Supplementary Material

Highly Diastereoselective Chelation-controlled 1,3-*anti*-Allylation of (*S*)-3-(Methoxymethyl)hexanal Enabled by Hydrate of Scandium Triflate

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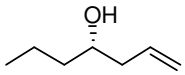
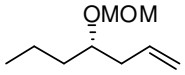
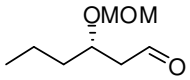
1. Synthesis of aldehyde 3.



(*S*)-Hept-1-en-4-ol (**SI-1**). Titanium(IV) isopropoxide (1.10 mL, 3.78 mmol) and CF_3COOH (28.0 μL, 0.37 mmol) were added in a sequence to a mixture of (*R*)-BINOL (2.16 g, 7.56 mmol) and 6.75 g of activated molecular sieves (4 Å) in anhydrous CH_2Cl_2 (155 mL). The reaction mixture was refluxed under inert atmosphere (argon) at vigorous stirring for 1 h. The obtained solution of titanium catalyst was cooled to –78°C (acetone-dry ice bath) and then a solution of butyraldehyde (4.86 mL, 54.0 mmol) in anhydrous CH_2Cl_2 (40 mL) was added at stirring. After 15 min, a solution of allyltributylstannane (36.0 g, 109 mmol) in anhydrous CH_2Cl_2 (70 mL) was added at the same temperature and the resulted mixture was kept in a refrigerator at –25°C for 120 h. The reaction mixture was treated at vigorous stirring with saturated aqueous solution of $NaHCO_3$ (300 mL). The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), the combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the title compound was isolated by column chromatography (SiO_2, eluent PE:EtOAc, 20:1). Colorless oil (5.40 g, 88%). R_f = 0.48 (PE:EtOAc, 4:1). $[\alpha]_D^{20}$= –12.2 (*c* 1.18, $CHCl_3$). IR (neat): ν = 3362, 1642, 1465, 1123 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.89–5.76 (m, 1H), 5.17–5.07 (m, 2H), 3.69–3.61 (m, 1H), 2.33–2.25 (m, 1H), 2.19–2.07 (m, 1H), 1.63 (br.s, 1H), 1.52–1.28 (m, 4H), 0.93 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 134.90, 118.00, 70.38, 41.93, 38.94, 18.82, 14.04. HRMS (ESI) calcd. for $C_7H_{15}O^+$ $[M+H]^+$ 115.1117, found *m/z* 115.1115. The enantiomeric excess (ee > 99%) was determined by Mosher's method [1].



(*S*)-4-(Methoxymethoxy)hept-1-ene (**SI-2**). A solution of methoxymethyl chloride (2 M in toluene, 45.0 mL, 90.0 mmol, prepared as described in [2]) was added to a solution of (*S*)-hept-1-en-4-ol (**SI-1**) (5.13 g, 45.0 mmol), *N*,*N*-diisopropylethylamine (10.5 mL, 60.2 mmol) and catalytic amount of Bu_4NI in anhydrous CH_2Cl_2 (55 mL). The reaction mixture was stirred at room temperature for 4 h. Afterwards, the mixture was quenched at vigorous stirring with saturated aqueous solution of $NaHCO_3$ (100 mL) and additionally stirred for 1h. The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL), the combined organic extracts were washed with brine (50 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the title compound was isolated by column chromatography (SiO_2, eluent PE:EtOAc, 50:1). Colorless oil (6.80 g, 96%). R_f = 0.53 (PE:EtOAc, 10:1). $[\alpha]_D^{20}$ = –33.1 (*c* 2.08, $CHCl_3$). IR (neat): ν = 1641, 1466, 1378, 1213, 1145, 1101, 1043 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.82 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.13– 5.01 (m, 2H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 3.65–3.57 (m, 1H), 3.38 (s, 3H), 2.28 (ddt, *J* = 7.1, 5.8, 1.3 Hz, 2H), 1.54–1.26 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 134.86, 116.98, 95.36, 76.59, 55.47, 38.90, 36.39, 18.57, 14.12. HRMS (ESI) calcd. for $C_9H_{18}O_2Na^+$ $[M+Na]^+$ 181.1199, found *m/z* 181.1204.



(*S*)-3-(Methoxymethoxy)hexanal (**3**). Ozonated oxygen was passed through a stirred solution of (*S*)-4-(methoxymethoxy)hept-1-ene (**SI-2**) (6.64 g, 42.0 mmol) in CH_2Cl_2 (150 mL) at –78°C until a persistent blue color appeared (ca. 2 h). Then, pure oxygen gas was passed through the solution to remove excess of ozone. Triphenylphosphine (22.0 g, 84.0 mmol) was added portion wise at –78°C and the reaction mixture was stirred until it warmed to room temperature (ca. 2 h). After treating with saturated

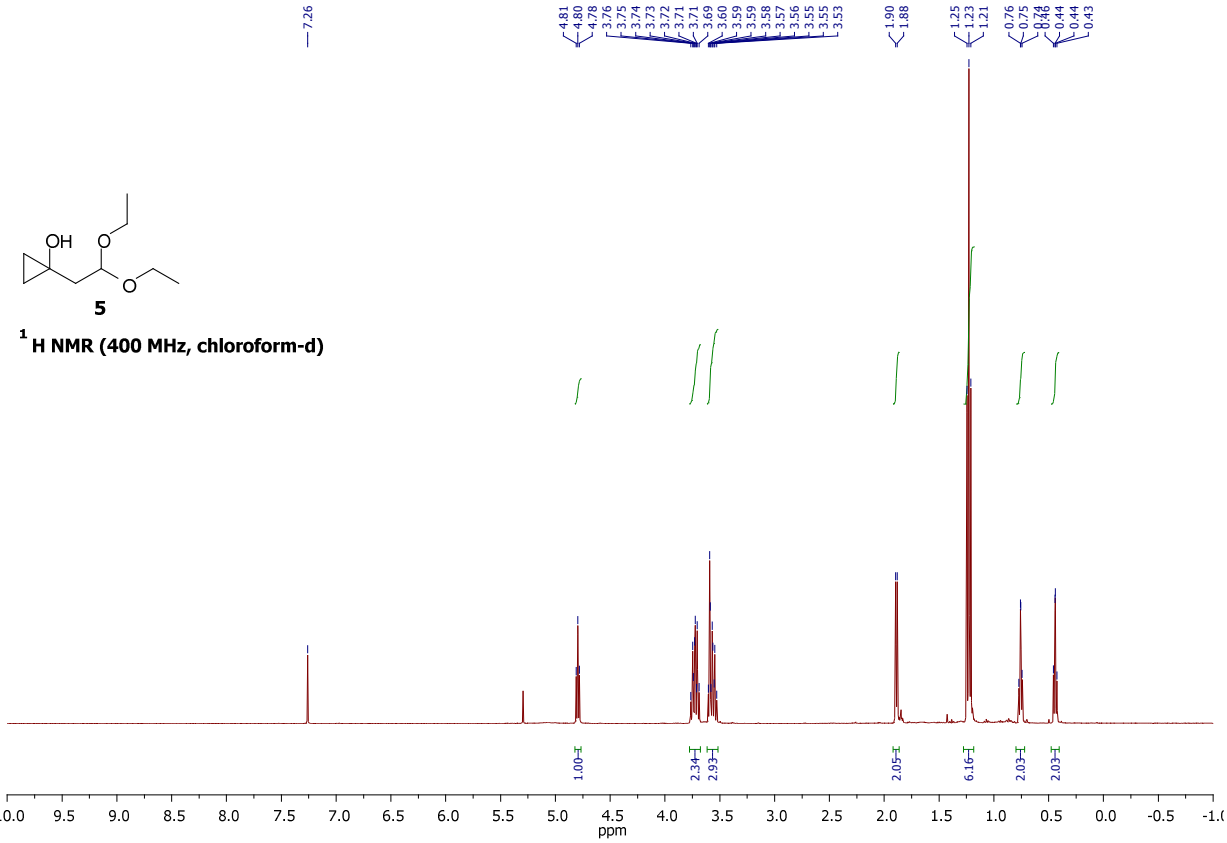
aqueous solution of $NaHCO_3$ (50 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure, and the title compound was isolated by column chromatography (SiO_2, PE:EtOAc, 20:1). Colorless oil (6.25 g, 93%). R_f = 0.47 (PE:EtOAc, 4:1). $[\alpha]_D^{20}$ = +20.1 (*c* 1.48, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (dd, *J* = 2.8, 1.8 Hz, 1H), 4.68 (d, *J* = 7.0 Hz, 1H), 4.64 (d, *J* = 7.0 Hz, 1H), 4.12–4.04 (m, 1H), 3.34 (s, 3H), 2.63 (ddd, *J* = 16.3, 7.0, 2.8 Hz, 1H), 2.55 (ddd, *J* = 16.3, 4.8, 1.8 Hz, 1H), 1.68– 1.56 (m, 1H), 1.56–1.29 (m, 3H), 0.93 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 201.47, 95.79, 72.91, 55.59, 48.73, 37.10, 18.44, 13.97. HRMS (ESI) calcd. for $C_8H_{16}O_3Na^+$ $[M+Na]^+$ 183.0992, found *m*/*z* 183.0990.

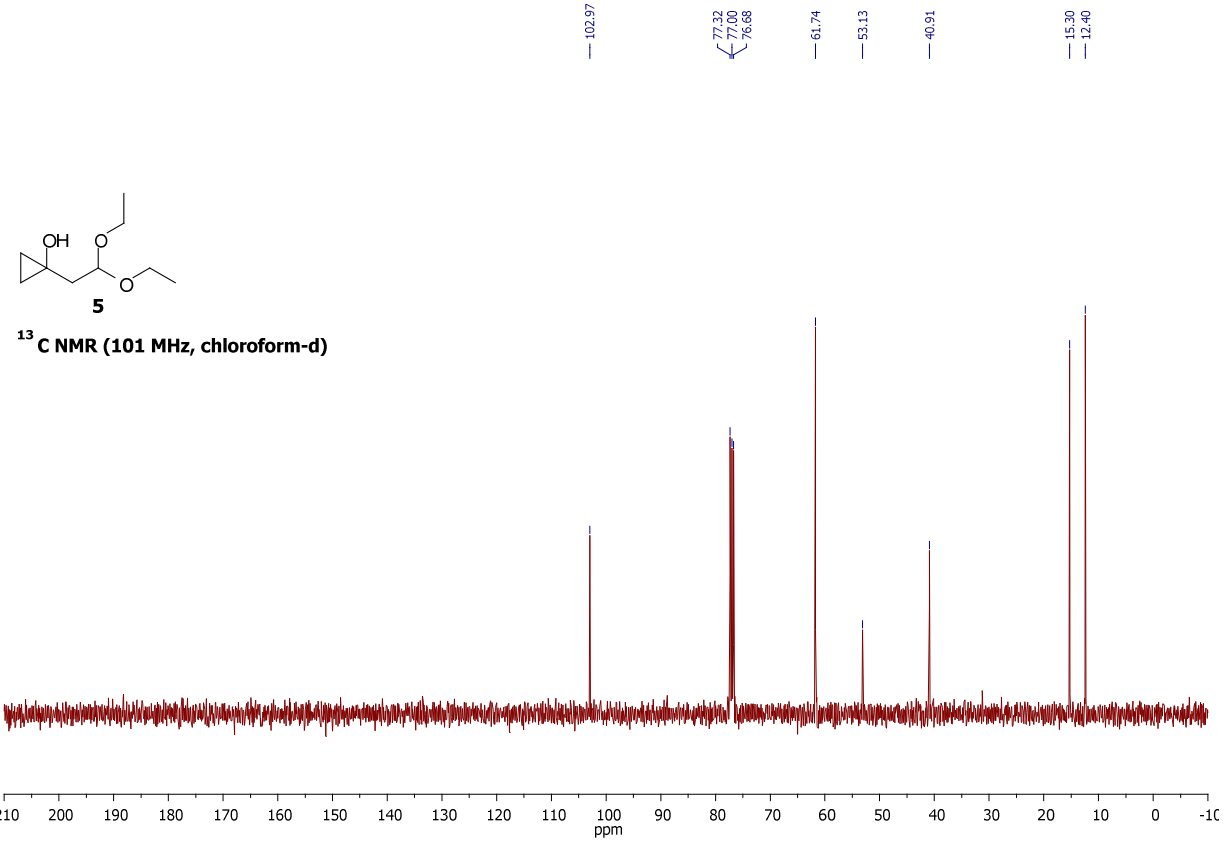
References

1. Dale, J.A.; Dull, D.L.; Mosher, H.S.; α-Methoxy-α-trifluoromethylphenylacetic acid, a versatile reagent for the determination of enantiomeric composition of alcohols and amines. *J. Org. Chem*. **1969**, *34*, 2543–2549.
2. Berliner, M.A.; Belecki, K.; Simple, rapid procedure for the synthesis of chloromethyl methyl ether and other chloro alkyl ethers. *J. Org. Chem*. **2005**, *70*, 9618–9621.

2. Copies of ^{1}H and ^{13}C NMR spectra

^{1}H and ^{13}C NMR spectra of 5





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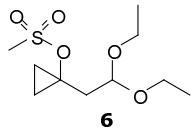

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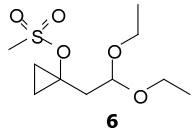
^{1}H NMR (400 MHz, chloroform-d)



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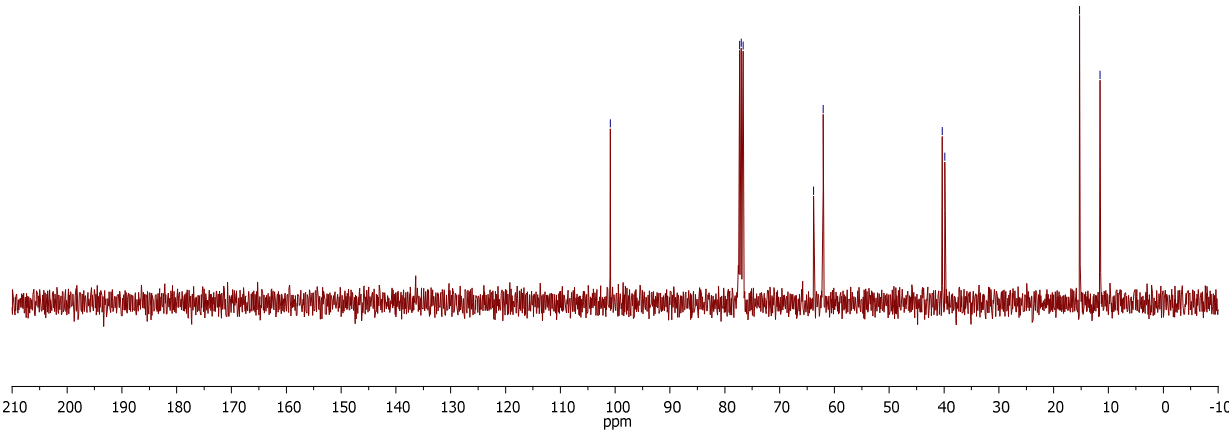

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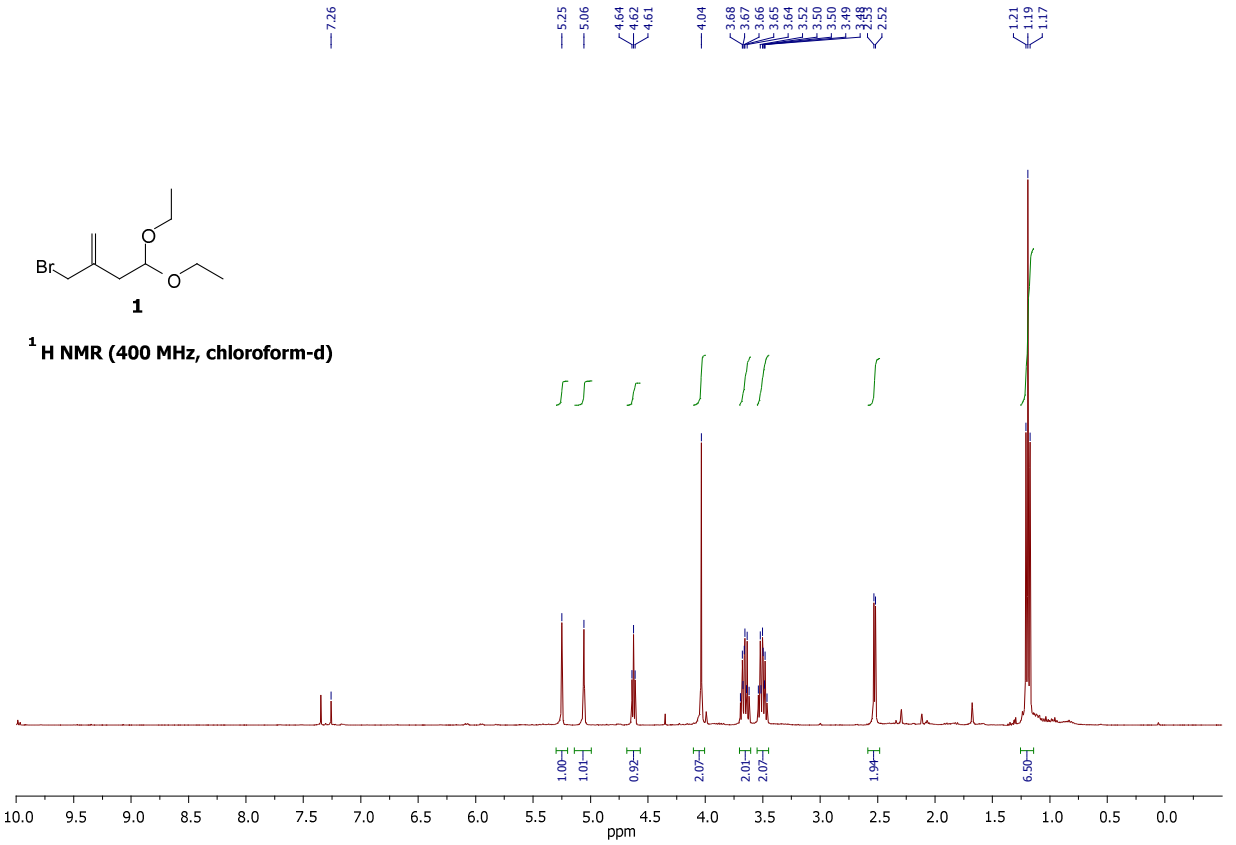

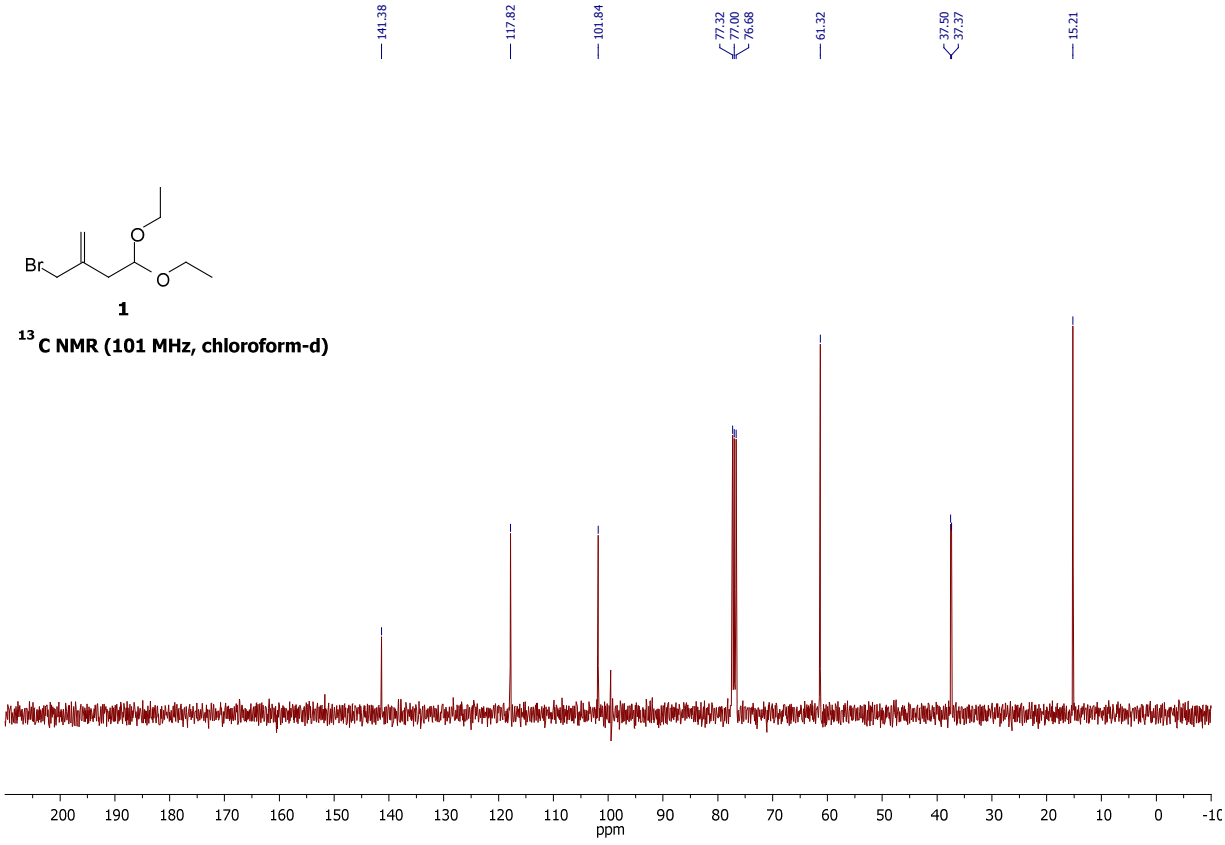

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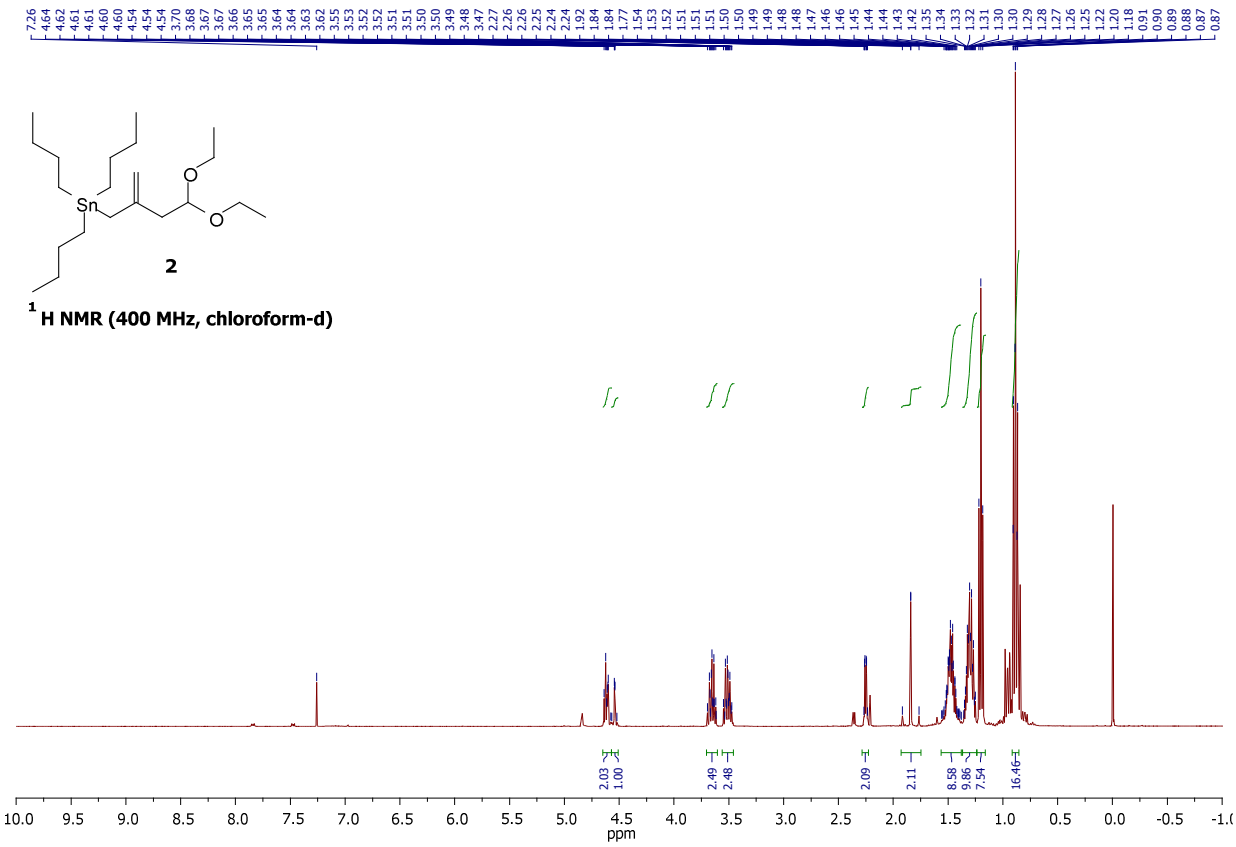

