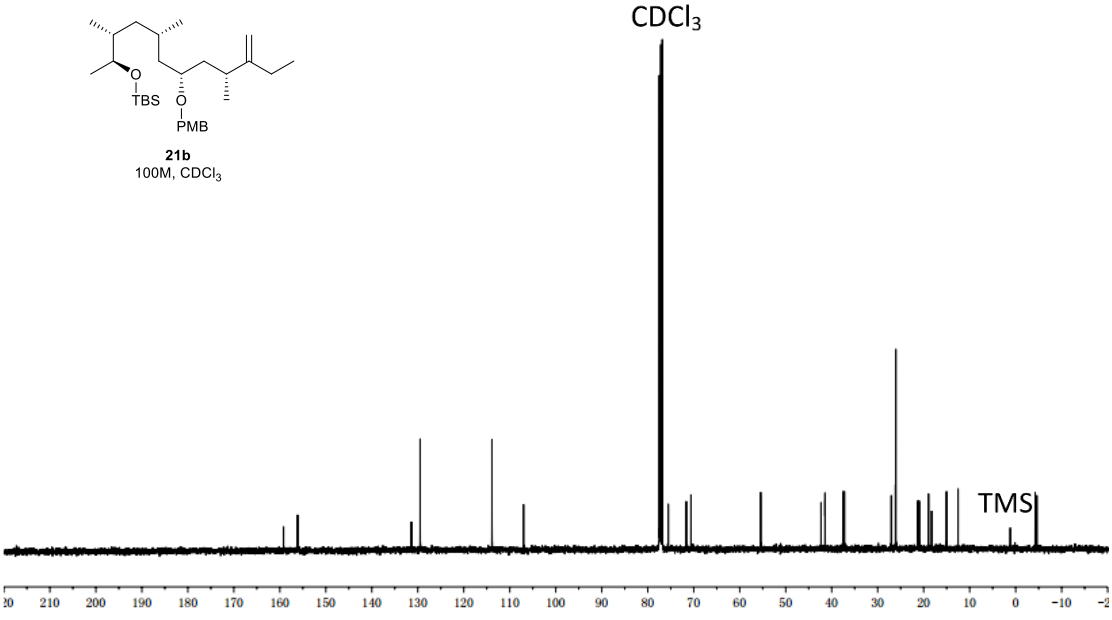


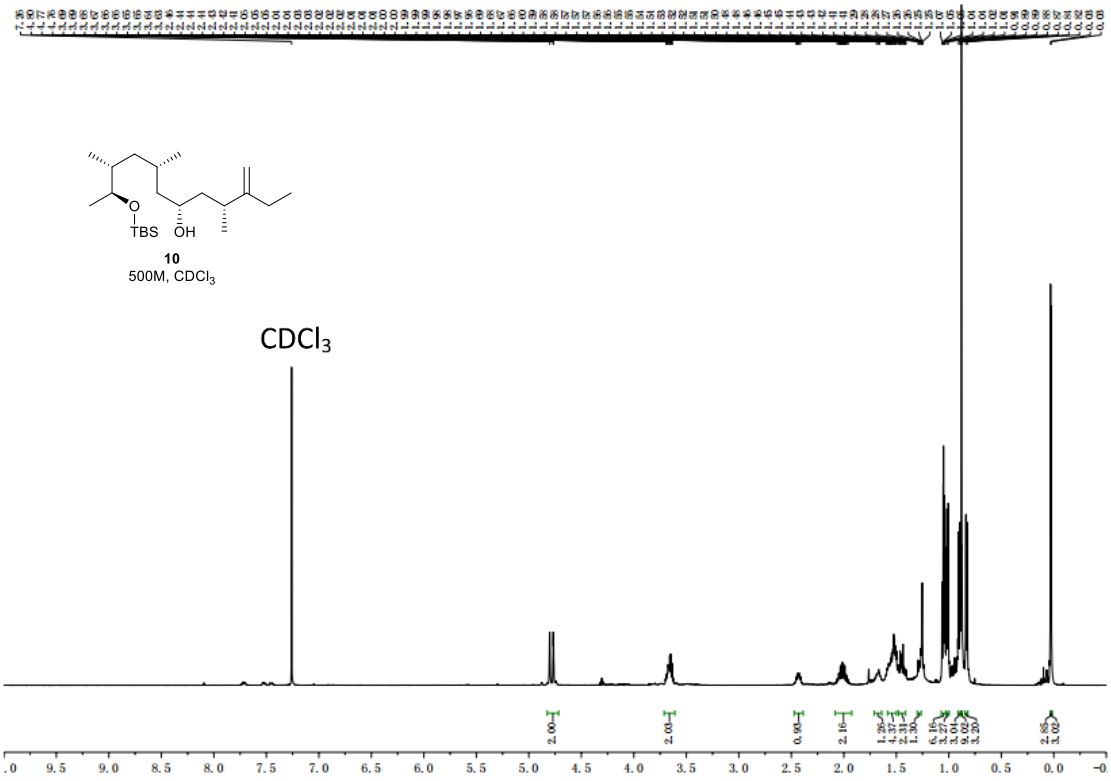
21a
400M, $CDCl_3$

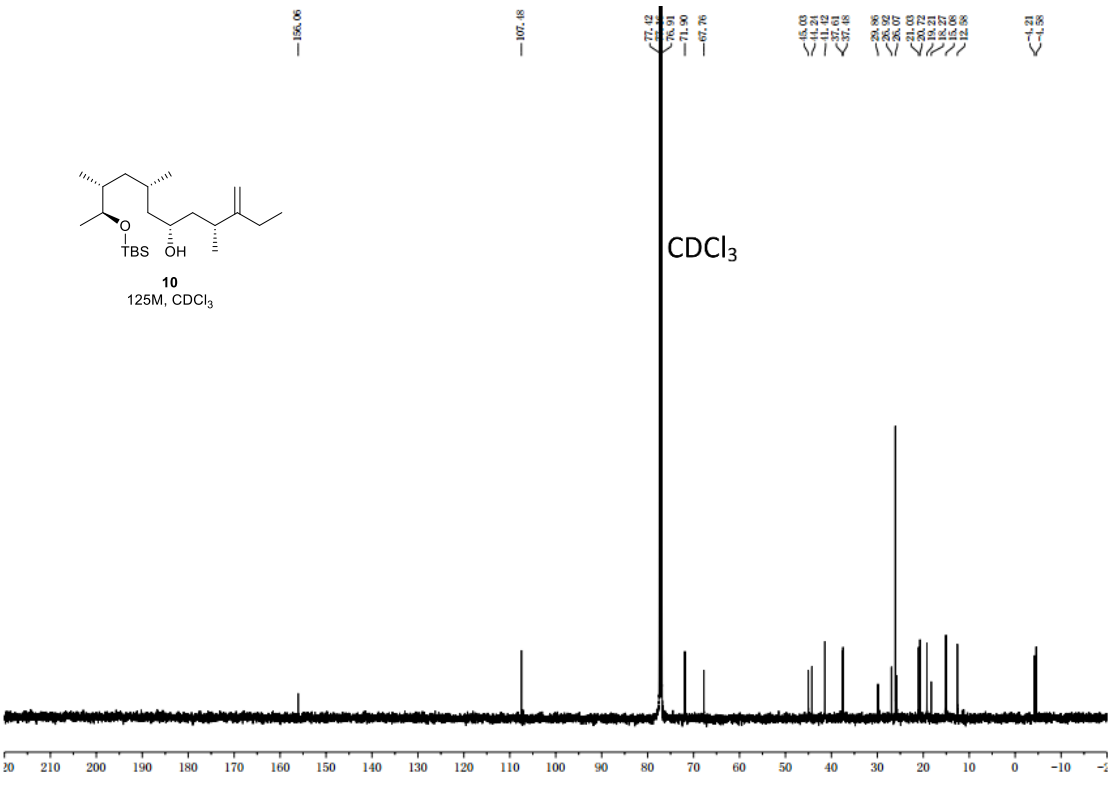


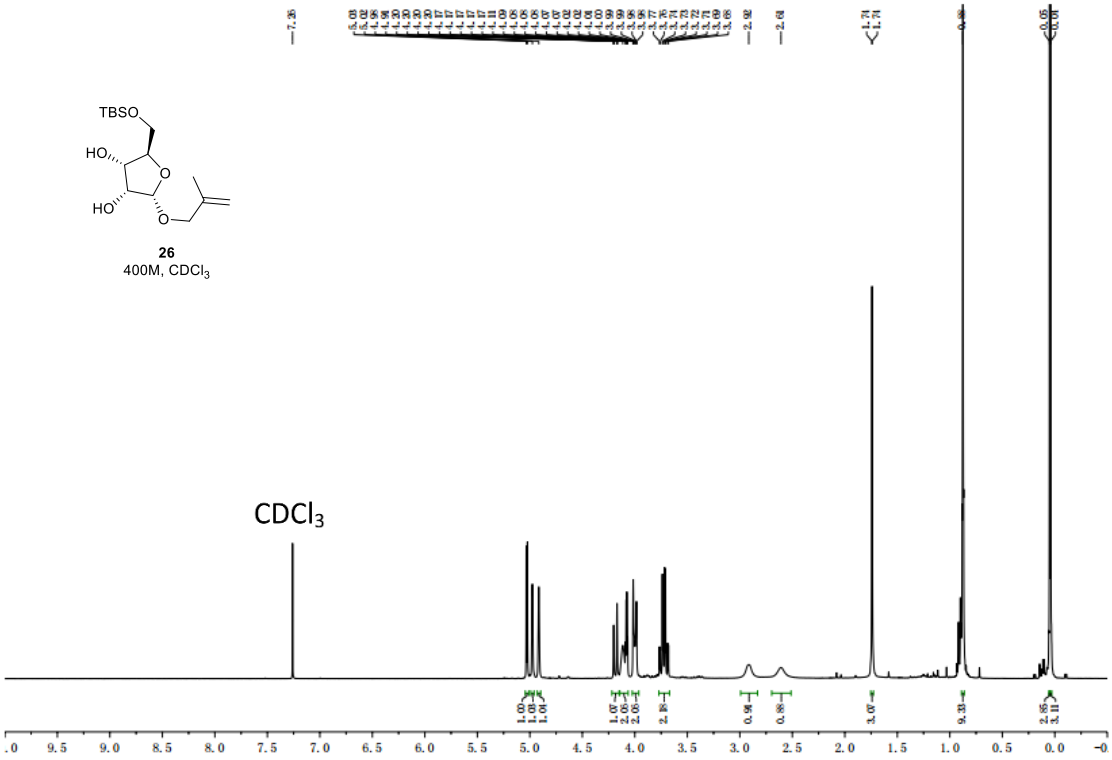
21a
100M, $CDCl_3$


TBS
O
O
PMB
21b
400M, CDCl3
CDCl3
TMS

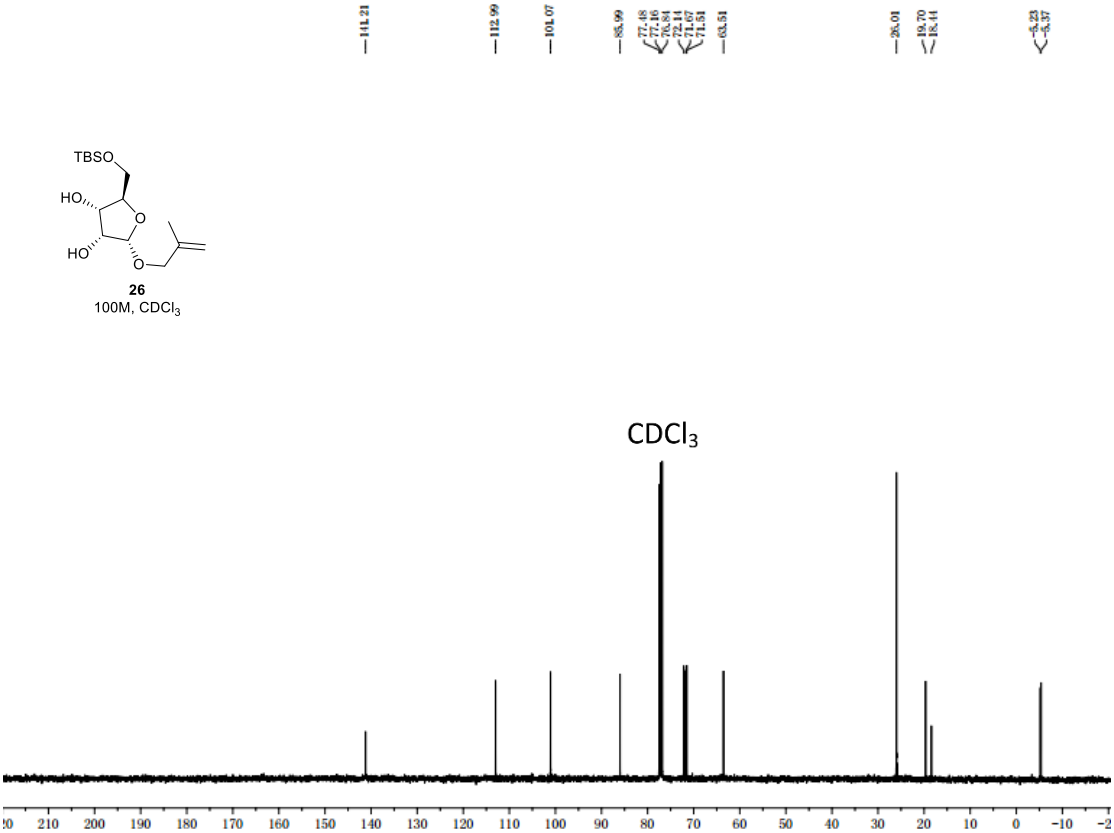

TBS
O
O
PMB
21b
100M, CDCl3
