Total Synthesis of Stemaphylline *N*-oxide and Related C9a-Epimeric Analogs.

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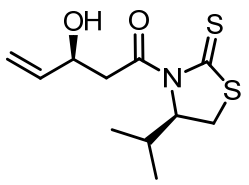
General Experimental

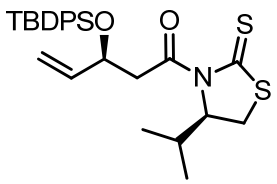
All reagents were purchased from commercial suppliers and purified as needed according to the procedures of Armarego and Chai[1]. Analytical thin-layer chromatography (TLC) was performed on 250 μm silica gel plates from Sorbent Technologies. Visualization was accomplished via UV light, and/or the use of potassium permanganate and phosphomolybdic acid solutions followed by application of heat. Chromatography was performed using Silica Gel 60 (230-400 mesh) from Sorbent Technologies or Silica RediSep Rf flash columns on a CombiFlash Rf automated flash chromatography system. All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 (400 MHz and 100 MHz respectively). All ^{1}H and ^{13}C chemical shifts are reported in ppm relative to residual solvent peaks as an internal standard set to δ 7.26 and δ 77.16 ($CDCl_3$) and δ 7.16 and δ 128.06 (C_6D_6). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constant (Hz), integration. Low resolution mass spectra (LCMS) were obtained on an Agilent 1200 LCMS with electrospray ionization. High resolution mass spectra (HRMS) were recorded on a Waters Qtof-API-US plus Acquity system with ES as the ion source. Crystals for x-ray structure determination were mounted on a cryoloop and maintained at 100 K using a Bruker KryoFlex cryostat. Data were collected using a Bruker Microstar rotating-anode X-ray generator operated at 2.7 kW. Diffraction data were collected using Montel multi-layer confocal optics and a Bruker X8 kappa axis goniometer with a Bruker Proteum PT135 CCD area detector. Diffraction data scans were calculated using Cosmo software and the diffraction data integrated and scaled using Proteum2 software. Absorption correction was applied using SADABS (Sheldrick, 2006). The space group was determined using XPREP (Sheldrick, 2006). Diffraction data were phased and a molecular model was built using SIR2011 (Burla, et al., 2012). Refinement was performed using SHELXL (Sheldrick, 2006). Manual inspection of the refinement was done using COOT (Emsley & Cowtan, 2004) and PLATON (Spec, 2006).

(*S*)-3-hydroxy-1-((*R*)-4-isopropyl-2-thioxothiazolidin-3-yl)pent-4-en-1-one.



To a solution of (*R*)-1-(4-isopropyl-2-thioxothiazolidin-3-yl)ethanone (11.23 g, 55.21 mmol, 1.0 eq) in CH_2Cl_2 (0.25 M) under argon at -48 °C was added $TiCl_4$ (10.8 mL, 98.27 mmol, 1.78 eq) dropwise followed by *N*,*N*-diisopropylethylamine (17.02 mL, 97.72 mmol, 1.77 eq) dropwise. After stirring at –48 °C for 2 h, the reaction mixture is cooled to -78 °C and acrolein (3.80 mL, 55.21 mmol, 1.0 eq) is added dropwise. The reaction stirred at -78 °C for 30 min. The reaction is quenched by addition of pH 7 phosphate buffer and warmed to room temperature. The aqueous layer is extracted with CH_2Cl_2 and the combined organic extracts are dried over $NaSO_4$ and concentrated *in vacuo*. Purification via flash chromatography (Hex:EtOAc 4:1) affords the desired product as a yellow oil in 90% overall yield and 5:1 dr. The pure desired diastereomer can be isolated in 75% yield (10.74 g). $[\alpha]_D^{20}$ = -358.3 (c = 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.85 (ddd, J_1 = 17.2 Hz, J_2 = 10.5 Hz, J_3 = 5.4 Hz, 1H); 5.24 (d, J = 17.2 Hz, 1H); 5.11-5.04 (m, 2H); 4.63-4.56 (m, 1H); 3.56-3.44 (m, 2H); 3.25 (dd, J_1 = 17.5 Hz, J_2 = 8.8 Hz, 1H); 3.12 (br, 1H); 2.98 (d, J = 11.6 Hz, 1H); 2.29 (oct, J = 6.7 Hz, 1H); 0.99 (d, J = 6.9 Hz, 3H); 0.91 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 202.90; 172.04; 138.90; 115.00; 71.30; 68.52; 44.94; 30.67; 30.61; 18.94; 17.66. HRMS (TOF, ES+) $C_{11}H_{17}NO_2S_2$ [M+Na]+ calc. mass 282.0598, found 282.0596.

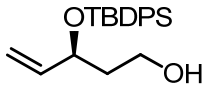
(*S*)-3-((*tert*-butyldiphenylsilyl)oxy)-1-((*R*)-4-isopropyl-2-thioxothiazolidin-3-yl)pent-4-en-1-one, (11).



To a solution of (S)-3-hydroxy-1-((R)-4-isopropyl-2-thioxothiazolidin-3-yl)pent-4-en-1-one

(20.1 g, 77.49 mmol, 1.0 eq) in CH_2Cl_2 (0.2 M) at 0 ºC was added imidazole (5.54 g, 81.36 mmol, 1.05 eq) followed by TBDPS-Cl (21.16 mL, 81.36 mmol, 1.05 eq). The reaction was allowed to warm to rt and continue stirring overnight. The reaction was filtered through celite and concentrated under vacuum. Purification via silica chromatography (Hex:EtOAc 4:1) afforded the desired product as a yellow oil in 95% yield (36.64 g). $[\alpha]_D^{20}$ = -139.7 (c = 0.69, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.70-7.65 (m, 4H); 7.45-7.33 (m, 6H); 5.90 (ddd, J_1 = 17.0 Hz, J_2 = 10.3 Hz, J_3 = 6.5 Hz, 1H); 5.03 (dt, J_1 = 17.2 Hz, J_2 = 1.4 Hz, 1H); 4.96 (dt, J_1 = 10.3 Hz, J_2 = 1.3 Hz, 1H); 4.89-4.83 (m, 1H); 4.78-4.71 (m, 1H); 3.73 (dd, J_1 = 17.0 Hz, J_2 = 6.7 Hz, 1H); 3.35 (dd, J_1 = 11.4 Hz, J_2 = 8.0 Hz, 1H), 3.27 (dd, J_1 = 17.0 Hz, J_2 = 5.8 Hz, 1H), 2.94 (dd, J_1 = 11.4 Hz, J_2 = 1.0 Hz, 1H); 2.29 (oct, J = 6.7 Hz, 1H); 1.03 (s, 9H); 1.00 (d, J = 6.7 Hz, 3H); 0.90 (d, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 202.76; 170.94; 139.80; 136.07; 136.01; 134.14; 133.85; 129.69; 127.58; 127.54; 115.31; 71.64; 71.56; 46.27; 30.84; 30.58; 27.11; 19.44; 19.20; 17.78. HRMS (TOF, ES+) $C_{27}H_{35}NO_2S_2Si$ [M+H]+ calc. mass 498.1957, found 498.1960.

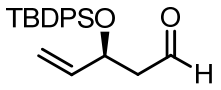
(*S*)-3-((*tert*-butyldiphenylsilyl)oxy)pent-4-en-1-ol.



To a solution of (S)-3-((tert-butyldiphenylsilyl)oxy)-1-((R)-4-isopropyl-2-thioxothiazolidin-3-yl)pent-4-en-1-one (15.45 g, 31.04 mmol, 1.0 eq) in THF (0.1 M) under argon at 0 °C is added methanol (5.0 mL, 124 mmol, 4.0 eq) followed by 2.0 M $LiBH_4$ solution in THF (46.5 mL, 93.11 mmol, 3.0 eq) dropwise. The reaction was allowed to stir for 45 min at 0 °C. The reaction was quenched with NH_4Cl solution, extracted 3x with EtOAc, dried over Na_2SO_4, and concentrated under vacuum. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 93% yield (9.83 g). $[\alpha]_D^{20}$ = 0.7 (c = 0.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.75-7.66 (m, 4H); 7.48-7.34 (m, 6H); 5.86 (ddd, J_1 = 16.9 Hz, J_2 = 10.5 Hz, J_3 = 6.2 Hz, 1H); 5.06 (dt, J_1 = 17.2 Hz, J_2 = 1.4 Hz, 1H); 5.01 (dt, J_1 = 10.4 Hz, J_2 = 1.3 Hz, 1H); 4.44 (m, 1H); 3.75 (m, 1H); 3.65 (m, 1H); 1.92 (br, 1H); 1.81 (m, 1H); 1.70 (m, 1H); 1.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 140.18; 136.12; 136.03; 133.91;

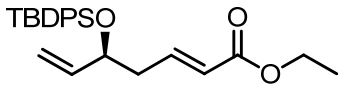
133.74; 129.94; 129.82; 127.77; 127.60; 114.99; 73.35; 59.56; 39.45; 27.16; 19.43. HRMS (TOF, ES+) $C_{21}H_{28}O_2Si$ [M+H]+ calc. mass 341.1937, found 341.1935.

(*S*)-3-((*tert*-butyldiphenylsilyl)oxy)pent-4-enal.



To a flame-dried flask equipped with a stir bar, under argon, was added CH_2Cl_2 (71 mL) followed by $(COCl)_2$ (3.12 mL, 35.66 mmol, 1.2 eq). The reaction was cooled to -78 ^oC and DMSO (4.64 mL, 65.38 mmol, 2.2 eq) was added dropwise. After stirring at -78 ^oC for 30 min, a solution of (*S*)-3-((*tert*-butyldiphenylsilyl)oxy)pent-4-en-1-ol (10.12 g, 29.72 mmol, 1.0 eq) in CH_2Cl_2 (0.25 M) was added dropwise. The reaction was allowed to stir at -78 ^oC for 30 min after which NEt_3 (5.0 eq) was added followed by warming to rt. The reaction was quenched with NH_4Cl, extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated *in vacuo*. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 98% yield (9.86 g). $[\alpha]_D^{20}$ = 6.7 (c = 0.73, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.71 (t, J = 2.6 Hz, 1H); 7.72-7.65 (m, 4H); 7.48-7.35 (m, 6H); 5.91 (ddd, J_1 = 17.0 Hz, J_2 = 10.4 Hz, J_3 = 5.9 Hz); 5.15 (dt, J_1 = 17.1 Hz, J_2 = 1.3 Hz, 1H); 5.07 (dt, J_1 = 10.5 Hz, J_2 = 1.3 Hz, 1H); 4.67 (m, 1H); 2.53-2.48 (m, 2H); 1.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 201.57; 139.30; 136.00; 133.61; 133.50; 130.07; 129.90; 127.86; 127.68; 115.60; 70.36; 50.84; 27.07; 19.41. HRMS (TOF, ES+) $C_{21}H_{26}O_2Si$ [M+H]+ calc. mass 339.1780, found 339.1777.

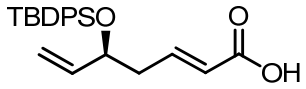
(*S,E*)-ethyl 5-((*tert*-butyldiphenylsilyl)oxy)hepta-2,6-dienoate, (12).



To a suspension of dried LiCl (1.40 g, 33.11 mmol, 1.2 eq) in MeCN (0.1 M) in a flame-dried flask under argon was added DBU (4.21 mL, 27.59 mmol, 1.0 eq), triethyl phosphonoacetate (6.77 mL, 33.11 mmol, 1.2 eq), and (*S*)-3-((tert-butyldiphenylsilyl)oxy)pent-4-enal (9.34 g,

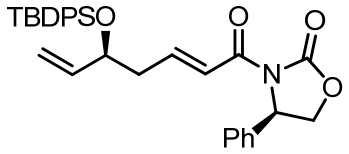
27.59 mmol, 1.0 eq). The reaction stirred at rt for 2 h. The reaction is quenched by the addition of pH 7 buffer followed by extraction with EtOAc. The organic extracts were dried over Na_2SO_4 and concentrated under vacuum. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 90% yield (10.14 g). $[\alpha]_D^{20}$ = 53.9 (c = 0.87, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.75-7.66 (m, 4H); 7.48-7.35 (m, 6H); 6.91 (dt, J_1 = 7.5 Hz, J_2 = 15.7 Hz, 1H); 5.84 (ddd, J_1 = 16.9 Hz, J_2 = 10.4 Hz, J_3 = 6.2 Hz, 1H); 5.76 (d, J = 15.7 Hz, 1H); 5.14-5.02 (m, 2H); 4.32 (q, J = 5.9 Hz, 1H); 4.20 (q, J = 7.1 Hz, 2H); 2.39-2.33 (m, 2H); 1.30 (t, J = 7.1 Hz, 3H); 1.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.30; 144.66; 139.66; 136.00; 135.97; 134.01; 133.79; 129.85; 129.73; 127.69; 127.55; 123.79; 115.30; 73.57; 60.16; 40.63; 27.08; 19.40; 14.34. HRMS (TOF, ES+) $C_{25}H_{32}O_3Si$ [M+H]+ calc. mass 409.2199, found 409.2202.

(*S*,*E*)-5-((*tert*-butyldiphenylsilyl)oxy)hepta-2,6-dienoic acid.



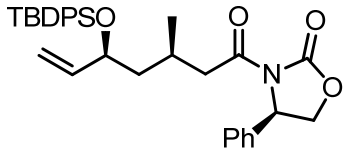
To a solution of (*S*,*E*)-ethyl 5-((tert-butyldiphenylsilyl)oxy)hepta-2,6-dienoate (9.76 g, 23.89 mmol, 1.0 eq) in 3:1 THF/H_2O (0.2 M) under argon was added LiOH (5.72 g, 238.88 mmol, 10.0 eq). The resulting solution was heated to 55 ^{o}C for 18 hrs. The reaction was cooled to rt and acidified to pH 2 by slow addition of HCl. The solution was then extracted with EtOAc, dried over Na_2SO_4, and concentrated *in vacuo*. Purification via flash chromatography (Hex:EtOAc 1:1) afforded the desired product as a clear, colorless oil in 89% yield (8.09 g). $[\alpha]_D^{20}$ = 58.1 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.74-7.63 (m, 4H); 7.49-7.34 (m, 6H); 7.00 (dt, J_1 = 7.3 Hz, J_2 = 15.7 Hz, 1H); 5.82 (ddd, J_1 = 16.8 Hz, J_2 = 10.3 Hz, J_3 = 6.2 Hz, 1H); 5.74 (d, J = 15.7 Hz, 1H); 5.14-5.03 (m, 2H); 4.36-4.29 (m, 1H); 2.36 (t, J = 6.4 Hz, 2H); 1.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 172.00; 147.84; 139.59; 136.07; 136.03; 134.01; 133.79; 129.97; 129.81; 127.80; 127.63; 123.19; 115.51; 73.22; 40.70; 27.13; 19.44. HRMS (TOF, ES+) $C_{23}H_{28}O_3Si$ [M+Na]+ calc. mass 403.1705, found 403.1708.

(*R*)-3-((*S*,*E*)-5-((*tert*-butyldiphenylsilyl)oxy)hepta-2,6-dienoyl)-4-phenyloxazolidin-2-one, (9).



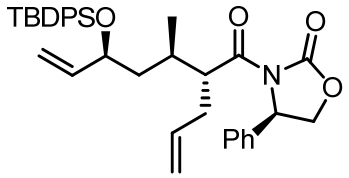
To a solution of (*S*,*E*)-5-((tert-butyldiphenylsilyl)oxy)hepta-2,6-dienoic acid (7.23 g, 19.00 mmol, 1.0 eq), in THF (0.1 M), under argon at -78 ^{o}C, was added NEt_3 (3.18 mL, 22.79 mmol, 1.2 eq) followed by dropwise addition of pivaloyl chloride (2.62 mL, 21.28 mmol, 1.12 eq). The reaction was allowed to stir at -78 ^{o}C for 15 min followed by stirring at 0 ^{o}C for 15 min. In a separate flame-dried flask under argon at -78 ^{o}C was added (*R*)-(−)-4-Phenyl-2-oxazolidinone (3.10 g, 19.00 mmol, 1.0 eq) followed by THF (0.1 M). *n*-BuLi (7.98 mL, 19.90 mmol, 1.05 eq) was added dropwise followed by continued stirring at -78 ^{o}C for 30 min. The solution of mixed anhydride was cooled back down to – 78 ^{o}C and the oxazolidinone was added via cannula. After stirring at -78 ^{o}C for 20 min, the reaction warmed to rt and continued stirring for 1 h. The reaction was quenched by addition of saturated NH_4Cl, extracted with EtOAc, dried over Na_2SO_4, and concentrated. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 95% yield (9.49 g). $[\alpha]_D^{20}$ = -8.6 (c = 0.90, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.68-7.59 (m, 4H); 7.44-7.28 (m, 11H); 7.20 (d, *J* = 15.5 Hz, 1H); 7.03 (m, 1H); 5.77 (ddd, J_1 = 16.90 Hz, J_2 = 10.3 Hz, J_3 = 6.1 Hz, 1H); 5.47 (dd, J_1 = 8.6 Hz, J_2 = 3.8 Hz, 1H); 5.09-4.98 (m, 2H); 4.69 (t, *J* = 8.7 Hz, 1H); 4.32-4.24 (m, 2H); 2.44-2.31 (m, 2H); 1.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.24; 153.75; 147.67; 139.61; 139.31; 136.04; 134.03; 133.80; 129.88; 129.74; 129.32; 128.79; 127.75; 127.59; 126.04; 122.50; 115.41; 73.25; 70.07; 57.85; 40.98; 27.13; 19.42. HRMS (TOF, ES+) $C_{32}H_{35}NO_4Si$ [M+Na]+ calc. mass 526.2414, found 526.2416.

(*R*)-3-((3*R*,5*S*)-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-enoyl)-4-phenyloxazolidin-2-one.



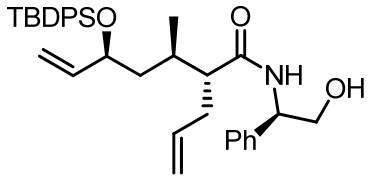
To a solution of copper iodide dimethyl sulfide complex (2.47 g, 10.40 mmol, 2.0 eq) in THF (0.23 M) under argon at -78 ^{o}C was slowly added MeLi (7.2 mL, 10.14 mmol, 1.95 eq). The reaction stirred at rt for 30 min. TMS-I (1.44 mL, 10.14 mmol, 1.95 eq) was added followed by stirring at -78 ^{o}C for an additional 5 min. A solution of (*R*)-3-((*S*,*E*)-5-((tert-butyldiphenylsilyl)oxy)hepta-2,6-dienoyl)-4-phenyloxazolidin-2-one (2.73 g, 5.20 mmol,1.0 eq) in THF (0.15 M) was cooled to -78 ^{o}C and transferred to the cuprate solution via cannula. After stirring at -78 ^{o}C overnight, NEt_3 (7.75 mL) was added and the reaction stirred for an additional hour. The reaction was quenched by the addition of pH 10 ammonia buffer, extracted with EtOAc, dried over Na_2SO_4, and concentrated. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 90% yield (2.53 g) and 17:1 d.r. $[\alpha]_D^{20}$ = -20.0 (c = 0.98, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) d 7.67-7.63 (m, 4H), 7.41-7.29 (m, 11H), 5.73 (ddd, *J* = 17.1, 10.4, 7.1 Hz, 1H), 5.40 (dd, *J* = 8.6, 3.6 Hz, 1H), 4.94-4.87 (m, 2H), 4.65 (t, *J* = 8.8 Hz, 1H), 4.26 (dd, J = 8.9, 3.6 Hz, 1H), 4.13-4.08 (m, 1H), 2.82-2.67 (m, 2H), 2.01-1.92 (m, 1H), 1.52-1.46 (m, 1H), 1.41-1.35 (m, 1H), 1.04 (s, 9H), 0.63 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 153.6, 140.8, 139.1, 136.04, 135.99, 134.2, 134.1, 129.5, 129.4, 129.1, 128.6, 127.5, 127.3, 125.8, 114.6, 73.0, 69.8, 57.6, 44.6, 42.6, 27.1, 26.0, 19.7, 19.3. HRMS (TOF, ES+) $C_{33}H_{39}NO_4Si$ [M+Na]+ calc. mass 564.2546, found 564.2546.

***(R)*-3-((2*R*,3*R*,5*S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-enoyl)-4-phenyloxazolidin-2-one, (14).**



To a solution of (R)-3-((3R,5S)-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-enoyl)-4-phenyloxazolidin-2-one (3.1 g, 5.72 mmol, 1.0 eq) in THF (0.1 M) under argon at -78 ^{o}C under argon was added 1.0 M LiHMDS (6.3 mL, 6.29 mmol, 1.1 eq). The reaction continued stirring for 2 h at -78 ^{o}C. In a separate flask a solution of allyl iodide (1.57 mL, 17.16 mmol, 3.0 eq) and HMPA (3.0 mL, 17.16 mmol, 3.0 eq) in THF (0.5 M) was prepared and transferred to the enolate solution at -78 ^{o}C. The reaction was warmed to -45 ^{o}C and continued stirring overnight. The reaction was quenched by the addition of saturated NH_4Cl, extracted with EtOAc, dried over Na_2SO_4, and concentrated. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 87% yield (2.89 g) and 15:1 d.r. $[\alpha]_D^{20}$ = -29.6 (c = 0.63, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4H), 7.46-7.31 (m, 9 H), 7.27-25 (m, 2H), 5.75 (ddd, *J* = 17.2, 10.3, 7.3 Hz, 1H), 5.53-5.43 (m, 1H), 5.35 (dd, *J* = 8.6, 3.4 Hz, 1H), 5.00-4.92 (m, 2H), 4.77-4.72 (m, 2H), 4.55 (t, *J* = 8.8 Hz, 1H), 4.22 (dd, *J* = 8.9, 3.5 Hz, 1H), 4.15-4.10 (m, 1H), 3.82-3.77 (m, 1H), 2.29-2.21 (m, 1H), 2.13-2.09 (m, 1H), 1.72-1.66 (m, 2H), 1.33-1.27 (m, 1H), 1.08 (s, 9H), 0.66 (d, *J* = 6.6. Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 153.3, 140.1, 139.0, 135.8, 135.8, 134.8, 134.2, 133.9, 129.5, 129.4, 128.8, 128.4, 127.4, 127.3, 125.9, 116.7, 115.2, 73.3, 69.3, 57.7, 47.3, 40.8, 32.9, 30.9, 26.9, 19.1, 17.2. HRMS (TOF, ES+) $C_{36}H_{43}NO_4Si$ [M+H]+ calc. mass 582.3040, found 582.3035.

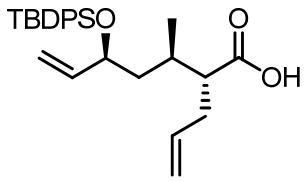
(2R,3R,5S)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-N-((R)-2-hydroxy-1-phenylethyl)-3-methylhept-6-enamide, (15).



To a solution of Weinreb salt (301 mg, 3.09 mmol, 3.0 eq) in THF (0.5 M) under argon at 0 ^{o}C, was added $AlMe_3$ (1.55 mL, 3.09 mmol, 3.0 eq) dropwise. The reaction stirred at 0 ^{o}C for 15 min then warmed to rt and stirred for an additional 15 min. The reaction was recooled to 0 ^{o}C and a solution of (R)-3-((2R,3R,5S)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-enoyl)-4-phenyloxazolidin-2-one (600 mg, 1.03 mmol, 1.0 eq) in THF (0.1 M) was added. The reaction was warmed to 50 ^{o}C and stirred overnight. The product was partitioned between water and EtOAc, extracted with EtOAc (3x), dried over Na_2SO_4, and concentrated *in vacuo*. Purification via flash chromatography (Hex/EtOAc 1:1) did not afford the desired Weinreb amide, however the product of ring opening of the oxazolidinone (**15**) was isolated in 59% yield (338 mg). Crystals of (2R,3R,5S)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-N-((R)-2-hydroxy-1-phenylethyl)-3-methylhept-6-enamide (**15**) were obtained as thin, colorless needles. Due to significant positional disorder in the structure, diffraction quality was poor at high angles requiring the use of a rotating-anode to obtain sufficient completeness for determination of the absolute structure. The molecule crystallized in the orthorhombic space group $P2_12_12_1$ with 2 molecules in the asymmetric unit. The absolute configuration was determined with a Flack parameter of -0.0032, with an e.s.d. of 0.0383. $[\alpha]_D^{20}$ = 4.3 (c = 0.43, $CHCl_3$). 1H NMR (400MHz, $CDCl_3$) δ (ppm): 7.72-7.62 (m, 4H); 7.44-7.27 (m, 9H); 7.25-7.19 (m, 2H); 5.94 (d, *J* = 6.7 Hz, 1H); 5.80 (ddd, J_1 = 17.3 Hz, J_2 = 10.4 Hz, J_3 = 7.1 Hz, 1H); 5.67-5.55 (m, 1H); 5.05-4.88 (m, 5H); 4.16 (m, 1H); 3.83-3.72 (m, 2H); 2.82 (br, 1H); 2.33-2.22 (m, 1H); 2.17-2.08 (m, 1H); 1.86 (ddd, J_1 = 10.6 Hz, J_2 = 6.5 Hz, J_3 = 4.2 Hz, 1H); 1.71-1.60 (m, 2H); 1.37 (ddd, J_1 = 14.0 Hz, J_2 = 10.5 Hz, J_3 = 4.7 Hz, 1H); 1.08 (s, 9H); 0.70 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.70; 140.40; 139.05; 136.12; 136.08; 136.05; 134.41; 134.09; 129.79; 129.69; 128.86; 127.92; 127.67; 127.51; 126.92; 116.80; 115.44; 77.36; 73.51; 66.70; 55.97;

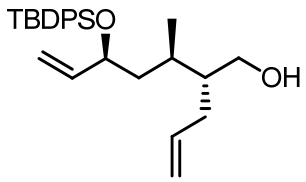
52.89; 42.74; 34.45; 31.69; 27.15; 19.37; 16.88.. HRMS (TOF, ES+) $C_{35}H_{45}NO_3Si$ [M+Na]+ calc. mass 578.3066, found 578.3065.

(2*R*,3*R*,5*S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-enoic acid.



To a solution of (*R*)-3-((*2R,3R,5S*)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-enoyl)-4-phenyloxazolidin-2-one (4.74 g, 8.14 mmol, 1.0 eq) in 3:1 THF/H_2O (0.2 M) under argon at 0 ^oC was added 30% H_2O_2 (3.65 mL, 32.15 mmol, 3.95 eq) followed by LiOH (390 mg, 16.28 mmol, 2.02 eq). The reaction was warmed to rt and continued stirring overnight. The reaction was quenched with saturated $NaHSO_4$ and NH_4Cl, extracted with EtOAc, dried over Na_2SO_4, and concentrated *in vacuo*. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 96% yield (3.42 g). $[\alpha]_D^{20}$ = 19.8 (c = 0.75, $CHCl_3$). ^1H NMR (400MHz, $CDCl_3$) d 7.75-7.70 (m, 4H), 7.47-7.38 (m, 6H), 5.86-5.68 (m, 2H), 5.10-4.98 (m, 4H), 4.24-4.19 (m, 1H), 2.38-2.29 (m, 2H), 2.17-2.13 (m, 1H), 1.74-1.66 (m, 2H), 1.46-1.39 (m, 1H), 1.12 (s, 9H), 0.72 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 140.2, 136.0, 135.9, 135.5, 134.2, 134.0, 129.6, 129.5, 127.5, 127.4, 116.7, 115.2, 73.3, 50.4, 42.3, 33.5, 31.0, 27.0, 19.2, 16.5. HRMS (TOF, ES+) $C_{27}H_{36}O_3Si$ [M+H]+ calc. mass 437.2512, found 437.2514.

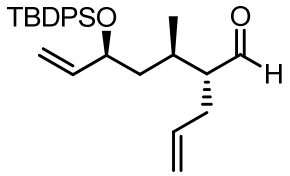
(*2R,3R,5S*)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-en-1-ol.



To a solution of (*2R,3R,5S*)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-enoic acid

(1.87 g, 4.27 mmol, 1.0 eq) in 4:1 THF/Et_2O (0.1 M) under argon at 0 ^oC was added $LiAlH_4$ (594 mg, 14.96 mmol, 3.5 eq). The reaction was allowed to warm to rt and continue stirring for 7 h. The reaction was cooled to 0 ^oC and quenched with H_2O. The reaction was then warmed to rt and diluted with Et_2O. Rochelle's Salt and 1.0 M NaOH were added followed by stirring for 30 min. The reaction was then filtered through Celite, extracted with EtOAc, dried over Na_2SO_4, and concentrated. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 84% yield (1.51 g). $[\alpha]_D^{20}$ = 35.6 (c = 0.59, $CHCl_3$). ^1H NMR (400MHz, $CDCl_3$) d 7.70-7.65 (m, 4H), 7.45-7.34 (m, 6H), 5.83-5.69 (m, 2H), 5.04-4.95 (m, 4H), 4.16-4.11 (m, 1H), 3.47 (dd, *J* = 5.8, 2.1 Hz, 2H), 2.03-1.91 (m, 2H), 1.59-1.49 (m, 2H), 1.43-1.39 (m, 1H), 1.34-1.27 (m, 1H), 1.23 (bs, 1H), 1.07 (s, 9H), 0.59 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 137.9, 135.95, 135.90, 134.4, 134.1, 115.8, 114.9, 73.7, 63.3, 45.7, 41.7, 33.3, 29.0, 27.0, 19.2, 16.2. HRMS (TOF, ES+) $C_{27}H_{38}O_2Si$ [M+H]+ calc. mass 423.2719, found 423.2723.

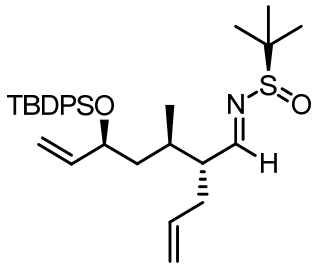
(*2R,3R,5S*)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-enal, (16).



To a solution of (*2R,3R,5S*)-2-allyl-5-((tert-butyldiphenylsilyl)oxy)-3-methylhept-6-en-1-ol (1.35 g, 3.18 mmol, 1.0 eq) in CH_2Cl_2 (0.1 M) under argon was added 4Å molecular sieves (0.5g/mmol) followed by NMO (551.8 mg, 4.71 mmol, 1.48 eq). The reaction was stirred at rt for 10 min after which TPAP (112 mg, 0.32 mmol, 0.1 eq) was added. The reaction continued to stir at rt for 5 h. The reaction was filtered through Celite and concentrated *in vacuo*. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 85% yield (1.14 g). $[\alpha]_D^{20}$ = 11.2 (c = 0.55, $CHCl_3$). ^1H NMR (400MHz, $CDCl_3$) δ 9.52 (d, J = 2.6 Hz,1H), 7.68-7.63 (m, 4H), 7.44-7.33 (m, 6H), 5.76 (ddd, J = 17.3, 10.3, 7.0 Hz, 1H), 5.70-5.60 (m, 1H), 5.02-4.95 (m, 4H), 4.18-4.13 (m, 1H), 2.37-2.31 (m, 1H), 2.20-2.15 (m, 1H), 2.07-2.01 (m, 1H), 1.82-1.79 (m, 1H), 1.59-1.53 (m, 1H), 1.42-1.35 (m, 1H), 1.06 (s, 9H), 0.66 (d, J =

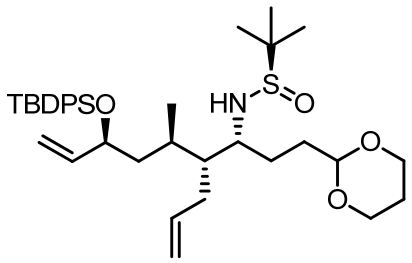
6.9 Hz, 3H); 13C NMR (100 MHz, $CDCl_3$) δ 204.9, 140.1, 136.0, 135.9, 135.7, 134.2, 134.0, 120.7, 129.6, 127.5, 127.4, 116.7, 115.4, 73.3, 56.3, 41.9, 30.4, 29.3, 27.0, 19.2, 16.5. HRMS (TOF, ES+) $C_{27}H_{36}O_2Si$ [M+Na]+ calc. mass 443.2382, found 443.2383.

(*R*)-*N*-((*2R,3R,5S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-en-1-ylidene)-2-methylpropane-2-sulfinamide, (18).



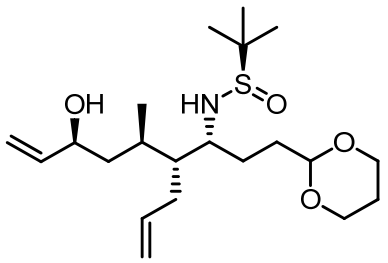
To a solution of (2*R*,3*R*,5*S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-enal (897 mg, 2.13 mmol, 1.0 eq) in THF (0.2 M) under argon was added $Ti(OEt)_4$ (1.11 mL, 5.33 mmol, 2.5 eq) followed by (S)-2-methylpropane-2-sulfinamide (284 mg, 2.34 mmol, 1.1 eq). The reaction was allowed to stir at 40 ^oC overnight. The reaction was quenched by the addition of saturated $NaHCO_3$, extracted with EtOAc, dried over sodium sulfate, and concentrated under vacuum. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 92% yield (1.03 g). $[\alpha]_D^{20}$ = -88.6 (c = 0.76, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.83 (d, J = 6.2 Hz, 1H); 7.70-7.62 (m, 4H); 7.45-7.32 (m, 6H); 5.75 (ddd, J_1 = 17.2 Hz, J_2 = 10.2 Hz, J_3 = 7.0 Hz, 1H); 5.64 (dddd, J_1 = 17.0 Hz, J_2 = 13.9 Hz, J_3 = 10.2 Hz, J_4 = 7.0 Hz, 1H); 5.04-4.96 (m, 2H); 4.96-4.88 (m, 2H); 4.16 (q, J = 7.2 Hz, 1H); 2.48-2.40 (m, 1H); 2.38-2.27 (m, 1H); 2.18-2.08 (m, 1H); 1.83-1.72 (m, 1H); 1.57 (ddd, J_1 = 13.2 Hz, J_2 = 8.4 Hz, J_3 = 4.8 Hz, 1H); 1.39 (ddd, J_1 = 14.1, J_2 = 9.3 Hz, J_3 = 5.3 Hz, 1H); 1.17 (s, 9H); 1.06 (s, 9H); 0.65 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.65; 140.49; 136.14; 136.07; 134.33; 134.21; 129.81; 129.66; 127.68; 127.51; 116.89; 115.25; 73.42; 56.60; 50.06; 42.68; 34.00; 31.40; 27.18; 22.65; 19.39; 16.09. HRMS (TOF, ES+) $C_{31}H_{45}NO_2SSi$ [M+Na]+ calc. mass 546.2838, found 546.2841.

(*R*)-*N*-((*3S,4R,5R,7S*)-4-allyl-7-((tert-butyldiphenylsilyl)oxy)-1-(1,3-dioxan-2-yl)-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide, (21).



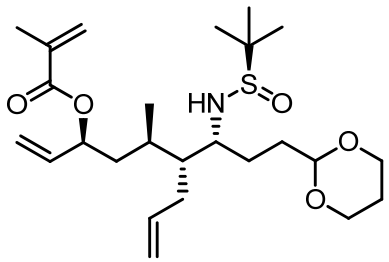
To a solution of (*R*)-*N*-((*2R,3R,5S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-en-1-ylidene)-2-methylpropane-2-sulfinamide (723 mg, 1.38 mmol, 1.0 eq) in CH_2Cl_2 (0.1 M) under argon at -45 ^oC was added (2-(1,3-dioxan-2-yl)ethyl)magnesium bromide (27.6 mL, 1.0 M in THF, 20.0 equiv) dropwise via cannula. The reaction was allowed to warm to room temperature and continue stirring for 24 h. The reaction was quenched with NH_4Cl, extracted with EtOAc, dried over sodium sulfate, and concentrated. Purification via flash chromatography (Hex:EtOAc 50-100%) afforded the desired product as a clear, colorless oil in 86% yield and 10:1 dr. The pure desired diastereomer can be isolated in 78% yield (689 mg). $[\alpha]_D^{20}$ = -9.7 (c = 0.38, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.70-7.61 (m, 4H); 7.45-7.31 (m, 6H); 5.84-5.69 (m, 2H); 5.09-4.92 (m, 4H); 4.44 (t, J = 4.6 Hz, 1H); 4.08 (dd, J_1 = 11.0 Hz, J_2 = 5.2 Hz, 3H); 3.78-3.68 (m, 2H); 3.41 (d, J = 6.0 Hz, 1H); 3.31-3.23 (m, 1H); 2.13-1.97 (m, 2H); 1.71-1.63 (m, 1H); 1.63-1.48 (m, 5H); 1.48-1.39 (m, 2H); 1.36-1.29 (m, 1H); 1.29-1.20 (m, 2H); 1.16 (s, 9H); 1.06 (s, 9H); 0.61 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.60; 139.36; 136.11; 136.07; 134.51; 134.29; 129.75; 129.62; 127.66; 127.50; 116.37; 115.36; 102.22; 73.92; 67.00; 66.98; 57.94; 55.97; 46.91; 40.99; 31.74; 31.25; 28.80; 27.80; 27.18; 25.92; 22.98; 19.35; 18.22. HRMS (TOF, ES+) $C_{37}H_{57}NO_4SSi$ [M+H]+ calc. mass 640.3852, found 640.3856.

(*R*)-*N*-((3*R*,4*R*,5*R*,7*S*)-4-allyl-1-(1,3-dioxan-2-yl)-7-hydroxy-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide.



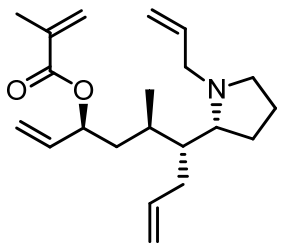
To a solution of (*R*)-*N*-((*3S,4R,5R,7S*)-4-allyl-7-((tert-butyldiphenylsilyl)oxy)-1-(1,3-dioxan-2-yl)-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide (930 mg, 1.45 mmol, 1.0 eq) in THF (0.1 M) under argon at 0 ^{o}C was added 1.0 M TBAF (5.0 mL, 5.08 mmol, 3.5 eq). The reaction was warmed to rt and continued stirring overnight. The reaction was quenched by the addition of saturated NH_4Cl, extracted with EtOAc, dried over sodium sulfate, and concentrated *in vacuo*. Purification via flash chromatography (EtOAc 100%) afforded the desired product as a clear, colorless oil in 97% yield (565 mg). $[\alpha]_D^{20}$ = -45.8 (c = 1.01, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 5.89-5.76 (m, 2H); 5.23 (d, *J* = 17.2 Hz, 1H); 5.14-5.06 (m, 2H); 5.04 (d, *J* = 10.2 Hz, 1H); 4.48 (t, *J* = 3.9 Hz, 1H); 4.16 (q, *J* = 6.6 Hz, 1H); 4.07 (dd, J_1 = 11.0, J_2 = 5.0, 2H); 3.78-3.68 (m, 2H); 3.52 (d, *J* = 6.6 Hz, 1H); 3.39-3.31 (m, 1H); 2.25-2.18 (m, 2H); 2.05 (qt, J_1 = 13.1 Hz, J_2 = 5.1 Hz, 1H); 1.94 (br, 1H); 1.84-1.73 (m, 1H); 1.70-1.49 (m, 6H); 1.42 (ddd, J_1 = 14.3 Hz, J_2 = 9.3 Hz, J_3 = 5.9 Hz, 1H); 1.36-1.29 (m, 1H); 1.18 (s, 9H); 1.02 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.13; 139.18; 116.54; 115.49; 102.16; 72.29; 67.00; 58.31; 56.10; 46.87; 40.58; 31.83; 31.74; 29.93; 28.71; 25.89; 22.99; 19.17. HRMS (TOF, ES+) $C_{21}H_{39}NO_4S$ [M+H]+ calc. mass 402.2678, found 402.2681.

(3*S*,5*R*,6*R*)-6-((*R*)-1-((*R*)-1,1-dimethylethylsulfinamido)-3-(1,3-dioxan-2-yl)propyl)-5-methylnona-1,8-dien-3-yl methacrylate.



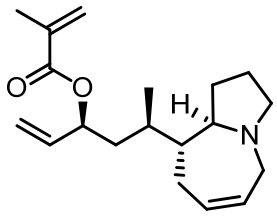
To a solution of (*R*)-*N*-((3*R*,4*R*,5*R*,7*S*)-4-allyl-1-(1,3-dioxan-2-yl)-7-hydroxy-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide (490 mg, 1.22 mmol, 1.0 eq) in CH_2Cl_2 (0.1 M) under argon at 0 ^oC was added NEt_3 (0.43 mL, 3.05 mmol, 2.5 eq) and DMAP (15 mg, 0.12 mmol, 0.1 eq). Methacrylic anhydride (0.4 mL, 2.68 mmol, 2.2 eq) was added dropwise and the reaction was warmed to rt and continued stirring for 3.5 hours. The reaction was quenched by the addition of saturated NH_4Cl, extracted with EtOAc, dried over sodium sulfate, and concentrated *in vacuo*. Purification via flash chromatography (EtOAc 50-100%) afforded the desired product as a clear, colorless oil in 82% yield (467 mg). $[\alpha]_D^{20}$ = -32.8 (c = 1.05, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 6.10 (s, 1H); 5.87-5.73 (m, 2H); 5.55 (s, 1H); 5.36-5.25 (m, 2H); 5.20 (d, J = 10.5 Hz, 1H); 5.10 (dd, J_1 = 17.3 Hz, J_2 = 1.6 Hz, 1H); 5.04 (dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz, 1H); 4.48 (t, J = 4.3 Hz, 1H); 4.08 (dd, J_1 = 10.7 Hz, J_2 = 5.0 Hz, 2H); 3.78-3.69 (m, 2H); 3.51 (d, J = 5.9 Hz, 1H); 3.41-3.33 (m, 1H); 2.24-2.16 (m, 2H); 2.05 (qt, J_1 = 13.2 Hz, J_2 = 5.0 Hz, 1H); 1.93 (s, 3H); 1.83-1.48 (m, 9H); 1.36-1.29 (m, 1H); 1.18 (s, 9H); 1.04 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.68; 139.07; 136.73; 136.38; 125.52; 117.76; 116.72; 102.12; 74.49; 67.02; 66.99; 57.59; 56.04; 46.44; 37.49; 31.72; 31.36; 29.74; 28.43; 25.91; 23.00; 18.45; 18.38. HRMS (TOF, ES+) $C_{37}H_{57}NO_4SSi$ [M+Na]+ calc. mass 470.2940, found 470.2943.

(3*S*,5*R*,6*R*)-6-((*R*)-1-allylpyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl methacrylate, (23).



To a vial containing (3*S*,5*R*,6*R*)-6-((*R*)-1-((*R*)-1,1-dimethylethylsulfinamido)-3-(1,3-dioxan-2-yl)propyl)-5-methylnona-1,8-dien-3-yl methacrylate (440 mg, 0.94 mmol, 1.0 eq), was added 95:5 TFA/H_2O (0.2 M). The reaction was allowed to stir at rt for 5 min, followed by dilution in 5 mL of toluene. The resulting crude imine was concentrated *in vacuo* and resuspended in 5 mL toluene and concentrated. The crude imine was then dissolved in DCE (0.1 M) followed by addition of PS-$BH(OAc)_3$ (2.0 g, 4.7 mmol, 5.0 eq). The reaction mixture was rotated at rt for 2 h. The crude pyrrolidine was then filtered through celite eluting with DCM and MeOH. The solution was concentrated and dissolved in DMF (0.2 M). K_2CO_3 (260 mg, 1.88 mmol, 2.0 eq) and allyl iodide (0.086 mL, 0.94 mmol, 1.0 eq) were added and the reaction was stirred at rt for 2 h, after which an additional 0.5 eq of allyl iodide (0.043 mL) was added. After stirring at rt for an additional hour, the reaction was filtered through celite eluting with DCM and MeOH, concentrated in vacuo, and purified by reverse phase chromatography (10-90% H_2O/MeCN) to afford the pure product in 46% isolated yield (143 mg). $[\alpha]_D^{20}$ = 80.5 (c = 0.49, $CHCl_3$). ^{1}H NMR (400MHz, C_6D_6) δ 6.20 (s, 1H); 5.93-5.73 (m, 3H); 5.68-5.60 (m, 1H); 5.29 (d, *J* = 17.2 Hz, 1H); 5.22 (t, *J* = 1.6 Hz, 1H); 5.14 (dd, J_1 = 17.2 Hz, J_2 = 1.1 Hz, 1H); 5.07-4.96 (m, 4H); 3.34-3.26 (m, 1H); 3.07-2.99 (m, 1H); 2.60 (dd, J_1 = 14.0, J_2 = 7.6 Hz, 1H); 2.42-2.35 (m, 1H); 2.18-1.96 (m, 4H); 1.87 (s, 3H); 1.83 (ddd, J_1 = 12.1 Hz, J_2 = 8.8 Hz, J_3 = 3.3 Hz, 1H); 1.68-1.58 (m, 1H); 1.58-1.38 (m, 5H); 1.04 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 166.20; 139.56; 137.39; 137.30; 137.06; 124.93; 117.27; 115.92; 115.22; 74.85; 66.25; 58.43; 54.23; 45.57; 38.46; 33.84; 29.04; 27.53; 23.34; 20.06; 18.50. HRMS (TOF, ES+) $C_{21}H_{34}NO_2$ [M+H]+ calc. mass 332.2590, found 332.2589.