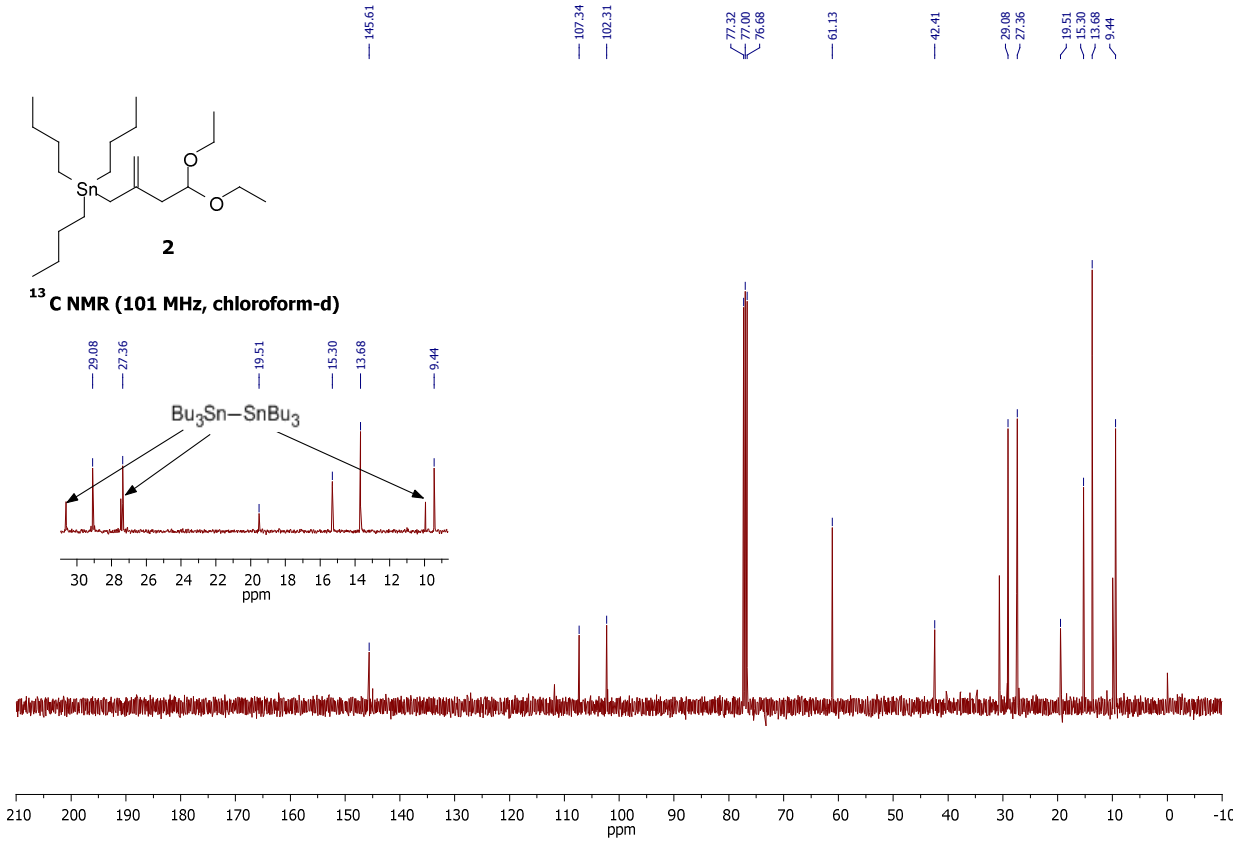

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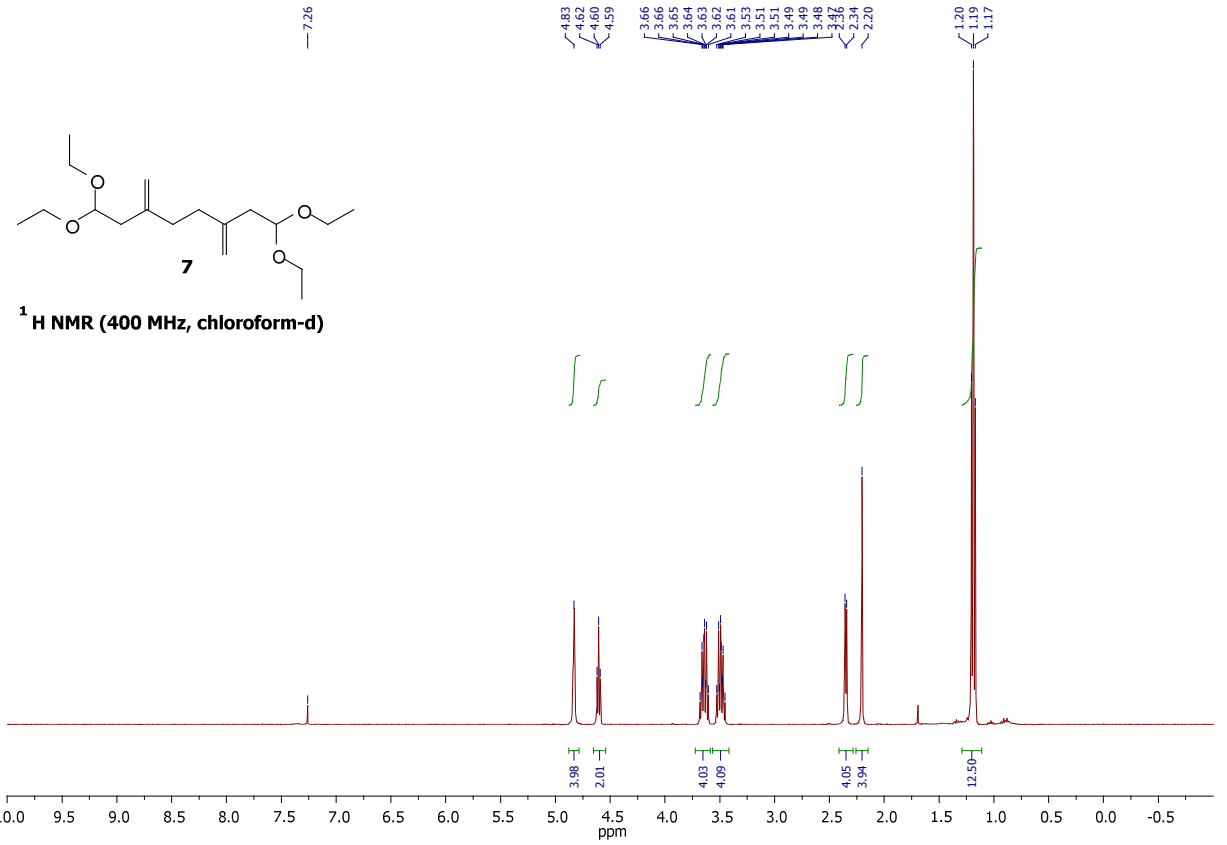

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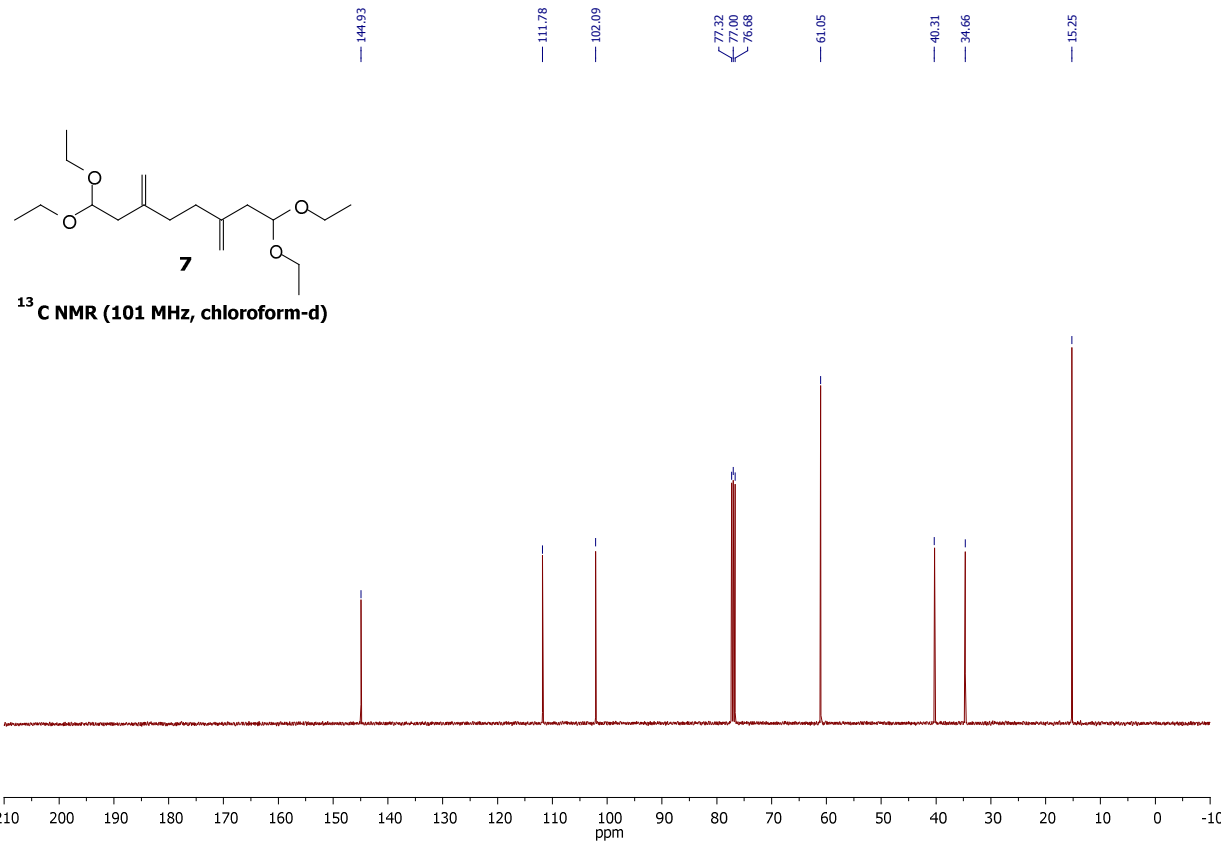
^{1}H NMR (400 MHz, chloroform-d)



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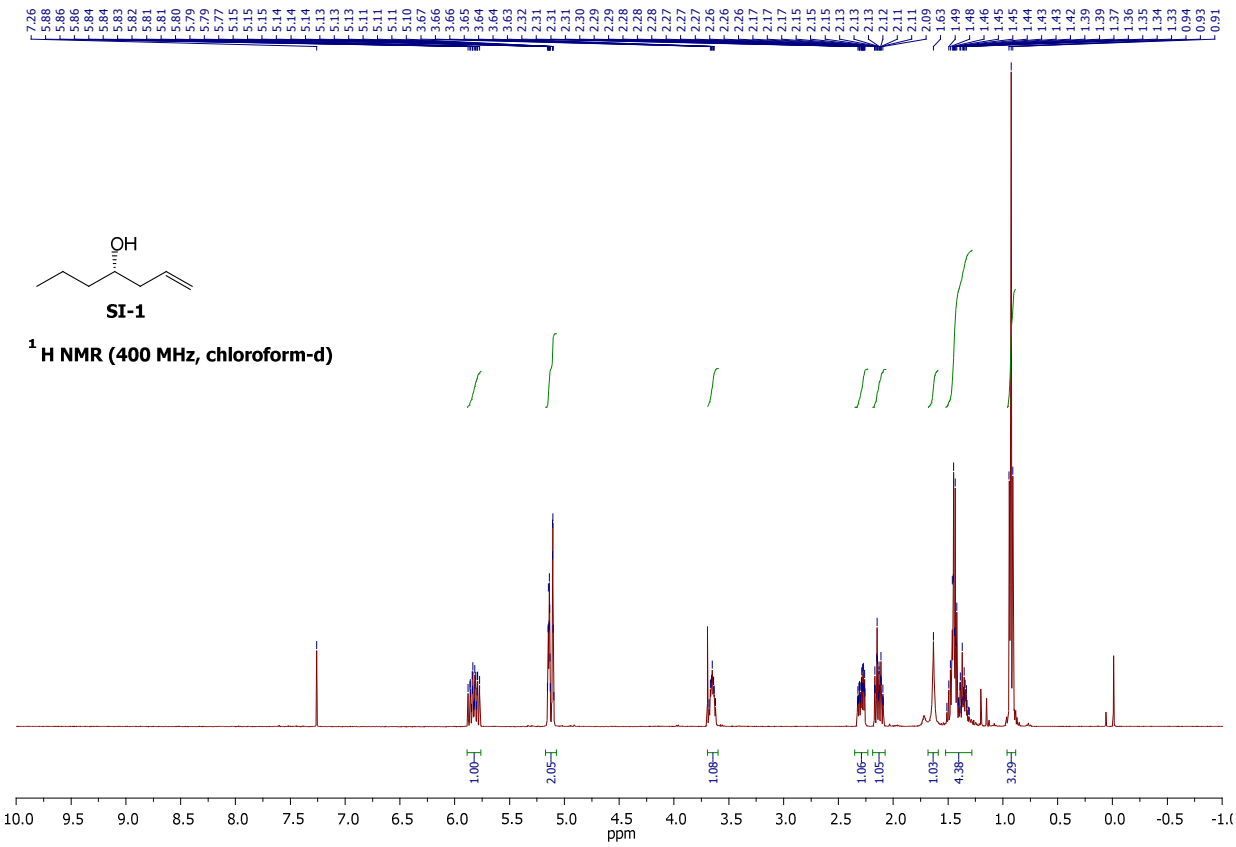
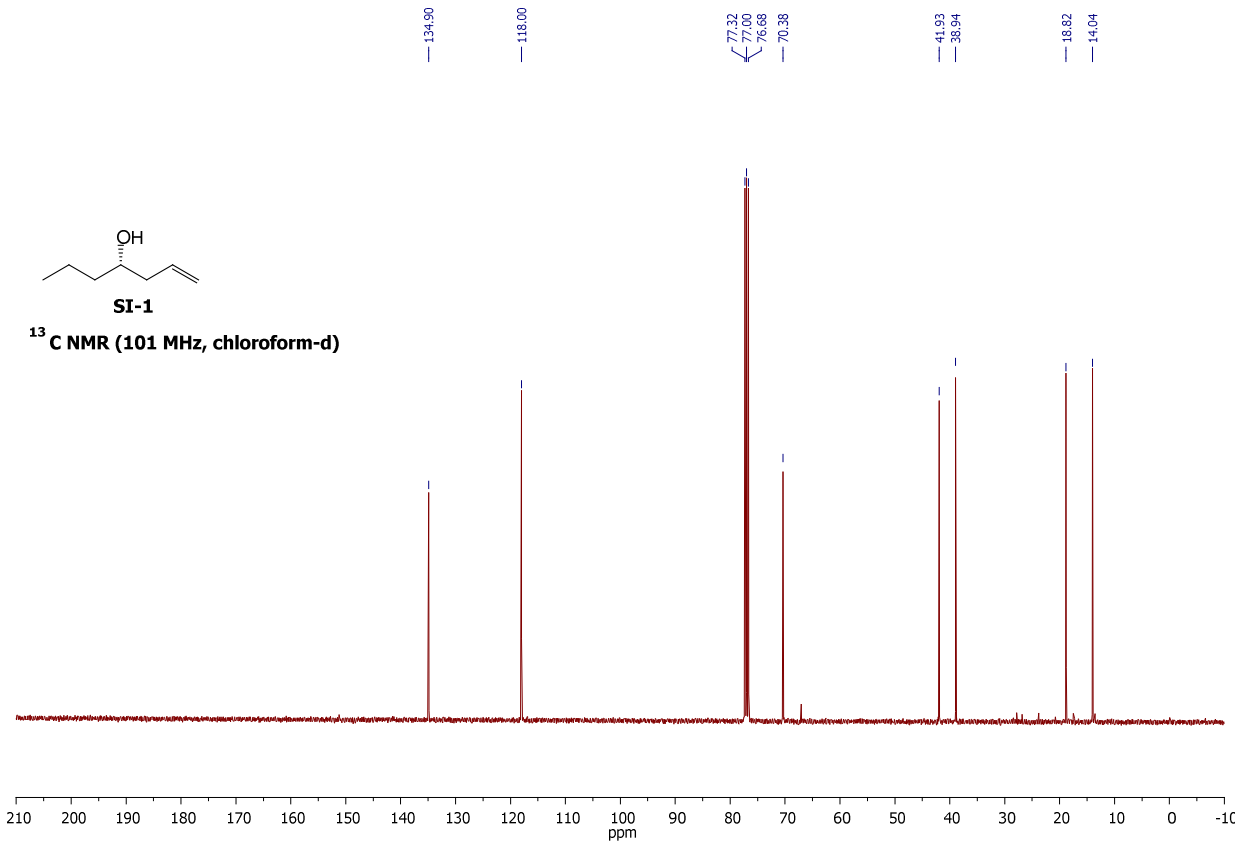
^{13}C NMR (101 MHz, chloroform-d)

^{1}H and ^{13}C NMR spectra of SI-1





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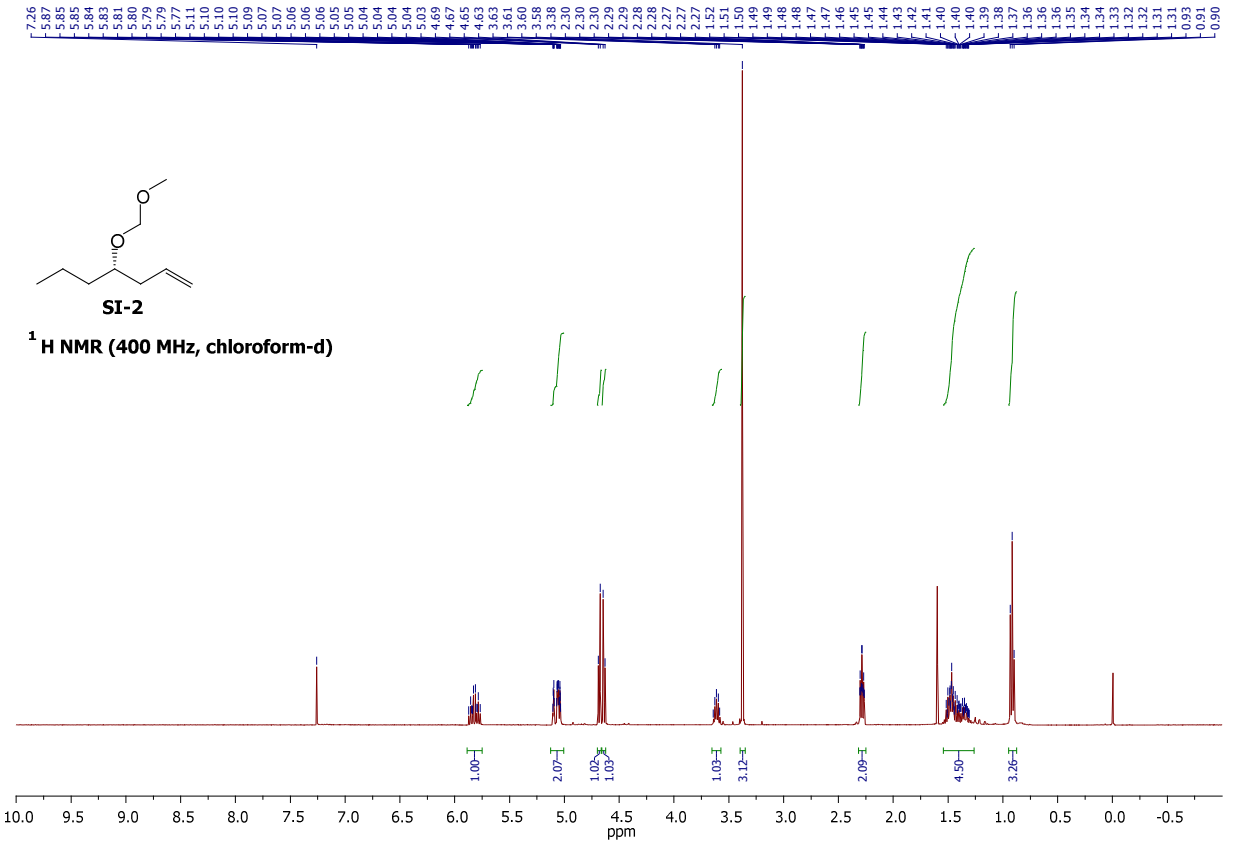