CDCl3
TMS


TBS
OH
10
500M, CDCl3
CDCl3

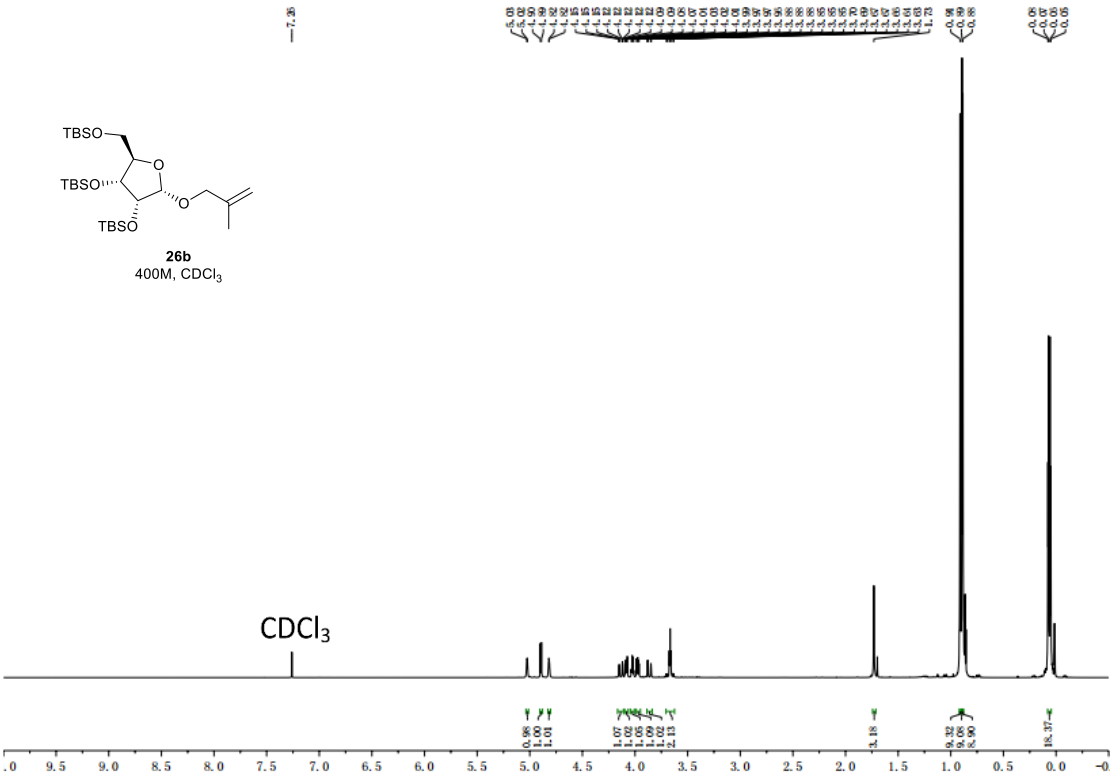

TBS
OH
10
125M, CDCl3
CDCl3



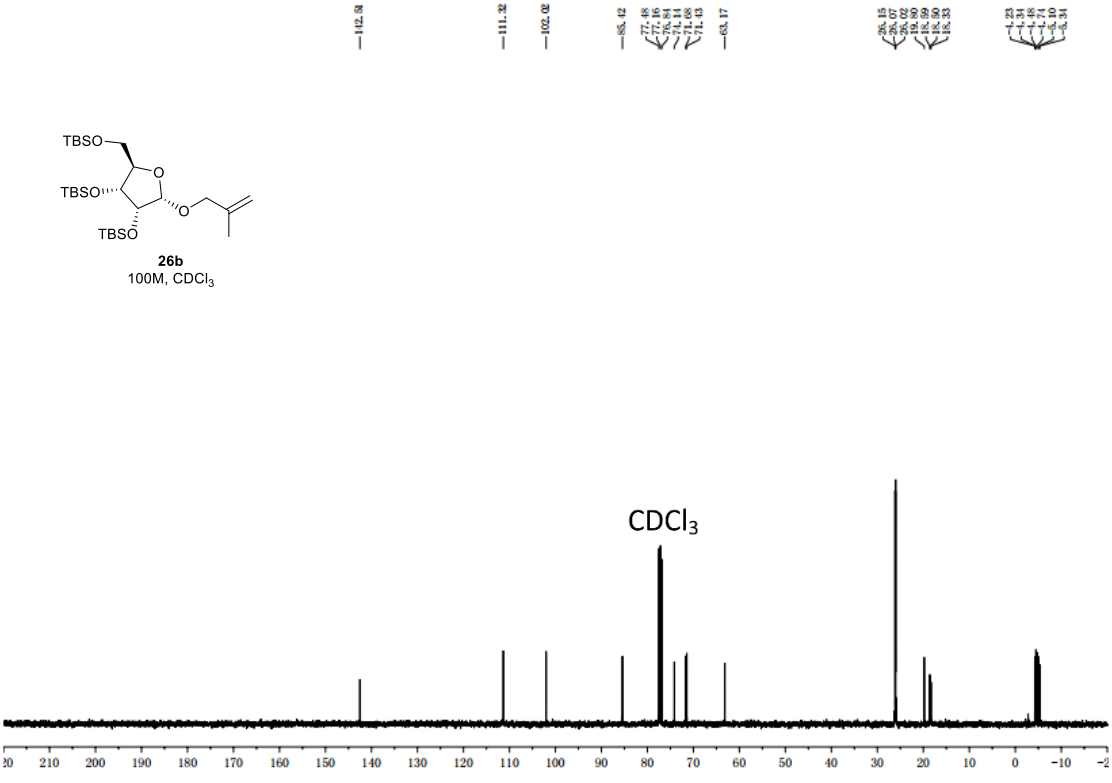
26
400M, $CDCl_3$



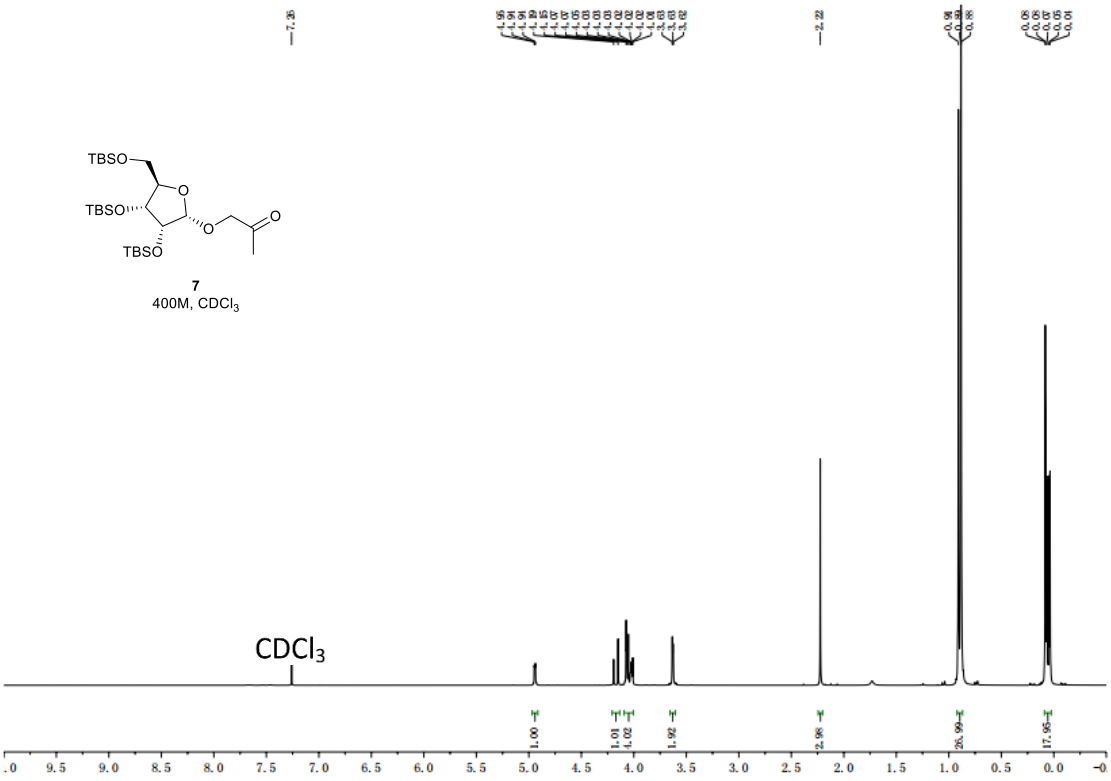
26
100M, $CDCl_3$

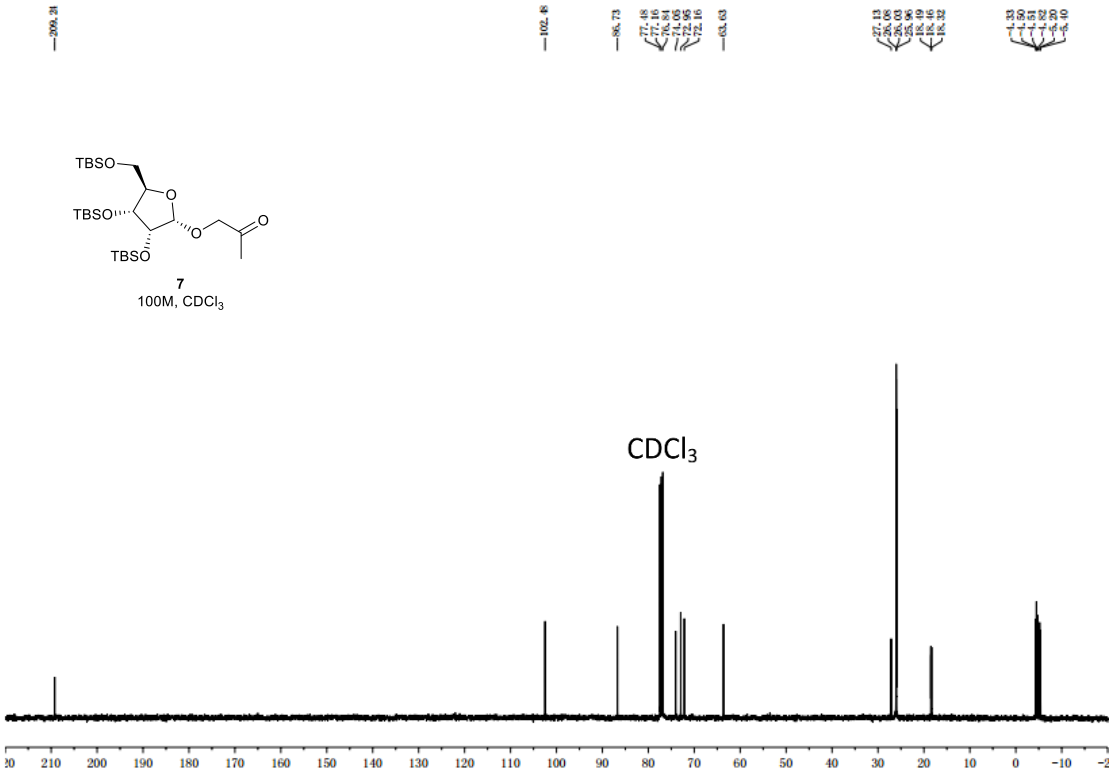


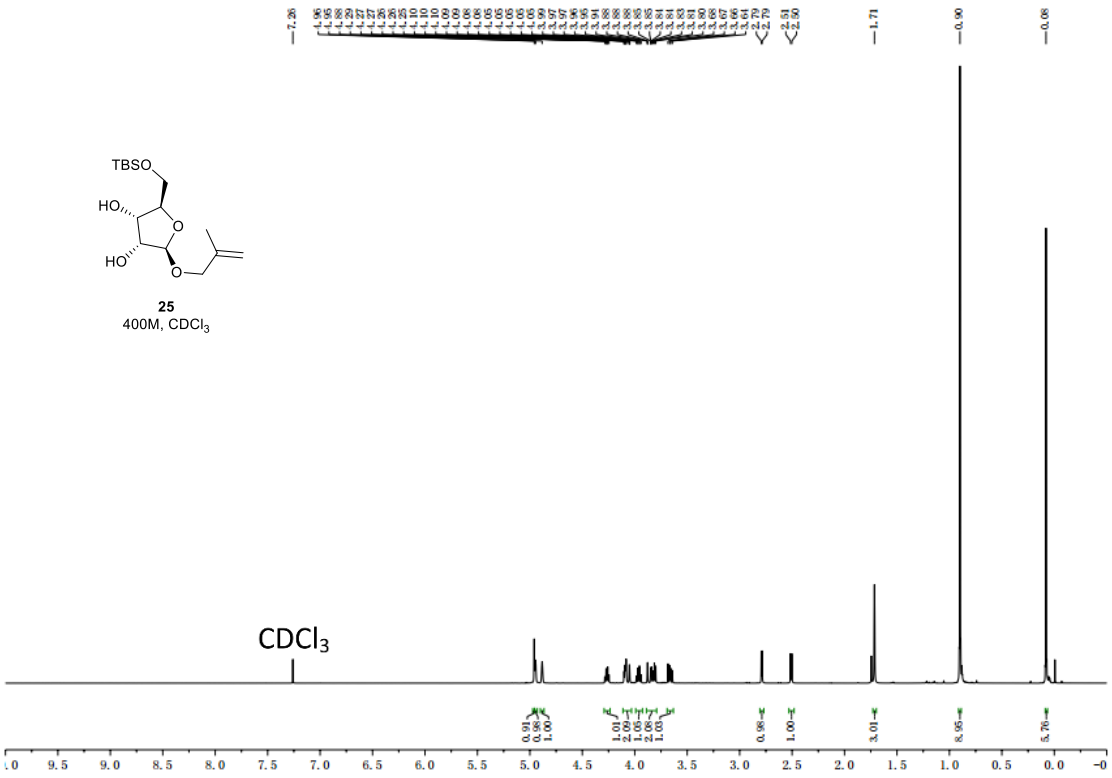