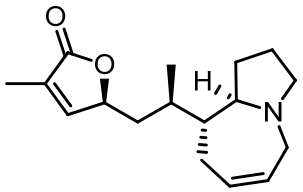
(3*S*,5*R*)-5-((9*R*,9a*R*)-2,3,5,8,9,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-9-yl)hex-1-en-3-yl methacrylate, (25).



To a solution of (3*S*,5*R*,6*R*)-6-((*R*)-1-allylpyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl methacrylate (27 mg, 0.081 mmol, 1.0 eq) in toluene (0.005 M) under argon was added CSA (37.6 mg, 0.162 mmol, 2.0 eq) and Grela catalyst (5.5 mg, 0.0081 mmol, 0.1 eq). The reaction

continued stirring for 6 h at rt before being concentrated *in vacuo*. The reaction was purified via reverse phase chromatography (MeCN/H_2O 10-90%) to afford the pure product of single ring closure in 65% yield (16.0 mg). $[\alpha]_D^{20}$ = 11.9 (c = 0.26, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 6.10 (s, 1H); 5.91-5.81 (m, 1H); 5.81-5.69 (m, 2H); 5.55 (s, 1H); 5.34-5.25 (m, 2H); 5.21 (d, *J* = 10.3 Hz, 1H); 3.41 (dd, J_1 = 15.2 Hz, J_2 = 6.6 Hz, 1H); 3.09 (t, *J* = 8.2 Hz, 1H); 2.87 (d, *J* = 15.2 Hz, 1H); 2.40-2.24 (m, 4H); 2.05-1.87 (m, 2H); 1.94 (s, 3H); 1.82-1.50 (m, 5H); 1.46-1.31 (m, 2H); 1.00 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 166.70; 136.82; 136.27; 132.07; 128.84; 125.44; 118.02; 74.93; 71.23; 57.81; 54.09; 49.77; 35.71; 32.27; 31.66; 26.00; 21.54; 19.17; 18.45. HRMS (TOF, ES+) $C_{19}H_{30}NO_2$ [M+H]+ calc. mass 304.2277, found 304.2278.

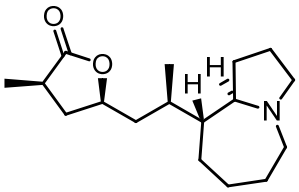
(*S*)-5-((*R*)-2-((9*R*,9a*R*)-2,3,5,8,9,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-9-yl)propyl)-3-methylfuran-2(5H)-one, (26).



To a solution of (3*S*,5*R*,6*R*)-6-((*R*)-1-allylpyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl methacrylate (27.5 mg, 0.083 mmol, 1.0 eq) in toluene (0.005 M) under argon was added CSA (38.5 mg, 0.166 mmol, 2.0 eq) followed by stirring for 10 min at rt. Grela catalyst (5.6 mg, 0.0083 mmol, 0.1 eq) was added and the reaction was allowed to stir at rt for 7.5 h. An additional 10 mol% catalyst (5.6 mg) was added and the reaction continued stirring for 15 h at 90 ^{o}C. An additional 10 mol% catalyst (5.6 mg) was then added and the reaction continued stirring for an additional 8 h. The reaction was then concentrated *in* vacuo and purified via reverse phase chromatography (MeCN/H_2O 10-90%) to afford the pure product of *bis*-ring closure in 52% yield (11.9 mg). $[\alpha]_D^{20}$ = 76.9 (c = 0.20, $CHCl_3$). ^{1}H NMR (500MHz, $CDCl_3$) δ (ppm): 7.05 (s, 1H); 5.83-5.75 (m, 1H); 5.73-5.65 (m, 1H); 4.90 (m, 1H); 3.45 (dd, J_1 = 15.5 Hz, J_2 = 6.0 Hz, 1H); 3.08 (t, *J* = 8.3 Hz, 1H); 2.86 (d, *J* = 15.5 Hz, 1H); 2.42 (dd, J_1 = 12.8 Hz, J_2 = 4.3 Hz, 1H); 2.34-2.23 (m, 2H); 2.04-1.95 (m, 1H); 1.92 (s, 3H); 1.93-1.85 (m, 1H); 1.83-1.63 (m, 4H); 1.61-1.53 (m, 1H); 1.52-1.46 (m, 1H); 1.45-1.39 (m, 1H); 1.05 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, CDCl3) δ (ppm): 174.23; 148.60; 130.93; 130.20; 129.14; 80.76; 70.46; 57.75; 54.79; 50.30; 35.82; 32.61; 32.49; 25.71; 21.87; 19.87; 10.85. HRMS (TOF, ES+) $C_{17}H_{26}NO_2$ [M+H]+

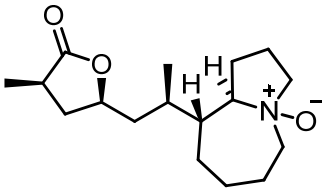
calc. mass 276.1964, found 276.1964.

(3*R*,5*S*)-3-methyl-5-((*R*)-2-((9*R*,9a*R*)-octahydro-1H-pyrrolo[1,2-a]azepin-9-yl)propyl)dihydrofuran-2(3H)-one (9a-*epi*-stemaphylline), (27).



To a solution of (*S*)-5-((*R*)-2-((9*R*,9a*R*)-2,3,5,8,9,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-9-yl)propyl)-3-methylfuran-2(5H)-one (18.1 mg, 0.066 mmol, 1.0 eq) in THF (0.025 M) at rt was added $Pd(OH)_2/C$ (4.5 mg, 0.25 eq). The reaction was then bubbled with hydrogen gas for 3 min, placed under an atmosphere of hydrogen (via balloon) and stirred at rt for 12 h. The reaction was then filtered through a pad of Celite and concentrated. Purification via reverse phase chromatography ($MeCN/H_2O$ 10-90%) afforded the pure product in 95% yield (17.5 mg). $[\alpha]_D^{20}$ = 27.7 (c = 0.68, $CHCl_3$). ^{1}H NMR (500MHz, $CDCl_3$) δ (ppm): 4.39-4.32 (m, 1H); 3.12-3.05 (m, 1H); 3.04-2.97 (m, 1H); 2.70-2.60 (m, 1H); 2.51 (ddd, J_1 = 12.5 Hz, J_2 = 8.4 Hz, J_3 = 5.3 Hz, 1H); 2.47-2.38 (m, 1H); 2.37-2.27 (m, 1H); 2.26-2.16 (m, 1H); 2.08-1.96 (m, 1H); 1.86-1.75 (m, 2H); 1.73-1.51 (m, 9H); 1.45-1.31 (m, 3H); 1.27 (d, J = 7.1 Hz, 3H); 1.00 (d, J = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, CDCl3) δ (ppm): 179.51; 78.33; 70.33; 58.53; 54.78; 51.85; 37.80; 36.86; 35.98; 32.34; 28.24; 25.28; 22.29; 19.67; 15.22. HRMS (TOF, ES+) $C_{17}H_{29}NO_2$ [M+H]+ calc. mass 280.2277, found 280.2275.

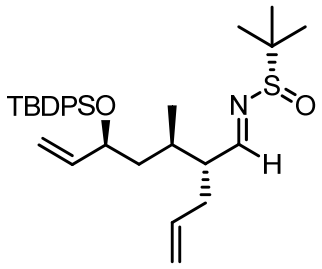
(9*R*,9a*R*)-9-((*R*)-1-((2*S*,4*R*)-4-methyl-5-oxotetrahydrofuran-2-yl)propan-2-yl)decahydropyrrolo[1,2-a]azepine 4-oxide (9a-*epi*-stemaphylline-*N*-oxide), (28).



To a solution of 9a-*epi*-stemaphylline (16.3 mg, 0.058 mmol, 1.0 eq) in DCM (0.005 M), was bubbled ozone for 3 min. Upon completion, the reaction was concentrated and purified via

reverse phase chromatography (MeCN/H_2O 10-90%) to afford the pure *N*-oxide in 53% yield (9.1 mg). $[\alpha]_D^{20}$ = 18.1 (c = 0.33, $CHCl_3$). ^{1}H NMR (600MHz, $CDCl_3$) δ (ppm): 4.40-4.33 (m, 1H); 3.69-3.62 (m, 1H); 3.61-3.54 (m, 1H); 3.53-3.46 (m, 1H); 3.26-3.15 (m, 2H); 2.71-2.63 (m, 1H); 5.56-2.45 (m, 3H); 2.43-2.35 (m, 1H); 2.21 (ddd, J_1 = 5.4 Hz, J_2 = 11.4 Hz, J_3 = 23.4 Hz, 1H); 2.15-2.10 (m, 1H); 2.09-2.00 (m, 1H); 1.94-1.79 (m, 3H); 1.75-1.65 (m, 3H); 1.64-1.57 (m, 1H); 1.46-1.33 (m, 3H); 1.30-1.22 (m, 1H); 1.27 (d, *J* = 7.2 Hz, 3H); 1.05 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (125 MHz, CDCl3) δ (ppm): 179.29; 81.12; 77.77; 72.24; 66.26; 42.96; 37.74; 36.65; 35.98; 31.92; 28.68; 25.47; 24.47; 21.73; 20.06; 19.16; 15.15. HRMS (TOF, ES+) $C_{17}H_{30}NO_3$ [M+H]+ calc. mass 296.2226, found 296.2226.

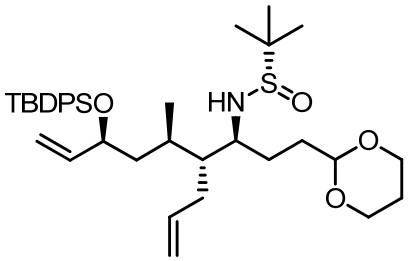
(*S*)-*N*-((*2R,3R,5S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-en-1-ylidene)-2-methylpropane-2-sulfinamide, (8).



To a solution of (2*R*,3*R*,5*S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-enal (990 mg, 2.35 mmol, 1.0 eq) in THF under argon was added $Ti(OEt)_4$ (1.23 mL, 5.88 mmol, 2.5 eq) followed by (*S*)-2-methylpropane-2-sulfinamide (313 mg, 2.59 mmol, 1.1 eq). The reaction was allowed to stir at 40 ^oC overnight. The reaction was quenched by the addition of saturated $NaHCO_3$, extracted with EtOAc, dried over sodium sulfate, and concentrated under vacuum. Purification via flash chromatography (Hex:EtOAc 4:1) afforded the desired product as a clear, colorless oil in 92% yield (1.13 g). $[\alpha]_D^{20}$ = 108.8 (c = 0.76, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.87 (d, *J* = 6.0 Hz, 1H); 7.68-7.62 (m, 4H); 7.45-7.32 (m, 6H); 5.73 (ddd, J_1 = 17.4 Hz, J_2 = 10.4 Hz, J_3 = 7.3 Hz, 1H); 5.64 (dddd, J_1 = 17.0 Hz, J_2 = 13.7 Hz, J_3 = 10.2 Hz, J_4 = 6.8 Hz, 1H); 5.03-4.93 (m, 3H); 4.89 (d, *J* = 17.2 Hz, 1H); 4.17-4.09 (m, 1H); 2.50-2.42 (m, 1H); 2.38-2.28 (m, 1H); 2.19-2.09 (m, 1H); 1.82-1.72 (m, 1H); 1.55 (ddd, J_1 = 13.3 Hz, J_2 = 8.7 Hz, J_3 = 4.4 Hz, 1H); 1.44-1.35 (m, 1H); 1.17 (s, 9H); 1.05 (s, 9H); 0.66 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.50; 140.42; 136.13; 136.06; 134.30; 134.19; 129.81; 129.67; 127.70;

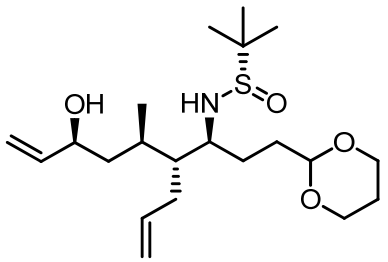
127.51; 116.82; 115.45; 73.50; 56.78; 50.24; 42.78; 33.78; 31.42; 27.17; 22.64; 19.39; 16.07. HRMS (TOF, ES+) $C_{31}H_{45}NO_2SSi$ [M+H]+ calc. mass 524.3019, found 524.3018.

(S)-N-((3S,4R,5R,7S)-4-allyl-7-((tert-butyldiphenylsilyl)oxy)-1-(1,3-dioxan-2-yl)-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide, (20a).



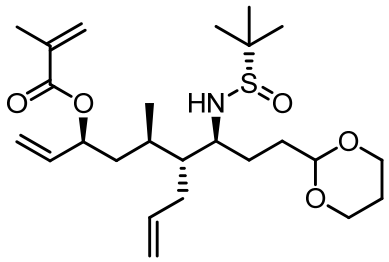
To a solution of (*S*)-*N*-((*2R,3R,5S*)-2-allyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-methylhept-6-en-1-ylidene)-2-methylpropane-2-sulfinamide (867 mg, 1.66 mmol, 1.0 eq) in CH_2Cl_2 (0.1 M) under argon at -45 ^oC was added (2-(1,3-dioxan-2-yl)ethyl)magnesium bromide (16.5 mL, 1.0 M in THF, 10.0 equiv) dropwise. The reaction was allowed to warm to room temperature and continue stirring for 24 h. The reaction was quenched with NH_4Cl, extracted with EtOAc, dried over sodium sulfate, and concentrated. Purification via flash chromatography (Hex:EtOAc 50-100%) afforded the desired product as a clear, colorless oil in 95% yield and 1.2:1 dr. The pure desired diastereomer can be isolated in 51% yield (542 mg). $[\alpha]_D^{20}$ = 35.9 (c = 1.68, $CHCl_3$). ^1H NMR (400MHz, $CDCl_3$) δ 7.70-7.62 (m, 4H); 7.44-7.31 (m, 6H); 5.93-5.82 (m, 1H); 5.77 (ddd, J_1 = 17.5 Hz, J_2 = 10.5 Hz, J_3 = 7.3 Hz, 1H); 5.08-4.90 (m, 4H); 4.46 (t, J = 4.6 Hz, 1H); 4.11-4.03 (m, 3H); 3.77-3.66 (m, 2H); 3.56 (d, J = 9.3 Hz, 1H); 3.27-3.19 (m, 1H); 2.13-1.97 (m, 3H); 1.81-1.62 (m, 4H); 1.54-1.42 (m, 2H); 1.40-1.28 (m, 3H); 1.27-1.20 (m, 1H); 1.17 (s, 9H); 1.05 (s, 9H); 0.57 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.59; 140.36; 136.06; 136.01; 134.38; 134.25; 129.66; 129.53; 127.59; 127.42; 115.78; 115.25; 102.33; 102.03; 73.95; 66.93; 66.89; 59.70; 56.07; 48.76; 43.11; 35.23; 32.35; 30.94; 27.10; 26.08; 25.91; 25.83; 23.97; 22.89; 19.29; 17.78. HRMS (TOF, ES+) $C_{37}H_{57}NO_4SSi$ [M+Na]+ calc. mass 640.3852, found 640.3856.

(S)-N-((3S,4R,5R,7S)-4-allyl-1-(1,3-dioxan-2-yl)-7-hydroxy-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide.



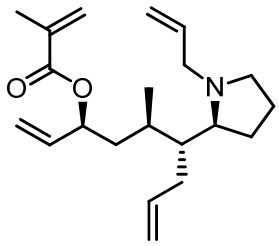
To a solution of (S)-N-((3S,4R,5R,7S)-4-allyl-7-((tert-butyldiphenylsilyl)oxy)-1-(1,3-dioxan-2-yl)-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide (595 mg, 0.93 mmol, 1.0 eq) in THF (0.1 M) under argon at 0 ^{o}C was added TBAF (3.25 mL, 3.25 mmol, 3.5 eq). The reaction was warmed to rt and continued stirring overnight. The reaction was quenched by the addition of saturated NH_4Cl, extracted with EtOAc, dried over sodium sulfate, and concentrated *in vacuo*. Purification via flash chromatography (EtOAc 100%) afforded the desired product as a clear, colorless oil in 97% yield (362 mg). $[\alpha]_D^{20}$ = 28.4 (c = 0.80, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 5.95-5.81 (m, 2H); 5.25 (d, J = 17.3 Hz, 1H); 5.15-5.07 (m, 2H); 5.04 (d, J = 10.1 Hz, 1H); 4.50 (t, J = 4.8 Hz, 1H); 4.33-4.25 (m, 1H); 4.09 (dd, J_1 = 11.0 Hz, J_2 = 5.1 Hz, 2H); 3.80-3.70 (m, 3H); 3.34 (tt, J_1 = 9.5 Hz, J_2 = 3.1 Hz, 1H); 2.31-2.13 (m, 2H); 2.13-1.99 (m, 2H); 1.97-1.88 (m, 1H); 1.82 (ddd, J_1 = 13.6 Hz, J_2 = 6.7 Hz, J_3 = 4.3 Hz, 1H); 1.78-1.67 (m, 2H); 1.66-1.50 (m, 4H); 1.49-1.37 (m, 2H); 1.36-1.30 (m, 1H); 1.20 (s, 9H); 0.97 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.24; 139.73; 116.26; 114.99; 102.19; 72.02; 67.05; 59.21; 56.30; 48.09; 41.23; 32.48; 32.28; 30.43; 27.34; 25.93; 23.03; 19.34. HRMS (TOF, ES+) $C_{21}H_{40}NO_4S$ [M+H]+ calc. mass 402.2678, found 402.2681.

(3S,5R,6R)-6-((S)-1-((S)-1,1-dimethylethylsulfinamido)-3-(1,3-dioxan-2-yl)propyl)-5-methylnona-1,8-dien-3-yl methacrylate, (22).



To a solution of (S)-N-((3S,4R,5R,7S)-4-allyl-1-(1,3-dioxan-2-yl)-7-hydroxy-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide (563 mg, 1.4 mmol, 1.0 eq) in CH_2Cl_2 (0.1 M) under argon at 0 ^oC was added NEt_3 (0.49 mL,. 3.5 mmol, 2.5 eq) and DMAP (85.5 mg, 0.70 mmol, 0.5 eq). Methacrylic anhydride (0.46 mL, 3.08 mmol, 2.2 eq) was added dropwise and the reaction was warmed to rt and continued stirring for 3.5 hours. The reaction was quenched by the addition of saturated NH_4Cl, extracted with EtOAc, dried over sodium sulfate, and concentrated *in vacuo*. Purification via flash chromatography (EtOAc 50-100%) afforded the desired product as a clear, colorless oil in 73% yield (483 mg). $[\alpha]_D^{20}$ = 36.6 (c = 0.80, $CHCl_3$). ^1H NMR (400MHz, $CDCl_3$) δ 6.11 (s, 1H); 5.97-5.84 (m, 1H); 5.78 (ddd, J_1 = 17.4 Hz, J_2 = 10.4 Hz, J_3 = 7.0, 1H); 5.55 (t, J = 1.7 Hz, 1H); 5.35-5.25 (m, 2H); 5.20 (d, J = 10.4 Hz, 1H); 5.11 (d, J = 17.3 Hz, 1H); 5.04 (d, J = 10.0 Hz, 1H); 4.51 (t, J = 5.0 Hz, 1H); 4.09 (dd, J_1 = 10.7 Hz, J_2 = 5.0 Hz, 2H); 3.79-3.69 (m, 2H); 3.56 (d, J = 9.6 Hz, 1H); 3.35 (tt, J_1 = 9.6 Hz, J_2 = 2.7 Hz, 1H); 2.27-2.14 (m, 2H); 2.07 (qt, J_1 = 13.4 Hz, J_2 = 5.0 Hz, 1H); 2.02-1.92 (m, 1H); 1.94 (s, 3H); 1.89-1.82 (m, 1H); 1.80-1.71 (m, 1H); 1.65-1.46 (m, 6H); 1.46-1.39 (m, 1H); 1.37-1.30 (m, 1H); 1.19 (s, 9H); 1.00 (d, J = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.53; 139.74; 136.61; 136.34; 125.36; 117.58; 116.12; 101.92; 74.68; 66.89; 66.86; 59.35; 56.11; 48.69; 39.26; 32.40; 32.24; 31.55; 26.41; 25.77; 22.83; 18.32; 17.81. HRMS (TOF, ES+) $C_{25}H_{44}NO_5S$ [M+H]+ calc. mass 470.2940, found 470.2943.

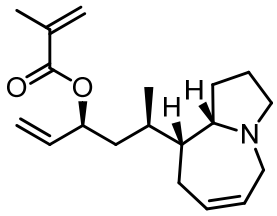
(3S,5R,6R)-6-((S)-1-allylpyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl methacrylate, (7).



To a vial containing (3S,5R,6R)-6-((S)-1-((S)-1,1-dimethylethylsulfinamido)-3-(1,3-dioxan-2-yl)propyl)-5-methylnona-1,8-dien-3-yl methacrylate (287 mg, 0.61 mmol, 1.0 eq), was added 95:5 TFA/H_2O (0.2 M). The reaction was allowed to stir at rt for 5 min, followed by dilution in 5 mL of toluene. The resulting crude imine was concentrated *in vacuo* and resuspended in 5 mL

toluene and concentrated. The crude imine was then dissolved in DCE (0.1 M) followed by addition of PS-$BH(OAc)_3$ (1.32 g, 3.05 mmol, 5.0 eq). The reaction mixture was rotated at rt for 2 h. The crude pyrrolidine was then filtered through celite eluting with DCM and MeOH. The solution was concentrated and dissolved in DMF (0.2 M). K_2CO_3 (253 mg, 1.83 mmol, 3.0 eq) and allyl iodide (0.056 mL, 0.61 mmol, 1.0 eq) were added and the reaction was stirred at rt for 2 h, after which an additional 0.5 eq of allyl iodide (0.028 mL) was added. After stirring at rt for an additional hour, the reaction was filtered through celite eluting with DCM and MeOH, concentrated in vacuo, and purified by reverse phase chromatography (10-90% H_2O/MeCN) to afford the pure product in 47% isolated yield (97 mg). $[\alpha]_D^{20}$ = -36.2 (c = 0.48, $CHCl_3$). ^{1}H NMR (400MHz, C_6D_6) δ 6.20-6.17 (m, 1H); 5.96-5.80 (m, 2H); 5.80-5.71 (m, 1H); 5.67 (q, J = 7 Hz, 1H); 5.28 (dt, J_1 = 17.0 Hz, J_2 = 1.4 Hz, 1H); 5.23-5.15 (m, 2H); 5.08-4.96 (m, 4H); 5.07-4.96 (m, 4H); 3.52-3.44 (m, 1H); 3.06-2.99 (m, 1H); 2.65 (dd, J_1 = 13.6, J_2 = 7.7 Hz, 1H); 2.57-2.49 (m, 1H); 2.30 (td, J_1 = 8.7 Hz, J_2 = 2.6 Hz, 1H); 1.98-1.89 (m, 2H); 1.87 (s, 3H); 1.85-1.74 (m, 1H); 1.74-1.64 (m, 3H); 1.56-1.34 (m, 5H); 0.83 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 166.26; 139.79; 137.32; 137.22; 125.01; 116.93; 116.02; 115.20; 73.79; 63.41; 57.41; 53.70; 43.23; 40.25; 31.61; 30.38; 26.88; 23.95; 18.48; 16.67. HRMS (TOF, ES+) $C_{21}H_{34}NO_2$ [M+H]+ calc. mass 332.2590, found 332.2588.

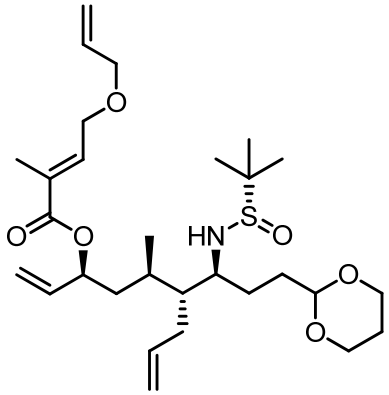
(3S,5R)-5-((9R,9aS)-2,3,5,8,9,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-9-yl)hex-1-en-3-yl methacrylate, (29).



To a solution of (3S,5R,6R)-6-((S)-1-allylpyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl methacrylate (10 mg, 0.03 mmol, 1.0 eq) in toluene (0.005 M) under argon was added CSA (14 mg, 0.06 mmol, 2.0 eq) and benzoquinone (0.8 mg, 0.0075 mmol, 0.25 eq). After stirring at rt for 10 min, Hoveyda Grubbs II catalyst (1.9 mg, 0.003 mmol, 10 mol%) was added and the

reaction continued stirring for 15 h at rt. An additional 10 mol % catalyst (1.9 mg) was added followed by stirring at rt for an additional 8.5 h. After addition of 10 mol% catalyst (1.9 mg) and stirring for 15 additional h the reaction was concentrated *in vacuo*. The reaction was purified via reverse phase chromatography (MeCN/H_2O 10-90%) followed by additional purification via flash chromatography (DCM/MeOH/NH_4OH 94.9:5:0.1) to afford the product of a single ring closure in 48% yield (4.4 mg). $[\alpha]_D^{20}$ = -38.1 (c = 0.89, $CHCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 6.11 (s, 1H); 5.94-5.85 (m, 2H); 5.73-5.68 (m, 1H); 5.59-5.53 (m, 2H); 5.17 (d, *J* = 17.3 Hz, 1H); 5.07 (d, *J* = 9.8 Hz, 1H); 3.38-3.2 (m, 1H); 3.12-3.06 (m, 1H); 2.69 (dd, J_1 = 13.1 Hz, J_2 = 7.5 Hz, 1H); 2.58 (dd, J_1 = 14.0 Hz, J_2 = 8.9 Hz, 1H); 2.53-2.46 (m, 1H); 2.16-2.08 (m, 1H); 1.95 (s, 3H); 1.93-1.87 (m, 1H); 1.85 (dt, J_1 = 13.1 Hz, J_2 = 2.5 Hz, 1H); 1.79-1.71 (m, 1H); 1.70-1.58 (m, 4H); 1.55-1.47 (m, 1H); 1.42-1.34 (m, 1H); 1.01 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 166.94; 136.88; 136.59; 133.58; 131.31; 125.39; 116.51; 73.83; 65.25; 56.93; 54.21; 43.65; 41.66; 36.55; 25.51; 24.40; 22.60; 21.75; 18.49. HRMS (TOF, ES+) $C_{19}H_{30}NO_2$ [M+H]+ calc. mass 304.2277, found 304.2275.

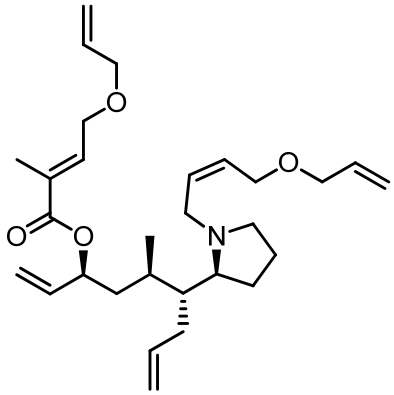
(*E*)-(3*S*,5*R*,6*R*)-6-((*S*)-1-((*S*)-1,1-dimethylethylsulfinamido)-3-(1,3-dioxan-2-yl)propyl)-5-methylnona-1,8-dien-3-yl 4-(allyloxy)-2-methylbut-2-enoate, (31).



To a solution of triethylamine (0.347 mL, 3.43 mmol, 5.0 eq) in CH_2Cl_2 (0.1 M) under argon was added DMAP (84 mg, 0.686 mmol, 1.0 eq), 2-methyl-6-nitrobenzoic anhydride (MNBA) (590 mg, 1.715 mmol, 2.5 eq) and carboxylic acid **30** (268 mg, 1.715 mmol, 2.5 eq) at room temperature. After stirring for 10 min, (S)-N-((3S,4R,5R,7S)-4-allyl-1-(1,3-dioxan-2-yl)-7-hydroxy-5-methylnon-8-en-3-yl)-2-methylpropane-2-sulfinamide (275.6 mg, 0.686 mmol, 1.0 eq) was added. The mixture was refluxed with stirring for 3 h. The mixture was cooled down to 0

°C, and a saturated aqueous solution of NH_4Cl was added. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with sat. $NaHCO_3$ and dried over MgSO4. Concentration under vacuum gave the crude product, and purification by silica gel column chromatography (1:1 Hex/EtOAc) afforded the desired product as a colorless oil in 98% yield (361 mg). $[\alpha]_D^{20}$ = 60.5 (c = 0.58, $CHCl_3$) ^{1}H NMR (400MHz, $CDCl_3$) δ 6.83 (td, J_1 = 5.9 Hz, J_2 = 1.3 Hz, 1H); 5.98-5.84 (m, 2H); 5.76 (ddd, J_1 = 17.3 Hz, J_2 = 10.4 Hz, J_3 = 7.1 Hz, 1H); 5.35-5.24 (m, 3H); 5.20 (t, J = 10.3 Hz, 2H); 5.10 (d, J = 17.3 Hz, 1H); 5.03 (d, J = 10.0 Hz, 1H); 4.51 (t, J = 4.9 Hz, 1H); 4.16 (d, J = 5.9 Hz, 2H); 4.08 (dd, J_1 = 10.9 Hz, J_2 = 4.9 Hz, 2H); 4.01 (d, J = 5.7 Hz, 2H); 3.74 (t, J = 12.3 Hz, 2H); 3.56 (d, J = 9.5 Hz, 1H); 3.34 (t, J = 10.0 Hz, 1H); 2.27-2.13 (m, 2H); 2.06 (qt, J_1 = 12.6 Hz, J_2 = 4.9 Hz, 1H); 2.00-1.92 (m, 1H); 1.83 (s, 3H); 1.80-1.70 (m, 1H); 1.68 (s, 1H); 1.63-1.38 (m, 5H); 1.33 (d, J = 13.6 Hz, 1H); 1.18 (s, 9H); 0.99 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.71; 139.90; 138.18; 136.45; 134.48; 129.61; 117.81; 117.67; 116.22; 102.06; 74.92; 71.83; 67.03; 67.00; 66.93; 59.53; 56.25; 48.83; 39.39; 32.51; 32.38; 31.71; 26.48; 25.89; 22.95; 17.91; 12.97. HRMS (TOF, ES+) $C_{29}H_{50}NO_6S$ [M+H]+ calc. mass 540.3359, found 540.3354.

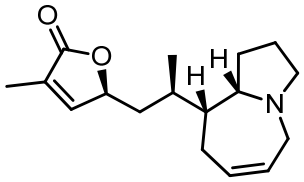
(E)-(3S,5R,6R)-6-((S)-1-((Z)-4-(allyloxy)but-2-en-1-yl)pyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl 4-(allyloxy)-2-methylbut-2-enoate, (33).



To a vial containing (E)-(3S,5R,6R)-6-((S)-1-((S)-1,1-dimethylethylsulfinamido)-3-(1,3-dioxan-2-yl)propyl)-5-methylnona-1,8-dien-3-yl 4-(allyloxy)-2-methylbut-2-enoate (276.4 mg, 0.512 mmol, 1.0 eq), was added 95:5 TFA/H_2O (0.2 M). The reaction was allowed to stir at rt for 5 min, followed by dilution in 5 mL of toluene. The resulting crude imine was concentrated *in vacuo* and resuspended in 5 mL toluene and concentrated. The crude imine was then dissolved in DCE (0.1 M) followed by addition of PS-$BH(OAc)_3$ (1.11 g, 2.56 mmol, 5.0 eq). The reaction

mixture was rotated at rt for 2 h. The crude pyrrolidine was then filtered through celite eluting with DCM and MeOH. The solution was concentrated and dissolved in DMF (0.2 M). K_2CO_3 (212 mg, 1.54 mmol, 3.0 eq) and allylic bromide **32** (118 mg, 0.61 mmol, 1.1 eq) were added and the reaction was stirred at rt for 2 h, after which, the reaction was filtered through celite eluting with DCM and MeOH, concentrated in vacuo, and purified by reverse phase chromatography (10-90% H_2O/MeCN) to afford the pure product in 40% isolated yield (97 mg). $[\alpha]_D^{20}$ = -36.2 (c = 0.48, $CHCl_3$). $[\alpha]_D^{20}$ = -42.7 (c = 1.26, $CDCl_3$). ^{1}H NMR (400MHz, $CDCl_3$) δ 6.83 (td, J_1 = 5.9 Hz, J_2 = 1.3 Hz, 1H); 5.96-5.88 (m, 2H); 5.76 (ddd, J_1 = 17.2 Hz, J_2 = 10.5 Hz, J_3 = 6.7 Hz, 1H); 5.73-5.62 (m, 3H); 5.34 (q, J = 6.9 Hz, 1H); 5.32-5.20 (m, 4H); 5.20-5.15 (m, 2H); 4.96 (d, J = 17.0 Hz, 1H); 4.91 (d, J = 10.0 Hz, 1H); 4.17 (dd, J_1 = 5.9 Hz, J_2 = 1.0 Hz, 2H); 4.12 (dd, J_1 = 12.2 Hz, J_2 = 6.0 Hz, 1H); 4.06 (dd, J_1 = 12.0 Hz, J_2 = 5.4 Hz, 1H); 4.01 (dt, J_1 = 5.7 Hz, J_2 = 1.3 Hz, 2H); 3.99-3.97 (m, 2H); 3.37 (dd, J_1 = 13.7 Hz, J_2 = 4.6 Hz, 1H); 3.07-3.00 (m, 1H); 2.79 (dd, J_1 = 13.8 Hz, J_2 = 7.2 Hz, 1H); 2.42-2.30 (m, 2H); 2.06-1.96 (m, 1H); 1.92 (dt, J_1 = 14.1 Hz, J_2 = 9.0 Hz, 1H); 1.84 (s, 3H); 1.74-1.53 (m, 9H); 0.86 (d, J = 6.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.74; 139.37; 138.07; 136.69; 135.00; 134.47; 131.04; 129.59; 128.22; 117.73; 117.21; 117.17; 115.21; 74.18; 71.90; 71.31; 67.00; 66.05; 63.92; 53.71; 50.92; 43.10; 39.98; 31.19; 30.10; 26.56; 23.55; 16.47; 12.99. HRMS (TOF, ES+) $C_{29}H_{46}NO_4$ [M+H]+ calc. mass 472.3427, found 472.3429.

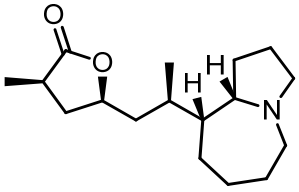
(S)-5-((R)-2-((9R,9aS)-2,3,5,8,9,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-9-yl)propyl)-3-methylfuran-2(5H)-one, (6).



(E)-(3S,5R,6R)-6-((S)-1-((Z)-4-(allyloxy)but-2-en-1-yl)pyrrolidin-2-yl)-5-methylnona-1,8-dien-3-yl 4-(allyloxy)-2-methylbut-2-enoate (90 mg, 0.19 mmol, 1.0 eq) was placed under argon and dissolved in toluene (0.02 M). CSA (88.7 mg, 0.38 mmol, 2.0 equiv) was added and the solution was stirred for 10 min at rt. In a two neck flask equipped with a reflux condenser a solution of

Hoveyda Grubbs II catalyst (23.8 mg, 0.038 mmol, 0.2 eq) was dissolved in toluene (0.007 M relative to tetraene **33**) and heated to vigorous reflux. After the solution was brought to reflux the reaction mixture was sparged with argon through the second neck of the flask. The solution of tetraene **33** and CSA in toluene was then added dropwise via syringe over ~10 min. After 20 minutes of additional heating under argon sparge the reaction mixture was concentrated *in vacuo* and purified by reverse phase chromatography (10-90% H_2O/MeCN) to afford the pure product in 37% isolated yield (19.3 mg) and with minimal epimerization (10:1). $[\alpha]_D^{20}$ = -13.0 (c = 1.26, $CHCl_3$) ^{1}H NMR (400MHz, $CDCl_3$) δ 6.14 (m, 1H); 5.72-5.67 (m, 1H); 5.49-5.44 (m, 1H); 4.47-4.42 (m, 1H); 4.47-4.42 (m, 1H); 3.20 (dd, J_1 = 16.7 Hz, J_2 = 6.2 Hz, 1H); 2.98 (d, J = 16.7 Hz, 1H); 2.81 (td, J_1 = 8.2 Hz, J_2 = 3.5 Hz, 1H); 2.54-5.48 (m, 1H); 229-2.18 (m, 2H); 1.75-1.70 (m, 1H); 1.70-1.59 (m, 6H); 1.58-1.52 (m, 1H); 1.52-1.44 (m, 2H); 1.44-1.38 (m, 1H); 1.14 (ddd, J_1 = 14.0 Hz, J_2 = 8.8 Hz, J_3 = 7.5 Hz, 1H); 0.81 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.31; 148.25; 131.15; 129.69; 128.35; 127.98; 80.16; 67.21; 54.79; 54.74; 52.43; 46.81; 39.02; 32.33; 28.10; 27.44; 23.03; 19.70; 10.64. HRMS (TOF, ES+) $C_{37}H_{57}NO_4SSi$ [M+Na]+ calc. mass 470.2940, found 470.2943.

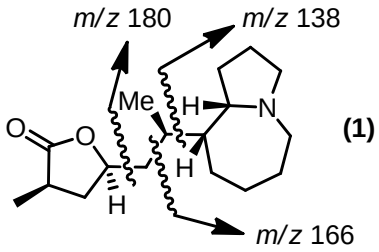
(3*R*,5*S*)-3-methyl-5-((*R*)-2-((9*R*,9a*S*)-octahydro-1H-pyrrolo[1,2-a]azepin-9-yl)propyl)dihydrofuran-2(3H)-one (stemaphylline), (1).



To a solution of (S)-5-((R)-2-((9R,9aS)-2,3,5,8,9,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-9-yl)propyl)-3-methylfuran-2(5H)-one (17.9 mg, 0.065 mmol, 1.0 eq) in THF (0.025 M) at rt was added $Pd(OH)_2$/C (5.4 mg, 0.16 eq). The reaction was then bubbled with hydrogen gas for 3 minutes, placed under an atmosphere of hydrogen (via balloon) and stirred at rt for 12 h. An additional portion of $Pd(OH)_2$ (5.4 mg, 0.16 eq) was added and the reaction was again bubbled with hydrogen gas for 3 min, placed under an atmosphere of hydrogen (via balloon) and stirred at rt for 8 h. The reaction was then filtered through a pad of Celite and concentrated *in vacuo*.

Purification via reverse phase chromatography (MeCN/H_2O 10-90%) afforded the pure product in 62% yield (11.3 mg). $[\alpha]_D^{20}$ = -36.2 (c = 0.70, $CHCl_3$). ^{1}H NMR (600MHz, $CDCl_3$) δ (ppm): 4.46-4.40 (m, 1H); 3.08-2.91 (m, 3H); 2.72-2.54 (m, 3H); 2.54-2.48 (m, 1H); 2.00-1.94 (m, 1H); 1.84-1.77 (m, 2H); 1.77-1.68 (m, 3H); 1.68-1.55 (m, 5H); 1.53-1.43 (m, 3H); 1.38-1.30 (m, 1H); 1.26 (d, *J* = 7.0 Hz, 3H); 0.98 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, CDCl3) δ (ppm): 179.65; 78.08; 64.87; 53.94; 52.22; 46.12; 39.59; 37.81; 35.80; 33.01; 28.15; 28.07; 27.73; 26.15; 23.73; 18.94; 14.99. HRMS (TOF, ES+) $C_{17}H_{29}NO_2$ [M+H]+ calc. mass 280.2277, found 280.2279.

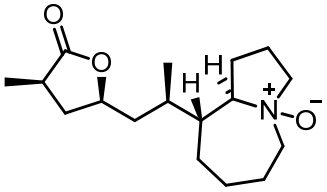
The observed fragmentation pattern of synthetic stemaphylline matched that reported by Lie and co-workers for stemaphylline.



(1)

$C_{12}H_{22}N^{\bullet}$: calc mass 180.1752, found 180.1750.
$C_{11}H_{20}N^{\bullet}$: calc mass 166.1596, found 166.1603.
$C_{19}H_{16}N^{\bullet}$: calc mass 138.1283, found 138.1321.

(9*R*,9a*R*)-9-((*R*)-1-((2*S*,4*R*)-4-methyl-5-oxotetrahydrofuran-2-yl)propan-2-yl)decahydropyrrolo[1,2-a]azepine 4-oxide (stemaphylline-*N*-oxide), (2).



To a solution of stemaphylline (7.0 mg, 0.025 mmol, 1.0 eq) in CH_2Cl_2 (0.02 M) at 0 °C under argon was added mCPBA (6.8 mg, 0.028 mmol, 1.1 eq). The reaction stirred at 0 °C for 30 min, then concentrated *in vacuo*, and purified via reverse phase chromatography (MeCN/H_2O 10-90%) to afford the pure product in 74% yield (5.5 mg). $[\alpha]_D^{20}$ = -42.3 (c = 0.22, $CHCl_3$). ^{1}H NMR (600MHz, $CDCl_3$) δ (ppm): 4.71-4.65 (m, 1H); 3.70-3.60 (m, 1H); 3.60-3.53 (m, 2H); 3.40-3.35 (m, 2H); 2.70-2.62 (m, 2H); 2.60-2.54 (m, 1H); 2.41-2.30 (m, 1H); 2.30-2.20 (m, 1H); 2.12-2.04 (m 1H); 2.00-1.88 (m, 2H); 1.87-1.80 (m, 1H); 1.80-1.71 (m, 2H); 1.70-1.64 (m, 2H); 1.62-1.50 (m, 3H); 1.44 (q, *J* = 12.2 Hz, 1H); 1.25 (d, *J* = 7.0 Hz, 3H); 0.90 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, CDCl3) δ (ppm): 179.94; 81.85; 76.73; 71.31; 67.48; 40.84; 38.05; 35.97; 35.42; 35.18; 25.66; 25.36; 25.32; 20.95; 19.62; 17.53; 15.21. HRMS (TOF, ES+) $C_{17}H_{30}NO_3$ [M+H]+ calc. mass 296.2226, found 296.2225.

References:

1) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 6th Ed.; Elsevier: Burlington, MA, 2009.

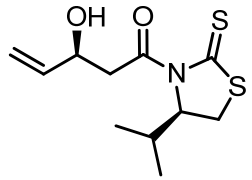
2) Burla, M.C., Caliandro, R., Camalli, M., Carrozini, G., Cascarano, G.L., De Caro, L., Giacovazzo, C., Polidori, G., & Spagna, R. 2005. SIR2004: an improved tool for crystal structure determination and refinement. Journal of Applied Crystallography, 38, 381-388.