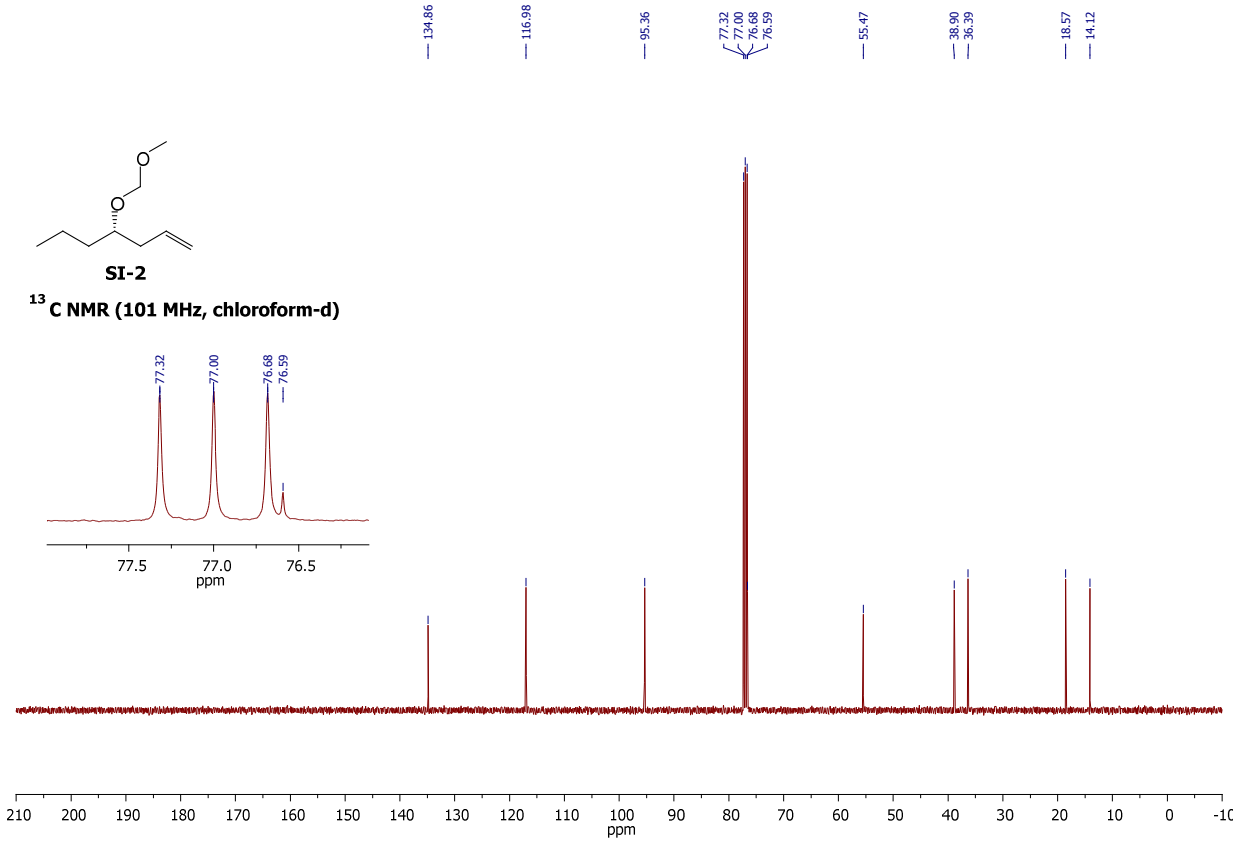

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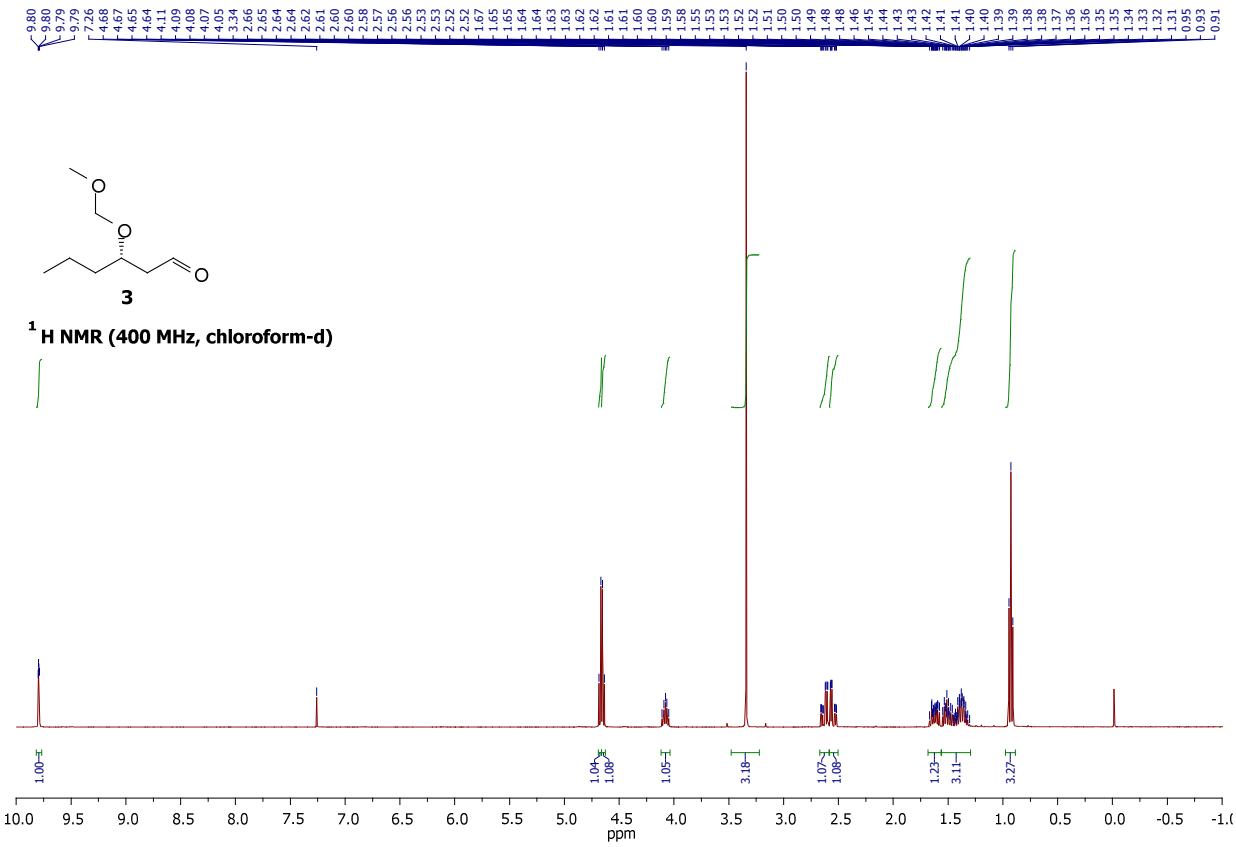

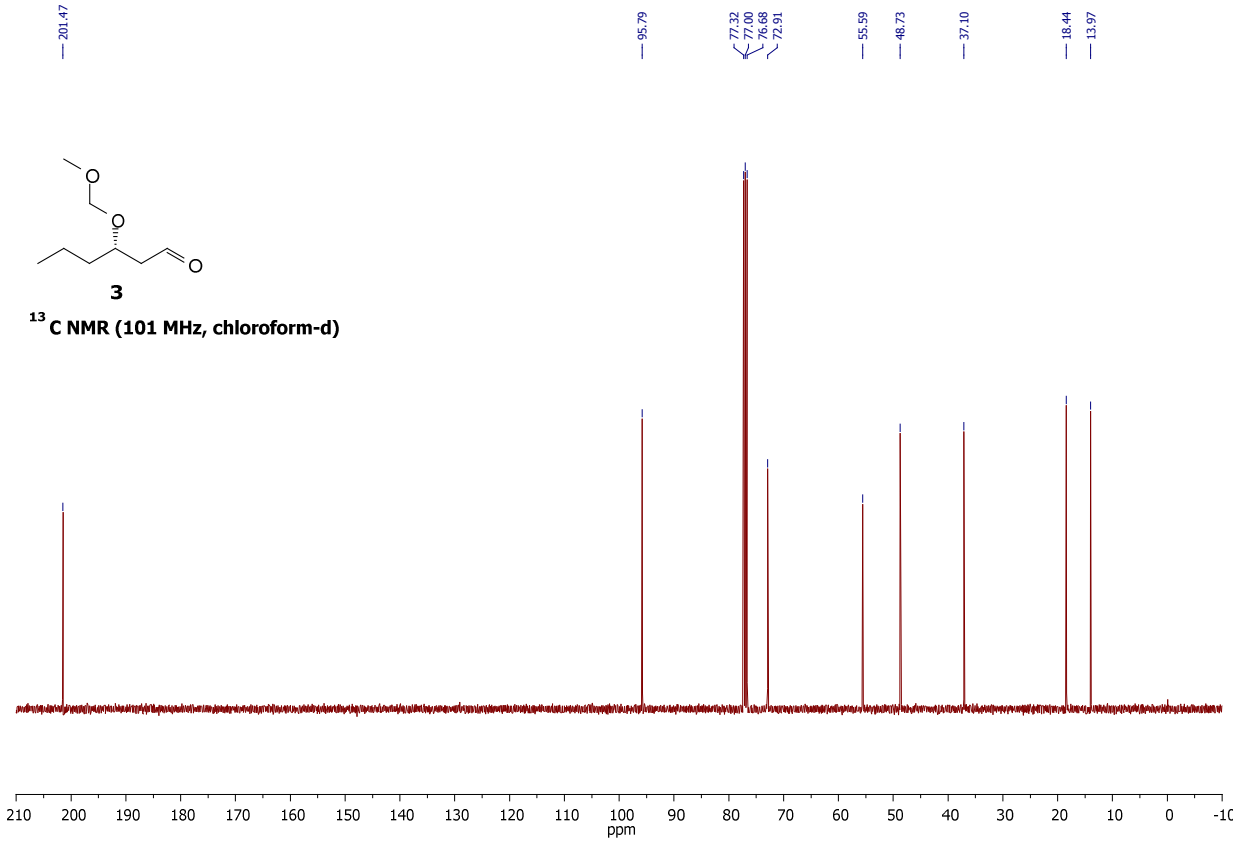

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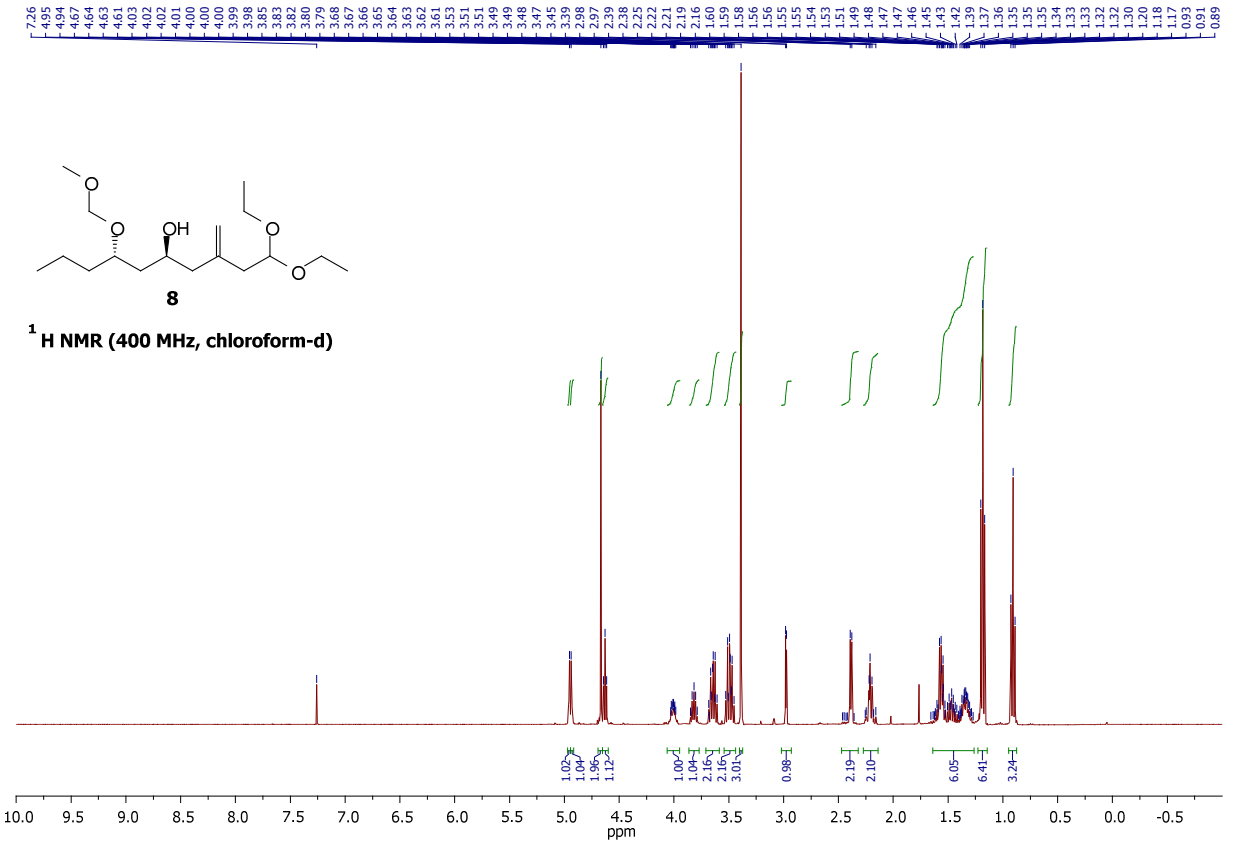
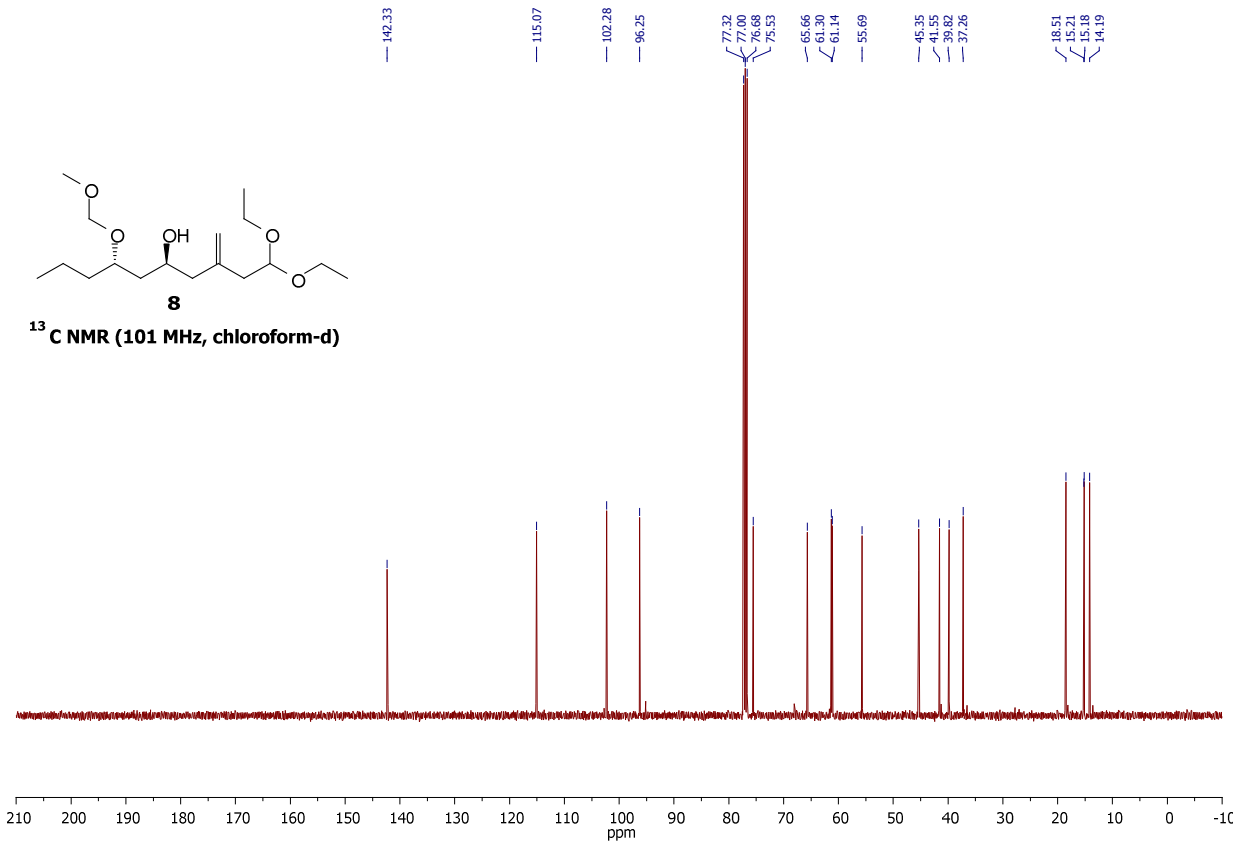


8

^{1}H NMR (400 MHz, chloroform-d)



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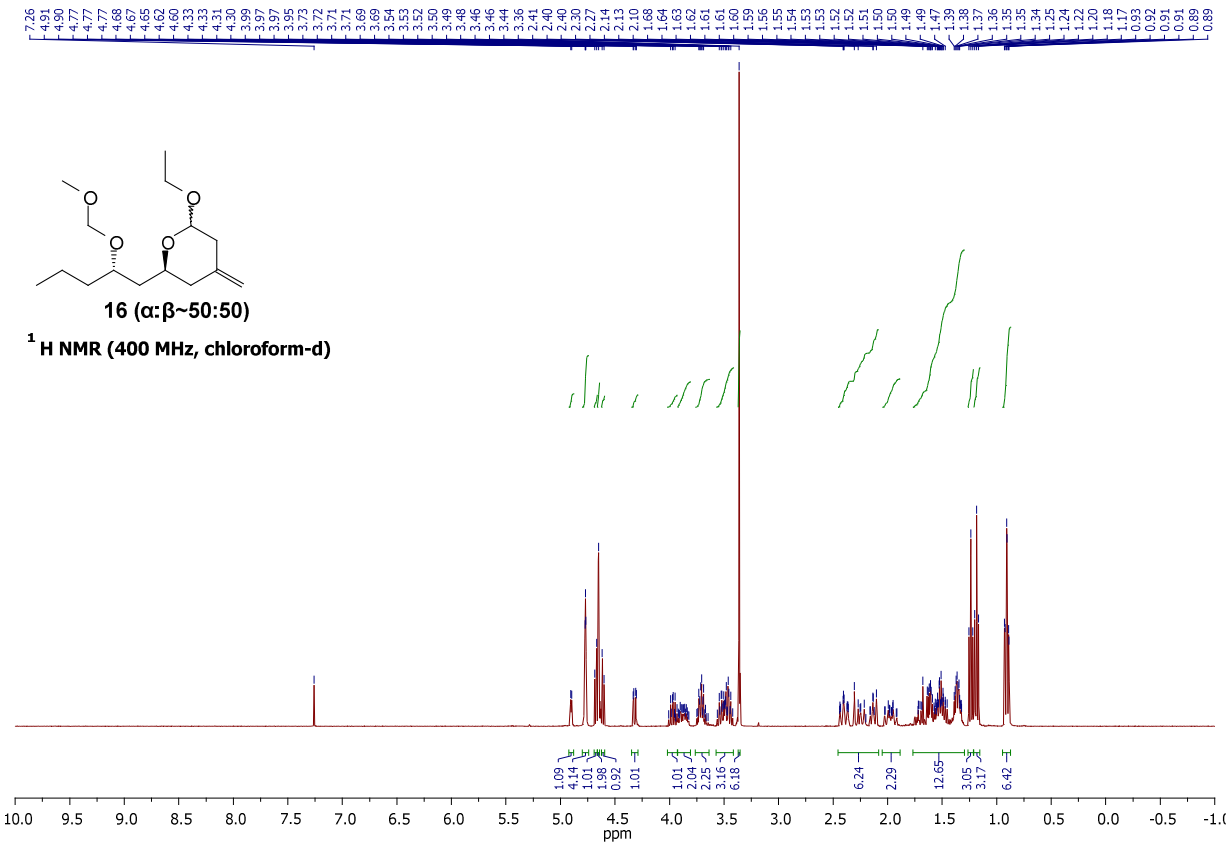
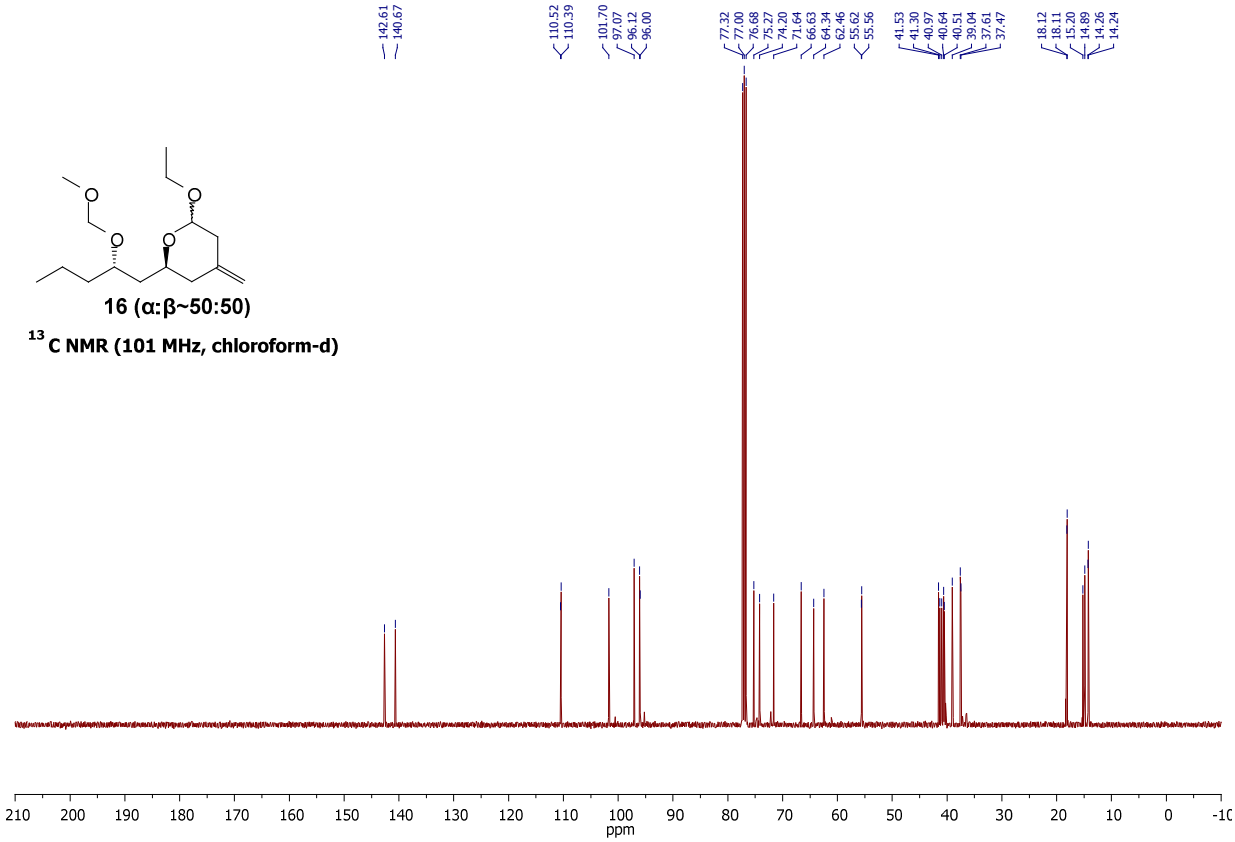
^{1}H and ^{13}C NMR spectra of 16





