Construction of the Tricyclic Core of *Steenkrotin*-Type Diterpenoids via Intramolecular [3+2] Cycloaddition

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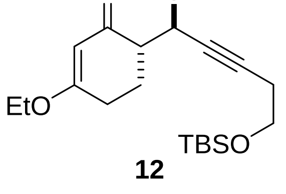
Supporting Information Available

I) Experimental Section

Experimental Data for Compounds

General Procedures. All reactions were carried out under a nitrogen or argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry acetonitrile (MeCN), 1,4-dioxane, tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), toluene and triethylamine (Et_3N) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Methanol (MeOH), benzene, *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were purchased in anhydrous form and used without further purification. Water, ethyl acetate (EtOAc), diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), acetone and hexanes were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of ammonium molybdate, anisaldehyde, and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. NMR spectra were recorded on a Bruker AV-400 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, pent = pentet, hex = hexet, br = broad. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI TOF (time of flight) mass spectrometer at 3500 V emitter voltage.



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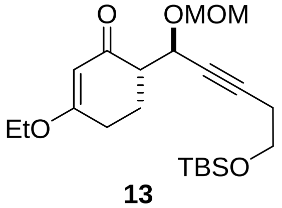
Alcohol 12: To a stirred solution of *i*-Pr$_2$NH (15.25 g, 0.15 mol) in THF (150 mL) at –78°C was added *n*-BuLi (2.5 M in hexane,55 mL, 0.14 mol). The resulting mixture was stirred at –78 °C for 0.5 h before it was added a solution of 3-ethoxy-2-cyclohexenone **10**[1] (14.8 g, 0.11 mol) in THF (20 mL). After stirring at –78 °C for further 0.5 h, the resulting mixture was added a solution of aldehyde **11**[2] (27 g, 0.13 mol) in THF (30 mL) at –78 °C. The resulting mixture was stirred at –78 °C for 15 min before it was diluted with EtOAc (50 mL) and quenched with NH_4Cl (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 50 mL).The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 6:1) afforded alcohol **12** (34.8 g, 90%, dr = 1.5:1) as a light yellow oil. **12**: $R_f = 0.25$ (hexanes:EtOAc 5:1); IR (film) ν_{max} 3437, 2933, 2859, 1644, 1603, 1468, 1382, 1359, 1250, 1193, 1104, 916, 837, 770, 740, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.35$ (d, $J = 11.7$ Hz, 1 H), 4.71–4.57 (m, 1 H), 3.98–3.86 (m, 2 H), 3.70 (dt, $J = 10.9, 7.1$ Hz, 2 H), 2.61–2.23 (m, 6 H), 2.11–1.96 (m, 1 H), 1.77–1.60 (m, 1 H), 1.36 (t, $J = 7.0$ Hz, 3 H), 0.87 (d, $J = 2.8$ Hz, 9 H), 0.05 ppm (d, $J = 2.7$ Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.0$, 200.7, 179.0, 178.6, 103.2, 102.5, 83.7, 83.5, 80.1, 79.8, 64.9, 64.7, 64.4, 63.6, 62.0, 61.9, 50.3, 49.9, 29.0, 28.9, 26.0 (6C), 24.3, 23.3 (2C), 23.0, 18.4 (2C), 14.2 (2C), -5.2 ppm (4C); HRMS(ESI): calcd for $C_{19}H_{33}O_4Si^+[M+H^+]$ 353.2143, found 353.2146.

MOM ether 13: To a stirred solution of alcohol **12** (22.0 g, 0.063 mol) in CH_2Cl_2 (100 mL) at 0 °C was added *i*-Pr_2NEt (44.0 mL, 0.25 mol) and MOMCl (14.4 mL, 0.19 mol). The resulting mixture was warmed to room temperature and stirred for 12 h before it was quenched with $NaHCO_3$ (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL).The combined organic layers were dried



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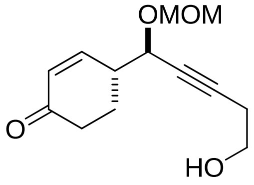
(Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 12:1) afforded MOM ether **13** (22.8 g, 92%) as a colorless oil. **13**: R_f =0.25 (hexanes:EtOAc 8:1); IR (film) ν_{max} 2933, 2887, 1655, 1606, 1467, 1380, 1360, 1250, 1189, 1099, 1034, 915, 836, 777, 734, 664 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.34 (s, 1 H), 5.11–5.04 (m, 1 H), 4.93 (d, *J* = 6.6 Hz, 1 H), 4.58 (d, *J* = 6.6 Hz, 1 H), 3.89 (dd, *J* = 6.9, 4.6 Hz, 2 H), 3.66 (t, *J* = 7.2 Hz, 2 H), 3.35 (s, 3 H), 2.64–2.54 (m, 1 H), 2.46 (d, *J* = 4.5 Hz, 2 H), 2.38 (t, *J* = 6.5 Hz, 2 H), 2.24–2.08 (m, 2 H), 1.35 (t, *J* = 7.0 Hz, 3 H), 0.86 (s, 9 H), 0.03 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.3, 177.4, 102.7, 94.2, 84.7, 65.6, 64.3, 61.8, 55.7, 49.9, 28.4, 25.8 (4C), 23.2, 22.1, 18.2, 14.1, -5.2 ppm (2C); HRMS(ESI): calcd for $C_{21}H_{37}O_5Si^+[M+H^+]$ 397.2405, found 397.2408.

Enone 9: To a stirred solution of MOM ether **13** (8.1 g, 20.5 mmol) in THF (50 mL) at –78°C was added Dibal-H (1.5 M in toluene, 20.5 mL, 30.8 mmol). The resulting mixture was warmed to –20°C and stirred for 0.5 h before it was acidified (HCl, 2.0 M aq.) to pH 1.The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL).The combined organic layers were washed with $NaHCO_3$ (20 mL, sat. aq.) and brine (20 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded the crude alcohol as a colorless oil.



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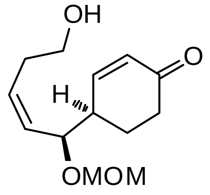
To a stirred solution of the alcohol (crude, obtained above) in THF/H_2O (20:1, v/v, 30 mL) at room temperature was added n-$Bu_4NF\cdot 3H_2O$ (5.38 g, 17.0 mmol). The resulting mixture was stirred for 2 h before it was quenched with NH_4Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo.* Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone **9** (3.2 g , 65% over the two steps) as a colorless oil. **9**: $R_f = 0.25$ (hexanes:EtOAc 1:1); IR (film) ν_{max} 3409, 2959, 2886, 2235, 1673, 1390, 1332, 1213, 1147, 1097, 1024, 921, 844, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.03$ (d, $J = 10.2$ Hz, 1 H), 6.05 (dd, $J = 10.2, 2.0$ Hz, 1 H), 4.95 (d, $J = 6.9$ Hz, 1 H), 4.59 (d, $J = 6.8$ Hz, 1 H), 4.35 (dd, $J = 4.0, 1.8$ Hz, 1 H), 3.69 (dd, $J = 8.4, 4.2$ Hz, 2 H), 3.36 (s, 3 H), 2.73 (dd, $J = 4.7, 2.3$ Hz, 1 H), 2.63–2.27 (m, 5 H), 2.20–2.12 (m, 1 H), 1.99 ppm (ddd, $J = 13.4, 10.6, 4.4$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 199.6$, 150.3, 130.4, 94.2, 85.2, 78.1, 68.2, 60.9, 55.9, 41.6, 36.8, 25.2, 23.0 ppm; HRMS(ESI): calcd for $C_{13}H_{19}O_4^+$ [$M+H^+$] 239.1278, found 239.1280.

Alkene 14: To a stirred solution of alkyne **9** (2.6 g, 10.9 mmol) in toluene (20 mL) at room temperature was added $Pd/CaCO_3$ (260 mg). The resulting mixture was stirred under hydrogen atmosphere (1 atm) for 0.5 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded alkene **14** (2.5 g, 95%) as a colorless oil. **14:** $R_f = 0.25$ (hexanes:EtOAc 1:1); IR (film) ν_{max} 3436, 2947, 2887, 1673, 1390, 1349, 1216, 1147, 1094, 1030, 923, 878, 845, 749cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.15$ (d, $J = 10.2$ Hz, 1 H), 6.07 (dd, $J = 10.2, 2.1$ Hz, 1 H), 5.86–5.76 (m, 1 H), 5.44 (t, $J = 10.4$ Hz, 1 H), 4.79 (d, $J = 6.8$



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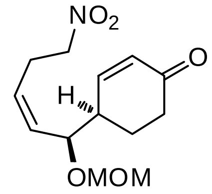
Hz, 1 H), 4.54 (d, J = 6.8 Hz, 1 H), 4.3–4.23 (m, 1 H), 3.69 (ddt, J = 13.3, 10.4, 5.3 Hz, 2 H), 3.38 (s, 3 H), 2.59–2.43 (m, 3 H), 2.41–2.34 (m, 1 H), 2.34–2.25 (m, 1 H), 2.04 (ddd, J = 22.2, 9.8, 5.1 Hz, 2 H), 1.80–1.68 ppm (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.5, 151.0, 132.9, 130.0, 129.6, 93.5, 72.9, 61.8, 55.7, 41.1, 37.0, 31.4, 25.4 ppm; HRMS(ESI): calcd for $C_{13}H_{21}O_4^+$ [M+H$^+$] 241.1434, found 241.1436.

Nitro compound 8: To a stirred solution of alcohol **14** (1.23 g, 5.13 mmol) in CH_2Cl_2 (15 mL) at 0 °C were added PPh_3 (2.01 g, 7.69 mmol), imidazole (5.23 g, 7.69 mmol) and iodine (1.95 g, 7.69 mmol). The resulting mixture was warmed to room temperature and stirred for 4 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded the crude iodide as a corless oil, which was used directly without further purification.



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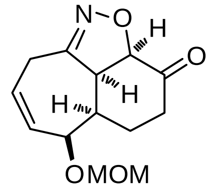
To a stirred solution of iodide (crude, obtained above) in Et_2O/H_2O (1:3, v/v, 15 mL) at room temperature was added $AgNO_2$ (3.2 g, 20.6 mmol). The resulting mixture was stirred for 12 h before it was filtered through a short pad of celite. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded nitro compound **8** (677 mg, 55% over the two steps) as a colorless oil. **8:** R_f = 0.45 (hexanes:EtOAc 2:1); IR (film) ν_{max} 3491, 2949, 2892, 2362, 1678, 1553, 1382, 1215, 1147, 1095, 1030, 921, 791, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.12 (d, J = 10.3 Hz, 1 H), 6.08 (dd, J = 10.3, 2.2 Hz, 1 H), 5.73 (dt, J = 11.0, 7.4 Hz, 1 H), 5.49 (dd, J = 10.9, 9.9 Hz, 1 H), 4.67 (d, *J* = 6.8 Hz, 1 H), 4.51 (d, *J* = 6.8 Hz, 1 H), 4.44 (dd, *J* = 13.1, 6.5 Hz, 2 H), 4.32–4.23 (m, 1 H), 3.38 (s, 3 H), 2.83 (d, *J* = 7.1 Hz, 2 H), 2.53 (ddd, *J* = 12.7, 9.3, 4.8 Hz, 2 H), 2.44–2.27 (m, 1 H), 2.09–1.98 (m, 1 H), 1.82–1.66 ppm (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 150.4, 131.4, 130.2, 129.2, 93.4, 74.5, 72.1, 55.8, 41.0, 37.0, 25.7, 25.4 ppm; HRMS(ESI): calcd for $C_{13}H_{20}NO_5^+$[M+H$^+$] 270.1336, found 270.1334.

Tricyclic isoxazoline 15: To a stirred solution of nitro compound **8** (600 mg, 2.23 mmol) in toluene (20 mL) at room temperature was added Boc_2O (2.43 g, 11.1 mmol) and 4-DMAP (134 mg, 1.1 mmol). The resulting mixture was stirred at 90 °C for 5 h before it was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded tricyclic isoxazoline **15** (420 mg, 75%) as a white solid. **15:** R_f = 0.48 (hexanes:EtOAc 1:1); m.p. = 131–133 ^{o}C; IR (film) ν_{max} 3437, 2947, 2892, 2360, 1724, 1604, 1280, 1220, 1148, 1101, 1037, 917, 840, 744, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85–5.75 (m, 1 H), 5.69 (d, *J* = 10.9 Hz, 1 H), 4.76–4.65 (m, 3 H), 4.59 (s, 1 H), 3.90 (dd, *J* = 10.9, 5.8 Hz, 1 H), 3.43–3.32 (m, 4 H), 2.94 (d, *J* = 15.8 Hz, 1 H), 2.74–2.63 (m, 1 H), 2.44–2.28 (m, 2 H), 2.03 (d, *J* = 8.0 Hz, 1 H), 1.77–1.67 ppm (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.8, 152.6, 134.9, 123.2, 95.0, 83.1, 74.9, 55.8, 55.6, 39.0, 36.8, 25.7, 20.1 ppm; HRMS(ESI): calcd for $C_{13}H_{18}NO_4^+$[M+H$^+$] 252.1230, found 252.1234.



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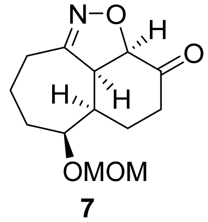
Isoxazoline 7: To a stirred solution of tricyclic isoxazoline **15** (246 mg, 0.98 mmol) in EtOAc (10 mL) at room temperature was added Pd/C (10% wt/wt, 26.5 mg). The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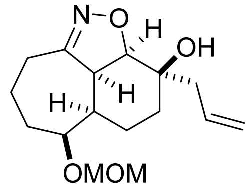
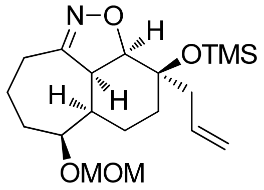
resulting mixture was stirred under hydrogen atmosphere (1 atm) for 0.5 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded isoxazoline **7** (238 mg, 96%) as a colorless oil. **7:** R_f = 0.25 (hexanes:EtOAc 1:1); IR (film) ν_{max} 3851, 3634, 2942, 2886, 2360, 1725, 1452, 1279, 1223, 1148, 1099, 1035, 918, 840, 746 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.68 (d, *J* = 7.4 Hz, 2 H), 4.64 (d, *J* = 7.0 Hz, 1 H), 3.82 (d, *J* = 6.5 Hz, 1 H), 3.73 (dd, *J* = 7.6, 3.2 Hz, 1 H), 3.38 (s, 3 H), 2.81–2.68 (m, 2 H), 2.53 (dd, *J* = 12.4, 3.1 Hz, 1 H), 2.44 (dd, *J* = 10.2, 6.0 Hz, 2 H), 2.35–2.26 (m, 1 H), 2.25–2.17 (m, 1 H), 2.06–1.83 (m, 3 H), 1.50 ppm (d, *J* = 5.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.7, 160.1, 95.4, 83.2, 79.7, 55.8, 53.6, 39.5, 38.1, 31.2, 26.7, 21.4, 20.7 ppm; HRMS(ESI): calcd for $C_{13}H_{20}NO_4^+$ [$M+H^+$] 254.1387, found 254.1386.

Alcohol 16: To a stirred solution of isoxazoline **7** (556 mg, 2.20 mmol) in THF (50 mL) at –78 °C was added allylmagnesium bromide (0.35 M in THF, 6.8 mL, 2.40 mmol). The resulting mixture was stirred for 20 min before it was quenched with NH_4Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded alcohol **16** (591 mg, 91%) as a colorless oil. **16**: R_f = 0.50 (hexanes:EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$)：δ = 5.85 (td, *J* = 16.7, 8.5 Hz, 1 H), 5.12 (t, *J* = 13.4 Hz, 2 H), 4.66 (s, 2 H), 4.46 (d, *J* = 9.5 Hz, 1 H), 3.79–3.67 (m, 1 H), 3.47–3.40 (m, 1 H), 3.38 (s, 3 H),


16

2.61 (dd, J = 16.1, 8.5 Hz, 1 H), 2.55–2.41 (m, 1 H), 2.31 (dd, J = 13.6, 6.4 Hz, 1 H), 2.25–2.13 (m, 2 H), 2.07 (d, J = 9.6 Hz, 2 H), 1.92 (d, J = 14.0 Hz, 1 H), 1.85–1.66 (m, 3 H), 1.54 (dd, J = 12.5, 9.9 Hz, 2 H), 1.23 ppm (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 133.0, 120.6, 94.9, 83.8, 79.8, 72.0, 55.4, 50.1, 43.9, 33.3, 30.8, 29.2, 26.8, 21.3, 16.5 ppm; HRMS(ESI): calcd for $C_{16}H_{26}NO_4^+[M+H^+]$ 296.1856, found 296.1854.

TMS ether 17: To a stirred solution of alcohol **16** (591 mg, 2.0 mmol) in CH_2Cl_2 (50 mL) at –78 °C was added 2,6-lutidine (2.3 mL, 20 mmol) and TMSOTf (1.8 mL, 10 mmol). The resulting mixture was stirred for 0.5 h before it was quenched with NH_4Cl (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded TMS ether **17** (631 mg, 86%) as a colorless oil. **17**: R_f = 0.50 (hexanes:EtOAc 5:1); IR (film) ν_{max} 3783, 2947, 2884, 2361, 1725, 1640, 1445, 1251, 1147, 1100, 1037, 918, 842, 756, 686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91 (ddt, J = 17.2, 10.3, 7.0 Hz, 1 H), 5.21–5.05 (m, 2 H), 4.64 (q, J = 6.9 Hz, 2 H), 4.51 (d, J = 11.0 Hz, 1 H), 3.70 (dt, J = 11.2, 3.8 Hz, 1 H), 3.45 (d, J = 11.0 Hz, 1 H), 3.37 (s, 3 H), 2.99–2.88 (m, 1 H), 2.71 (d, J = 17.6 Hz, 1 H), 2.56–2.34 (m, 2 H), 2.27 (dd, J = 14.7, 6.7 Hz, 1 H), 1.97 (d, J = 7.3 Hz, 1 H), 1.86–1.73 (m, 2 H), 1.69–1.63 (m, 3 H), 1.51 (dd, J = 18.6, 7.0 Hz, 1 H), 1.40 (td, J = 13.1, 6.6 Hz, 1 H), 0.16 ppm (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 131.3, 115.6, 92.1, 81.2, 76.9, 74.0, 53.0, 47.6, 40.7, 30.4, 28.1, 26.9, 24.4,



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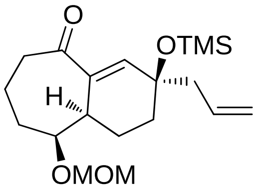
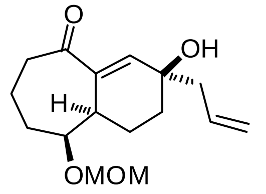
18.9, 14.3, 0.0 ppm (3C); HRMS(ESI): calcd for $C_{19}H_{34}NO_4Si^+[M+H^+]$ 368.2252, found 368.2255.



18

Enone 18: To a stirred solution of TMS ether **17** (587 mg, 1.6 mmol) in MeCN (30 mL) at room temperature was added $Mo(CO)_6$ (522 mg, 2.0 mmol). The resulting mixture was stirred at 90 °C for 1.5 h before it was added H_2O (3 mL). The resulting mixture was stirred at 90 °C for further 5 h before it was filtered through a short pad of celite. The filtrate was extracted with Et_2O (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone **18** (237 mg, 42%) as a colorless oil. **18:** $R_f = 0.25$ (hexanes:EtOAc 1:1); IR (film) ν_{max} 3880, 3696, 3637, 3430, 2926, 2858, 2362, 1735, 1689, 1629, 1461, 1377, 1152, 1073, 1042, 917, 845, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.52$ (s, 1 H), 5.76 (ddt, $J = 17.4, 10.4, 7.2$ Hz, 1 H), 5.04 (dd, $J = 9.8, 8.9$ Hz, 2 H), 4.63 (d, $J = 6.9$ Hz, 1 H), 4.51 (d, $J = 6.9$ Hz, 1 H), 3.88 (d, $J = 4.9$ Hz, 1 H), 3.33 (s, 3 H), 2.59–2.43 (m, 3 H), 2.38 (dd, $J = 13.7, 7.2$ Hz, 1 H), 2.32–2.22 (m, 2 H), 1.97 (ddd, $J = 24.3, 13.2, 2.5$ Hz, 1 H), 1.88–1.66 (m, 4 H), 1.60 (d, $J = 5.6$ Hz, 1 H), 1.42 (td, $J = 13.3, 2.7$ Hz, 1 H), 0.13 ppm (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 203.5, 140.2, 139.2, 133.8, 117.8, 95.3, 79.0, 71.5, 55.9, 47.7, 43.8, 41.3, 34.7, 33.8, 25.7, 20.1, 2.6 ppm (3C); HRMS(ESI): calcd for $C_{19}H_{33}O_4Si^+[M+H^+]$ 353.2143, found 353.2146.

