Supporting Information

Synthesis and Evaluation of a Linkable Functional Group-Equipped Analog of the Epothilones

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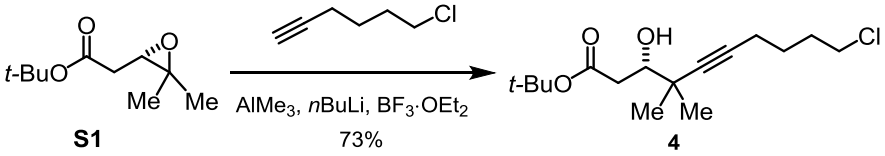
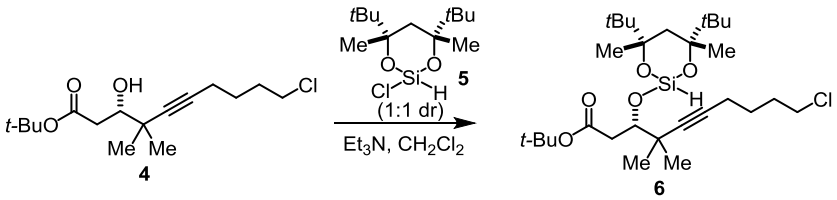
General Information. All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Degassed solvents were purified by passage through an activated alumina column. Thin-layer chromatography was carried out on glass backed silica gel TLC plates (250 mm) from Silicycle. Visualization was accomplished with UV light (254 nm), followed by heating after staining the plate with phosphomolybdic acid (PMA), potassium permanganate ($KMnO_4$) or *p*-anisaldehyde solution. Optical rotations were recorded on a Jasco DIP-1000 digital polarimeter. Infrared spectra were recorded on a Perkin-Elmer Spectrum Two (Diamond ATR) IR spectrometer. ^{1}H NMR spectra were recorded on a Bruker DPX-400 (400 MHz), Bruker AVIII 500 (500 MHz) or AVIII 500 Ascend (500 MHz) spectrometer and are reported in ppm, relative to residual protonated solvent peak ($CHCl_3$, 7.26 ppm). Data are reported as follows: (bs= broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration). Proton decoupled ^{13}C NMR spectra were recorded on a Bruker AVIII 500 (125 MHz) or AVIII 500 Ascend (125 MHz) spectrometer, relative to $CDCl_3$ (77.16 ppm). High-resolution mass spectra were obtained from the Columbia University Mass Spectrometry Facility on a Waters XEVO G2XS QToF mass spectrometer equipped with a UPC2 SFC inlet, electrospray ionization (ESI) probe, atmospheric pressure chemical ionization (APCI) probe. pH 7.00 buffered silica gel: A 1000 mL round bottom flask charged with silica gel (250 g) and 25.0 mL of buffer solution pH 7.00 (potassium dihydrogen phosphate/sodium hydroxide, Fluka Analytical) was stirred on rotavapor under atmospheric pressure overnight.

Experimental Procedures and Spectroscopic Data of Compounds



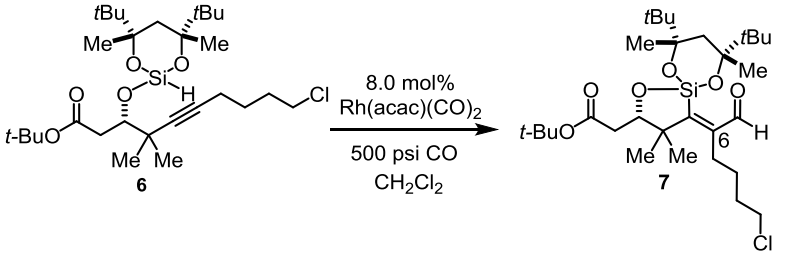
To a cooled (0 ℃) solution of 6-chloro-1-hexyne (13.5 mL, 111.1 mmol) in Et_2O (300 mL) was added *n*-BuLi (44.2 mL, 2.5 M in hexanes, 110.6 mmol) dropwise. After 5 minutes, $AlMe_3$ (53.0 mL, 106.0 mmol, 2.0 M in toluene) was added dropwise. The reaction was warmed to room temperature and stirred for 20 minutes. The reaction was then cooled to −78 ℃ and **S1**[1] (9.40 g, 50.5 mmol) was added as a solution in Et_2O (50 mL), followed by $BF_3 OEt_2$ (12.5 mL, 101.0 mmol). After 2h, the reaction was slowly quenched with MeOH (30.0 mL). The mixture was stirred for 10 minutes then poured into saturated aqueous $NaHCO_3$ (100 mL) solution of pH 10.0. After stirring for about 45 minutes, the layers were separated and the aqueous layer extracted with Et_2O Et_2O (3 × 80 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by silica gel flash column chromatography (EtOAc/hexanes = 1:10) to provide **4** as a clear, yellow oil (11.2 g, 73% yield). $\mathbf{[\alpha]^{20}_D}$ −28.7 (*c* 1.2, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.75 (ddd, *J* = 10.4, 4.5, 2.3 Hz, 1H), 3.56 (t, *J* = 6.6 Hz, 2H), 2.91 (d, *J* = 4.5 Hz, 1H), 2.62 (dd, *J* = 16.0, 2.4 Hz, 1H), 2.39 (dd, *J* = 16.0, 10.4 Hz, 1H), 2.21 (t, *J* = 7.0 Hz, 2H), 1.92 – 1.82 (m, 2H), 1.69 – 1.60 (m, 2H), 1.47 (s, 9H), 1.20 (s, 3H), 1.18 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.8, 85.4, 81.6, 81.3, 74.6, 44.7, 38.8, 36.2, 31.7, 28.3, 26.4, 26.3, 24.9, 18.2; **IR** (film): 3494, 2974, 2934, 2868, 1712, 1455, 1392, 1367, 1302, 1254, 1151, 1079, 1041, 950, 762, 651 cm^{-1}; **HRMS** (ESI+) calcd for $C_{16}H_{27}ClO_3Na$ [M+Na]+: 325.1546, found 325.1547.



To a cooled (0 ℃) solution of silane **5**[1] (817 mg, 2.93 mmol) in CH_2Cl_2 (28 mL) was added homopropargyl alcohol **4** (845 mg, 2.79 mmol) as a solution in CH_2Cl_2 (10 mL), followed by Et_3N (0.58 mL, 4.19 mmol). The reaction was warmed to room temperature after 30 minutes. ^{1}H NMR analysis was used to determine the conversion of the reaction mixture. Additional silane **5** was added

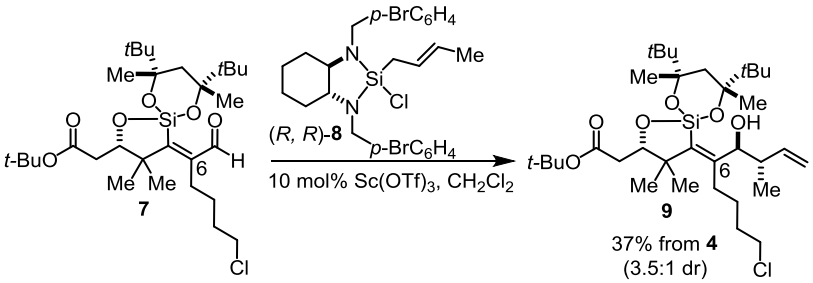
[1] Foley, C. N.; Leighton, J. L. *Org. Lett.* **2015**, *17*, 5858–5861.

if starting material remained. Once complete, the reaction was concentrated and the residue filtered with Et_2O through an oven-dried frit. The filtrate was concentrated to provide **6** as a 1:1 mixture of diastereomers, which was used directly in the next step. Since silylether **6** is difficult to purify due to hydrolytic sensitivity, and both diastereomers useful for our purposes, characterization reflects the mixture we obtained. Observed spectra: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.47 (m, 2H), 4.13 (m, 2H), 3.55 (t, *J* = 6.6 Hz, 4H), 2.76 (m, 2H), 2.44 (m, 2H), 2.19 (t, *J* = 6.9 Hz, 4H), 1.92 – 1.81 (m, 4H), 1.69 (m, 4H), 1.67 – 1.57 (m, 4H), 1.47 (m, 18H), 1.37 – 1.28 (m, 12H), 1.21 (m, 6H), 1.12 (m, 6H), 0.94 – 0.87 (m, 36H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.24, 171.20, 86.3, 86.2, 81.2, 81.1, 80.7, 80.6, 80.0, 79.8, 79.6, 79.3, 76.1, 75.9, 44.8, 40.5, 40.1, 39.19, 39.2, 39.1, 39.0, 38.3, 38.2, 36.2, 36.1, 31.7, 31.6, 28.4, 28.3, 27.3, 27.11, 27.07, 26.2, 25.8, 25.7, 24.92, 24.87, 23.7, 23.4, 18.2, 18.1.

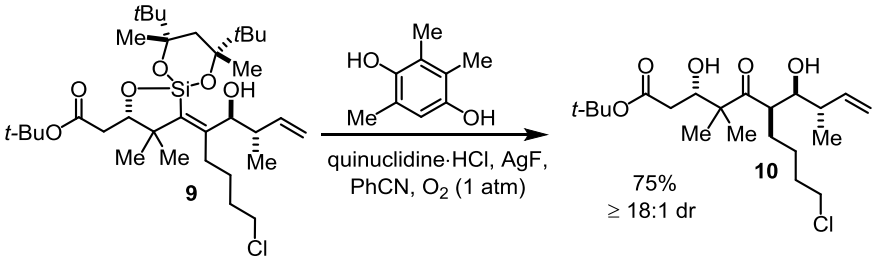


A glass liner for a Parr bomb was charged with the crude **6** as a solution in CH_2Cl_2 (5.6 mL). The bomb was assembled and pressurized with CO to approximately 500 psi and then vented. This procedure was repeated two more times, then the bomb was pressurized again to 500 psi and stirred for about fifteen minutes. the bomb was carefully vented and opened, then $Rh(acac)(CO)_2$ (0.223 mmol, 58 mg) was added. The bomb was reassembled and pressurized to 500 psi with CO then stirred at ambient temperature. After 24 hours, the bomb was carefully vented and opened. ^{1}H NMR analysis indicated complete consumption of starting material and clean formation of product **7** as a 1:1 mixture of diastereomers. This reaction solution was used directly in the following crotylation reaction. Observed spectra of the diastereomeric mixture were as follows: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.09 (s, 1H), 10.04 (s, 1H), 4.16 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.10 (dd, *J* = 10.0, 2.8 Hz, 1H), 3.57 (m, 4H), 2.59 – 2.40 (m, 6H), 2.35 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.15 (dd, *J* = 14.6, 10.4 Hz, 1H), 1.93 – 1.80 (m, 8H), 1.48 (m, 18H), 1.46 (s, 3H), 1.43 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H), 1.27 (m, 6H), 1.14 (s, 3H), 0.98 (s, 9H), 0.97 – 0.93 (m, 28H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 195.8, 195.6, 171.1, 170.6, 165.1, 163.1, 152.3, 151.6, 81.3, 81.2, 80.7, 80.6, 80.5, 80.1, 80.0, 78.2, 48.2, 47.3, 44.6, 41.7, 39.6, 39.5, 39.3, 39.2, 38.5, 37.9, 37.9, 33.0, 32.9, 28.1, 27.9,

27.8, 27.5, 27.0, 26.9, 26.7, 26.6, 25.8, 25.6, 24.9, 24.9, 24.9, 24.5, 23.8, 21.3.

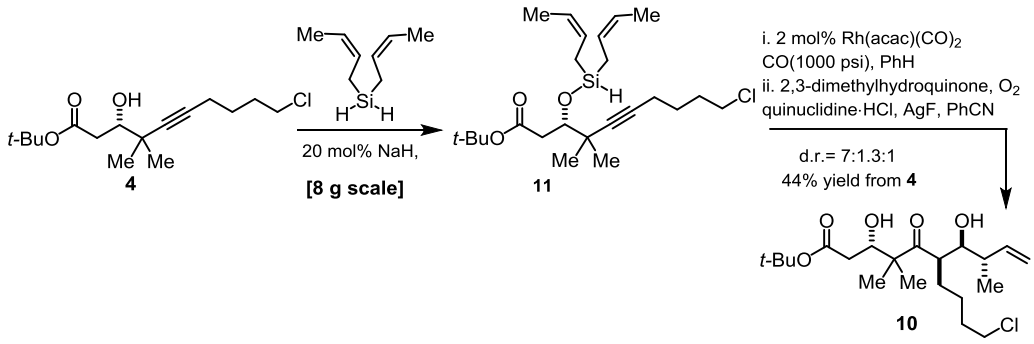


To a solution of the reaction mixture from aldehyde **7** formation in CH_2Cl_2 (28.0 mL) was added (*R*, *R*)-*trans*-crotylsilane diamine reagent **8** (2.38 g, 4.19 mmol) and $Sc(OTf)_3$ (138 mg, 0.279 mmol). After 24 hours at room temperature, additional $Sc(OTf)_3$ and reagent **8** were added. After another 16 hours, the reaction was still incomplete as judged by ^{1}H NMR. The solution was then cooled to 0 ℃ and tetrabutylammonium fluoride (TBAF) trihydrate (879 mg, 2.79 mmol) was added portion-wise over 20 minutes. After about 3 hours, the reaction was concentrated and the residue purified via silica gel chromatography (5% EtOAc/hexanes) to afford **9** (658 mg, 37% over 3 steps, 3.5:1 dr) as a viscous yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.76 (m, 3H), 5.06 – 4.89 (m, 6H), 4.39 (d, *J* = 2.3 Hz, 2H), 4.34 (d, *J* = 2.3 Hz, 1H), 4.19 – 4.11 (m, 3H), 3.58 (m, 6H), 2.99 (d, *J* = 3.4 Hz, 1H), 2.95 (d, *J* = 3.1 Hz, 2H), 2.83 (m, 3H), 2.52 (m, 6H), 2.30 (m, 3H), 1.99 (m, 3H), 1.82 (m, 12H), 1.76 – 1.61 (m, 5H), 1.57 – 1.48 (m, 4H), 1.47 (m, 34H), 1.44 (m, 13H), 1.34 – 1.25 (m, 17H), 1.26 – 1.17 (m, 13H), 1.00 – 0.97 (m, 57H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 173.3, 173.1, 162.2, 138.9, 138.8, 134.6, 114.9, 114.8, 80.7, 80.6, 80.4, 80.1, 79.9, 79.9, 79.7, 74.2, 74.1, 44.7, 41.8, 41.4, 41.3, 39.9, 39.8, 39.5, 39.4, 38.7, 38.4, 38.3, 37.9, 37.6, 32.8, 32.7, 31.6, 29.8, 28.4, 28.2, 28.1, 28.1, 27.9, 27.7, 27.1, 26.4, 26.1, 25.9, 25.5, 25.2, 25.1, 25.1, 25.0, 24.7, 24.4, 22.7, 18.3, 18.2, 14.1. **HRMS** (DART+) calcd $C_{34}H_{61}O_6ClSi$ $[M+H]^+$: 629.3986, found 629.4004.



To a solution of trimethylhydroquinone (515 mg, 3.39 mmol), quinuclidine hydrochloride (450 mg, 3.05 mmol), and silver fluoride (459 mg, 3.62 mmol) in benzonitrile (5.0 mL) was added **9** (711 mg,

1.13 mmol) as a solution in benzonitrile (6.3 mL). The solution was purged with O_2 then the reaction was heated to 60 ℃ (oil bath, external temperature) and stirred overnight under a balloon of O_2. After 22 hours, the reaction was cooled to room temperature and diluted with $CHCl_3$ (15 mL). The solution was filtered through Celite, then washed with distilled water. The aqueous layer was extracted with CHCl3 (3 x 15 mL). The combined organics were washed with brine, dried over MgSO4, filtered, and concentrated. The residue was purified via silica gel chromatography (stepwise: 10% EtOAc/hexanes, 30% EtOAc/hexanes) to provide **10** (345 mg, 75%) as a brown oil with >18:1 dr with respect to the newly formed stereocenter at C(6). Further purification by flash chromatography on silica gel allowed us to obtain an analytically pure sample of **10** for characterization. **$[\alpha]^{20}_{D}$** −46.7 (*c* 0.45, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 17.8, 10.4, 7.7 Hz, 1H), 5.12 (dd, *J* = 8.4, 1.5 Hz, 1H), 5.09 – 5.05 (m, 1H), 4.24 (dt, *J* = 10.0, 3.2 Hz, 1H), 3.61 (dt, *J* = 8.1, 2.6 Hz, 1H), 3.53 (td, *J* = 6.6, 3.4 Hz, 2H), 3.36 (d, *J* = 3.5 Hz, 1H), 3.23 (dt, *J* = 8.8, 3.2 Hz, 1H), 2.54 (d, *J* = 2.6 Hz, 1H), 2.40 (dd, *J* = 16.1, 2.9 Hz, 1H), 2.31 (dd, *J* = 16.2, 9.7 Hz, 2H), 1.89 – 1.71 (m, 3H), 1.53 – 1.61 (m, 1H), 1.47 (s, 9H), 1.43 – 1.29 (m, 2H), 1.23 (s, 3H), 1.10 (s, 3H), 1.03 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 219.7, 172.5, 141.2, 115.4, 81.8, 73.7, 72.9, 52.0, 48.4, 44.8, 41.3, 37.4, 33.0, 28.3, 25.5, 24.7, 22.2, 19.2, 16.9; **IR** (film): 3494, 2971, 2932, 2872, 1706, 1457, 1392, 1368, 1303, 1253, 1221, 1153, 1033, 997, 915, 765, 727, 650 cm^{-1}; **HRMS** (ESI+) calcd $C_{21}H_{37}ClO_5Na$ $[M+Na]^+$: 427.2227, found 427.2232.



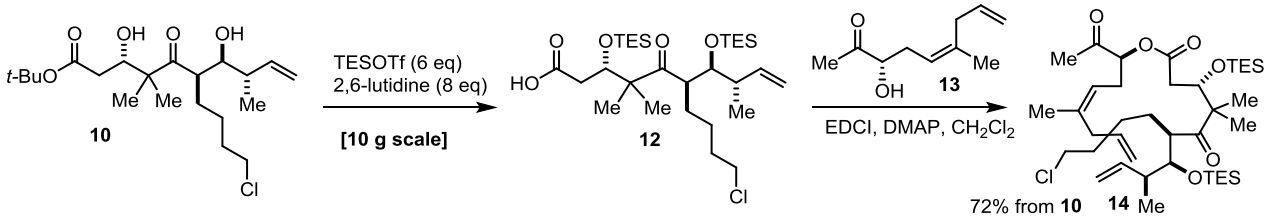
The NaH catalyzed silylation of alcohol with di-*cis*-crotylsilane was carried out according to our published procedure.[2] To a solution of alcohol **4** (8.00 g, 26.42 mmol) and di-*cis*-crotylsilane (5.56 g, 39.63 mmol) in anhydrous hexane was added sodium hydride (0.127 g, 3.28 mmol, 60% wt. dispersion in mineral oil). After the solution was heated at 60 ℃ (oil bath, external temperature) for

[2] a) Zacuto, M. J.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7890-7891; b) Harrison, T. J.; Rabbbat, P. M. A.; Leighton, J. L. *Org. Lett.* **2012**, *14*, 4890-4893.

45−60 min (monitored by TLC analysis), cooled, diluted with hexane, and filtered through a pad of celite, eluted with EtOAc/Hexanes = 1:10. The filtrate was concentrated to afford **11** as colorless oil which was generally of sufficient purity for use in the tandem silylformylation-crotylsilylation reaction. Analytical samples of the di-*cis*-crotylsilyl ether could be obtained by flash silica gel column chromatography (EtOAc/Hexanes = 1:50); **[α]$^{23}_{D}$** −9.3 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.49 – 5.35 (m, 4H), 4.49 (m, 1H), 4.04 (dd, *J* = 9.1, 2.1 Hz, 1H), 3.55 (t, *J* = 6.6 Hz, 2H), 2.75 (dd, *J* = 16.4, 2.2 Hz, 1H), 2.37 (dd, *J* = 16.4, 9.1 Hz, 1H), 2.19 (t, *J* = 7.0 Hz, 2H), 1.86 (dq, *J* = 7.8, 6.6 Hz, 2H), 1.79 – 1.70 (m, 2H), 1.69 – 1.59 (m, 10H), 1.47 (s, 9H), 1.17 (s, 3H), 1.09 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.8, 124.3, 124.1, 123.3, 123.2, 86.4, 81.0, 80.6, 77.3, 44.70, 44.67, 40.3, 36.6, 31.7, 28.3, 27.0, 26.2, 23.6, 18.2, 15.5, 15.2, 12.9; **IR** (film): 2971, 2925, 2871, 2128, 1727, 1648, 1455, 1380, 1366, 1297, 1247, 1154, 1096, 1057, 989, 951, 906, 853, 795, 761, 728, 690, 665, 555 cm^{-1}; **HRMS** (ESI+) calcd for $C_{24}H_{41}ClNaO_3Si$ $[M+Na]^+$: 463.2411; found 463.2416.