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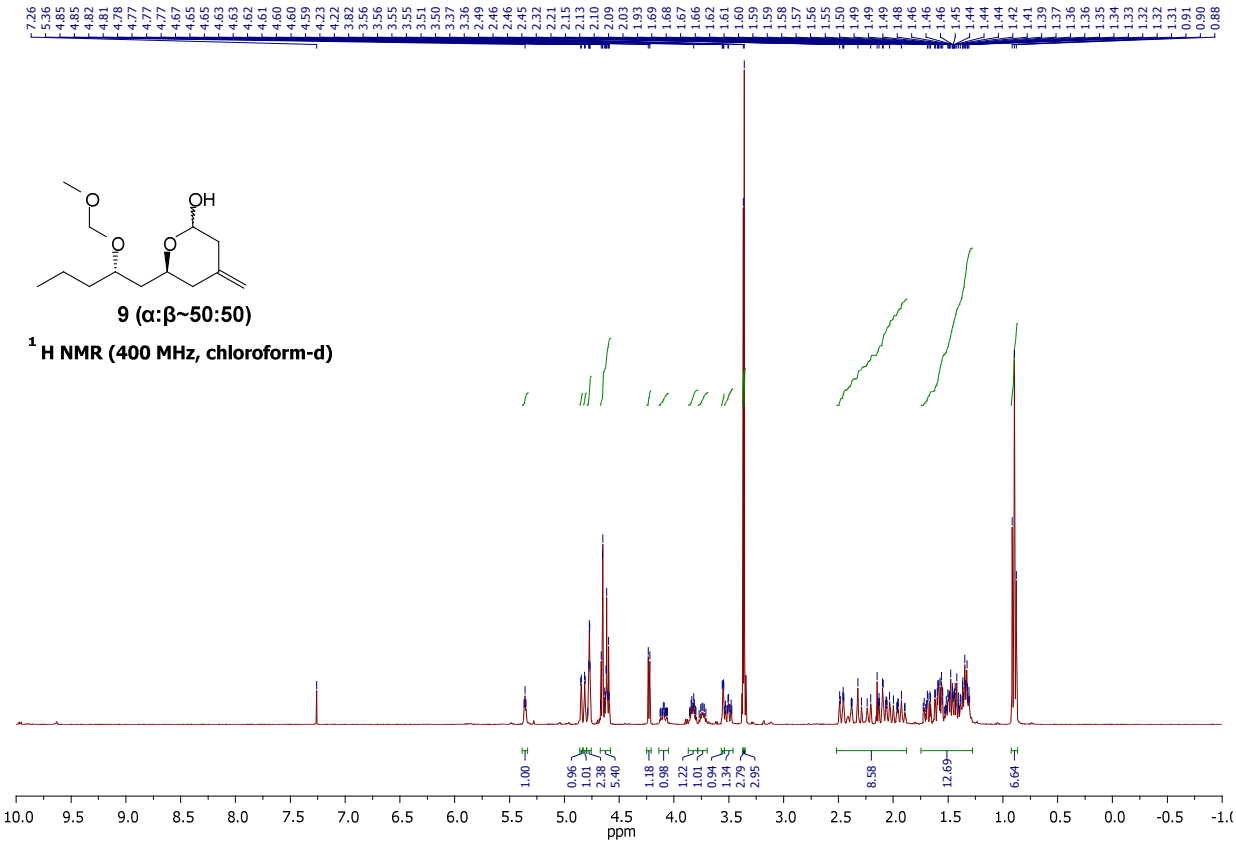

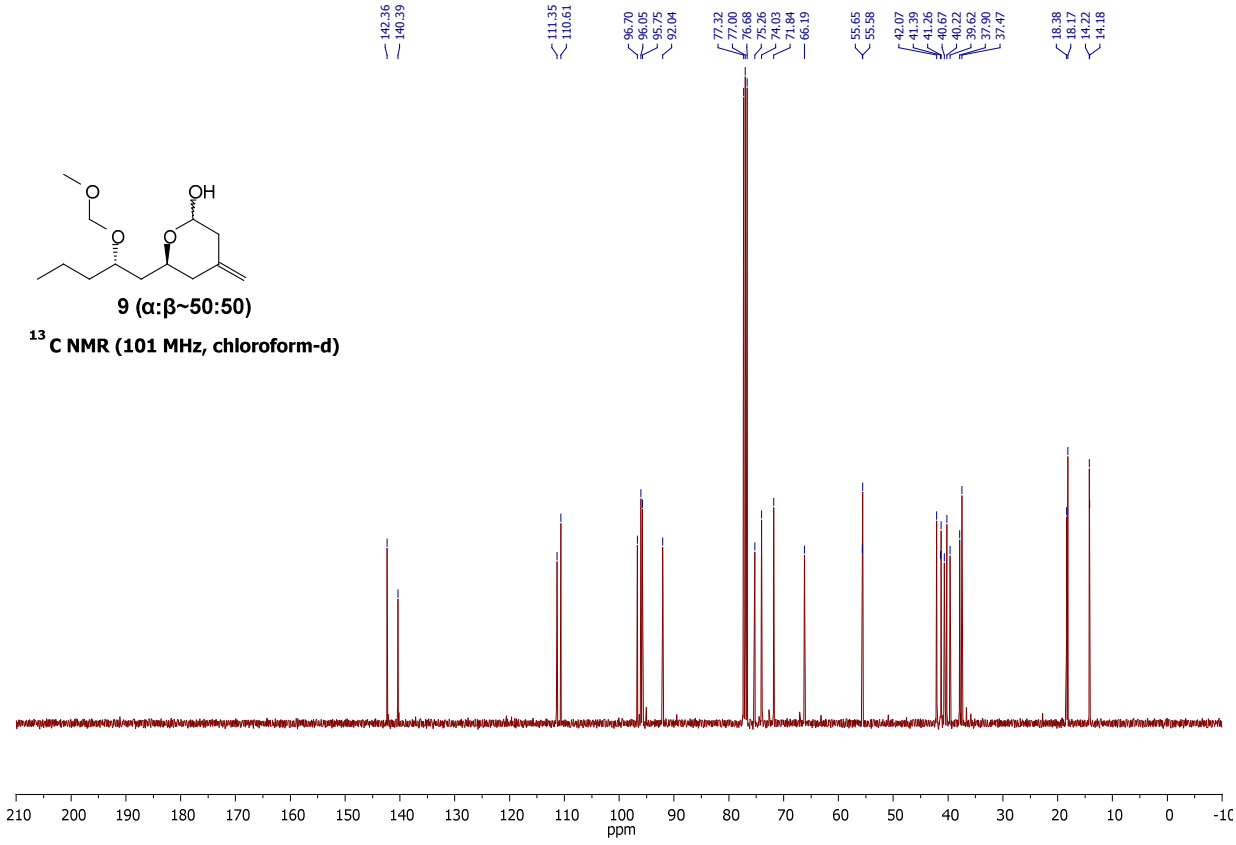

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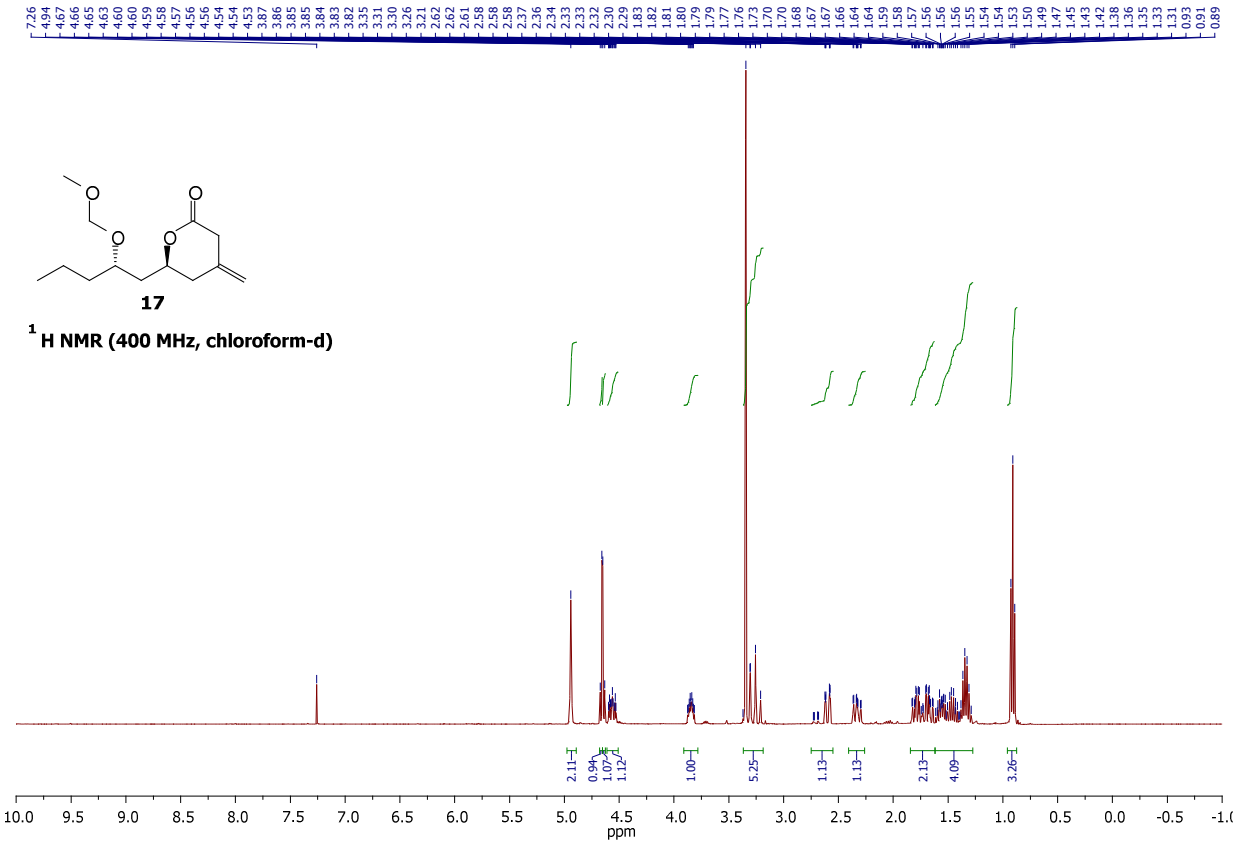

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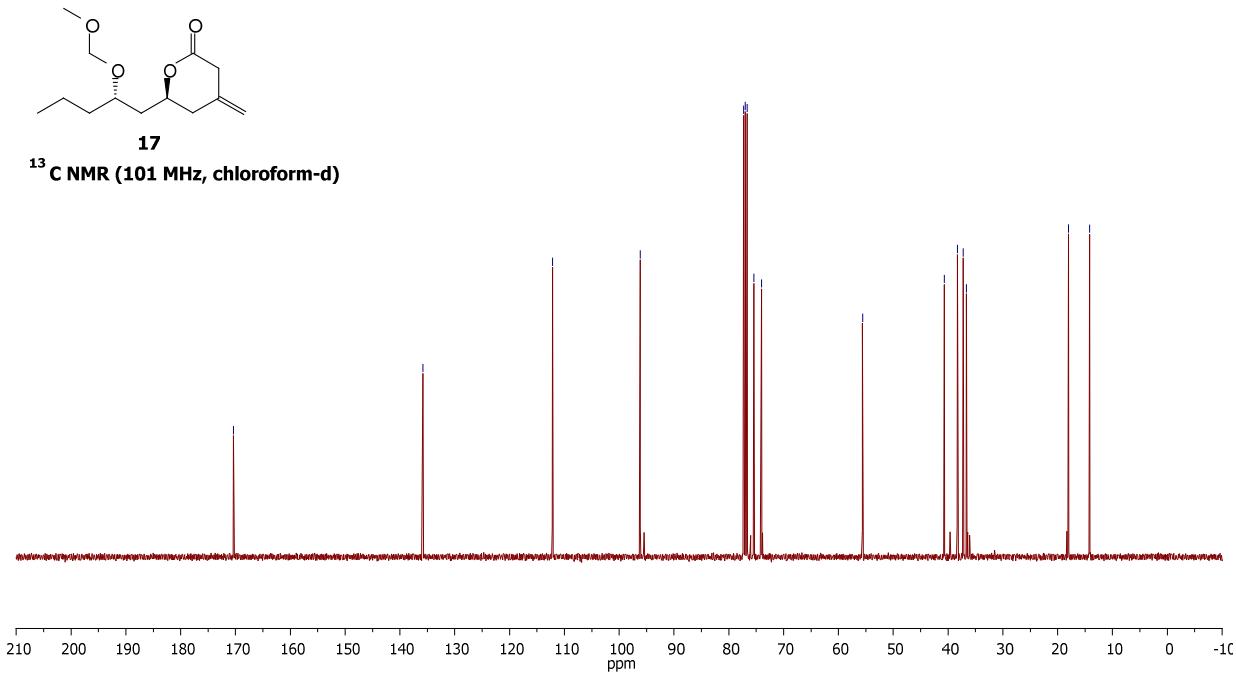
^{1}H NMR (400 MHz, chloroform-d)



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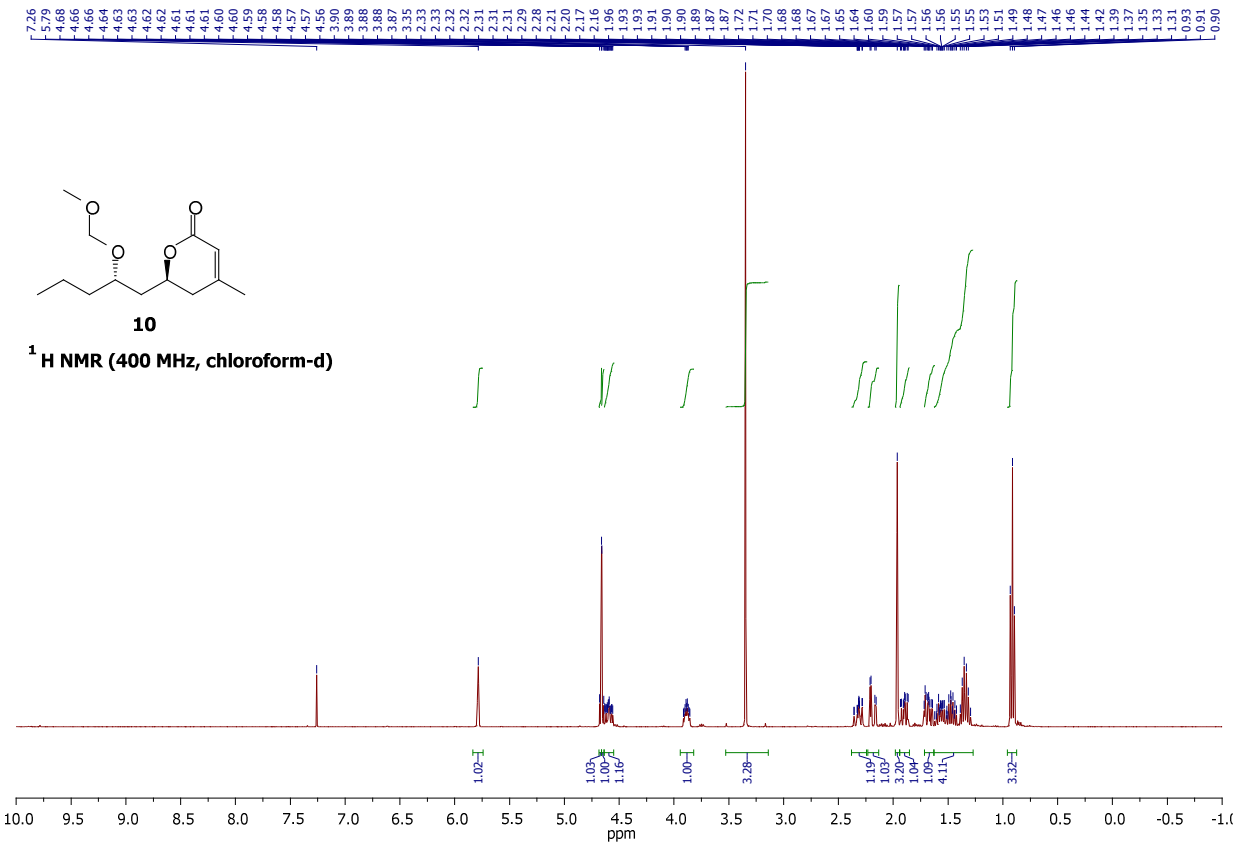
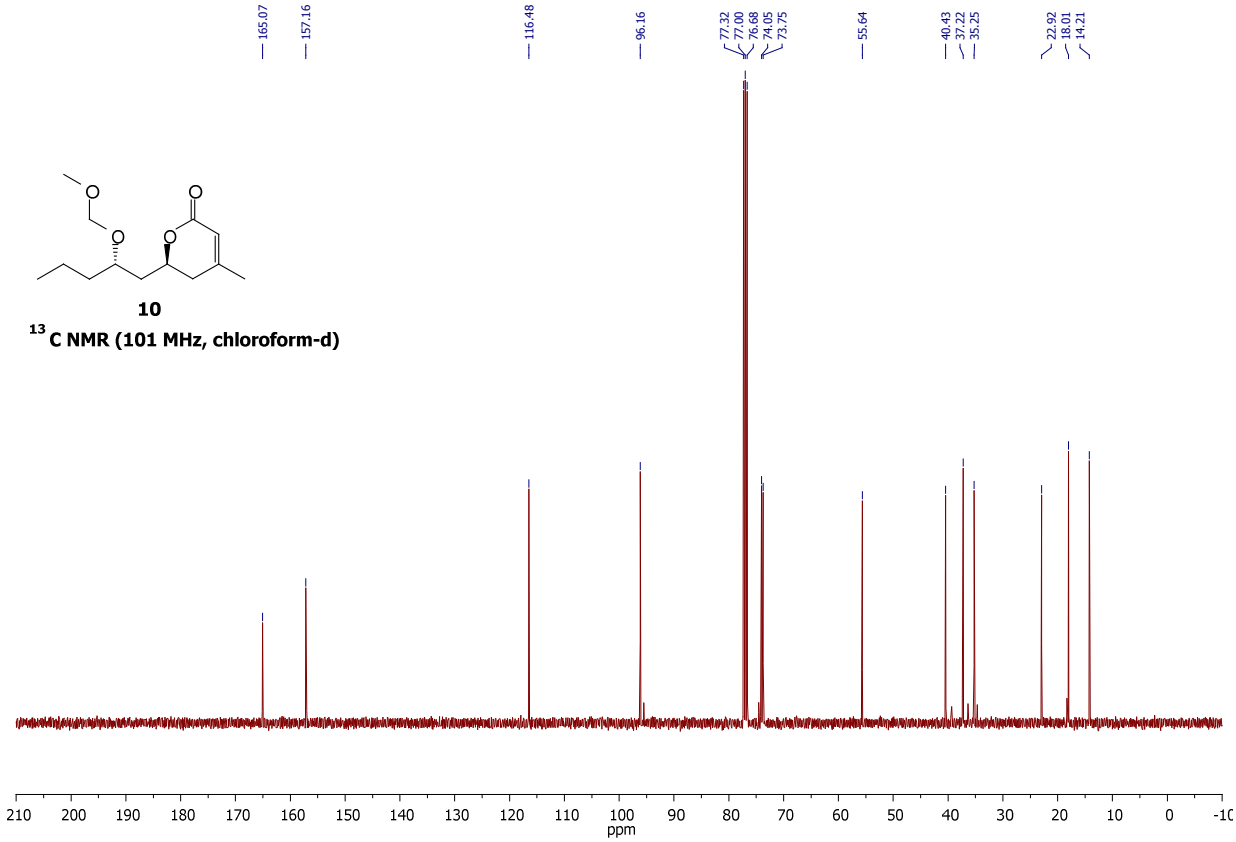
^{13}C NMR (101 MHz, chloroform-d)

^{1}H and ^{13}C NMR spectra of 10





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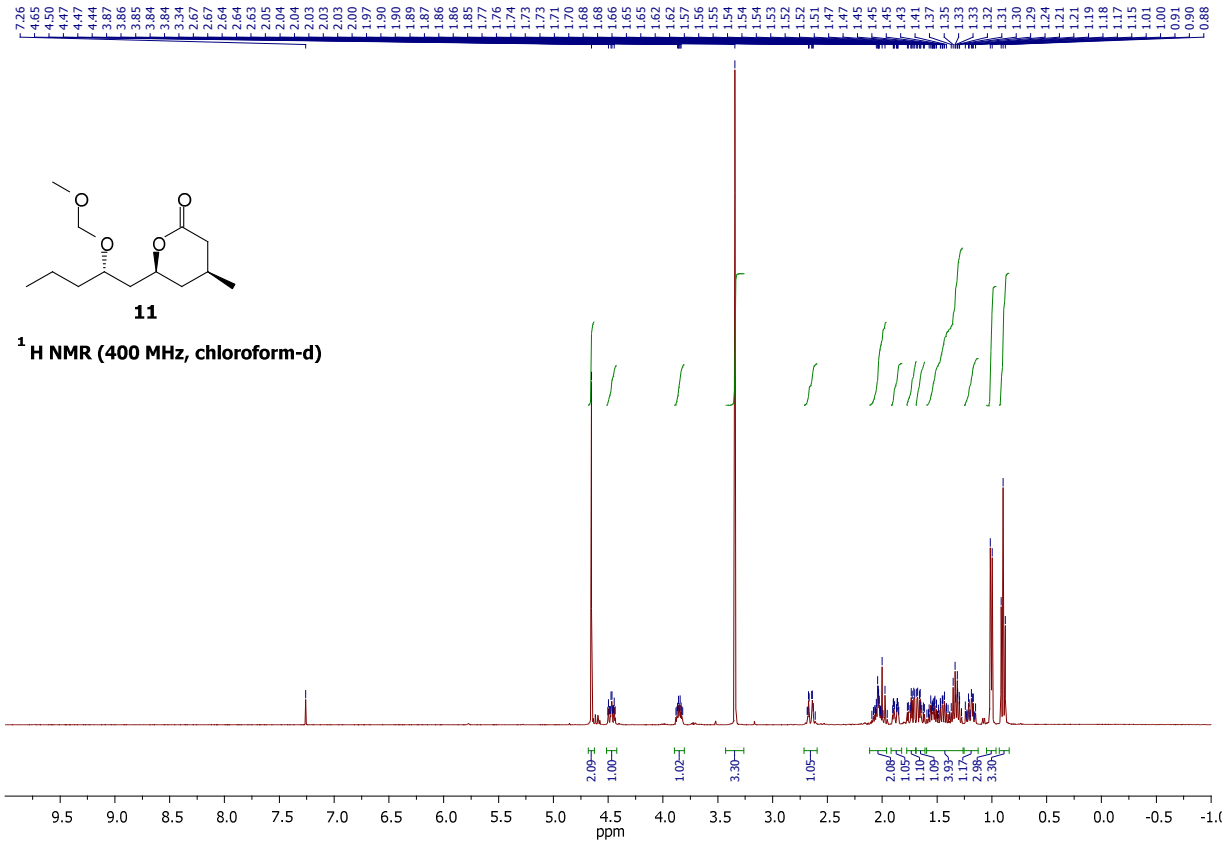

