Total Syntheses of (±)-Platencin and (–)-Platencin

K. C. Nicolaou,* G. Scott Tria, David J. Edmonds, and Moumita Kar

Contribution from the Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, and the Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, California 92093.

Email: *kcn@scripps.edu*

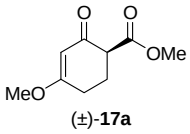
Supporting Information Available

I. Experimental Section

General Methods

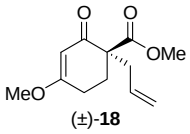
All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry toluene, diethyl ether (Et_2O), acetonitrile (CH_3CN), dimethyl formamide (DMF), methanol, triethylamine (Et_3N), methylene chloride (CH_2Cl_2), and tetrahydrofuran (THF) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Dimethylsulfoxide (DMSO), 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU), and ethanol (EtOH) were purchased in anhydrous form and used without further purification. HMPA was distilled under reduced pressure from CaH_2 and degassed by three cycles of freezing under argon followed by thawing under high vacuum. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on S-2 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and ethanolic *p*-anisaldehyde, aqueous ammonium cerium nitrate/ammonium molybdate or basic aqueous potassium permanganate as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker AV-400, DRX-500 or DRX-600 instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, quint = quintet, br = broad. IR spectra were recorded on a Perkin–Elmer Spectrum 100 FT-IR spectrometer. Melting points (m.p.) are uncorrected and were recorded on a Thomas Hoover Uni-Melt apparatus. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI-TOF (time of flight) mass spectrometer at a 4000 V emitter voltage. Optical rotations were recorded on a Perkin–Elmer Model 343 polarimeter at 589 nm, and are reported in units of 10^{-1}(deg cm^2 g^{-1}).

Methyl ester [(±)-**17a**]. To a stirred solution of 3-methoxy-2-cyclohexen-1-one (**17**, 2.0 g, 15.85 mmol) in THF (50 mL) at –78 °C was added LiHMDS (1.0 M solution in THF, 19.0 mL, 19.02 mmol) dropwise over 10 min. The mixture was stirred at –78 °C for 30 min and then methyl cyanoformate (1.38 ml, 17.44 mmol) was added. The solution was stirred at –78 °C for 1 h and then at 0 °C for an additional 1.5 h before the addition of sat. aq. $NaHCO_3$ (50 mL). The resulting mixture was extracted with EtOAc (3 × 60 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 30% → 60% EtOAc in hexanes) to afford (±)-**17a** (2.68 g, 92% yield) as a pale yellow oil. [(±)-**17a**]: R_f = 0.12 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3708, 3681, 2951, 2923, 2865, 2844, 2076, 1733, 1655, 1602, 1455, 1435, 1383, 1366, 1315, 1254, 1227, 1194, 1169, 1082, 1055, 1033, 1009, 982, 931, 908, 895, 860, 827, 801, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 5.40 (s, 1 H), 3.75 (s, 3 H), 3.70 (s, 3 H), 3.34 (dd, *J* = 8.9, 5.0 Hz, 1 H), 2.57 (ddd, *J* = 16.9, 6.3, 4.8 Hz, 1 H), 2.45 (dd, *J* = 8.3, 4.9 Hz, 1 H), 2.35 (tdd, *J* = 13.5, 8.6, 4.9 Hz, 1 H), 2.21–2.11 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.46, 178.37, 170.60, 101.53, 55.75, 52.16, 52.00, 26.94, 23.96 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_9H_{13}O_4^+$ 185.0808, found 185.0811.



(±)-**17a**

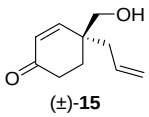
Allyl methyl ester [(±)-**18**]. To a stirred solution of methyl ester (±)-**17a** (2.3 g, 12.5 mmol) in THF (70 mL) at 25 °C was added NaH (60% in mineral oil, 750 mg, 18.74 mmol). The reaction mixture was stirred for 30 min, and then allyl bromide (1.62 ml, 18.74 mmol) was added dropwise. The resulting mixture was stirred for 2 h at 25 °C and then quenched with sat. aq. NH_4Cl solution (50 mL). The resulting suspension was extracted with EtOAc (3 × 60 mL) and dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 30% → 50% EtOAc in hexanes) to afford allyl methyl ester (±)-**18** (2.22 g, 79% yield) as a pale yellow oil. [(±)-**18**]: R_f = 0.31 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3708, 3681, 2967, 2950, 2923, 2865, 2844, 2075, 1730, 1660, 1608, 1454, 1383, 1347, 1322, 1279, 1250, 1237, 1193, 1172, 1055, 1033, 1014, 923, 867, 839, 815, 779, 751 cm^{-1};



(±)-**18**

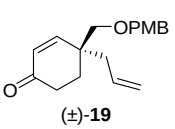
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.79–5.69 (m, 1 H), 5.38 (d, *J* = 1.2 Hz, 1 H), 5.13–5.06 (m, 2 H), 3.71 (s, 3 H), 3.69 (s, 3 H), 2.72 (ddt, *J* = 13.9, 7.4, 1.1 Hz, 1 H), 2.68–2.58 (m, 1 H), 2.55 (ddt, 13.6, 7.2, 1.2 Hz, 1 H), 2.42–2.38 (m, 2 H), 1.98–1.92 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.37, 177.18, 171.25, 133.08, 118.19, 100.97, 55.33, 55.17, 51.82, 38.09, 27.67, 25.56 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{17}O_4^+$ 225.1121, found 225.1124.

Allyl hydroxy enone [(±)-**15**]. To a solution of allyl methyl ester (±)-**18** (2.23 g, 9.94 mmol) in Et_2O (50 mL) at 0 °C was added $LiAlH_4$ (1.0 M solution in THF, 12.0 mL, 11.93 mmol) dropwise over 10 min. The reaction mixture was stirred at 0 °C for 1 h and then allowed to warm to 25 °C and stirred for 2 h, after which time it was cooled to 0 °C and MeOH (10 mL, 246.88 mmol) was added slowly to quench the excess $LiAlH_4$. The reaction mixture was then allowed to reach 25 °C and acidified with 2 M methanolic HCl (30 mL, 60.00 mmol) and stirred vigorously for 16 h. The reaction mixture was diluted with H_2O (100 mL) and extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ solution (250 mL) and brine (250 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 50% → 60% EtOAc in hexanes) to afford allyl hydroxy enone (±)-**15** (1.35 g, 82% yield) as a colorless oil. [(±)-**15**]: R_f = 0.31 (silica, 60% EtOAc in hexanes); IR (film): ν_{max} = 3413, 3076, 2922, 2869, 1661, 1448, 1417, 1390, 1330, 1249, 1220, 1185, 1110, 1086, 1058, 1034, 995, 973, 917, 887, 868, 799, 759, 716 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.77 (dd, *J* = 10.3, 0.7 Hz, 1 H), 6.03 (d, *J* = 10.3 Hz, 1 H), 5.86–5.75 (m, 1 H), 5.19–5.15 (m, 1 H), 5.15–5.12 (m, 1 H), 3.62 (d, *J* = 10.7 Hz, 1 H), 3.56 (d, *J* = 10.9 Hz, 1 H), 2.58–2.42 (m, 2 H), 2.30 (dt, *J* = 7.5, 1.1 Hz, 2 H), 1.98 (dddd, *J* = 13.9, 8.0, 5.9, 0.7 Hz, 1 H), 1.90 (dddd, *J* = 13.9, 8.0, 5.9, 0.8 Hz, 1 H), 1.80 (br s, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.67, 154.36, 133.19, 129.88, 119.00, 67.36, 40.98, 39.95, 33.82, 28.44 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{10}H_{15}O_2^+$ 167.1067, found 167.1068.



(±)-**15**

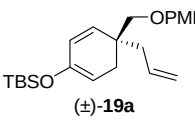
PMB allyl enone [(±)-**19**]. To a stirred solution of allyl hydroxy enone (±)-**15** (0.93 g, 5.59 mmol) in CH_2Cl_2 (35 mL) at 0 °C was added a solution of $PMBOC(NH)CCl_3$ (3.19 g, 11.17 mmol) in CH_2Cl_2 (10



(±)-**19**

mL) followed by TsOH•H_20 (111 mg, 0.58 mmol).[1] The reaction mixture was allowed to warm to 25 °C and stirred at that temperature for 2.5 h after which time the reaction mixture was diluted with Et_2O:pentane (1:1, 100 mL) and filtered through Celite™. The resulting filtrate was washed with sat. aq. $NaHCO_3$ solution (100 mL) and brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 15% → 25% EtOAc in hexanes) to afford PMB allyl enone (±)-**19** (1.34 g, 85% yield) as a colorless oil. [(±)-**19**]: R_f = 0.61 (silica, 60% EtOAc in hexanes); IR (film): ν_{max} = 3345, 3074, 3002, 2934, 2859, 1731, 1676, 1638, 1612, 1586, 1512, 1442, 1420, 1387, 1361, 1302, 1246, 1173, 1090, 1033, 998, 920, 819, 756, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.23 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 6.77 (d, *J* = 10.3 Hz, 1 H), 5.98 (d, *J* = 10.3 Hz, 1 H), 5.73 (ddt, *J* = 16.5, 10.5, 7.5 Hz, 1 H), 5.14–5.06 (m, 2 H), 4.46 (d, *J* = 12.0 Hz, 1 H), 4.43 (d, *J* = 11.8 Hz, 1 H), 3.81 (s, 3 H), 3.35 (d, *J* = 9.0 Hz, 1 H), 3.30 (d, *J* = 9.0 Hz, 1 H), 2.44 (t, *J* = 7.0 Hz, 2 H), 2.35–2.25 (m, 2 H), 1.96 (dt, *J* = 13.8, 7.0 Hz, 1 H), 1.87 (dt, *J* = 13.8, 6.9 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.47, 159.22, 154.97, 133.27, 130.08, 129.25, 129.10, 118.81, 113.78, 73.92, 73.04, 55.25, 40.15, 33.84, 28.83 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{23}O_3^+$ 287.1642, found 287.1646.

TBS enol ether [(±)-**19a**]. To a stirred solution of PMB allyl enone (±)-**19** (1.4 g, 4.89 mmol) in

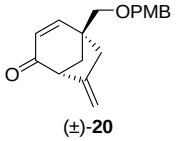


(±)-**19a**

THF (25 mL) at 0 °C was added Et_3N (2.73 mL, 19.56 mmol) followed by dropwise addition of TBSOTf (2.8 mL, 12.22 mmol). The resulting mixture was stirred at 0 °C for 1 h before it was quenched with sat. aq. $NaHCO_3$ solution (35 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated, and the resulting residue was purified by flash column chromatography (silica, 2% → 5% Et_2O in hexanes with 2% Et_3N) to afford pure TBS enol ether (±)-**19a** (1.79 g, 91% yield) as a colorless oil. [(±)-**19a**]: R_f = 0.56 (silica, 20% EtOAc in hexanes); IR (film): ν_{max} = 2954, 2929, 2856, 2897, 1652, 1612, 1587, 1512, 1463, 1439, 1401, 1361, 1329, 1301, 1246, 1207, 1181, 1087, 1037, 1004, 939, 911, 889, 836, 805, 779, 693, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J*

= 8.7 Hz, 2 H), 5.82–5.71 (m, 1 H), 5.67 (d, *J* = 2.1 Hz, 1 H), 5.60 (d, *J* = 0.7 Hz, 1 H), 5.06–4.97 (m, 2 H), 4.74 (dd, *J* = 2.1, 0.6 Hz, 1 H), 4.43 (s, 2 H), 3.81 (s, 3 H), 3.27 (d, *J* = 8.8 Hz, 1 H), 3.20 (d, *J* = 8.8 Hz, 1 H), 2.32–2.16 (m, 3 H), 2.11 (dd, *J* = 17.1, 4.8 Hz, 1 H), 0.93–0.91 (m, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.01, 147.26, 134.91, 134.08, 130.74, 128.93, 126.10, 117.28, 113.64, 101.13, 73.72, 72.83, 55.13, 39.84, 38.74, 29.64, 25.69, 18.00, –2.97, –4.51 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{37}O_3Si^+$ 401.2506, found 401.2500.

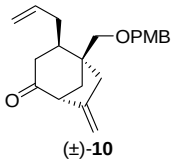
Bicyclo enone [(±)-**20**]. To a stirred solution of TBS enol ether (±)-**19a** (1.78 g, 4.44 mmol) in



(±)-**20**

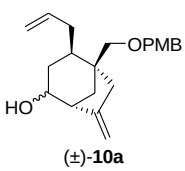
DMSO (45 mL) at 25 °C was added $Pd(OAc)_2$ (100 mg, 0.44 mmol). The resulting mixture was warmed to 45 °C and stirred under an oxygen atmosphere (balloon) at that temperature for 16 h and then cooled to room temperature and diluted with Et_2O (50 mL). The resulting suspension was filtered through Celite™ and rinsed with further Et_2O (50 mL). To the filtrate was added H_2O (150 mL) and the separated aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with 10% aq. HCl (250 mL), sat. aq. $NaHCO_3$ solution (250 mL), and brine (250 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated, and the residue was purified by flash column chromatography (silica, 15% → 25% EtOAc in hexanes) to afford bicyclo enone (±)-**20** (1.08 g, 85% yield) as a colorless oil. [(±)-**20**]: R_f = 0.35 (silica, 30% EA in hexanes); IR (film): ν_{max} = 3707, 3681, 3665, 2981, 2967, 2938, 2923, 2865, 2844, 2075, 2053, 1679, 1611, 1586, 1512, 1455, 1431, 1360, 1346, 1331, 1302, 1245, 1209, 1172, 1143, 1054, 1032, 1012, 886, 843, 819, 765, 710 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 (d, *J* = 8.8 Hz, 2 H), 7.13 (dd, *J* = 9.7, 2.0 Hz, 1 H), 6.90 (d, *J* = 8.7 Hz, 2 H), 5.82 (dd, *J* = 9.7, 1.6 Hz, 1 H), 5.27 (s, 1 H), 5.04 (d, *J* = 0.7 Hz, 1 H), 4.51 (s, 2 H), 3.81 (s, 3 H), 3.57–3.41 (m, 3 H), 2.41 (ddd, *J* = 17.6, 15.9, 7.5 Hz, 2 H), 2.12 (dd, *J* = 11.1, 2.3 Hz, 1 H), 1.81 (ddd, *J* = 11.1, 5.0, 2.0 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 198.75, 159.29, 156.39, 145.00, 130.07, 129.19, 126.57, 113.84, 112.33, 73.95, 73.13, 58.53, 55.27, 47.67, 42.87, 39.62 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{21}O_3^+$ 285.1485, found 285.1483.

Allyl bicyclo ketone [(±)-**10**]. To a stirred solution of CuBr•Me_2S (1.56 g, 7.60 mmol) in THF (20 mL) at –78 °C was added allyl magnesium chloride (1.7 M solution in THF, 8.94 mL, 15.19 mmol) dropwise over a period of 10 min and the mixture was stirred for an additional 1 h at that temperature. A solution of bicyclo enone (±)-**20** (1.08 g, 3.80 mmol) in THF (10 mL) was then added dropwise at –78 °C over 10 min, and the mixture was stirred for an additional 1 h at that temperature before it was allowed to slowly warm to –40 °C over a period of 1 h. The reaction was quenched with sat. aq. NH_4Cl solution (30 mL, adjusted to pH 8 with aq. NH_4OH) and, after allowing the mixture to warm to room temperature, extracted with EtOAc (3 × 70 mL). The combined organic extracts were washed with brine (200 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 5% → 10% EtOAc in hexanes) to afford allyl ketone (±)-**10** (1.07 g, 86% yield) as a colorless oil. [(±)-**10**]: R_f = 0.5 (silica, 30% EtOAc in hexanes); IR (film): ν_{max} = 3707, 3681, 3665, 2966, 2937, 2923, 2865, 2844, 2074, 1713, 1654, 1639, 1612, 1586, 1512, 1455, 1437, 1422, 1361, 1301, 1246, 1212, 1173, 1151, 1056, 1033, 1012, 915, 888, 820, 757, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 8.8 Hz, 2 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 5.72–5.62 (m, 1 H), 5.07–4.99 (m, 3 H), 4.90 (s, 1 H), 4.49 (d, *J* = 11.6 Hz, 1 H), 4.43 (d, *J* = 11.6 Hz, 1 H), 3.81 (s, 3 H), 3.59 (d, *J* = 9.2 Hz, 1 H), 3.26 (d, *J* = 9.2 Hz, 1 H), 3.18 (d, *J* = 5.0 Hz, 1 H), 2.66–2.63 (m, 2 H), 2.55 (ddd, *J* = 15.75, 7.92, 1.11 Hz, 1 H), 2.24–2.14 (m, 3 H), 1.82 (dd, *J* = 12.4 Hz, 1 H), 1.76–1.71 (m, 1 H), 1.67 (ddd, *J* = 12.0, 4.8, 1.6 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 210.02, 159.12, 148.47, 136.59, 130.24, 129.04, 117.04, 113.68, 108.21, 73.87, 72.89, 59.73, 55.15, 46.55, 42.56, 40.79, 38.38, 35.30, 34.32 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{27}O_3Na^+$ 349.1780, found 349.1774.



(±)-**10**

Alcohol [(±)-**10a**]. To a stirred solution of allyl ketone (±)-**10** (1.04 g, 3.19 mmol) in MeOH (32 mL) at –5 °C was added $NaBH_4$ (300 mg, 7.96 mmol), and the reaction mixture was allowed to warm to 25 °C. After 30 min, the reaction mixture was cooled to 0 °C and H_2O (75 mL) was added carefully. The mixture was extracted with EtOAc (3 × 75 mL) and the



(±)-**10a**

combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (silica, 10% EtOAc in hexanes → 30% EtOAc in hexanes) afforded alcohol (±)-**10a** (1.02 g, 97% yield, *ca*. 2:1 diastereomeric ratio) as a colorless oil. [(±)-**10aa**] (major, more polar): R_f = 0.38 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3707, 3681, 3665, 3432, 2981, 2973, 2937, 2923, 2865, 2844, 2075, 2053, 1655, 1639, 1611, 1586, 1512, 1455, 1440, 1389, 1360, 1346, 1331, 1321, 1301, 1244, 1209, 1172, 1054, 1033, 1014, 945, 910, 881, 846, 819, 735, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.23 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.80–5.64 (m, 1 H), 5.04–5.02 (m, 1 H), 5.01–4.99 (m, 1 H), 4.93–4.91 (m, 2 H), 4.46 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 3.80 (s, 3 H), 3.69 (ddd, *J* = 11.3, 5.5, 3.1 Hz, 1 H), 3.51 (d, *J* = 9.2 Hz, 1 H), 3.16 (d, *J* = 9.2 Hz, 1 H), 2.60 (t, *J* = 4.0 Hz, 1 H), 2.39 (dt, *J* = 17.3, 2.6 Hz, 1 H), 2.32 (dd, *J* = 17.4, 1.8 Hz, 1 H), 2.21–2.12 (m, 1 H), 1.93–1.83 (m, 3 H), 1.48 (dd, *J* = 11.8, 1.7 Hz, 1 H), 1.41 (ddd, *J* = 11.9, 5.4, 1.0 Hz, 1 H), 1.15 (ddd, *J* = 13.7, 9.2, 5.1 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.10, 150.95, 138.10, 130.62, 129.03, 115.92, 113.71, 106.29, 74.71, 72.88, 69.03, 55.24, 50.77, 46.40, 43.42, 39.26, 33.84, 33.76, 31.94 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{29}O_3^+$ 329.2117, found 329.2114.

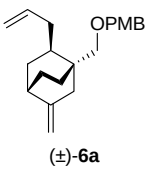
[(±)-**10ab**] (minor, less polar): R_f = 0.48 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3707, 3681, 3665, 3459, 2981, 2973, 2937, 2923, 2865, 2844, 2075, 2053, 1654, 1638, 1612, 1586, 1512, 1454, 1441, 1359, 1332, 1321, 1301, 1245, 1172, 1055, 1033, 1012, 910, 880, 847, 819, 760, 706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.24 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 5.84–5.73 (m, 1 H), 5.08–5.02 (m, 1 H), 5.01 (dd, *J* = 1.7, 0.9 Hz, 1 H), 4.86 (dd, *J* = 3.1, 1.9 Hz, 1 H), 4.81 (s, 1 H), 4.46 (d, *J* = 11.9 Hz, 1 H), 4.41 (d, *J* = 11.9 Hz, 1 H), 3.84–3.82 (m, 1 H), 3.81 (s, 3 H), 3.57 (d, *J* = 9.1 Hz, 1 H), 3.15 (d, *J* = 9.1 Hz, 1 H), 2.66 (t, *J* = 4.7 Hz, 1 H), 2.45 (dd, *J* = 17.3, 1.9 Hz, 1 H), 2.39–2.29 (m, 2 H), 2.27–2.21 (m, 1 H), 2.02 (dd, *J* = 11.6, 2.1 Hz, 1 H), 1.85–1.80 (m, 1 H), 1.73–1.66 (m, 1 H), 1.60 (dd, *J* = 15.4, 1.1 Hz, 1 H), 1.11 (dd, *J* = 11.7, 5.0 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.07, 152.53, 139.37, 130.78, 129.04, 115.70, 113.70, 105.40, 75.48, 72.90, 72.87, 55.26, 49.88,

46.81, 42.60, 38.43, 34.79, 28.78, 28.45 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{29}O_3^+$ 329.2117, found 339.2221.

Xanthate [(±)-**9a**]. To a stirred solution of a mixture of alcohols (±)-**10a** (*ca*. 2:1 diastereomeric ratio, 1.04 g, 3.17 mmol) in THF (65 mL) at –78 °C was added sequentially CS_2 (1.9 mL, 31.66 mmol) and KHMDS (0.5 M solution in toluene, 31.7 mL, 15.83 mmol). After stirring for 20 min at –78 °C, the cooling bath was removed and the mixture was stirred for an additional 1 h at 25 °C. Methyl iodide (0.99 mL, 15.83 mmol, freshly filtered through anhydrous K_2CO_3) was added dropwise and the reaction mixture was allowed to stir for an additional 30 min. The reaction was quenched by addition of H_2O (75 mL) and the resulting mixture was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were washed with brine (2 × 200 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Flash column chromatography (silica, 5% EtOAc in hexanes) of the residue afforded xanthates (±)-**9a** (1.23 mg, 92% yield *ca*. 2:1 diastereomeric ratio) as a pale yellow oil. Samples of the individual xanthate diastereoisomers (±)-**9aa** and (±)-**9ab** were prepared in an analogous fashion from the diastereoisomerically pure alcohols **10aa** and **10ab**, respectively. [(±)-**9aa**] [from more polar isomer (±)-**10aa**]: R_f = 0.34 (silica, 10% EtOAc in hexanes); IR (film): ν_{max} = 3072, 2929, 2853, 1658, 1639, 1612, 1586, 1512, 1462, 1440, 1361, 1336, 1301, 1229, 1208, 1172, 1048, 997, 965, 914, 885, 846, 820, 758, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.24 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 5.80–5.66 (m, 1 H), 5.61 (ddd, *J* = 11.5, 5.6, 2.9 Hz, 1 H), 5.11–4.98 (m, 2 H), 4.98–4.87 (m, 2 H), 4.46 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz), 3.81 (s, 3 H), 3.53 (d, *J* = 9.2 Hz, 1 H), 3.17 (d, *J* = 9.2 Hz, 1 H), 2.96 (d, *J* = 3.2 Hz, 1 H), 2.52 (s, 3H), 2.40 (t, *J* = 2.1 Hz, 2 H), 2.25–2.14 (m, 1 H), 2.02 (dd, *J* = 13.6, 5.9 Hz, 1 H), 1.98–1.87 (m, 2 H), 1.72–1.60 (m, 1 H), 1.59–1.51 (m, 2 H), 1.42 (ddd, *J* = 12.0, 5.8, 1.4 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 214.62, 159.08, 149.27, 137.61, 130.48, 129.02, 116.40, 113.67, 107.74, 81.98, 74.46, 72.85, 55.19, 46.68, 46.42, 43.24, 39.25, 33.76, 33.56, 26.56, 18.31 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{23}H_{30}O_3S_2Na^+$ 441.1534, found 441.1507.

[(±)-**9ab**] [from less polar isomer (±)-**10ab**]: R_f = 0.34 (silica, 10% EtOAc in hexanes); IR (film): ν_{max} = 3071, 2933, 2855, 1656, 1638, 1612, 1586, 1512, 1441, 1359, 1301, 1245, 1227, 1213, 1197, 1171, 1125, 1051, 1036, 949, 911, 887, 847, 819, 761, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.26 (d, *J* = 8.7 Hz, 2 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 5.76–5.66 (m, 1 H), 5.54 (t, *J* = 4.1 Hz, 1 H), 5.09–4.98 (m, 3 H), 4.91 (s, 1 H), 4.48 (d, *J* = 11.9 Hz, 1 H), 4.42 (d, *J* = 11.9 Hz, 1 H), 3.82 (s, 3 H), 3.59 (d, *J* = 9.1 Hz, 1 H), 3.19 (d, *J* = 9.2 Hz, 1 H), 3.03 (t, *J* = 4.7 Hz, 1 H), 2.58 (s, 3 H), 2.49 (dd, *J* = 17.3, 1.7 Hz, 1 H), 2.42 (dt, *J* = 4.6, 2.6 Hz, 1 H), 2.28–2.19 (m, 1 H), 2.19 – 2.07 (m, 1 H), 1.96 (d, *J* = 15.7 Hz, 1 H), 1.93–1.74 (m, 3 H), 1.23 (dd, *J* = 11.8, 5.1 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 214.76, 159.11, 150.51, 138.17, 130.61, 129.08, 116.41, 113.71, 107.32, 84.13, 75.09, 72.88, 55.24, 46.38, 46.27, 42.55, 38.26, 34.17, 29.94, 25.06, 18.87 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{31}O_3S_2^+$ 419.1715, found 419.1685.

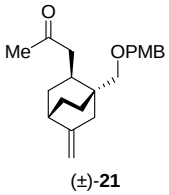
Bicyclo diene [(±)-**6a**]. To a degassed stirred solution of xanthates (±)-**9a** (*ca*. 2:1 diastereomeric ratio, 940 mg, 2.25 mmol) in toluene (274 mL) at 25 °C was added AIBN (36 mg, 0.22 mmol, recrystallized from acetone) followed by *n*-Bu_3SnH (1.5 mL, 4.49 mmol). The mixture was heated to 110 °C and stirred at that temperature for 8 h. Upon cooling to room temperature, the reaction mixture was diluted with Et_2O (400 mL). The organic phase was washed with 1 N aq. HCl (400 mL), sat. aq. $NaHCO_3$ solution (400 mL), and brine (400 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography (silica, 2% → 5% EtOAc in hexanes) to afford bicyclo diene (±)-**6a**, along with an inseparable impurity (575 mg, 92% combined yield; *ca*. 4:1 ratio), as a colorless oil. [(±)-**6a**]: R_f = 0.43 (silica, 10% EtOAc in hexanes); IR (film): ν_{max} = 3086, 2931, 2859, 1639, 1612, 1586, 1512, 1464, 1361, 1301, 1245, 1207, 1171, 1082, 1036, 994, 959, 909, 873, 846, 819, 757, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 8.2 Hz, 2 H), 6.88 (d, *J* = 8.3 Hz, 2 H), 5.83–5.69 (m, 1 H), 5.04–4.99 (m, 1 H), 4.99–4.95 (m, 1 H), 4.72 (dd, *J* = 4.4, 2.1 Hz, 1 H), 4.59 (dd, *J* = 4.1, 2.1 Hz, 1 H), 4.43 (d, *J* = 11.9 Hz, 1 H), 4.39 (d, *J* = 11.8 Hz, 1 H), 3.81 (s, 3 H), 3.22 (d, *J* = 9.1 Hz, 1 H), 3.04 (d, *J* = 9.1 Hz, 1 H), 2.40 (dd, *J* = 16.8, 2.4 Hz, 1 H), 2.28–2.15 (m, 3 H), 1.84–1.69 (m, 3 H), 1.64–1.52 (m,



(±)-**6a**

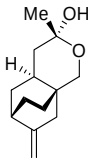
2 H), 1.51–1.42 (m, 1 H), 1.25–1.15 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.00, 151.97, 137.91, 130.89, 128.93, 115.30, 113.66, 104.65, 75.43, 72.88, 55.25, 39.75, 37.02, 36.32, 36.01, 33.85, 26.29, 23.16 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{29}O_2^+$ 313.2168, found 313.2125.

Ketone [(±)-**21**]. To a stirred solution of bicyclo diene (±)-**6a** (549 mg, 1.76 mmol) in DMF (12.2 mL) at 25 °C were added sequentially CuCl (348 mg, 3.51 mmol), H_2O (1.8 mL), and $PdCl_2$ (156 mg, 0.88 mmol). The reaction mixture was stirred under an oxygen atmosphere (balloon) for 24 h at 25 °C and then filtered through a pad of Celite™. The filtrate was diluted with Et_2O (100 mL) and H_2O (100 mL) and the separated aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was subjected to flash column chromatography (silica, 20% → 30% Et_2O in hexanes) to afford ketone (±)-**21** (468 mg, 81% yield) as a pale yellow oil. [(±)-**21**]: R_f = 0.23 (silica, 25% EtOAc in hexanes); IR (film): ν_{max} = 2920, 2858, 1709, 1648, 1611, 1586, 1512, 1464, 1443, 1357, 1301, 1245, 1208, 1172, 1087, 1033, 930, 874, 818, 757, 708 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 4.73 (dd, *J* = 4.4, 2.2 Hz, 1 H), 4.61 (dd, *J* = 4.0, 2.0 Hz, 1 H), 4.39 (d, *J* = 11.8 Hz, 1 H), 4.31 (d, *J* = 11.8 Hz, 1 H), 3.80 (s, 3 H), 3.10 (d, *J* = 9.2 Hz, 1 H), 3.02 (d, *J* = 9.2 Hz, 1 H), 2.54 (dd, *J* = 14.3, 3.6 Hz, 1 H), 2.42 (ddd, *J* = 16.8, 4.8, 2.2 Hz, 1 H), 2.25–2.09 (m, 4 H), 2.06 (s, 3 H), 1.93–1.86 (m, 1 H), 1.62–1.55 (m, 2 H), 1.52–1.44 (m, 1 H), 1.21–1.14 (m, 1 H), 1.06 (ddd, *J* = 13.1, 6.3, 2.1 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 209.04, 159.06, 150.95, 130.63, 129.02, 113.67, 105.21, 75.29, 72.69, 55.24, 46.88, 39.59, 36.73, 36.02, 34.57, 32.73, 29.78, 26.13, 23.12 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{29}O_3^+$ 329.2117, found 329.2017.



(±)-**21**

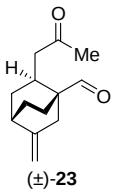
Hemiketal [(±)-**22**]. To a stirred solution of ketone (±)-**21** (28 mg, 0.085 mmol) in 2.5 mL CH_2Cl_2:H_2O (20:1) at 0 °C was added 2,3-dichloro-5,6-dicyanobenzoquinone (24 mg, 0.102 mmol). The resulting suspension was stirred for 1 h at that temperature before it was quenched with sat. aq. $NaHCO_3$ solution (7 mL) and extracted with CH_2Cl_2 (4 × 8 mL). The combined



(±)-**22**

organic extracts were washed with sat. aq. $NaHCO_3$ solution (15 mL) and brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by preparative TLC (silica, 10% Et_2O in CH_2Cl_2) to give hemiketal (±)-**22** (9.4 mg, 53% yield) as a white solid. [(±)-**22**]: R_f = 0.43 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3378, 2929, 2861, 1646, 1474, 1451, 1431, 1396, 1367, 1200, 1147, 1085, 1073, 1044, 1032, 939, 864 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 4.77 (q, *J* = 2.2 Hz, 1 H), 4.63 (q, *J* = 2.0 Hz, 1 H), 3.68 (d, *J* = 11.0 Hz, 1 H), 3.14 (d, *J* = 11.0 Hz, 1 H), 2.19–2.16 (m, 1 H), 2.13–2.06 (m, 1 H), 2.03 (dt, *J* = 16.1, 2.2 Hz, 1 H), 1.99 (d, *J* = 2.2 Hz, 1 H), 1.94–1.88 (m, 3 H), 1.78 (dd, *J* = 13.2, 4.1 Hz, 1 H), 1.64–1.58 (m, 2 H), 1.41 (s, 3 H), 1.16–1.10 (m, 1 H), 1.01–0.98 (m, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.8, 105.9, 95.6, 69.3, 39.7, 38.7, 35.7, 34.7, 31.8, 31.0, 30.3, 26.7, 23.5 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{21}O_2^+$ 209.1536, found 209.1536.

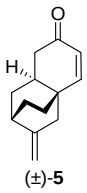
Keto aldehyde [(±)-**23**]. To a stirred solution of hemiketal (±)-**22** (37 mg, 0.177 mmol) in CH_2Cl_2 (6.0 mL) at 25 °C were added sequentially NMO (136 mg, 1.16 mmol) and TPAP (2 mg, 0.006 mmol). The reaction mixture was stirred at 25 °C for 4 h and then filtered through a silica plug and concentrated. Flash column chromatography (silica, 10% → 25% Et_2O in hexanes) of the residue afforded keto aldehyde (±)-**23** (20 mg, 54% yield) as a volatile colorless oil.



(±)-**23**

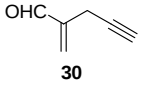
[(±)-**23**]: R_f = 0.32 (silica, 20% EtOAc in hexanes); IR (film): ν_{max} = 3068, 2938, 2867, 2713, 1714, 1651, 1469, 1429, 1405, 1355, 1233, 1180, 1161, 1135, 880, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 9.41 (s, 1 H), 4.84 (s, 1 H), 4.73 (s, 1 H), 2.56–2.46 (m, 3 H), 2.36 (dd, *J* = 17.9, 10.5 Hz, 1 H), 2.29–2.26 (m, 2 H), 2.11 (s, 3 H), 2.08–2.05 (m, 1 H), 1.84–1.77 (m, 1 H), 1.65–1.62 (m, 2 H), 1.57–1.51 (m, 1 H), 1.13 (ddd, *J* = 13.3, 5.1, 2.4 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 207.32, 205.20, 147.50, 107.13, 48.36, 47.40, 36.43, 36.00, 34.38, 31.23, 30.33, 25.51, 20.21 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{19}O_2^+$ 207.1379, found 207.1377.

Enone [(±)-**5**]. To a stirred solution of keto-aldehyde (±)-**23** (70 mg, 0.34 mmol) in EtOH (5 mL) at 25 °C was added solid NaOH (81 mg, 2.04 mmol), and the resulting mixture was stirred at that


(±)-**5**

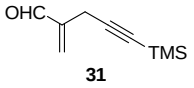
temperature for 8 h. The reaction mixture was concentrated and the residue was dissolved in Et_2O (20 mL) and washed with 1 N aq. HCl (2 × 10 mL), sat. aq. $NaHCO_3$ solution (10 mL), and brine (10 mL), and then dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (silica, 10% EtOAc in hexanes) afforded enone (±)-**5** (63 mg, 99% yield) as a colorless oil. [(±)-**5**]: R_f = 0.44 (silica, 20% EtOAc in hexanes); IR (film): ν_{max} = 2938, 2865, 1682, 1466, 1428, 1391, 1269, 1250, 887 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.56 (d, *J* = 10.0 Hz, 1 H), 5.87 (dd, *J* = 10.0, 1.0 Hz, 1 H), 4.82 (dd, *J* = 4.50, 1.84 Hz, 1 H), 4.68 (dd, *J* = 3.92, 1.80 Hz, 1 H), 2.47–2.40 (m, 2 H), 2.34–2.28 (m, 2 H), 2.18–2.08 (m, 2 H), 2.01–1.96 (m, 1 H), 1.81–1.67 (m, 3 H), 1.53–1.47 (m, 1 H), 1.19 (ddd, *J* = 12.63, 7.77, 1.29 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.0, 156.7, 148.9, 127.8, 106.9, 41.7, 40.9, 36.0, 35.6, 35.5, 34.9, 26.4, 24.5 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{17}O^+$ 189.1274, found 189.1272.

Aldehyde (**30**). To a stirred solution of 5-pentyn-1-ol (**27**, 10.0 mL, 107.7 mmol) in CH_2Cl_2 (270


30

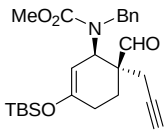
mL) at 25 °C were added Et_3N (75.0 mL, 538 mmol), DMSO (38.2 mL, 538 mmol), and py•SO_3 (34.3 g, 216 mmol). The mixture was stirred for 2 h, at which point *N*,*N*-dimethyl(methylene)iminium chloride (15.1 g, 161.5 mmol) was added in a single portion. The resulting suspension was stirred for 14 h before the addition of sat. aq. $NaHCO_3$ solution (150 mL). The phases were separated and the aqueous portion was extracted with Et_2O (4 × 150 mL). The combined organic extracts were washed with 10% aq. $CuSO_4$ (100 mL), 1 M HCl (100 mL), and brine (100 mL), and dried over anhydrous $MgSO_4$. The solution was filtered and concentrated at atmospheric pressure by distillation through a vigreux column, purified by passing through a short silica plug, eluting with 25% Et_2O in hexanes, and reconcentrated to give aldehyde **30** (5.35 g, 53% yield) as a volatile colorless oil. **30**: R_f = 0.55 (silica, 25% Et_2O in hexanes); IR (film): ν_{max} = 3291, 2827, 1688, 1652, 1431, 1415, 1347, 1241, 957 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.61 (s, 1 H), 6.69 (t, *J* = 2.0 Hz, 1 H), 6.20 (t, *J* = 1.5 Hz, 1 H), 3.17–3.16 (m, 2H), 2.20 (t, *J* = 2.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.6, 144.7, 135.0, 79.4, 72.0, 18.1 ppm. HRMS (*m/z*): $[M - H]^-$ calcd for $C_6H_5O^-$ 93.0346, found 93.0347.

Aldehyde (**31**). To a stirred solution of 5-trimethylsilyl-4-pentyn-1-ol (**28**, 5.11 g, 32.69 mmol) in DMSO (11.6 mL) at 25 °C were added Et_3N (22.8 mL, 163.47 mmol) and py•SO_3 (10.4 g, 65.39 mmol). The mixture was stirred for 40 min and then diluted with CH_2Cl_2 (150 mL) before *N*,*N*-dimethyl(methylene)iminium chloride (4.6 g, 93.55 mmol) was added in one portion. The resulting suspension was stirred for 2 h at ambient temperature before sat. aq. $NaHCO_3$ solution (200 mL) was added. The phases were separated and the aqueous layer was extracted with Et_2O (2 × 200 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ solution (300 mL), 0.5 M aq. HCl (2 × 300 mL), and brine (300 mL), and then dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 5% → 15% Et_2O in hexanes) to afford aldehyde **31** (5.01 g, 92% yield) as a volatile colorless oil. **31**: R_f = 0.53 (silica, 20% EtOAc in hexanes); IR (film): ν_{max} = 2960, 2899, 2815, 2180, 1969, 1629, 1428, 1411, 1346, 1249, 1097, 1069, 1039, 957, 919, 837, 759, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 9.61 (s, 1 H), 6.68 (t, *J* = 1.9 Hz, 1 H), 6.20 (t, *J* = 1.6 Hz, 1 H), 3.20 (t, *J* = 1.7 Hz, 2 H), 0.18 (s, *J* = 0.5 Hz, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.70, 144.93, 135.05, 101.66, 88.91, 19.46, 0.00 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_9H_{15}OSi^+$ 167.0887, found 167.0887.



31

Aldehyde [(–)-**33**]. To a stirred solution of catalyst **32** (1.25 g, 1.50 mmol) and oven-dried powdered 4Å molecular sieves (2.5 g) in CH_2Cl_2 (12 mL) at –60 °C was added dienophile **30** (2.82 g, 29.96 mmol). Diene **26** (17.7 g, 50.94 mmol) was added dropwise over 1 h as a solution in CH_2Cl_2 (18 mL) *via* syringe pump. The reaction mixture was stirred at that temperature for 60 h, then filtered though Celite™ (rinsed with further CH_2Cl_2, 40 mL). The resulting solution was concentrated and subjected to flash column chromatgraphy (1% → 4% EtOAc in hexanes with 5% Et_3N) to afford aldehyde (–)-**33** (8.65 g, 92% yield) as a pale yellow oil. [(–)-**33**]: R_f = 0.38 (silica, 20% EtOAc in hexanes); $[\alpha]_D^{35}$ = –89.3 (*c* = 1.12, $CHCl_3$); IR (film): ν_{max} = 3286, 2951, 2930, 2857, 1719, 1693, 1665, 1451, 1391, 1374, 1260, 1205, 839 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.79 (br s, 1 H), 7.29–7.26 (m, 2 H), 7.19 (br t, *J* = 7.5 Hz, 1 H), 7.08 (br s, 2 H), 4.95 (br s, 1 H), 4.58



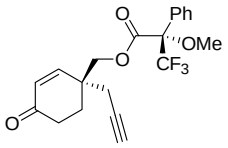
(–)-**33**

(d, J = 5.5 Hz, 1 H), 4.53 (br d, J = 16.0 Hz, 1 H), 4.39 (br d, J = 16.0 Hz, 1 H), 3.59 (br s, 3 H), 2.77 (br d, J = 17.5 Hz, 1 H), 2.47 (br d, J = 17.5 Hz, 1 H), 2.17–2.12 (m, 1 H), 2.03–2.10 (m, 1 H), 2.06 (t, J = 2.5 Hz, 1 H), 2.00–1.96 (m, 1 H), 1.92–1.86 (m, 1 H), 0.83 (br s, 9 H), –0.06 (br s, 3 H), –0.14 (br s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 203.14, 128.26, 126.62, 126.03, 99.58, 99.48, 79.09, 71.84, 56.76, 52.90, 48.10, 25.64, 25.60, 25.45, 22.58, 21.73, 17.83, –3.58, –4.78 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{25}H_{36}NO_4Si^+$ 442.2408, found 442.2427.

Hydroxy enone [(–)-**16**]. To a stirred solution of aldehyde (–)-**33** (8.39 g, 19.0 mmol) in Et_2O (95 mL) at –78 °C was added $LiAlH_4$ (1.0 M solution in THF, 28.5 mL, 28.5 mmol) dropwise over 10 min. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm up to –40 °C over 1 h, after which time the excess $LiAlH_4$ was quenched by addition of EtOAc (15.0 mL, 171 mmol). The reaction mixture was then warmed to 25 °C and acidified by addition of HCl (2 M in MeOH, 95 mL, 190.00 mmol), and then stirred vigorously for 16 h. The reaction mixture was diluted with H_2O (200 mL) and extracted with EtOAc (3 × 250 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ solution (500 mL) and brine (500 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 45% EtOAc in hexanes) to afford hydroxy enone (–)-**16** (1.96 g, 63% yield) as white needles. Mosher ester analysis found the enantiopurity to range from 86–93%, see below for preparation of the corresponding Mosher ester. [(–)-**16**]: R_f = 0.26 (silica, 50% EtOAc in hexanes); m.p. 100–102 °C; $[\alpha]_D^{35}$ = –11.3 (c = 0.97, $CHCl_3$); IR (film): ν_{max} = 3404, 3287, 2932, 2870, 2116, 1661, 1451, 1427, 1390, 1331, 1248, 1218, 1085, 1040, 1006, 980, 939, 887, 867, 798, 762 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.84 (dd, J = 10.3, 0.7 Hz, 1 H), 6.04 (d, J = 10.3 Hz, 1 H), 3.71 (dd, J = 10.9, 5.3 Hz, 1 H), 3.67 (dd, J = 10.9, 5.8 Hz, 1 H), 2.53–2.46 (m, 2 H), 2.43 (dd, J = 7.5, 2.7 Hz, 2 H), 2.22 (t, J = 5.6 Hz, 1 H), 2.07 (td, J = 2.7, 0.7 Hz, 1 H), 2.07–1.94 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.02, 152.80, 130.25, 79.87, 71.54, 66.08, 40.56, 33.67, 28.45, 25.25 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{10}H_{13}O_2^+$ 165.0910, found 165.0912.

(–)-**16**

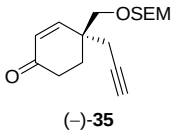
(*S*)-Mosher ester (**16a**). To a stirred solution of hydroxy enone (–)-**16** (10.2 mg, 0.062 mmol) in



16a

CH_2Cl_2 (1.0 mL) at 25 °C were added Et_3N (13 μL, 0.093 mmol) and 4-DMAP (2 mg, 0.006 mmol). The resulting mixture was cooled to 0 °C after which time (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride (CAS no.: 20445-33-4, 18 μL, 0.093 mmol) was added and the reaction mixture was stirred for 5 min at that temperature. The reaction mixture was allowed to warm to 25 °C and stirred for 20 min before it was quenched with sat. aq. $NaHCO_3$ solution (5 mL) and extracted with Et_2O (3 × 3 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by preparative TLC (30% EtOAc in hexane) to afford (*S*)-Mosher ester **16a** (23.1 mg, 98% yield) as a colorless oil. **16a**: R_f = 0.56 (silica, 50% EtOAc in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.47 (m, 2 H), 7.44–7.38 (m, 3 H), 6.71 (d, *J* = 10.3 Hz, 1 H), 6.04 (d, *J* = 10.3 Hz, 1 H), 4.49 (d, *J* = 11.1 Hz, 1 H), 4.27 (d, *J* = 11.1 Hz, 1 H), 3.53 (s, 3 H), 2.45 (t, *J* = 6.9 Hz, 2 H), 2.40 (dd, *J* = 16.9, 2.6 Hz, 1 H), 2.33 (dd, *J* = 16.9, 2.6 Hz, 1 H), 2.11 (t, *J* = 2.7 Hz, 1 H), 2.02–1.91 (m, 2 H).

SEM ether [(–)-**35**]. To a stirred solution of hydroxy enone (–)-**16** (4.45 g, 27.10 mmol) in THF (90

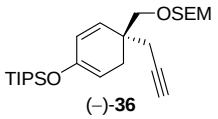


(–)-**35**

mL) was added Et_3N (15.1 mL, 108.40 mmol) and 4-DMAP (332 mg, 2.71 mmol) at 25 °C. The reaction mixture was cooled to 0 °C and 2-(trimethylsilyl)ethoxymethyl chloride (5.76 mL, 32.52 mmol) was added dropwise, after which time the mixture was heated at reflux for 16 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ solution (200 mL) and the resulting mixture was extracted with EtOAc (3 × 200 mL). The combined organic extracts were washed with brine (400 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 5% → 25% EtOAc in hexanes) to afford SEM ether (–)-**35** (7.49 g, 94% yield) as a colorless oil. [(–)-**35**]: R_f = 0.57 (silica, 40% EtOAc in hexanes); $[\alpha]_D^{35}$ = –14.7 (*c* = 1.31, $CHCl_3$); IR (film): ν_{max} = 3309, 2952, 2886, 1683, 1421, 1386, 1248, 1190, 1158, 1107, 1056, 1035, 859, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (d, *J* = 10.0 Hz, 1 H), 6.03 (d, *J* = 10.0 Hz,

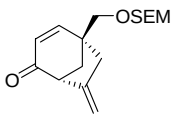
1 H), 4.69 (s, 2 H), 3.64–3.59 (m, 2 H), 3.60 (d, J = 9.6 Hz, 1 H), 3.55 (d, J = 9.6 Hz, 1 H), 2.51–2.45 (m, 4 H), 2.06–2.00 (m, 3 H), 0.96–0.92 (m, 2 H), 0.02 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.7, 152.7, 130.0, 95.0, 79.9, 71.4, 70.6, 65.2, 39.5, 33.7, 28.9, 25.7, 18.1, –1.5 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{26}O_3SiNa^+$ 317.1543, found 317.1538.

Enol ether [(–)-**36**]. To a stirred solution of SEM ether (–)-**35** (7.48 g, 25.40 mmol) in CH_2Cl_2 (130 mL) at 25 °C was added Et_3N (10.6 mL, 76.21 mmol). The reaction mixture was cooled to –78 °C and TIPSOTf (10.3 mL, 38.10 mmol) was added dropwise. The resulting mixture was stirred at –78 °C for 15 min, after which time it was allowed to warm slowly to 0 °C. The reaction mixture was diluted with Et_2O:hexanes (2:1, 400 mL) and washed with sat. aq. $NaHCO_3$ solution (250 mL) and brine (250 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography (silica, 2% → 4% Et_2O in hexanes with 2% Et_3N) to afford pure enol ether (–)-**36** (11.1 g, 97% yield) as a colorless oil. [(–)-**36**]: R_f = 0.59 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = –1.5 (c = 1.00, $CHCl_3$); IR (film): ν_{max} = 2945, 2867, 1652, 1597, 1464, 1402, 1329, 1247, 1206, 1148, 1108, 1056, 1038, 882, 859, 834 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.81 (dd, J = 10.0, 2.0 Hz, 1 H), 5.71 (d, J = 10.0 Hz, 1 H), 4.80–4.78 (m, 1 H), 4.68 (s, 2 H), 3.62 (t, J = 8.6 Hz, 2 H), 3.54 (d, J = 9.0 Hz, 1 H), 3.46 (d, J = 9.0 Hz, 1 H), 2.39 (dd, J = 16.5, 2.6 Hz, 1 H), 2.34 (dd, J = 16.5, 2.6 Hz, 1 H), 2.29–2.22 (m, 2 H), 1.99 (t, J = 2.6 Hz, 1 H), 1.20–1.14 (m, 3 H), 1.08 (d, J = 7.0 Hz, 18 H), 0.97–0.94 (m, 2 H), 0.03 (s, 9 H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.6, 132.7, 127.1, 99.7, 95.0, 81.5, 70.4, 70.3, 64.9, 38.1, 29.5, 24.6, 18.1, 18.0, 12.5, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{25}H_{47}O_3Si_2^+$ 451.3058, found 451.3063.



(–)-**36**

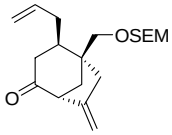
Bicyclo enone [(+)-**37**]. To a stirred solution of enol ether (–)-**36** (5.30 g, 11.76 mmol) in toluene (31 mL) at 25 °C was added solid $AuCl(PPh_3)$ (116 mg, 0.24 mmol, 2 mol%). A solution of $AgBF_4$ (46 mg, 0.24 mmol, 2 mol%) in MeOH (3.1 mL) was then added over 1 min, after which time the reaction mixture was stirred in the dark for 30 min, then diluted with Et_2O (40 mL), filtered through a short silica plug, and rinsed with further Et_2O (175 mL). The resulting solution was



(+)-**37**

concentrated and the residue was purified by flash column chromatography (silica, 5% → 25% Et_2O in hexanes) to afford bicyclo enone (+)-**37** (3.25 g, 94% yield) as a colorless oil. [(+)-**37**]: R_f = 0.29 (silica, 30% Et_2O in hexanes); $[\alpha]_D^{35}$ = +71.9 (*c* = 0.99, $CHCl_3$); IR (film): ν_{max} = 2952, 2892, 1685, 1376, 1284, 1153, 1108, 1055, 1034, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.11 (dd, *J* = 9.5, 2.0 Hz, 1 H), 5.84 (dd, *J* = 9.5, 1.8 Hz, 1 H), 5.28 (br s, 1 H), 5.05 (br s, 1 H), 4.70 (s, 2 H), 3.67 (d, *J* = 9.5 Hz, 1 H), 3.62 (d, *J* = 9.5 Hz, 1 H), 3.64–3.61 (m, 2 H), 3.47 (d, *J* = 5.0 Hz, 1 H), 2.46 (dt, *J* = 16.0, 2.5 Hz, 1 H), 2.38–2.35 (m, 1 H), 2.13 (dd, *J* = 11.0, 2.5 Hz, 1 H), 1.82 (ddd, *J* = 11.0, 5.0, 2.0 Hz, 1 H), 0.96–0.93 (m, 2 H), 0.02 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.5, 156.0, 144.8, 126.7, 112.4, 95.1, 71.9, 65.2, 58.5, 47.4, 42.8, 39.5, 18.1, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{27}O_3Si^+$ 295.1724, found 295.1723.

Diene [(+)-**38**]. To a stirred solution of CuBr•Me_2S (8.71 g, 42.38 mmol) in THF (130 mL) at –78 °C

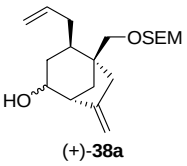


(+)-**38**

was added allyl magnesium chloride (1.7 M solution in THF, 49.9 mL, 84.83 mmol) dropwise over a period of 10 min and the resulting mixture was stirred for an additional 1 h at that temperature. A solution of bicyclo enone (+)-**37** (6.24 g, 21.19 mmol) in THF (33 mL) was then added dropwise at –78 °C over 15 min, and the mixture was stirred for an additional 1 h before it was allowed to slowly warm to –40 °C over a period of 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (120 mL, adjusted to pH 8 with aq. NH_4OH). After allowing to warm to room temperature, the reaction mixture was extracted with Et_2O (3 × 200 mL) and the combined organic extracts were washed with brine (300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 10% → 20% Et_2O in hexanes) to afford diene (+)-**38** (5.27 g, 74% yield) as a colorless oil. [(+)-**38**]: R_f = 0.49 (silica, 25% EtOAc in hexanes); $[\alpha]_D^{35}$ = +88.7 (*c* = 0.98, $CHCl_3$); IR (film): ν_{max} = 2953, 2916, 1717, 1655, 1640, 1437, 1377, 1248, 1105, 1056, 1035, 859, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.70–5.61 (m, 1 H), 5.06–5.02 (m, 3 H), 4.91 (br s, 1 H), 4.66 (s, 2 H), 3.73 (d, *J* = 9.5 Hz, 1 H), 3.62–3.59 (m, 2 H), 3.39 (d, *J* = 9.5 Hz, 1 H), 3.20 (d, *J* = 5.0 Hz, 1 H), 2.63–2.62 (m, 2 H), 2.55 (ddd, *J* =

16.0, 8.0, 1.0 Hz, 1 H), 2.34–2.28 (m, 1 H), 2.20 (d, *J* = 16.0 Hz, 1 H), 2.18–2.14 (m, 1 H), 1.85 (d, *J* = 12.5 Hz, 1 H), 1.79 (ddd, *J* = 13.8, 10.9, 8.7 Hz, 1 H), 1.69 (ddd, *J* = 12.5, 5.5, 2.5 Hz, 1 H), 0.95–0.92 (m, 2 H), 0.01 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.9, 148.4, 136.4, 117.3, 108.4, 95.0, 71.9, 65.2, 59.8, 46.4, 42.4, 40.9, 38.4, 35.3, 34.3, 18.1, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{33}O_3Si^+$ 337.2193, found 337.2194.

Alcohol [(+)-**38a**]. To a stirred solution of diene (+)-**38** (5.26 g, 15.63 mmol) in MeOH (65 mL) at –5 °C was added $NaBH_4$ (1.48 g, 39.07 mmol), and the reaction mixture was allowed to warm to 25 °C. After 30 min, the reaction mixture was cooled to 0 °C and H_2O (200 mL) was added carefully. The mixture was extracted with Et_2O (3 × 250 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (silica, 5% → 20% Et_2O in hexanes) afforded a mixture of alcohols (+)-**38a** (5.12 g, 97% yield, *ca*. 2:1 diastereomeric ratio) as a colorless oil. [(+)-**38aa**] (major, more polar): R_f = 0.22 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = +4.2 (*c* = 0.98, $CHCl_3$); IR (film): ν_{max} = 3432, 3074, 2931, 2865, 1658, 1640, 1457, 1431, 1413, 1386, 1249, 1106, 1056, 1035, 835 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.68 (dddd, *J* = 16.9, 10.2, 8.5, 5.3 Hz, 1 H), 5.02–4.97 (m, 1 H), 4.90 (br s, 1 H), 4.88 (br s, 1 H), 4.60 (s, 2 H), 3.71–3.65 (m, 1 H), 3.62 (d, *J* = 9.6 Hz, 1 H), 3.58–3.55 (m, 2 H), 3.26 (d, *J* = 9.6 Hz, 1 H), 2.58 (br t, *J* = 3.7 Hz, 1 H), 2.34 (dt, *J* = 17.2, 2.5 Hz, 1 H), 2.28–2.19 (m, 2 H), 1.94–1.86 (m, 2 H), 1.78–1.75 (m, 1 H), 1.70 (d, *J* = 9.8 Hz, 1 H), 1.47 (dd, *J* = 11.9, 2.0 Hz, 1 H), 1.41 (ddd, *J* = 11.8, 5.4, 1.9 Hz, 1 H), 1.17–1.10 (m, 1 H), 0.93–0.90 (m, 2 H), –0.01 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.6, 137.8, 116.0, 106.4, 94.9, 72.5, 68.9, 64.9, 50.7, 46.0, 43.2, 39.2, 33.7, 33.6, 31.7, 18.0, –1.5 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{35}O_3Si^+$ 339.2350, found 339.2348.

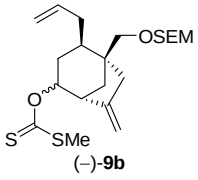


(+)-**38a**

[(+)-**38ab**] (minor, less polar): R_f = 0.29 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = +1.2 (*c* = 1.06, $CHCl_3$); IR (film): ν_{max} = 3472, 3068, 2928, 2870, 1656, 1639, 1444, 1375, 1249, 1105, 1056, 1031, 835 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.74 (dddd, *J* = 17.0, 10.1, 7.5, 5.3 Hz, 1 H), 5.05–4.99 (m, 2

H), 4.85 (br s, 1 H), 4.73 (br s, 1 H), 4.63 (s, 2 H), 3.80 (br s, 1 H), 3.69 (d, J = 9.5 Hz, 1 H), 3.60–3.57 (m, 2 H), 3.26 (d, J = 9.5 Hz, 1 H), 2.66 (t, J = 4.8 Hz, 1 H), 2.41–2.26 (m, 4 H), 2.03 (dd, J = 11.5, 1.6 Hz, 1 H), 1.76–1.72 (m, 1 H), 1.69 (br s, 1 H), 1.69–1.63 (m, 1 H), 1.59 (br d, J = 15.3 Hz, 1 H), 1.11 (dd, J = 11.5, 5.0 Hz, 1 H), 0.94–0.91 (m, 2 H), 0.00 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.3, 139.1, 115.8, 105,4. 94.9, 73.3, 72.7, 64.9, 49.9, 46.5, 42.4, 38.5, 34.6, 28.7, 28.3, 18.0, –1.5 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{35}O_3Si^+$ 339.2350, found 339.2354.