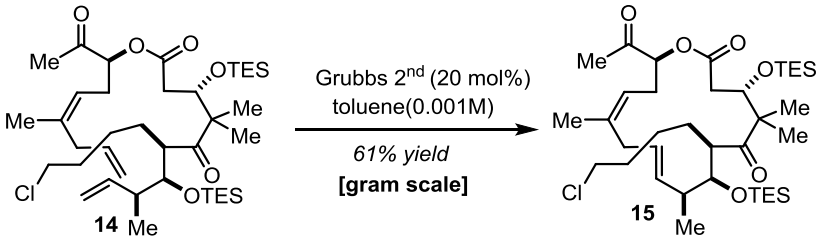
A glass liner for a 300 mL capacity Parr bomb was charged with crude **11** (1.0 equiv) and benzene (105 mL). The vessel was cooled to −78 ℃ to freeze the benzene solution under Ar. $Rh(acac)(CO)_2$ (0.136 g, 0.528 mmol) was added on top of the frozen benzene solution. The bomb was assembled (pressure inlet, and guage), immersed in the −78 ℃ bath, and charged with 500 psi CO and vented 3 times. The bomb was charged with 980 psi CO, and then immersed in an oil bath set at 60 ℃ (the pressure rose and topped out at 1000 psi). After 24 h, the bomb apparatus was allowed to cool to room temperature and then vented. The reaction mixture was transferred to a 250 mL round bottom flask (with CH_2Cl_2 washes) and concentrated. To the residue was added 2,3-dimethylhydroquinone (9.12 g, 66.1 mmol), quinuclidine ⋅HCl (10.5 g, 71.3 mmol), and AgF (10.7 g, 84.5 mmol). PhCN (260 mL) was added and the brown mixture was then heated at 60 ℃ (oil bath, external temperature) under an atmosphere of O_2 (balloon). After 24 h, the mixture was allowed to cool to room temperature, diluted with $CHCl_3$ (150 mL) and filtered. The filtrate was washed with water (200 mL). The water layer was extracted with $CHCl_3$ (3 x 80 mL), dired over $MgSO_4$, filtered and concentrated (to remove the $CHCl_3$) to afford a red liquid. The bulk of the PhCN was then removed by distillation under reduced pressure, and the residue was passed through a plug of silica gel column (EtOAc/Hexanes = 1:20 to elute residual PhCN, and then a gradient EtOAc/Hexanes = 1:5 to 1:3 to elute **10**). The eluent was concentrated to afford **10** as the major product of a mixture of

diastereomers (4.71 g total, 44% yield from **4**, 7:1.3:1 dr). It proved most convenient to partially separate the diastereomers at this stage, and a single chromatographic purification was found to improve the ratio to 9:1:0.5. Further separation proved straightforward over the following several steps as noted in the following procedures.



To a cooled (−78 ℃) solution of **10** (10.0 g, 24.7 mmol, 9:1:0.5 dr) in CH_2Cl_2 (250 mL) was added 2,6-lutidine (22.9 mL, 197.5 mmol). Followed by the first portion of TESOTf (16.8 mL, 74.1 mmol) was then added dropwise. After 30 minutes, a second portion of TESOTf (16.8 mL, 74.1 mmol) was added and the cold bath was removed, allowing the reaction to warm to room temperature. After 3 hours, the reaction was diluted with Et_2O (300 mL), washed with 5% aqueous $KHSO_4$ (2 x 80 mL), then brine (80 mL), dried over Na_2SO_4, and concentrated. The residue was dissolved in aqueous THF (100 mL, 6:1 THF/H_2O) and treated with saturated aqueous $NaHCO_3$ (30.0 mL). After stirring at room temperature for 20 minutes, the mixture was diluted with Et_2O (50.0 mL) and acidified with 5% aqueous $KHSO_4$ (30.0 mL). The layers were separated then the aqueous layer extracted with Et_2O (2 x 80 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated to provide **12**. The crude product was used directly in the next step. For characterization purpose, purification via silica gel chromatography (EtOAc/hexanes = 1:20, pH 7.0 buffered silica gel) provided **12** as a light yellow oil. $\mathbf{[\alpha]^{24}_D}$ −22.6 (*c* 1.43, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.73 (bs, 1H), 5.94 – 5.79 (m, 1H), 5.11 – 4.98 (m, 2H), 4.32 (dd, *J* = 7.4, 2.9 Hz, 1H), 3.86 (dd, *J* = 5.3, 3.3 Hz, 1H), 3.50 (t, *J* = 6.6 Hz, 2H), 3.03 – 3.00 (m, 1H), 2.60 (dd, *J* = 16.6, 2.9 Hz, 1H), 2.33 (dd, *J* = 16.6, 7.3 Hz, 1H), 2.20 – 2.13 (m, 1H), 1.76 – 1.59 (m, 3H), 1.51 – 1.45 (m, 1H), 1.39 – 1.28 (m, 2H), 1.21 (s, 3H), 1.12 (s, 3H), 1.05 (s, 3H), 0.98 – 0.94 (m, 18H), 0.71 – 0.52 (m, 12H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 216.6, 177.0, 140.2, 115.5, 75.8, 74.3, 53.3, 51.6, 45.0, 44.3, 39.6, 33.2, 27.0, 25.4, 24.2, 19.5, 18.7, 7.3, 7.1, 5.6, 5.3; **IR** (film): 2955, 2877, 2916, 1709, 1692, 1458, 1416, 1302, 1238, 1093, 1003, 914, 731 cm^{-1}; **HRMS** (ESI+) calcd $C_{29}H_{57}ClNaO_5Si_2$ $[M+Na]^+$:599.3331, found 599.3344.

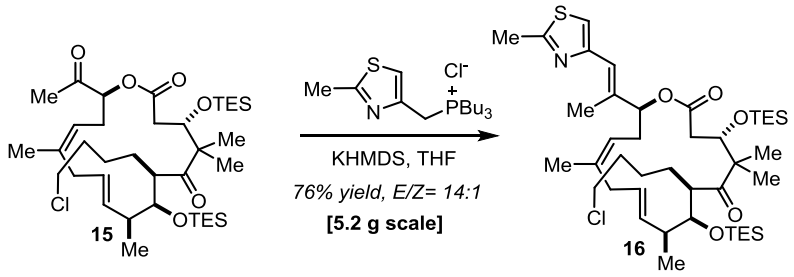
To a cooled (0 ℃) solution of **13**[3] (5.81 g, 34.6 mmol) in CH_2Cl_2 (300 mL) was added solid DMAP (172 mg, 39.5 mmol) and EDCI (270 mg, 39.5 mmol). After stirring for 15 minutes, the above crude **12** was added slowly as a solution in CH_2Cl_2 (80.0 mL). After completion of addition, the mixture was stirred for 5 minutes, the cooling bath was removed and the reaction was allowed to warm to ambient temperature. After 5 hours, the reaction mixture was filtered directly though a plug of silica gel (EtOAc/hexanes = 1:10). Further purification via pH 7.0 buffered silica gel column chromatography (EtOAc/hexanes = 1:30) provided **14** (12.9 g, 72% over 2 steps, 12:1 dr). $\mathbf{[\alpha]^{24}_D}$ −24.5 (*c* 0.84, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.86 (ddd, J = 17.2, 10.6, 8.1 Hz, 1H), 5.83 – 5.64 (m, 1H), 5.19 (t, *J* = 7.2 Hz, 1H), 5.07 – 4.99 (m, 4H), 4.97 (t, *J* = 6.2 Hz, 1H), 4.28 (dd, *J* = 7.3, 2.8 Hz, 1H), 3.84 (dd, *J* = 4.9, 3.5 Hz, 1H), 3.50 (t, *J* = 6.6 Hz, 2H), 3.04 – 3.01 (m, 1H), 2.80 – 2.73 (m, 2H), 2.70 (dd, *J* = 17.2, 2.9 Hz, 1H), 2.48 (t, *J* = 6.8 Hz, 2H), 2.39 (dd, *J* = 17.2, 7.4 Hz, 1H), 2.21 – 2.15 (m, 1H), 2.13 (s, 3H), 1.76 – 1.62 (m, 6H), 1.50 – 1.46(m, 1H), 1.34 (d, *J* = 8.0 Hz, 2H), 1.24 (s, 3H), 1.10 (s, 3H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.98 – 0.92 (m, 18H), 0.61 (q, *J* = 8.2 Hz, 12H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 216.1, 205.3, 172.1, 140.3, 137.4, 135.4, 119.0, 115.8, 115.4, 78.8, 75.8, 74.7, 53.0, 51.8, 45.0, 44.4, 39.5, 36.5, 33.3, 29.2, 26.8, 26.6, 25.4, 24.0, 23.7, 20.4, 18.6, 7.3, 7.2, 5.6, 5.2; **IR** (film): 2955, 2877, 2911, 1731, 1693, 1638, 1458, 1416, 1379, 1295, 1238, 1161, 1092, 1003, 913, 728 cm^{-1}; **HRMS** (ESI+) calcd $C_{39}H_{71}ClO_6NaSi_2$ $[M+Na]^+$: 749.4375, found 749.4380.



To a refluxing solution of diene **14** (1.00 g, 1.37 mmol) in dry and degassed toluene (1.50 L) was added a solution of Grubbs second generation catalyst (0.233 g, 0.274 mmol, 20 mol%) in toluene (10.0 mL). The mixture was stirred for 30 min under reflux and immediately cooled to 0 ℃ and kept at 0 ℃ before filtration through a pad of silica gel. A second batch of diene **14** (1.00 g) was processed identically and simultaneously in another flask. The combined reaction mixture were

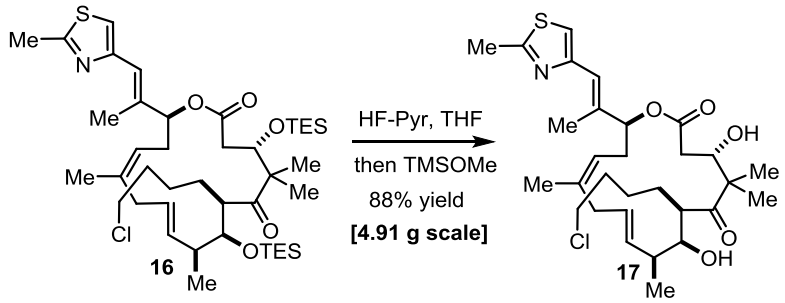
[3] a) Chappell, M. D.; Stachel, S. J.; Lee, C. B.; Danishefsky, S. J. *Org. Lett.* **2000**, *2*, 1633; b) Rivkin, A.; Yoshimura, F.; Gabarda, A. E.; Chou, T. C.; Dong, H.; Tong, W. P.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 2899; c) Rivkin, A.; Yoshimura, F.; Gabarda, A. E.; Cho, Y. S.; Chou, T.-C.; Dong, H.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 10913.

filtered through a pad of silica gel, which was rinsed with hexane, then CH_2Cl_2, the combine filtrate was concentrated and purified by flash column chromatography (EtOAc/hexanes = 1:30 to 1:10) to provide **15** (1.17 g, 61%) as a colorless amorphous oil. **$[\alpha]^{22}_D$** −10.0 (*c* 0.71, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.58 (dd, *J* = 15.8, 8.1 Hz, 1H), 5.34 (t, *J* = 5.9 Hz, 1H), 5.19 (t, *J* = 8.0 Hz, 1H), 4.96 (dd, *J* = 9.2, 2.4 Hz, 1H), 4.17 (dd, *J* = 9.7, 2.5 Hz, 1H), 4.10 (d, *J* = 9.7 Hz, 1H), 3.61 – 3.42 (m, 2H), 3.17 – 3.04 (m, 1H), 3.03 – 2.89 (m, 2H), 2.72 (dd, *J* = 15.4, 2.6 Hz, 1H), 2.62 – 2.52 (m, 1H), 2.52 – 2.43 (m, 1H), 2.38 (dd, *J* = 14.5, 7.5 Hz, 1H), 2.29 (p, *J* = 7.1 Hz, 1H), 2.21 (s, 3H), 1.78 – 1.67 (m, 3H), 1.66 (s, 3H), 1.54 – 1.38 (m, 2H), 1.27 – 1.19 (m, 1H), 1.17 (s, 3H), 1.11 (s, 3H), 1.05 (d, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.9 Hz, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.67 (q, *J* = 7.9 Hz, 6H), 0.57 (q, *J* = 8.1 Hz, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 213.9, 204.8, 171.4, 140.3, 132.6, 129.7, 118.6, 79.2, 77.0, 75.8, 54.0, 53.7, 44.8, 41.0, 40.3, 34.9, 33.1, 29.1, 28.3, 26.6, 23.8, 23.7, 23.6, 23.5, 21.4, 7.3, 7.1, 5.8, 5.4. **IR** (film): 2955, 2877, 2911, 1744, 1730, 1692, 1459, 1415, 1380, 1357, 1305, 1239, 1158, 1102, 1007, 855, 728 cm^{-1}; **HRMS** (ESI+) calcd $C_{37}H_{67}ClO_6NaSi_2$ $[M+Na]^+$: 721.4062, found 721.4072.



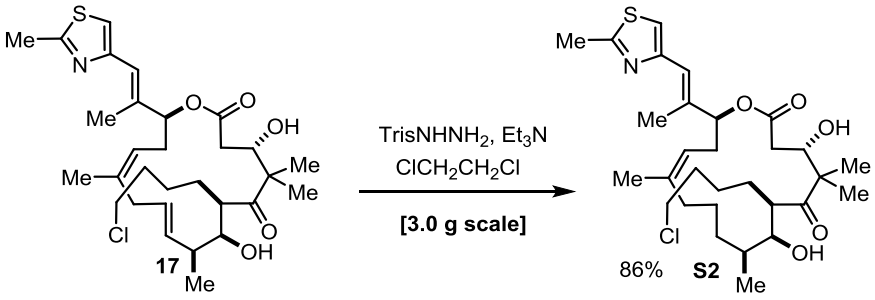
To a cooled (0 ℃) solution of Wittig salt reagent (15.6, 44.6 mmol) in THF (450 mL) was added KHMDS (90.0 mL, 45.0 mmol, 0.5 M in toluene) slowly by additional funnel. The mixture was stirred for 30 minutes, then cooled to −78 ℃. To the solution was added **15** (5.20 g, 7.43 mmol) as a solution in THF (100 mL), and the resulting mixture allowed to warm to −20 ℃ over the course of 3 hours. The reaction was quenched with sat. aq. NH_4Cl (120 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified via silica gel chromatography (EtOAc/hexanes = 1:30) to afford colorless oil **16** (4.49 g, 76%) as a 14:1 (*E/Z*) mixture. Pure *E*-configured compound was obtained through further silica gel chromatography for characterization purposes. **$[\alpha]^{21}_D$** −11.5 (*c* 0.66, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.56 (s, 1H), 5.66 (dd, *J* = 15.7, 8.1 Hz, 1H), 5.40 – 5.28 (m, 2H), 5.22 (dd, *J* = 10.0, 5.7 Hz, 1H), 4.31 (dd, *J* = 9.5, 1.8 Hz, 1H), 4.11 (d, *J* = 9.7 Hz, 1H), 3.56 – 3.40 (m, 2H), 3.15 (dd, *J* = 14.5, 6.8 Hz, 1H), 3.00 (dt, *J* = 9.6, 4.0 Hz, 1H), 2.71 (s, 3H), 2.71 – 2.62 (m, 2H), 2.47

(dd, *J* = 14.6, 2.1 Hz, 1H), 2.41 (dd, *J* = 14.6, 5.7 Hz, 1H), 2.24 – 2.13 (m, 2H), 2.13 (d, *J* = 1.3 Hz, 3H), 1.90 – 1.78 (m, 1H), 1.75 – 1.61 (m, 5H), 1.54 – 1.37 (m, 2H), 1.22 – 1.12 (m, 1H), 1.11 (s, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.04 (s, 3H), 1.01 (t, *J* = 7.9 Hz, 9H), 0.88 (t, *J* = 7.9 Hz, 9H), 0.68 (q, J = 8.0 Hz, 6H), 0.56 (qd, *J* = 8.3, 7.9, 1.7 Hz, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 214.9, 170.7, 164.7, 152.7, 138.1, 132.0, 129.6, 120.9, 120.4, 116.3, 79.3, 76.3, 74.8, 53.9, 53.8, 44.8, 41.2, 41.1, 35.4, 33.3, 33.2, 28.1, 24.5, 23.7, 23.5, 21.9, 21.7, 19.4, 15.1, 7.4, 7.1, 5.9, 5.5; **IR** (film): 2956, 2877, 2911, 1739, 1690, 1459, 1414, 1379, 1240, 1181, 1100, 1031, 1009, 971, 731 cm^{-1}; **HRMS** (ESI+) calcd $C_{42}H_{73}ClNO_5SSi_2$ $[M+H]^+$: 794.4437, found 794.4439.

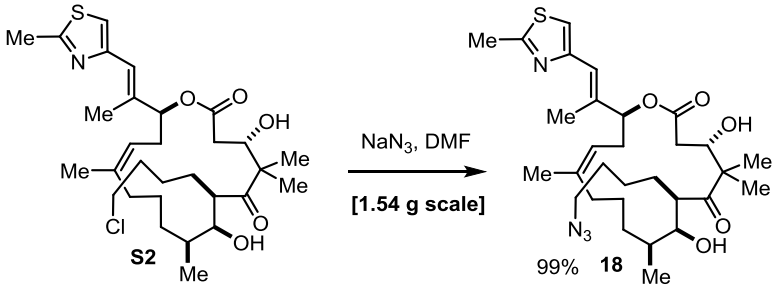


To a cooled (0 ℃) solution of **16** (4.91 g, 6.18 mmol) in THF (125 mL) in a polyethylene tube was added HF pyridine (30.9 mL). After addition, the reaction was warmed to ambient temperature and stirred for 3 hours. The reaction was cooled to 0 ℃ and TMSOMe (90.0 mL) was added dropwise. After the addition, the reaction was warmed to ambient temperature and stirred for 30 minutes. The reaction was concentrated and dried under high vacuum, then the residue purified by silica gel chromatography (EtOAc/Hexanes = 1:2) to provide **17** (3.08 g, 88%, 25:1 dr) as a white foam solid. **$[\alpha]^{22}_D$** −82.4 (*c* 0.75, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.97 (s, 1H), 6.54 (s, 1H), 5.58 (ddd, *J* = 15.7, 7.6, 5.0 Hz, 1H), 5.47 (dd, *J* = 15.7, 7.3 Hz, 1H), 5.33 (dd, *J* = 9.0, 2.9 Hz, 1H), 5.12 (dd, *J* = 9.2, 5.3 Hz, 1H), 4.29 (dt, *J* = 8.2, 3.6 Hz, 1H), 3.77 – 3.67 (m, 1H), 3.51 (td, *J* = 6.6, 4.1 Hz, 2H), 3.36 – 3.24 (m, 1H), 3.21 (d, *J* = 4.8 Hz, 1H), 2.94 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.70 (s, 3H), 2.68 – 2.56 (m, 2H), 2.53 (dd, *J* = 20.7, 4.1 Hz, 1H), 2.48 – 2.40 (m, 2H), 2.42 – 2.30 (m, 2H), 2.08 (s, 3H), 1.95 – 1.85 (m, 1H), 1.80 – 1.67 (m, 5H), 1.55 – 1.37 (m, 1H), 1.39 – 1.26 (m, 5H), 1.09 (d, *J* = 6.9 Hz, 3H), 1.01 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 217.3, 170.8, 165.1, 152.3, 138.0, 137.8, 131.3, 129.9, 120.5, 119.7, 116.2, 78.4, 75.5, 72.7, 53.0, 51.1, 44.8, 39.3, 39.2, 35.3, 32.9, 32.3, 28.0, 24.6, 23.9, 21.6, 20.6, 19.4, 19.3, 15.9; **IR** (film): 3460, 2964, 2930, 2871, 1730, 1687, 1506, 1446, 1377, 1293, 1252, 1187, 1155, 1044, 977, 755 cm^{-1}; **HRMS** (ESI+) calcd $C_{30}H_{45}ClNO_5S$ $[M+H]^+$:

566.2707, found 566.2712.