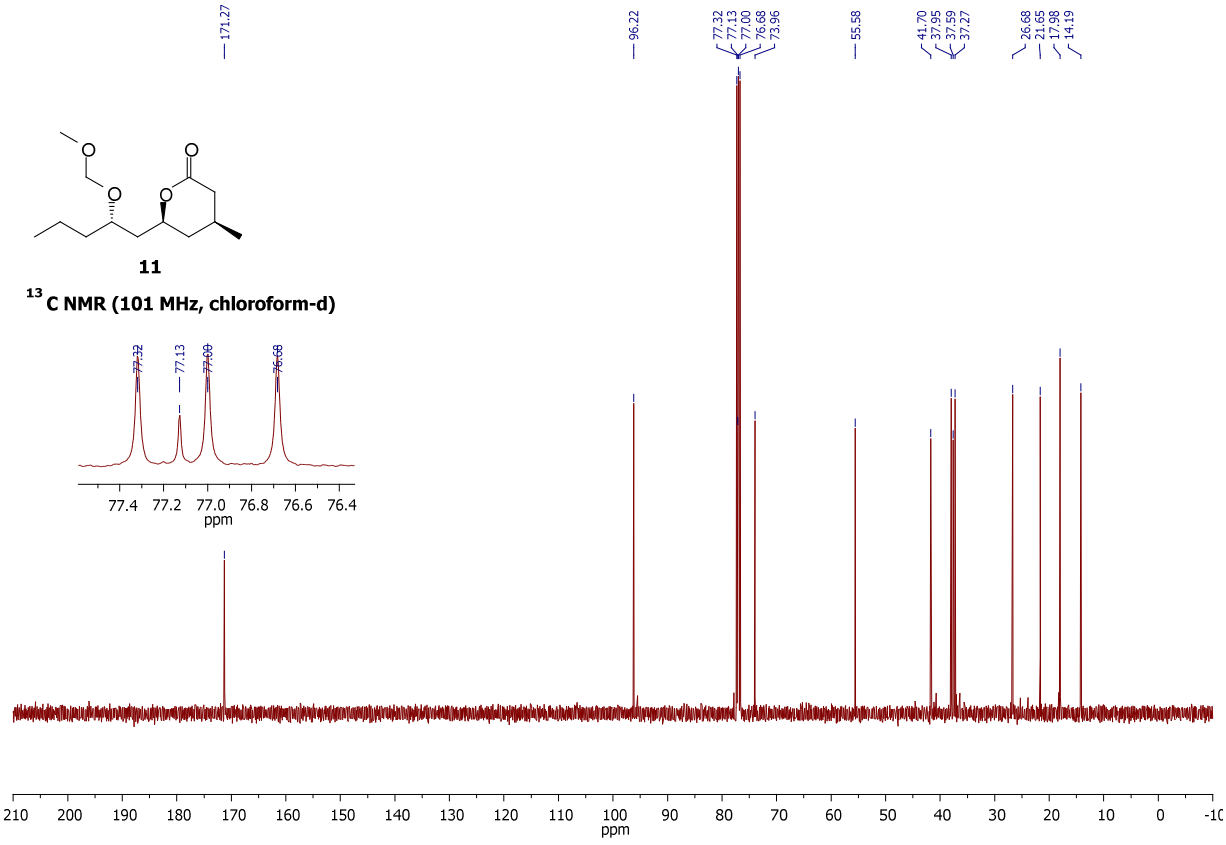

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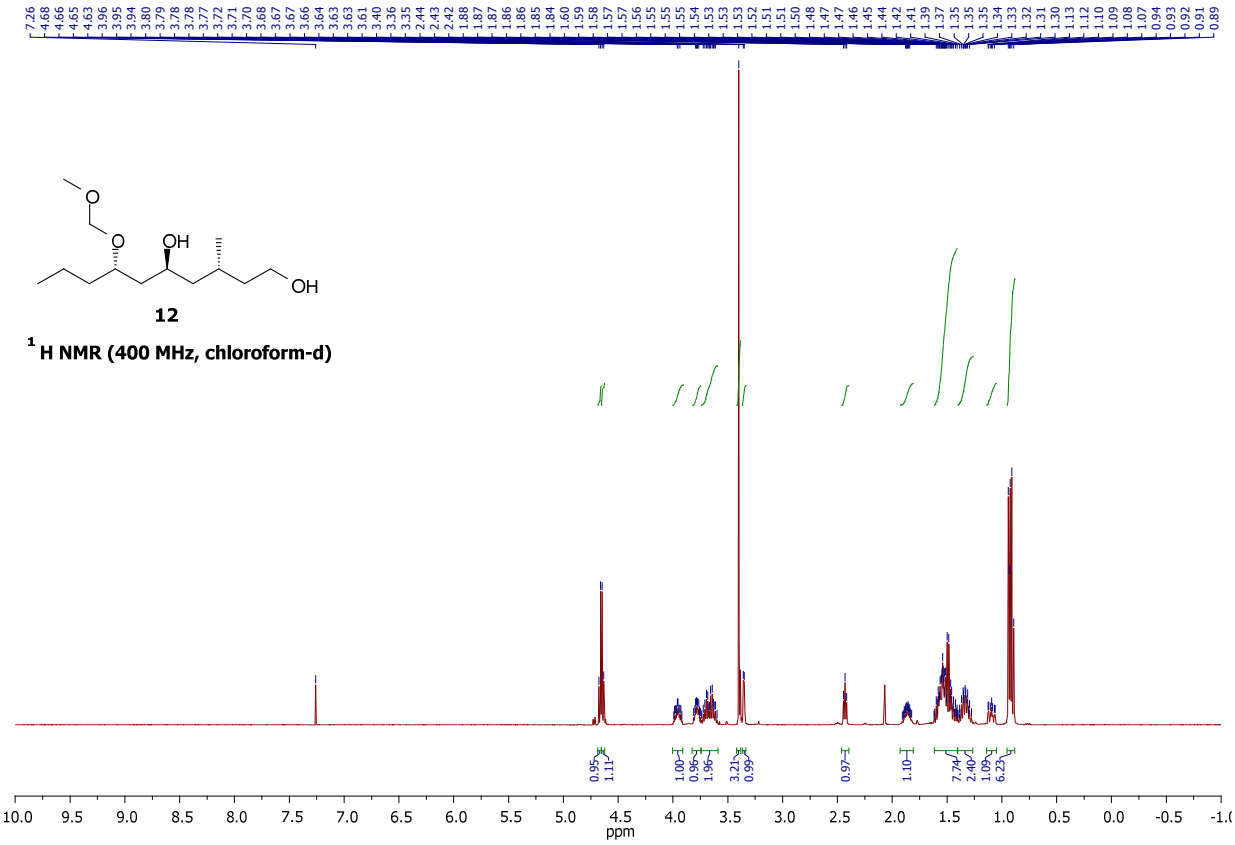

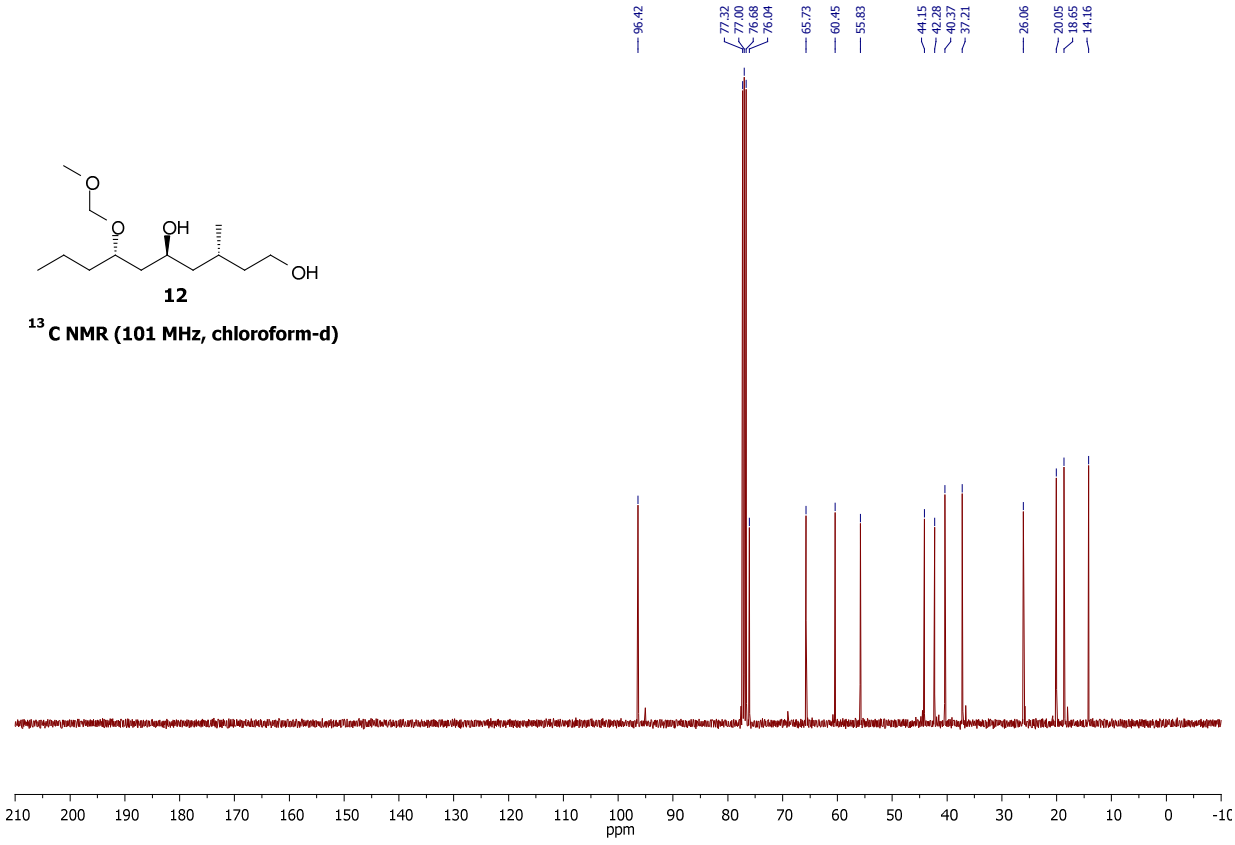

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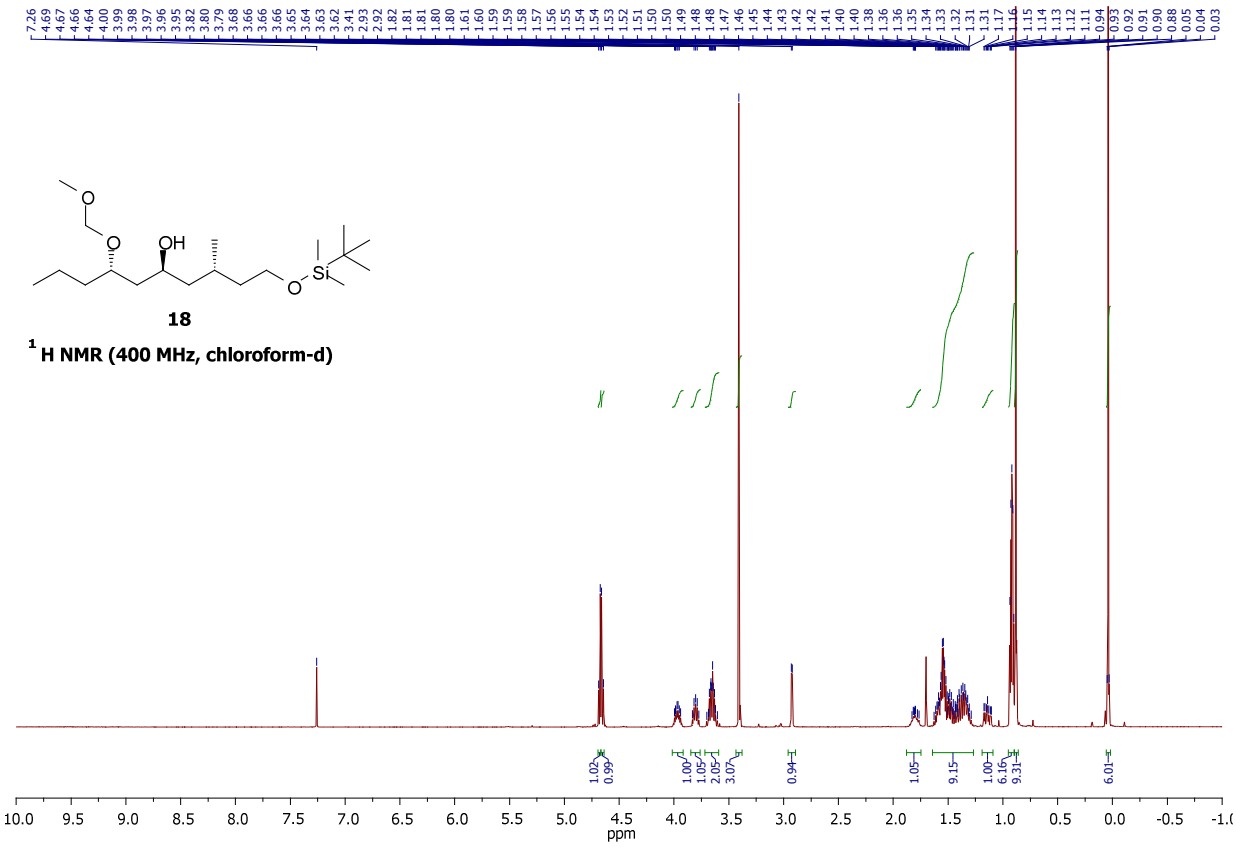

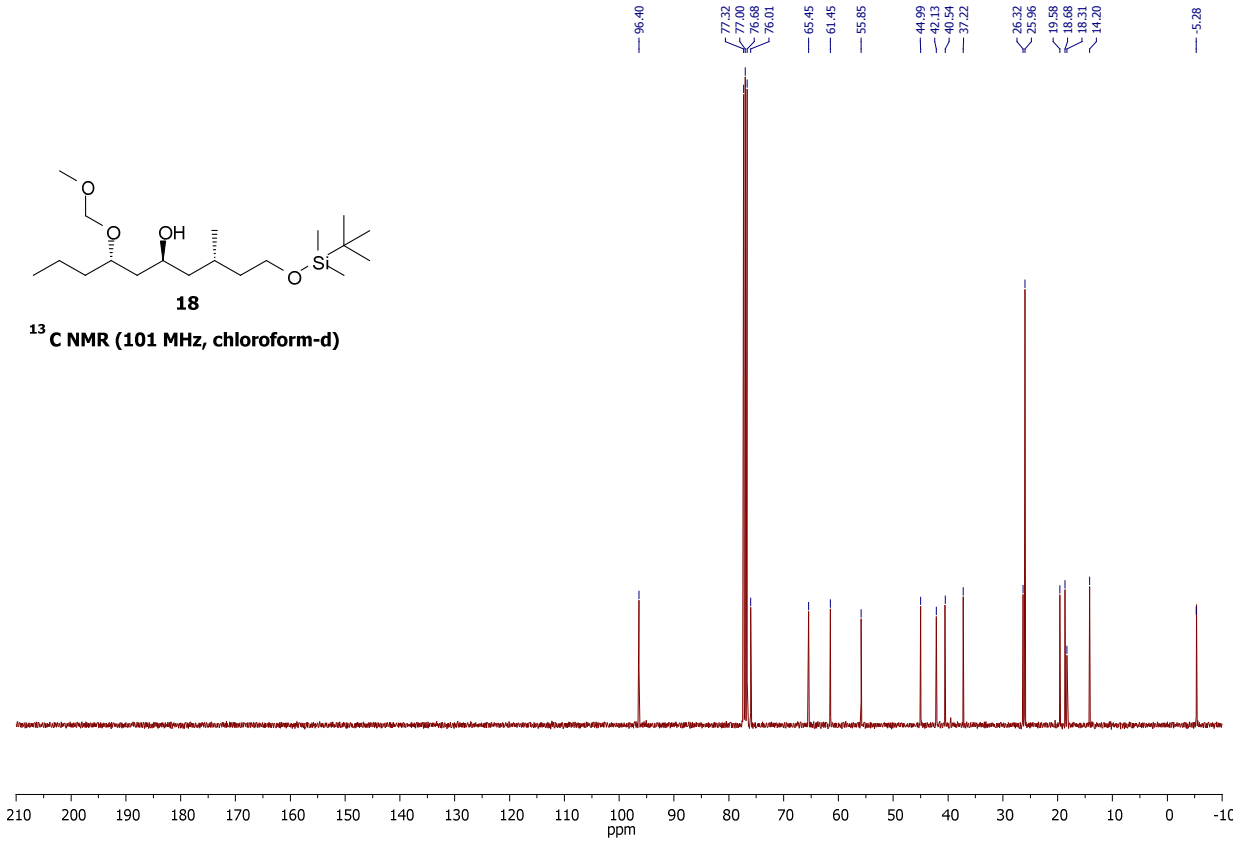

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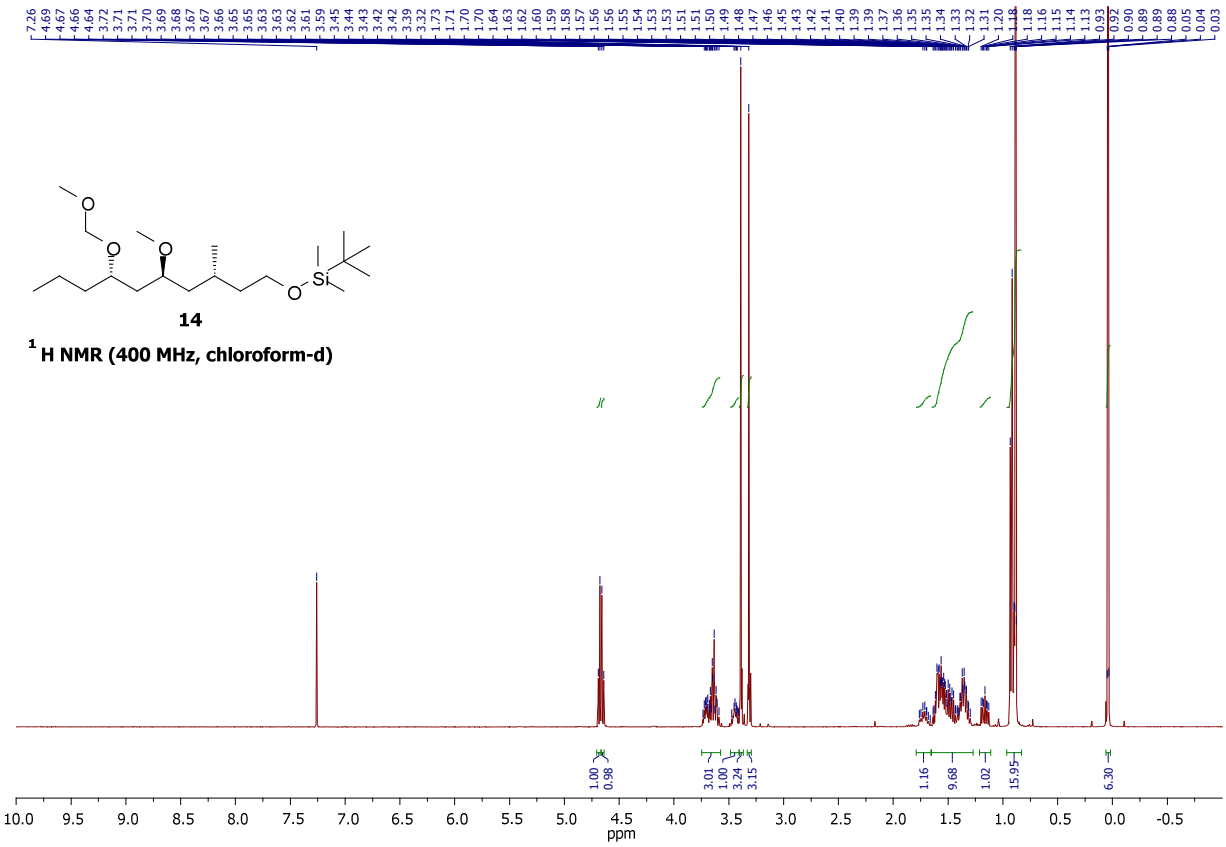
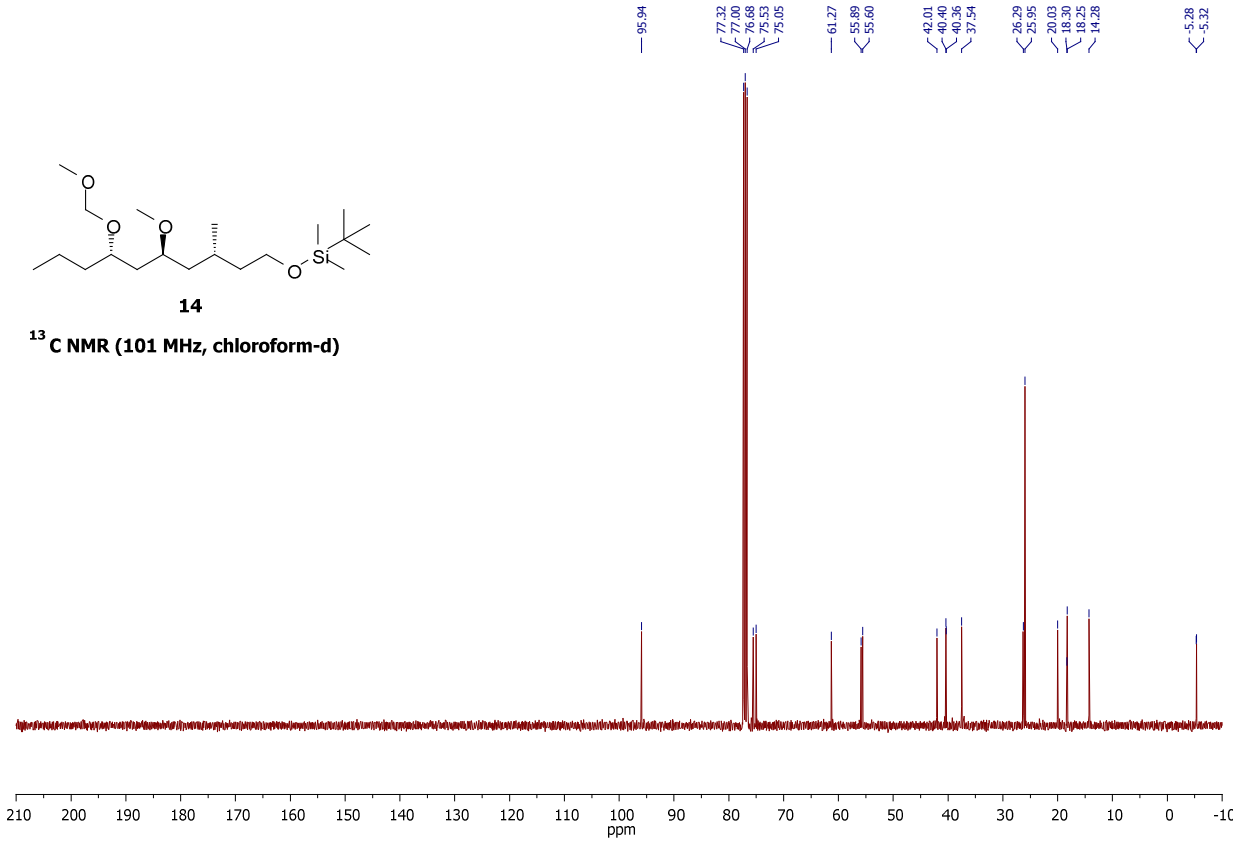


14

^{1}H NMR (400 MHz, chloroform-d)