Xanthate [(–)-**9b**]. To a stirred solution of a mixture of alcohols (+)-**38a** (*ca*. 2:1 diastereomeric ratio, 1.40 g, 4.14 mmol) in THF (80 mL) at –78 °C was added sequentially CS_2 (2.49 mL, 41.4 mmol) and KHMDS (0.5 M solution in toluene, 41.4 mL, 20.7 mmol). After stirring for 20 min at –78 °C, the cooling bath was removed and the mixture was stirred for an additional 1 h at 25 °C. Methyl iodide (1.28 mL, 20.7 mmol, freshly filtered through anhydrous K_2CO_3) was added dropwise and the reaction mixture was allowed to stir for an additional 1 h at that temperature. The reaction mixture was quenched with H_2O (100 mL) and the resulting mixture was extracted with Et_2O (4 × 100 mL). The combined organic extracts were washed with brine (2 × 100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. Flash column chromatography (silica, 2% → 6% Et_2O in hexanes) of the resulting residue afforded xanthates (–)-**9b** (1.80 g, 100% yield, *ca*. 2:1 diastereomeric ratio) as a pale yellow oil. Samples of the individual xanthate diastereoisomers(–)-**9ba** and (–)-**9bb** were prepared in an analogous fashion from the diastereoisomerically pure alcohols (+)-**38aa** and (+)-**38ab**, respectively. [(–)-**9ba**] (from more polar isomer (+)-**38aa**): R_f = 0.54 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = –25.7 (c = 1.04, $CHCl_3$); IR (film): ν_{max} = 3073, 2952, 2870, 1658, 1638, 1458, 1428, 1413, 1373, 1230, 1208, 1108, 1052 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.72 (dddd, J = 17.1, 10.1, 8.5, 5.3 Hz, 1 H), 5.63 (ddd, J = 11.6, 5.6, 2.8 Hz, 1 H), 5.08 (dd, J = 17.1, 0.9 Hz, 1 H), 5.04 (d, J = 10.1 Hz, 1 H), 4.95 (br s, 1 H), 4.93 (br s, 1 H), 4.65 (s, 2 H), 3.68 (d, J = 9.3 Hz, 1 H), 3.62–3.58 (m, 2 H), 3.31 (d, J = 9.3 Hz, 1 H), 3.00–2.96 (m, 1 H), 2.52 (s, 3 H), 2.44–2.35 (m, 2 H), 2.32–2.26 (m, 1 H), 2.04 (dd, J = 13.2, 5.7 Hz, 1 H), 2.00–1.88 (m, 2 H), 1.66 (td, J = 12.3, 6.2 Hz,

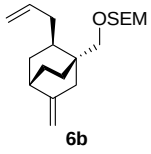


(–)-**9b**

1 H), 1.59 (dd, J = 12.0, 1.4 Hz, 1 H), 1.46 (ddd, J = 12.0, 5.8, 1.7 Hz, 1 H), 0.96–0.92 (m, 2 H), 0.00 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.7, 149.2, 137.5, 116.6, 107.9, 95.0, 81.9, 72.4, 65.1, 46,8, 46.2, 43.1, 39.4, 33.8, 33.5, 26.6, 18.4, 18.1, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{37}O_3S_2Si^+$ 429.1948, found 429.1949.

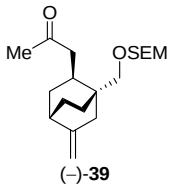
[(–)-**9bb**] (from less polar isomer (+)-**38ab**): R_f = 0.54 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = –25.8 (*c* = 1.49, $CHCl_3$); IR (film): ν_{max} = 3068, 2950, 2870, 1656, 1635, 1441, 1228, 1215, 1055, 1034 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.68 (dddd, J = 17.1, 10.1, 9.1, 5.1 Hz, 1 H), 5.56–5.53 (m, 1 H), 5.08–5.00 (m, 3 H), 4.91 (br s, 1 H), 4.66 (s, 2 H), 3.73 (d, J = 9.5 Hz, 1 H), 3.63–3.60 (m, 2 H), 3.32 (d, J = 9.5 Hz, 1 H), 3.05 (t, J = 4.8 Hz, 1 H), 2.58 (s, 3 H), 2.49–2.39 (m, 2 H), 2.36–2.30 (m, 1 H), 2.22–2.16 (m, 1 H), 1.97 (d, J = 15.1 Hz, 1 H), 1.93 (dd, J = 11.8, 1.5 Hz, 1 H), 1.85–1.77 (m, 2 H), 1.26 (dd, J = 12.1, 5.0 Hz, 1 H), 0.97–0.93 (m, 2 H), 0.03 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.8, 150.4, 138.0, 116.6, 107.5, 95.0. 84.0, 73.0, 65.1, 46.3, 46.1, 42.4, 38.4, 34.1, 29.9, 25.0, 18.9, 18.1, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{37}O_3S_2Si^+$ 429.1948, found 429.1949.

Diene (**6b**). To a degassed stirred solution of xanthates (–)-**9b** (*ca*. 2:1 diastereomeric ratio, 1.16 g, 2.71 mmol) in toluene (270 mL) at 25 °C were added AIBN (36 mg, 0.22 mmol, recrystallized from acetone) and *n*-Bu_3SnH (1.46 mL, 5.41 mmol). The mixture was heated to 100 °C and stirred at that temperature for 20 min. Upon cooling to room temperature, the reaction mixture was diluted with Et_2O (600 mL). The organic phase was washed with 1 N aq. HCl (500 mL), sat. aq. $NaHCO_3$ solution (500 mL), and brine (500 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography (silica, 100% hexanes → 4% Et_2O in hexanes) to afford diene **6b**, along with an inseparable impurity (800 mg, 92% combined yield; *ca*. 5.5:1 ratio), as a colorless oil. This mixture was used in the next step without further purification. **6b**: R_f = 0.39 (silica, 5% EtOAc in hexanes).



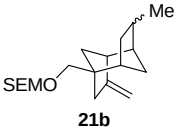
6b

Ketone [(–)-**39**]. To a stirred solution of diene **6b** (800 mg, 2.48 mmol; *ca*. 5.5:1 ratio **6b**:by-product impurity) in DMF (16.5 mL) at 25 °C were added sequentially CuCl (368 mg, 3.72 mmol), H_2O (2.5 mL), and $PdCl_2$ (110 mg, 0.62 mmol). The reaction mixture was stirred under an oxygen atmosphere (balloon) for 24 h at 25 °C and then filtered through a pad of Celite™. The filtrate was diluted with hexanes (250 mL) and H_2O (100 mL), and the separated aqueous layer was extracted with hexanes (5 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was subjected to flash column chromatography (silica, 20% → 30% Et_2O in hexanes) to afford ketone (–)-**39** [455 mg, 50% from xanthate (–)-**39**] as a pale yellow oil along with the unreacted by-product from the previous radical rearrangement reaction as a pale yellow oil (**21b**). [(–)-**39**]: R_f = 0.36 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = –8.1 (*c* = 1.23, $CHCl_3$); IR (film): ν_{max} = 2934, 2867, 1716, 1652, 1469, 1428, 1408, 1373, 1354, 1157, 1105, 1056, 1030, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 4.74–4.73 (m, 1 H), 4.62–4.60 (m, 1 H), 4.59 (s, 2 H), 3.60–3.56 (m, 2 H), 3.24 (d, *J* = 9.7 Hz, 1 H), 3.14 (d, *J* = 9.7 Hz, 1 H), 2.62 (dd, *J* = 15.1, 3.5 Hz, 1 H), 2.40–2.34 (m, 1 H), 2.25 (dd, *J* = 15.1, 10.4 Hz, 1 H), 2.21–2.14 (m, 3 H), 2.12 (s, 3 H), 1.96–1.89 (m, 1 H), 1.62–1.57 (m, 2 H), 1.52–1.44 (m, 1 H), 1.25–1.18 (m, 1 H), 1.07 (ddd, *J* = 12.9, 6.2, 2.2 Hz, 1 H), 0.94–0.91 (m, 2 H), 0.02 (s, 9 H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 208.8, 150.8, 105.3, 95.0, 73.1, 65.0, 46.7, 39.4, 36.4, 35.9, 34.5, 32.7, 30.0, 26.1, 23.1, 18.1, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{35}O_3Si^+$ 339.2350, found 339.2350.



(–)-**39**

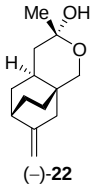
5-*exo*-trig by-product (**21b**). Spectroscopically pure material was obtained as a pale yellow oil, *ca.* 4:1 diastereomeric ratio, from the purification of (–)-**39** discussed directly above. **21b**: R_f = 0.39 (silica, 5% EtOAc in hexanes). IR (film): ν_{max} = 3058, 2946, 2923, 1653, 1471, 1451, 1376, 1248, 1155, 1107, 1057, 1034, 922, 859, 835, 693; ^1H NMR (500 MHz, C_6D_6): δ = 4.90 (s, 1 H), 4.81 (s, 1 H), 4.61 (d, *J* = 6.6 Hz, 1 H), 4.59 (d, *J* = 6.6 Hz, 1 H), 3.70–3.60 (m, 2 H), 3.32 (d, *J* = 9.3 Hz, 1 H), 3.27 (d, *J* = 9.3 Hz, 1 H), 2.55 (ddd, *J* = 15.2, 5.2, 2.5 Hz, 1 H), 2.31–2.25 (m, 1 H), 2.15 (d, *J* = 15.1 Hz, 1 H), 1.85–1.74 (m, 1 H), 1.68–1.62 (m, 1 H), 1.54–1.48 (m, 1 H), 1.48–1.44 (m, 2



21b

H), 1.41 (t, J = 6.2 Hz, 1 H), 1.31 (dd, J = 12.4, 2.9 Hz, 1 H), 1.25–1.13 (m, 2 H), 0.98 (dd, J = 8.5, 7.6 Hz, 2 H), 0.87 (d, J = 6.8 Hz, 3 H), 0.02 (d, J = 1.2 Hz, 9 H) ppm; ^{13}C NMR (125 MHz, C_6D_6): δ = 152.42, 105.90, 65.68, 73.16, 65.26, 41.14, 38.79, 38.12, 37.19, 33.04, 31.07, 29.10, 28.78, 27.92, 18.94, 18.71, –0.89 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{35}O_2Si^+$ 323.2401, found 323.2398.

Hemiketal [(–)-**22**]. To a stirred solution of ketone (–)-**39** (126 mg, 0.37 mmol) in DMPU (10.0 mL) at 25 °C was added tris(dimethylamino)sulfonium difluorotrimethyl-silicate (TASF, 1.03 g, 3.72 mmol). The reaction mixture was heated to 80 °C and stirred for 1.5 h, after which time it was quenched with sat. aq. $NaHCO_3$ solution (10 mL). The resulting mixture was extracted with Et_2O (5 × 15 mL) and the combined organic extracts were washed with 1 M aq. HCl:brine (1:1, 20 mL) and brine (20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was subjected to flash column chromatography (silica, 10% → 25% Et_2O in hexanes) to afford recovered **21** (32 mg, 25%) and hemiketal (–)-**22** (48.7 mg, 63% yield; 84% yield based on recovered starting material) as a white solid. Hemiketal (–)-**22** crystallized from a CH_2Cl_2/$CDCl_3$ solution on standing to give colorless needles (m.p. 115–117 °C), from which an X-ray crystal structure was obtained. $[\alpha]_D^{35}$ = –106.2 (c = 0.66, $CHCl_3$).

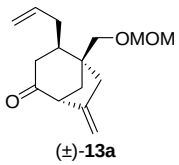


(–)-**22**

Keto aldehyde [(–)-**23**]. The preparation of (–)-**23** was exactly as that described for (±)-**23** earlier in this supplementary information. [(–)-**23**]: $[\alpha]_D^{35}$ = –52.5 (c = 0.8, $CHCl_3$).

Enone [(+)-**5**]. The preparation of (+)-**5** was exactly as that described for (±)-**5** earlier in this supplementary information. [(+)-**5**]: $[\alpha]_D^{35}$ = +25.89 (c = 0.97, $CHCl_3$).

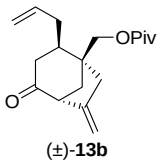
MOM ether [(±)-**13a**]. To a stirred solution of hydroxy ketone (±)-**13** (49 mg, 0.24 mmol) in CH_2Cl_2 (3 mL) at 0 °C was added *i*-Pr_2NEt (83 μL, 0.48 mmol) followed by MOMCl (54 μL, 0.71 mmol). The resulting mixture was allowed to warm to 25 °C and stirred for 15 h before it was quenched with sat. aq. $NaHCO_3$ solution (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (30 mL), dried over



(±)-**13a**

anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (silica, 10% → 20% EtOAc in hexanes) afforded ketone (±)-**13a** (50 mg, 84% yield) as a colorless oil. [(±)-**13a**]: R_f = 0.38 (silica, 40% Et_2O in hexanes); IR (film): γ_{max} = 3076, 2928, 2875, 1714, 1654, 1640, 1438, 1386, 1296, 1216, 1184, 1147, 1105, 1040, 994, 967, 915, 886, 833, 764, 681; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.72–5.61 (m, 1 H), 5.07–5.00 (m, 3 H), 4.91 (s, 1 H), 4.62 (d, *J* = 6.6 Hz, 1 H), 4.60 (d, *J* = 6.6 Hz, 1 H), 3.71 (d, *J* = 9.6 Hz, 1 H), 3.38 (d, *J* = 9.6 Hz, 1 H), 3.35 (s, 3 H), 3.19 (d, *J* = 5.1 Hz, 1 H), 2.64 (t, *J* = 2.1 Hz, 2 H), 2.55 (ddd, *J* = 15.9, 8.1, 1.0 Hz, 1 H), 2.35–2.27 (m, 1 H), 2.24–2.14 (m, 2 H), 1.84 (d, *J* = 12.2 Hz, 1 H), 1.82–1.74 (m, 1 H), 1.69 (ddd, *J* = 12.2, 5.1, 2.2 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.85, 148.29, 136.40, 117.28, 108.42, 96.63, 71.82, 59.78, 55.31, 46.32, 42.35, 40.89, 38.39, 35.27, 34.32; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{15}H_{23}O_3^+$ 251.1642, found 251.1641.

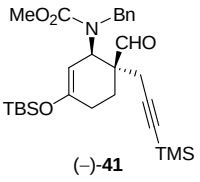
Piv ester [(±)-**13b**]. To a stirred solution of hydroxy ketone (±)-**13** (50 mg, 0.24 mmol) in CH_2Cl_2 (3 mL) at 25 °C were added Et_3N (37 μL, 0.36 mmol) and 4-DMAP (3 mg, 0.024 mmol). The resulting mixture was cooled to 0 °C after which time pivaloyl chloride (45 μL, 0.036 mmol) was added and the reaction mixture was stirred at that temperature for 5 min. The reaction mixture was allowed to warm to 25 °C and stirred for 8 h before it was quenched with sat. aq. $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (25 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 5% → 15% EtOAc in hexanes) to afford ketone (±)-**13b** (64.3 mg, 91% yield) as a colorless oil. [(±)-**13b**]: R_f = 0.44 (silica, 30% Et_2O in hexanes); IR (film): ν_{max} = 3077, 2972, 2911, 1717, 1655, 1640, 1479, 1460, 1438, 1397, 1365, 1282, 1214, 1147, 1034, 993, 914, 885, 833, 769, 676; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.65 (dddd, *J* = 16.7, 10.3, 8.4, 5.5 Hz, 1 H), 5.09–5.01 (m, 3 H), 4.94 (s, 1 H), 4.27 (d, *J* = 11.3 Hz, 1 H), 4.00 (d, *J* = 11.4 Hz, 1 H), 3.24 (d, *J* = 5.1 Hz, 1 H), 2.62 (t, *J* = 2.2 Hz, 2 H), 2.59 (ddd, *J* = 15.9, 8.1, 1.0 Hz, 1 H), 2.32–2.26 (m, 1 H), 2.24 (d, *J* = 16.0 Hz, 1 H), 2.12 (dd, *J* = 10.6, 8.1 Hz, 1 H), 1.91 (d, *J* = 12.3 Hz, 1



(±)-**13b**

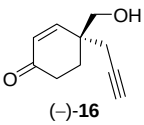
H), 1.82 (ddd, J = 13.9, 10.9, 8.4 Hz, 1 H), 1.74 (ddd, J = 12.2, 5.2, 2.3 Hz, 1 H), 1.22 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.19, 178.13, 147.62, 136.02, 117.57, 108.92, 67.89, 59.61, 46.03, 42.26, 41.31, 38.98, 38.47, 35.18, 34.48, 27.22 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{27}O_3^+$ 291.1955, found 291.1946.

Aldehyde [(–)-**41**]. To a stirred solution of aldehyde **31** (2.9 g, 17.44 mmol) and oven-dried powdered 4Å molecular sieves (3.0 g) in CH_2Cl_2 (10 mL) at 0 °C was added catalyst **40** (15 mg, 0.18 mmol) followed by solid diene **26** (6.67 g, 19.18 mmol) in one portion. The reaction mixture was stirred at 0 °C for 30 min and then filtered through Celite™ (rinsed with further CH_2Cl_2, 30 mL). The resulting solution was concentrated and subjected to flash column chromatgraphy (2% → 5% EtOAc in hexanes with 2% Et_3N) to afford aldehyde (–)-**41** (8.68 g, 97% yield) as a pale yellow oil. [(–)-**41**]: R_f = 0.47 (silica, 20% EtOAc in hexanes); $[\alpha]_D^{35}$ = –87.59 (*c* = 1.00, $CHCl_3$); IR (film): ν_{max} = 2956, 2931, 2896, 2858, 2176, 1719, 1696, 1665, 1494, 1451, 1391, 1373, 1350, 1335, 1294, 1251, 1205, 1165, 1102, 1026, 988, 943, 841, 799, 779, 761, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C): δ = 9.76 (s, 1 H), 7.28 (t, J = 7.5 Hz, 2 H), 7.20 (t, J = 7.3 Hz, 1 H), 7.12 (d, J = 5.5 Hz, 2 H), 4.88 (br s, 1 H), 4.59 (br d, J = 5.1 Hz, 1 H), 4.49 (t, J = 14.53 Hz, 1 H), 4.47–4.43 (m, 1 H), 3.63 (br s, 3 H), 2.78 (br d, J = 17.0 Hz, 1 H), 2.51 (d, J = 17.4 Hz, 1 H), 2.18 (d, J = 15.9 Hz, 1 H), 2.13–2.03 (m, 1 H), 2.03–1.94 (m, 1 H), 1.94–1.85 (m, 1 H), 0.86 (s, 9 H), 0.15 (s, 9 H), –0.01 (s, 3 H), –0.07 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ = 202.78, 139.27, 128.27, 126.71, 101.64, 99.66, 88.80, 57.22, 52.72, 25.81, 25.52, 24.24, 17.89, –0.02, –4.68 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{28}H_{44}NO_4Si_2^+$ 514.2803, found 514.2794.



(–)-**41**

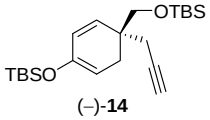
Hydroxy enone [(–)-**16**]. To a stirred solution of aldehyde (–)-**41** (9.5 g, 18.49 mmol) in Et_2O (95 mL) at –78 °C was added $LiAlH_4$ (1.0 M solution in THF, 27.7 mL, 27.73 mmol) dropwise over 10 min. The reaction mixture was stirred at –78 °C for 30 min and then allowed to warm up to –40 °C and stirred for 2 h at that temperature, after which time the excess $LiAlH_4$ was quenched by addition of MeOH (40 mL, 987.52 mmol) and the reaction mixture was warmed to 25 °C.



(–)-**16**

K_2CO_3 (12.8 g, 92.44 mmol) was added in one portion and the reaction mixture was stirred at 25 °C for 5 h, and then acidified with HCl (4 M in MeOH, 95 mL, 380.00 mmol) and stirred vigorously for 16 h. The reaction mixture was diluted with H_2O (200 mL) and extracted with EtOAc (3 × 250 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ solution (500 mL) and brine (500 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 35% → 45% EtOAc in hexanes) to afford hydroxy enone (–)-**16** (4.02 g, 92% yield) as a white solid. This material was recrystallized from 5:1 hexanes:EtOAc (150 mL) to give white needles from which Mosher ester analysis, as before, revealed > 98% *ee*, see Supporting Information Section **IV** for corresponding ^{1}H NMR.

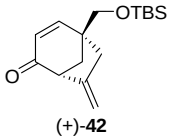
Enol ether [(–)-**14**]. To a stirred solution of hydroxy enone (–)-**16** (1.56 g, 9.50 mmol) in CH_2Cl_2 (35 mL) at 25 °C were added sequentially Et_3N (5.3 mL, 38.00 mmol), 4-DMAP (116 mg, 0.95 mmol), and TBSCl (2.15 g, 14.25 mmol). The reaction mixture was heated to 45 °C and stirred at that temperature for 10 h. The mixture was cooled to 0 °C and TBSOTf (3.27 mL, 14.25 mmol) was added dropwise followed by stirring at the same temperature for 3 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ solution (70 mL), and the resulting mixture was extracted with Et_2O (3 × 80 mL). The combined organic extracts were washed with brine (300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 100% hexanes with 5% Et_3N → 5% Et_2O in hexanes with 5% Et_3N) to afford enol ether (–)-**14** (3.62 g, 97% yield) as a colorless oil. [(–)-**14**]: R_f = 0.63 (silica, 10% EtOAc in hexanes); $[\alpha]_D^{35}$ = –22.54 (*c* = 1.14, $CHCl_3$); IR (film): ν_{max} = 3313, 2955, 2930, 2897, 2857, 1652, 1596, 1472, 1463, 1403, 1361, 1328, 1252, 1231, 1206, 1183, 1098, 1006, 938, 915, 887, 835, 775, 688, 668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.73 (dd, *J* = 12.9, 0.7 Hz, 1 H), 5.69 (dt, *J* = 10.0, 0.8 Hz, 1 H), 4.79–4.76 (m, 1 H), 3.54 (d, *J* = 9.4 Hz, 1 H), 3.42 (d, *J* = 9.4 Hz, 1 H), 2.35 (dd, *J* = 16.5, 2.6 Hz, 1 H), 2.28 (dd, *J* = 16.4, 2.7 Hz, 1 H), 2.21 (d, *J* = 4.6 Hz, 2 H), 1.96 (td, *J* = 2.7, 0.8 Hz, 1 H), 0.92 (d, *J* = 0.9 Hz, 9 H), 0.89 (d, *J* = 0.9 Hz, 9 H), 0.13 (s, 6 H), 0.04 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ



(–)-**14**

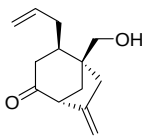
= 147.51, 133.06, 126.80, 100.97, 81.96, 70.25, 65.00, 39.42, 28.84, 25.86, 25.69, 18.28, 18.06, –2.94, –4.46, –4.50 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{41}O_2Si_2^+$ 393.2639, found 393.2639.

Bicyclo enone [(+)-**42**]. To a stirred solution of enol ether (–)-**14** (4.25 g, 10.82 mmol) in toluene (27 mL) at 25 °C was added solid $AuCl(PPh_3)$ (107 mg, 0.22 mmol, 2 mol%). A solution of $AgBF_4$ (42 mg, 0.22 mmol, 2 mol%) in MeOH (2.7 mL) was then added over 5 min and stirring continued in the dark for 30 min. The resulting mixture was diluted with Et_2O (50 mL), filtered through a short silica plug, and rinsed with further Et_2O (200 mL). The solution was concentrated and the residue was purified by flash column chromatography (silica, 5% → 10% EtOAc in hexanes) to afford bicyclo enone (+)-**42** (2.87 g, 95% yield) as a colorless oil. [(+)-**42**]: R_f = 0.30 (silica, 10% EtOAc in hexanes); $[\alpha]_D^{35}$ = +84.74 (*c* = 2.49, $CHCl_3$); IR (film): ν_{max} = 2954, 2929, 2886, 2856, 1685, 1656, 1471, 1431, 1386, 1361, 1311, 1253, 1219, 1153, 1141, 1084, 1046, 1006, 962, 939, 924, 884, 834, 815, 775, 738, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.12 (dd, *J* = 9.7, 1.8 Hz, 1 H), 5.83 (dd, *J* = 9.7, 1.4 Hz, 1 H), 5.27 (s, 1 H), 5.05 (s, 1 H), 3.71 (d, *J* = 9.9 Hz, 1 H), 3.68 (d, *J* = 9.9 Hz, 1 H), 3.46 (d, *J* = 4.9 Hz, 1 H), 2.46 (dt, *J* = 15.8, 2.5 Hz, 1 H), 2.31 (d, *J* = 15.9 Hz, 1 H), 2.02 (dd, *J* = 11.1, 2.0 Hz, 1 H), 1.81 (ddd, *J* = 11.1, 5.0, 1.9 Hz, 1 H), 0.90 (d, *J* = 1.4 Hz, 9 H), 0.07 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.01, 156.29, 145.34, 126.58, 112.25, 66.96, 58.60, 49.02, 42.28, 39.12, 25.81, 18.25, –5.50 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{27}O_2Si^+$ 279.1775, found 279.1774.



(+)-**42**

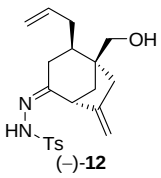
Alcohol [(+)-**13**]. To a stirred solution of CuBr•Me_2S (3.81 g, 18.53 mmol) in THF (60 mL) at –78 °C was added allyl magnesium chloride (1.7 M solution in THF, 21.9 mL, 37.06 mmol) dropwise over a period of 10 min, and the resulting mixture was stirred at that temperature for an additional 1 h. A solution of bicyclo enone (+)-**42** (2.58 g, 9.27 mmol) in THF (30 mL) was then added dropwise at –78 °C over 15 min, and the resulting mixture was stirred for an additional 1 h before it was allowed to slowly warm to –40 °C over a period of 1 h. The reaction mixture was quenched with 2 M aq. HCl (50 mL, 100.00 mmol), warmed to 25 °C, and stirred for 4 h. The reaction mixture was then diluted with H_2O (100 mL) and extracted with EtOAc (3 × 120 mL).



(+)-**13**

The combined organic extracts were washed with sat. aq. $NaHCO_3$ solution (400 mL) and brine (400 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 30% → 40% EtOAc in hexanes) to afford alcohol (+)-**13** (1.62 g, 85% yield) as a colorless oil. [(+)-**13**]: R_f = 0.18 (silica, 30% EtOAc in hexanes); $[\alpha]_D^{35}$ = +182.76 (*c* = 2.5, $CHCl_3$); IR (film): ν_{max} = 3427, 3073, 2956, 2926, 2870, 1701, 1653, 1638, 1436, 1226, 1183, 1140, 1031, 1011, 993, 916, 887 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 5.75–5.67 (m, 1 H), 5.08–5.04 (m, 3 H), 4.93 (s, 1 H), 3.85 (d, *J* = 10.9 Hz, 1 H), 3.57 (d, *J* = 10.9 Hz, 1 H), 3.22 (d, *J* = 5.0 Hz, 1 H), 2.67–2.62 (m, 2 H), 2.58 (dd, *J* = 15.9, 8.1 Hz, 1 H), 2.34 (br d, *J* = 13.81 Hz, 1 H), 2.26–2.16 (m, 2 H), 1.84–1.78 (m, 2 H), 1.69 (ddd, *J* = 12.2, 5.1, 2.2 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 210.27, 148.11, 136.47, 117.36, 108.62, 66.81, 59.86, 47.58, 41.72, 40.66, 38.63, 34.96, 34.47 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{19}O_2^+$ 207.1379 found 207.1372.

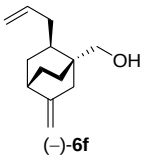
Tosyl hydrazone [(–)-**12**]. To a stirred solution of alcohol (1.76 g, 8.53 mmol) in CH_2Cl_2 (70 mL) were added tosyl hydrazone (1.67 g, 8.96 mmol) and *p*-toluenesulfonic acid (8 mg, 0.04 mmol) and the resulting mixture was refluxed at 45 °C for 3 h. The reaction mixture was concentrated to afford tosyl hydrazone (–)-**12** as a colorless oil which was used directly in the next step without any further purification (3.14 g, 98% yield, *E*:*Z ca.* 1.5:1). [(–)-**12**]: R_f = 0.31 (silica, 60% EtOAc in hexanes); $[\alpha]_D^{35}$ = –38.15 (*c* = 0.8, $CHCl_3$); IR (film): ν_{max} = 3508, 3218, 3068, 2956, 2925, 2875, 1704, 1656, 1638, 1598, 1437, 1400, 1334, 1304, 1289, 1164, 1093, 1019, 918, 890, 814, 705, 665 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.88–7.76 (m, 4 H), 7.63 (br s, 0.5 H), 7.35–7.27 (m, 4 H), 7.23 (br s, 1 H), 5.71–5.57 (m, 2 H), 5.07 (dt, *J* = 10.1, 1.5 Hz, 1 H), 4.99–4.94 (m, 1 H), 4.91 (dt, *J* = 4.7, 1.6 Hz, 1 H), 4.87–4.86 (m, 2 H), 4.82–4.77 (m, 2 H), 3.75 (d, *J* = 10.9 Hz, 1 H), 3.71 (d, *J* = 10.9 Hz, 0.68 H), 3.66 (d, *J* = 5.1 Hz, 0.68 H), 3.45 (d, *J* = 10.9 Hz, 1 H), 3.44 (d, *J* = 10.9 Hz, 0.68 Hz), 3.30 (d, *J* = 4.8 Hz, 1 H), 2.51–2.46 (m, 3 H), 2.43 (s, 3 H), 2.42 (s, 1 H), 2.24 (d, *J* = 13.9 Hz, 1 H), 2.14 (d, *J* = 14.7 Hz, 1 H), 2.07–2.01 (m, 2 H), 1.97 (dd, *J* = 15.5, 7.2 Hz, 1 H), 1.94–1.89 (m, 1 H), 1.88 (d, *J* = 5.4 Hz, 1 H), 1.76 (d, *J* = 5.5 Hz, 0 H), 1.60–1.55 (m, 1 H), 1.53–1.51 (m, 1 H), 1.50–1.44



(–)-**12**

(m, 3 H), 1.38 (d, J = 12.4 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 149.80, 148.85, 148.77, 137.41, 136.81, 135.43, 135.25, 129.64, 129.61, 129.49, 129.41, 128.02, 127.99, 127.91, 127.89, 117.52, 116.83, 108.41, 108.02, 67.08, 66.72, 52.69, 48.32, 47.61, 44.55, 41.58, 40.50, 39.62, 35.40, 35.14, 34.19, 32.80, 32.47, 24.36, 21.58, 21.56 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{20}H_{27}N_2O_3S^+$ 375.1737 found 375.1735.

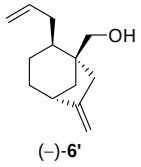
Hydroxy diene [(–)-**6**]. To a stirred solution of tosyl hydrazone (–)-**12** (417 mg, 1.11 mmol) in



(–)-**6f**

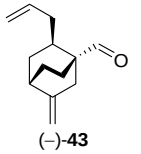
CH_2Cl_2:MeOH (20:1, 6 mL) at 45 °C was added $NaBH_4$ (84 mg, 2.27 mmol). The mixture was stirred at that temperature for 1 h, after which time another portion of $NaBH_4$ (84 mg, 2.27 mmol) was added. The $NaBH_4$ addition/stirring was repeated twice more (total 4 × $NaBH_4$, 84 mg, 2.27 mmol), after which time the reaction mixture was cooled to room temperature and quenched with sat. aq. $NaCHO_3$ solution (25 mL). The mixture was extracted with Et_2O (3 × 30 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting residue was purified by flash column chromatography (silica, 10% → 30% Et_2O in hexanes) to afford hydroxy diene (–)-**6** (159 mg, 74%) as a colorless oil contaminated with < 5% impurity. Chiral HPLC separation of the resulting mixture (Chiralcel OD-H, 0.5% *i*-PrOH in Hexanes) gave spectroscopically pure material $R_{t(major)}$ = 20.80 min, $R_{t(minor)}$ = 26.98 min. [(–)-**6**]: R_f = 0.67 (silica, 60% EtOAc in hexanes); $[\alpha]_D^{35}$ = –44.17 (*c* = 1.03, $CHCl_3$); IR (film): ν_{max} = 3362, 3069, 2972, 2932, 2864, 1640, 1466, 1429, 1332, 1297, 1249, 1213, 1180, 1140, 1117, 1089, 1054, 1031, 1014, 994, 910, 874 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.84–5.73 (m, 1 H), 5.06 (ddd, J = 17.1, 3.4, 1.7 Hz, 1 H), 5.00 (ddd, J = 10.1, 1.9, 1.1 Hz, 1 H), 4.75 (dd, J = 4.4, 2.2 Hz, 1 H), 4.62 (dd, J = 4.0, 2.0 Hz, 1 H), 3.48 (d, J = 11.4 Hz, 1 H), 3.28 (d, J = 11.1 Hz, 1 H), 2.38–2.25 (m, 2 H), 2.25–2.12 (m, 2 H), 1.91–1.74 (m, 2 H), 1.74–1.64 (m, 1 H), 1.65–1.53 (m, 2 H), 1.53–1.44 (m, 1 H), 1.31–1.13 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.38, 137.70, 115.70, 105.11, 68.21, 38.94, 37.73, 36.27, 35.97, 35.83, 34.04, 26.25, 22.69 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{21}O^+$ 193.1587, found 193.1582.

Deoxygenation by-product [(–)-**6′**]. [(–)-**6′**]: R_f = 0.67 (silica, 60% EtOAc in hexanes). $[\alpha]_D^{35}$ = –13.68 (*c* = 0.9 $CHCl_3$); IR (film): ν_{max} = 3351, 3086, 2928, 2860, 1656, 1635, 1458, 1446, 1433, 1352, 1259, 1140, 1094, 1023, 993, 907, 875, 796 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 5.81–5.73 (m, 1 H), 5.04–4.99 (m, 2 H), 4.84 (s, 1 H), 4.79 (s, 1 H), 2.62 (t, *J* = 4.6 Hz, 1 H), 2.38–2.32 (m, 2 H), 2.29–2.25 (m, 1 H), 2.04–1.96 (m, 1 H), 1.73–1.71 (m, 1 H), 1.65–1.57 (m, 2 H), 1.51–1.41 (m, 3 H), 1.25–1.19 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 154.91, 138.76, 115.51, 103.84, 68.46, 47.90, 43.48, 42.47, 38.64, 34.95, 33.23, 29.90, 21.79 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{21}O^+$ 193.1587, found 193.1590.



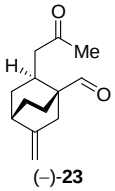
(–)-**6'**

Aldehyde [(–)-**43**]. To a stirred solution of hydroxy diene (–)-**6** (81 mg, 0.42 mmol) in CH_2Cl_2 (5.0 mL) at 25 °C was added pyridine (34 μL, 0.004 mmol) followed by Dess–Martin periodinane (357 mg, 0.84 mmol). The reaction mixture was stirred at 25 °C for 2 h and then quenched with sat. aq. $NaHCO_3$ solution:sat. aq. Na_2SO_3 (1:1, 20 mL) and extracted with Et_2O (3 × 10 ml). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated, and the resulting residue was purified by flash column chromatography (silica, 10% → 20% Et_2O in hexanes) to afford aldehyde (–)-**43** (72 mg, 90% yield) as a colorless oil. [(–)-**43**]: R_f = 0.61 (silica, 30% EtOAc in hexanes); $[\alpha]_D^{35}$ = –58.34 (*c* = 1.45, $CHCl_3$); IR (film): ν_{max} = 3073, 2934, 2866, 2701, 1720, 1641, 1469, 1429, 1137, 993, 914, 879, 711 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 9.50 (s, 1 H), 5.75–5.67 (m, 1 H), 5.05–4.00 (m, 2 H), 4.83 (dd, *J* = 3.9, 2.3 Hz, 1 H), 4.70 (dd, *J* = 3.7, 1.9 Hz, 1 H), 2.44 (ddd, *J* = 16.5, 5.2, 2.4 Hz, 1 H), 2.30–2.28 (m, 1 H), 2.19 (dt, *J* = 16.5, 2.2 Hz, 1 H), 2.15–2.10 (m, 1 H), 2.06–1.93 (m, 2 H), 1.91–1.84 (m, 2 H), 1.67–1.53 (m, 3 H), 1.31 (ddd, *J* = 13.1, 5.2, 2.5 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.61, 148.32, 136.38, 116.60, 106.69, 48.87, 37.73, 36.69, 36.23, 33.34, 25.56, 20.01 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{19}O^+$ 191.1430, found 191.1430.



(–)-**43**

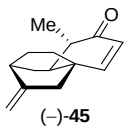
Keto aldehyde [(–)-**23**]. To a stirred solution of aldehyde (–)-**43** (72 mg, 0.38 mmol) in DMF (4 mL) at 25 °C were added sequentially CuCl (56 mg, 0.57 mmol), H_2O (0.6 mL), and $PdCl_2$ (17 mg, 0.09


(–)-**23**

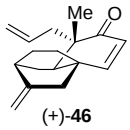
mmol). The reaction mixture was stirred under an oxygen atmosphere (balloon) for 24 h at 25 °C and then filtered through a pad of Celite™. The filtrate was diluted with Et_2O (10 mL) and H_2O (50 mL), and the separated aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was subjected to flash column chromatography (silica, 20% → 30% Et_2O in hexanes) to afford keto aldehyde (–)-**23** (70 mg, 90% yield) as a colorless oil.

Enone (+)-(**5**). The preparation of (+)-**5** was exactly as that described for (±)-**5** earlier in this supplementary information.

Methyl enone [(–)-**45**]. To a stirred solution of enone (+)-**5** (38.8 mg, 0.21 mmol) in THF (3.5 mL) and HMPA (0.88 mL) at –78 °C was added KHMDS (0.5 M solution in toluene, 0.62 mL, 0.31 mmol). The reaction mixture was allowed to stir at –78 °C for 35 min, after which time methyl iodide (103 μL, 1.65 mmol, freshly filtered through anhydrous K_2CO_3) was added. The reaction mixture was then allowed to warm slowly to 0 °C over a period of 1 h, and then quenched with sat. aq. $NaHCO_3$ solution (4 mL) and extracted with Et_2O (4 × 5 mL). The combined organic extracts were washed with brine (3 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was subjected to flash column chromatography (silica, 5% → 10% Et_2O in hexanes) to afford methyl enone (–)-**45** (37.4 mg, 90% yield) as a colorless oil. [(–)-**45**]: R_f = 0.59 (silica, 40% Et_2O in hexanes); $[\alpha]_D^{35}$ = –14.85 (*c* = 1.28, $CHCl_3$); IR (film): ν_{max} = 2934, 2864, 1675, 1450, 1428, 1390, 1374, 1204, 1165, 873, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.49 (d, *J* = 10.0 Hz, 1 H), 5.87 (d, *J* = 10.0 Hz, 1 H), 4.83–4.82 (m, 1 H), 4.68–4.67 (m, 1 H), 2.40 (dt, *J* = 16.3, 2.6 Hz, 1 H), 2.34–2.36 (m, 1 H), 2.27 (dq, *J* = 13.2, 6.7 Hz, 1 H), 2.16–2.12 (m, 1 H), 2.03–1.97 (m, 1 H), 1.83–1.69 (m, 4 H), 1.53–1.48 (m, 1 H), 1.30 (ddd, *J* = 12.7, 8.3, 1.4 Hz, 1 H), 1.12 (d, *J* = 6.7 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 202.0, 155.4, 148.9, 127.2, 106.7, 43.7, 42.6, 41.2, 36.0, 35.6, 34.3, 26.3, 24.9, 11.3 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{14}H_{19}O^+$ 203.1430, found 203.1422.

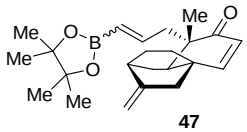

(–)-**45**

Allyl enone [(+)-**46**]. To a stirred solution of methyl enone (–)-**45** (27 mg, 0.134 mmol) in THF (1.1 mL) and HMPA (0.25 mL) at –78 °C was added KHMDS (0.5 M solution in toluene, 1.06 mL, 0.53 mmol). The reaction mixture was allowed to stir at –78 °C for 45 min, after which time allyl iodide (0.10 mL, 1.09 mmol, freshly filtered through anhydrous K_2CO_3) was added. The reaction mixture was allowed to stir for an additional 45 min at –78 °C and then allowed to slowly warm up to 0 °C over a period of 1.5 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ solution (3 mL) and extracted with Et_2O (4 × 4 mL). The combined organic extracts were washed with brine (3 × 2 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Flash column chromatography (silica, 5% → 10% Et_2O in hexanes) of the residue afforded allyl enone (+)-**46** (28 mg, 86% yield) as a colorless oil. [(+)-**46**]: R_f = 0.43 (silica, 15% EtOAc in hexanes); $[\alpha]_D^{35}$ = +50.1 (*c* = 0.69, $CHCl_3$); IR (film): ν_{max} = 3068, 2972, 2933, 2865, 1675, 1466, 1451, 1428, 1388, 1373, 1279, 998, 912, 880, 824 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.47 (d, *J* = 10.1 Hz, 1 H), 5.85 (d, *J* = 10.1 Hz, 1 H), 5.64 (dtd, *J* = 16.8, 9.6, 5.1 Hz, 1 H), 5.05–5.00 (m, 1 H), 4.98–4.96 (m, 1 H), 4.84–4.82 (m, 1 H), 4.67–4.66 (m, 1 H), 2.65 (ddt, *J* = 13.9, 5.0, 1.7 Hz, 1 H), 2.43–2.39 (m, 1 H), 2.29 (dt, *J* = 16.1, 2.4 Hz, 1 H), 2.10–2.09 (m, 1 H), 2.08–2.04 (m, 1 H), 2.00–1.90 (m, 1H), 1.92 (dd, *J* = 13.7, 9.7 Hz, 1 H), 1.74–1.71 (m, 3 H), 1.51–1.47 (m, 2 H), 1.13 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.2, 154.6, 149.1, 134.8, 126.3, 117.2, 106.9, 48.0, 44.3, 40.0, 39.6, 36.2, 36.0, 27.7, 26.7, 26.1, 20.7 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{23}O^+$ 243.1743, found 243.1735.



(+)-**46**

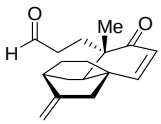
Boronate (**47**). To a stirred solution of allyl enone (+)-**46** (22 mg, 0.091 mmol) and benzoquinone (1 mg, 0.009 mmol) in degassed benzene (1.8 mL) at 25 °C was added boronic acid pinacol ester (**48**, 77 μL, 0.454 mmol). The mixture was heated to 70 °C and a solution of the Hoveyda–Grubbs second generation catalyst (**49**, CAS no.: 301224-40-8, 5.7 mg, 0.009 mmol) in degassed benzene (0.5 mL) was added dropwise over 10 min. The mixture was stirred at 70 °C for a further 1 h, and then cooled to room temperature and concentrated. Flash column chromatography of the residue (100% CH_2Cl_2 → 2% EtOAc in CH_2Cl_2) afforded boronate **47** (25 mg,



47

75% yield, *E*:*Z ca*. 3:1) as a pale brown film. (**47*E***): R_f = 0.40 (silica, 20 % EtOAc in hexanes). (**47*Z***): R_f = 0.33 (silica, 20 % EtOAc in hexanes); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.47–6.40 (M, 1 H), 6.45 (d, *J* = 10.2 Hz, 1 H), 5.85 (d, *J* = 10.1 Hz, 1 H), 5.43 (d, *J* = 17.8 Hz, 1 H), 4.81 (s, 1 H), 4.64 (s, 1 H), 2.76 (dd, *J* = 14.2, 4.6 Hz, 1 H), 2.46–2.35 (m, 2 H), 2.24 (br d, *J* = 16.2 Hz, 1 H), 2.11 (br dd, *J* = 16.2, 1.5 Hz, 1 H), 2.00 (t, *J* = 10.0 Hz, 1 H), 1.97–1.92 (m, 1 H), 1.74–1.60 (m, 3 H), 1.55 (s, 3 H), 1.50–1.45 (m, 2 H), 1.24 (s, 12 H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 203.9, 154.5, 150.2, 149.0, 126.3, 106.9, 83.4, 83.0, 48.1, 44.0, 42.6, 40.1, 36.1, 36.0, 27.6, 26.8, 26.1, 24.8, 24.6, 20.8 ppm.

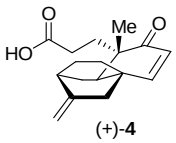
Aldehyde (**47a**). To a stirred solution of boronate **47** (25 mg, 0.068 mmol) in THF (2.0 mL) at 25 °C



47a

was added anhydrous trimethylamine *N*-oxide (25 mg, 0.339 mmol). The vessel was sealed and the mixture was heated at 70 °C for 1 h. The reaction mixture was then cooled to room temperature and partitioned between brine (2 mL) and Et_2O (5 mL). The layers were separated and the aqueous phase was extracted with Et_2O (4 × 5 mL). The combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Flash column chromatography of the residue (25% Et_2O in pentane) afforded aldehyde **47a** (11.1 mg, 63% yield) as a pale yellow oil which was used directly in the next step without further purification. (**47a**): R_f = 0.27 (silica, 20% EtOAc in hexanes).

Carboxylic acid [(+)-**4**]. To a vigorously stirred solution of aldehyde **47a** (11.1 mg, 0.043 mmol) and

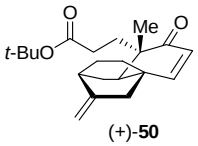


(+)-**4**

2-methyl-2-butene (50 μL, 0.471 mmol) in *t*-BuOH (0.56 mL) at 25 °C were added solutions of NaH_2PO_4 (26.1 mg, 0.218 mmol) in H_2O (0.28 mL) and $NaClO_2$ (11.6 mg, 0.129 mmol) in H_2O (0.28 mL). The resulting mixture was stirred for 20 min, after which time brine (0.5 mL) was added. The mixture was extracted with $CHCl_3$ (5 × 2 mL). The aqueous layer was acidified to pH 2 (1 M aq. HCl) and re-extracted with $CHCl_3$ (2 × 2 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the residue by flash column chromatography (60% EtOAc in hexanes → 60% EtOAc in hexanes with 0.5% AcOH) afforded carboxylic acid (+)-**4** (9.7 mg, 82% yield, 39% overall yield from allyl enone (+)-**46**) as a

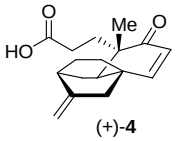
colorless oil. [(+)-**4**]: R_f = 0.3 (silica, 50% Et_2O in hexanes + 0.1% AcOH); $[\alpha]_D^{35}$ = +13.29 (*c* = 0.70, $CHCl_3$); IR (film): ν_{max} = 3068, 2929, 2865, 1708, 1673, 1454, 1438, 1428, 1410, 1390, 1375, 1307, 1293, 1259, 1226, 1180, 1153, 1122, 1092, 1077, 1014, 882, 872, 827 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.47 (d, *J* = 10.1 Hz, 1 H), 5.85 (d, *J* = 10.1 Hz, 1 H), 4.85 (s, 1 H), 4.69 (s, 1 H), 2.43 (d, *J* = 2.8 Hz, 1 H), 2.34–2.24 (m, 3 H), 2.15–2.04 (m, 2 H), 2.01–1.95 (m, 2 H), 1.75–1.67 (m, 3 H), 1.63–1.58 (m, 1 H), 1.55 (d, *J* = 11.3 Hz, 1 H), 1.52–1.48 (m, 1 H), 1.17 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.16, 178.53, 154.41, 148.67, 126.18, 107.42, 47.14, 44.49, 39.56, 36.11, 35.86, 29.49, 29.05, 28.05, 26.58, 25.83, 21.06 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{23}O_3^+$ 275.1642, found 275.1641

***t*-Butyl ester** [(+)-**50**]. To a stirred solution of methyl enone (–)-**45** (12.8 mg, 0.063 mmol) in THF (1.6 mL) at 25 °C was added *t*-BuOK (1.0 M in *t*-BuOH, 127 μL, 0.127 mmol) dropwise. The resulting mixture was stirred at that temperature for 15 min, after which time a solution of *t*-butyl acrylate (19 μL, 0.127 mmol) in THF (300 μL) was added and the reaction mixture was stirred at 25 °C for 30 min. The resulting mixture was quenched with sat. aq. NH_4Cl solution (3 mL) and extracted with Et_2O (4 × 3 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue by preparative TLC (40% Et_2O in hexane) afforded *t*-butyl ester (+)-**50** (19.5 mg, 92% yield) as a colorless oil. [(+)-**50**]: R_f = 0.29 (silica, 10% EtOAc in hexanes); $[\alpha]_D^{35}$ = +8.53 (*c* = 1.01, $CHCl_3$); IR (film): ν_{max} = 3068, 2972, 2933, 2865, 1729, 1675, 1466, 1453, 1438, 1390, 1367, 1304, 1292, 1256, 1226, 1150, 1077, 1051, 1031, 1014, 1003, 953, 880, 824 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.45 (d, *J* = 10.1 Hz, 1 H), 5.84 (s, 1 H), 4.84 (dd, *J* = 3.9, 2.2 Hz, 1 H), 4.67 (dd, *J* = 3.2, 2.0 Hz, 1 H), 2.42 (dd, *J* = 7.3, 4.3 Hz, 1 H), 2.31 (dt, *J* = 16.1, 2.3 Hz, 1 H), 2.18–2.02 (m, 4 H), 2.02–1.91 (m, 2 H), 1.77–1.67 (m, 3 H), 1.60–1.44 (m, 3 H), 1.42 (s, 9 H), 1.15 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.17, 172.91, 154.24, 148.92, 126.31, 107.24, 80.11, 47.18, 44.55, 39.48, 36.05, 35.93, 30.53, 29.80, 28.10, 28.00, 26.65, 25.91, 21.22 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{30}O_3Na^+$ 353.2087, found 353.2090.



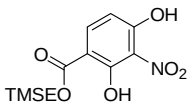
(+)-**50**

Carboxylic acid [(+)-**4**]. To a stirred solution of *t*-butyl ester (+)-**50** (10.1 mg, 0.031 mmol) in MeOH (0.5 mL) at 25 °C was added aq. LiOH (1 N, 0.5 mL). The resulting suspension was warmed to 50 °C and stirred at that temperature for 6 h, after which time the reaction mixture was concentrated under vacuum to remove MeOH; then H_2O (1 mL) was added and the aqueous solution was washed with EtOAc (2 mL) to remove organic impurities. The aqueous layer was then acidified with aq. HCl (1 N, 2.5 mL) and extracted with EtOAc (3 × 3 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (60% EtOAc in hexanes → 60% EtOAc in hexanes with 0.5% AcOH) afforded carboxylic acid (+)-**4** (8.1 mg, 97% yield) as a colorless oil.



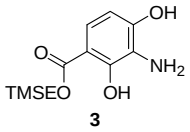
(+)-**4**

TMSE Ester (**51a**). To a stirred solution of methyl 2,4-dihydroxy-3-nitrobenzoate[2] (**51**, 500 mg, 2.35 mmol) in 2-(trimethylsilyl)-ethanol (5 mL, 34.88 mmol) at 25 °C was added *n*-Bu_2SnO (875 mg, 3.52 mmol). The vessel was sealed and the mixture was heated at 70 °C for 3 h. A further portion of *n*-Bu_2SnO (100 mg, 0.402 mmol) was then added and heating was continued for a further 2 h, after which time the mixture was allowed to cool to room temperature. The solvent was removed by vacuum distillation and the residue was suspended in a mixture of EtOAc and CH_2Cl_2 (1:1, 5 mL). This suspension was filtered through a pad of Celite™ and concentrated. Purification of the residue by flash column chromatography (50% EtOAc in hexanes with 0.5% AcOH) afforded TMSE ester **51a** (430 mg, 61% yield) as a pale yellow solid. (**51a**): pale yellow needles (m.p. 66–66.5 °C, hexanes); R_f = 0.25 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3434, 3341, 2953, 2896, 1666, 1617, 1578, 1532, 1463, 1395, 1371, 1333, 1263, 1250, 1176, 1151, 1137, 1064, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 9.2 Hz, 1 H), 6.62 (d, *J* = 9.2 Hz, 1 H), 4.49–4.45 (m, 2 H), 1.17–1.13 (m, 2 H), 0.09 (s, 9 H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.8, 160.7, 160.3, 136.7, 125.3, 109.1, 106.1, 64.9, 17.4, –1.5 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{17}NO_6SiNa^+$ 322.0717, found 322.0711.



51a

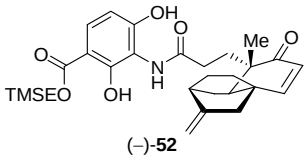
Aniline (**3**). To a stirred solution of nitro ester **51a** (100 mg, 0.334 mmol) in EtOAc (5.0 mL) and



3

MeOH (1 mL) at 25 °C was added AcOH (20 μL) followed by 10% Pd/C (18 mg, 0.017 mmol). The reaction vessel was evacuated (water aspirator) and purged with H_2. The mixture was stirred vigorously under an H_2 atmosphere (balloon) at 25 °C for 16 h. The solution was then purged with argon and the catalyst was removed by filtration though a pad of Celite™. Concentration of the resulting solution afforded aniline **3** (92 mg, 100% yield) as a grey solid, which was crystallized from hexanes. (**3**): colorless cubes (mp 102–103 °C, hexanes); R_f = 0.29 (silica, 40% EtOAc in hexanes); IR (film): ν_{max} = 3383, 3317, 3100, 2955, 2896, 1669, 1624, 1504, 1465, 1385, 1347, 1300, 1274, 1195, 1158, 1140, 1061, 958, 827 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.17 (s, 1 H), 7.33 (d, *J* = 8.6 Hz, 1 H), 6.38 (d, *J* = 8.6 Hz, 1 H), 4.43–4.40 (m, 2 H), 1.56 (br s, 2 H), 1.14–1.11 (m, 2 H), 0.08 (s, 9 H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6, 153.2, 151.2, 122.0, 121.0, 106.6, 106.1, 63.4, 17.4, –1.4 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{20}NO_4Si^+$ 270.1156, found 270.1152.

Amide [(–)-**52**]. To a stirred solution of carboxylic acid (+)-**4** (9.3 mg, 0.034 mmol) and aniline **3** (29

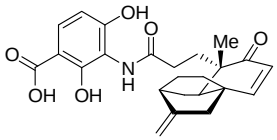


(–)-**52**

mg, 0.108 mmol) in DMF (120 μL) at 25 °C were added Et_3N (20 μL, 0.143 mmol) and HATU (41 mg, 0.108 mmol). The mixture was stirred for 13 h, after which time brine (0.2 mL) was added. The resulting mixture was extracted with $CHCl_3$ (10 × 1.5 mL), and the combined organic extracts were dried over anhydrous Na_2SO_4 (CAUTION: do not use $MgSO_4$!), filtered, and concentrated. Flash column chromatography of the resulting residue (10% EtOAc in hexanes) afforded amide (–)-**52** (10.9 mg, 61% yield) as a white film. [(–)-**52**]: R_f = 0.66 (silica, 50% EtOAc in hexanes); $[\alpha]_D^{35}$ = –18.4 (*c* = 0.50, $CDCl_3$); IR (film): ν_{max} = 3392, 3316, 3063, 2951, 2926, 2582, 1655, 1597, 1533, 1387, 1332, 1257, 1147, 1061, 933, 859, 838, 789 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.81 (s, 1 H), 11.09 (s, 1 H), 8.14 (s, 1 H), 7.55 (d, *J* = 9.0 Hz, 1 H), 6.51 (d, *J* = 10.4 Hz, 1 H), 6.50 (d, *J* = 9.0 Hz, 1 H), 5.89 (d, *J* = 10.4 Hz, 1 H), 4.86 (s, 1 H), 4.68 (s, 1 H), 4.43–4.40 (m, 2 H), 2.48–2.43 (m, 1 H), 2.41–2.38 (m, 2 H), 2.34 (d, *J* = 16.0 Hz, 1 H), 2.20–2.15 (m, 1 H), 2.09 (d, *J* = 16.3 Hz, 1 H), 2.05–1.98 (m, 2 H), 1.81–1.75 (m, 4 H), 1.60–1.49

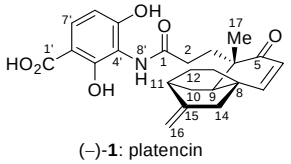
(m, 2 H), 1.21 (s, 3 H), 1.15–1.12 (m, 2 H), 0.09 (s, 9 H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 204.6, 174.0, 170.5, 154.7, 154.6, 153.9, 148.5, 127.3, 126.1, 114.4, 111.1, 107.6, 104.4, 63.7, 47.6, 44.4, 39.6, 36.2, 35.8, 32.4, 30.9, 28.0, 26.5, 25.8, 21.0, 17.4, –1.5 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{29}H_{40}NO_6Si^+$ 526.2619, found 526.2621.

Platencin [(–)-**1**]. To a stirred solution of amide (–)-**52** (13.1 mg, 0.025 mmol) in DMF (220 μL) at 25 °C was added tris(dimethylamino)sulfonium difluorotrimethyl-silicate (TASF, 13.7 mg, 0.050 mmol), and the resulting mixture was heated at 40 °C for 40 min. The solution was then cooled to room temperature and brine (0.4 mL) added. The mixture was extracted with $CHCl_3$ (10 × 1.5 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4 (CAUTION: do not use $MgSO_4$!), filtered, and concentrated. Flash column chromatography of the resulting residue (EtOAc:hexanes:MeOH:H_2O:AcOH 80:20:0.5:0.5:0.5) afforded synthetic (–)-platencin [(–)-**1**, 9.9 mg, 93% yield] as a white film. Synthetic platencin (–)-**1** crystallized from acetone on standing to give cubic colorless crystals (m.p. 194–197 °C dec.). [(–)-**1**]: R_f = 0.26 (silica, EtOAc:hexanes:MeOH:H_2O:AcOH 80:20:0.5:0.5:0.5); $[\alpha]_D^{35}$ = –12.5 (*c* = 0.39, MeOH) [Lit.[3] $[\alpha]_D^{23}$ = –7.0 (c = 0.85, MeOH)]; IR (film): ν_{max} = 3068, 2926, 2587, 1651, 1598, 1534, 1453, 1377, 1292, 1235, 1152, 1059, 908, 791, 733 cm^{-1}; ^{1}H NMR (600 MHz, C_5D_5N): δ = 10.55 (s, 1 H), 8.12 (d, *J* = 8.7 Hz, 1 H), 6.89 (d, *J* = 8.7 Hz, 1 H), 6.34 (d, *J* = 10.0 Hz, 1 H), 5.92 (d, *J* = 10.0 Hz, 1 H), 4.86 (s, 1 H), 4.70 (s, 1 H), 2.78–2.68 (m, 2 H), 2.57–2.52 (m, 1 H), 2.25 (s, 1 H), 2.18 (d, *J* = 16.1 Hz, 1 H), 2.01 (t, *J* = 9.9 Hz, 1 H), 1.97–1.89 (m, 2 H), 1.83–1.77 (m, 1 H), 1.62–1.58 (m, 1 H), 1.55 (t, *J* = 7.5 Hz, 2 H), 1.39–1.35 (m, 1 H), 1.34–1.29 (m, 1 H), 1.08 (s, 3 H) ppm; ^{13}C NMR (150 MHz, C_5D_5N): δ = 204.13, 175.12, 175.04, 158.69, 158.39, 154.87, 149.73, 129.77, 126.73, 115.71, 110.37, 107.71, 107.47, 47.98, 44.85, 40.33, 36.59, 36.54, 32.11, 31.70, 28.41, 26.98, 26.38, 21.49 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{28}NO_6^+$ 426.1911, found 426.1920.