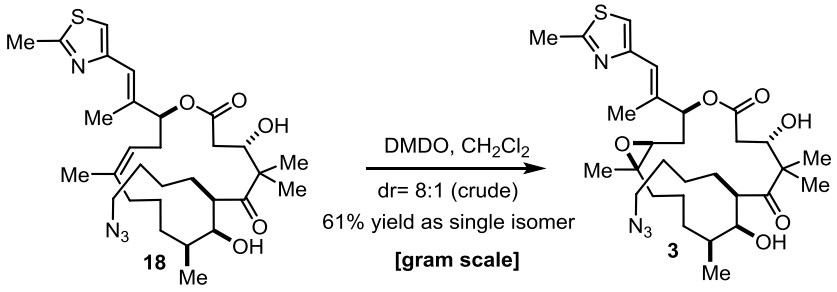


To a solution of **17** (3.0 g, 5.29 mmol) and $TrisNHNH_2$ (63.2 g, 211.6 mmol) in $ClCH_2CH_2Cl$ (1.50 L) at 50 ℃ (external temp, oil bath) was added Et_3N (29.4 mL, 211.6 mmol). After 8 hours, the reaction was cooled to ambient temperature and diluted with EtOAc, then filtered through a plug of silica gel (rinsed with EtOAc). The filtrate was concentrated, then the residue purified via silica gel chromatography (EtOAc/hexanes = 1:3 to 1:2) to provide **S2** (2.59 g, 86%) as a white foam solid. $[\alpha]^{23}_{D}$ −55.0 (*c* 0.70, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.95 (s, 1H), 6.56 (s, 1H), 5.23 (dd, J = 10.3, 2.1 Hz, 1H), 5.12 (dd, *J* = 10.0, 4.6 Hz, 1H), 4.25 (d, *J* = 10.6 Hz, 1H), 3.77 – 3.68 (m, 1H), 3.58 – 3.42 (m, 3H), 3.29 (dt, *J* = 7.9, 4.1 Hz, 1H), 2.70 (s, 3H), 2.68 – 2.60 (m, 1H), 2.57 (d, *J* = 3.7 Hz, 1H), 2.48 (dd, *J* = 14.8, 10.4 Hz, 1H), 2.39 (dd, *J* = 14.8, 2.8 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.27 – 2.21 (m, 1H), 2.07 (s, 3H), 1.91 – 1.70 (m, 6H), 1.69 (s, 3H), 1.66 – 1.56 (m, 1H), 1.48 – 1.37 (m, 3H), 1.33 (s, 3H), 1.29 – 1.21 (m, 2H), 1.08 (s, 3H), 1.04 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 219.2, 170.7, 165.2, 152.2, 139.6, 139.2, 120.4, 119.5, 115.9, 79.4, 74.4, 72.6, 53.5, 48.9, 44.8, 39.6, 36.2, 33.0, 32.8, 32.3, 30.7, 27.0, 25.1, 25.0, 23.8, 22.1, 19.7, 19.3, 17.1, 15.9; **IR** (film): 3474, 2960, 2932, 2871, 1731, 1686, 1507, 1464, 1446, 1377, 1337, 1291, 1252, 1187, 1151, 1072, 1029, 981, 755 cm^{-1}; **HRMS** (ESI+) calcd $C_{30}H_{47}ClNO_5S$ $[M+H]^+$: 568.2863, found 568.2869.



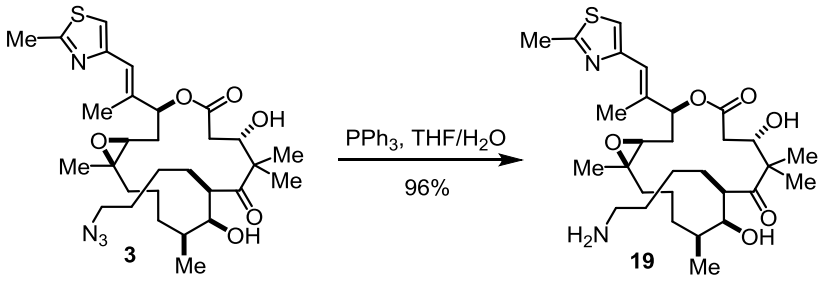
To a solution of **S2** (1.54 g, 2.71 mmol) in DMF (27.0 mL) was added NaN_3 (0.211 g, 3.25 mmol). The reaction was heated to 60 ℃ (external temp, oil bath) and stirred overnight. After 18 hours, the reaction was cooled to ambient temperature, then diluted with EtOAc and deionized water. The

layers were separated and the aqueous layer extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified via silica gel chromatography to provide **18** (1.54 g, 99%) as a white solid. **$[\alpha]^{21}_D$** −51.0 (*c* 0.68, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.95 (s, 1H), 6.56 (s, 1H), 5.22 (d, *J* = 9.8 Hz, 1H), 5.11 (dd, *J* = 10.0, 4.8 Hz, 1H), 4.31 – 4.23 (m, 1H), 3.75 – 3.65 (m, 1H), 3.59 (d, J = 5.6 Hz, 1H), 3.32 – 3.23 (m, 3H), 2.69 (s, 3H), 2.67 – 2.61 (m, 1H), 2.62 – 2.56 (m, 1H), 2.48 (dd, *J* = 14.8, 10.4 Hz, 1H), 2.38 (dd, *J* = 14.8, 2.9 Hz, 1H), 2.33 – 2.18 (m, 2H), 2.06 (d, *J* = 1.3 Hz, 3H), 1.88 – 1.71 (m, 4H), 1.69 (s, 3H), 1.66 – 1.52 (m, 5H), 1.37 – 1.28 (m, 6H), 1.07 (s, 3H), 1.04 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 219.1, 170.7, 165.1, 152.2, 139.6, 139.2, 120.4, 119.5, 115.9, 79.3, 74.4, 72.5, 53.4, 51.3, 48.9, 39.6, 36.2, 32.8, 32.3, 30.7, 29.5, 27.3, 25.0, 23.7, 22.0, 19.7, 19.2, 17.1, 15.9; **IR** (film): 3464, 2955, 2927, 2854, 2096, 1733, 1685, 1463, 1378, 1289, 1261, 1184, 1148, 1075, 1029, 803 cm^{-1}; **HRMS** (ESI+) calcd $C_{30}H_{47}N_4O_5S$ $[M+H]^+$: 575.3267, found 575.3266.

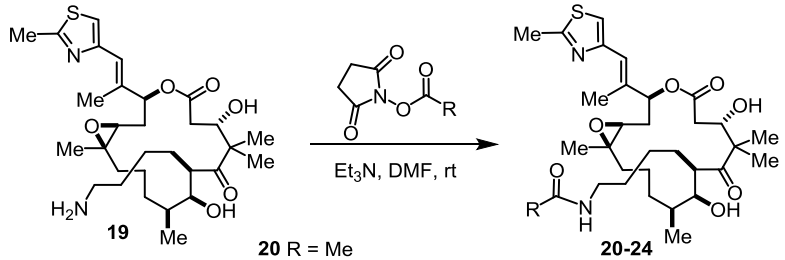


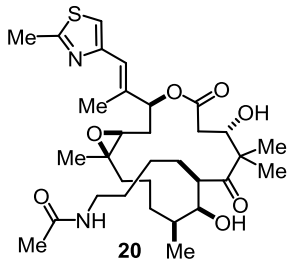
To a cooled (−78 ℃) solution of **18** (1.00 g, 1.74 mmol) in CH_2Cl_2 (90.0 mL) was added a cooled (−78 ℃) solution of DMDO (108 mL, 4.35 mmol, 0.04 M in acetone) via cannula. After the addition was complete, the solution was warmed to −50 ℃ and stirred for 5 hours. The saturated $Na_2S_2O_3$ aqueous (30.0 mL) was added to quench the remaining DMDO, the reaction mixture was extracted with CH_2Cl_2 (3 x 20 mL), dried over Na_2SO_4 and concentrated to give as a 8:1 mixture of diastereomers. The residue was purified via silica gel chromatography (EtOAc/hexanes = 1:2 to 1:1) to provide desired isomer **3** (0.627 g, 61%) as a white solid. **$[\alpha]^{23}_D$** −71.6 (*c* 0.53, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.97 (s, 1H), 6.55 (s, 1H), 5.46 (t, *J* = 5.0 Hz, 1H), 4.61 (d, *J* = 5.7 Hz, 1H), 4.27 (ddd, *J* = 10.2, 5.5, 2.5 Hz, 1H), 3.63 (q, *J* = 5.3 Hz, 1H), 3.44 (dt, *J* = 8.3, 3.9 Hz, 1H), 3.26 (td, *J* = 6.7, 4.1 Hz, 2H), 2.87 (d, *J* = 5.8 Hz, 1H), 2.80 (t, *J* = 6.2 Hz, 1H), 2.70 (s, 3H), 2.56 (dd, *J* = 14.3, 10.3 Hz, 1H), 2.41 (dd, *J* = 14.3, 2.6 Hz, 1H), 2.10 (d, *J* = 1.3 Hz, 3H), 2.02 (t, *J* = 5.7 Hz, 2H), 1.92 – 1.77 (m, 1H), 1.78 – 1.69 (m, 1H), 1.64 – 1.50 (m, 5H), 1.53 – 1.41 (m, 3H), 1.37 (s, 3H), 1.33 – 1.22 (m, 6H), 1.03 (s, 3H), 0.99 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 219.8,

170.6, 165.1, 152.0, 137.0, 119.4, 116.3, 76.7, 75.3, 73.4, 61.3, 61.0, 53.1, 51.2, 50.3, 39.0, 34.8, 32.1, 31.7, 30.0, 29.3, 28.1, 25.0, 22.3, 21.2, 21.0, 20.4, 19.2, 17.5, 16.1; **IR** (film): 3446, 2960, 2926, 2859, 2095, 1735, 1685, 1504, 1463, 1379, 1345, 1289, 1259, 1183, 1144, 1050, 1025, 978, 803, 735 cm^{-1}; **HRMS** (ESI+) calcd $C_{30}H_{47}N_4O_6S$ $[M+H]^+$: 591.3216, found 591.3214.



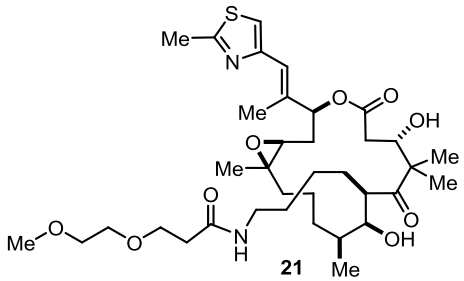
To a solution of **3** (0.102 g, 0.173 mmol) in THF/H_2O (v/v = 10:1, 2.2 mL) was added PPh_3 (90.7 mg, 0.346 mmol). After stirred for 18 hours at 30 ℃, the solvent was removed under vacuum, and the residual was directly subjected to silica gel chromatography (CH_2Cl_2/MeOH/ Et_3N= 10:1:0.1) to afford the amine **19** (93.8 mg, 96%) as a white solid. **$[\alpha]^{23}_D$** −40.4 (*c* 0.36, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.56 (s, 1H), 5.44 (dd, *J* = 7.1, 3.2 Hz, 1H), 4.23 (dd, *J* = 10.0, 3.1 Hz, 1H), 3.73 (t, *J* = 5.1 Hz, 1H), 3.37 (ddd, *J* = 7.5, 5.4, 4.0 Hz, 1H), 2.80 (t, *J* = 6.2 Hz, 1H), 2.71–2.67 (m, 5H), 2.57 – 2.51 (m, 2H), 2.41 (dd, *J* = 14.3, 3.1 Hz, 1H), 2.09 (d, *J* = 1.4 Hz, 3H), 2.07 – 1.92 (m, 2H), 1.84 (dddd, *J* = 13.8, 11.8, 7.6, 4.5 Hz, 1H), 1.69 – 1.52 (m, 3H), 1.52 – 1.36 (m, 7H), 1.33 – 1.30 (m, 4H), 1.29 – 1.16 (m, 4H), 1.05 – 1.01 (m, 4H), 0.99 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 219.6, 170.8, 165.1, 152.1, 137.1, 119.6, 116.4, 76.7, 75.0, 73.4, 61.5, 61.2, 53.1, 50.3, 46.3, 41.4, 39.2, 35.0, 32.9, 32.1, 31.9, 29.9, 27.9, 24.0, 22.4, 21.8, 21.0, 20.7, 19.3, 17.8, 16.0, 11.6; **IR** (film): 3363, 2958, 2925, 2855, 1733, 1686, 1465, 1380, 1293, 1260, 1187, 1146, 1053, 978, 752, 666 , 570 cm^{-1}; **HRMS** (ESI+) calcd for $C_{30}H_{49}N_2O_6S$ $[M+H]^+$: 565.3311, found 565.3323.





20

To a solution of **19** (12.0 mg, 0.021 mmol) and 2,5-dioxopyrrolidin-1-yl acetate (3.3 mg, 0.021 mmol) in DMF (0.2 mL) was added Et_3N (0.0029 mL, 0.021 mmol) and stirred for 1 hour at room temperature, then the mixture was purified by silica gel chromatography (CH_2Cl_2/MeOH = 30:1) to give the **20** (10.4 mg, 82%) as a white solid. **[α]$^{23}_{D}$** −36.4 (*c* 0.66, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.97 (s, 1H), 6.56 (s, 1H), 5.52 (d, *J* = 6.6 Hz, 1H), 5.47 – 5.41 (m, 1H), 4.52 (d, *J* = 5.8 Hz, 1H), 4.23 (dd, *J* = 10.4, 5.2 Hz, 1H), 3.65 (d, *J* = 5.1 Hz, 1H), 3.41 (dt, *J* = 8.5, 4.5 Hz, 1H), 3.27 (dq, *J* = 13.6, 6.9 Hz, 1H), 3.19 (dq, *J* = 13.2, 6.4 Hz, 1H), 3.05 (d, *J* = 5.5 Hz, 1H), 2.81 (t, *J* = 6.2 Hz, 1H), 2.70 (s, 3H), 2.56 (dd, *J* = 14.3, 10.1 Hz, 1H), 2.42 (dd, *J* = 14.3, 2.9 Hz, 1H), 2.10 (s, 3H), 2.02 (q, *J* = 6.6, 5.2 Hz, 2H), 1.96 (s, 3H), 1.92 – 1.82 (m, 1H), 1.73 – 1.63 (m, 1H), 1.58 (app. q, *J* = 9.4, 8.7 Hz, 2H), 1.56 – 1.48 (m, 3H), 1.48 – 1.40 (m, 4H), 1.35 (s, 3H), 1.32 – 1.15 (m, 5H), 1.03 (s, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 220.0, 170.8, 170.4, 165.2, 152.0, 137.0, 119.5, 116.4, 76.6, 75.2, 73.5, 61.4, 61.1, 53.1, 50.6, 39.1, 39.0, 34.9, 32.0, 31.7, 30.0, 29.8, 28.0, 24.5, 23.5, 22.4, 21.5, 21.2, 20.4, 19.3, 17.7, 16.1; **IR** (film): 3342, 2956, 2924, 2853, 1733, 1657, 1551, 1463, 1378, 1288, 1251, 1184, 1144, 1052, 976, 755, 666, 574 cm^{-1}; **HRMS** (ESI+) calcd for $C_{32}H_{51}N_2O_7S$ $[M+H]^+$: 607.3417, found 607.3417.



21

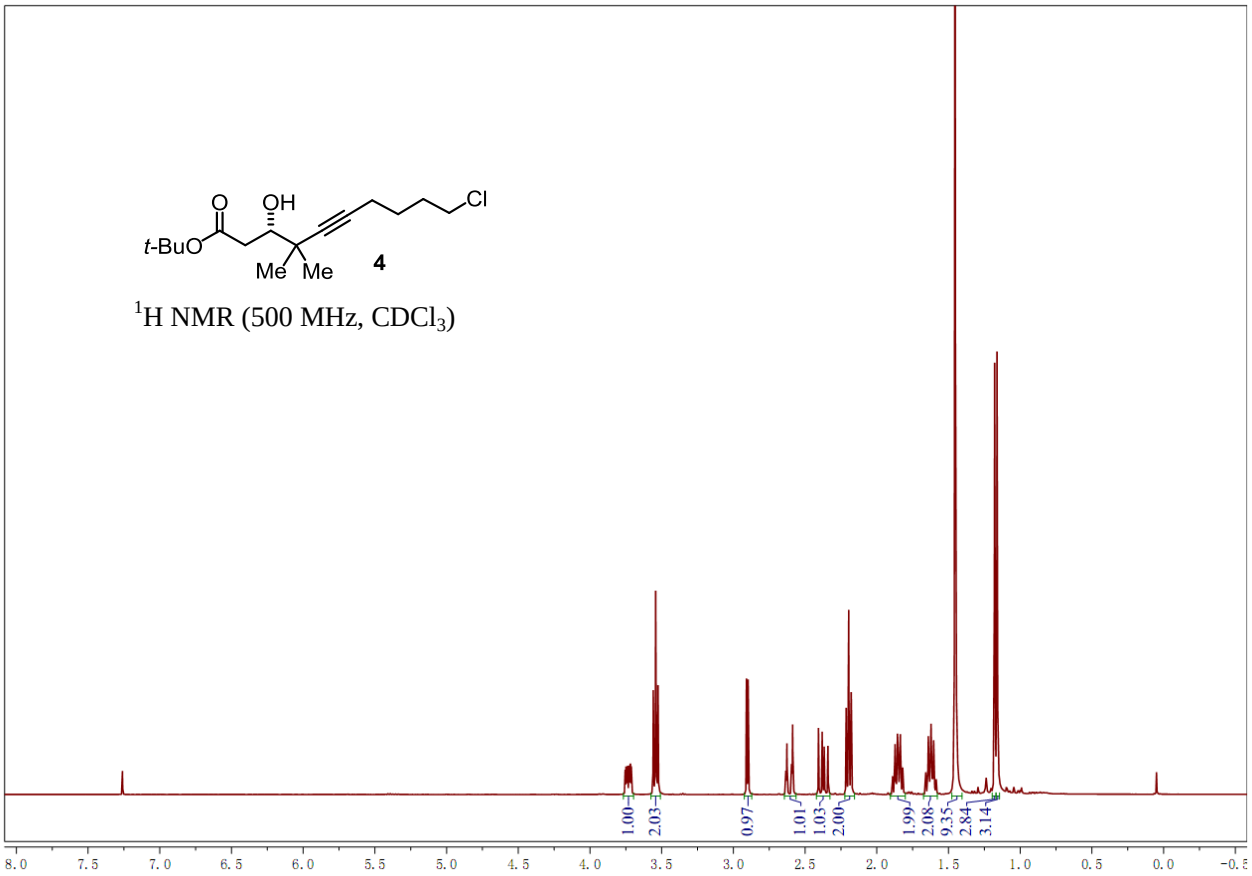
To a solution of **19** (10.0 mg, 17.7 μmol) and m-dPEG2-NHS ester (4.34 mg, 17.7 μmol) in DMF (0.4 mL) was added Et_3N (2.5 μL, 17.7 μmol) and stirred for 30 minutes at room temperature, then the mixture was purified by silica gel chromatography (CH_2Cl_2/MeOH = 30:1) to afford the analog **21** (11.2 mg, 91%). **[α]$^{25}_{D}$** −42.6 (*c* 0.77, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.57 – 6.52 (m, 2H), 5.44 (dd, *J* = 7.1, 3.1 Hz, 1H), 4.37 (d, *J* = 6.2 Hz, 1H), 4.22 (ddd, *J* = 9.6, 6.2, 3.1 Hz,

1H), 3.70 (t, *J* = 5.7 Hz, 2H), 3.67 (q, *J* = 5.4 Hz, 1H), 3.63 – 3.61 (m, 2H), 3.55 – 3.53 (m, 2H), 3.38 (s, 4H), 3.30 (dq, *J* = 13.5, 6.9 Hz, 1H), 3.16 (dq, *J* = 13.3, 7.5, 6.9 Hz, 2H), 2.80 (t, *J* = 6.2 Hz, 1H), 2.70 (s, 3H), 2.55 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.46 (t, *J* = 5.7 Hz, 2H), 2.41 (dd, *J* = 14.4, 3.1 Hz, 1H), 2.10 (d, *J* = 1.3 Hz, 3H), 2.08 – 1.95 (m, 2H), 1.92 – 1.83 (m, 1H), 1.69 (s, 2H), 1.67 – 1.38 (m, 10H), 1.35 (s, 3H), 1.27 (s, 3H), 1.03 (s, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 219.7, 172.0, 170.8, 165.2, 152.1, 137.1, 119.7, 116.4, 77.4, 76.7, 75.0, 73.6, 71.7, 70.2, 67.4, 61.5, 61.3, 59.1, 53.0, 50.6, 39.2, 38.7, 37.0, 35.0, 32.1, 32.0, 30.0, 29.9, 28.1, 24.2, 22.4, 21.8, 21.1, 20.6, 19.3, 17.8, 16.0; **IR** (film): 3347, 2958, 2924, 2863, 1735, 1677, 1646, 1550, 1510, 1462, 1378, 1289, 1250, 1192, 1136, 1097, 1050, 1026, 977, 881, 751, 665, 569 cm^{-1}; **HRMS** (ESI+) calcd for $C_{36}H_{58}N_2O_9NaS$ $[M+Na]^+$: 717.3761, found 717.3771.

