SUPPORTING INFORMATION

Stereoselective Heterocycle Synthesis through a Reversible Allylic Alcohol Transposition and Nucleophilic Addition Sequence

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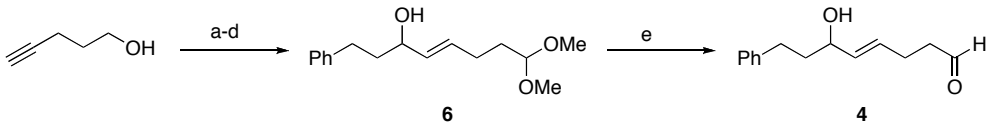
General

^{1}H NMR and ^{13}C NMR spectra were taken on a Bruker Avance 300 spectrometer at 300 MHz and 75 MHz respectively, a Bruker Avance 400 spectrometer at 400 MHz and 100 MHz, or a Bruker Avance 500 spectrometer at 500 MHz and 125 MHz, as specified. The chemical shifts are reported in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.27 ppm, CD_2Cl_2 = 5.31 ppm, C_6D_6 = 7.16 ppm, for ^{13}C NMR: $CDCl_3$ = 77.23, $CDCl_3$ = 53.52, C_6D_6 = 128.37 . Data are reported as follows: m = multiplet, s = singlet; d = doublet; t = triplet; q = quartet; p = pentet; dd = doublet of doublets; dt = doublet of triplets; br = broad. High resolution mass spectra were recorded on a Micromass UK Limited Q-Tof Ultima API or a Fissions VG Autospec spectrometer. Infrared (IR) spectra were taken on a Mattson Cygnus 100 spectrometer. Samples for IR were prepared as thin films on a NaCl plates by dissolving the corresponding compounds in CH_2Cl_2 followed by evaporation of the CH_2Cl_2. Methylene chloride was distilled under N_2 from CaH_2. Analytical TLC was performed on E. Merck pre-coated (25 mm) silica gel 60F-254 plates. Visualization was done under UV (254 nm). Flash chromatography was done using ICN SiliTech 32-63 60 Å silica gel. Reagent grade ethyl acetate, diethyl ether, pentane and hexanes (commercial mixture) were purchased from EM Science and used as is for chromatography. All reactions were performed in oven or flame-dried glassware under a positive pressure of N_2 with magnetic stirring unless otherwise noted.

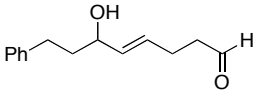
General procedure for the Re_2O_7-mediated cyclization

To a solution of the substrate in CH_2Cl_2 (~0.05-0.10M) was added Re_2O_7 (0.05 equiv). The reaction mixture was stirred at rt (unless otherwise mentioned) until the starting was completely consumed as determined by TLC, then the reaction was quenched with a few drops of pyridine or triethylamine and the solvent was removed under vacuum The final products were isolated after purification by flash chromatography or preparative TLC.



Reagents and conditions
a) DIBAL-H, THF, –78 °C, then I_2, 52%. b) IBX, DMSO, 84%. c) $(MeO)_3CH$, PPTs, MeOH, 88%. d) *t*BuLi, THF, –78 °C, then $PhCH_2CH_2CHO$, 50%. d) HOAc, H_2O, 100%.

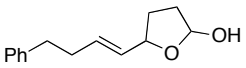
Scheme 1. Synthesis of substrates **4** and **6**.



(*E*)-6-hydroxy-8-phenyloct-4-enal (4)

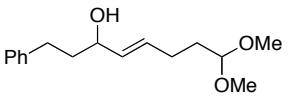
^{1}H NMR (400 MHz, CD_2Cl_2) δ 9.73 (t, *J* = 1.2 Hz, 1H), 7.26-7.29 (m, 2H), 7.15-7.21 (m, 3H), 5.65 (dtd, *J* = 0.4, 6.4, 15.6 Hz, 1H), 5.54 (tdd, *J* = 1.2, 6.4, 15.6 Hz, 1H), 4.04 (app q, *J* = 5.6 Hz, 1H), 2.59-2.73 (m, 2H), 2.51 (t, *J* = 8.0 Hz, 2H), 2.35 (q, *J* = 4.8 Hz, 2H), 1.70-1.87 (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 202.3, 142.6, 134.7, 129.8, 128.8, 128.7, 126.1, 72.3, 43.5, 39.3, 32.1, 25.1; IR (neat) 3439, 3063, 3031, 2954, 2925, 2867, 1605, 1496,

1453, 1375, 1179, 1121,1024 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}O_2Na$ $[M+Na]^+$ 241.1204, found 241.1211.



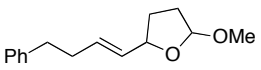
5-(4-phenylbut-1-en-1-yl)tetrahydrofuran-2-ol (5)

The general cyclization procedure was followed with **5** (50 mg, 0.23 mmol), Re_2O_7 (5.5 mg, 0.011 mmol), and CH_2Cl_2 (3 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (10-20% ethyl acetate in hexanes) to give the product (10 mg, 20%, dr = 1.2:1). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.24-7.28 (m, 2H), 7.14-7.19 (m, 3H), 5.70 (app q, J = 6.4 Hz, 0.45H), 5.67 (app q, J = 6.4 Hz, 0.55H), 5.54 (dt, J = 1.2, 7.6 Hz, 0.45H), 5.49-5.52 (m, 0.55H), 5.44 (dt, J = 1.2, 7.2, Hz 0.45H), 5.39-5.41 (m, 0.55H), 4.54 (q, J = 6.8 Hz, 0.55H), 4.33 (q, J = 6.8, 0.45H), 2.65-2.72 (m, 2H), 2.57-2.63 (m, 1H), 2.30-2.43 (m, 2H), 1.82-2.16 (m, 2.4H), 1.70-1.82 (m, 1H), 1.46-1.55 (m, 0.6H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 141.9, 133.0, 131.6, 131.4, 131.0, 128.4, 128.2, 125.7, 98.5, 98.4, 81.4, 78.8, 35.5, 34.2, 34.0, 33.8, 33.2, 30.4, 30.0; IR (neat) 3402, 3060, 3025, 2933, 2857, 1603, 1495, 1453, 1191, 1018; HRMS (ESI) calcd for $C_{14}H_{18}O_2Na$ $[M+Na]^+$ 241.1204, found 241.1228.



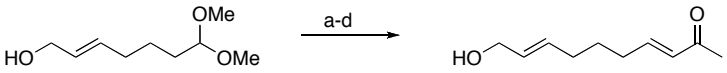
(*E*)-8,8-dimethoxy-1-phenyloct-4-en-3-ol (6)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.32 (m, 2H), 7.18-7.22 (m, 3H), 5.68 (ddt, J = 0.4, 6.4 Hz, 15.2, 1H), 5.55 (ddt, J = 1.2, 6.8, 15.2 Hz, 1H), 4.40 (t, J = 5.6 Hz, 1H), 4.09 (q, J = 5.7 Hz, 2H), 3.34 (s, 6H), 2.64-2.77 (m, 2H), 2.10-2.15 (q, J = 7.1 Hz, 2H), 1.77-1.94 (m, 2H), 1.74 (br, 1H), 1.70-1.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 133.4, 131.2, 128.5, 128.4, 125.8, 103.9, 72.2, 52.76, 53.74, 38.8, 32.0, 31.8, 27.3; IR (neat) 3426, 3060, 3025, 2941, 2857, 2831, 1669, 1602, 1495, 1452, 1385, 1190, 1127, 1058 969, 913, 747 cm^{-1}; HRMS (APCI) calcd for $C_{16}H_{24}O_3Na$ $[M+Na]^+$ 287.1623, found 287.1632.



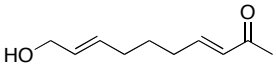
2-methoxy-5-(4-phenylbut-1-en-1-yl)tetrahydrofuran (8)

The general cyclization procedure was followed with **6** (50 mg, 0.19 mmol), Re_2O_7 (4.6 mg, 0.010 mmol), DCM (3 mL), the reaction was stirred at rt for 30 min, then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (36 mg, 83%, dr = 6:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ. 7.28-7.35 (m, 2H), 7.18-7.25 (m, 3H), 5.69-5.84 (m, 1H), 5.43-5.65 (m, 1H), 5.08 (dd, J = 2.0, 5.2 Hz, 0.6H), 4.99 (d, J = 4.4 Hz, 0.4H), 4.50 (q, J = 7.1 Hz, 0.6H), 4.45 (q, J = 7.7 Hz, 0.4H), 3.39 (s, 1.8H), 3.37 (s, 1.2H), 2.62-2.82 (m, 2H), 2.26-2.53 (m, 2H), 1.70-2.20 (m, 3.4H), 1.50-1.62 (m, 0.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 132.8, 132.3, 131.8, 130.6, 128.5, 128.4,128.32, 128.30, 125.9, 125.8, 105.3, 105.0, 81.5, 78.7, 54.9, 54.5, 35.53, 35.49, 34.1, 34.0, 33.5, 32.4, 30.3, 30.1; IR (neat) 3061, 3026, 2984, 2928, 2828, 1684, 1603, 1495, 1453, 1363, 1203, 1098, 1034, 966, 746 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$ 255.1361, found 25.1374.



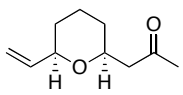
Reagents and conditions
a) HOAc, H_2O. b) TBDPSCl, imidazole, DMAP, DMF. c) $(EtO)_2P(O)CH_2C(O)CH_3$, NaH, THF. d) HF•pyridine, THF.

Scheme 2. Synthesis of substrate **9**.



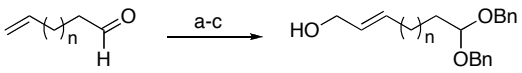
(3*E*,8*E*)-10-hydroxydeca-3,8-dien-2-one (9)

^{1}H NMR (400 MHz, CH_2Cl_2) δ 6.77 (dt, J = 7.2, 16.0 Hz, 1H), 6.03 (dt, J = 1.4, 16.0 Hz, 1H), 5.59-5.70 (m, 2H), 4.04 (d, J = 3.6 Hz, 2H), 2.22 (dt, J = 1.4, 7.2 Hz, 2H), 2.19 (s, 3H), 2.03-2.11 (m, 2H), 1.56 (p, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, CH_2Cl_2) δ 198.3, 147.9, 131.7, 131.4, 130.1, 63.4, 31.8, 31.6, 27.6, 26.6; IR (neat) 3427, 3004, 2928, 2857, 1672, 1625, 1431, 1362, 1431,1362, 1257, 1089, 972 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{16}O_2Na$ $[M+Na]^+$ 191.1048, found 191.1066.



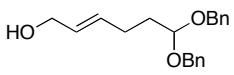
1-((2S,6R)-6-vinyltetrahydro-2H-pyran-2-yl)propan-2-one (10)

The general rearrangement procedure was followed with **9** (14.2 mg, 0.084 mmol), Re_2O_7 (2.1 mg, 0.004 mmol), and CD_2Cl_2 (1.5 mL). The reaction was stirred at 20 °C for 10 min, after which the catalyst was removed by filtration through a small pad of Celite. ^{1}H NMR was taken directly to show a quantative conversion. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.90 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.16 (dt, J = 1.6, 17.2 Hz, 1H), 5.02 (dt, J = 1.6, 10.4 Hz, 1H), 3.75-3.85 (m, 2H), 2.63 (dd, J = 7.6, 15.6 Hz, 1H), 2.42 (dd, J = 5.2, 15.6 Hz, 1H), 2.13 (s, 3H), 1.79-1.87 (m, 1H), 1.51-1.65 (m, 3H), 1.13-1.29 (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) 207.1, 139.6, 113.7, 78.1, 74.1, 50.3, 31.19, 31.16, 30.6, 20.3; IR (neat) 2934, 2857, 1717, 1438, 1358, 1199, 1089, 1045, 989, 916 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{15}O_2$ [M–H]$^+$ 167.1072, found 167.1100.



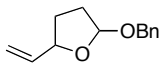
Reagents and conditions
a) BnOH, *p*-TsOH, Na_2SO_4, CH_2Cl_2, 64% (n = 1), 51% (n = 2), 52% (n = 3). b) Methyl acrylate, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 89% (n = 1), 97% (n = 2), 99% (n = 3). c) DIBAL-H, CH_2Cl_2, –78 °C, 90% (n = 1), 89% (n = 2), 86% (n = 3).

Scheme 3. Synthesis of substrates **11**, **13**, and **15**.



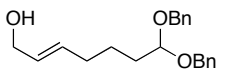
(*E*)-6,6-bis(benzyloxy)hex-2-en-1-ol (11)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.45 (m, 10H), 5.62-5.76 (m, 2H), 4.83 (t, *J* = 6.0 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 2H), 4.64 (d, *J* = 12.0 Hz, 2H), 4.07 (d, *J* = 4.8 Hz, 2H), 2.40 (br, 1H), 2.24 (q, *J* = 7.0 Hz, 2H), 1.93 (q, *J* = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 131.6, 129.8, 128.6, 127.9, 127.8, 101.6, 67.4, 63.4, 32.8, 27.6; IR (neat) 3401, 3087, 3062, 3030, 2930-2868, 1670, 1605, 1496, 1453, 1385, 1353, 1208, 1124, 1023,737 cm^{-1}; HRMS (APCI) calcd for $C_{20}H_{24}O_3Na$ [M+Na]$^+$ 355.1623, found 355.1608.



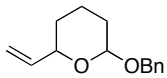
2-(Benzyloxy)-5-vinyltetrahydrofuran (12)

The general cyclization procedure was followed with **11** (100 mg, 0.32 mmol), Re_2O_7 (7.8 mg, 0.016 mmol), and CH_2Cl_2 (5 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (55 mg, 84%, dr = 6:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.40 (m, 5H), 5.95 (ddd, *J* = 7.2, 10.0, 17.2 Hz, 0.4H), 5.90 (ddd, *J* = 6.8, 10.4, 17.2 Hz, 0.6H), 5.23-5.33 (m, 2H), 5.13-5.18 (m, 1H), 4.82 (d, *J* = 12.0 Hz, 0.4H), 4.81 (d, *J* = 12.0 Hz, 0.6H), 4.81 (q, *J* = 6.8 Hz, 0.6H), 4.50-4.55 (m, 1.4H), 2.20-2.30 (m, 0.6H), 2.08-2.16 (m, 1.5H), 1.88-2.04 (m, 1.5H), 1.61-1.70 (m,0.8H); ^{13}C NMR (100 MHz, $CDCl_3$) 140.5, 138.5, 138.34, 138.32, 128.4, 127.94, 127.88, 127.5, 115.7, 115.6, 103.5, 103.2, 81.8, 78.9, 69.0, 68.6, 33.5, 32.1, 30.02, 30.0; IR (neat) 3064,3030, 2924, 2853, 1605, 1455,1273, 1205, 1025, 733 cm^{-1}; HRMS (APCI) calcd for $C_{13}H_{16}O_2Na$ [M+Na]$^+$ 227.1048, found 227.1049.



(*E*)-7,7-bis(benzyloxy)hept-2-en-1-ol (13)

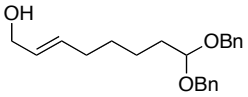
^{1}H NMR (300 MHz, $CDCl_3$) 7.33-7.44 (m, 10H), 5.62-5.76 (m, 2H), 4.83 (t, *J* = 6.0 Hz, 1H), 4.75 (d, *J* = 11.7 Hz, 2H), 4.65 (d, *J* = 11.7 Hz, 2H), 2.14 (q, *J* = 6.5 Hz, 2H), 1.86 (q, *J* = 7.2 Hz, 2H), 1.95 (p, *J* = 7.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 132.1, 129.8, 128.6, 127.9, 127.8, 102.1, 67.3,63.4, 32.9, 32.1, 24.4; IR 3403, 3062, 3030, 2932, 2865, 1669, 1605,1496, 1454,1384, 1351, 1208, 1124, 1023, 736 (neat) cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{26}O_3Na$ [M+Na]$^+$ 349.1780, found 349.1754.



2-(benzyloxy)-6-vinyltetrahydro-2H-pyran (14)

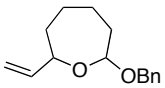
The general rearrangement procedure was followed with **13** (100 mg, 0.31 mmol), Re_2O_7 (7.4 mg, 0.015 mmol), and DCM (5 mL). The reaction was stirred at rt for 30 min and then

was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (55 mg, 81%, dr = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.41 (m, 5H), 5.95 (ddd, *J* = 5.2, 10.4, 17.2 Hz, 0.3H), 5.88 (ddd, *J* = 6.0, 10.8, 17.2 Hz, 0.7), 5.31 (dt, *J* = 1.6, 17.2 Hz, 0.3H), 5.26 (dt, *J* = 1.6, 17.6 Hz, 0.7H), 5.14 (dt, *J* = 1.4, 10.8 Hz, 0.3H), 5.13 (dt, *J* = 1.4, 10.4 Hz, 0.7H), 5.00 (d, *J* = 1.6 Hz, 0.7H), 4.95 (d, *J* = 12.0 Hz, 0.3H), 4.76 (d *J* = 12.0 Hz, 0.7H), 4.65 (d, *J* = 12.0 Hz, 0.3H), 4.55 (dd, *J* = 2.0, 9.2 Hz, 0.3H), 4.52 (d, *J* = 12.0 Hz, 0.7H), 4.31(ddddd, *J* = 1.6, 1.6, 1.6, 5.6, 10.4 Hz, 0.7H), 3.93 (ddddd, *J* = 1.2, 1.6, 2.4, 5.2, 11.2 Hz, 0.3H), 1.25-2.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 138.6, 138.4, 138.1, 128.4, 128.0, 127.8, 127.6, 127.5, 114.8, 114.6, 101.0, 96.7, 76.5, 69.8, 69.7, 68.5, 31.1, 31.0, 30.8, 29.5, 22.0, 18.0; IR (neat) 3065, 3030, 2940, 2867, 1646, 1604, 1496, 1454, 1357, 1261, 1205, 1121, 1023, 736 cm^{-1}; HRMS (APCI) calcd for $C_{14}H_{18}O_2Na$ $[M+Na]^+$ 241.1204, found 241.1184.



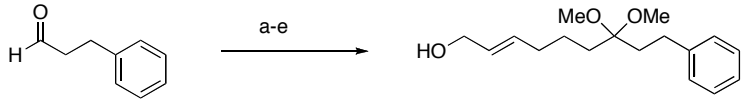
(*E*)-8,8-bis(benzyloxy)oct-2-en-1-ol (15)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.46 (m, 10H), 5.64-5.76 (m, 2H), 4.83 (t, *J* = 5.6 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 2H), 4.65 (d, *J* = 12.0 Hz, 2H), 4.09 (d, *J* = 4.8 Hz, 2H), 2.64 (br, 1H), 2.12 (q, *J* = 6.1 Hz, 2H), 1.86 (q, *J* = 6.8 Hz, 2H), 1.41-1.58 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 132.5, 129.5, 128.5, 127.9, 127.7, 102.2, 67.3, 63.4, 33.2, 32.2, 29.0, 24.3; IR (neat) 3406, 3062, 3030, 2932, 2861, 1669, 1605, 1494, 1454, 1384, 1351, 1205, 1125, 1022, 736 cm^{-1}; HRMS (APCI) calcd for $C_{22}H_{28}O_3Na$ $[M+Na]^+$ 363.1936, found 363.1925.