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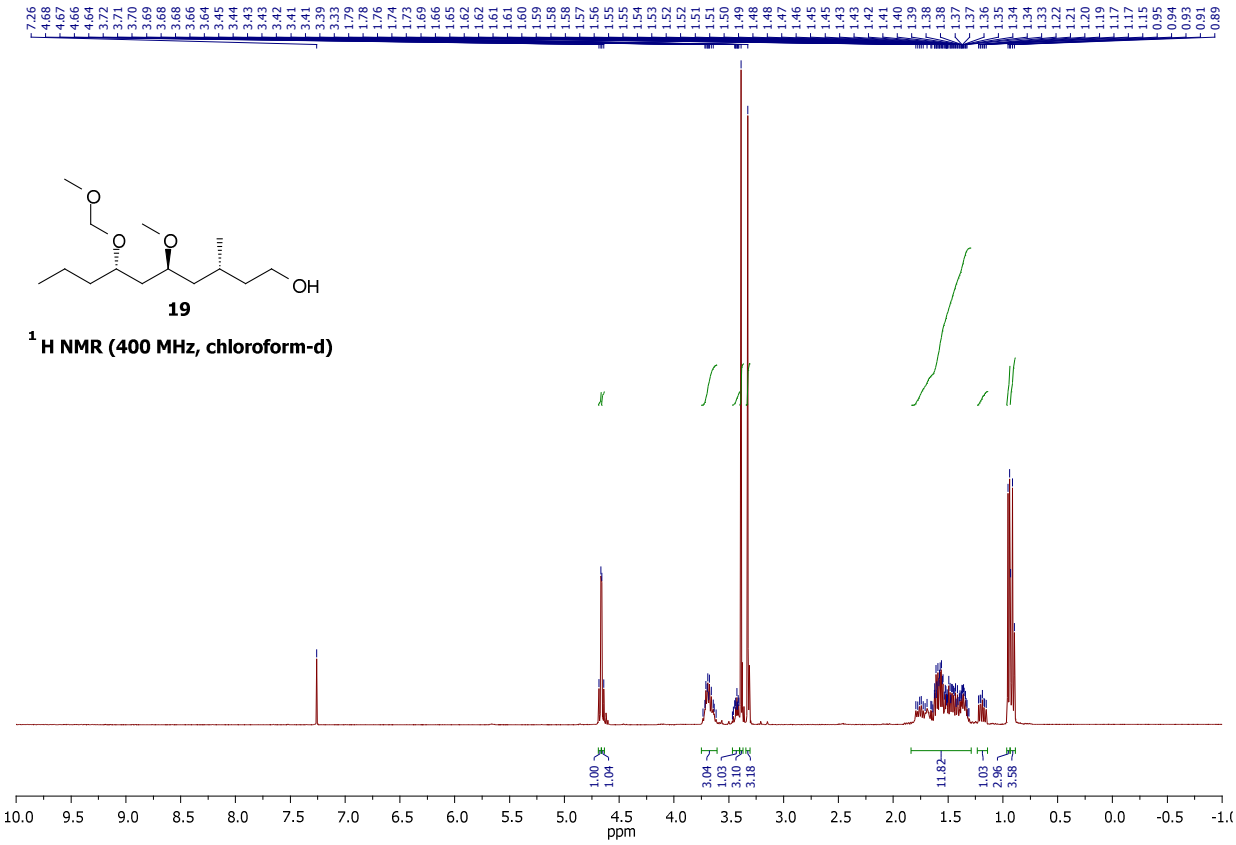
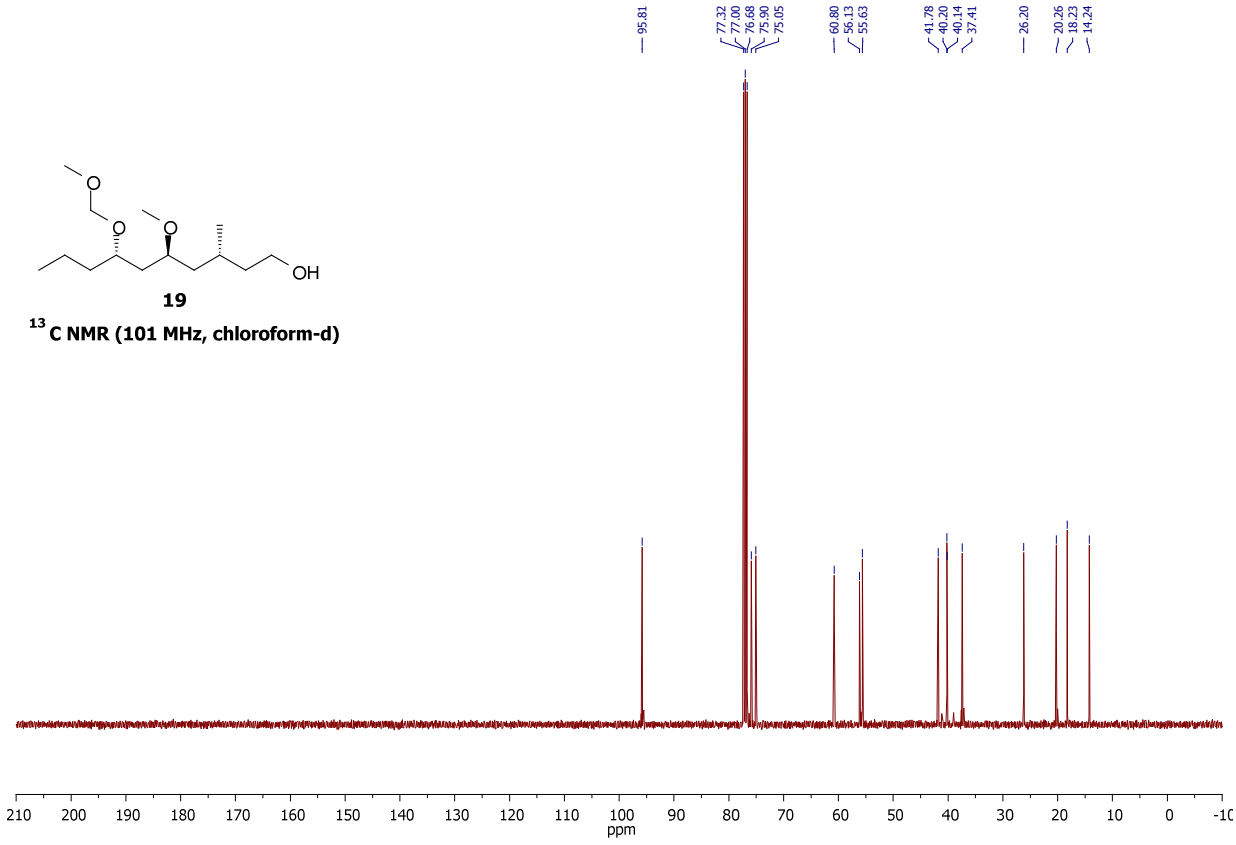
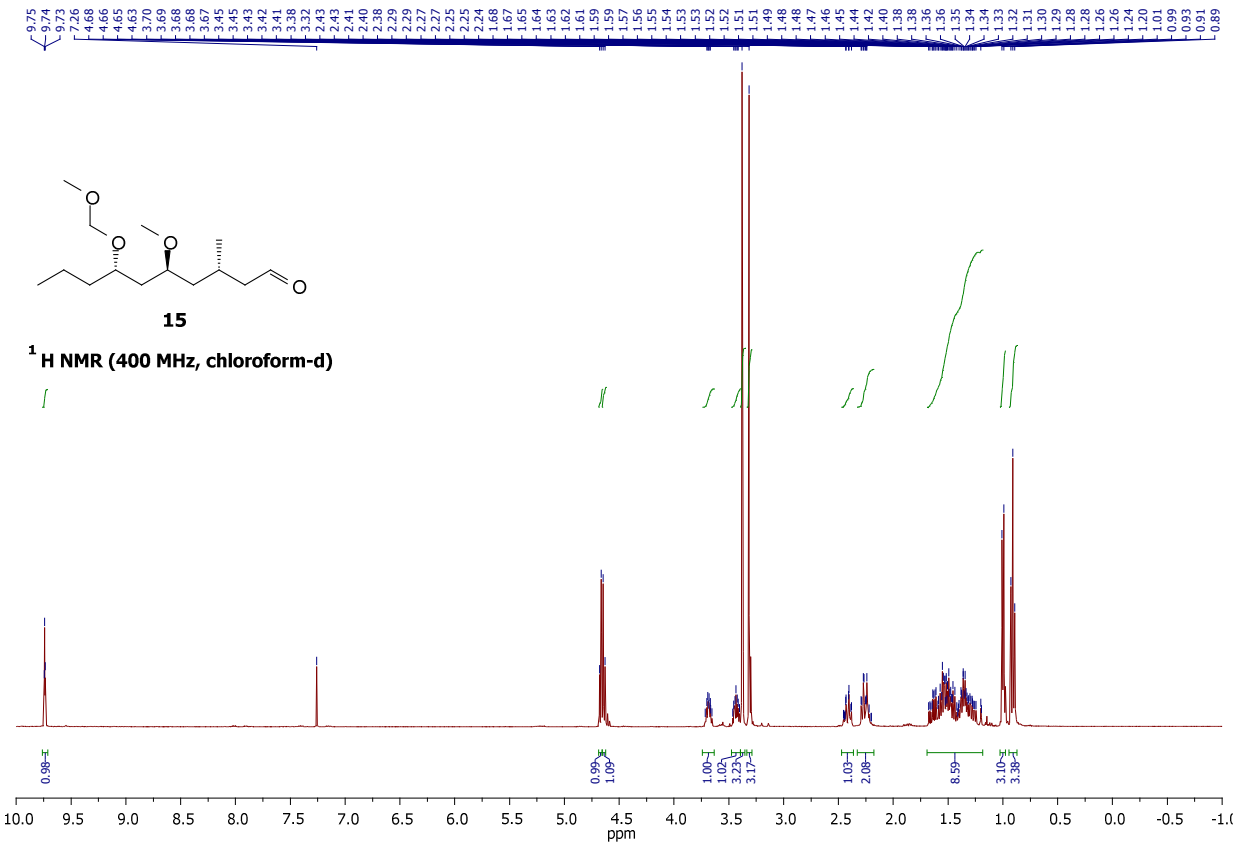
^{13}C NMR (101 MHz, chloroform-d)