26b
400M, $CDCl_3$

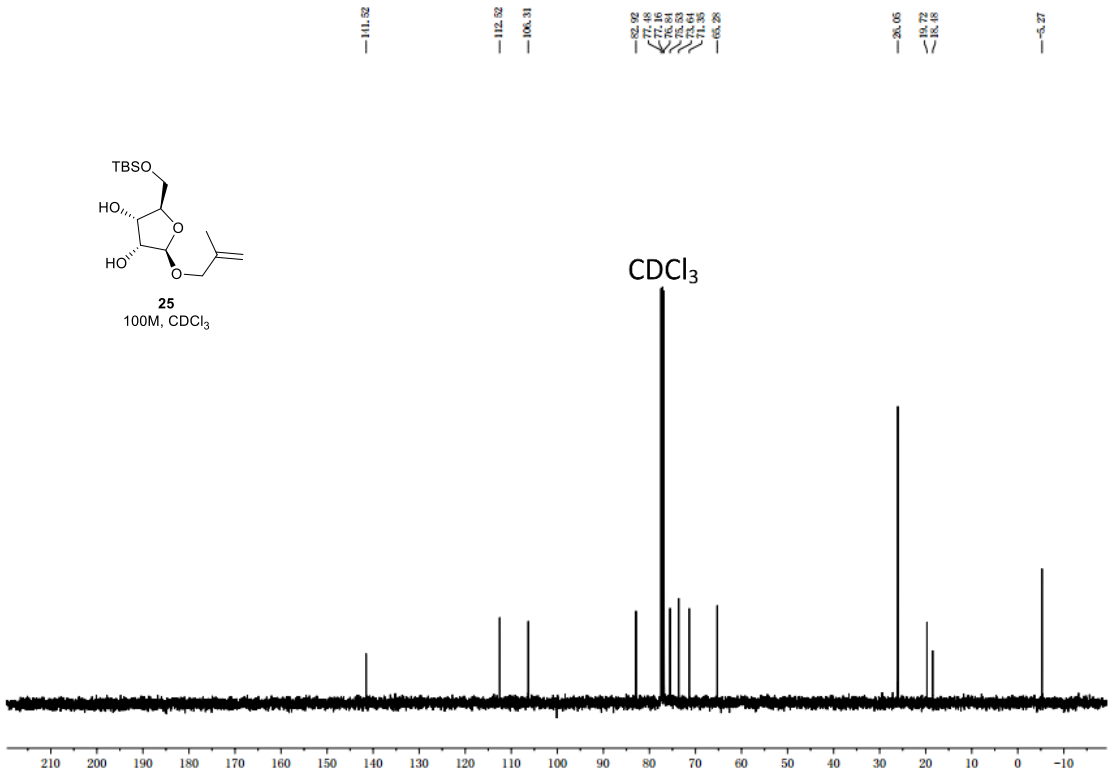


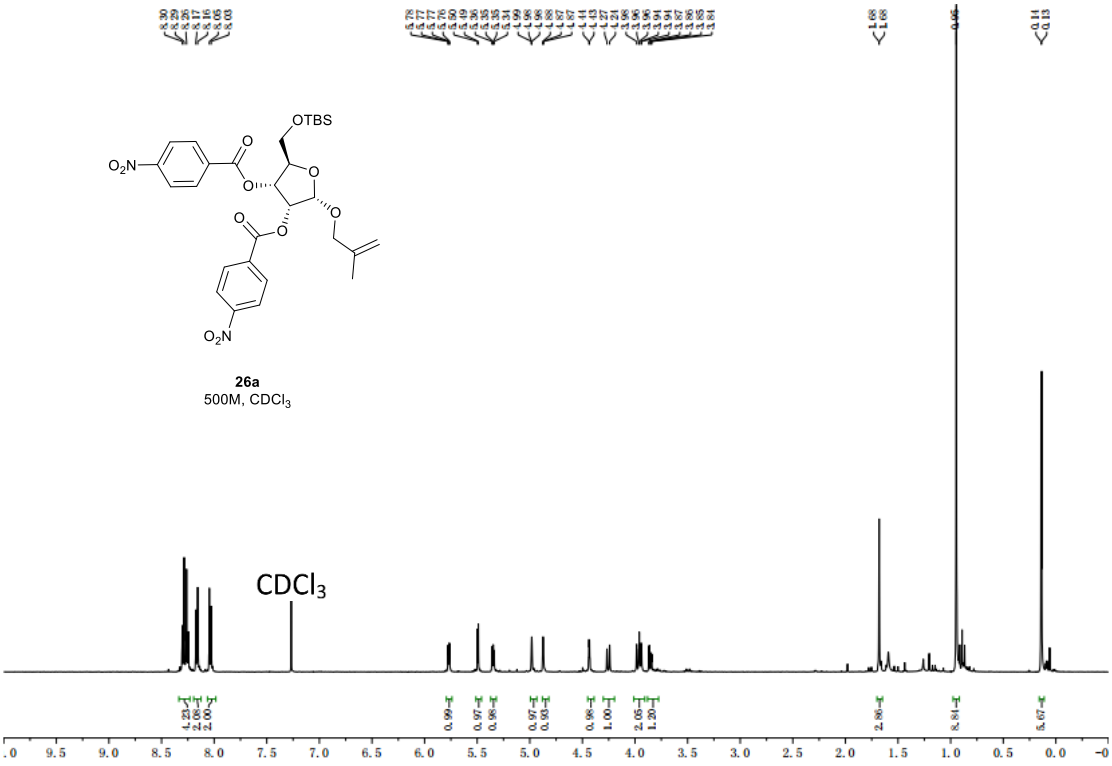
26b
100M, $CDCl_3$


TBSO
TBSO
TBSO
O
O
O
7
400M, CDCl3
CDCl3

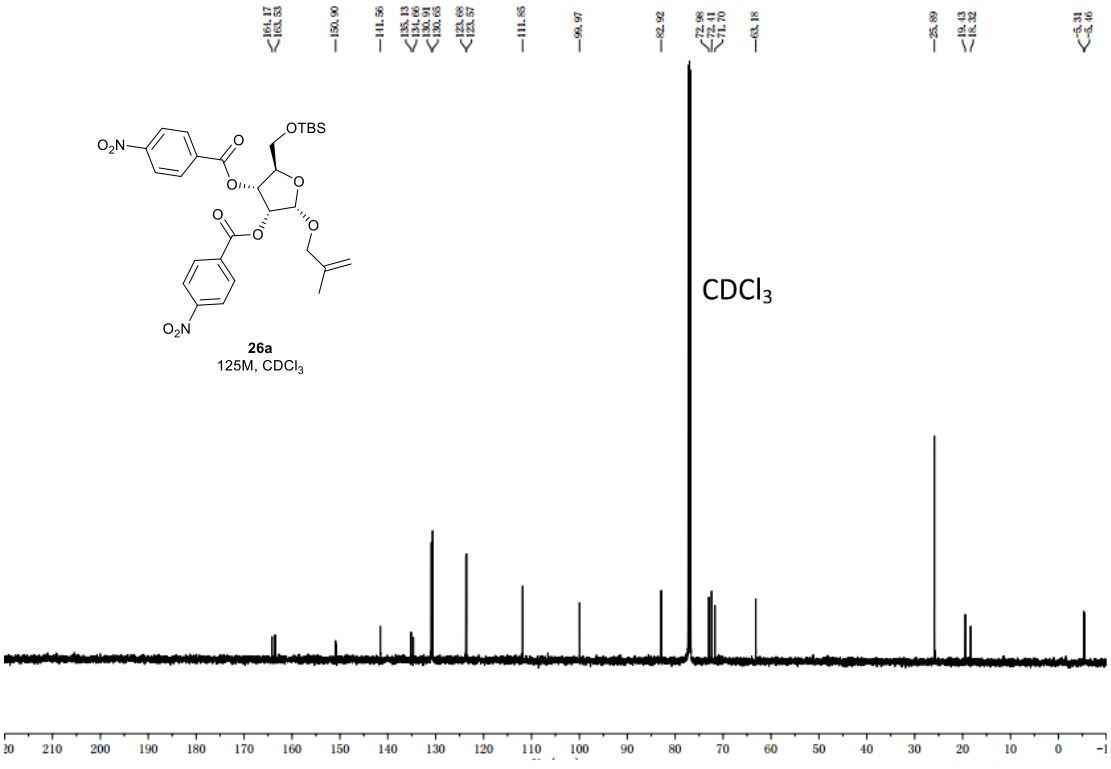

TBSO
TBSO
TBSO
O
O
O
7
100M, CDCl3
CDCl3


TBSO
HO
HO
O
O
25
400M, CDCl3
CDCl3


TBSO
HO
HO
O
O
25
100M, CDCl3
