

Cross metathesis of (-)- β -pinene, (-)-limonene and terpenoids derived from limonene with internal olefins

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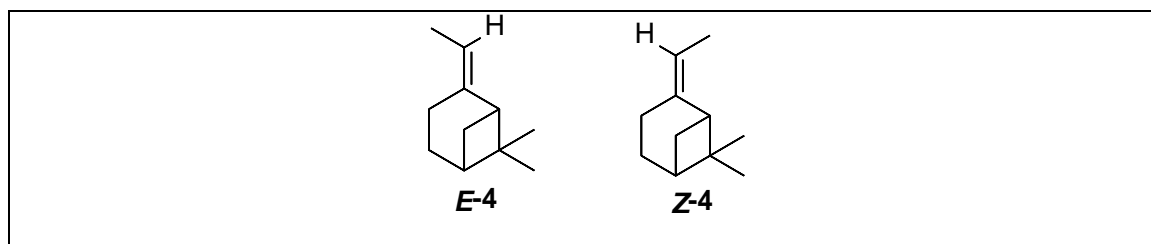
1. General information

All reactions were carried out with exclusion of air using Schlenk tube techniques. DMC was distilled and stored over activated 3 Å molecular sieves. NMR spectra were recorded at 400 MHz for ^1H and 100 MHz for ^{13}C on a Bruker Ascend - Av III spectrometer. Chemical shifts are given in ppm vs TMS using the residual solvent signal as reference. Reactions were monitored using a Shimadzu 2014 gas chromatograph equipped with a 30 m x 0.25 mm x 0.25 μm Equity TM – 1 Fused Silica capillary column. Pure products were obtained by column chromatography on silica gel (Merck Silica Gel 60) or alumina using mixtures of heptane and ethyl acetate as the eluent. Products were further analyzed by GC-MS on a Shimadzu QP2010S apparatus.

The indexation of signals in ^1H and ^{13}C NMR were based on COSY, HSQC and HMBC sequences and NOESY (800 ms mixing time) for structure determination.

2. Product synthesis and characterization

- β -pinene/2-methylbut-2-ene cross metathesis product **4**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of β -pinene was added in 1 mL of 2-methylbut-2-ene (neat reaction). **Ru2** catalyst (0.018 mmol, 11.5 mg, 2.5 mol%) was then added and the reaction mixture was stirred at 40 °C for 15 h. After this time, another 1 mol% of catalyst (5 mg) was added and the reaction stirred for an additional 8 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by filtration with pentane, which was later evaporated by simple distillation to give 61 mg of **4** as colorless oil (56% isolated yield).

The determination of configuration of the major isomer (*E*) was made by 1D gradient selective NOESY (800 ms mixing time) (see spectra section). The accurate chemical shifts of protons was determined using HSQC and 1D selective TOCSY sequences.

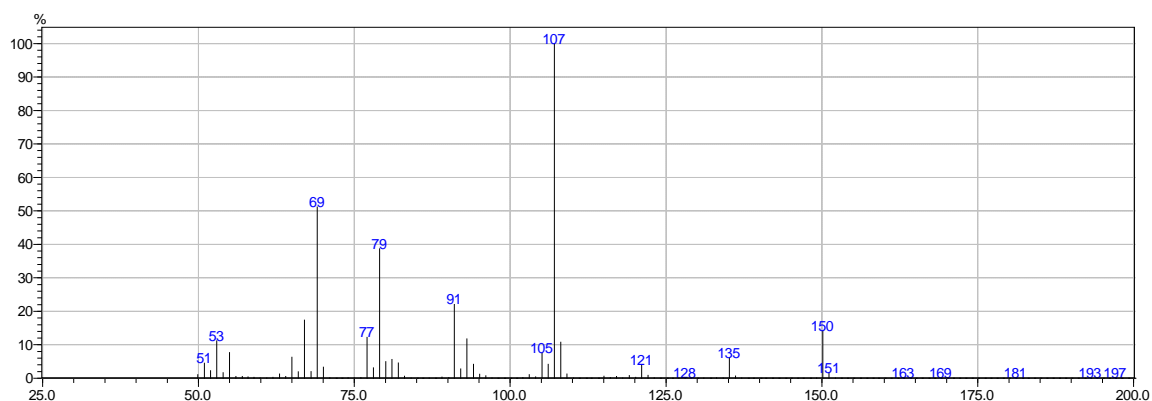
¹H NMR (400 MHz, CDCl₃) δ ppm:

Major (*E*) isomer: 0.70 (s, 3H, C(9)H₃); 1.21 (s, 3H, C(8)H₃); 1.31 (d, ¹J= 8.7 Hz, 1H, C(7a)HH); 1.55 (d, 3H, J= 6.7 Hz, C(11)H₃); 1.82-1.90 (m, 2H, C(4)H₂); 1.93-2.02 (m, 1H, C(5)H); 2.28-2.39 (m, 4H, C(3a)HH)+ C(1)H+ C(7a)HH)+ C(3s)HH); 5.00-5.08 (m, 1H, C(10)H).

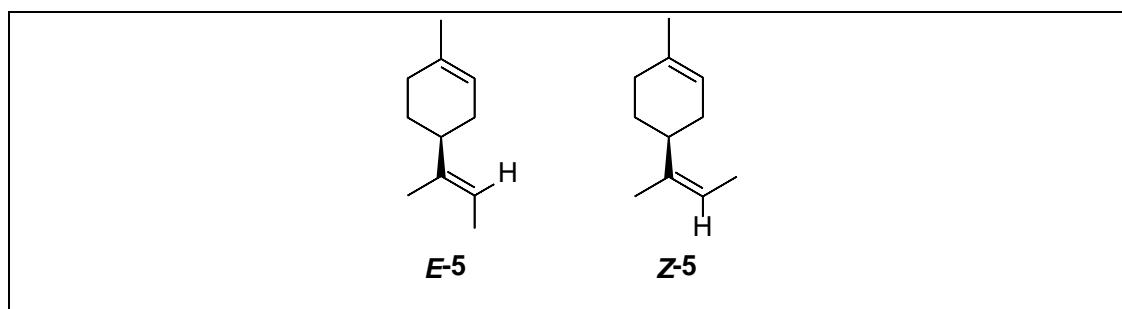
¹³C NMR (100 MHz, CDCl₃) δ ppm:

Major (*E*) isomer: 12.7 (C(11)); 19.7 (C(3)); 22.2 (C(9)); 23.9 (C(4)); 26.2 (C(8)); 28.2 (C(7)); 40.8 (C(6)); 41.1 (C(5)); 52.7 (C(1)); 115.3 (C(10)); 143.1 (C(2)).

MS spectra – m/z th = 150



- (-)-limonene / 2-methylbut-2-ene cross metathesis product **5**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of limonene was added to 1 mL of 2-methylbut-2-ene (neat reaction). **Ru2** catalyst (0.018 mmol, 11.5 mg, 2.5 mol%) was then added and the reaction mixture was stirred at 40 °C for 15 h. After this time, another 2.5 mol% of catalyst was added and the reaction stirred for an additional 8 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by filtration with pentane, which was later evaporated by simple distillation to give 66 mg of **5** as colorless oil (60% isolated yield).

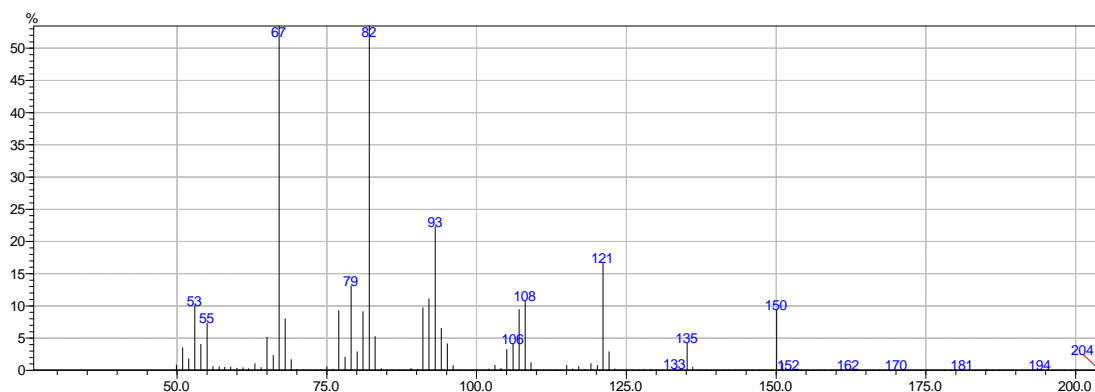
¹H NMR (400 MHz, CDCl₃) δ ppm

Major (E) isomer: 1.41-1.55 (m, 1H, C(5)HH); 1.58 (d, 3H, J= 5.8 Hz, C(11)H₃); 1.59 (s, 3H, C(10)H₃), 1.65 (broad s, 3H, C(7)H₃); 1.67-1.76 (m, 1H, C(5)HH); 1.84-2.14 (m, 5H, C(6)H₂, C(3)H₂, C(4)H); 5.20-5.29 (m, 1H, C(9)H); 5.37-5.44 (m, 1H, C(2)H).

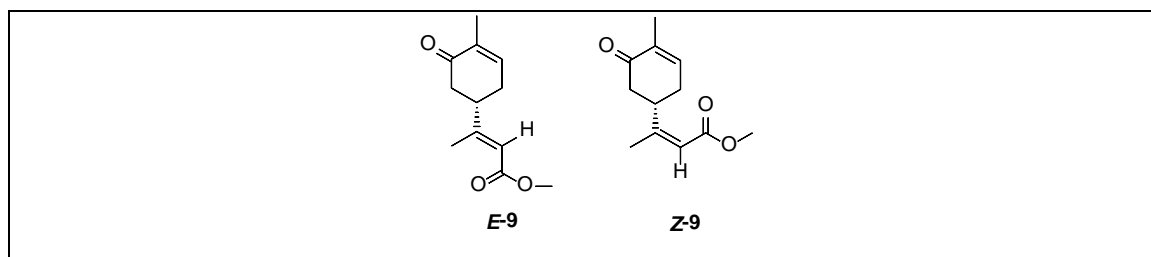
¹³C NMR (100 MHz, CDCl₃) δ ppm:

(E) isomer: 13.4 (C(11)); 13.9 (C(10)); 23.6 (C(7)); 28.1 (C(5)); 30.9 (C(3) and C(6)); 43.0 (C(4)); 116.9 (C(9)); 121.1 (C(2)); 133.8 (C(1)); 140.3 (C(8)).

MS spectra – m/z th = 150



- (+)-carvone / dimethyl maleate cross metathesis product **9**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of (+)-Carvone and 380 μ L of dimethyl maleate (2.8 mmol) were dissolved in 1 mL of distilled dimethyl carbonate (with tetradecane as internal standard), **Ru2** catalyst (0.037 mmol, 23 mg, 5 mol%) was then added and the reaction mixture was stirred at 100 °C for 15 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by column chromatography on silica gel (1.5 cm x 12 cm) using a mixture of heptane/diethyl ether (98:2) as eluent to give 52 mg of **9** as colorless oil (37% isolated yield).

¹H NMR (400 MHz, CDCl₃) δ ppm:

Major isomer (E)-isomer: 1.75-1.81 (m, 3H, C(7)H₃); 2.17 (s, 3H, C(10)H₃); 2.27-2.49 (m, 3H, C(5)H and C(3)H₂), 2.51-2.61 (m, 1H, C(5)H), 2.73-2.85 (m, 1H, C(4)H); 3.69 (s, 3H, C(12)H₃); 5.68-5.73 (m, 1H, C(9)H); 6.71-6.77 (m, 1H, C(2)H).

Minor isomer (Z)-isomer: 1.75-1.81 (m, 3H, C(7)H₃); 1.87 (s, 3H, C(10)H₃); 2.27-2.49 (m, 3H, C(5)H and C(3)H₂); 2.51-2.61 (m, 1H, C(5)H), 4.35-4.48 (m, 1H, C(4)H); 3.66 (s, 3H, C(12)H₃); 5.68-5.73 (m, 1H, C(9)H); 6.71-6.77 (m, 1H, C(2)H).

¹H NMR (400 MHz, CDCl₃) δ ppm:

Major isomer (E): 1.32 (broad s, 3H, C(7)H₃); 1.28-1.40; 1.41-1.54; 1.64-1.81; 1.89-2.12 (m, 7H, C(5)H₂,C(6)H₂,C(3)H₂,C(4)H); 2.09 (d, 3H, J= 1.2 Hz, C(10)H₃); 2.97-3.03 (m, 1H, C(2)H); 3.67 (s, 3H, C(12)H₃); 5.65 (s, 1H, C(9)H).

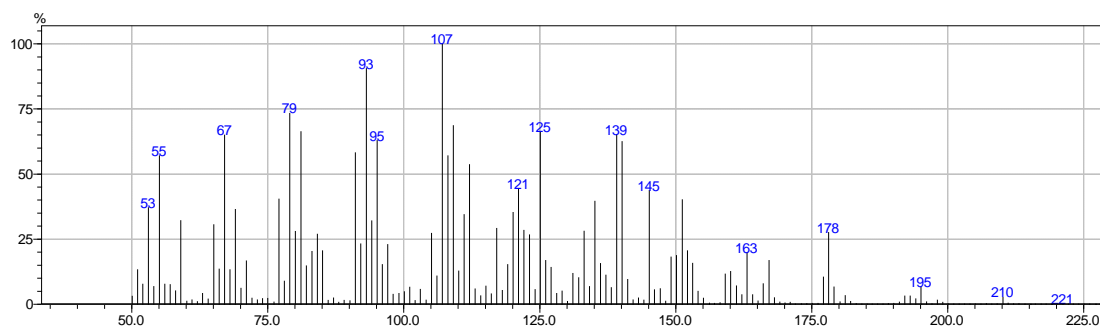
Minor isomer (Z): 1.31 (broad s, 3H, C(7)H₃); 1.28-1.40; 1.41-1.54; 1.64-1.81; 1.89-2.12 (m, 7H, C(5)H₂,C(6)H₂,C(3)H₂,C(4)H); 1.77 (d, 3H, J= 1.4 Hz, C(10)H₃); 2.97-3.03 (m, 1H, C(2)H); 3.66 (s, 3H, C(12)H₃); 5.61 (s, 1H, C(9)H).

¹³C NMR (100 MHz, CDCl₃) δ ppm:

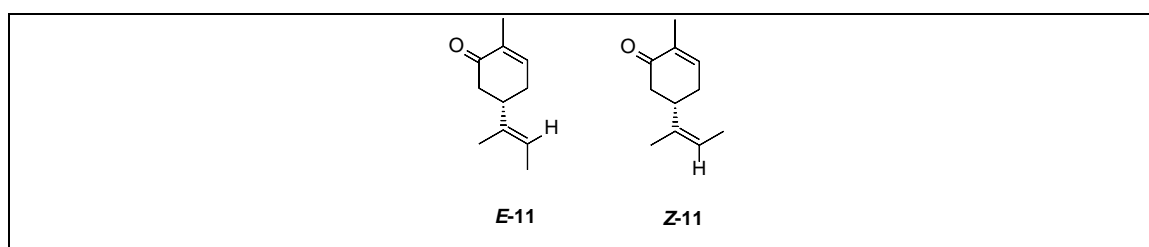
Major isomer (E): 16.7 (C(10)); 23.1 (C(7)); 23.9, 29.4, 30.6 (C(3),C(5),C(6)); 43.9 (C(4)); 51.0 (C(12)); 57.5 (C(1)); 58.8 (C(2)); 114.7 (C(9)); 163.1 (C(8)); 167.4 (C(11)).

Minor isomer (Z): 20.5 (C(10)); 23.1 (C(7)); 23.9, 29.4, 30.6 (C(3),C(5),C(6)); 43.9 (C(4)); 50.9 (C(12)); 57.5 (C(1)); 59.2 (C(2)); 115.9 (C(9)); 163.1 (C(8)); 167.4 (C(11)).

MS spectra – m/z th = 210



- **(+)-carvone / 2-methylbut-2-ene cross metathesis product 11**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of (+)-carvone was added in 1 mL of 2-methylbut-2-ene (neat reaction). **Ru2** catalyst (0.018 mmol, 11.5 mg, 2.5 mol%) was then added and the reaction mixture was stirred at 40 °C for 15 h. After this time, another 1% of catalyst (5 mg) was added for an additional 8 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by filtration with heptane,

which was later evaporated in the vacuum line to give 79 mg of **11** as colorless oil (73% isolated yield).

^1H NMR (400 MHz, CDCl_3) δ ppm

Major (*E*) isomer: 1.56 (d, 3H, $J = 6.6$ Hz, $\text{C}(11)\text{H}_3$), 1.58 (broad s, 3H, $\text{C}(10)\text{H}_3$); 1.75 (broad s, 3H, $\text{C}(7)\text{H}_3$); 2.18-2.37 (m, 3H, $\text{C}(3)\text{H}_2$, $\text{C}(5)\text{HH}$); 2.48 (ddd, 1H, $J = 16.0, 3.7, 1.2$ Hz, $\text{C}(5)\text{HH}$); 2.55-2.68 (m, 1H, $\text{C}(4)\text{H}$); 5.26 (q, 1H, $J = 6.6$ Hz, $\text{C}(9)\text{H}$); 6.67-6.77 (m, 1H, $\text{C}(2)\text{H}$).