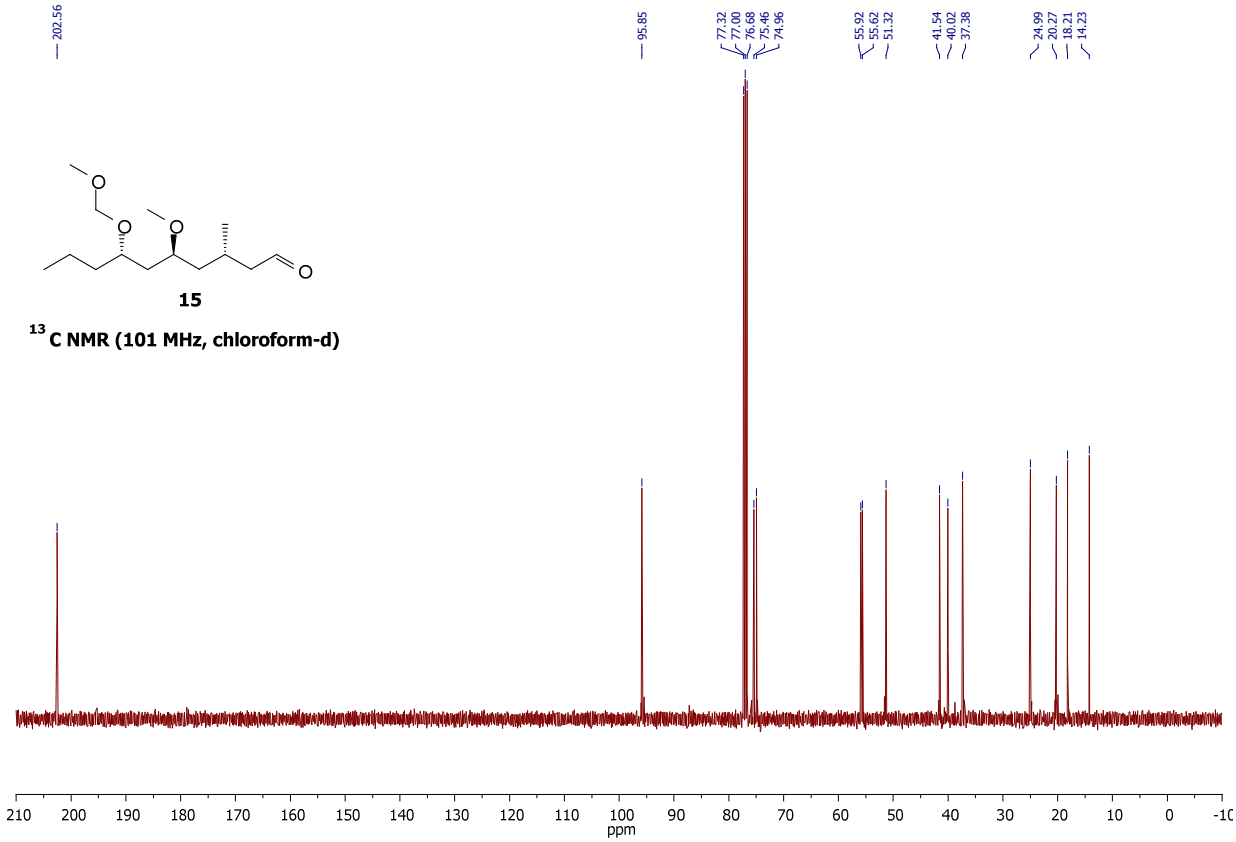
^{1}H and ^{13}C NMR spectra of 19



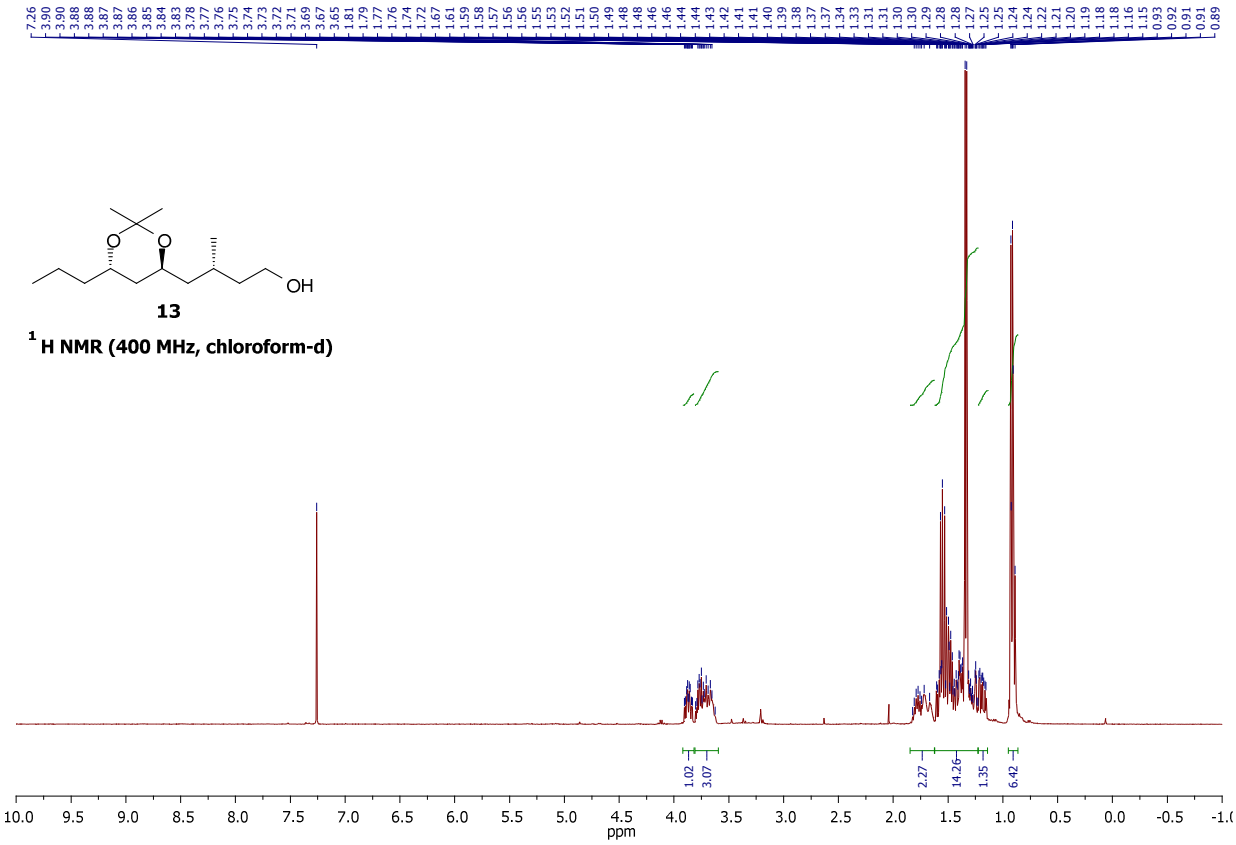


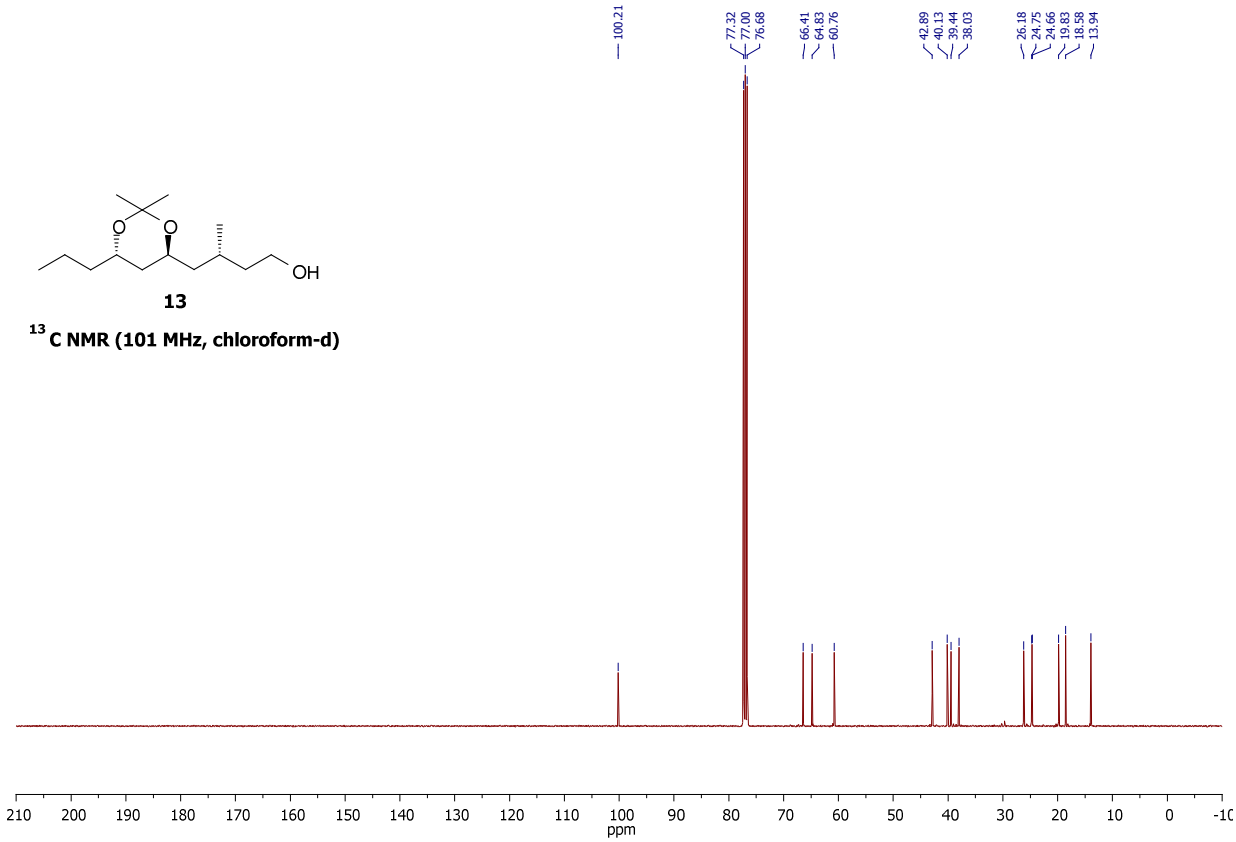
^{1}H and ^{13}C NMR spectra of 15



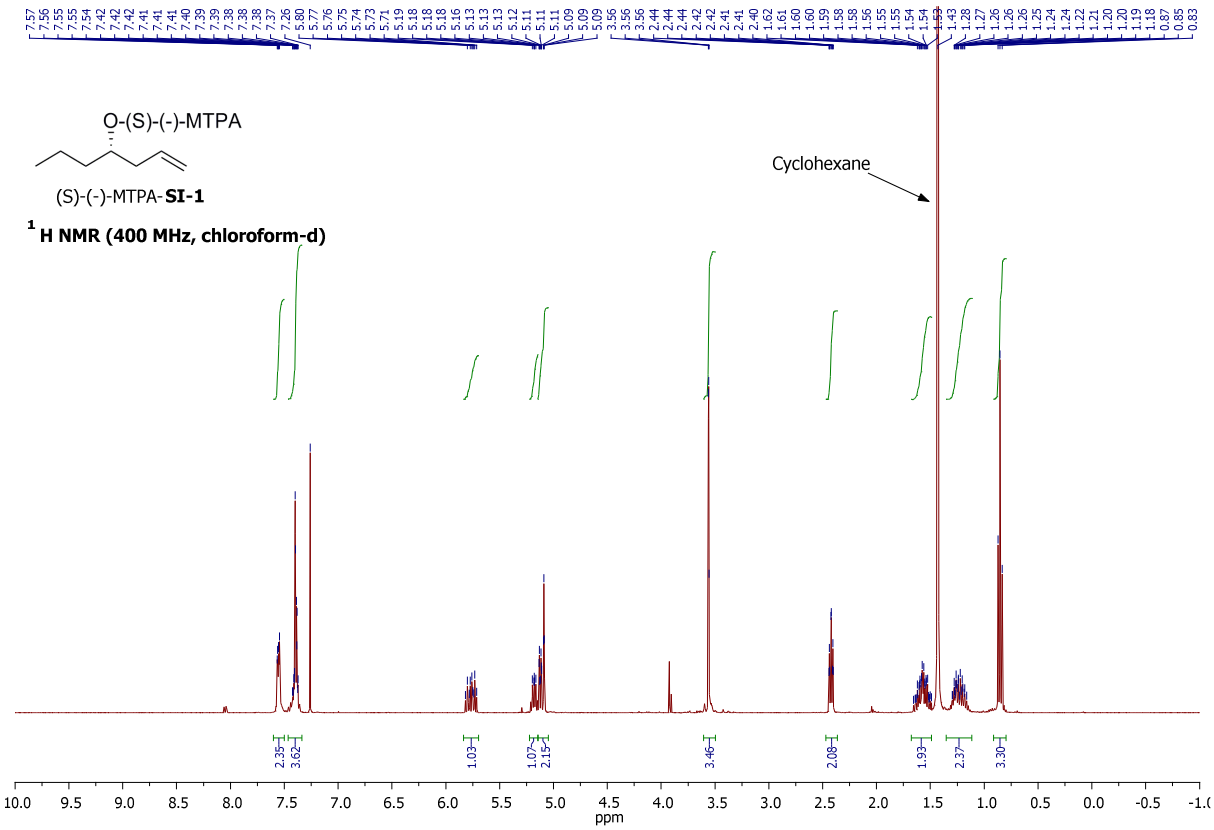


^{1}H and ^{13}C NMR spectra of 13

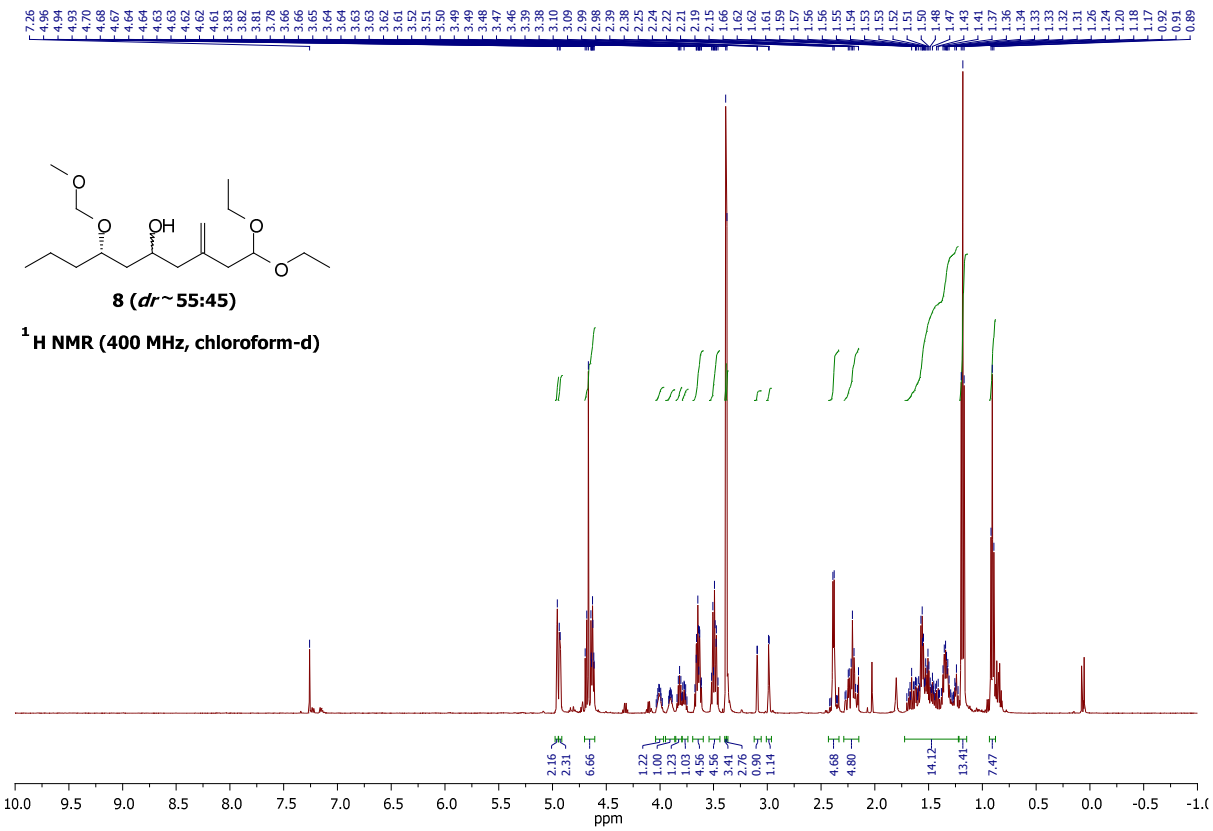




^{1}H NMR spectrum of (S)-(-)-Mosher ester of SI-1

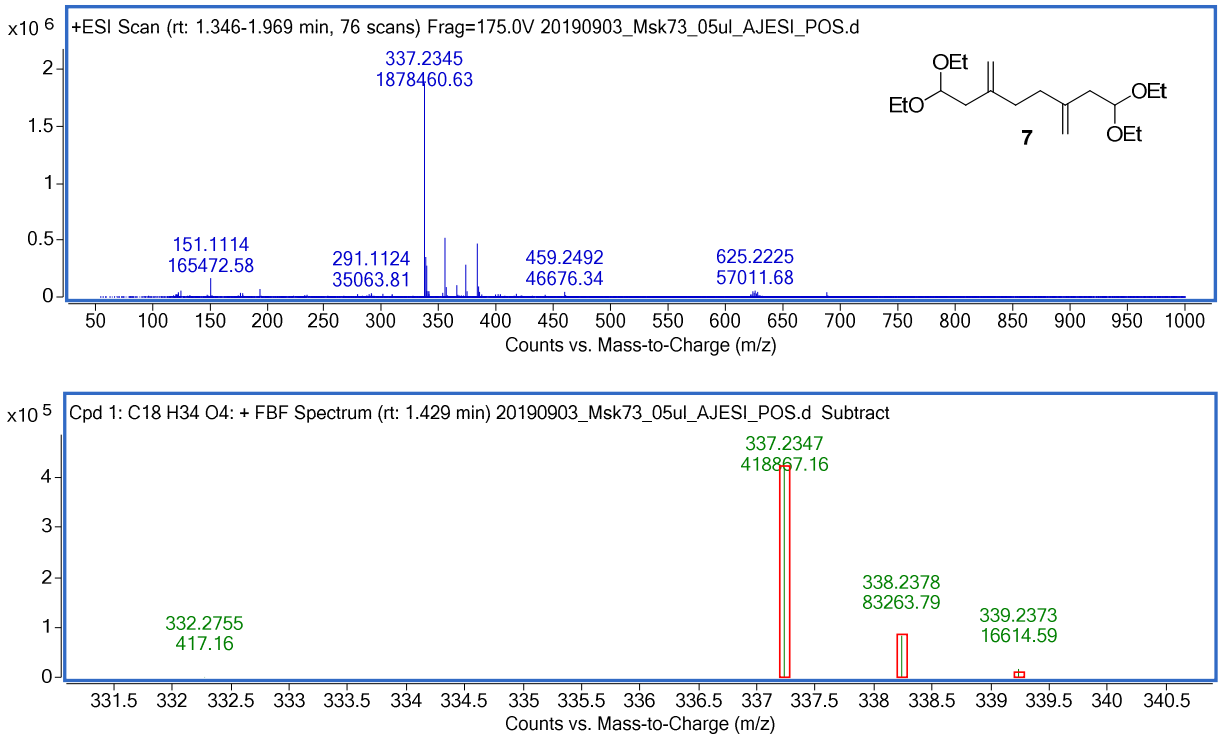


^{1}H NMR spectrum of 8 (mixture of diastereomers)