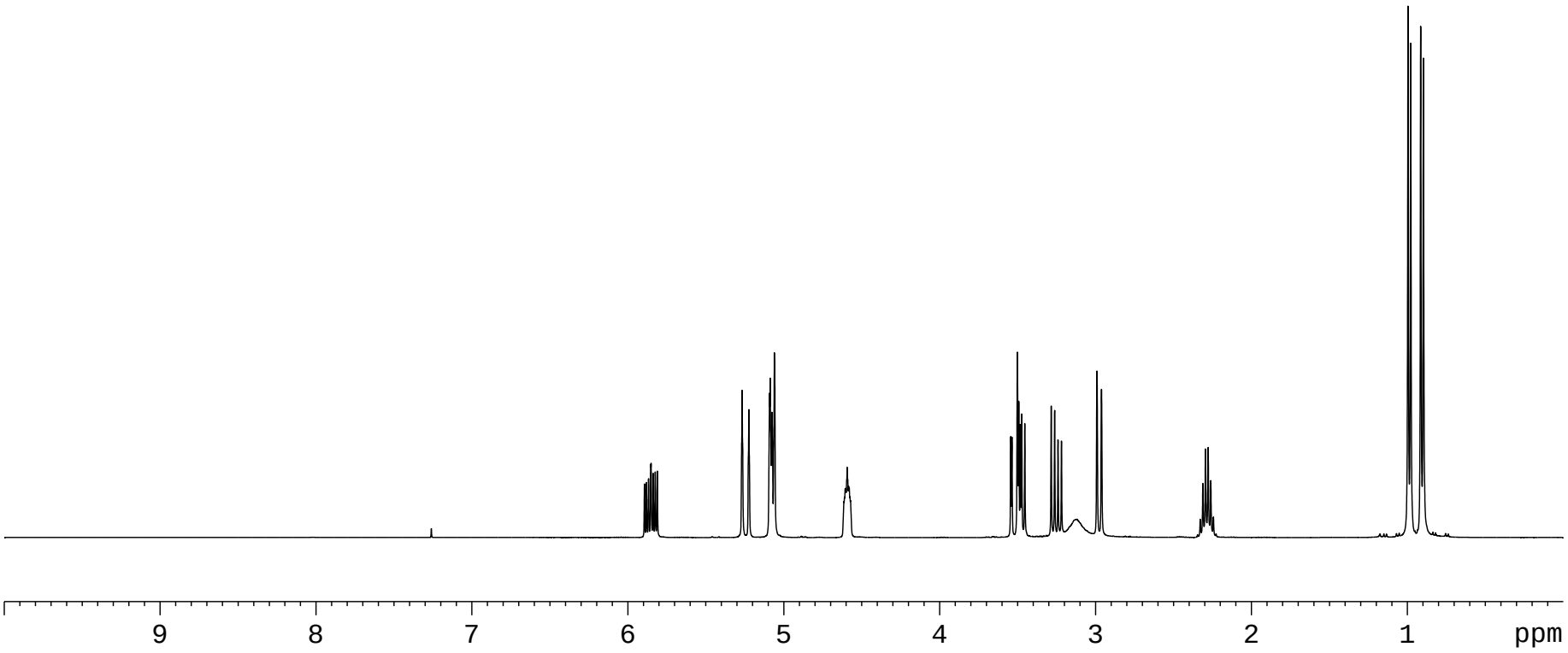
3) Emsley, P. & Cowtan, K. 2004. COOT: model-building tools for molecular graphics. Acta Crystallographica, D60, 2126-2132.

4) Sheldrick, G. 2006. A short history of SHELX. Acta Crystallographica, A64, 112-122.

5) Spec, A. L. 2006. PLATON: A multipurpose crystallographic tool. Utrecht University.

^{1}H NMR





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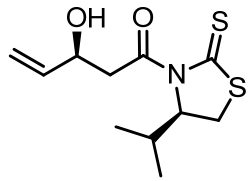

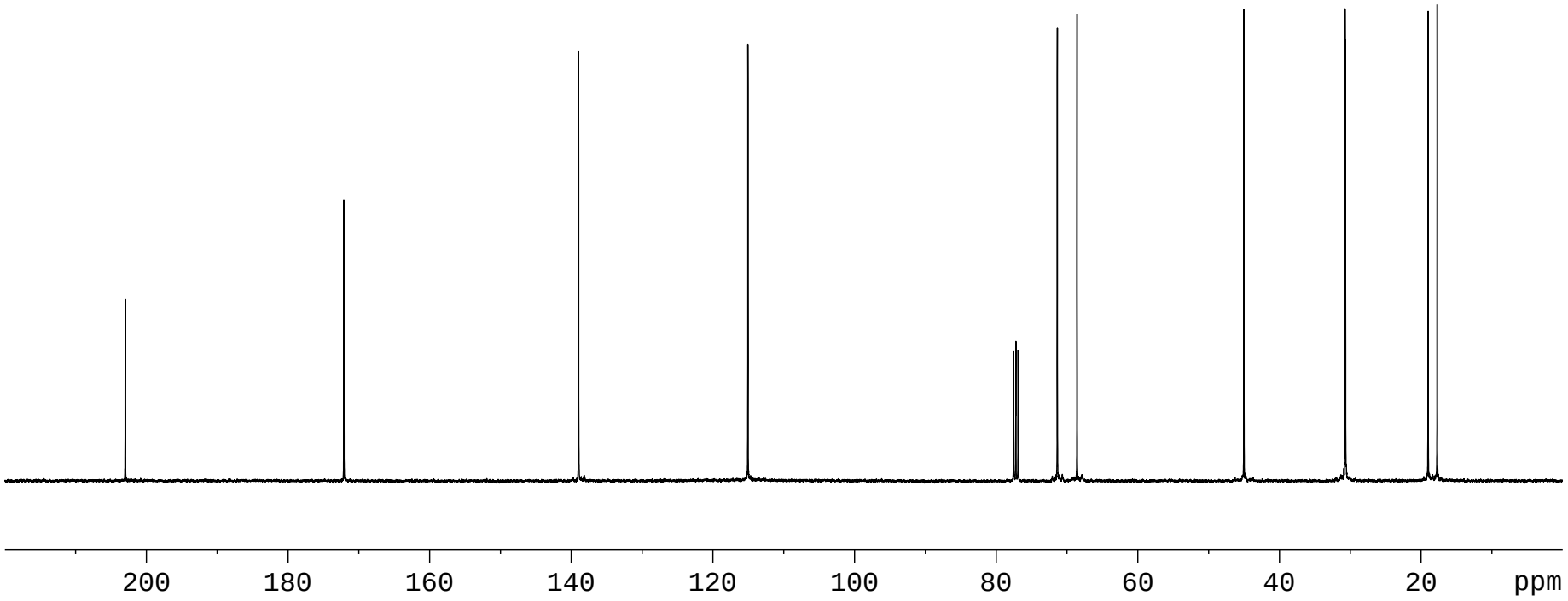

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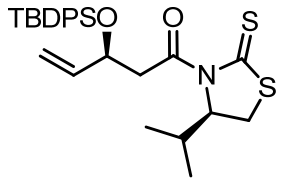

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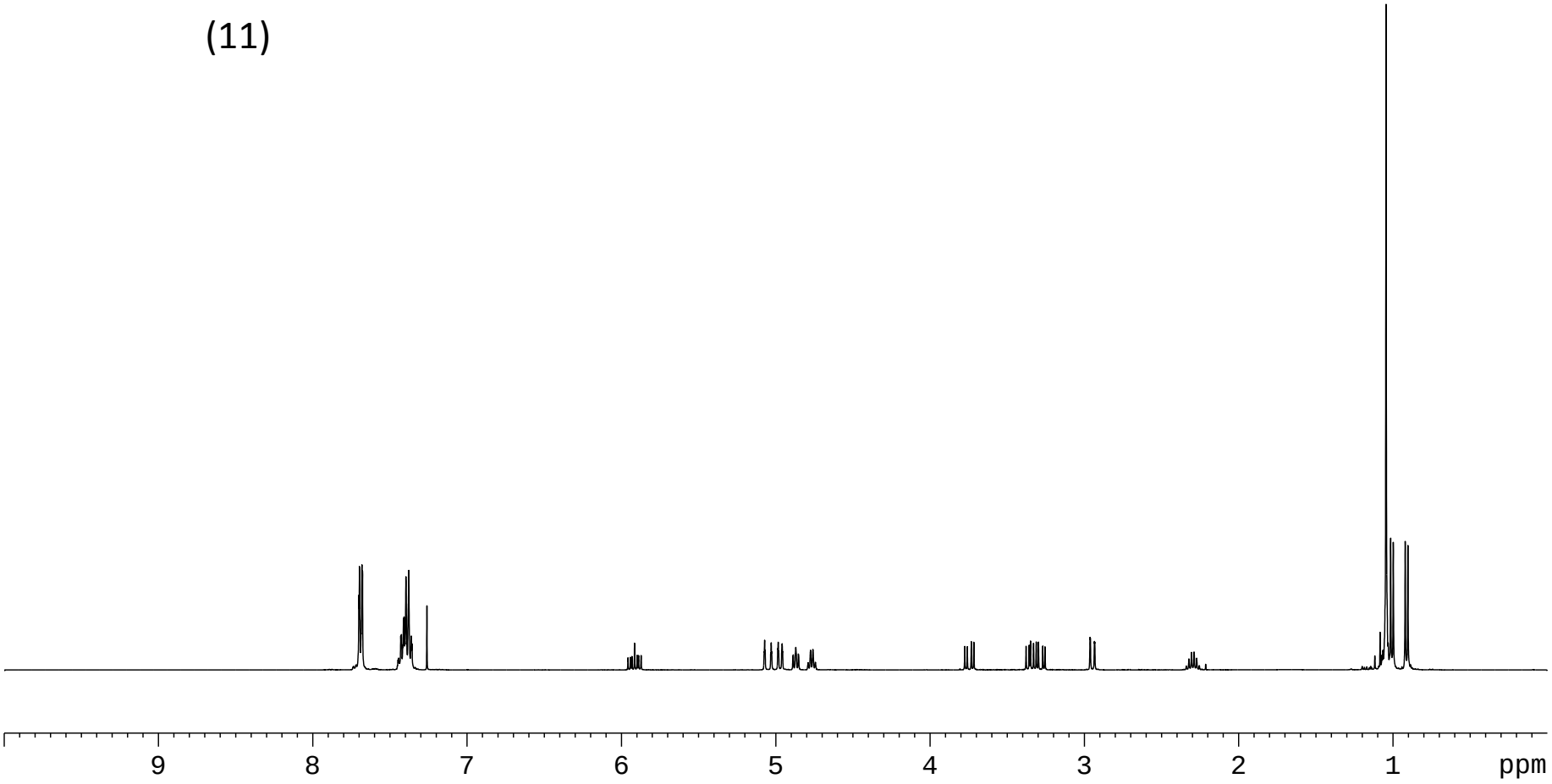

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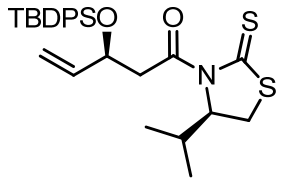

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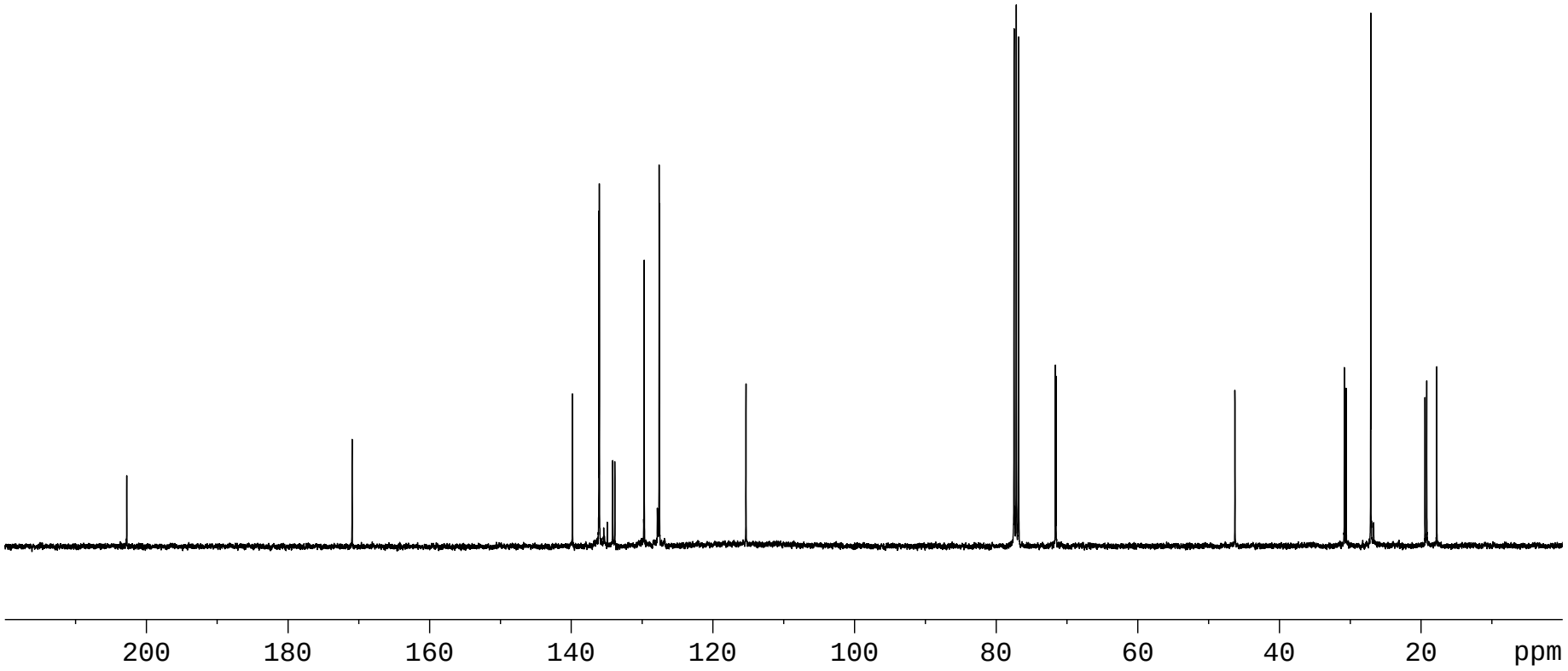

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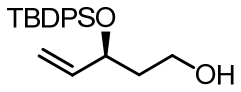

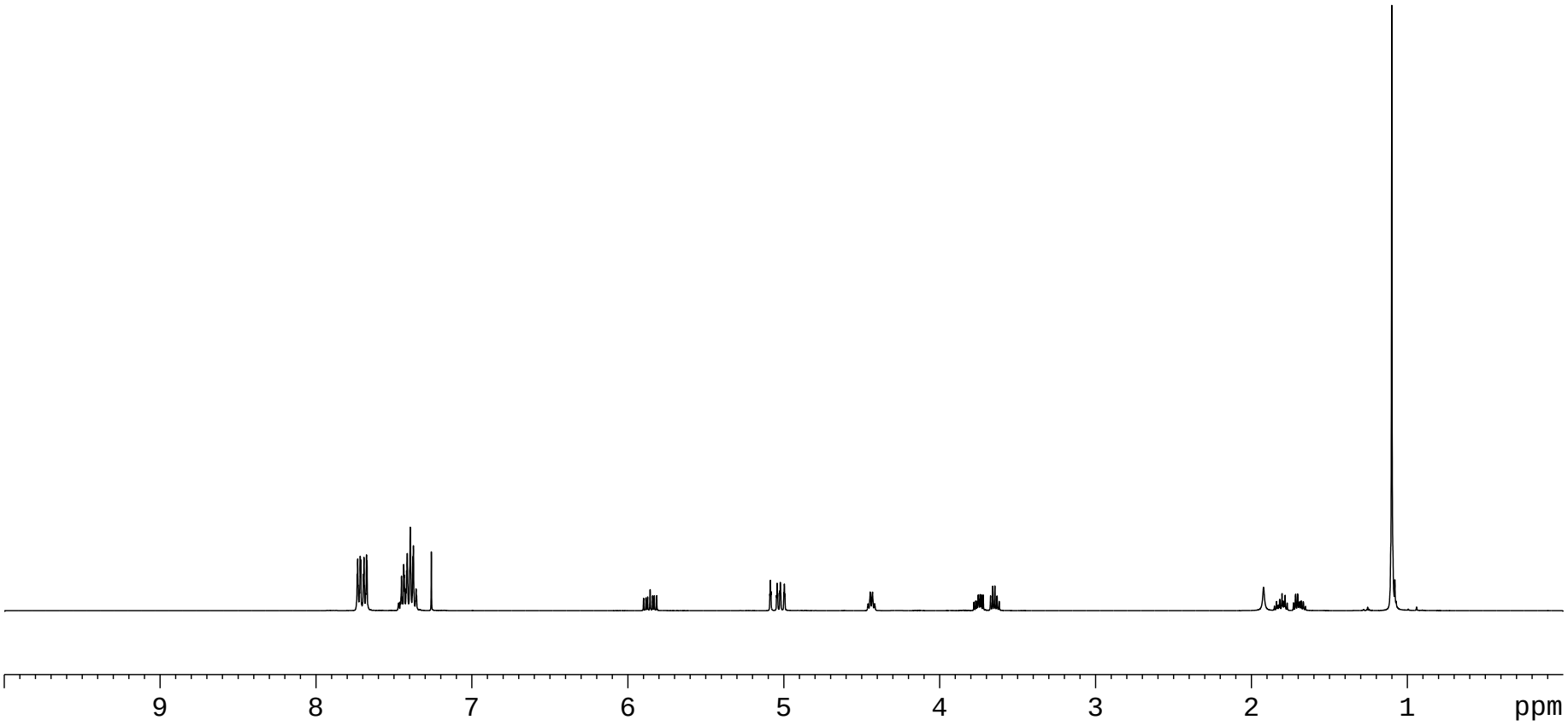

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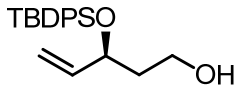

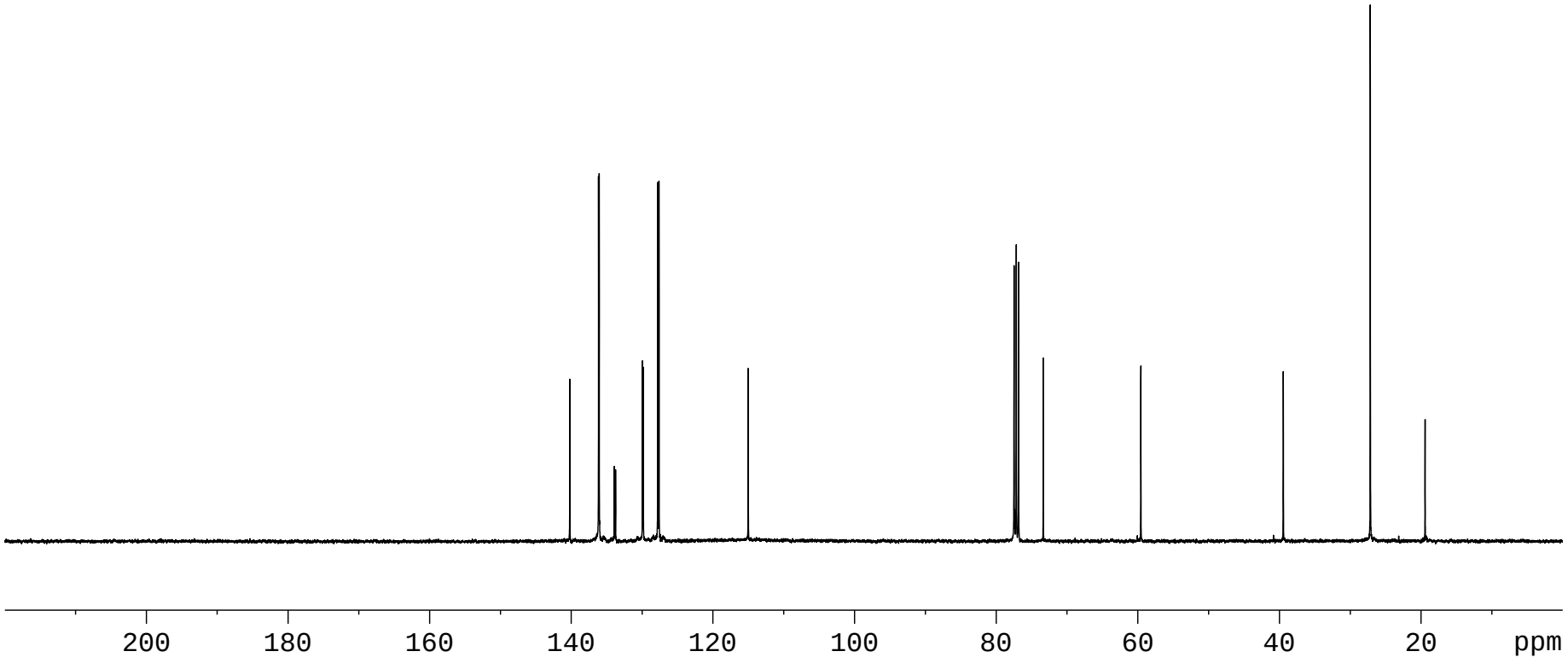

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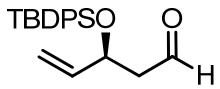

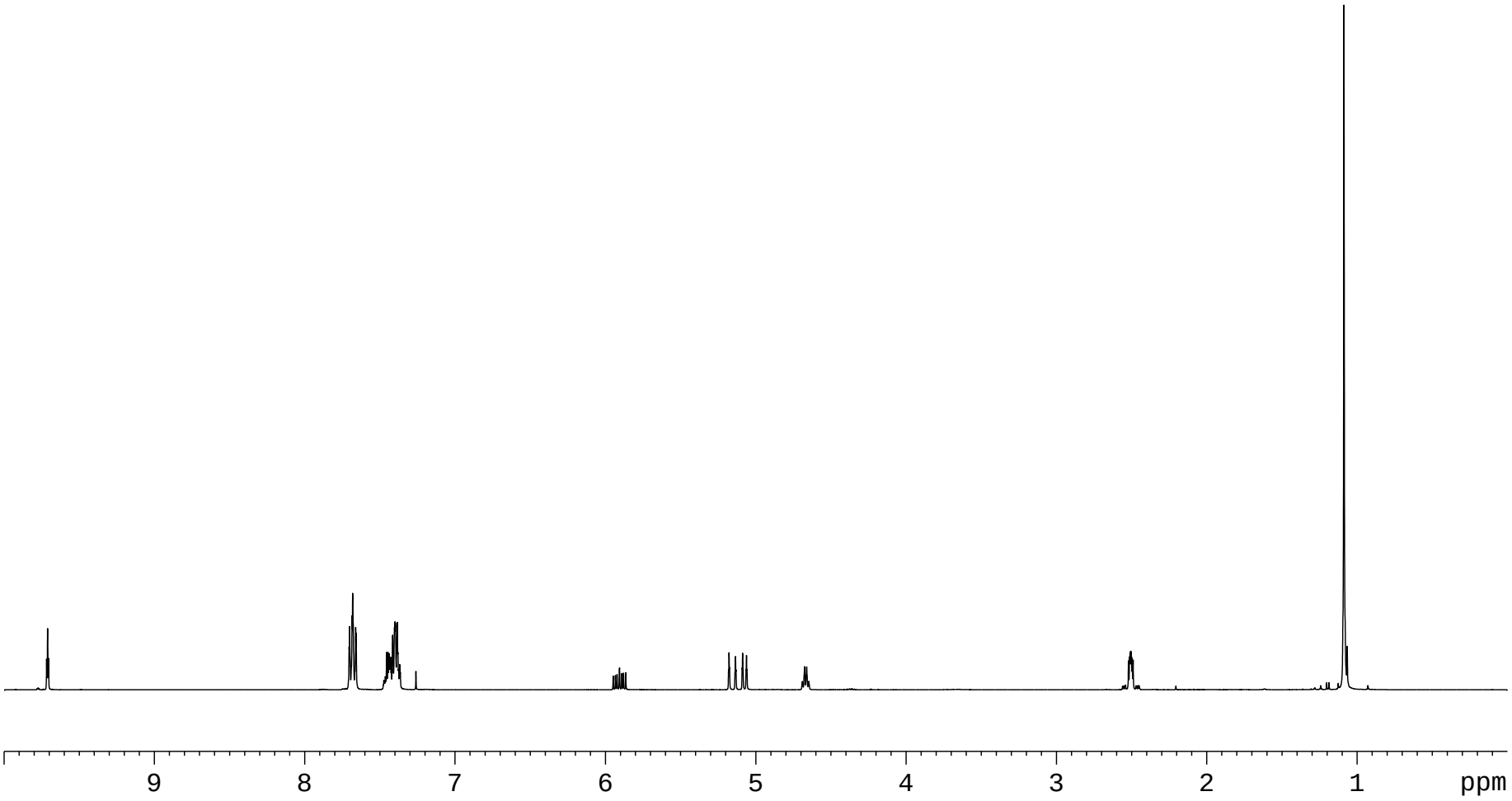

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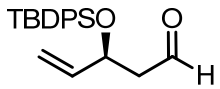

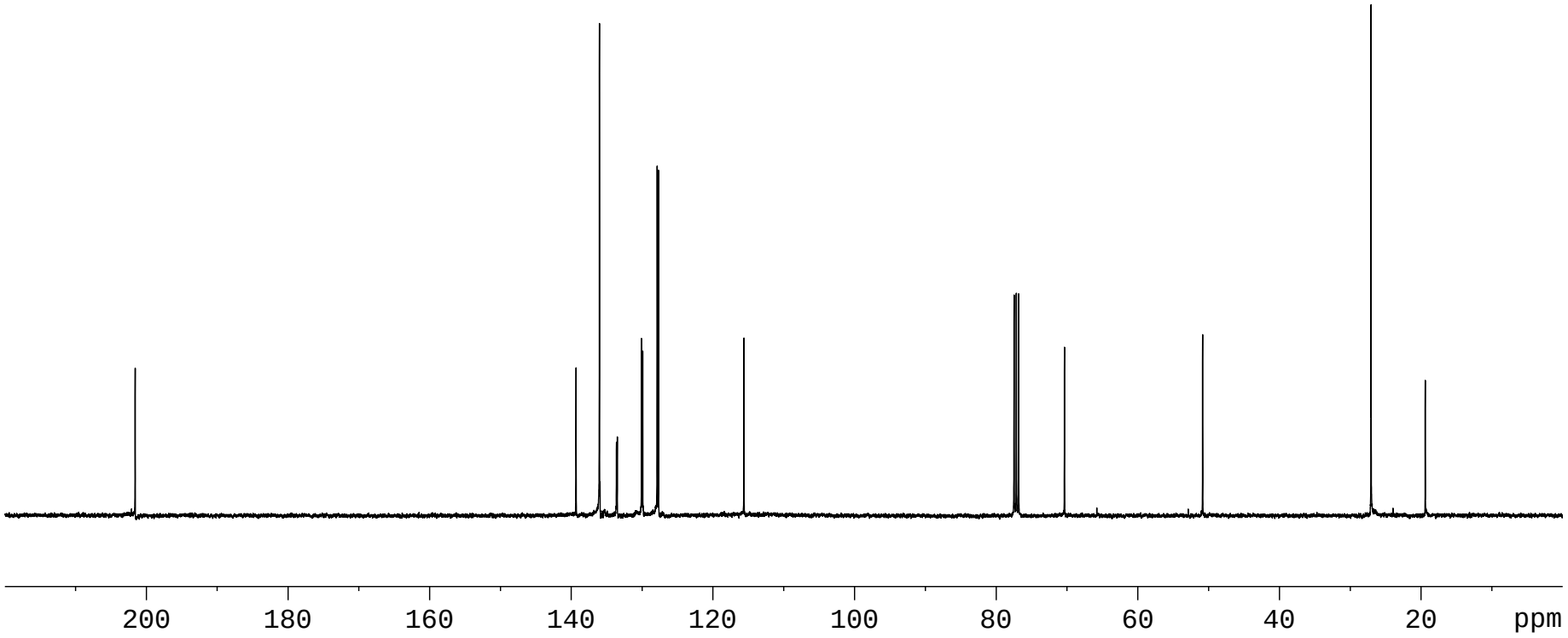

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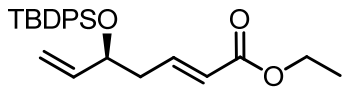

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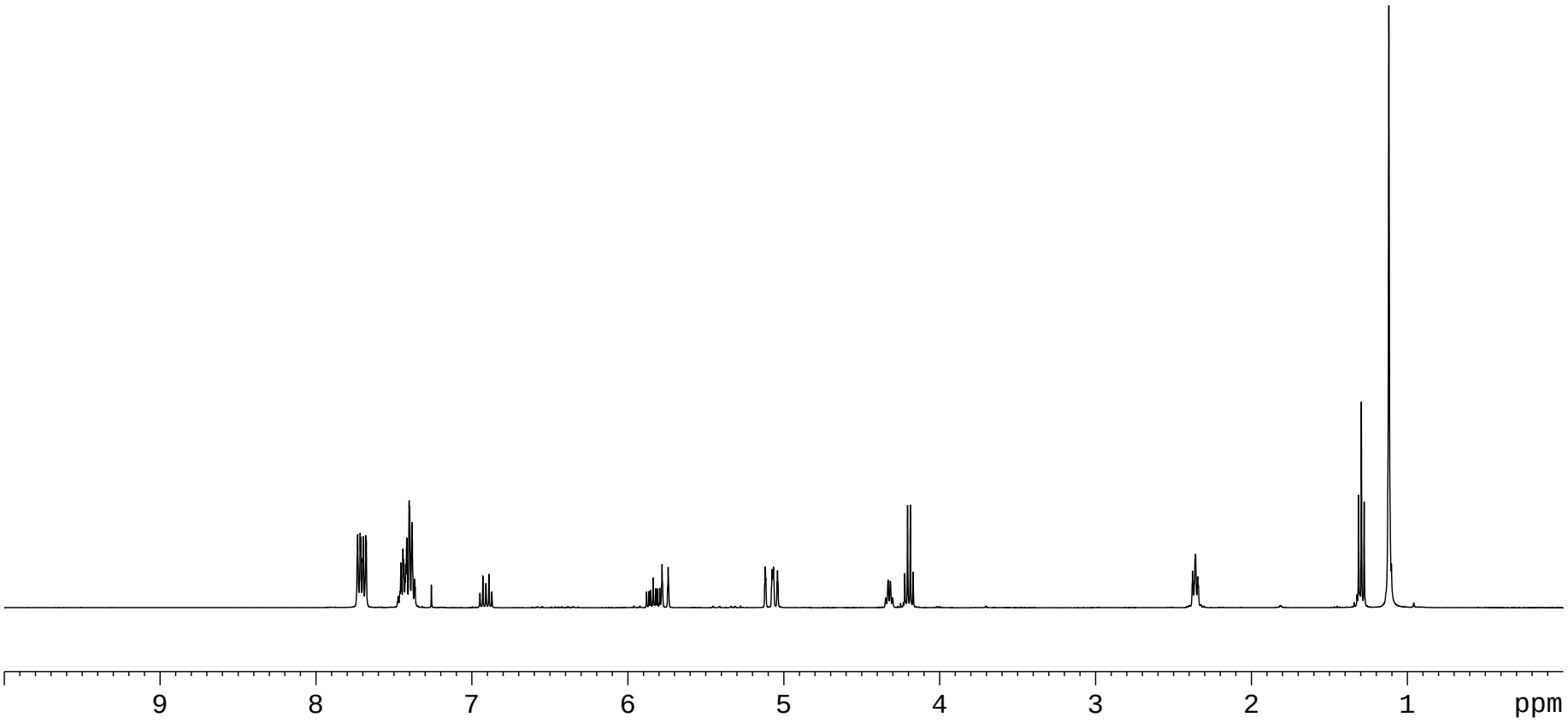

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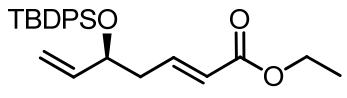

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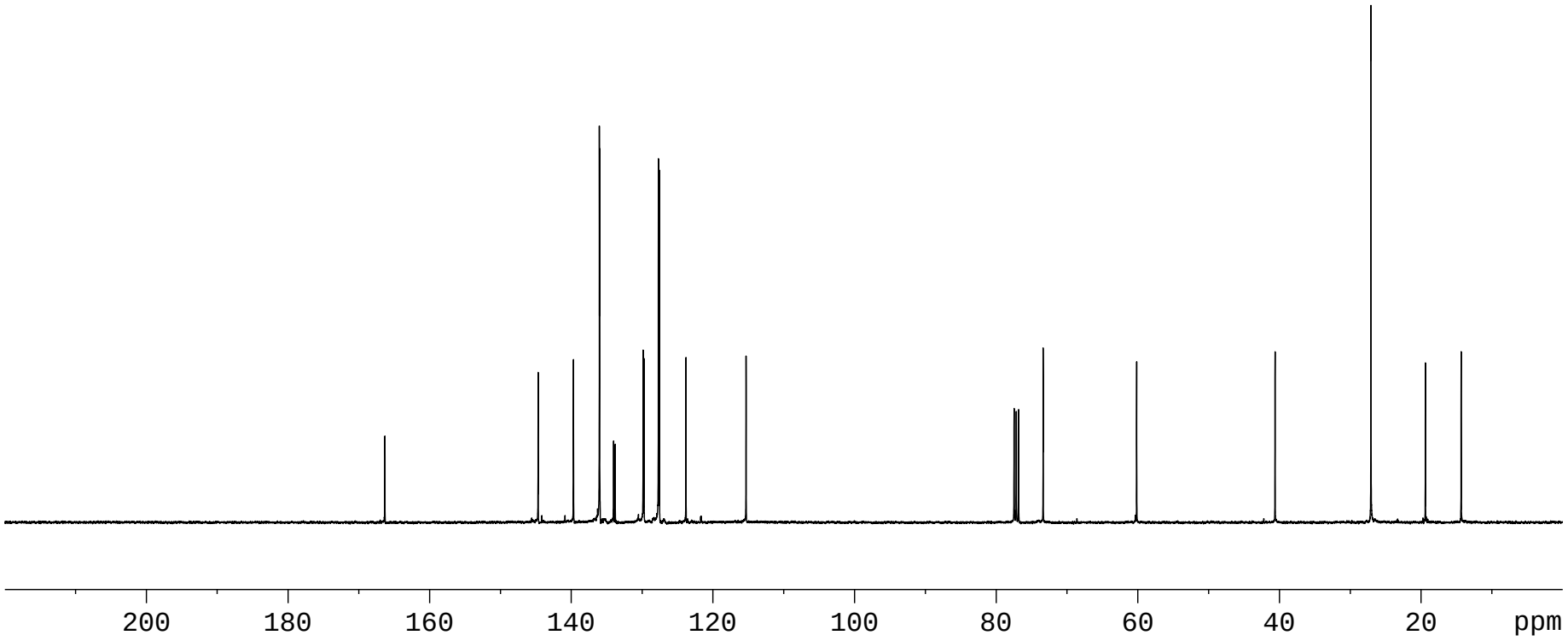

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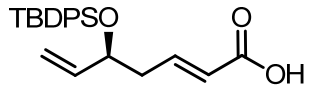

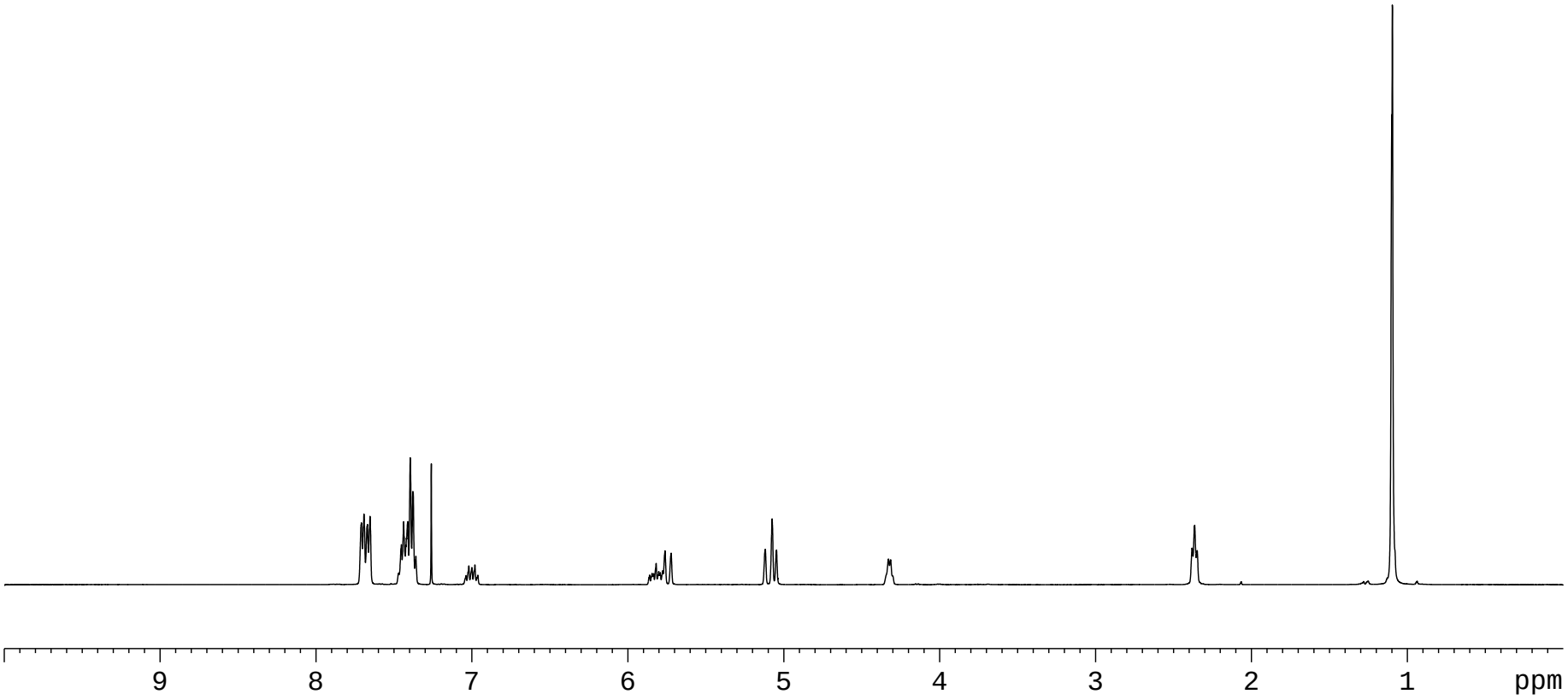

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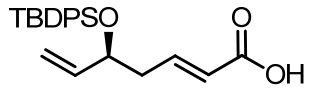

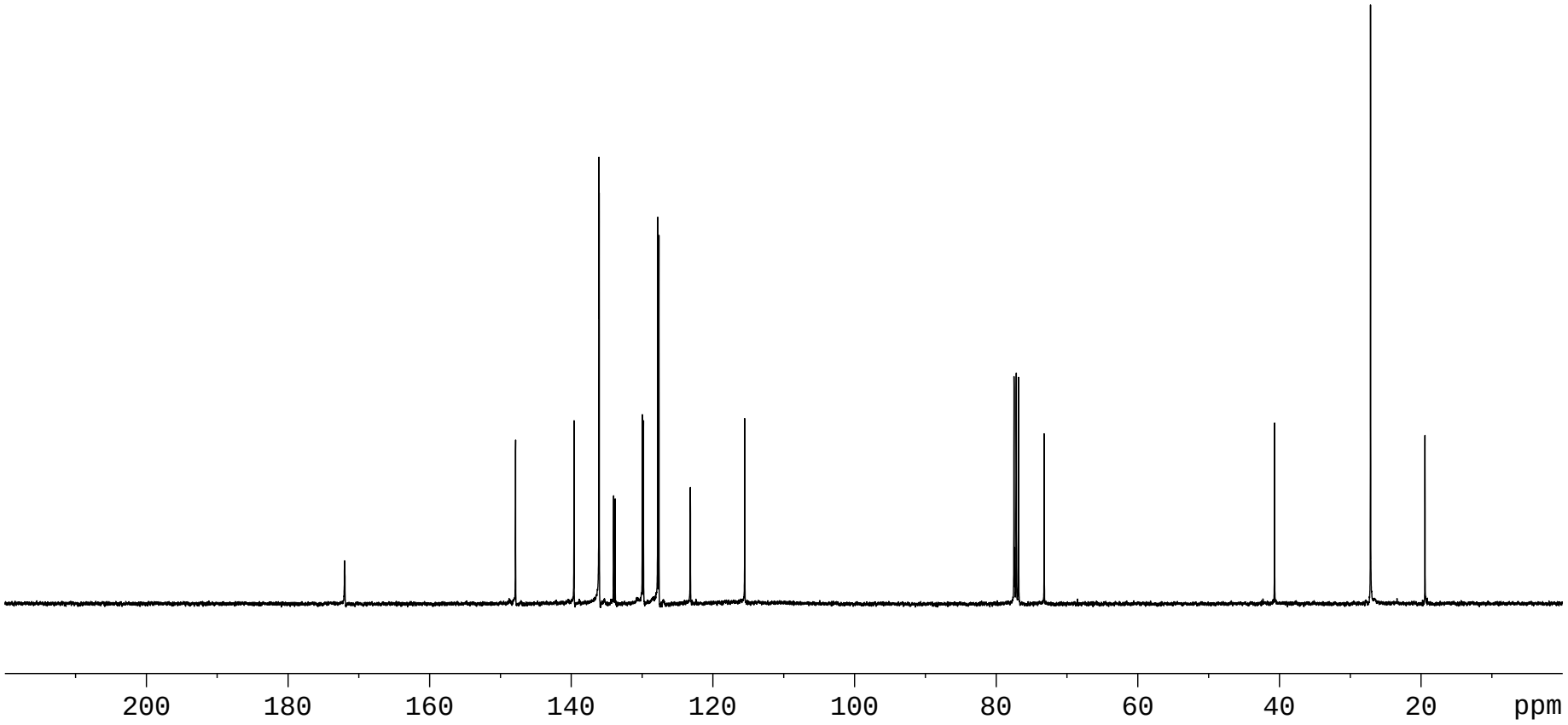

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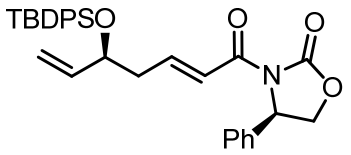

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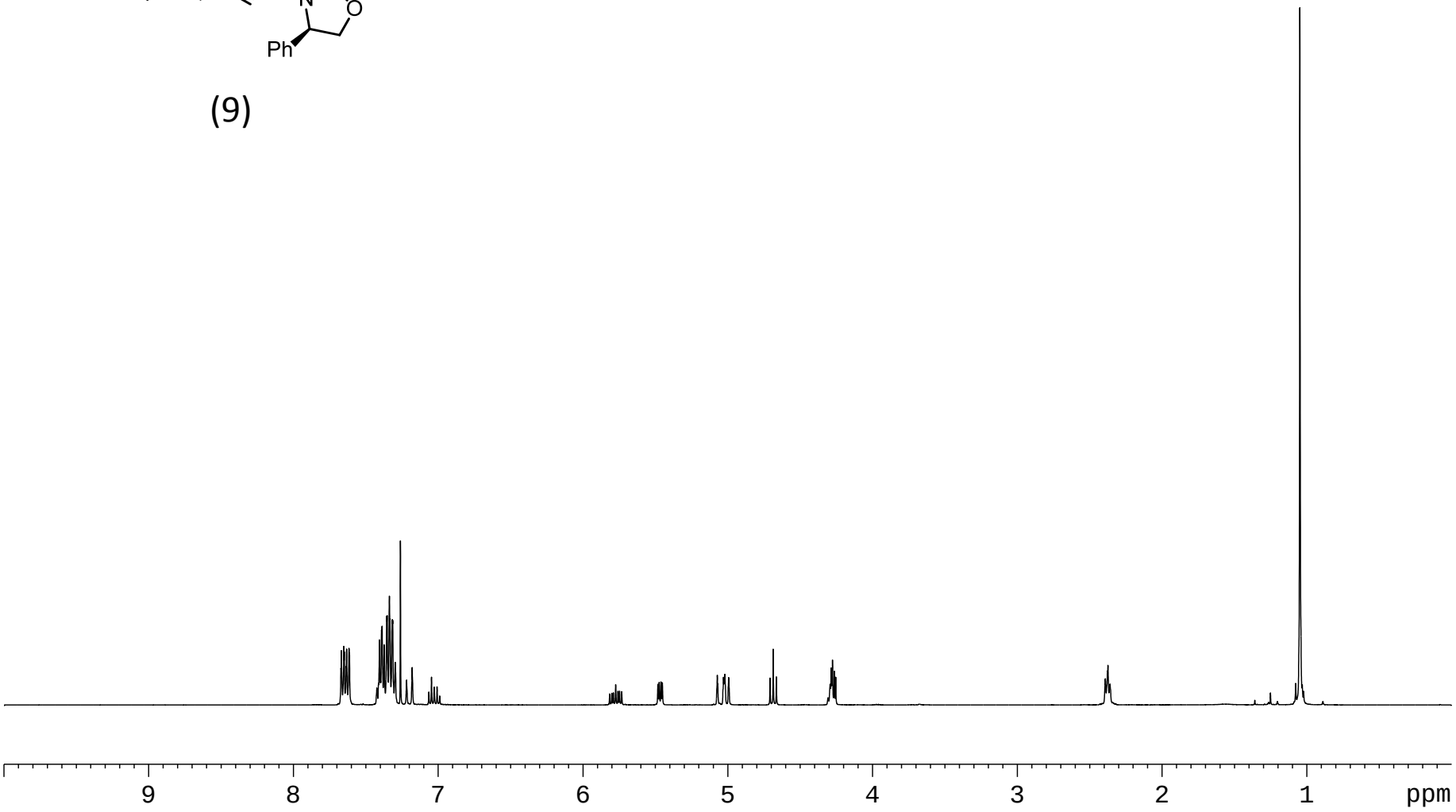

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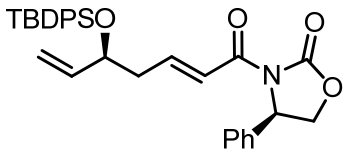