^{13}C NMR (1005 MHz, CDCl_3) δ ppm

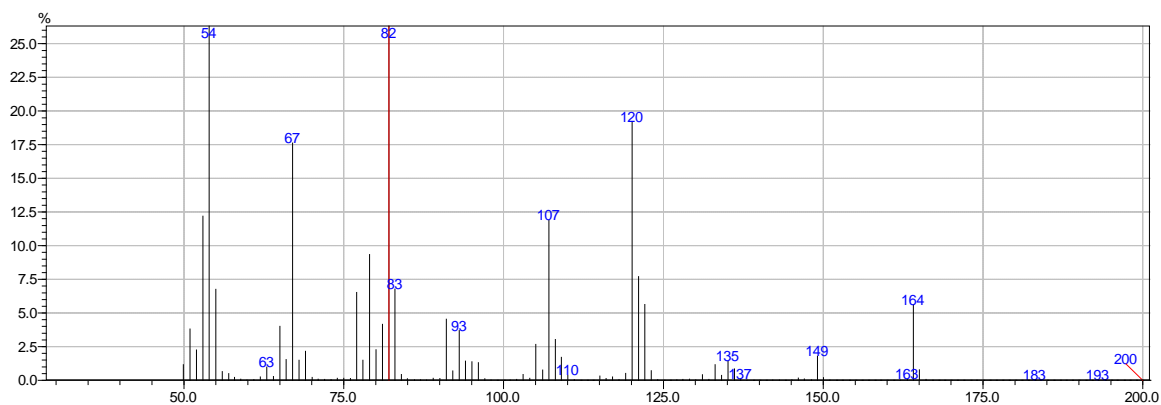
(*E*) isomer: 13.4 ($\text{C}(11)$); 13.7 ($\text{C}(10)$); 15.8 ($\text{C}(7)$); 31.5 ($\text{C}(3)$); 43.4 ($\text{C}(5)$); 44.41 ($\text{C}(4)$); 119.1 ($\text{C}(9)$); 135.3 ($\text{C}(1)$); 137.0 ($\text{C}(8)$); 145.0 ($\text{C}(2)$); 200.3 ($\text{C}(6)$).

Minor (*Z*)- isomer : only the $\text{C}(4)\text{-H}$ entity shows visible different chemical shifts

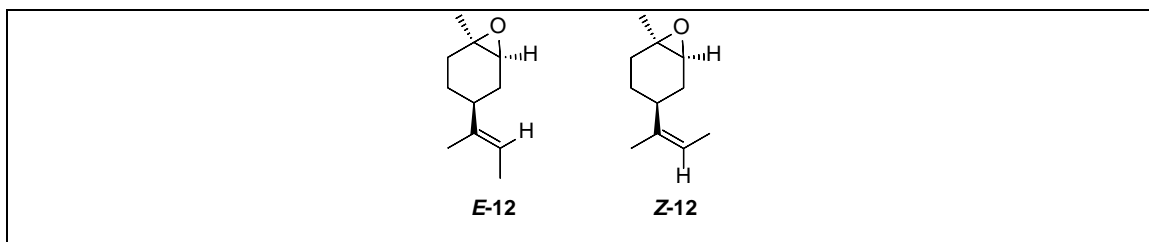
^1H NMR (400 MHz, CDCl_3) δ ppm: 3.15-3.28 (m, 1H, $\text{C}(4)\text{-H}$)

^{13}C NMR (75.5 MHz, CDCl_3) δ ppm: 36.5 ($\text{C}(4)$)

MS spectra – m/z th = 164



- (+)-*trans*-limonene epoxide / 2-methylbut-2-ene cross metathesis product **12**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of (+)-*trans*-limonene epoxide was added in 1 mL of 2-methylbut-2-ene (neat reaction). **Ru2** catalyst (0.018 mmol, 11.5 mg, 2.5 mol%) was then added and the reaction mixture was stirred at 40 °C for 15 h. After this time, another 2.5% of catalyst was added and the reaction stirred for an additional 8 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by filtration with heptane, which was later evaporated in the vacuum line to give 37 mg of **12** as colorless oil (34% isolated yield).

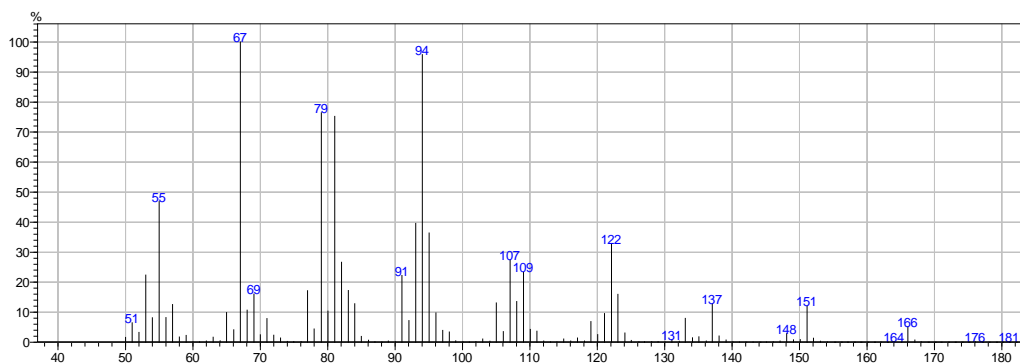
¹H NMR (400 MHz, CDCl₃) δ ppm:

Major isomer (E): 1.26-1.43 (m, 2H, C(5)H₂); 1.30 (s, 3H, C(7)H₃); 1.52 (s, 3H, C(10)H₃); 1.54 (d, J= 6.7 Hz, C(11)H₃); 1.60-1.75 (m, 2H, C(3)H₁, C(6)H₁); 1.78-2.07 (m, 3H, C(3)H₁, C(4)-H, C(6)H₁); 2.99 (d, 1H, J= 5.2 Hz, C(2)H); 5.19 (q, 1H, J= 6.5 Hz, C(9)H).

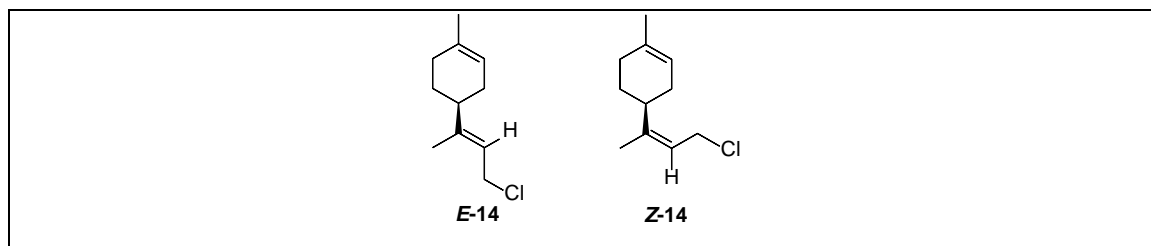
¹³C NMR (100 MHz, CDCl₃) δ ppm:

13.36 (C(10) and C(11)); 23.3 (C(7)); 24.5 (C(5)); 29.9 (C(6)); 31.0 (C(3)); 42.7 (C(4)); 57.7 (C(1)); 59.6 (C(2)); 117.6 (C(9)); 139.3 (C(8)).

MS spectra – m/z th = 166



- (-)-limonene / *cis*-1,4-dichlorobut-2-ene cross metathesis product **14**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of (-)-limonene and 163 μ L of *cis*-1,4-dichlorobut-2-ene (1.4 mmol) were dissolved in 1 mL of distilled dimethyl carbonate (with tetradecane as internal standard). **Ru2** catalyst (0.018 mmol, 11.5 mg, 2.5 mol%) was then added and the reaction mixture was stirred at 50 °C for 15 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by filtration with pentane, which was later evaporated by simple distillation to give 38 mg of **14** as colorless oil (28% isolated yield).

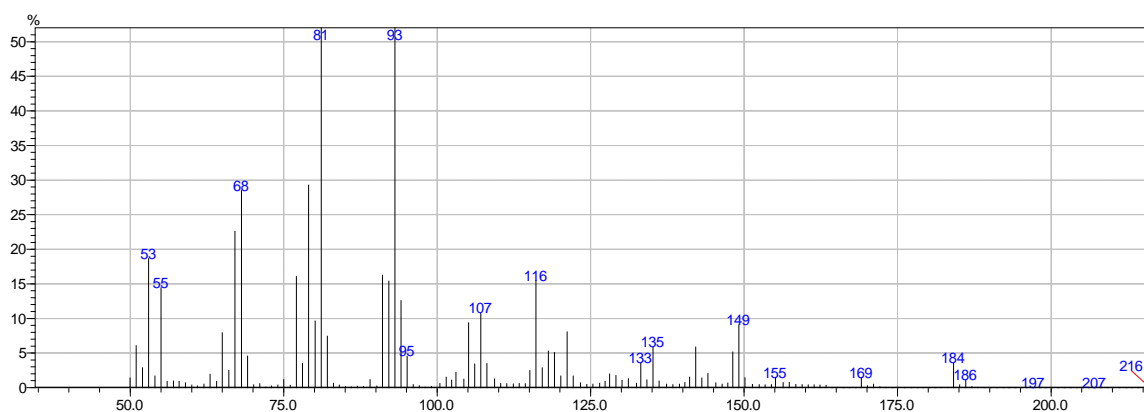
¹H NMR (400 MHz, CDCl₃) δ ppm

Major (E) isomer: 1.42-1.60 (m, 1H, C(5)HH); 1.65 (broad s, 3H, C(7)H₃); 1.72 (s, 3H, C(10)H₃); 1.68-1.80 (m, 1H, C(5)HH); 1.84-2.22 (m, 5H, C(6)H₂, C(3)H₂, C(4)H) ; 4.12 (d, 2H, *J*= 7.9 Hz, C(11)H₂); 5.34-5.43 (m, 1H, C(2)H); 5.43-5.54 (m, 1H, C(9)H).

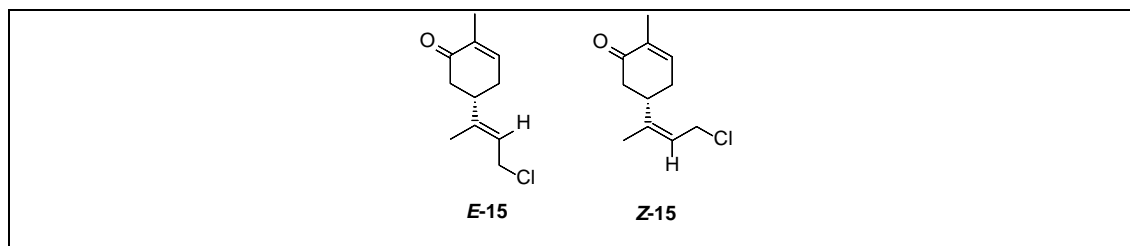
¹³C NMR (100 MHz, CDCl₃) δ ppm:

(*E*) isomer: 14.4 (C(10)); 23.6 (C(7)); 27.6 (C(5)); 30.5 and 30.6 (C(3) and C(6)); 41.4 (C(11)); 42.8 (C(4)); 119.1 (C(9)); 120.5 (C(2)); 134.0 (C(1)); 147.1 (C(8)).

MS spectra – m/z th = 184



- (+)-carvone / *cis*-1,4-dichlorobut-2-ene cross metathesis product **15**



In a Schlenk tube under argon, 100 mg (0.7 mmol) of (+)-carvone and 163 μ L of *cis*-1,4-dichlorobut-2-ene (1.4 mmol) were dissolved in 1 mL of distilled dimethyl carbonate (with tetradecane as internal standard). **Ru2** catalyst (0.037 mmol, 23 mg, 5 mol%) was then added and the reaction mixture was stirred at 50 °C for 15 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by column chromatography on alumina (1.5 cm x 12 cm) using a heptane/diethyl ether (98:2) mixture as eluent to give 15 mg of **15** as colorless oil (12% isolated yield).

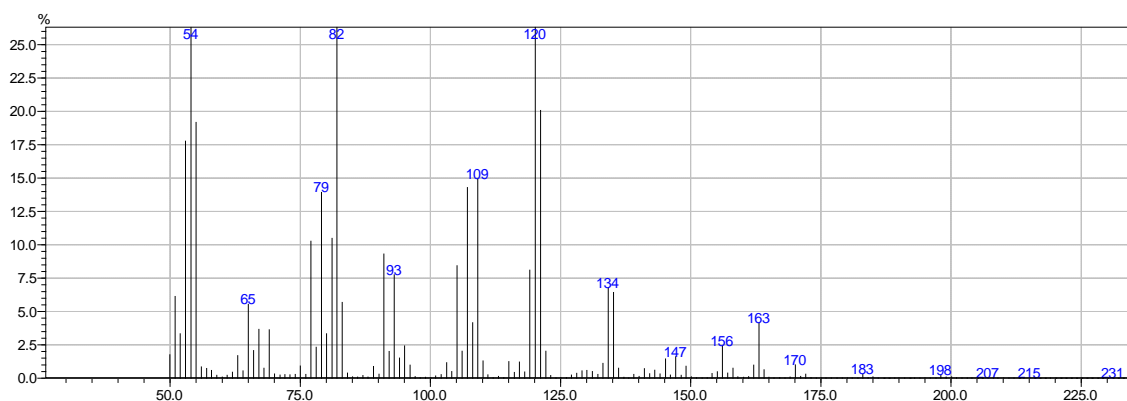
¹H NMR (400 MHz, CDCl₃) δ ppm

Major (E) isomer: 1.74 (broad s, 3H, C(10)H₃); 1.78 (broad s, 3H, C(7)H₃); 2.22-2.47 (m, 3H, C(3)HH, C(5)HH, C(3)HH); ; 2.50-2.60 (m, 1H, C(5)HH); 2.62-2.79 (m, 1H, C(4)H); 4.09 (d, 2H, J= 7.7 Hz, C(11)H₂); 5.50 (t, 1H, J= 7.4 Hz C(9)H); 6.71-6.79 (m, 1H, C(2)H).

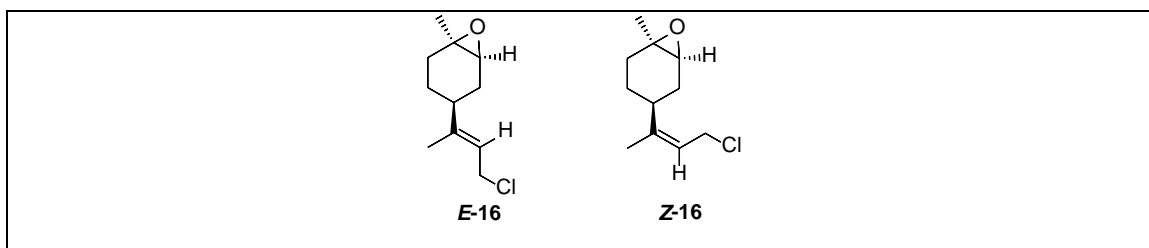
¹³C NMR (100 MHz, CDCl₃) δ ppm:

(E) isomer: 14.3 (C(10)); 15.8 (C(7)); 31.0 (C(3)); 40.6 (C(11)); 42.8 (C(5)); 44.1 C(4)); 121.1 (C(9)); 135.7 (C(1)); 143.2 (C(8)); 144.4 (C(2)); 199.3 (C(6)).

MS spectra – m/z th = 198



- (+)-*trans*-limonene epoxide / *cis*-1,4-dichlorobut-2-ene cross metathesis product
16



In a Schlenk tube under argon, 100 mg (0.7 mmol) of (+)-*trans*-limonene epoxide and 163 μ L of *cis*-1,4-dichlorobut-2-ene (1.4 mmol) were dissolved in 1 mL of distilled dimethyl carbonate (with tetradecane as internal standard). **Ru2** catalyst (0.037 mmol, 23 mg, 5 mol%) was then added and the reaction mixture was stirred at 50 °C for 15 h. A sample of the reaction mixture was taken and analyzed by gas chromatography. The product was purified by column chromatography on alumina (1.5 cm x 12 cm) using a heptane/diethyl ether (98:2) mixture as eluent to give 21 mg of **16** as colorless oil (15% isolated yield).

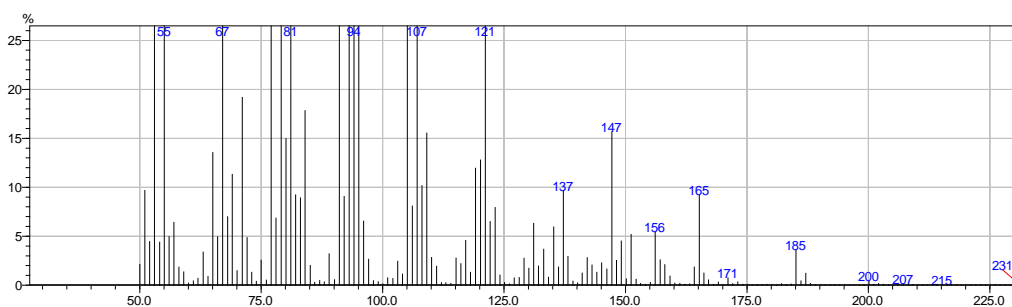
^1H NMR (400 MHz, CDCl_3) δ ppm:

Major isomer: (E) 1.32 (s, 3H, C(7)H₃); 1.15-1.48 (m, 2H, C(5)H₂); 1.66 (s, 3H, C(10)H₃); 1.67-1.73 (m, 2H, C(3)H, C(6)H); 1.84-2.08 (m, 3H, C(3)H, C(4)H, C(6)H); 2.99 (d, 1H, J= 5.1 Hz, C(2)H); 4.07 (d, 2H, J= 7.9 Hz, C(11)H₂); 5.43 (t, 1H, J= 7.9 Hz, C(9)H).