CDCl3

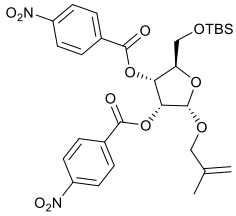


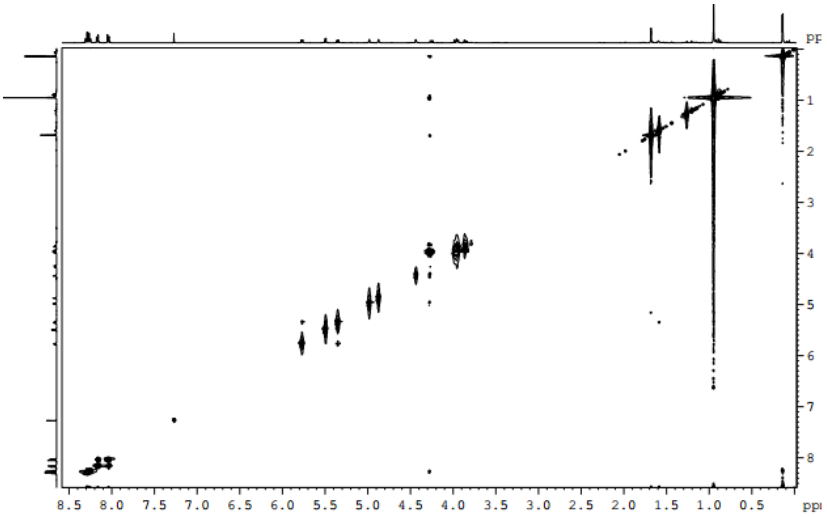
26a
500M, $CDCl_3$



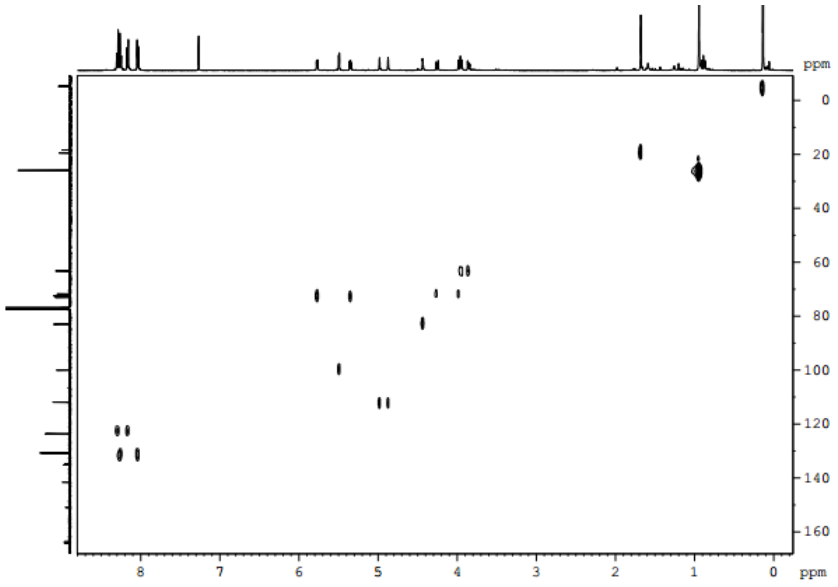
26a
125M, $CDCl_3$

COSY (500 MHz, $CDCl_3$)

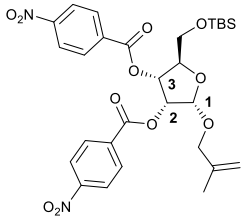


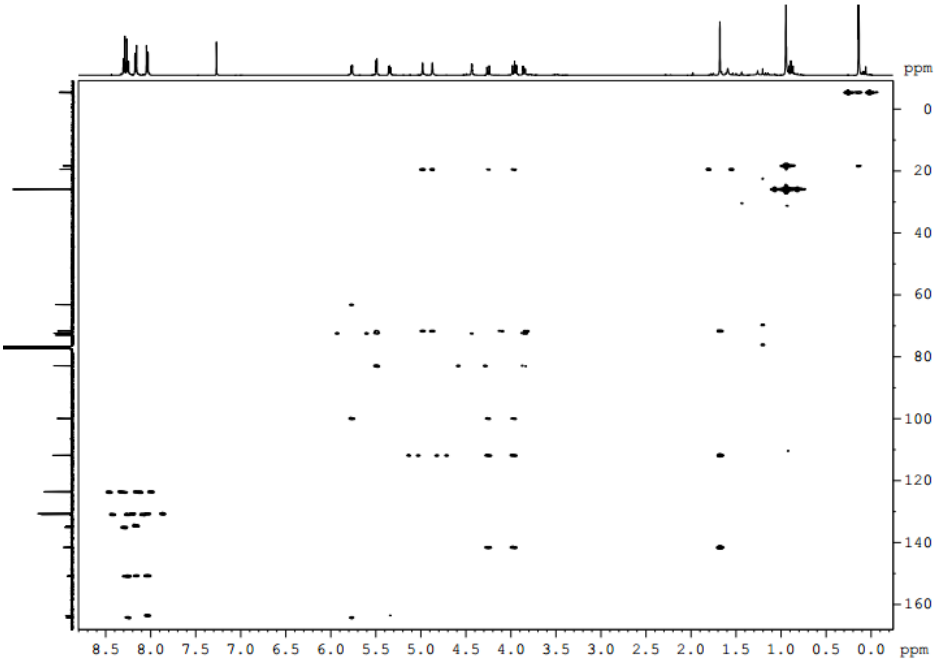


HSQC (500 MHz, $CDCl_3$)