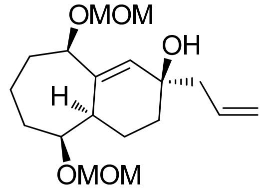
Alcohol 6: To a stirred solution of enone **18** (106 mg, 0.30 mmol) in THF (20 mL) at room temperature was added *n*-Bu_4NF (1.0 M in toluene, 0.43 mL, 0.43 mmol). The



6

resulting mixture was stirred at room temperature for 0.5 h before it was quenched with NH_4Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded alcohol **6** (72 mg, 90%) as a colorless oil. **6**: $R_f = 0.25$ (hexanes:EtOAc 1:1); IR (film) ν_{max} 3786, 3697, 3636, 3440, 2926, 2858, 2362, 1729, 1687, 1627, 1460, 1152, 1040, 991, 916, 752, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.56$ (s, 1 H), 5.85 (ddt, *J* = 17.6, 10.5, 7.3 Hz, 1 H), 5.19–5.02 (m, 2 H), 4.66 (d, *J* = 7.1 Hz, 1 H), 4.54 (d, *J* = 7.1 Hz, 1 H), 3.87 (d, *J* = 4.9 Hz, 1 H), 3.33 (s, 3 H), 2.62–2.51 (m, 3 H), 2.34 (d, *J* = 7.3 Hz, 2 H), 2.31–2.23 (m, 1 H), 2.19 (s, 1 H), 2.00–1.88 (m, 1 H), 1.88–1.68 (m, 4 H), 1.57–1.53 (m, 1 H), 1.49 ppm (dd, *J* = 13.2, 3.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 203.7$, 140.7, 137.9, 133.0, 119.0, 95.9, 79.8, 68.2, 56.1, 46.4, 43.6, 40.8, 34.2, 33.9, 25.2, 20.2 ppm; HRMS(ESI): calcd for $C_{16}H_{25}O_4^+[M+H^+]$ 281.1747, found 281.1746.

MOM ether 19: To a stirred solution of alcohol **6** (78 mg, 0.28 mmol) in THF (20 mL) at 0 °C was added $NaBH_4$ (11 mg, 0.28 mmol) and $CeCl_3 \cdot 7H_2O$ (104 mg, 0.28 mmol). The resulting mixture was stirred at 0 °C for 0.5 h before it was quenched with NH_4Cl (10 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:2)

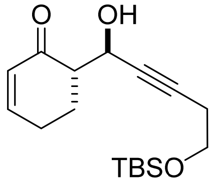


19

afforded crude diol as a colorless oil, which was used directly without further purification.

To a stirred solution of the diol (crude, obtained above) in CH_2Cl_2 (20 mL) at 0 °C was added *i*-Pr_2NEt (0.24 mL, 1.40 mmol) and MOMCl (64 μL, 0.84 mmol). The resulting mixture was warmed to room temperature and stirred for 12 h before it was quenched with $NaHCO_3$ (10 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded MOM ether **19** (74 mg, 81% over the two steps) as a colorless oil. **19**: R_f = 0.25 (hexanes:EtOAc 1:1); IR (film) ν_{max} 3876, 3790, 3638, 3467, 2929, 2361, 1725, 1639, 1445, 1278, 1149, 1100, 1037, 995, 946, 915, 748, 646 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91 (s, 1 H), 5.88–5.74 (m, 1 H), 5.16–5.01 (m, 2 H), 4.63 (dd, *J* = 15.1, 6.8 Hz, 2 H), 4.56 (d, *J* = 6.7 Hz, 1 H), 4.47 (d, *J* = 6.7 Hz, 1 H), 4.15–4.02 (m, 1 H), 3.92–3.82 (m, 1 H), 3.36 (d, *J* = 5.2 Hz, 6 H), 2.54–2.47 (m, 1 H), 2.36–2.28 (m, 2 H), 2.10–2.01 (m, 2 H), 1.93–1.77 (m, 3 H), 1.72 (s, 1 H), 1.63 (ddd, *J* = 14.0, 8.7, 2.6 Hz, 2 H), 1.48 (dd, *J* = 15.7, 6.9 Hz, 2 H), 1.43 ppm (d, *J* = 4.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 133.9, 128.0, 118.7, 95.0, 93.9, 74.4, 69.2, 55.7, 55.6, 47.7, 41.7, 37.8, 34.8, 29.9 (2C), 23.8, 19.7 ppm; HRMS(ESI): calcd for $C_{18}H_{31}O_5^+$[M+H$^+$] 327.2166, found 327.2165.

Alcohol 21: To a stirred solution of *i*-Pr_2NH (28.9 mL, 0.21 mol) in THF (150 mL) at –78 °C was added *n*-BuLi (2.5 M in hexane, 75 mL, 0.19 mol). The resulting mixture was stirred at –78 °C for 0.5 h before it was



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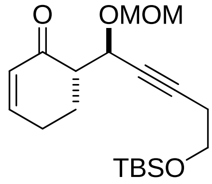
added a solution of cyclohexenone **20** (13.9 g, 0.14 mol) in THF (20 mL). After stirring at –78 °C for further 0.5 h, the resulting mixture was added a solution of aldehyde **11** (35 g, 0.17 mol) in THF (30 mL). The resulting mixture was stirred at –78 °C for 15 min before it was diluted with EtOAc (50 mL) and quenched with NH_4Cl (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded alcohol **21** (32.3 g, 75%, dr = 3:1) as a yellow oil. **21**: $R_f = 0.25$ (hexanes:EtOAc 4:1); IR (film) ν_{max} 3461, 2932, 2859, 1674, 1467, 1390, 1333, 1252, 1223, 1105, 1053, 991, 915, 839, 778, 666 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (dt, *J* = 4.5, 4.0 Hz, 1 H), 6.02 (dd, *J* = 9.2, 7.8 Hz, 1 H), 4.80–4.55 (m, 1 H), 3.98 (d, *J* = 2.6 Hz, 1 H), 3.70 (dd, *J* = 11.4, 4.3 Hz, 2 H), 2.63–2.27 (m, 6 H), 1.85–1.67 (m, 1 H), 0.88 (s, 9 H), 0.05 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.0, 200.8, 151.7, 151.4, 130.0, 129.5, 83.8, 83.4, 79.8, 79.3, 63.7, 62.9, 61.8, 61.7, 51.9, 51.4, 25.9 (6C), 25.8, 25.3 (2C), 24.0, 23.2 (2C), 18.3 (2C), -5.3 ppm (4C); HRMS(ESI): calcd for $C_{17}H_{29}O_3Si^+[M+H^+]$ 309.1880, found 309.1883.

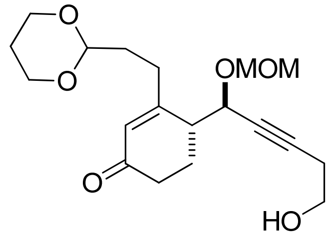
MOM ether 22: To a stirred solution of alcohol **21** (30 g, 0.097 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added *i*-Pr_2NEt (85.3 mL, 0.49 mol) and MOMCl (22.6 mL, 0.29 mol). The resulting mixture was warmed to room temperature and stirred for 12 h before it was quenched with $NaHCO_3$ (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4)



22

and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 12:1) afforded MOM ehter **22** (32.4 g, 95%) as a light yellow oil. **22**: R_f = 0.50 (hexanes:EtOAc 4:1); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.03–6.88 (m, 1 H), 6.00 (d, *J* = 10.1 Hz, 1 H), 5.05–5.00 (m, 1 H), 4.94 (d, *J* = 6.7 Hz, 1 H), 4.58 (d, *J* = 6.7 Hz, 1 H), 3.66 (t, *J* = 7.1 Hz, 2 H), 3.35 (s, 3 H), 2.68 (dt, *J* = 12.1, 4.7 Hz, 1 H), 2.47–2.33 (m, 4 H), 2.26 (ddd, *J* = 12.9, 8.4, 4.2 Hz, 1 H), 2.20–2.05 (m, 1 H), 0.86 (s, 9 H), 0.03 ppm (s, 6 H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 197.7, 150.2, 129.7, 94.1, 84.7, 76.9, 64.9, 61.8, 55.7, 51.3, 25.8 (3C), 25.2, 23.7, 23.1, 18.2, -5.3 ppm (2C); HRMS(ESI): calcd for $C_{19}H_{33}O_4Si^+[M+H^+]$ 353.2143, found 353.2146.

Enone 24: To a stirred solution of MOM ether **22** (6.0 g, 0.017 mol) in THF (20 mL) at –20 °C was added **23** (0.65M in THF, 41.3 mL, 0.026 mol). The resulting mixture was stirred for 0.5 h before it was quenched with NH$_4$Cl (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried (Na$_2$SO$_4$) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded the crude alcohol as a colorless oil, which was used directly without further purification.

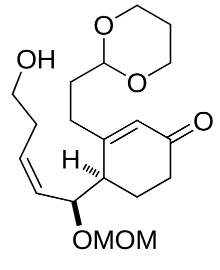


24

To a stirred solution of the alcohol (crude, obtained above) in CH$_2$Cl$_2$ (20 mL) at room temperature was added silica gel (7.25 g) and pyridinium chloroformate (7.25 g, 0.034 mol). After stirring for 12 h, the resulting mixture was quenched with Et$_2$O (100 mL). The resulting mixture was stirred for further 0.5 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded the crude enone as a yellow oil, which was used directly without further purification.

To a stirred solution of the enone (crude, obtained above) in THF/H_2O (20:1, v/v, 20 mL) at room temperature was added *n*-$Bu_4NF\cdot 3H_2O$ (4.1 g, 13.0 mmol). The resulting mixture was stirred for 2 h before it was quenched with NH_4Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo.* Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone **24** (3.0 g, 50% over the three steps) as a colorless oil. **24**: $R_f = 0.25$ (hexanes:EtOAc 1:1); IR (film) ν_{max} 3785, 3461, 2950, 2854, 2361, 2232, 1663, 1379, 1335, 1246, 1145, 1032, 900, 853, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.94$ (s, 1 H), 4.95 (d, *J* = 6.8 Hz, 1 H), 4.64 (dd, *J* = 16.4, 6.2 Hz, 2 H), 4.55 (t, *J* = 4.6 Hz, 1 H), 4.09 (d, *J* = 7.8 Hz, 2 H), 3.74 (t, *J* = 11.1 Hz, 2 H), 3.67 (dd, *J* = 11.6, 5.7 Hz, 2 H), 3.36 (s, 3 H), 2.77–2.58 (m, 2 H), 2.47 (dd, *J* = 15.3, 8.0 Hz, 4 H), 2.36–2.23 (m, 2 H), 2.21–1.99 (m, 4 H), 1.87–1.75 (m, 1 H), 1.34 ppm (d, *J* = 13.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 199.6$, 164.3, 127.4, 101.1, 94.3, 85.7, 78.2, 67.4, 66.9 (2C), 60.9, 55.9, 43.0, 34.6, 32.6, 30.4, 25.7, 24.4, 23.2 ppm; HRMS(ESI): calcd for $C_{19}H_{29}O_6^+[M+H^+]$ 353.1959, found 353.1963.

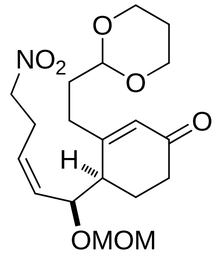
Alkene 25: To a stirred solution of alkyne **24** (1.2 g, 3.4 mmol) in toluene (20 mL) at room temperature was added $Pd/CaCO_3$ (300 mg). The resulting mixture was stirred under the hydrogen atmosphere for 0.5 h



25

before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded alkene **25** (1.2 g, 100%) as a colorless oil. **25**: R_f = 0.25 (hexanes:EtOAc 1:1); IR (film) ν_{max} 3459, 2950, 2861, 2732, 2361, 1662, 1347, 1283, 1211, 1143, 1080, 1027, 971, 898, 752, 641 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.89 (s, 1 H), 5.79 (td, *J* = 9.9, 6.3 Hz, 1 H), 5.36 (t, *J* = 10.5 Hz, 1 H), 4.72 (d, *J* = 6.8 Hz, 1 H), 4.61–4.51 (m, 2 H), 4.45 (d, *J* = 6.8 Hz, 1 H), 4.08 (dd, *J* = 11.0, 3.9 Hz, 2 H), 3.71 (dd, *J* = 31.1, 19.3 Hz, 4 H), 3.26 (s, 3 H), 2.60–2.34 (m, 5 H), 2.32–2.18 (m, 2 H), 2.09–1.96 (m, 3 H), 1.83 (dd, *J* = 13.6, 9.5 Hz, 2 H), 1.74 (dd, *J* = 9.0, 5.4 Hz, 1 H), 1.33 ppm (d, *J* = 13.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 168.5, 133.3, 129.7, 126.0, 101.3, 93.0, 73.0, 66.9 (2C), 61.8, 55.4, 42.3, 33.8, 32.7, 32.4, 31.4, 25.7, 25.0 ppm; HRMS(ESI): calcd for $C_{19}H_{31}O_6^+[M+H^+]$ 355.2115, found 355.2116.

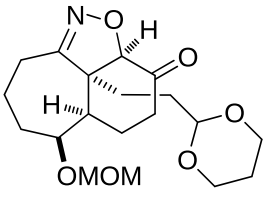
Nitro compound 26: To a stirred solution of alcohol **25** (0.99 g, 2.8 mmol) in CH_2Cl_2 (10 mL) at 0 °C were added PPh_3 (1.1 g, 4.2 mmol), imidazole (0.29 g, 4.2 mmol) and iodine (1.1 g, 4.2 mmol). The resulting mixture was warmed to room temperature and stirred for 4 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded the crude iodide as a corless oil, which was used directly without further purification.



26

To a stirred solution of iodide (crude, obtained above) in Et_2O/H_2O (1:3, v/v, 10 mL) at room temperature was added $AgNO_2$ (1.73 g, 11.2 mmol). The resulting mixture was stirred for 12 h before it was filtered through a short pad of celite. The filtrate was extracted with Et_2O (3 × 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) afforded **26** (676 mg, 63% over the two steps) as a colorless oil. **26**: $R_f = 0.50$ (hexanes:EtOAc 2:1); IR (film) ν_{max} 3778, 3492, 2951, 2857, 2733, 2361, 1665, 1622, 1551, 1431, 1378, 1283, 1247, 1210, 1143, 1082, 1027, 898, 745, 642 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.92 (s, 1 H), 5.74–5.62 (m, 1 H), 5.44 (t, *J* = 10.4 Hz, 1 H), 4.64–4.51 (m, 3 H), 4.49–4.37 (m, 3 H), 4.09 (dd, *J* = 11.4, 4.2 Hz, 2 H), 3.74 (td, *J* = 12.1, 2.0 Hz, 2 H), 3.26 (s, 3 H), 2.82 (qd, *J* = 15.2, 7.8 Hz, 2 H), 2.59–2.45 (m, 3 H), 2.36 (dd, *J* = 11.0, 6.1 Hz, 2 H), 2.02 (dtd, *J* = 12.6, 9.5, 4.5 Hz, 3 H), 1.84 (ddd, *J* = 15.0, 10.3, 5.3 Hz, 1 H), 1.79–1.69 (m, 1 H), 1.34 ppm (d, *J* = 12.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 167.6, 131.6, 129.2, 126.4, 101.2, 93.1, 74.5, 72.2, 66.9 (2C), 55.5, 42.3, 33.8, 32.7, 32.3, 25.7, 25.7, 24.8 ppm; HRMS(ESI): calcd for $C_{19}H_{30}NO_7^+$[M+H$^+$] 384.2017, found 384.2021.

Tricyclic isoxazoline 28: To a stirred solution of nitro compound **26** (532 mg, 1.39 mmol) in toluene (20 mL) at room temperature was added PhNCO (1.5 mL, 13.9 mmol) and Et_3N (0.19 mL, 1.39 mmol). The resulting mixture was stirred at 90 °C for 5 h before it was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded tricyclic isoxazoline **27** (315 mg, 65%) as a white solid, which was used immediately in the next step due to its instability.



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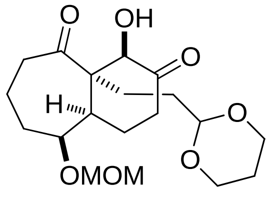
To a stirred solution of tricyclic isoxazoline **27** (315 mg, 0.90 mmol) in EtOAc (10 mL) at room temperature was added Pd/C (10% wt/wt, 20 mg). The resulting mixture was stirred under hydrogen atmosphere (1 atm) for 1 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded tricyclic isoxazoline **28** (284 mg, 90%) as a colorless oil. **28**: R_f = 0.25 (hexanes:EtOAc 1:1); IR (film) ν_{max} 3877, 3660, 2930, 2857, 2361, 2248, 1726, 1670, 1446, 1407, 1379, 1326, 1239, 1216, 1143, 1081, 1022, 919, 899, 735, 697, 646 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 4.61 (d, *J* = 7.0 Hz, 1 H), 4.55 (dd, *J* = 7.7, 3.9 Hz, 2 H), 4.30 (s, 1 H), 4.08 (dd, *J* = 11.2, 4.5 Hz, 2 H), 3.85 (d, *J* = 8.5 Hz, 1 H), 3.74 (t, *J* = 11.5 Hz, 2 H), 3.35 (s, 3 H), 2.74 (ddd, *J* = 15.2, 11.1, 5.2 Hz, 2 H), 2.42–2.28 (m, 2 H), 2.24 (d, *J* = 9.5 Hz, 1 H), 2.05 (ddd, *J* = 20.3, 12.6, 7.7 Hz, 1 H), 1.97–1.88 (m, 2 H), 1.88–1.78 (m, 3 H), 1.78–1.66 (m, 4 H), 1.53–1.41 (m, 1 H), 1.33 ppm (d, *J* = 13.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.7, 161.0, 101.0, 95.5, 88.0, 77.9, 66.9 (2C), 63.1, 56.0, 43.3, 36.2, 30.3, 29.5, 29.0, 25.7, 24.2, 21.1, 20.4 ppm; HRMS(ESI): calcd for $C_{19}H_{30}NO_6^+[M+H^+]$ 368.2068, found 368.2069.

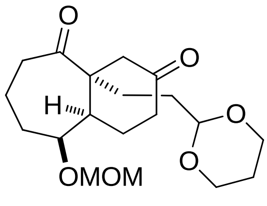
Hydroxyl ketone 29: To a stirred solution of isoxazoline **28** (570 mg, 1.63 mmol) in $MeCN/H_2O$ (10:1, v/v, 50 mL) at room temperature was added $Mo(CO)_6$ (517 mg, 1.94 mmol). The resulting mixture was heated to 90 °C and stirred for 1.5 h before it was filtered through a short pad of celite. The filtrate was extracted with Et_2O (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash



29

column chromatography (silica gel, hexanes:EtOAc 2:1) afforded hydroxyl ketone **29** (413 mg, 72%) as a colorless oil. **29**: R_f = 0.50 (CH_2Cl_2:Et_2O 1:1); IR (film) ν_{max} 3914, 3490, 2951, 2857, 2361, 2248, 1719, 1689, 1547, 1405, 1380, 1279, 1243, 1141, 1093, 1033, 912, 863, 843, 731, 696, 647 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.73 (d, *J* = 6.9 Hz, 1 H), 4.68 (d, *J* = 6.9 Hz, 1 H), 4.65–4.59 (m, 1 H), 4.19–4.00 (m, 4 H), 3.84–3.72 (m, 3 H), 3.67 (d, *J* = 4.9 Hz, 1 H), 3.40 (s, 3 H), 2.68 (dd, *J* = 16.2, 7.0 Hz, 1 H), 2.60 (dd, *J* = 15.5, 4.0 Hz, 1 H), 2.50–2.37 (m, 2 H), 2.31 (d, *J* = 12.9 Hz, 1 H), 2.26–2.10 (m, 4 H), 2.07 (dd, *J* = 11.1, 6.2 Hz, 1 H), 1.97–1.82 (m, 3 H), 1.56–1.42 (m, 2 H), 1.35 ppm (d, *J* = 13.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.8, 208.2, 101.9, 96.0, 77.4, 76.9, 67.1 (2C), 62.7, 55.7, 41.8, 41.1, 36.9, 29.0, 28.9, 25.9, 22.7, 20.7, 20.6 ppm ; HRMS(ESI): calcd for $C_{19}H_{31}O_7^+[M+H^+]$ 371.2064, found 371.2063.