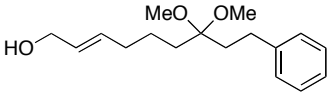
2-(Benzyloxy)-7-vinyloxepane (16)

The general rearrangement procedure was followed with **15** (100 mg, 0.29 mmol), Re_2O_7 (7.1 mg, 0.015 mmol), and CH_2Cl_2 (5 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (55 mg, 81%, dr = 9:1).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.40 (m, 5H), 5.94 (ddd, *J* = 5.2, 10.4, 17.2 Hz, 1H), 5.34 (dt, *J* = 1.6, 17.2 Hz, 1H), 5.14 (dt, *J* = 1.6, 10.4 Hz, 0.1H), 5.13 (dt, *J* = 1.6, 10.4 Hz, 0.9H), 4.93 (dd, *J* = 5.6, 8.8 Hz, 0.9H), 4.88 (d, *J* = 12.0 Hz, 0.1H), 4.81 (d, *J* = 11.6 Hz, 0.9H), 4.70 (dd, *J* = 3.6, 7.6 Hz, 0.1H), 4.57 (d, *J* = 12.0 Hz, 0.1H), 4.52 (d, *J* = 11.6 Hz, 0.9H), 4.45 (dd, *J* = 5.2, 9.6 Hz, 0.9H), 4.01-4.04 (m, 0.1H), 2.13-2.22 (m, 1H), 1.88-1.98 (m, 1H), 1.65-1.87 (m, 3H), 1.36-1.60 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 139.5, 138.4, 138.1, 128.4, 128.1, 128.0, 127.5, 113.6, 103.3, 100.3, 77.8, 71.1, 69.2, 69.1, 36.5, 35.9, 35.7, 35.4, 29.5, 24.7, 23.3, 22.5; IR (neat) 3064, 3030, 2931, 2856, 1645, 1605, 1496, 1452, 1356, 1206, 1131, 1055, 1024, 735 cm^{-1}; HRMS (APCI) calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$ 255.1361, found 255.1359.



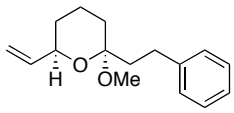
Reagents and conditions
a) Pentenylmagnesium bromide, THF, 0 °C, 89%. b) PCC, Celite, CH_2Cl_2, 96%. c) *p*-TsOH, $(MeO)_3CH$, MeOH, 50 °C, 93%. d) Ethyl acrylate, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux. e) DIBAL-H, CH_2Cl_2, –78 °C.

Scheme 4. Synthesis of substrate **17**.



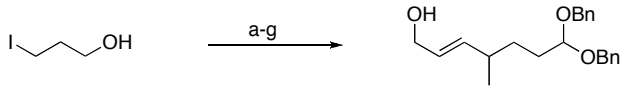
(*E*)-7,7-Dimethoxy-9-phenylnon-2-en-1-ol (17)

^{1}H NMR (400 MHz, C_6D_6) δ 7.04-7.18 (m, 5H), 5.47-5.57 (m, 2H), 3.87 (br, 2H), 3.05 (s, 6H), 2.58-2.63 (m, 2H), 1.94 -2.01 (m, 2H), 1.89-1.93 (m, 2H), 1.66-1.71 (m, 2H), 1.40 (p, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 142.1, 131.1, 130.3, 128.4, 128.2, 125.8, 102.8, 63.1, 47.2, 34.7, 32.3, 32.2, 30.4, 23.5; IR (neat) 3400, 3025, 2949, 2829, 1669, 1603, 1495, 1454, 1368, 1181, 1054, 971, 743 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{26}O_3Na$ $[M+Na]^+$ 301.1780, found 301.1811.



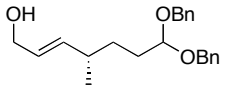
(±)-(2*S*, 6*R*)-2-methoxy-2-phenethyl-6-vinyltetrahydro-2H-pyran (18)

The general rearrangement cyclization procedure was followed with **17** (11 mg, 0.039 mmol), Re_2O_7 (2.0 mg, 0.004 mmol), and CD_2Cl_2 (1.0 mL). The reaction was stirred at 0 °C for 2 min, after which the cold bath was removed, and the reaction was stirred for another 8 min and then was quenched with pyridine (25 μL). $Me_2(Bn)SiH$ (5 μl) was added as an internal standard and crude NMR was used to determine the yield of 85%. ^{1}H NMR (400 MHz, C_6D_6) δ 7.12-7.19 (m, 2H), 7.04-7.11 (m, 3H), 5.88 (ddd, *J* = 5.6, 9.8, 17.2 Hz, 1H), 5.29 (dt, *J* = 1.8, 17.2 Hz, 1H), 5.03 (dt, *J* = 1.6, 17.2 Hz, 1H), 4.08 (ddddd, *J* = 1.2, 1.6, 2.4, 5.2, 11.6 Hz, 1H), 3.07 (s, 3H), 2.53-2.69 (m, 2H), 1.99-2.09 (m, 1H), 1.81-1.98 (m, 2H), 1.72 (dddd, *J* = 1.6, 1.6, 1.6, 12.8 Hz, 1H) 1.36-1.51 (m, 2H), 1.19-1.30 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 142.3, 139.8, 128.4, 128.3, 125.7, 113.3, 99.1, 70.7, 46.7, 38.4, 32.2, 31.0, 30.0 18.9; IR (neat) 3063, 3026, 2941, 2867, 1646, 1603, 1496, 1454, 1367, 1273, 1216, 1104, 1024, 924, 755, 738 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{22}O_2Na$ $[M+Na]^+$ 269.1517, found 269.1548.



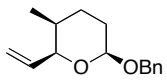
Reagents and conditions
a) IBX, DMSO, CH_2Cl_2. b) BnOH, *p*-TsOH, $Na_2S_2O_4$, CH_2Cl_2, 27% (two steps). c) LDA, propionic acid pseudoephedrine amide, LiCl, THF, 0 °C, 73%. d) BH_3•NH_3, LDA, THF. e) IBX, DMSO, 73% (two steps). e) NaH, triethyl phosphonoacetate, THF, 0 °C, 99%. f) DIBAL-H, CH_2Cl_2, –78 °C, 92%

Scheme 5. Synthesis of substrate **19**.



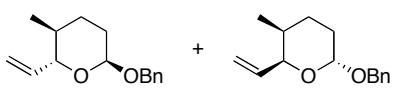
(*S*,*E*)-7,7-Bis(benzyloxy)-4-methylhept-2-en-1-ol (19)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.45 (m, 10H), 5.53-5.66 (m, 2H), 4.79 (t, *J* = 5.7 Hz, 1H), 4.73 (d, *J* = 11.7 Hz, 2H), 4.63 (d, *J* = 11.7 Hz, 2H), 4.10 (d, *J* = 4.2 Hz, 2H), 2.19 (heptet, *J* = 6.6 Hz, 1H), 1.94 (br, 1H), 1.74-1.88 (m, 2H), 1.40-1.54 (m, 2H), 1.06 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 138.1, 128.5, 127.9, 127.7, 102.3, 67.28, 67.26, 67.23, 63.6, 36.3, 31.7, 31.2, 20.5; IR (neat) 3403, 3063, 3030, 2926, 2867, 1667, 1605, 1493, 1454, 1380, 1349, 1208, 1122, 1022, 736 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{28}O_3Na$ $[M+Na]^+$ 363.1936, found 363.1973.



(2*S*,3*S*,6*S*)-6-(Benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran (20)

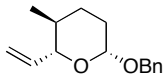
The general rearrangement procedure was followed with **19** (50 mg, 0.16 mmol), Re_2O_7 (2 mg, 0.004 mmol), and CH_2Cl_2 (5 mL). The reaction was stirred at rt for 20 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (33 mg, 100%, dr = 3:3:1:1). ^{1}H NMR (400 MHz, C_6D_6) δ 7.29-7.34 (m, 2H), 7.16-7.20 (m,2H), 7.07-7.12 (m, 1H), 5.74 (ddd, *J* = 4.8, 10.8, 17.2 Hz, 1H), 5.39 (dt, *J* = 2.0, 17.2 Hz, 1H), 5.10 (dt, *J* = 2.0, 10.8 Hz, 2H), 4.85 (d, *J* = 3.2 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.51(dddd, *J* = 0.5, 1.4, 1.6, 2.4 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 2.13 (dddd, *J* = 4.6, 4.6, 13.6, 13.6 Hz, 1H), 1.68 (dddd, *J* = 4.4, 4.4, 14.0, 14.0 Hz, 1H), 1.54 (m, 1H), 1.45 (dddd, *J* = 1.2, 2.8, 4.4, 14.0 Hz, 1H), 1.21 (dddd, *J* = 2.4, 2.8, 5.2, 13.6 Hz, 1H), 0.93 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.7,138.4, 128.2, 127.8, 127.3, 113.6, 96.4, 70.8, 68.3, 31.3, 25.3, 24.2, 11.4; IR (neat) 3065, 3030, 2938, 2892, 1645, 1606, 1453, 1351, 1211, 1126, 1019, 729 cm^{-1}; HRMS (APCI) calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$ 255.1361, found 255.1372.



(2*R*, 3*S*, 6*S*)-6-(Benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran and (2*S*, 3*S*, 6*R*)-6-(benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran

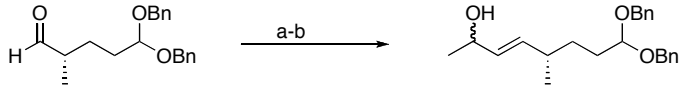
^{1}H NMR (400 MHz, C_6D_6) δ 7.28-7.36 (m, 2H), 7.13-7.19 (m, 2H), 7.05-7.11 (m, 1H), 5.87 (ddd, *J* = 6.8, 10.4, 17.2 Hz, 0.75H), 5.81 (ddd, *J* = 5.2, 10.8, 17.2 Hz, 0.25H), 5.35 (dt, *J* = 2, 17.2 Hz, 0.25H), 5.27 (ddd *J* = 0.8, 2.0, 17.2 Hz, 0.75H), 5.06-5.11 (m, 1H), 4.96 (d, *J* = 12.0 Hz, 0.25H), 4.89 (d, *J* = 3.2 Hz, 0.75H), 4.73 (d, *J* = 12.0 Hz, 0.75H), 4.53 (d, *J* = 12.0 Hz, 0.25H), 4.41 (dd, *J* = 2.8, 8.4 Hz, 0.25H), 4.40 (d, *J* = 12.0 Hz, 0.75H), 3.91 (dd, *J* = 7.2, 9.6 Hz, 0.75H), 3.84 (dddd, *J* = 1.6, 1.6, 3.8, 5.8 Hz, 0.25H), 1.45-1.85 (m, 3H), 1.25-1.45 (m, 2H), 0.87 (d, *J* = 6.4 Hz, 0.75H),

0.71 (d, J = 6.4 Hz, 2.25H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.8, 138.7, 138.2, 137.7, 128.21, 128.17, 127.8, 127.3, 116.0, 114.3, 100.9, 95.9, 69.3, 68.2, 35.1, 31.4, 30.2, 28.3, 26.8, 26.7, 17.7, 12.5; IR (neat) 3066, 3030, 2930, 2876, 1645, 1604, 1455, 1376, 1232, 1123, 1023, 923, 730 cm^{-1}; HRMS (APCI) calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$ 255.1361, found 255.1377.



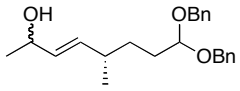
(2*R*, 3*S*, 6*R*)-6-(Benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran

^{1}H NMR (400 MHz, C_6D_6) δ 7.33-7.37 (m, 2H), 7.13-7.20 (m, 2H), 7.06-7.12 (m, 2H), 5.89 (ddd, J = 6.8, 10.4, 17.2 Hz, 1H), 5.29 (ddd, J = 1.2, 2.0, 17.2 Hz, 1H), 5.09 (ddd, J = 0.8, 2.0, 10.4 Hz, 1H), 4.98 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.37 (dd, J = 2.8, 8.8 Hz, 1H), 3.25 (dd, J = 2.8 Hz, 10), 1.60-1.75 (m, 2H), 1.41-1.48 (dt, J = 3.6, 13.6 Hz, 2H), 1.15-1.28 (m, 2H), 0.80-0.91 (m, 2H), 0.61 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.8, 137.6, 128.2, 127.8, 127.3, 115.8, 100.7, 82.7, 69.5, 34.7, 31.7, 31.1, 16.8; IR (neat) 3065, 3029, 2952, 2929, 2873, 2853, 1645, 1606, 1496, 1362, 1146, 1055, 1091, 920, 736 cm^{-1}; HRMS (APCI) calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$ 255.1361, found 255.1342.



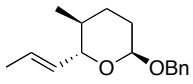
Reagents and conditions
a) Diethyl 2-oxopropylphosphonoacetate, NaH, THF, 83%. b) CBS-catalyst, BH_3•THF, THF, –25 °C, 80%.

Scheme 6. Synthesis of substrate **21**.



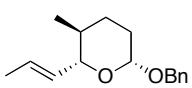
(5*S*,*E*)-8,8-Bis(benzyloxy)-5-methyloct-3-en-2-ol (21)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.44 (m, 10H), 5.44-5.56 (m, 2H), 4.76 (t, J = 5.6 Hz, 1H), 4.69 (d, J = 12.0 Hz, 2H), 4.59 (d, J = 12.0 Hz, 2H), 4.26 (p, J = 5.6 Hz, 1H), 2.07-2.18 (m, 1H), 1.72-1.82 (m, 2H), 1.65 (br, 1H) 1.37-11.49 (m, 2H), 1.27 (d, J = 6.4 Hz, 3H), 1.02 (d, J = 6.8 Hz, 1H) 1.01 (d, J =6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 136.1, 136.0, 133.08, 133.04, 128.5, 127.8, 127.7, 102.27, 102.25, 68.9, 68.8, 67.24, 67.15, 67. 13, 36.2, 36.1, 31.7, 31.6, 31.1, 23.6, 23.5, 20.6, 20.5 IR (neat) 3417, 3063, 3030, 2958, 2869, 1666, 1605, 1496, 1453, 1369, 1207, 1124, 1023, 972, 736 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{30}O_3Na$ $[M+Na]^+$ 377.2093, found 377.2063.



(2*S*, 3*S*, 6*S*)-6-(Benzyloxy)-3-methyl-2-((*E*)-prop-1-en-1-yl)tetrahydro-2H-pyran (22)

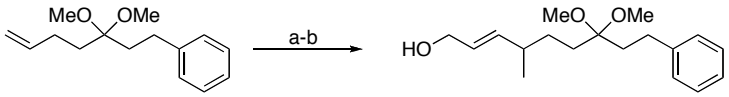
The general cyclization procedure was followed with **21** (50 mg, 0.14 mmol), Re_2O_7 (3 mg, 0.007 mmol), and CH_2Cl_2 (3 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (30 mg, 86%, dr = 3:1, *trans*: *cis* > 10:1 as determined by the ^{1}H NMR spectrum of the crude mixture). ^{1}H NMR (400 MHz, CD_2Cl_2) δ7.24-7.36 (m, 5H), 6.66 (dq, J = 6.4, 15.2 Hz, 1H), 5.39 (ddq, J = 1.6, 8, 15.2 Hz, 1H), 4.88 (dd, J = 2.0, 2.4 Hz, 1H), 4.67 (d, J = 12.0 Hz, 1H), 4.42 (d, J = 12.0 Hz, 1H), 3.74 (dd, J = 8.8, 9.2 Hz, 1H) 1.66-1.75 (m, 2H), 1.70 (dd, J = 1.6, 6.4 Hz, 3H), 1.48-1.58 (m, 2H), 1.35-1.47 (m, 1H), 0.77 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 138.8, 131.2, 128.8, 128.2, 127.8, 127.3, 96.4, 76.4, 68.3, 35.0, 30.2, 26.7, 17.8, 17.5. IR (neat) 3063, 3030, 2929, 2876, 1676, 1604, 1454, 1376, 1230, 1049, 1022, 972, 920, 730 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{22}O_2Na$ $[M+Na]^+$ 269.1517, found 269.1558 .



(2*S*, 3*S*, 6*R*)-6-(Benzyloxy)-3-methyl-2-((*E*)-prop-1-en-1-yl)tetrahydro-2H

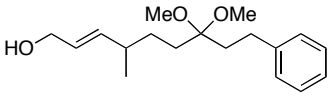
^{1}H NMR (400 MHz, C_6D_6) δ 7.35-7.38 (m, 2H), 7.14-7.19 (m, 2H), 7.05-7.11 (m, 1H), 5.67 (ddq, J = 0.8, 6.0, 15.2 Hz, 1H), 5.58 (ddq, J = 1.6, 6.8, 15.2 Hz, 1H), 5.01 (d, J =12.0 Hz, 1H), 4.59 (d, J = 12.0 Hz, 1H), 4.40 (dd, J = 2.8, 8.8 Hz, 1H), 3.28 (dd, J = 6.8, 9.6 Hz, 1H), 1.63-1.79 (m, 2H), 1.59 (d, J = 6.4 Hz, 3H), 1.49 (dq, J = 3.6, 13.2 Hz, 1H), 1.19-1.33 (m, 1H), 0.83-0.95 (m, 1H), 0.65 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.8, 131.3, 128.2, 127.8, 127.4, 127.2,

100.7, 82.6, 69.4, 34.9, 31.8, 31.2, 17.5, 17.1; IR (neat) 3030, 2950, 2929, 2853, 1676, 1606, 1454, 1365, 1146, 1102, 1078, 1031, 966, 735 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{22}O_2Na$ $[M+Na]^+$ 269.1517, found 269.1529.

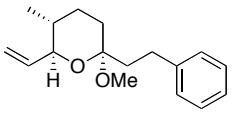


Reagents and conditions
a) Vinyl oxirane, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 25%. b) $Me_2CuCNLi$, THF, –78 °C to rt, 60%

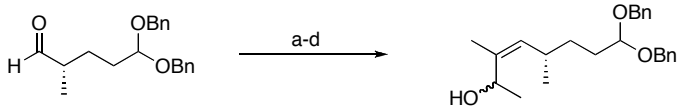
Scheme 7. Synthesis of substrate **23**.