(–)-**1**: platencin

Table 1. ^{1}H and ^{13}C NMR (600 MHz, C_5D_5N) Spectroscopic Comparison for Natural vs. Synthetic Platencin



(–)-**1**: platencin

No.	Natural δ ^{1}H [ppm, mult, *J* (Hz)] 600 MHz	Synthetic δ ^{1}H [ppm, mult, *J* (Hz)] 600 MHz	Natural δ ^{13}C (ppm) 600 MHz	Synthetic δ ^{13}C (ppm) 600 MHz
1			175.2	175.12
2	2.70 (m)	2.78–2.68 (m)	32.2	32.11
	2.68 (m)	–		
3	1.93 (ddd, 14.4, 10.8, 5.4)	1.97–1.89 (m)	31.7	31.70
	2.53 (ddd, 14.4, 10.8, 5.4)	2.57–2.52 (m)		
4			48.1	47.98
5			204.2	204.13
6	5.92 (d, 10)	5.92 (d, 10.0)	126.8	126.73
7	6.36 (d, 10)	6.34 (d, 10.0)	154.9	154.87
8			36.7	36.59
9	2.02 (t, 9.6)	2.01 (t, 9.9)	40.4	40.33
10	1.60 (m)	1.62–1.58 (m)	27.1	26.99
	1.36 (ddd, 12.0, 9.6, 1.2)	1.39–1.35		
11	2.26 (m)	2.25 (s)	36.6	36.54
12	1.78 (m)	1.83–1.58 (m)	26.5	26.38
	1.56 (m)	–		
13	1.30 (m)	1.29–1.34 (m)	28.5	28.41
14	1.95 (d, 16.0)	1.97–1.89 (m)	44.9	44.85
	2.19 (d, 16.0)	2.18 (d, 16.1)		
15			149.8	149.73
16	4.71 (br s)	4.70 (s)	107.8	107.71
	4.87 (br s)	4.86 (s)		
17	1.09 (s)	1.08 (s)	21.5	21.49
1′			175.2	175.04
2′			107.6	107.47
3′			158.8	158.69
4′			115.8	115.71
5′			158.3	158.39
6′	6.88 (d, 8.4)	6.89 (d, 8.7)	110.4	110.37
7′	8.12 (d, 8.4)	8.12 (d, 8.7)	129.8	129.77
8′-NH	10.5 (s)	10.55 (s)		

II. Abbreviations

Ac = acetate

AIBN = 2,2′-azobis(isobutyronitrile)

Bn = benzyl

DCE = 1,2-dichloroethane

DDQ = 2,3-dichloro-5,6-dicyanobenzoquinone

DMAP = 4-dimethylaminopyridine

DMF = *N*,*N*-dimethylformamide

DMP = Dess–Martin periodinane

DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone

DMSO = dimethyl sulfoxide

HATU = *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate

HMDS = hexamethyldisilazide

HMPA = hexamethylphosphoramide

MOM = methoxymethyl

M. S. = molecular sieves

NMO = *N*-methylmorpholine-*N*-oxide

Piv = pivalate

PMB = *p*-methoxy benzyl

py = pyridine

SEM = 2-(trimethylsilyl)ethoxymethyl

Tf = trifluoromethanesulfonyl

Ts = *p*-toluenesulfonyl

TsOH = *p*-toluenesulfonic acid

TASF = tris(dimethylamino)sulfonium difluorotrimethylsilicate

TBS = *tert*-butyldimethylsilyl

THF = tetrahydrofuran

TIPS = triisopropylsilyl

TMS = trimethylsilyl

TMSE = trimethysilylethyl

TPAP = tetra-*n*-propylammonium perruthenate

III. References

Complete references for article:

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(3) (b) Young, K.; Jayasuriya, H.; Ondeyka, J. G.; Herath, K.; Zhang, C.; Kodali, S.; Galgoci, A.; Painter, R.; Brown-Driver, V.; Yamamoto, R.; Silver, L. L.; Zheng, Y.; Ventura, J. I.; Sigmund, J.; Ha, S.; Basilio, A.; Vicente, F.; Rubén Tormo, J.; Pelaez, F.; Youngman, P.; Cully, D.; Barrett, J. F.; Schmatz, D.; Singh, S. B.; Wang, J. *Antimicrob. Agents Chemother.* **2006**, *50*, 519.

(5) (a) Wang, J.; Kodali, S.; Lee, S. H.; Galgoci, A.; Painter, R.; Dorso, K.; Racine, F.; Motyl, M.; Hernandez, L.; Tinney, E.; Colletti, S.; Herath, K.; Cummings, R.; Salazar, O.; Gonzalez, I.; Basilio, A.; Vicente, F.; Genilloud, O.; Pelaez, F.; Jayasuriya, H.; Young, K.; Cully, D.; Singh, S. B. *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 7612.

(6) (a) Wang, J.; Soisson, S. M.; Young, K.; Shoop, W.; Kodali, S.; Galgoci, A.; Painter, R.; Parthasarathy, G.; Tang, Y. S.; Cummings, R.; Ha, S.; Dorso, K.; Motyl, M.; Jayasuriya, H.; Ondeyka, J.; Herath, K.; Zhang, C.; Hernandez, L.; Allocco, J.; Basilio, A.; Tormo, J. R.; Genilloud, O.; Vicente,

F.; Pelaez, F.; Colwell, L.; Lee, S. H.; Michael, B.; Felcetto, T.; Gill, C.; Silver, L. L.; Hermes, J. D.; Bartizal, K.; Barrett, J.; Schmatz, D.; Becker, J. W.; Cully, D.; Singh, S. B. *Nature* **2006**, *441*, 358.

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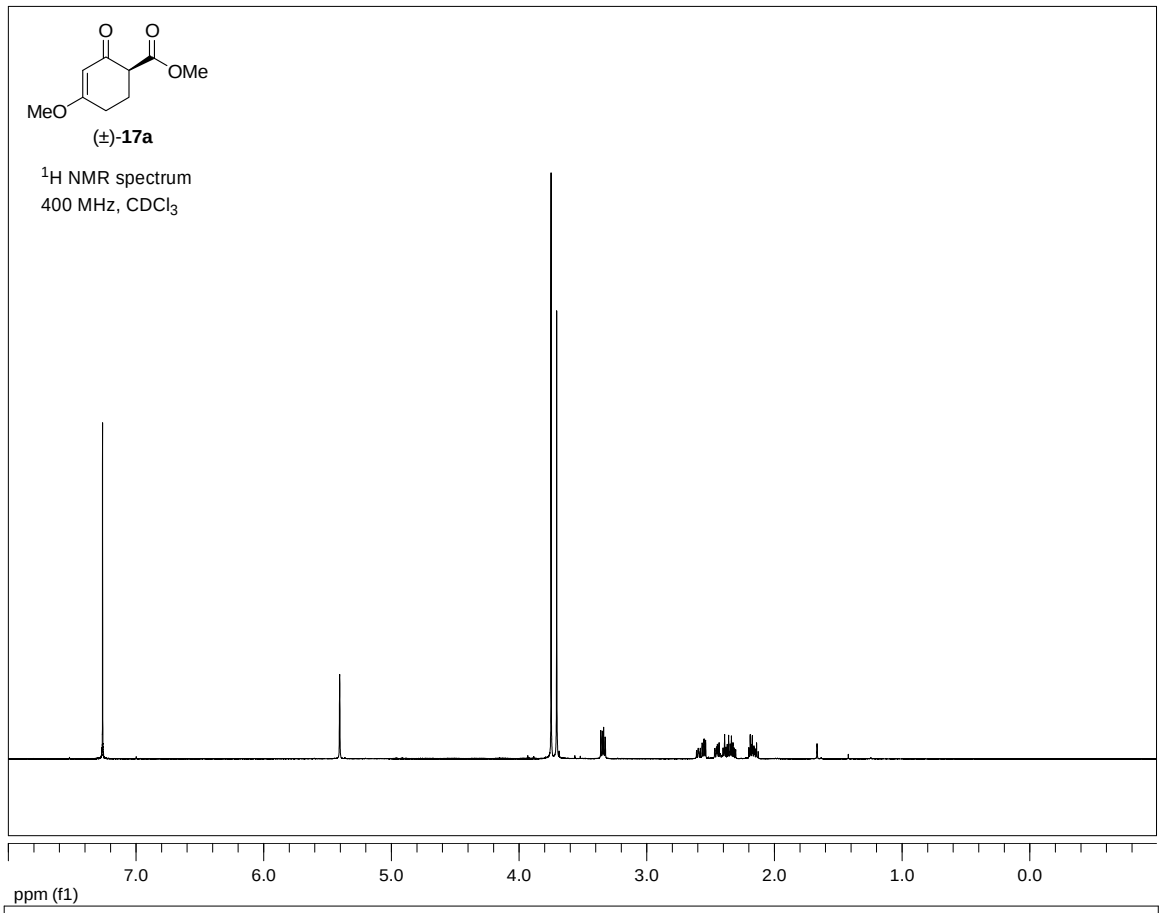
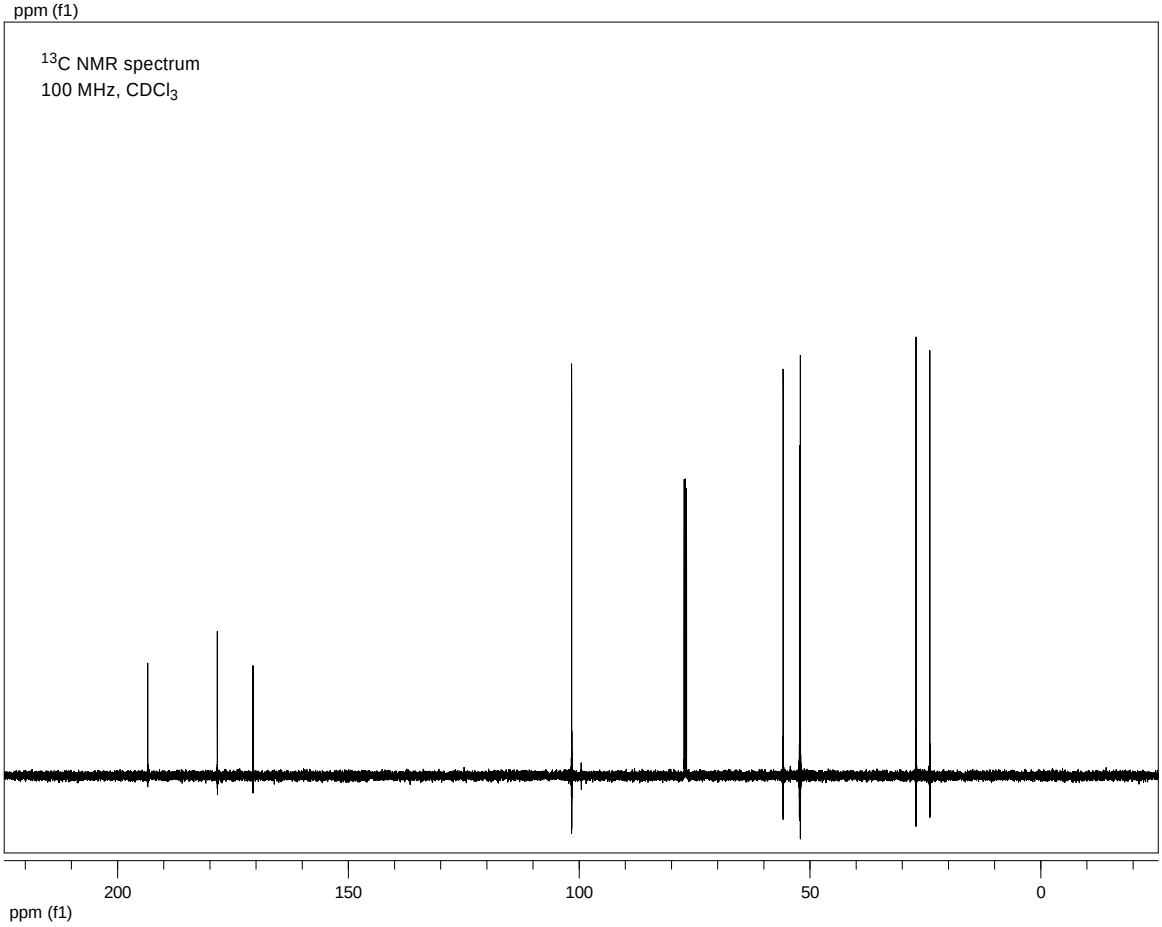
(1) Nakajima, N.; Horita, K.; Abe, R.; Yonemitsu, O. *Tetrahedron Lett.* **1988**, *29*, 4139

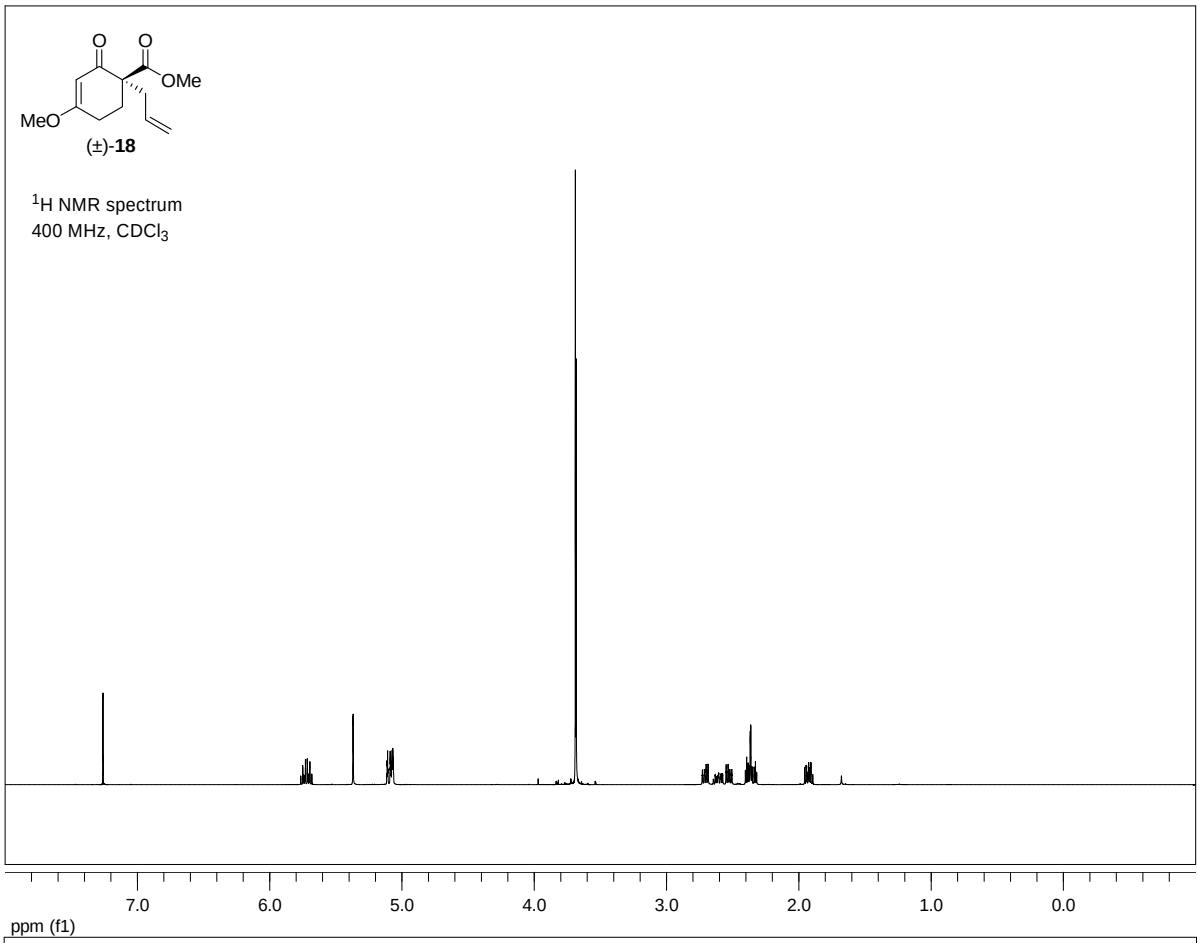
(2) Heretsch, P.; Giannis, A. *Synthesis* **2007**, *17*, 2614.

(3) Jayasuriya, H.; Herath, K. B.; Zhang, C.; Zink, D. L.; Basilio, A.; Genilloud, O.; Teresa Diez, M.; Vicente, F.; Gonzalez, I.; Salazar, O.; Pelaez, F.; Cummings, R.; Ha, S.; Wang, J.; Singh, S. B. *Angew. Chem., Int. Ed.* **2007**, *46*, 4684.

IV. ^{1}H and ^{13}C spectra of compounds



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O
OMe
MeO
(±)-18
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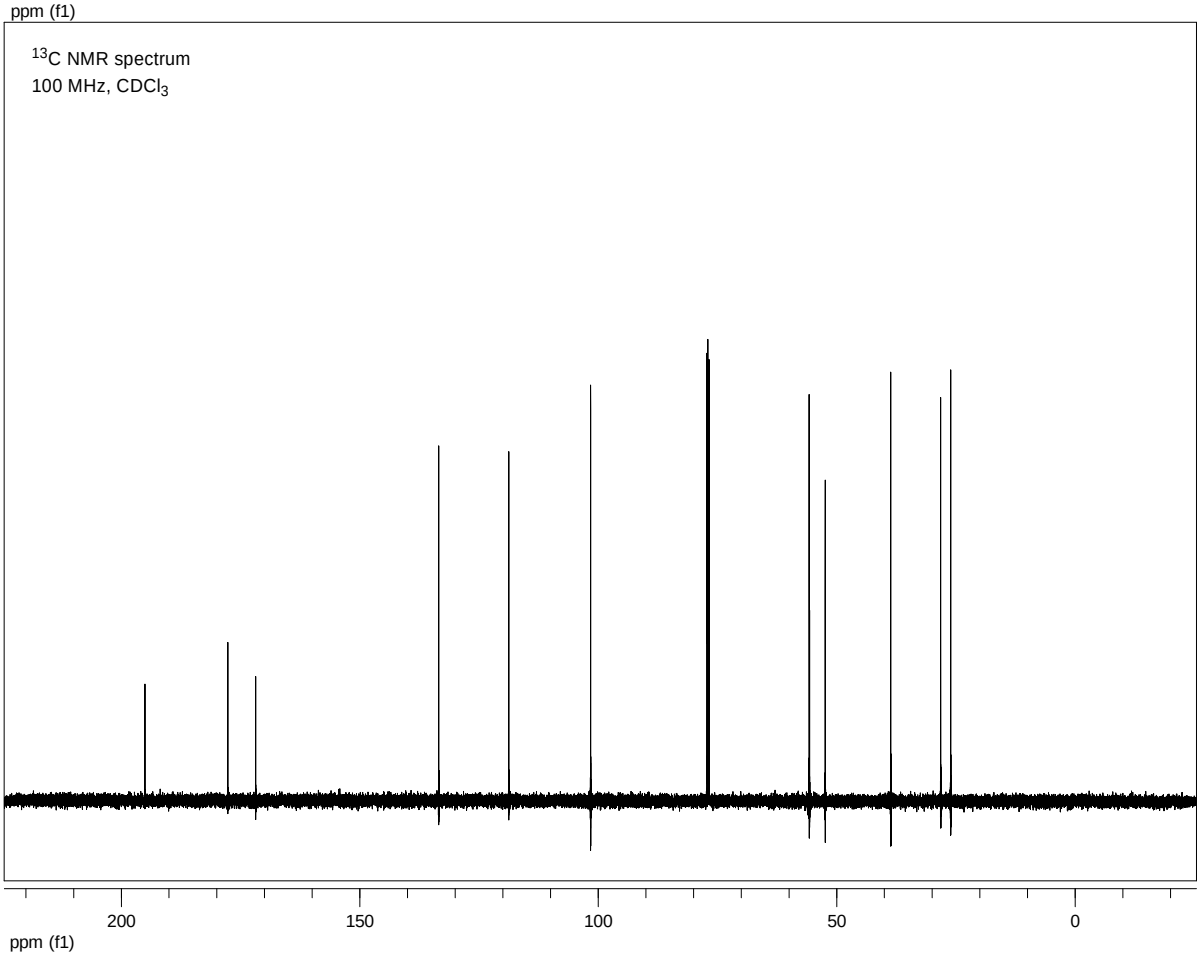
4.0
3.0
2.0
1.0
0.0
ppm (f1)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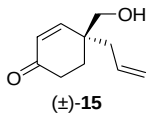
100 MHz, CDCl3
200
150
100
50
0
ppm (f1)



(±)-**15**

^{1}H NMR spectrum
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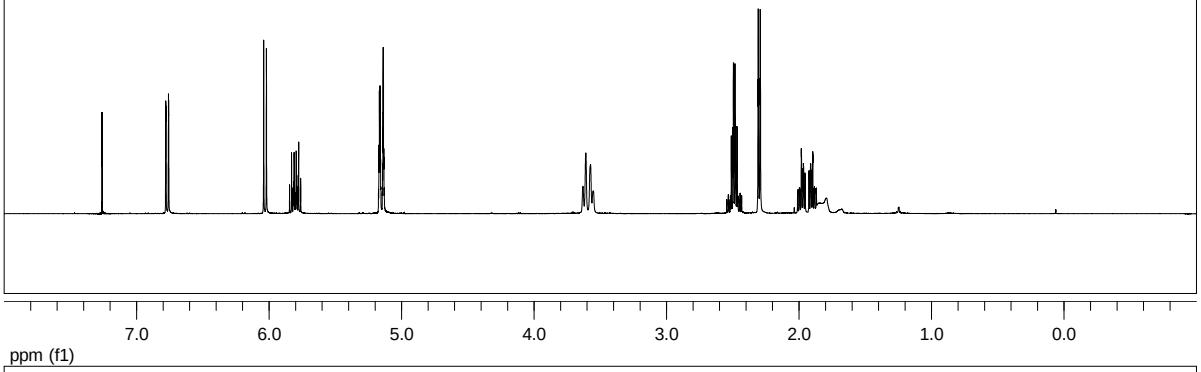

^{13}C NMR spectrum
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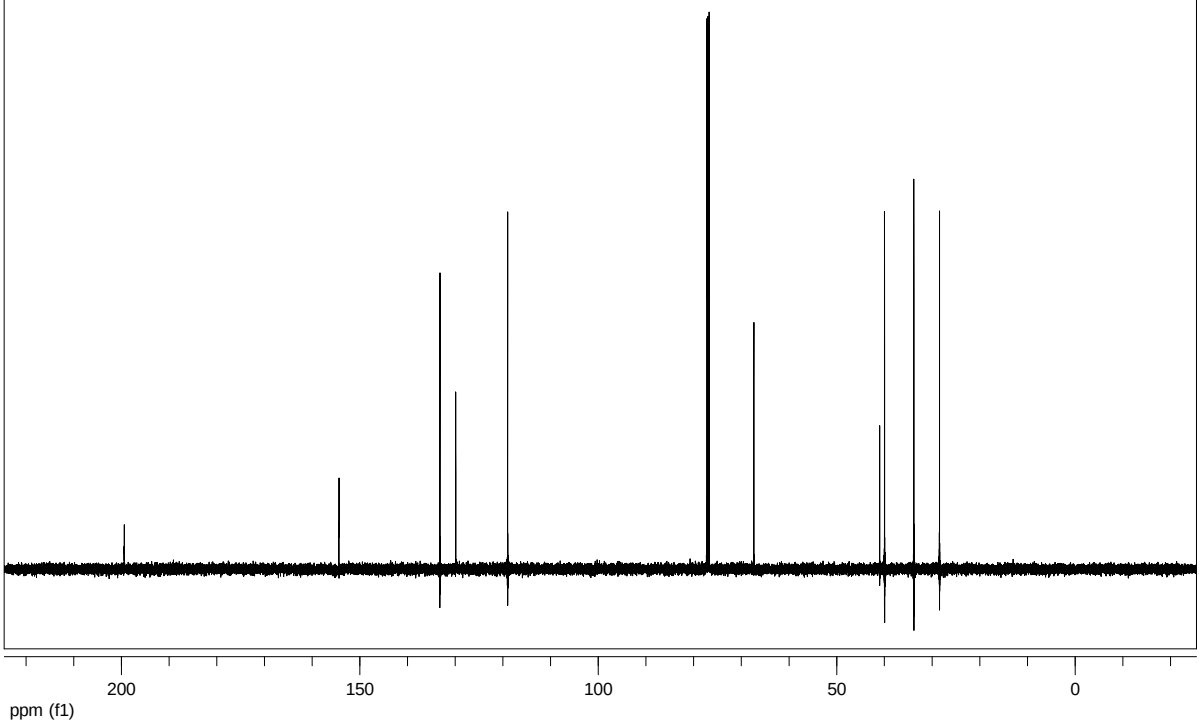

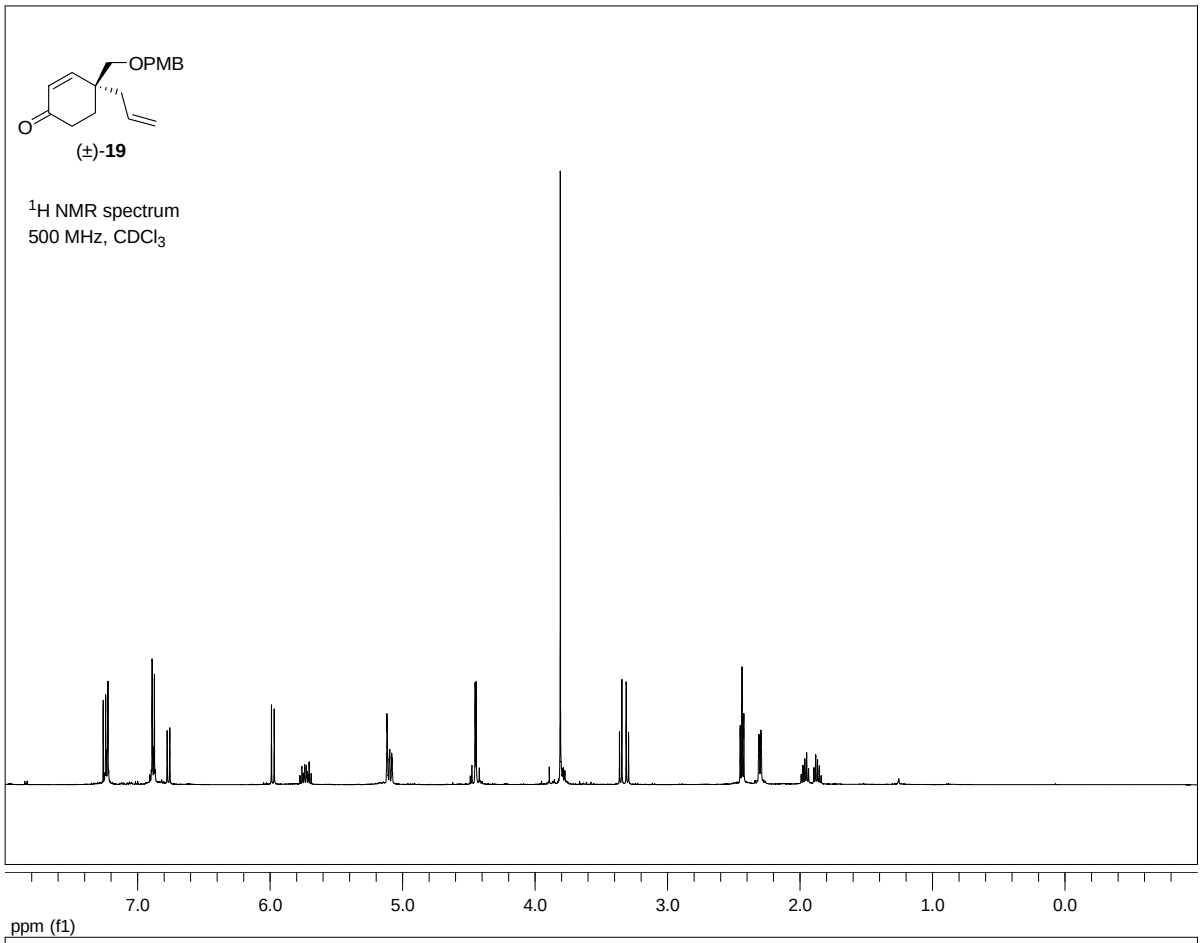
OPMB
O
(±)-19
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500 MHz, CDCl3
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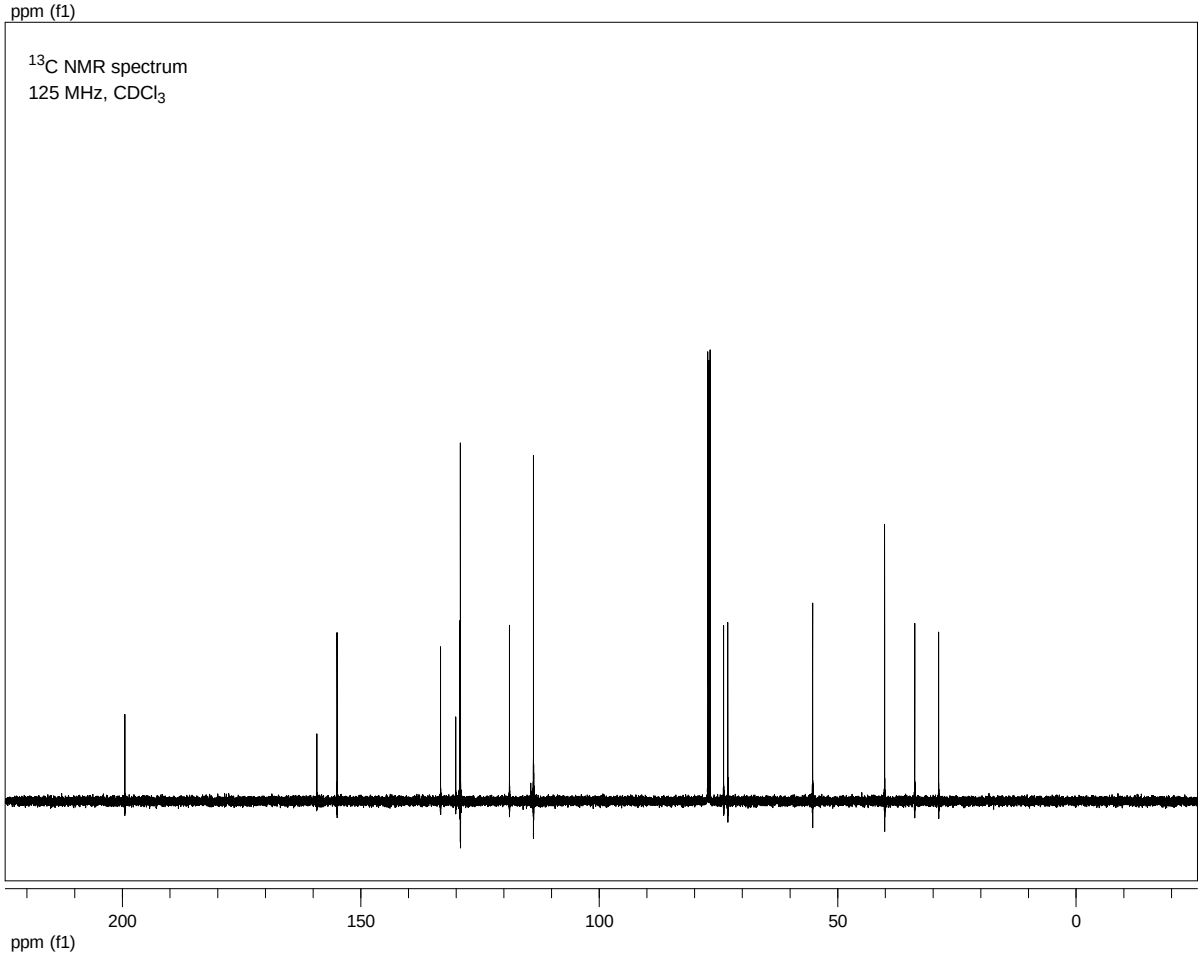
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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200
150
100
50
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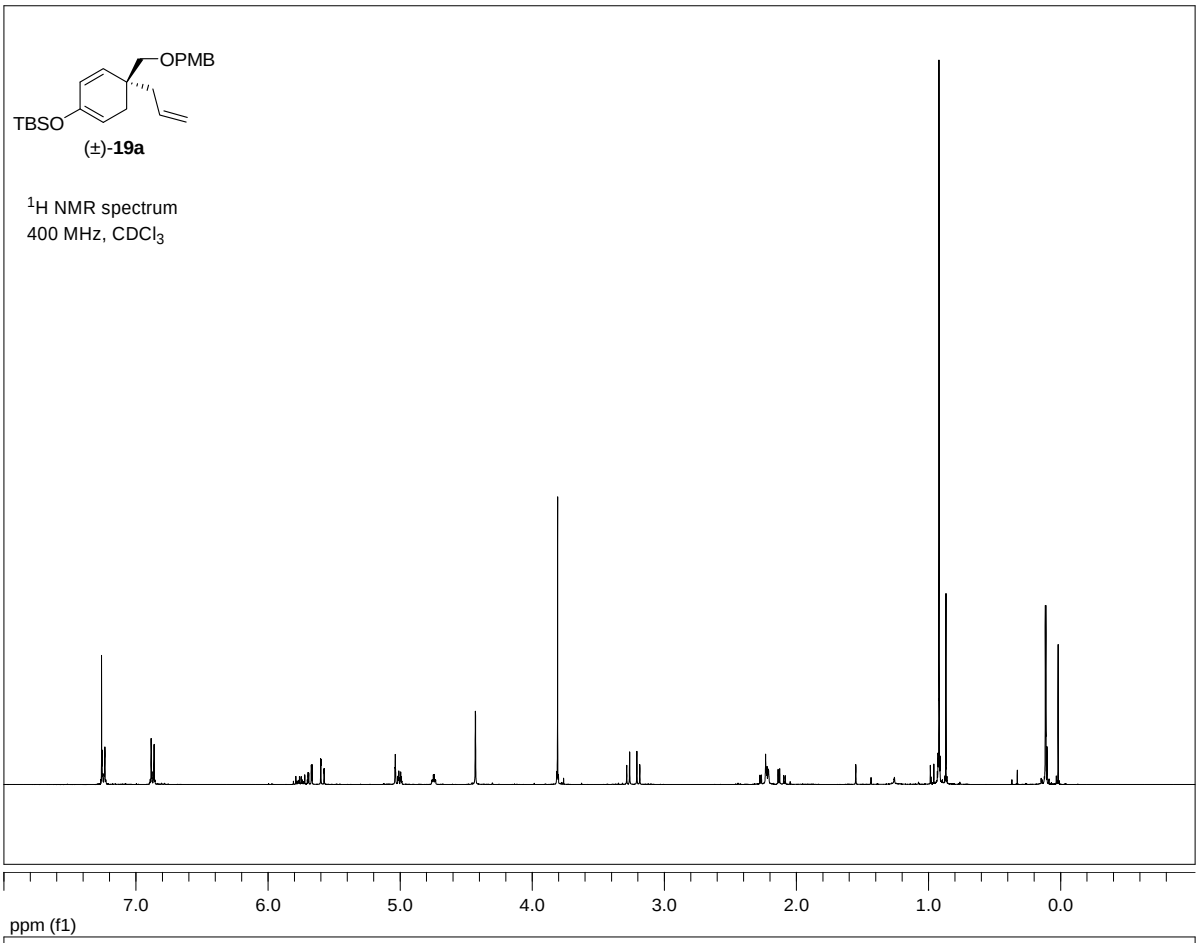
ppm (f1)


OPMB
TBSO
(±)-19a
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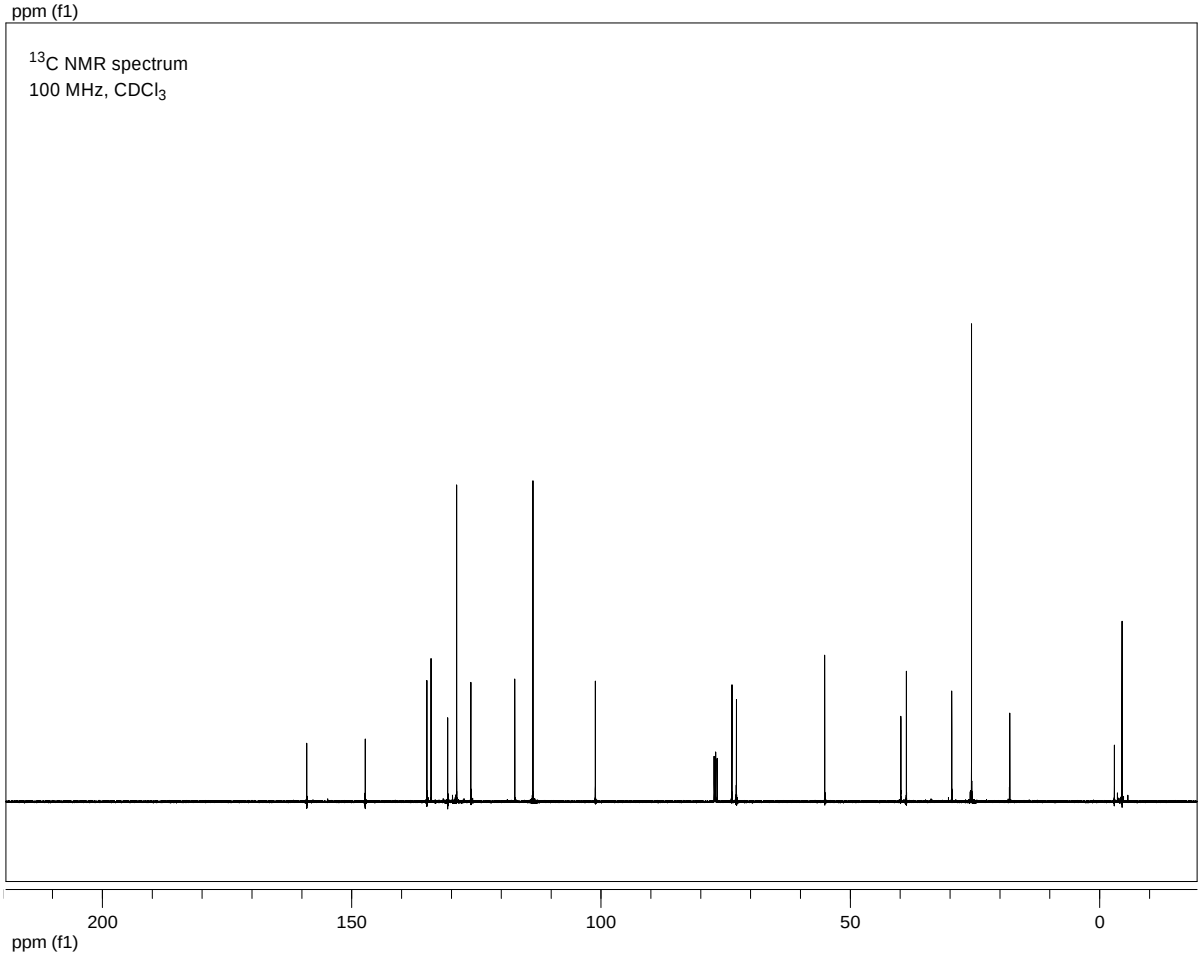
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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100 MHz, CDCl3
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150
100
50
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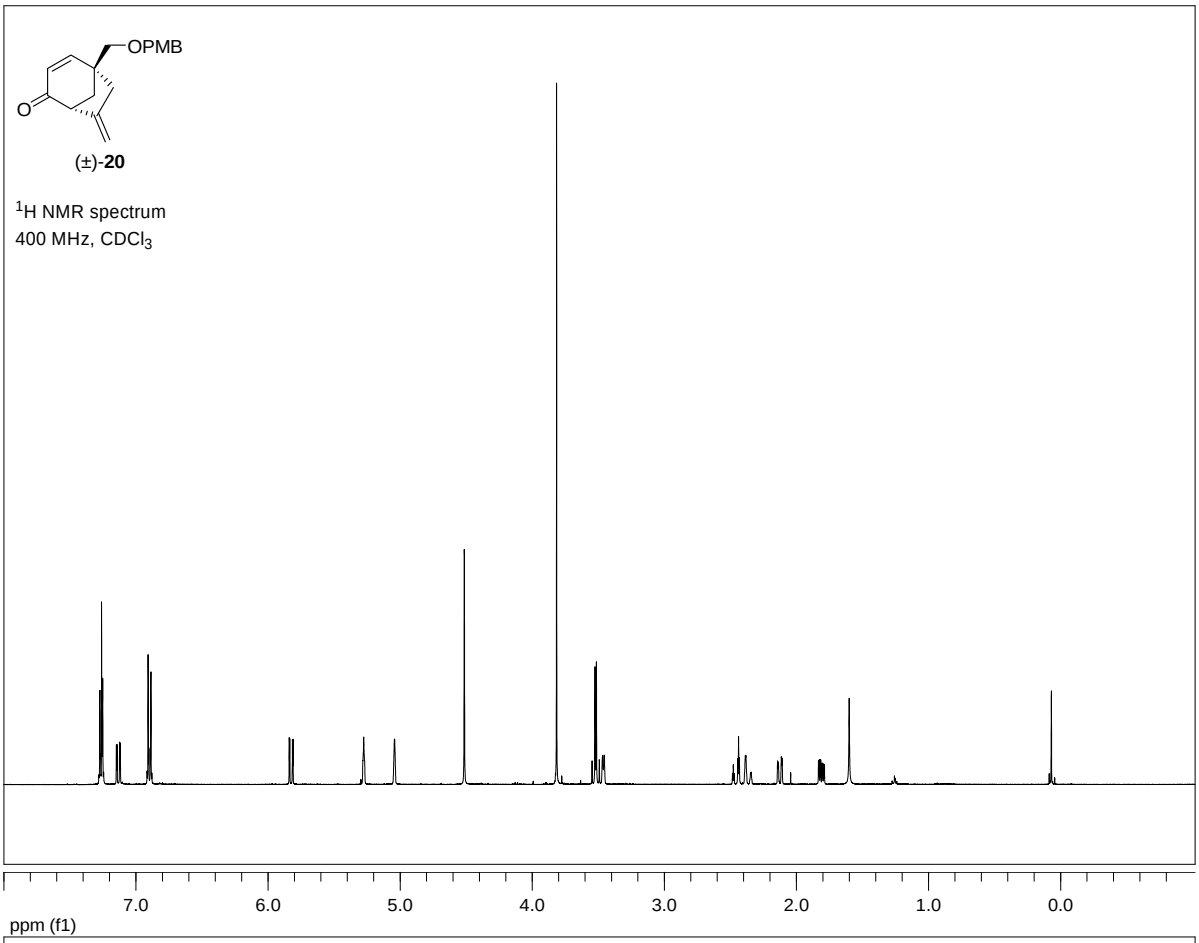
ppm (f1)


OPMB
O
(±)-20
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5.0
4.0
3.0
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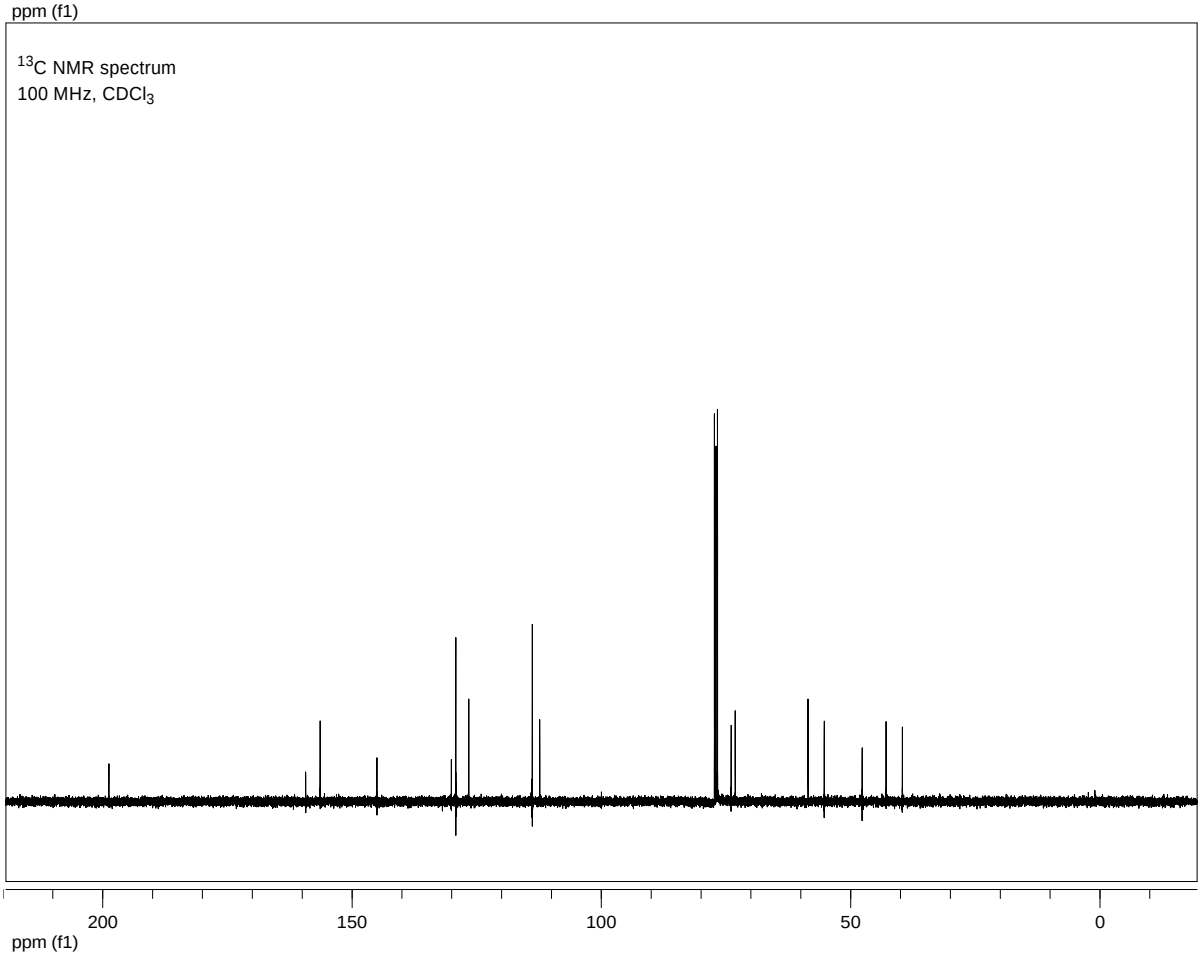
1.0
0.0
ppm (f1)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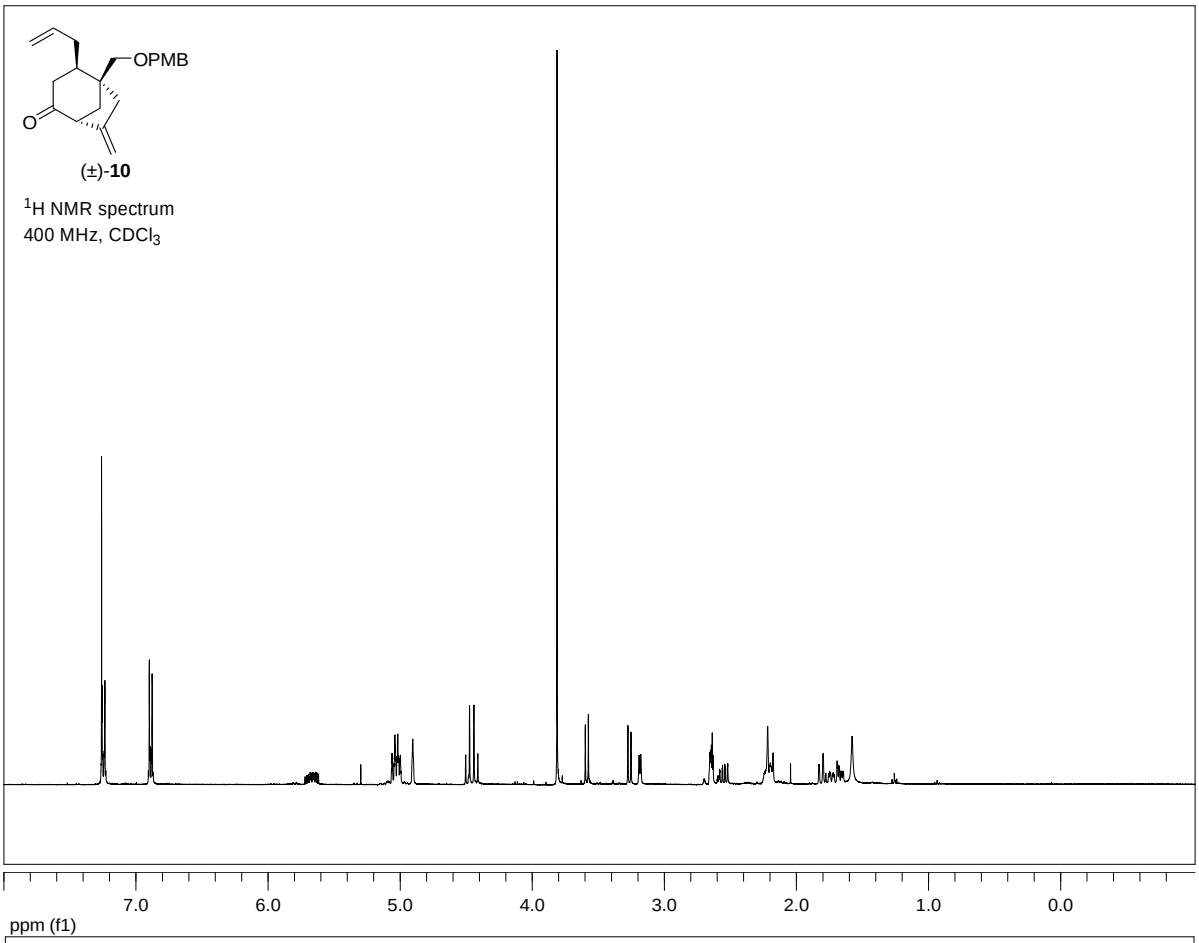
200
150
100
50
0
ppm (f1)