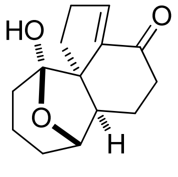
Ketone 30: To a stirred solution of hydroxyl ketone **29** (336 mg, 0.95 mmol) in CH_2Cl_2 (30 mL) at 0 °C were added Et_3N (0.65 mL, 4.68 mmol), Ac_2O (0.45 mL, 4.71 mmol) and DMAP (23 mg, 0.19 mmol). The resulting mixture was allowed to warmed to room temperature and stirred for 1 h before it was quenched with $NaHCO_3$ (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) afforded the crude acetate as a colorless oil, which was used directly without further purification.



30

To a stirred solution of acetate (crude, obtained above) in THF/MeOH (2:1, v/v, 15 mL) at –78 °C was added SmI_2[3] (0.1M in THF, 24 mL, 2.40 mmol). The resulting mixture was stirred for 15 min before it was quenched with NH_4Cl (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded ketone **30** (253 mg, 79%) as a colorless oil. **30**: $R_f = 0.50$ (hexanes:EtOAc 1:1); IR (film) ν_{max} 3912, 3789, 3637, 3490, 2945, 2885, 2361, 1708, 1463, 1407, 1379, 1239, 1215, 1144, 1097, 1077, 1036, 919, 884, 854, 744, 699, 644 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.69 (d, J = 6.9 Hz, 1 H), 4.64 (d, J = 6.9 Hz, 1 H), 4.47 (t, J = 4.4 Hz, 1 H), 4.17–3.99 (m, 3 H), 3.72 (t, J = 11.6 Hz, 2 H), 3.38 (s, 3 H), 2.84 (d, J = 15.2 Hz, 1 H), 2.71 (d, J = 14.8 Hz, 1 H), 2.59–2.36 (m, 2 H), 2.24–2.13 (m, 3 H), 2.11–1.94 (m, 3 H), 1.91–1.63 (m, 7 H), 1.37–1.27 ppm (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 213.0, 209.8, 101.3, 95.5, 79.1, 66.8 (2C), 56.0, 55.9, 47.0, 44.9, 41.1, 38.8, 31.1, 30.2, 29.5, 25.7, 24.2, 20.9 ppm; HRMS(ESI): calcd for $C_{19}H_{31}O_6^+[M+H^+]$ 355.2115, found 355.2117.

Core structure 4: To a stirred solution of ketone **30** (206 mg, 0.61 mmol) in THF (15 mL) at room temperature was added HCl (10% wt/wt, aq., 15 mL). The resulting mixture was heated to reflux and stirred for 0.5 h before it was quenched with $NaHCO_3$ (100 mL, sat. aq.) The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash



4

column chromatography (silica gel, hexanes:EtOAc 1:1) afforded core structure **4** (114 mg, 80%) as a colorless oil. **4**: R_f = 0.25 (hexanes:EtOAc 1:1); IR (film)ν_{max} 3912, 3853, 3660, 3410, 2938, 2862, 2361, 2247, 1682, 1612, 1334, 1284, 1254, 1217, 1081, 1027, 1002, 967, 938, 911, 881, 856, 824, 767, 740, 642 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (s, 1 H), 4.09 (s, 1 H), 2.80 (s, 1 H), 2.61–2.50 (m, 1 H), 2.39 (tdd, *J* = 11.4, 8.1, 4.6 Hz, 3 H), 2.26 (d, *J* = 18.8 Hz, 1 H), 2.22–2.12 (m, 2 H), 2.06–1.93 (m, 1 H), 1.91–1.74 (m, 6 H), 1.48 ppm (d, *J* = 10.0 Hz, 1 H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 200.1, 145.6, 143.6, 105.1, 78.3, 61.3, 45.8, 34.6 (2C), 33.4, 30.6, 29.2, 24.9, 17.7 ppm; HRMS(ESI): calcd for $C_{14}H_{19}O_3^+$[M+H$^+$] 235.1329, found 235.1330.

II) Abbreviations

MOMCl	chloromethylmethyl ether
PCC	pyridinium chlorochromate
DMAP	4-dimethylaminopyridine
Dibal-H	diisobutylaluminium hydride
THF	tetrahydrofuran
Tf	trifluoromethanesulfonyl
DIPEA	*N*,*N*-Diisopropylethylamine

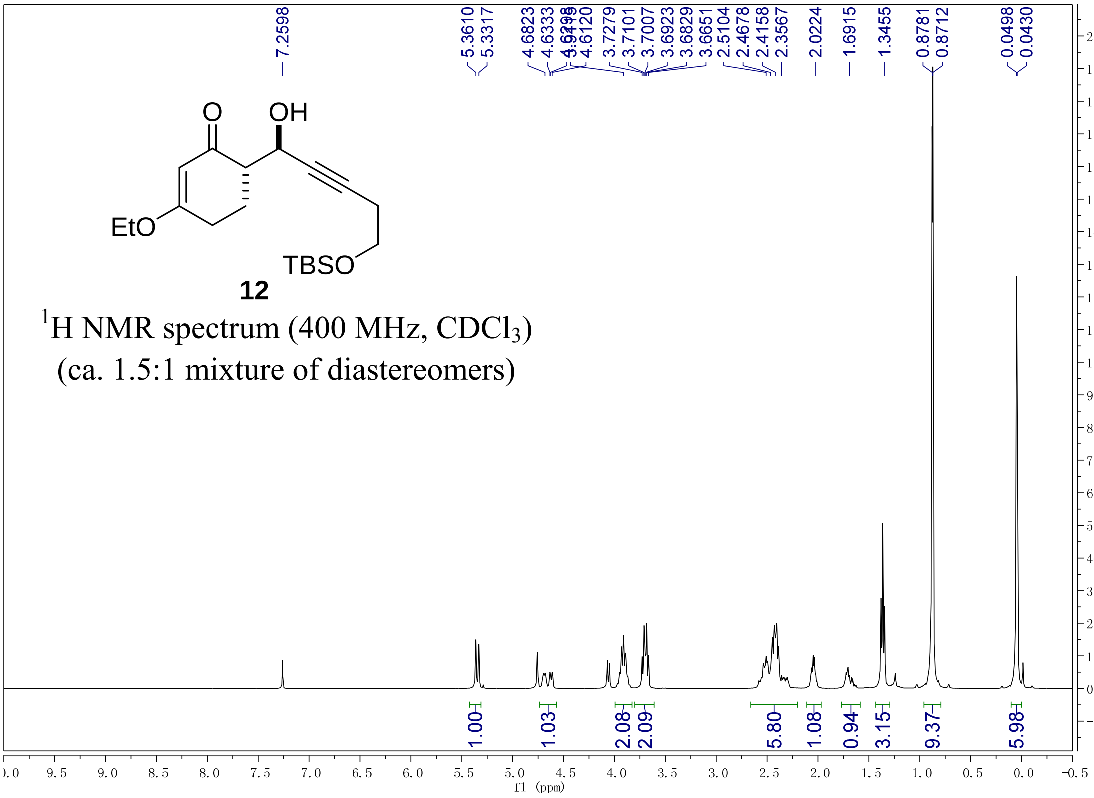
III) References

1 H. E. Zimmerman and E. E. Nesterov, *J. Am. Chem. Soc.*, 2003, **125**, 5422.

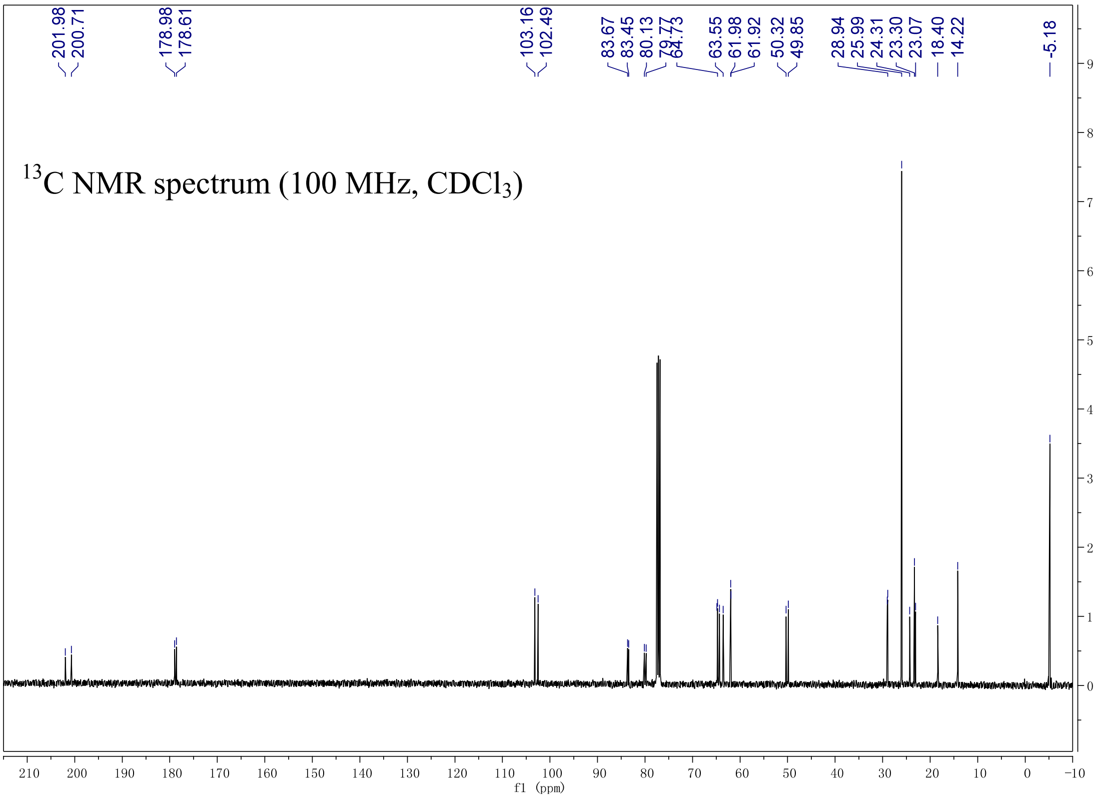
2 (*a*) C. Z. Rotsides and C. Hu, K. A. Woerpel, *Angew.Chem. Int. Ed.*, 2013, **52**, 13033; (*b*) T. Debnar, S. Dreisigacker and D. Menche, *Chem. Commun.*, 2013, **49**, 725.

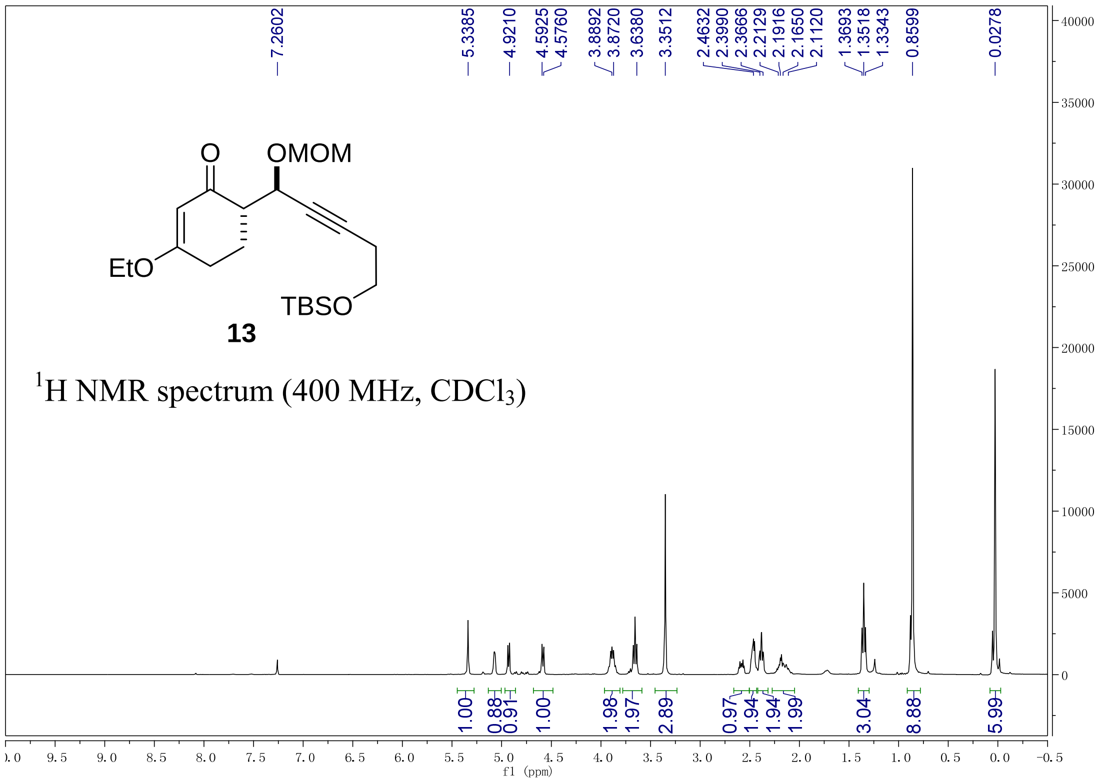
3 T. L. Fevig, R. L. Elliott and D. P. Curran, *J. Am. Chem. Soc.*, 1988, **110**, 5064.

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


12

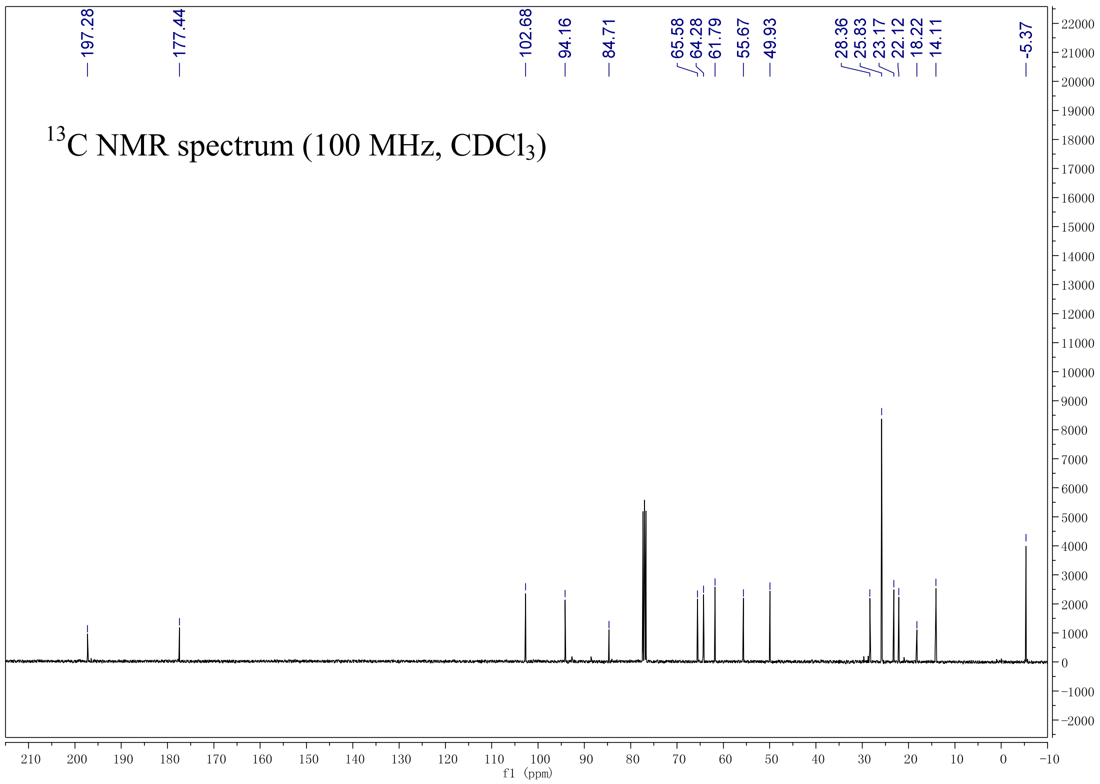
^{1}H NMR spectrum (400 MHz, $CDCl_3$)
(ca. 1.5:1 mixture of diastereomers)