(*E*)-7,7-dimethoxy-4-methyl-9-phenylnon-2-en-1-ol (23)
^1H NMR (500 MHz, C_6D_6) δ 7.05-7.21 (m, 5H), 5.48 (dt, J = 5.5, 15.5, 1H), 5.42 (ddt, J = 1.0, 7.5, 15.5 Hz, 1H), 3.86 (br, 2H), 3.07 (s, 3H), 3.06 (s, 3H), 2.62-2.66 (m, 2H), 1.95-2.04 (m, 3H), 1.65-1.80 (m, 2H), 1.34 (q, J = 7.0 , 2H), 0.95 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.1, 136.8, 128.6, 128.4, 128.3, 125.8, 102.9, 63.1, 47.2, 36.7, 34.6, 30.9, 30.4, 30.3, 20.4; IR (neat) 3403, 3025, 2955, 2869, 1667, 1603, 1454, 1374, 1299,1185, 1058, 972, 741 cm^{-1}; HRMS (APCI) calcd for $C_{18}H_{29}O_3$ $[M+H]^+$ 293.2117, found 293.2088.

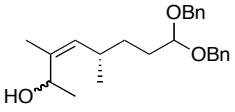


(±)-(2*S*, 5*R*, 6*S*)-2-Methoxy-5-methyl-2-phenethyl-6-vinyltetrahydro-2H-pyran (24)
The general rearrangement procedure was followed with **23** (50 mg, 0.17 mmol), Re_2O_7 (4 mg, 0.008 mmol), and CD_2Cl_2 (3.0 mL). The reaction was stirred at 0 °C for 30 min, after which the cold bath was removed, the reaction was stirred for another 10 min, then was quenced with pyridine (25 μL). $BnMe_2SiH$ (5 μl) was added as an internal standard, and a ^1H NMR spectrum was taken of the crude mixture to determine the yield (81%, dr = 10:1). ^1H NMR (500 MHz, CD_2Cl_2) δ 7.24-7.29 (m, 2H), 7.14-7.22 (m, 2H), 5.78 (ddd, J = 7.5, 10.0, 17.5 Hz, 1H), 5.23 (dd, J = 17.5, 2.0 Hz, 1H), 5.14 (dd, J = 10.0, 17.5 Hz, 1H), 3.60 (dd, J = 7.5, 10.0 Hz, 1H), 2.61 (m, 2H), 1.97 (ddd, J = 5.0, 12.0, 14.0 Hz, 2H), 1.81-1.85 (m, 1H), 1.76 (ddd, J = 4.5, 12.5, 14.0 Hz, 2H), 1.50-1.62 (m, 3H), 1.31-1.38 (m, 1H), 0.82 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) 142.4, 138.1,128.3, 128.2, 125.7, 116.5, 98.8, 78.1, 47.1, 38.0, 34.5, 32.9, 29.8, 27.6, 17.5; IR 3063, 3026, 2953, 2875, 1645, 1605, 1496, 1455, 1368, 1236, 1079, 1041, 932, 740 (neat) cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{24}O_2Na$ $[M+Na]^+$ 283.1674, found 283.1700.



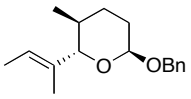
Reagents and conditions
a) Diethyl phosphonopropionate, NaH, THF, 65%. b) DIBAL-H, CH_2Cl_2, –78 °C, 95%.
c) IBX, DMSO, 100%. d) MeMgBr, THF, 0 °C, 100%, dr = 2.2:1.

Scheme 8. Synthesis of substrate **25**.

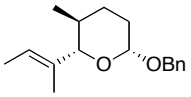


(5*S*, *Z*)-8,8-Bis(benzyloxy)-3,5-dimethyloct-3-en-2-ol (25)
Major isomer: ^1H NMR (400 MHz, C_6D_6) δ 7.31-7.36 (m, 2H), 7.16-7.21 (m, 2H), 7.09-7.12 (m, 1H), 4.83 (d, J = 10.0 Hz, 1H), 4.71 (t, J = 5.6 Hz, 1H), 4.61 (dd, J = 4.8, 12.0 Hz, 2 H), 4.52-4.58 (m, 1H), 4.49 (d, J = 12.0 Hz, 2H), 2.27-2.39 (m, 1H), 1.70-1.87 (m, 2H), 1.70 (d, J = 0.8 Hz, 3H), 1.38-1.46 (m, 1H), 1.22-1.34 (m, 1H), 1.13 (dd, J = 2.8, 6.4 Hz, 3H), 0.84 (d, J =6.4 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 138.62, 138.58, 137.2, 132.5, 128.3, 127.8, 127.9,127.50, 127.49, 102.55, 67.4, 67.2, 65.6, 32.5, 31.4, 31.3, 21.52, 21.49, 16.8; IR (neat) 3439, 3063, 3030, 2954, 2867, 1605, 1496, 1453, 1375, 1121, 1024, 736 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{32}O_3Na$ $[M+Na]^+$ 391.2249, found 391.2263. Minor isomer: ^1H NMR (400 MHz, C_6D_6) δ 7.29-7.35

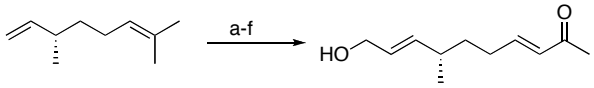
(m, 2H), 7.14-7.21 (m, 2H), 7.07-7.13 (m, 1H), 4.85 (d, J = 9.6 Hz, 1H), 4.68 (t, J = 5.6 Hz, 1H), 4.60 (dd, J = 3.6, 12.0 Hz, 2H), 5.53-4.60 (br, 1H), 4.47 (d, J = 12.0 Hz, 2H), 2.25-2.40 (m, 1H), 1.60-1.80 (m, 2H), 1.70 (s, 3H), 1.35-1.45 (m, 1H), 1.23-1.34 (m, 1H), 1.50 (dd, J = 1.2, 6.4 Hz, 3H), 0.60 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.8, 137.4, 132.2, 128.3, 127.6, 127.4, 102.1, 66.9, 66.8, 65.4, 32.6, 31.5, 31.4, 21.6, 21.5, 17.1; IR (neat) 3415, 3063, 3030, 2920, 1605, 1496, 1453, 1376, 1119, 1024, 898, 735 cm^{-1}; HRMS (APCI) calcd for $C_{24}H_{32}O_3Na$ [M+Na]$^+$ 391.2249, found 391.2242.



(2*S*, 3*S*, 6*S*)-6-(Benzyloxy)-2-((*E*)-but-2-en-2-yl)-3-methyltetrahydro-2H-pyran (26)
The general cyclization procedure was followed with **25** (50 mg, 0.14 mmol), Re_2O_7 (3 mg, 0.007 mmol), and CH_2Cl_2 (1.5 mL), the reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (32 mg, 91%, dr = 3:1). ^{1}H NMR (400 MHz, C_6D_6) δ 7.34-7.37 (m, 2H), 7.14-7.20 (m, 2H), 7.06-7.11 (m, 1H), 5.44 (qq, J = 1.2, 6.8 Hz, 1H), 4.92 (d, J = 3.2 Hz, 1H), 4.79 (d, J = 12.4 Hz, 1H), 4.43 (d, J = 12.4 Hz, 1H), 3.92 (d, J = 10.4 Hz, 1H), 1.66-1.78 (m, 2H), 1.71 (d, J = 1.2 Hz, 3H), 1.52-1.63 (m, 2H), 1.53 (dq, J = 1.2, 6.4 Hz, 3H), 1.39-1.46 (m, 1H), 0.68 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.0, 135.2, 128.2, 127.6, 127.2, 122.8, 96.1, 91.8, 68.1, 32.1, 20.4,27.0, 17.8, 12.7, 10.8; IR (neat) 3030, 2950, 2927, 2888, 1671, 1604, 1485, 1376, 1231, 1123, 1020, 920, 727 cm^{-1}; HRMS (APCI) calcd for $C_{17}H_{24}O_2Na$ [M+Na]$^+$ 283.1674, found 283.1665.

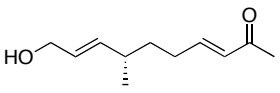


(2*S*, 3*S*, 6*R*)-6-(Benzyloxy)-2-((*E*)-but-2-en-2-yl)-3-methyltetrahydro-2H-pyran
^{1}H NMR (400 MHz, C_6D_6) δ 7.32-7.37 (m, 2H), 7.13-7.19 (m, 2H), 7.05-7.10 (m, 1H), 5.42 (q, J = 6.4 Hz, 1H), 4.97 (d, J = 12.o Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.20 (dd, J = 2.4, 9.2 Hz, 1H), 1.62-1.79 (m, 2H), 1,72 (s, 3H), 1.53 (d, J = 6.8 Hz, 3H), 1.48-1.56 (m, 1H), 1.37-1.48 (m, 1H), 0.85-0.97 (m, 1H), 0.58 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.9, 135.2, 128.1, 127.8, 127.2, 122.4, 101.0, 88.5, 69.4, 31.9, 31.7, 31.2, 17.0, 12.7, 12.7, 11.1; IR (neat) 3063, 3029, 2950, 2926 2854, 1672, 1607, 1454, 1375, 1308, 1148, 1056, 1021, 734 cm^{-1}; HRMS (APCI) calcd for $C_{17}H_{24}O_2Na$ [M+Na]$^+$ 283.1674, found 283.1685.

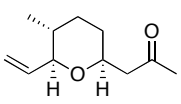


Reagents and conditions
a) O_3, CH_2Cl_2, –78 °C, then Me_2S, 33%. b) $(MeO)_3CH$, *p*-TsOH, MeOH, 50 °C, 52%.
c) Methyl acrylate, Grubbs-Hoveyda second generation metathesis catalyst, CH_2Cl_2, reflux, 85%. d) DIBAL-H, CH_2Cl_2, –78 °C, 58%. e) HOAc, H_2O, 95%.
f) $(EtO)_2P(O)CH_2C(O)CH_3$, NaH, THF, 58%.

Scheme 9. Synthesis of substrate **27**.

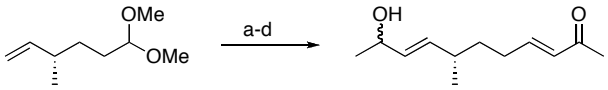


(7*S*,3*E*,8*E*)-10-hydroxy-7-methyldeca-3,8-dien-2-one (27)
^{1}H NMR (300 MHz, CD_2Cl_2) δ 6.77 (dt, J = 6.9, 15.9 Hz, 1H), 6.01 (dt, J = 1.5, 15.9 Hz, 1H), 5.45-5.64 (m, 2H), 4.03 (d, J = 5.1 Hz, 2H), 2.08-2.26 (m, 4H), 2.18 (s, 3H), 1.39-1.49 (m, 2H), 0.99 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 198.6, 148.5, 137.1, 131.2, 128.5, 63.2, 36.0, 35.0, 30.2, 26.6, 20.2; IR (neat) 3426, 2957, 2924, 2868, 1672, 1625, 1427, 1363, 1256, 975 (neat) cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{18}O_2Na$ [M+Na]$^+$ 205.1204, found 205.1235.



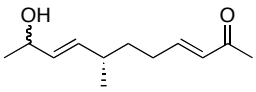
1-((2R,5S,6R)-5-methyl-6-vinyltetrahydro-2H-pyran-2-yl)propan-2-one (28)
The general rearrangement procedure was followed with **27** (26.5 mg, 0.145 mmol), Re_2O_7 (3.5 mg, 0.007 mmol), and CH_2Cl_2 (1.5 mL). The reaction was stirred at rt for 24hr and then quenched with pyridine (25 μL). $Me_2(Bn)SiH$ (5 μl) was added as an internal standard and crude NMR was used to determine the yield of 88%. ^{1}H NMR (400 MHz, CH_2Cl_2) δ 5.75 (ddd, J = 6.8, 10.4 Hz, 17.2, 1H), 5.18 (ddd, J = 1.2, 2.0, 17.2 Hz, 1H), 5.11 (ddd, J = 0.8, 2.0, 10.4 Hz, 1H) 3.71-3.78 (m, 1H) 3.36 (dd, J = 7.2, 8.8 Hz, 1H), 2.62 (dd, J = 7.6, 15.6 Hz, 1H), 2.42 (dd, J = 5.2, 15.6 Hz, 1H), 2.12 (s,

3H), 1.77-1.82 (m, 1H), 1.60-1.65 (m, 1H), 1.17-1.36 (m, 3H), 0.78 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CH_2Cl_2) δ 207.0, 137.9, 116.2, 85.1, 73.7, 50.2, 34.9, 32.3, 31.8, 30.5, 17.4; IR (neat) 3079, 2927, 2873, 2851,1716, 1457, 1425, 1356, 1225, 1152, 1072, 1018, 991, 923 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{18}O_2Na$ [M+Na]$^+$ 205.1204, found 205.1224.

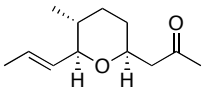


Reagents and conditions
a) Methyl vinyl ketone, Grubbs-Hoveyda second generation metathesis catalyst, CH_2Cl_2, reflux, 85%. b) DIBAL-H, CH_2Cl_2, –78 °C, 45%, two steps. c) HOAc, H_2O, 82%. d) $(EtO)_2P(O)CH_2C(O)CH_3$, NaH, THF, 53%.

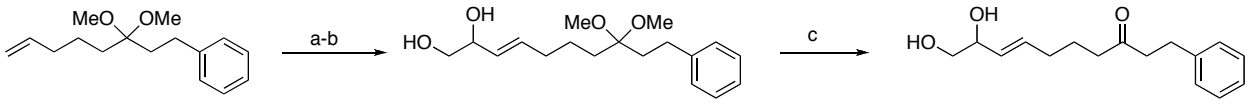
Scheme 10. Synthesis of substrate **29**.



(3*E*,7*S*,8*E*)-10-hydroxy-7-methylundeca-3,8-dien-2-one (29)
^{1}H NMR (300 MHz, CD_2Cl_2) δ 6.76 (dt, J = 6.9, 15.9 Hz, 1H), 6.03 (dd, J = 1.2, 15.9 Hz, 1H), 5.38-5.52 (m, 2H), 4.26 (q, J = 6.0 Hz, 2H), 2.21 (s, 3H), 2.04-2.21 (m, 3H), 1.38-1.47 (m, 2H), 1.23 (d, J = 6.3 Hz, 3H), 0.98 (d, J = 6.6 Hz, 1.5H), 0.97 (d, J = 6.6 Hz, 1.5H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 198.8, 148.47, 148.42, 135.4, 135.3, 133.5, 131.2, 68.7, 68.6, 35.89, 35.87, 35.0, 30.2, 26.9, 23.6, 23.56, 20.4; IR (neat) 3431, 2966, 2925, 2870, 1672, 1625, 1453, 1364, 1255, 1140, 1059, 975 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{20}O_2Na$ [M+Na]$^+$ 219.1361, found 219.1392.

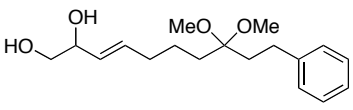


1-((2*R*,5*S*,6*S*)-5-methyl-6-((*E*)-prop-1-en-1-yl)tetrahydro-2H-pyran-2-yl)propan-2-one (30)
The general rearrangement procedure was followed with **29** (20.0 mg, 0.102 mmol), Re_2O_7 (2.5 mg, 0.005 mmol), and CH_2Cl_2 (1.5 mL). The reaction was stirred at rt for 50 min and then was quenched with pyridine (25 μL). $Me_2(Bn)SiH$ (5 μl) was added as an internal standard. Crude ^{1}H NMR was used to determine the yield of 90%. ^{1}H NMR (400 MHz, CH_2Cl_2) δ 5.68 (ddq, J = 0.8, 6.4, 15.2 Hz, 1H), 5.40 (ddq, J = 1.6, 7.6, 15.2 Hz, 1H), 3.77 (dddd, J = 2.4, 2.4, 6.4, 10.8 Hz, 1H) 3.35 (dd, J = 8.4, 8.8 Hz, 1H), 2.74 (dd, J = 6.4, 15.6 Hz, 1H), 2.47 (dd, J = 6.0, 15.6 Hz, 1H), 2.17 (s, 3H), 1.78-1.84 (m, 1H), 1.70 (dd, J = 1.6, 6.4 Hz, 3H), 1.64-1.69 (m, 1H), 1.20-1.37 (m, 3H), 0.78 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CH_2Cl_2) δ 207.5, 130.9, 129.0, 85.1, 73.6, 50.3, 35.0, 32.3, 31.9, 31.0, 17.9, 17.8; IR (neat) 2925, 2872, 2852, 1716, 1676, 1453, 1357, 1224, 1186, 1169, 1151, 1069, 1014, 965 cm^{-1}; HRMS (APCI) calcd for $C_{12}H_{20}O_2Na$ [M+Na]$^+$ 219.1361, found 219.1383.

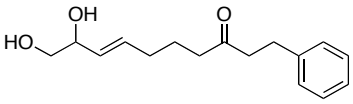


Reagents and conditions
a) Butenediol bis(triethylsilyl) ether, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 42%. b) Bu_4NF, THF, 97%. c) HOAc, H_2O, 85%.

Scheme 11. Synthesis of substrate **38** and **46**.

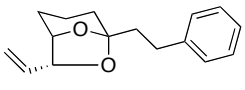


(*E*)-8,8-Dimethoxy-10-phenyldec-3-ene-1,2-diol (38)
^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.23-7.29 (m, 2H), 7.14-7.21 (m, 3H), 5.76 (ddt, J = 2.0, 7.0, 15.5 Hz, 1H), 5.47 (ddt, J = 1.2, 6.5, 5.0 Hz, 1H), 4.11-4.18 (m, 1H), 3.54-3.60 (m, 1H), 3.39-3.45 (m, 1H), 3.24 (s, 6H), 2.51-2.56 (m, 2H), 2.24 (br, 1H), 2.04-2.10 (q, J = 7.0 Hz, 2H), 2.04-2.10 (br, 1H), 1.81-1.86 (m, 2H), 1.59-1.64 (m, 2H), 1.34-1.41 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 142.2, 133.2, 129.4, 128.3, 128.2, 125.8, 102.8, 73.1, 66.6, 47.5, 34.2, 32.3, 31.8, 30.1, 23.2; IR (neat) 3399, 3061, 3025, 2949, 2828, 1669, 1603, 1495, 1454, 1303, 1182, 1072, 971, 742 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{28}O_4Na$ [M+Na]$^+$ 331.1885, found 331.1889.