OPMB
O
(±)-10
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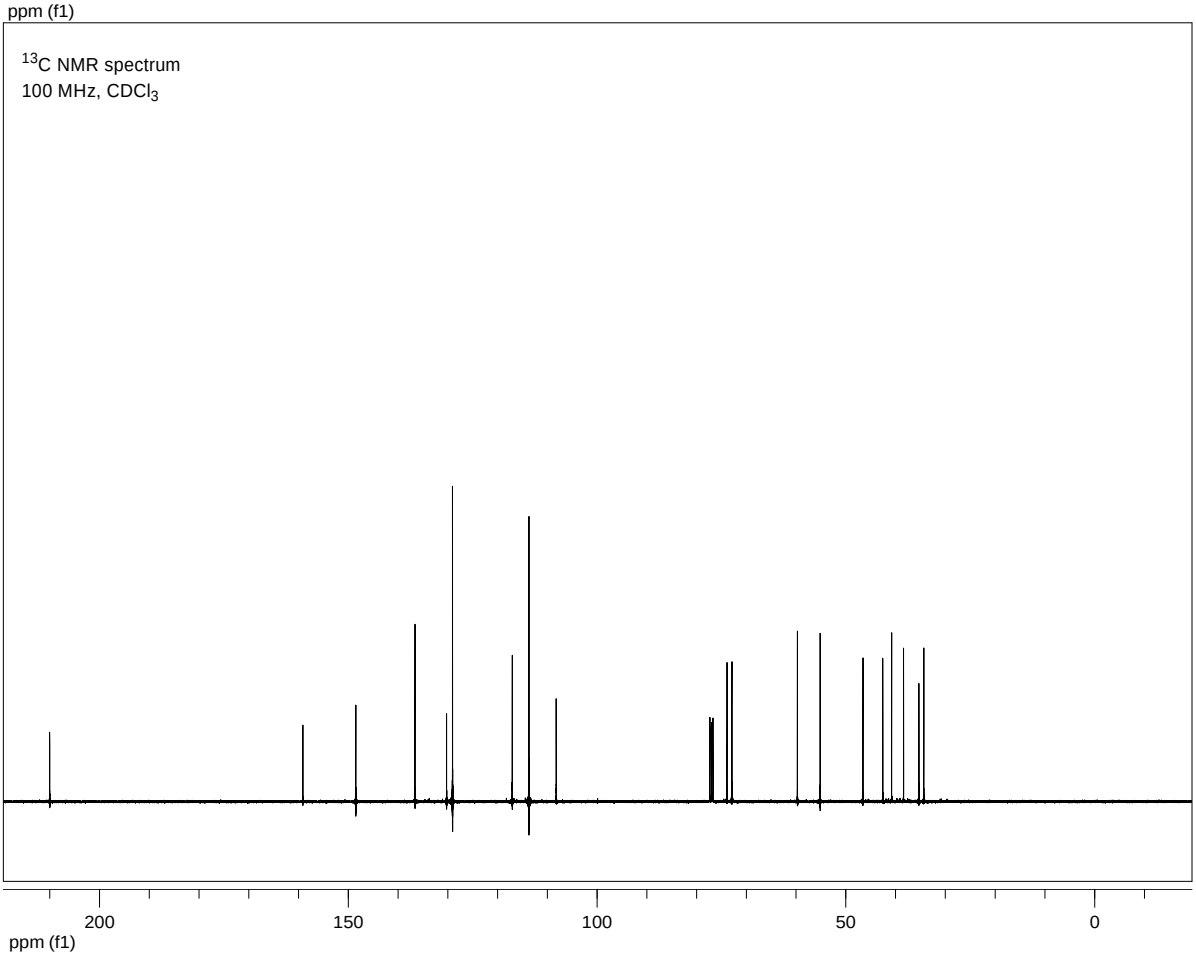
1.0
0.0
ppm (f1)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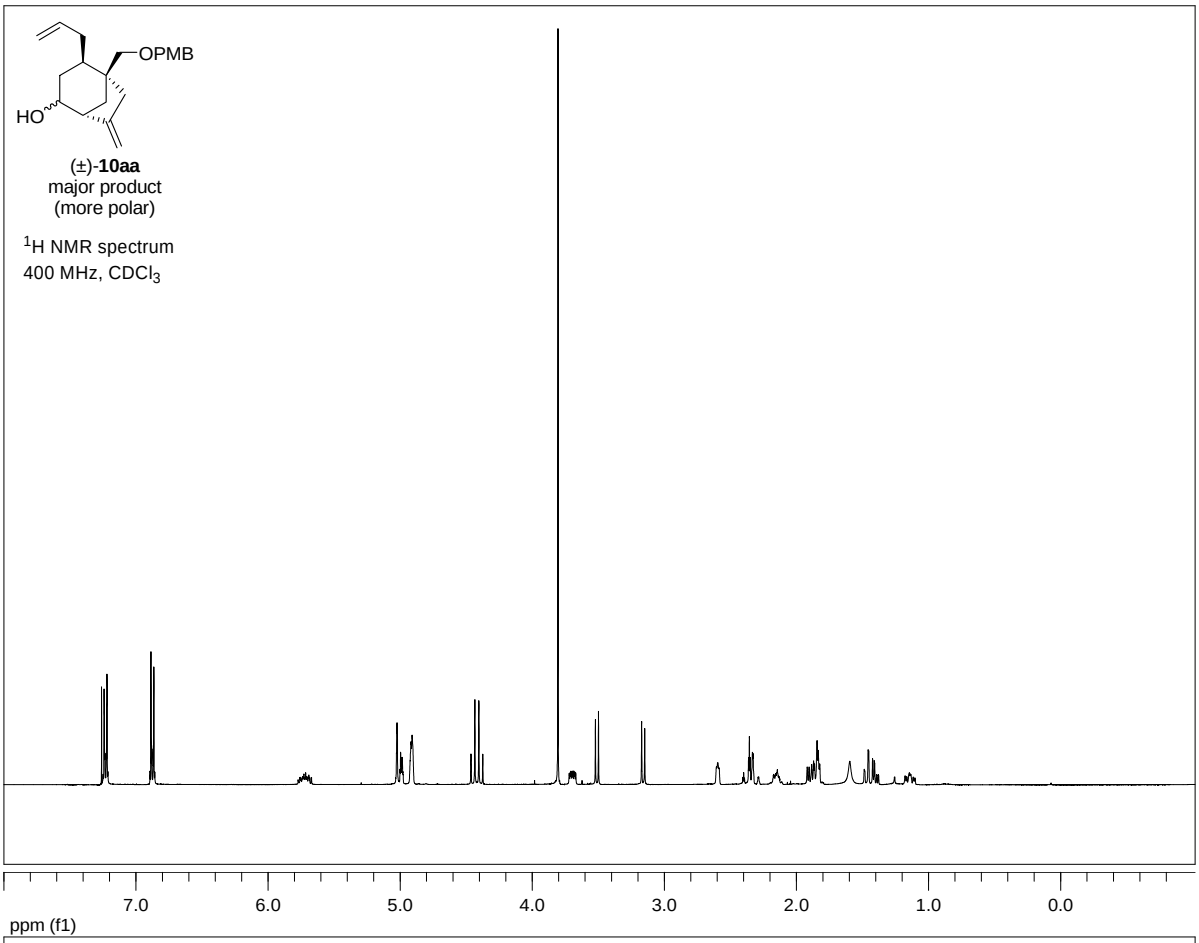
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HO
(±)-10aa
major product
(more polar)
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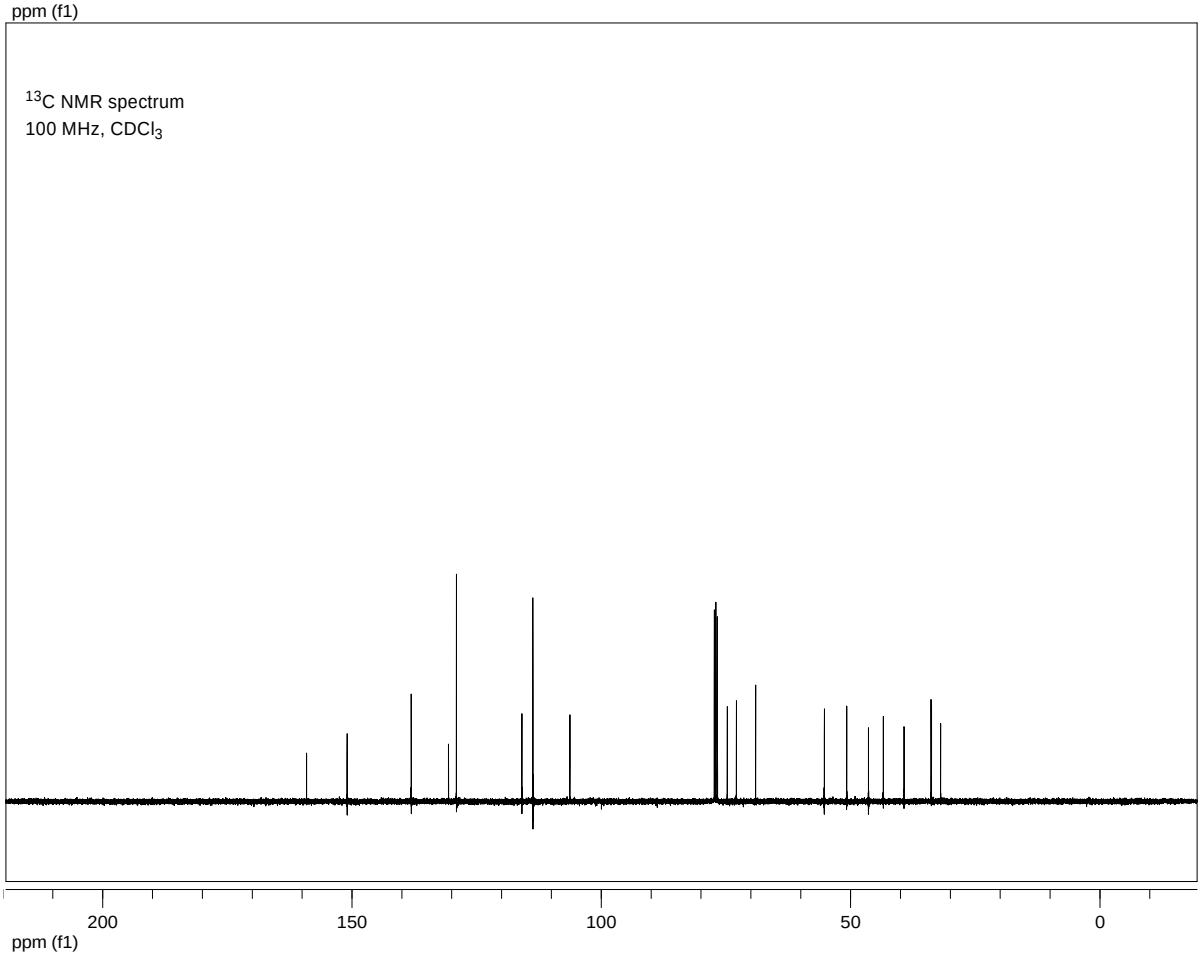
3.0
2.0
1.0
0.0
ppm (f1)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50
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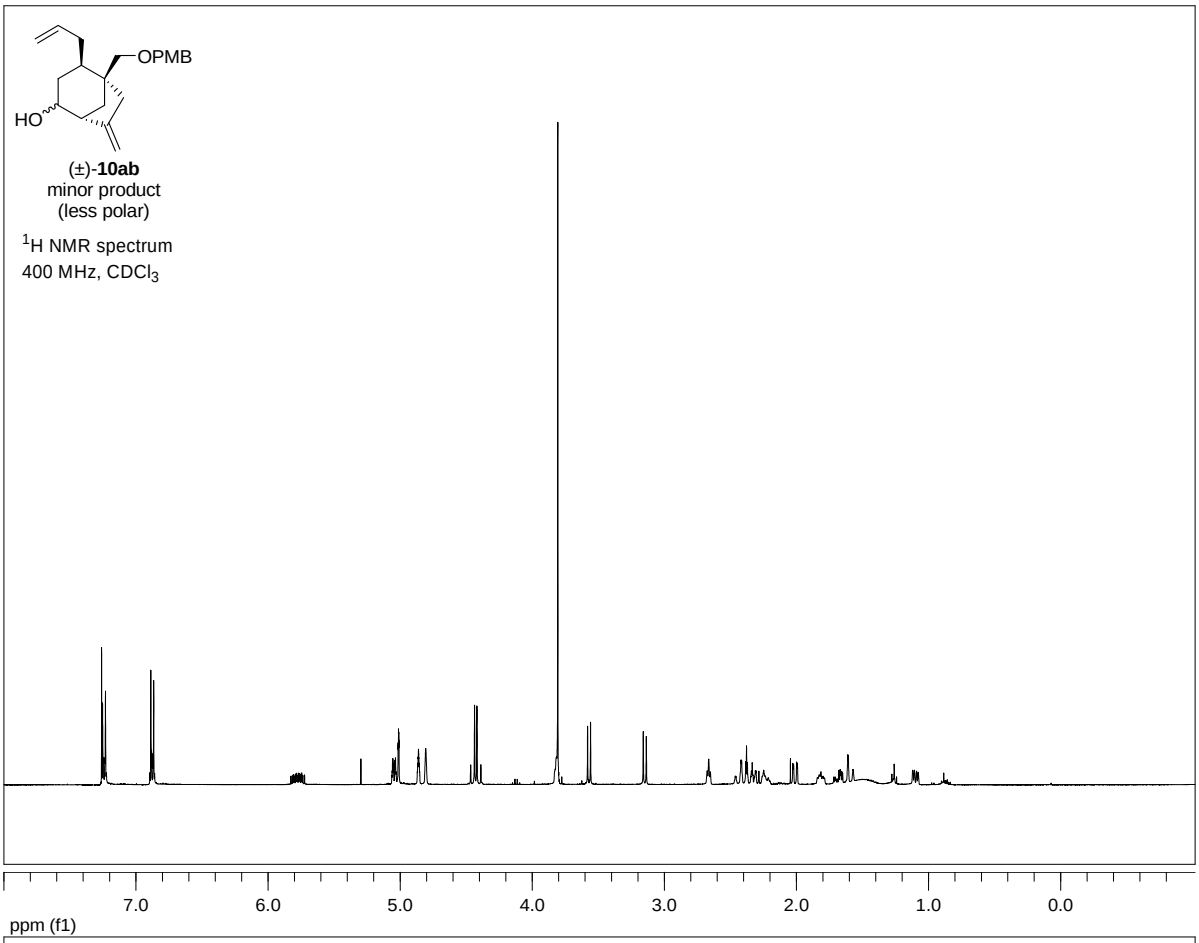
ppm (f1)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HO
(±)-10ab
minor product
(less polar)
1H NMR spectrum
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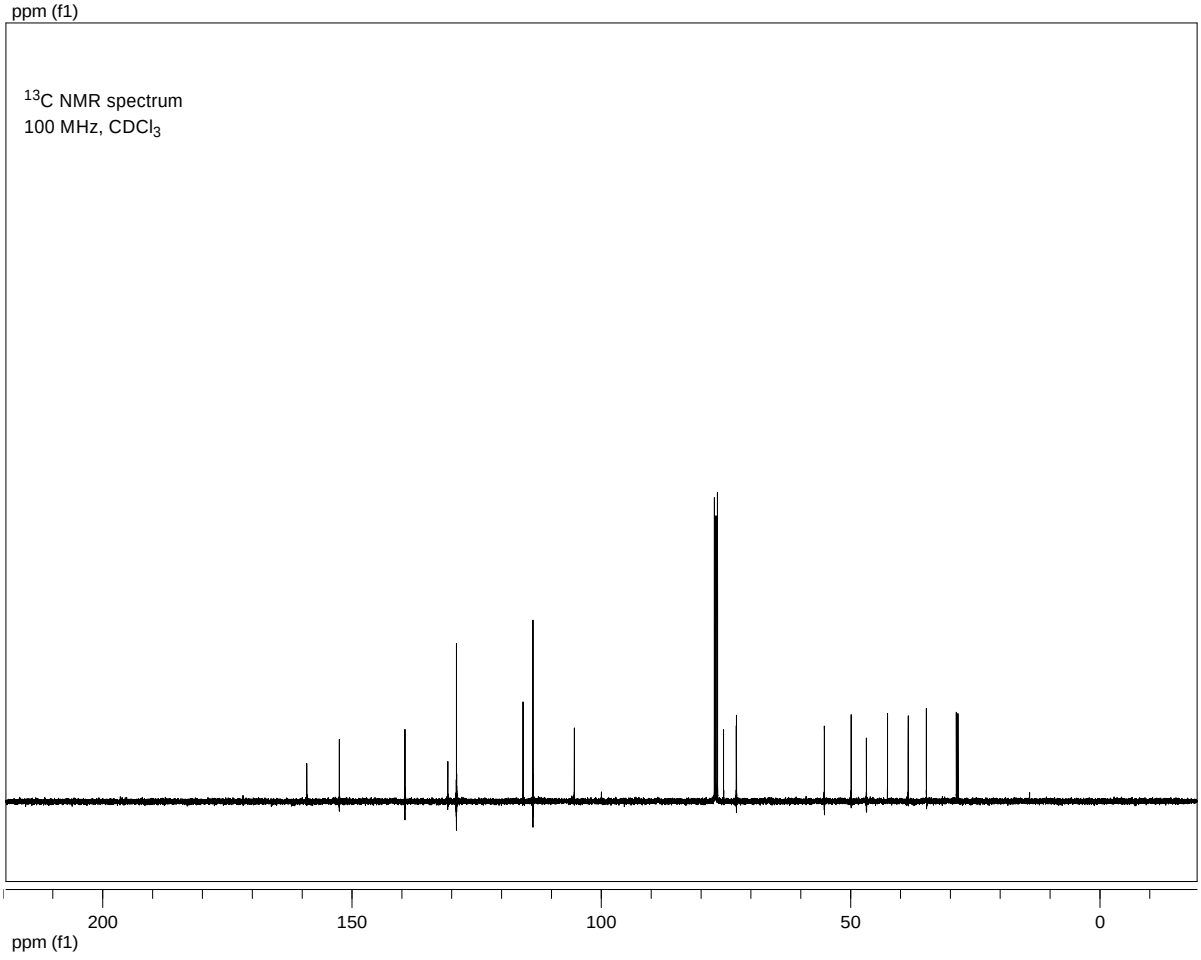
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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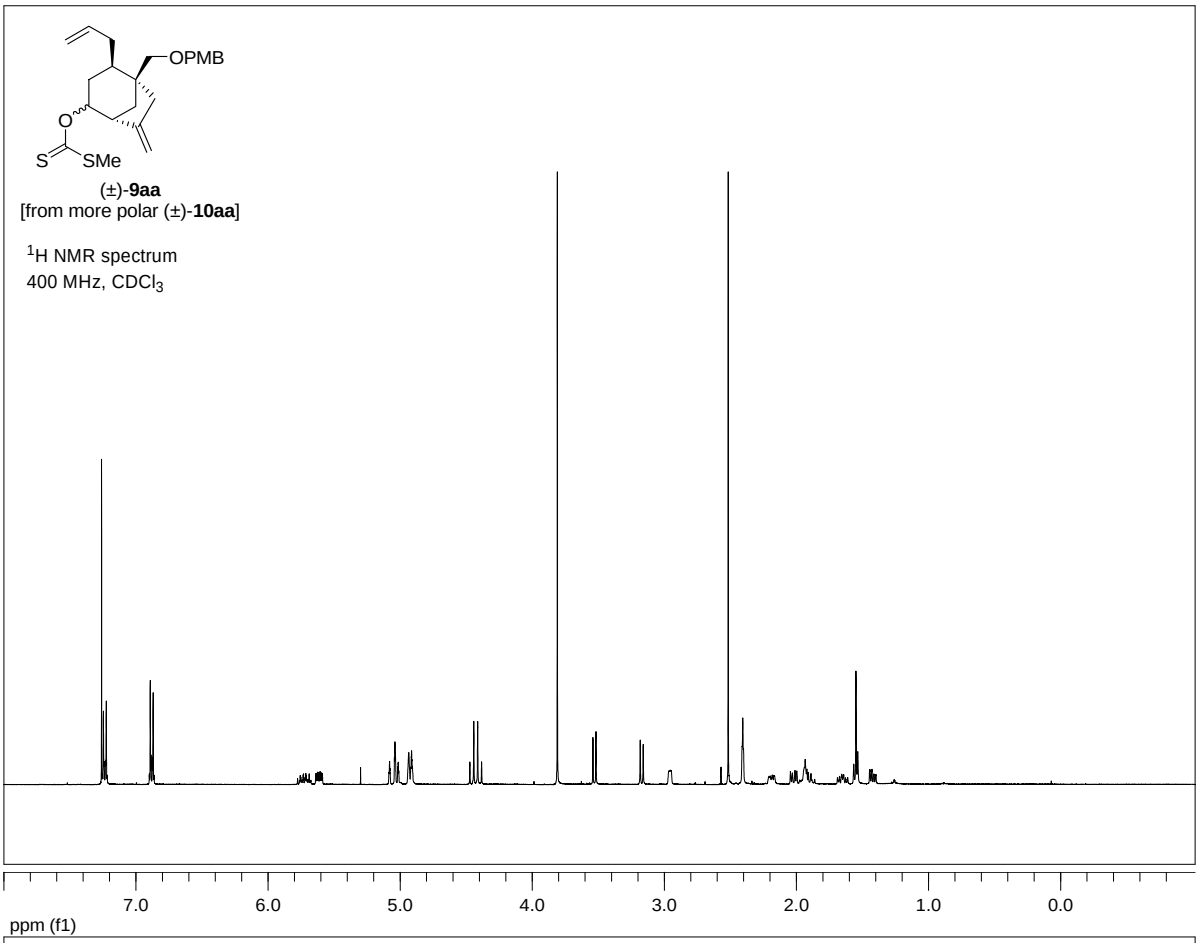
50
0
ppm (f1)


OPMB
O
S
SMe
(±)-9aa
[from more polar (±)-10aa]
1H NMR spectrum
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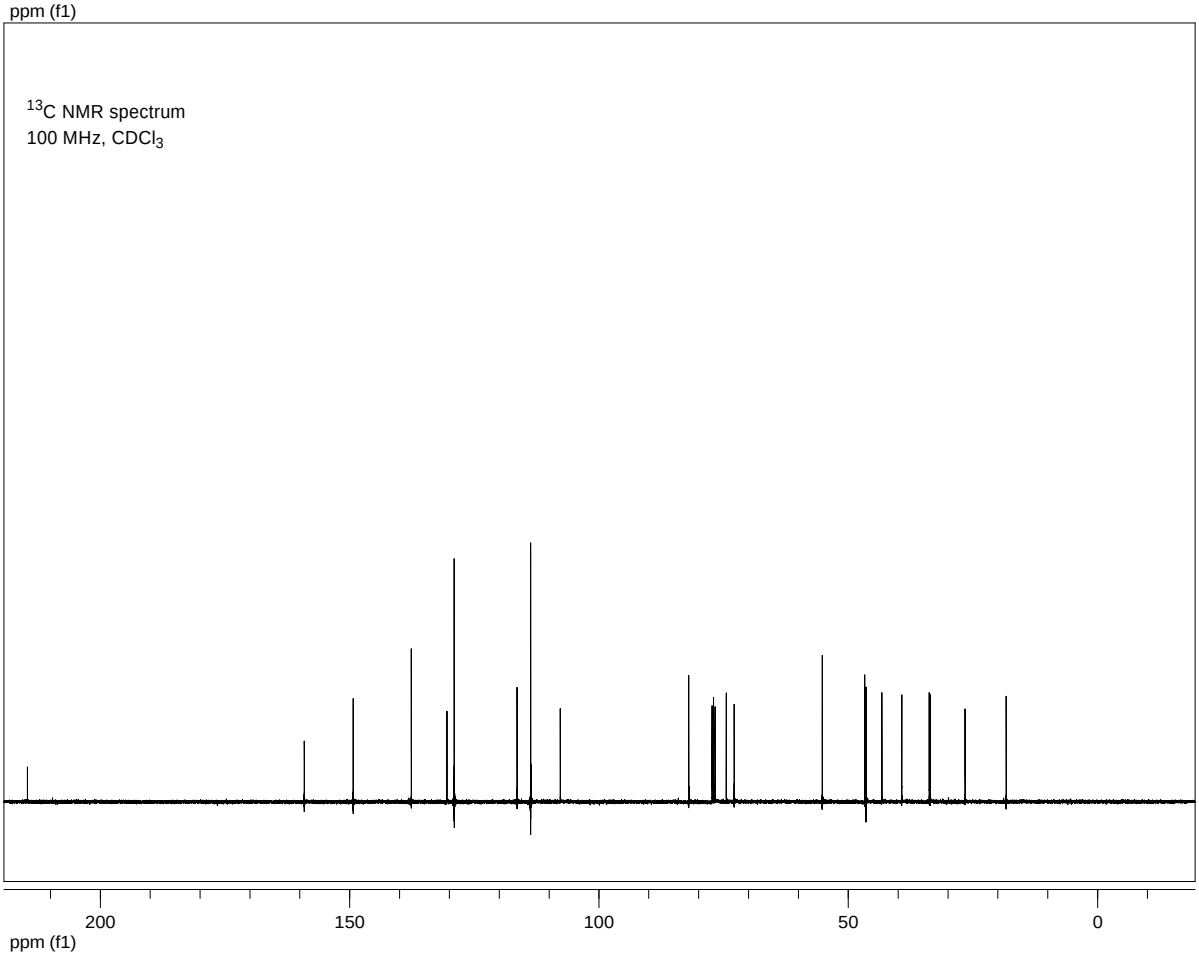
4.0
3.0
2.0
1.0
0.0
ppm (f1)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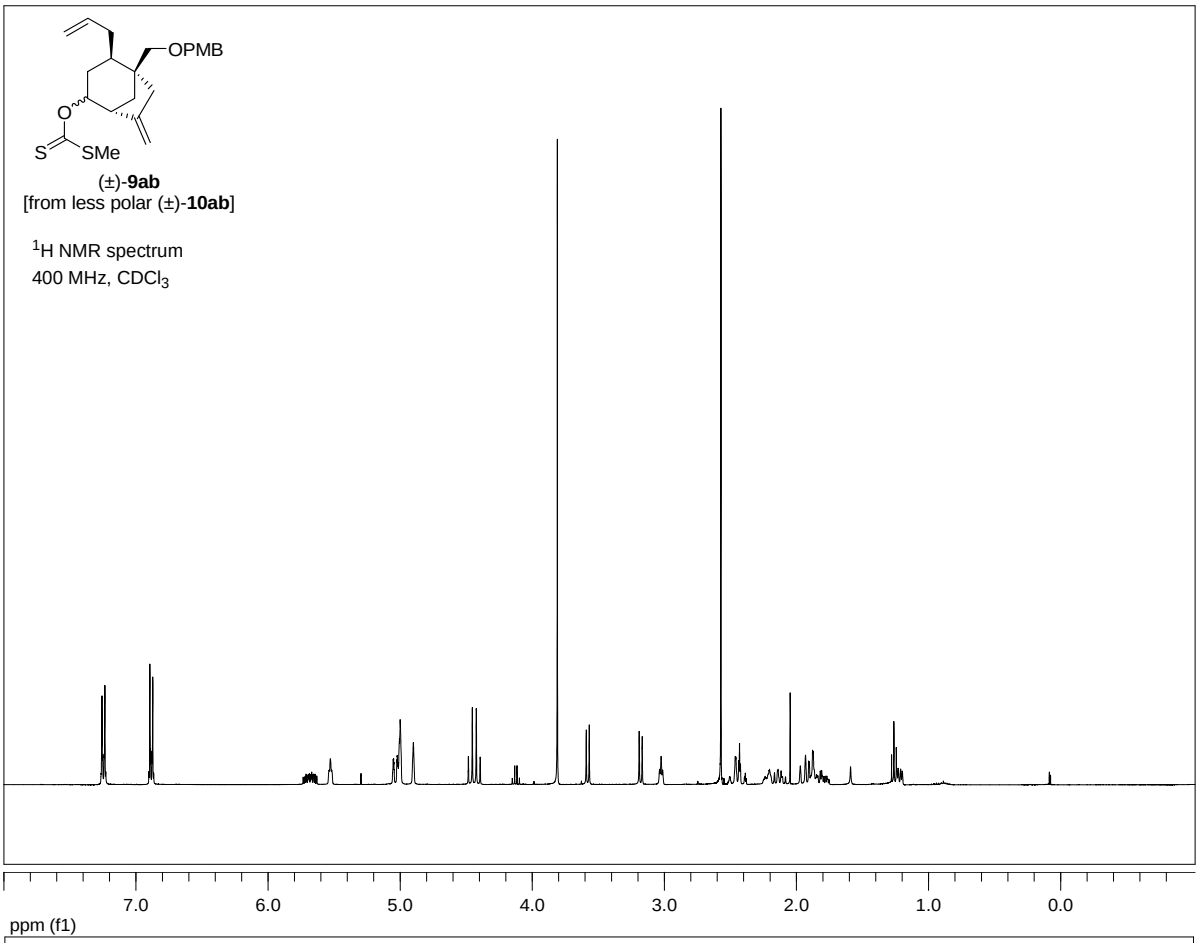
100
50
0
ppm (f1)


OPMB
O
S
SMe
(±)-9ab
[from less polar (±)-10ab]
1H NMR spectrum
400 MHz, CDCl3
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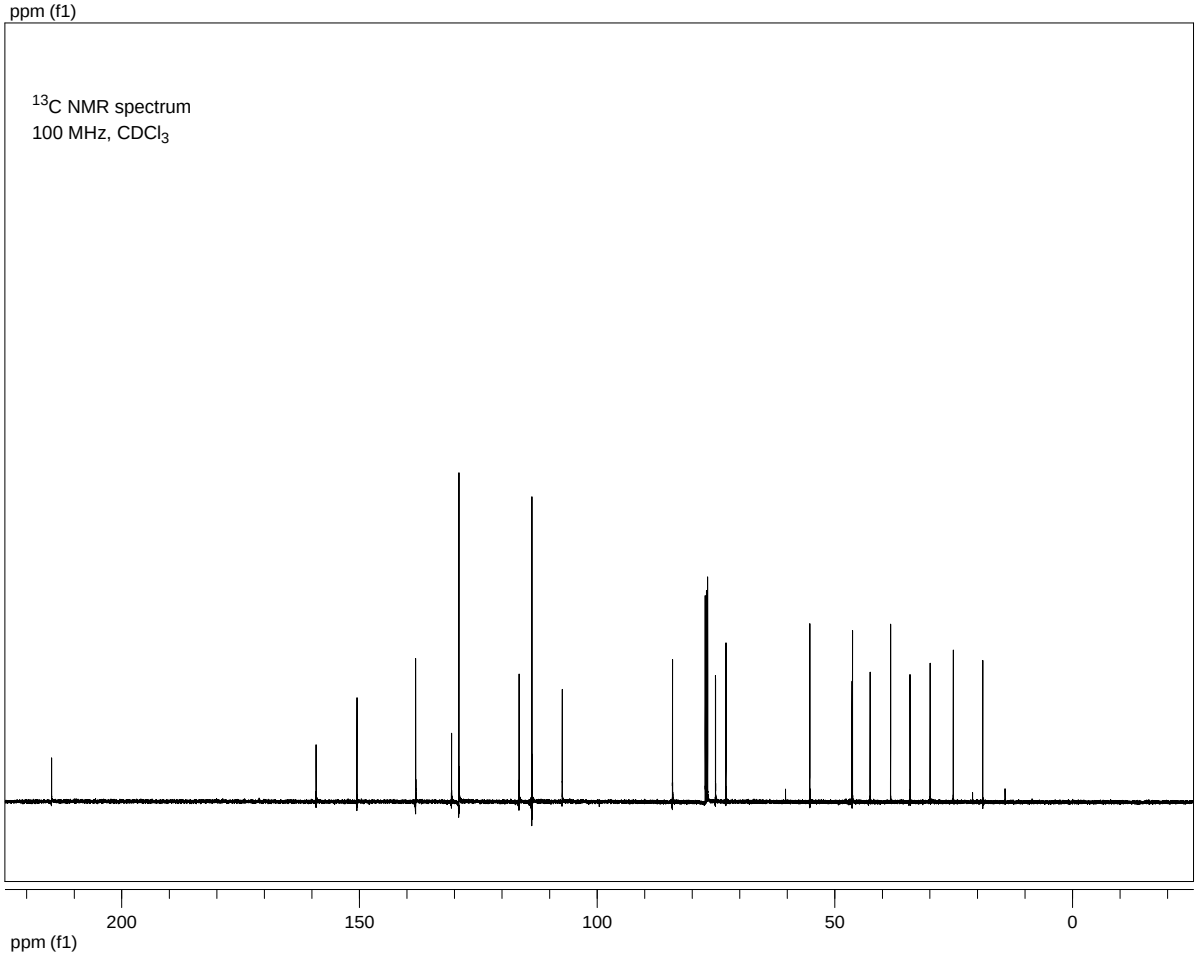
4.0
3.0
2.0
1.0
0.0
ppm (f1)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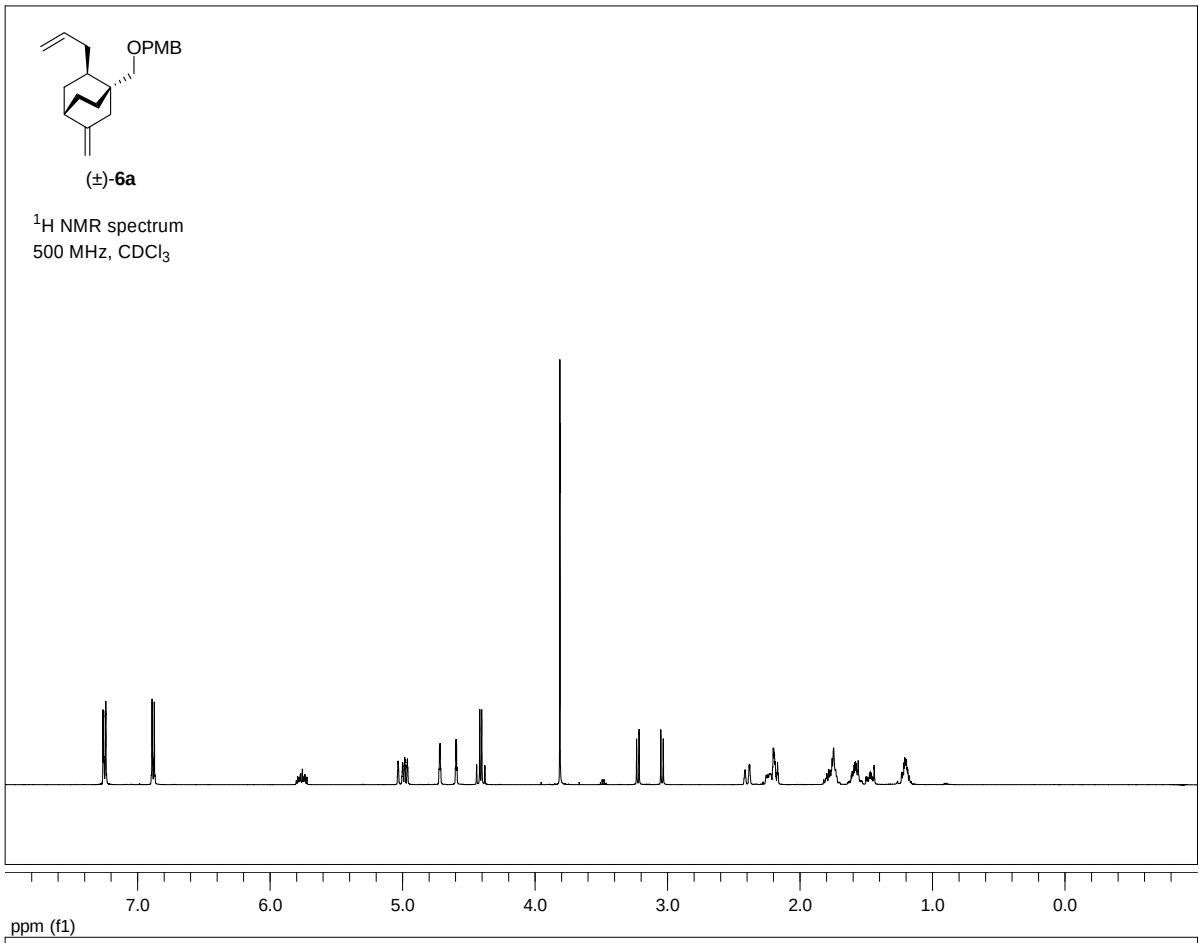
ppm (f1)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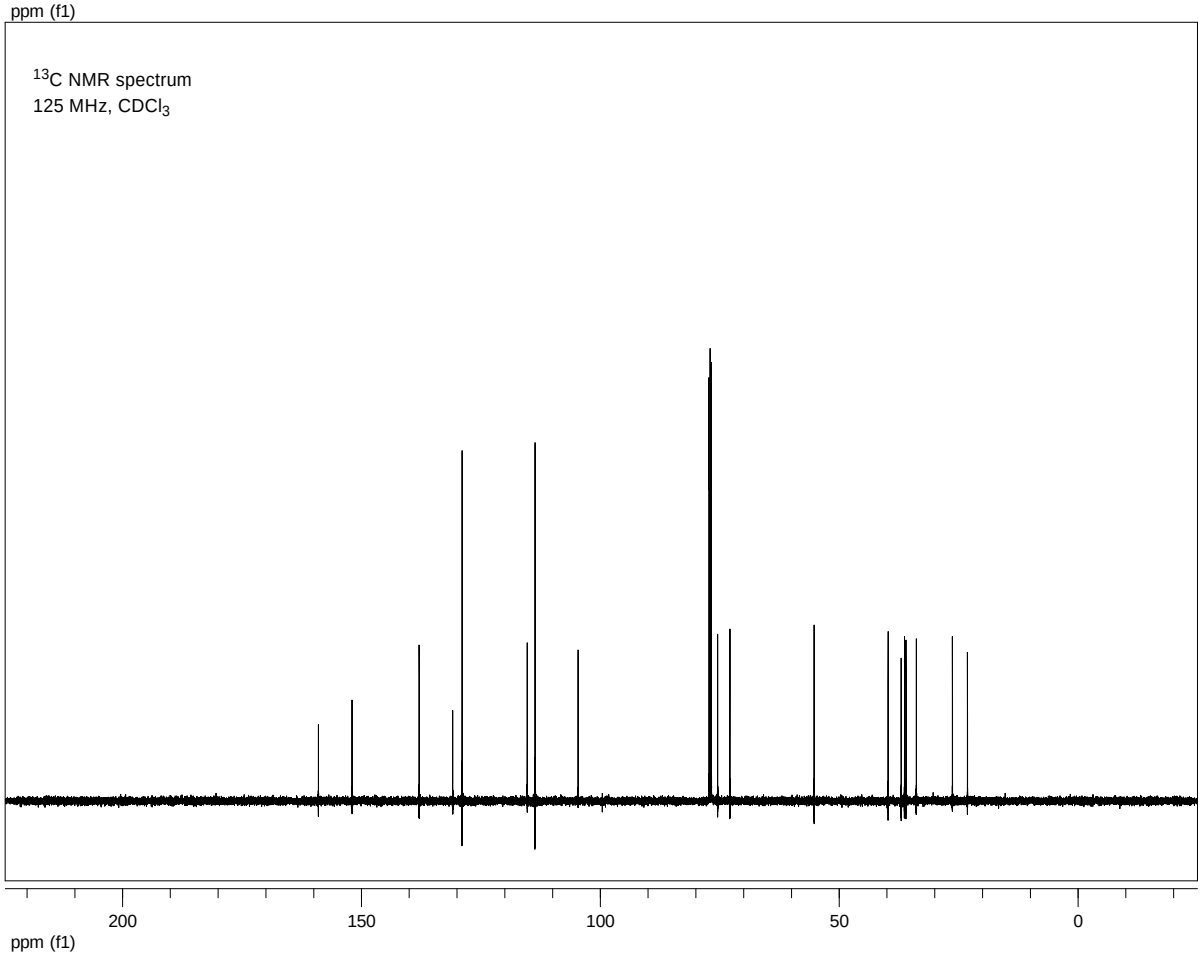
ppm (f1)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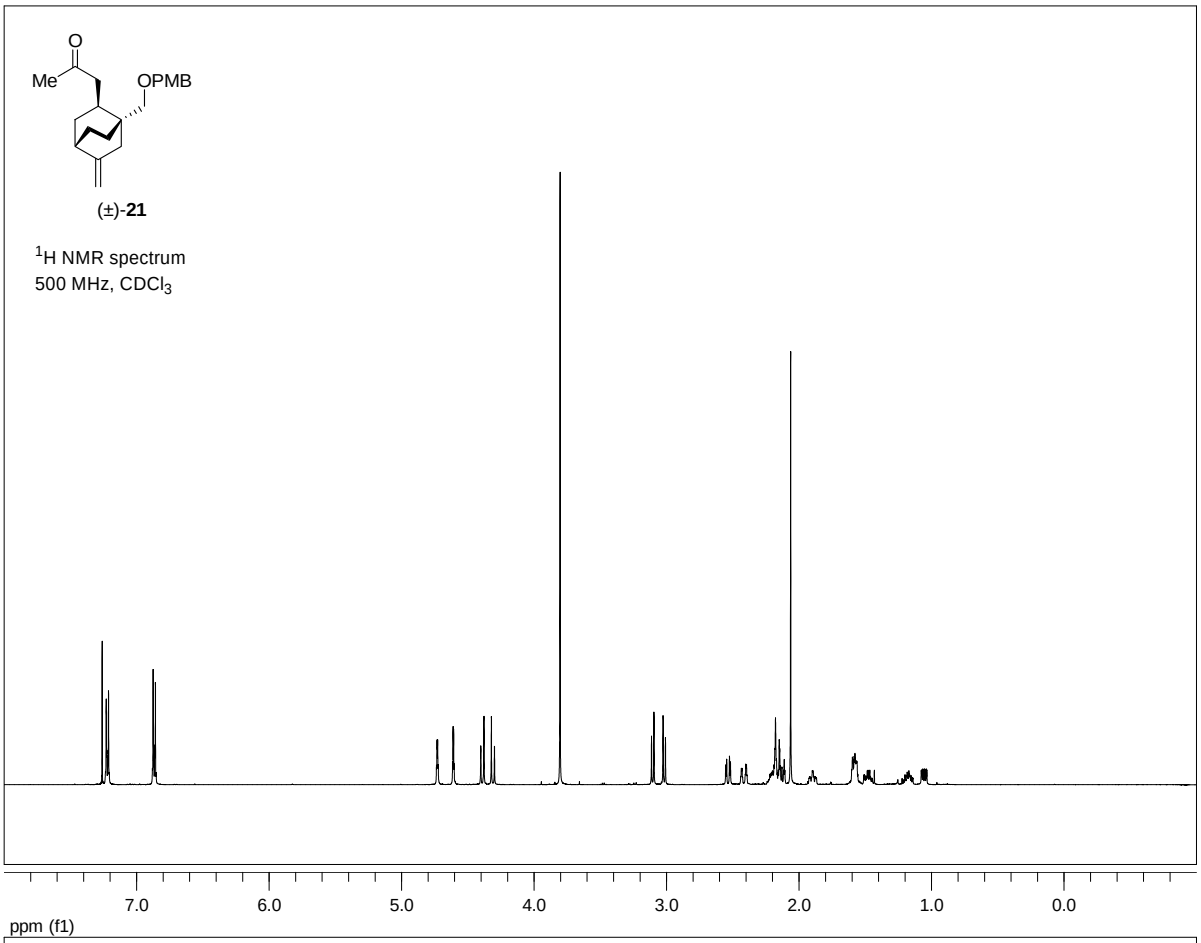
100
50
0
ppm (f1)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Me
OPMB
(±)-21
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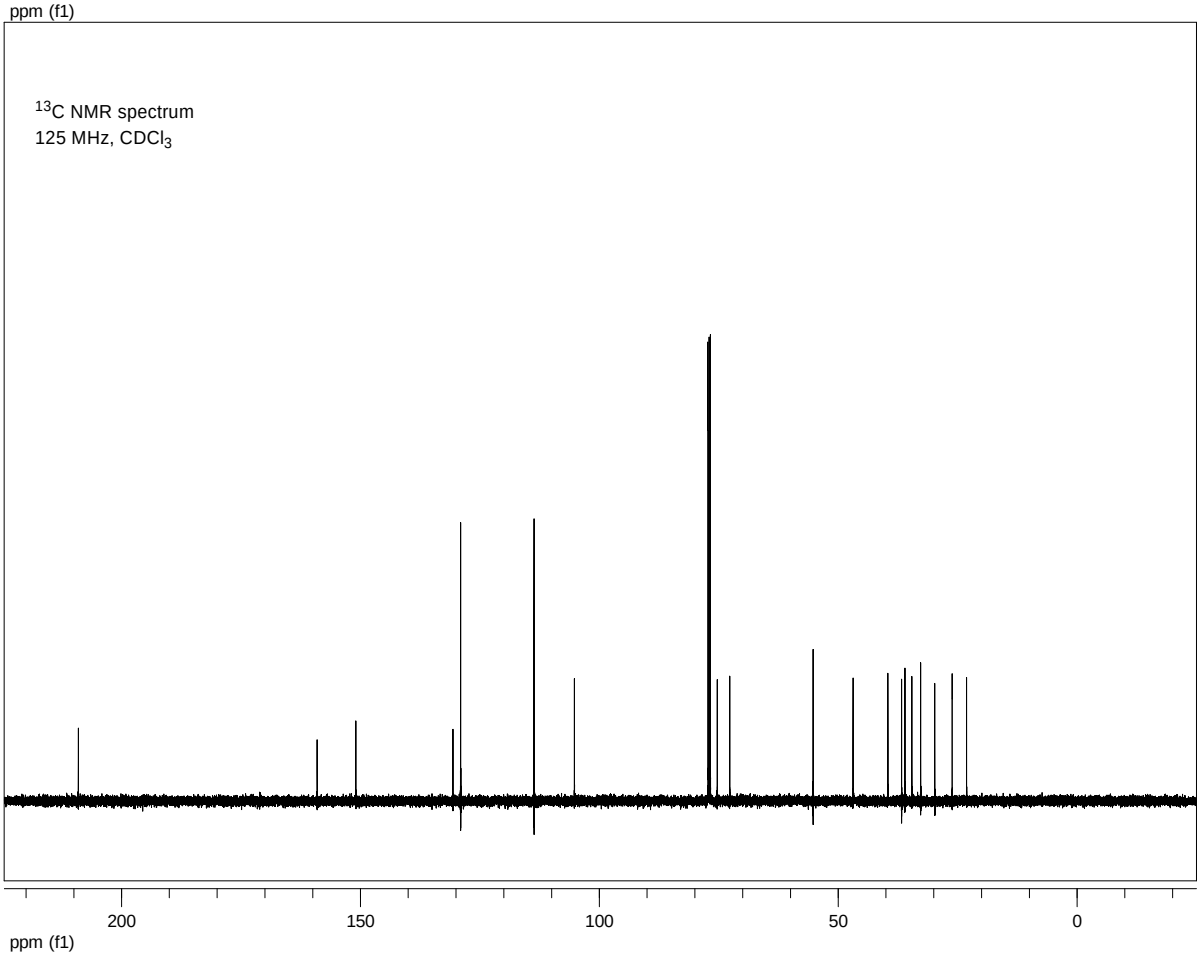
ppm (f1)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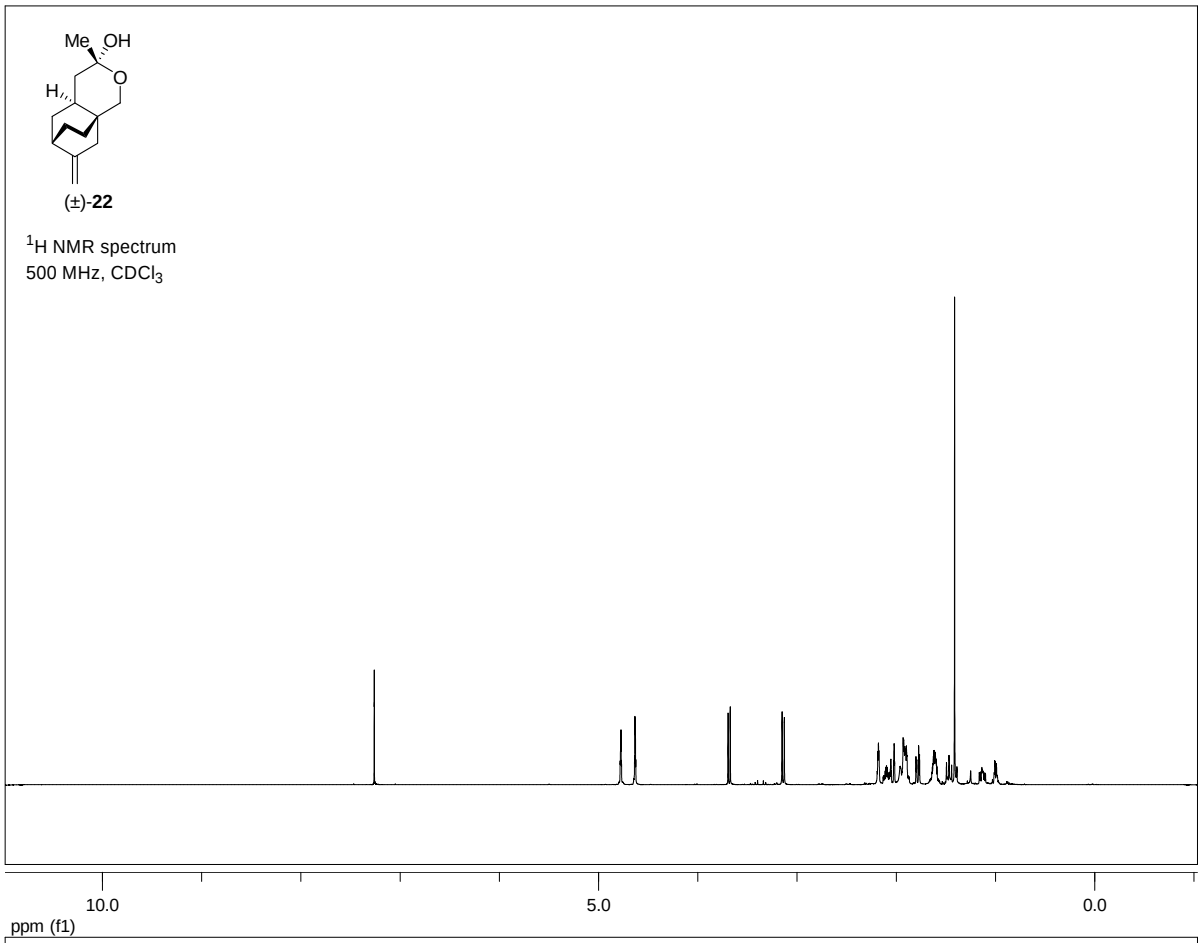
ppm (f1)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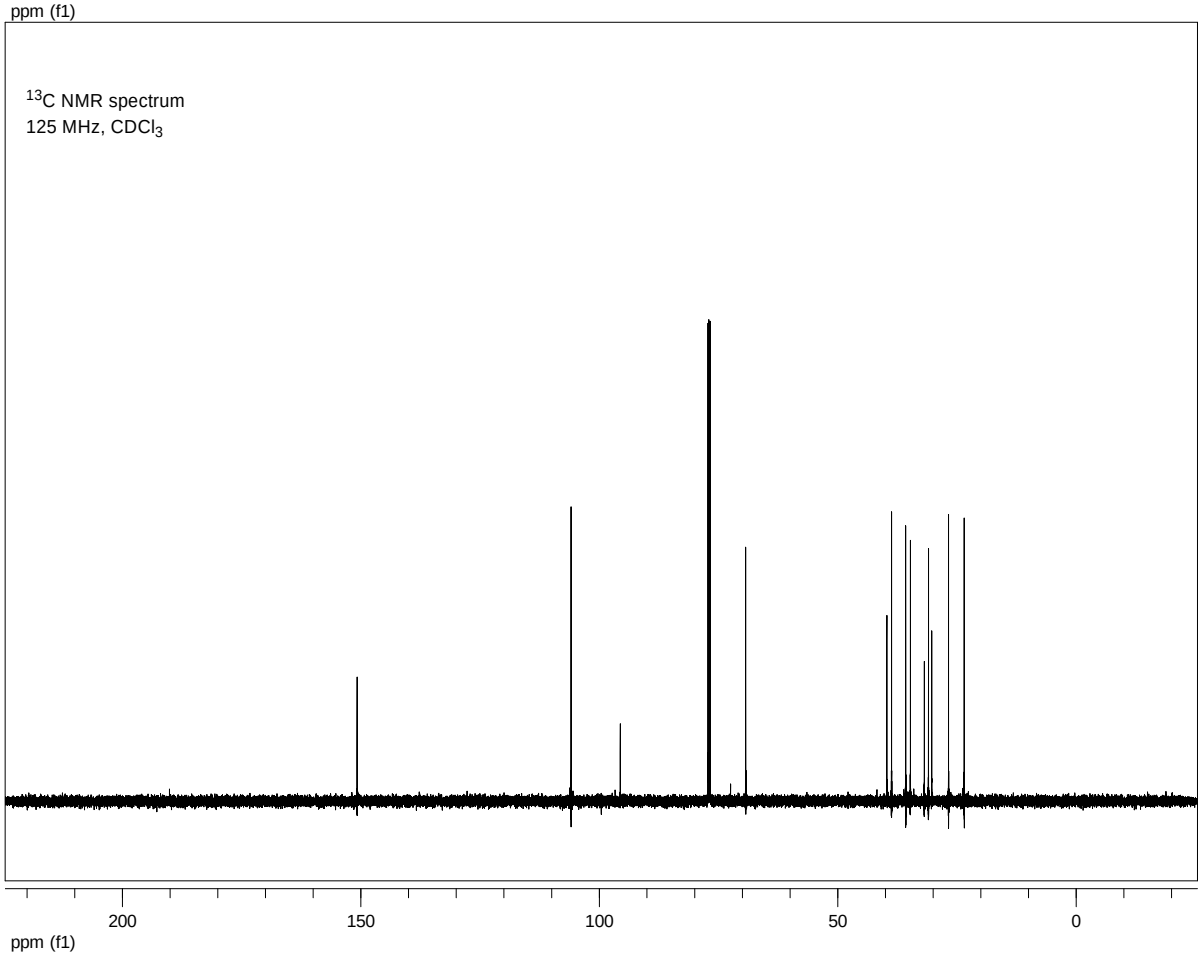
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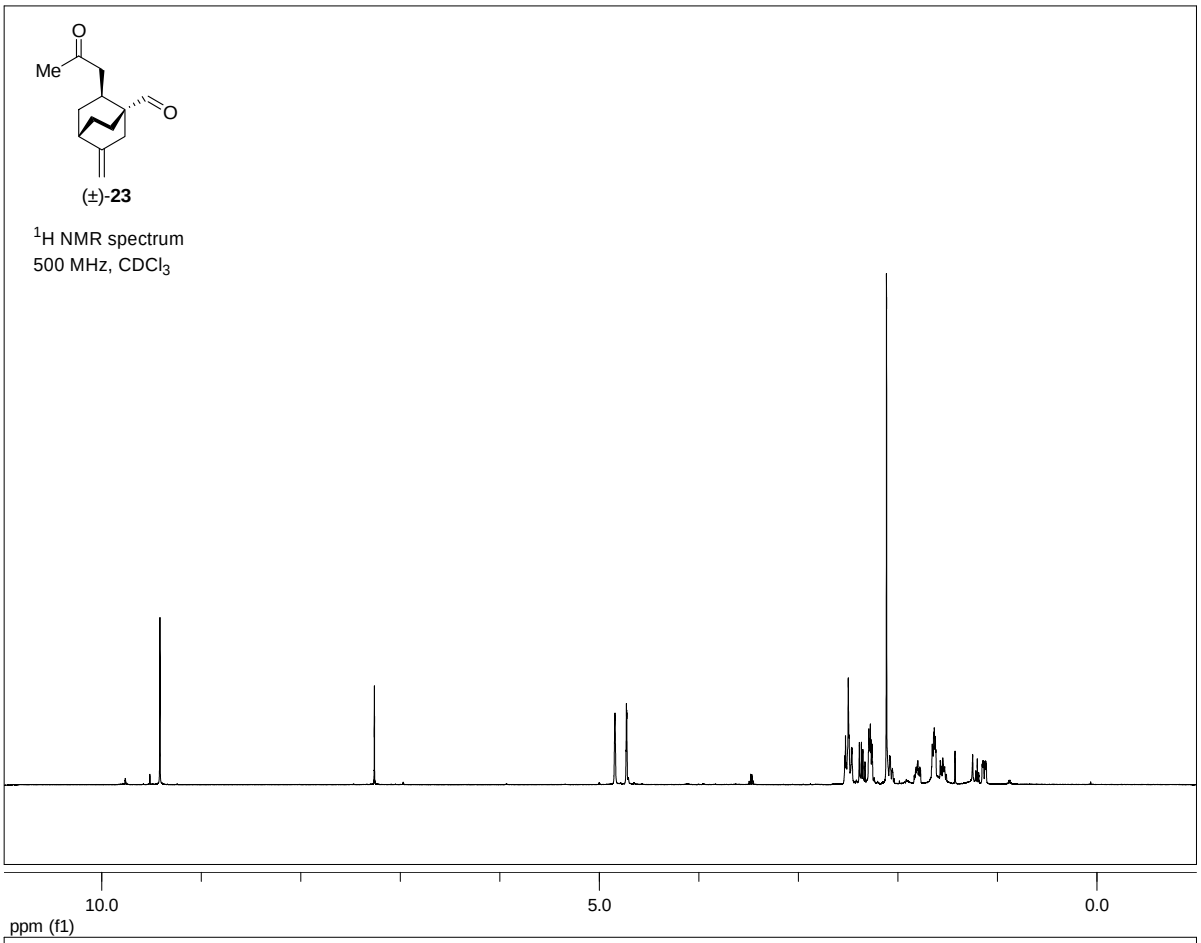
ppm (f1)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Me
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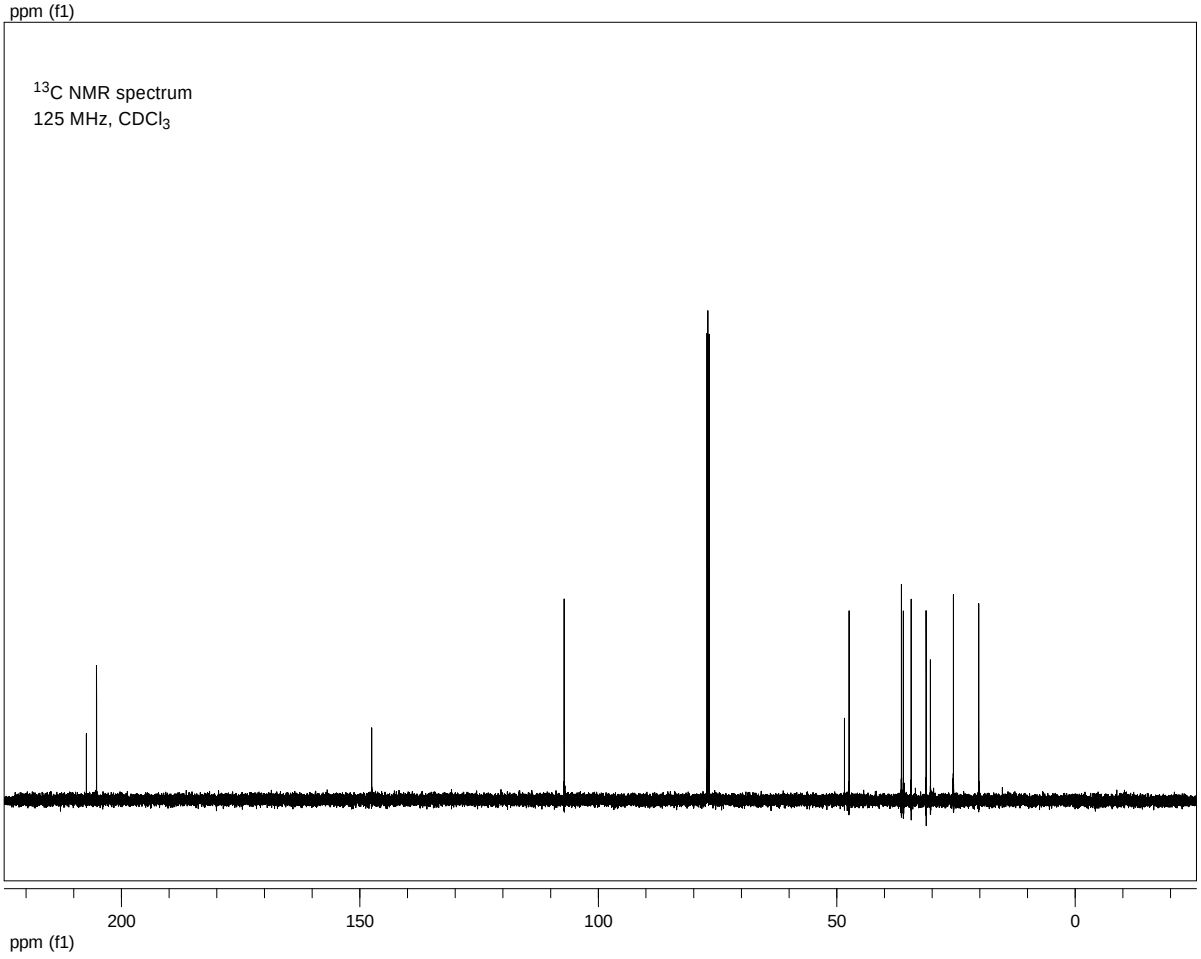
0.0
ppm (f1)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125 MHz, CDCl3
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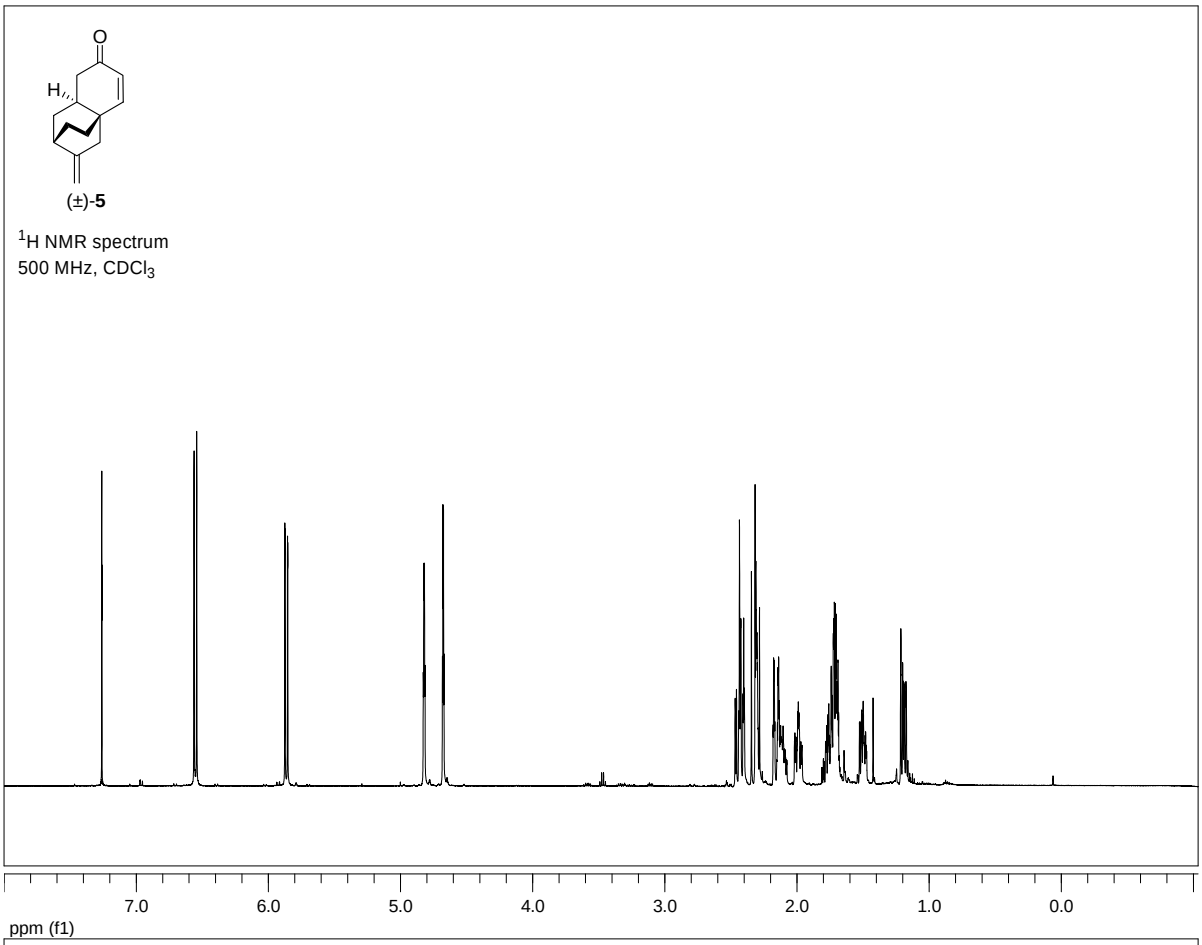
150
100
50
0
ppm (f1)