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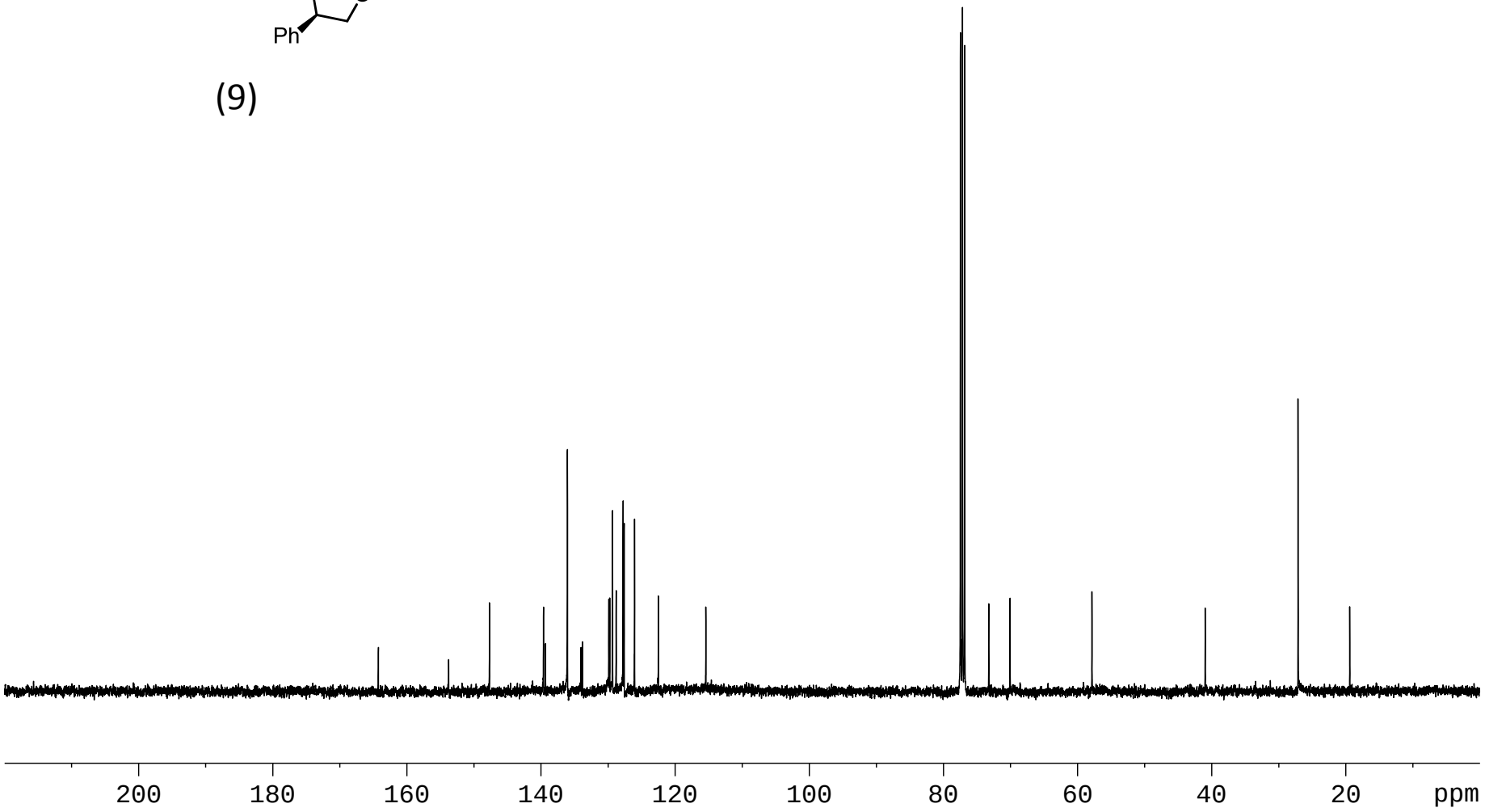

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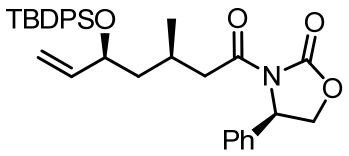

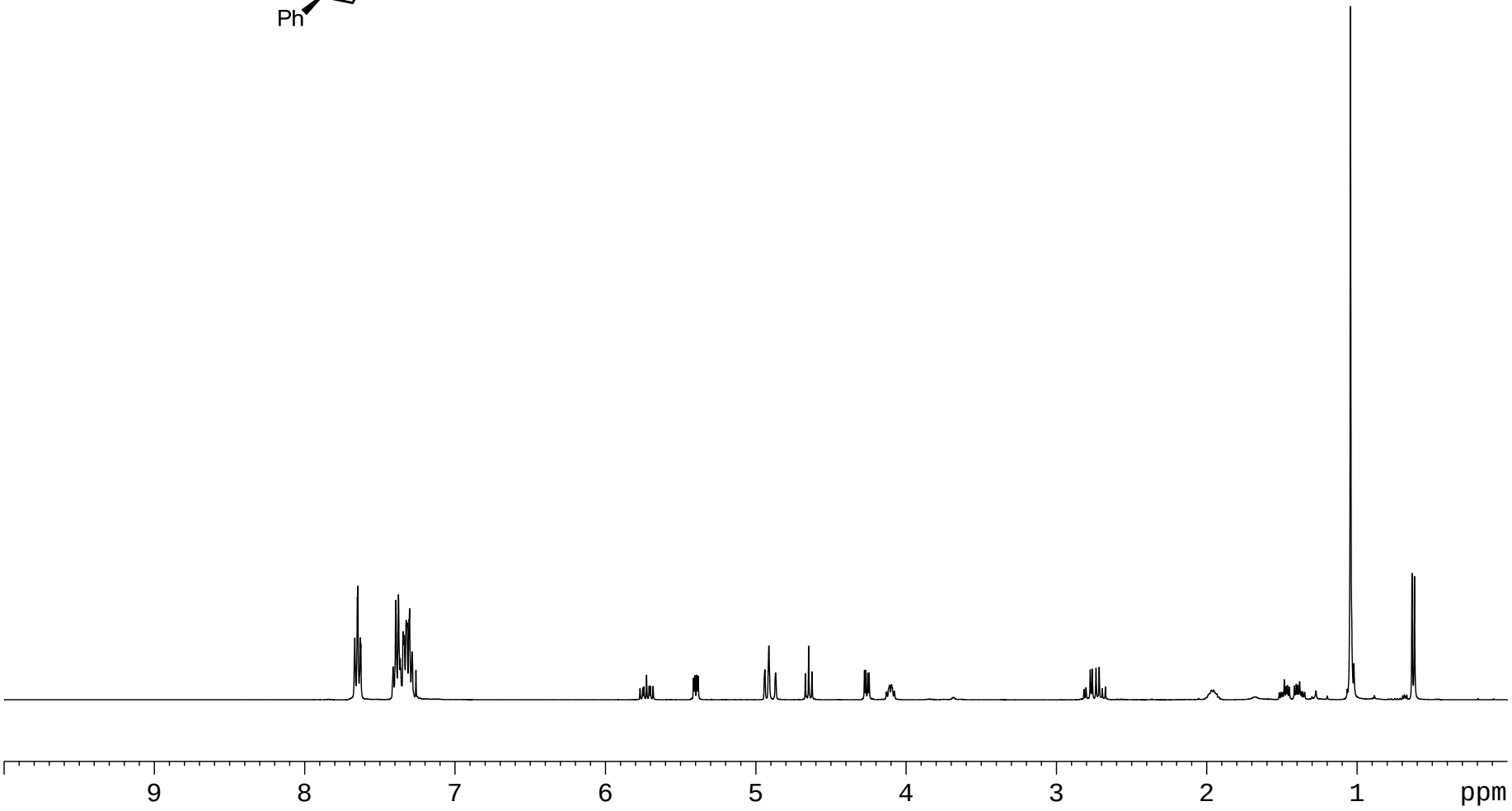

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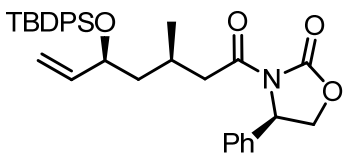

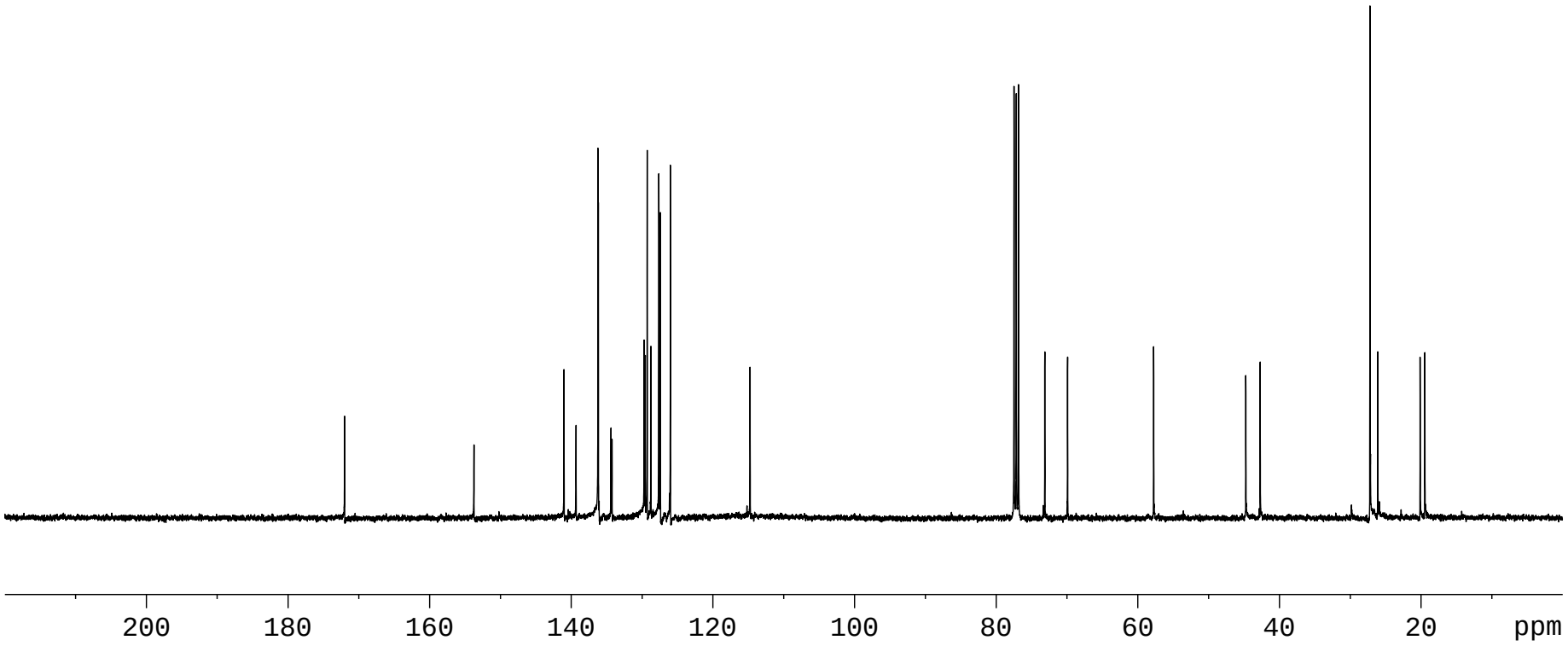

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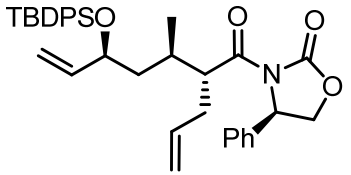

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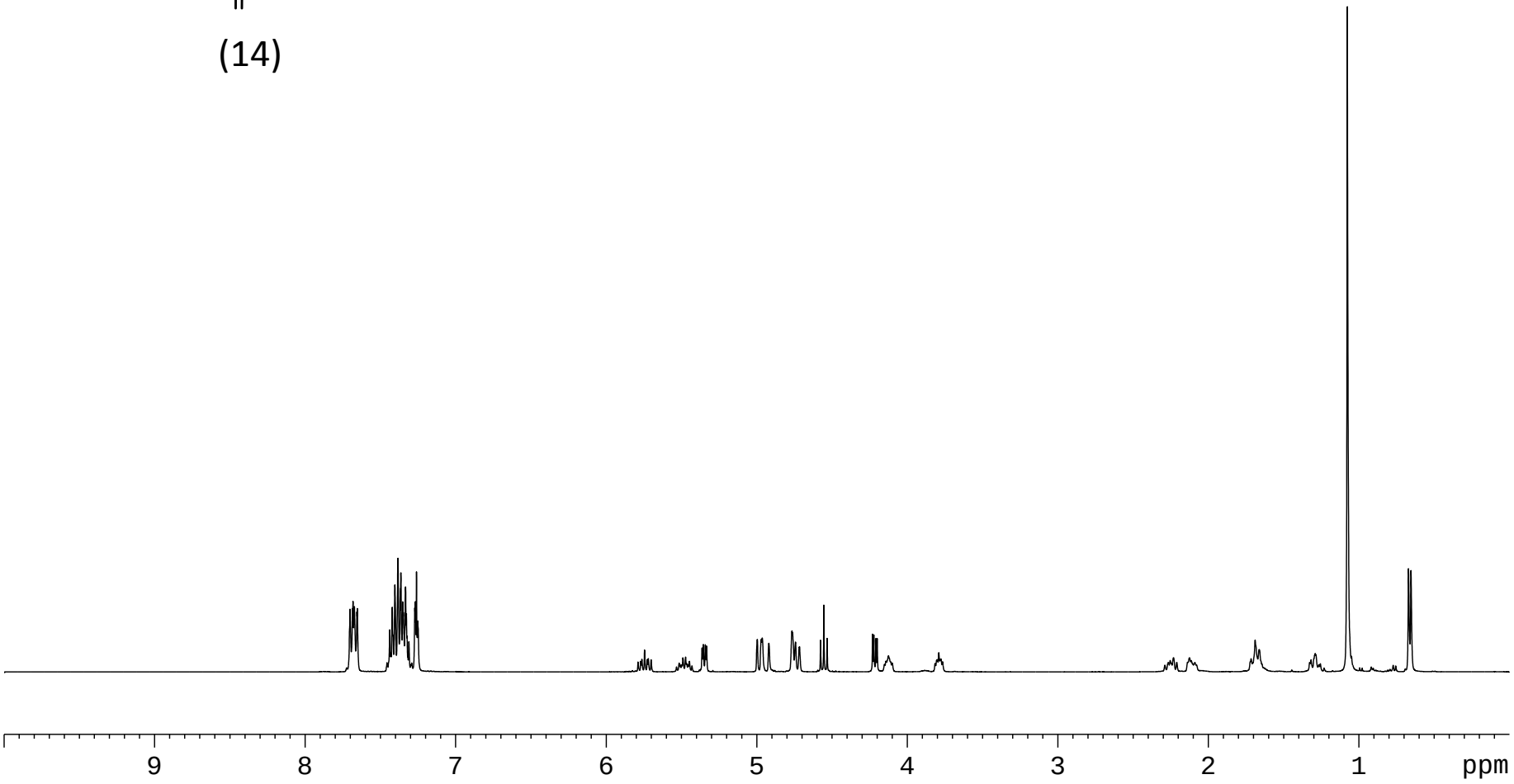

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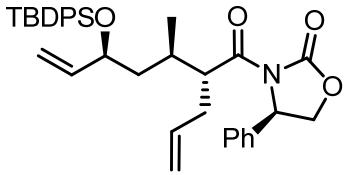

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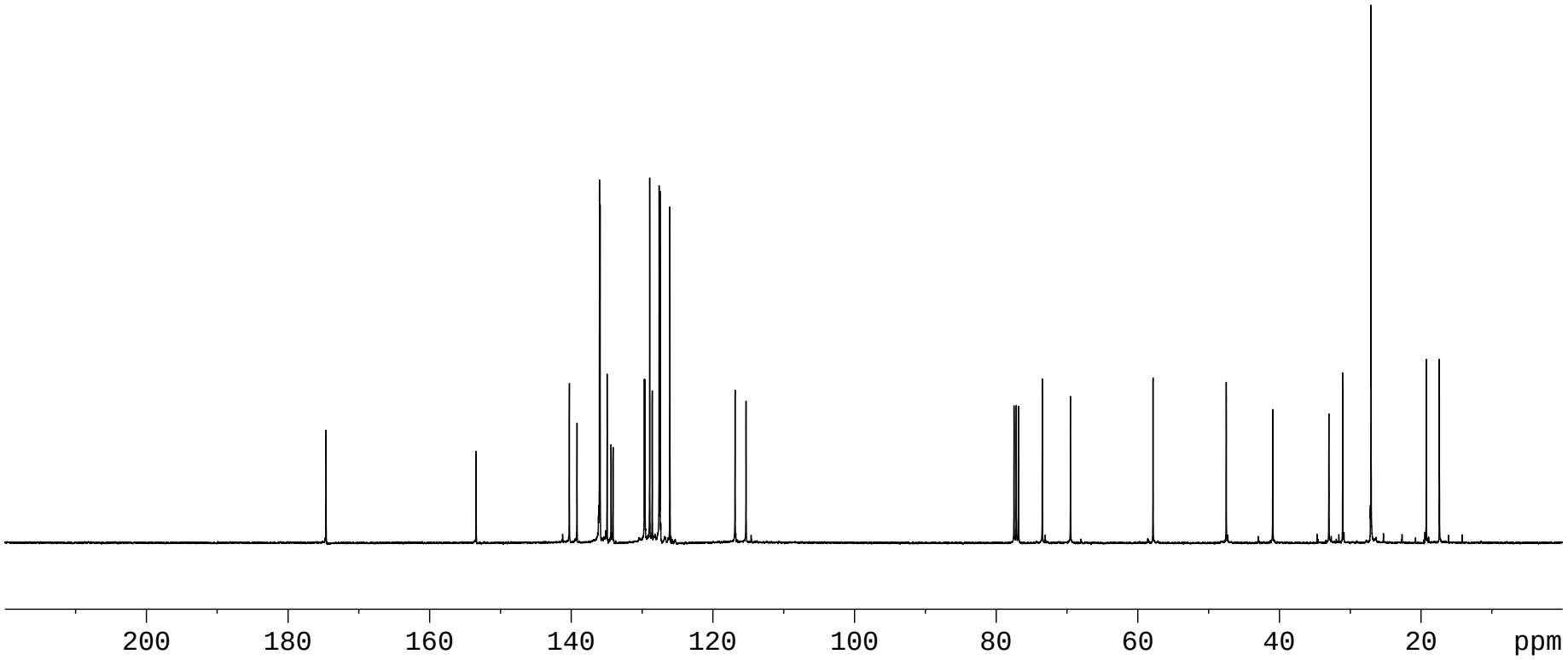

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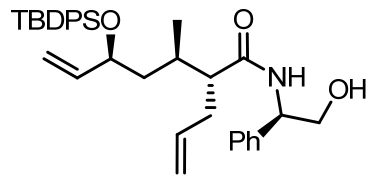

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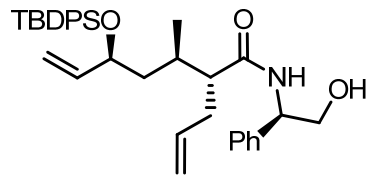

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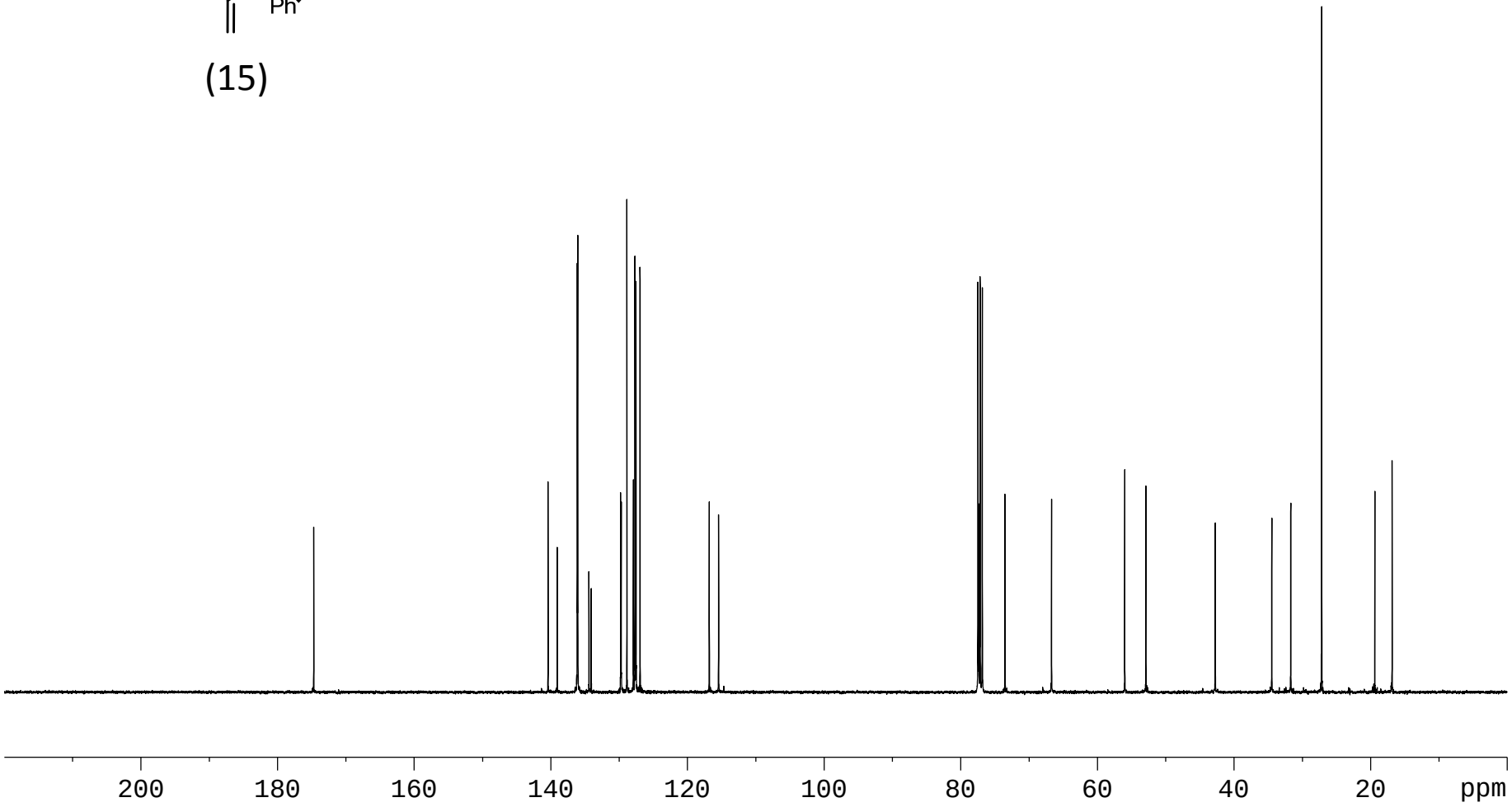

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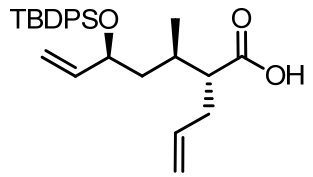

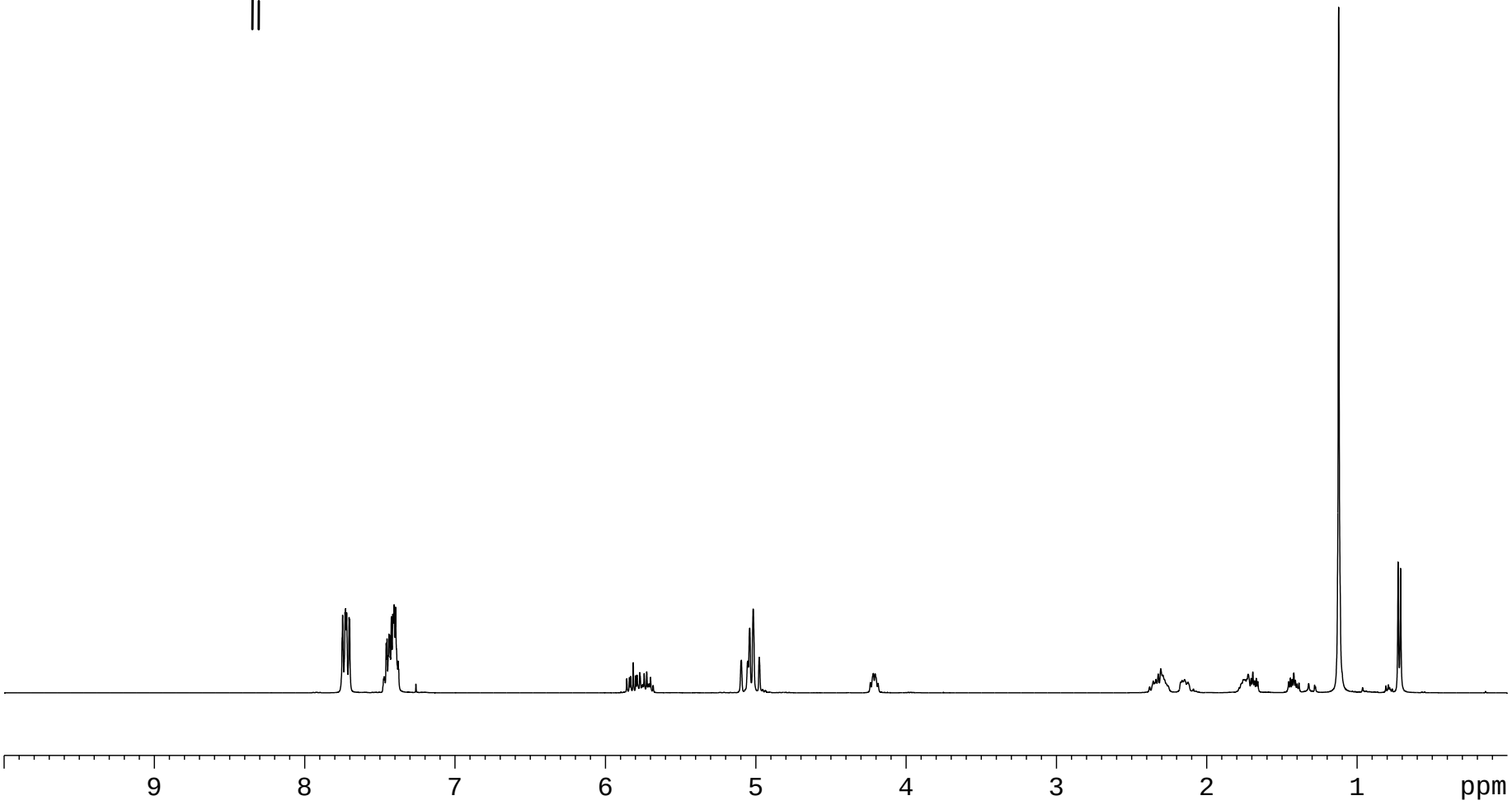

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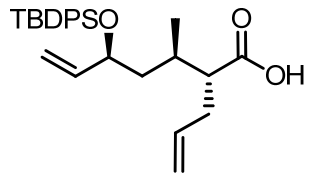

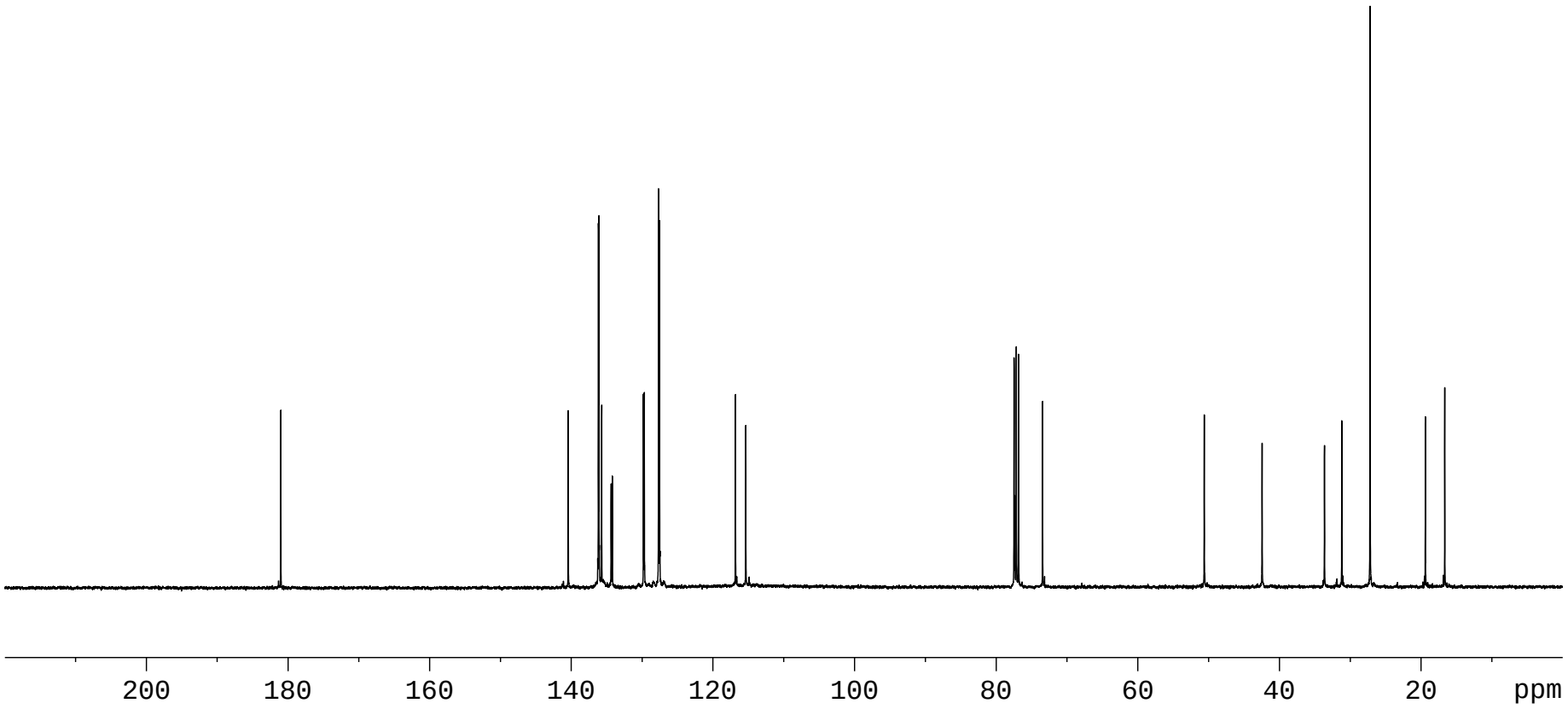

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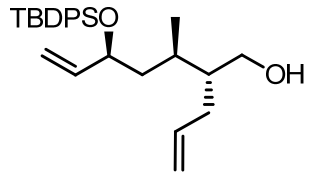

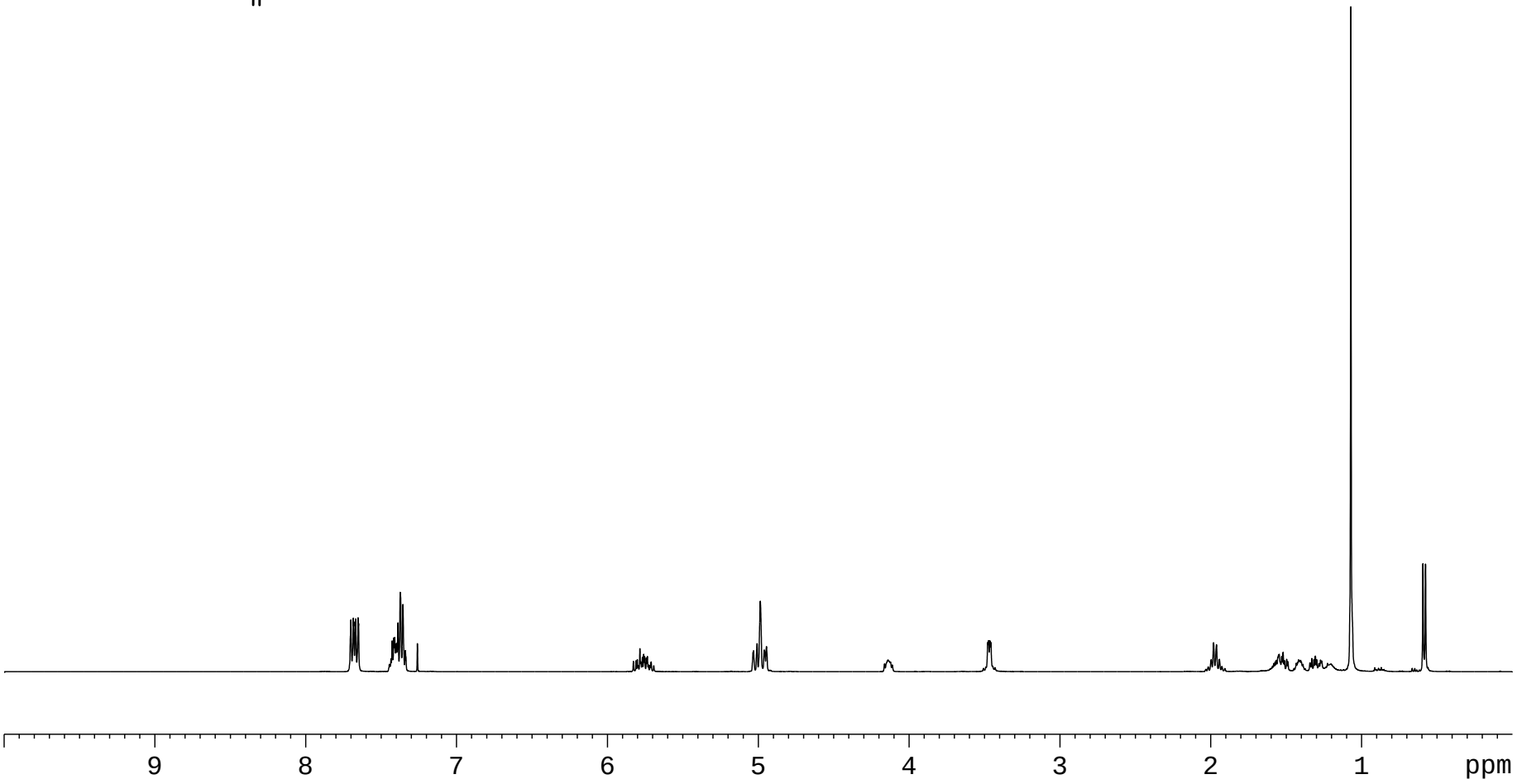

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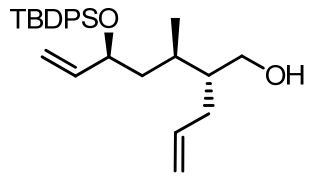

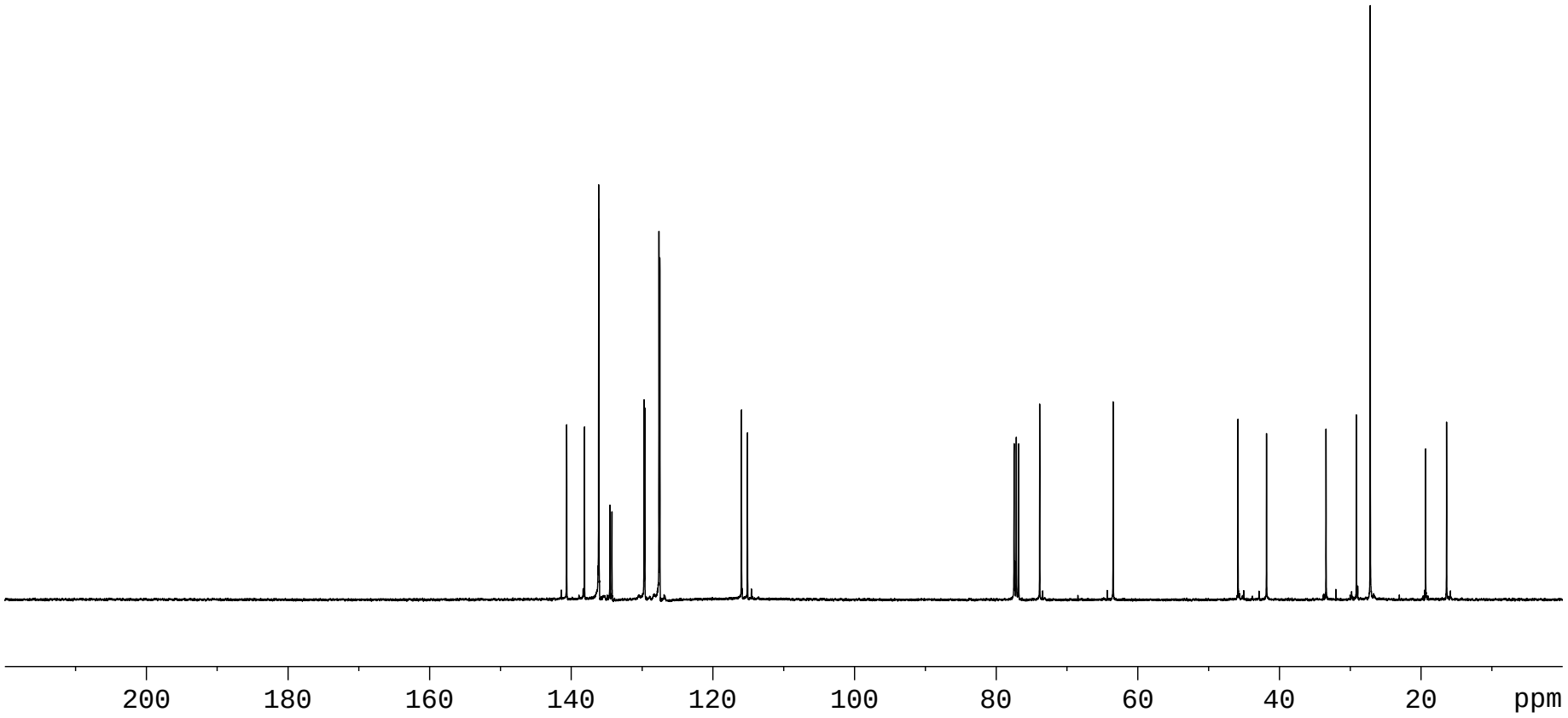

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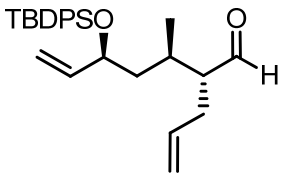

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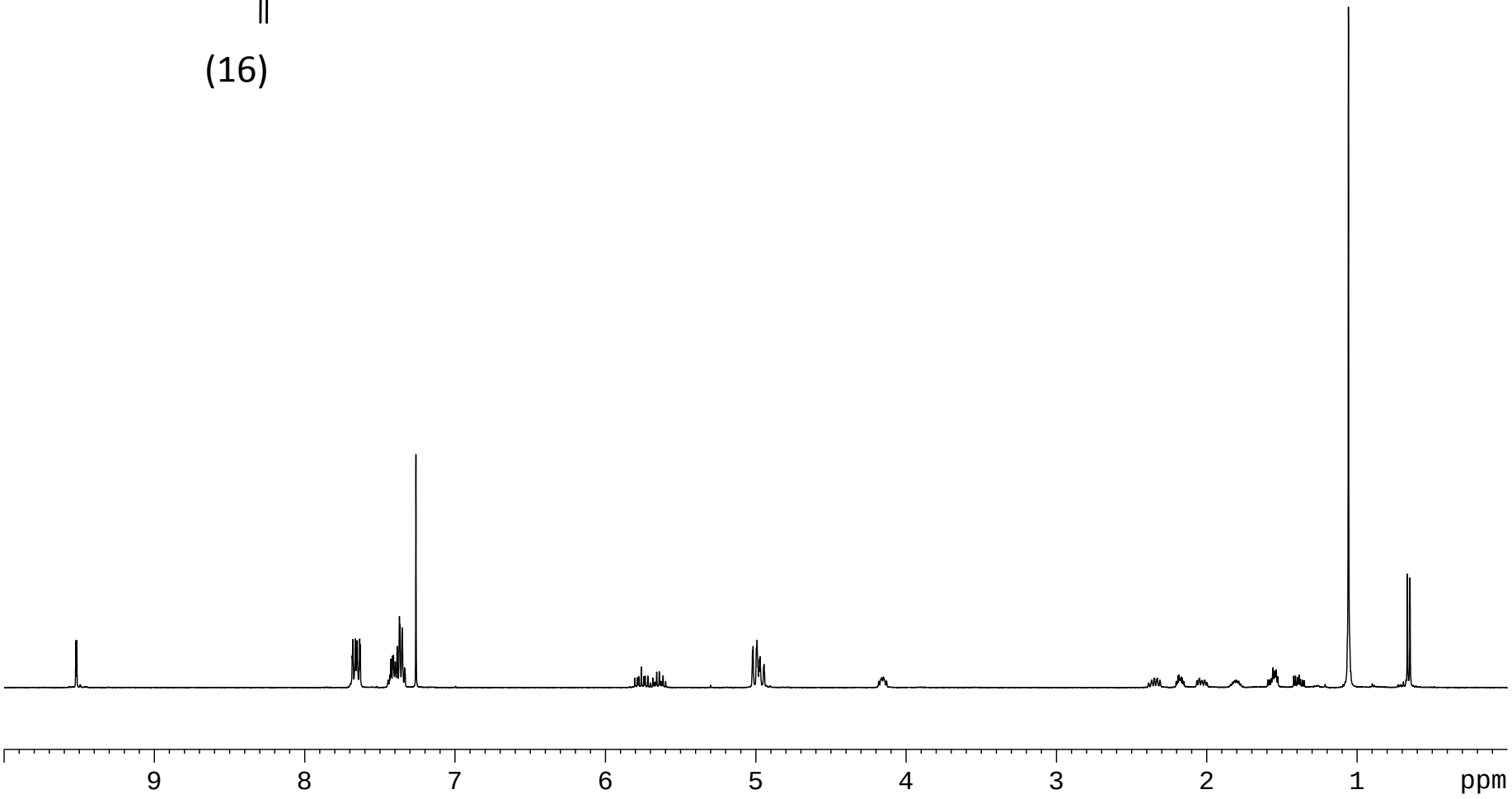

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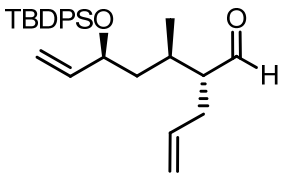

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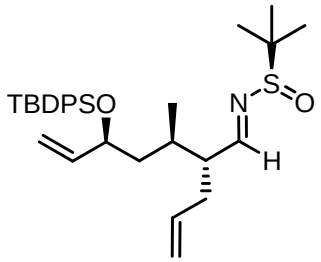

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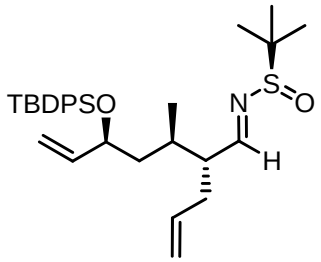