^{13}C NMR (100 MHz, CDCl_3) δ ppm: 13.8 (C(10)); 23.0 (C(7)); 23.9 (C(5)), 29.4 (C(3)), 30.6 C(6)); 40.9 (C(11)); 42.4 (C(4)); 57.5 (C(1)); 59.0 (C(2)); 119.7 (C(9)); 145.6 (C(8))*.

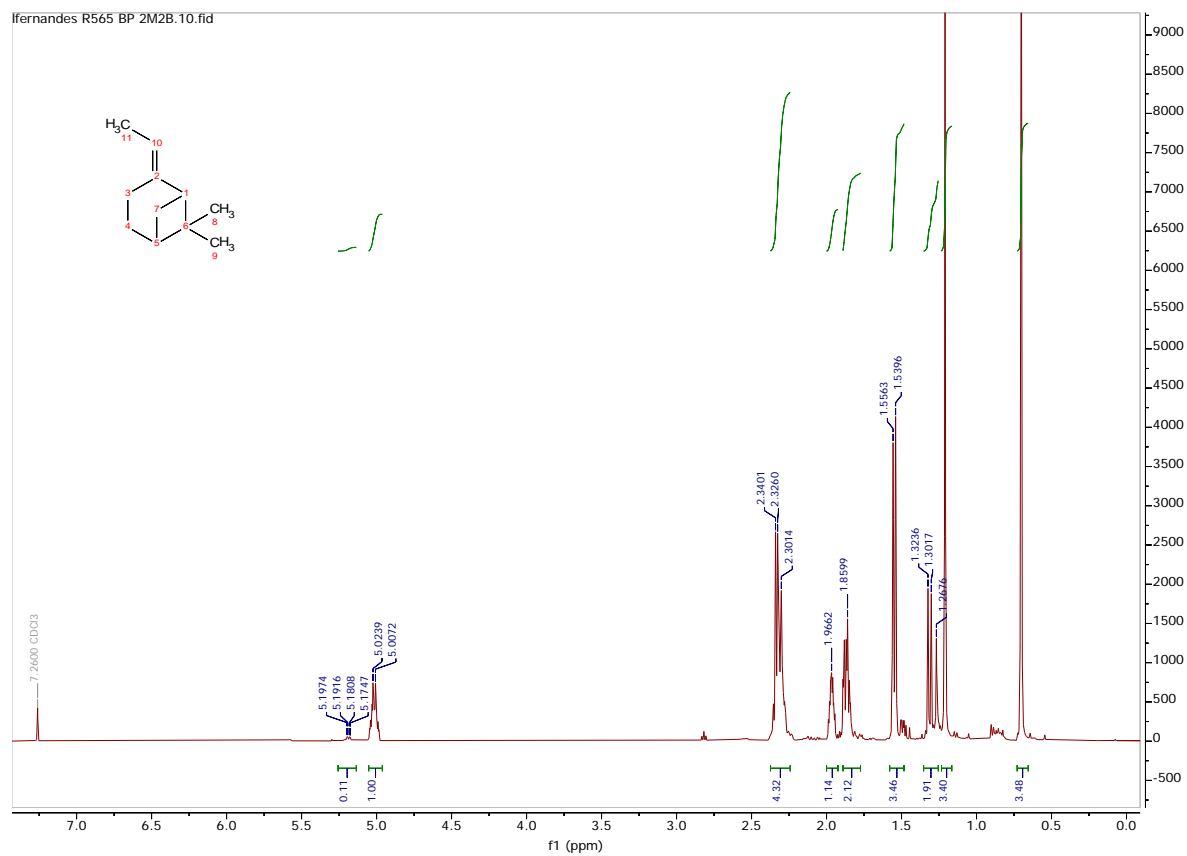
* This quaternary carbon was not detected under standard ^{13}C conditions due to long relaxation time. However, this quaternary carbon could be assigned thanks to HMBC experiment (see spectra section).

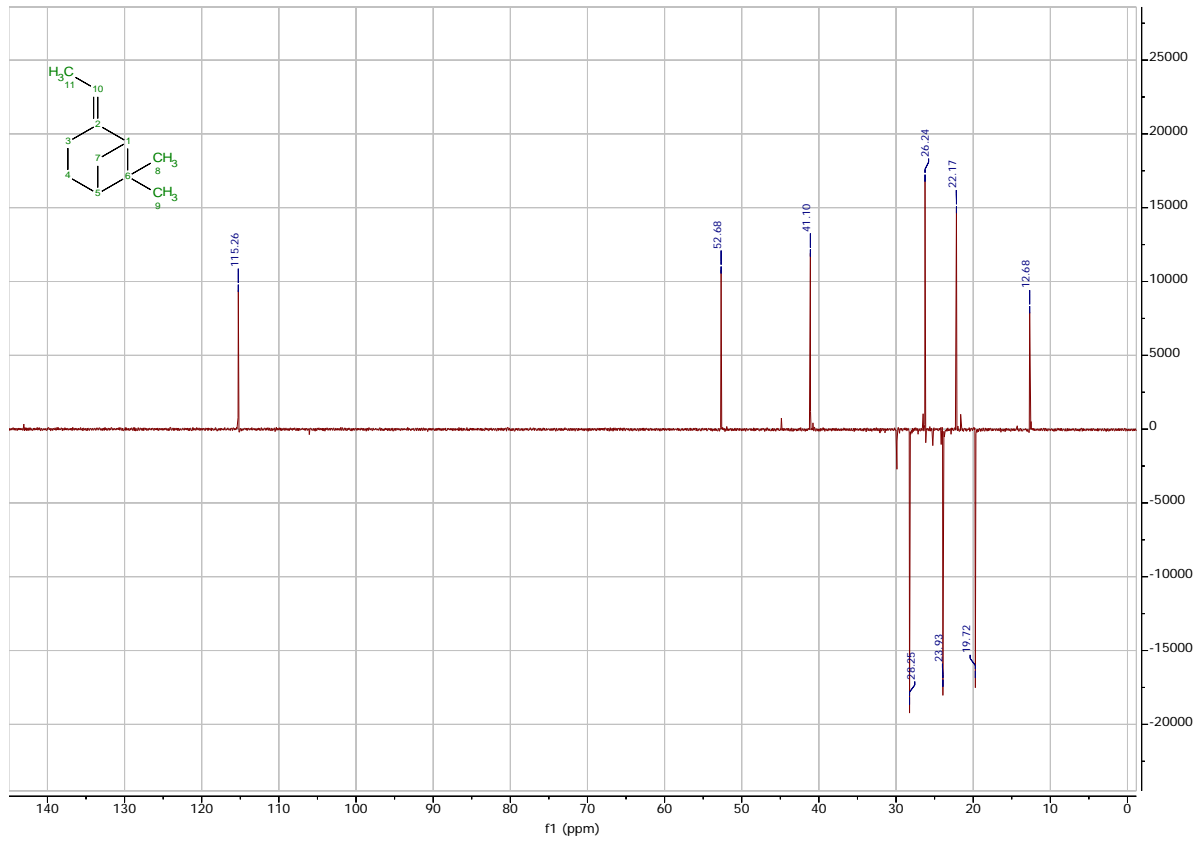
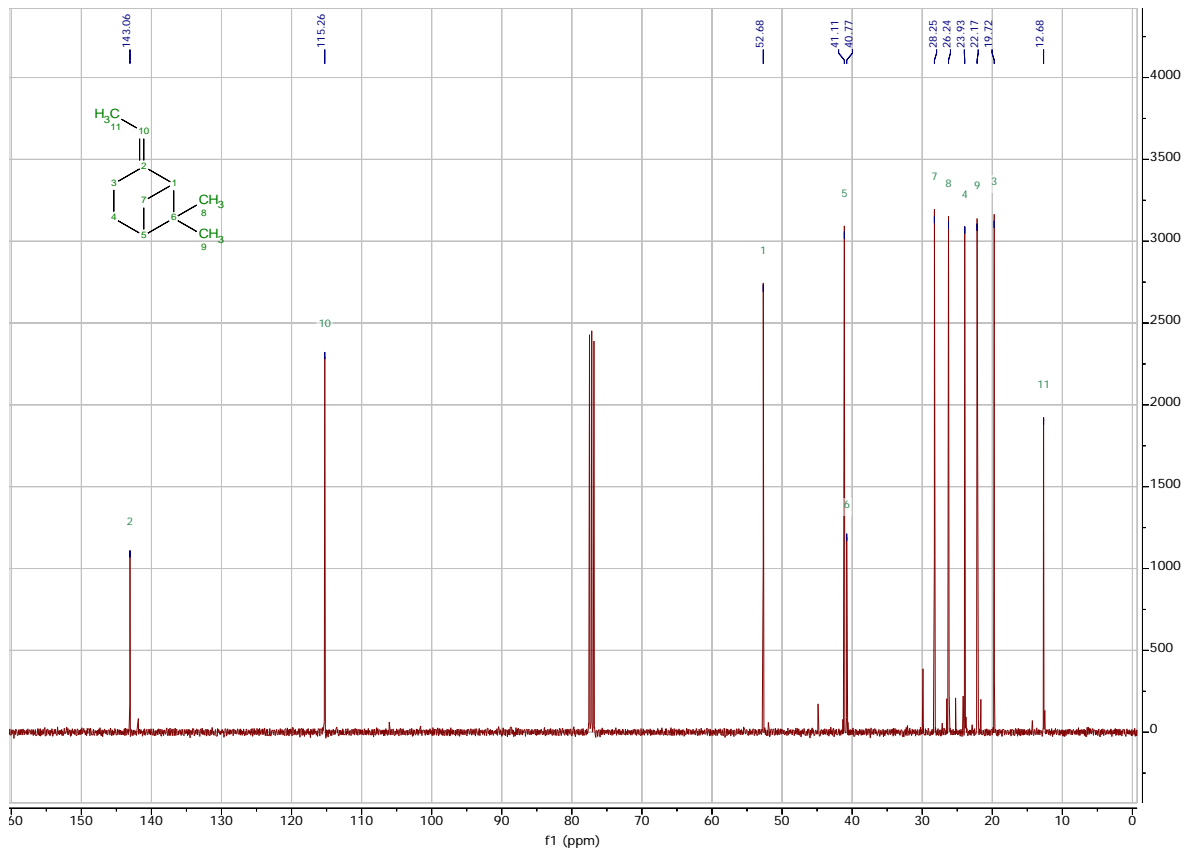
MS spectra – m/z th = 200

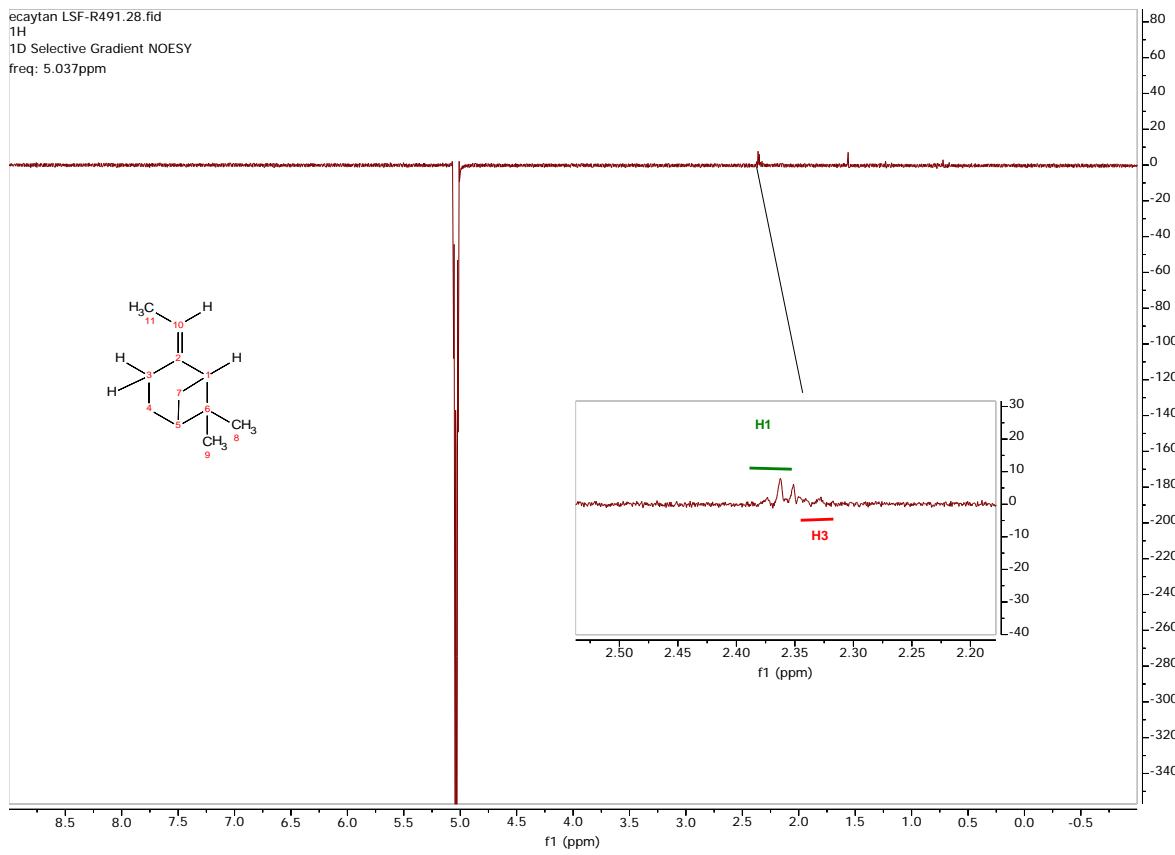
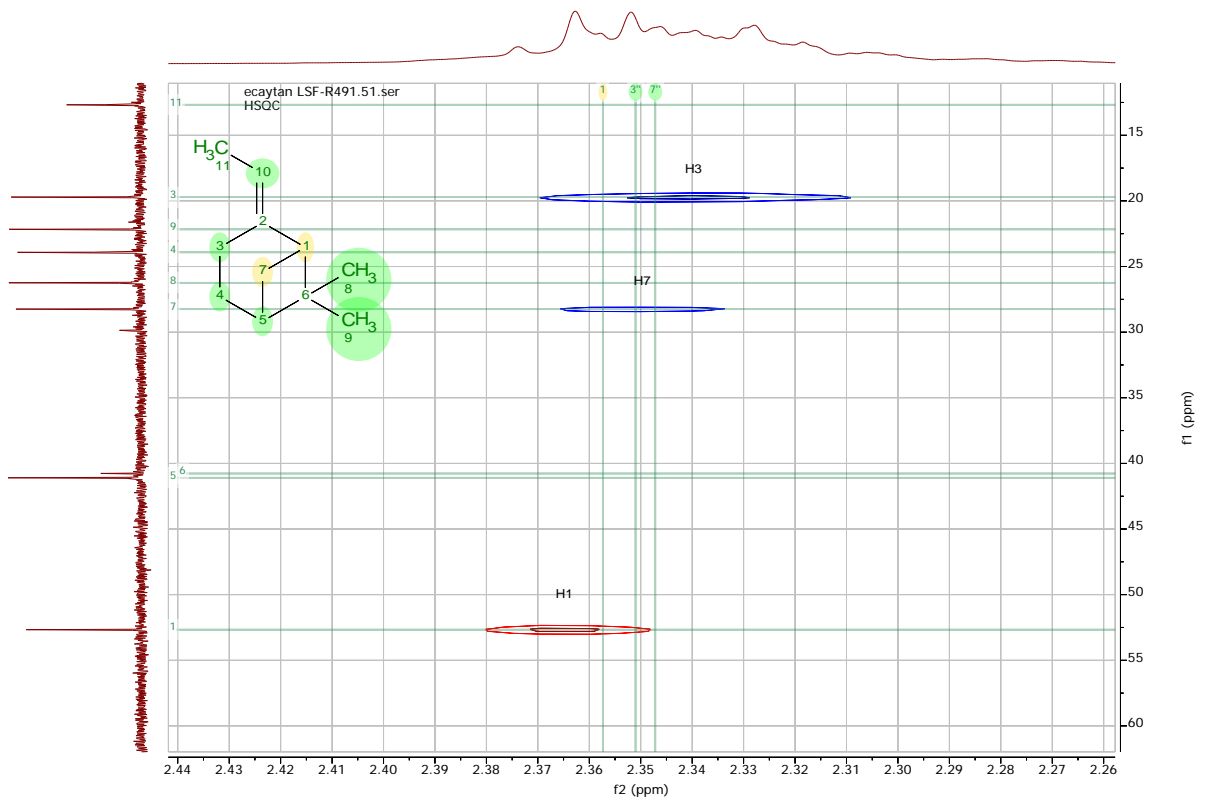