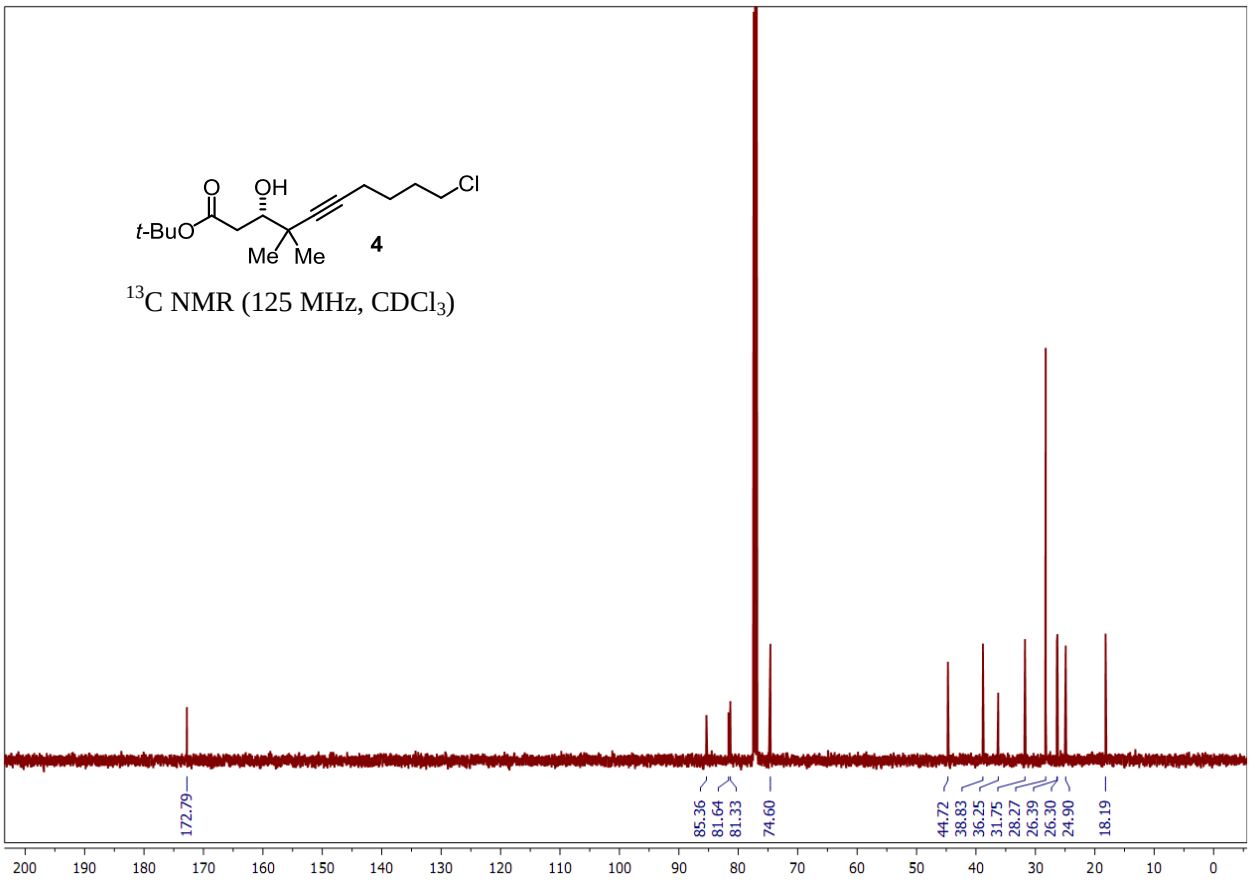
Cell Culture and Growth Inhibition

PC3 human prostate cancer and A549 human lung cancer cell lines were obtained from the NCI anticancer drug screen. All cells were maintained in RPMI medium supplemented with 10% fetal bovine serum. Growth inhibition was determined by the sulforhodamine B method, following exposure to serial dilutions of each compound for 4 days prior to fixation, staining and GI(50) determinations as described (1). The results presented are mean values based on two or more determinations. The standard deviation (for three or more determinations) or half-range (for two values) were between 10% and 50% of the mean for all values.

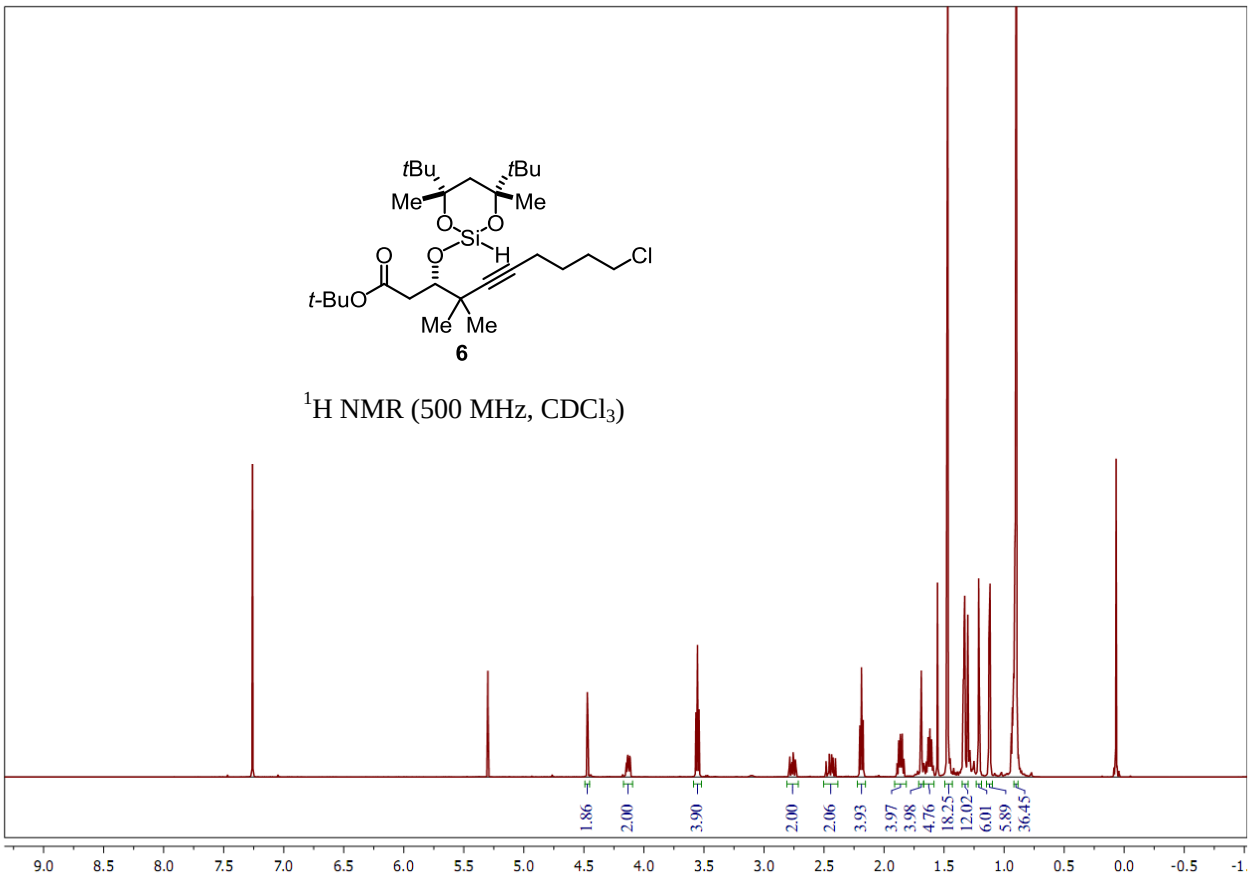
^{1}H NMR and ^{13}C NMR Spectra of New Compounds

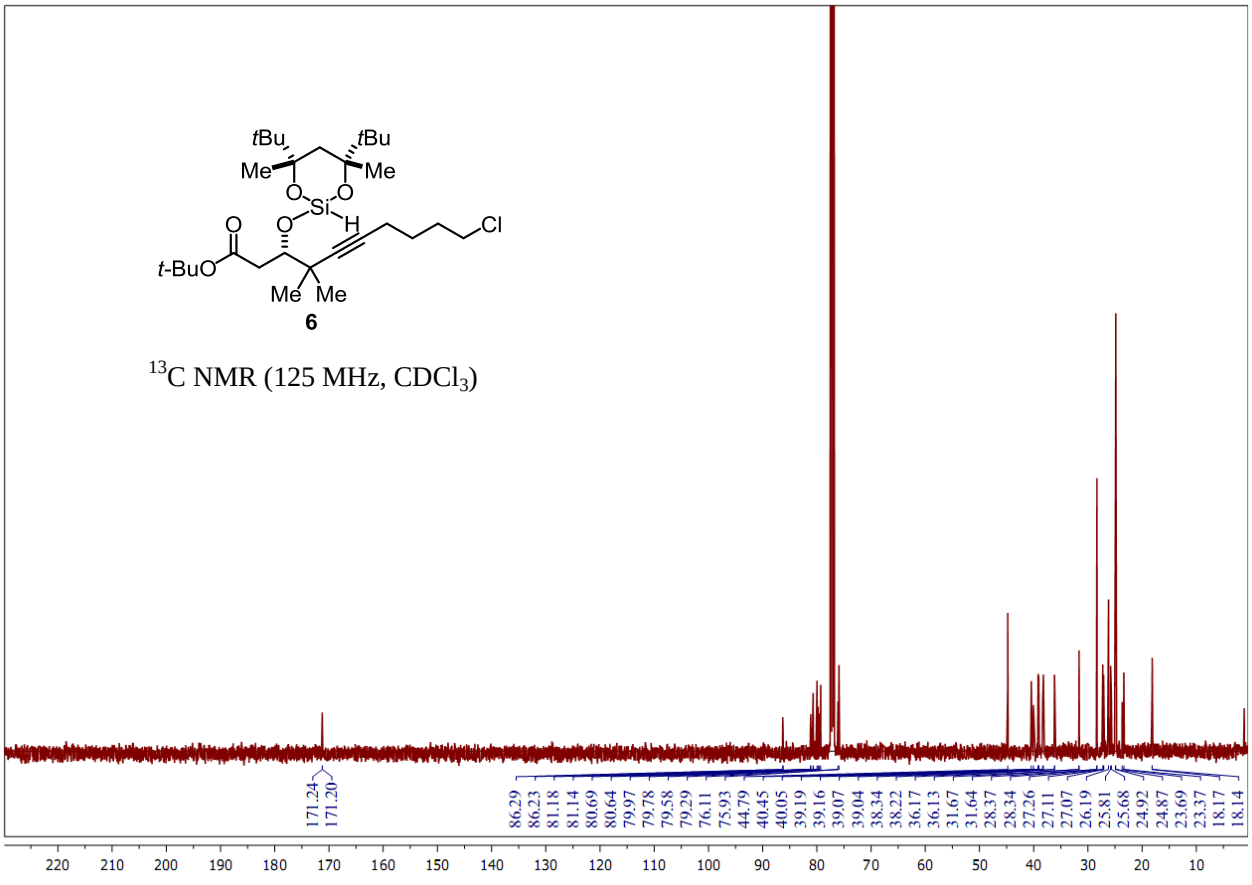


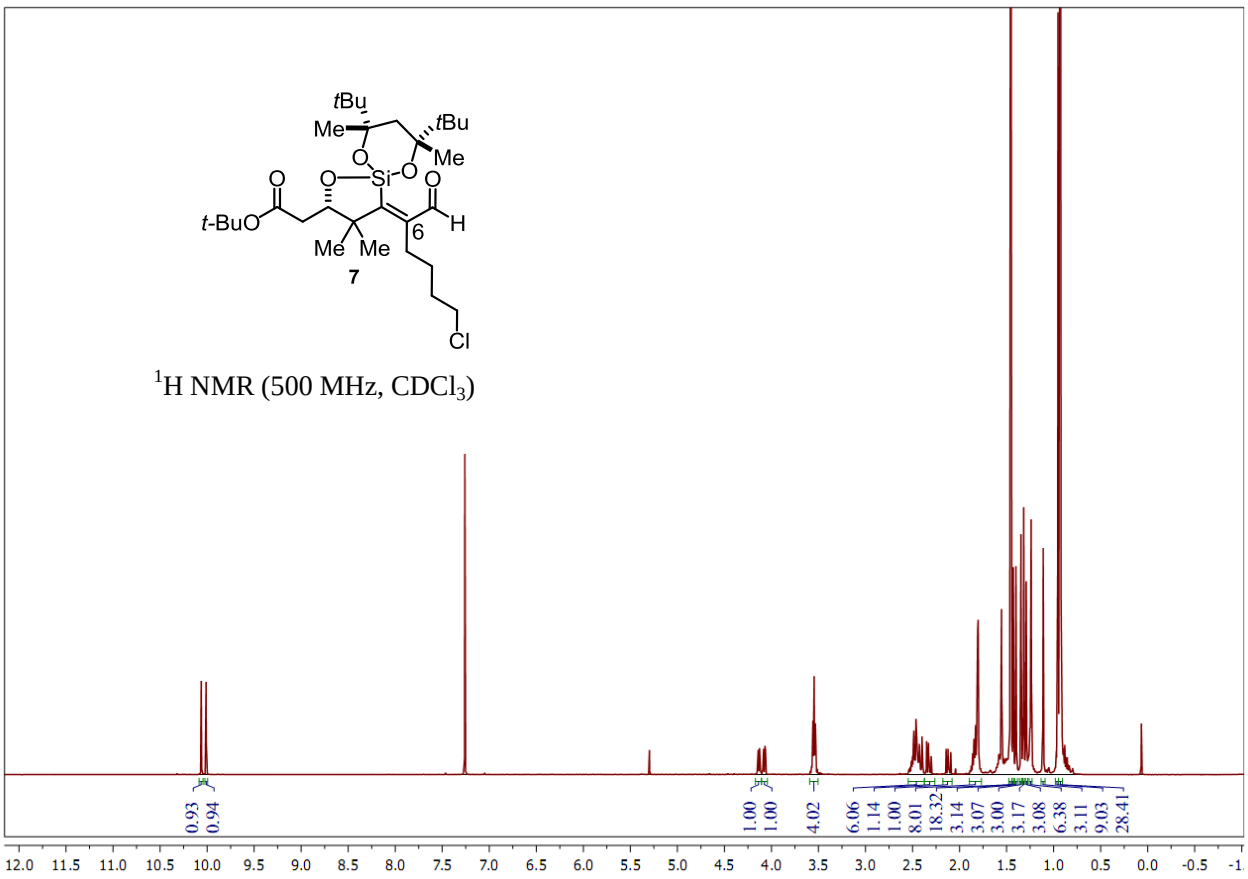
^{1}H NMR (500 MHz, $CDCl_3$)



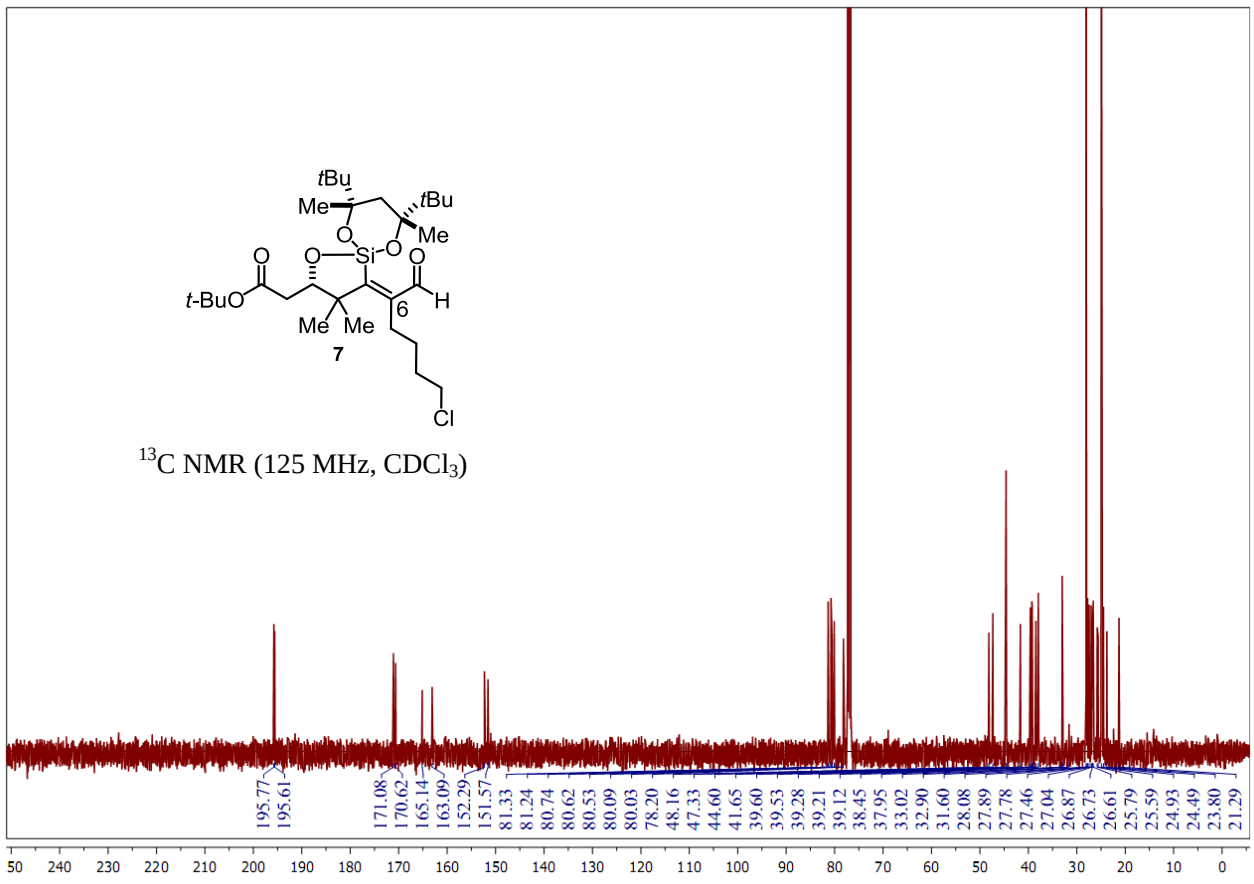
^{13}C NMR (125 MHz, $CDCl_3$)


tBu
tBu
Me
Me
O
Si
O
H
O
O
Cl
t-BuO
Me
Me
6
1H NMR (500 MHz, CDCl3)
1.86
2.00
3.90
2.00
2.06
3.93
3.97
3.98
4.76
18.25
12.02
6.01
5.89
36.45
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

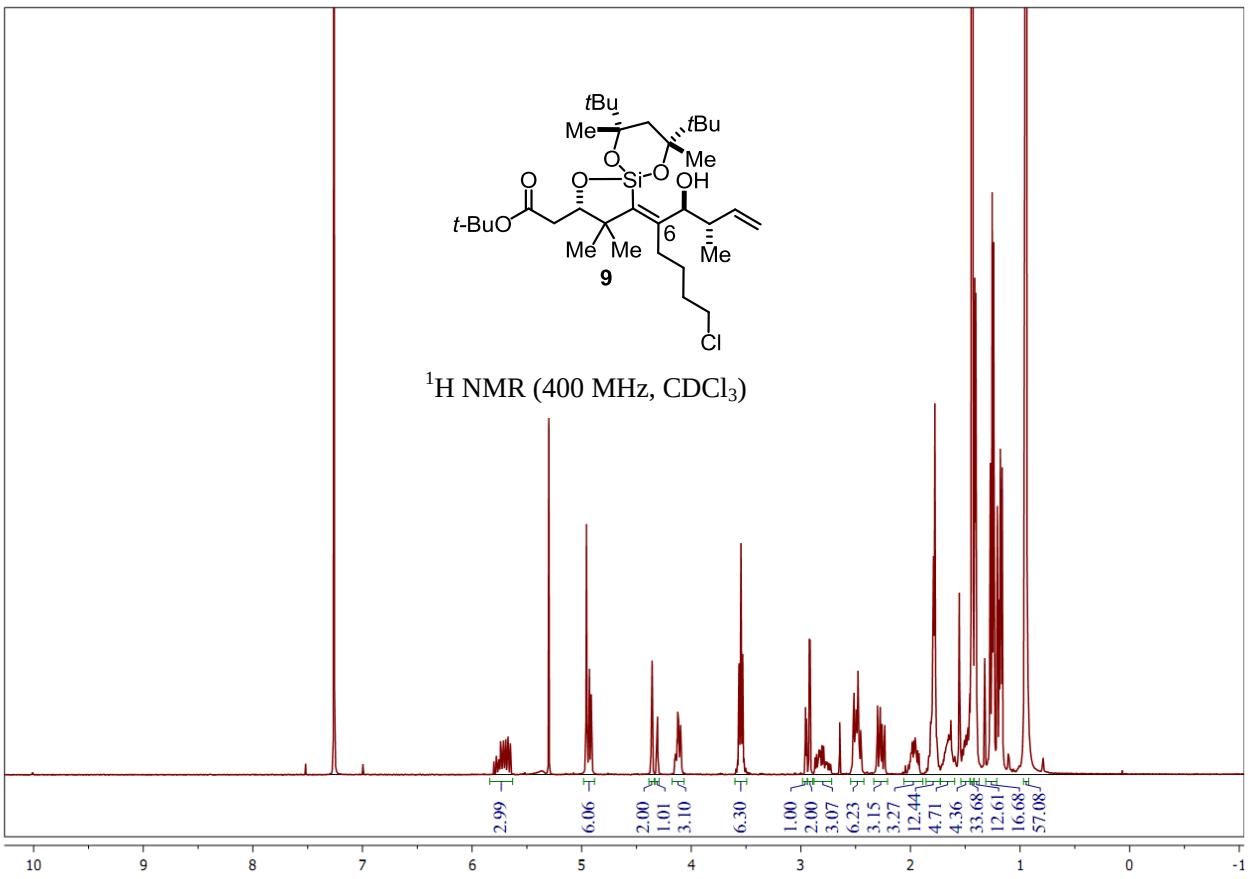

tBu
tBu
Me
Me
O
Si
O
H
O
O
Cl
t-BuO
Me
Me
6
13C NMR (125 MHz, CDCl3)
171.24
171.20
86.29
86.23
81.18
81.14
80.69
80.64
79.97
79.78
79.58
79.29
76.11
75.93
44.79
40.45
40.05
39.19
39.16
39.07
39.04
38.34
38.22
36.17
36.13
31.67
31.64
28.37
28.34
27.26
27.11
27.07
26.19
25.81
25.68
24.92
24.87
23.69
23.37
18.17
18.14
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10