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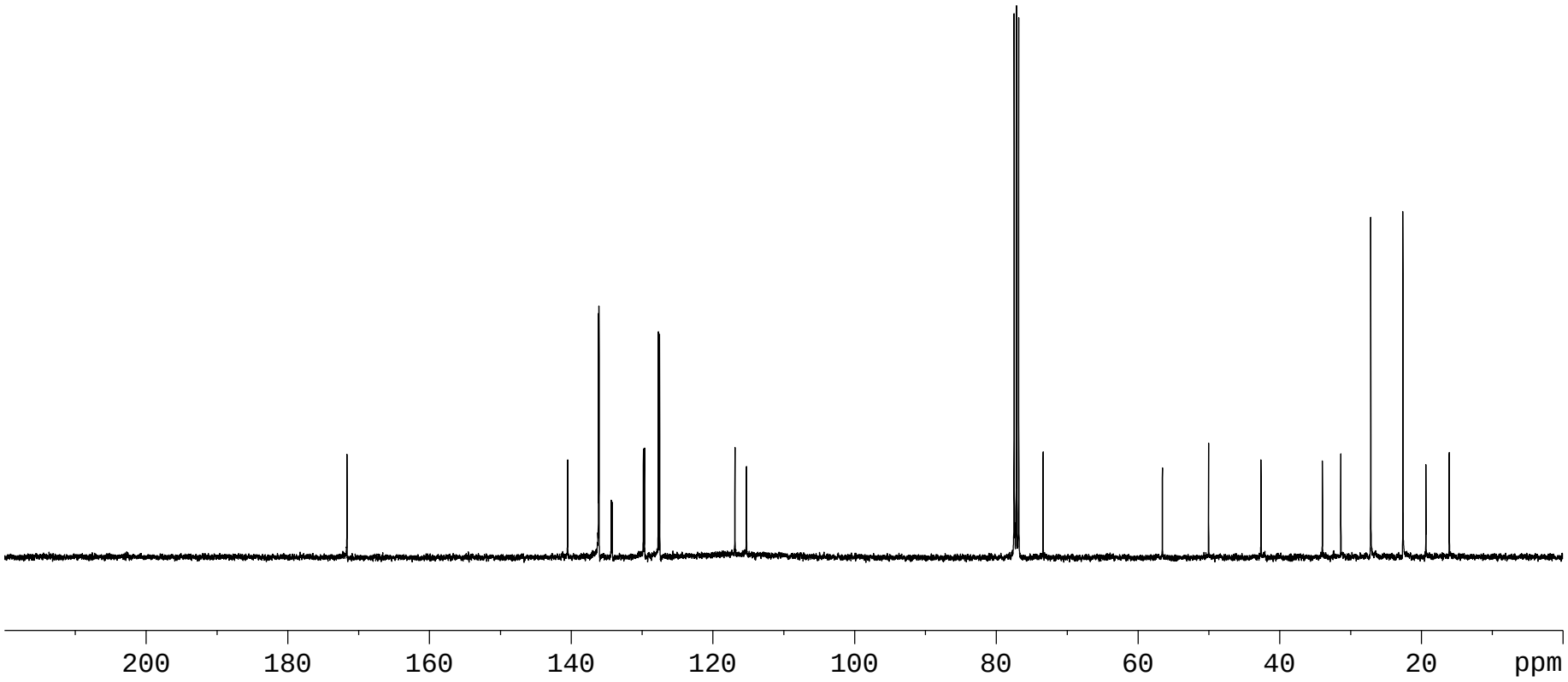

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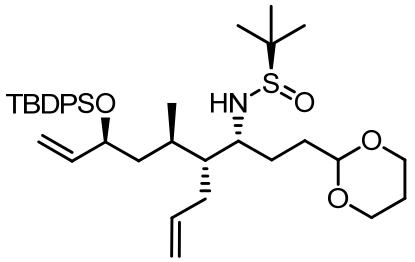

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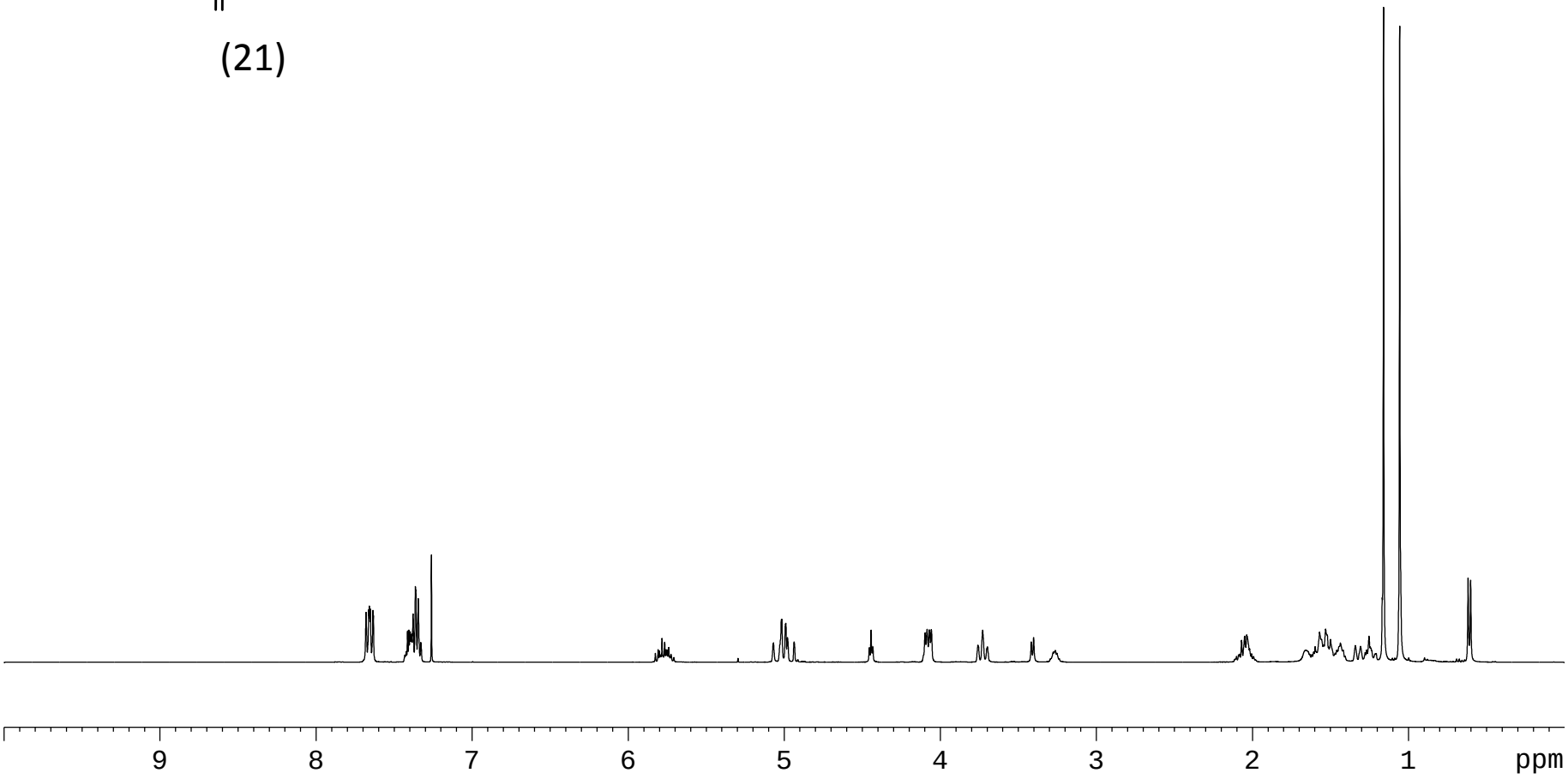

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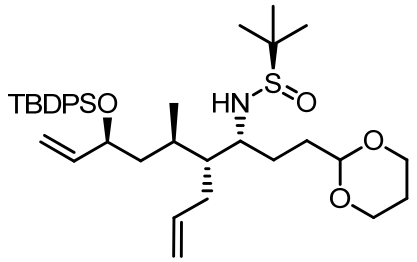

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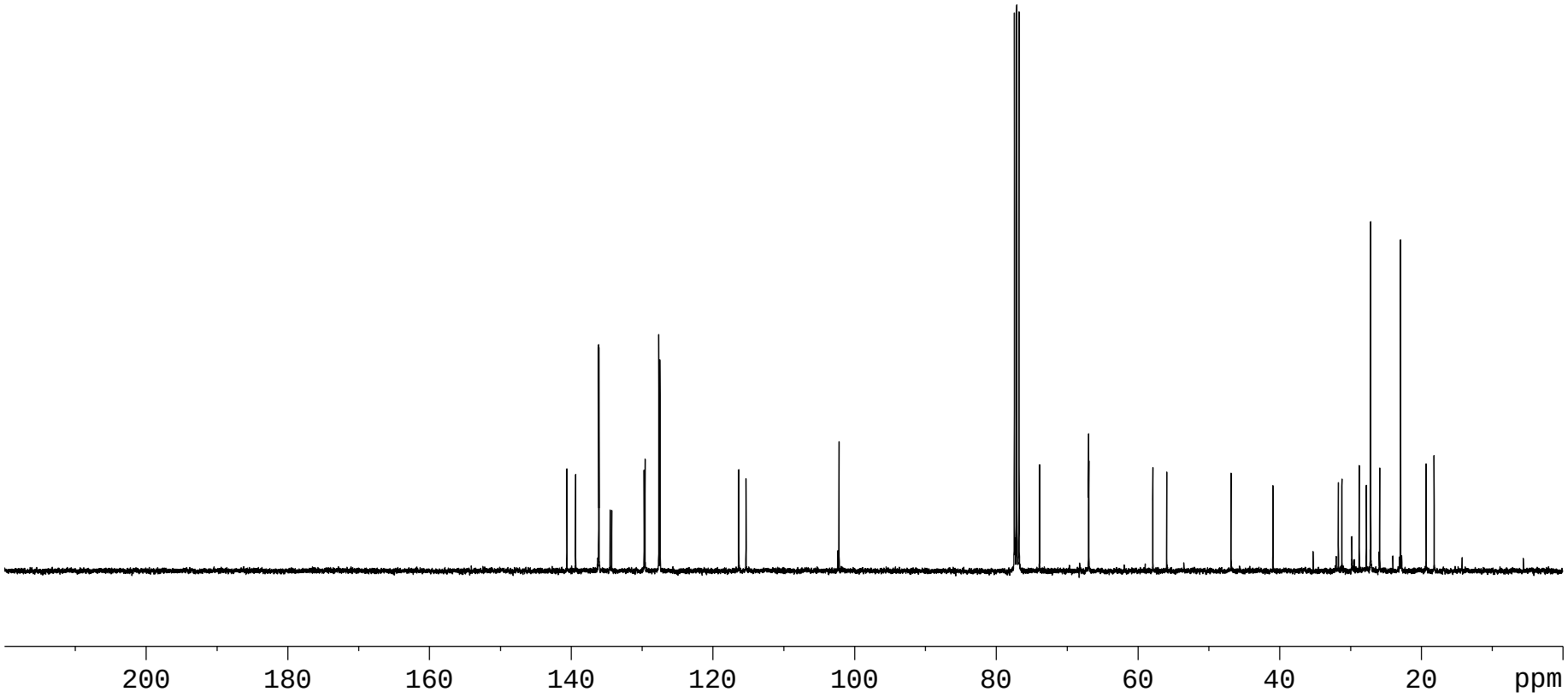

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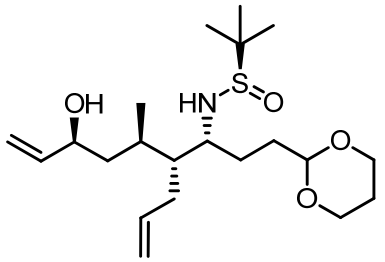
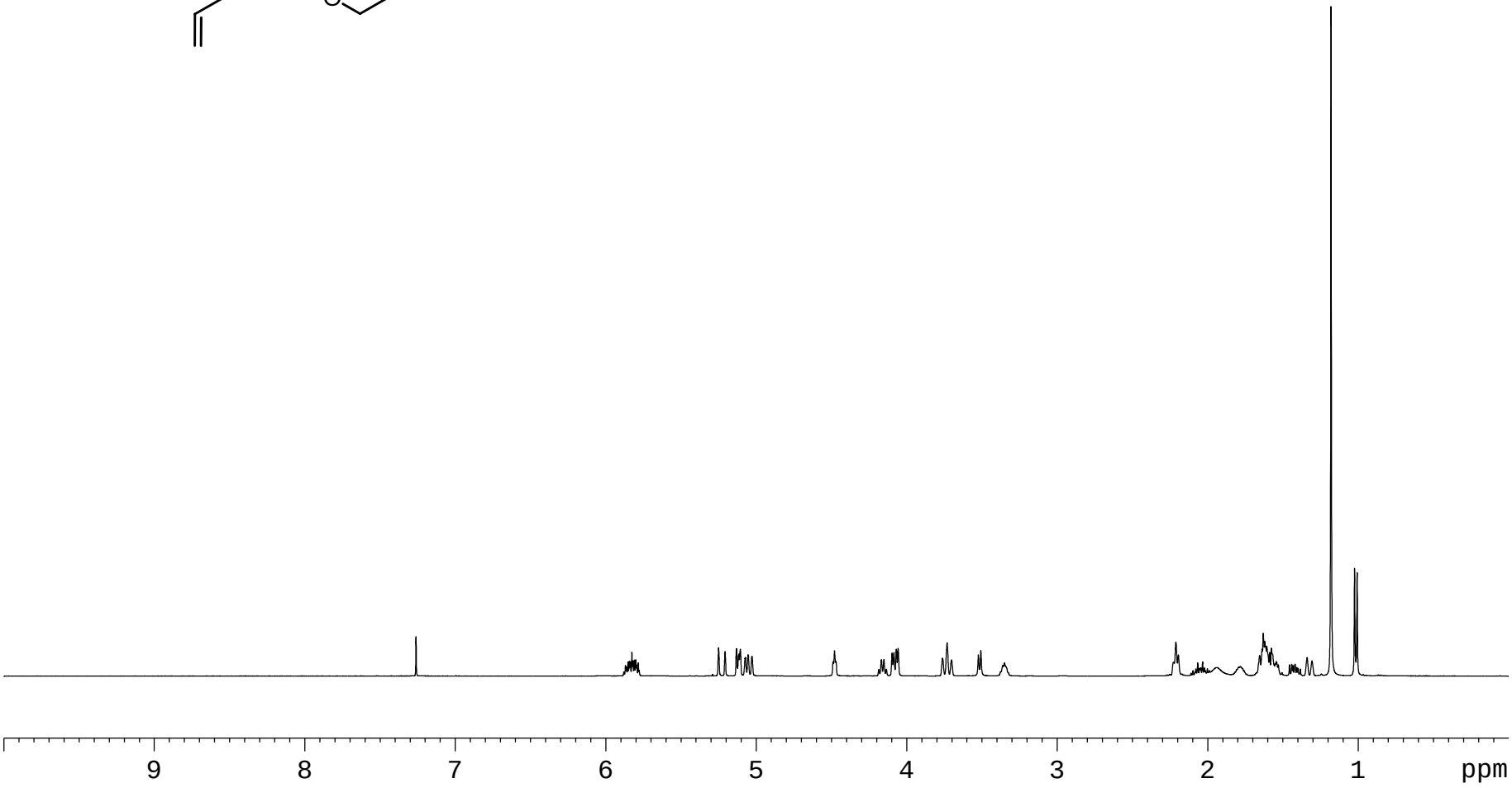
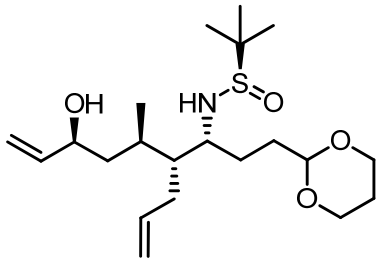
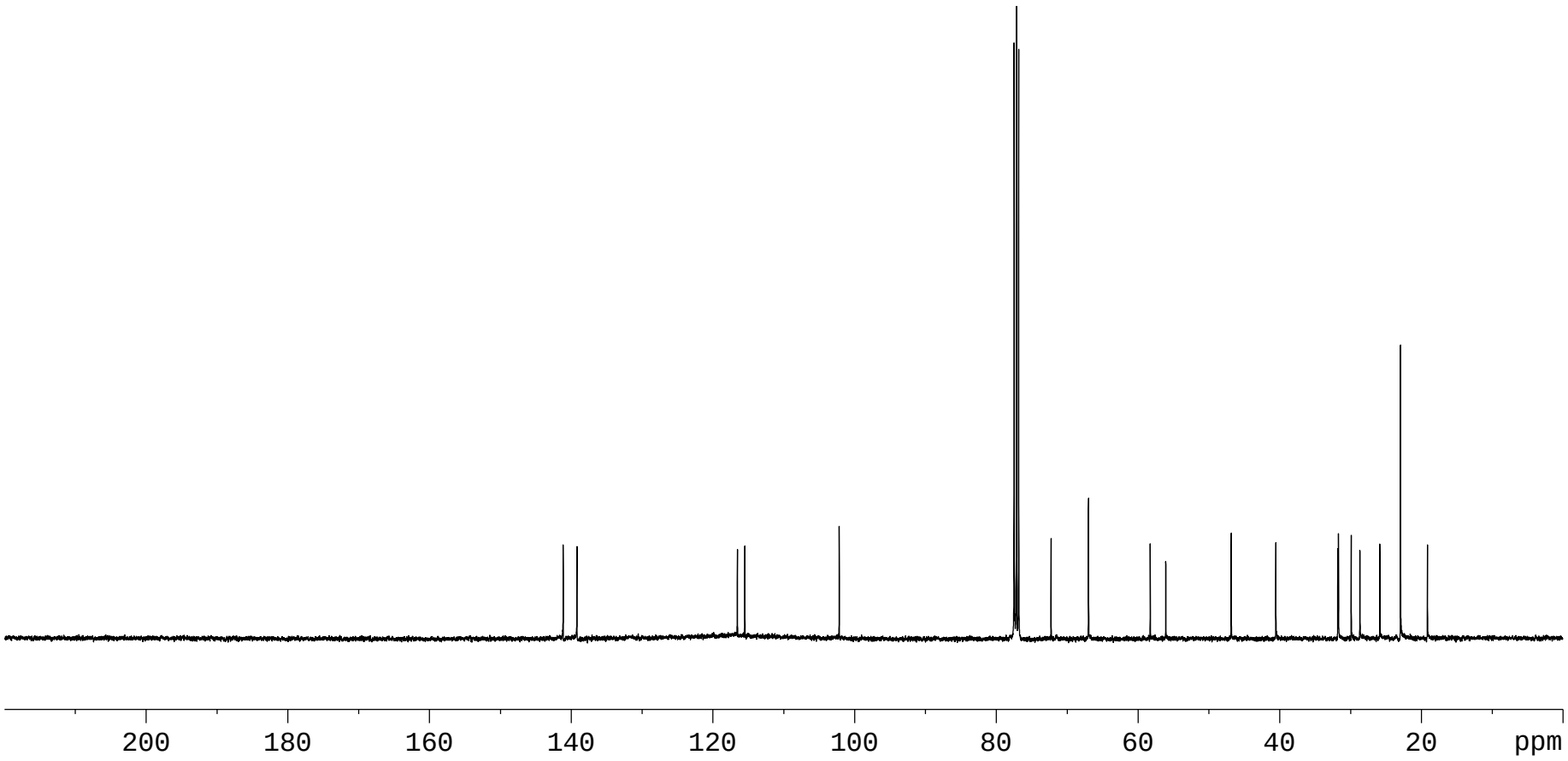


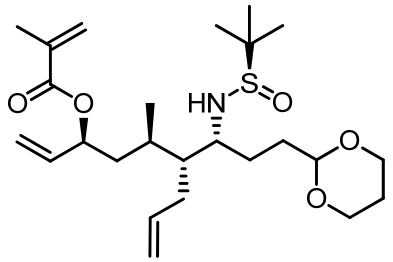


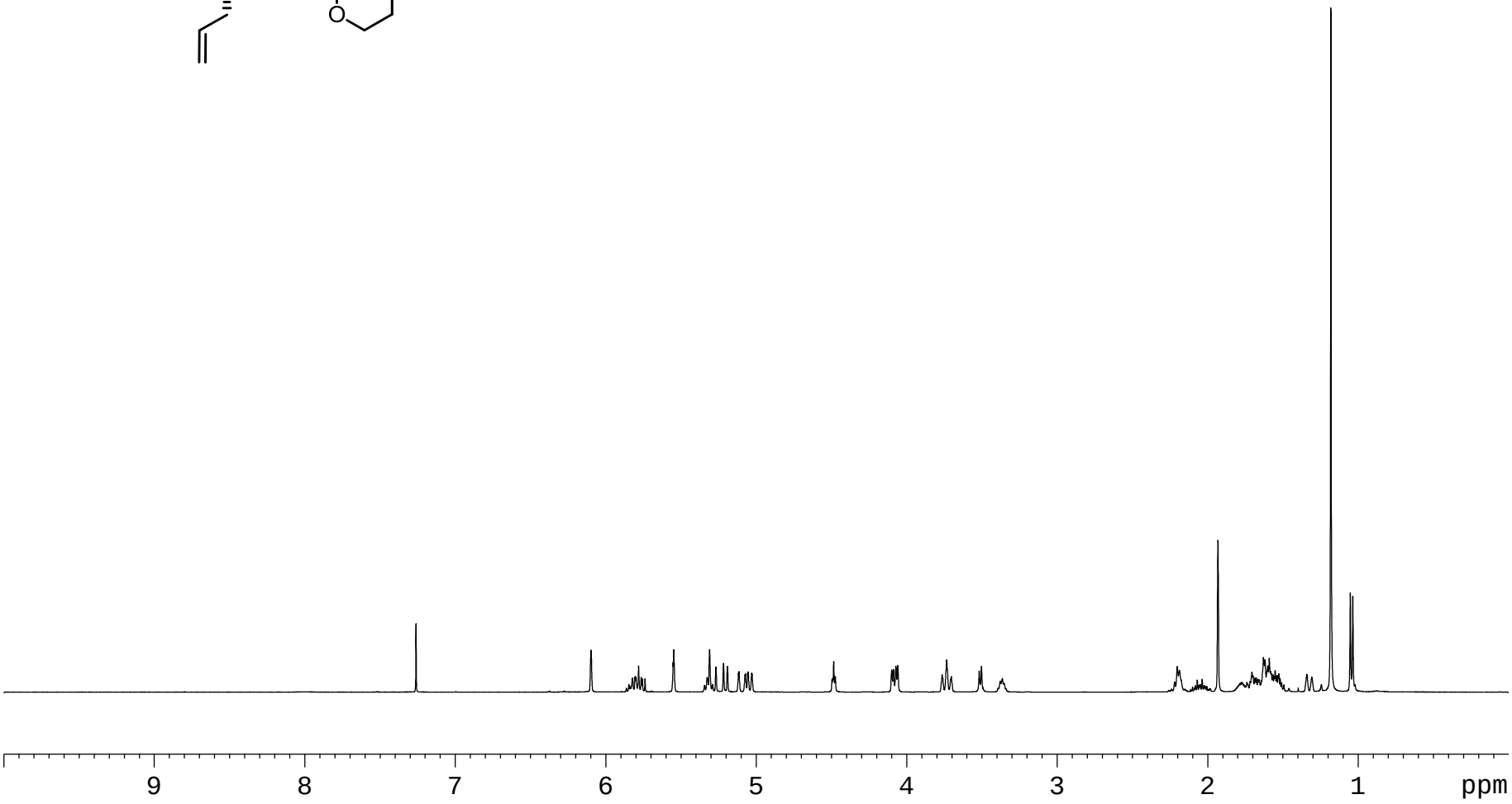
^{13}C NMR



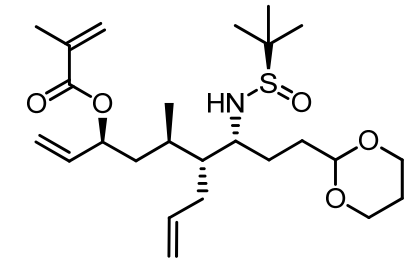


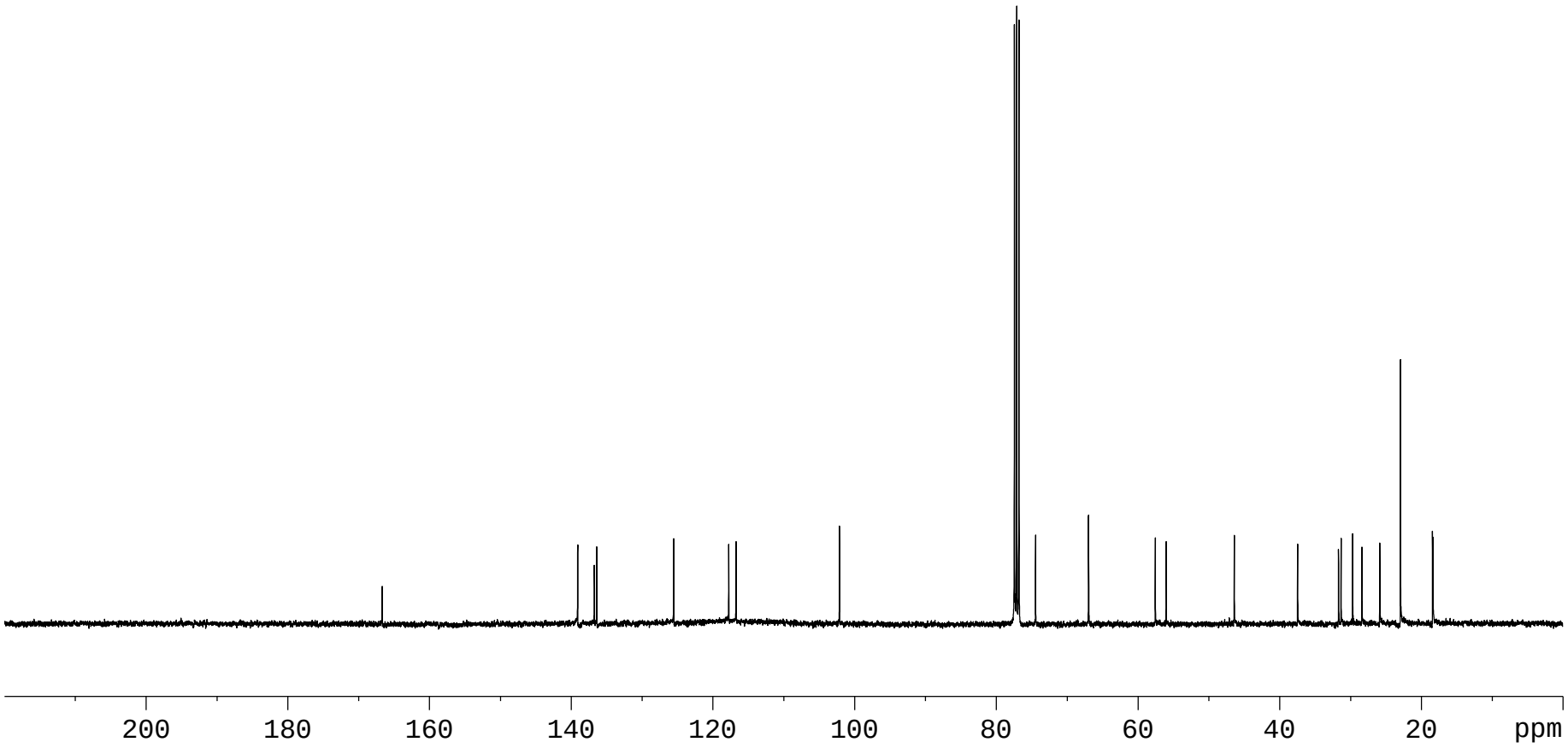
^{1}H NMR



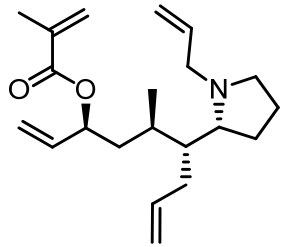


^{13}C NMR





^{1}H NMR



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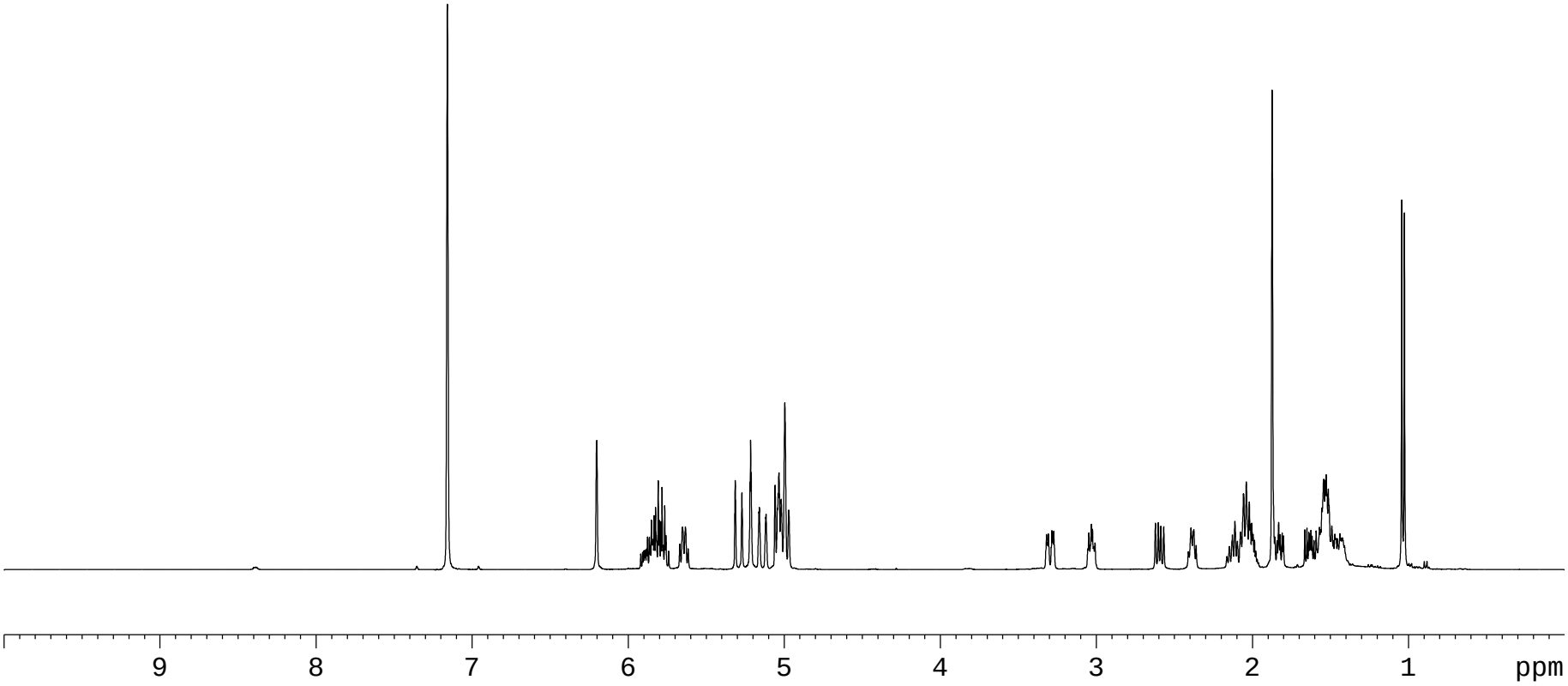
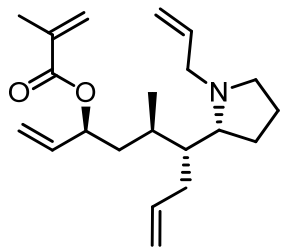


^{13}C NMR



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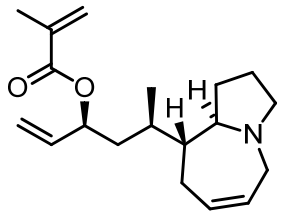
^{1}H NMR



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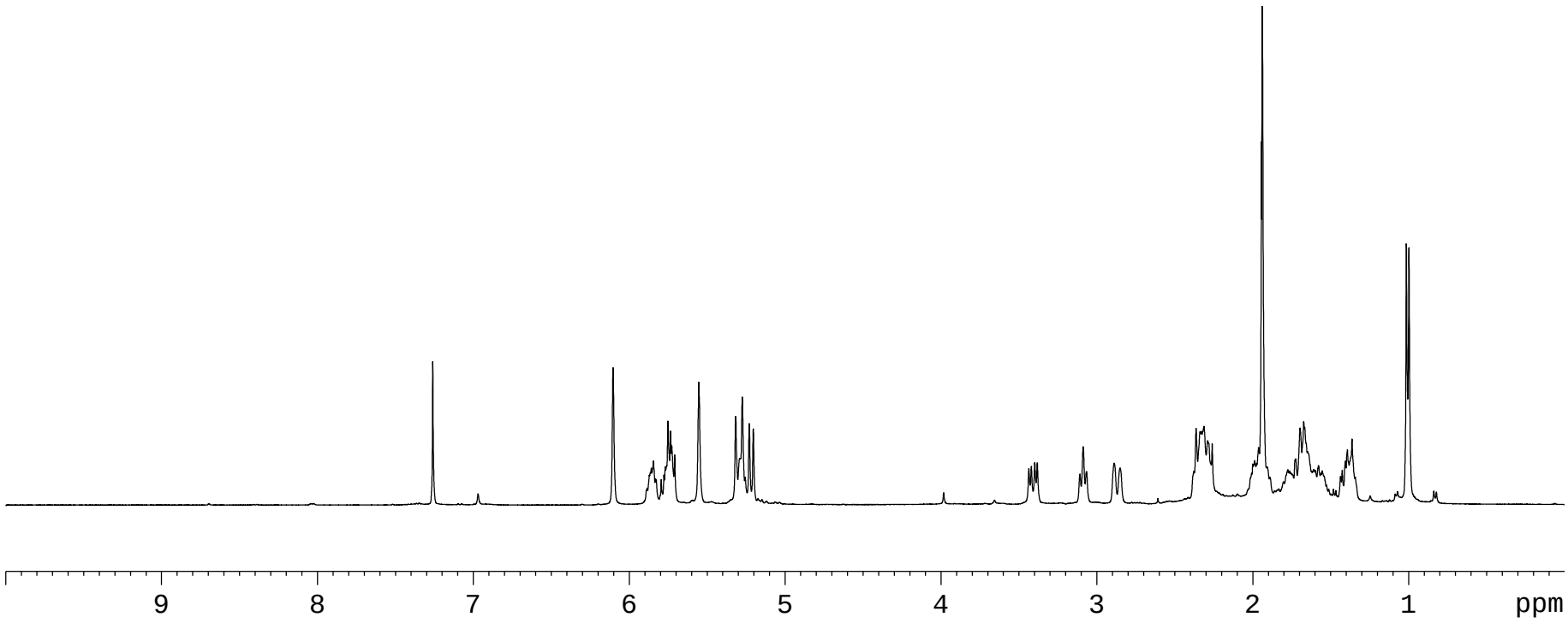
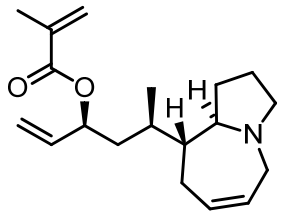
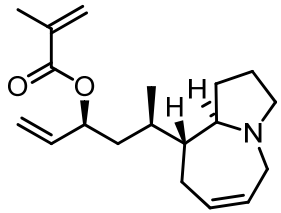


^{13}C NMR



(25)

COSY NMR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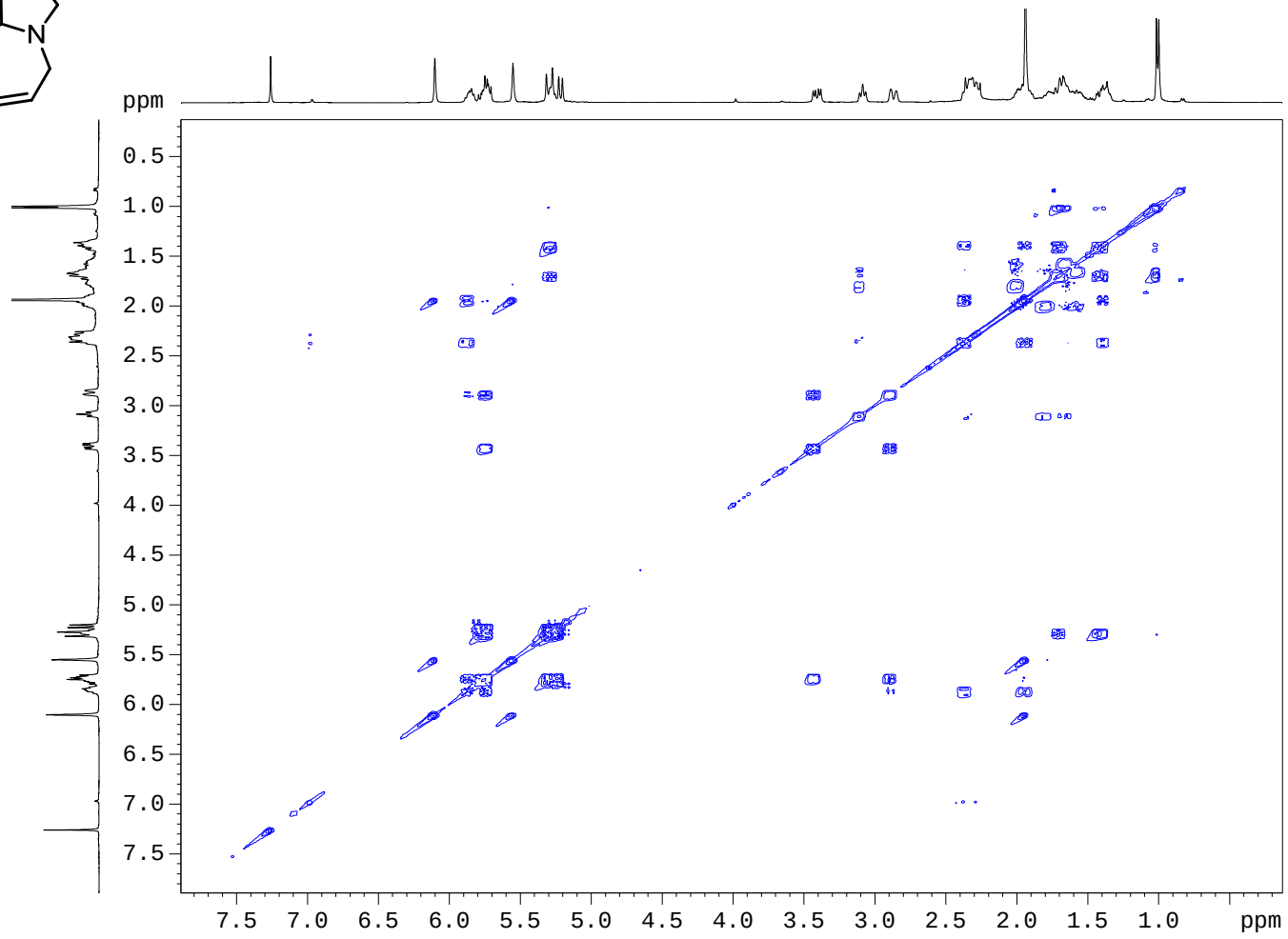
O
H
H
N

(25)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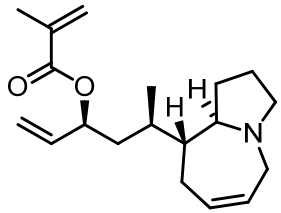
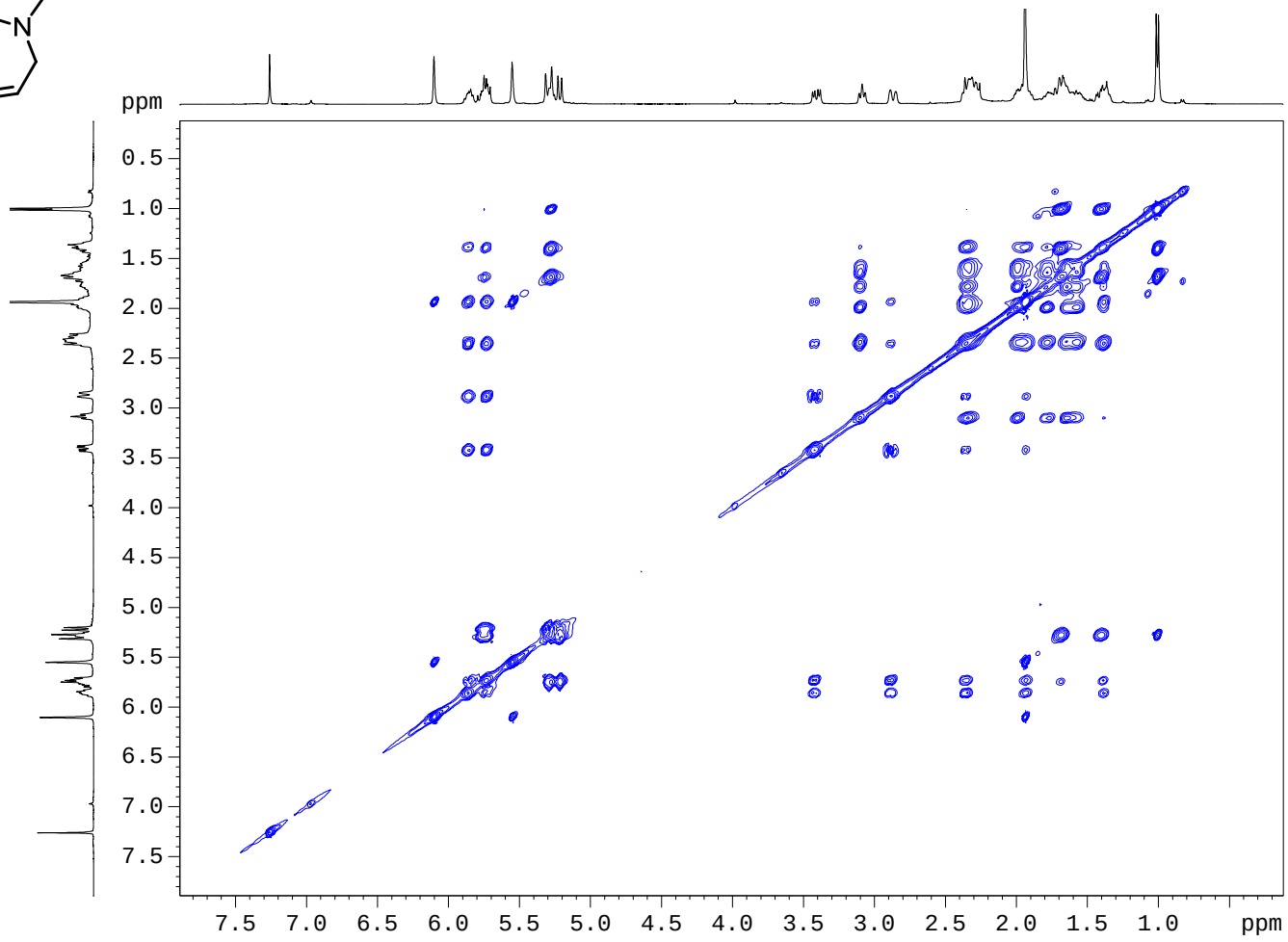
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

TOCSY NMR


O
O
H
H
N

(25)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3.5
4.0
4.5
5.0
5.5
6.0
6.5
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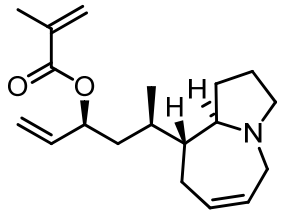
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