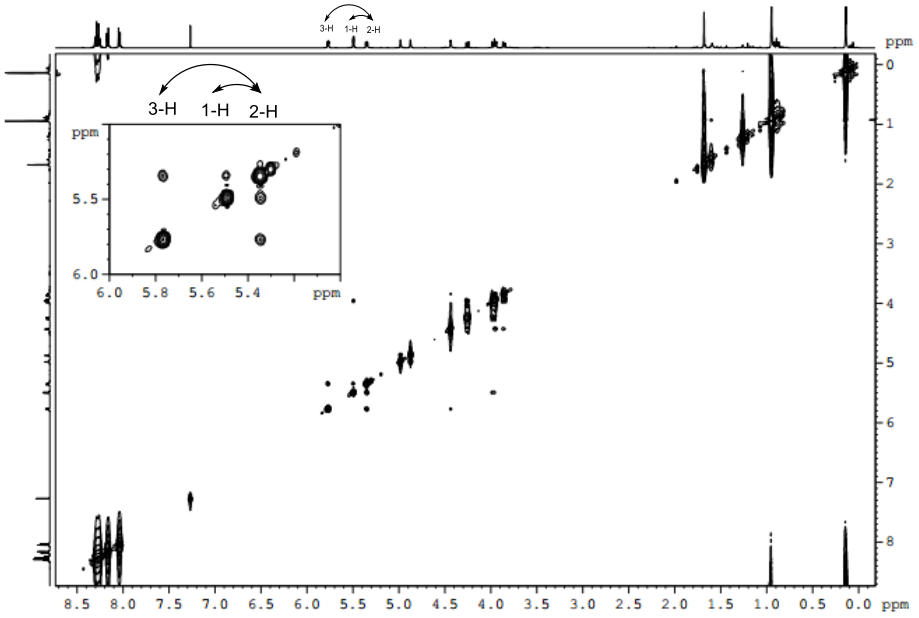


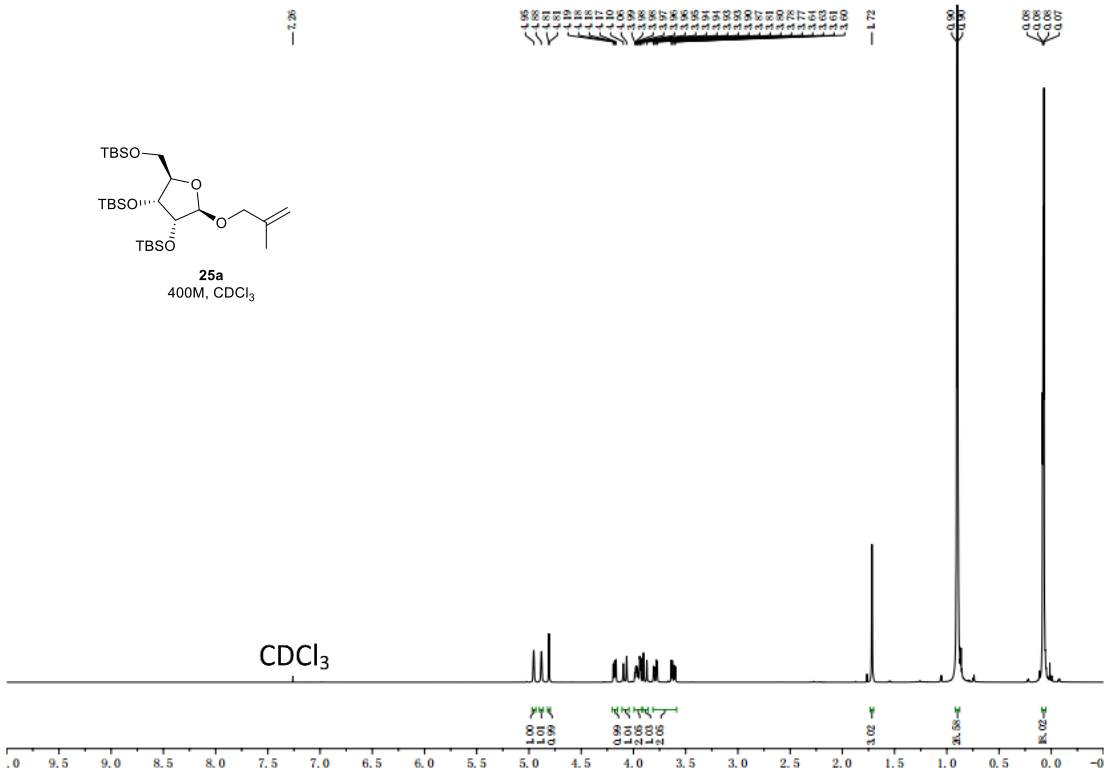
HMBC (500 MHz, $CDCl_3$)



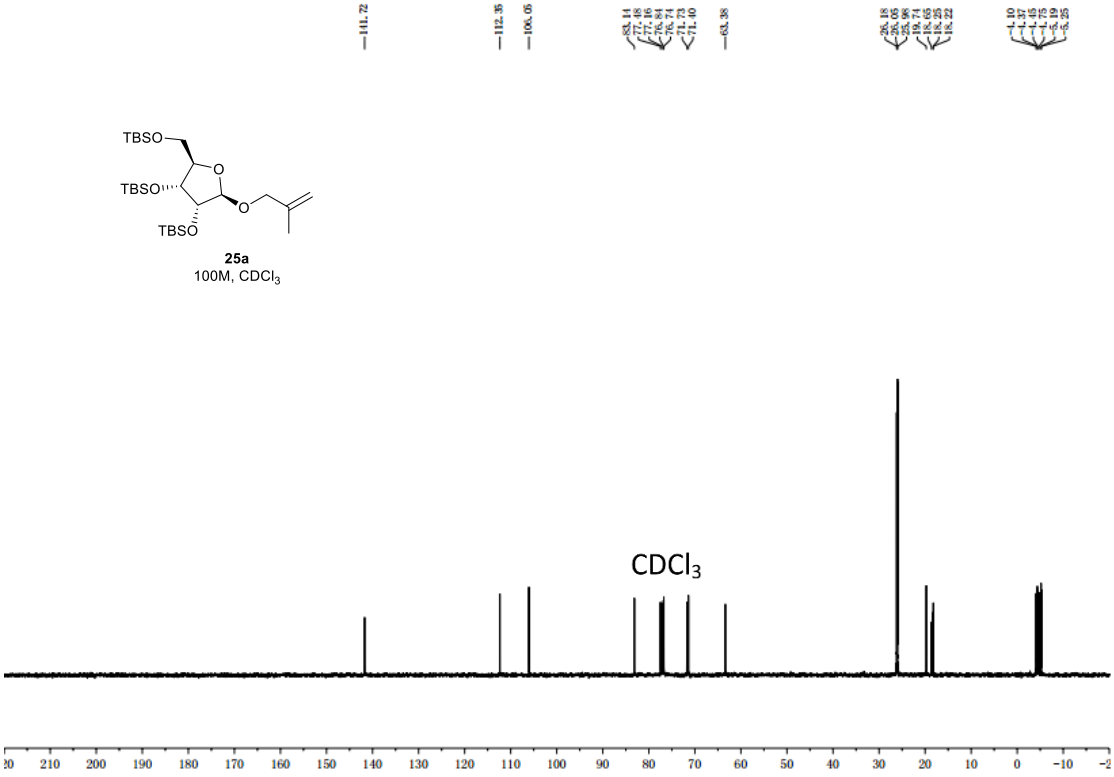


NOESY (500 MHz, $CDCl_3$)