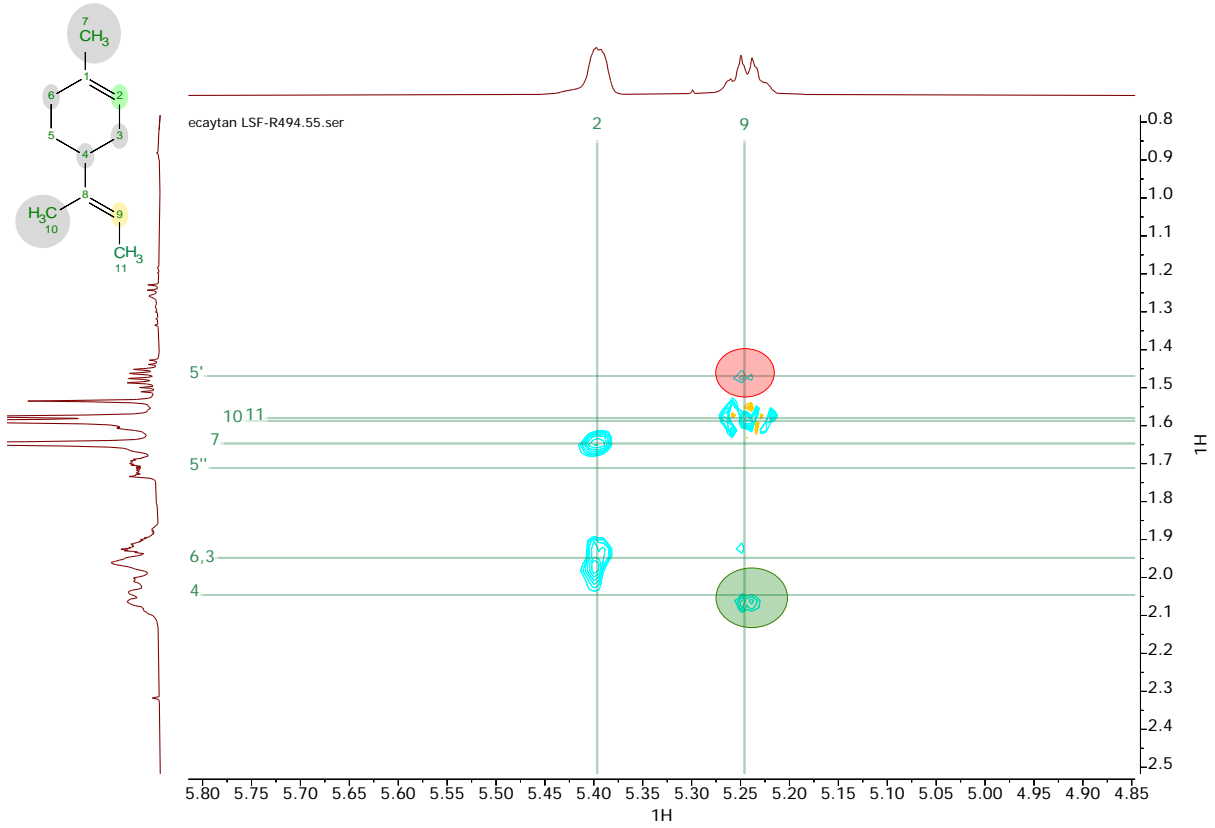
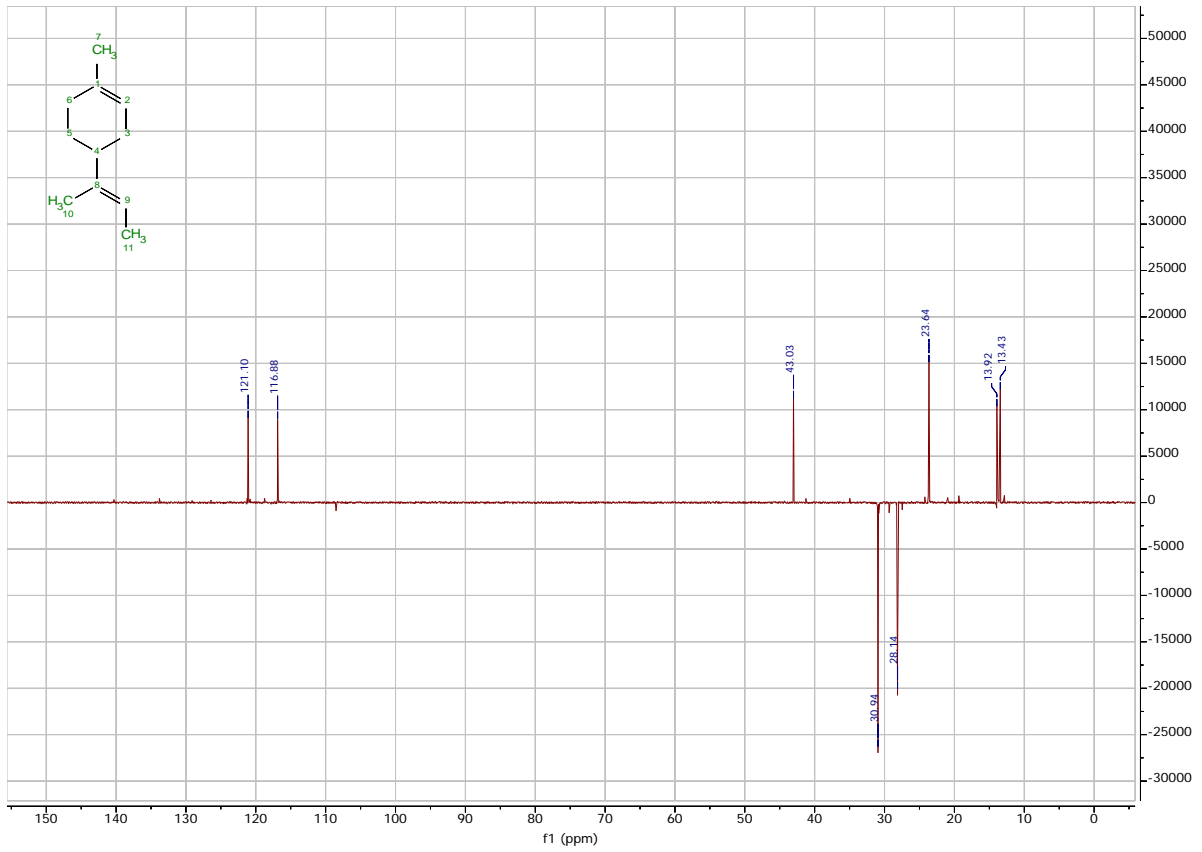
3. NMR spectra

Product 4

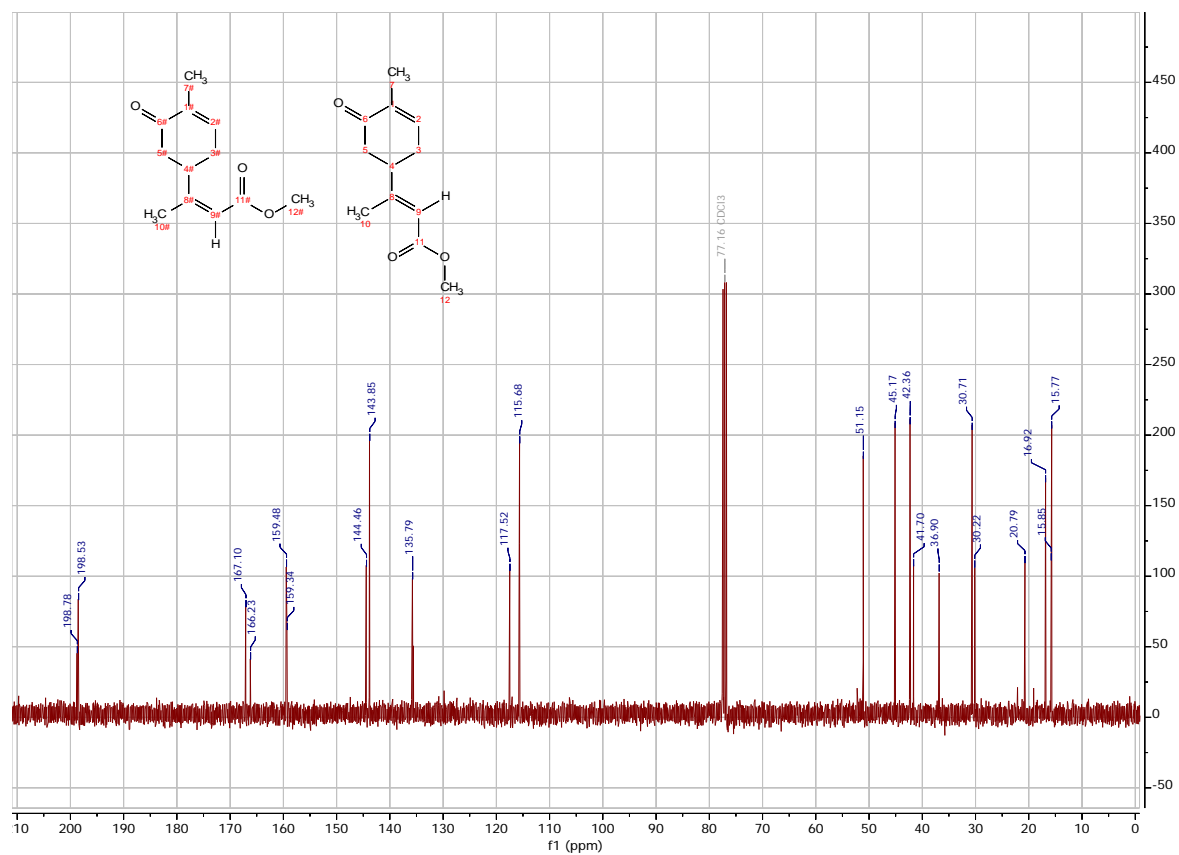
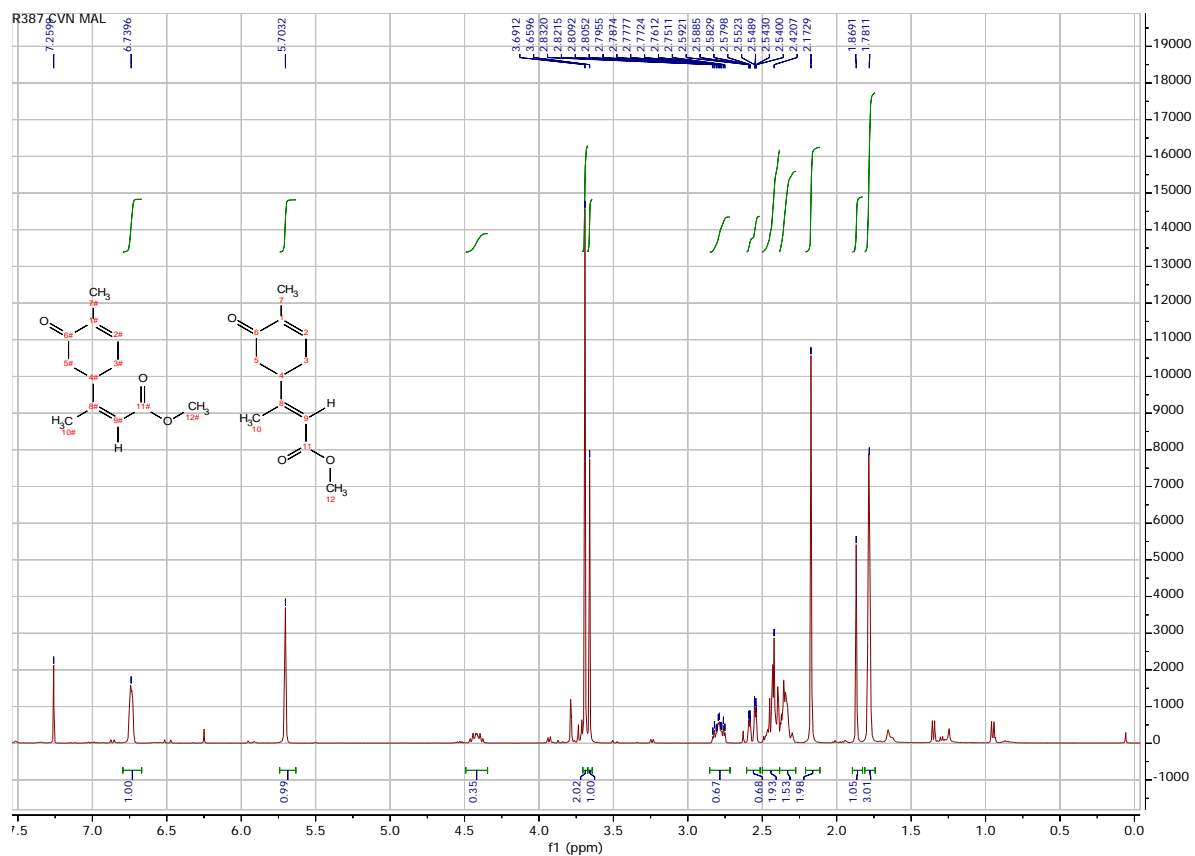