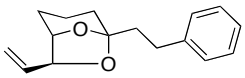
(*E*)-9,10-Dihydroxy-1-phenyldec-7-en-3-one (46)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.23-7.30 (m, 2H), 7.14-7.20 (m, 3H), 5.69 (ddt, *J* = 1.2, 6.8, 15.2 Hz, 1H), 5.43 (ddt, *J* = 1.4, 6.4, 15.2 Hz, 1H), 4.09-4.17 (m, 1H), 3.56 (dd, *J* = 2.0, 10.8 Hz, 1H), 3.41 (dd, *J* = 7.4, 11.2 Hz, 1H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.85 (br, 1H), 2.71 (t, *J* = 7.4 Hz, 2H), 2.71 (br, 1H), 2.38 (t, *J* = 7.4 Hz, 2H), 2.01 (q, *J* = 7.4 Hz, 2H), 1.62 (p, *J* = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 210.0, 141.4, 132.5, 129.6, 128.4, 128.3, 126.0, 73.0, 66.6, 44.1, 42.0, 31.6, 29.6, 23.0; IR (neat) 3378, 3030, 2929, 1709, 1603, 1495, 1453, 1408, 1372, 1074, 1029, 972, 748 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{22}O_3Na$ $[M+Na]^+$ 285.1467, found 285.1470.



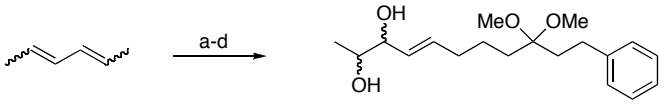
(±)-(1*R*, 5*S*, 7*S*)-5-Phenethyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (40)

The general rearrangement procedure was followed with **38** (100 mg, 0.32 mmol), Re_2O_7 (8 mg, 0.02 mmol), and CH_2Cl_2 (5.0 mL). The reaction was stirred at rt for 21 h then was quenched with pyridine (25 μL). The crude material was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (39 mg, 49%, dr = 4:3, for substrate **46**, 40%, dr = 4:3). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.22-7.29 (m, 2H), 7.18-7.22 (m, 2H), 7.12-7.18 (m, 1H), 6.05 (ddd, *J* = 6.8, 10.4, 17.2 Hz, 1H), 5.42 (dt, *J* = 1.6, 17.2 Hz, 1H), 5.29 (ddd, J = 1.2, 1.6, 10.4, 1H), 4.49 (ddq, J = 1.2, 4.4, 6.8, 1H), 4.30 (t, J = 4.0), 2.73-2.79 (m, 2H), 1.94-2.00 (m, 2H), 1.90-2.00 (m, 1H), 1.72-1.83 (m, 1H), 1.63-1.79 (m, 2H), 1.53-1.63 (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 142.7, 133.3, 128.34, 128.25, 125.6, 118.4, 108.7, 81.6, 77.7, 39.9, 33.4, 29.0, 24.6, 17.1; IR (neat) 3062, 2954, 2915, 1603, 1496, 1456, 1373, 1253, 1236, 1099, 1028, 988, 862,749 cm^{-1}; HRMS (APCI) calcd for $C_{16}H_{21}O_2$ $[M+H]^+$ 245.1442, found 245.1521.



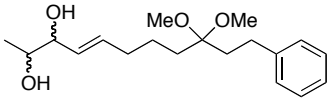
(±)-(1*R*, 5*S*, 7*R*)-5-Phenethyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (39)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.23-7.28 (m, 2H), 7.13-7.21 (m, 3H), 5.88 (ddd, *J* = 7.2, 10.0, 17.2 Hz, 1H), 5.24 (ddd, *J* = 1.2, 1.6, 17.2 Hz, 1H), 5.10 (ddd, *J* = 0.8, 1.6, 10.0 Hz, 1H), 4.44 (dd, *J* = 0.4, 3.6 Hz, 1H), 4.20 (br, 1H), 2.72-2.78 (m, 2H), 1.94-2.00 (m, 2H), 1.85-1.94 (m, 1H), 1.75-1.84 (m, 1H), 1.61-1.69 (m, 3H), 1.54-1.61 (m, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 142.6, 139.0, 128.32, 128.27, 125.6, 115.3, 109.3, 80.8, 79.8, 39.6, 33.9, 29.4, 28.1, 17.1; IR (neat) 3062, 3026, 2925, 2871, 1728, 1607, 1496, 1457, 1374, 1343, 1278, 1234, 1179, 1111, 1085, 1032, 1004, 924, 750 cm^{-1}; HRMS (APCI) calcd for $C_{16}H_{21}O_2$ $[M+H]^+$ 245.1442, found 245.1581.



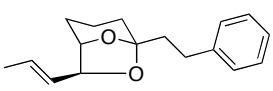
Reagents and conditions
a) AD-Mix β, $CH_3SO_2NH_2$, *t*BuOH, H_2O, 0 °C. b) TESCl, imidazole, DMAP, DMF, 74% (two steps). c) Alkenyl ketal, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 27%. d) Bu_4NF, THF, 75%,

Scheme 12. Synthesis of **43**.



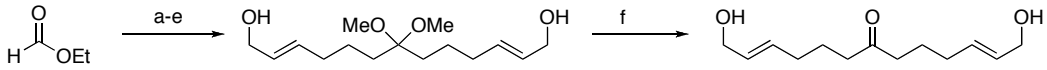
(*E*)-9,9-dimethoxy-11-phenylundec-4-ene-2,3-diol (43)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.25-7.30 (m, 2H), 7.15-7.21 (m, 3H), 5.75 (ddt, *J* = 0.8, 6.8, 15.2 Hz, 1H), 5.46 (ddt, *J* = 1.4, 7.2, 15.2 Hz, 1H), 3.74 (t, *J* = 6.8 Hz, 1H), 3.60 (t, *J* = 6.4 Hz, 1H), 3.15 (s, 6H), 2.51-2.56 (m, 2H), 2.08 (q, *J* = 6.8 Hz, 2H), 1.82-1.88 (m, 2H), 1.60-1.65 (m, 2H), 1.35-1.43 (m, 2H), 1.12 (d, *J* =6.0 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 142.2, 133.9, 130.0, 128.4, 128.2, 125.8, 102.9, 77.8, 70.8, 47.5, 34.2, 32.4, 31.9, 30.1, 23.2, 18.8; IR (neat) 3411, 3061, 3025, 2951, 2829, 1669, 1603, 1495, 1454, 1368, 1266, 1181, 1055, 972, 742 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{30}O_4Na$ $[M+Na]^+$ 345.2042, found 345.2051.



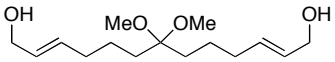
(1*R*, 5*S*, 7*R*)-5-Phenethyl-7-((*E*)-prop-1-en-1-yl)-6,8-dioxabicyclo[3.2.1]octane (44)

The general cyclization procedure was followed with **43** (50 mg, 0.16 mmol), Re_2O_7 (4 mg, 0.008 mmol), and CH_2Cl_2 (5.0 mL). The reaction was stirred at rt for 15 h and then was quenched with pyridine (25 μL). The crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (21 mg, 53%, dr = 7.5 : 1). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.23-7.29 (m, 2H), 7.18-7.22 (m, 2H), 7.12-7.18 (m, 1H), 5.67 (ddt, *J* = 0.4, 6.4, 15.2 Hz, 1H), 5.52 (ddt, *J* = 1.4, 8.0, 15.2 Hz, 1H), 4.40 (d, *J* = 8.0 Hz, 1H), 2.72-2.78 (m, 2H), 1.91-1.98 (m, 2H), 1.83-1.91 (m, 1H), 1.73-1.81 (m, 1H), 1.69 (dd, *J* = 1.6, 6.4 Hz, 3H), 1.59-1.66 (m, 3H), 1.52-1.58 (m, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 142.7, 132.1, 128.33, 128.25, 127.3, 125.6, 108.9, 80.7, 79.9, 39.6, 34.0, 29.4, 28.1, 17.3, 17.1; IR (neat) 3061, 3026, 2950, 1671, 1603, 1496, 1453, 1373, 1344, 1175, 1067, 1024, 990, 906, 751 cm^{-1}; HRMS (APCI) calcd for $C_{17}H_{23}O_2$ $[M+H]^+$ 259.1698, found 259.1673.



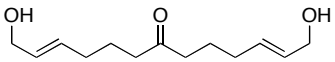
Reagents and conditions
a) Pentenylmagnesium bromide, THF, 0 °C, 82%. b) PCC, Celite, CH_2Cl_2, 81%. c) $(MeO)_3CH$, *p*-TsOH, MeOH, 50 °C, 92%. d) Methyl acrylate, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 68%. e) DIBAL-H, CH_2Cl_2, –78 °C, 77%. f) HOAc, H_2O, 84%.

Scheme 13. Synthesis of substrates **47** and **50**.



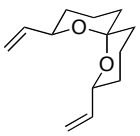
(2*E*,11*E*)-7,7-dimethoxytrideca-2,11-diene-1,13-diol (47)

^{1}H NMR (400 MHz, C_6D_6) δ 5.53-5.75 (m, 4H), 4.06 (br, 4H), 3.22-3.38 (br, 2H), 3.07 (s, 6H), 2.00 (q, *J* = 3.2 Hz, 4H), 1.65-1.71 (m, 4H), 1.42 (p, *J* = 7.6 Hz, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 131.2, 130.3, 103.3, 62.9, 47.2, 32.3, 32.1, 23.5; IR (neat) 3384, 2946, 1710, 1670, 1457, 1369, 1314, 1180, 1088, 970 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{28}O_4Na$ $[M+Na]^+$ 295.1885, found 295.1860.



(2*E*,11*E*)-1,13-dihydroxytrideca-2,11-dien-7-one (50)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.60-5.70 (m, 4H), 4.06 (br, 4H), 2.42 (t, *J* = 7.2 Hz, 4H), 2.25-2.35 (br, 2H), 2.02-2.09 (m, 4H), 1.66 (p, *J* = 7.2 Hz, 4H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 211.0, 131.5, 130.1, 63.2, 41.8, 31.5, 23.1; IR (neat) 3250, 3052, 3011, 2933, 2865, 1698, 1457, 1415, 1371, 1266, 1088, 1016, 970 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{22}O_3Na$ $[M+Na]^+$ 249.1467, found 249.1451.

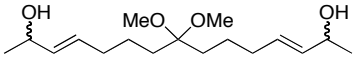


(±)-(2*R*, 6*R*, 8*R*)-2,8-Divinyl-1,7-dioxaspiro[5.5]undecane (48)

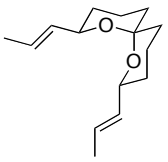
The general rearrangement procedure was followed with **47** (14 mg, 0.051 mmol), Re_2O_7 (1.2 mg, 0.0025 mmol), and CD_2Cl_2 (1.0 mL). The reaction was stirred at rt for 30 min. $BnMe_2SiH$ (5 μl) was added as an internal standard, and a ^{1}H NMR spectrum was taken of the crude mixture to show an 88% yield and 1:1 ratio of two stereoisomers. Additional stirring (>12 h) resulted in the mixture giving essentially a single diastereomer (dr > 20:1) with a decrease in overal yield (60%). The general rearrangement cyclization procedure was also followed with **50** (50 mg, 0.221 mmol), Re_2O_7 (5.4 mg, 0.011 mmol), and CD_2Cl_2 (3.0 mL). The reaction was stirred at rt for 30 min. $BnMe_2SiH$ (5 μl) was added as an internal standard, and a ^{1}H NMR spectrum was taken of the crude mixture to show a 94% yield and 1:1 ratio of two stereoisomers. Additional stirring (48 h) with the addition of MeOH showed isomerization of the mixture to give essentially a single stereoisomer with a decrease in overall yield (61%). ^{1}H NMR (400 MHz, C_6D_6) δ 5.89 (ddd, *J* = 5.2, 10.4, 17.2 Hz, 2H), 5.30 (dt, *J* = 1.6, 17.2 Hz, 2H), 5.02 (dt, *J* = 1.6, 10.4 Hz, 2H), 4.17 (ddddd, *J* = 1.2, 1.6, 2.4, 5.6, 11.2 Hz, 2H), 2.03 (dq, *J* = 4.0, 13.2 Hz, 2H), 1.63 (dddd, *J* = 1.6, 2.4, 4.0, 13.2 Hz, 2H), 1.41-1.49 (m, 2H), 1.34-1.41 (m, 2H), 1.17-1.34 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 140.0 113.2, 95.9, 69.7, 35.2, 31.1, 18.8; IR 3012, 2927, 2854, 1646, 456, 1374, 1279, 1220, 981, 917 (neat) cm^{-1}; HRMS (APCI) calcd for $C_{13}H_{21}O_2$ $[M+H]^+$ 209.1542, found 209.1567.

Reagents and conditions
a) Methyl vinyl ketone, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 44%. b) DIBAL-H, CH_2Cl_2, –78 °C, 81%.

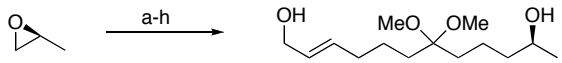
Scheme 14. Synthesis of substrate **51**.



(3*E*, 12*E*)-8,8-dimethoxypentadeca-3,12-diene-2,14-diol (51)
^{1}H NMR (400 MHz, C_6D_6) δ 5.52-5.62 (m, 4H), 4.21 (p, J = 5.2 Hz, 2H), 3.07 (s, 6H), 2.89 (br, 2H), 1.94-2.0 (m, 4H), 1.65-1.70 (m, 4H), 1.37-1.45 (m, 4H), 1.25 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 135.5, 129.1, 103.2, 68.1, 47.1, 32.1, 32.0, 23.6, 23.5; IR (neat) 3388, 2950, 1711, 1670, 1455, 1368, 1294, 1181, 1060, 969, 941, 864 cm^{-1}; HRMS (APCI) calcd for $C_{17}H_{32}O_4Na$ $[M+Na]^+$ 323.2198, found 323.2199.

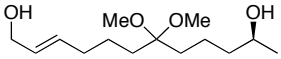


(±)-(2*R*, 6*R*, 8*R*)-2,8-Di((*E*)-prop-1-en-1-yl)-1,7-dioxaspiro[5.5]undecane (52)
The general rearrangement procedure was followed with **51** (44 mg, 0.15 mmol), Re_2O_7 (4 mg, 0.007 mmol), and CD_2Cl_2 (3.0 mL). The reaction was stirred at 0 °C for 60 min. $BnMe_2SiH$ (5 µl) was added as an internal standard, and a ^{1}H NMR spectrum was taken of the crude mixture to show a 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (ddq, J = 1.2, 6.4, 15.2 Hz, 2H), 5.52 (ddq, J = 1.6, 6.4, 15.2 Hz, 2H), 4.04 (ddp, J = 1.2, 6.4, 11.6 Hz, 2H), 1.94 (tq, J = 4.0, 13.2 Hz, 2H), 1.71 (dd, J = 1.6, 6.4 Hz, 6H), 1.52-1.67 (m, 6H), 1.36-1.45 (m, 2H), 1.25-1.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 126.4, 96.4, 69.6, 35.1, 31.0, 18.8, 17.9; IR 2937, 2867, 1731, 1676, 1452, 1438, 1377, 1279, 1219, 1201,1036, 979, 964 (neat) cm^{-1}; HRMS (APCI) calcd for $C_{15}H_{25}O_2$ $[M+H]^+$ 237.1855, found 237.1837.

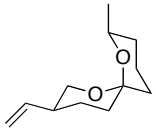


Reagents and conditions
a) Butenylmagnesium bromide, CuCN, Et_2O, 0 °C, 30%. b) $Me_3CC(O)Cl$, Et_3N, DMAP, CH_2Cl_2. c) O_3, CH_2Cl_2, –78 °C, then Me_2S, 27% (two steps). d) Pentenylmagnesium bromide, Et_2O, 0 °C, 56%. e) PCC, Celite, CH_2Cl_2, 86%. f) $(MeO)_3CH$, *p*-TsOH, MeOH, 100%. g) Methyl acrylate, Grubbs-Hoveyda second generation metathesis catalyst, CH_2Cl_2, reflux, 96%. h) DIBAL-H, CH_2Cl_2, –78 °C, 66%

Scheme 15. Synthesis of substrate **53**.

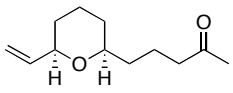


(*S*, *E*)-7,7-dimethoxydodec-2-ene-1,11-diol (53)
^{1}H NMR (400 MHz, C_6D_6) δ 5.58-5.71 (m, 2H), 4.04 (br, 2H), 3.63-3.70 (m, 1H), 3.09 (s, 3H), 3.08 (s, 3H), 1.95-2.05 (m, 2H), 1.62-1.76 (m, 4H), 1.28-1.60 (m, 6H), 1.12 (d, J = 6.0, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 131.1, 130.5, 103.4, 67.2, 62.9, 47.2, 39.4, 32.6, 32.1, 31.8, 23.6, 23.4, 20.1; IR (neat) 3396, 2949, 2871, 1669, 1458, 1372, 1131, 1041, 971 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{28}O_4Na$ $[M+Na]^+$ 283.1885, found 283.1915; $[\alpha]_D$ = + 6.26 (c 0.91, $CHCl_3$); ee>99% as determined by Mosher ester analysis.



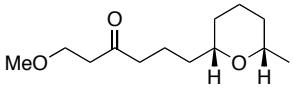
(2*S*, 6*R*, 8*R*)-2-methyl-8-vinyl-1,7-dioxaspiro[5.5]undecane (55)
The general rearrangement procedure was followed with **53** (50 mg, 0.19 mmol) and Re_2O_7 (5 mg, 0.01 mmol) in CD_2Cl_2 (3.0 mL), the reaction was stirred at rt for 24 h. $BnMe_2SiH$ (5 µl) was added as an internal standard, and a ^{1}H NMR spectrum was taken of the crude mixture to show a 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.26 (dt, J = 1.6, 17.2 Hz, 1H), 5.09 (dt, J = 1.6, 10.4 Hz, 1H), 4.08 (ddddd, J = 1.2, 1.6, 2.4, 5.2, 10.4 Hz, 1H)，3.72 (ddddd, J = 2.0, 6.0, 6.0, 6.0, 8.0 Hz, 1H), 1.86-2.02 (m, 2H), 1.49-1.70 (m, 6H), 1.35-1.46 (m 2H), 1.18-1.35 (m, 2H), 1.15 (d, J = 6.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 114.0, 96.3, 69.5, 65.2, 35.2, 35.1 32.7, 30.8, 21.9, 18.9, 18.8; IR (neat) 2924, 2853, 1658, 1459, 1377, 1224, 1087, 992 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{20}O_2Na$ $[M+Na]^+$ 219.1361, found 219.1387.

$[\alpha]_D$ = – 43.2 (c 0.31, $CHCl_3$); ee: 96% as determined by HPLC analysis using a Phenomenex Lux 5μ Cellulose-3 column (250 x 4.60 mm) with MeOH/H_2O (60/40, v/v) as the mobile phase.