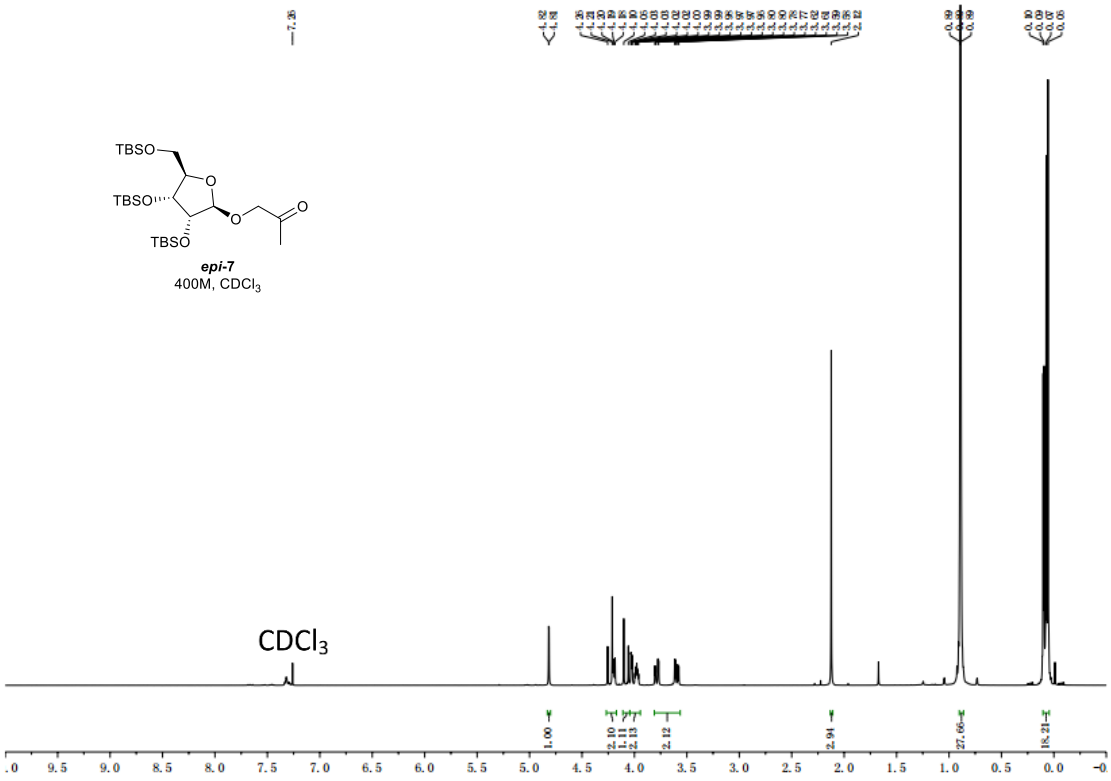




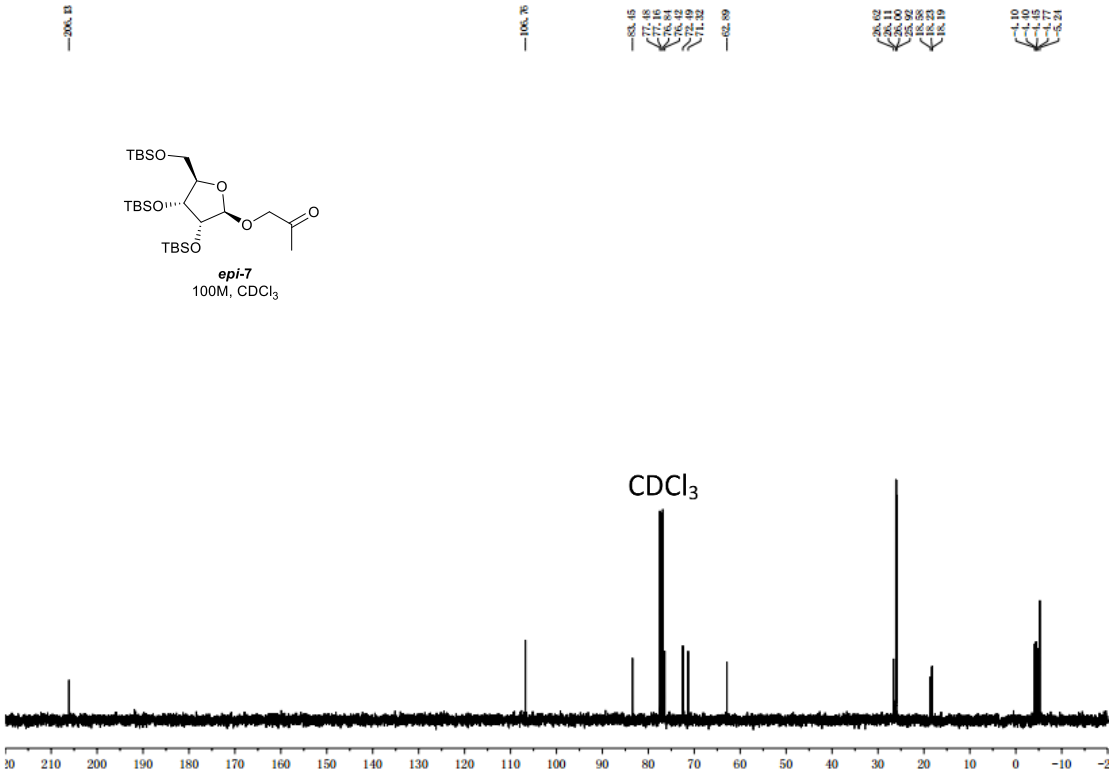
25a
400M, $CDCl_3$



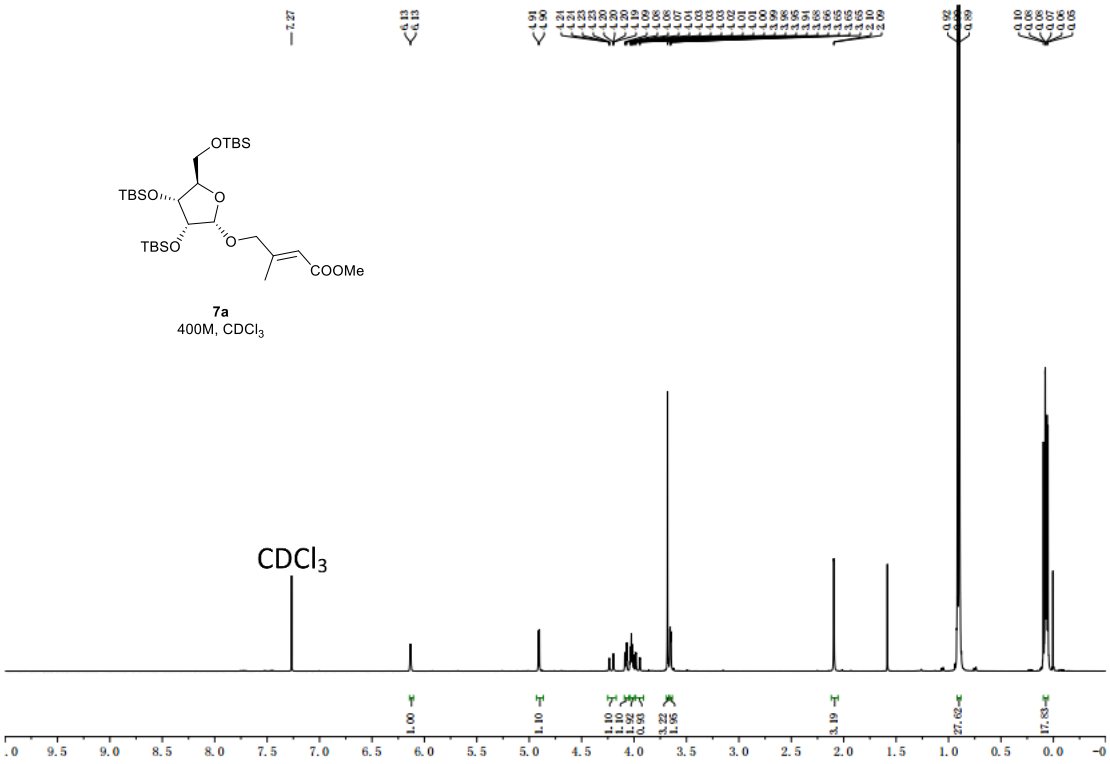
25a
100M, $CDCl_3$



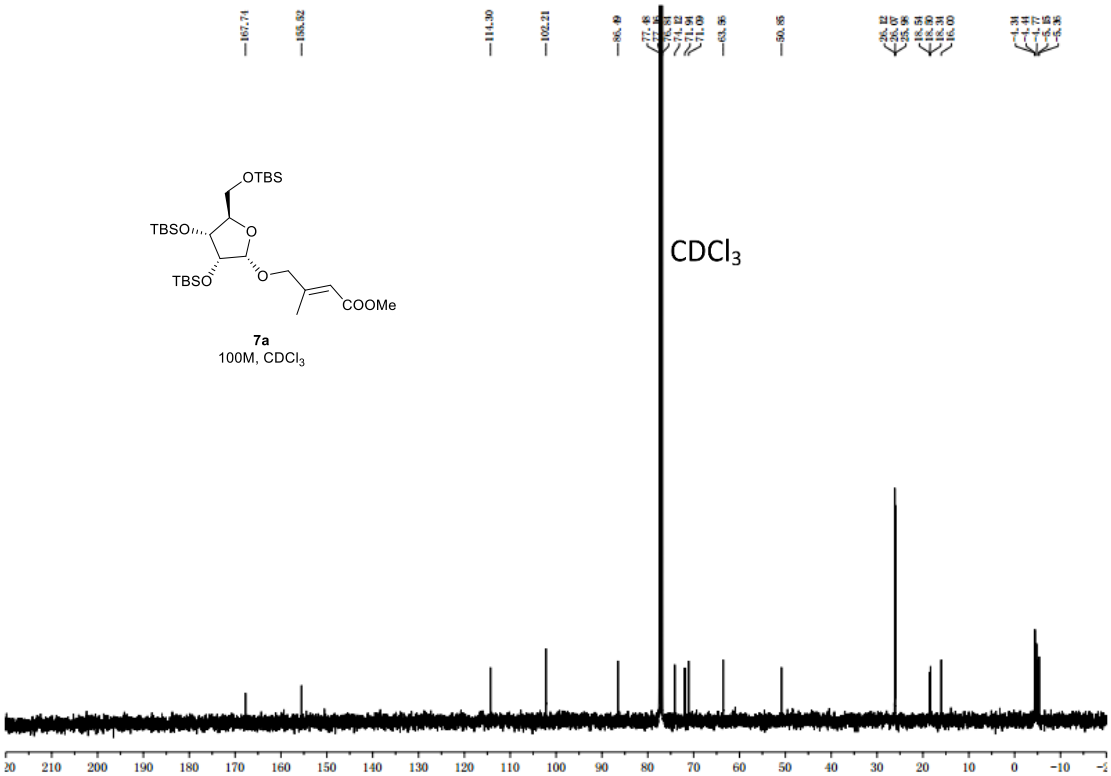
epi-7
400M, $CDCl_3$



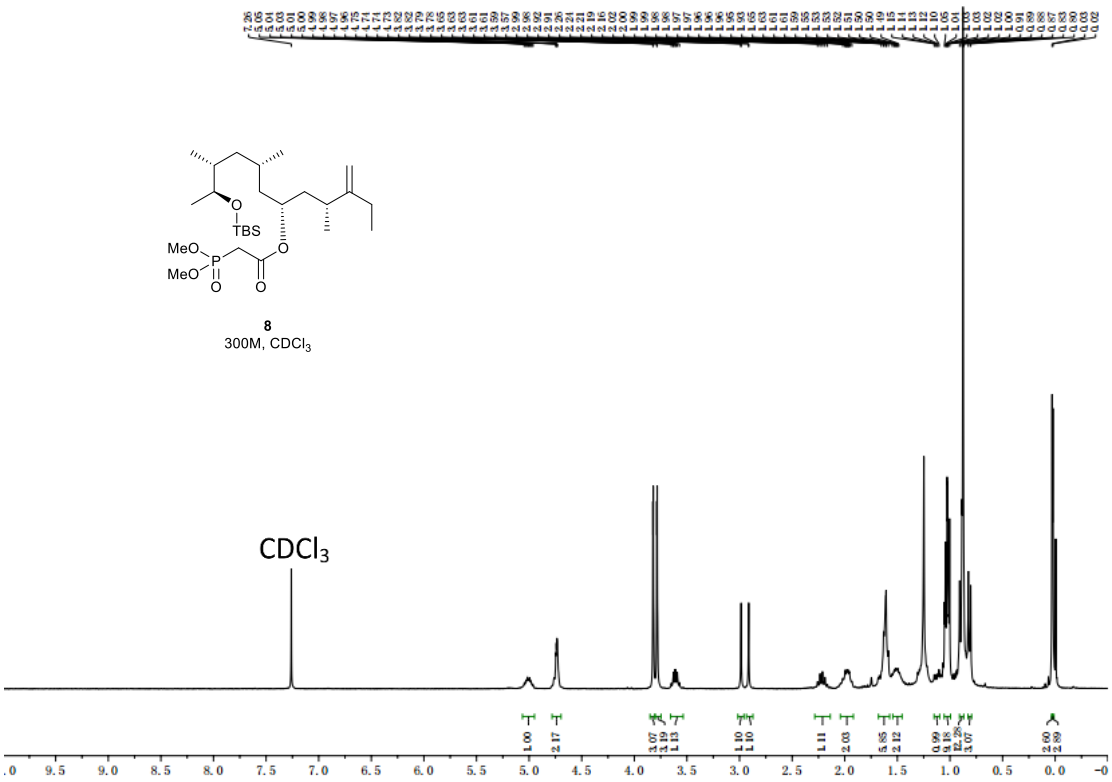
epi-7
100M, $CDCl_3$

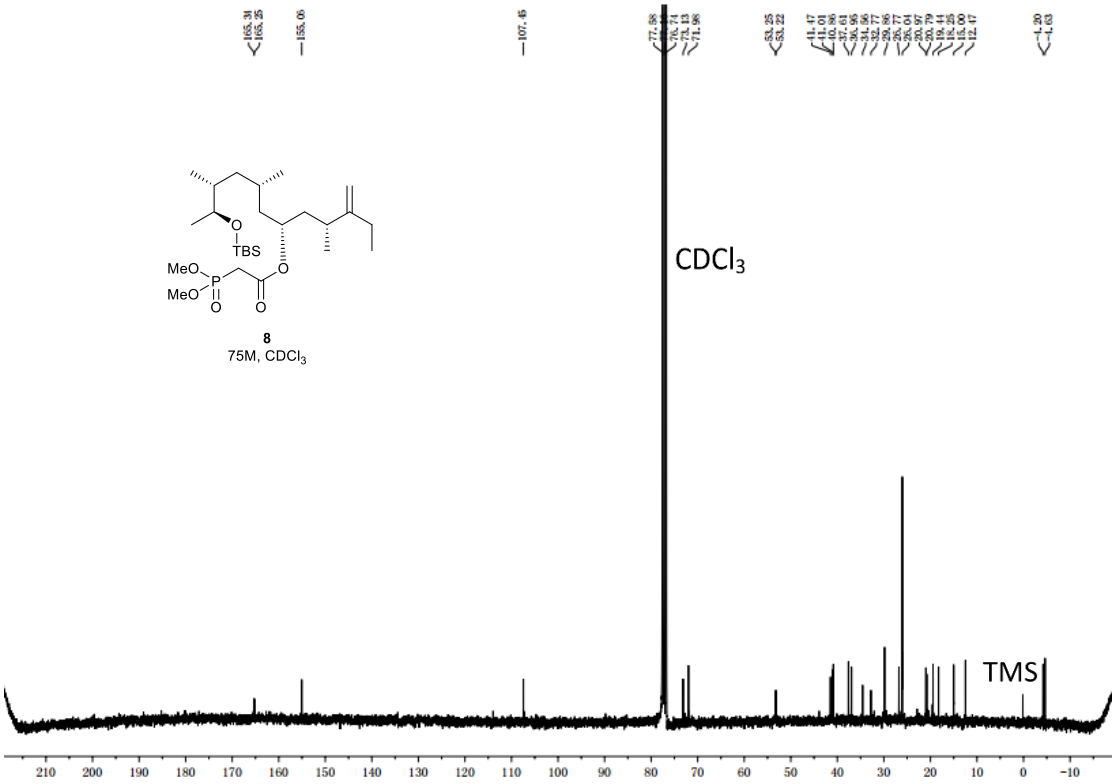


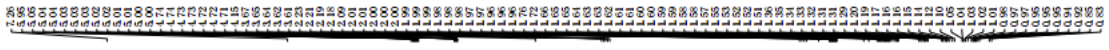
7a
400M, $CDCl_3$

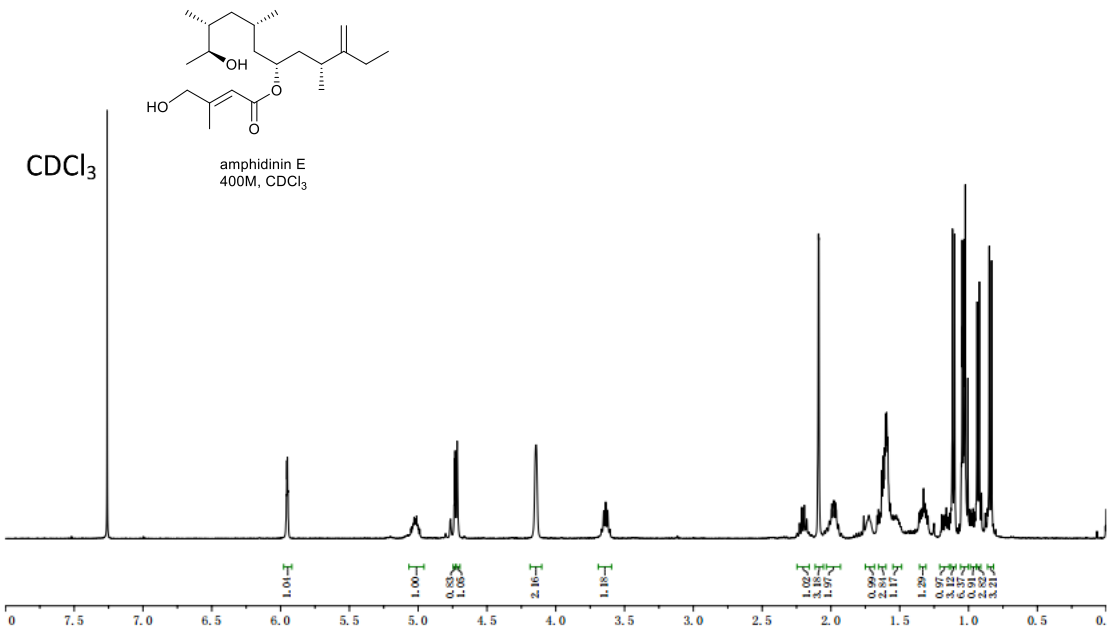


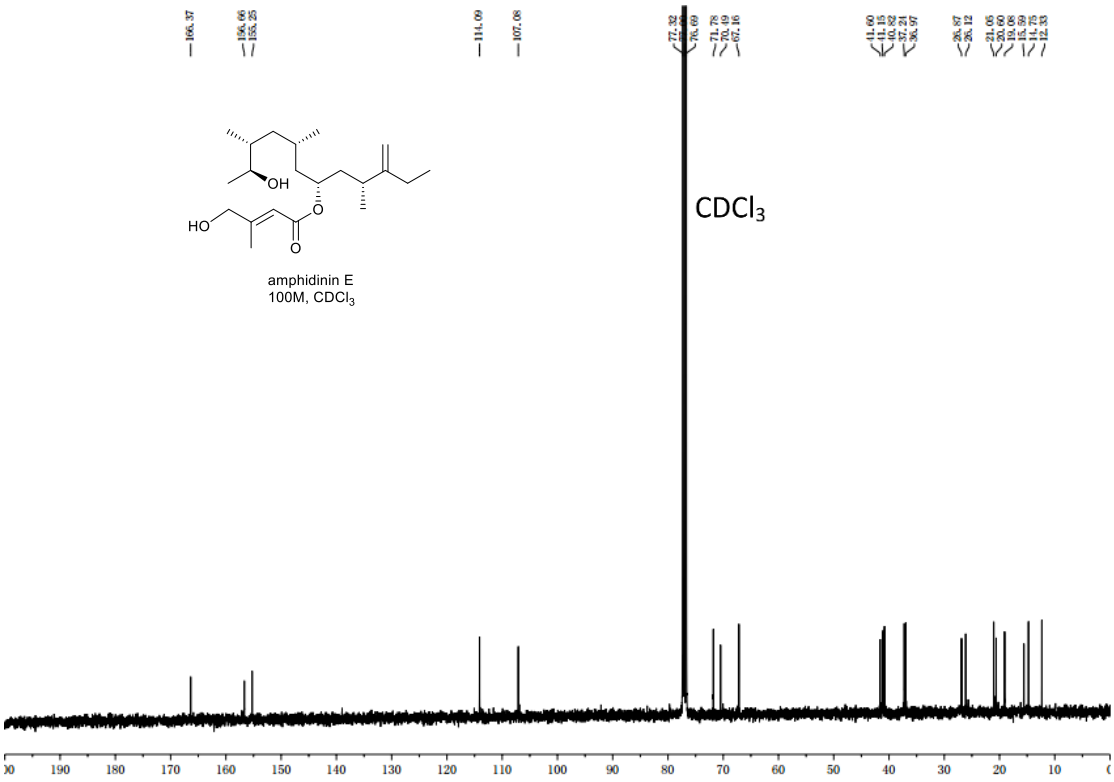