O
H
(±)-5
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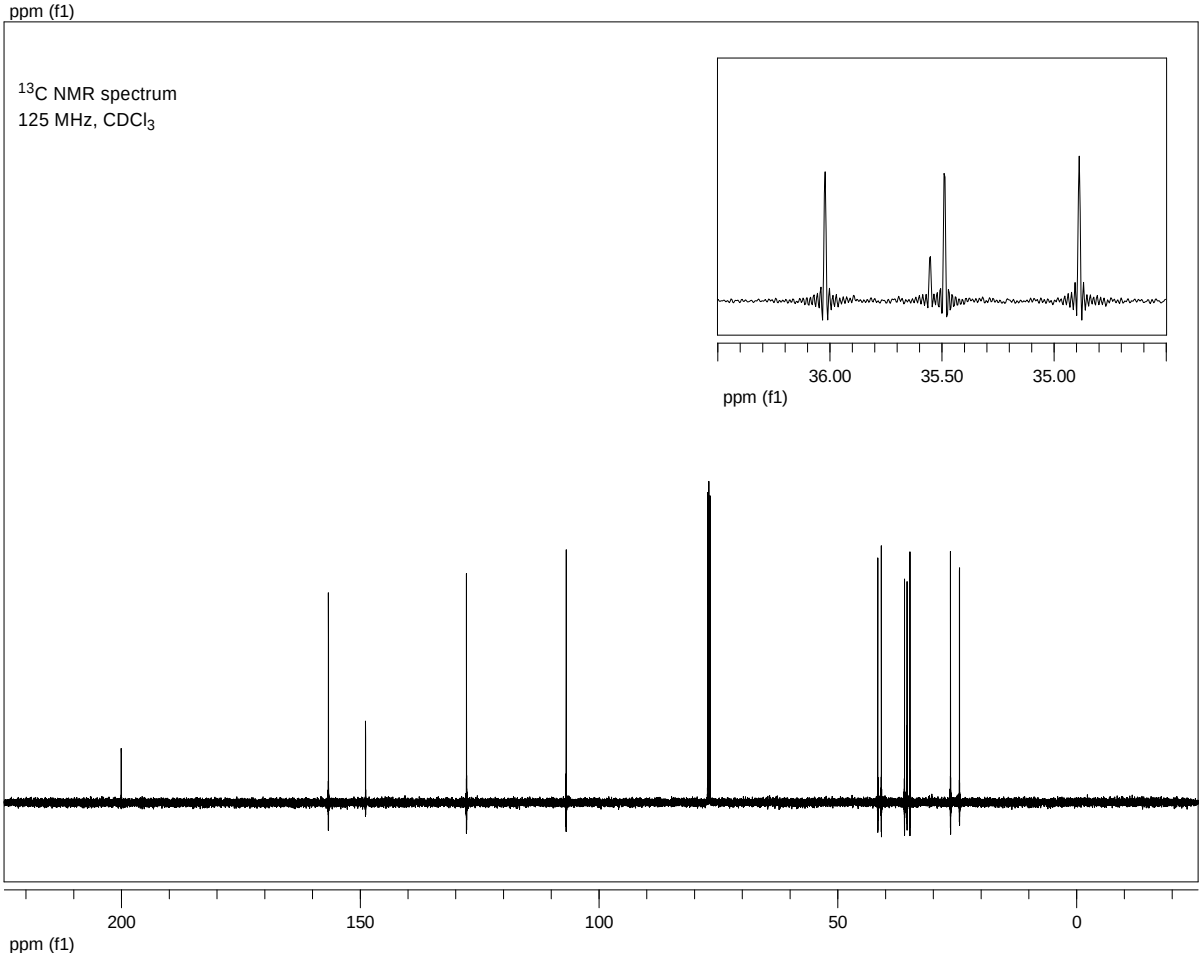
ppm (f1)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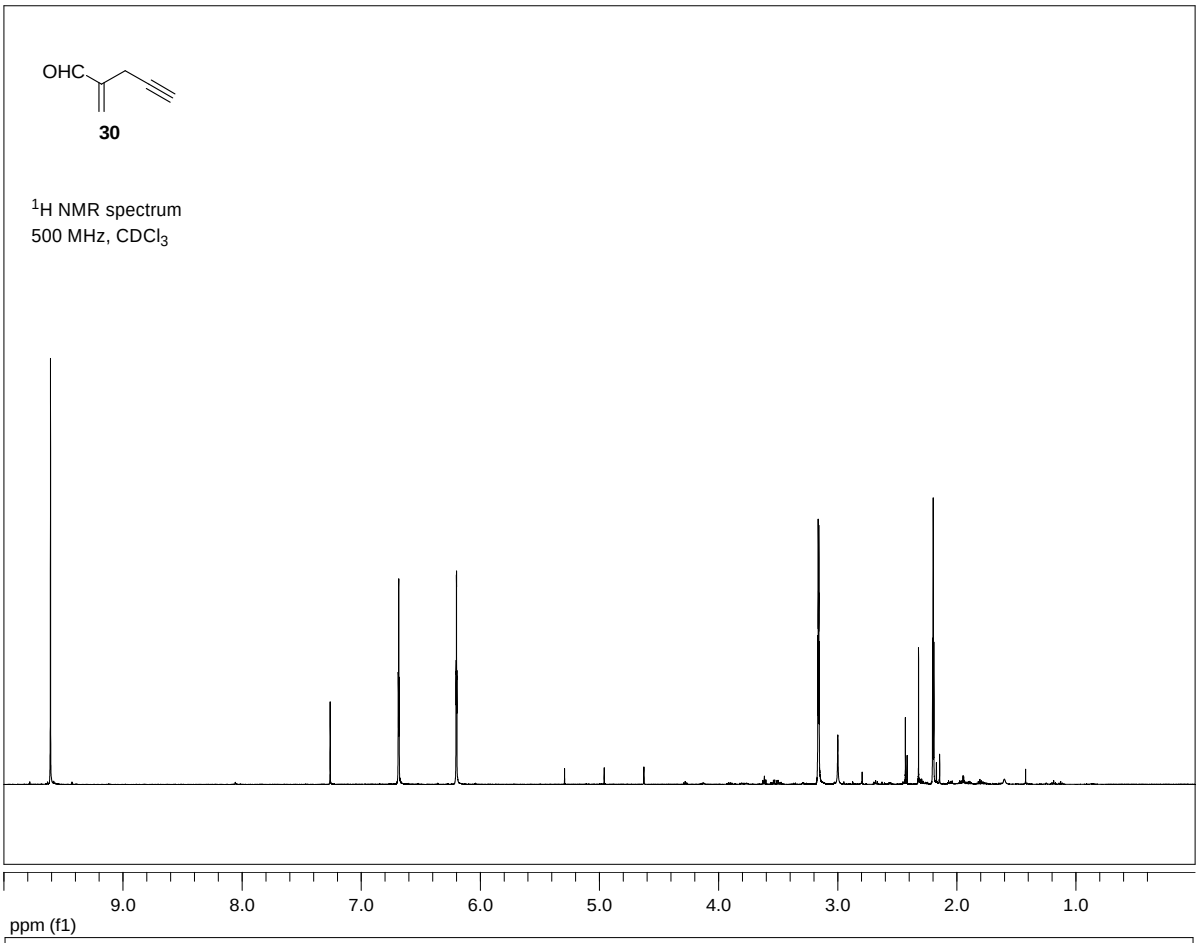
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30
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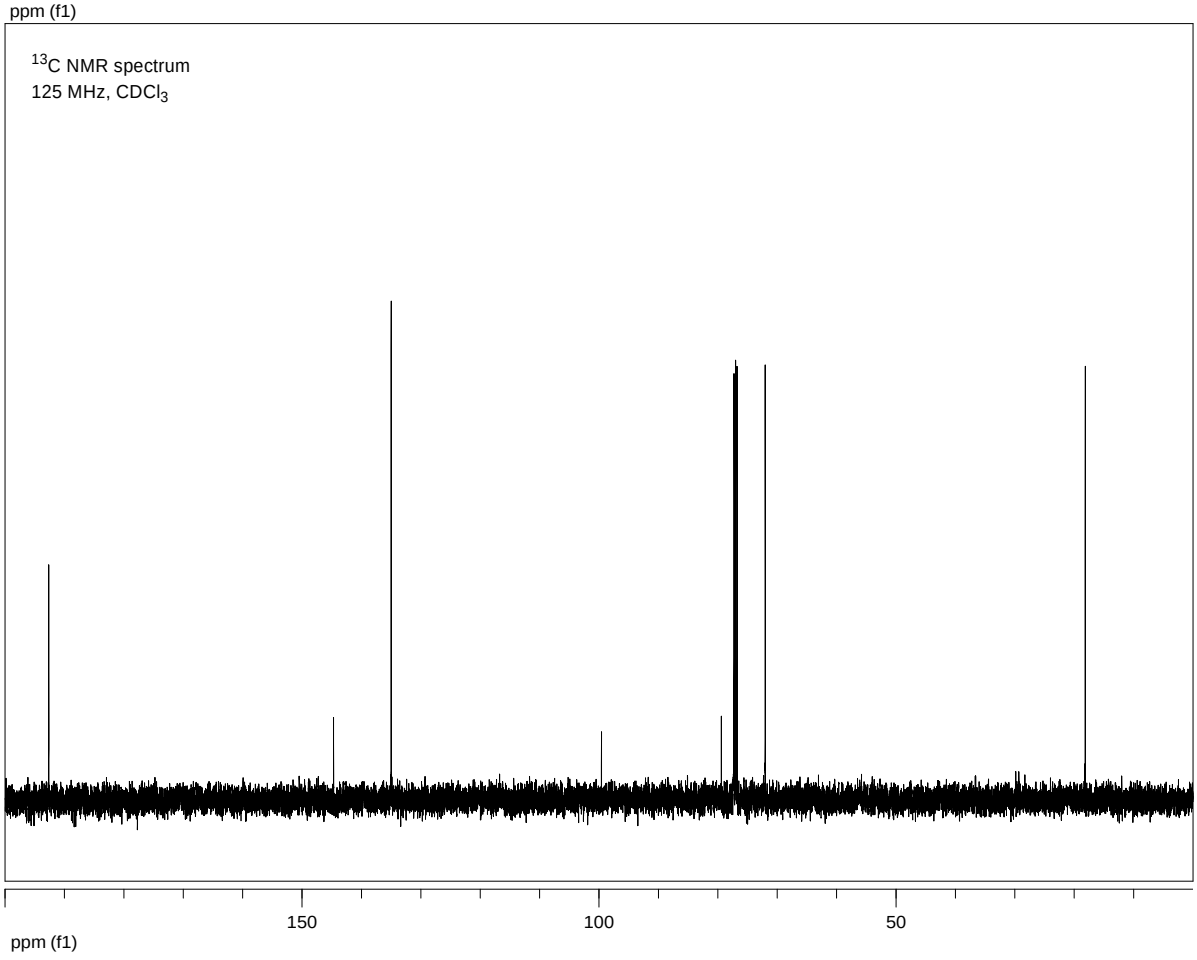
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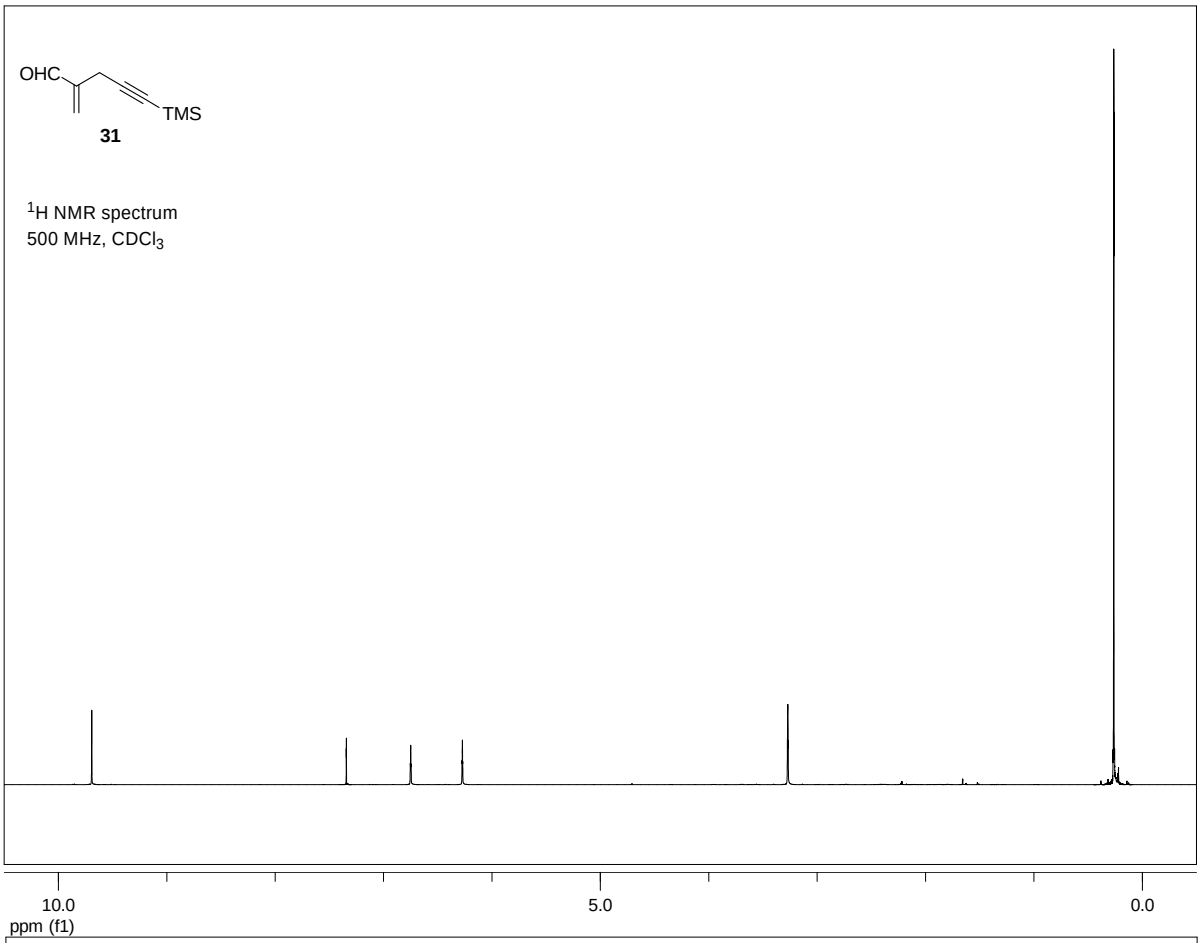
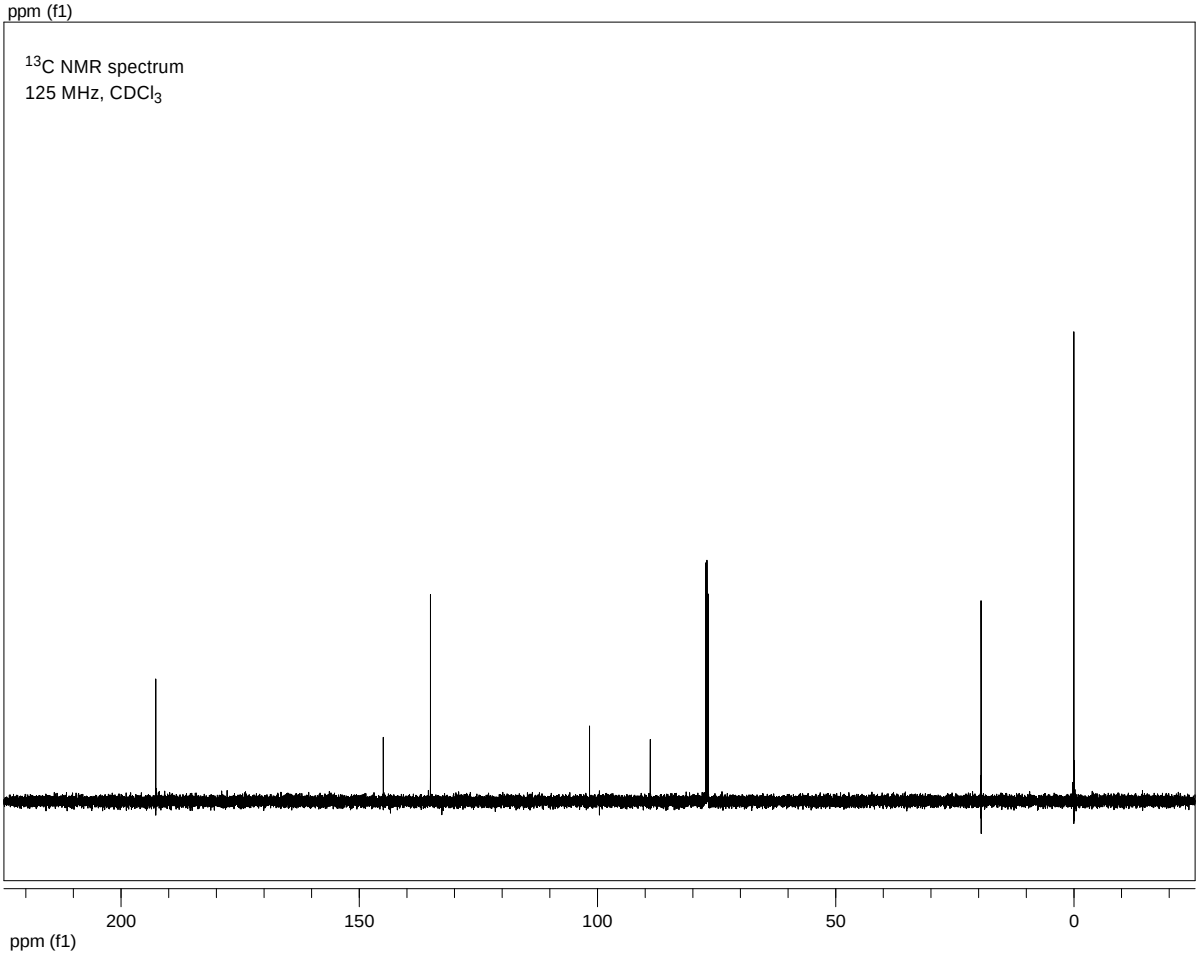
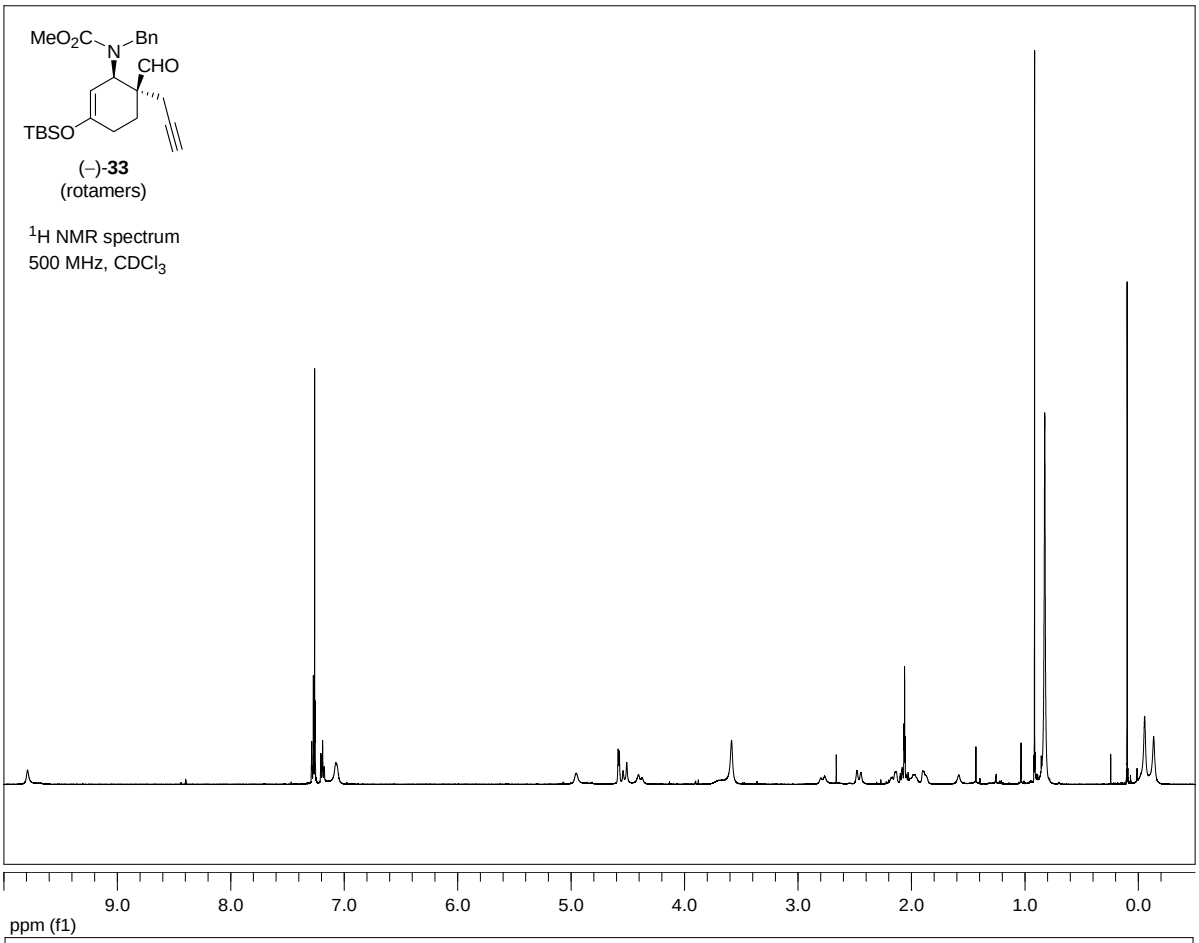
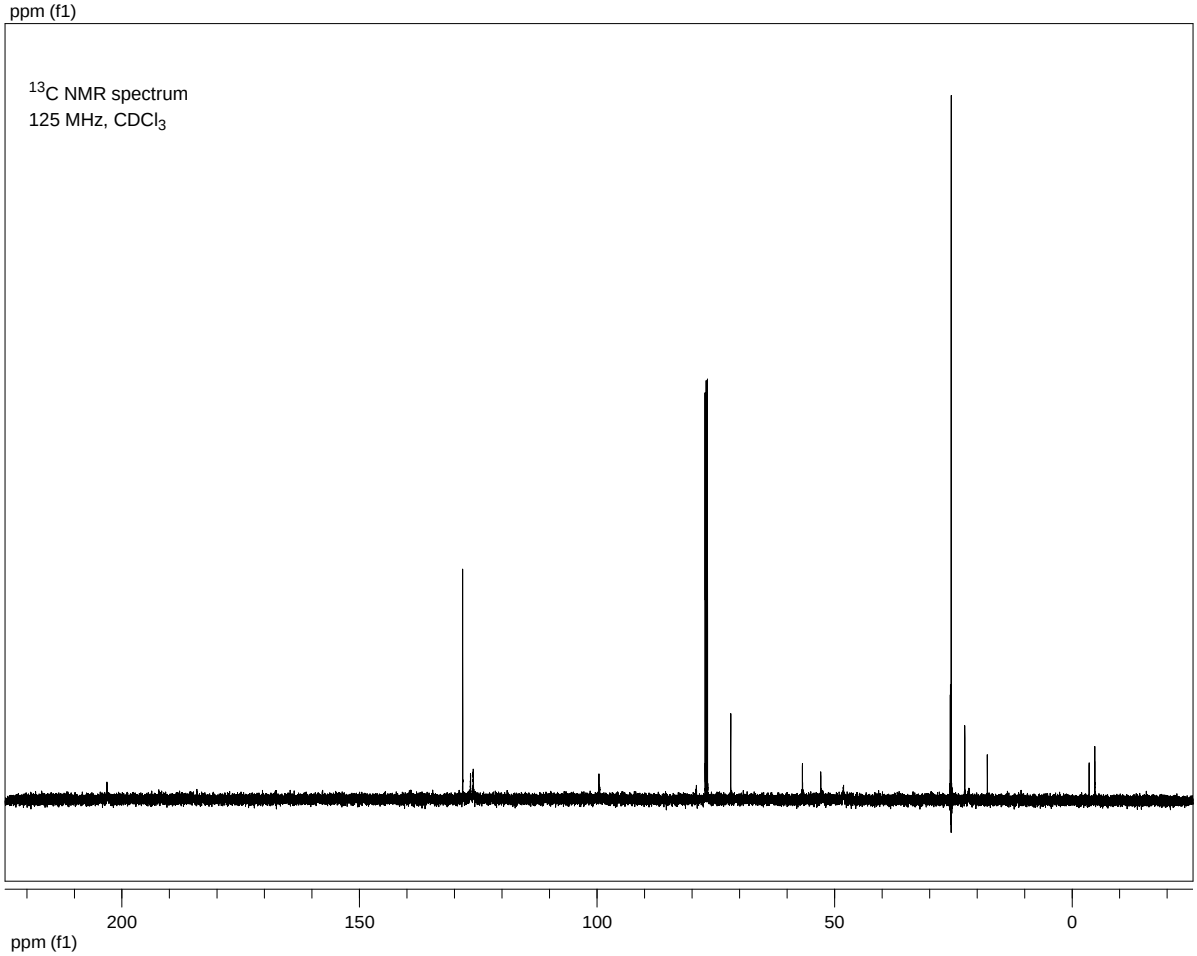
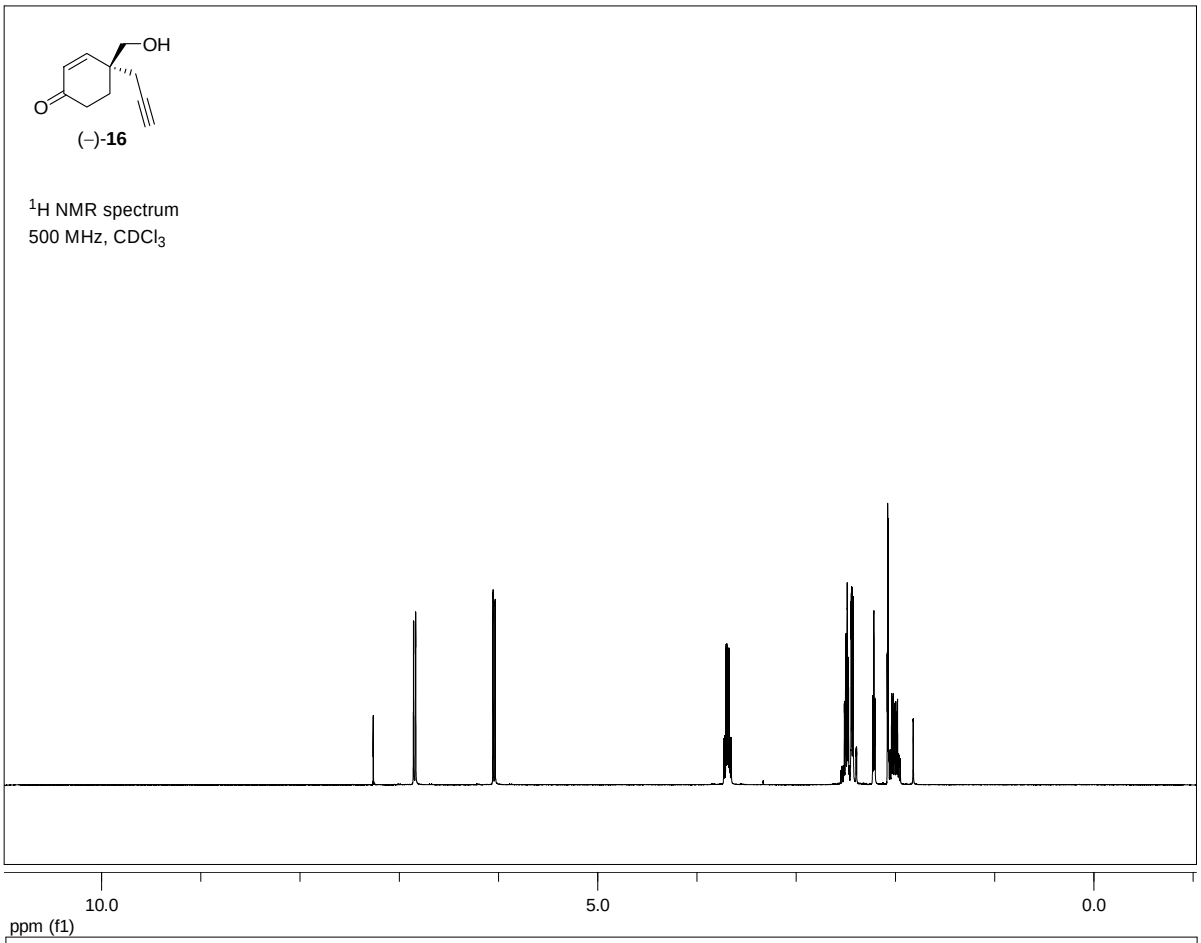
125 MHz, CDCl3
150
100
50
ppm (f1)

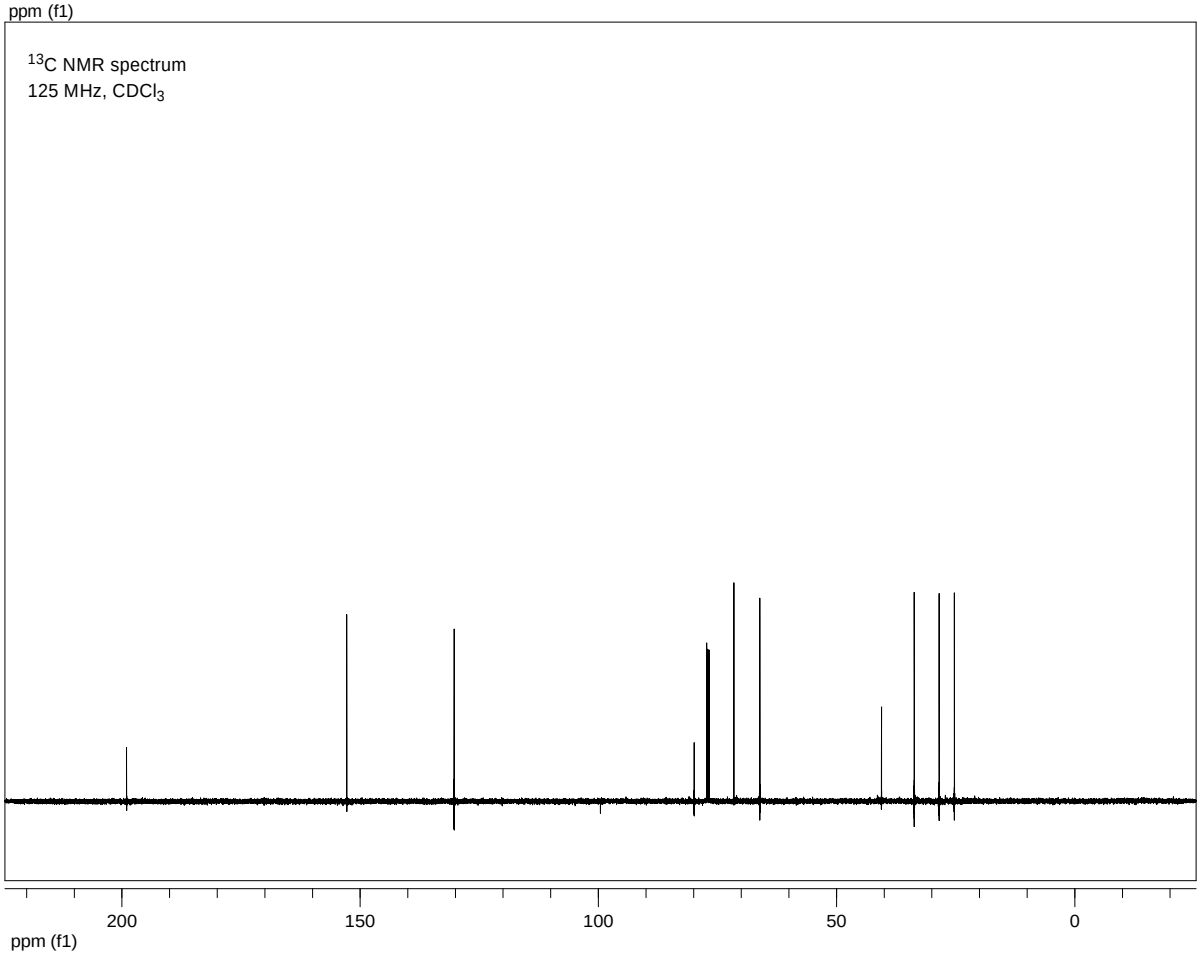

OHC
TMS
31
1H NMR spectrum
500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)

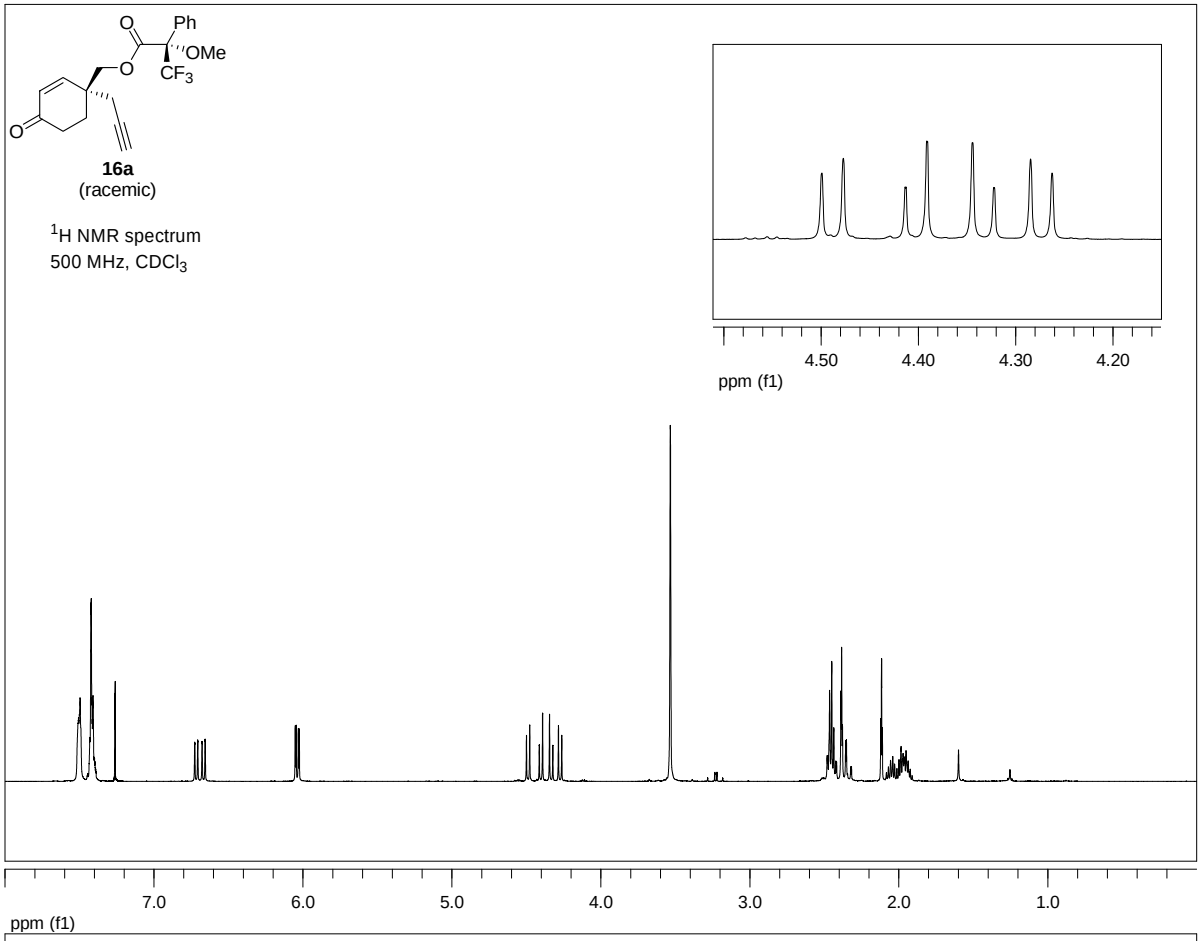

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

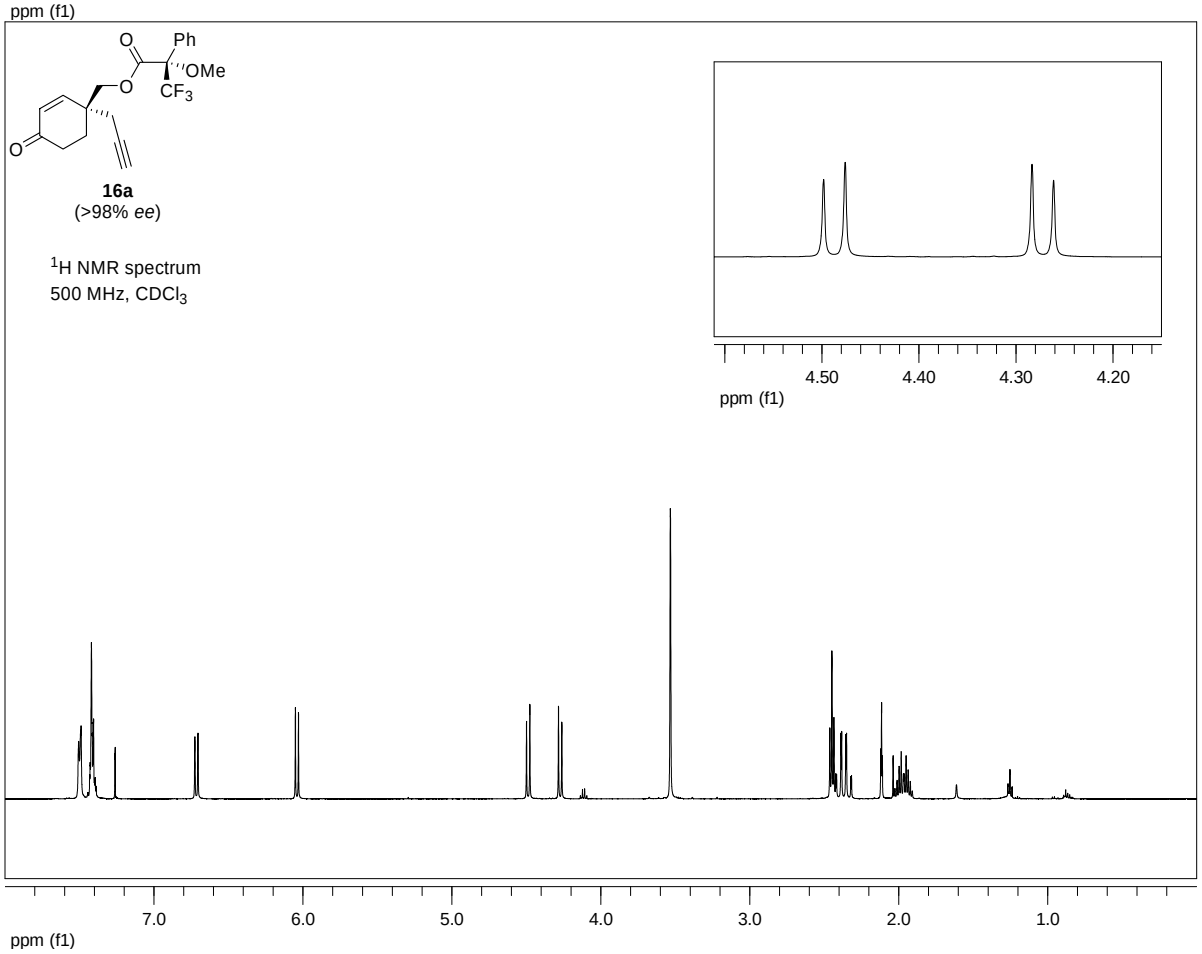

MeO2C
N
Bn
CHO
TBSO
(–)-33
(rotamers)
1H NMR spectrum
500 MHz, CDCl3
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

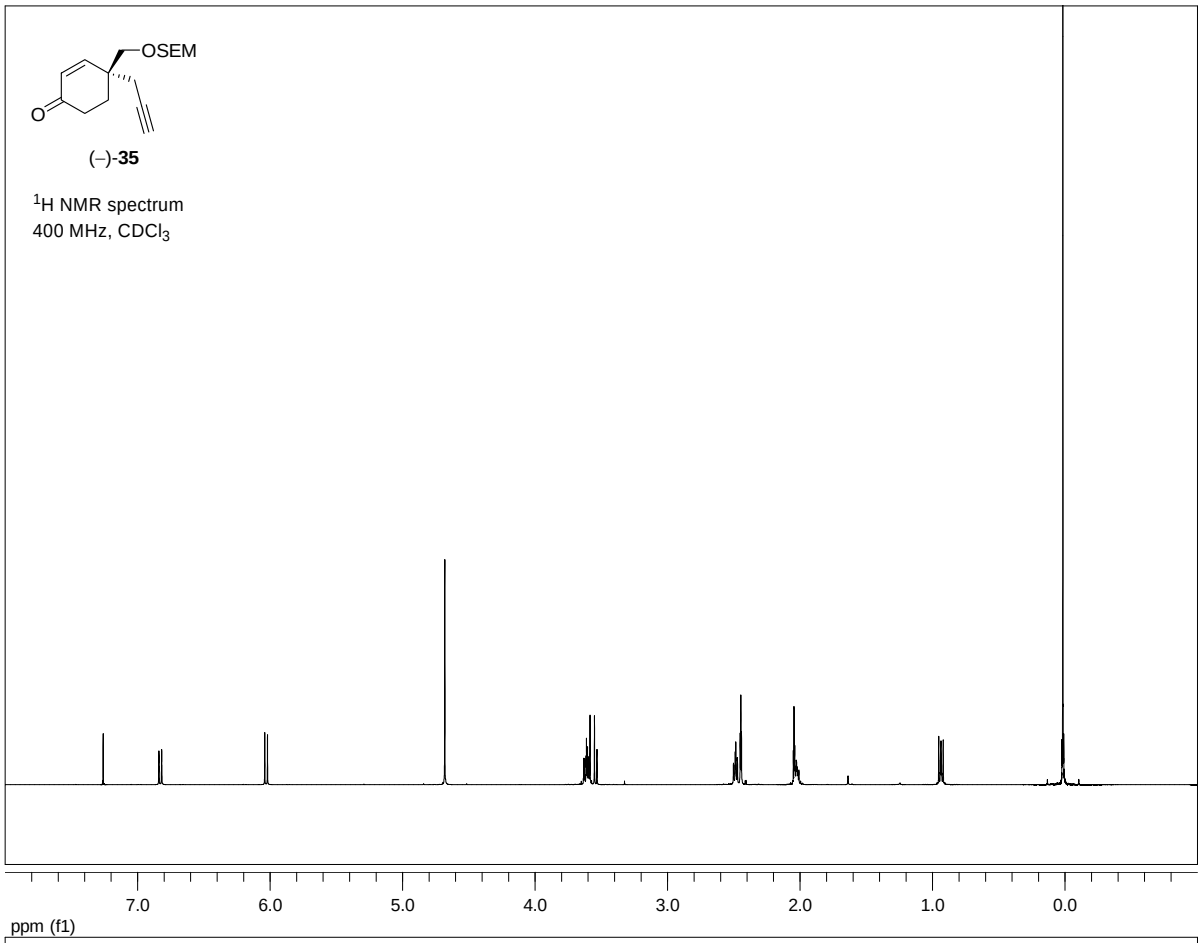

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


OH
O
(–)-16
1H NMR spectrum
500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)


13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


O
Ph
OMe
O
CF3
O
16a
(racemic)
1H NMR spectrum
500 MHz, CDCl3
4.50
4.40
4.30
4.20
ppm (f1)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)

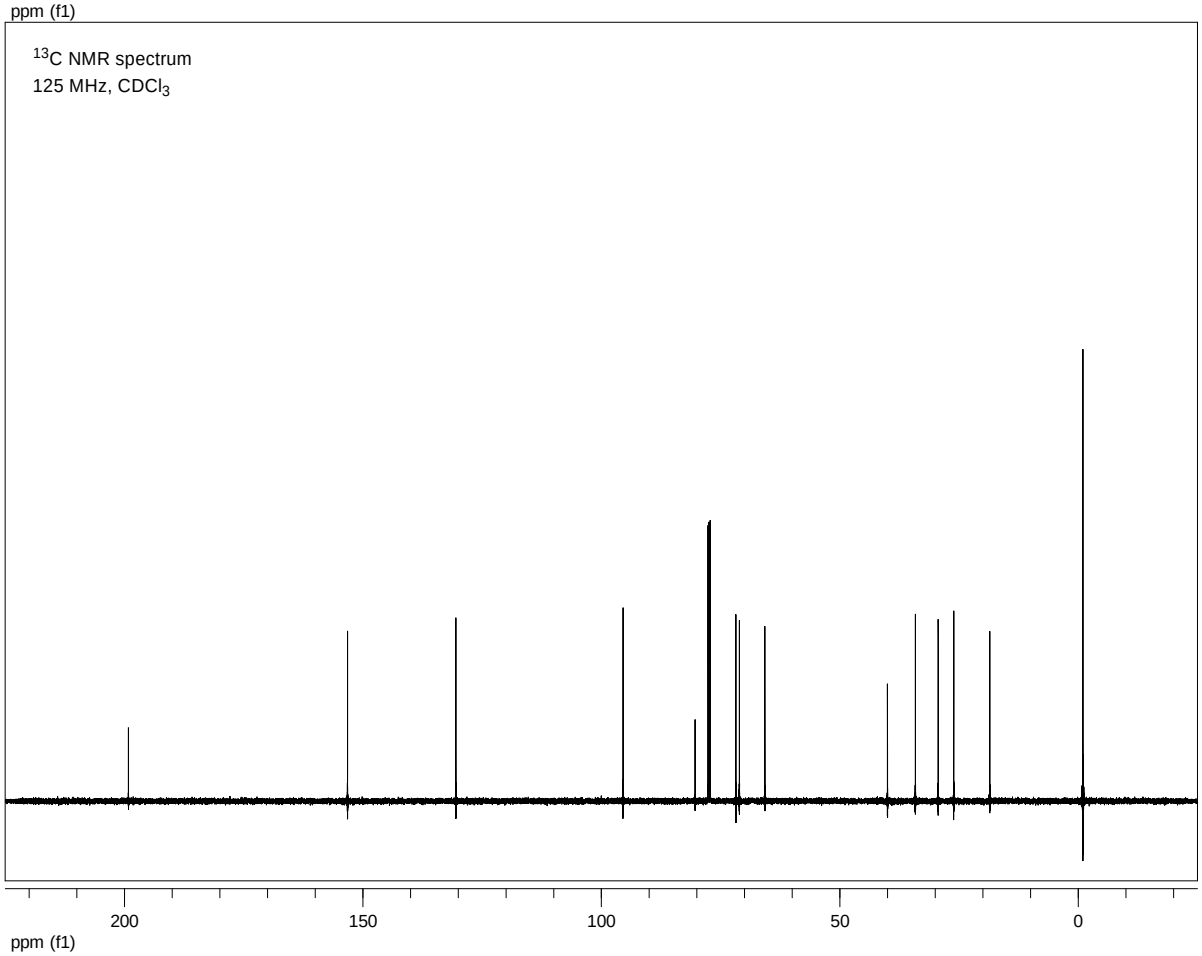

O
Ph
OMe
O
CF3
O
16a
(>98% ee)
1H NMR spectrum
500 MHz, CDCl3
4.50
4.40
4.30
4.20
ppm (f1)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)

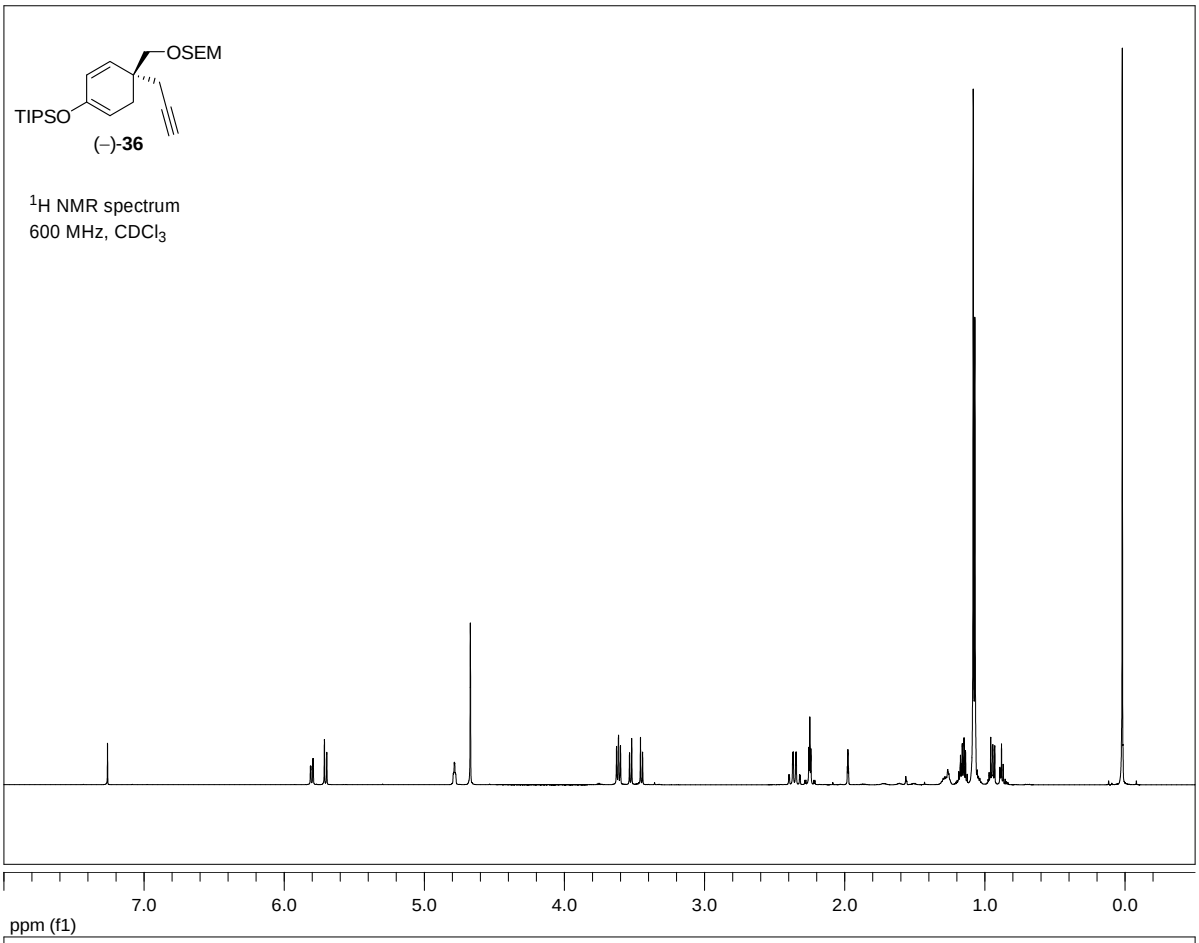


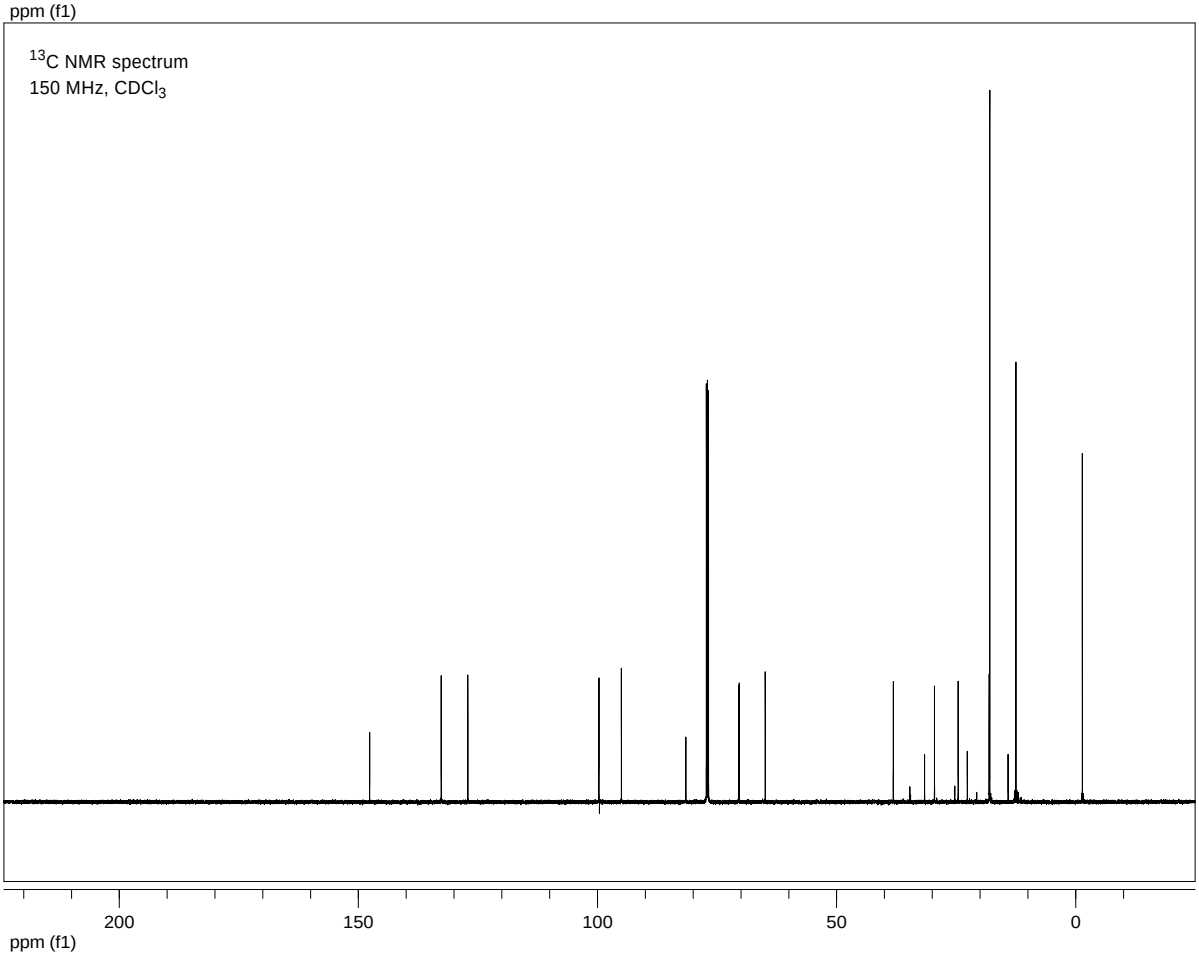
(–)-**35**

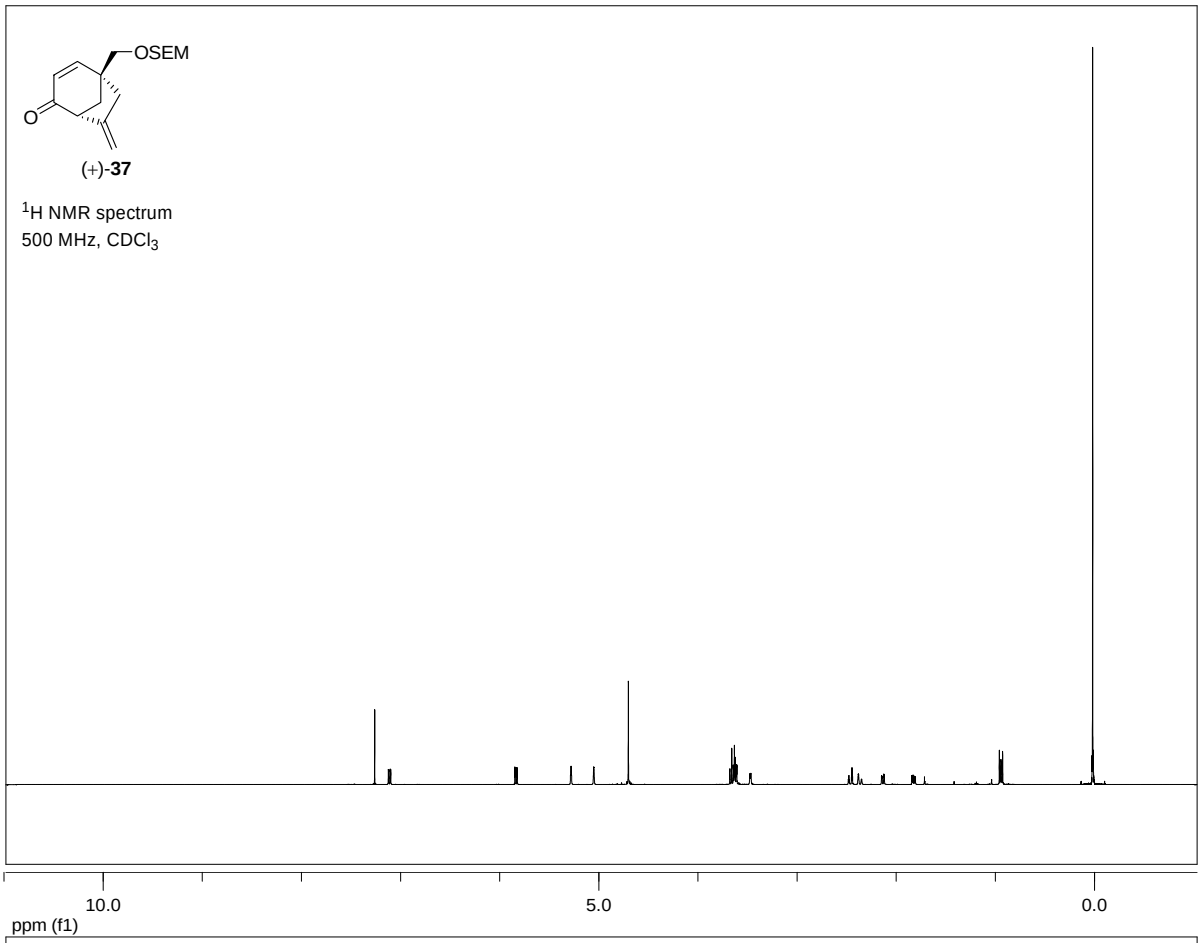
^{1}H NMR spectrum
400 MHz, $CDCl_3$

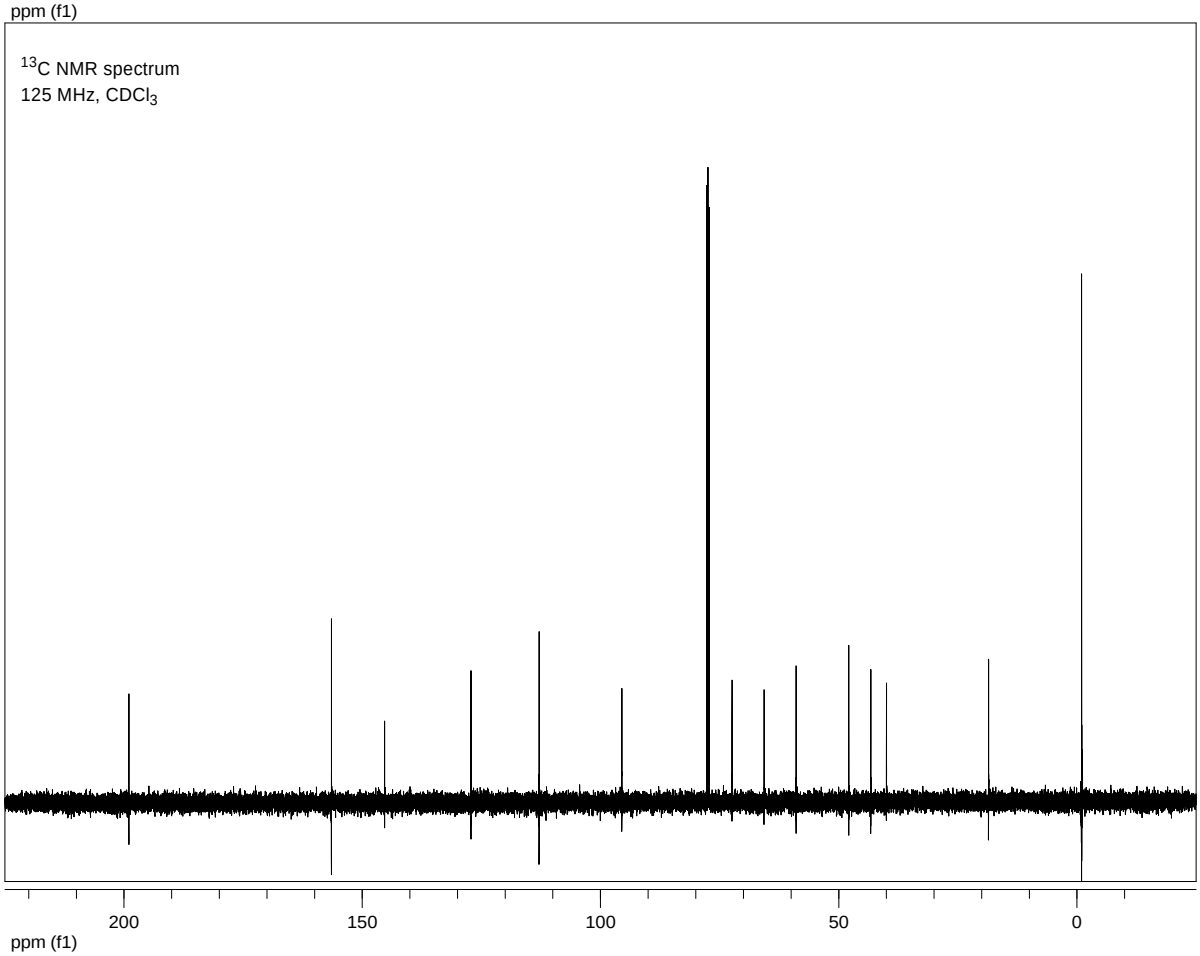
^{13}C NMR spectrum
125 MHz, $CDCl_3$

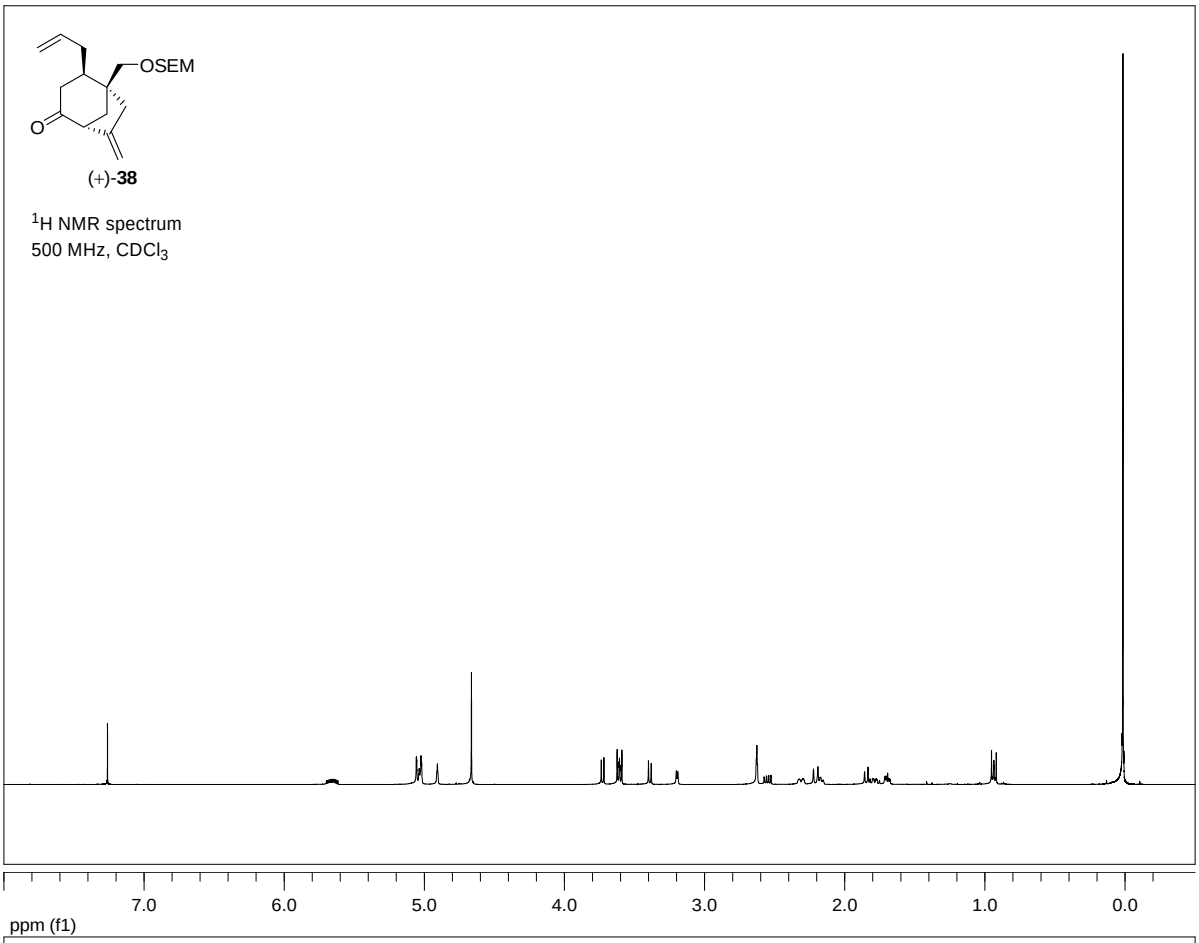


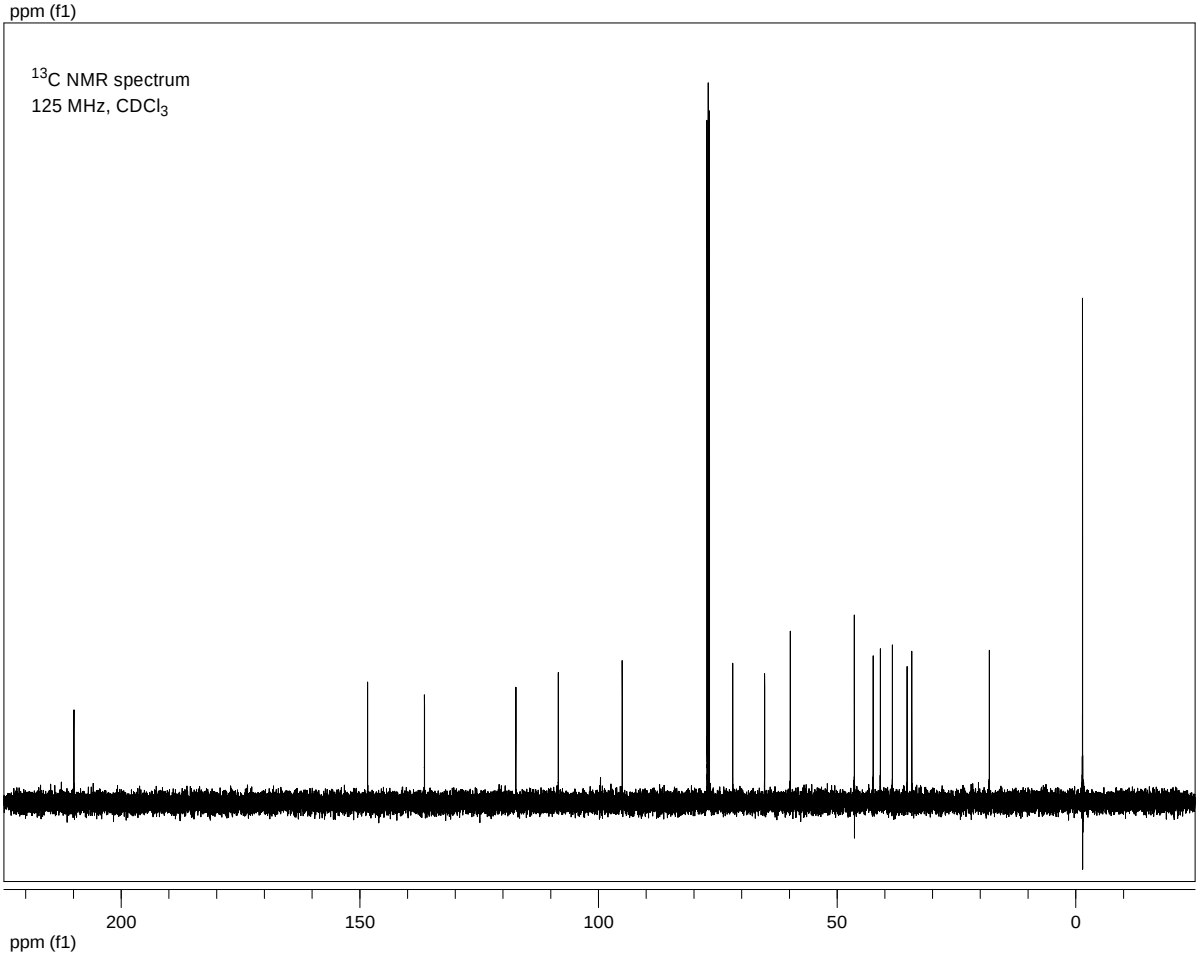

OSEM
TIPSO
(–)-36
1H NMR spectrum
600 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