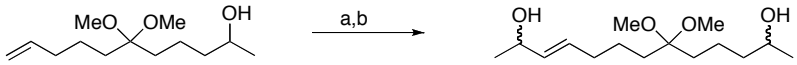
5-((2*S*, 6*R*)-6-vinyltetrahydro-2H-pyran-2-yl)pentan-2-one (57)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.82 (ddd, *J* = 5.2, 10.4, 17.2 Hz, 1H), 5.18 (dt, *J* = 1.6, 17.2 Hz, 1H), 5.02 (dt, *J* = 1.6, 10.4 Hz, 1H), 3.77 (ddddd, *J* = 1.2, 1.6, 2.4, 5.2, 10.8 Hz, 1H), 3.30 (dddd, *J* = 2.0, 5.2, 7.6, 10.8 Hz, 1H), 2.41 (t, *J* = 7.2 Hz, 2H), 2.08 (s, 3H), 1.78-1.85 (m, 2H), 1.35-1.70 (m, 6H), 1.08-1.27 (m, 4H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 208.7, 140.0, 113.5, 78.0, 77.3, 43.5, 35.8, 31.6, 31.3, 29.6, 23.5, 20.0; IR 3080, 2933, 2857, 1715, 1647, 1440, 1410, 1364, 1201, 1167, 1090, 1046, 990,919 (neat) cm^{-1}; HRMS (APCI) calcd for $C_{12}H_{21}O_2$ $[M+H]^+$ 197.1542, found 197.1566.



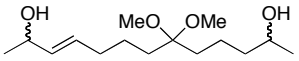
1-methoxy-6-((2S,6S)-6-methyltetrahydro-2H-pyran-2-yl)hexan-3-one (58)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 3.58 (t, *J* = 6.4, 2H), 3.36 (ddddd, *J* = 2.0, 6.0, 6.0, 6.0, 11.2, 1H), 3.22 (dddd, *J* = 2.0, 5.2, 7.2, 10.8, 1H), 1.72-1.81 (m, 1H), 1.58-1.78 (m, 1H), 1.47-1.58 (m, 4H), 1.27-1.47 (m, 3H), 1.09 (d, *J* = 6.4, 3H), 1.05-1.15 (m, 1H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 209.0, 77.3, 73.6, 67.6, 58.5, 43.1, 42.7, 35.9, 33.4, 31.3, 23.7, 22.0, 19.8. IR (neat) 2967, 2930, 2860, 1714, 1452, 1387, 1373, 1322, 1202, 1118, 1083, 1041, 963 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{24}O_3Na$ $[M+Na]^+$ 251.1623, found 251.1637.



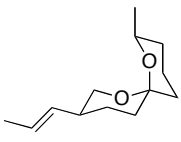
Reagents and conditions
a) Methyl vinyl ketone, Grubbs-Hoveyda metathesis catalyst, CH_2Cl_2, reflux, 53%. b) DIBAL-H, CH_2Cl_2, –78 °C, 61%.

Scheme 16. Synthesis of substrate **54**.



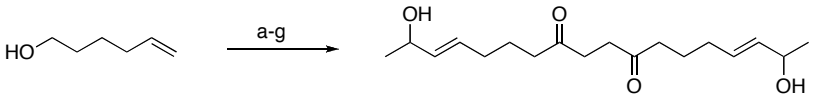
(*E*)-8,8-dimethoxytridec-3-ene-2,12-diol (54)

^{1}H NMR (400 MHz, C_6D_6) δ 5.48-5.64 (m, 2H), 4.20 (p, *J* = 6.0 Hz, 2H), 3.65 (q, *J* = 5.2 Hz, 1H), 3.091 (s, 3H), 3.087 (s, 3H), 2.79 (d, *J* = 14.8 Hz, 1H), 2.52 (d, *J* = 15.6 Hz, 1H), 1.95-2.02 (q, *J* = 7.2 Hz, 2H), 1.66-1.77 (m, 3H), 1.27-1.59 (m, 6H), 1.24 (d, *J* = 6.4 Hz, 3H), 1.10 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 135.73, 135.68, 129.1, 103.3, 68.12,68.09, 67.16, 67.10, 47.1, 39.4, 32.61, 32.59, 32.0, 31.8, 31.7, 23.7, 23.53. 23. 48, 23.44, 20.12, 20.08 IR (neat) 3391, 2952, 2830, 1170, 1670, 1457, 1370, 1313, 1126, 1064, 969, 941 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{30}O_4Na$ $[M+Na]^+$ 297.2042, found 297.2065.



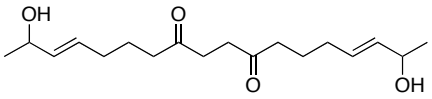
(2*S*, 6*R*, 8*R*)-2-methyl-8-((*E*)-prop-1-en-1-yl)-1,7-dioxaspiro[5.5]undecane (56)

The general cyclization procedure was followed with **54** (50 mg, 0.18 mmol) and Re_2O_7 (4 mg, 0.009 mmol) in $CDCl_3$ (3.0 mL). The mixture was stirred at rt for 30 min after which the reaction was quenched with pyridine (25 μL). $BnMe_2SiH$ (5 μl) was added as an internal standard, and a ^{1}H NMR spectrum was taken of the crude mixture to show a 65% yield. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.69 (ddq, *J* = 1.2, 6.4, 15.2 Hz, 1H), 5.51 (ddq, *J* = 1.6, 6.0, 15.2 Hz, 1H), 4.02 (ddp, *J* = 1.2, 6.0, 11.6 Hz, 1H), 3.72 (ddq, *J* = 2.0, 6.4, 11.2 Hz, 1H), 1.85-1.99 (m, 2H), 1.71 (dd, *J* = 2.4, 6.4, 3H), 1.49-1.66 (m, 6H), 1.41 (ddd, *J* = 4.4, 8.4, 13.2, 2H), 1.28-1.36 (m, 1H), 1.18-1.28 (m, 1H), 1.15 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.8, 126.2, 96.3, 69.5, 65.1, 35.21., 35.16, 32.8, 31.0, 21.9, 18.9, 18.8, 17.9; IR (neat) 2936, 2869, 1676, 1440, 1383, 1280, 1224, 1204,1087, 991, 964 cm^{-1}; HRMS (APCI) calcd for $C_{13}H_{23}O_2$ $[M+H]^+$ 211.1698, found 211.1716.

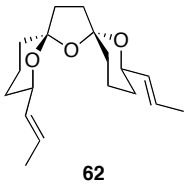


Reagents and conditions
a) PCC, Celite, CH_2Cl_2. b) MeMgBr, THF, 0 °C, 58% (two steps). c) PCC, Celite, CH_2Cl_2. d) (*Z*)-Hex-3-ene-2,5-diol, Grubbs-Hoveyda 2nd generation metathesis catalyst, CH_2Cl_2. e) TBDMSCl, imidazole, DMAP, DMF, 50% (three steps). f) LDA, THF, 0 °C, then $CuCl_2$, 26%. g) Bu_4NF, THF.

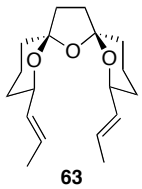
Scheme 17. Synthesis of substrate **61**.



***(3E,15E)*-2,17-dihydroxyoctadeca-3,15-diene-8,11-dione (61)**
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48-5.61 (m, 4H), 4.25 (q, *J* = 6.0 Hz, 2H), 2.65 (s, 4H), 2.46 (t, *J* = 7.2 Hz, 4H), 2.02 (q, *J* = 6.8 Hz, 4H), 1.67 (p, *J* = 7.2 Hz, 4H), 1.24 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.6, 135.2, 129.7, 68.8, 41.9, 36.1, 31.5, 23.4, 22.9; IR (neat) 3406, 2968, 2928, 1707, 1639, 1450, 1369, 1139, 1062, 970, 938 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{30}O_4Na$ $[M+Na]^+$ 333.2042, found 333.2075.



62



63

Spirotricycles 62 and 63
The general rearrangement procedure was followed with **61** (110 mg, 0.354 mmol), Re_2O_7 (8.6 mg, 0.018 mmol), and CH_2Cl_2 (3.0 mL). The reaction was stirred at 0 °C for 2 h and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (87 mg, 84%, dr = 1:1, **62**: 43 mg, **63**: 44 mg).
Faster eluting major isomer **62**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.60 (ddq, *J* = 0.8, 6.4, 15.2 Hz, 2H), 5.40 (ddq, *J* = 1.6, 6.8, 15.2 Hz, 2H), 4.21 (dd, *J* = 7.2, 11.2 Hz, 2H), 1.85-1.98 (m, 4H), 1.79-1.83 (m, 2H), 1.65 (d, *J* = 6.4 Hz, 6H), 1.54-1.70 (m, 8H), 1.20-1.31 (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 133.0, 125.8, 106.8, 71.4, 36.7, 34.8, 31.2, 20.3, 17.5; IR (neat) 3023, 2981, 2937, 2864, 1731, 1676, 1452, 1439, 1375, 1314, 1266, 1231,1072, 1028, 968, 874 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{28}O_3Na$ $[M+Na]^+$ 315.1936, found 315.1919. The stereochemical arrangement was established by HPLC analysis using a Phenomenex Lux 5μ Cellulose-3 column (250 x 4.60 mm) with MeOH/H_2O (Black line: 60/40 or Purple Line: 70/30, v/v) as the mobile phase.
Slower eluting minor isomer **63**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.58 (ddq, *J* = 0.8, 6.4, 15.6 Hz, 2H), 5.41 (ddq, *J* = 1.6, 6.8, 15.6 Hz, 2H), 4.28 (dd, *J* = 7.2, 10.8 Hz, 2H), 2.01-2.07 (m, 2H), 1.81-1.91 (m, 2H), 1.73-1.79 (m, 2H), 1.65 (d, *J* = 6.4 Hz, 6H), 1.48-1.63 (m, 8H), 1.22-1.33 (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 133.0, 126.2, 107.2, 72.6, 37.4, 34.8, 31.1, 20.1, 17.5; IR (neat) 3022, 2936, 2864, 1676, 1453, 1439, 1377, 1301, 1233, 1165, 1073, 1028, 964, 866 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{28}O_3Na$ $[M+Na]^+$ 315.1936, found 315.1918.
The two stereoisomers were resubjected to the following isomerization condition: 7.2 mg Re_2O_7 (0.015 mmol) and 1.5 ml CD_2Cl_2. After stirring at 0 °C for 4 h, the isomerizations were quenched with pyridine (25 μL). $BnMe_2SiH$ (5 μl) was added as an internal standard to each isomerization mixture, and a ^{1}H NMR spectrum was taken of the crude mixture to show that the equilibration of **62** provided 51% of 60 and 27% of **63**. The equilibration of 61 provided 52% of **62** and 29 % of **63**. Thus, after one cycle of isomerization: a total yield of 64% could be obtained for **62** and a total yield of 54% could be obtained for **63**.

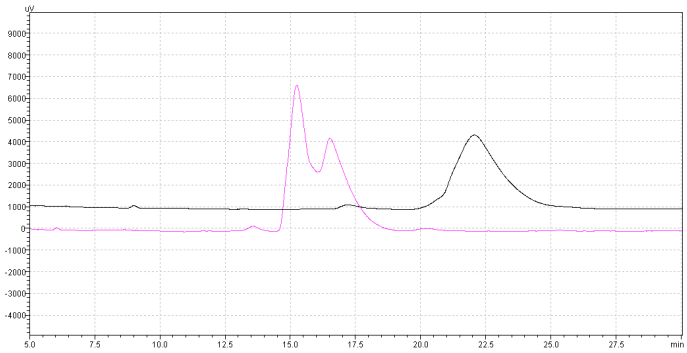
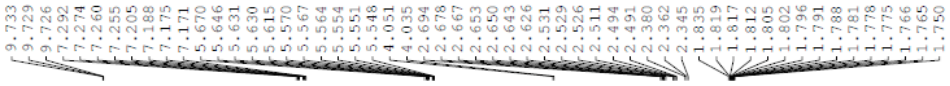


Figure 1. HPLC traces of **62** (pink) and **63** (black) using a chiral stationary phase.



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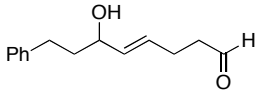
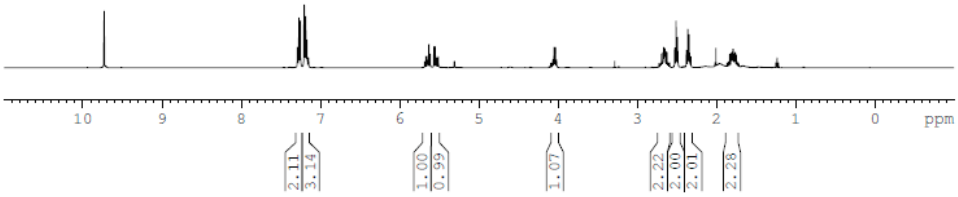
PROTON CD2C12 C:\Bruker\TOPSPIN floreancig 8





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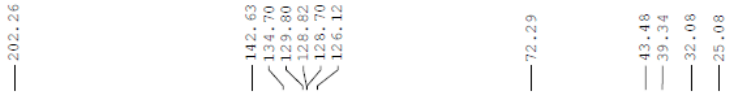
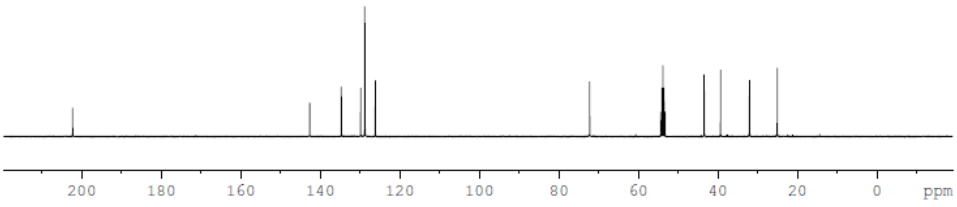
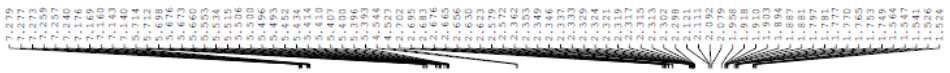
C13CPD CD2C12 C:\Bruker\TOPSPIN floreancig 13







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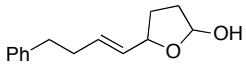