HSQC NMR



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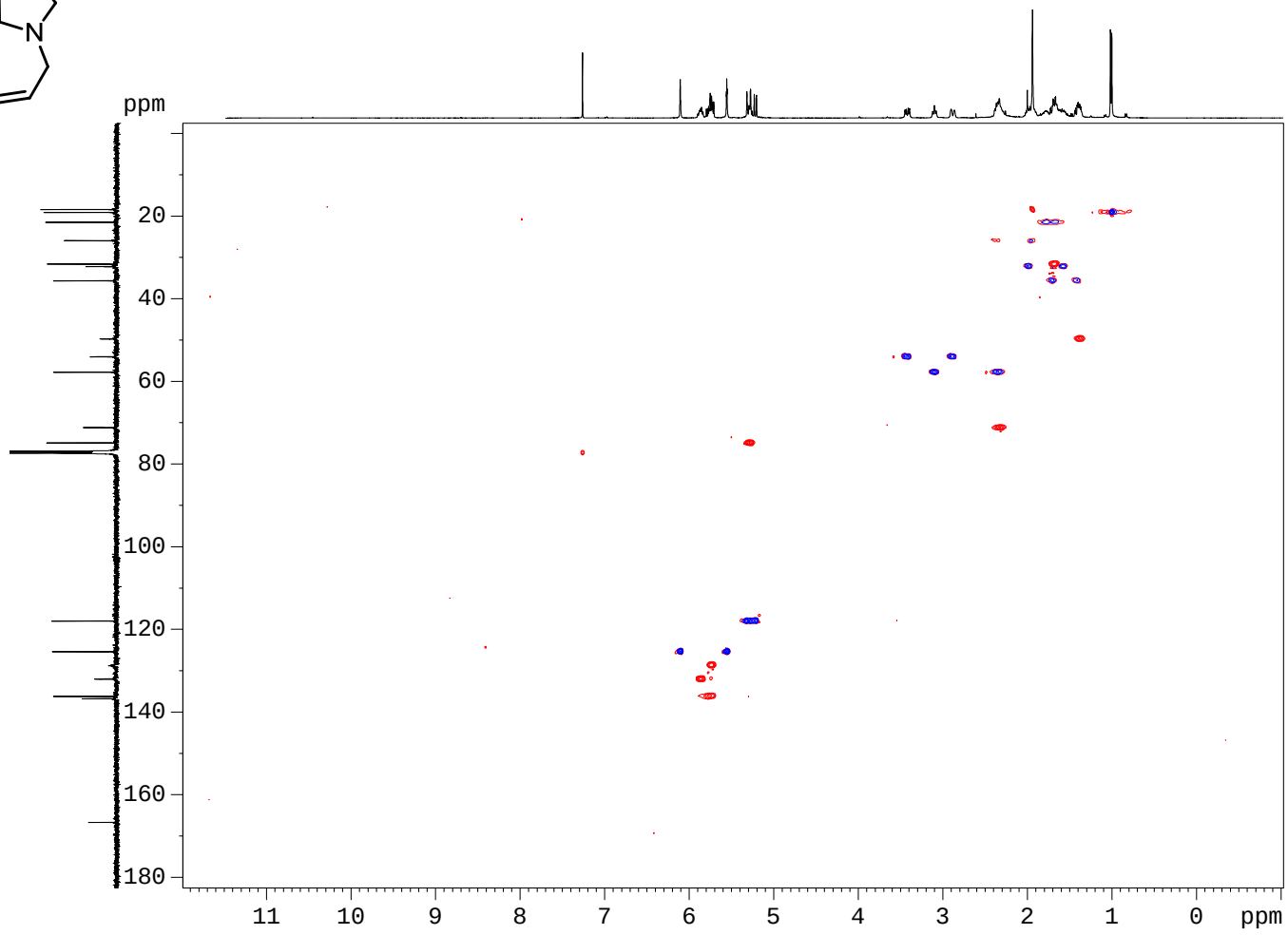
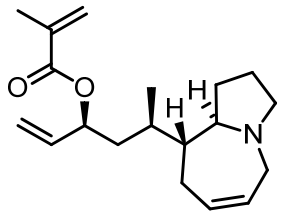
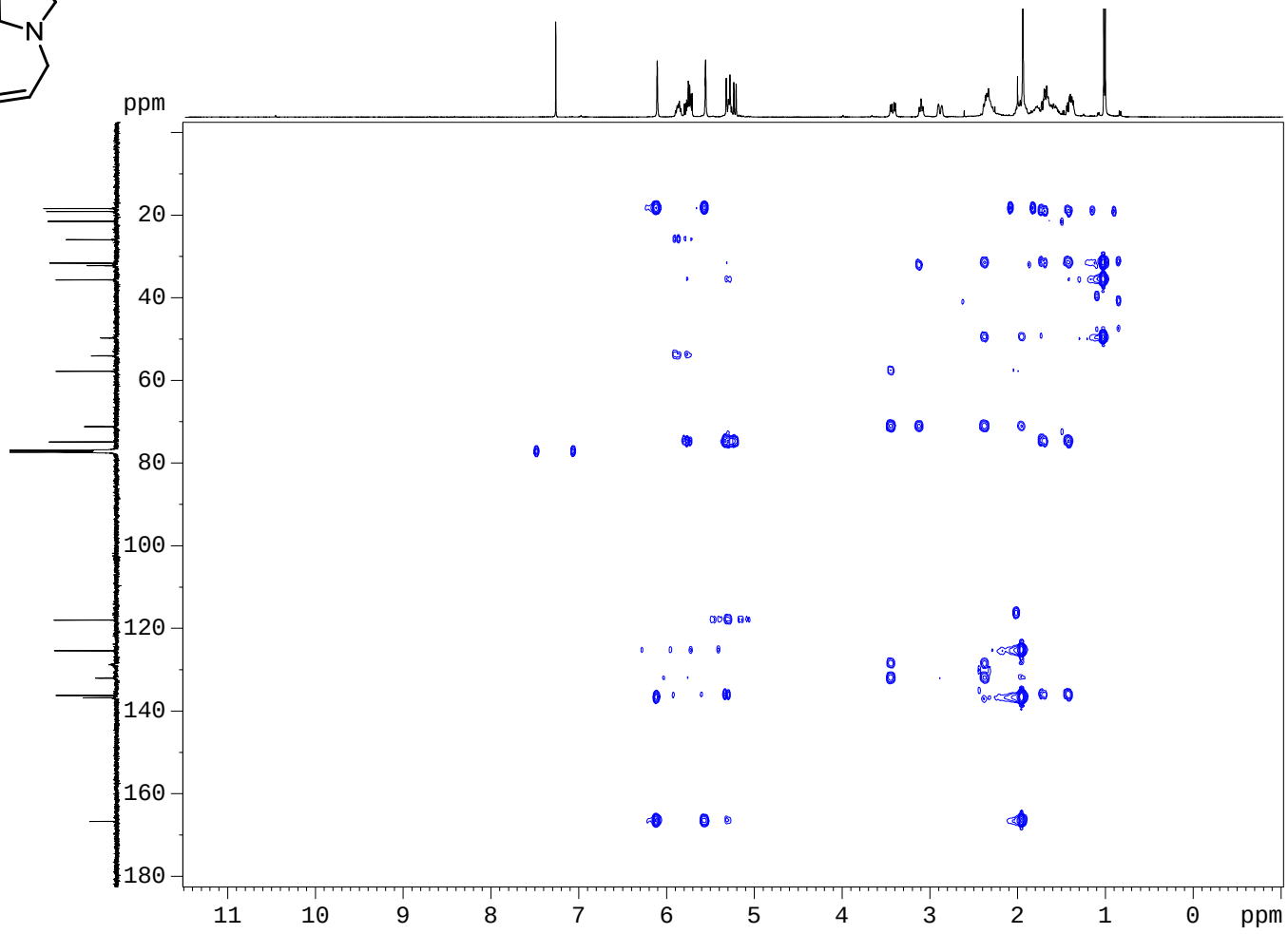


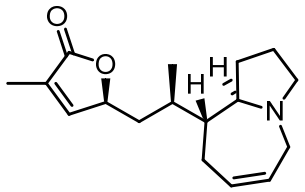
HMBC NMR



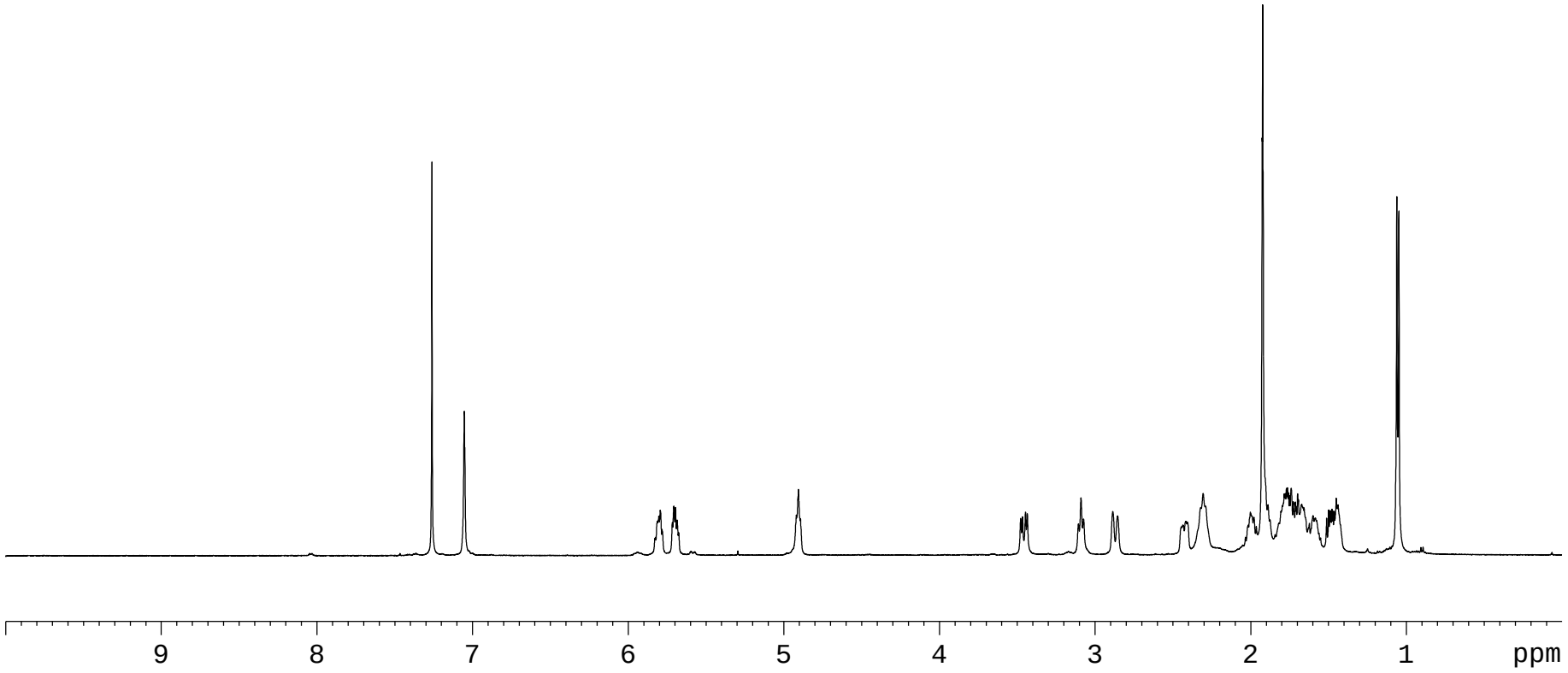
(25)



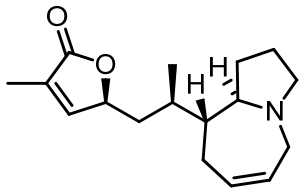
^{1}H NMR



(26)

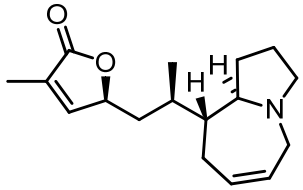


^{13}C NMR

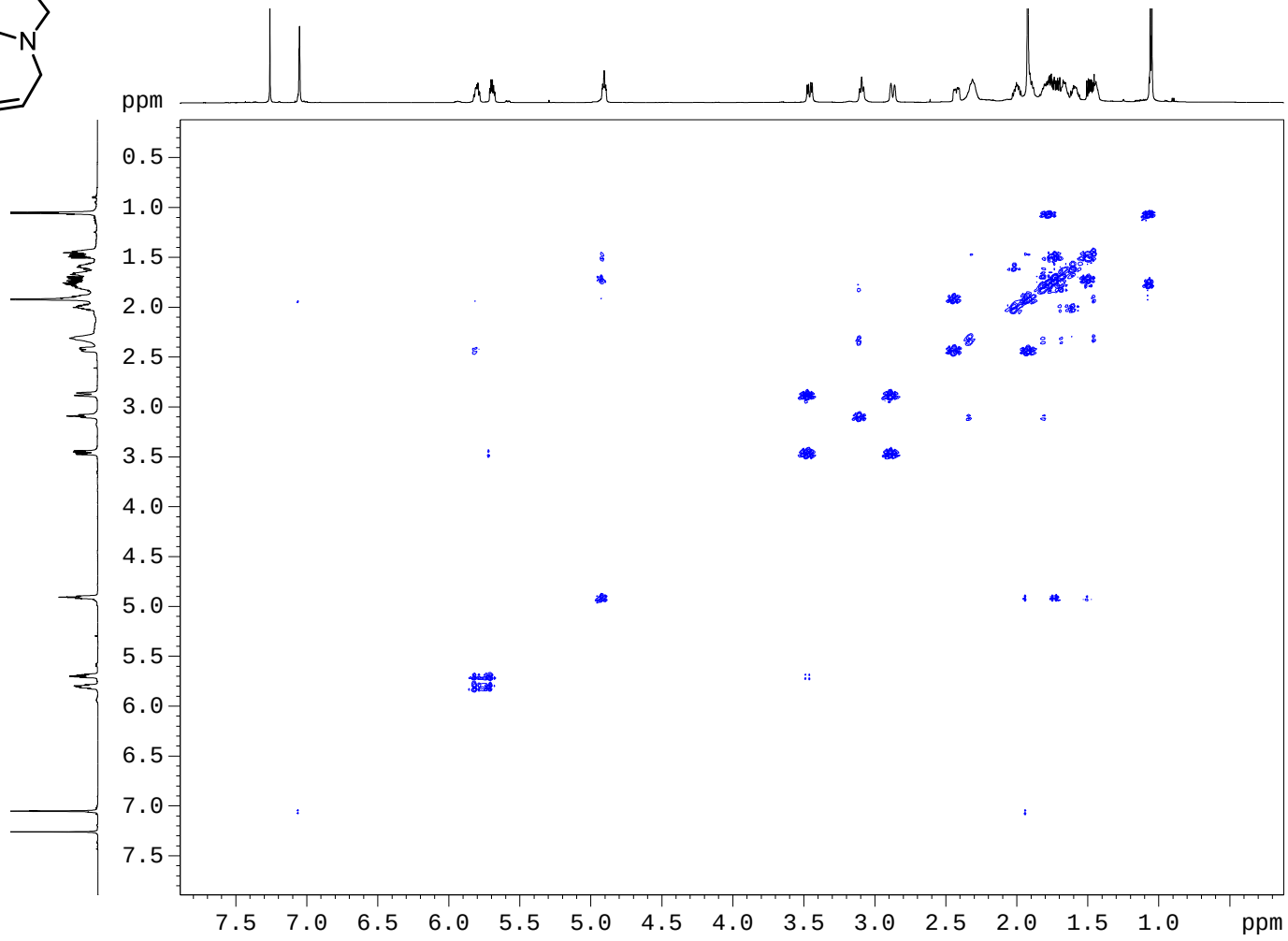


(26)

COSY NMR


O
O
H
H
N

(26)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3.0
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4.0
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5.5
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6.5
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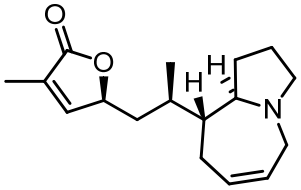
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

TOCSY NMR



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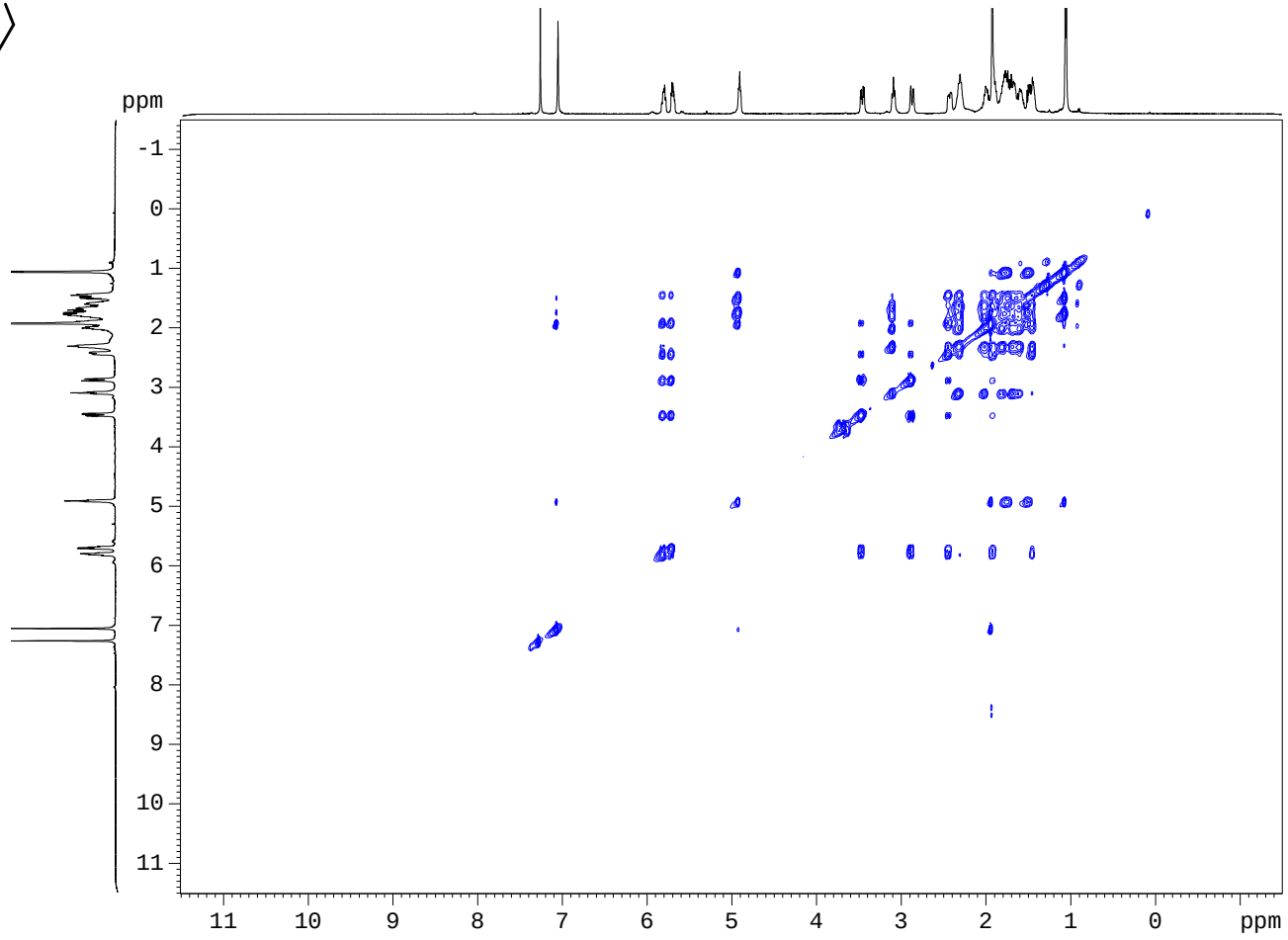
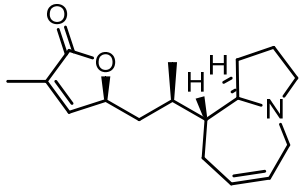


HSQC NMR



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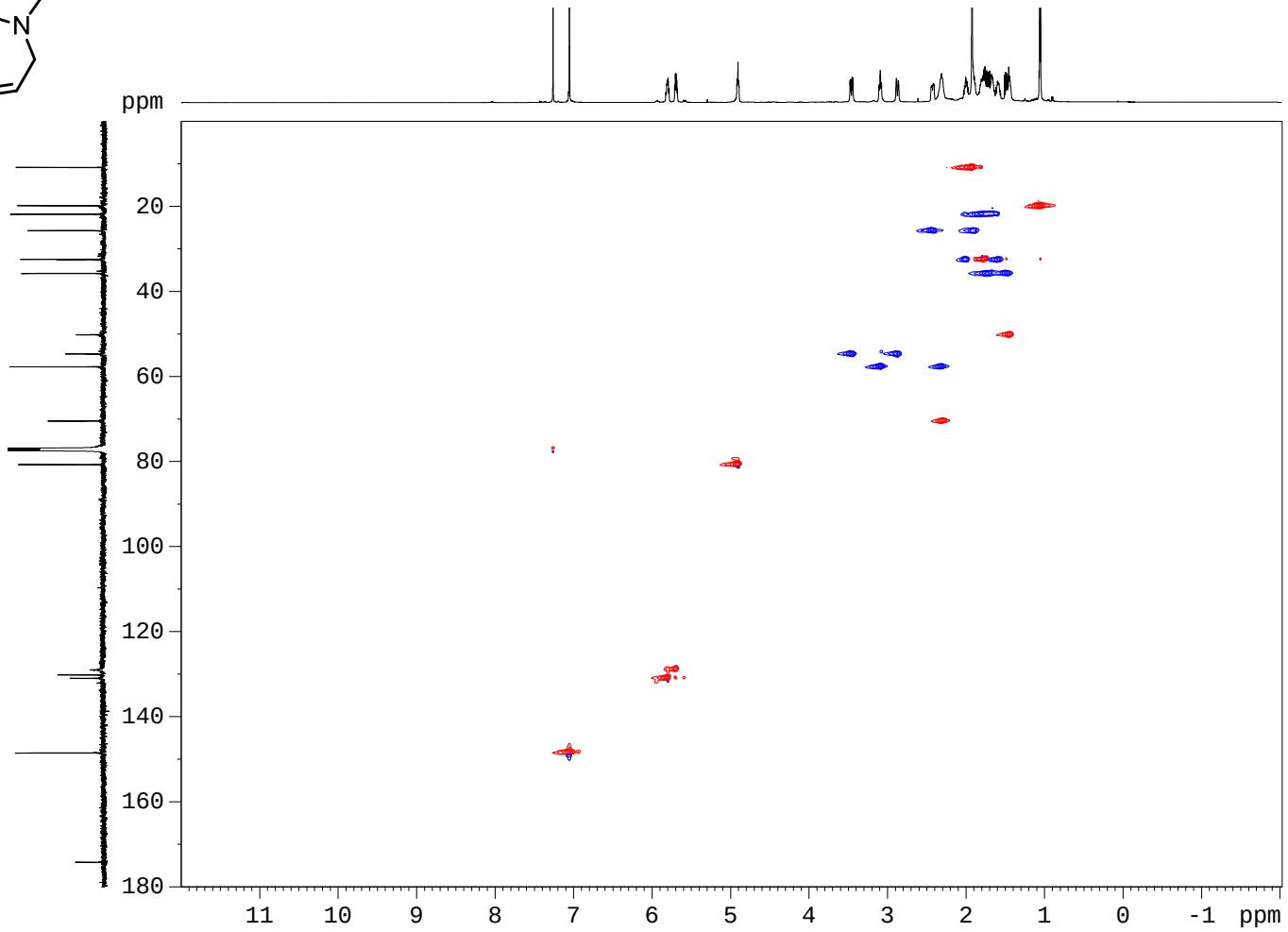
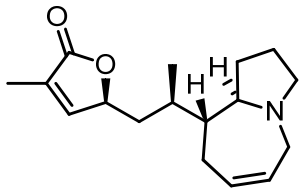
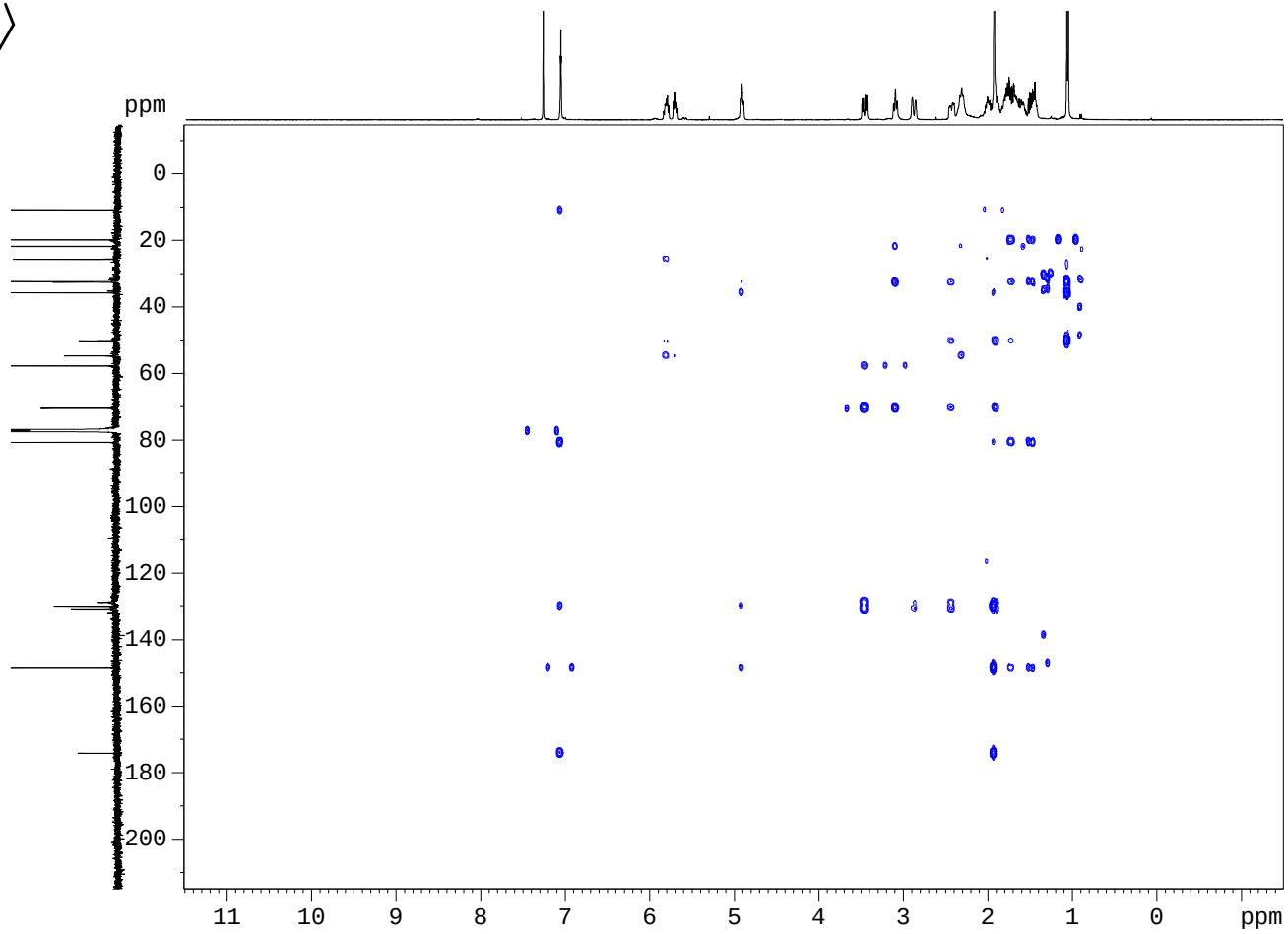


HMBC NMR


O
O
H
H
N

(26)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200
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8
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4
3
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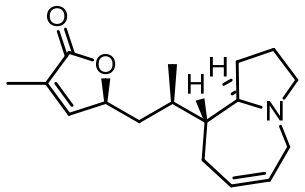
1
0
ppm

NOESY NMR



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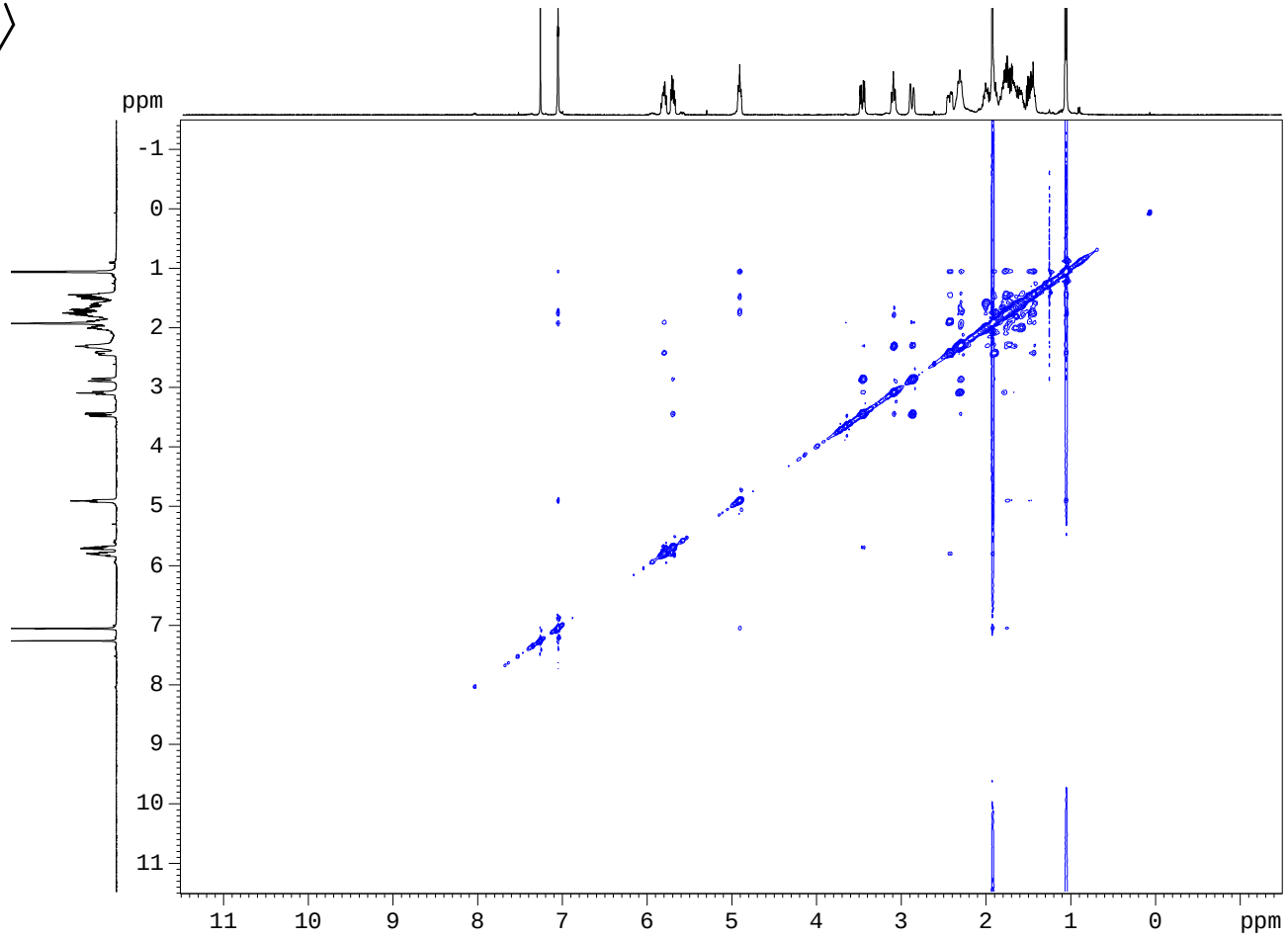
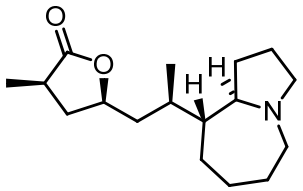


^{1}H NMR



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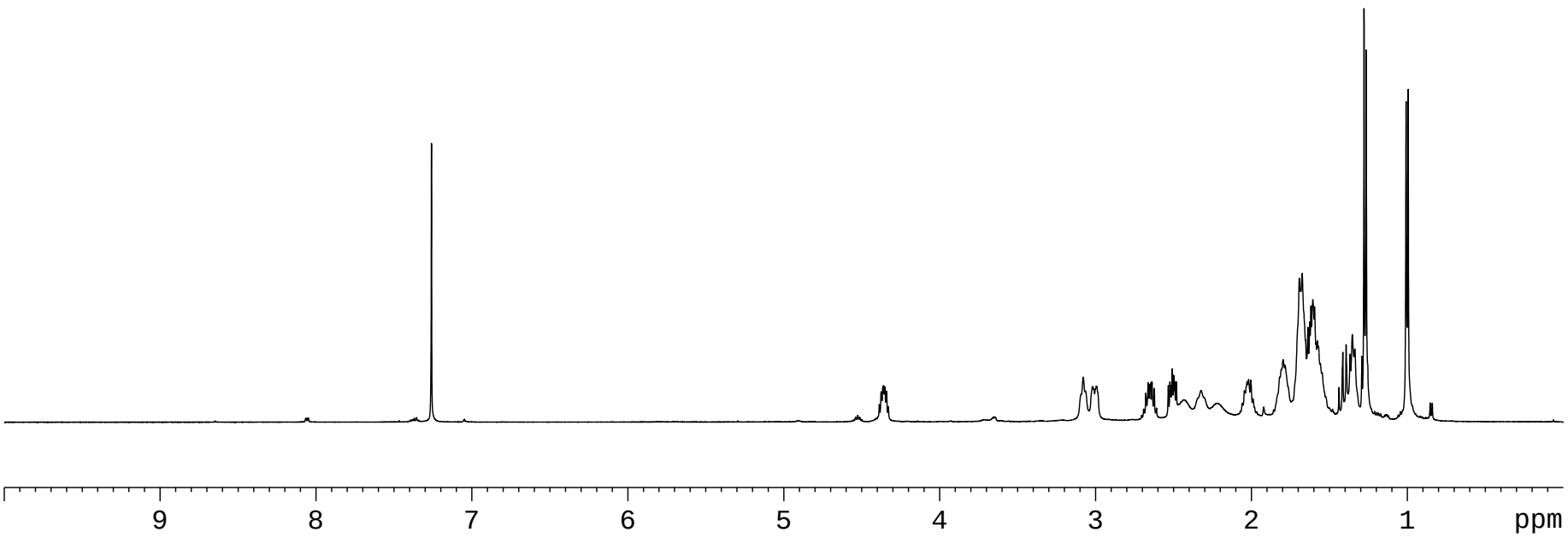
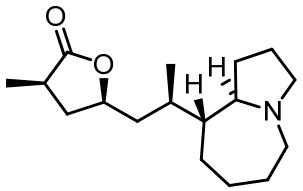
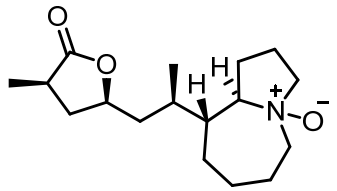


^{13}C NMR



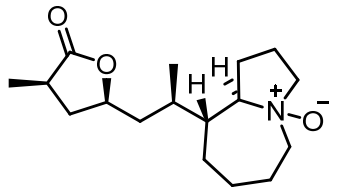
(27)

^{1}H NMR



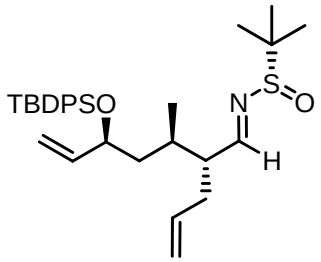
(28)

^{13}C NMR



(28)

^{1}H NMR



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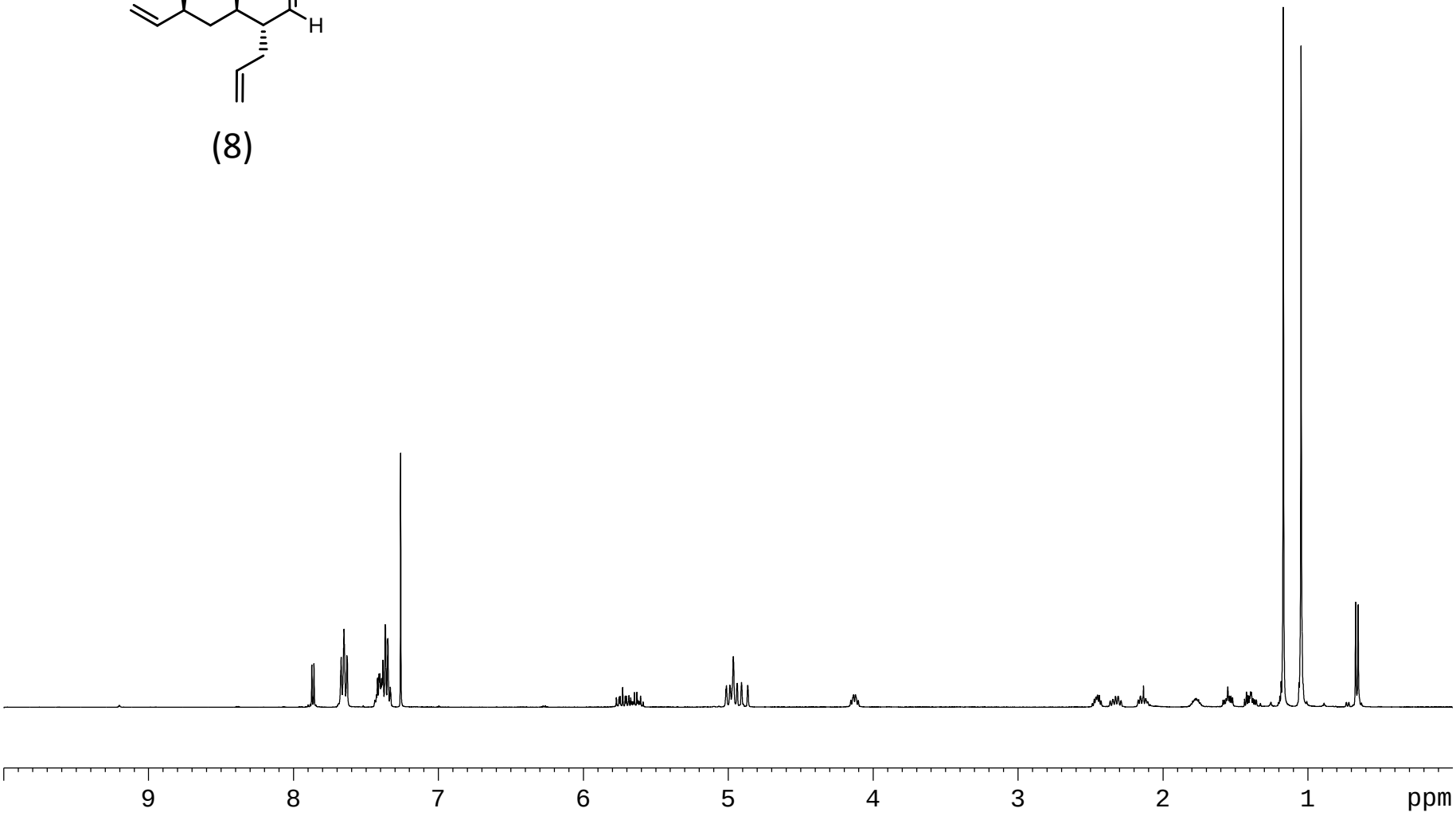
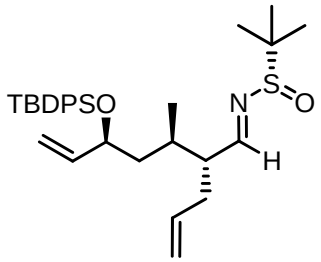
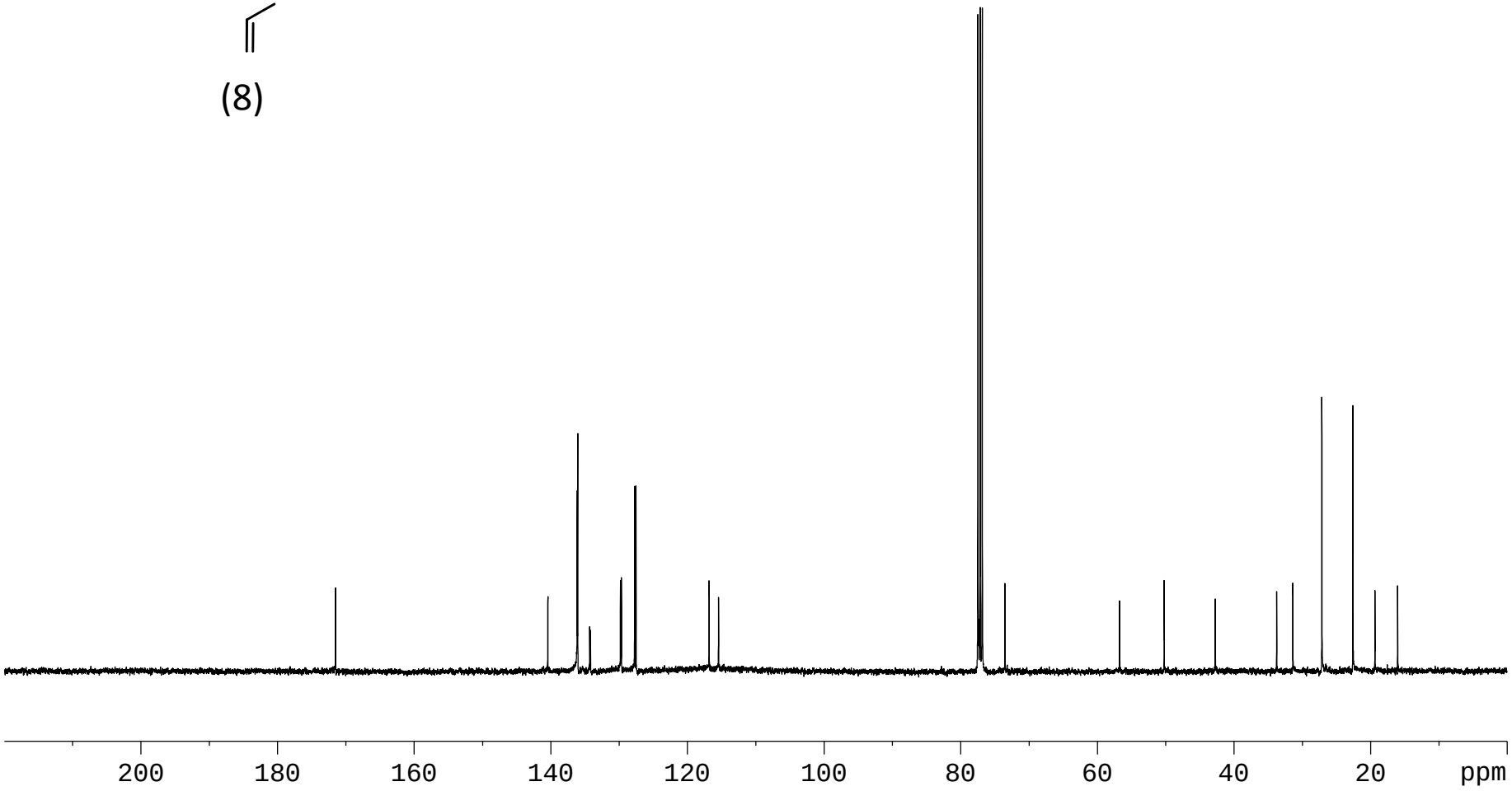


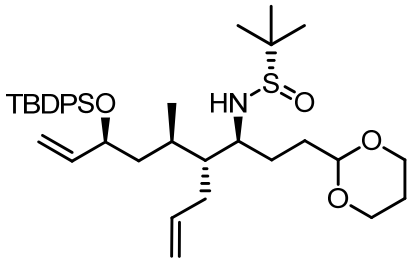
^{13}C NMR



(8)