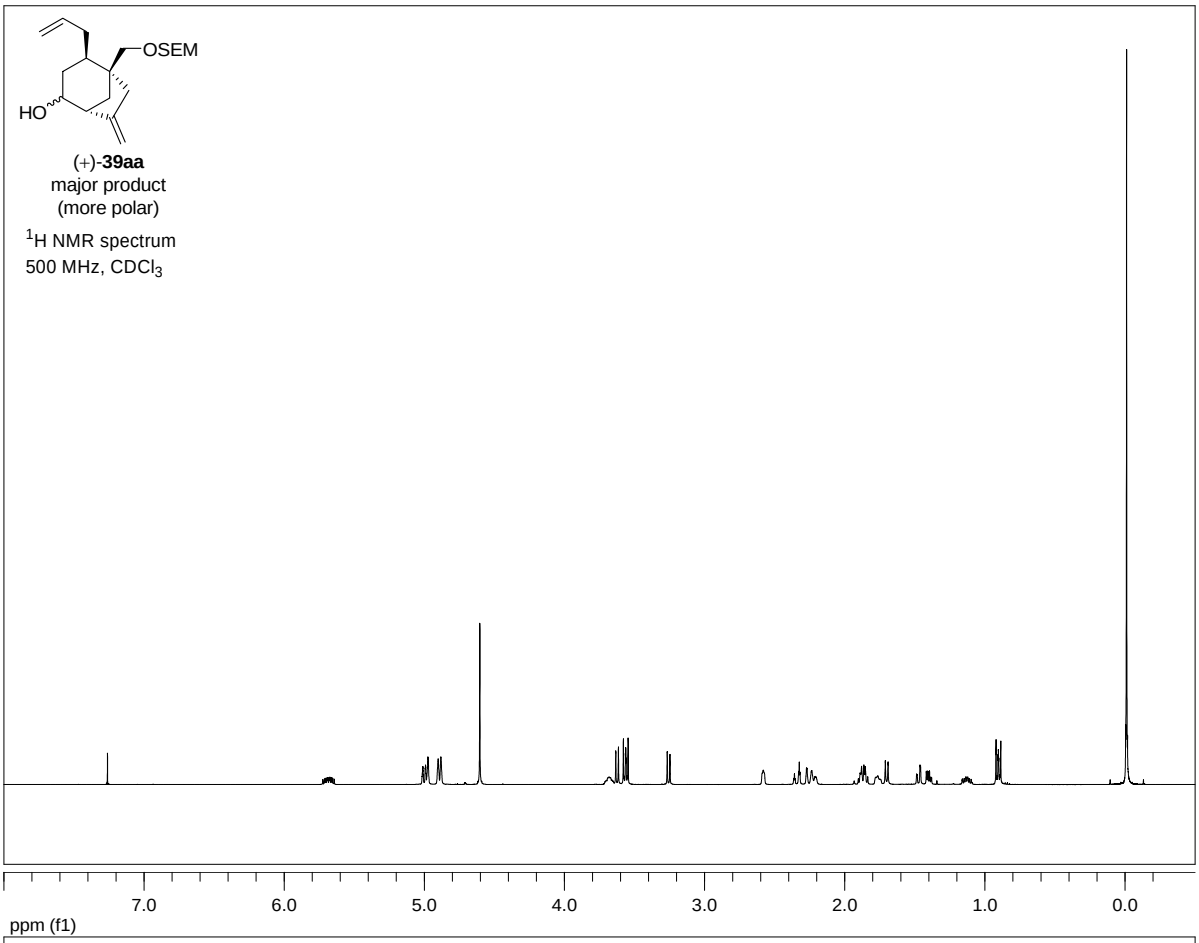

13C NMR spectrum
150 MHz, CDCl3
200
150
100
50
0
ppm (f1)

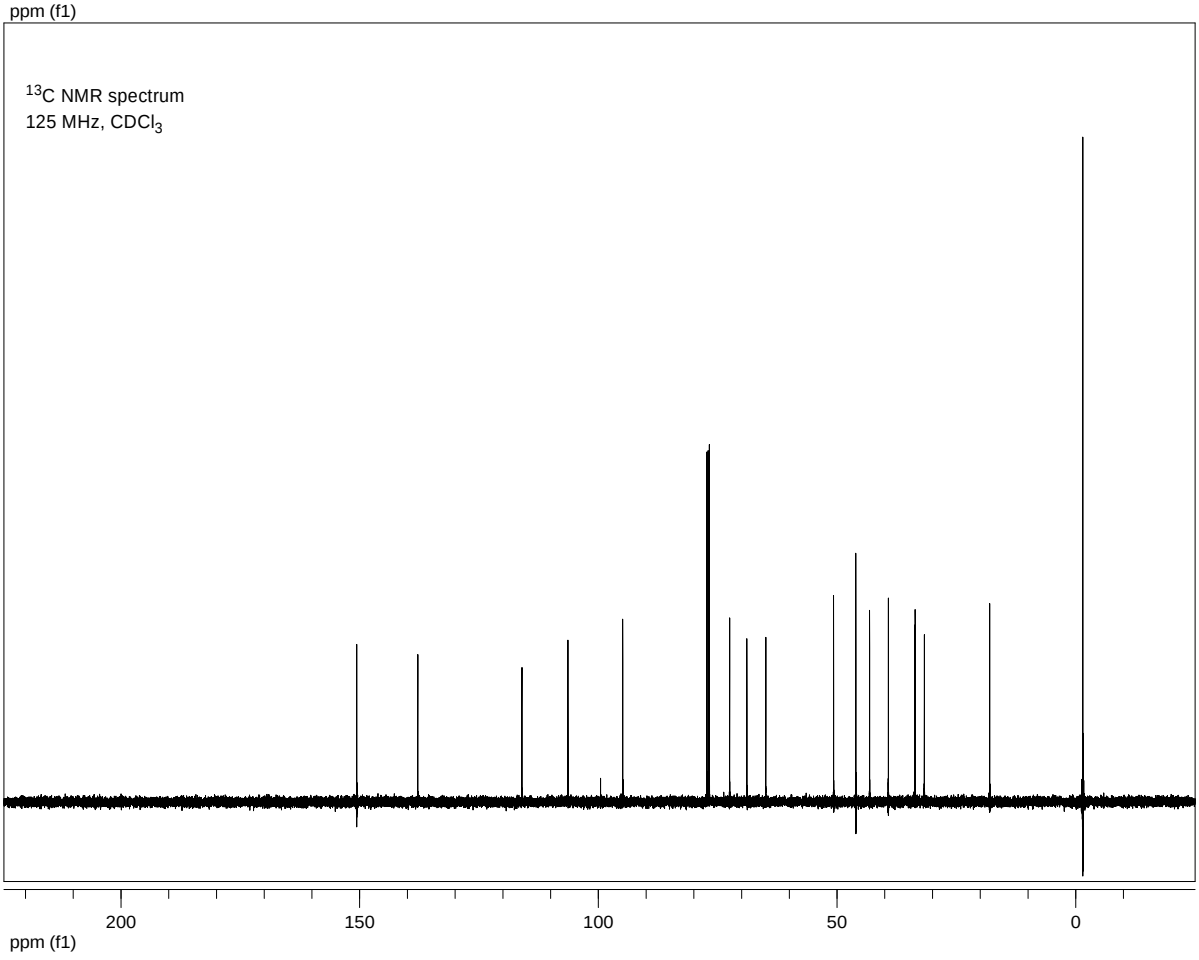

OSEM
O
(+)-37
1H NMR spectrum
500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)

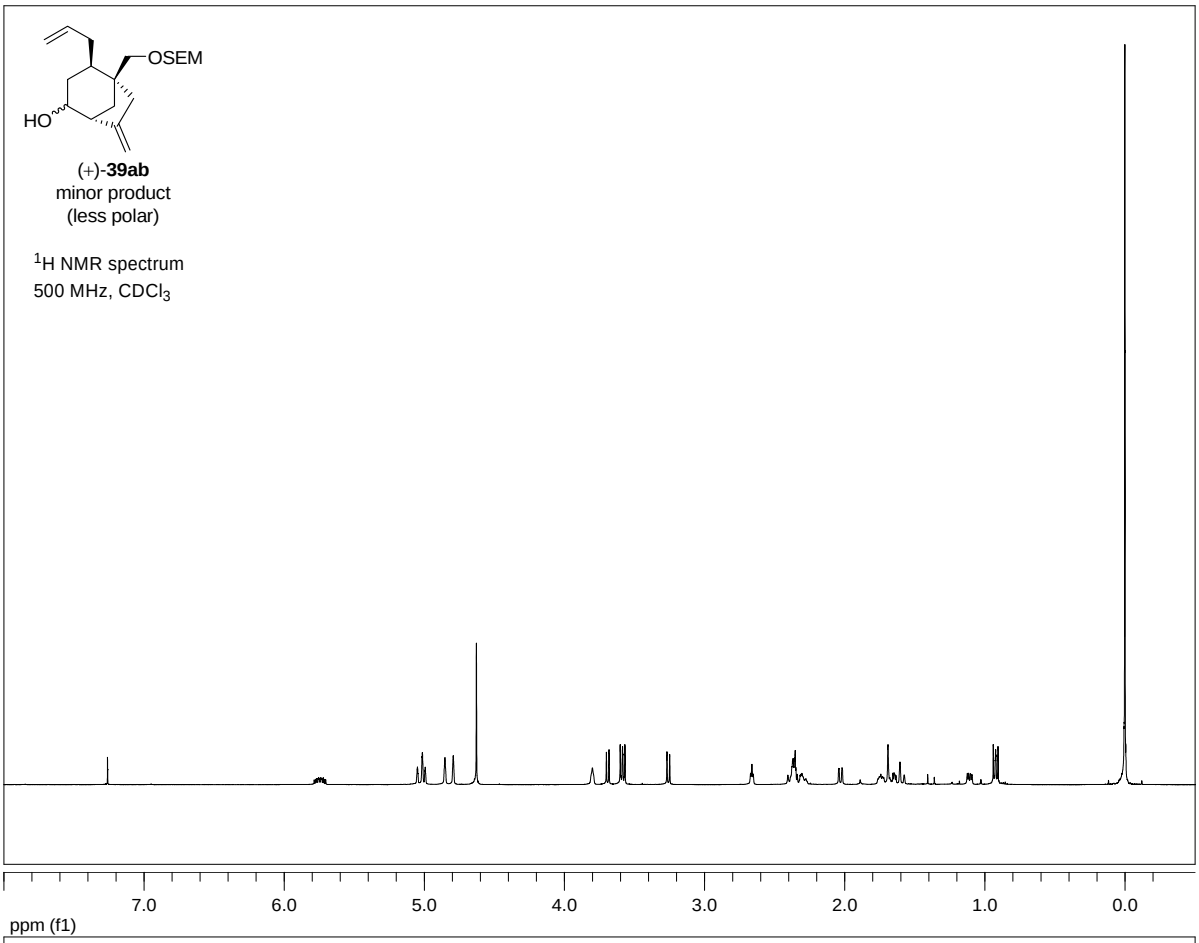

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

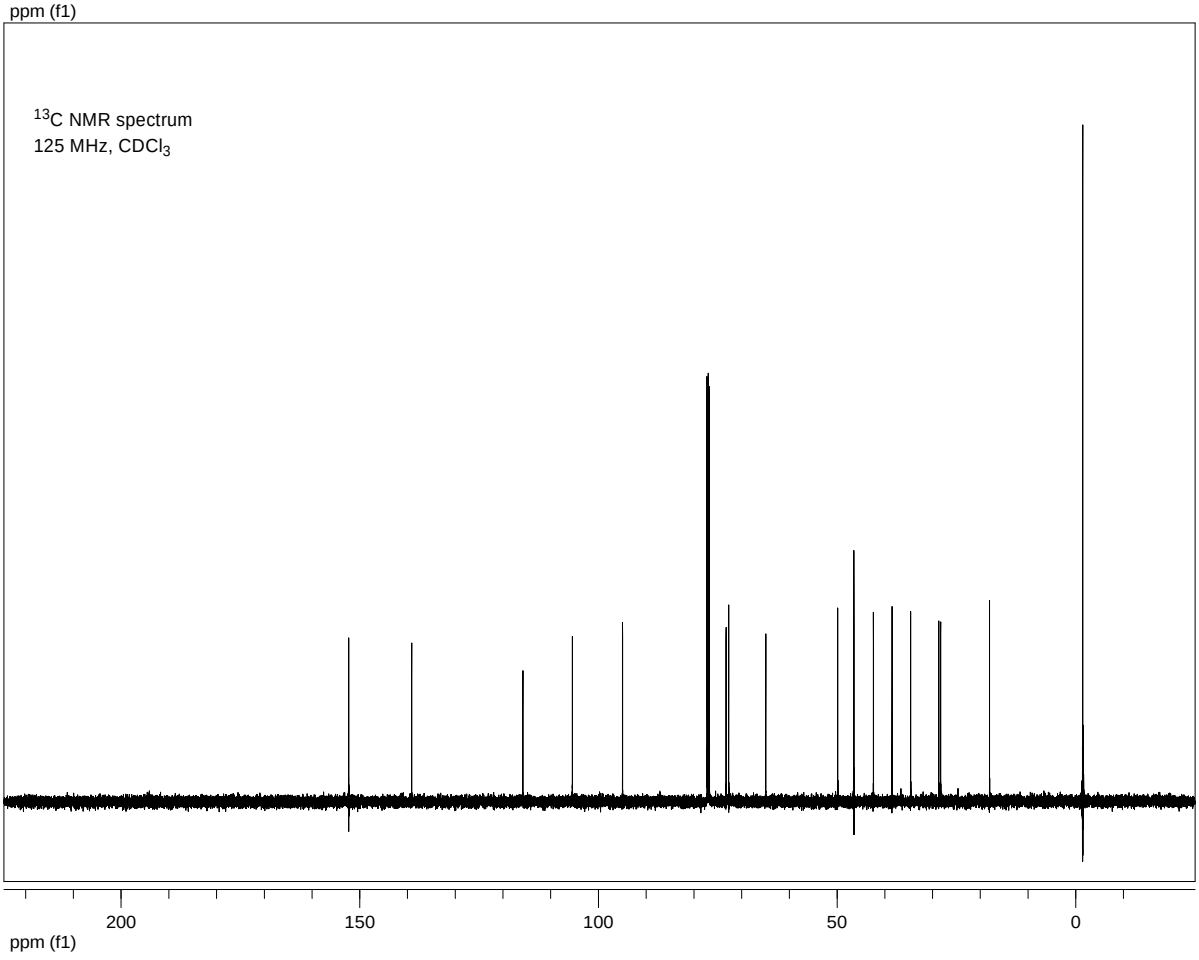

OSEM
O
(+)-38
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

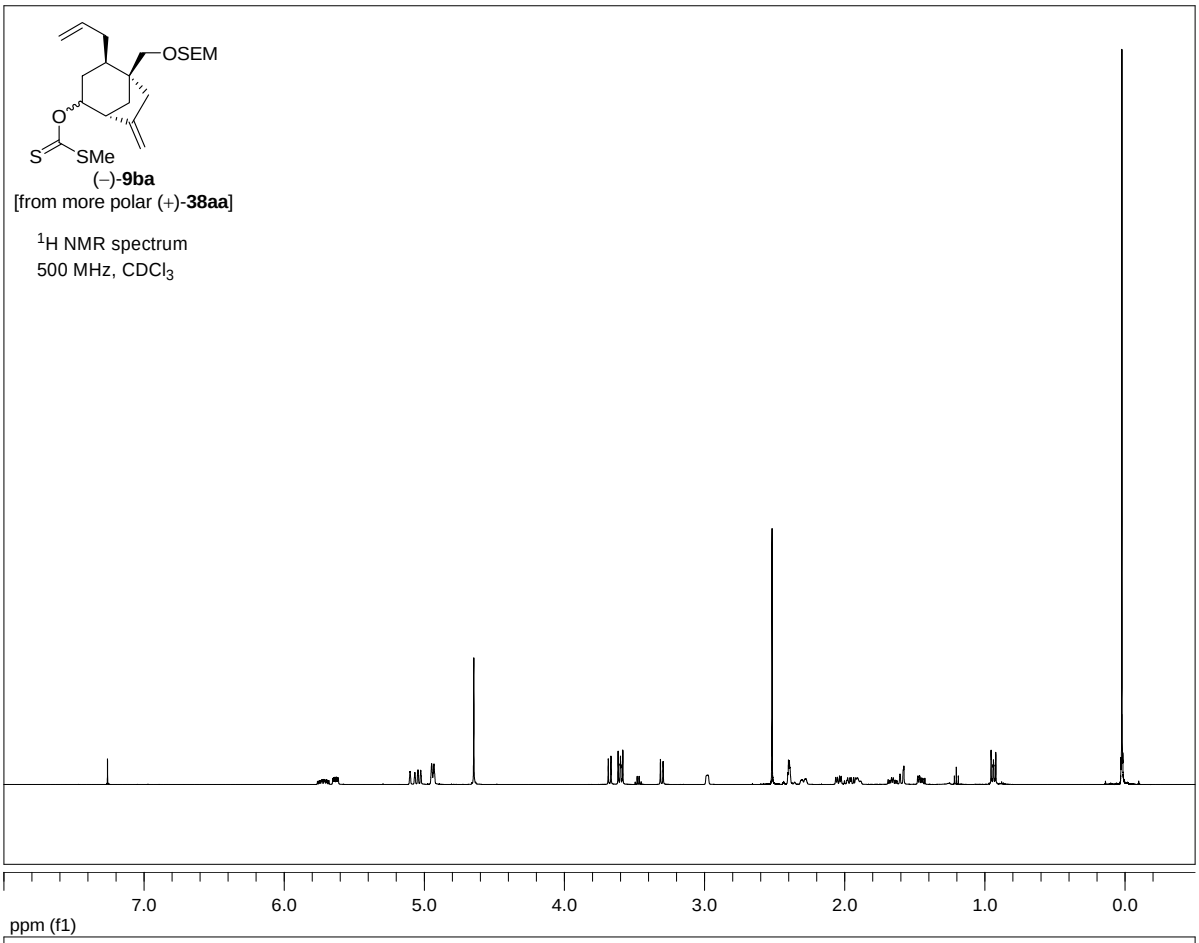

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


OSEM
HO
(+)-39aa
major product
(more polar)
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


OSEM
HO
(+)-39ab
minor product
(less polar)
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

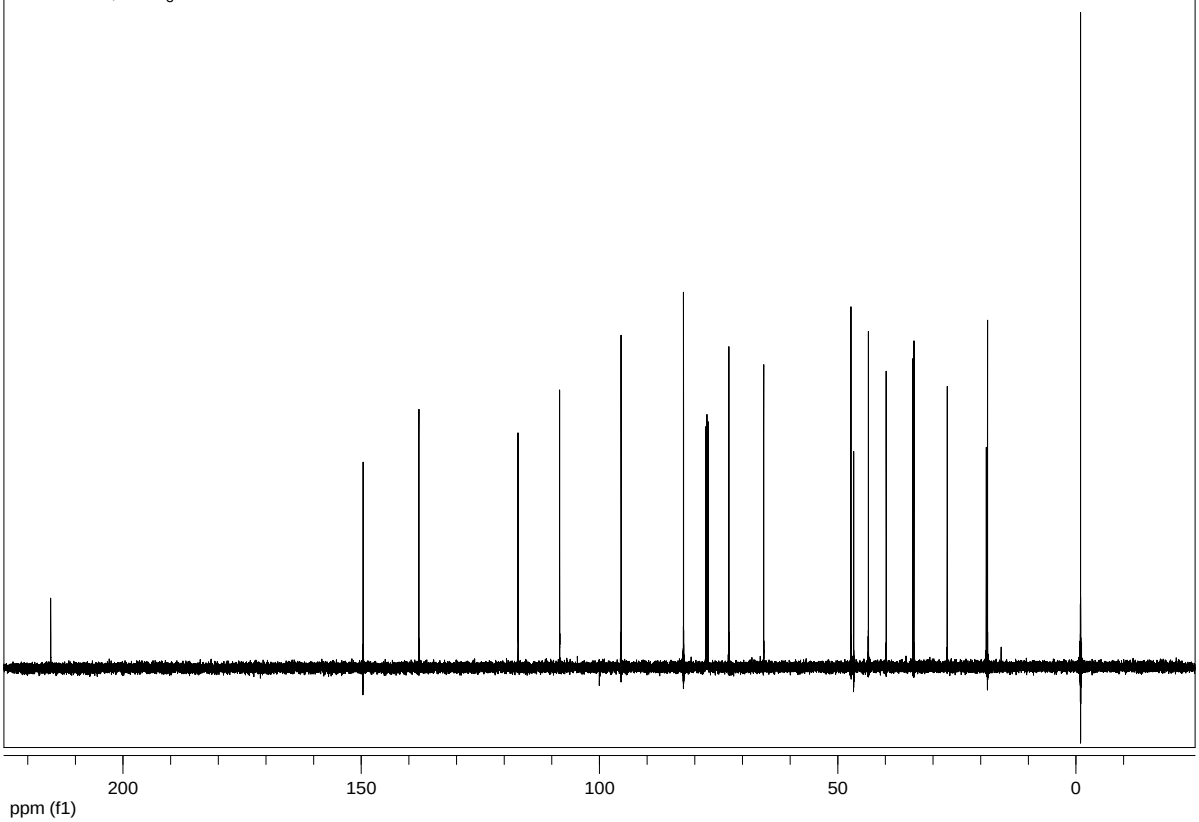

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

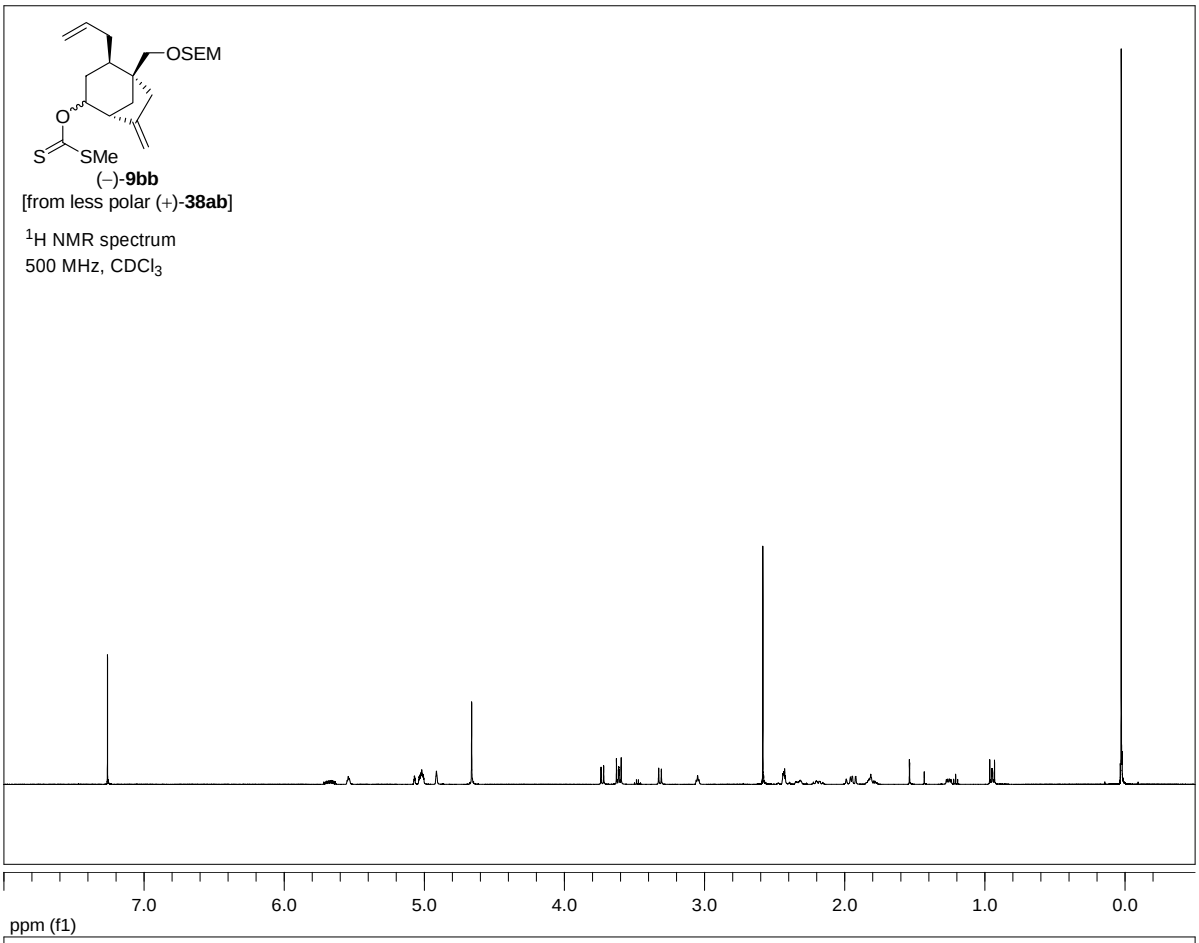


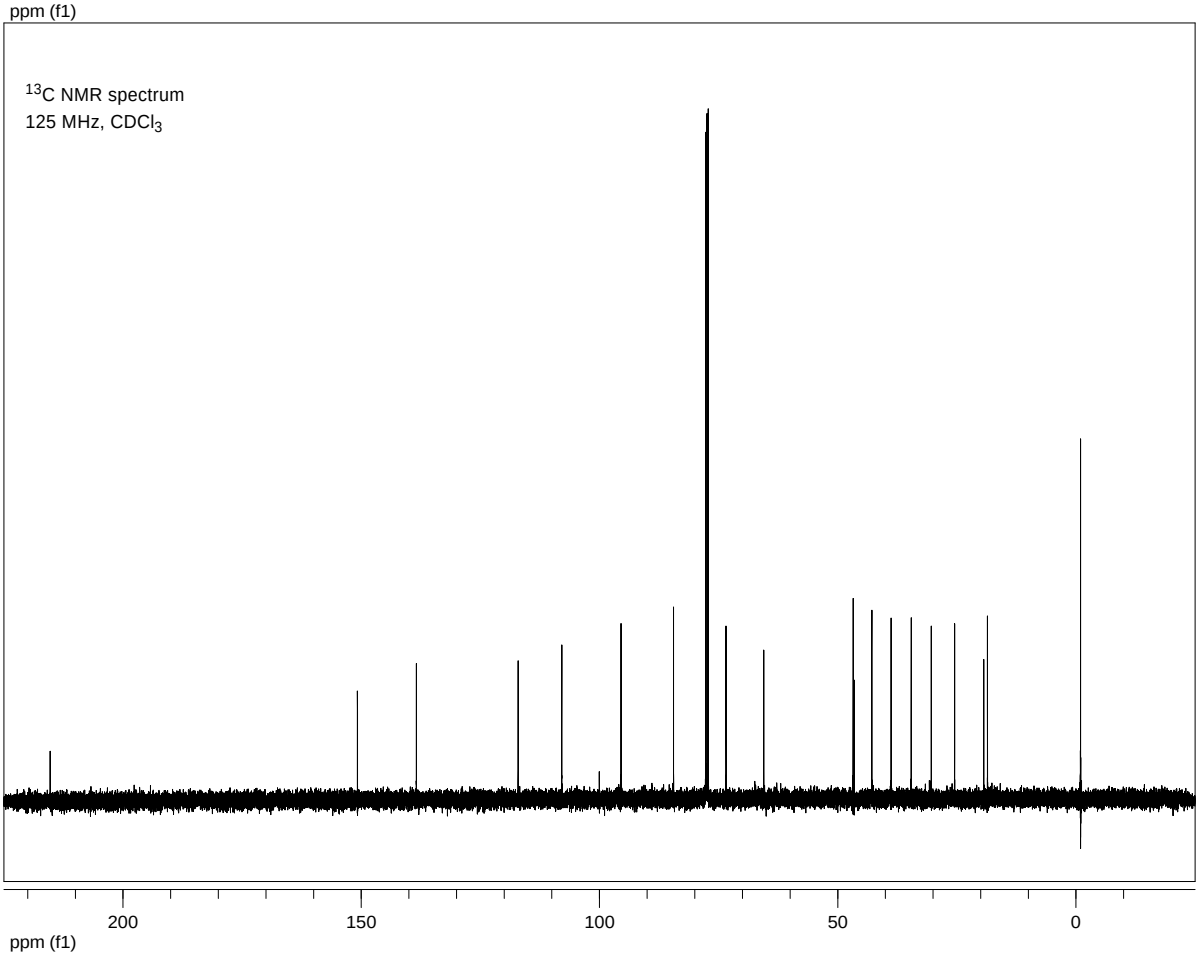
(–)-**9ba**
[from more polar (+)-**38aa**]

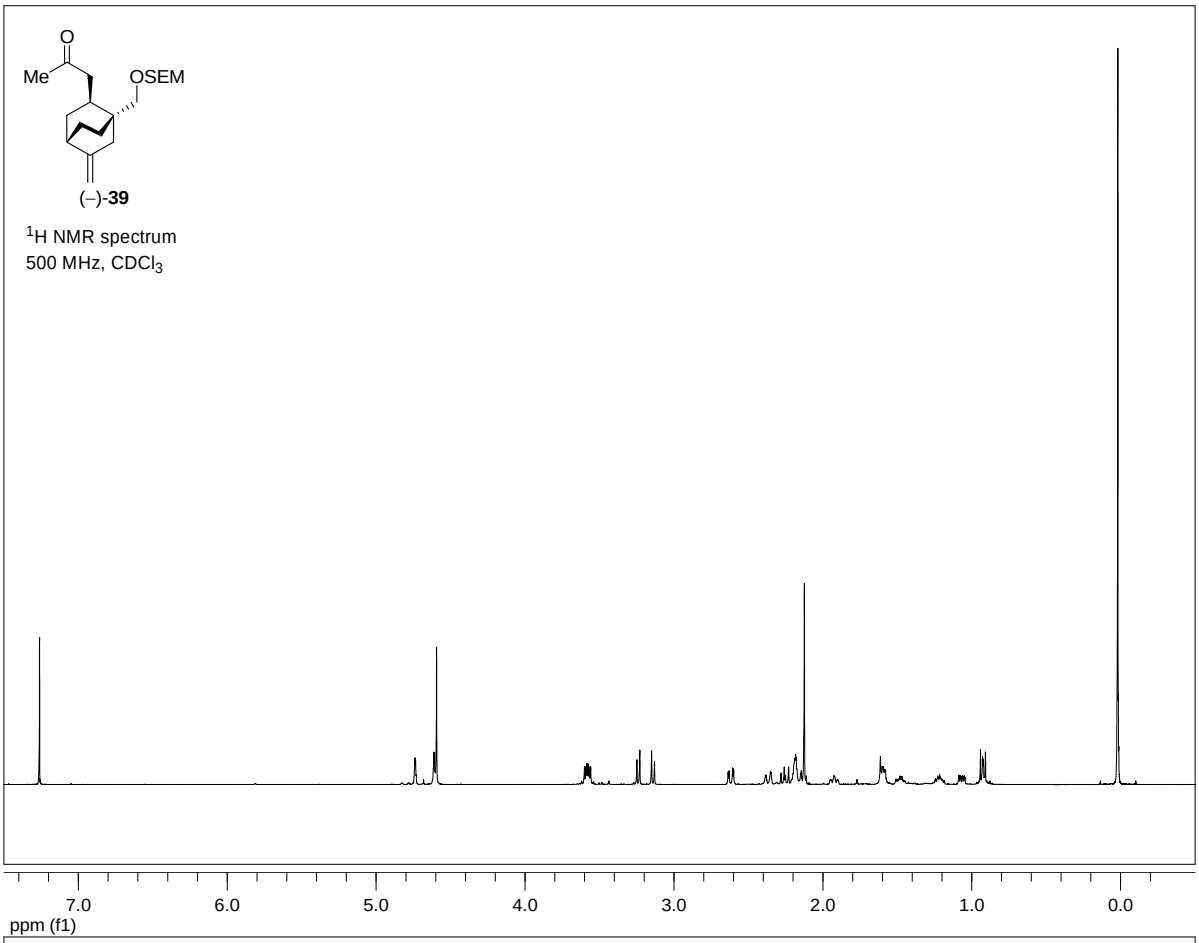
^{1}H NMR spectrum
500 MHz, $CDCl_3$

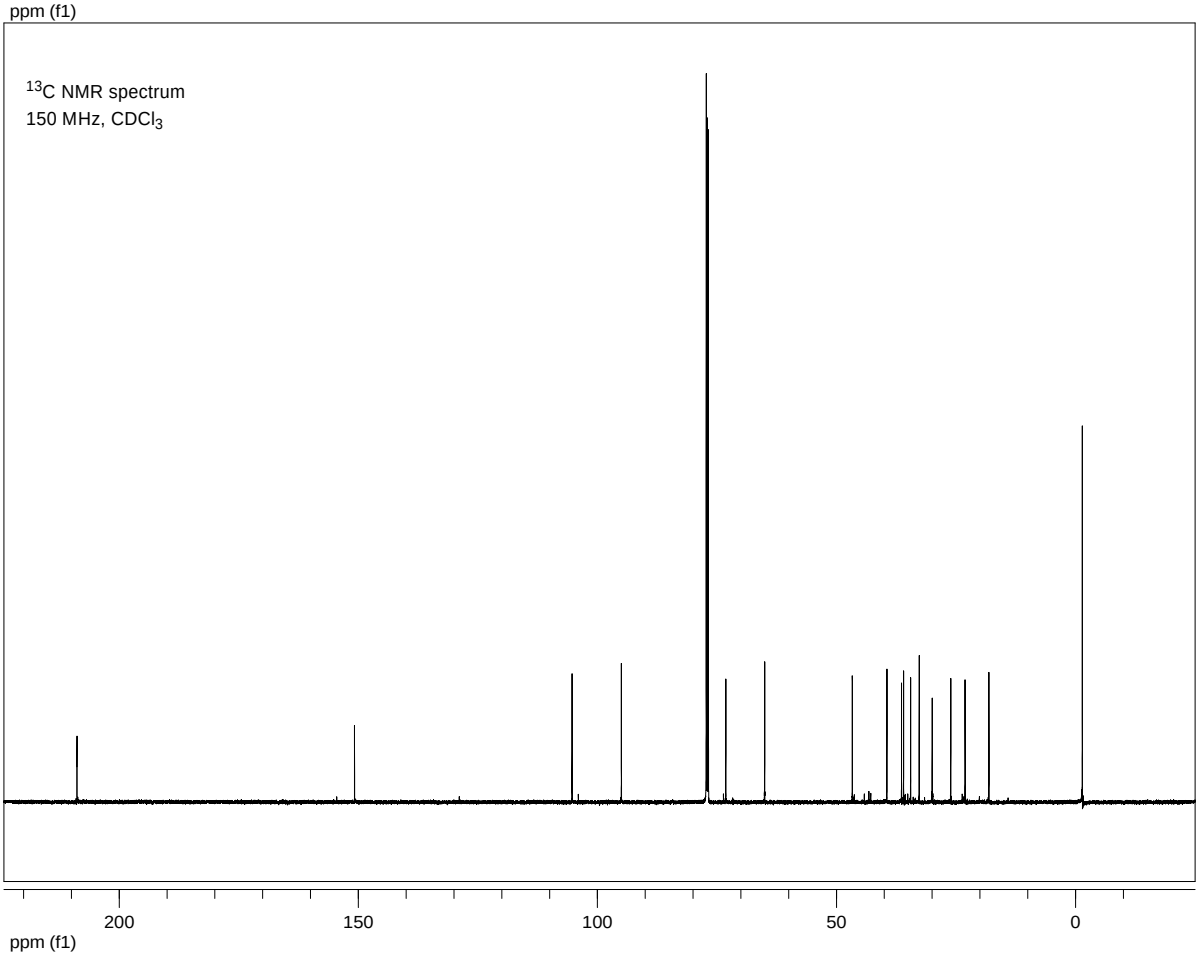
^{13}C NMR spectrum
125 MHz, $CDCl_3$

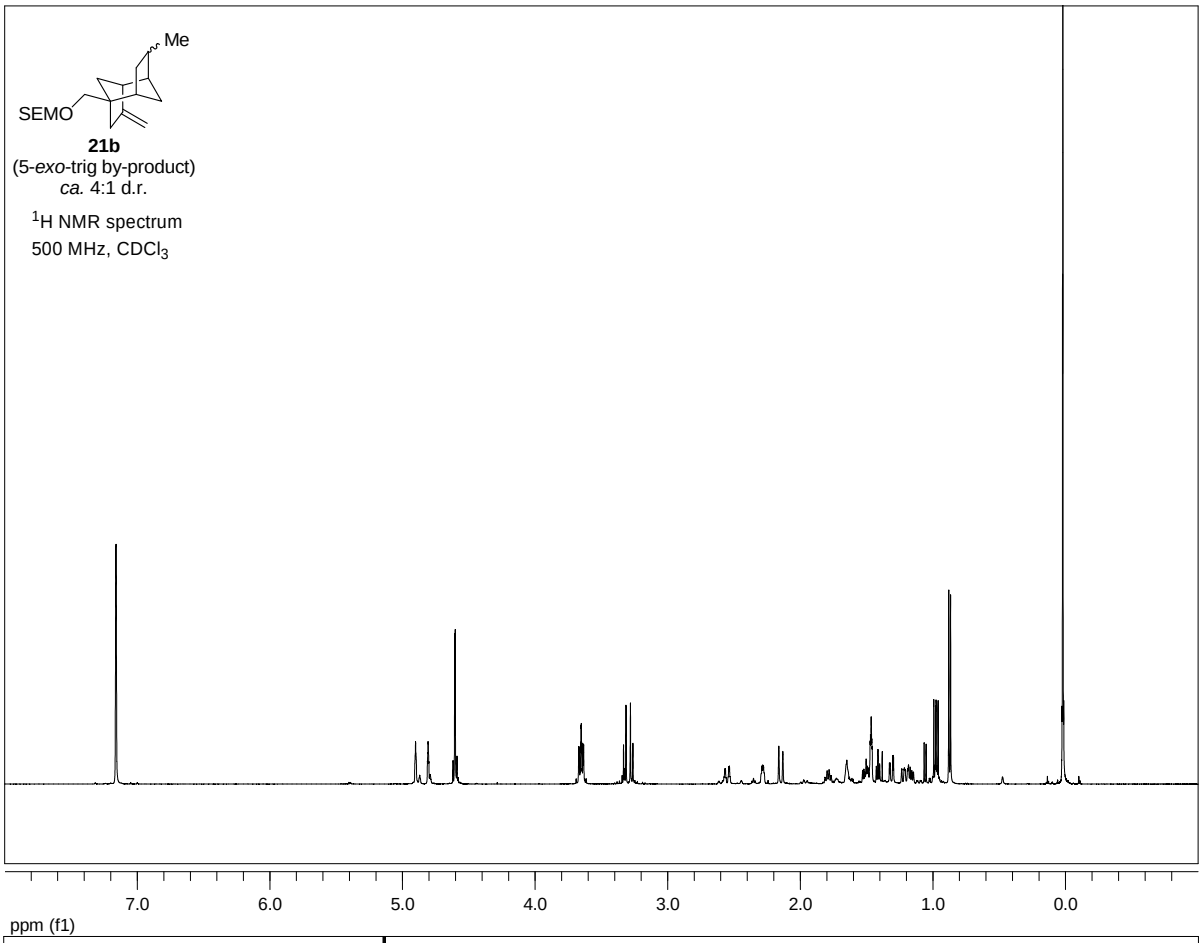


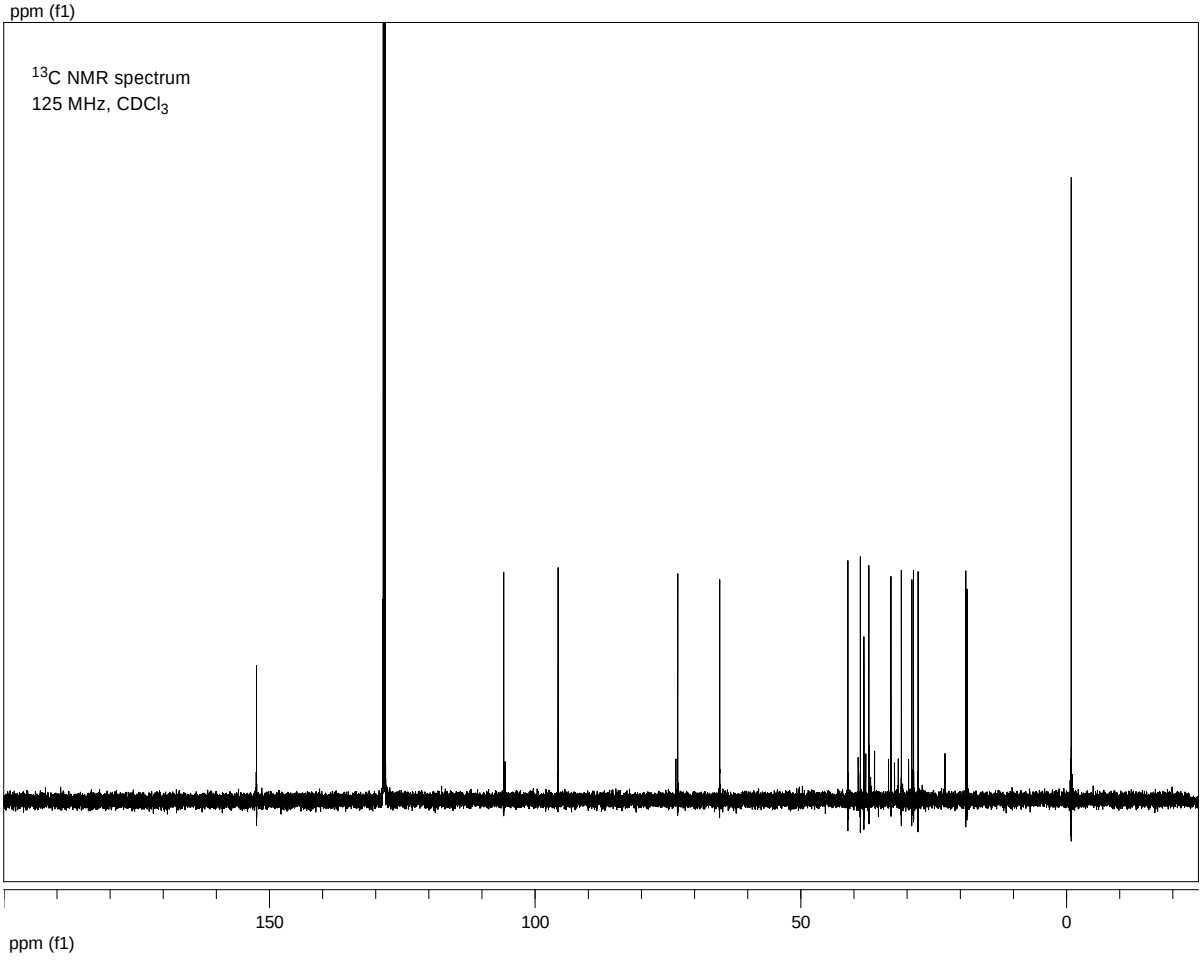

OSEM
O
S
SMe
(–)-9bb
[from less polar (+)-38ab]
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

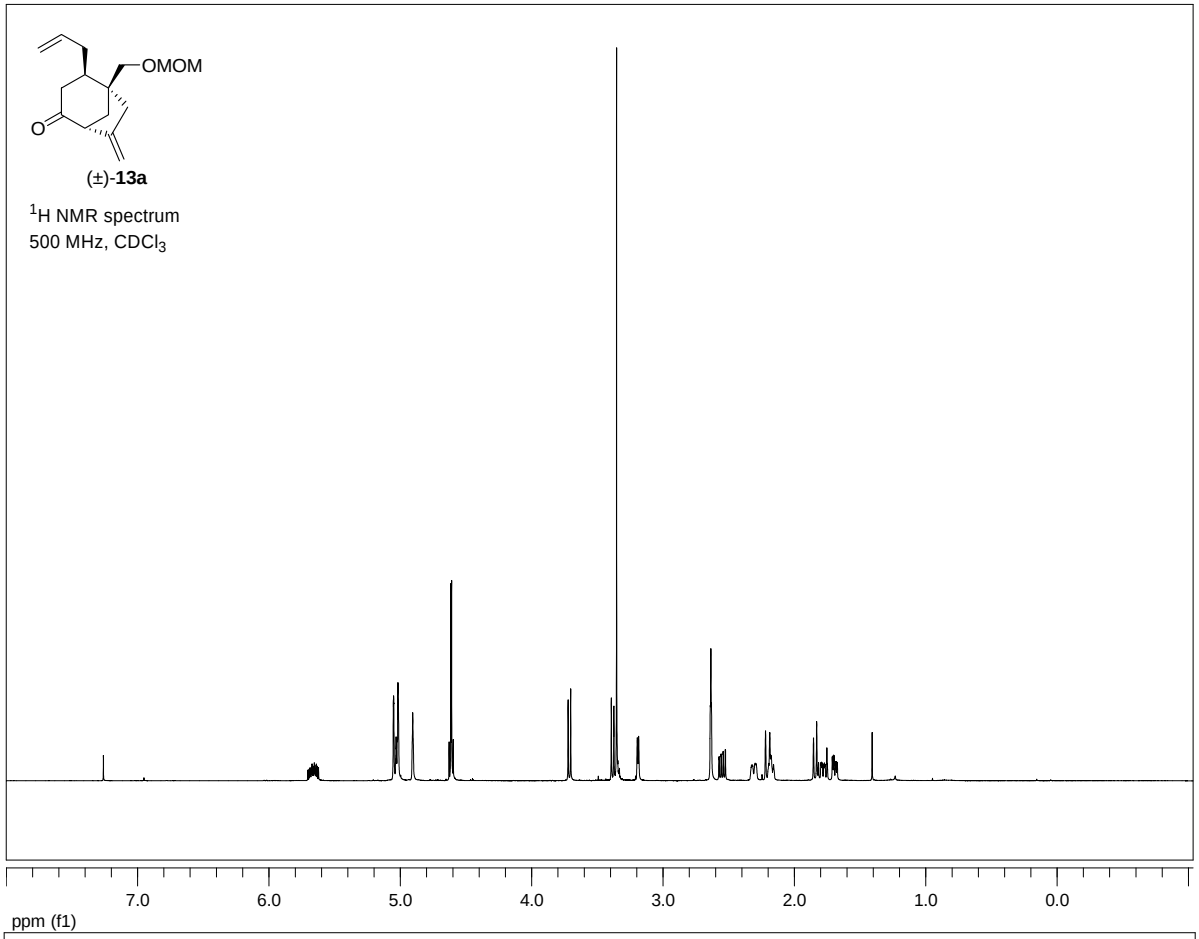

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

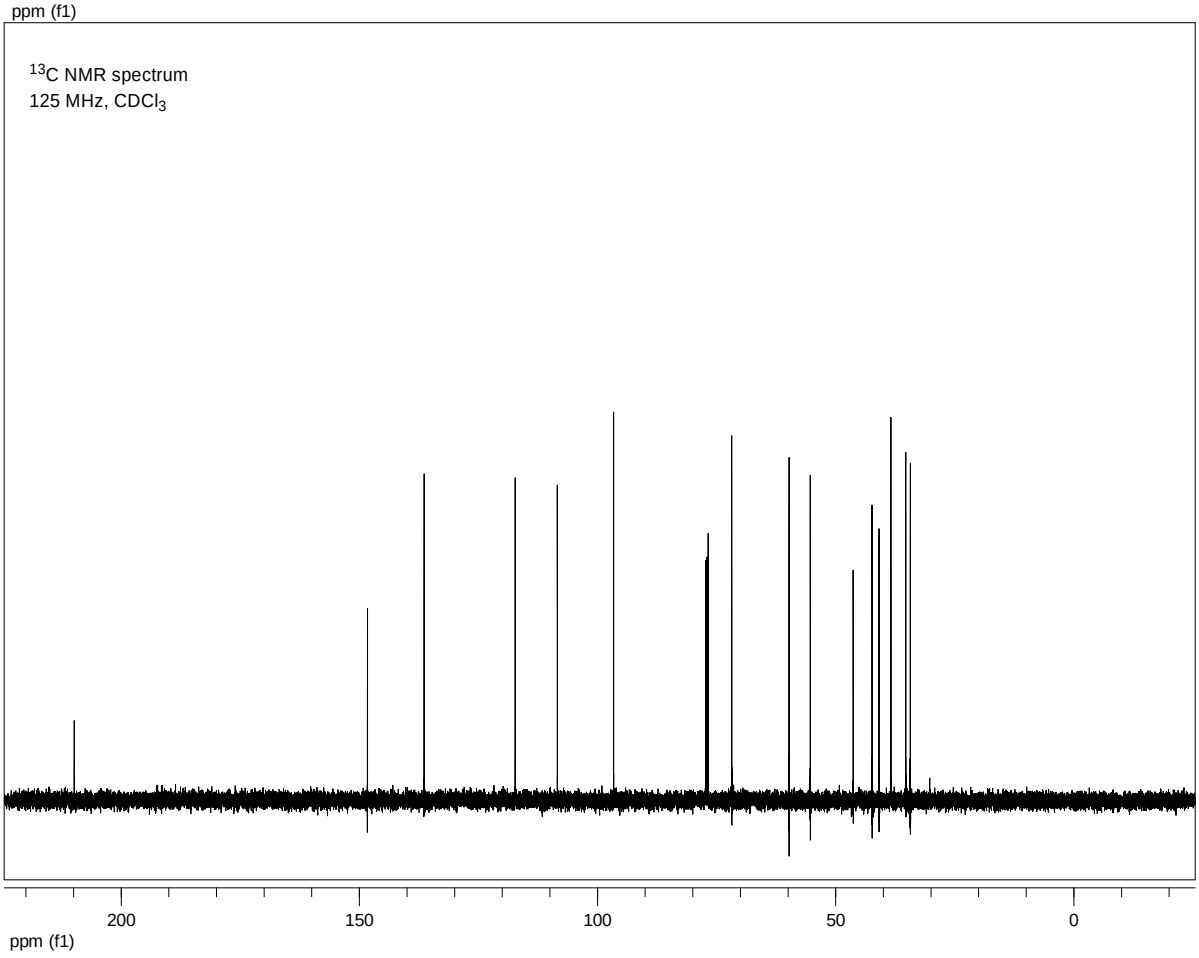

O
Me
OSEM
(–)-39
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

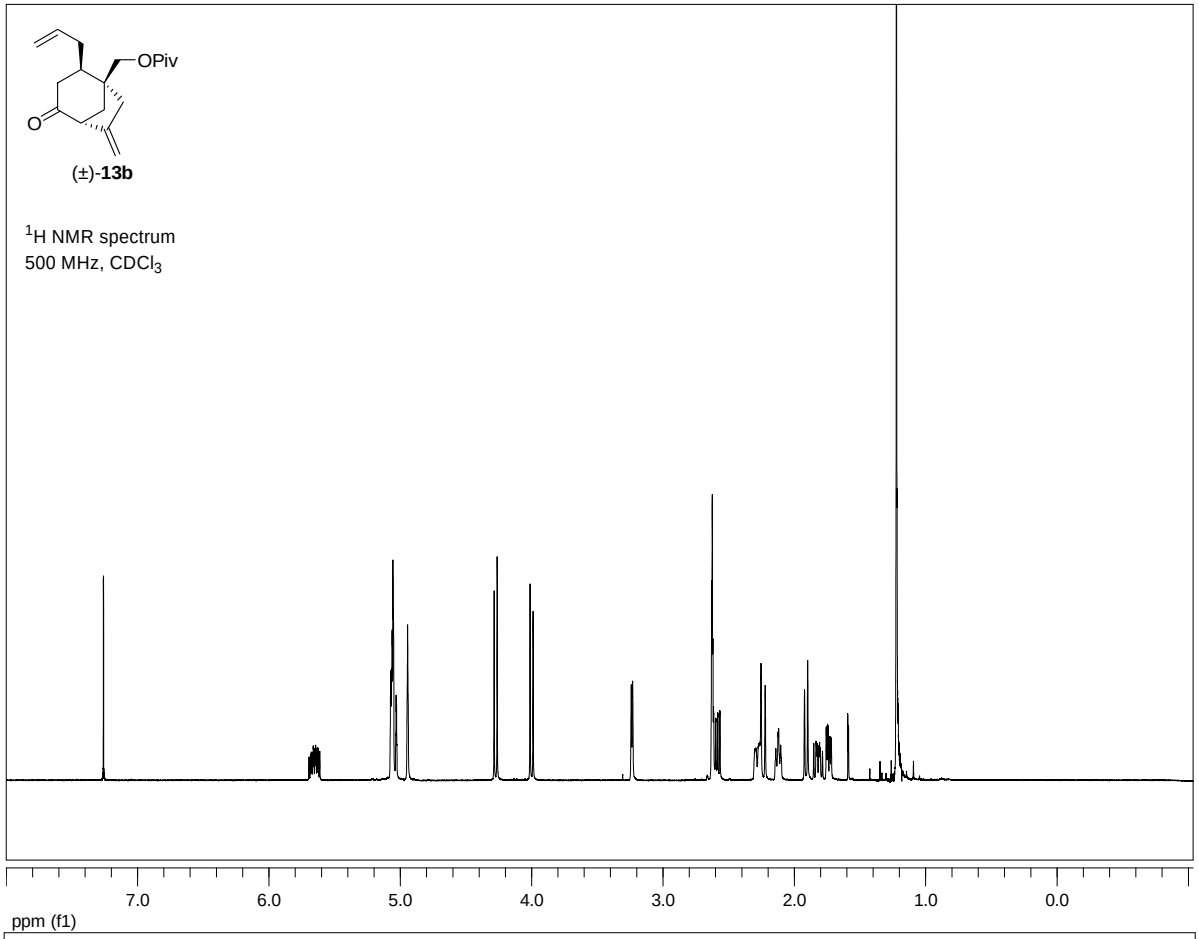

13C NMR spectrum
150 MHz, CDCl3
200
150
100
50
0
ppm (f1)