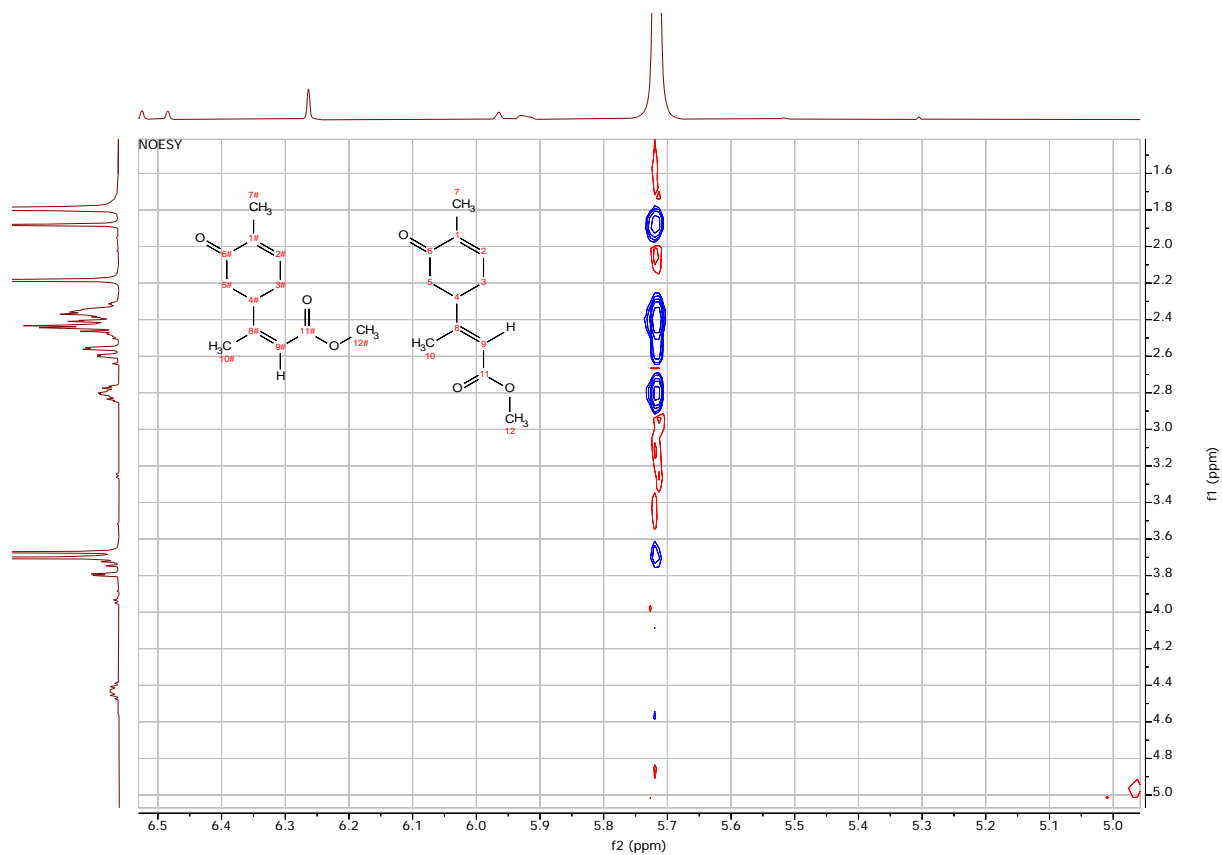




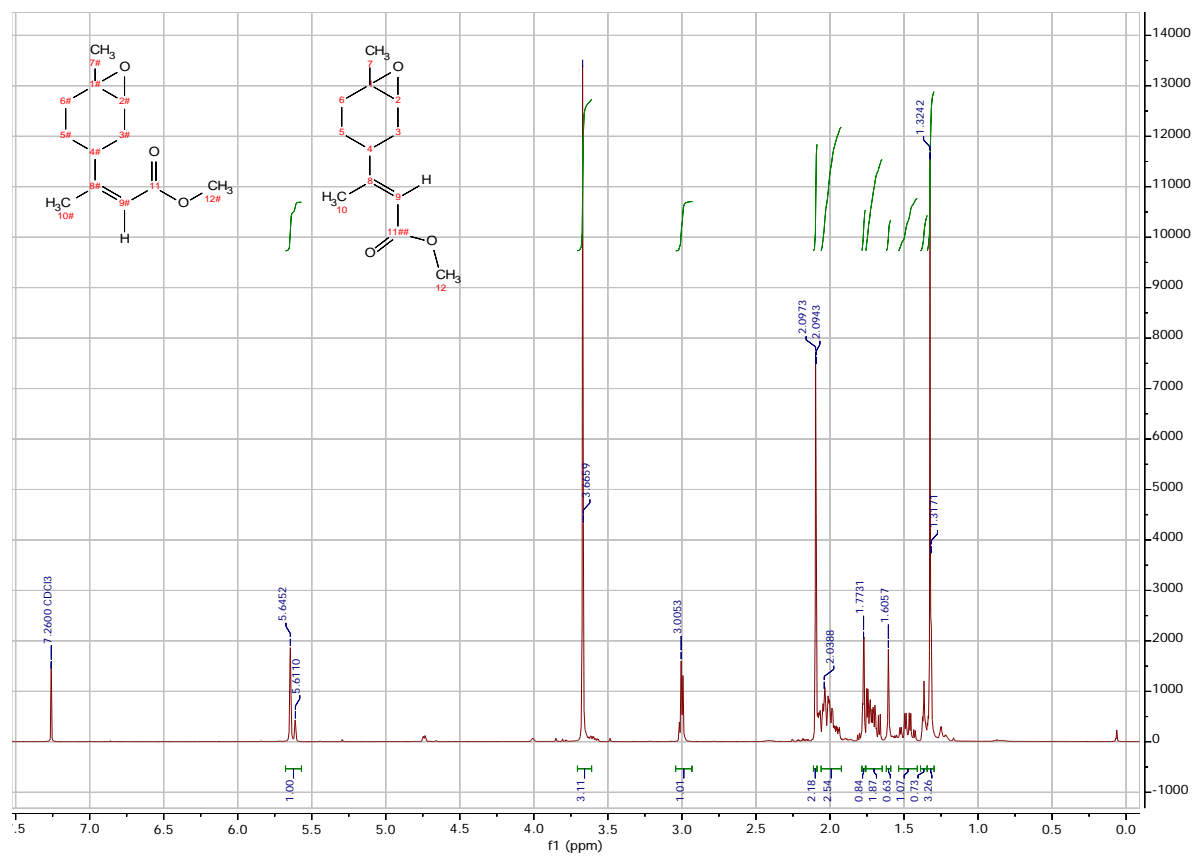


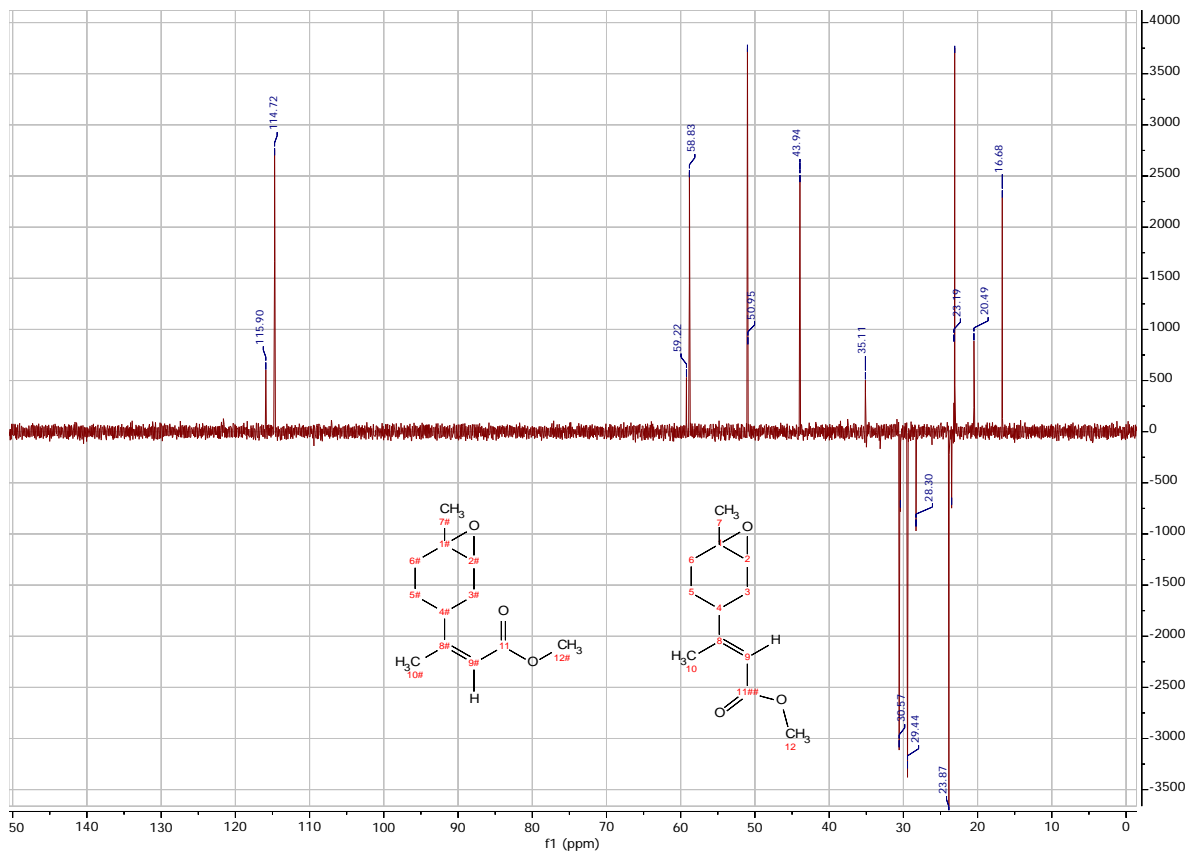
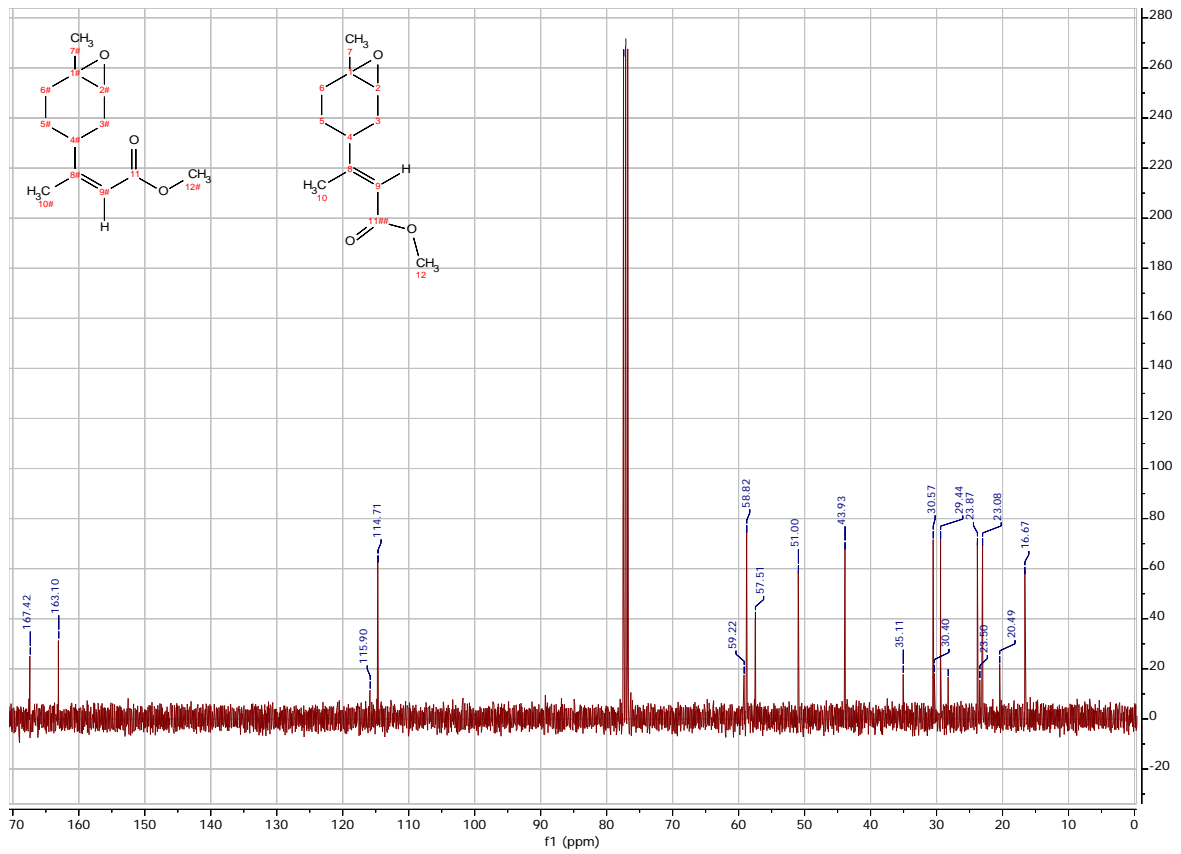
Product 9