^{1}H NMR



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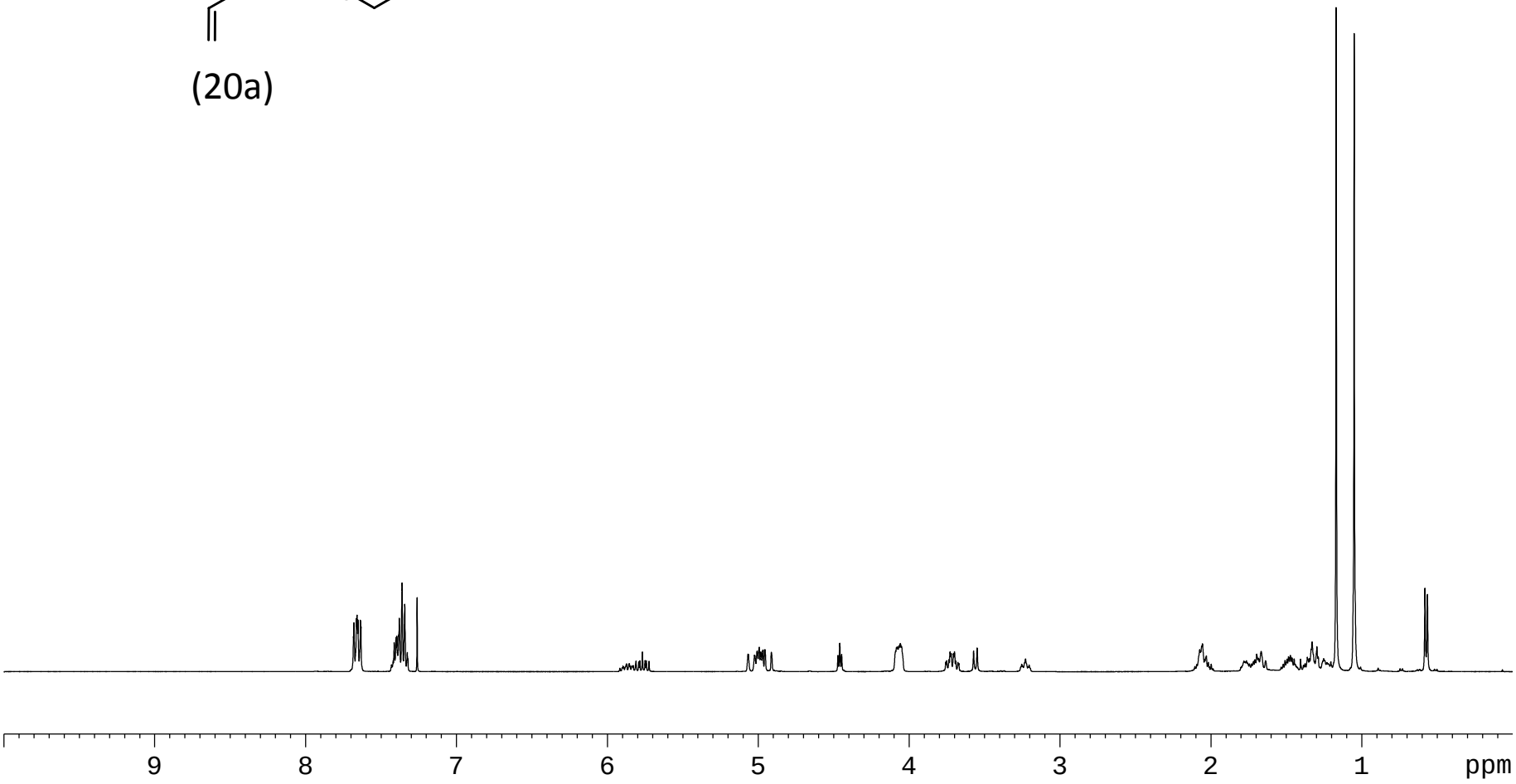
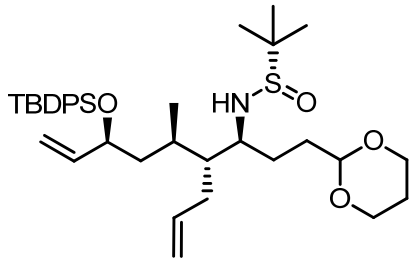
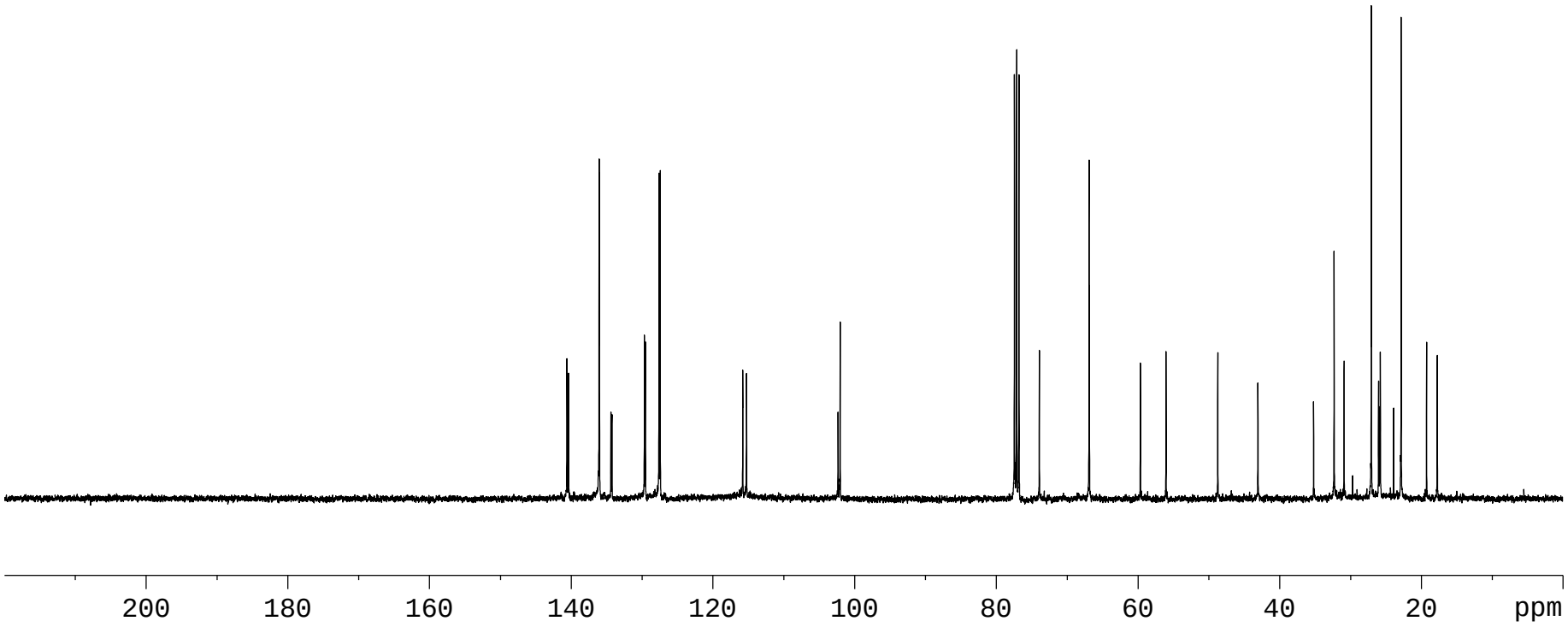


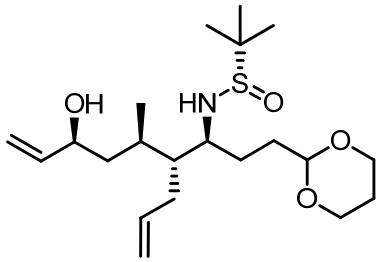
^{13}C NMR

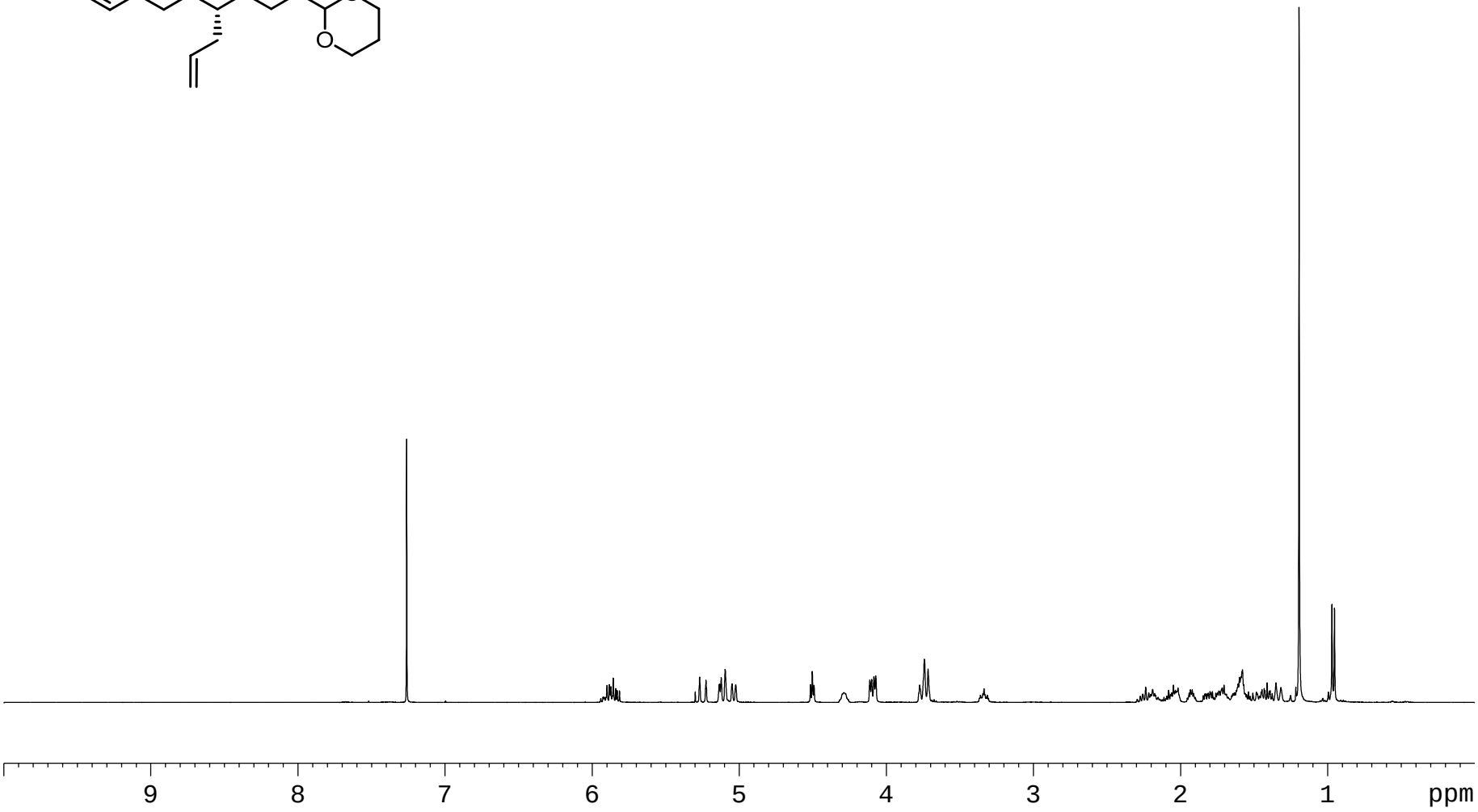


(20a)

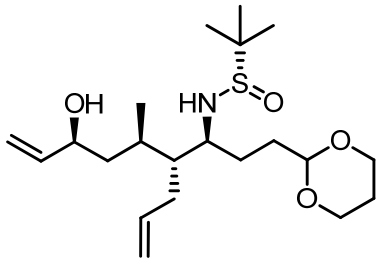


^{1}H NMR

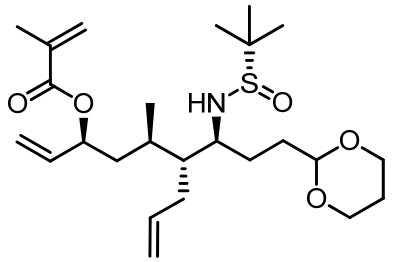




^{13}C NMR



^{1}H NMR



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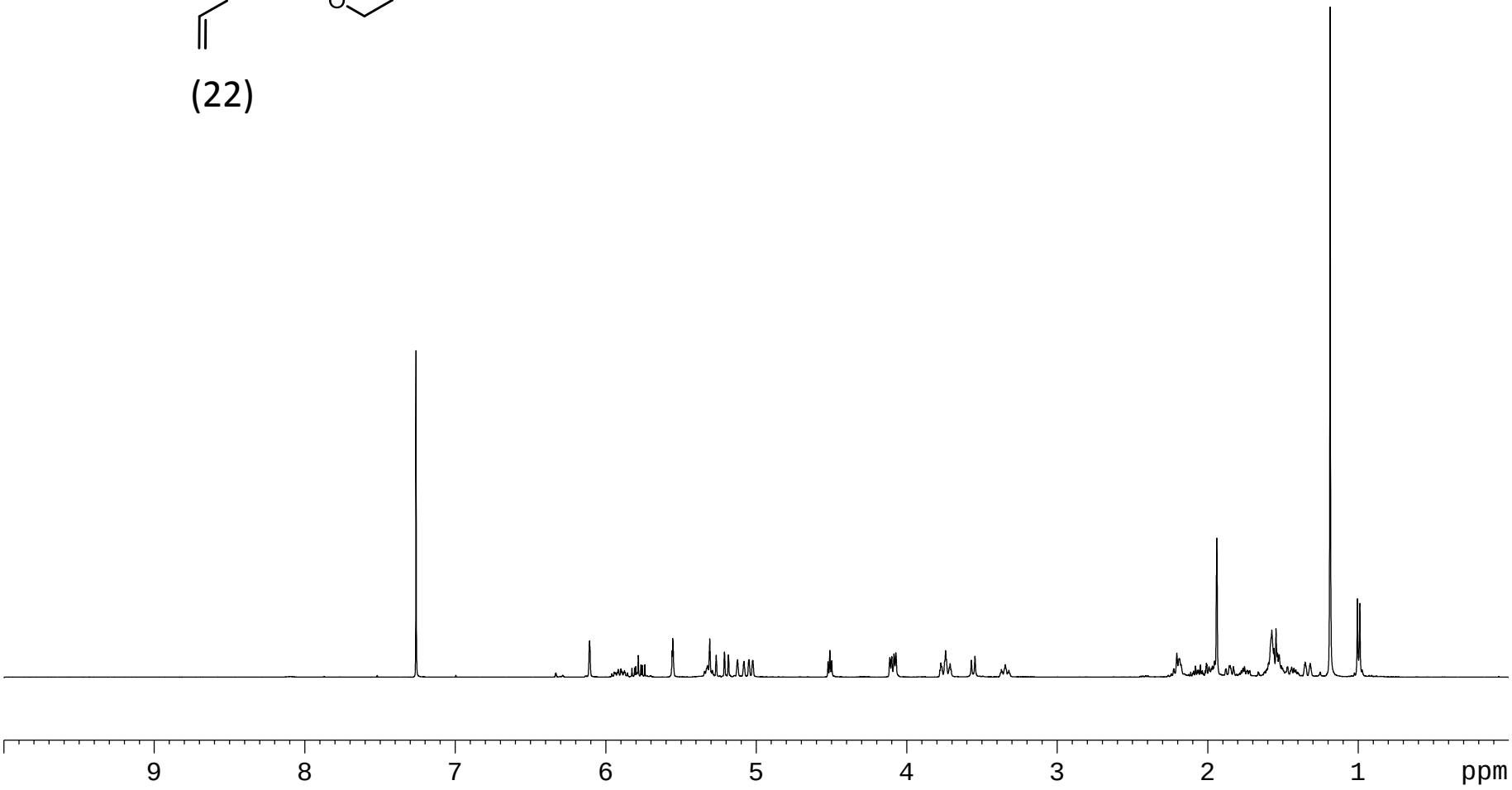

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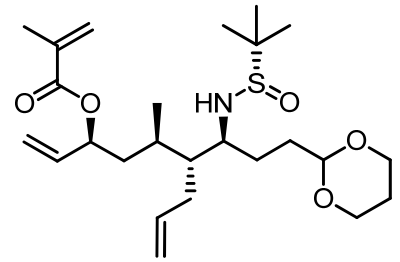

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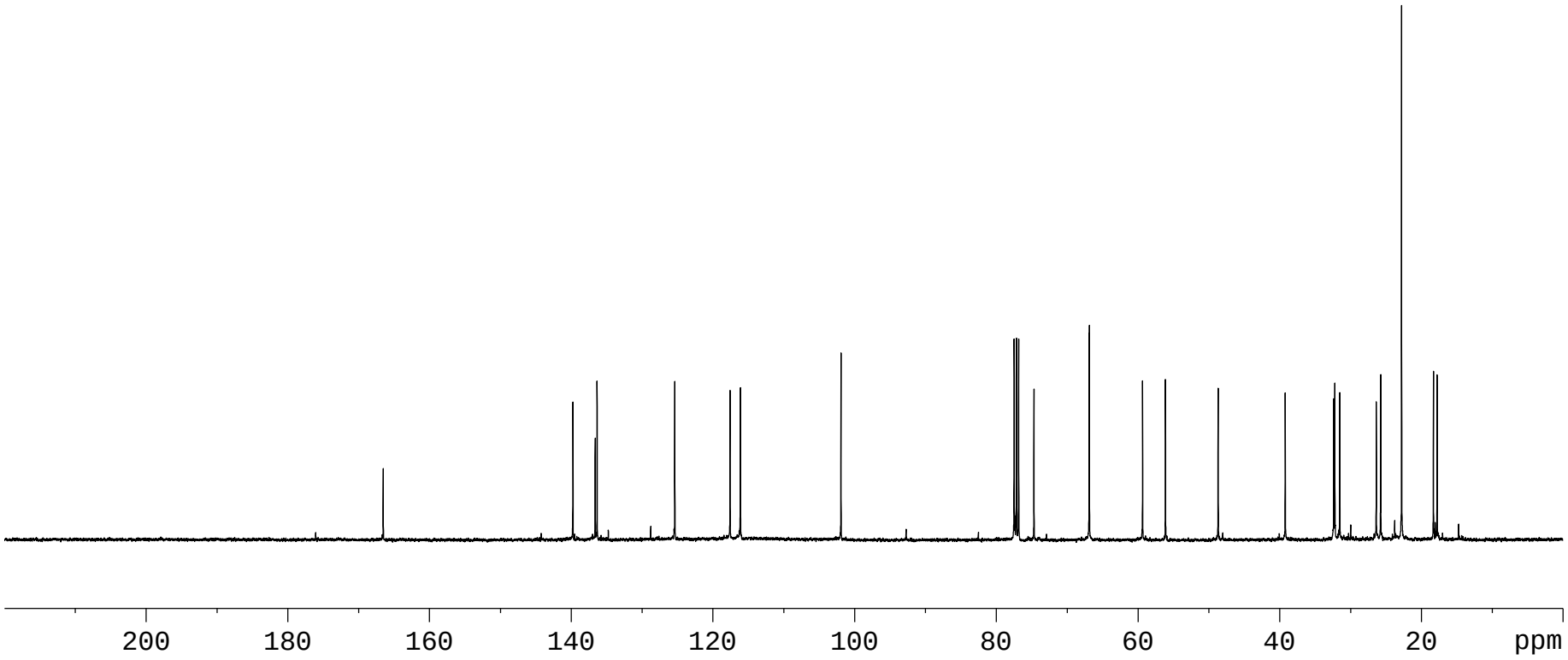
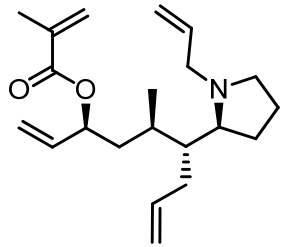


^{1}H NMR



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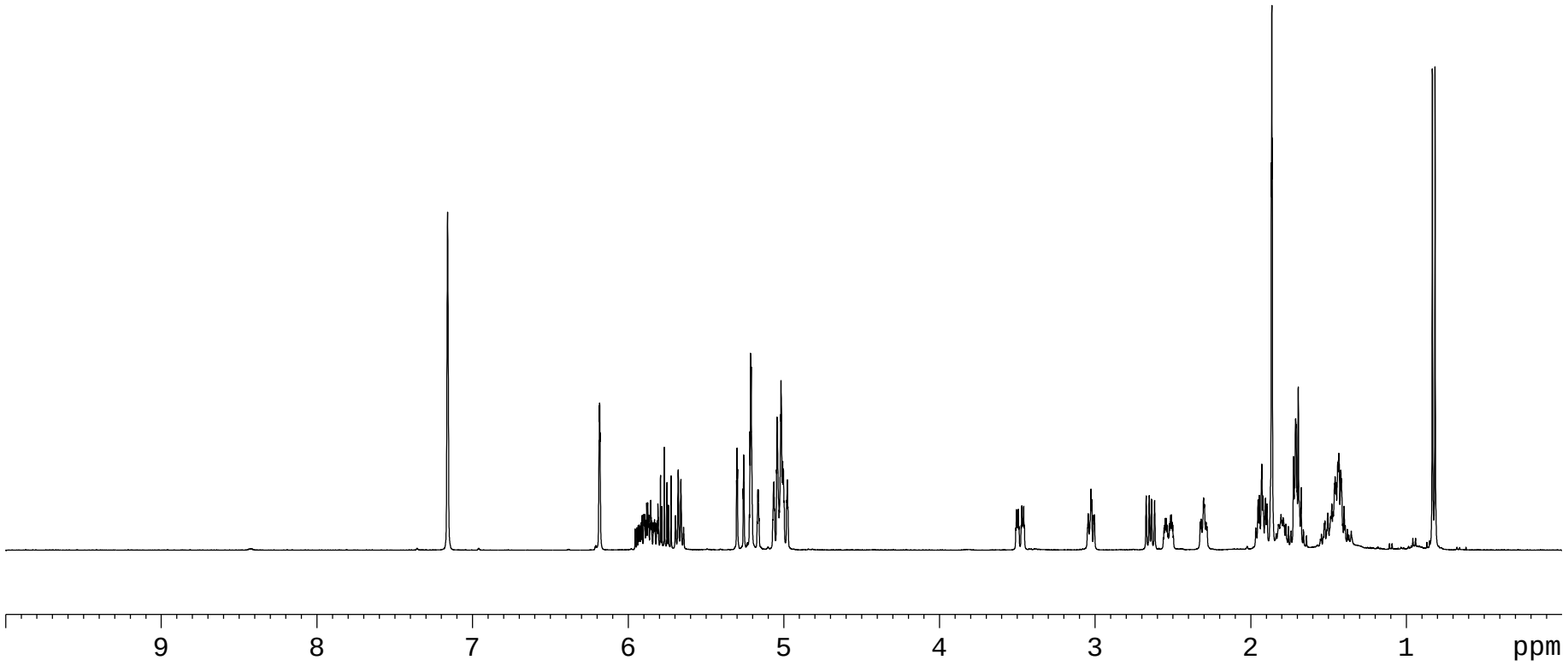
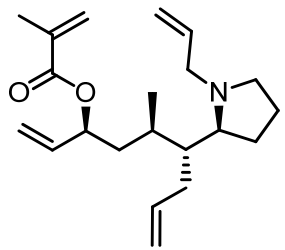


^{13}C NMR



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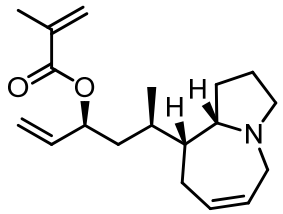

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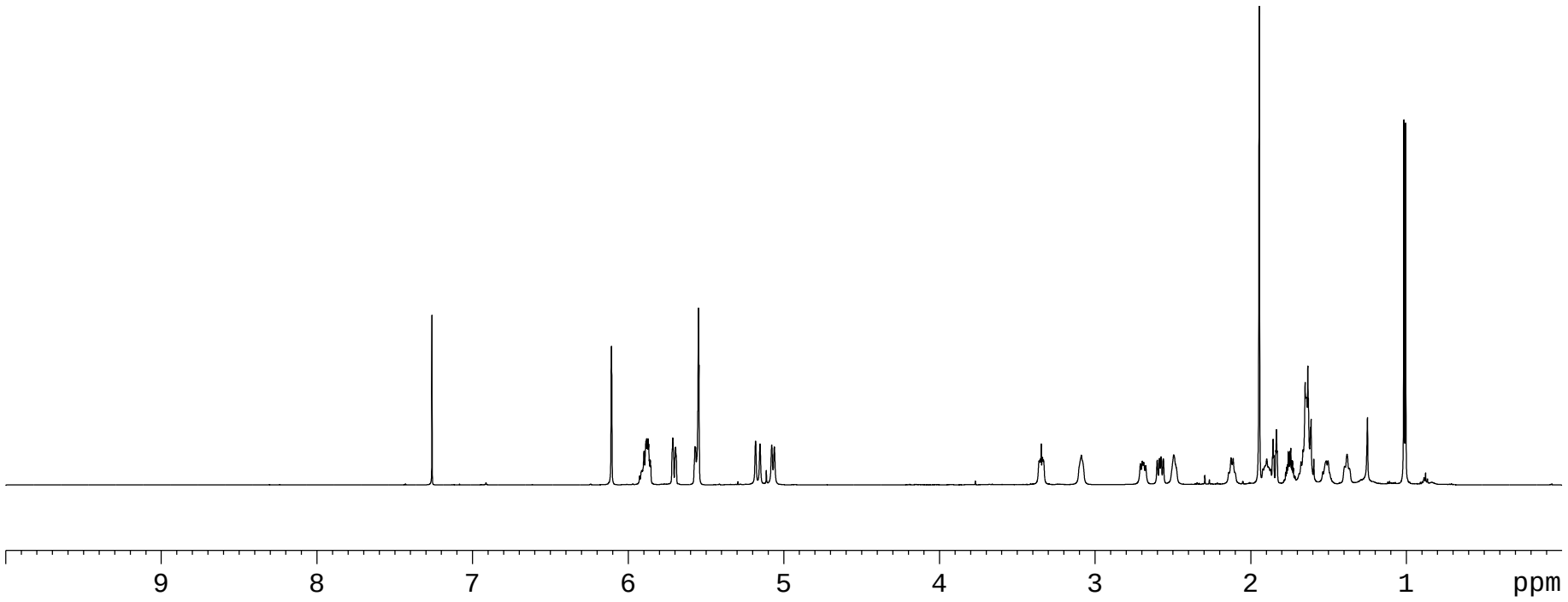

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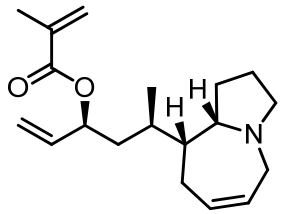

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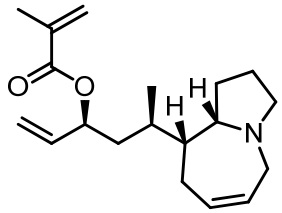
COSY NMR



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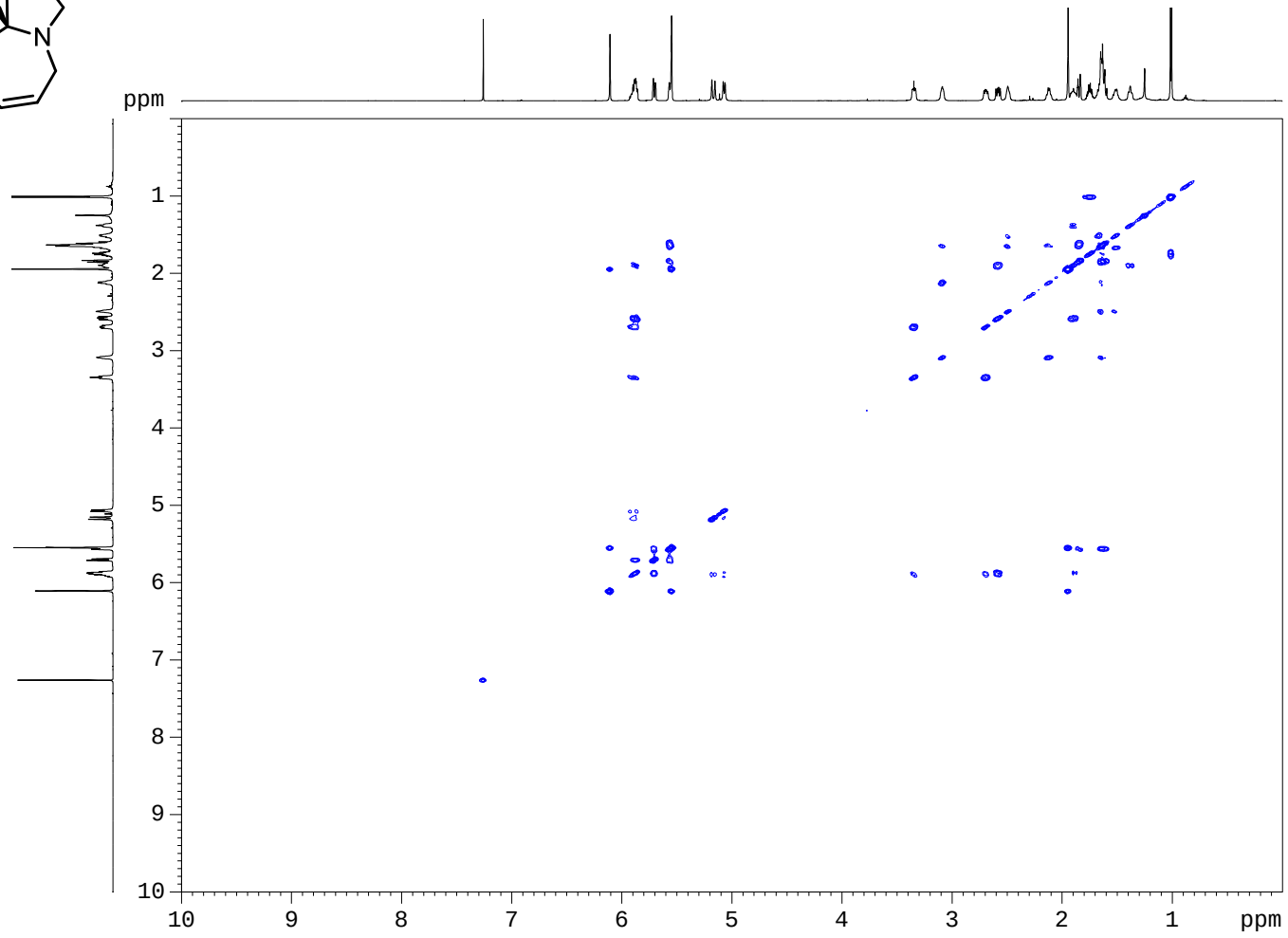
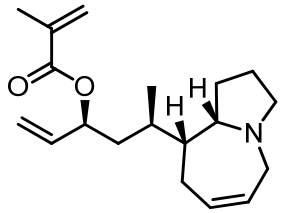


TOCSY NMR



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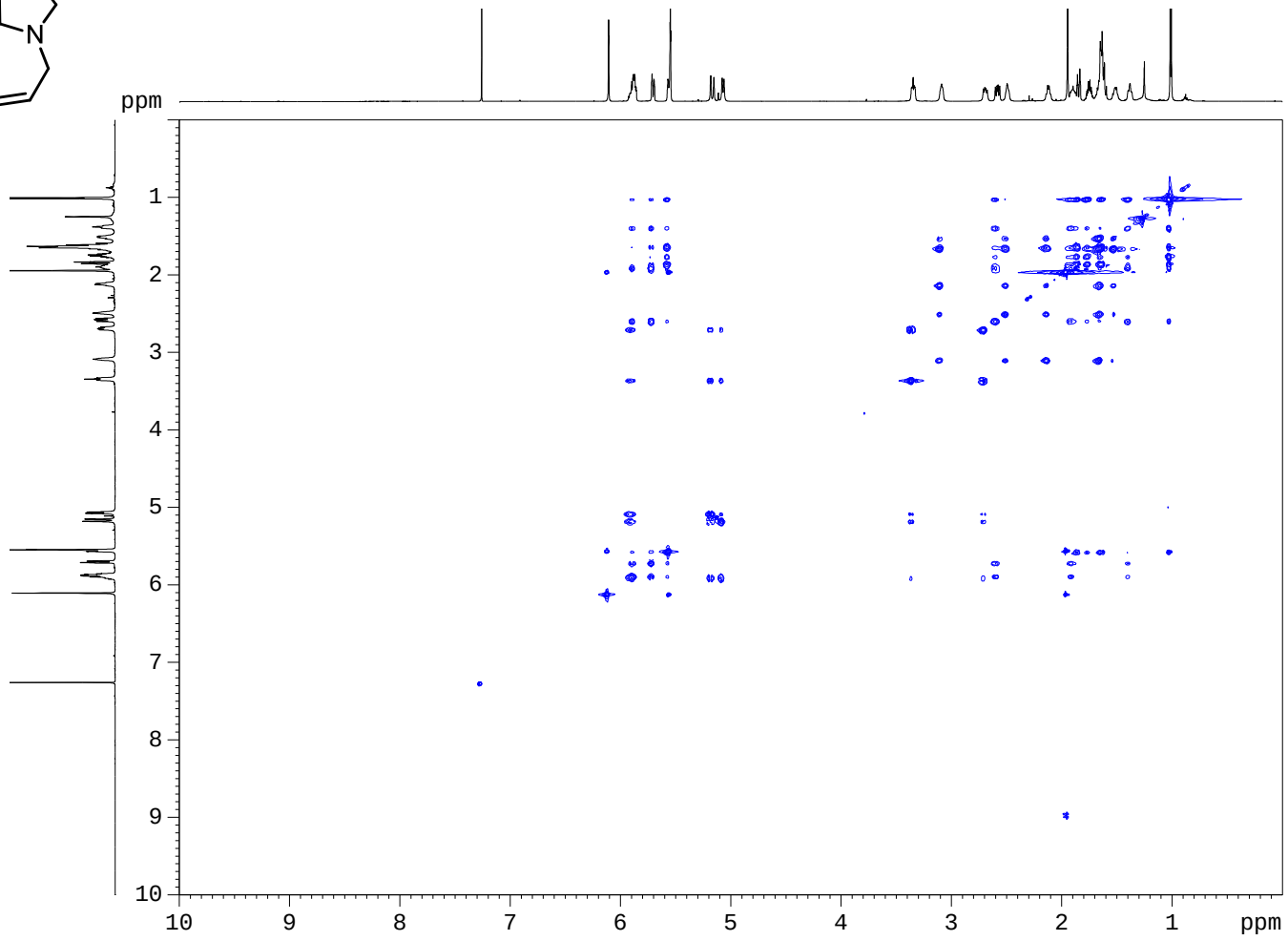
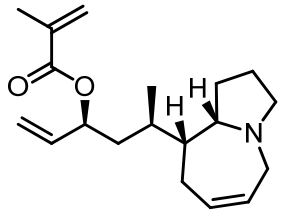


HSQC NMR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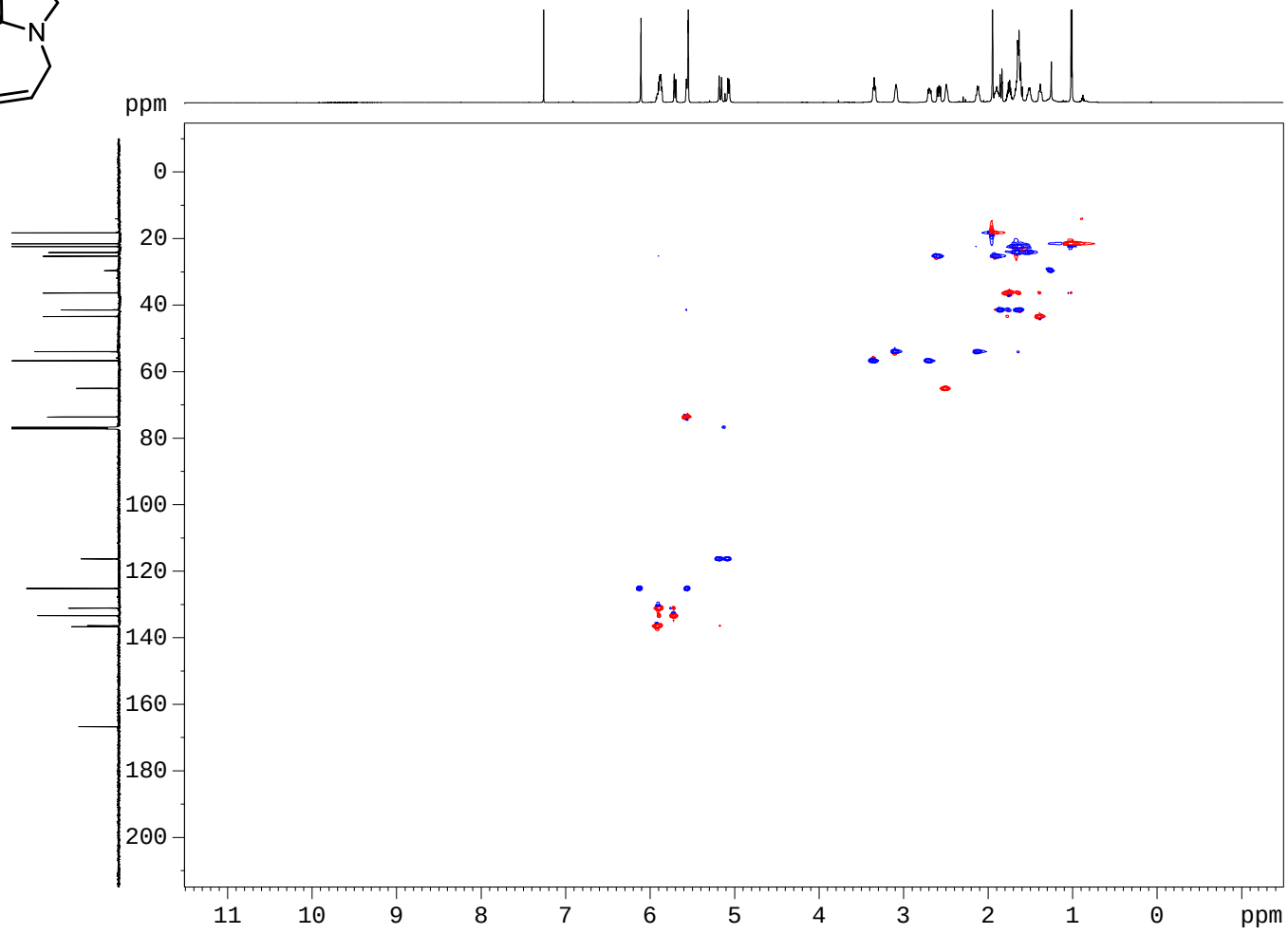
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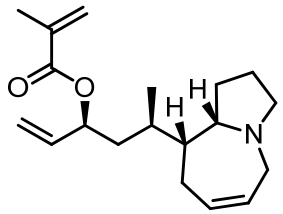
HMBC NMR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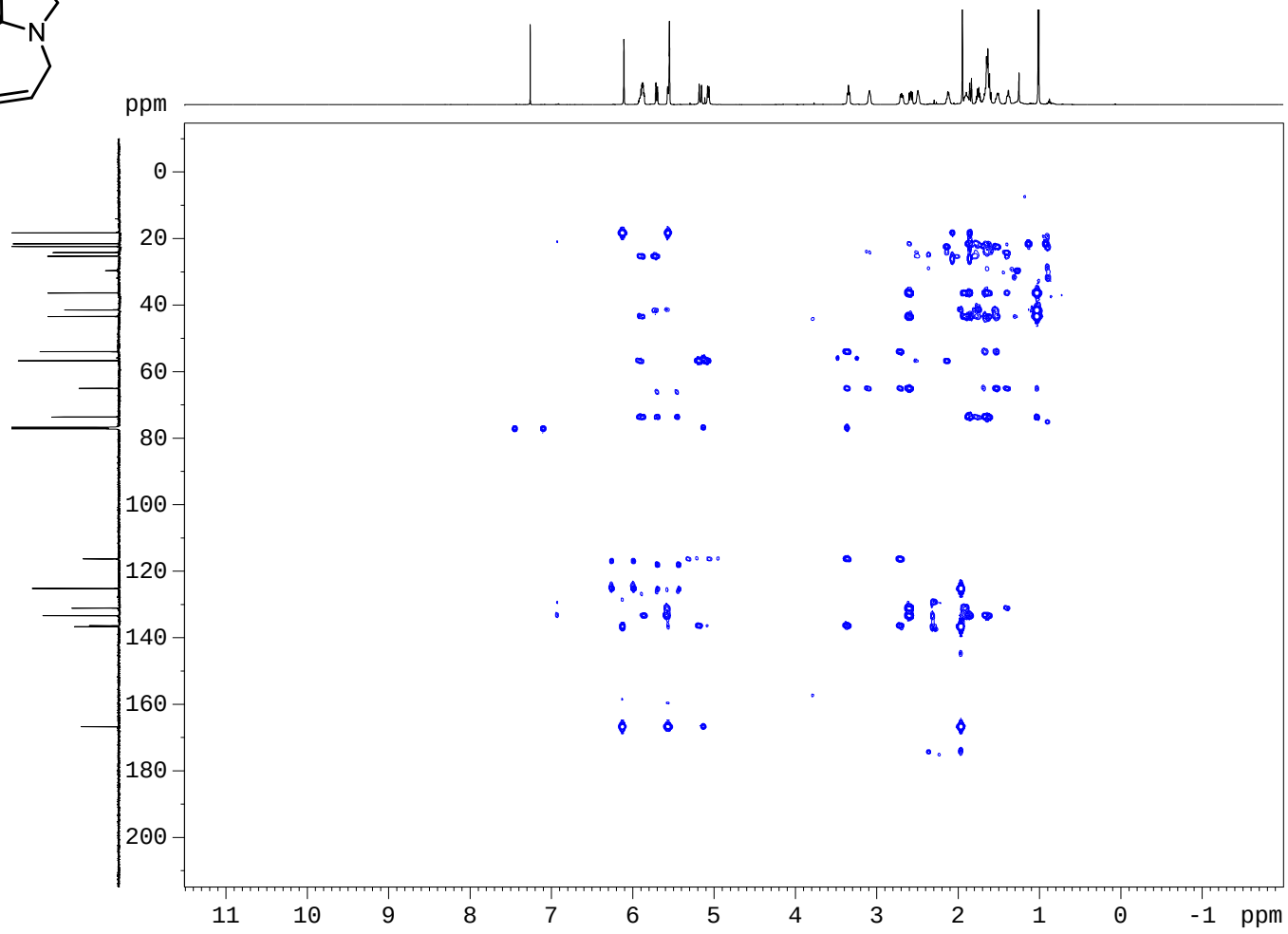
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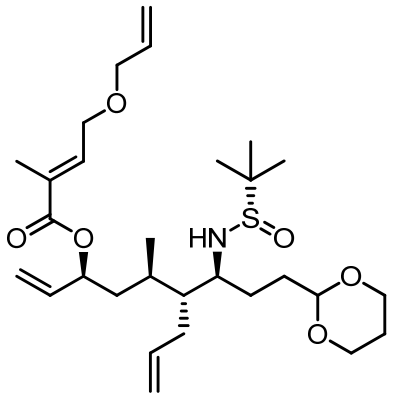
^{1}H NMR



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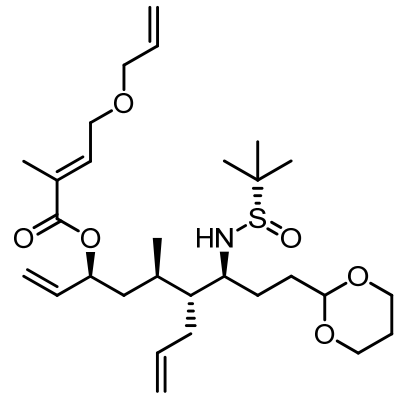
^{13}C NMR



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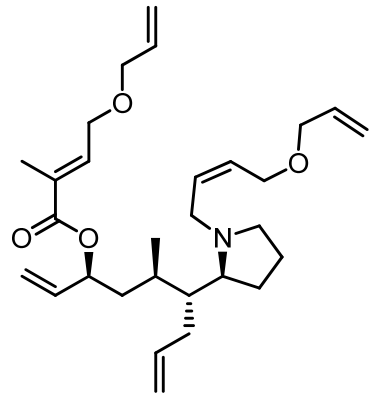

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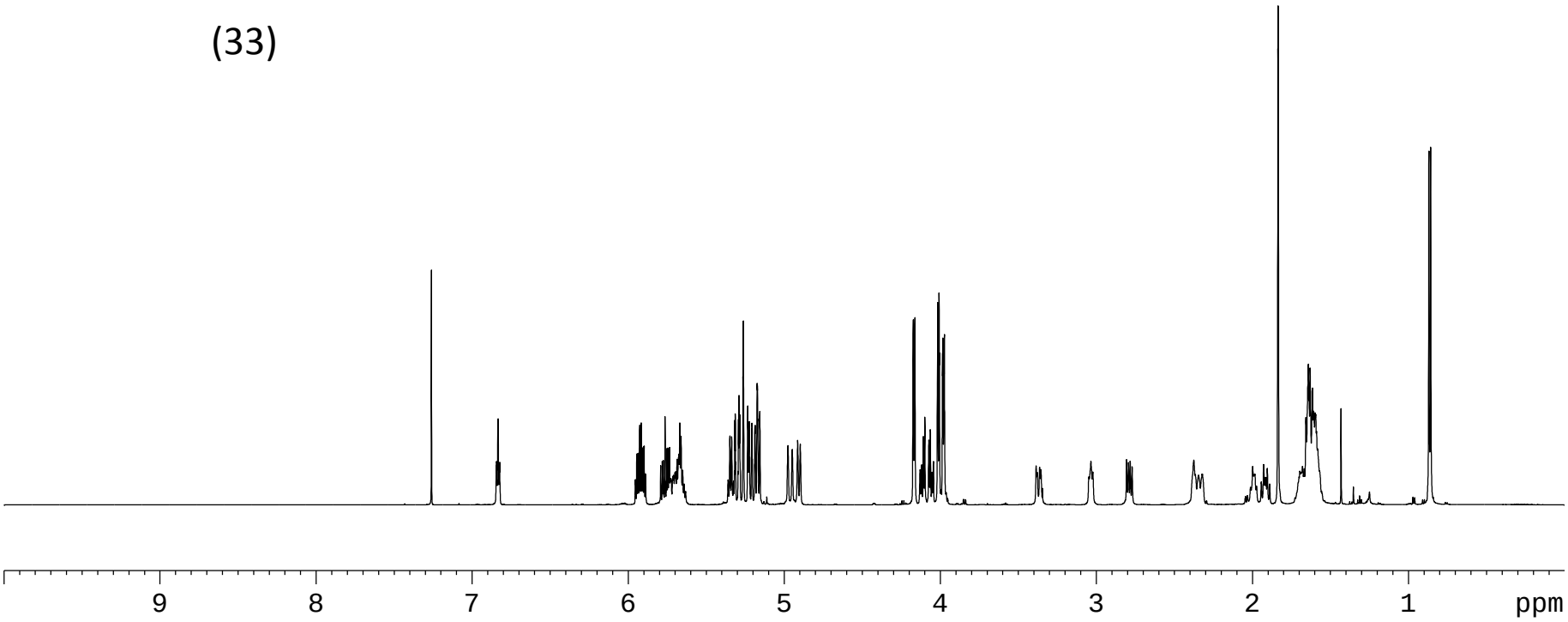

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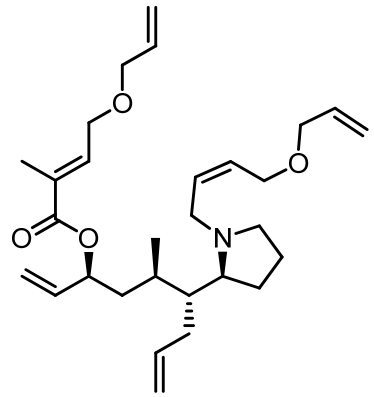