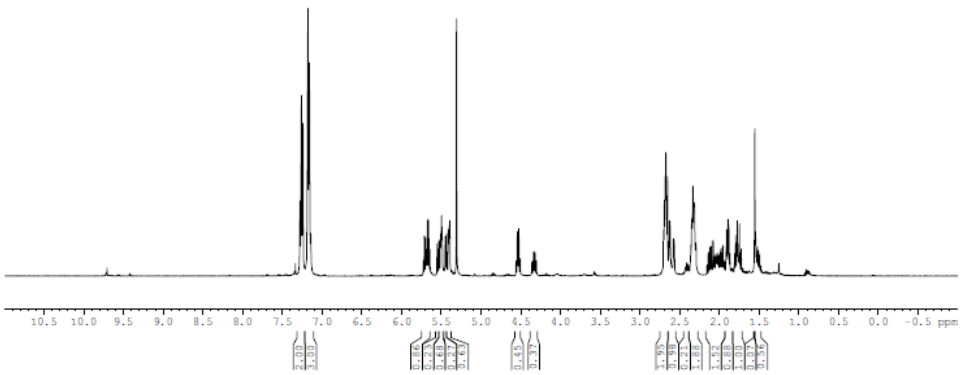

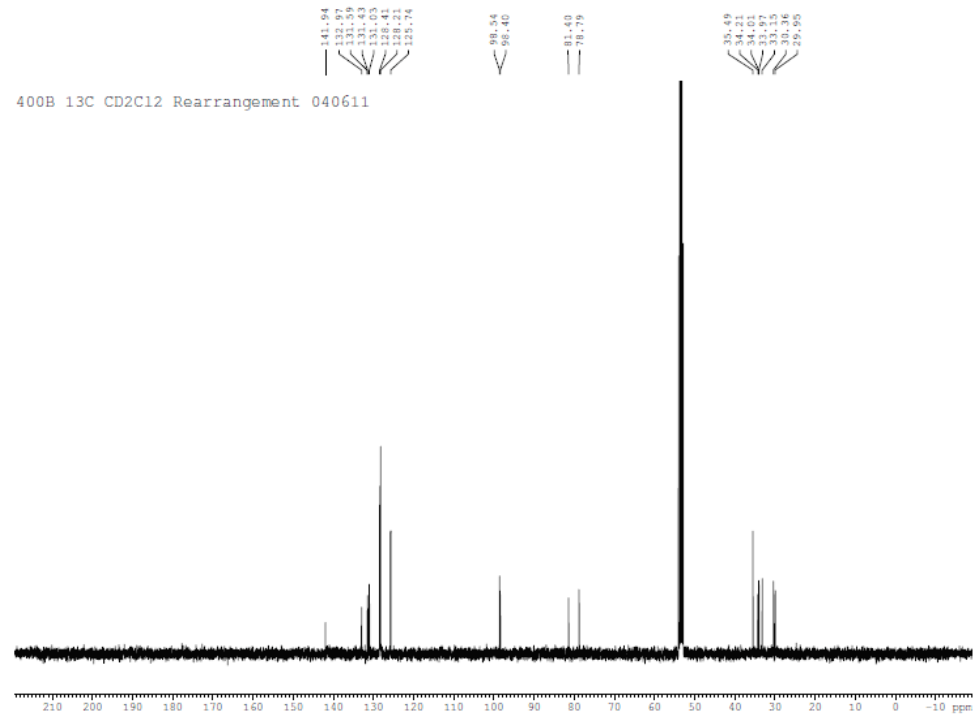

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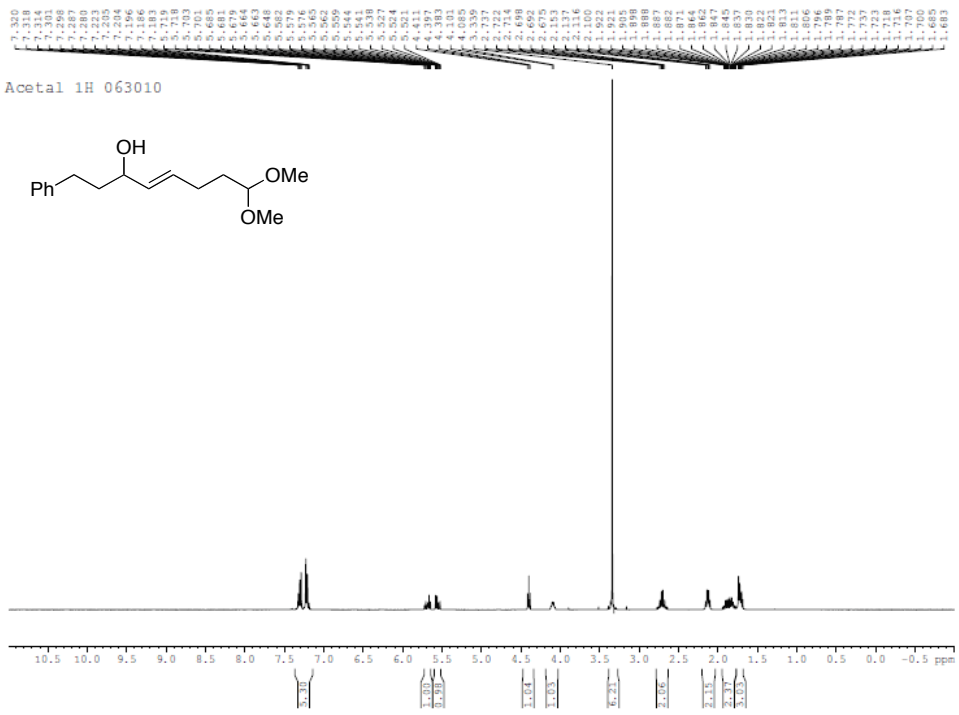
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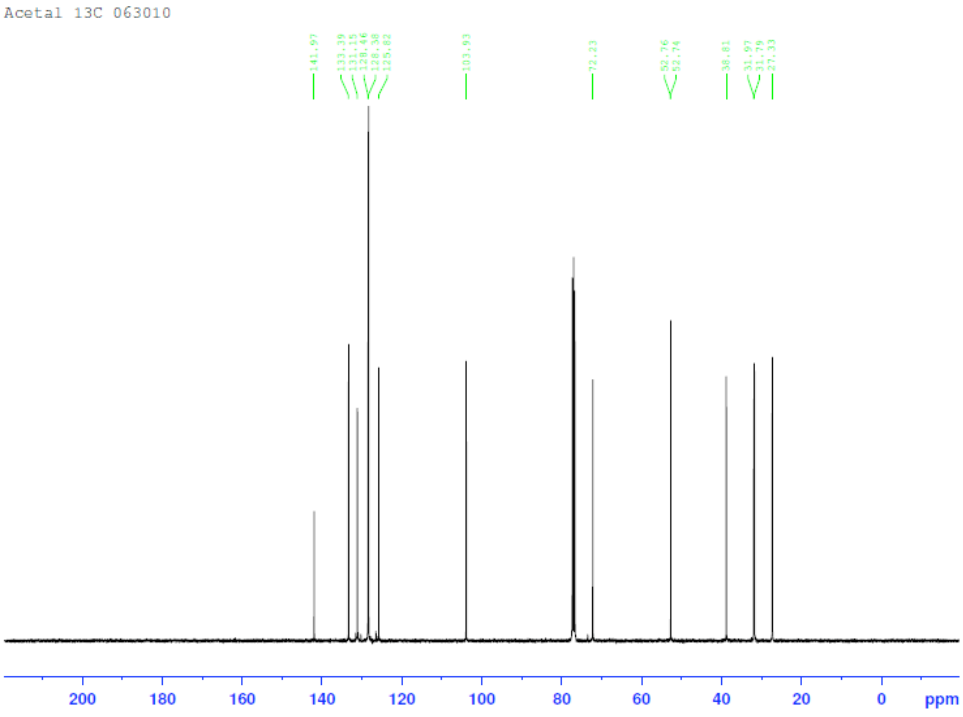
Ph
OMe
OMe
ppm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128.46
128.38
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103.93
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31.79
27.33
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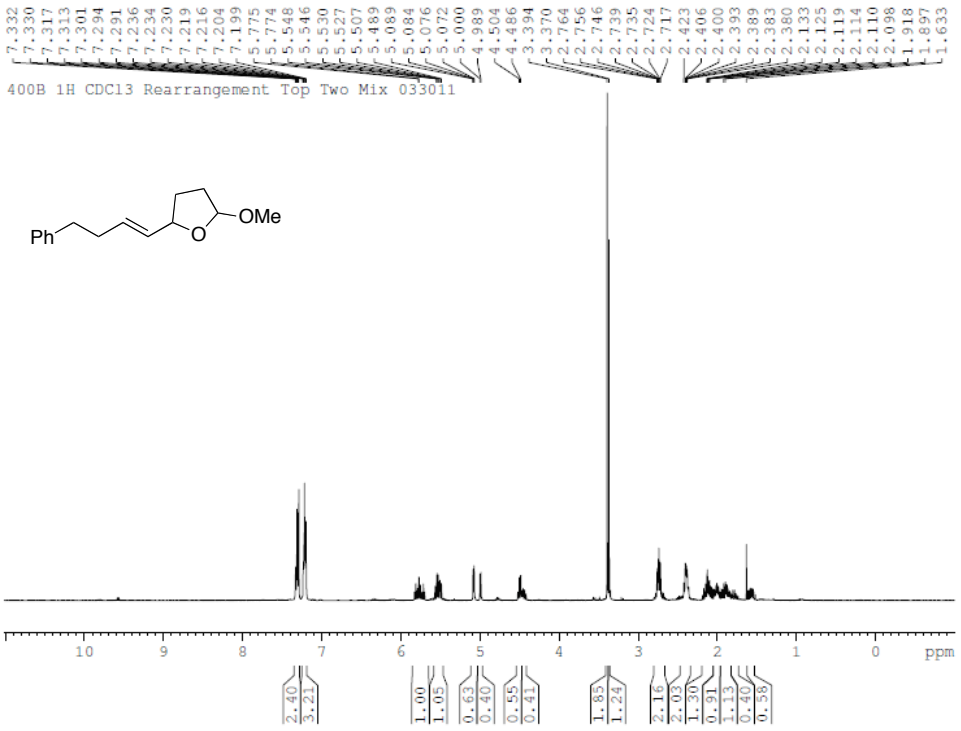
160
140
120
100
80
60
40
20
0
ppm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7.219
7.216
7.204
7.199
5.775
5.774
5.548
5.546
5.530
5.527
5.507
5.489
5.089
5.084
5.076
5.072
5.000
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4.504
4.486
3.394
3.370
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2.756
2.746
2.739
2.735
2.724
2.717
2.423
2.406
2.400
2.393
2.389
2.383
2.380
2.133
2.125
2.119
2.114
2.110
2.098
1.918
1.897
1.633
400B 1H CDC13 Rearrangement Top Two Mix 033011
Ph
OMe
O
10
9
8
7
6
5
4
3
2
1
0
ppm
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3.21
1.00
1.05
0.63
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2.16
2.05
1.30
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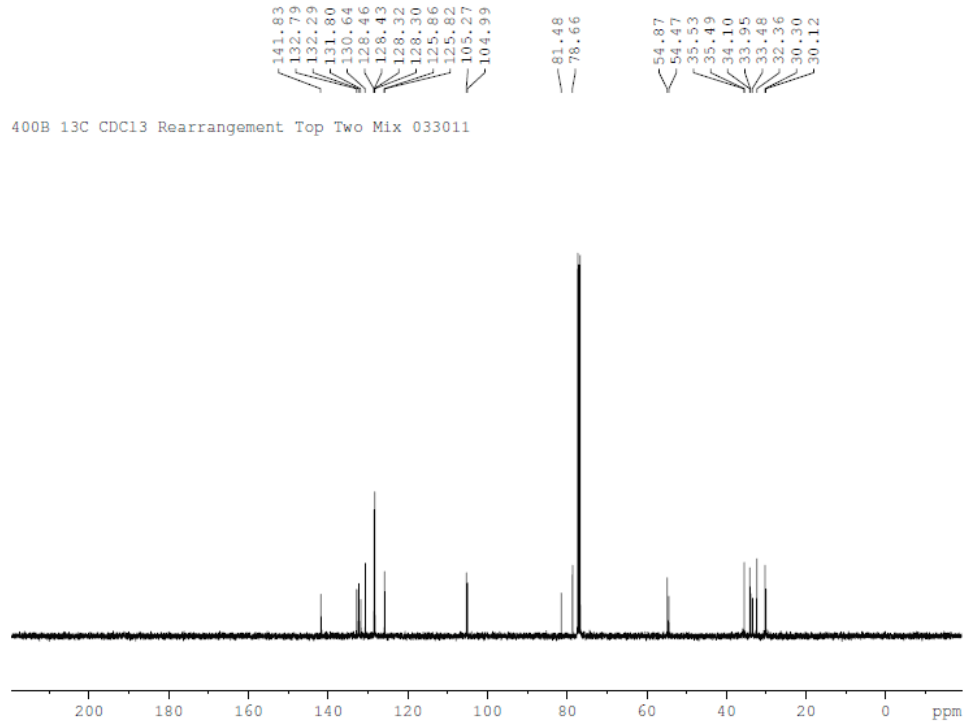
1.13
0.46
0.58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130.64
128.46
128.43
128.32
128.30
125.86
125.82
105.27
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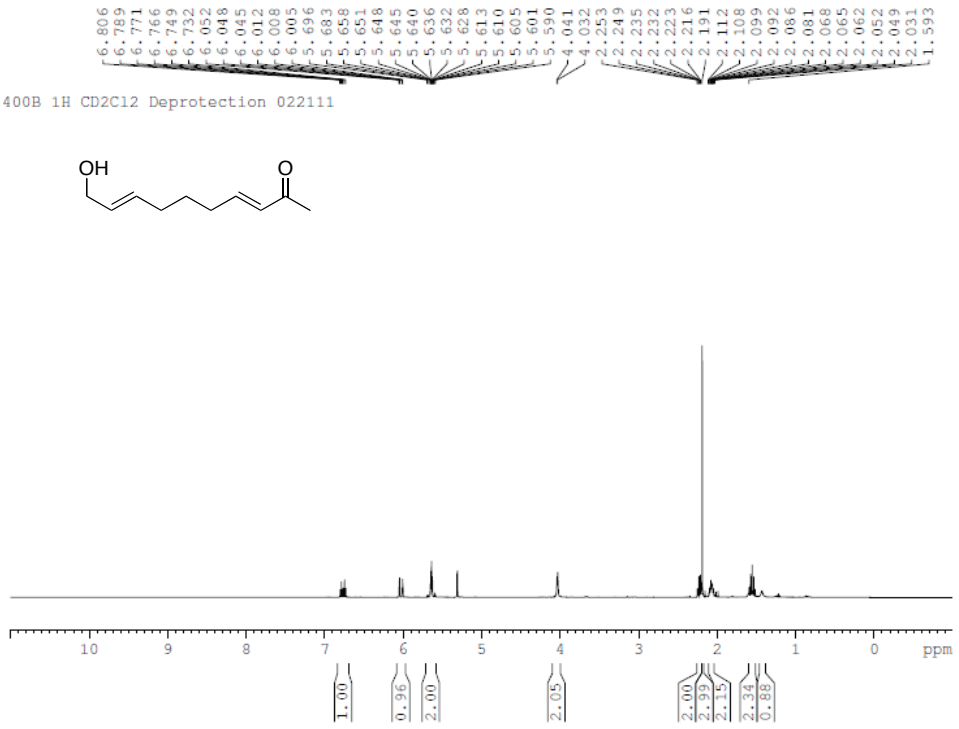
81.48
78.66
54.87
54.47
35.53
35.49
34.10
33.95
33.48
32.36
30.30
30.12
400B 13C CDC13 Rearrangement Top Two Mix 033011
200
180
160
140
120
100
80
60
40
20
0
ppm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2.031
1.593
400B 1H CD2Cl2 Deprotection 022111
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O
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9
8
7
6
5
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ppm
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2.00
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2.00
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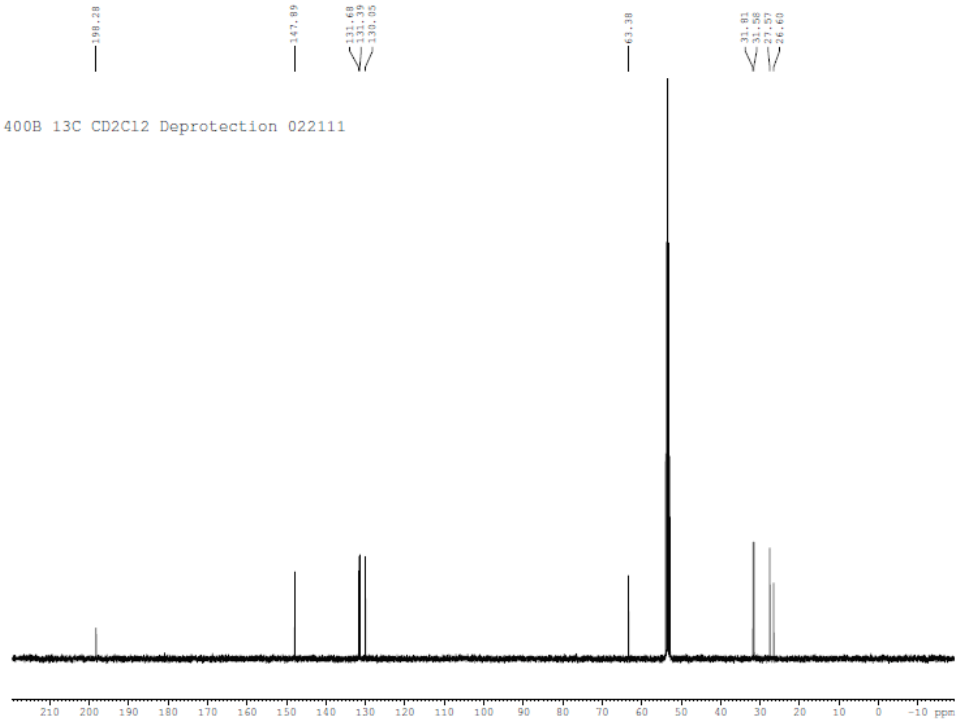
0.88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131.39
130.05
63.38
31.81
31.58
27.57
26.60
400B 13C CD2Cl2 Deprotection 022111
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200
190
180
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130
120
110
100
90
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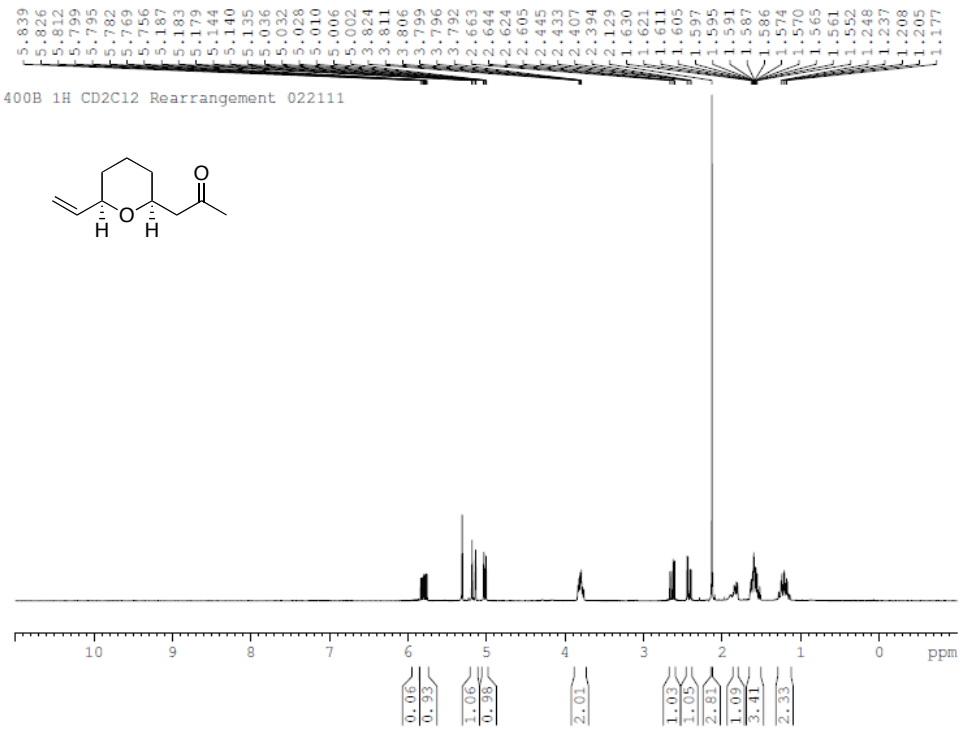
60
50
40
30
20
10
0
-10
ppm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H
O
H
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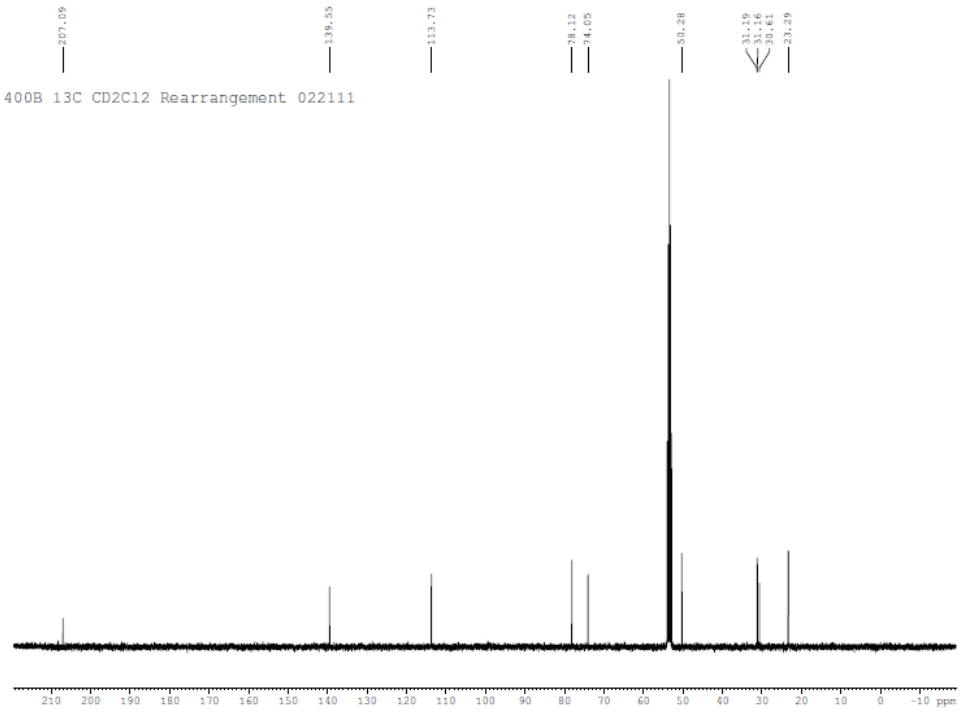
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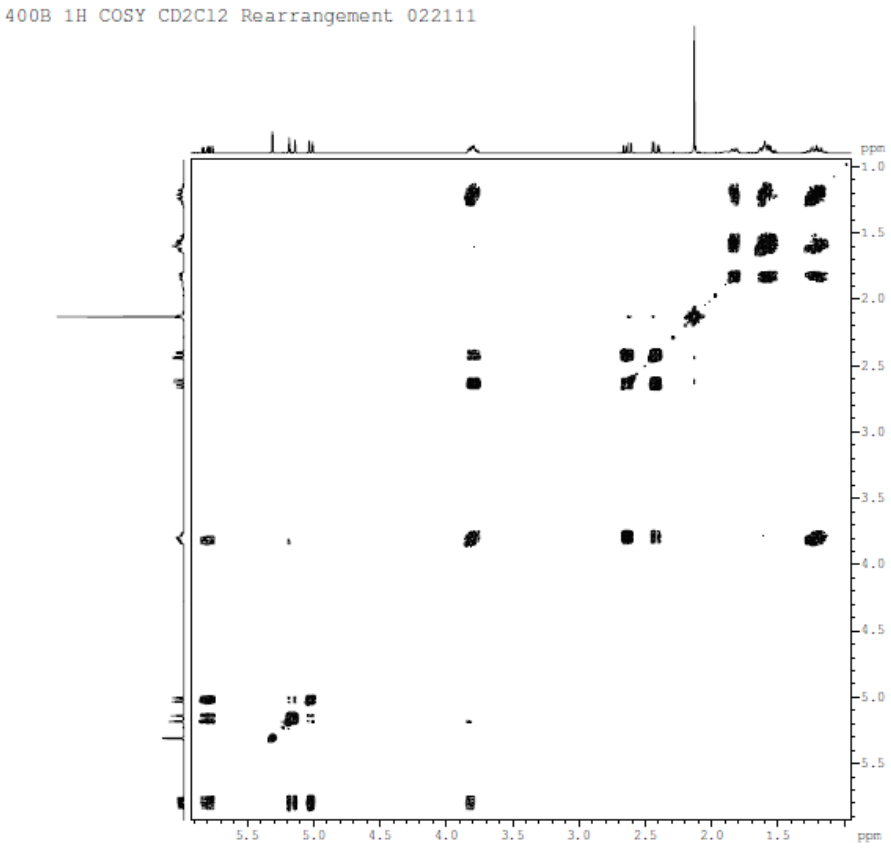
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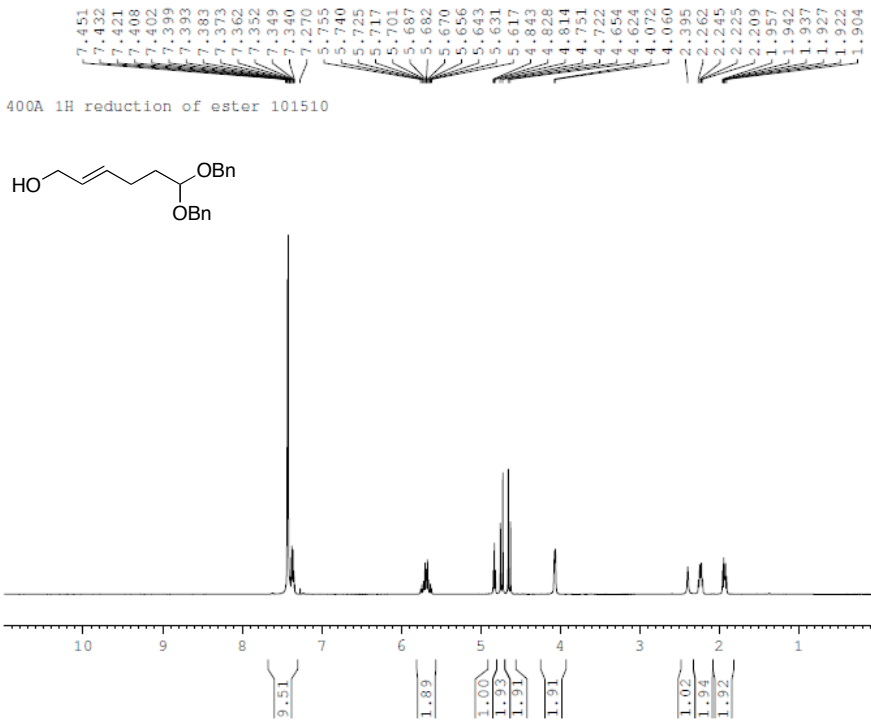
2.0
1.5
ppm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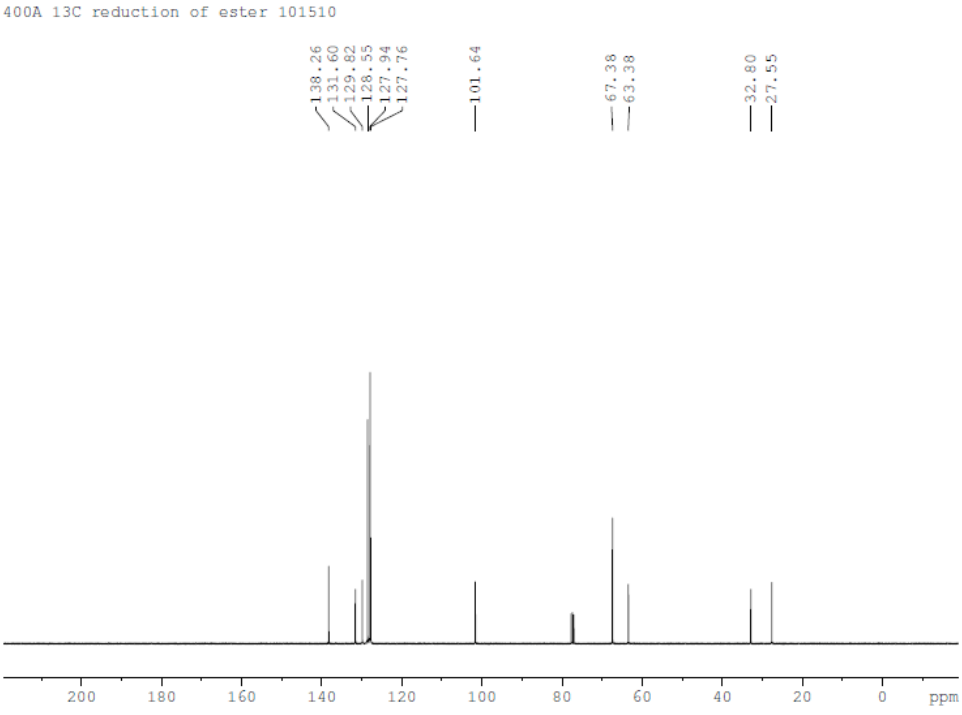
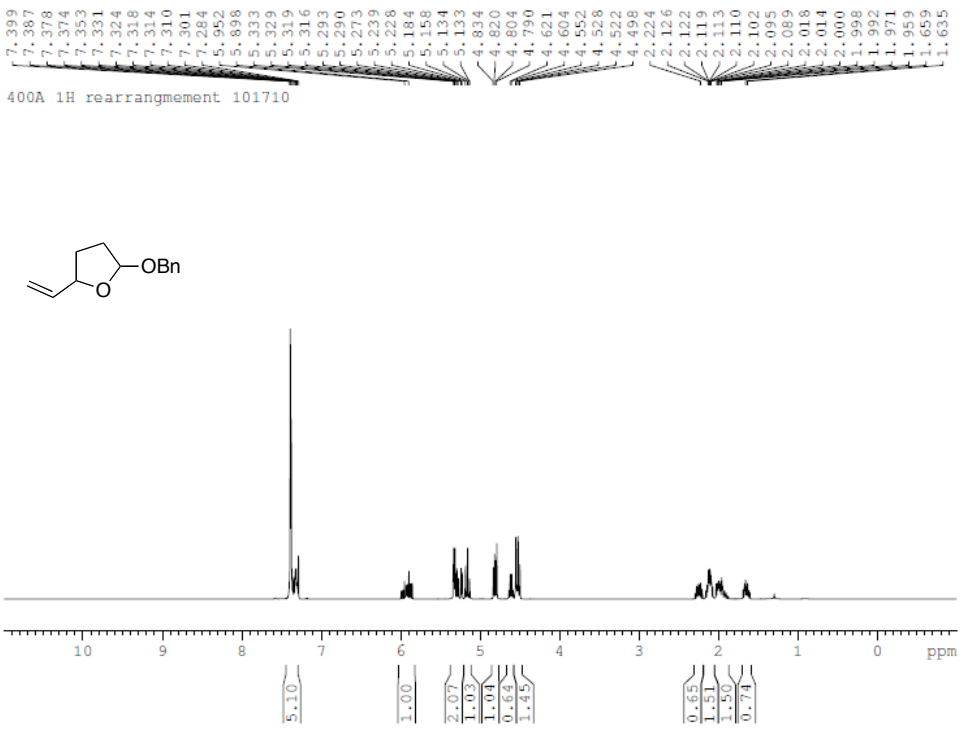
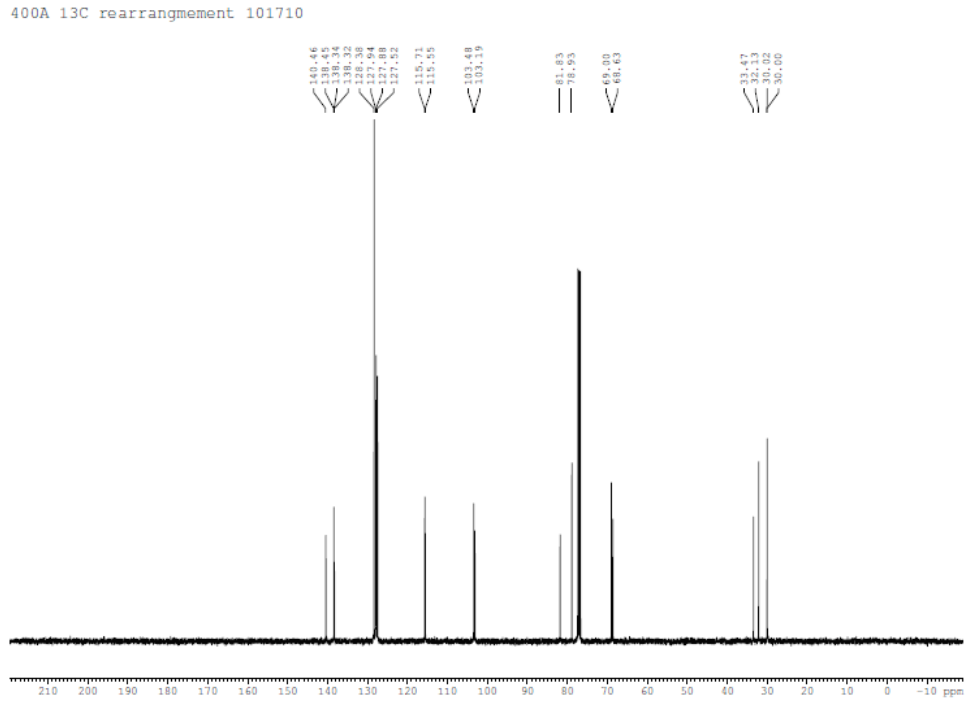
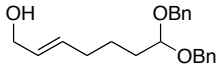
7.432
7.421
7.408
7.402
7.399
7.393
7.383
7.373
7.362
7.352
7.349
7.340
7.270
5.755
5.740
5.725
5.717
5.701
5.687
5.682
5.670
5.656
5.643
5.631
5.617
4.843
4.828
4.814
4.751
4.722
4.654
4.624
4.072
4.060
2.395
2.262
2.245
2.225
2.209
1.957
1.942
1.937
1.927
1.922
1.904
400A 1H reduction of ester 101510
HO
OBn
OBn
10
9
8
7
6
5
4
3
2
1
0
ppm
9.51
1.89
1.00
1.93
1.91
1.91
1.02
1.94
1.92