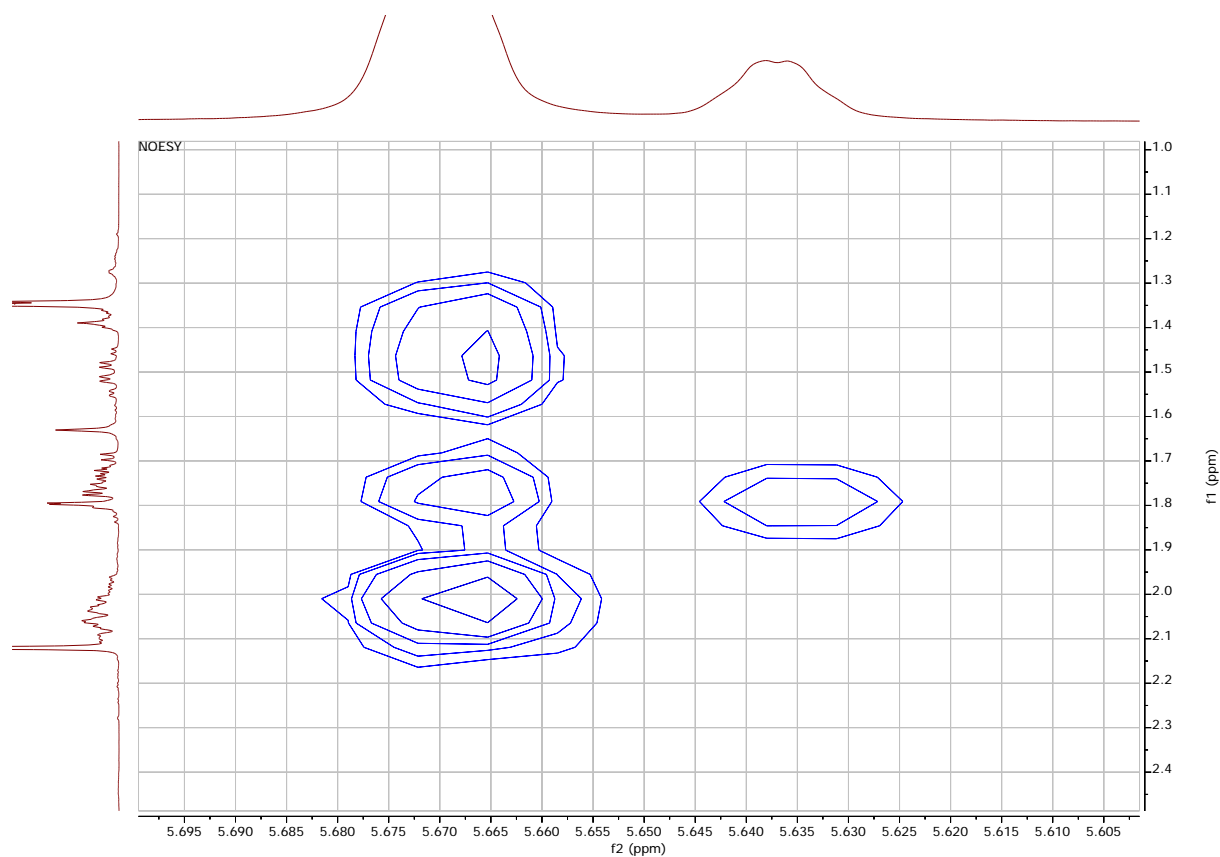




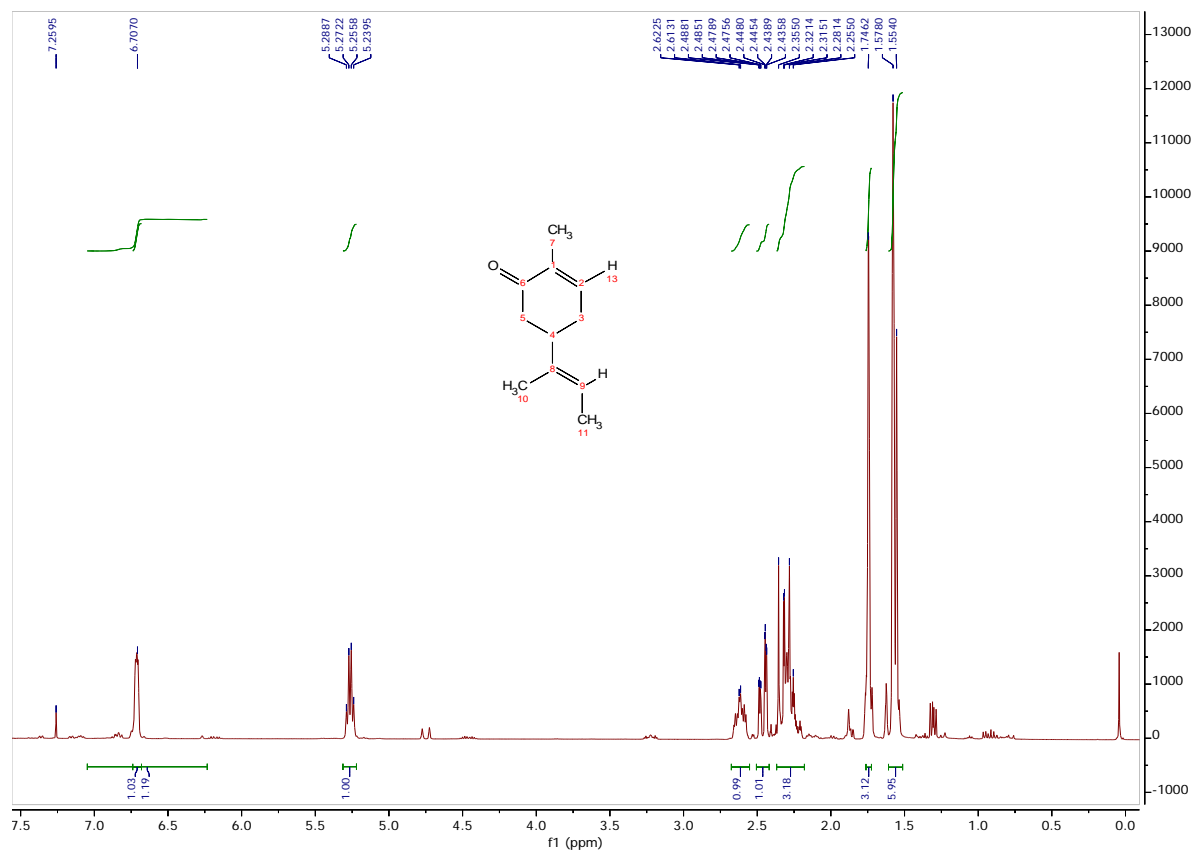
Product 10

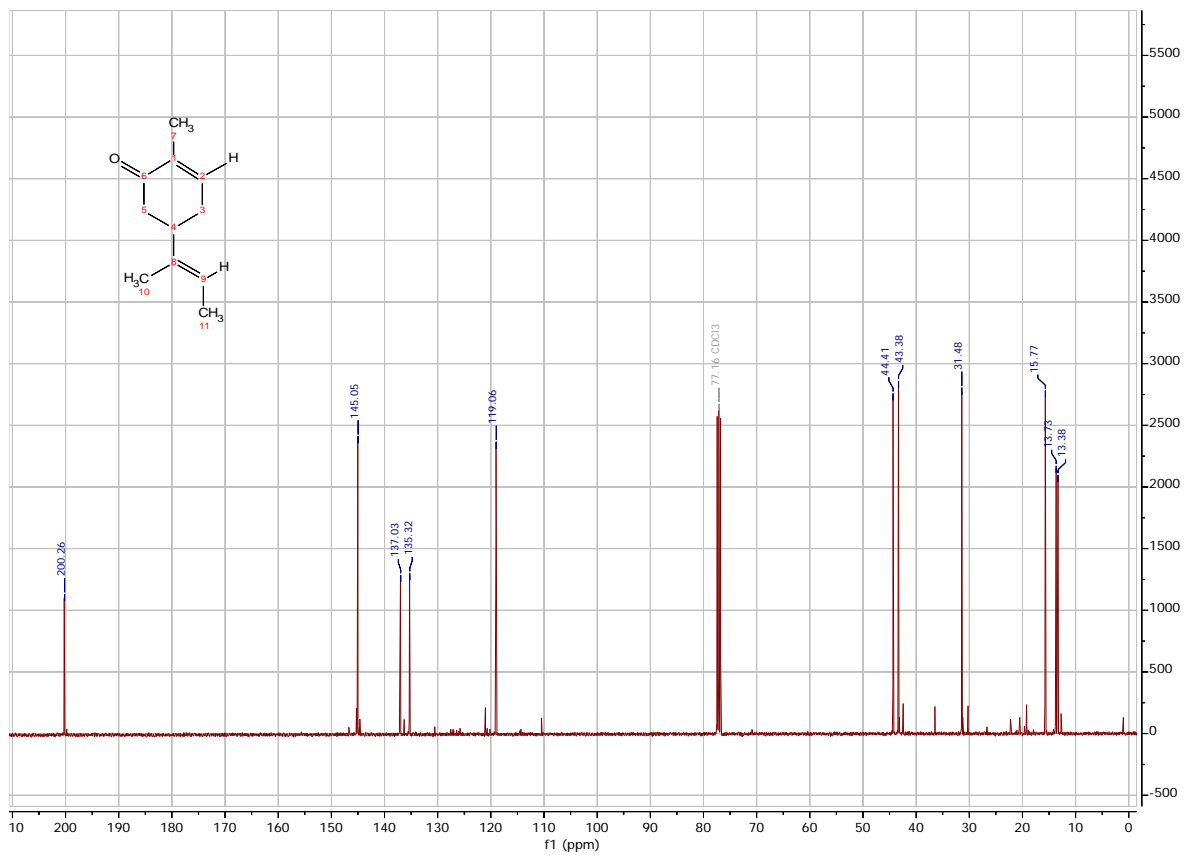
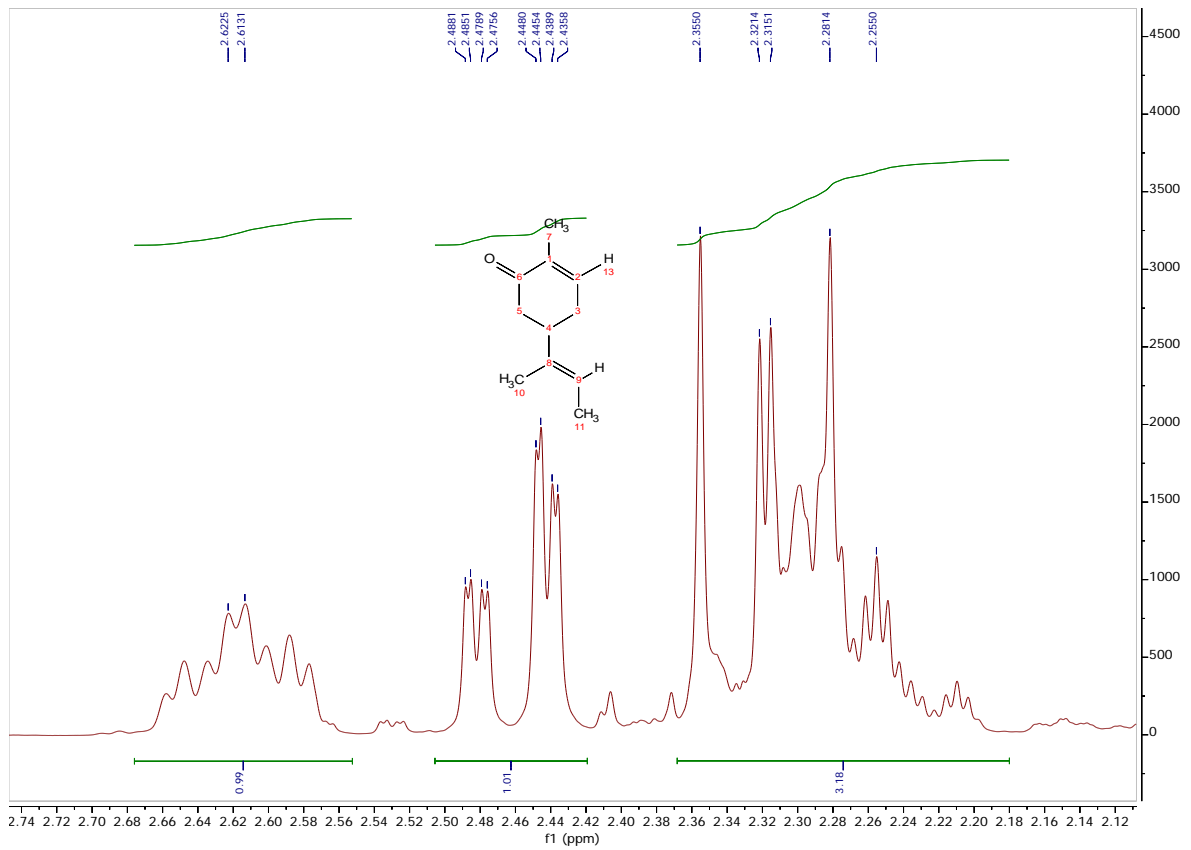


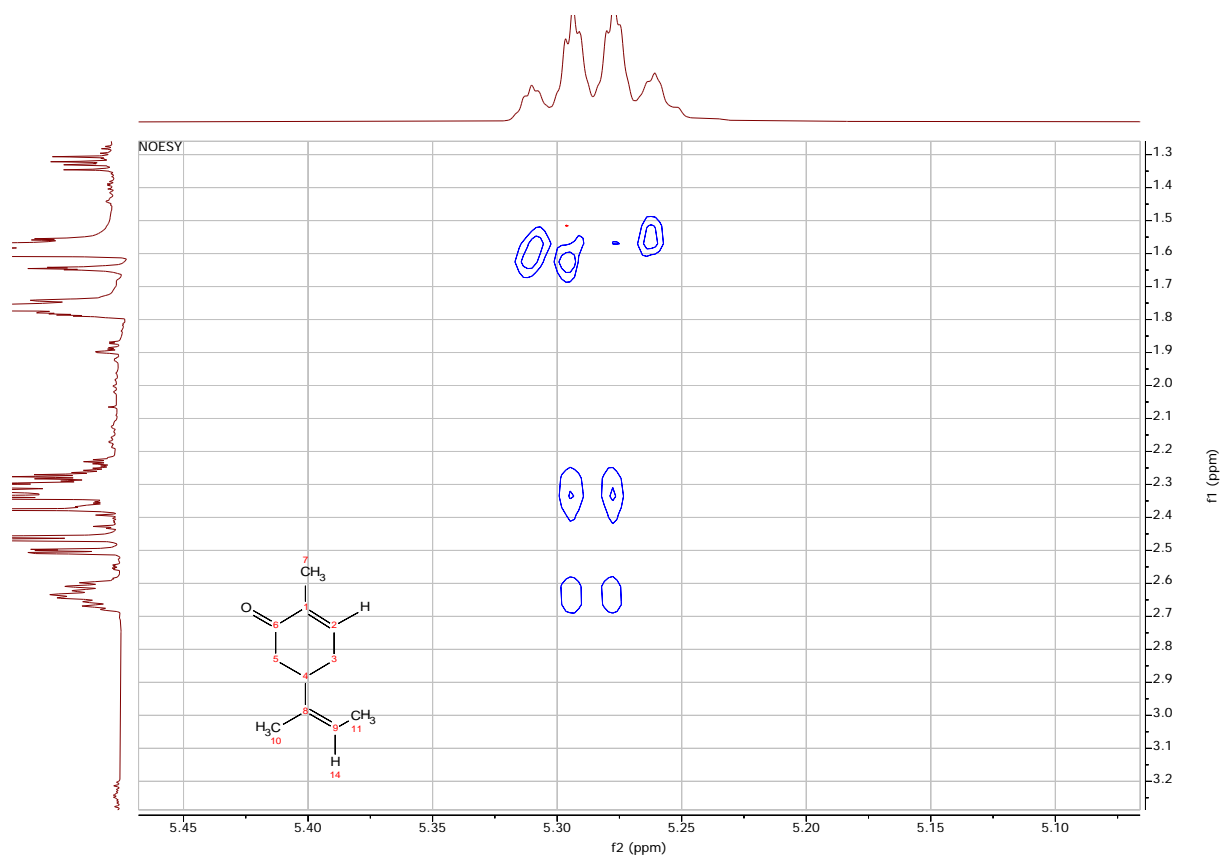




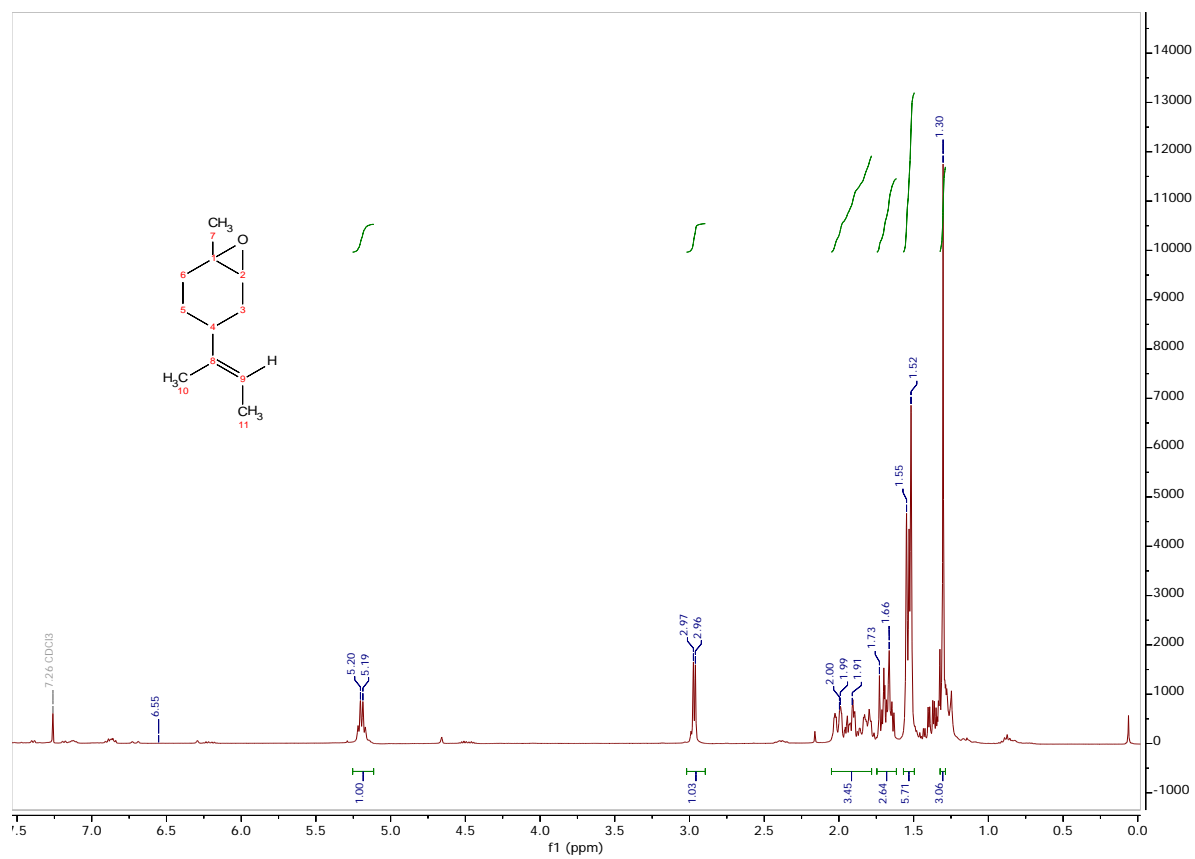
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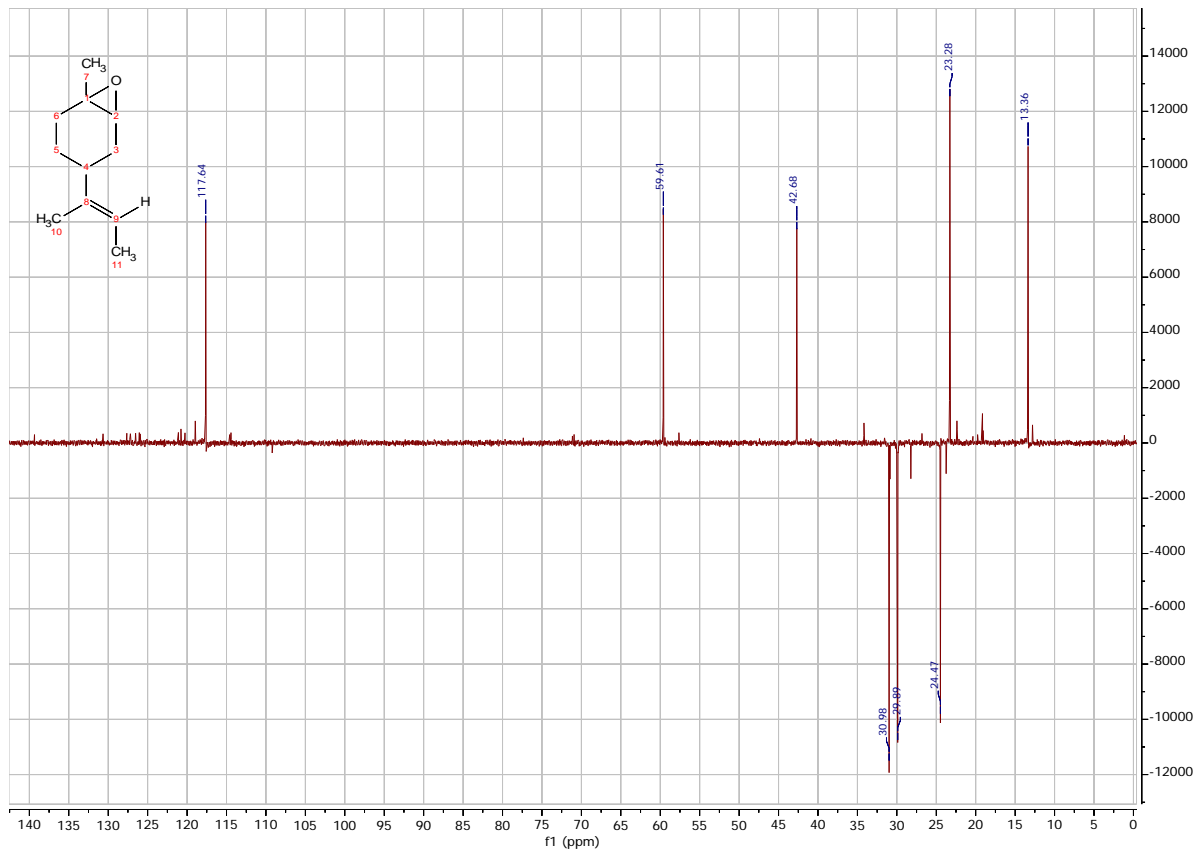
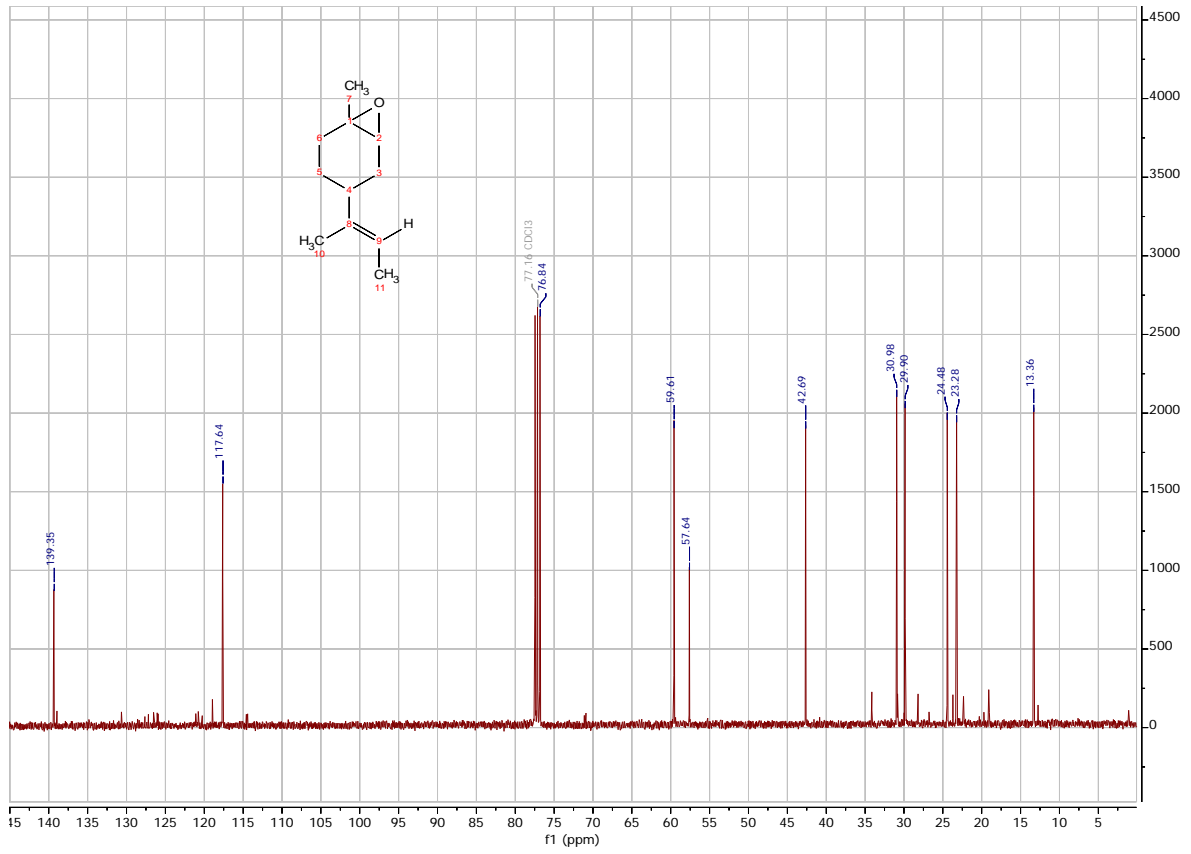