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

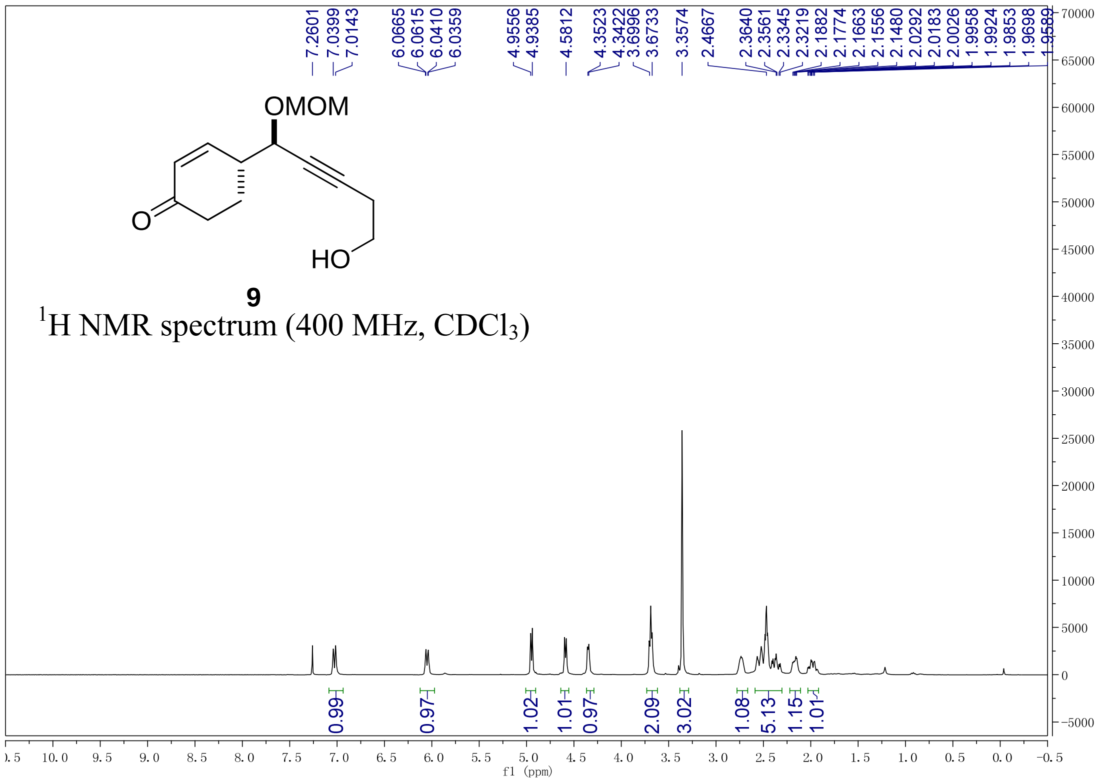


13

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

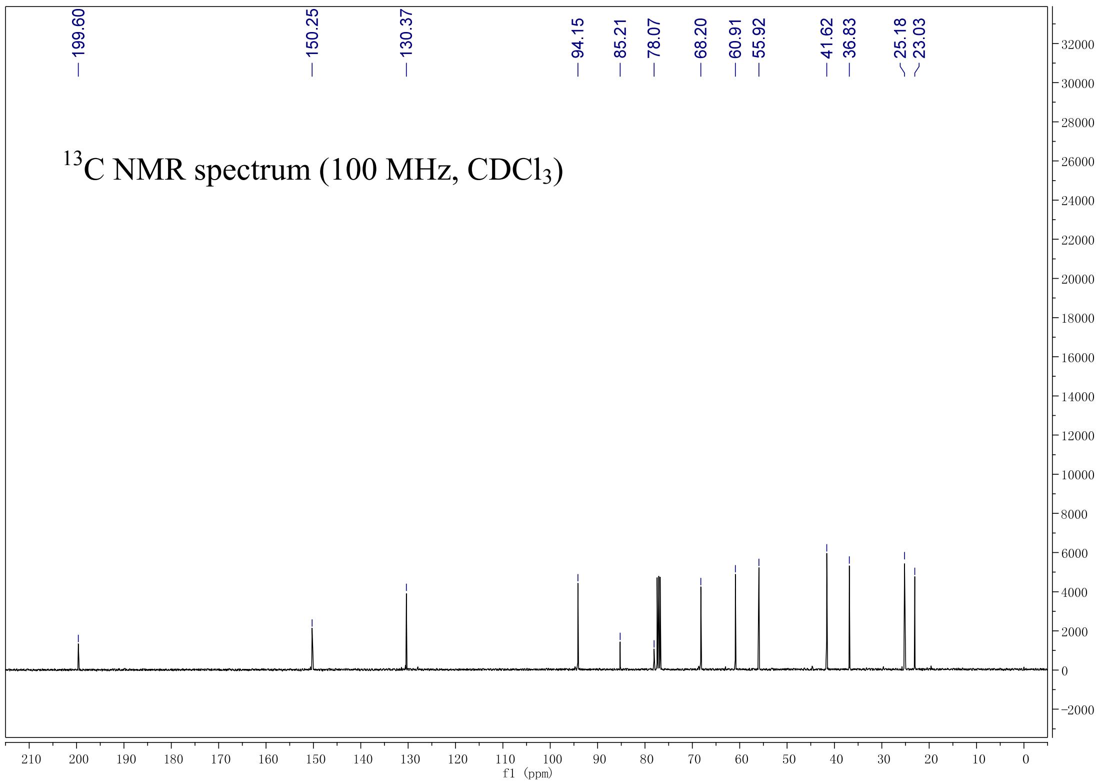


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

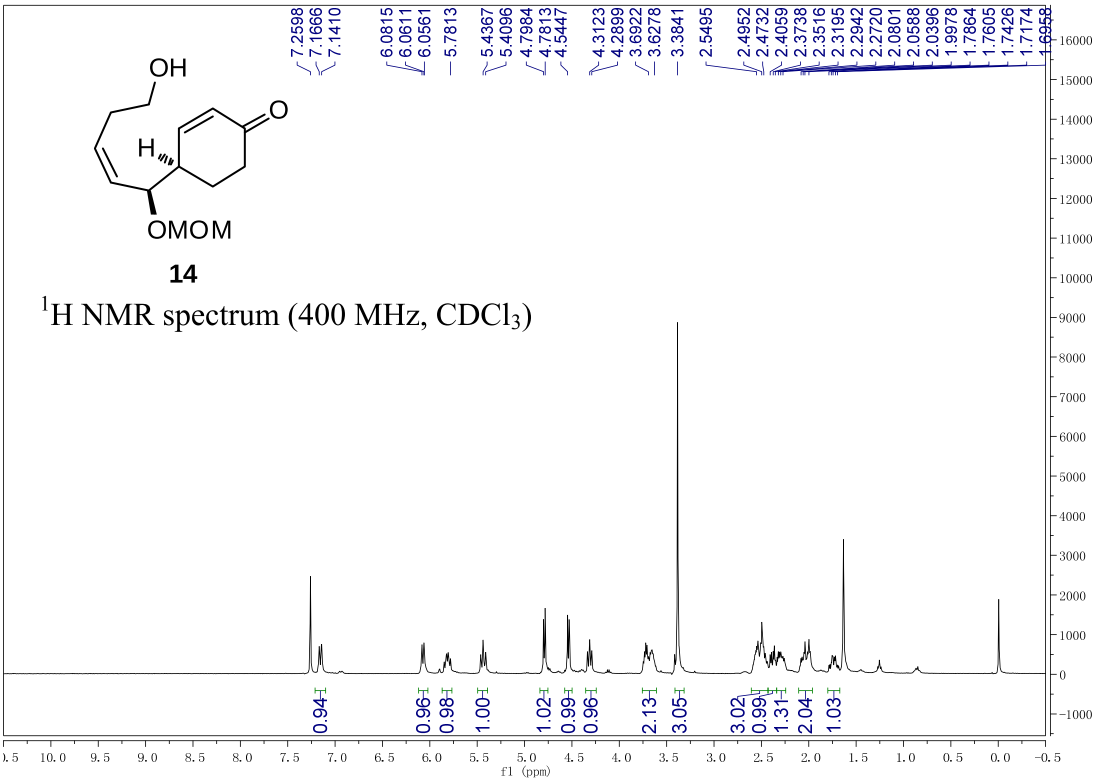


9

^{1}H NMR spectrum (400 MHz, CDCl$_3$)

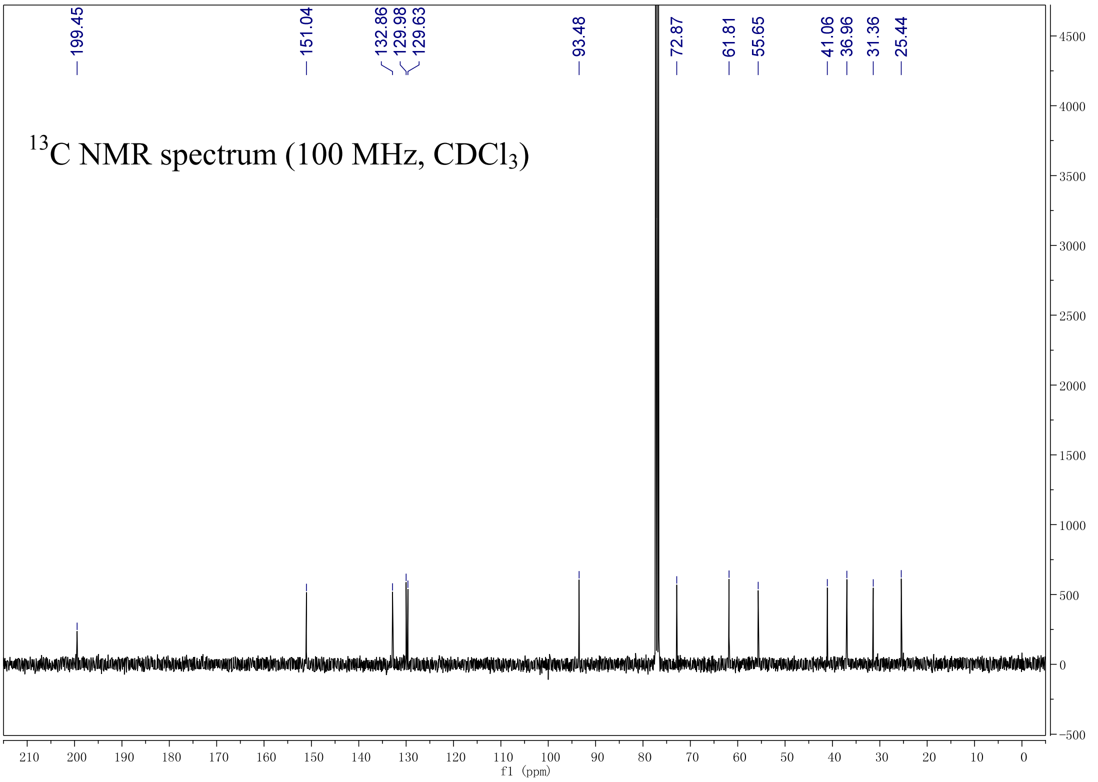


^{13}C NMR spectrum (100 MHz, CDCl$_3$)

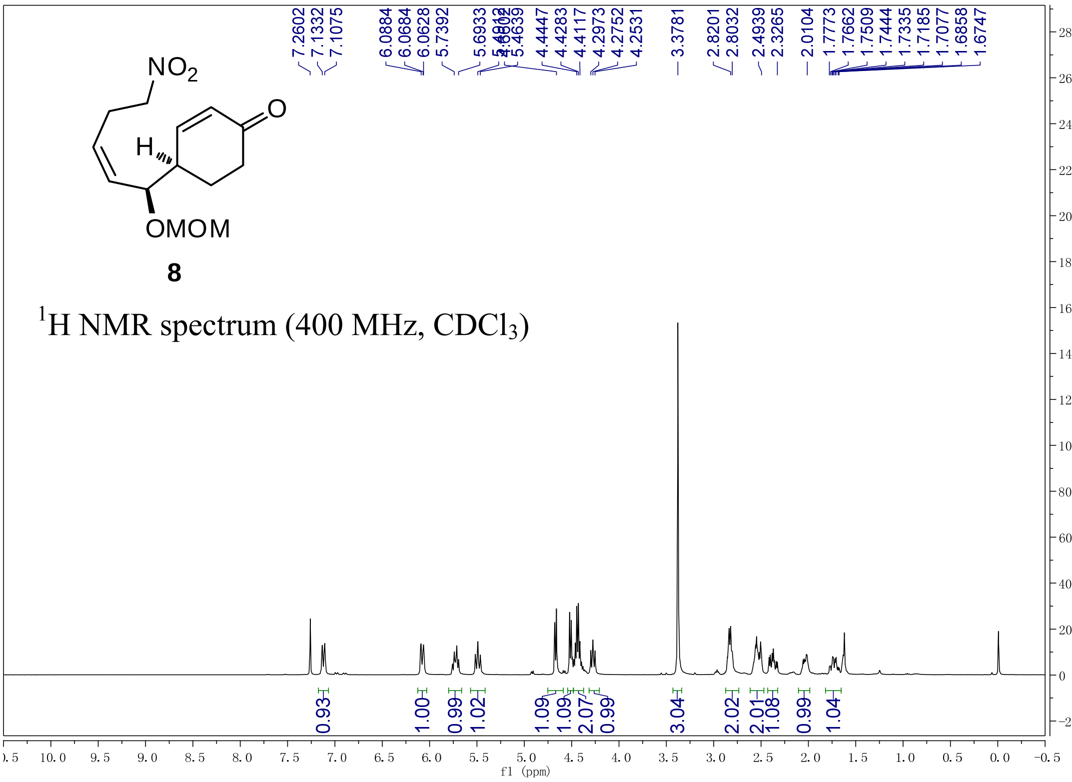


14

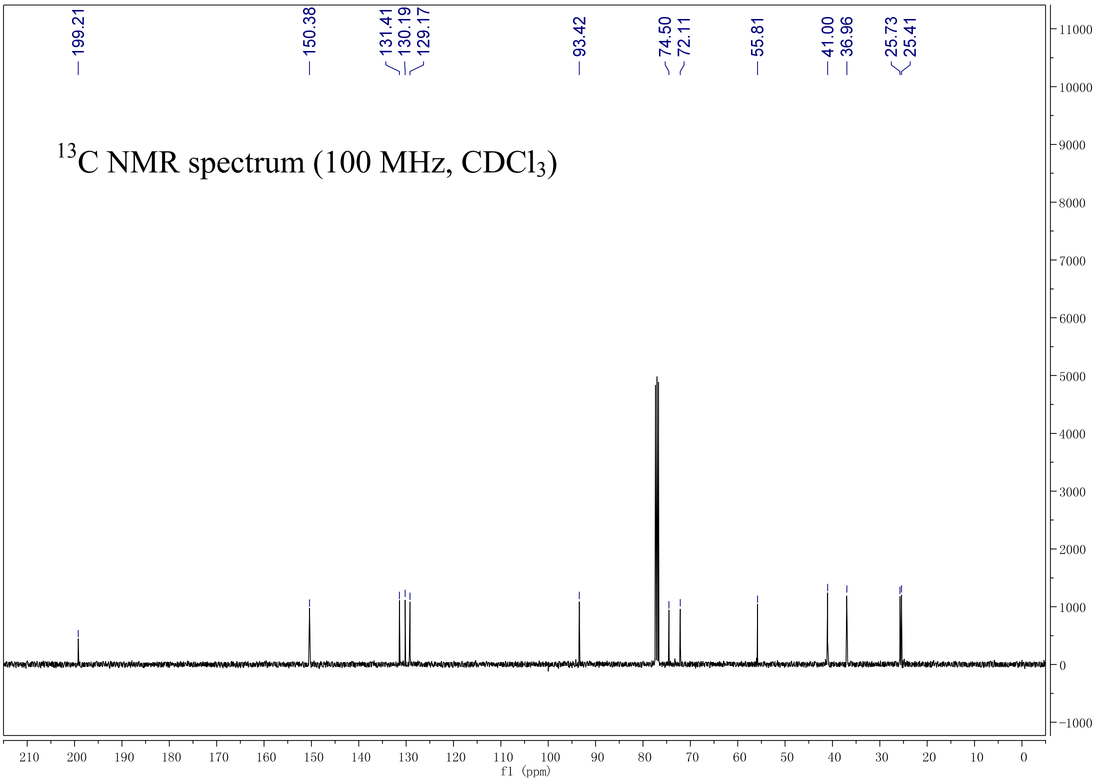
^{1}H NMR spectrum (400 MHz, CDCl$_3$)



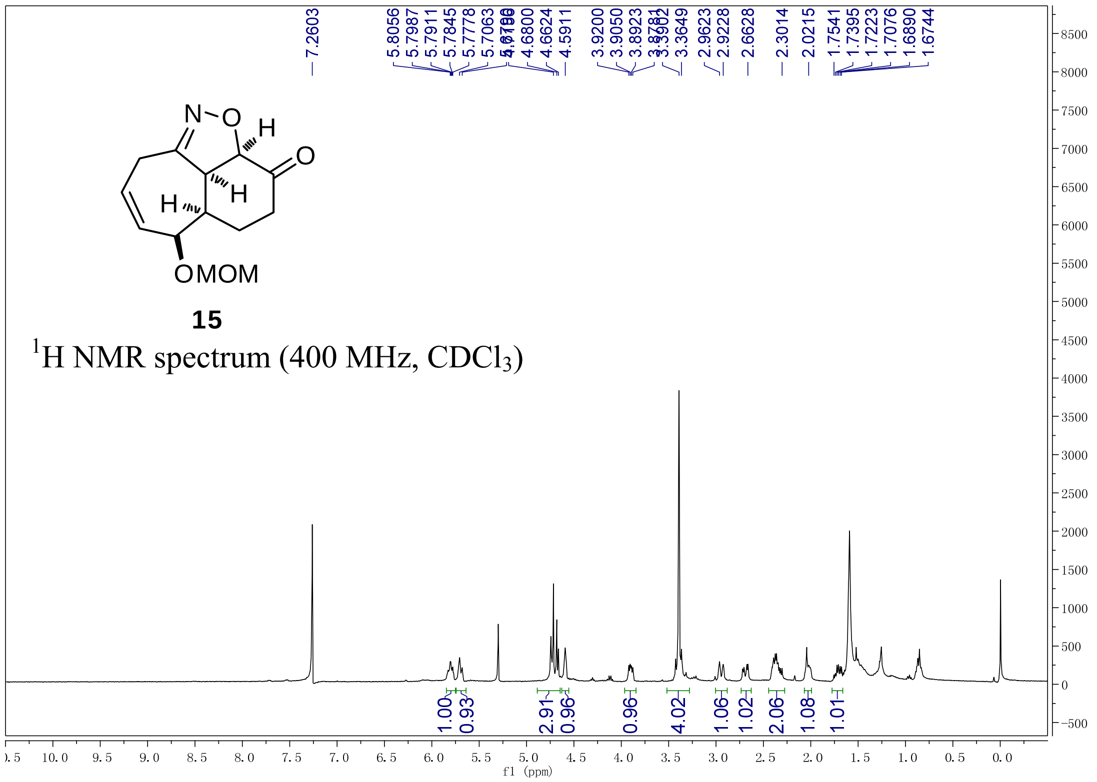
^{13}C NMR spectrum (100 MHz, CDCl$_3$)



^{1}H NMR spectrum (400 MHz, CDCl$_3$)

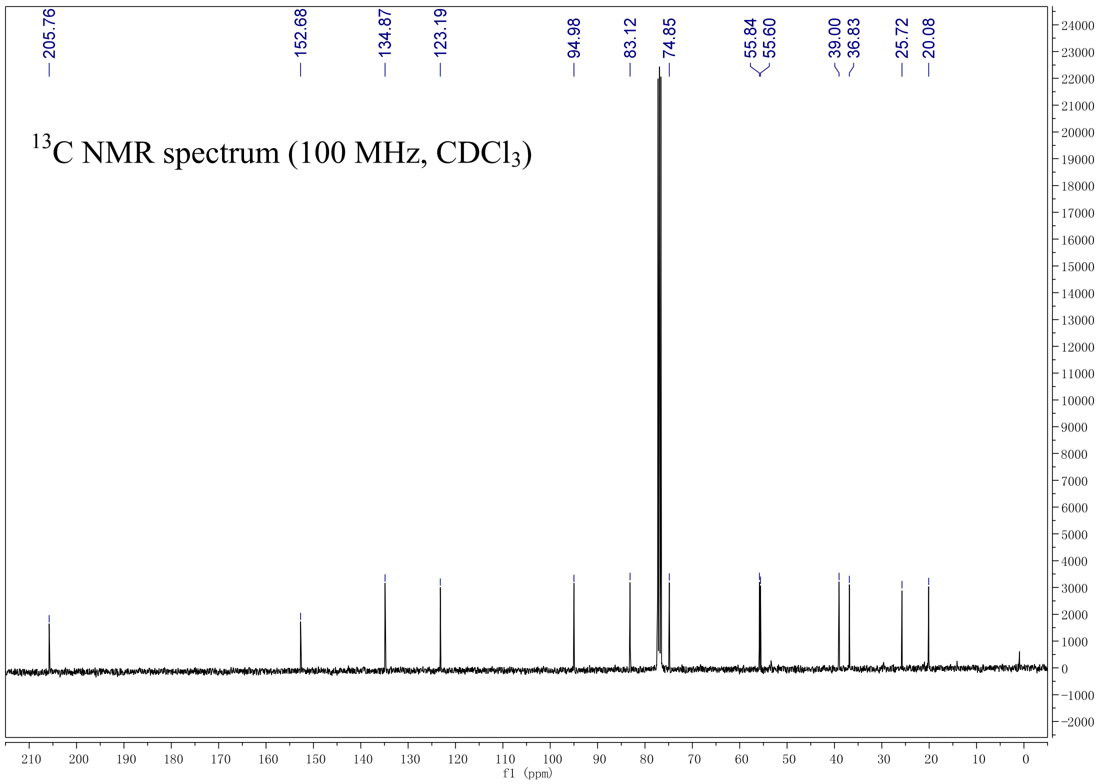


^{13}C NMR spectrum (100 MHz, CDCl$_3$)