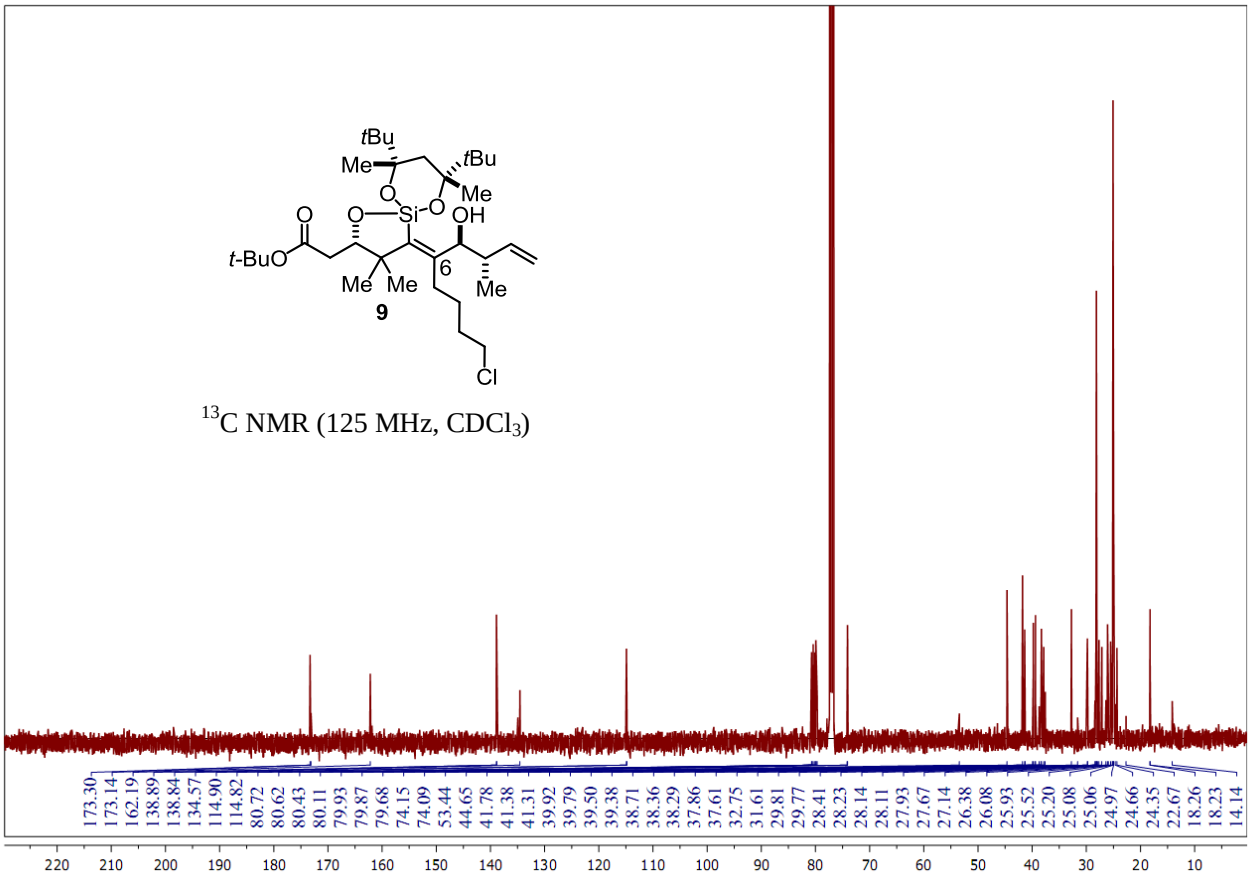
^{1}H NMR (500 MHz, $CDCl_3$)



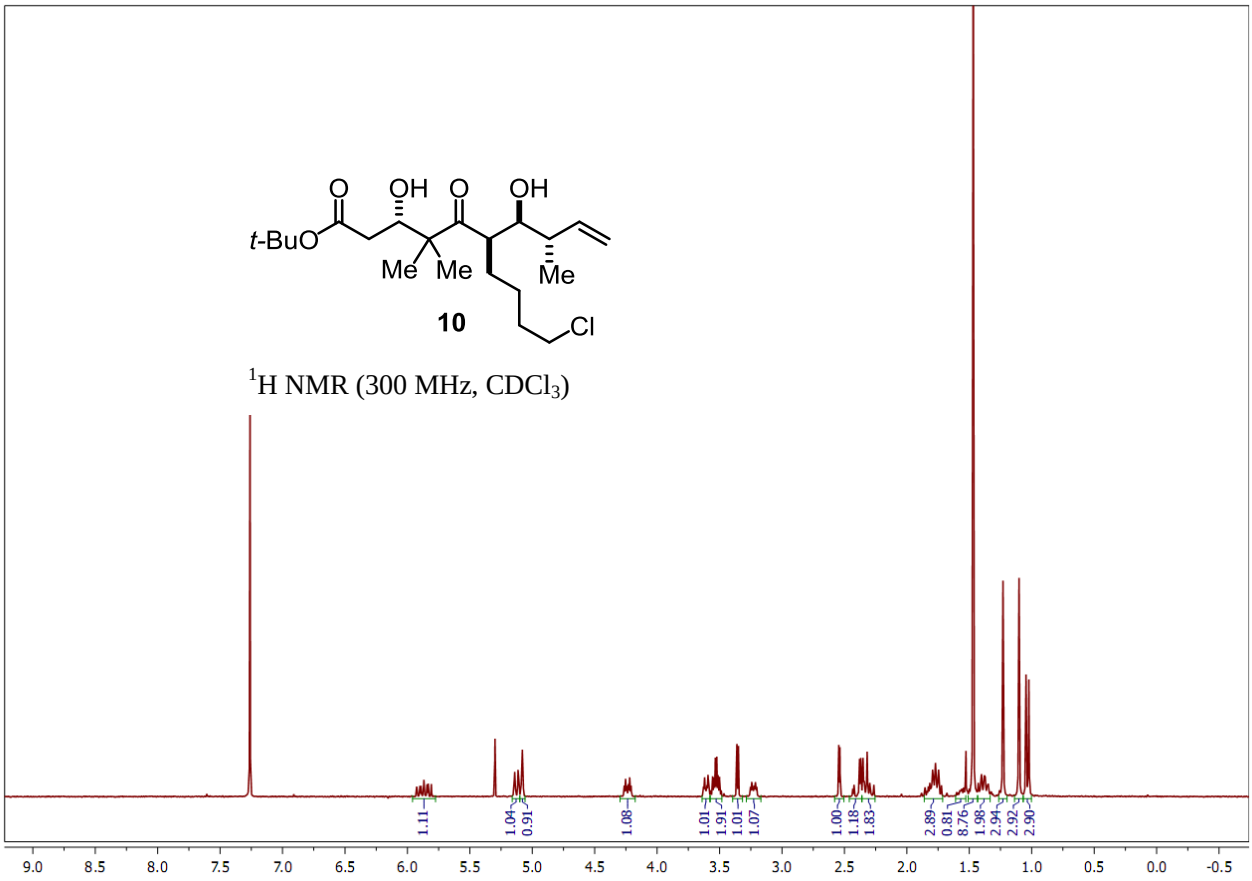
^{13}C NMR (125 MHz, $CDCl_3$)



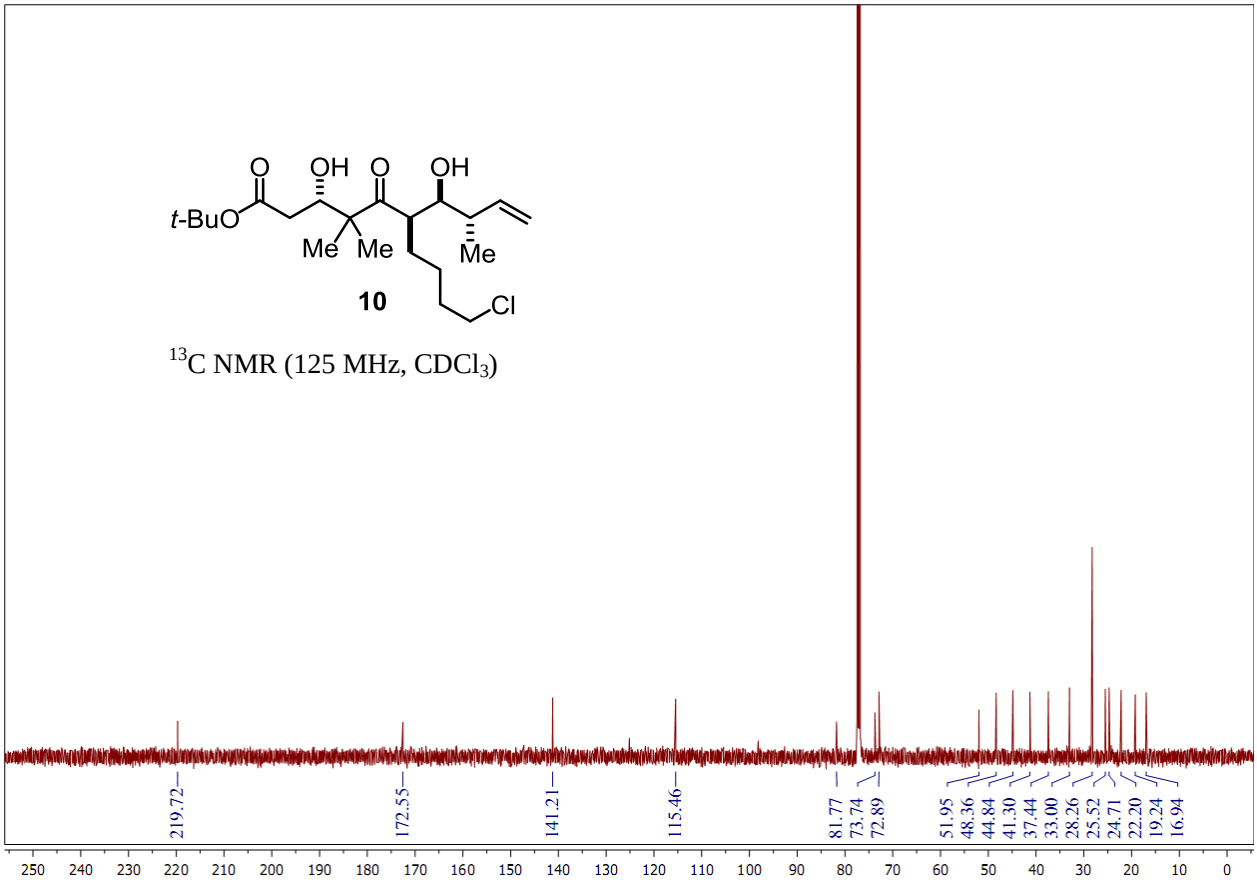
^{1}H NMR (400 MHz, $CDCl_3$)



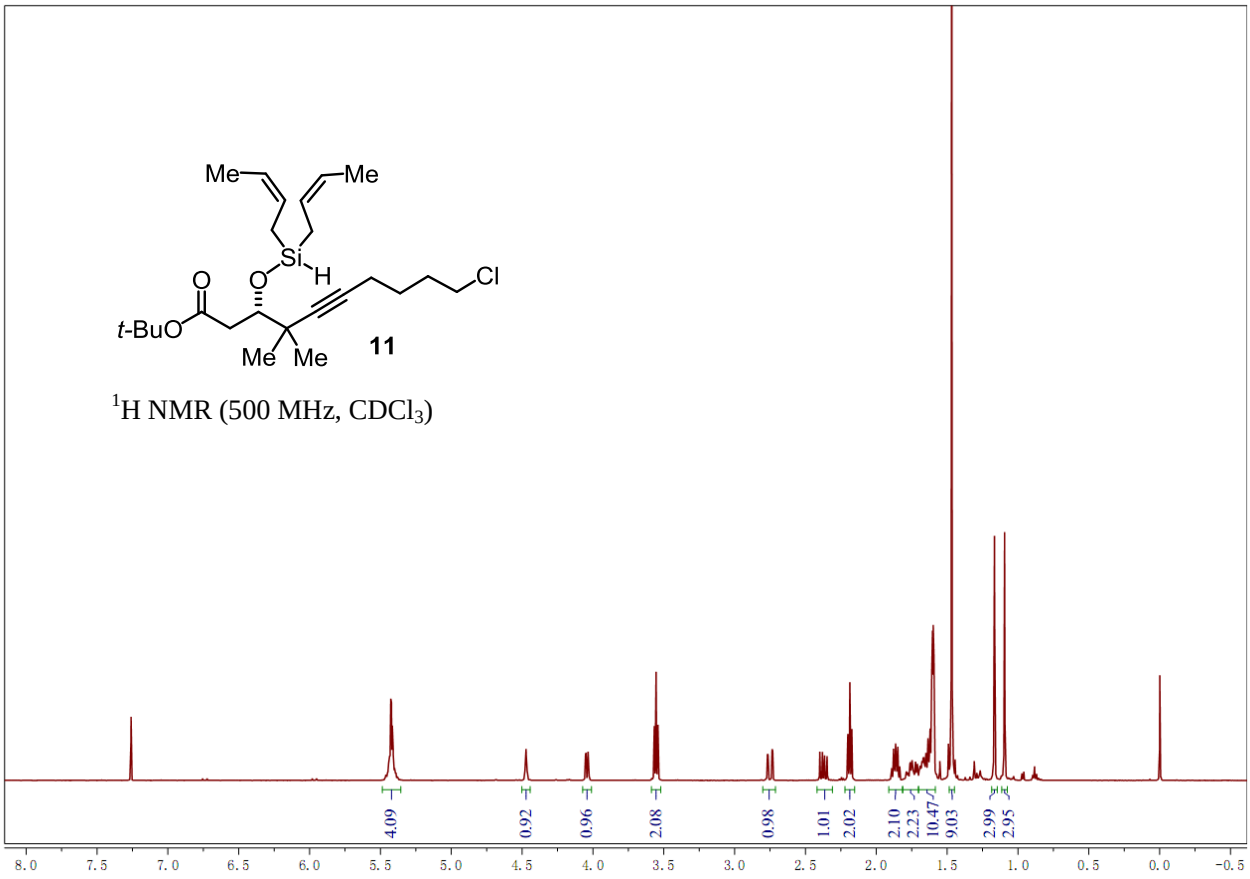
^{13}C NMR (125 MHz, $CDCl_3$)



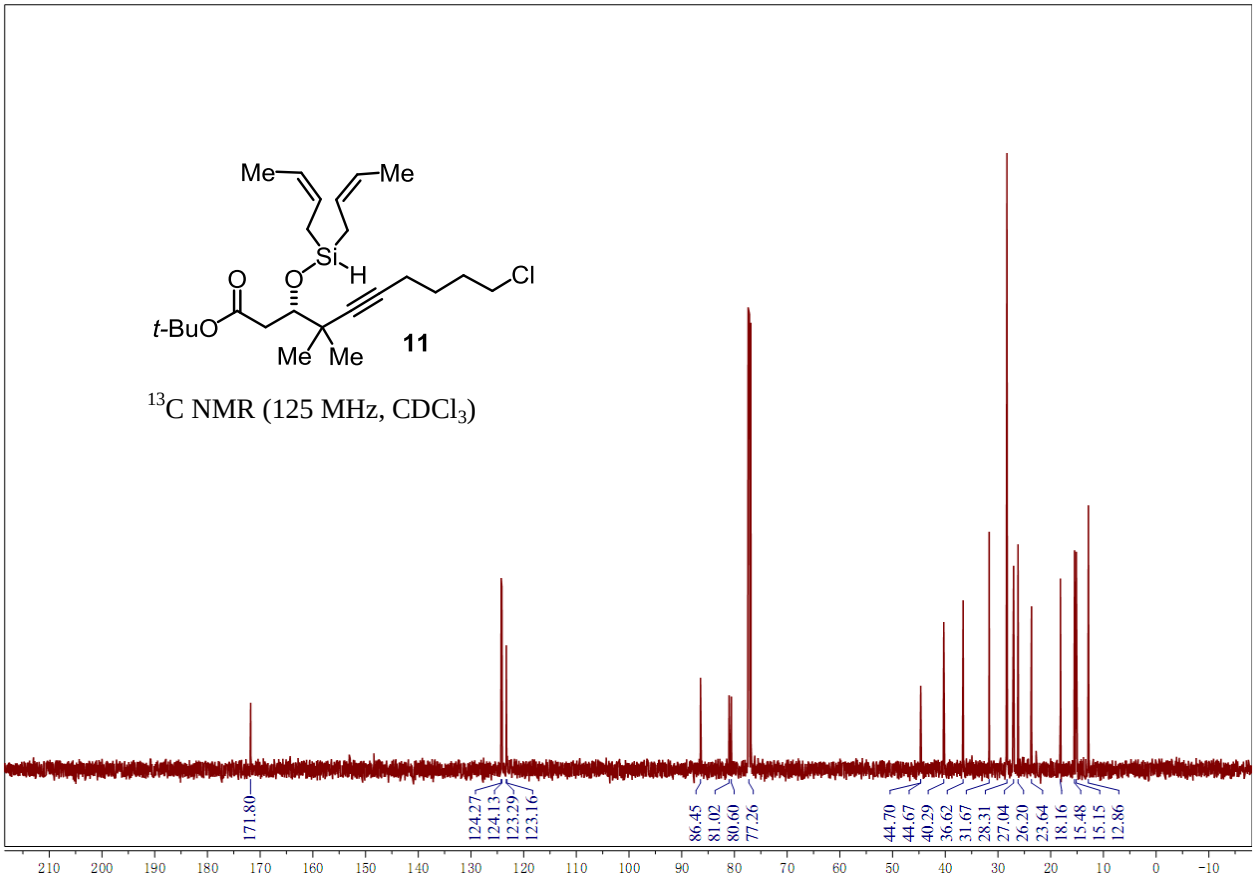
^{1}H NMR (300 MHz, $CDCl_3$)



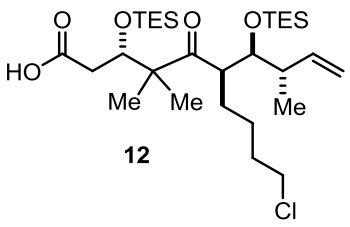
^{13}C NMR (125 MHz, $CDCl_3$)



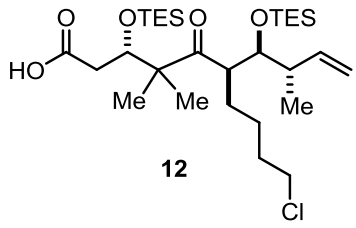
^{1}H NMR (500 MHz, $CDCl_3$)



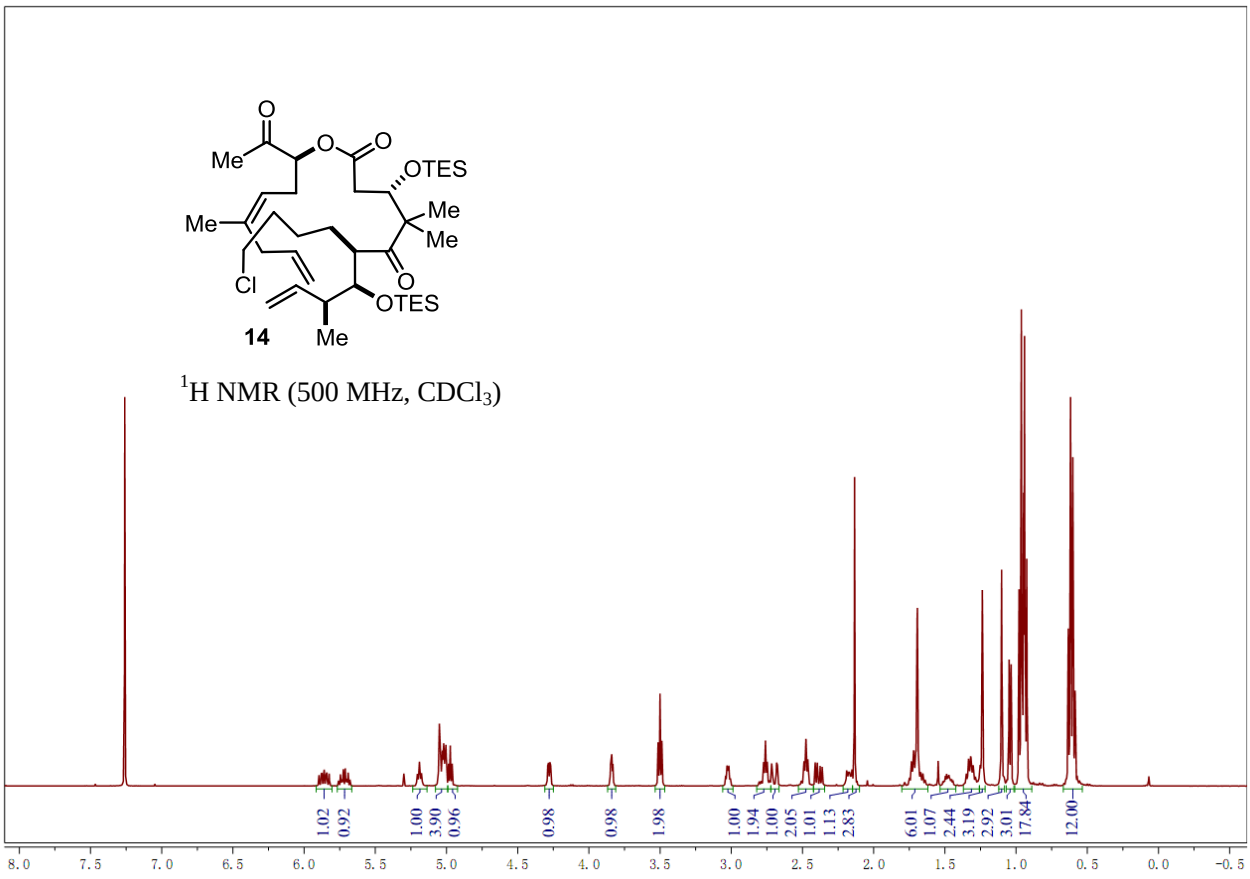
^{13}C NMR (125 MHz, $CDCl_3$)