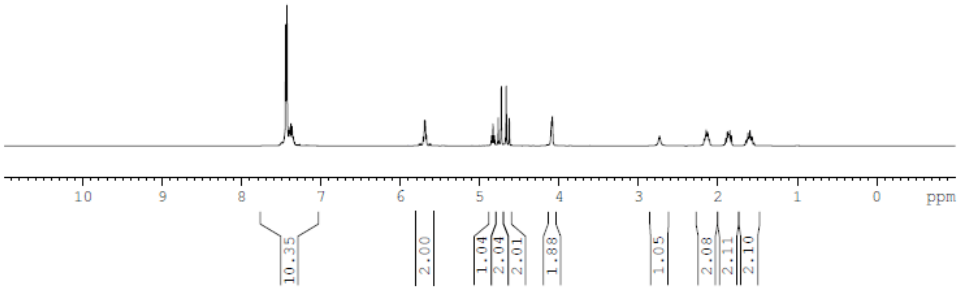

400A 13C reduction of ester 101510
138.26
131.60
129.82
128.55
127.94
127.76
101.64
67.38
63.38
32.80
27.55
200
180
160
140
120
100
80
60
40
20
0
ppm


7.399
7.387
7.378
7.374
7.353
7.331
7.324
7.318
7.314
7.310
7.301
7.284
5.952
5.898
5.333
5.329
5.319
5.316
5.293
5.290
5.273
5.239
5.228
5.184
5.158
5.134
5.133
4.834
4.820
4.804
4.790
4.621
4.604
4.552
4.528
4.522
4.498
2.224
2.126
2.122
2.119
2.113
2.110
2.102
2.095
2.089
2.018
2.014
2.000
1.998
1.992
1.971
1.959
1.659
1.635
400A 1H rearrangmement 101710
OBn
O
10
9
8
7
6
5
4
3
2
1
0
ppm
5.10
1.00
2.07
1.03
1.04
0.64
1.45
0.65
1.51
1.50
0.74

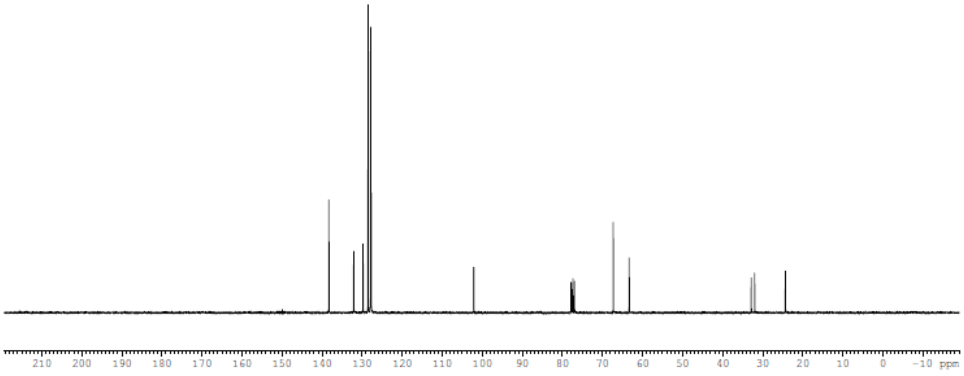

400A 13C rearrangmement 101710
140.46
138.45
138.34
138.32
128.38
127.94
127.88
127.52
115.71
115.55
103.48
103.19
81.83
78.93
69.00
68.63
33.47
32.13
30.02
30.00
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10 ppm