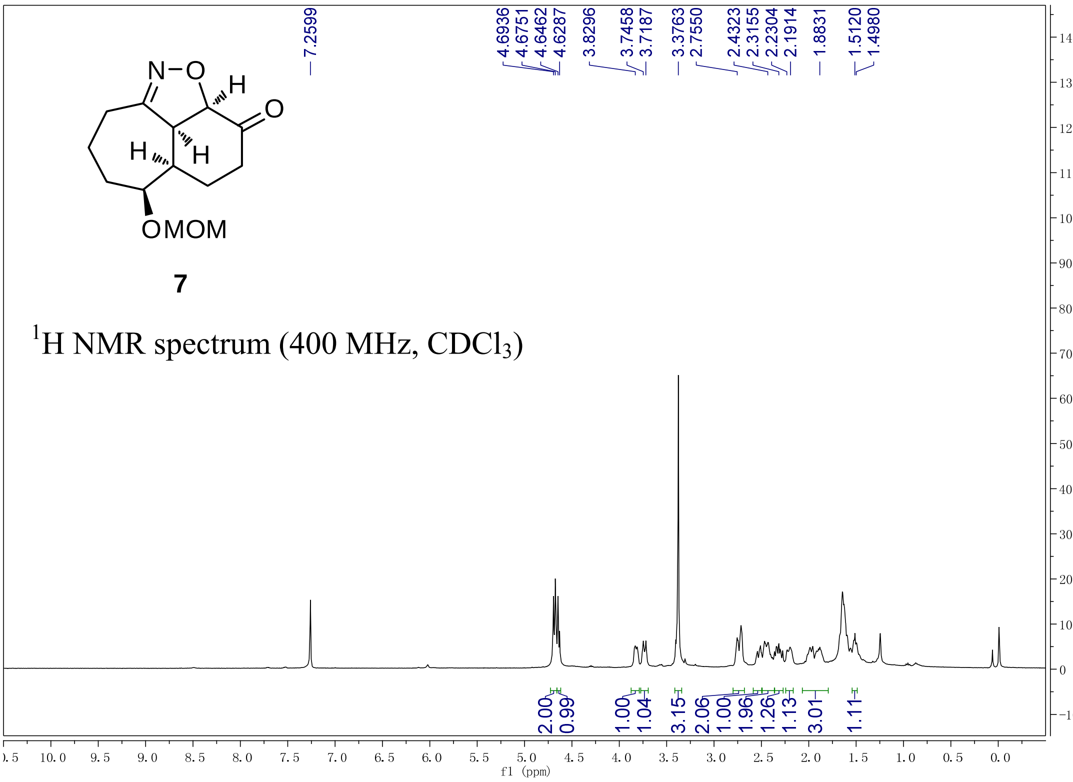


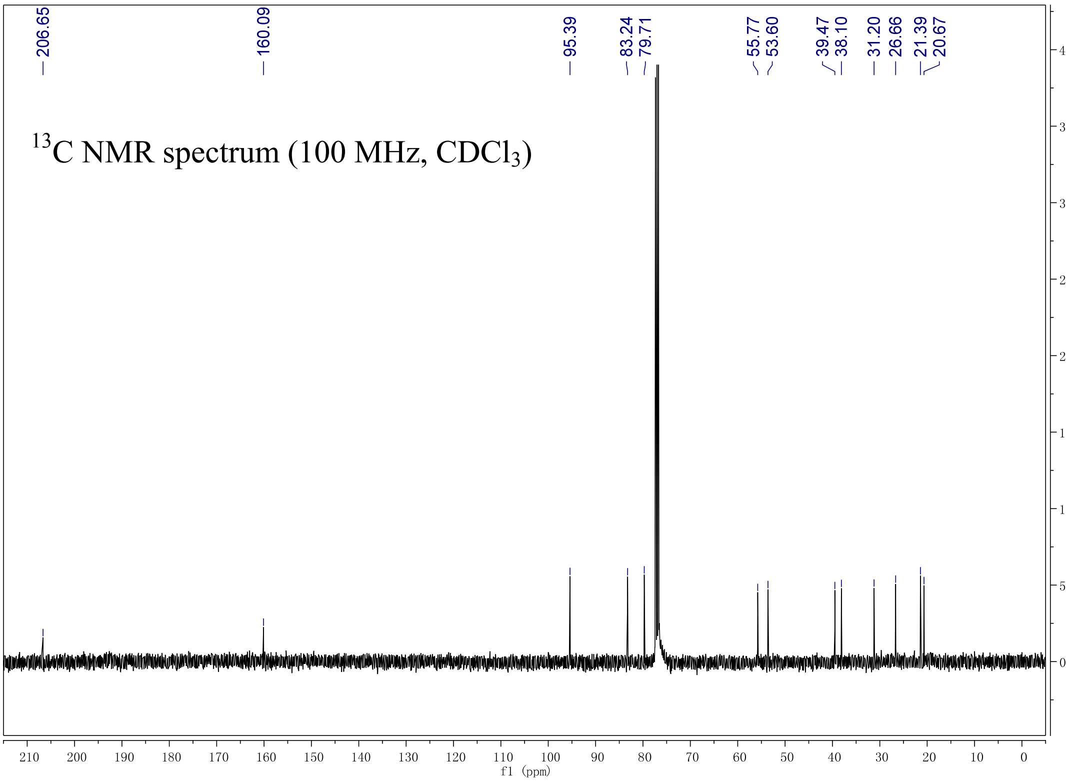
15

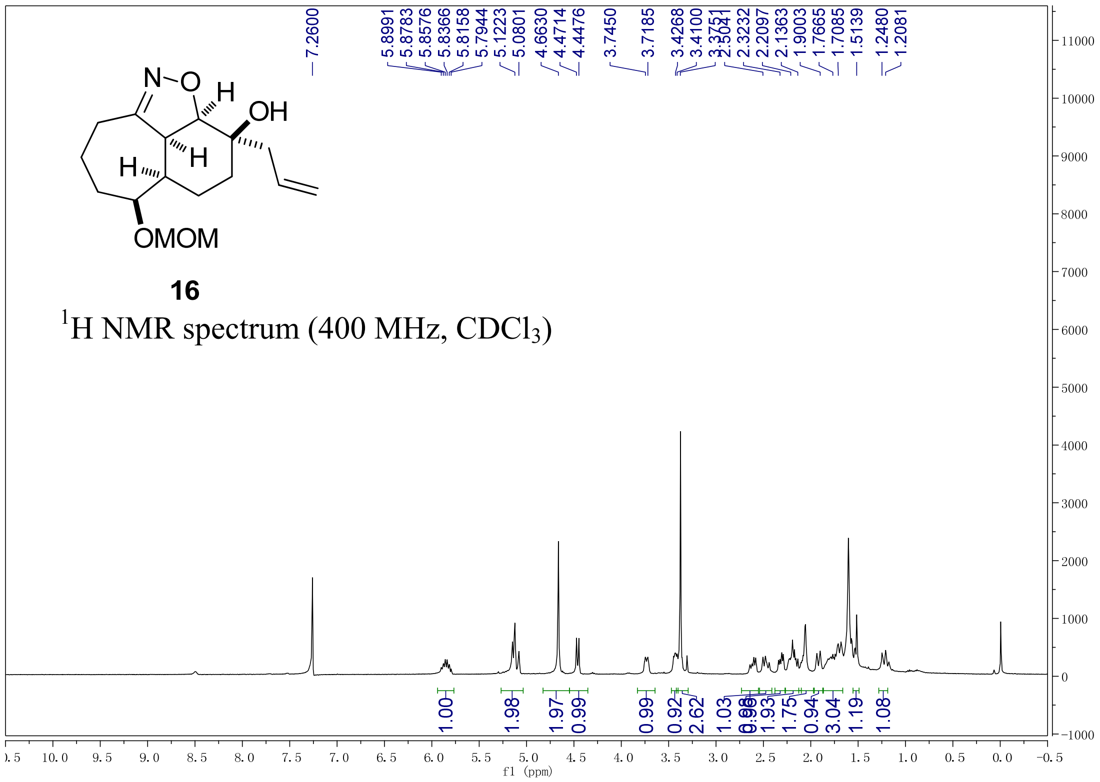
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



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

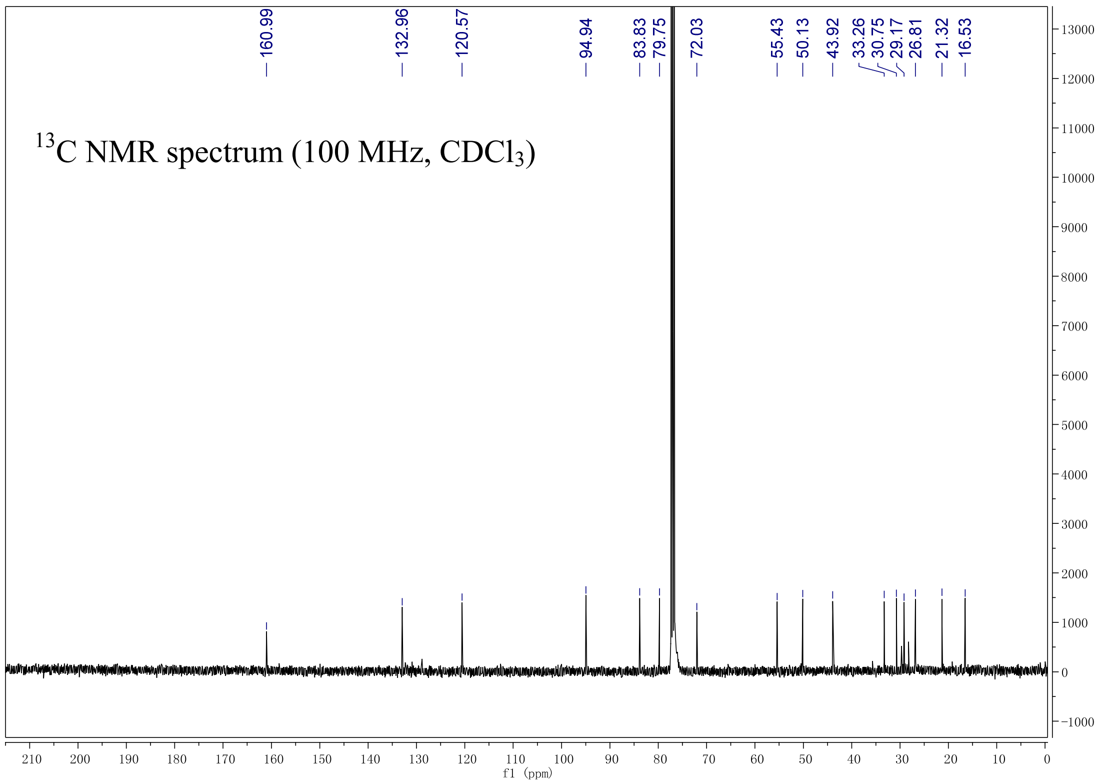

7.2599
4.6936
4.6751
4.6462
4.6287
3.8296
3.7458
3.7187
3.3763
2.7550
2.4323
2.3155
2.2304
2.1914
1.8831
1.5120
1.4980
N–O
H
O
H
H
OMOM
7
^{1}H NMR spectrum (400 MHz, CDCl$_3$)
2.00
0.99
1.00
1.04
3.15
2.06
1.00
1.96
1.26
1.13
3.01
1.11
f1 (ppm)


206.65
160.09
95.39
83.24
79.71
55.77
53.60
39.47
38.10
31.20
26.66
21.39
20.67
^{13}C NMR spectrum (100 MHz, CDCl$_3$)
f1 (ppm)

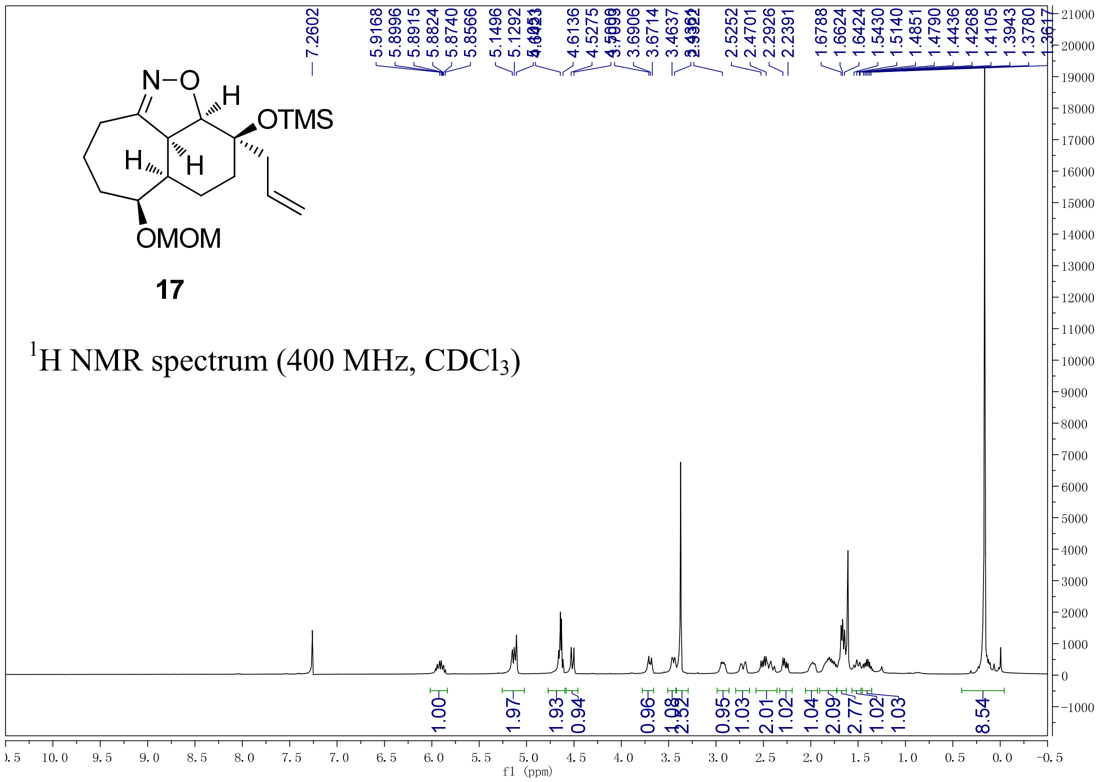


16

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

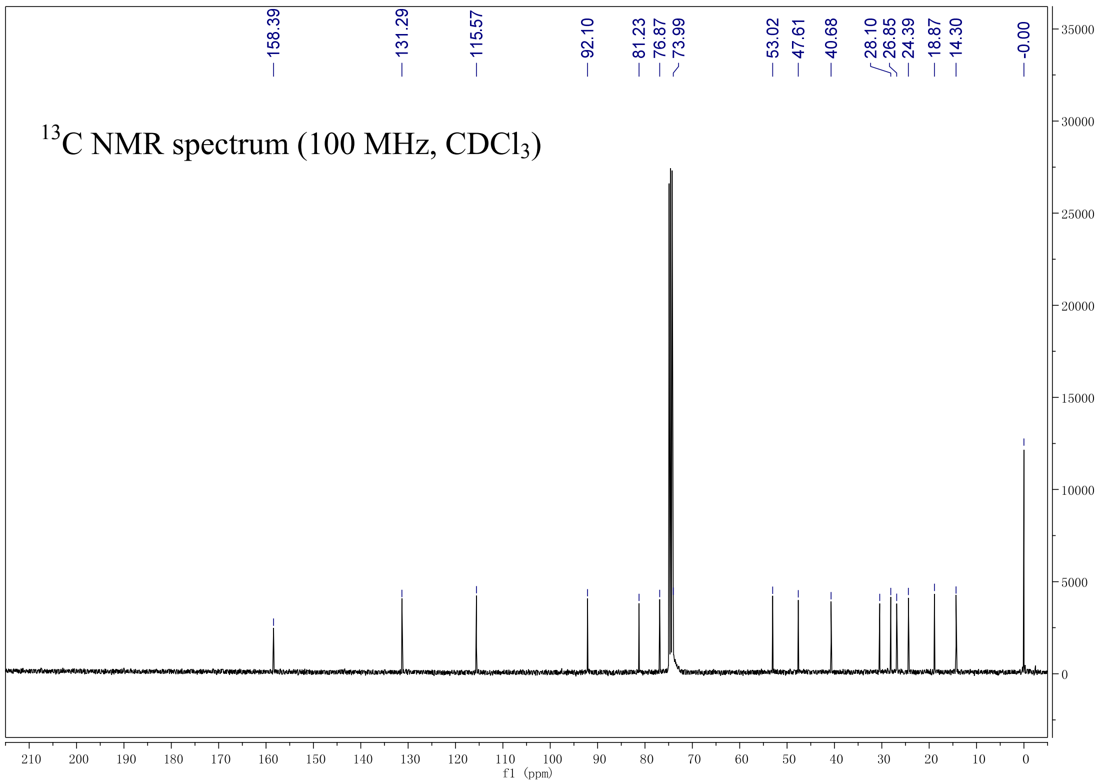


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



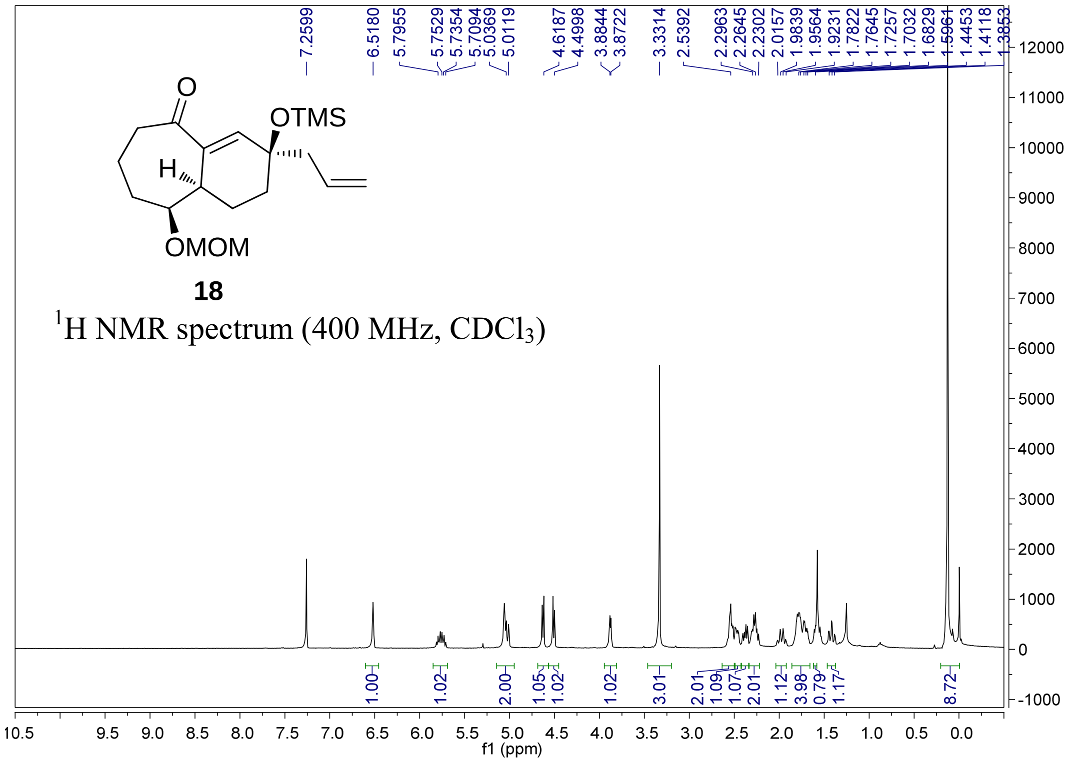
17

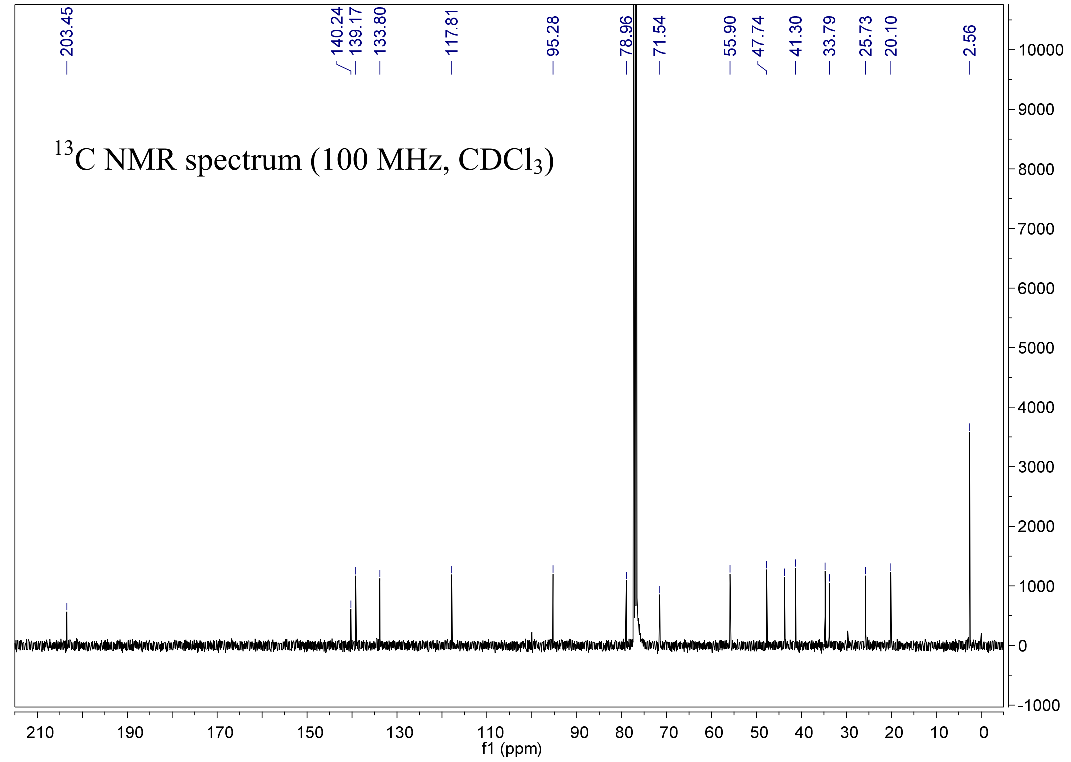
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