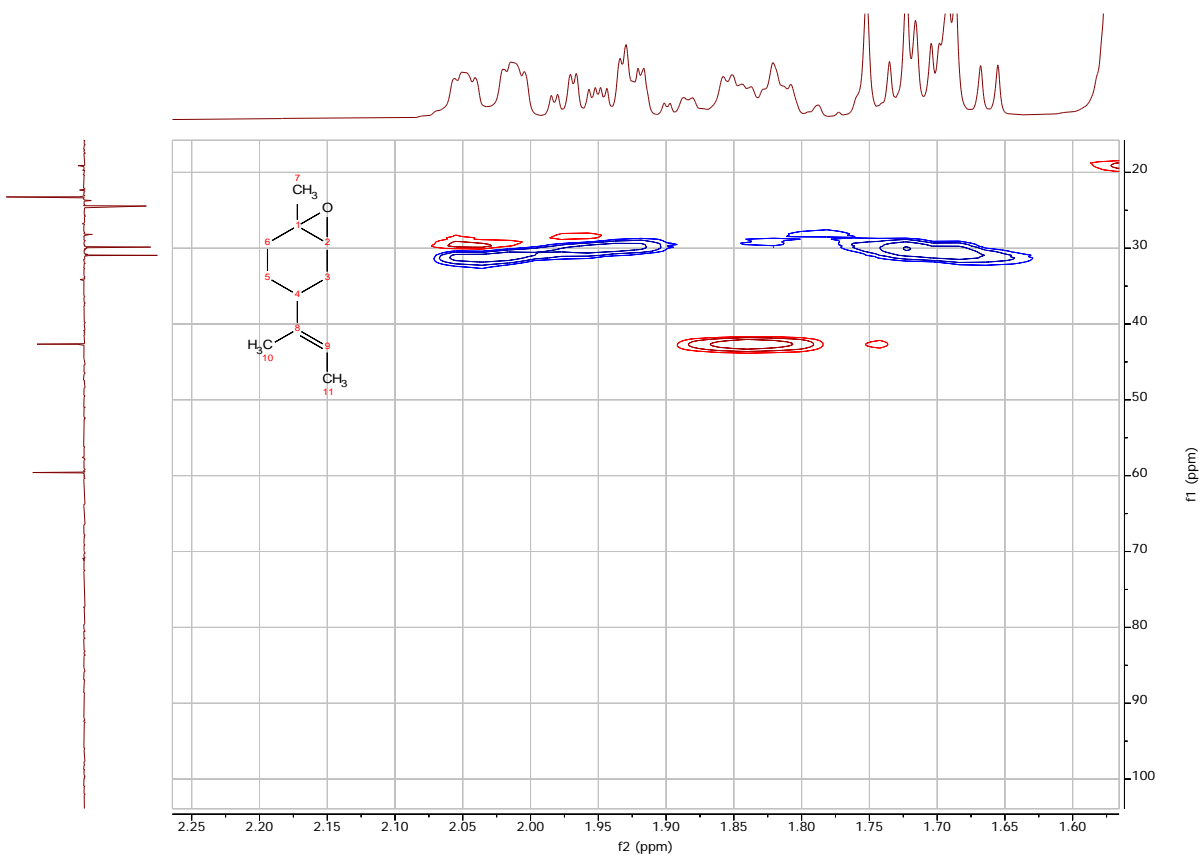
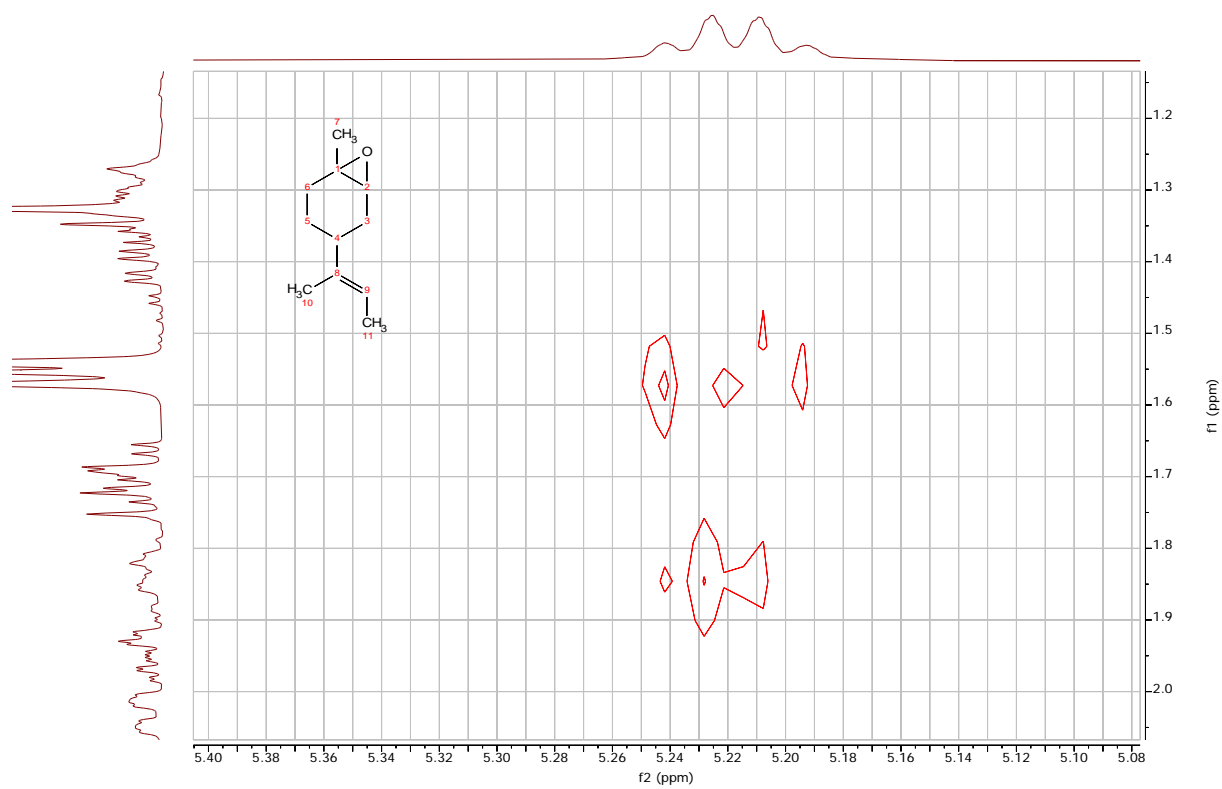




Product 12

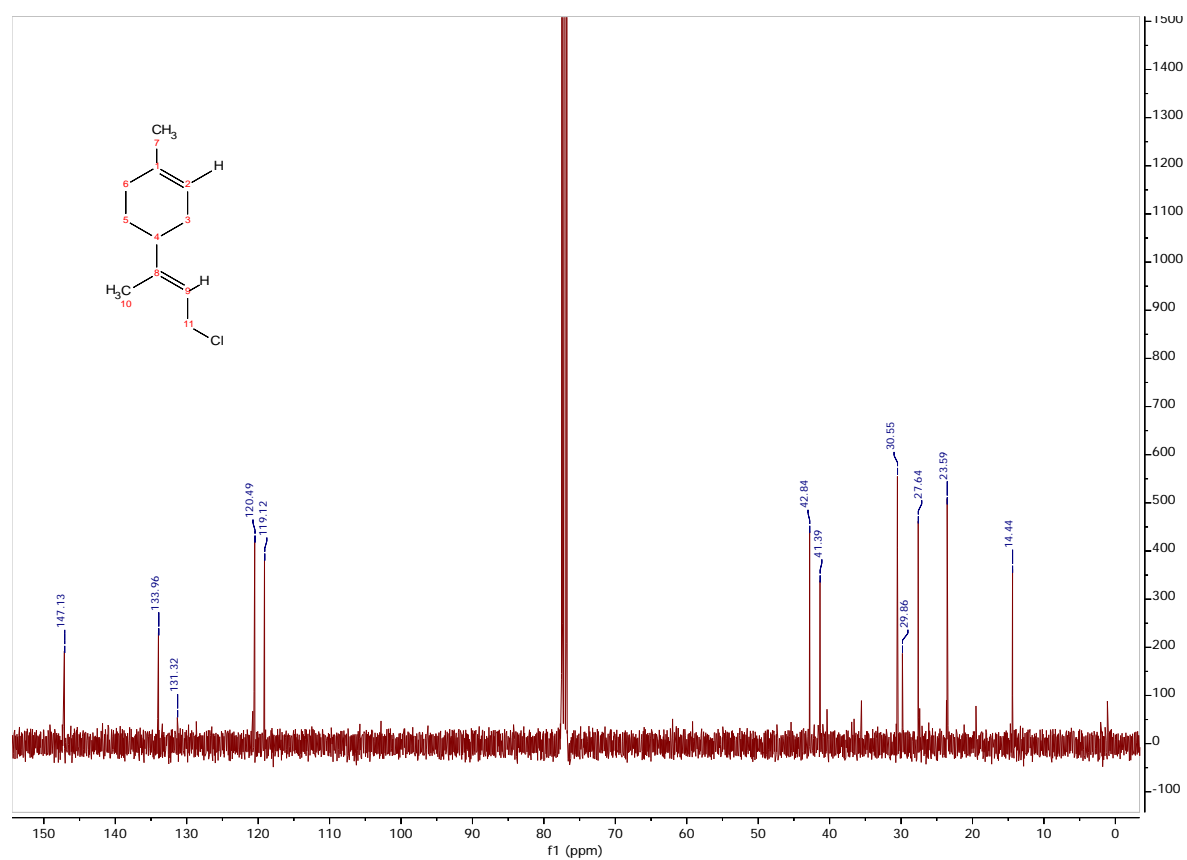
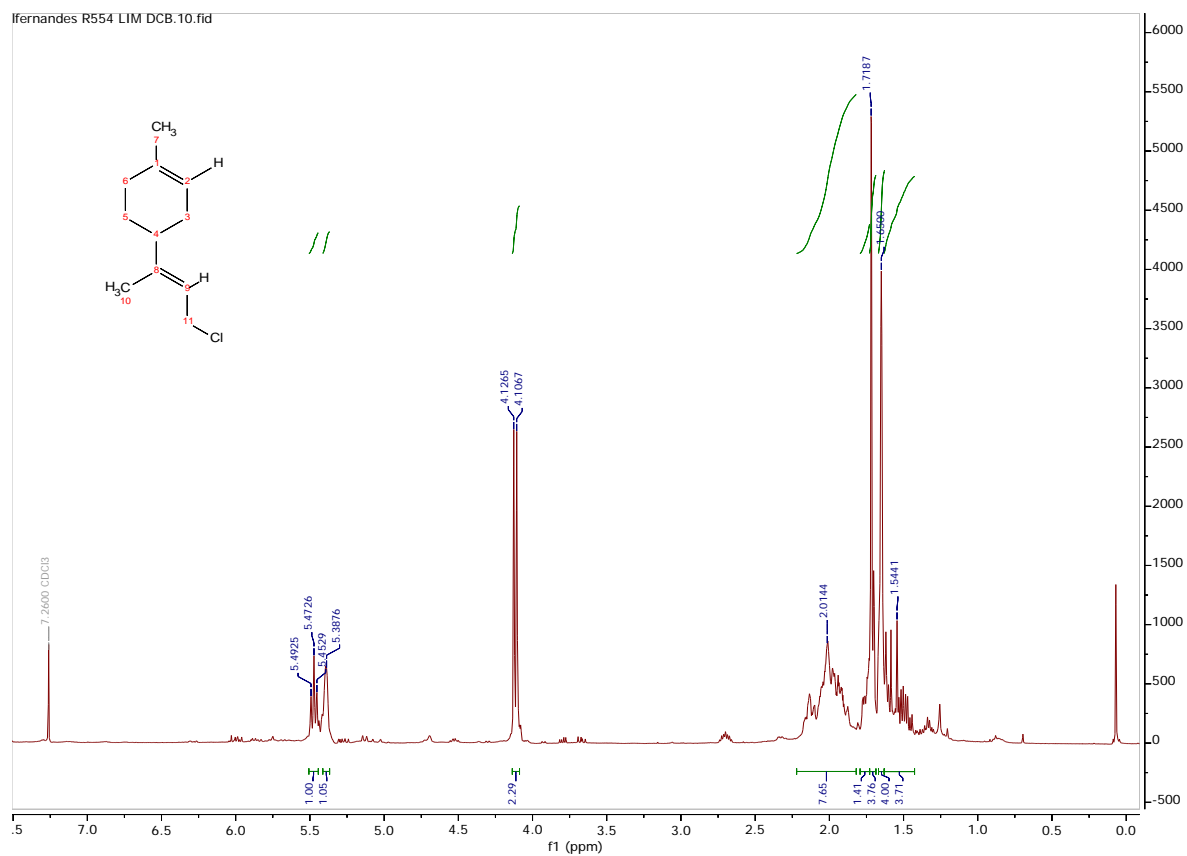