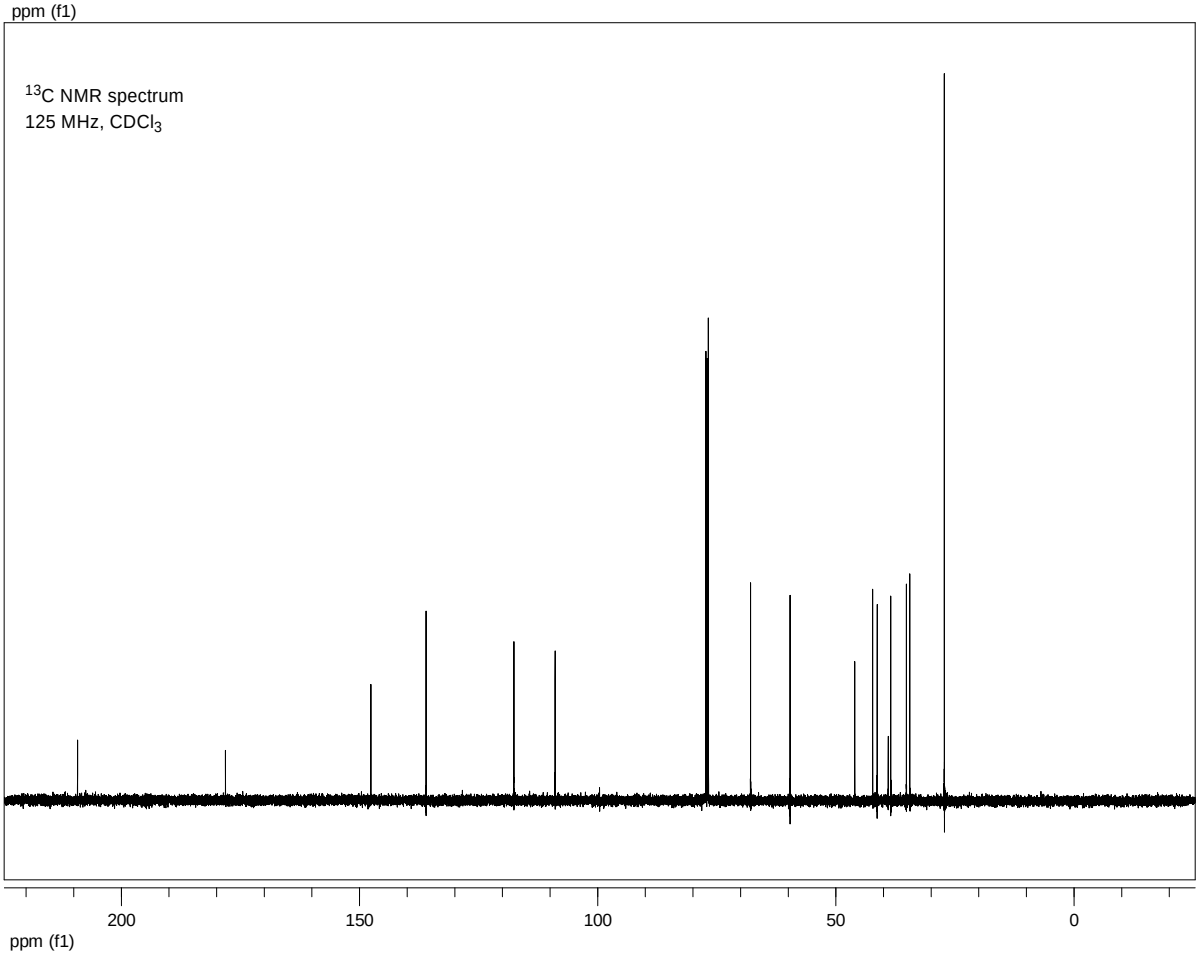

Me
SEMO
21b
(5-exo-trig by-product)
ca. 4:1 d.r.
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

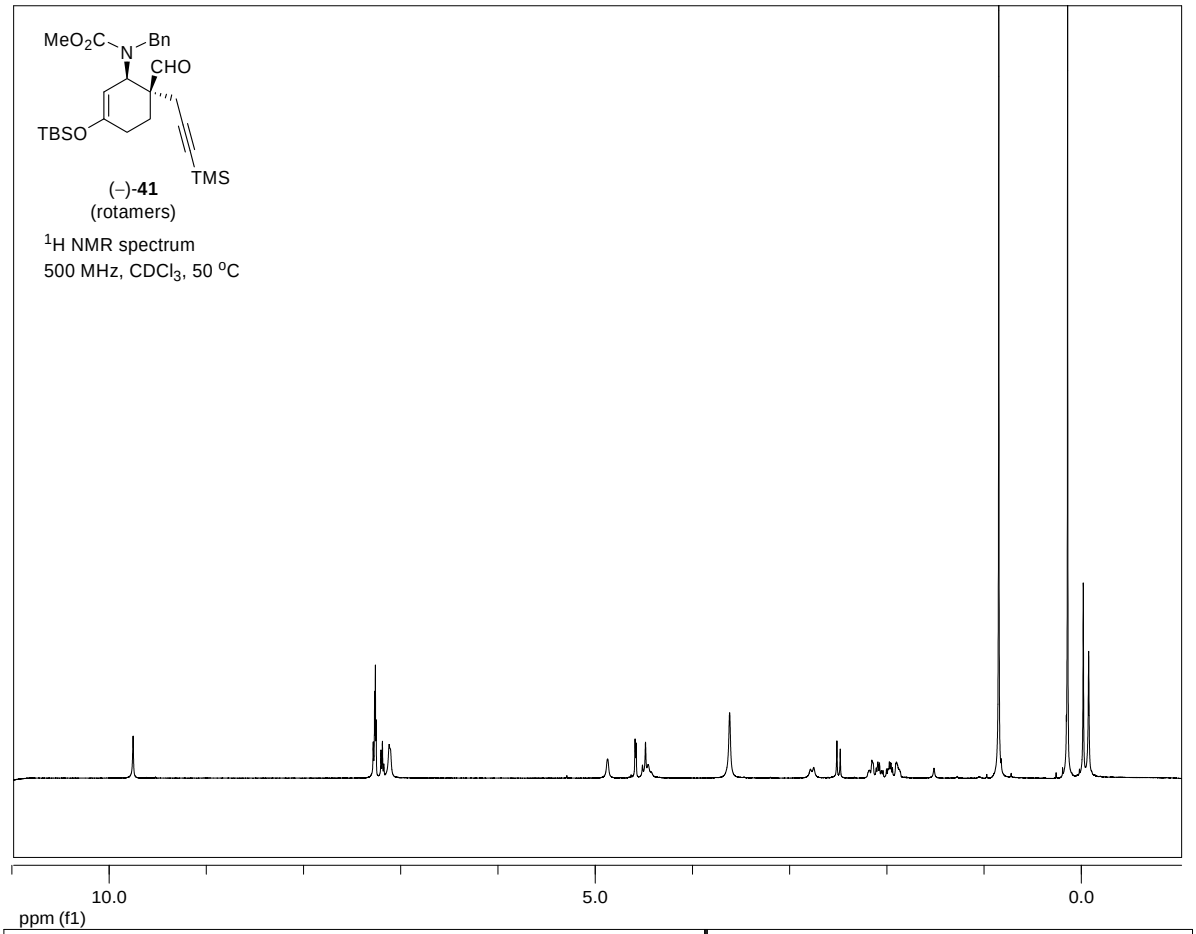

13C NMR spectrum
125 MHz, CDCl3
150
100
50
0
ppm (f1)

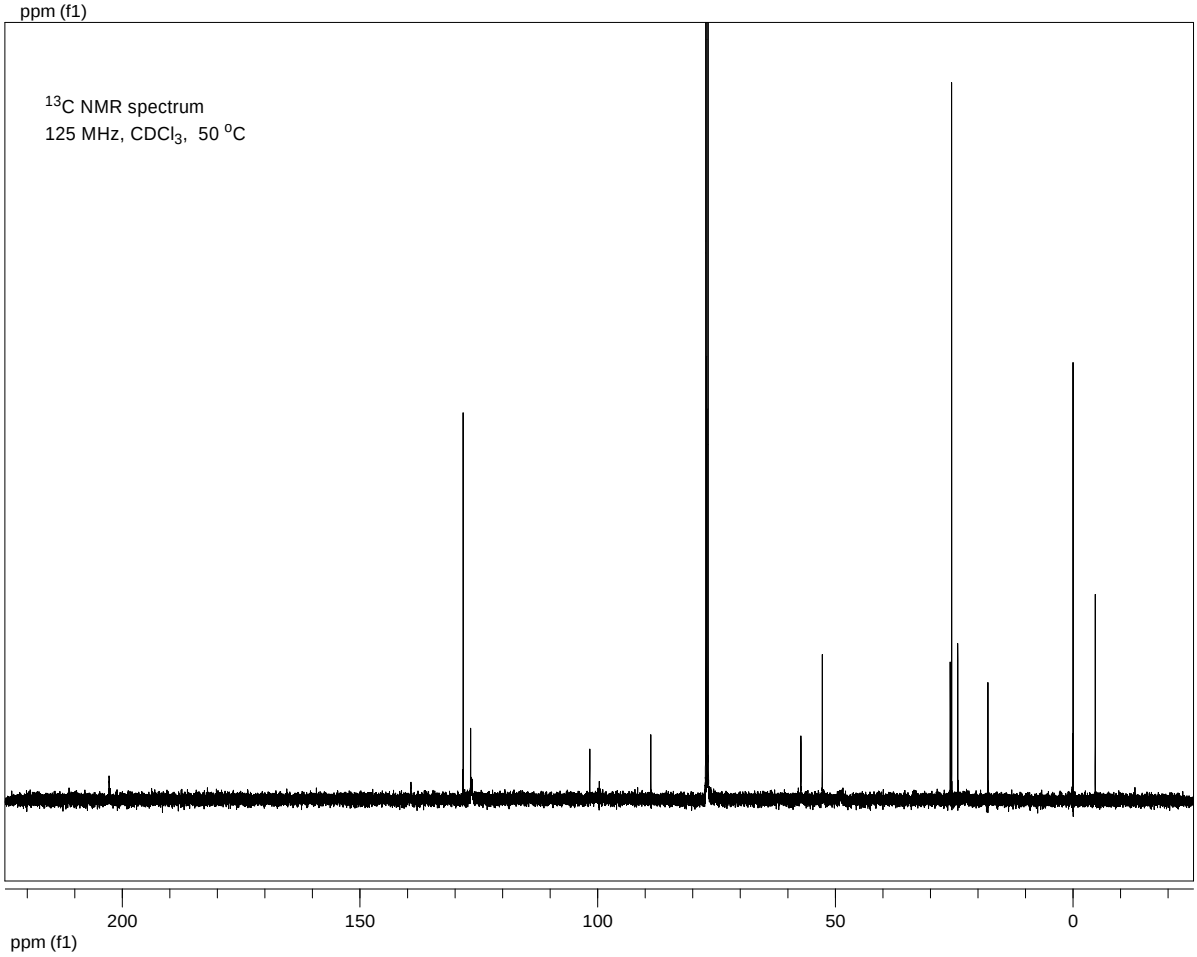

OMOM
O
(±)-13a
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

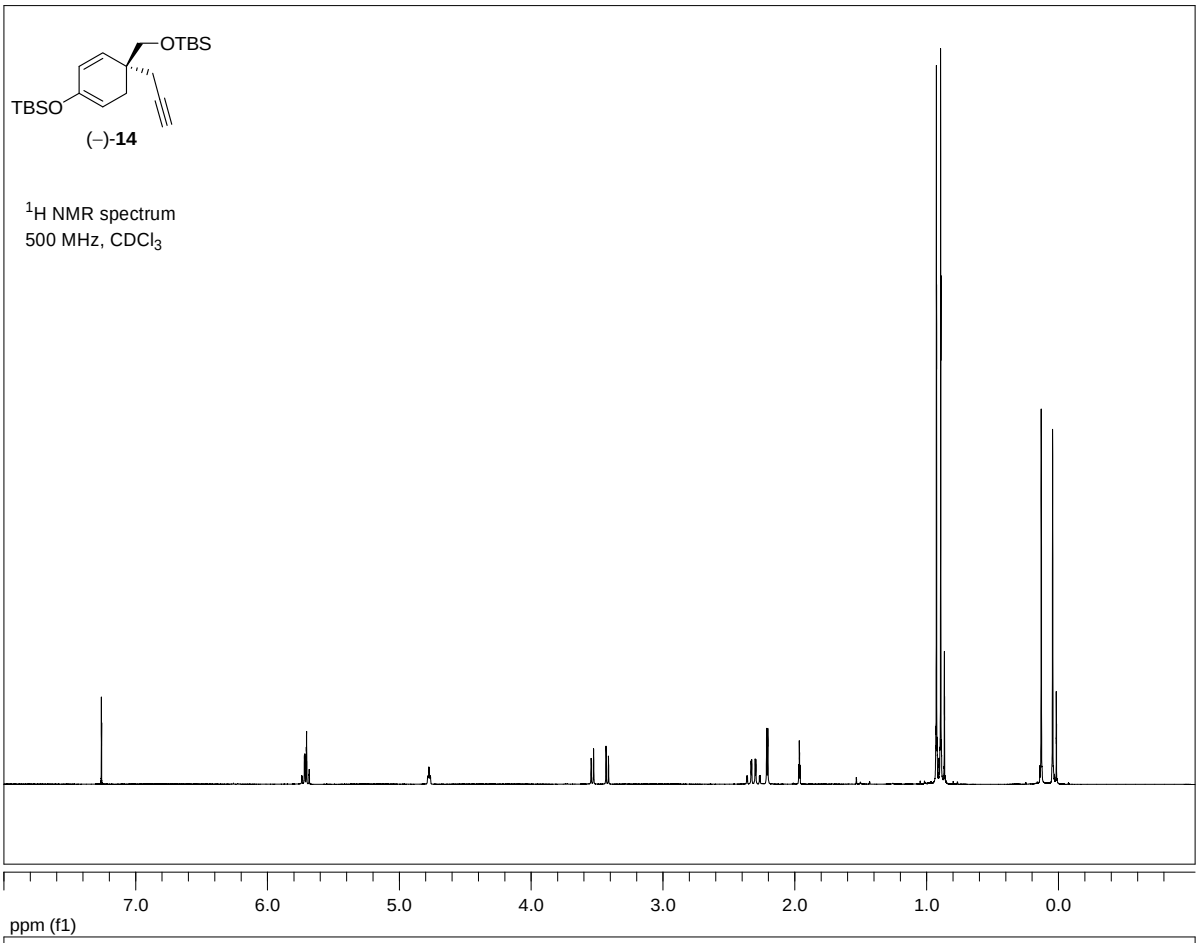

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

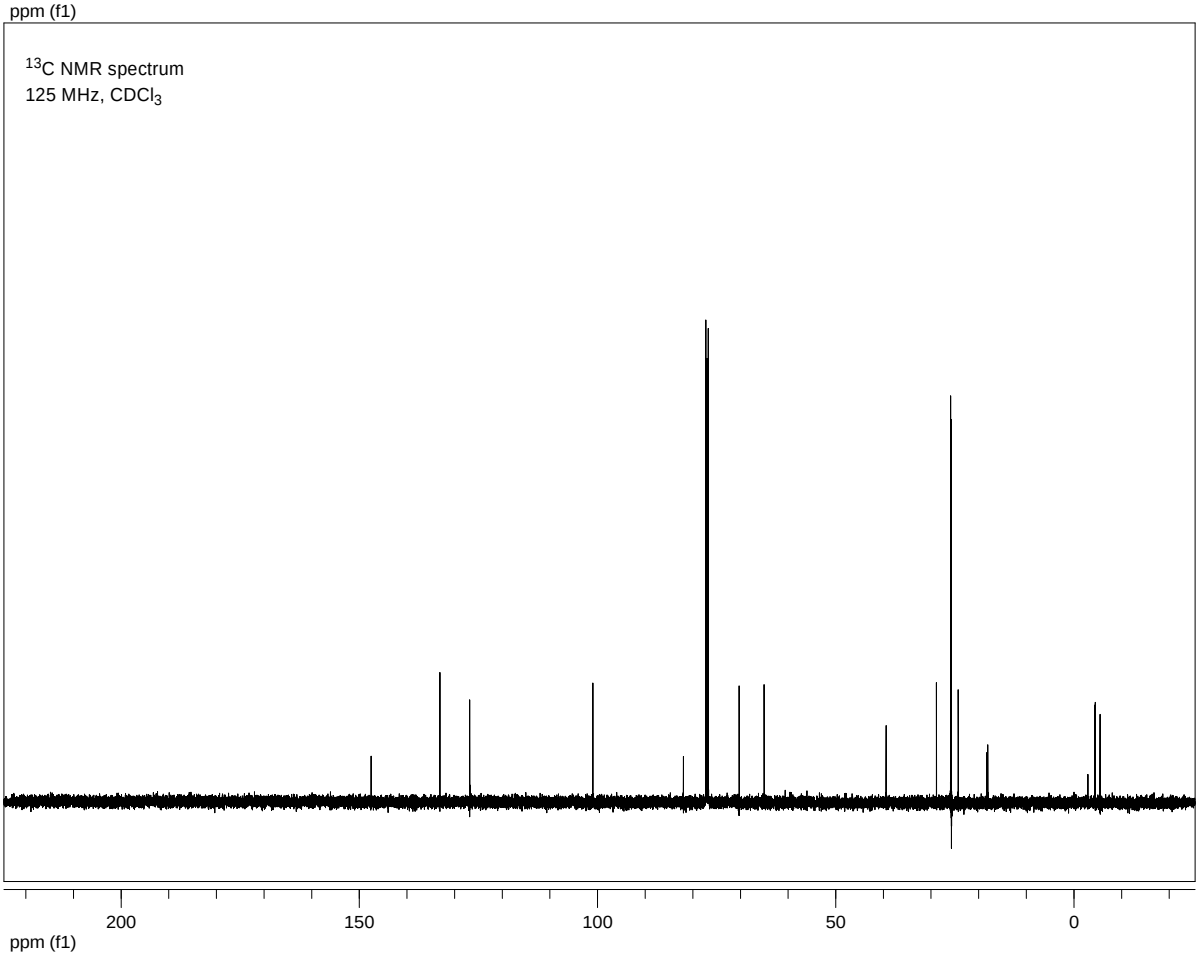

OPiv
O
(±)-13b
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

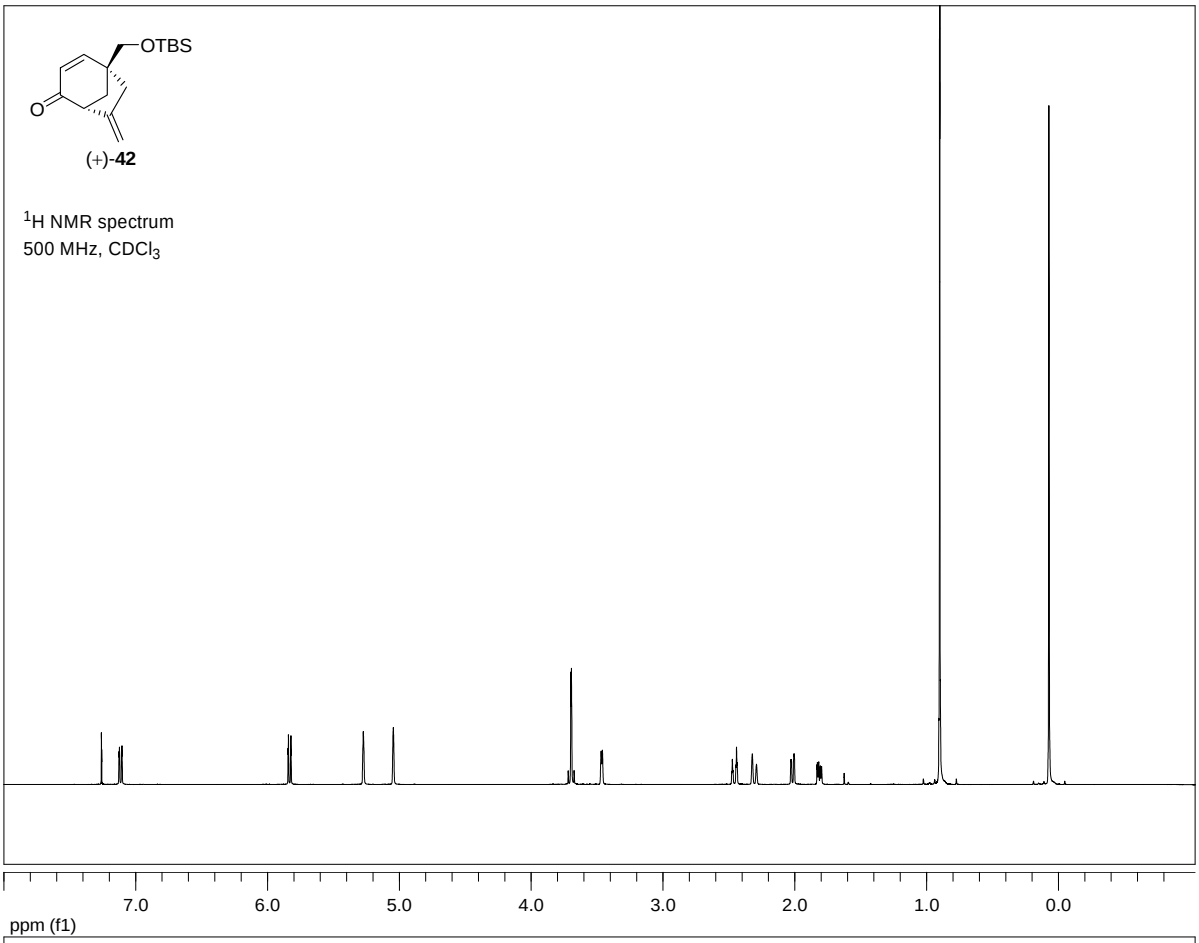

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

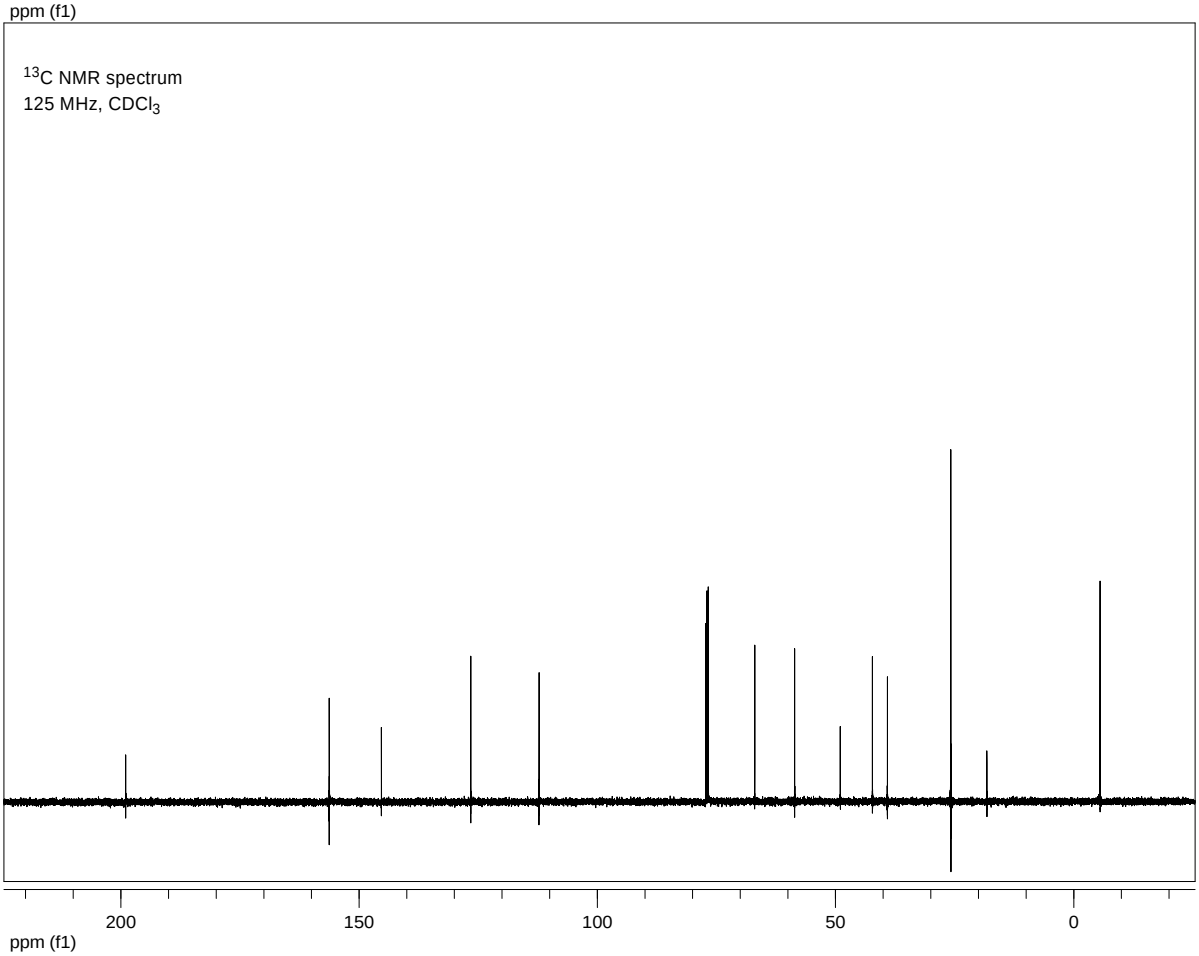

MeO2C
N
Bn
CHO
TBSO
TMS
(–)-41
(rotamers)
1H NMR spectrum
500 MHz, CDCl3, 50 °C
10.0
5.0
0.0
ppm (f1)

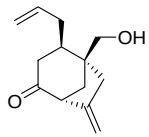

13C NMR spectrum
125 MHz, CDCl3, 50 °C
200
150
100
50
0
ppm (f1)


OTBS
TBSO
(–)-14
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

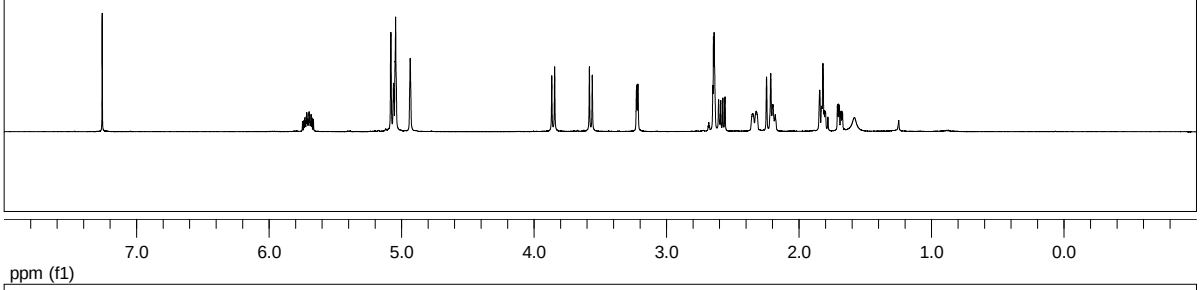

OTBS
O
(+)-42
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

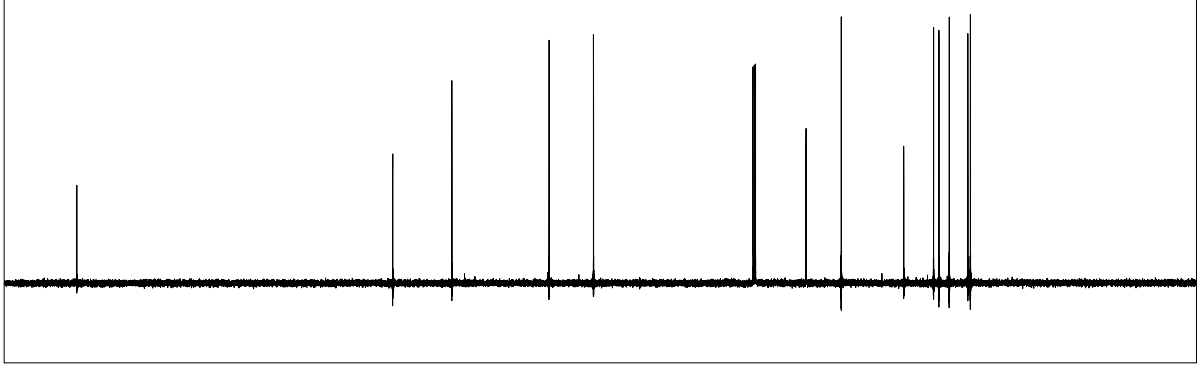


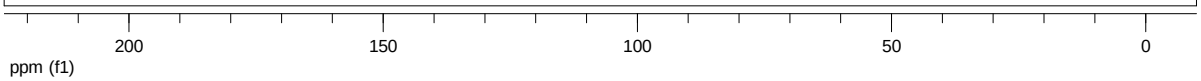
(+)-**13**

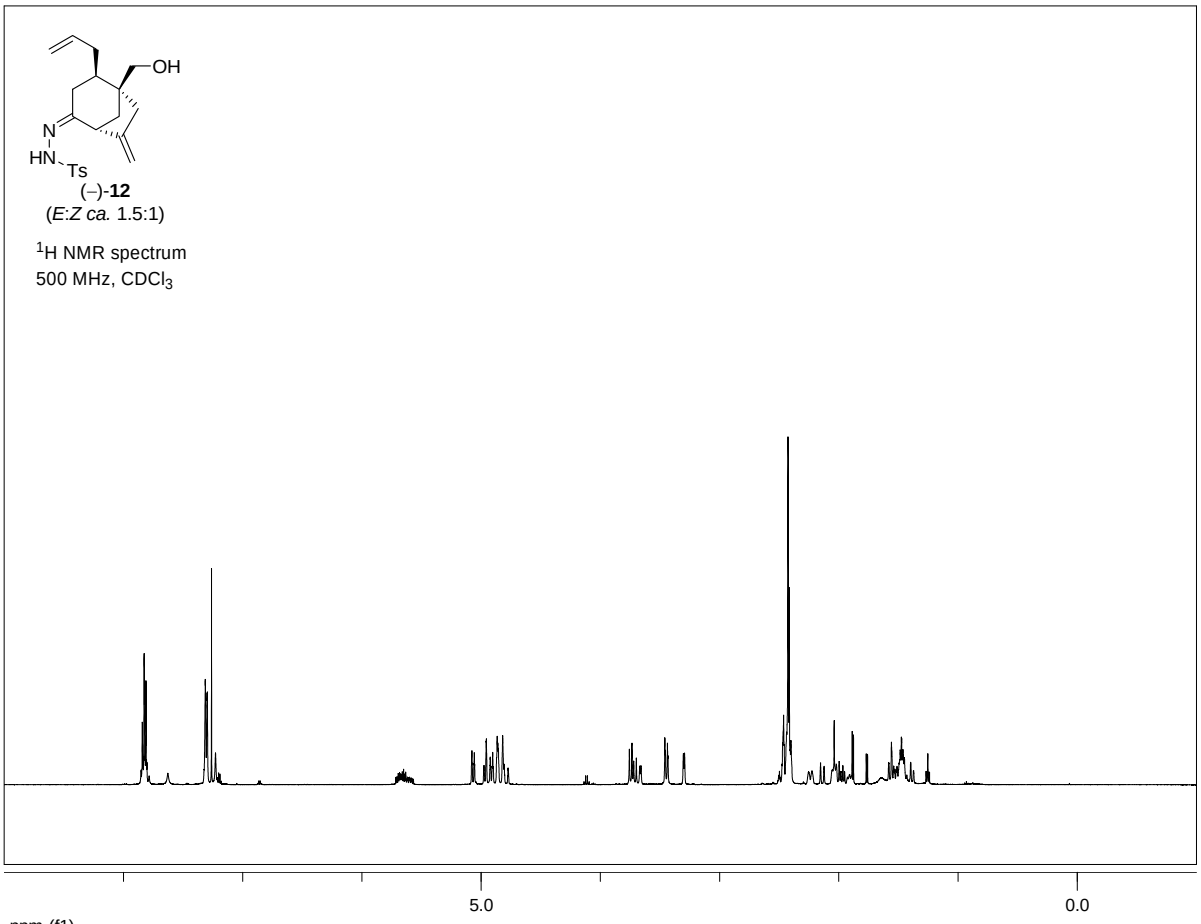
^{1}H NMR spectrum
500 MHz, $CDCl_3$



^{13}C NMR spectrum
125 MHz, $CDCl_3$







(–)-**12**

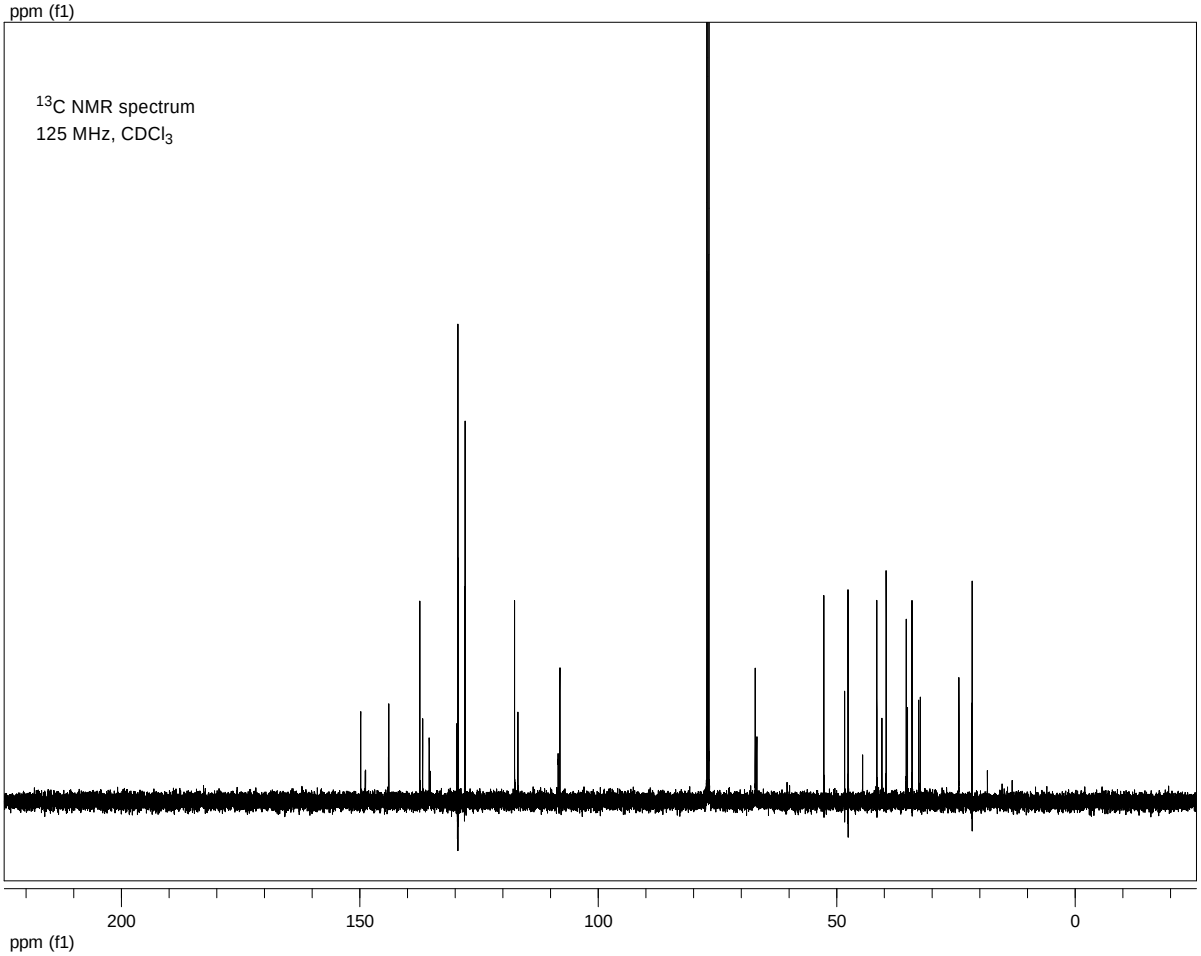
(*E*:*Z ca.* 1.5:1)

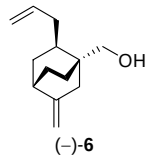
^{1}H NMR spectrum

500 MHz, $CDCl_3$

^{13}C NMR spectrum

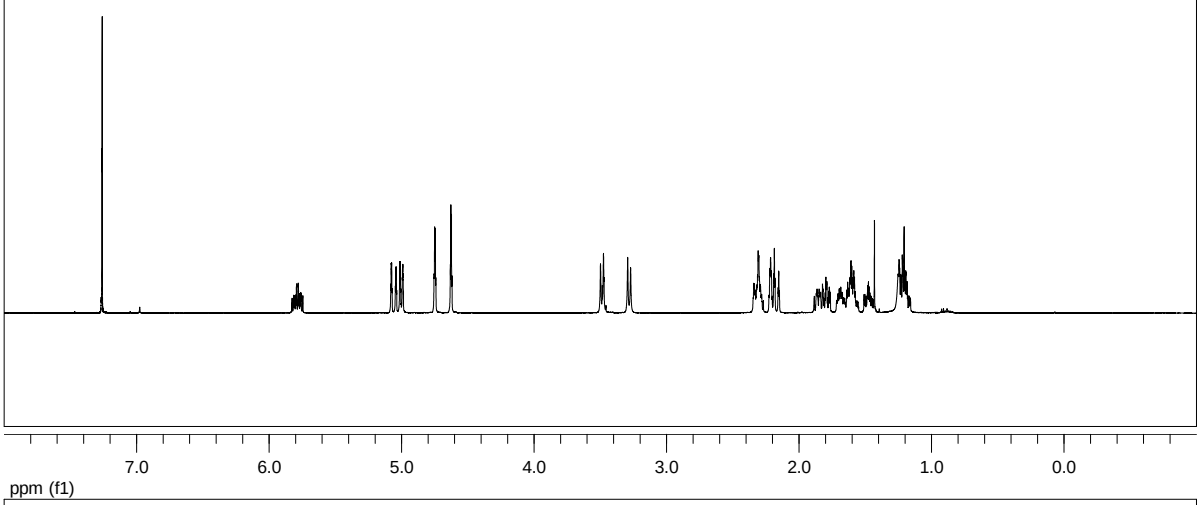
125 MHz, $CDCl_3$



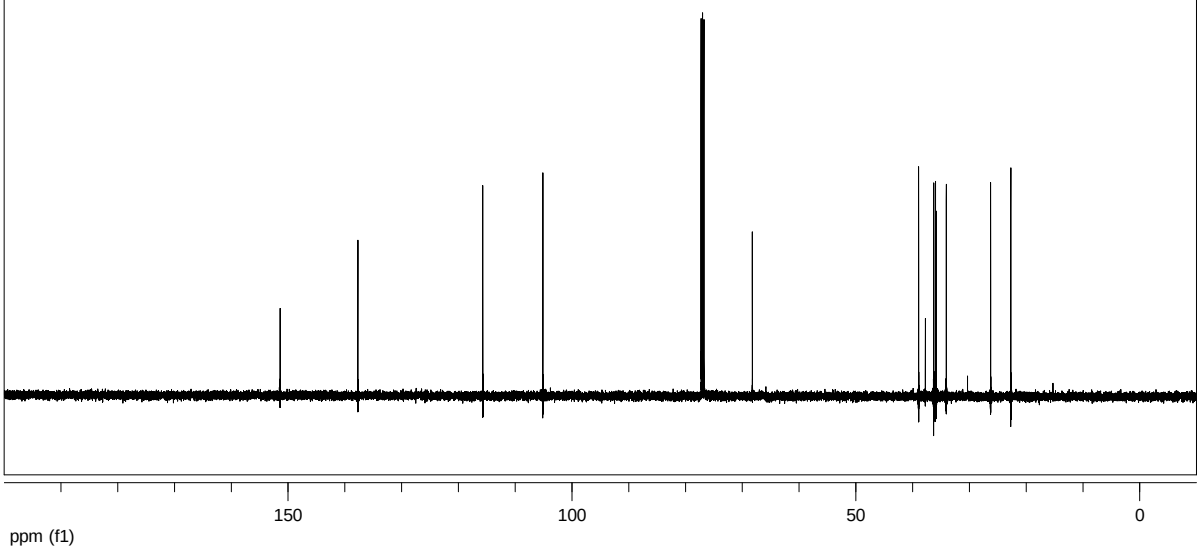


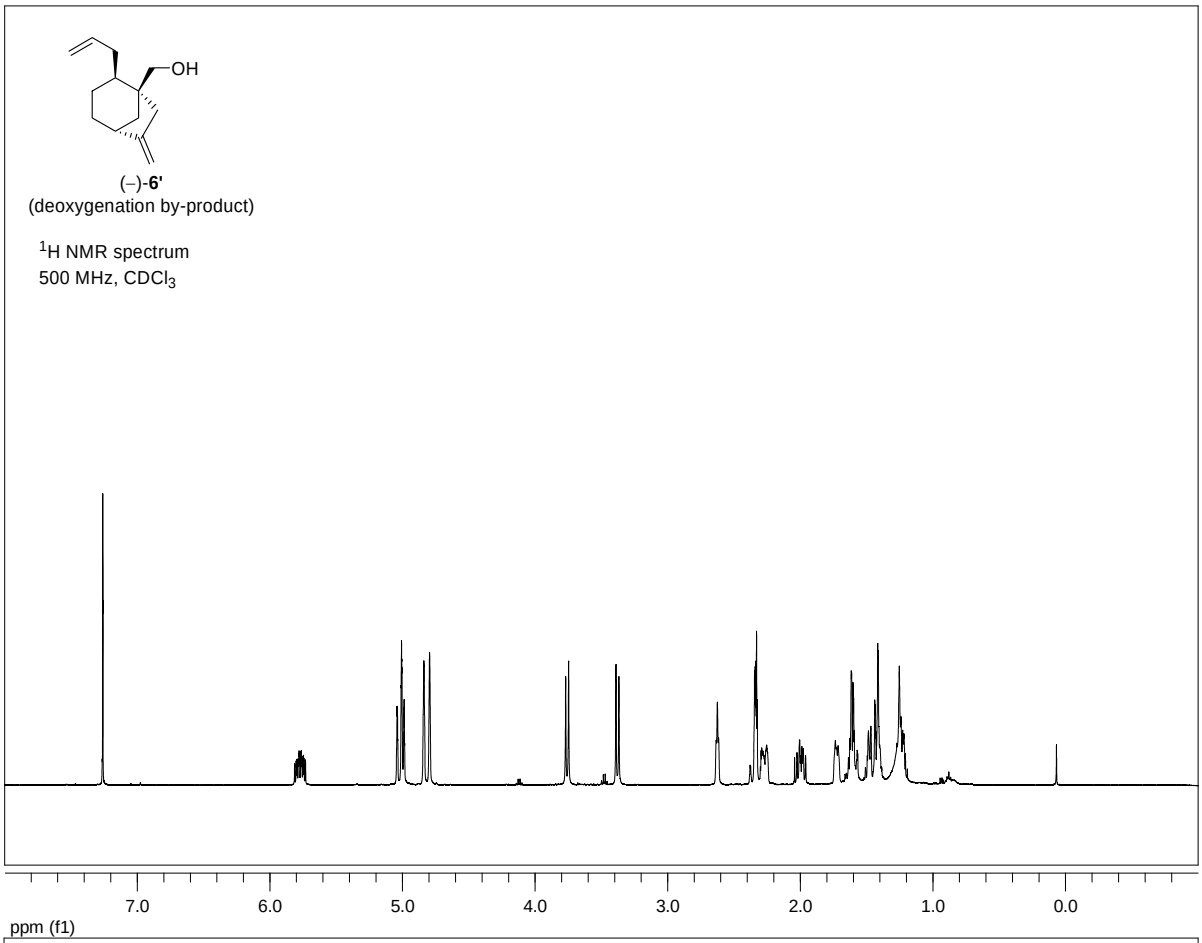
(–)-**6**

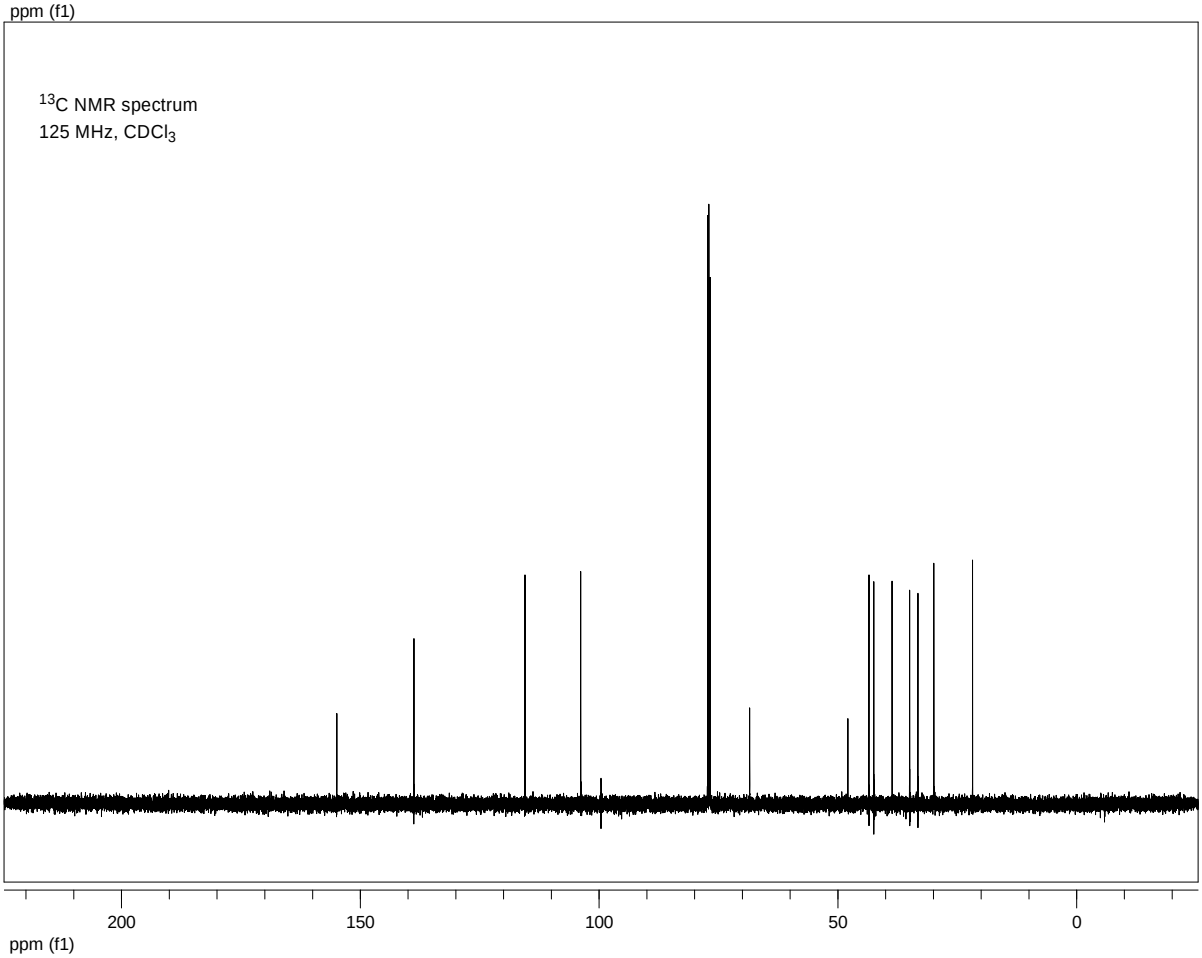
^{1}H NMR spectrum
500 MHz, $CDCl_3$

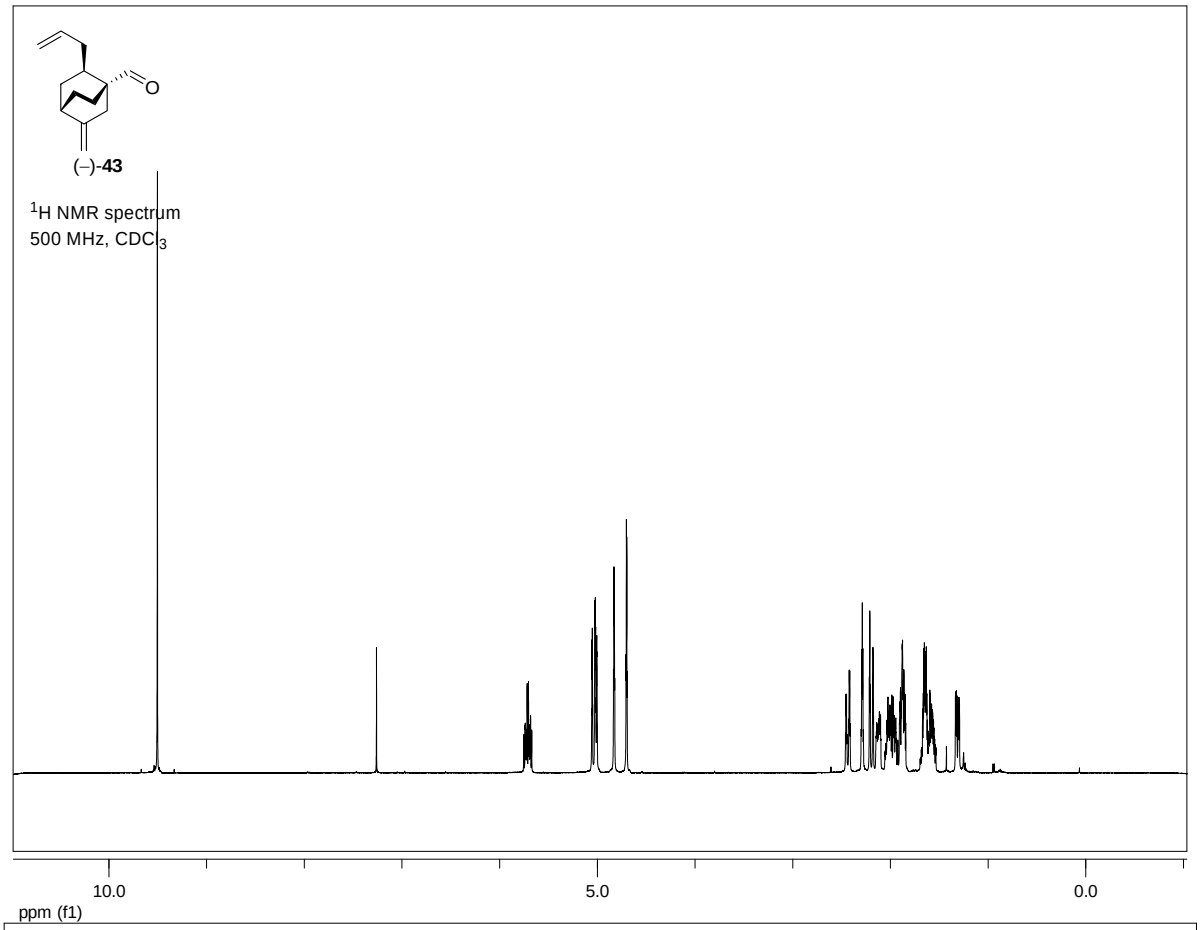


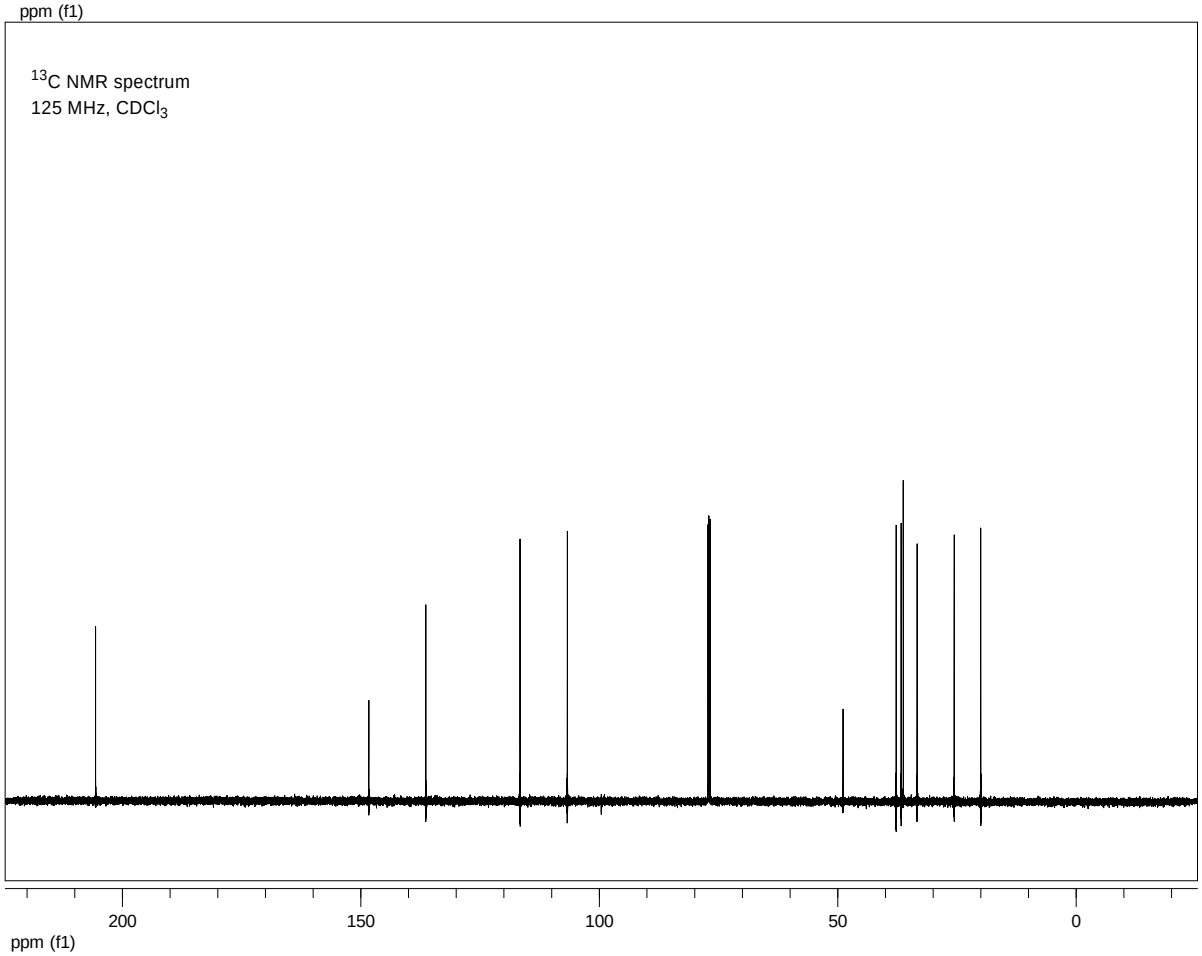
^{13}C NMR spectrum
125 MHz, $CDCl_3$

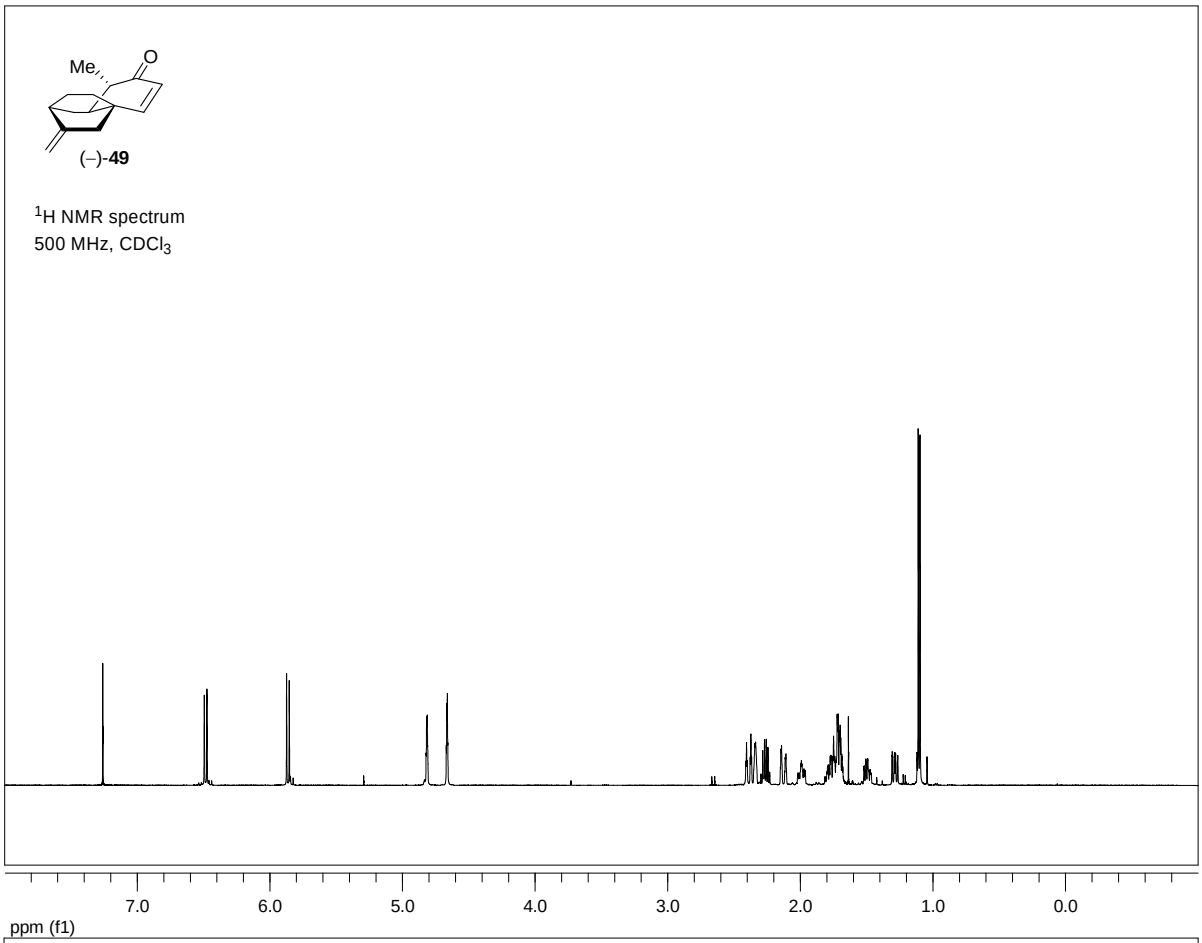


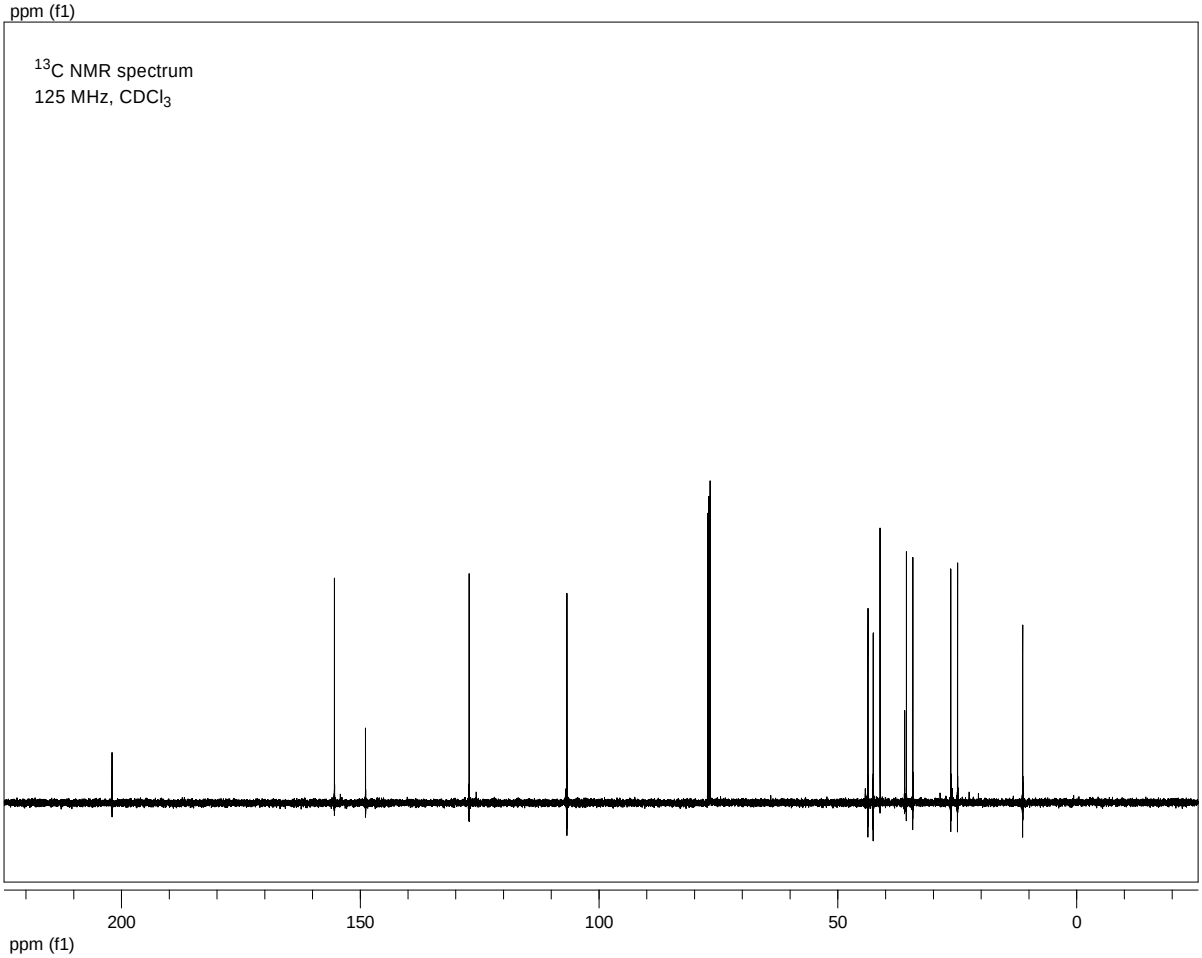

OH
(–)-6'
(deoxygenation by-product)
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