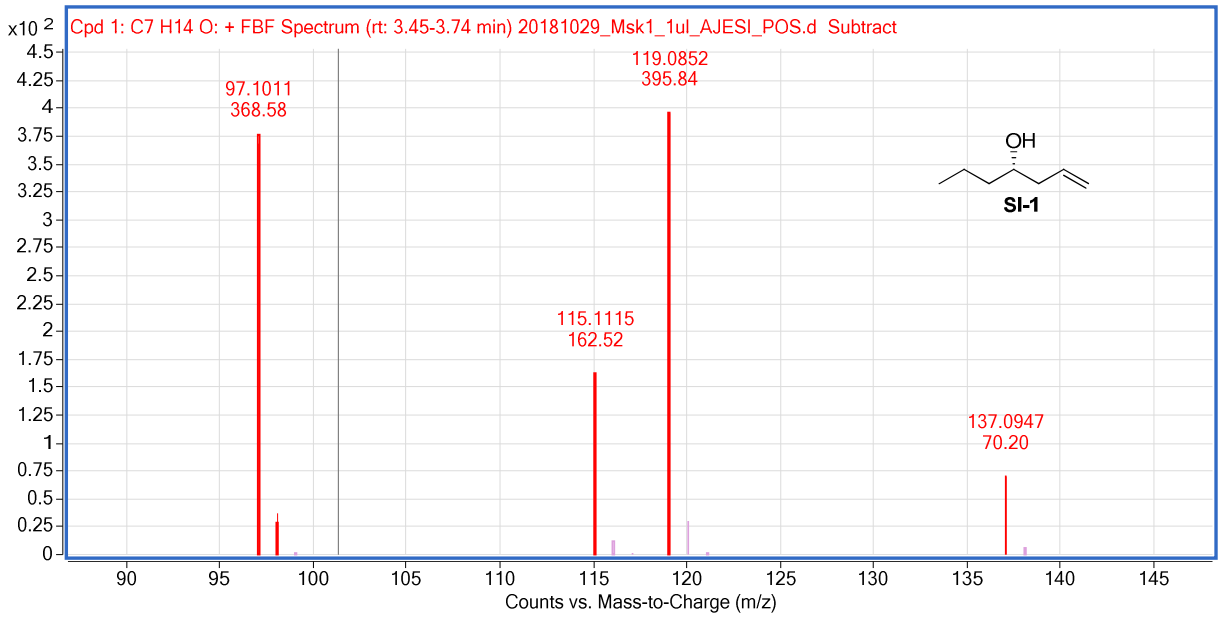


3. Copies of HRMS spectra

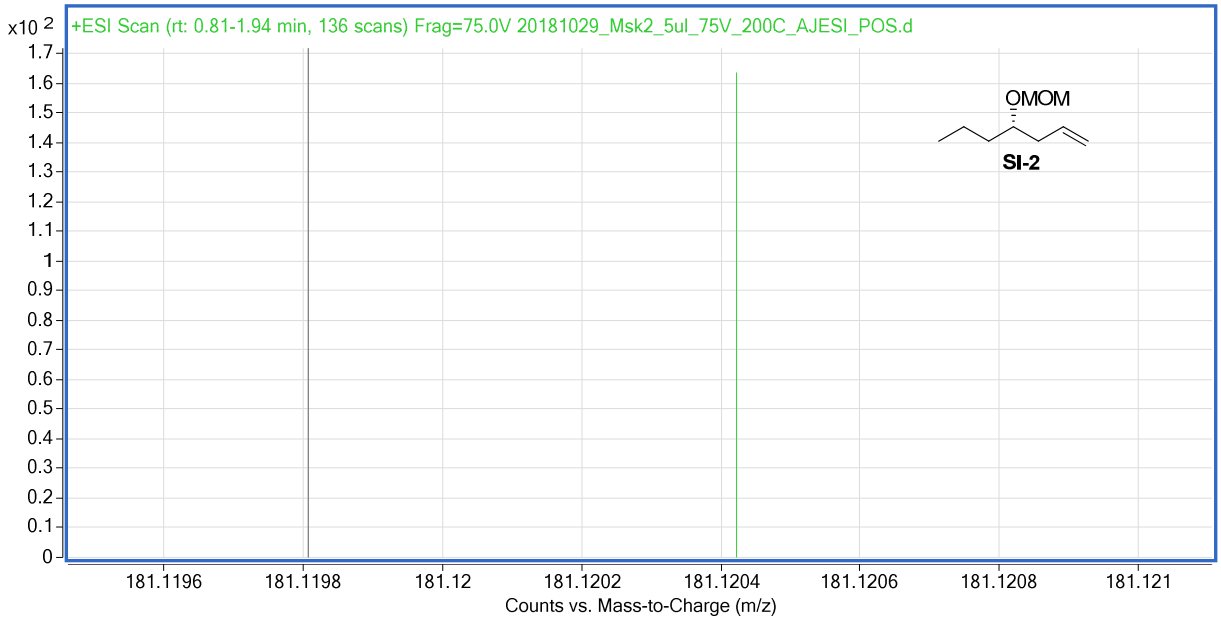
HRMS of compound 7



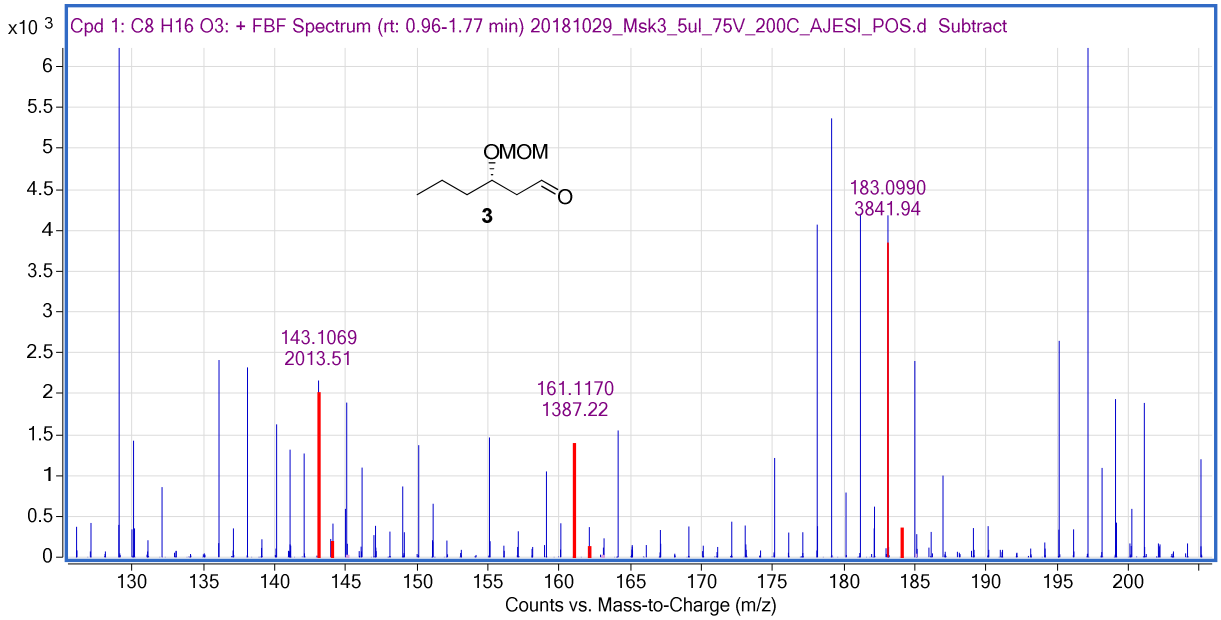
HRMS of compound SI-1

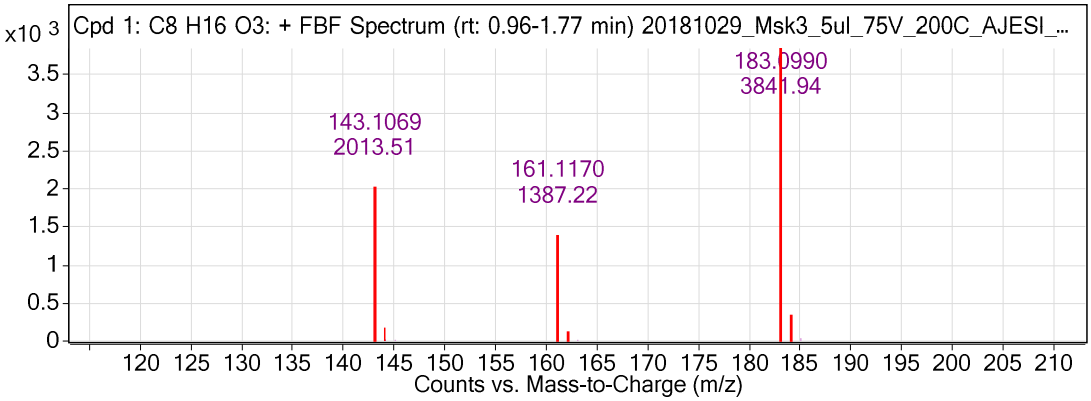


HRMS of compound SI-2

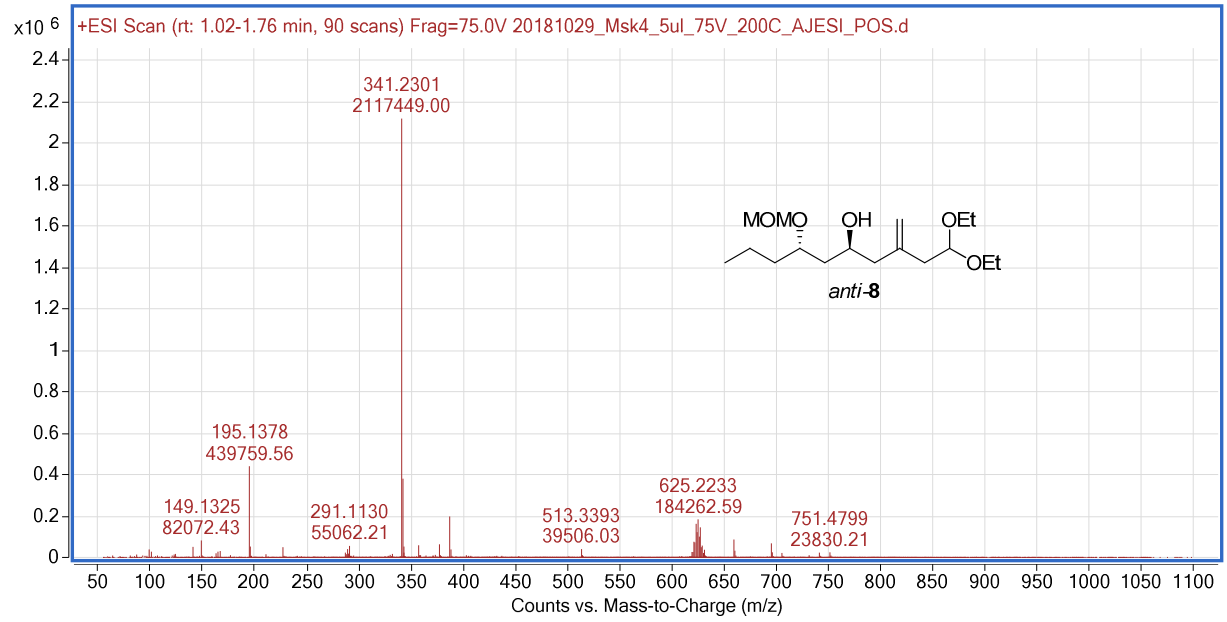


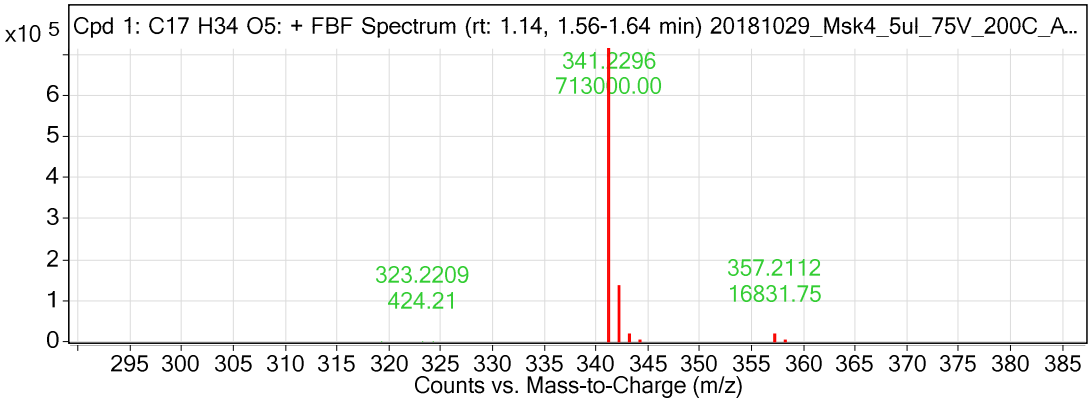
HRMS of compound 3



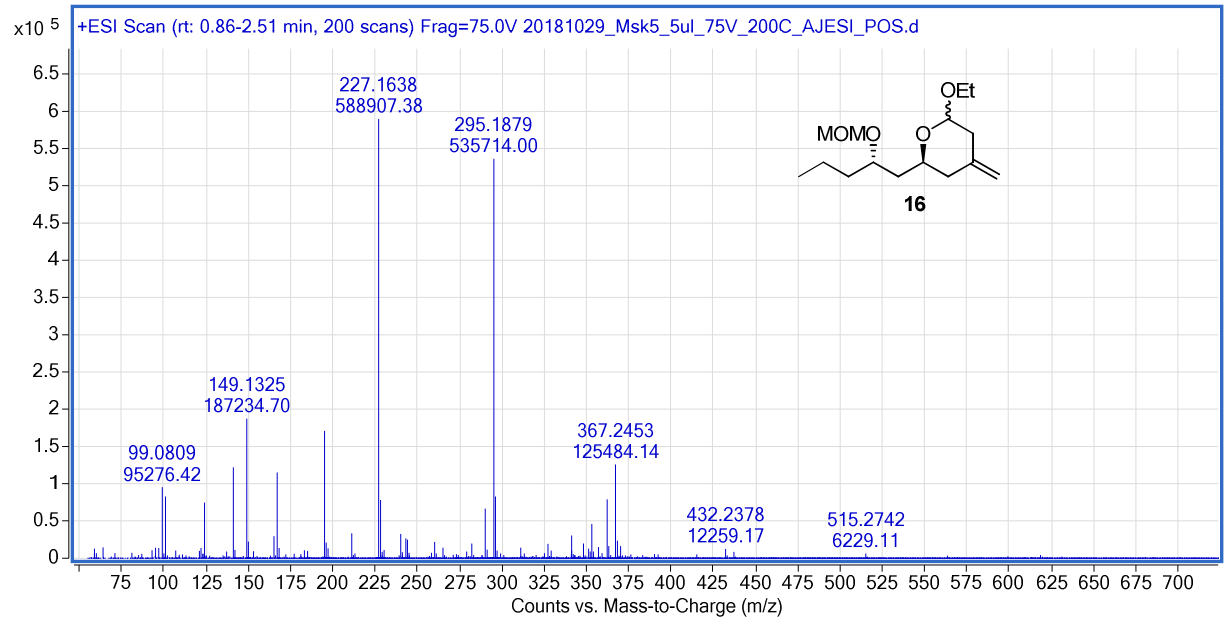


HRMS of compound 8

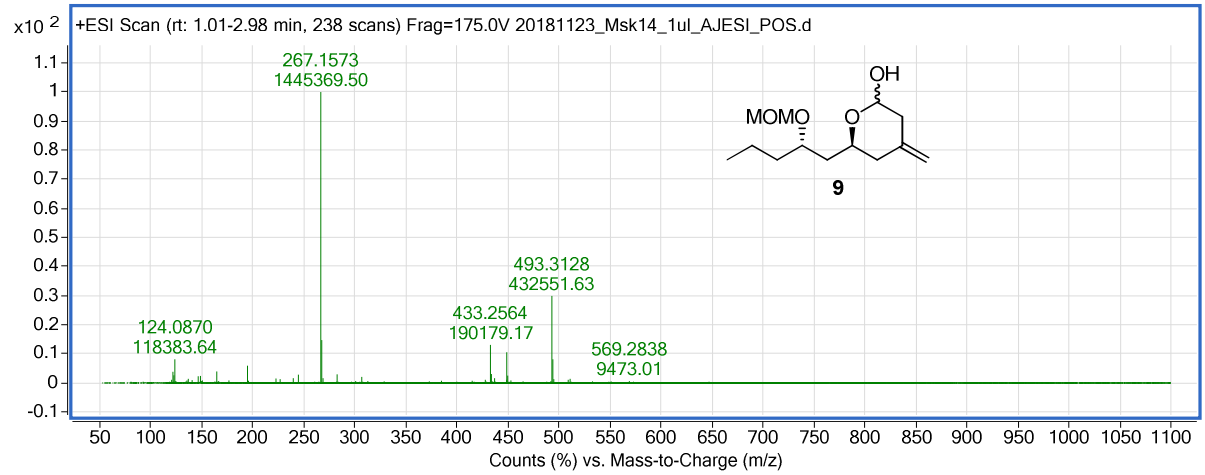


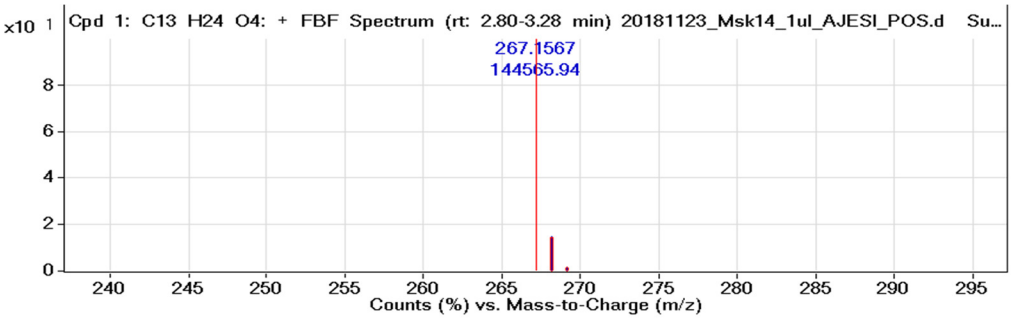


HRMS of compound 16

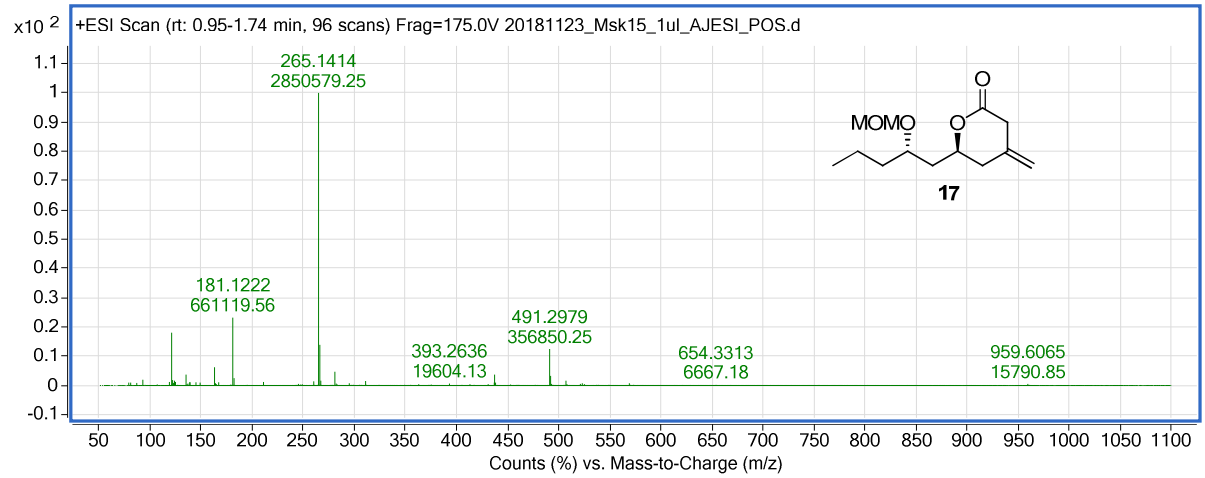


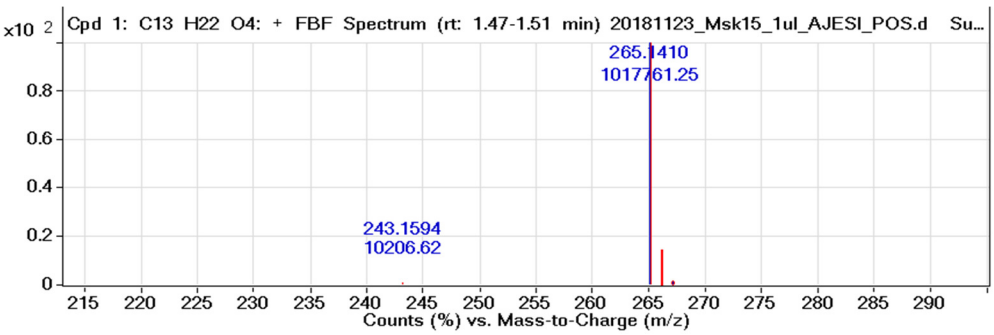
HRMS of compound 9



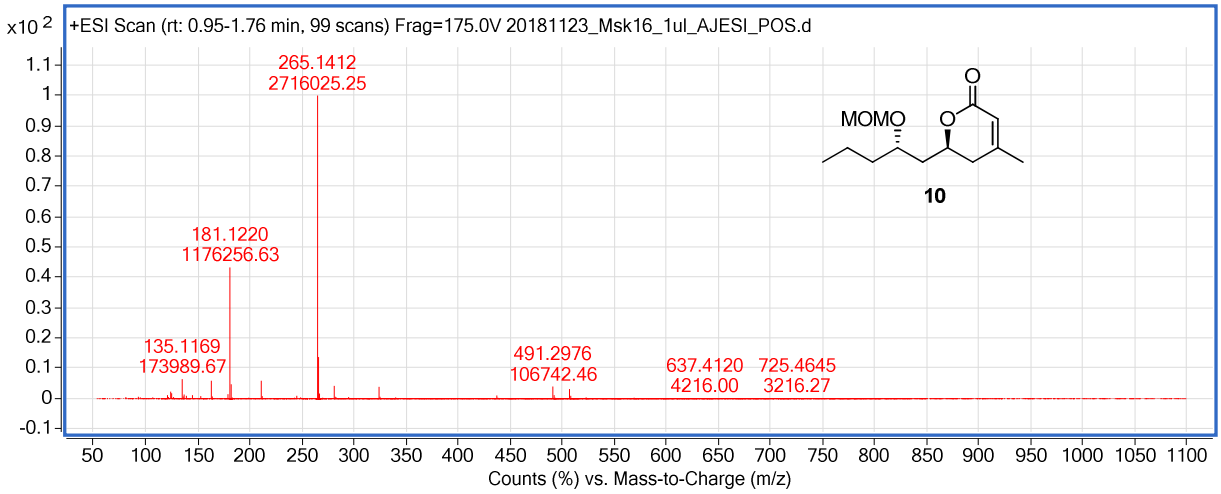


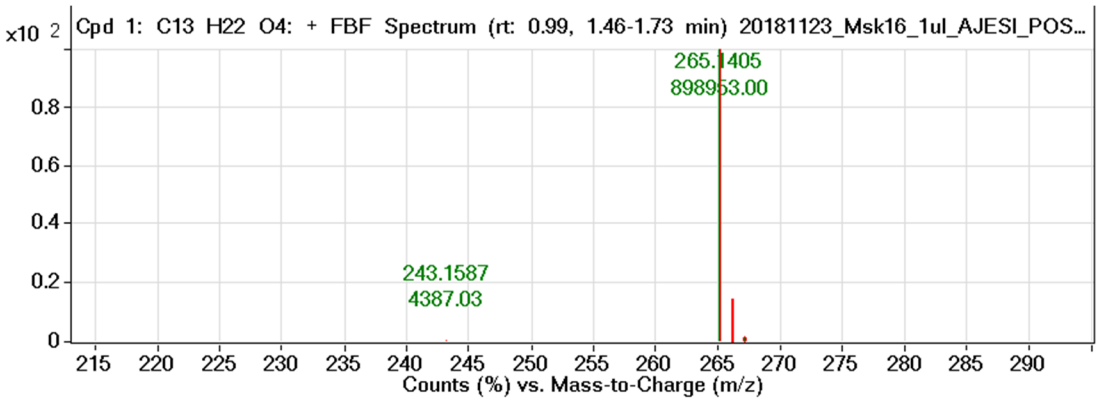
HRMS of compound 17



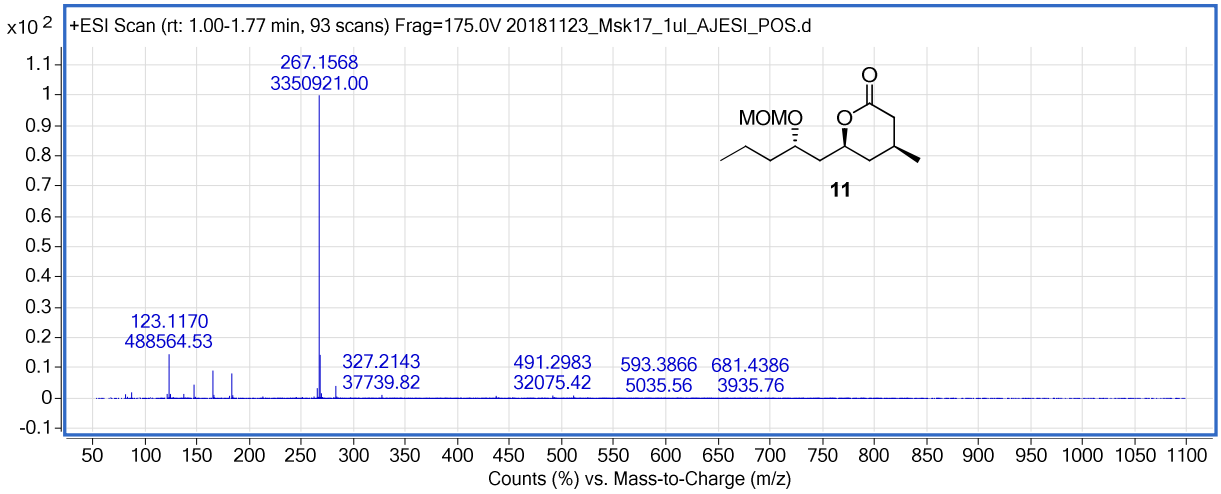


HRMS of compound 10

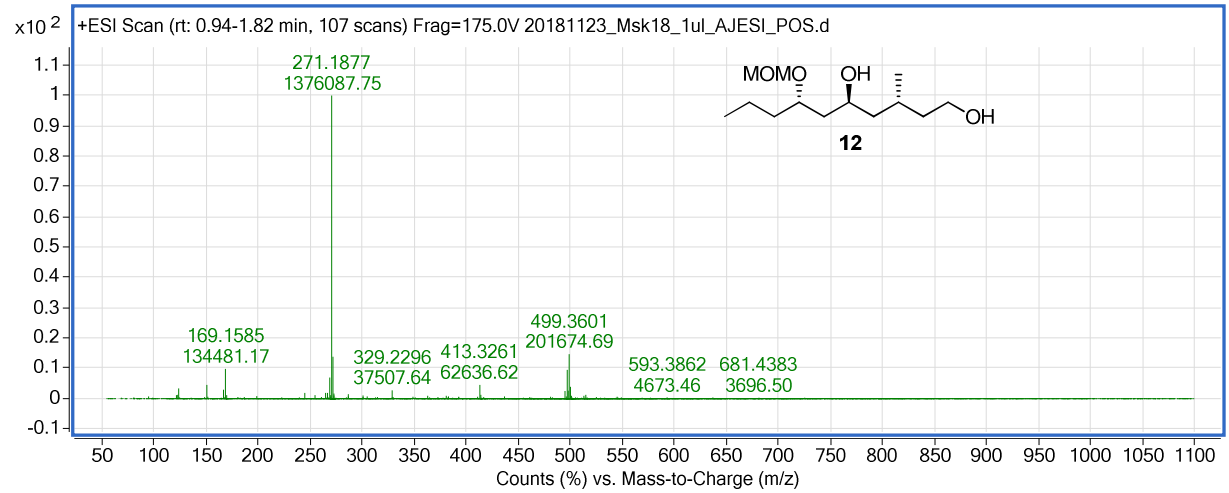


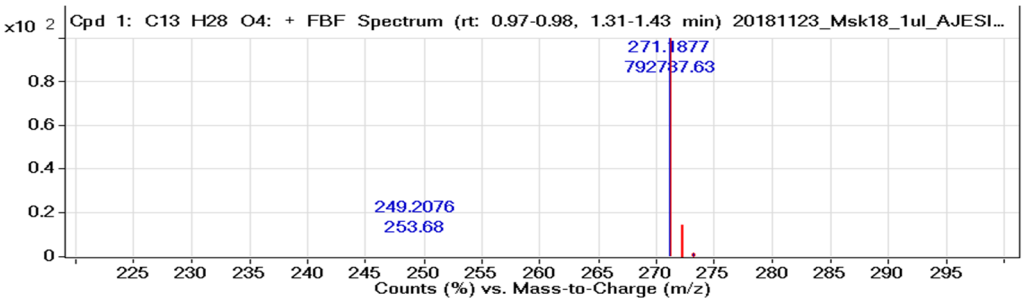


HRMS of compound 11

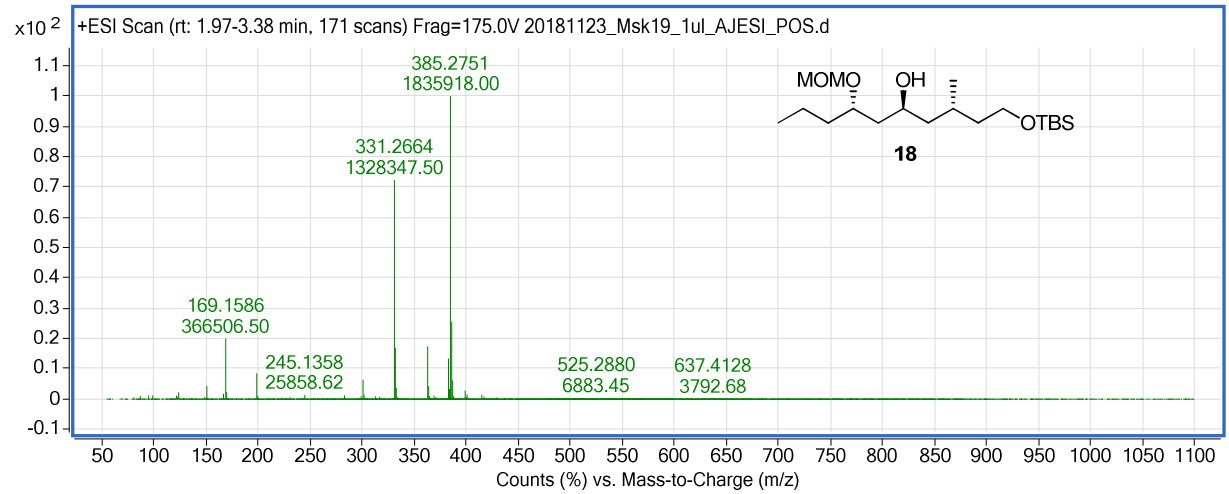


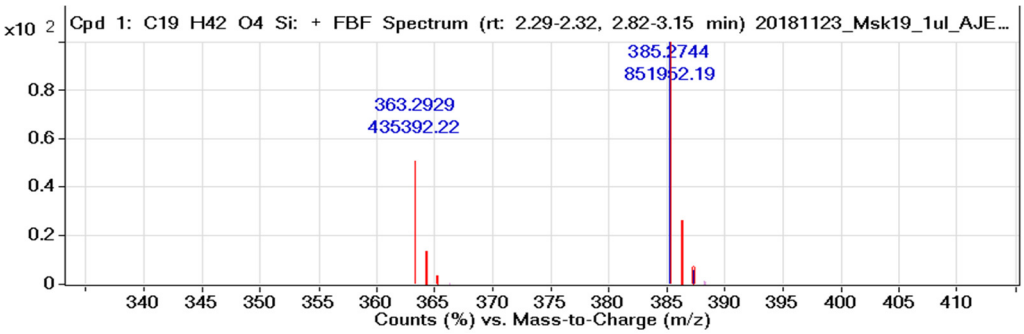
HRMS of compound 12



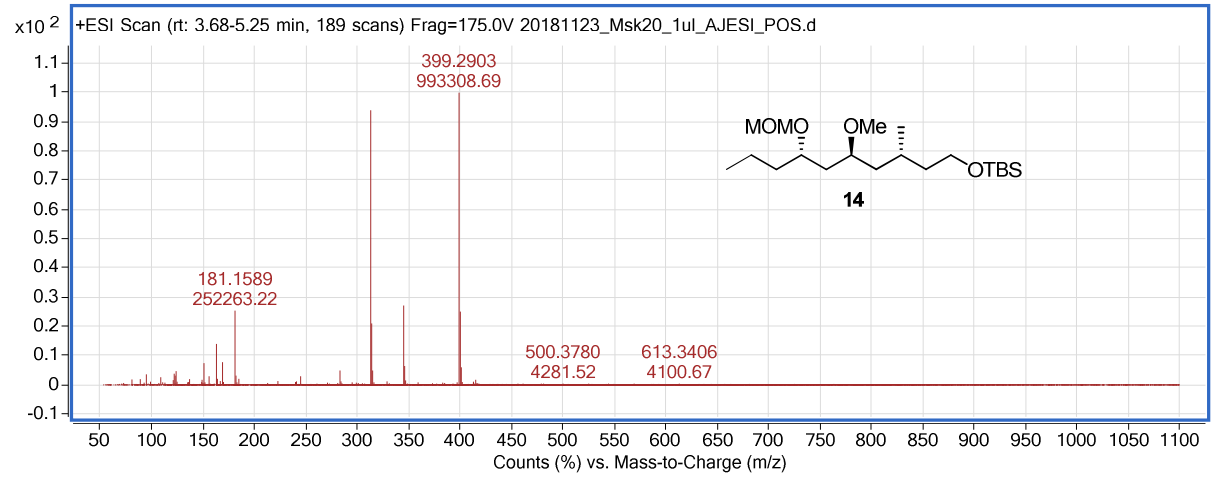


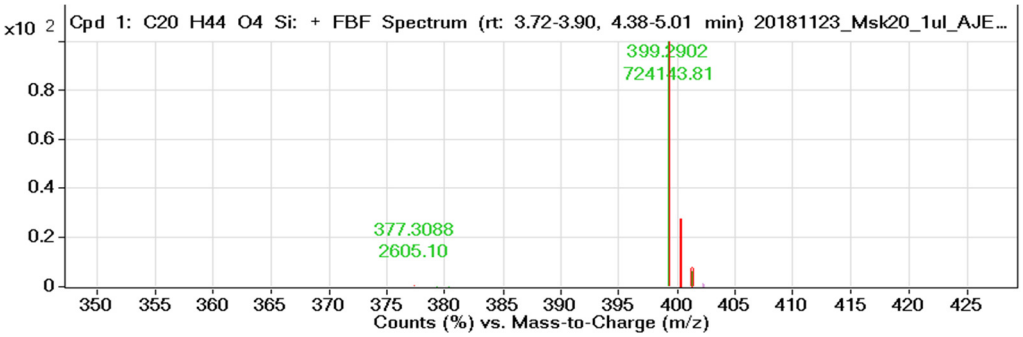
HRMS of compound 18



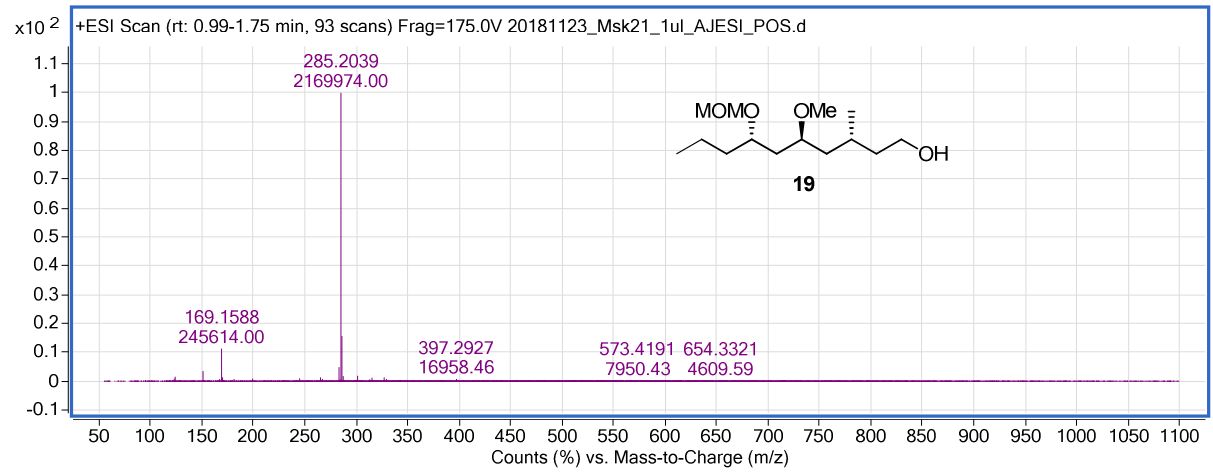


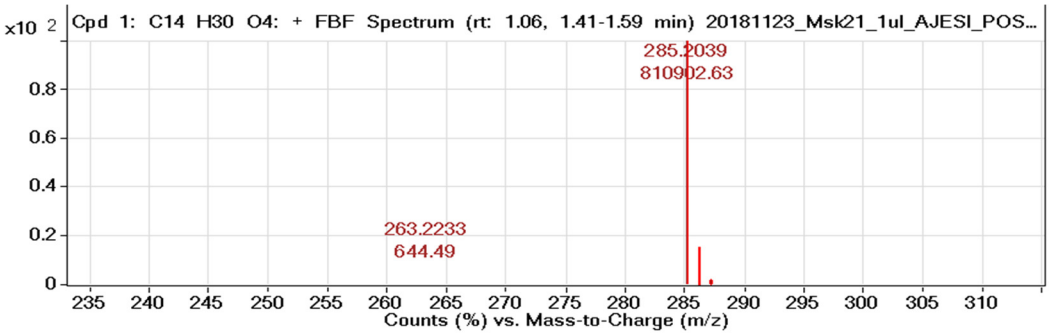
HRMS of compound 14



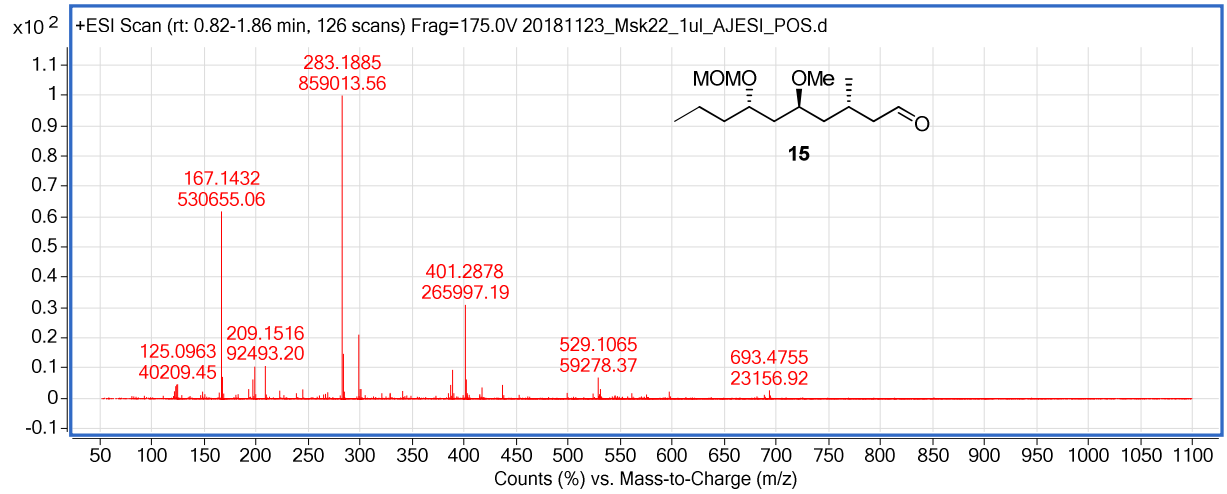


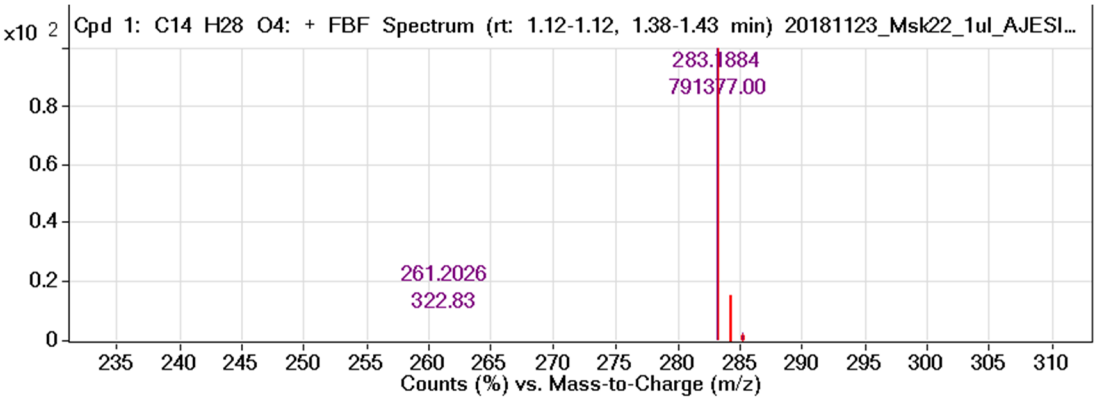
HRMS of compound 19





HRMS of compound 15





HRMS of compound 13