7a
100M, $CDCl_3$

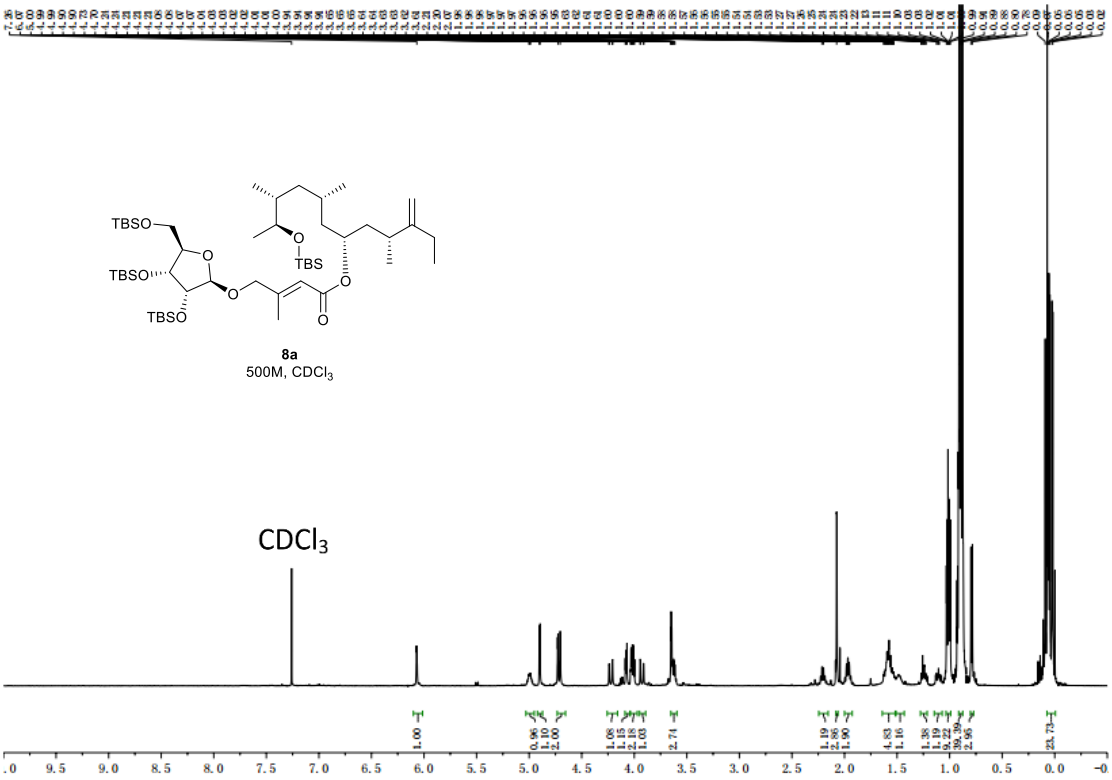

TBS
MeO
MeO
P
O
O
O
O
8
300M, CDCl3
CDCl3


TBS
MeO
MeO
P
O
O
O
O
8
75M, CDCl3
CDCl3
TMS

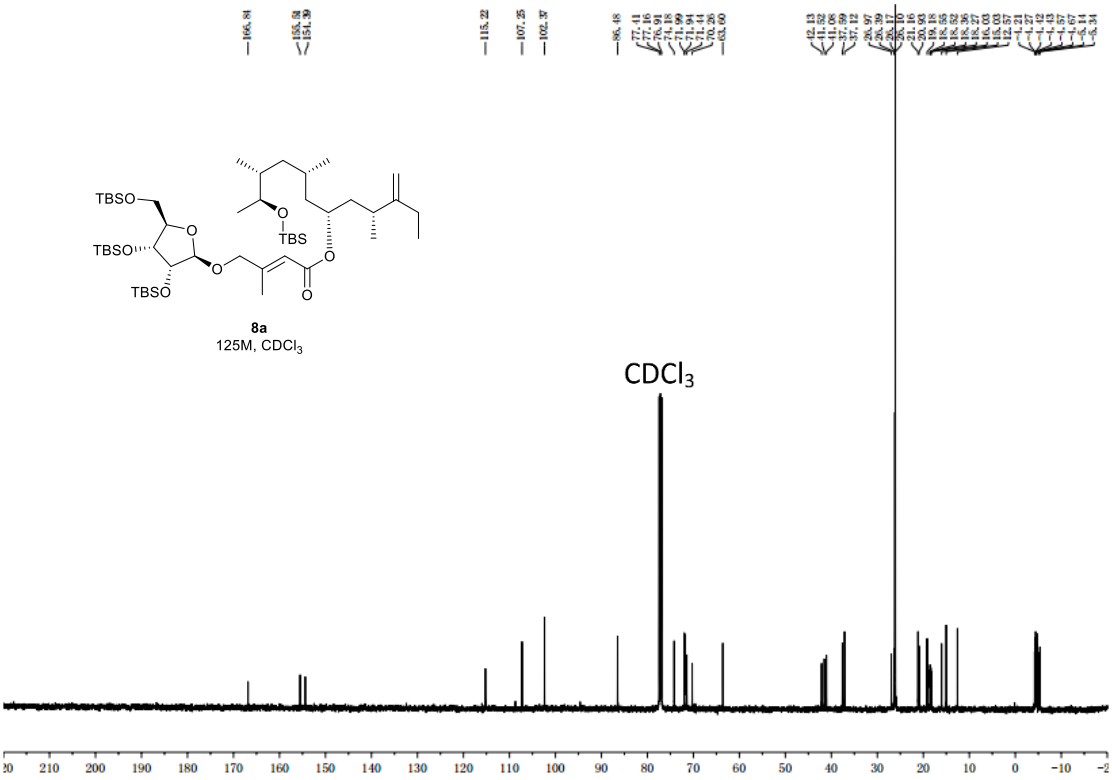



CDCl3
amphidinin E
400M, CDCl3

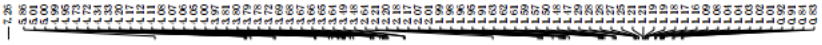

CDCl3
amphidinin E
100M, CDCl3

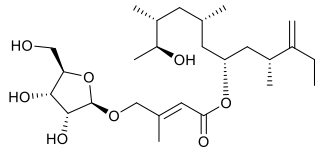


8a
500M, $CDCl_3$

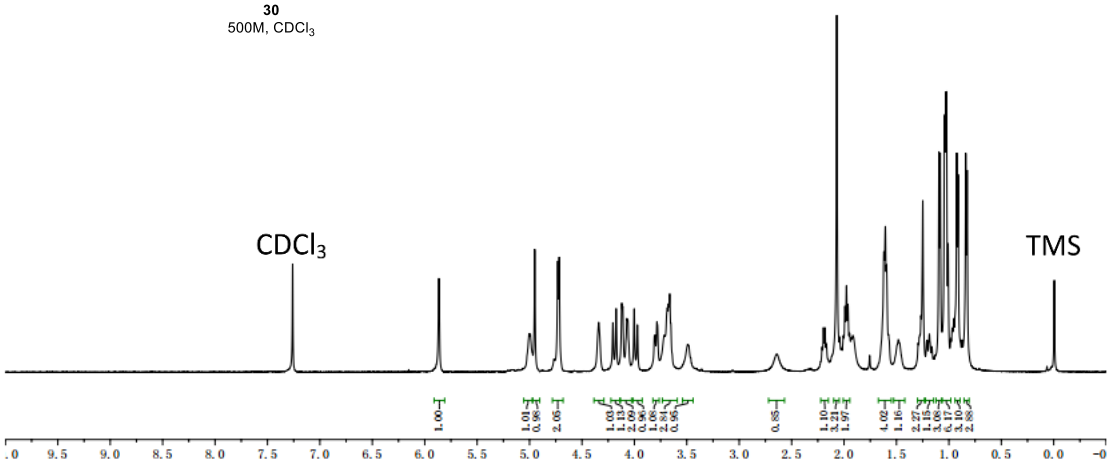


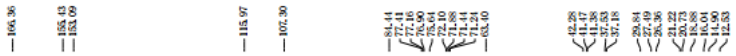
8a
125M, $CDCl_3$