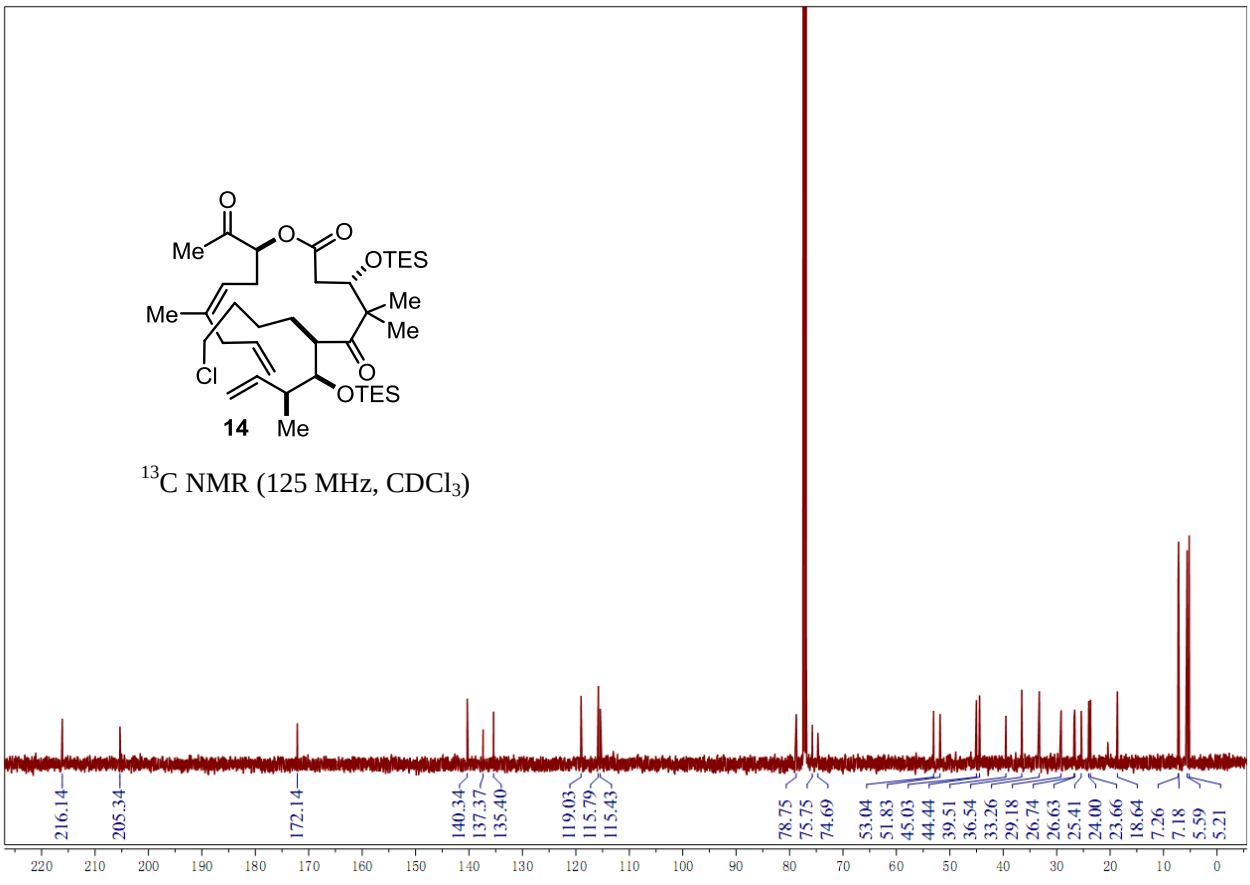
^{1}H NMR (500 MHz, $CDCl_3$)



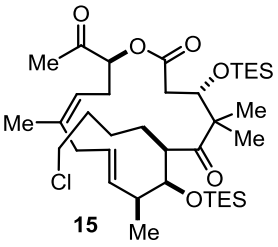
^{13}C NMR (125 MHz, $CDCl_3$)



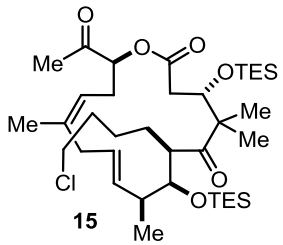
^{1}H NMR (500 MHz, $CDCl_3$)



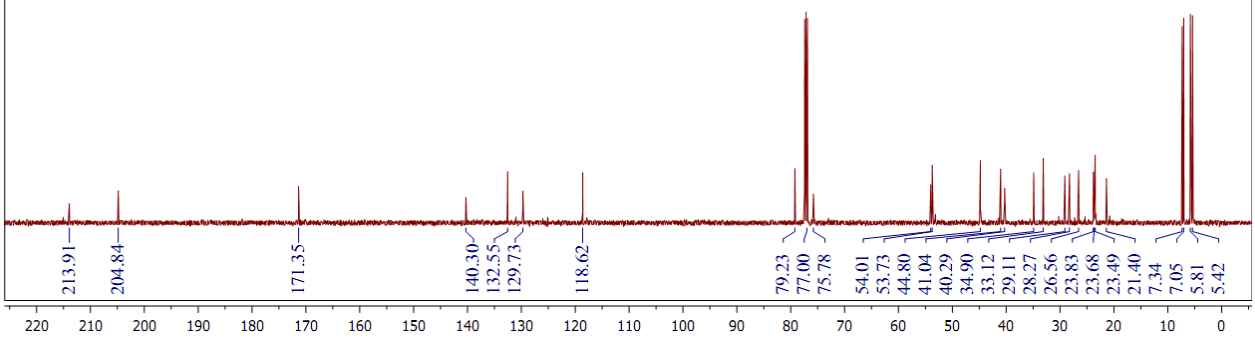
^{13}C NMR (125 MHz, $CDCl_3$)

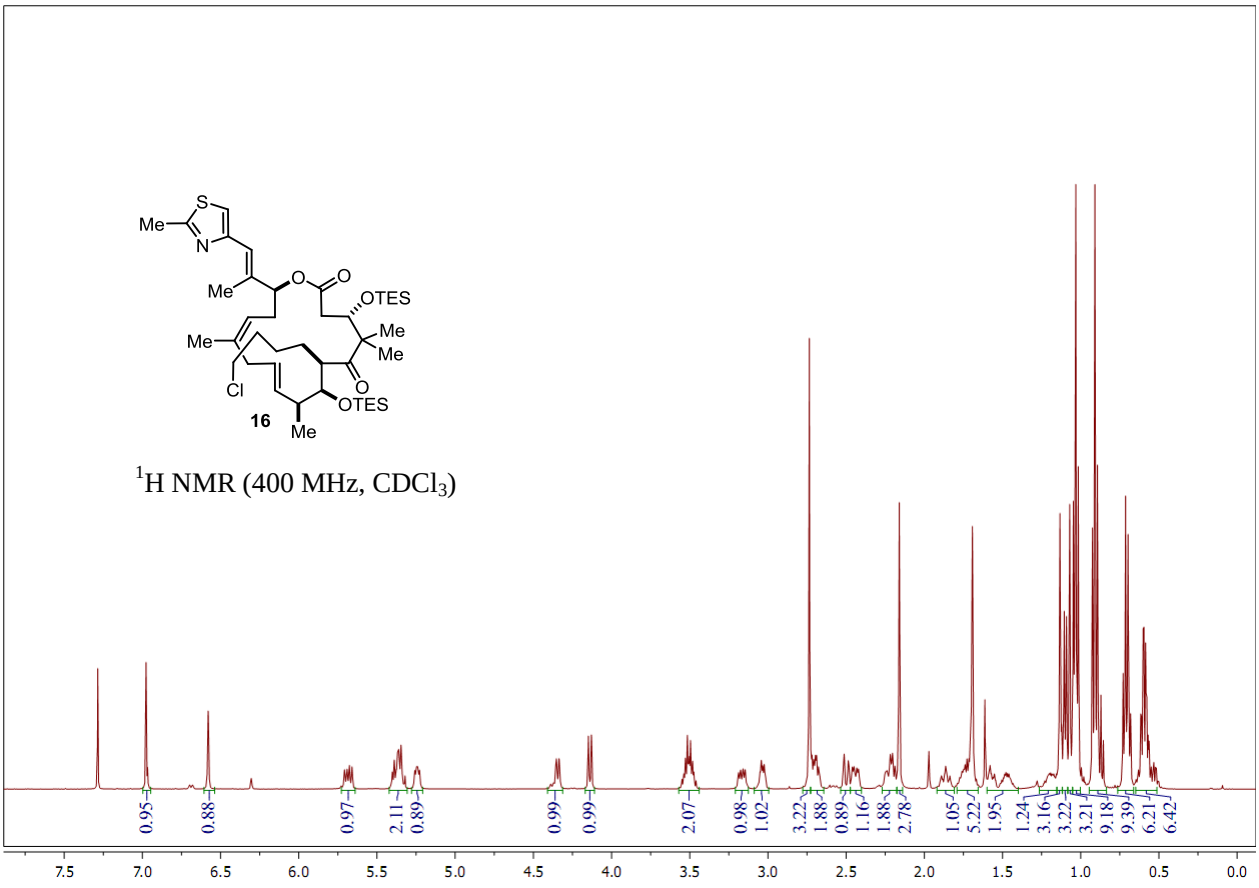


^{1}H NMR (400 MHz, $CDCl_3$)

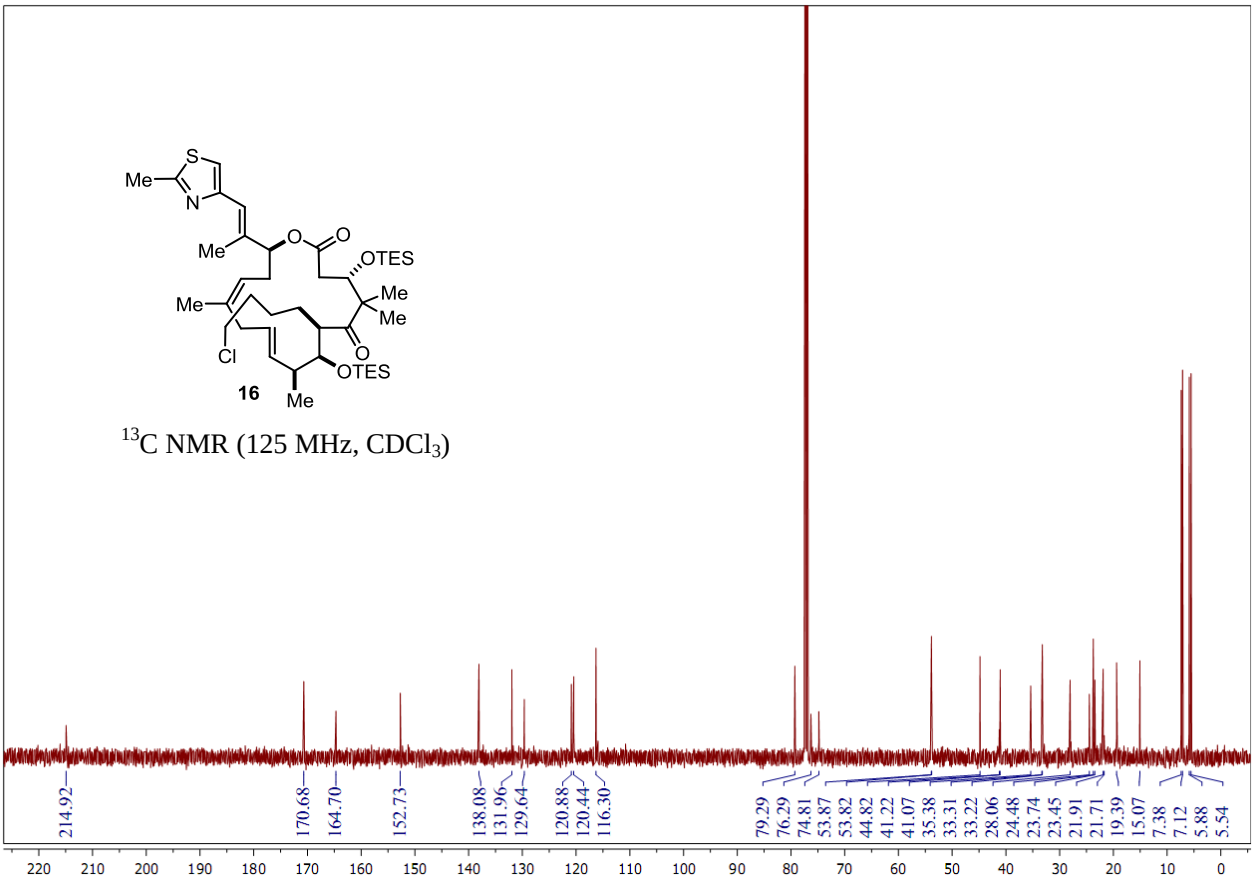


^{13}C NMR (125 MHz, $CDCl_3$)

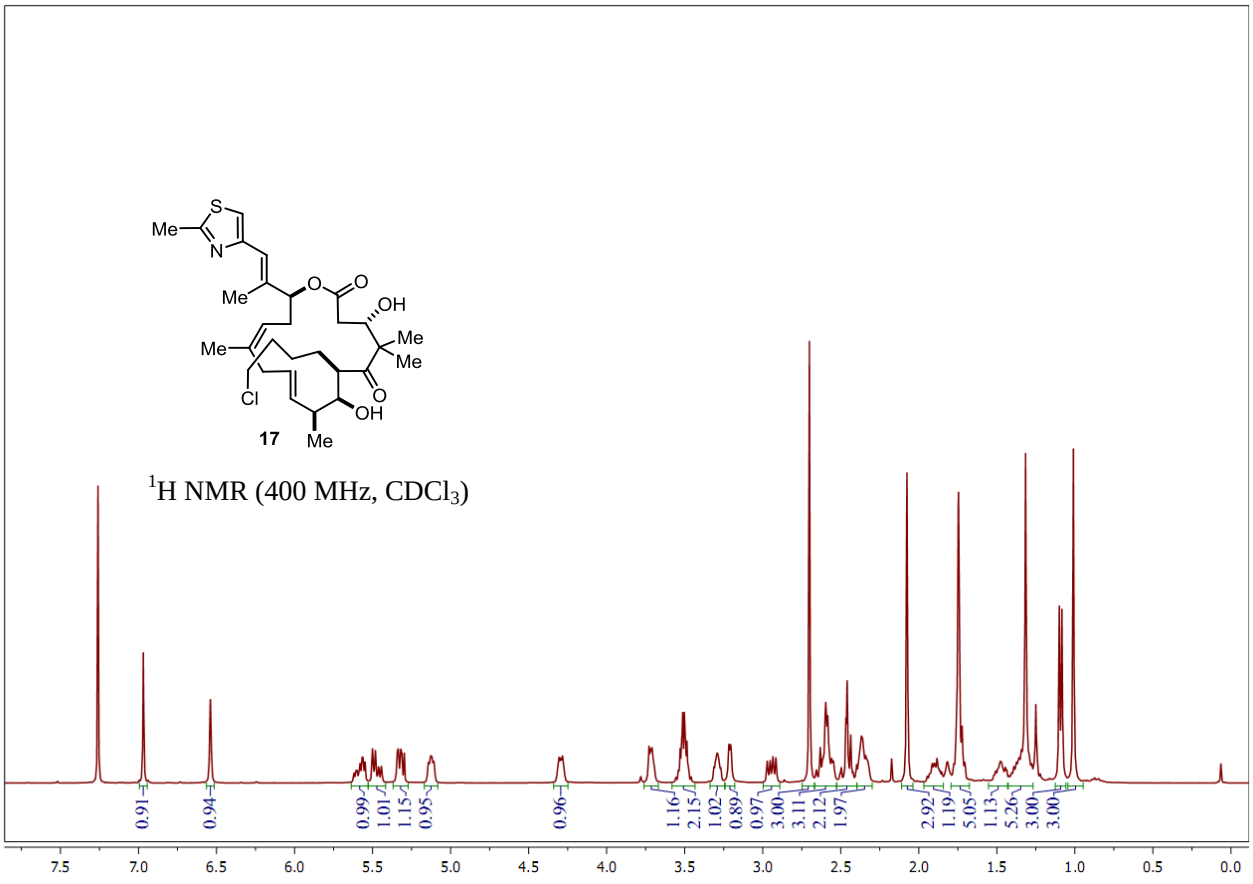




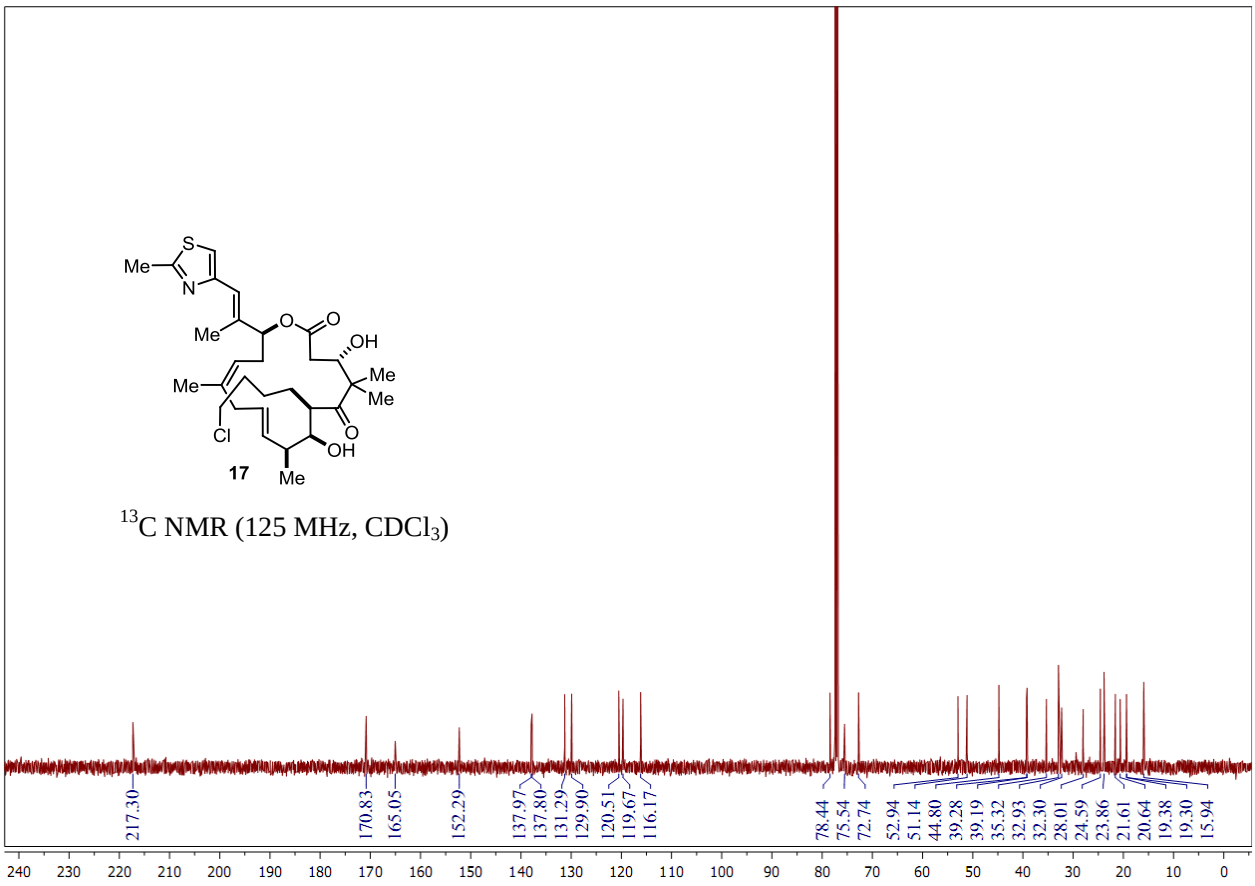
^{1}H NMR (400 MHz, $CDCl_3$)