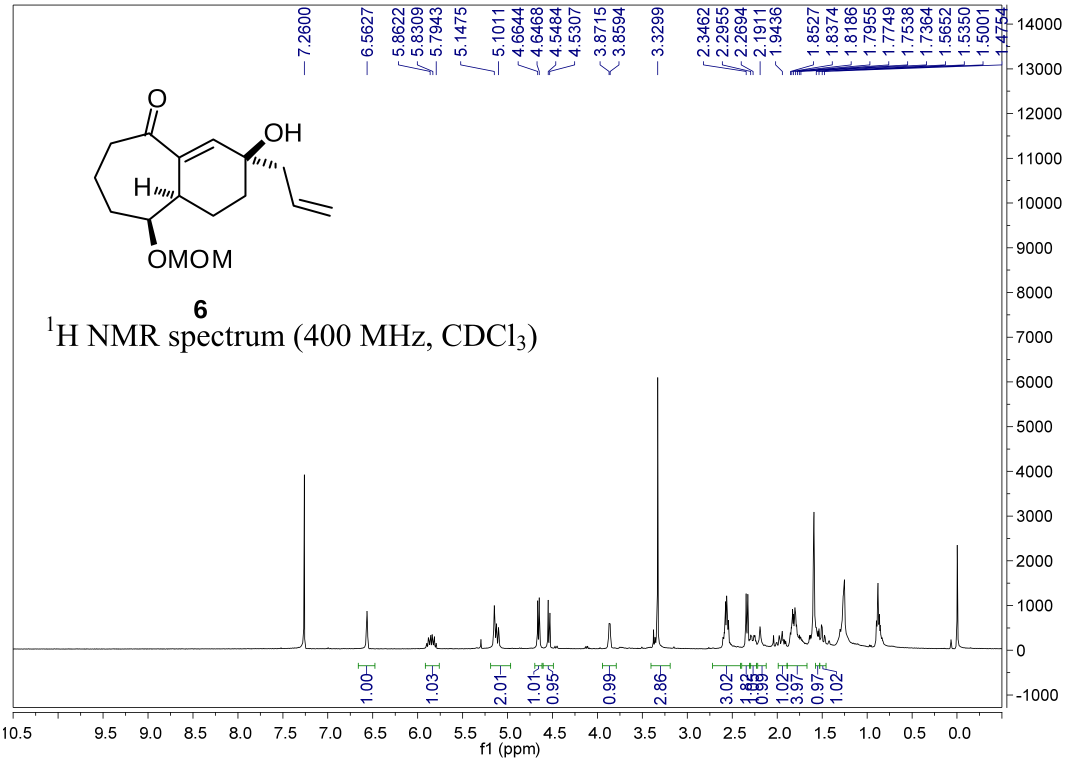


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

,

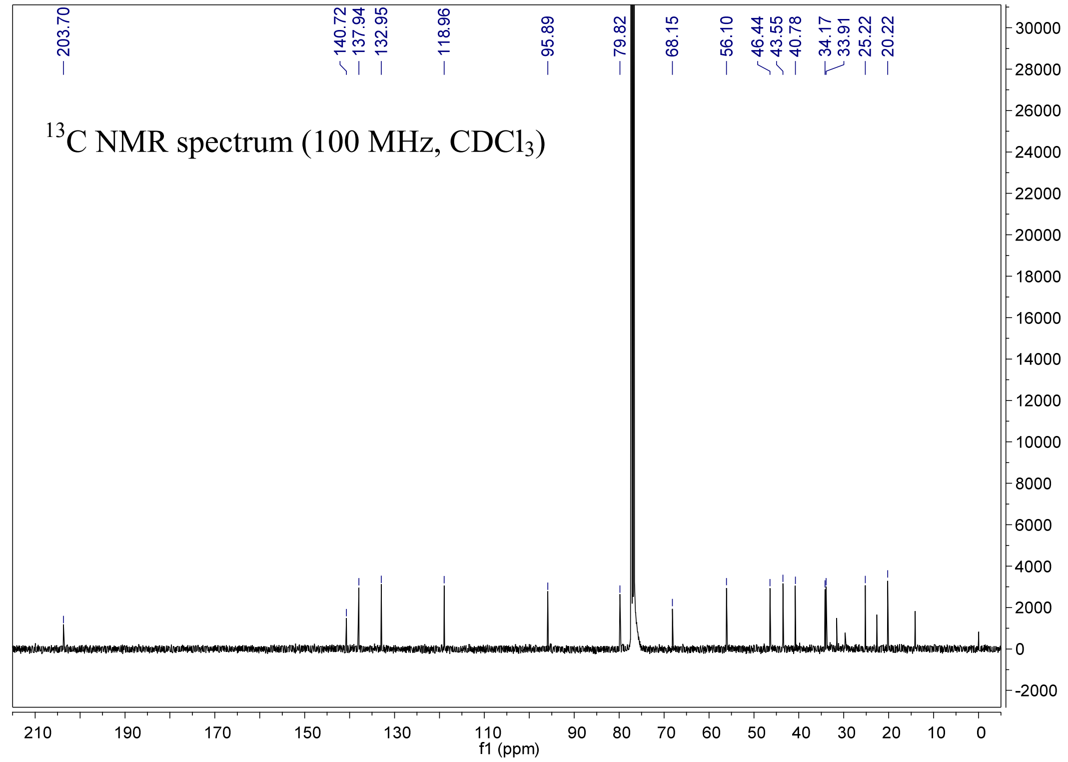

O
OTMS
H
OMOM
18
^{1}H NMR spectrum (400 MHz, CDCl$_3$)
7.2599
6.5180
5.7955
5.7529
5.7354
5.7094
5.0369
5.0119
4.6187
4.4998
3.8844
3.8722
3.3314
2.5392
2.2963
2.2645
2.2302
2.0157
1.9839
1.9564
1.9231
1.7822
1.7645
1.7257
1.7032
1.6829
1.5961
1.4453
1.4118
1.3853
1.00
1.02
2.00
1.05
1.02
1.02
3.01
2.01
1.09
1.07
2.01
1.12
3.98
0.79
1.17
8.72
f1 (ppm)


^{13}C NMR spectrum (100 MHz, CDCl$_3$)
203.45
140.24
139.17
133.80
117.81
95.28
78.96
71.54
55.90
47.74
41.30
33.79
25.73
20.10
2.56
f1 (ppm)

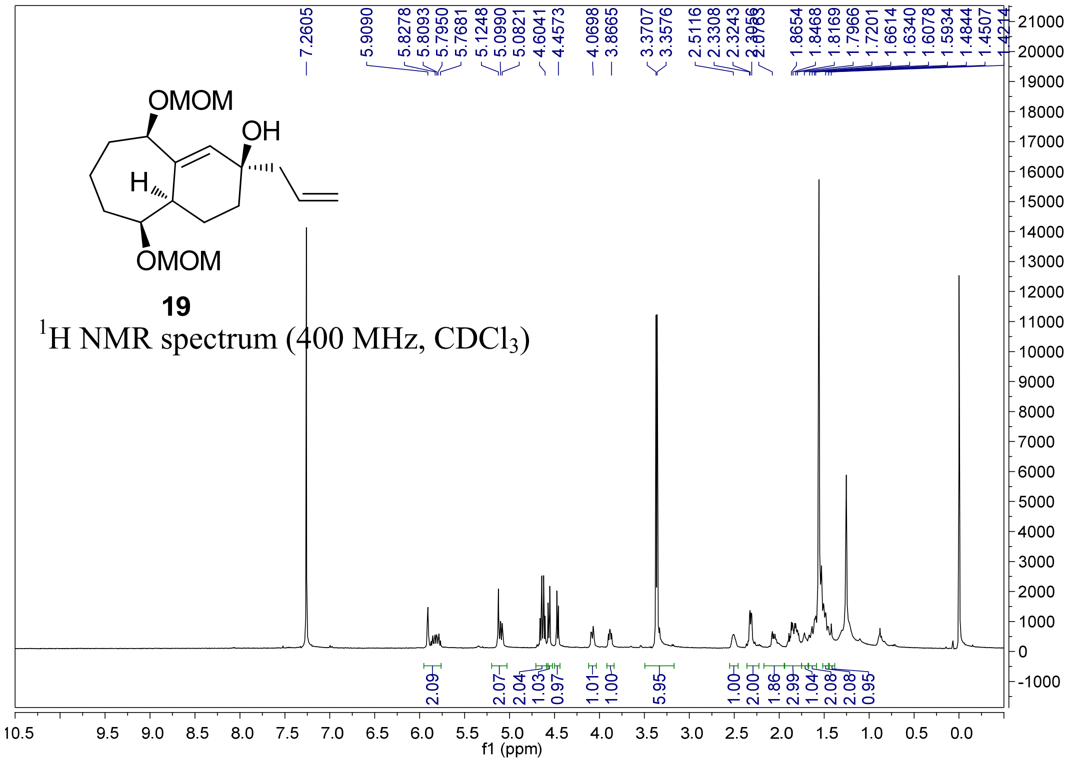


6

^{1}H NMR spectrum (400 MHz, CDCl$_3$)



^{13}C NMR spectrum (100 MHz, CDCl$_3$)


OMOM
OH
H
OMOM
19
^{1}H NMR spectrum (400 MHz, CDCl$_3$)
7.2605
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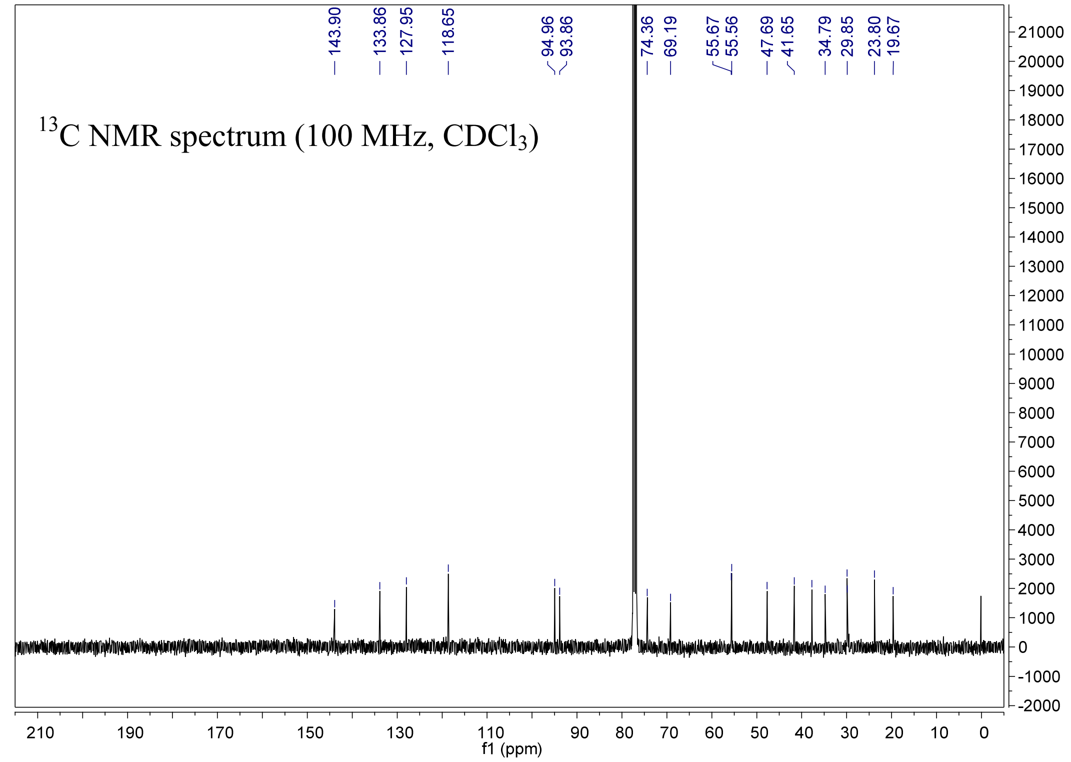
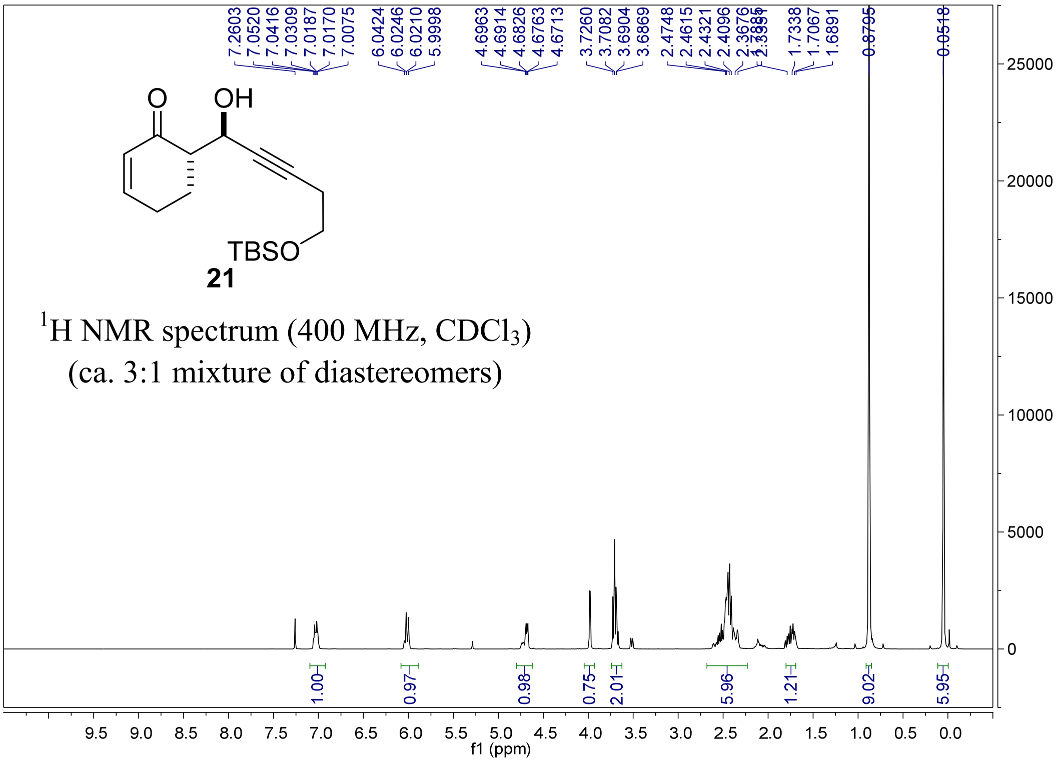
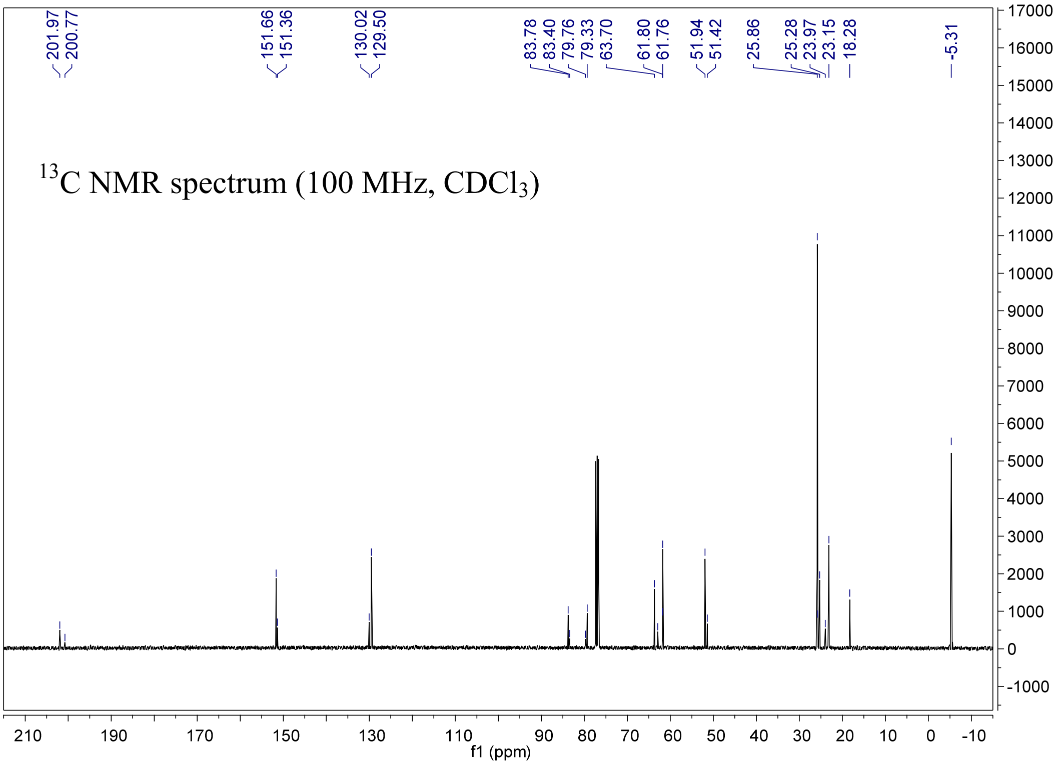
5.8278
5.8093
5.7950
5.7681
5.1248
5.0990
5.0821
4.6041
4.4573
4.0698
3.8665
3.3707
3.3576
2.5116
2.3308
2.3243
2.3056
2.0763
1.8654
1.8468
1.8169
1.7966
1.7201
1.6614
1.6340
1.6078
1.5934
1.4844
1.4507
1.4214
2.09
2.07
2.04
1.03
0.97
1.01
1.00
5.95
1.00
2.00
1.86
2.99
1.04
2.08
2.08
0.95
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

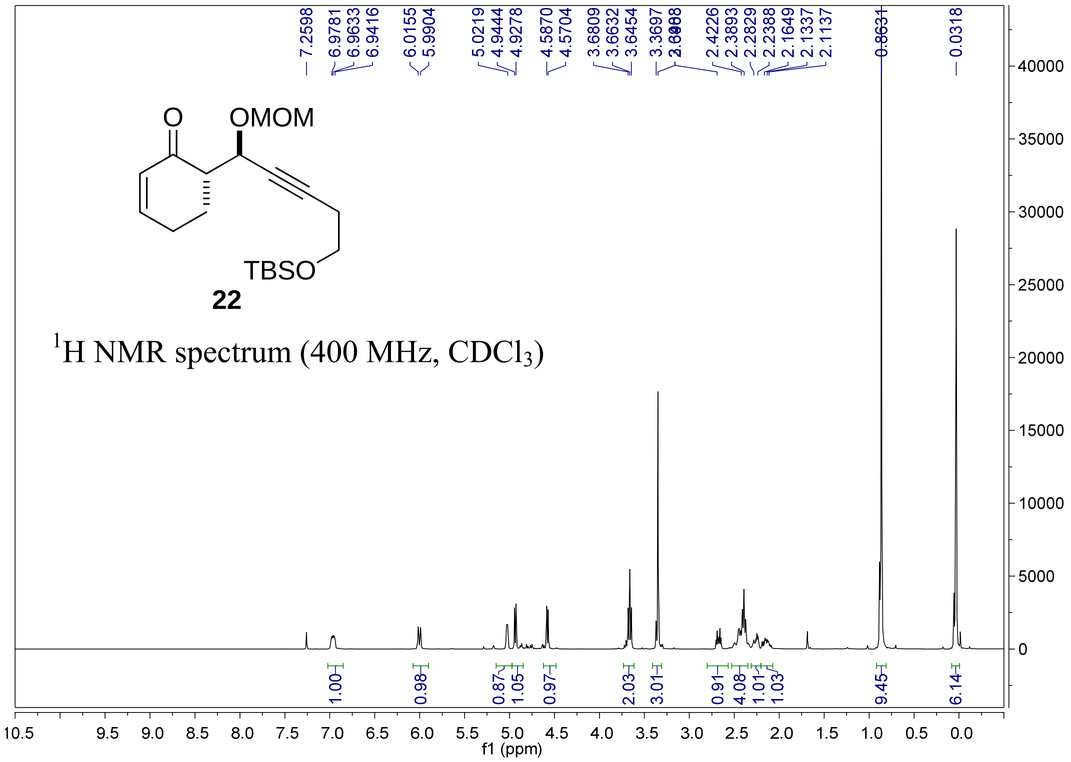

^{13}C NMR spectrum (100 MHz, CDCl$_3$)
143.90
133.86
127.95
118.65
94.96
93.86
74.36
69.19
55.67
55.56
47.69
41.65
34.79
29.85
23.80
19.67
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000