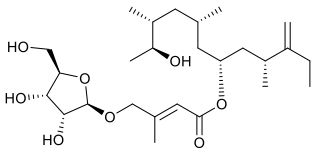




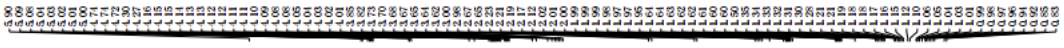
30
500M, $CDCl_3$

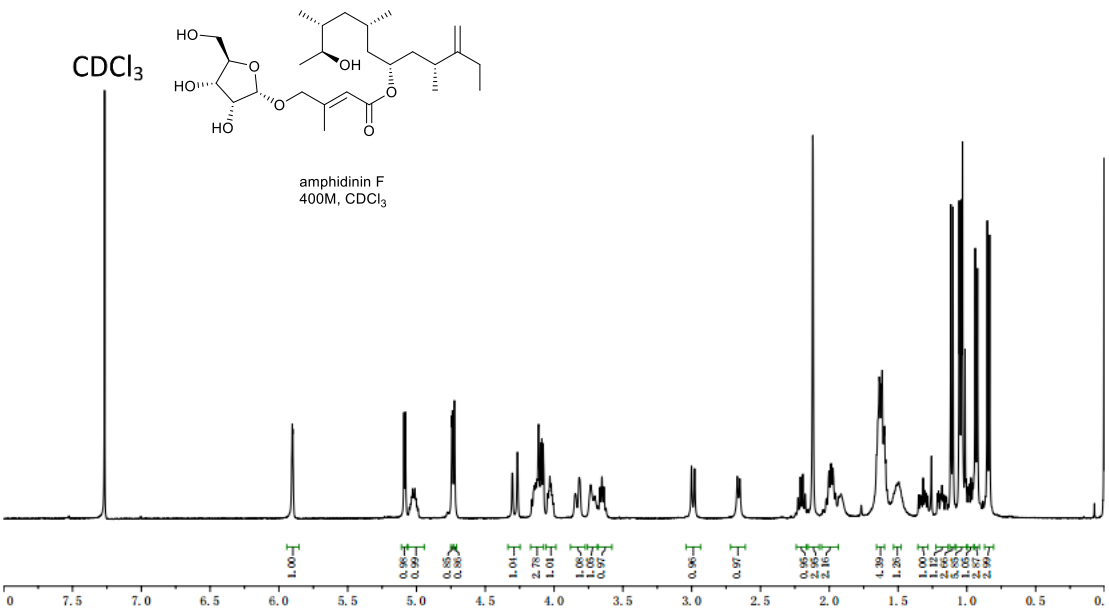


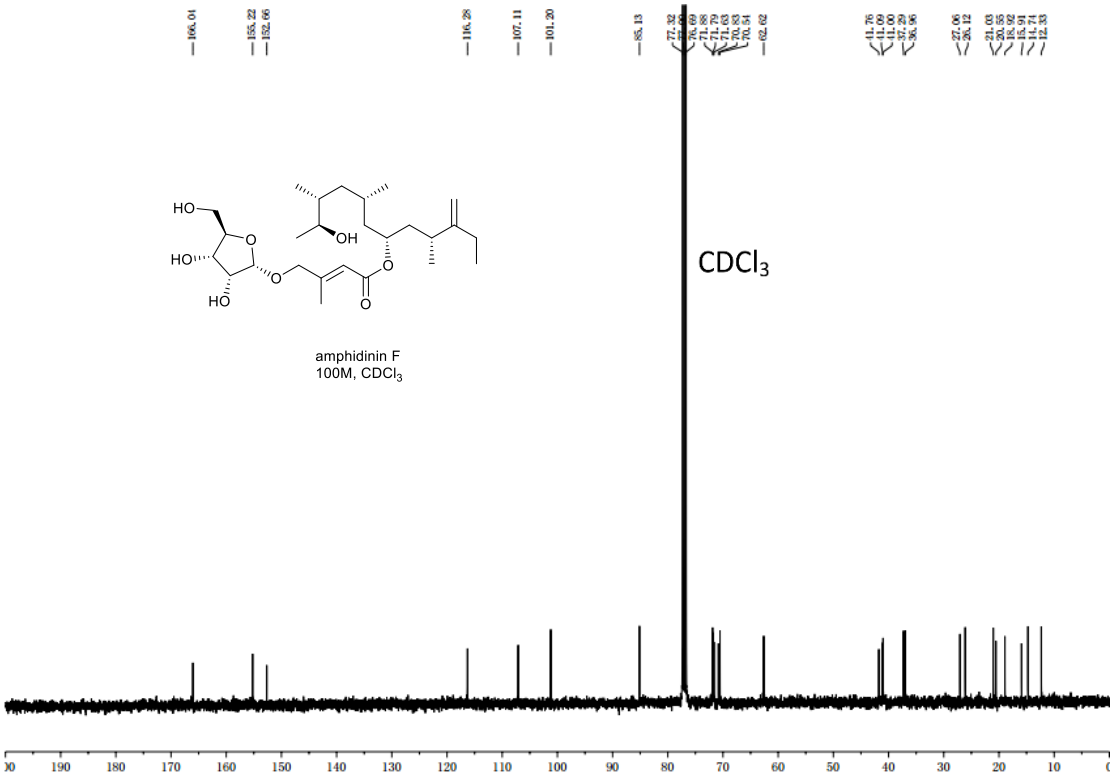


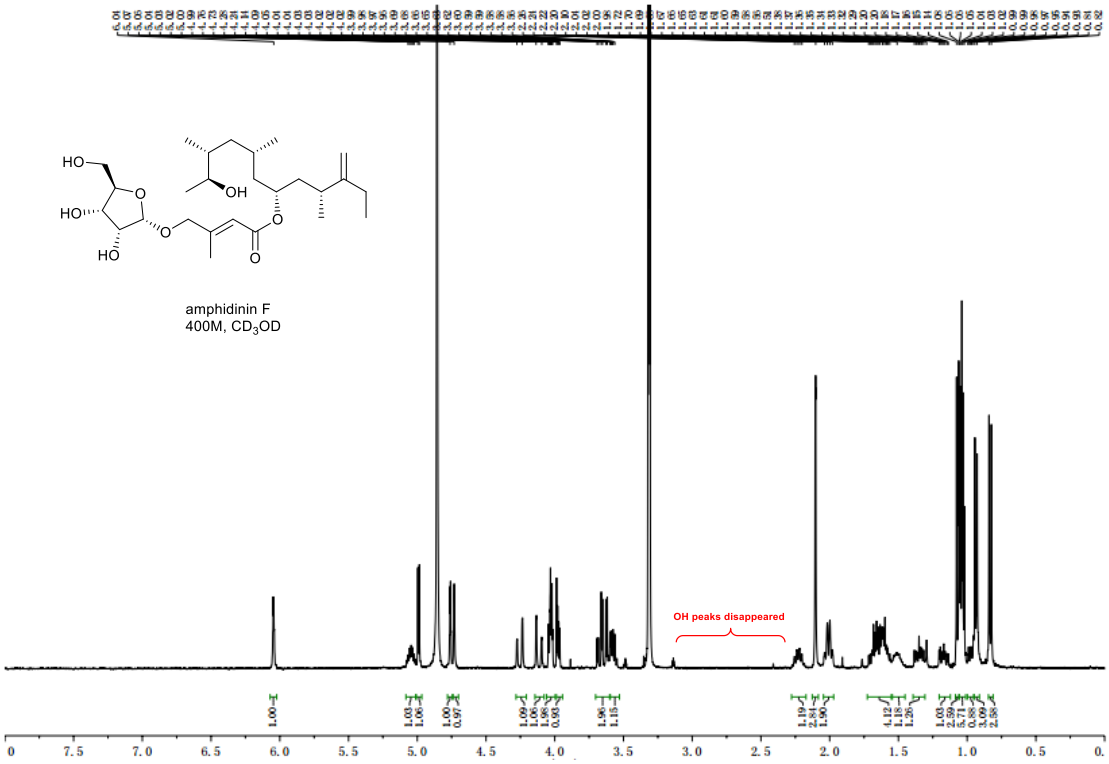


30
125M, $CDCl_3$




CDCl3
HO
HO
HO
O
OH
O
O
amphidinin F
400M, CDCl3


CDCl3
HO
HO
HO
O
OH
O
O
amphidinin F
100M, CDCl3


HO
HO
HO
O
O
OH
O
O
amphidinin F
400M, CD3OD
OH peaks disappeared
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