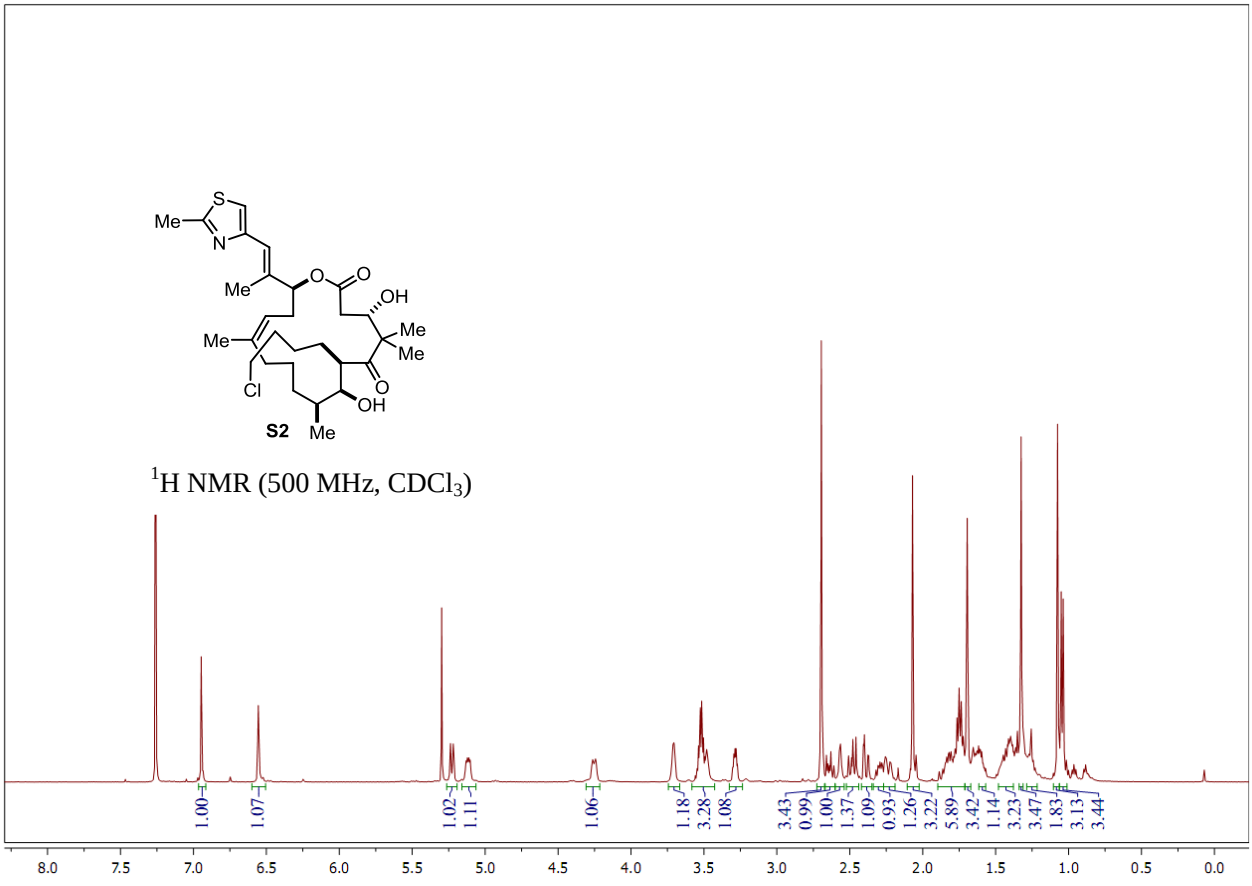
^{13}C NMR (125 MHz, $CDCl_3$)



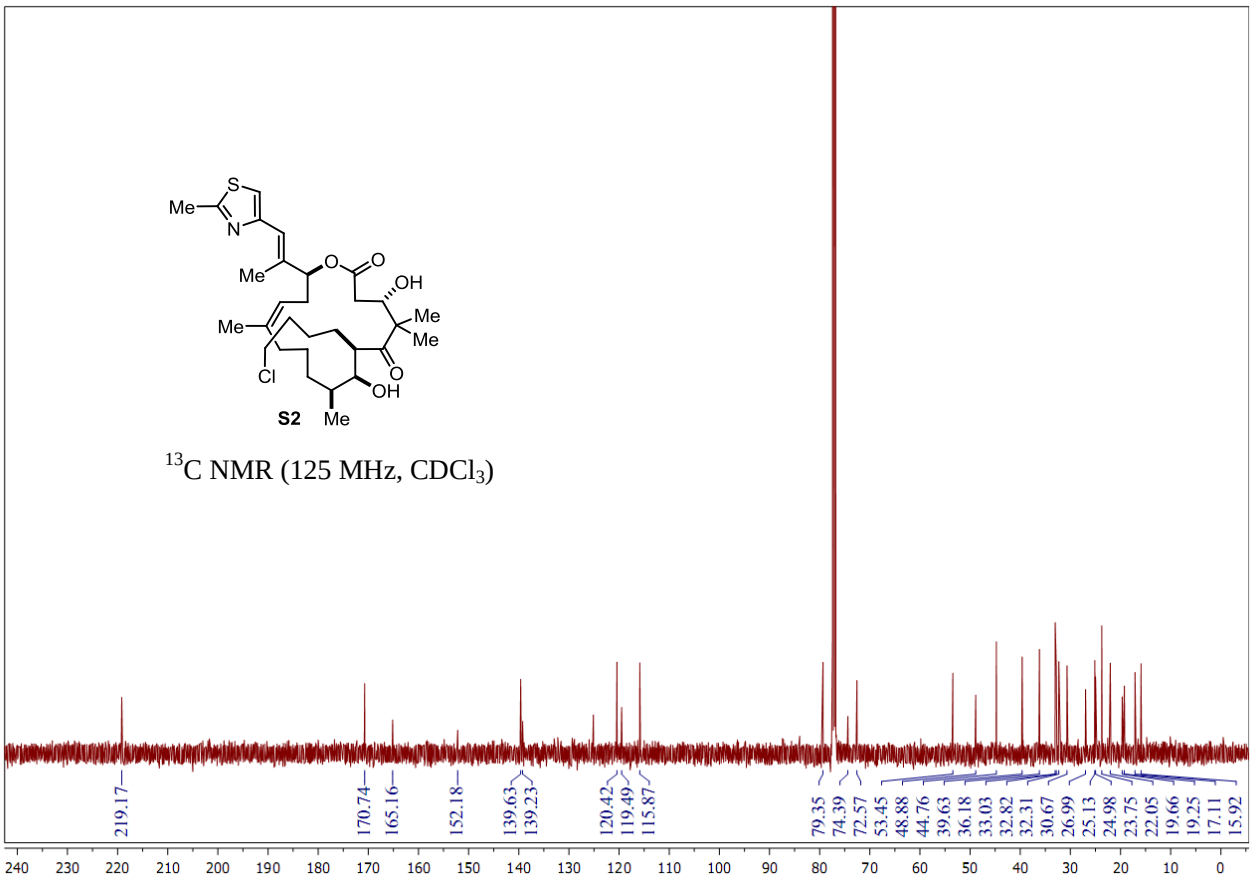
^{1}H NMR (400 MHz, $CDCl_3$)



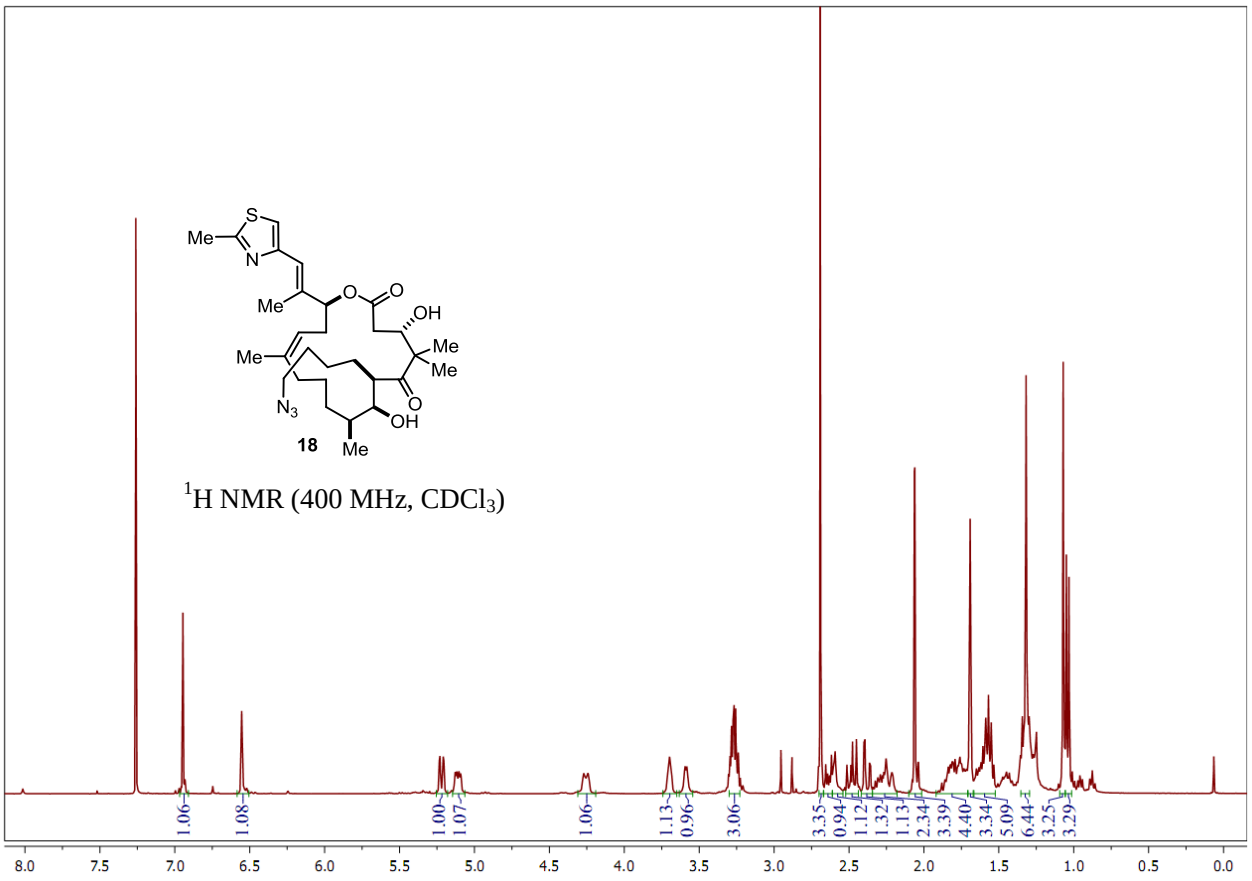
^{13}C NMR (125 MHz, $CDCl_3$)



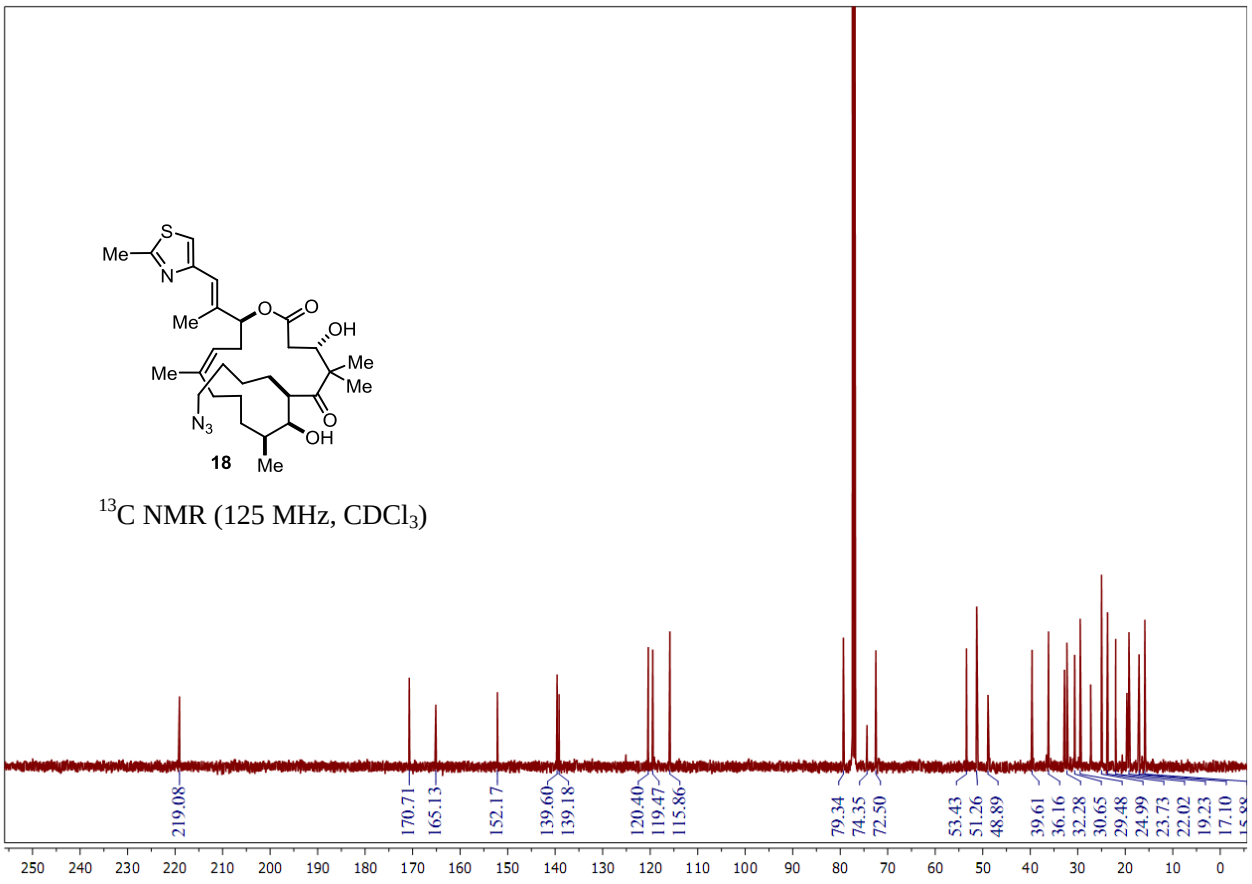
^{1}H NMR (500 MHz, $CDCl_3$)



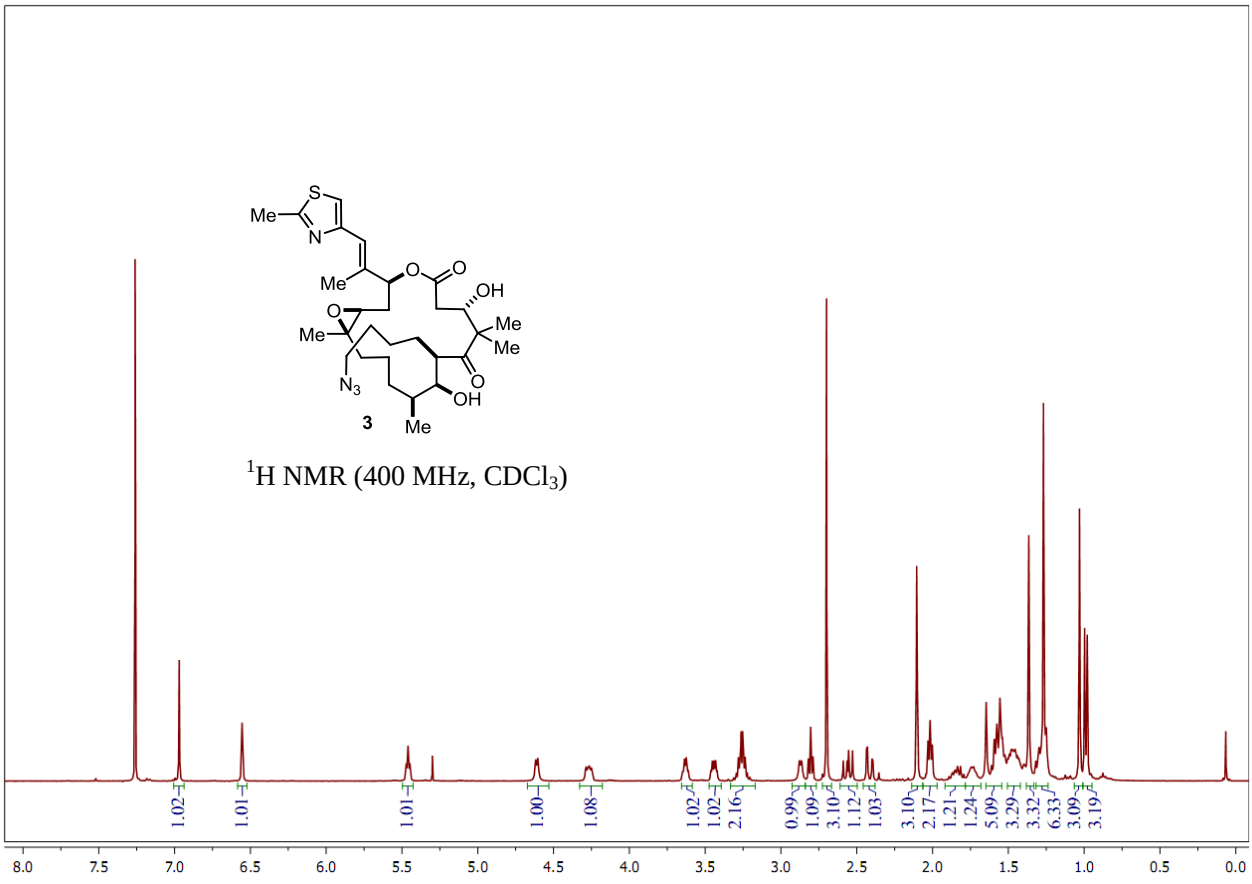
^{13}C NMR (125 MHz, $CDCl_3$)



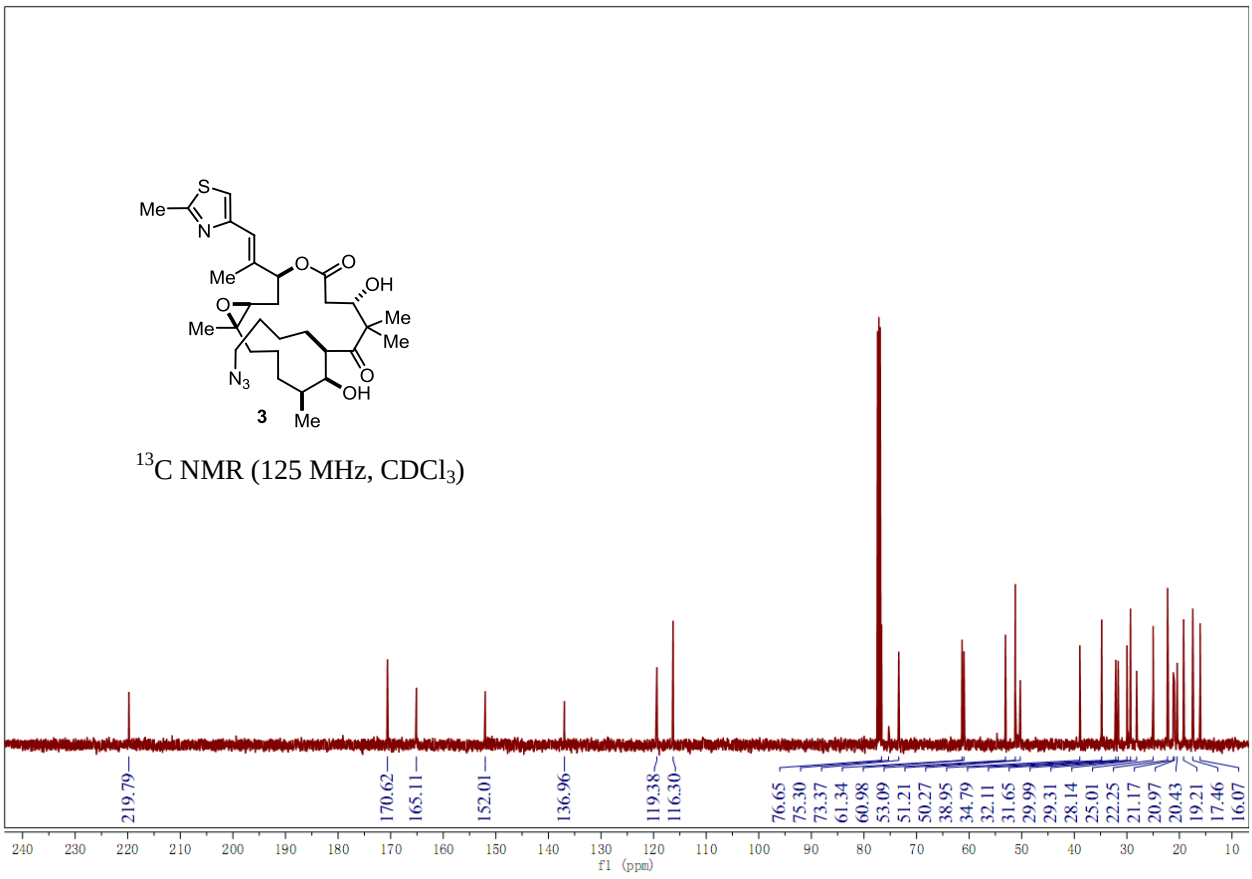
^{1}H NMR (400 MHz, $CDCl_3$)