^{1}H NMR spectrum (400 MHz, CDCl$_3$)
(ca. 3:1 mixture of diastereomers)

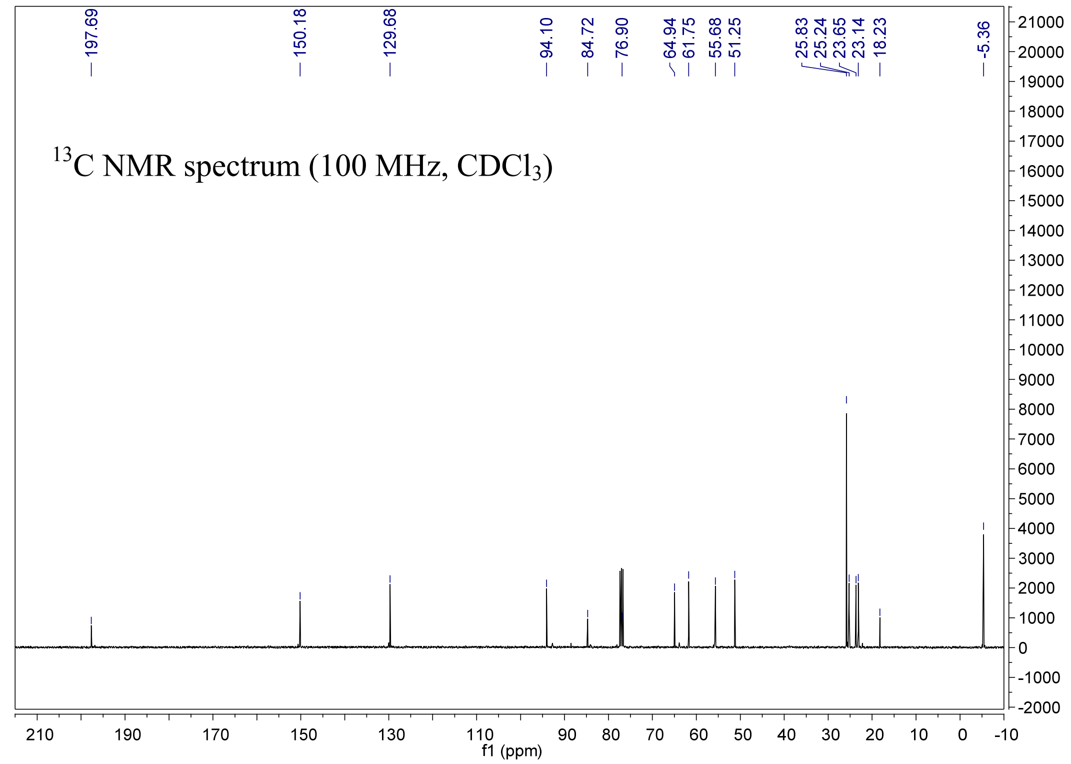


^{13}C NMR spectrum (100 MHz, CDCl$_3$)

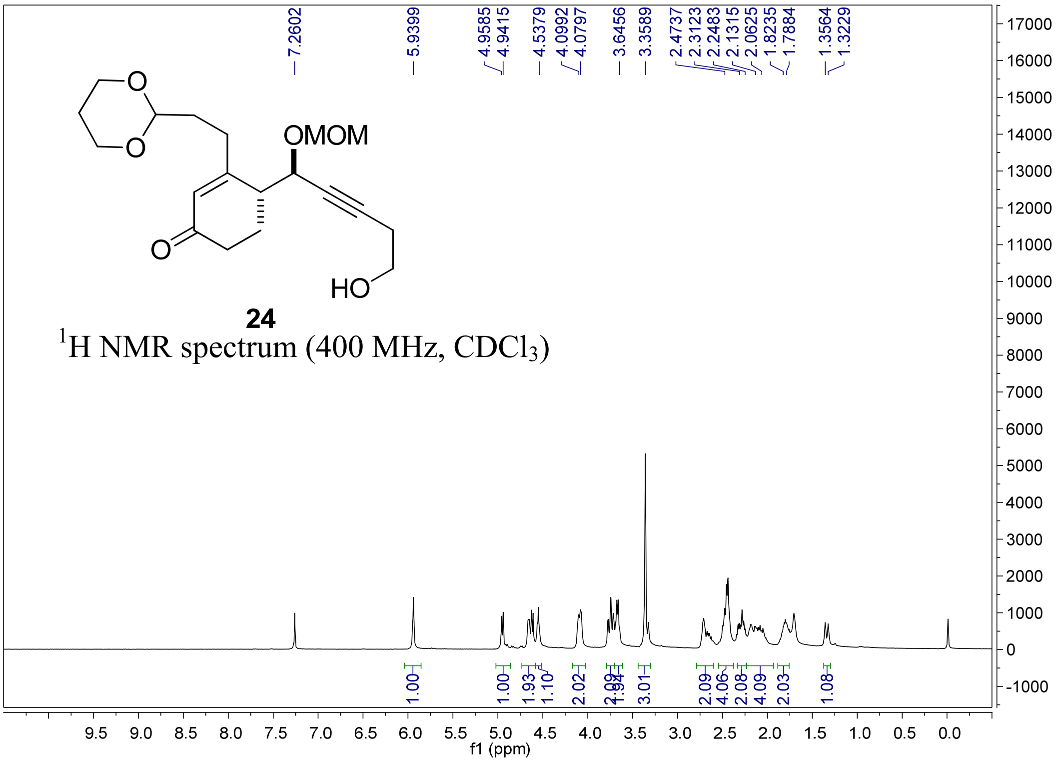


22

^{1}H NMR spectrum (400 MHz, CDCl$_3$)



^{13}C NMR spectrum (100 MHz, CDCl$_3$)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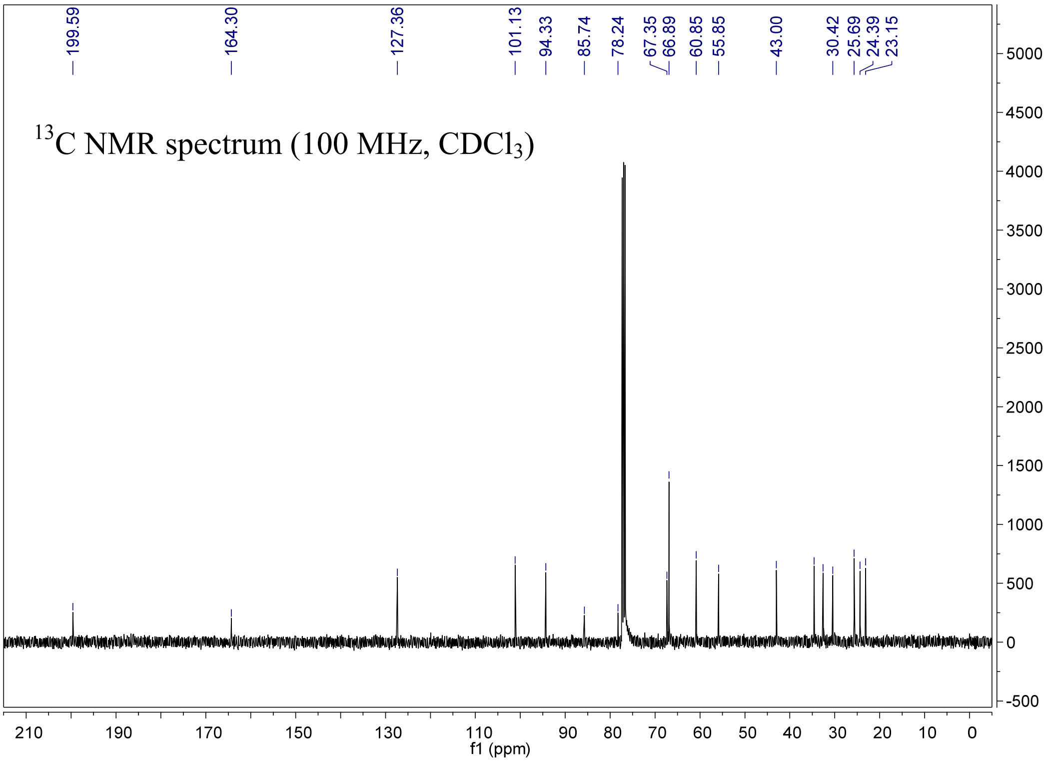
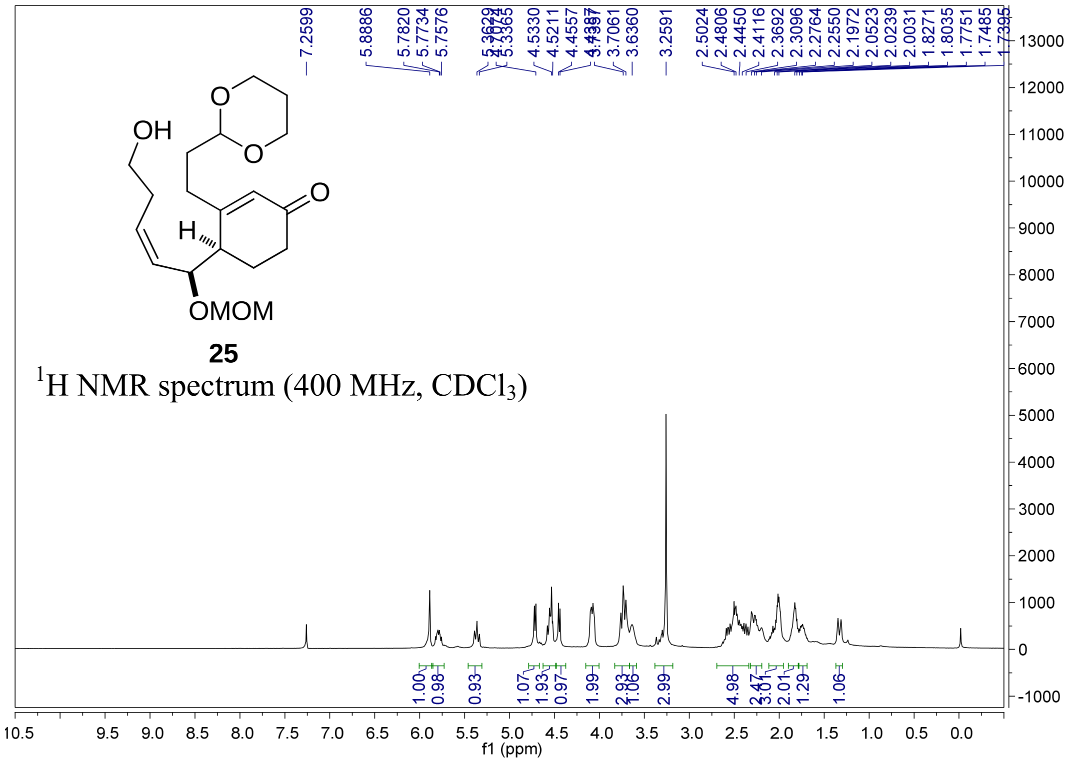
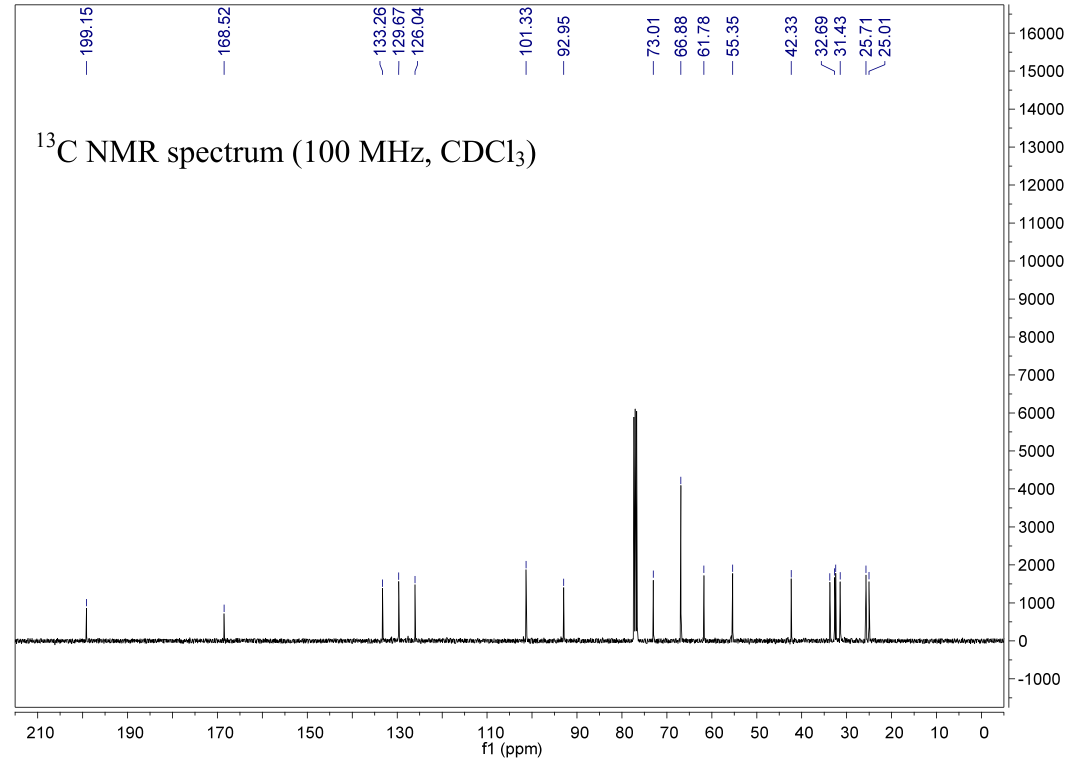
5.9399
4.9585
4.9415
4.5379
4.0992
4.0797
3.6456
3.3589
2.4737
2.3123
2.2483
2.1315
2.0625
1.8235
1.7884
1.3564
1.3229
OMOM
O
O
O
HO
24
^{1}H NMR spectrum (400 MHz, CDCl$_3$)
1.00
1.00
1.93
1.10
2.02
2.09
1.94
3.01
2.09
4.06
2.08
4.09
2.03
1.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000


199.59
164.30
127.36
101.13
94.33
85.74
78.24
67.35
66.89
60.85
55.85
43.00
30.42
25.69
24.39
23.15
^{13}C NMR spectrum (100 MHz, CDCl$_3$)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

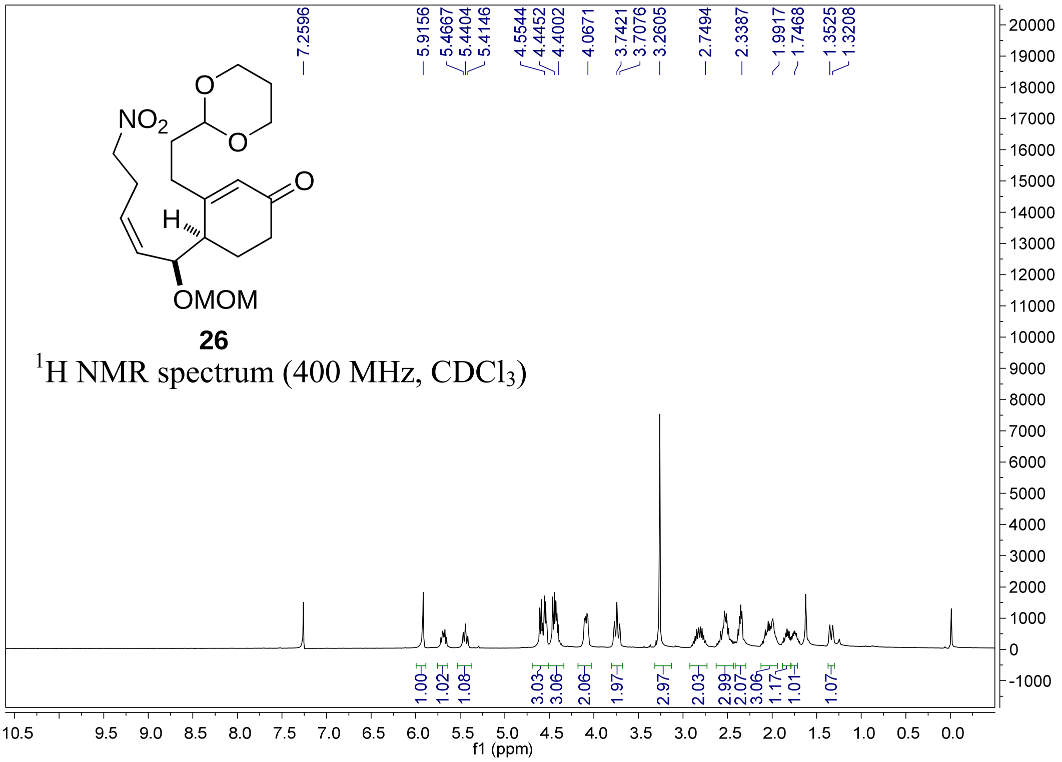


25

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

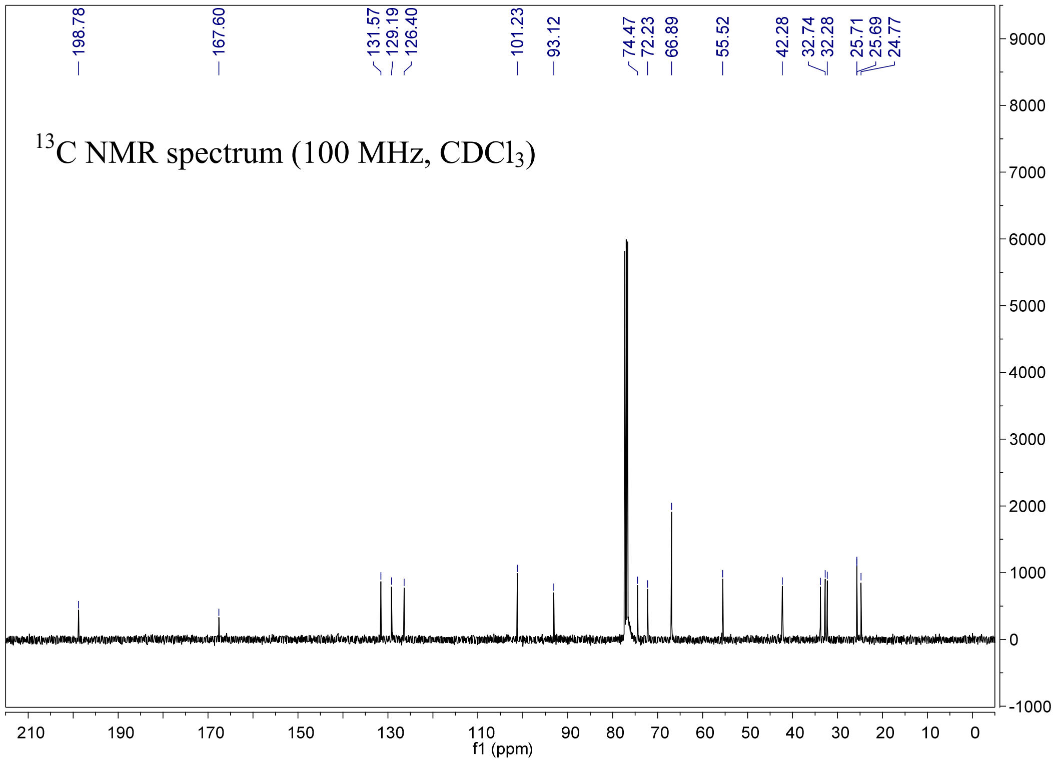


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

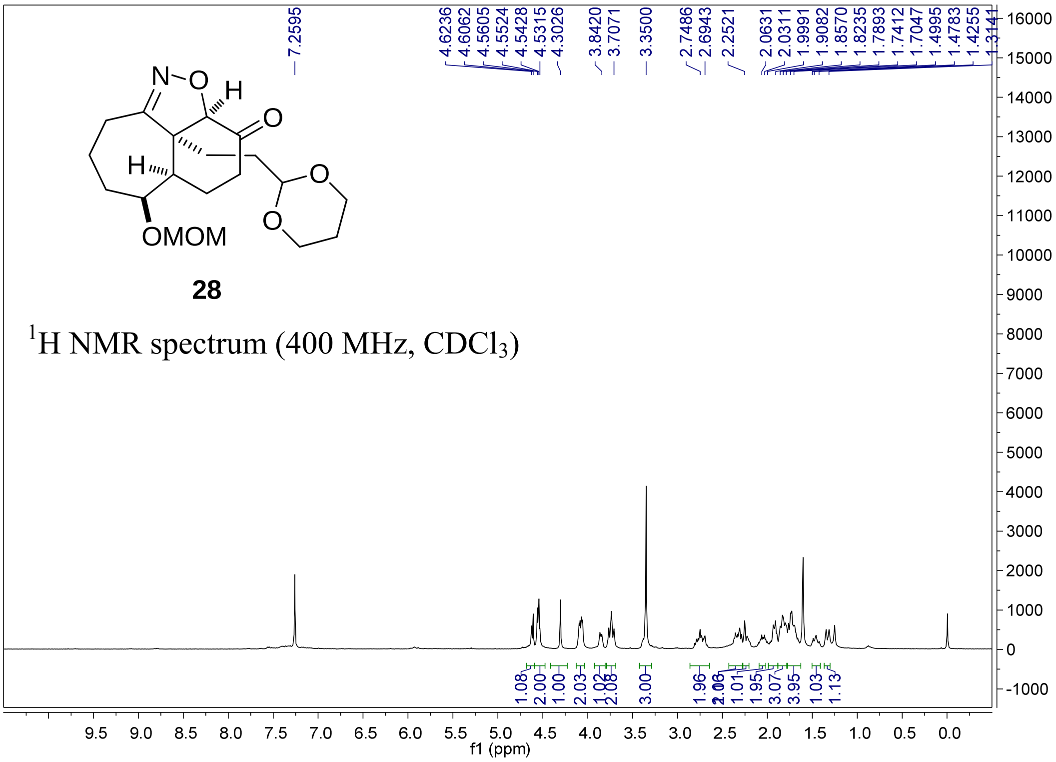


26

^{1}H NMR spectrum (400 MHz, CDCl$_3$)