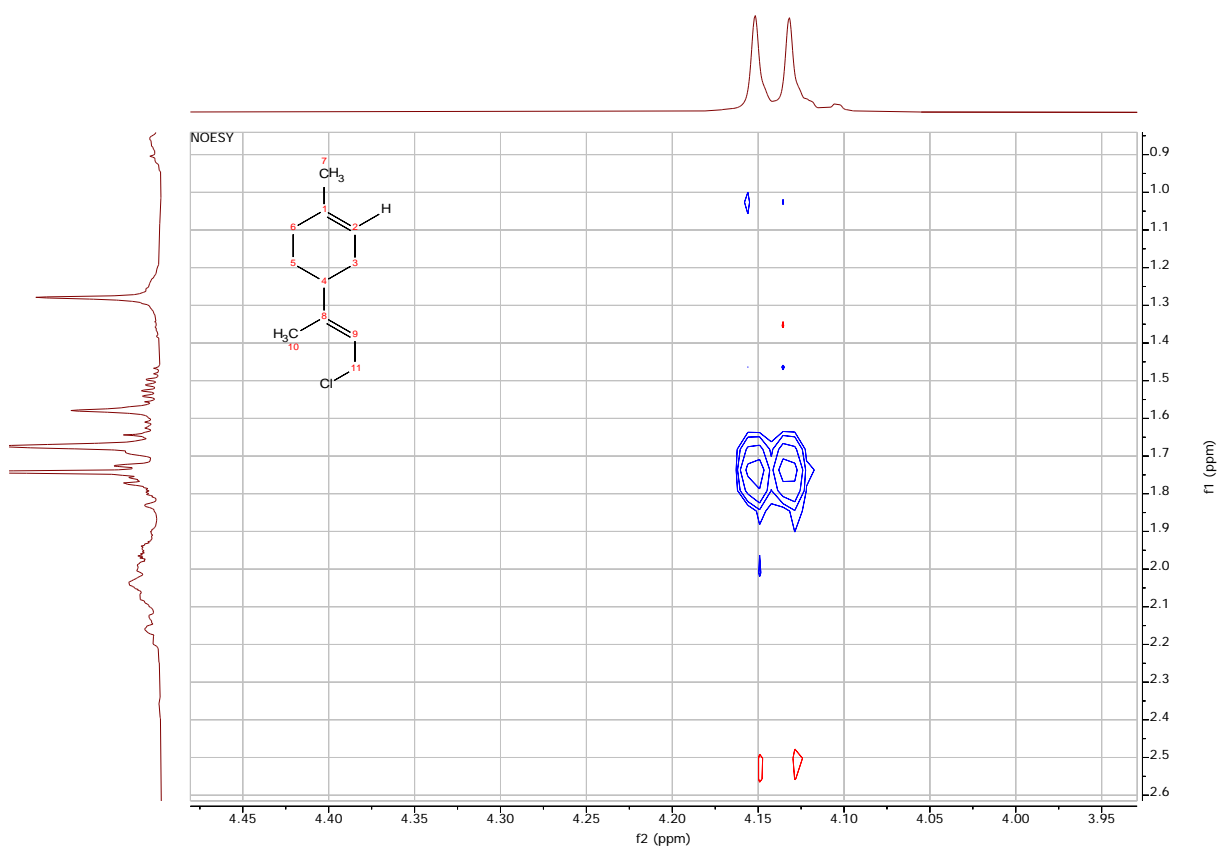
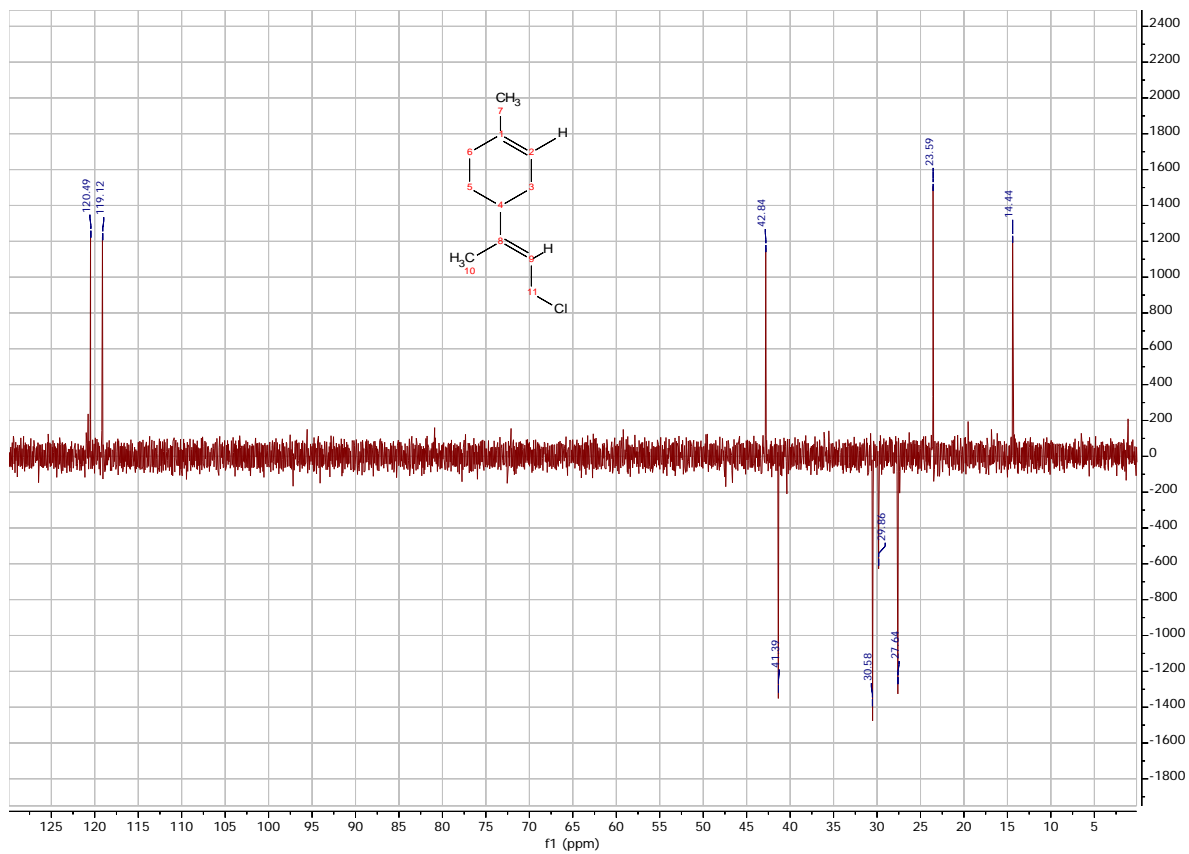




Product 14

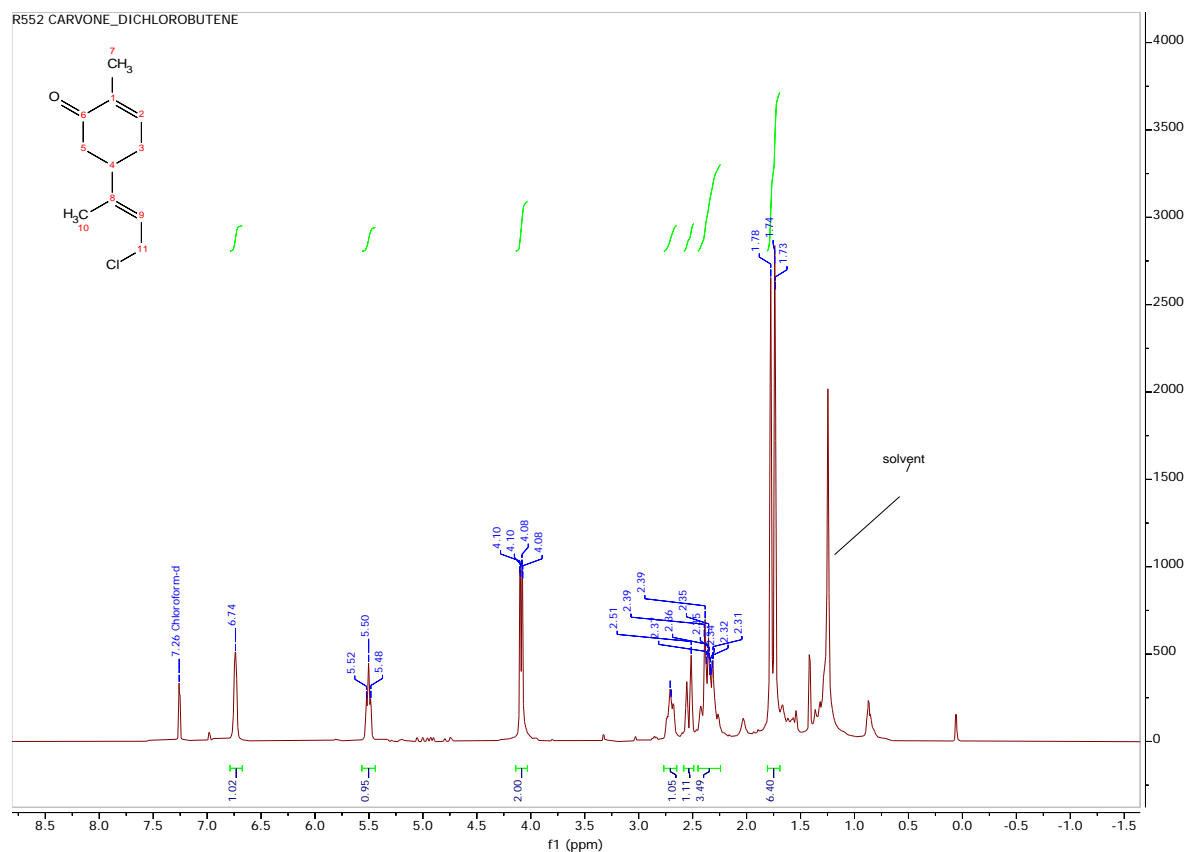
Ifernandes R554 LIM DCB.10.fid



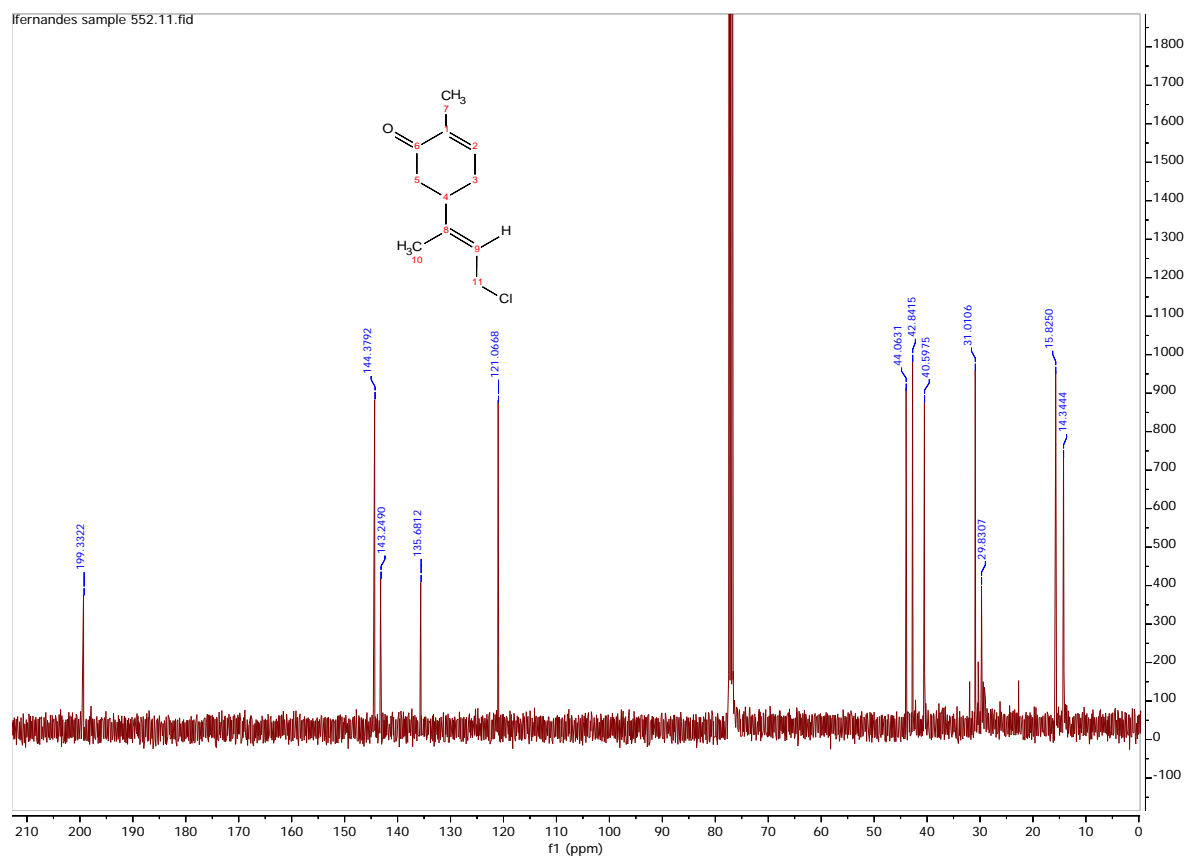


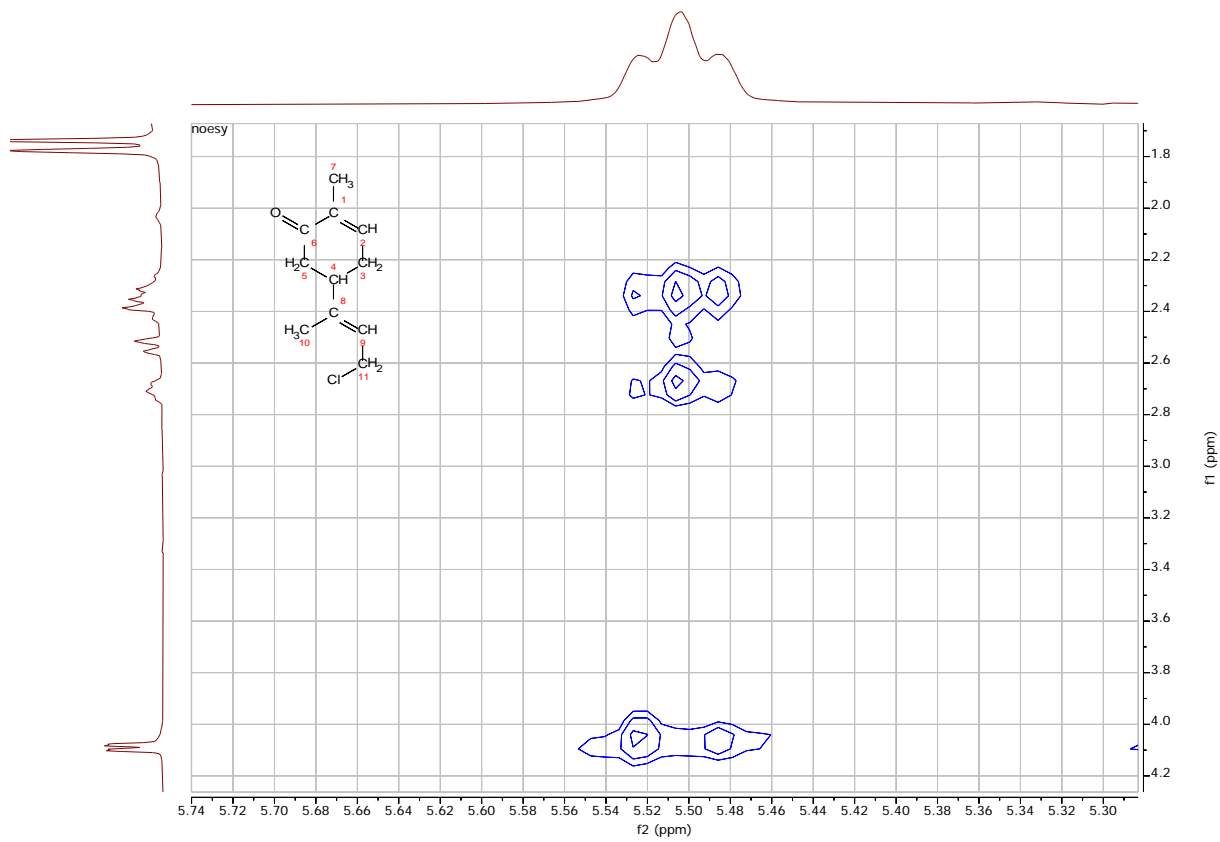
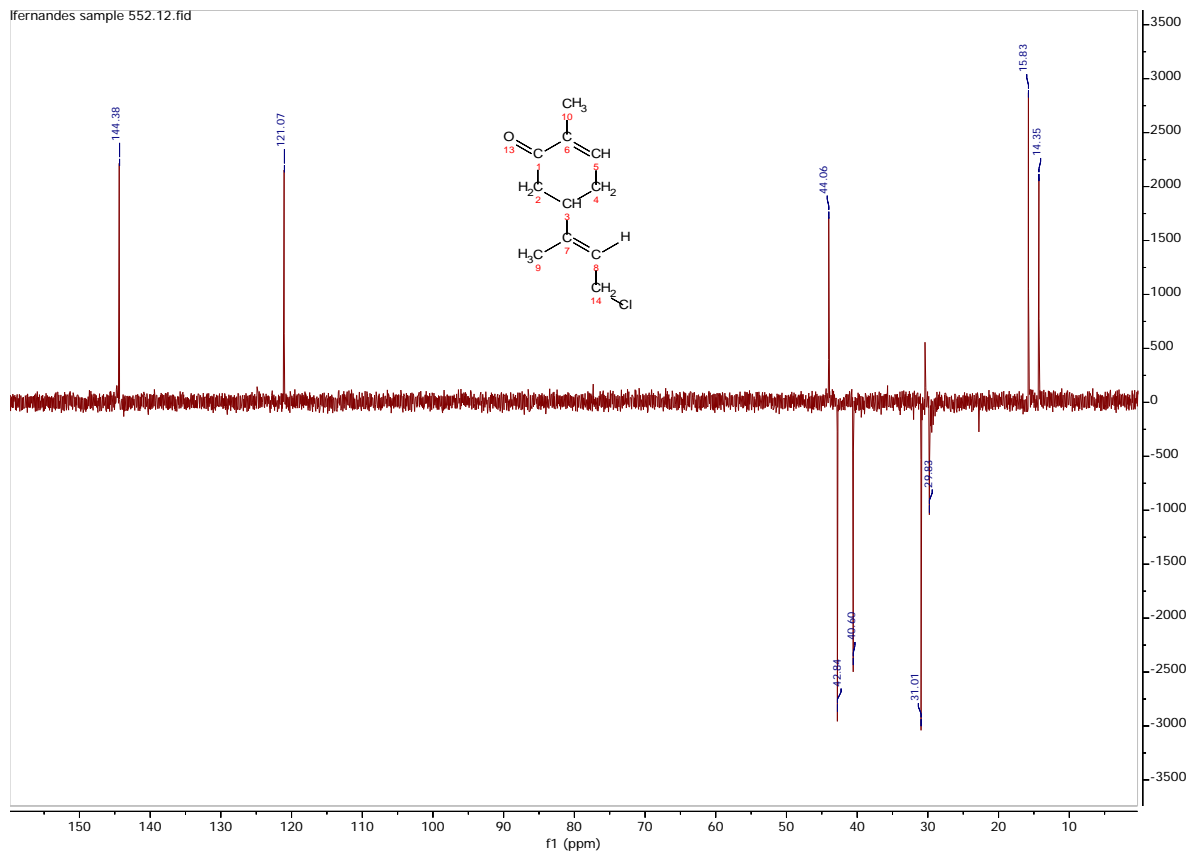
Product 15

R552 CARVONE_DICHLOROBUTENE



Ifernandes sample 552.11.fid





Product 16