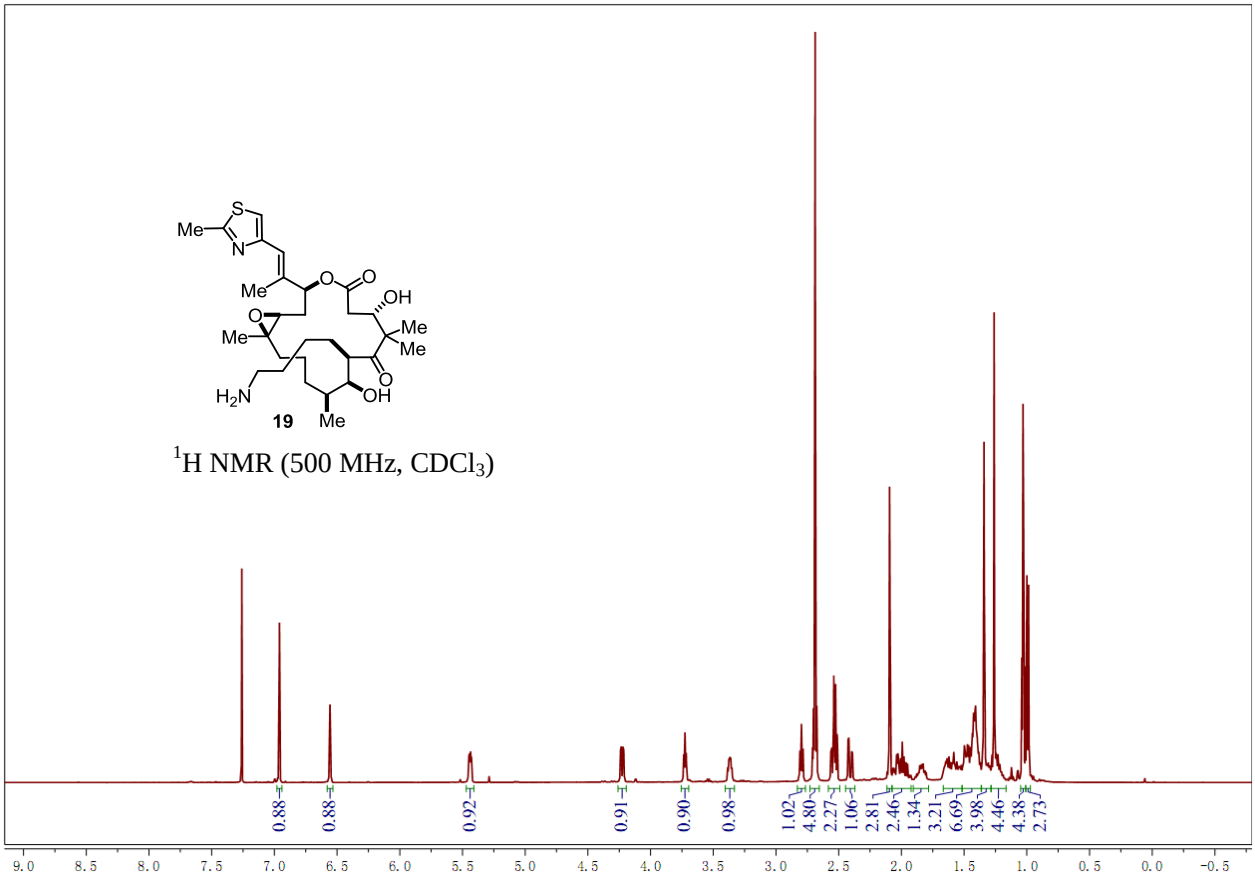
^{13}C NMR (125 MHz, $CDCl_3$)



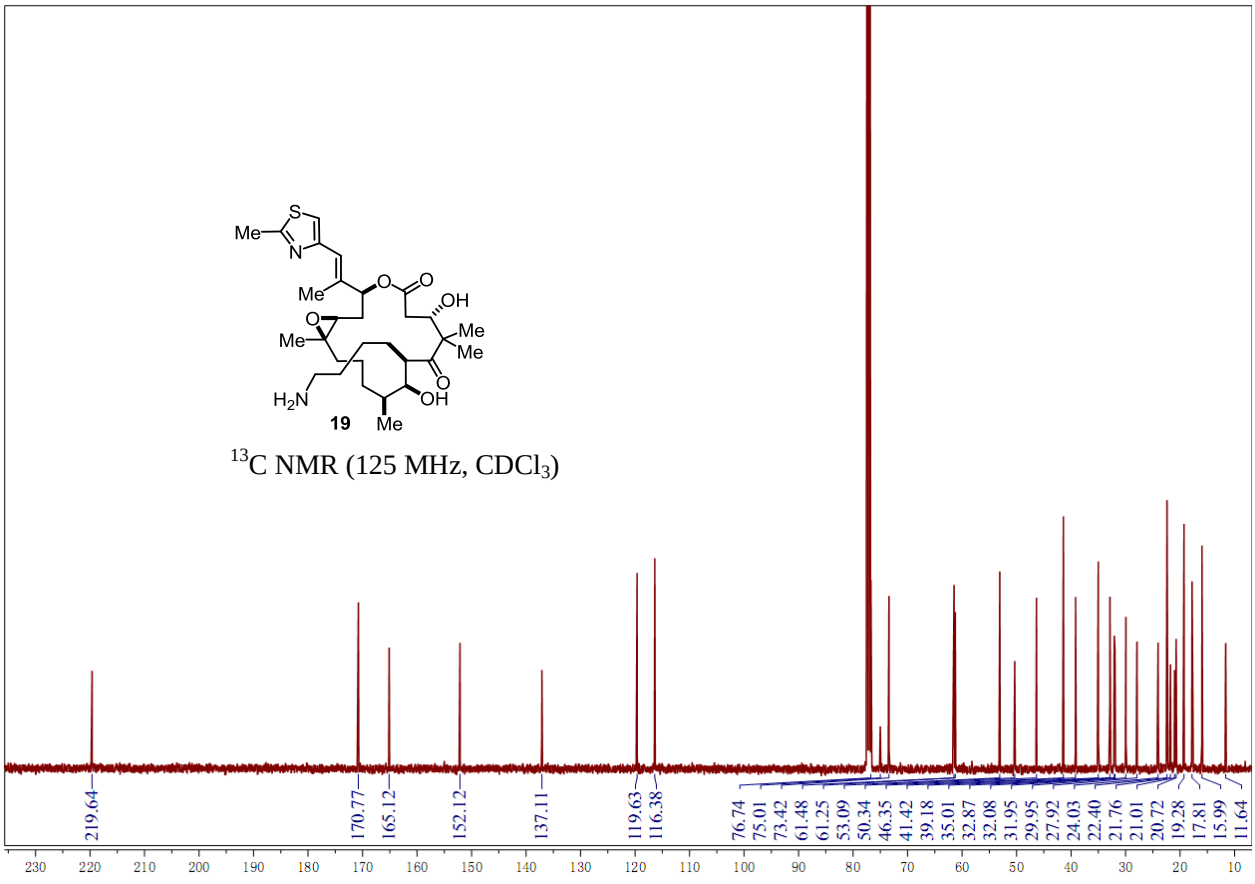
^{1}H NMR (400 MHz, $CDCl_3$)



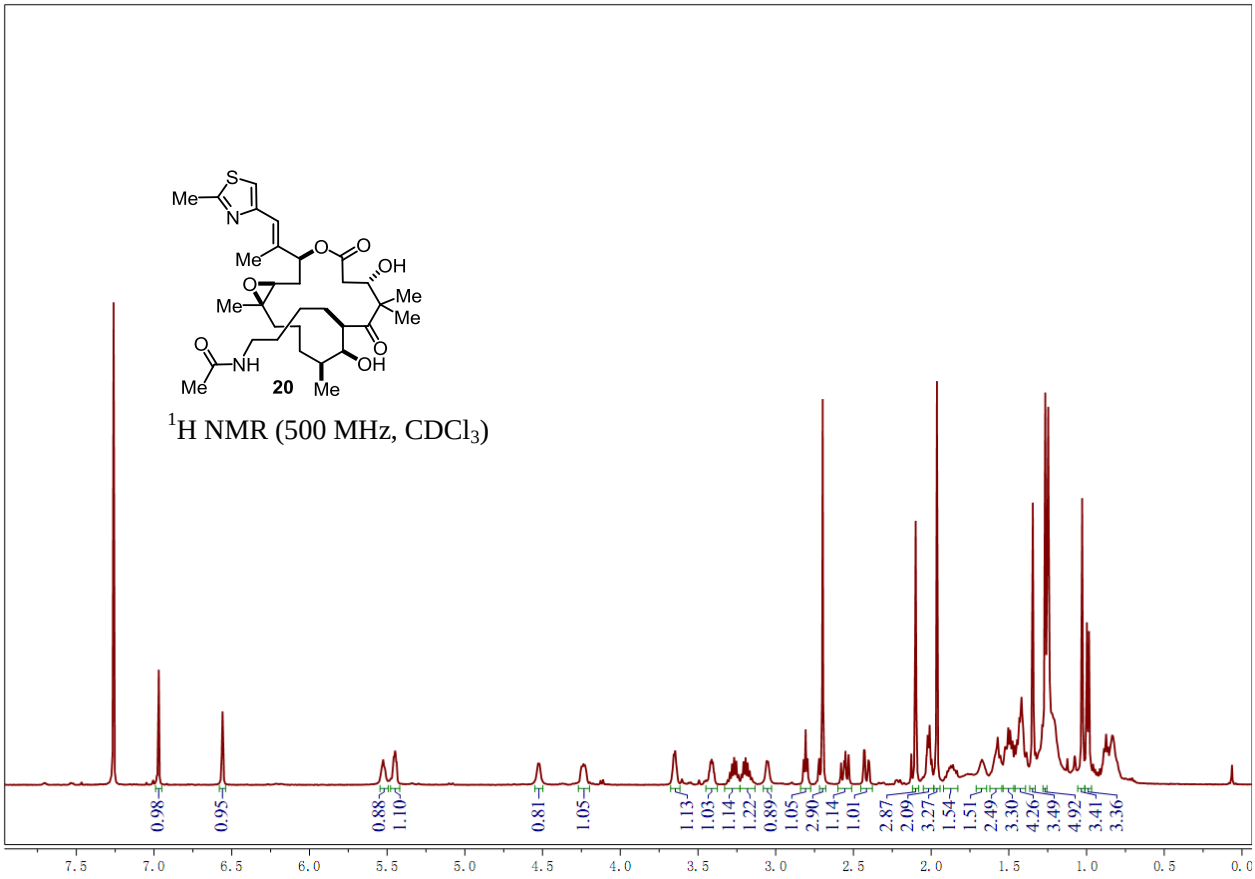
^{13}C NMR (125 MHz, $CDCl_3$)



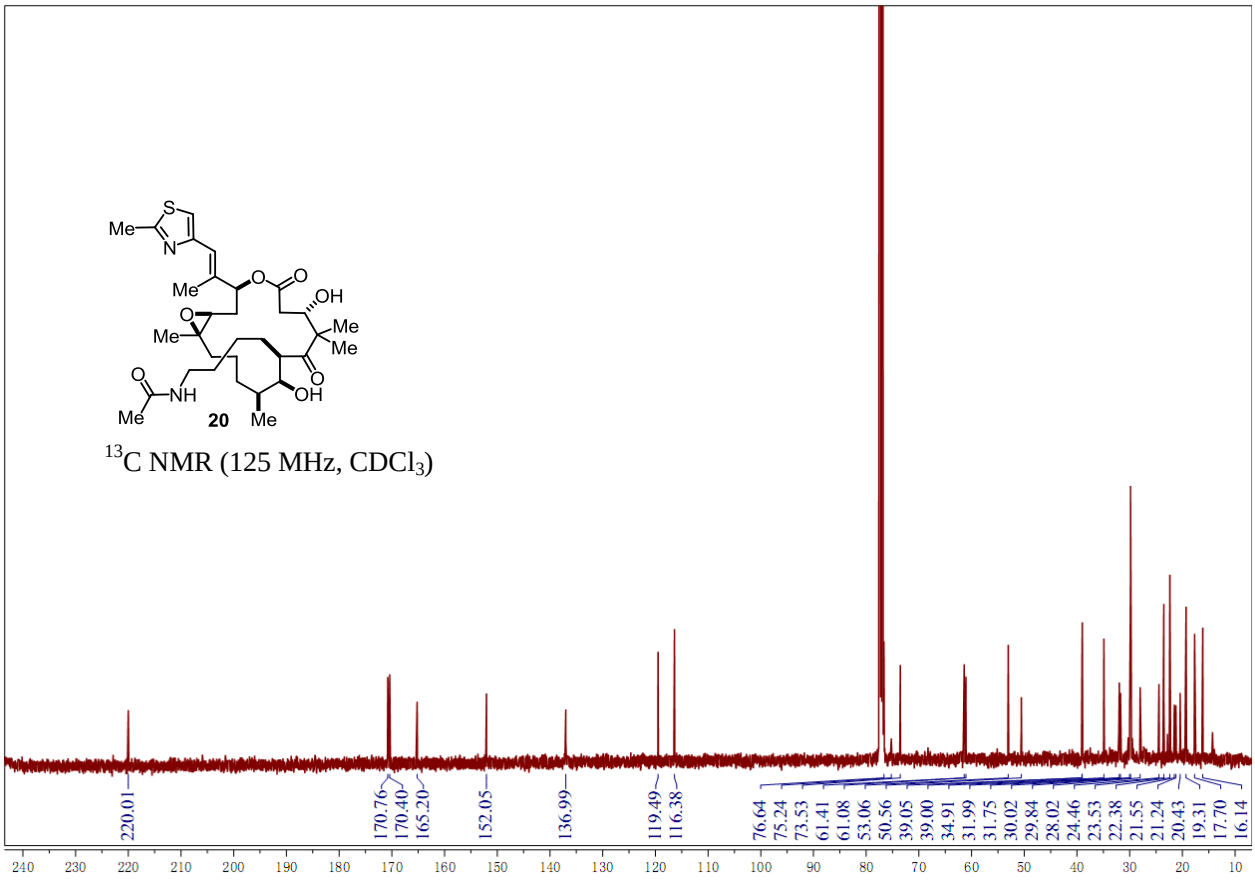
^{1}H NMR (500 MHz, $CDCl_3$)



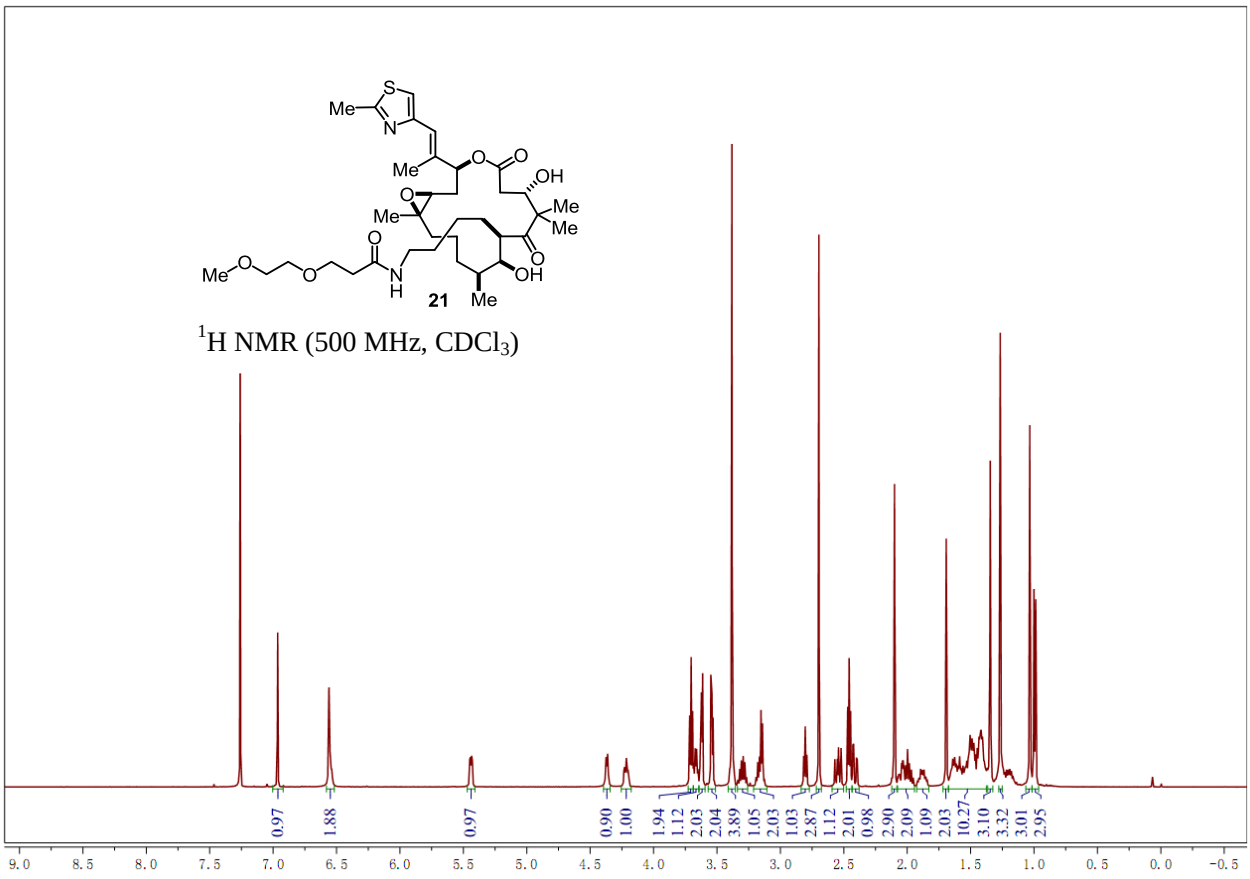
^{13}C NMR (125 MHz, $CDCl_3$)

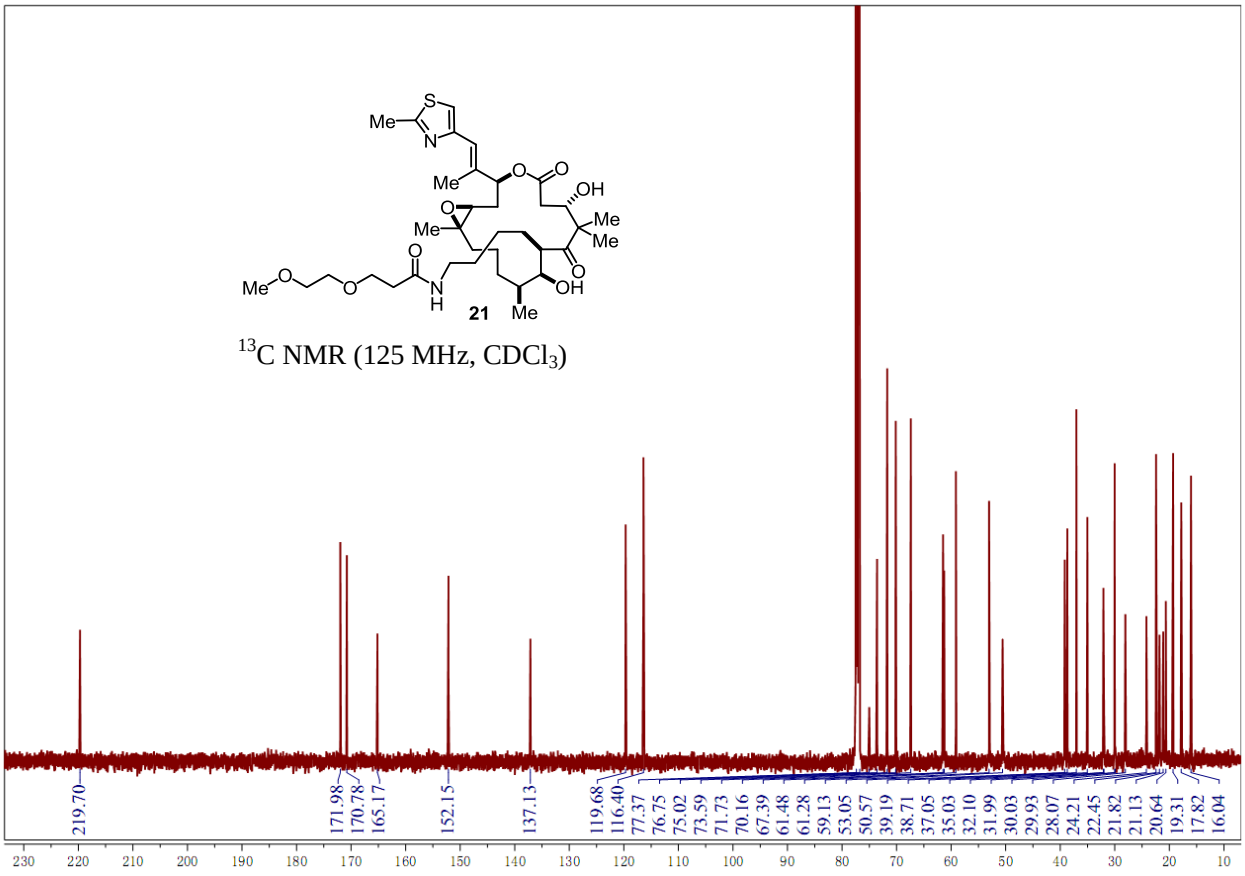


^{1}H NMR (500 MHz, $CDCl_3$)



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


21
^{1}H NMR (500 MHz, $CDCl_3$)
0.97 1.88 0.97 0.90 1.00 1.94 1.12 2.03 2.04 3.89 1.05 2.03 1.03 2.87 1.12 2.01 0.98 2.90 2.09 1.09 2.03 10.27 3.10 3.32 3.01 2.95
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


21
^{13}C NMR (125 MHz, $CDCl_3$)
219.70 171.98 170.78 165.17 152.15 137.13 119.68 116.40 77.37 76.75 75.02 73.59 71.73 70.16 67.39 61.48 61.28 59.13 53.05 50.57 39.19 38.71 37.05 35.03 32.10 31.99 30.03 29.93 28.07 24.21 22.45 21.82 21.13 20.64 19.31 17.82 16.04
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10