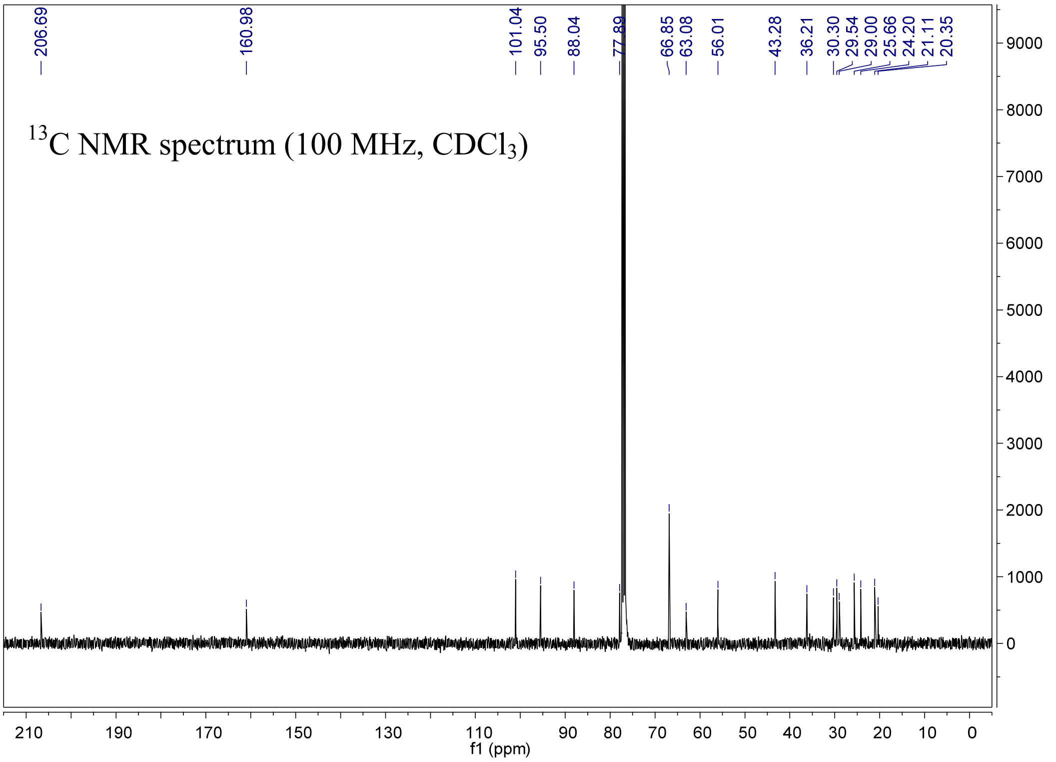


^{13}C NMR spectrum (100 MHz, CDCl$_3$)

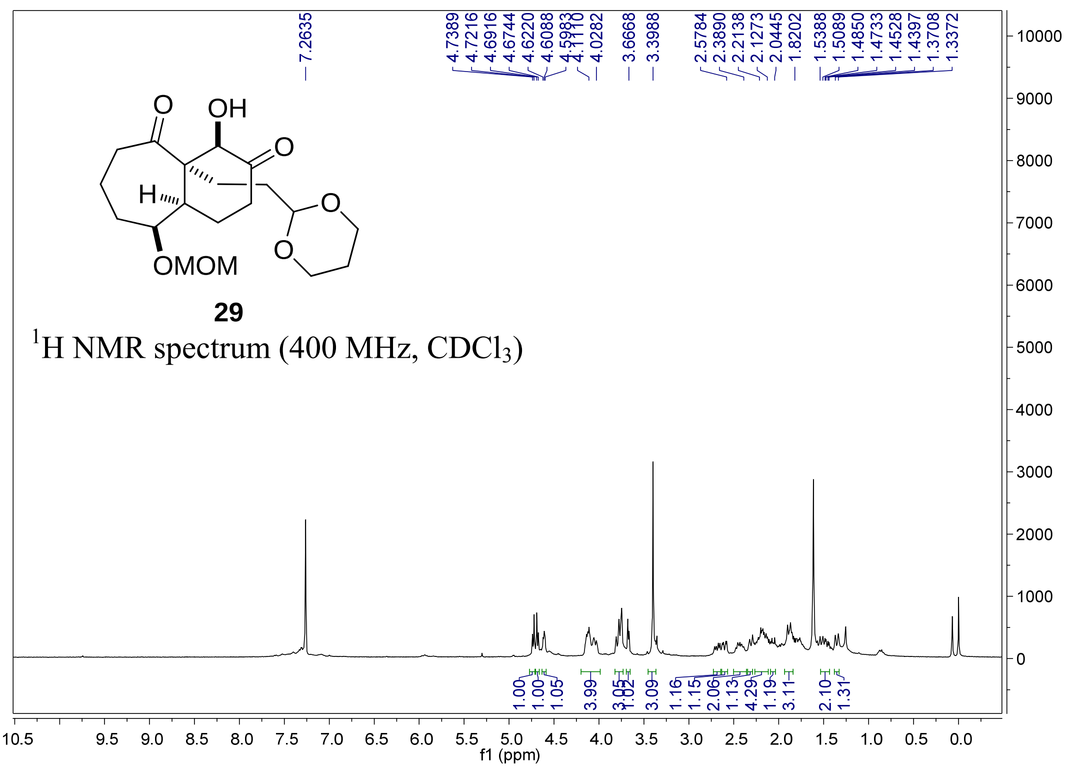


28

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

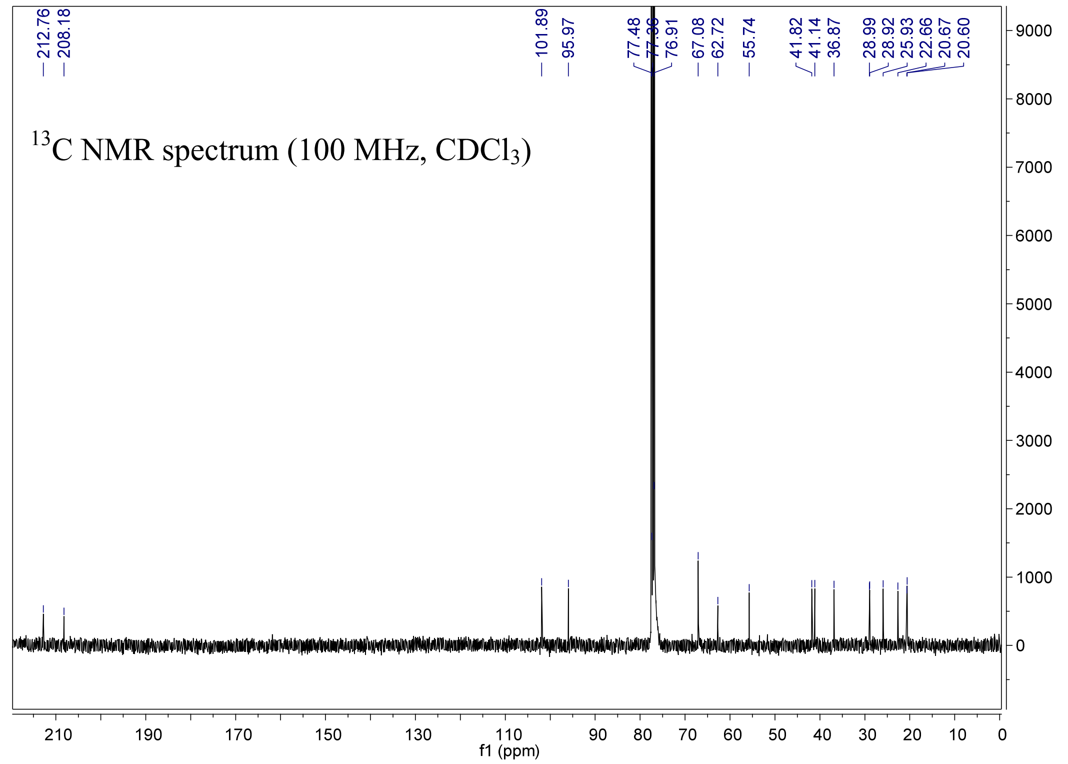


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

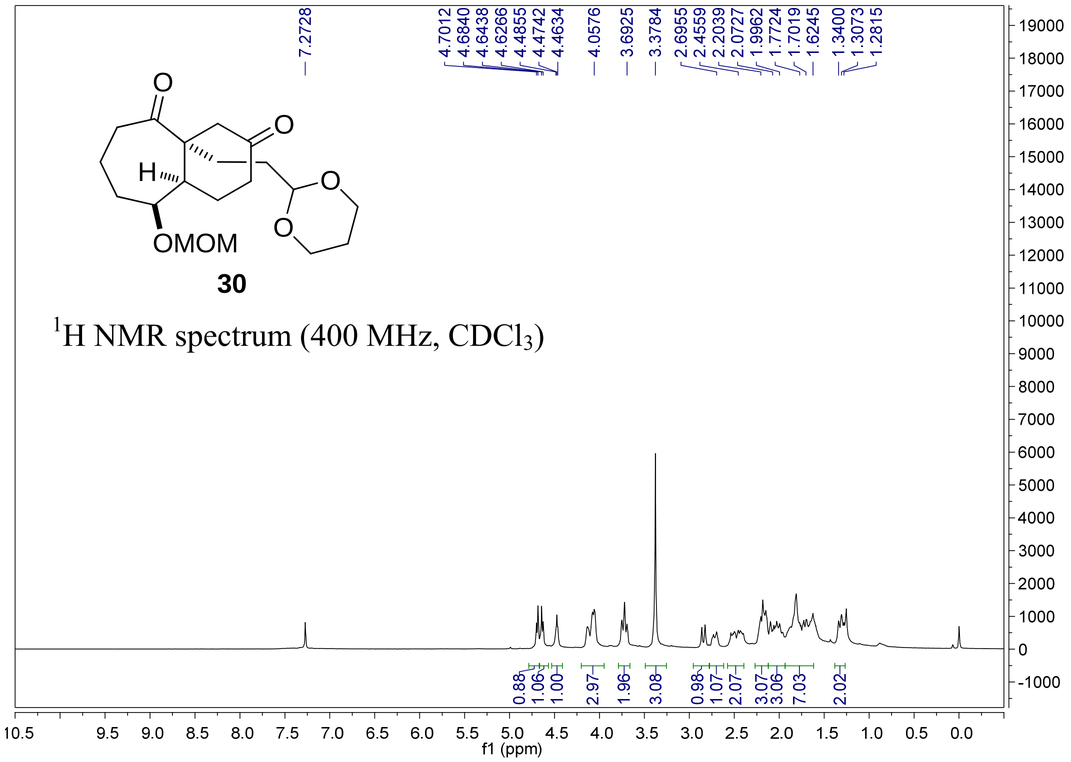


29

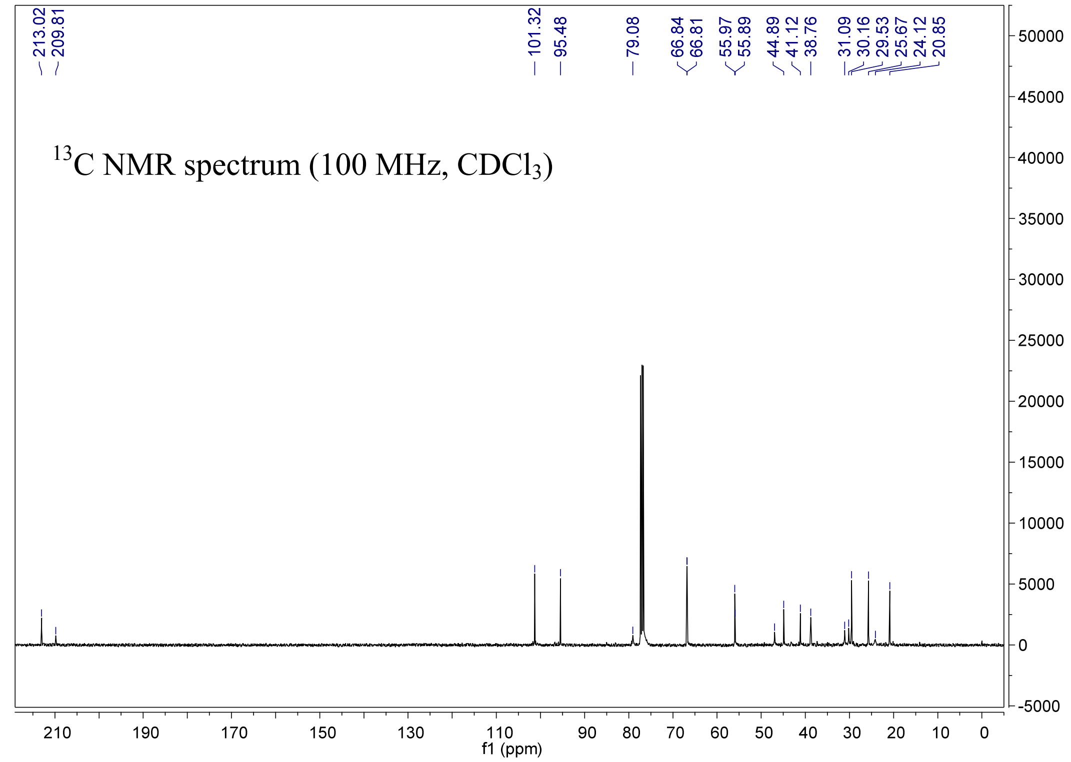
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



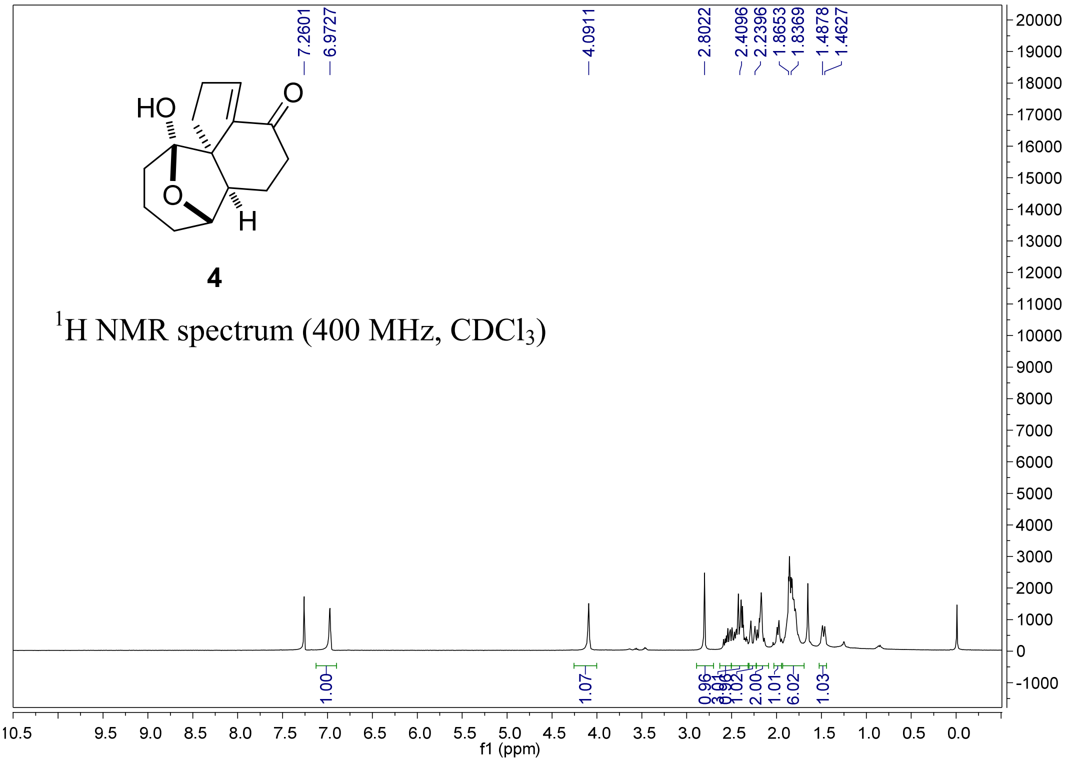
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



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

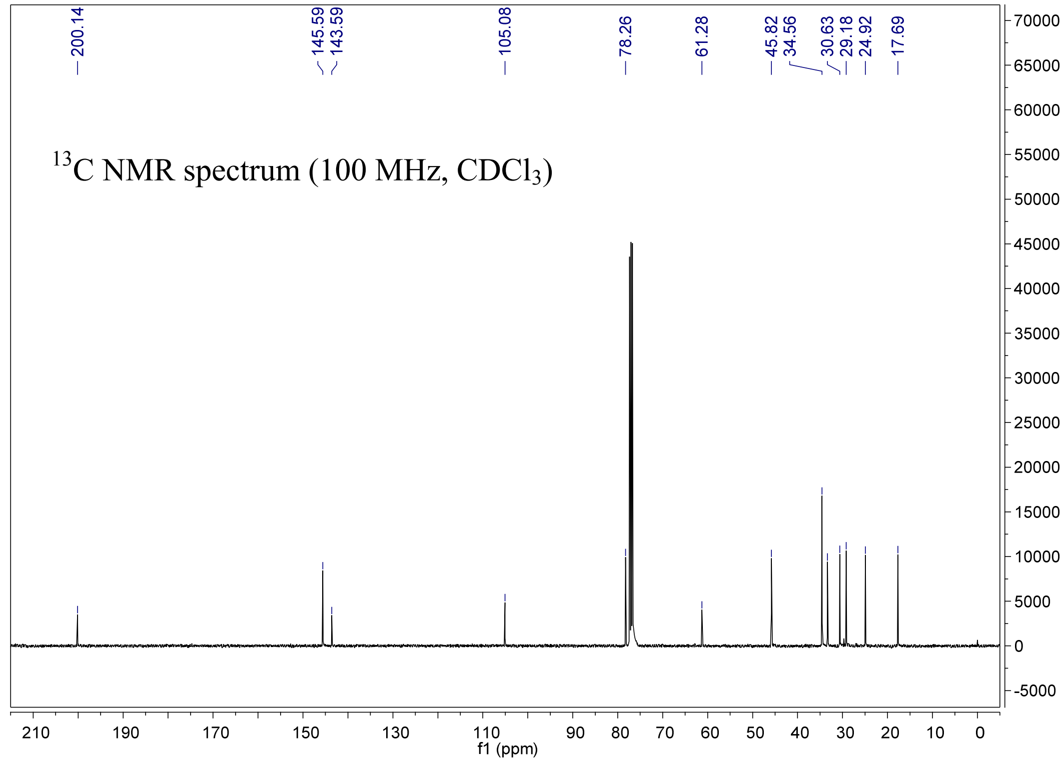


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



4

^{1}H NMR spectrum (400 MHz, CDCl$_3$)



^{13}C NMR spectrum (100 MHz, CDCl$_3$)