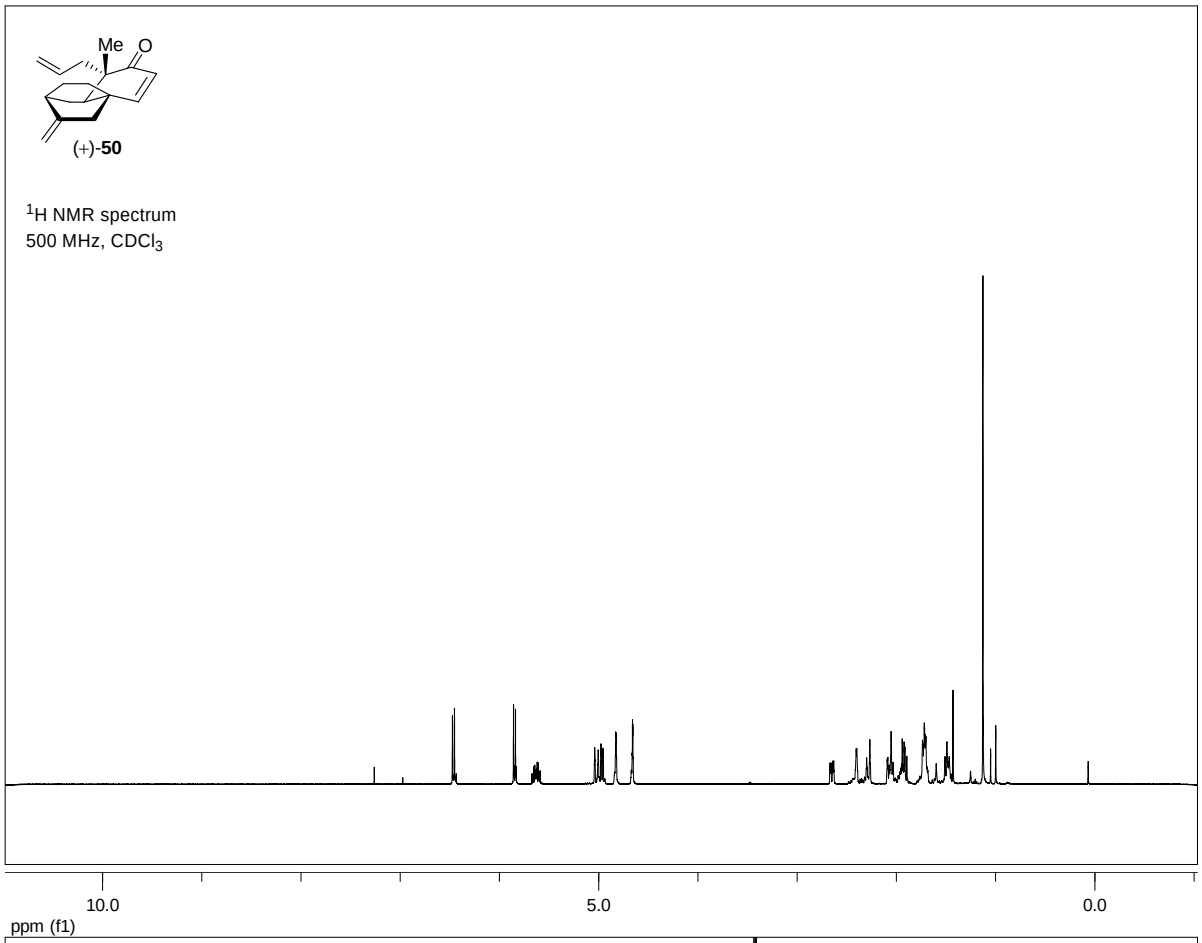

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

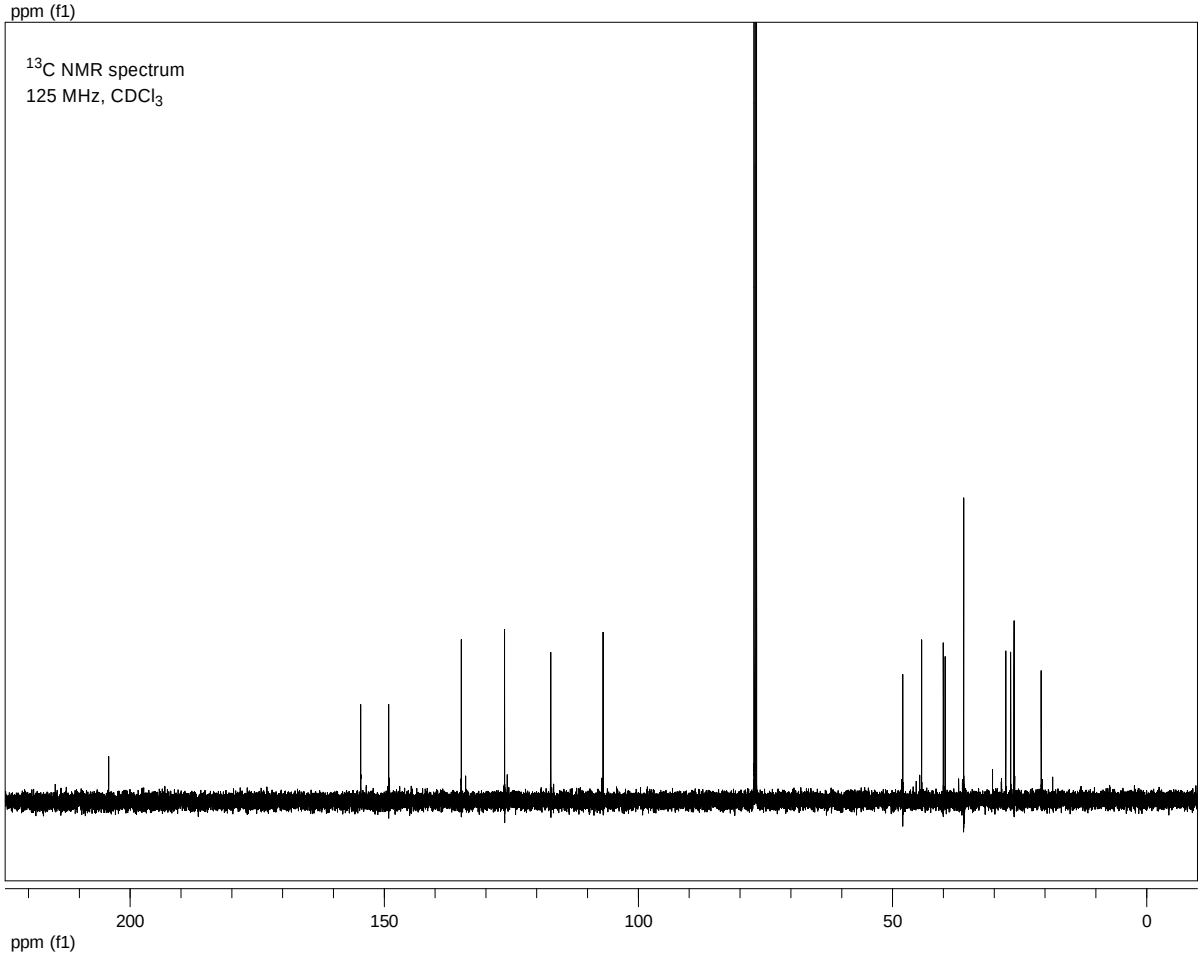

O
(–)-43
1H NMR spectrum
500 MHz, CDC3
10.0
5.0
0.0
ppm (f1)

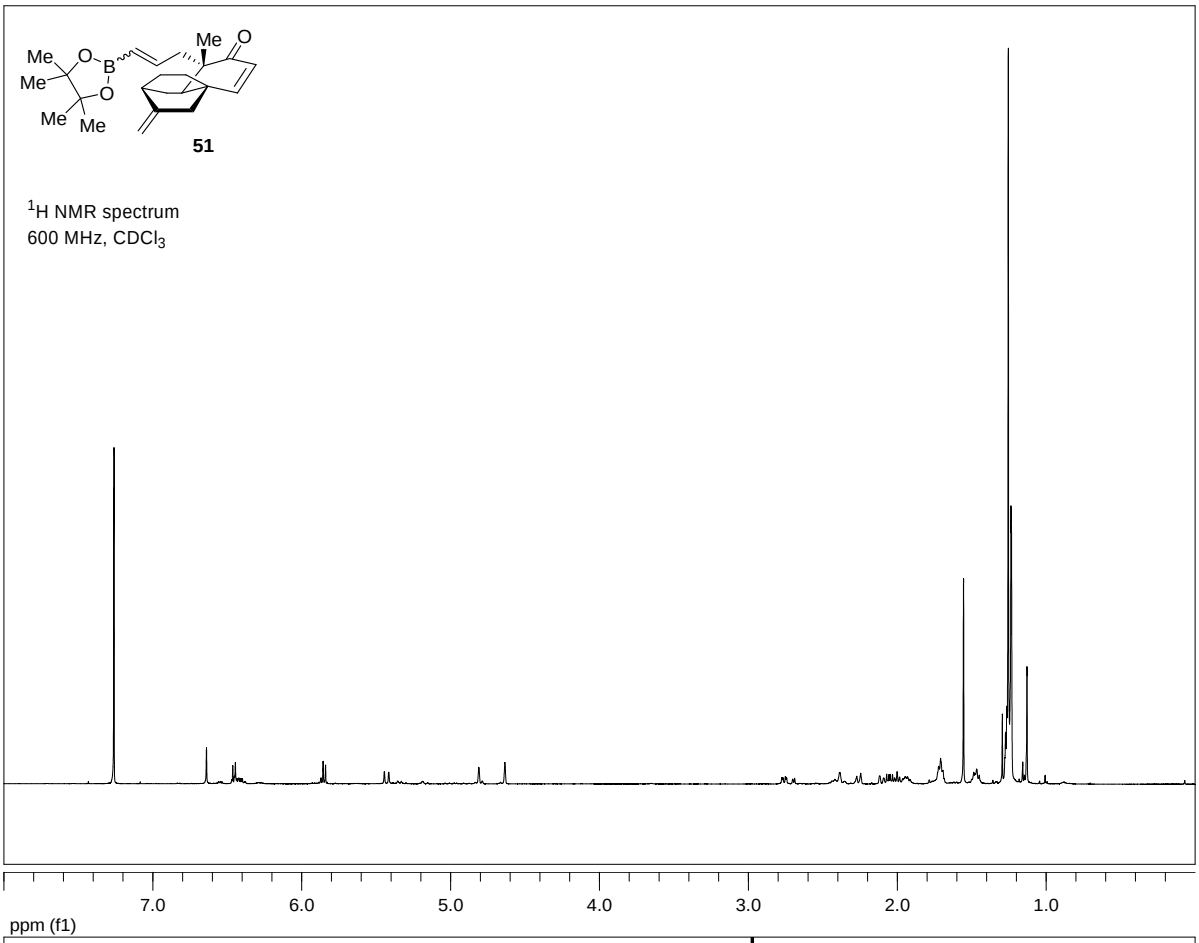

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

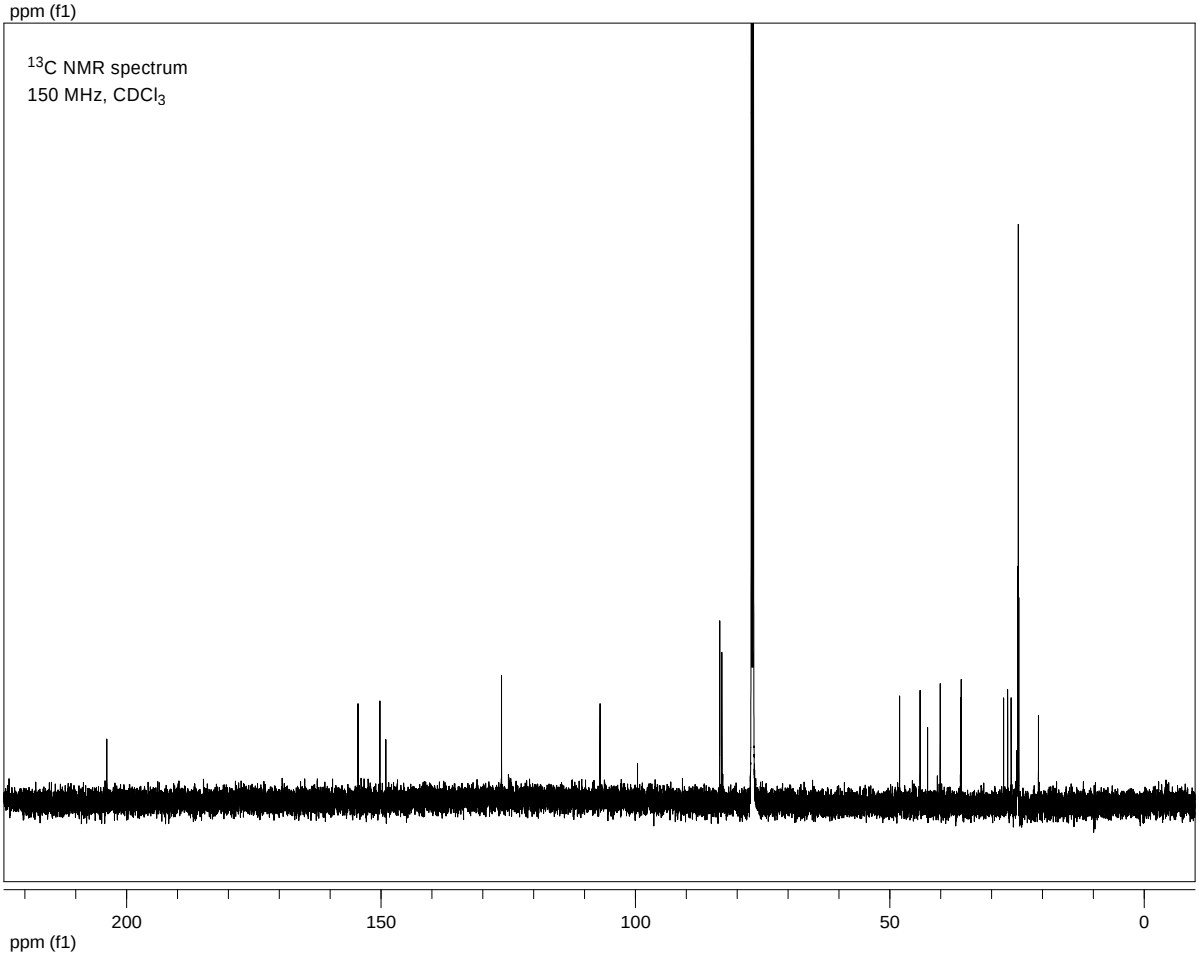

Me
O
(–)-49
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

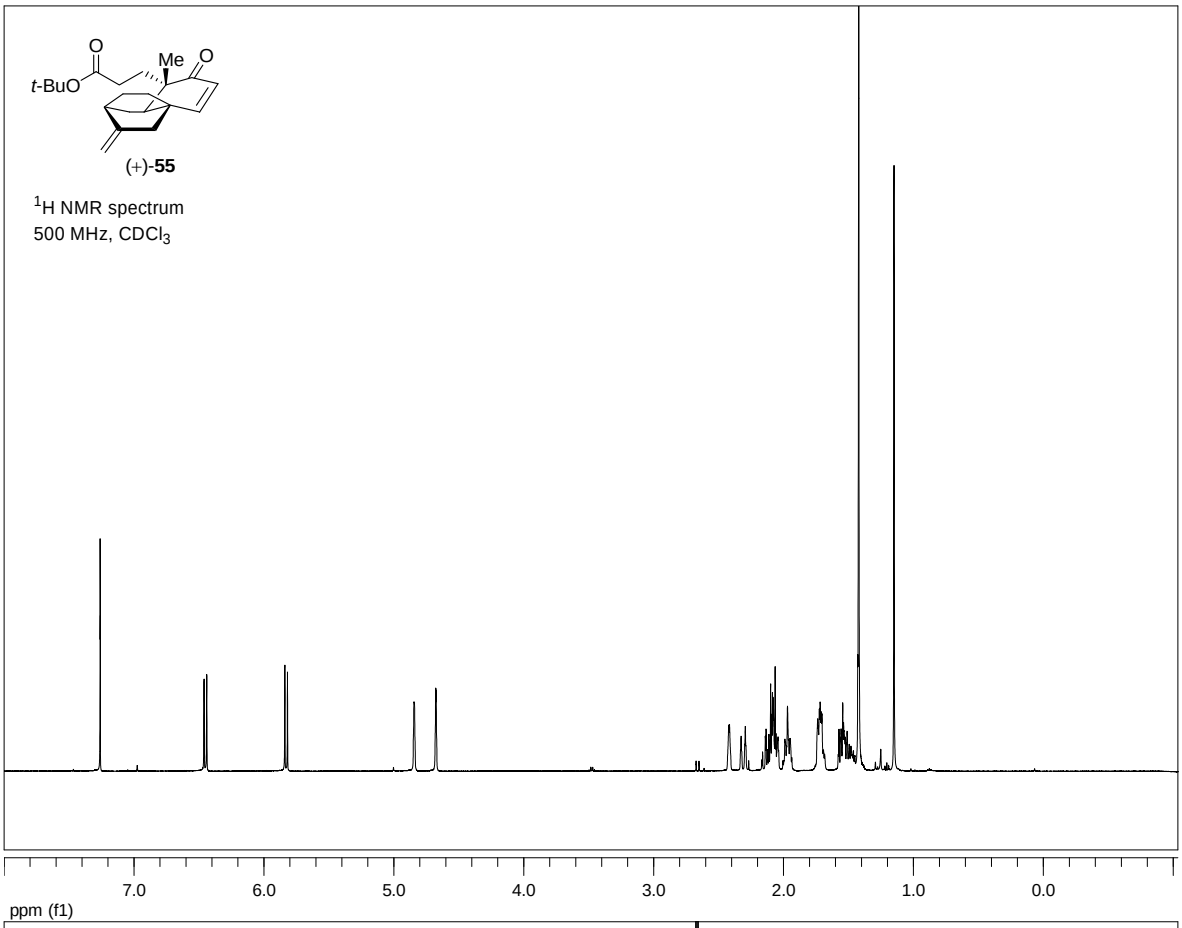

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


Me
O
(+)-50
1H NMR spectrum
500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)


13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

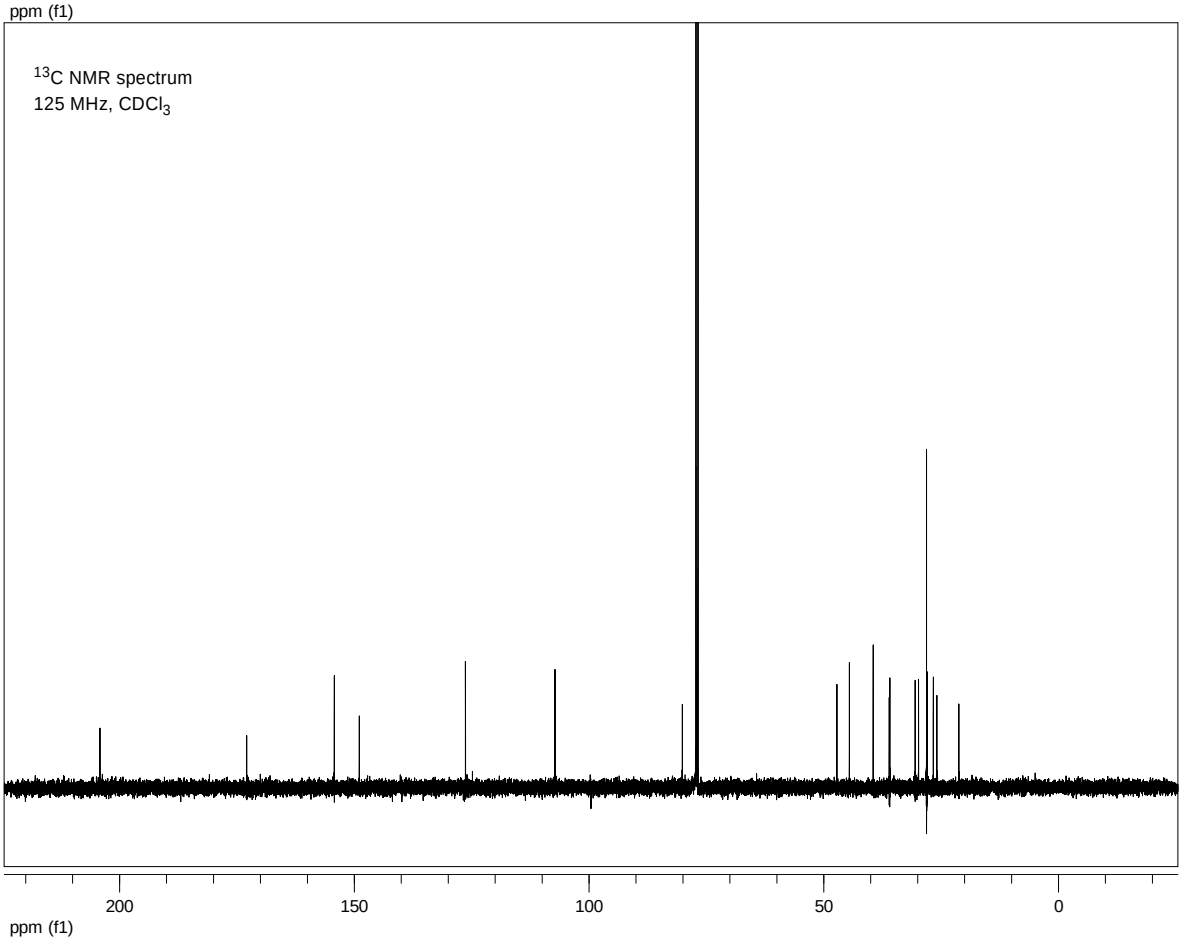

Me
O
Me
O
B
Me
O
Me
Me
51
1H NMR spectrum
600 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)


13C NMR spectrum
150 MHz, CDCl3
200
150
100
50
0
ppm (f1)

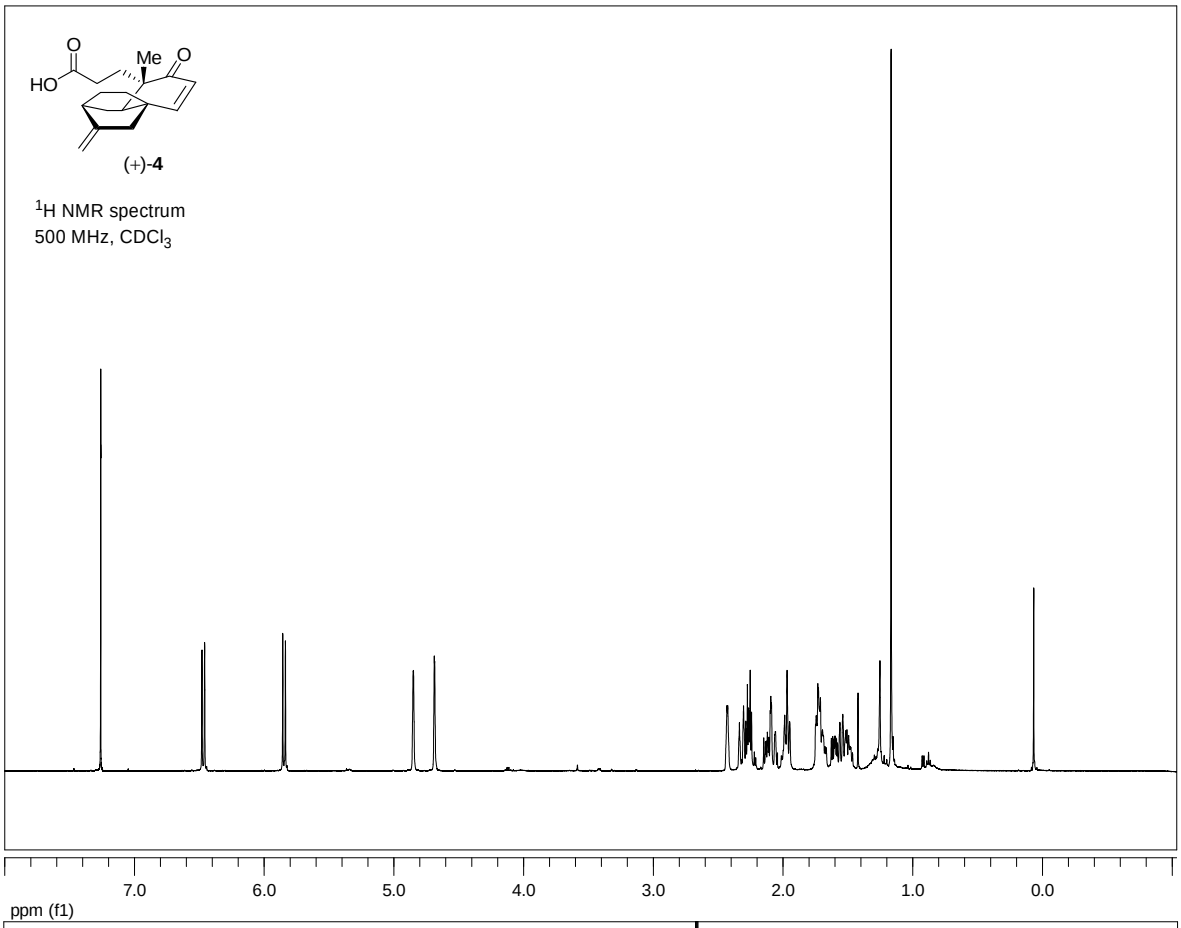


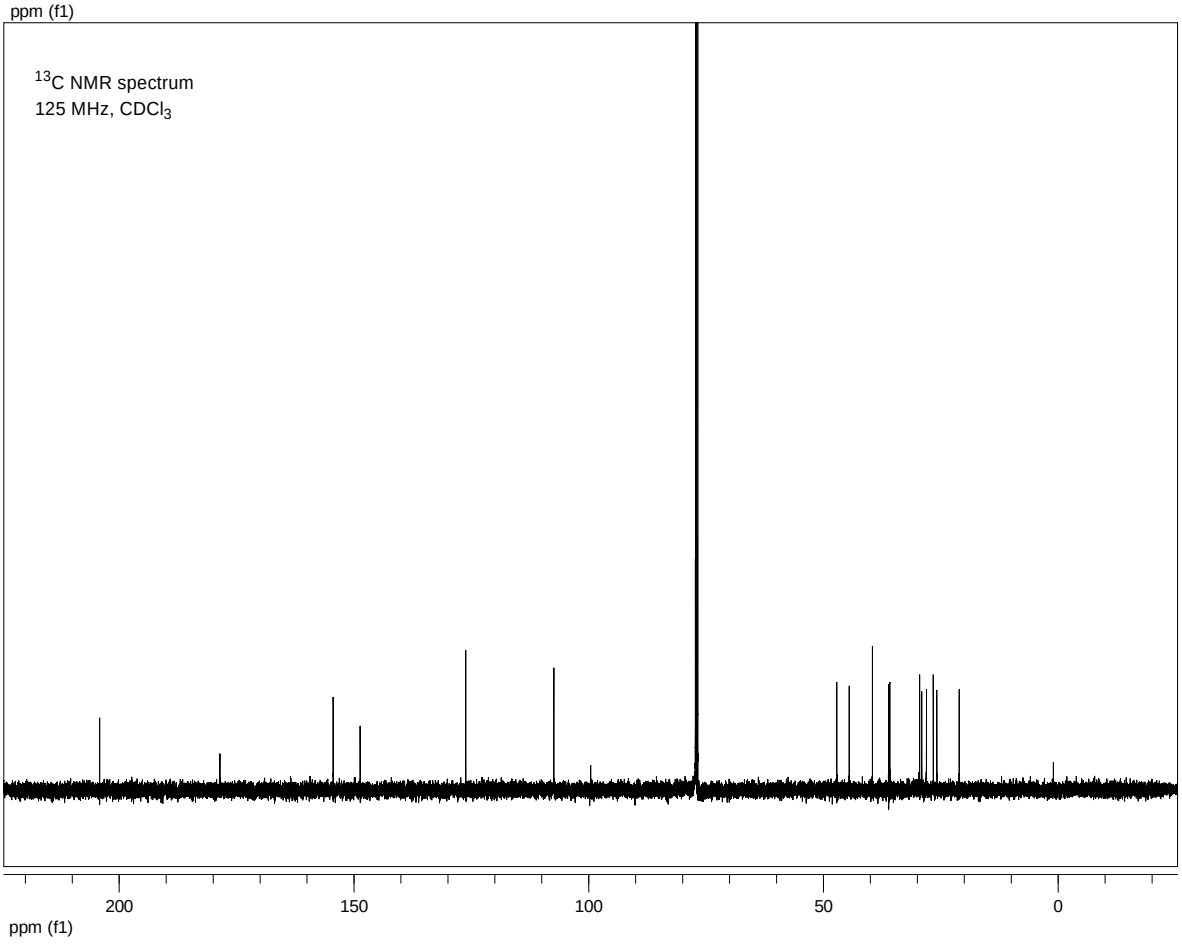
(+)-**55**

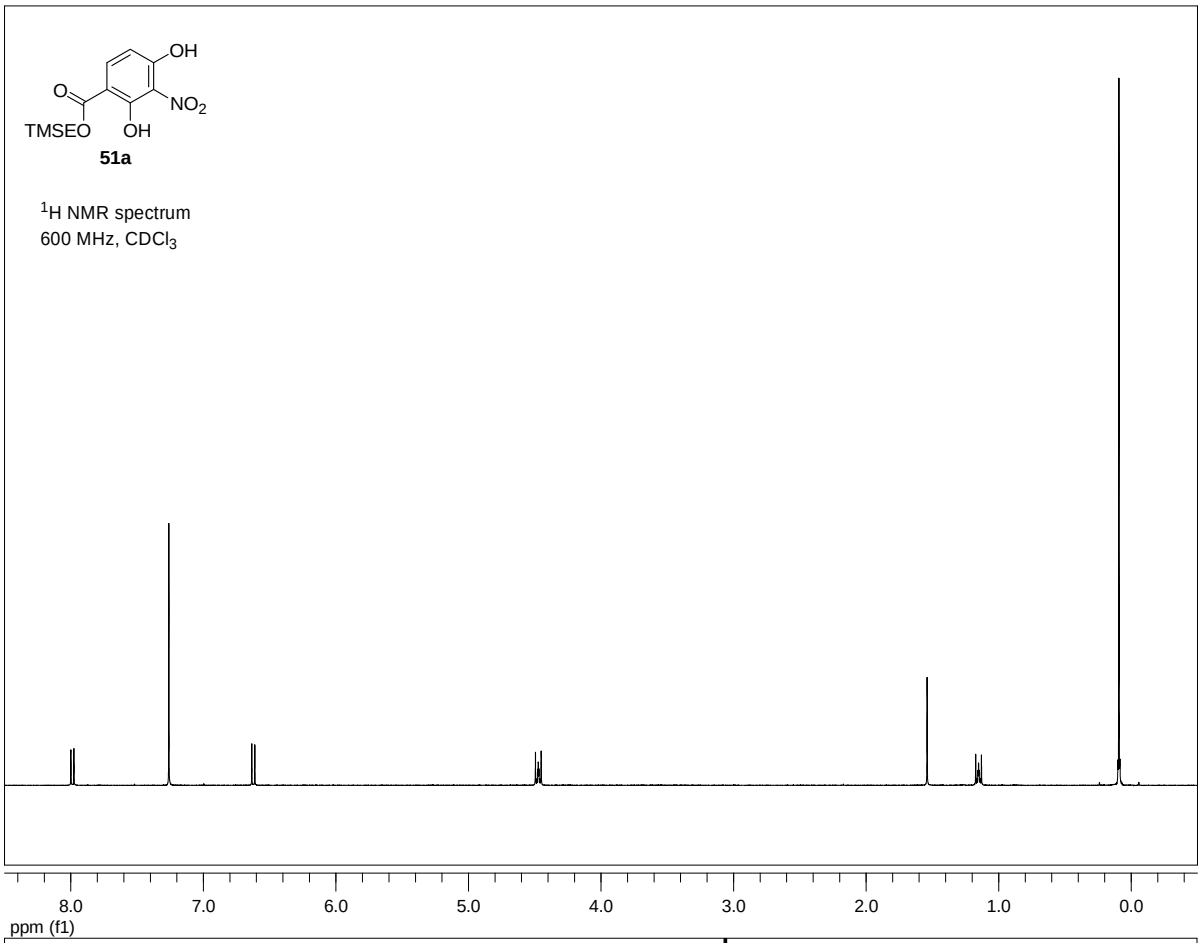
^{1}H NMR spectrum
500 MHz, $CDCl_3$

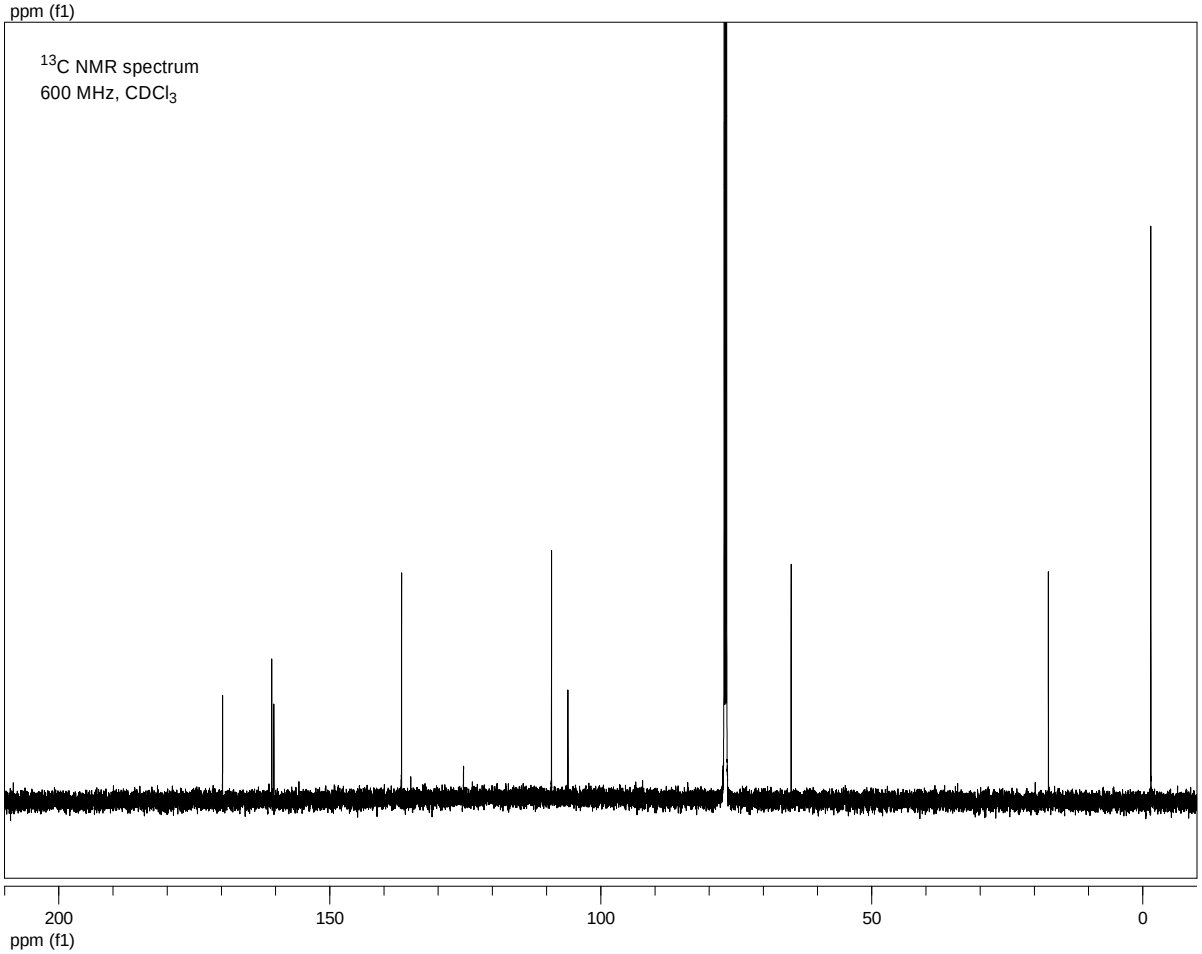


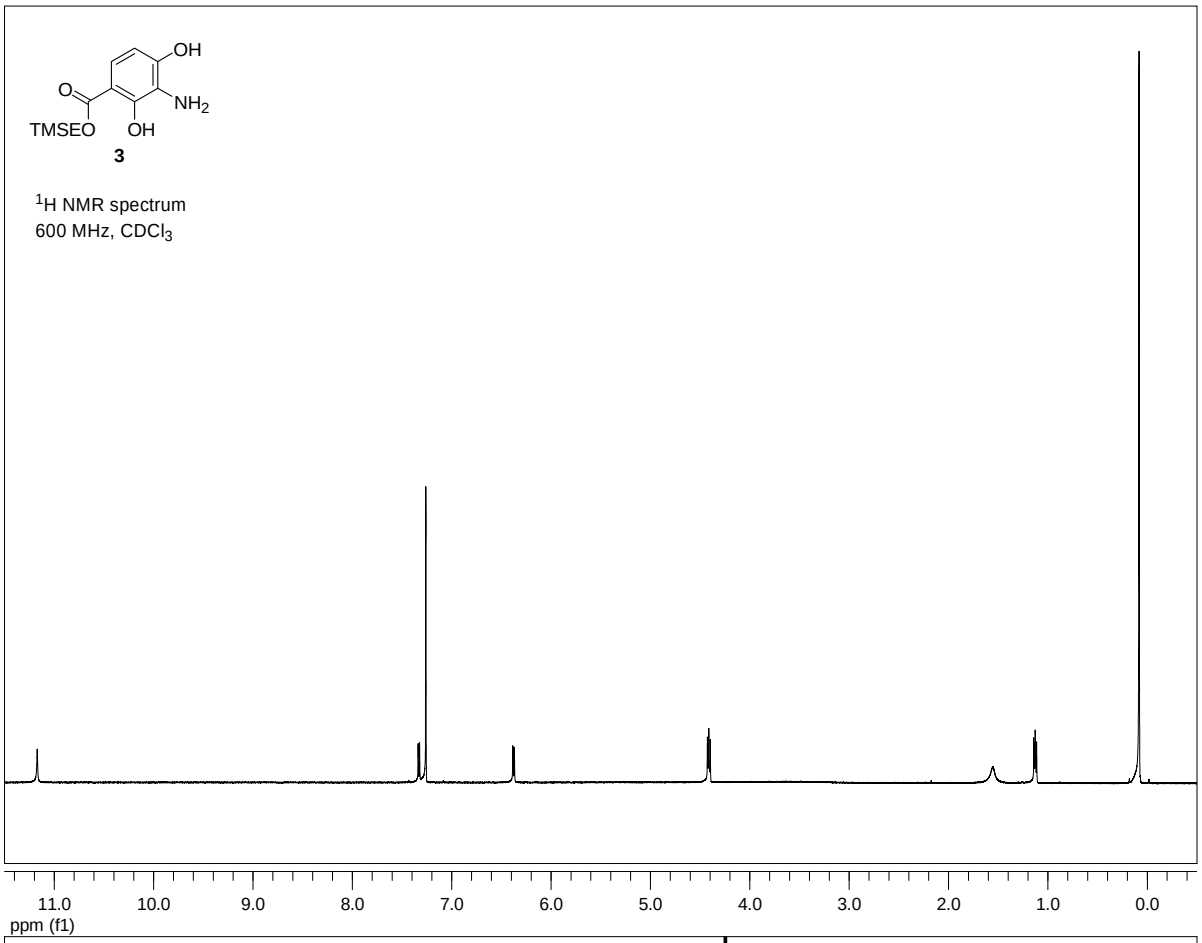
^{13}C NMR spectrum
125 MHz, $CDCl_3$

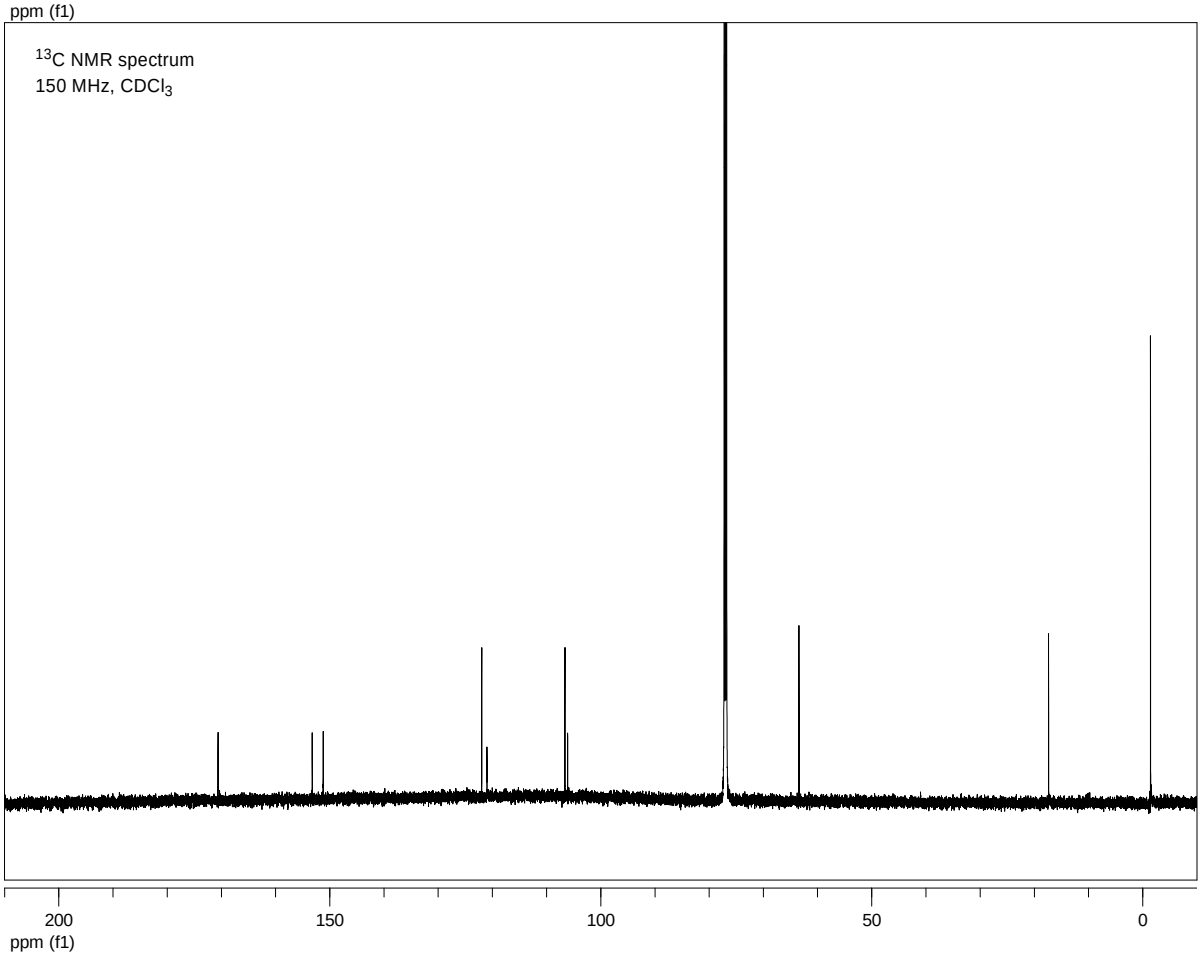

O
HO
Me
O
(+)-4
1H NMR spectrum
500 MHz, CDCl3
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

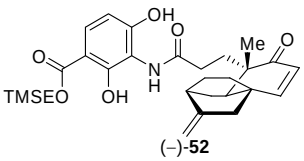

13C NMR spectrum
125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


OH
O
NO2
TMSEO
OH
51a
1H NMR spectrum
600 MHz, CDCl3
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


13C NMR spectrum
600 MHz, CDCl3
200
150
100
50
0
ppm (f1)


OH
O
NH2
TMSEO
OH
3
1H NMR spectrum
600 MHz, CDCl3
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

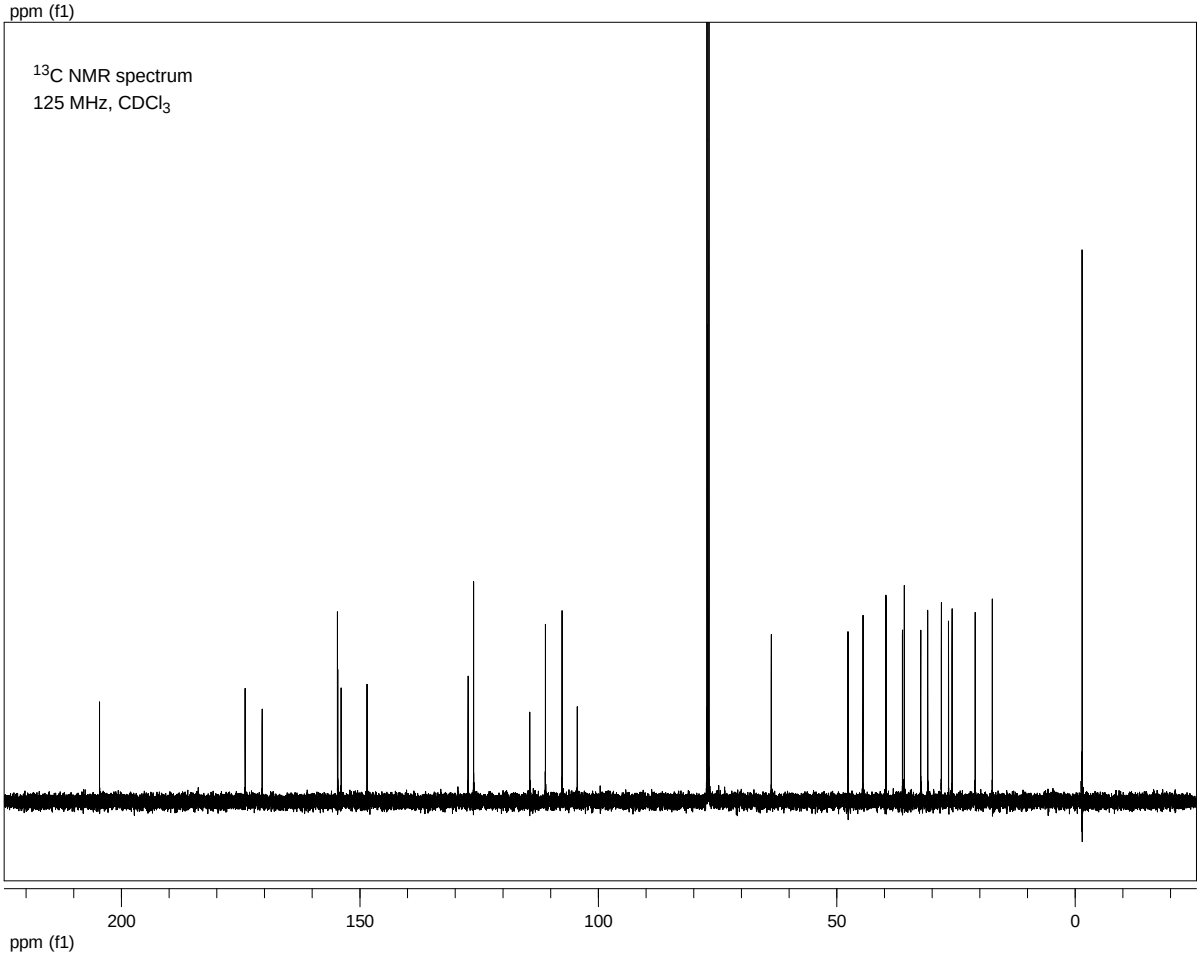

13C NMR spectrum
150 MHz, CDCl3
200
150
100
50
0
ppm (f1)

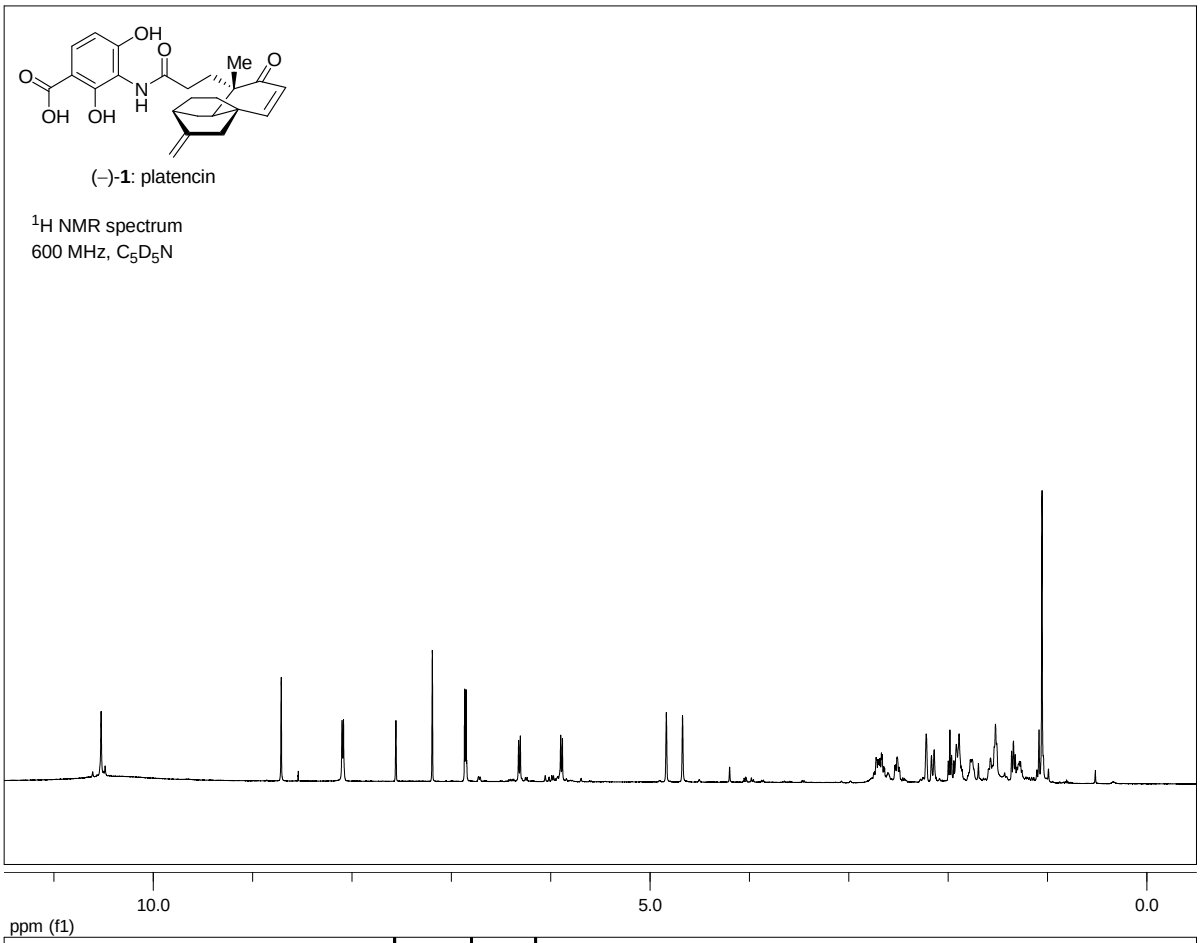


(–)-**52**

^{1}H NMR spectrum
500 MHz, $CDCl_3$

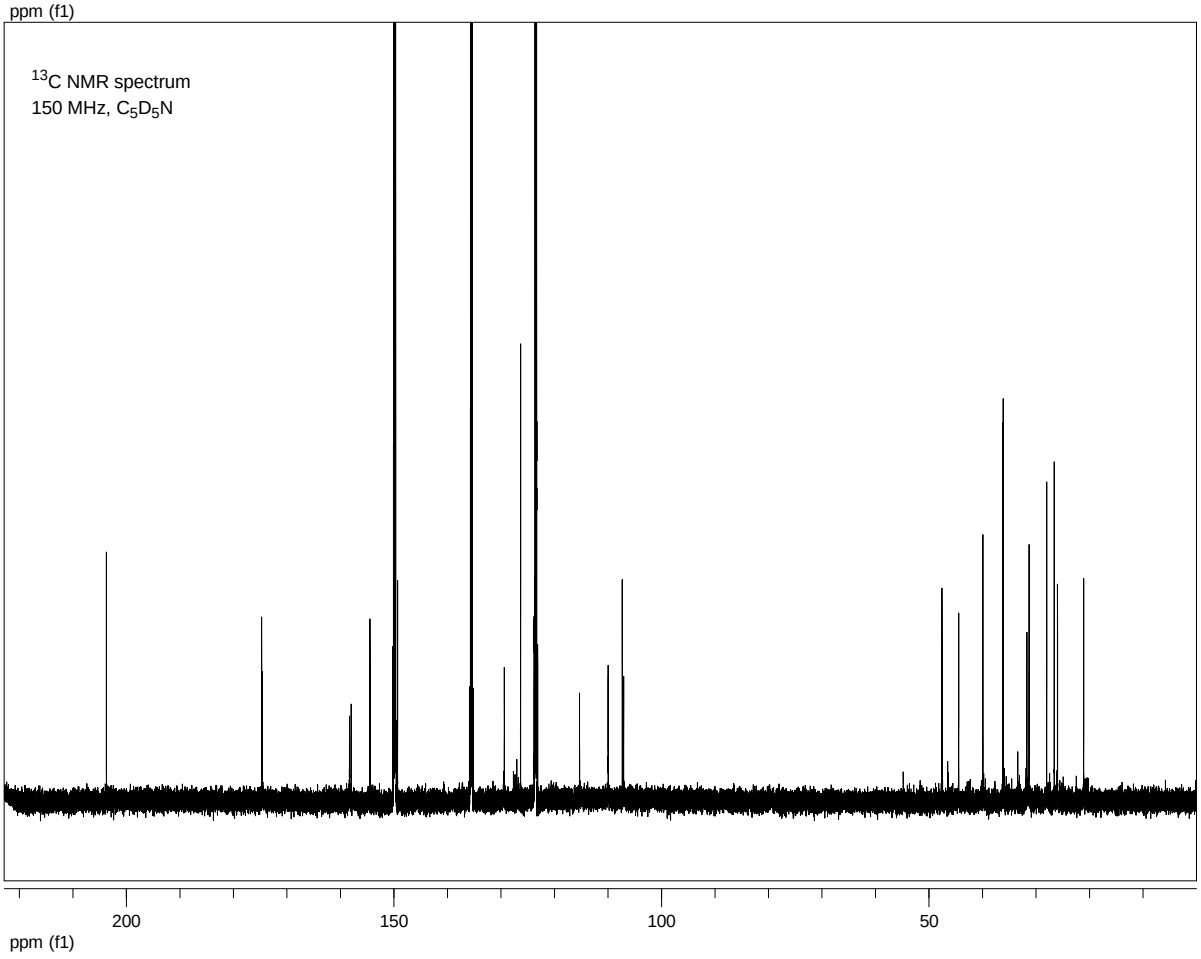
^{13}C NMR spectrum
125 MHz, $CDCl_3$





(–)-**1**: platencin

^{1}H NMR spectrum
600 MHz, C_5D_5N



^{13}C NMR spectrum
150 MHz, C_5D_5N