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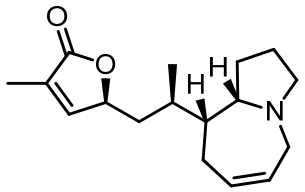

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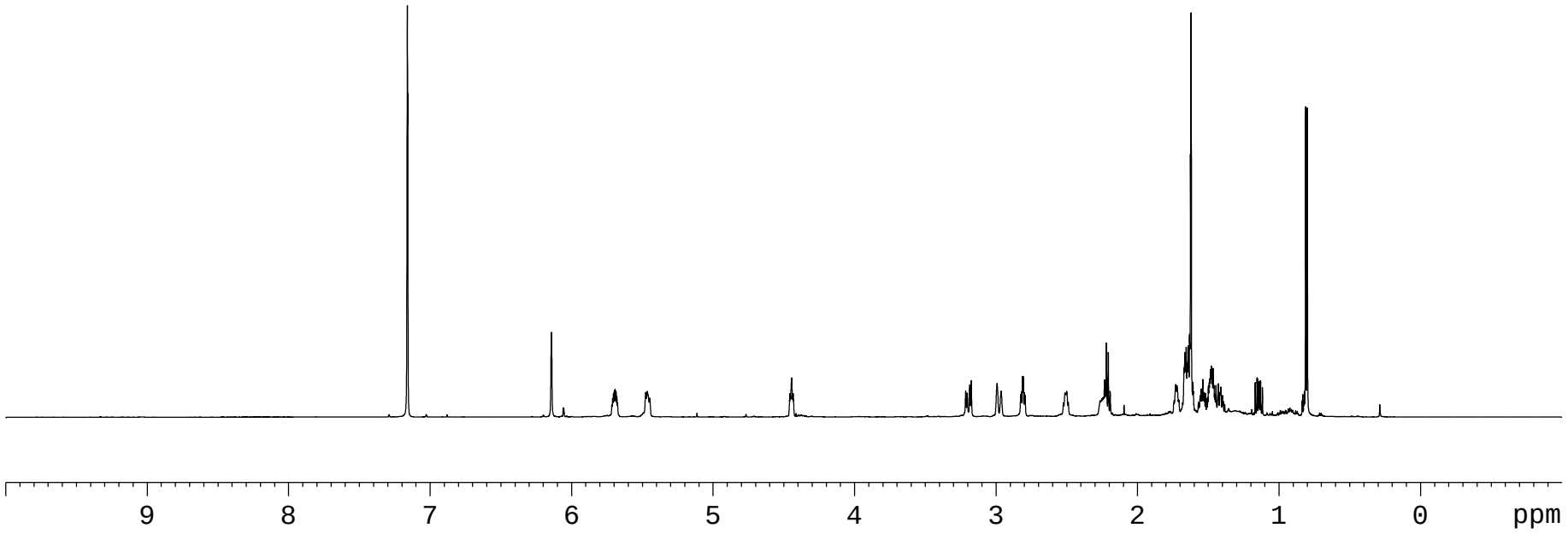

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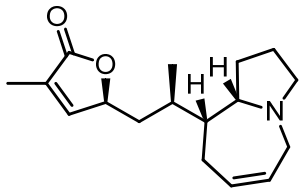

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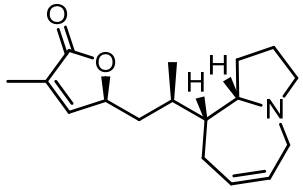
COSY NMR



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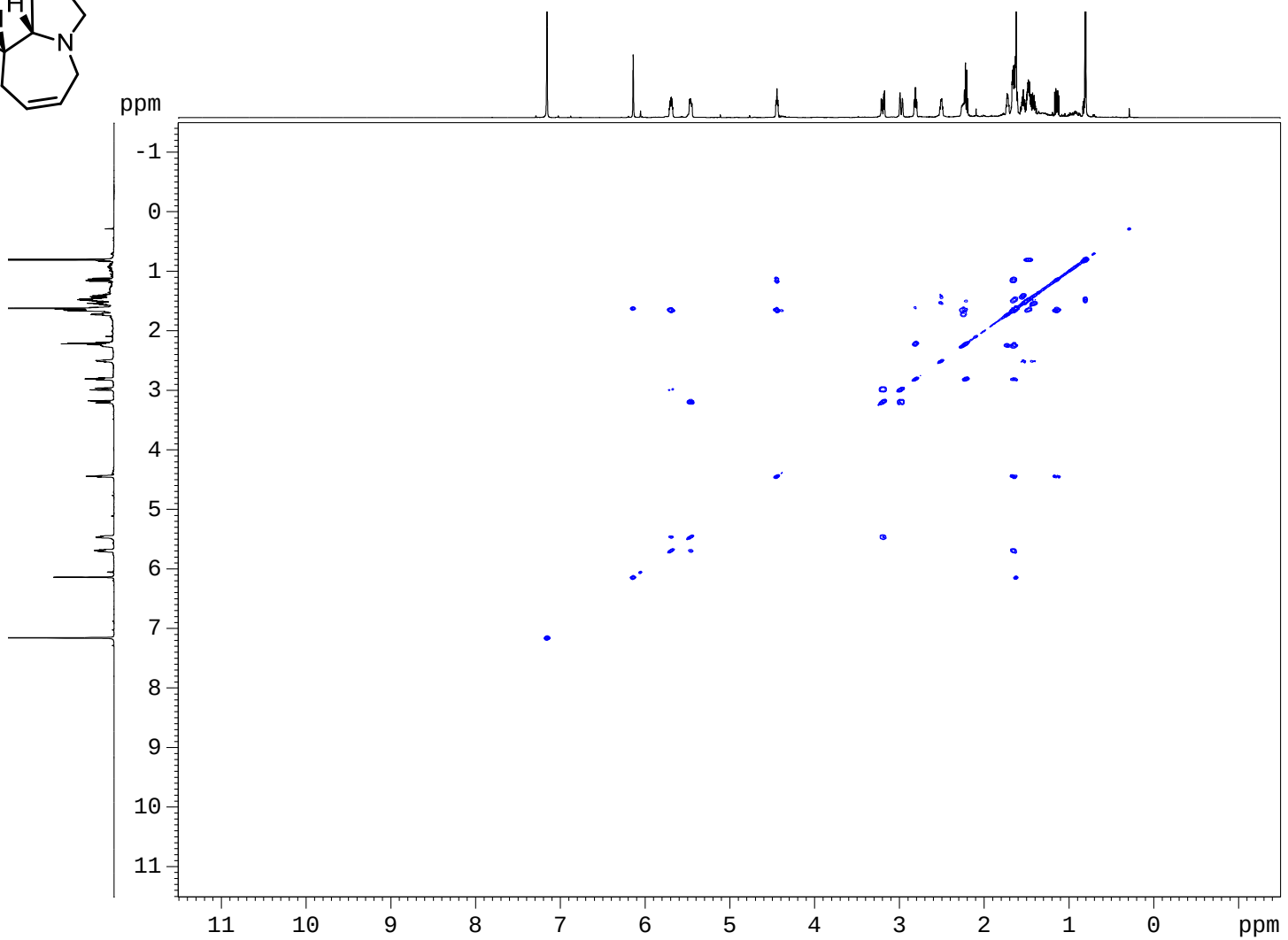

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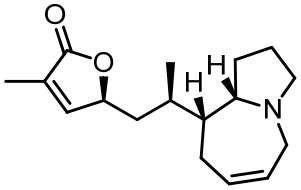

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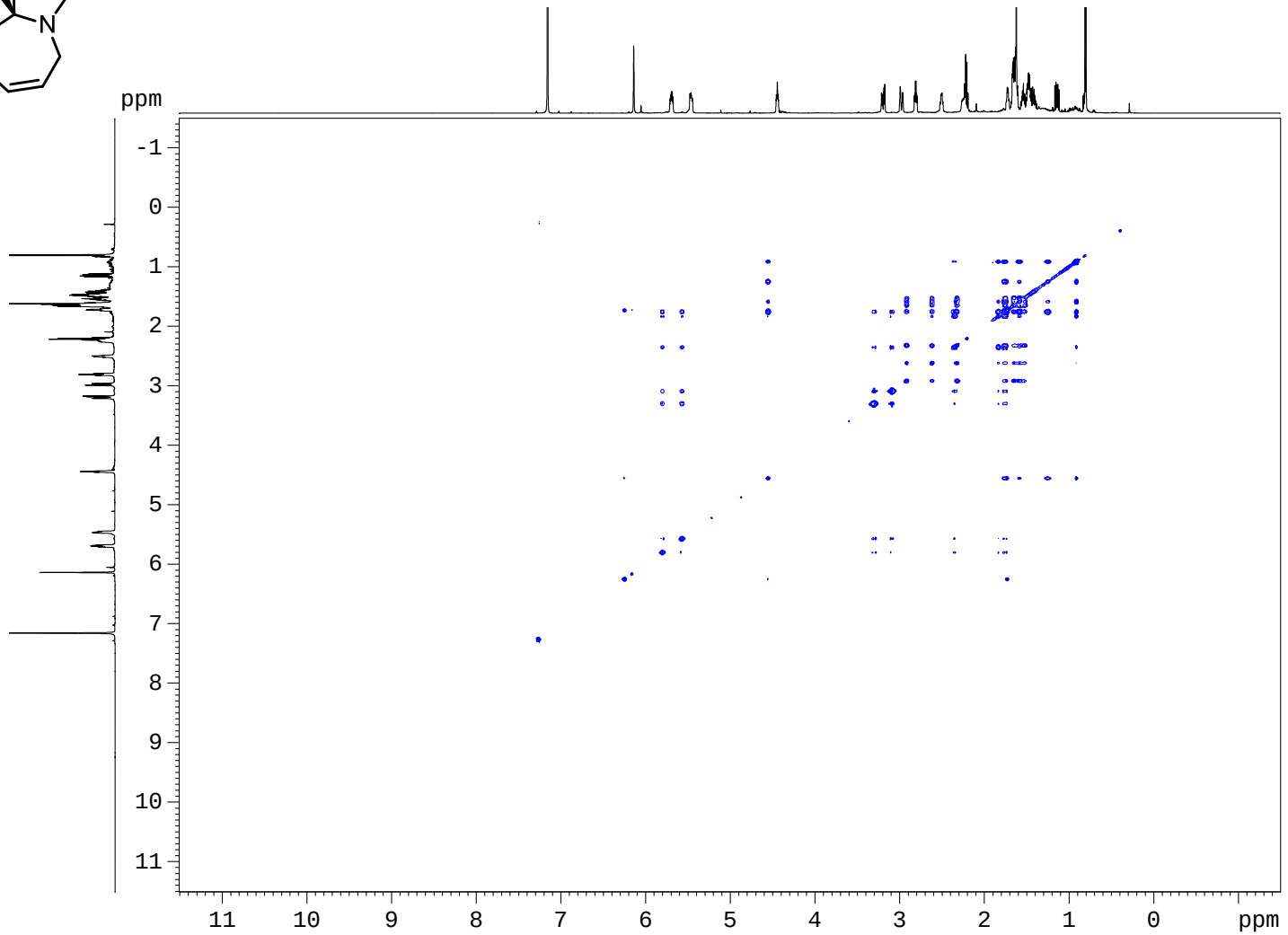
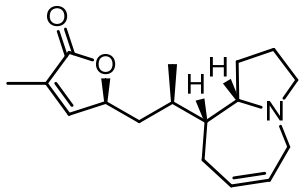


HSQC NMR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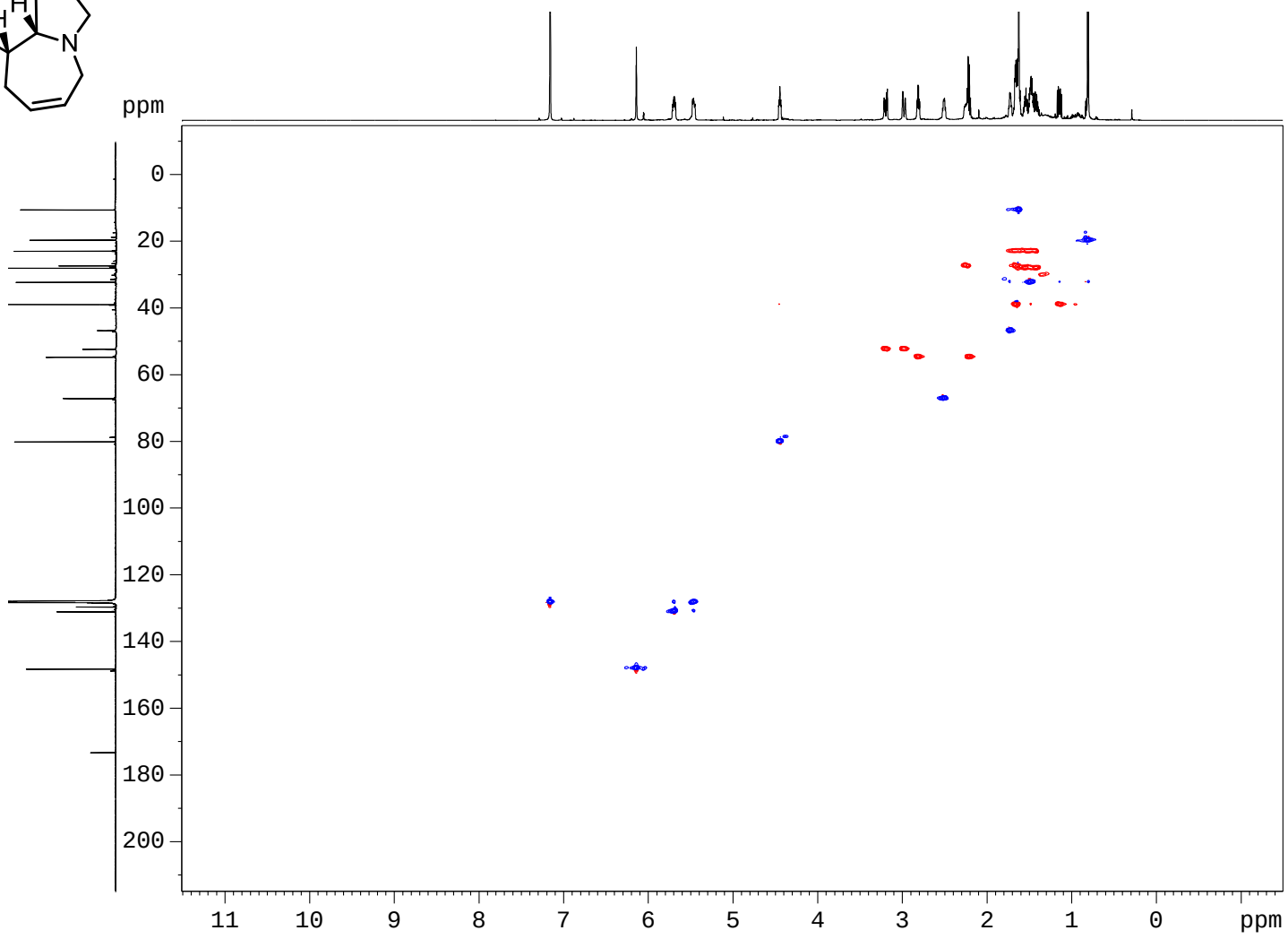
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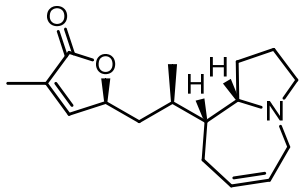
HMBC NMR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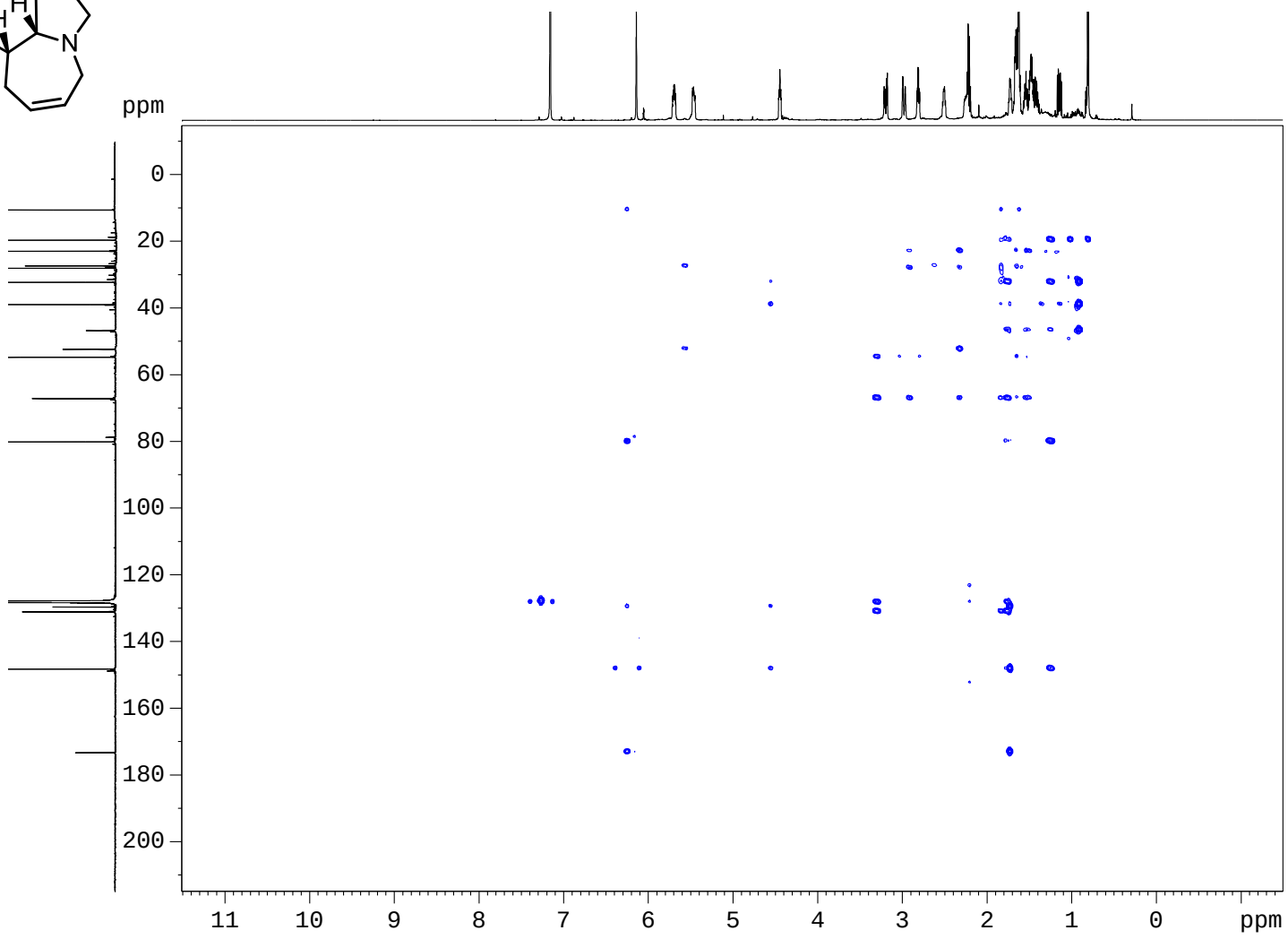
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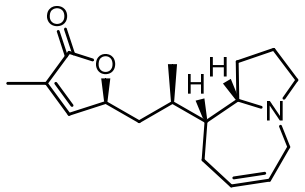
NOESY NMR



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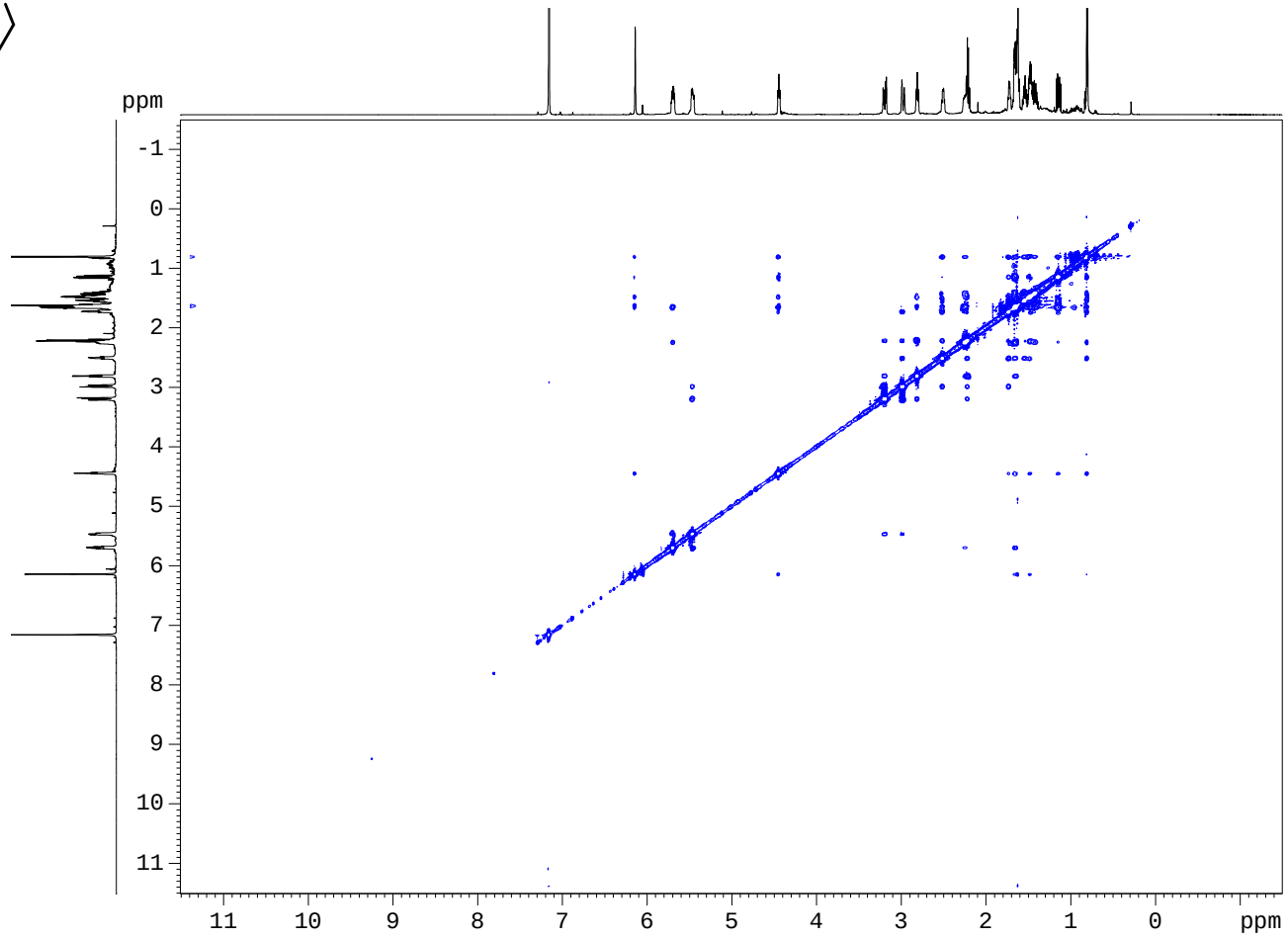
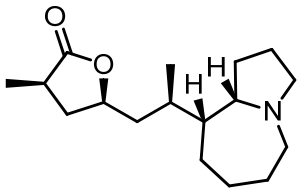


^{1}H NMR



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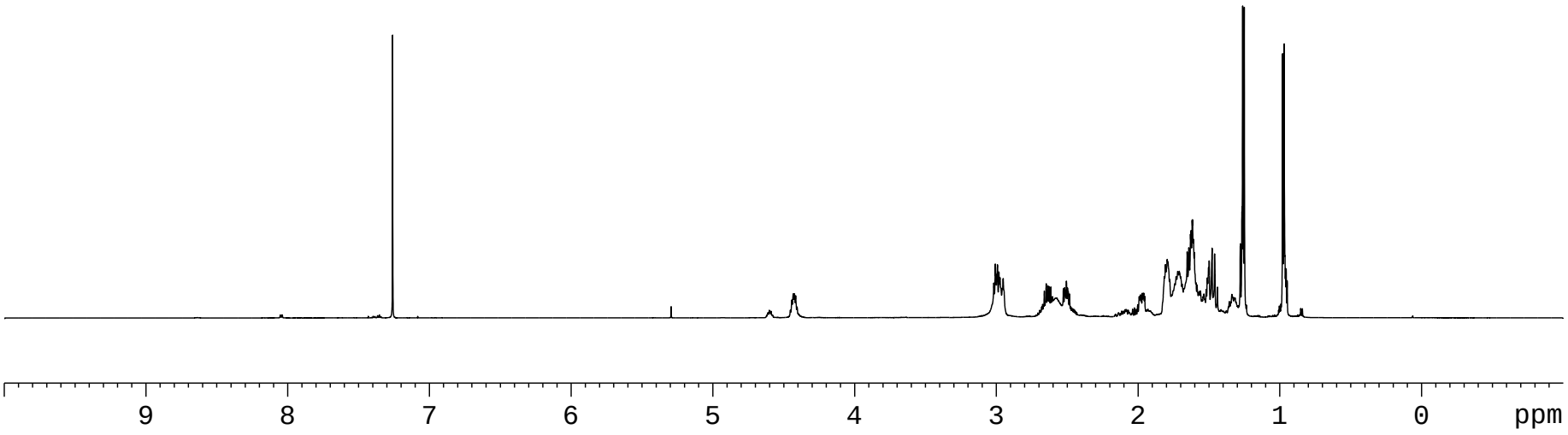
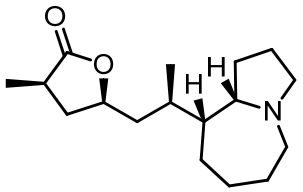


^{1}H NMR



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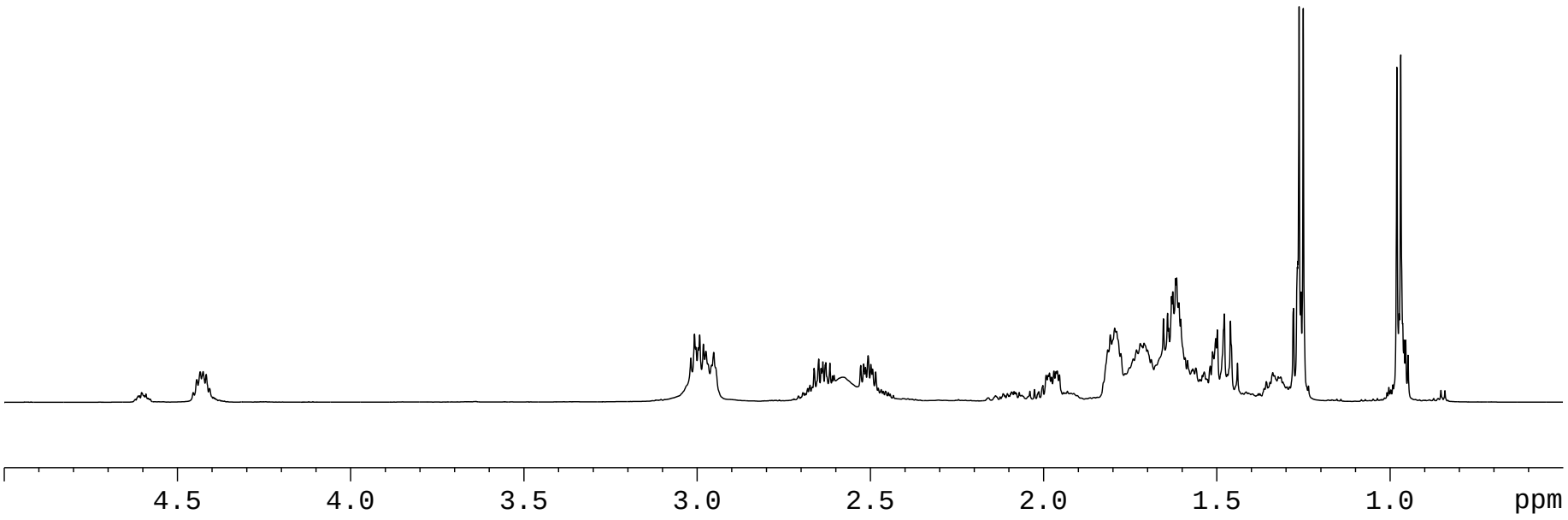
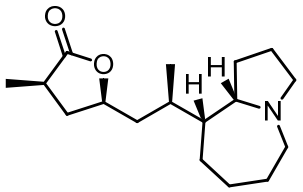
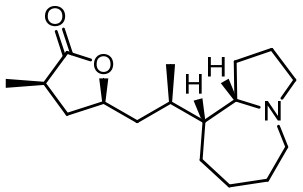


^{13}C NMR



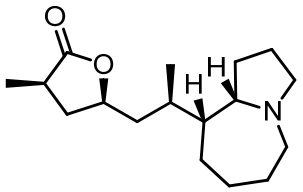
(1)

DEPT135 NMR



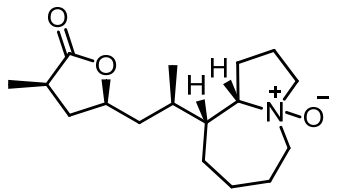
(1)

DEPT135 NMR



(1)

^{1}H NMR



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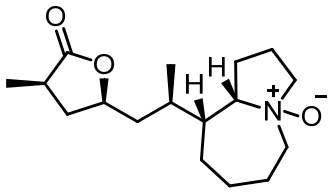
^{1}H NMR



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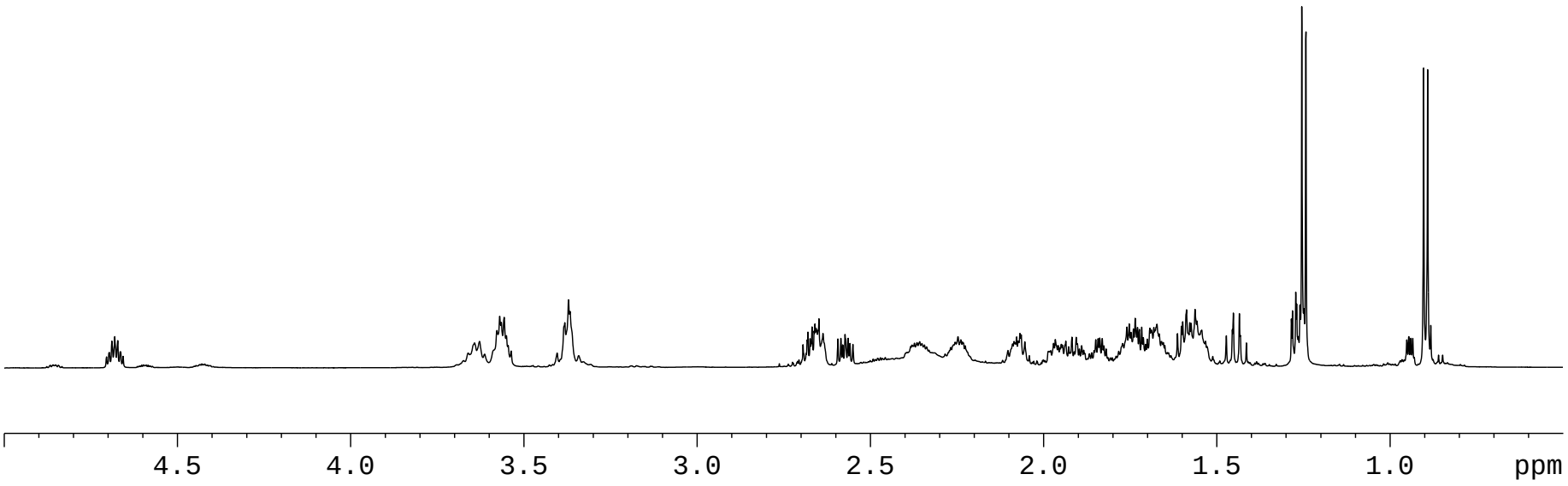
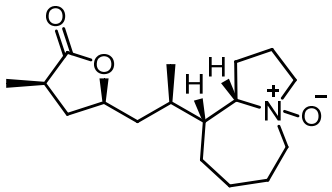


^{13}C NMR



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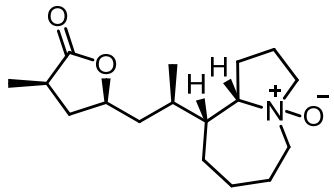
DEPT135 NMR



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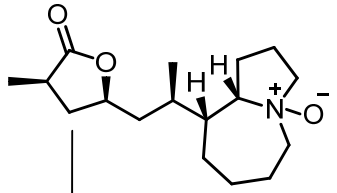

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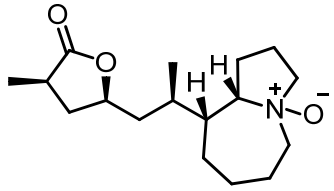
COSY NMR



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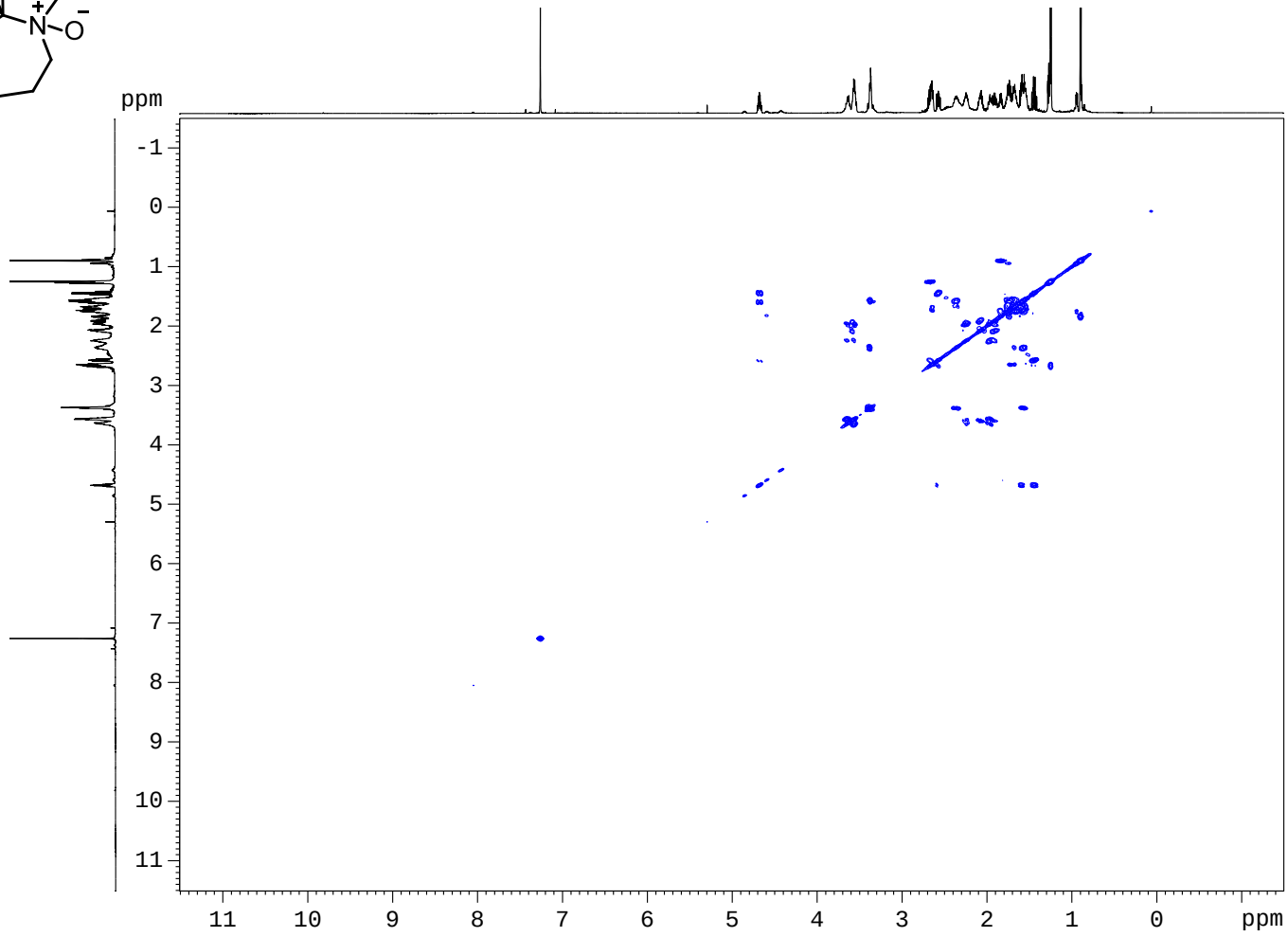

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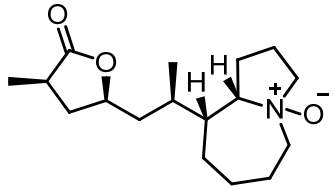

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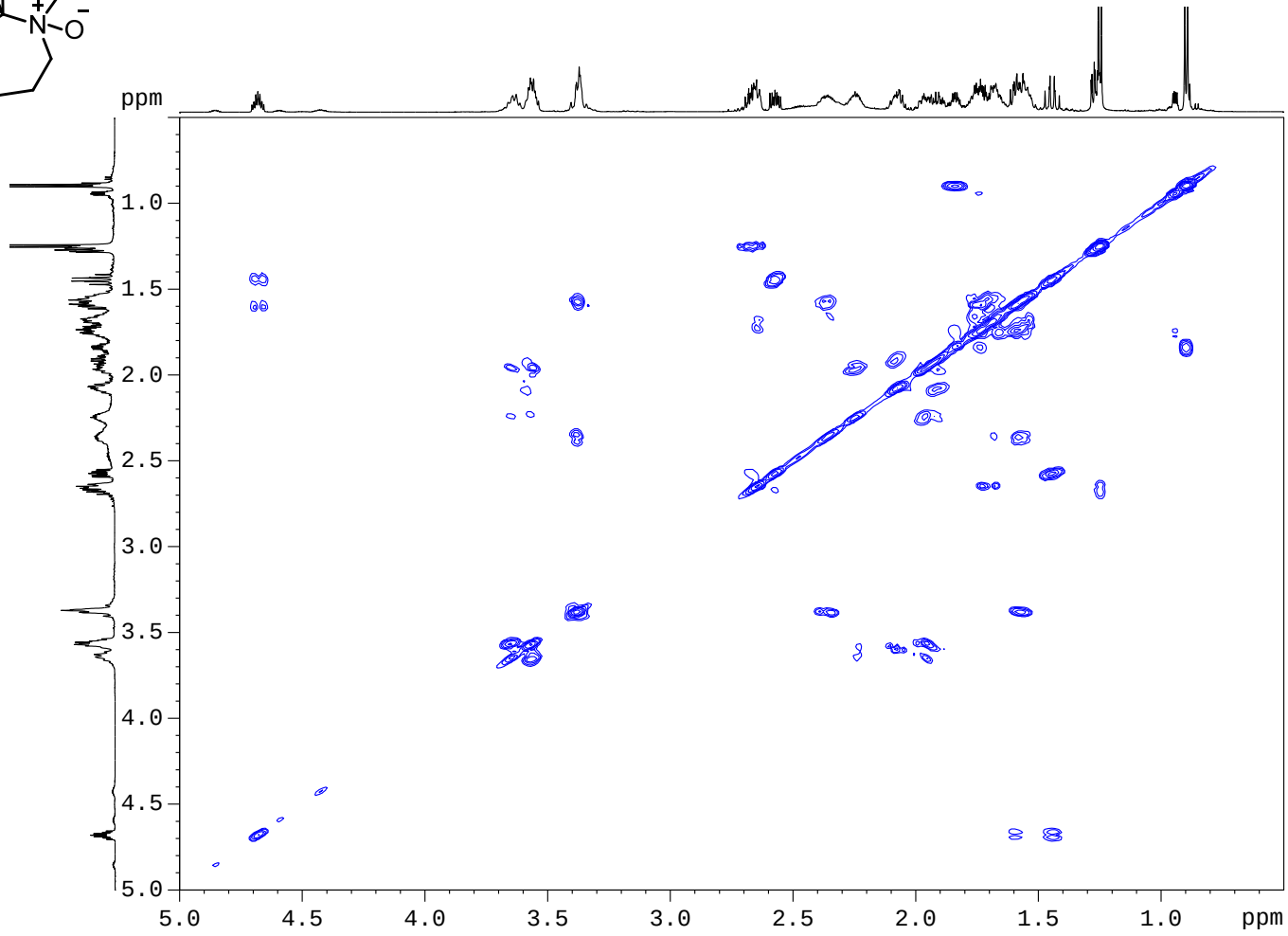
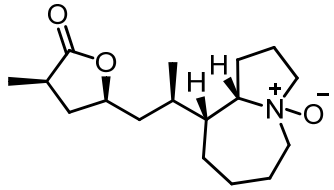


HSQC NMR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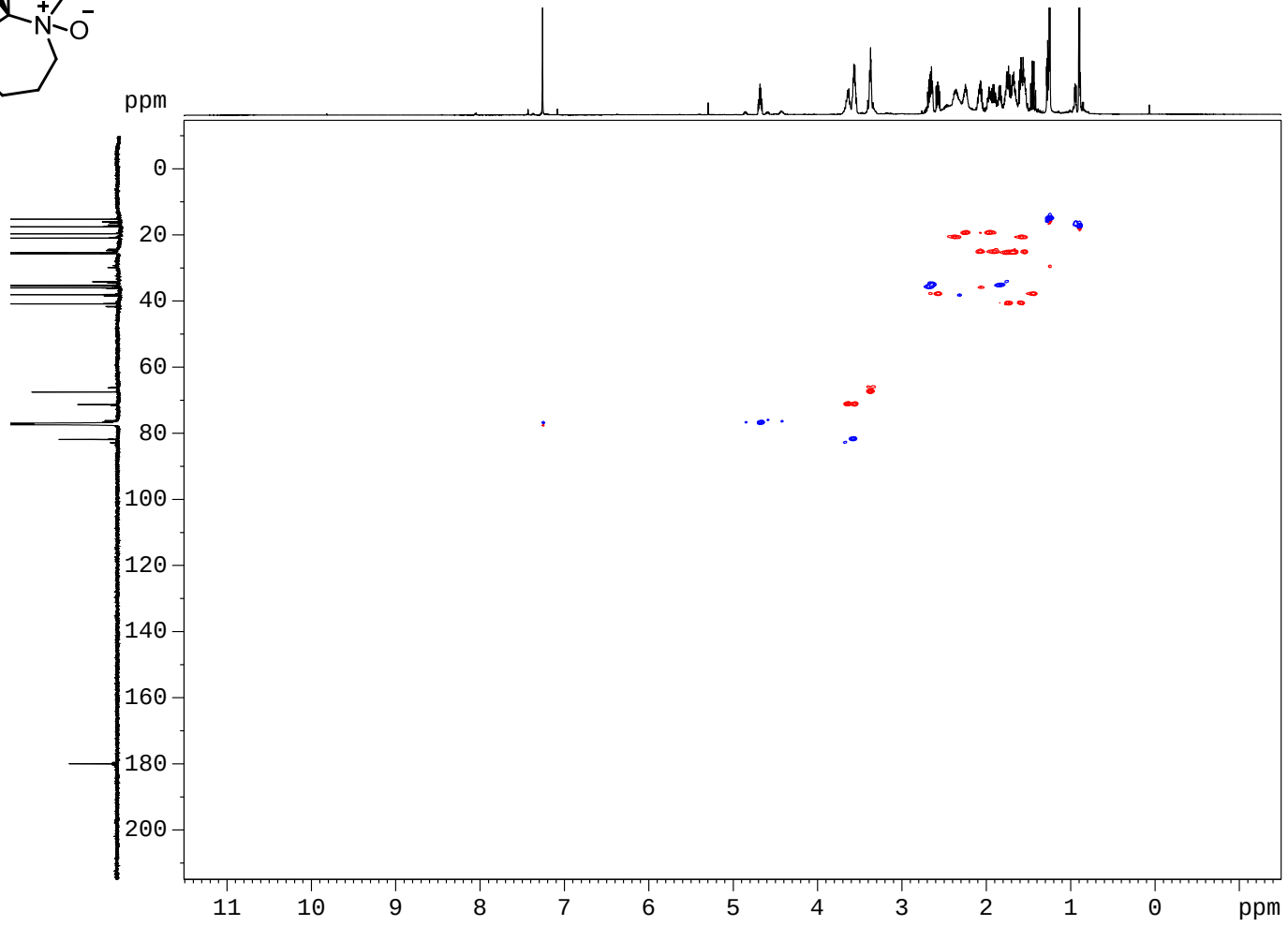
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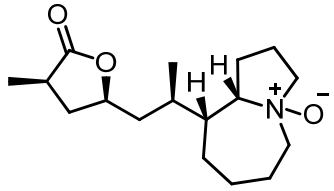
HSQC NMR



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