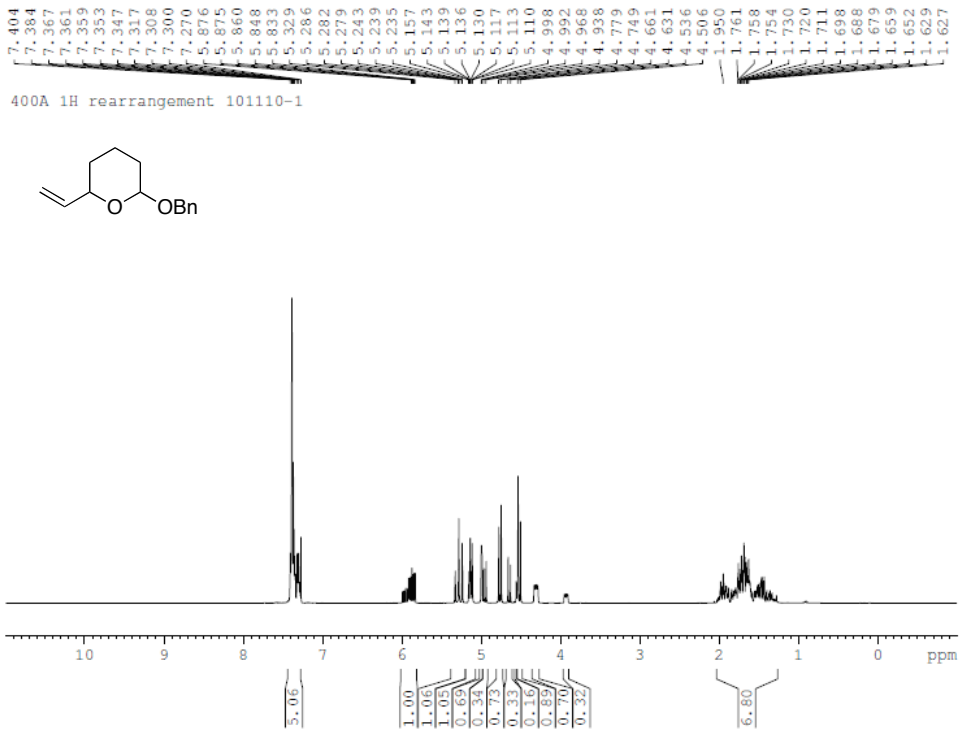
300 1H reduction of ester 100910

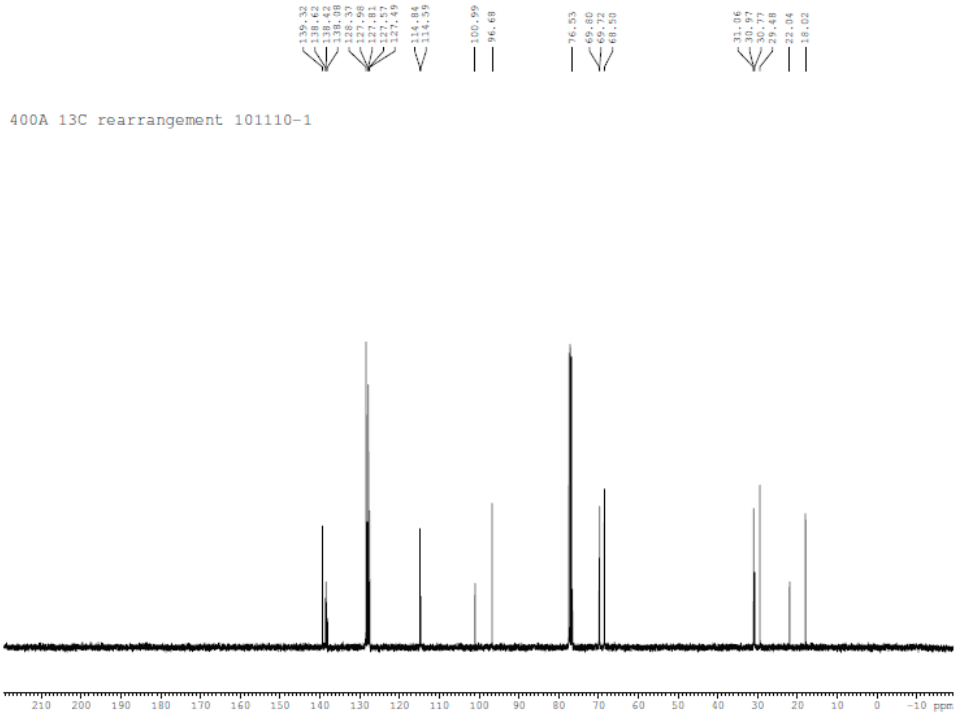


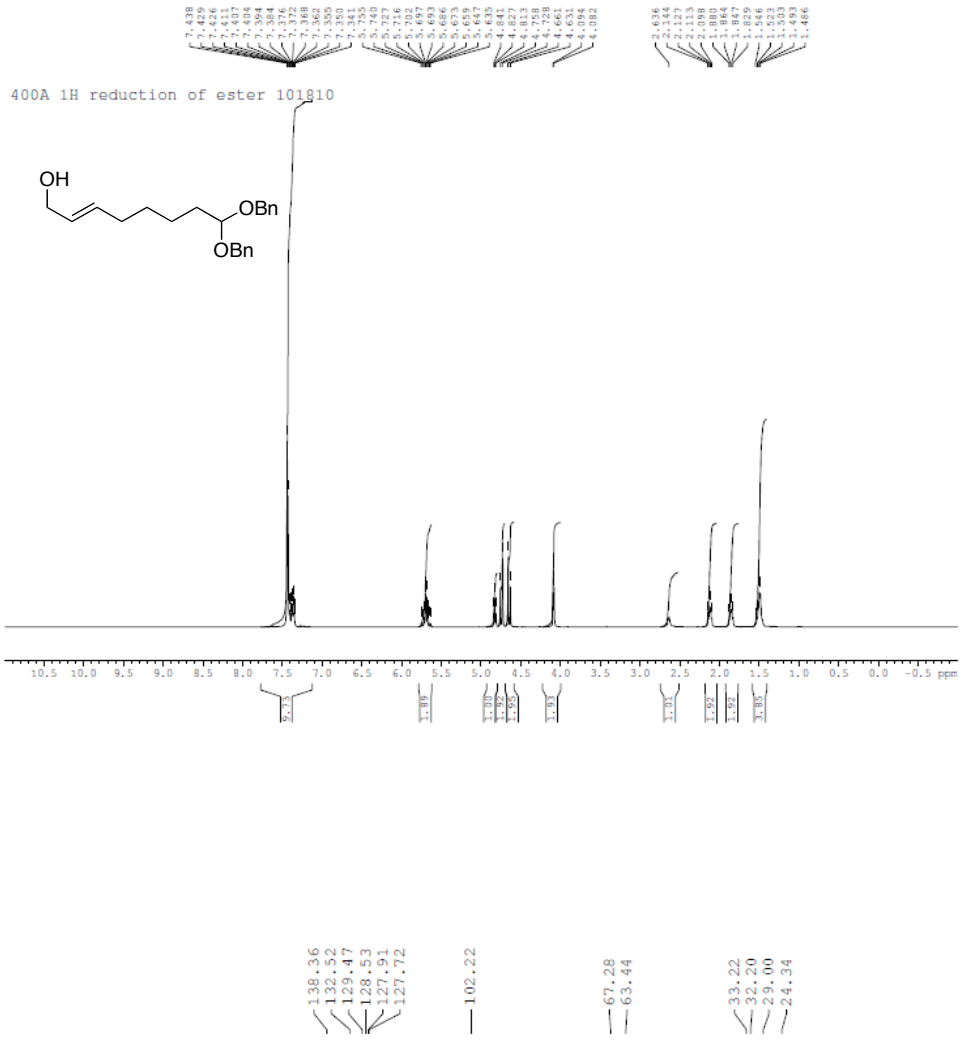


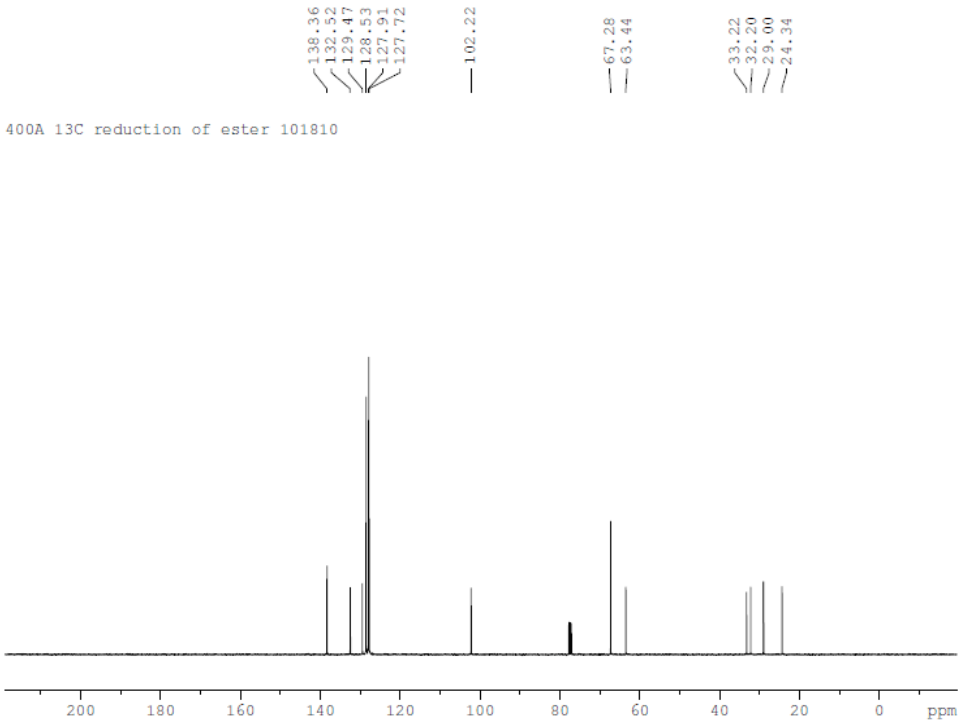
300 13C reduction of ester 100910

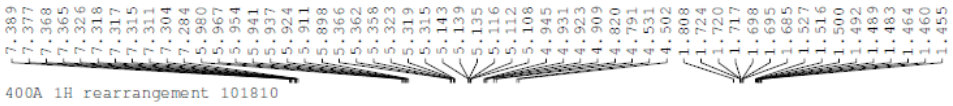



7.404
7.384
7.367
7.361
7.359
7.353
7.347
7.317
7.308
7.300
7.270
5.876
5.875
5.860
5.848
5.833
5.329
5.286
5.282
5.279
5.243
5.239
5.235
5.157
5.143
5.139
5.136
5.130
5.117
5.113
5.110
4.998
4.992
4.968
4.938
4.779
4.749
4.661
4.631
4.536
4.506
1.950
1.761
1.758
1.754
1.730
1.720
1.711
1.698
1.688
1.679
1.659
1.652
1.629
1.627
400A 1H rearrangement 101110-1
O
OBn
10
9
8
7
6
5
4
3
2
1
0
ppm
3.06
1.00
1.06
1.05
0.69
0.34
0.73
0.33
0.16
0.89
0.70
0.32
6.80

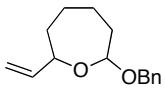

139.32
138.62
138.22
138.08
128.37
127.98
127.81
127.57
127.49
114.84
114.59
100.99
96.68
76.53
69.80
69.72
68.50
31.06
30.97
30.57
29.48
22.04
18.02
400A 13C rearrangement 101110-1
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10 ppm

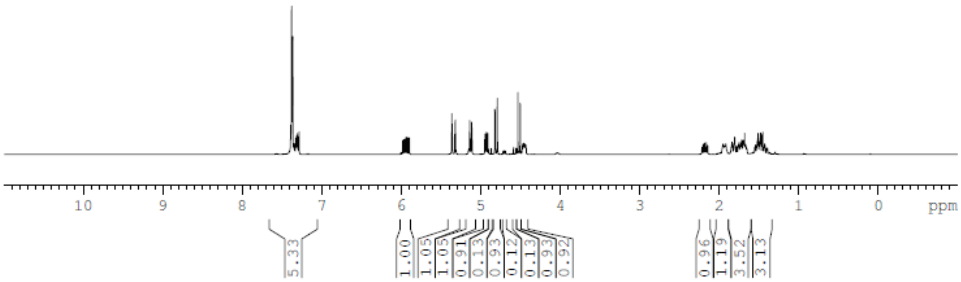

400A 1H reduction of ester 101810
OH
OBn
OBn
ppm

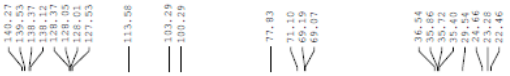

138.36
132.52
129.47
128.53
127.91
127.72
102.22
67.28
63.44
33.22
32.20
29.00
24.34
400A 13C reduction of ester 101810
ppm



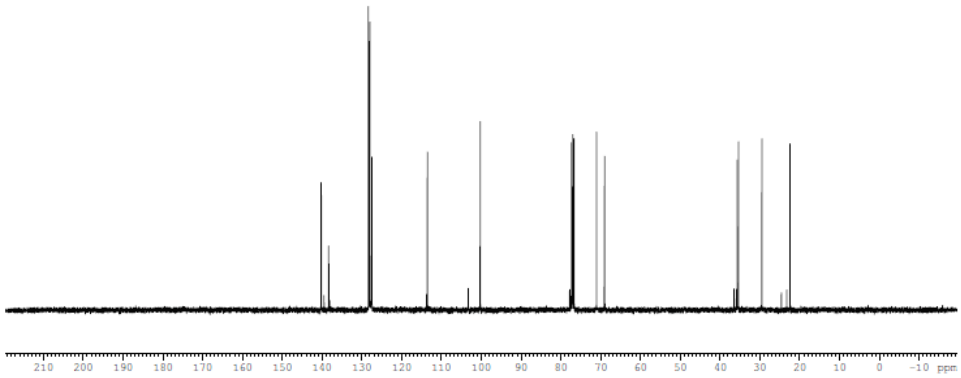
400A 1H rearrangement 101810

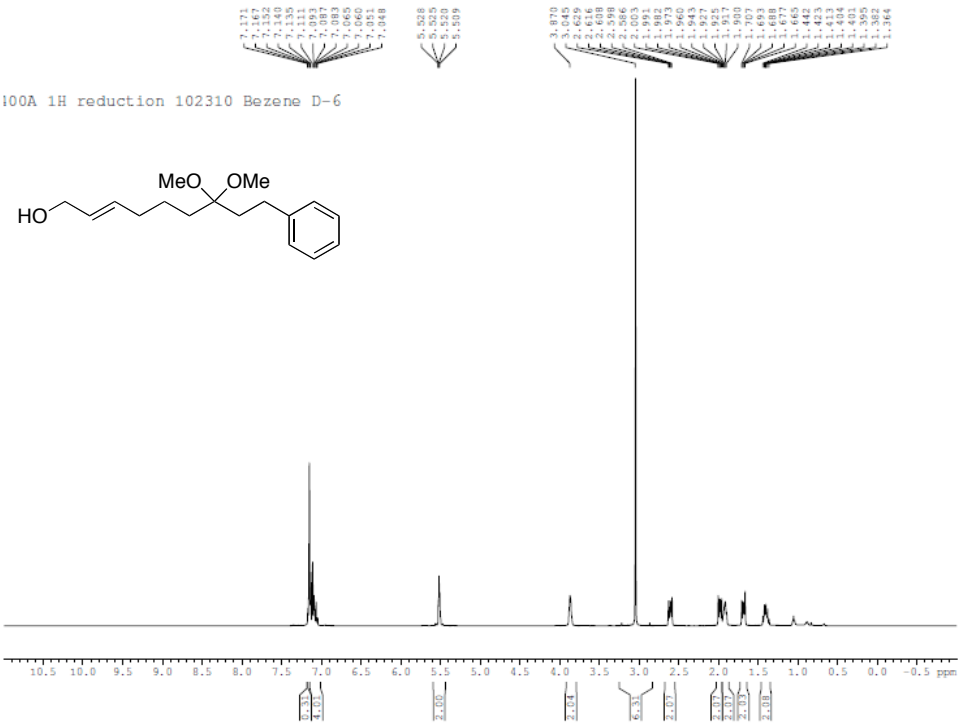


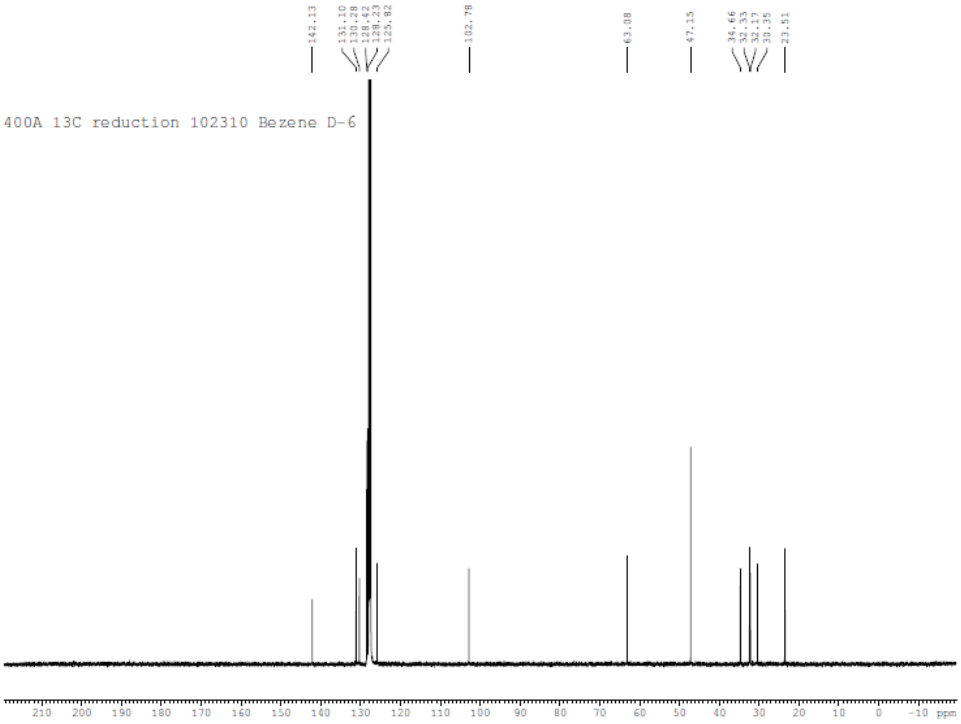


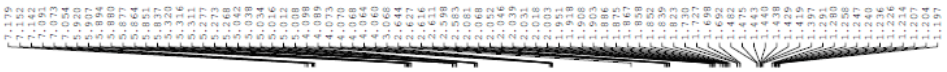


400A 13C rearrangement 101810

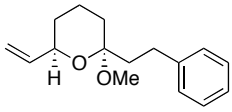


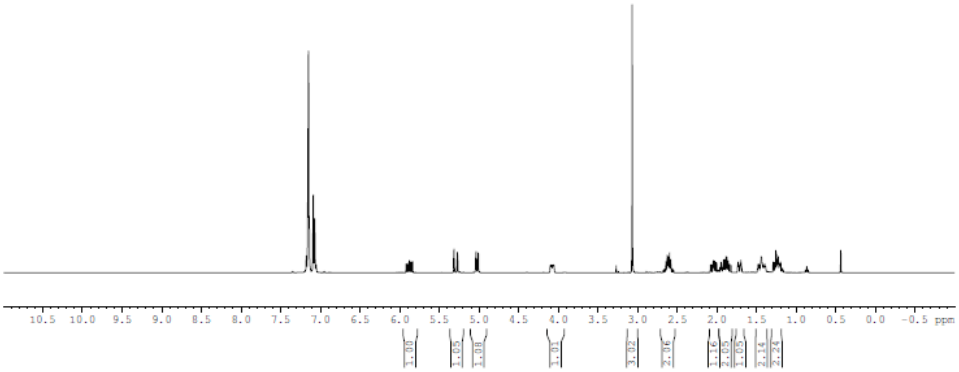

400A 1H reduction 102310 Bezene D-6
MeO
OMe
HO

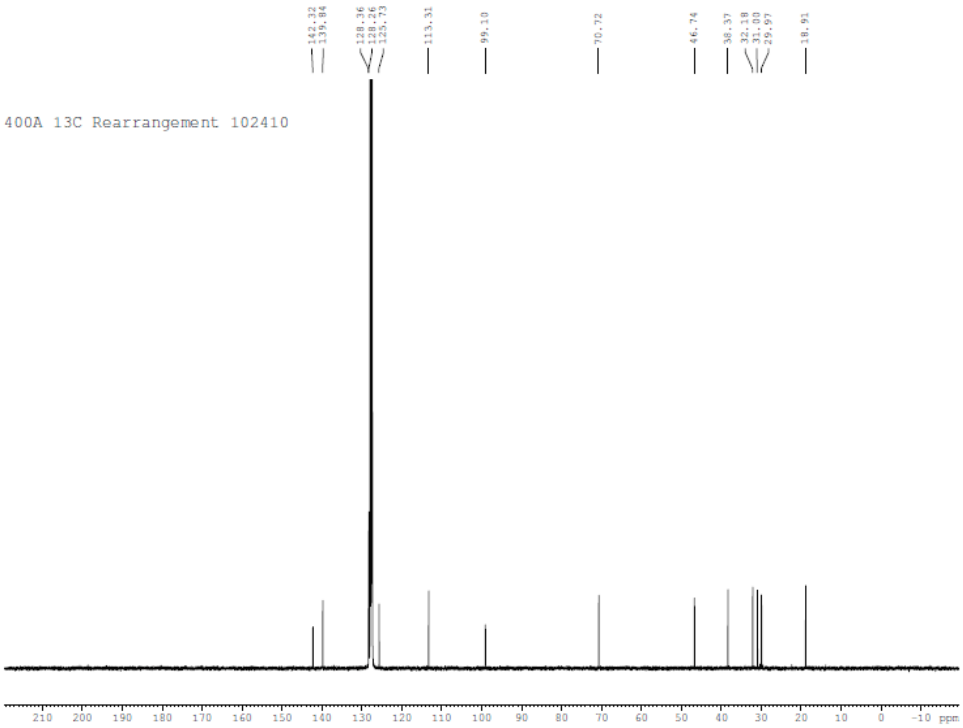

400A 13C reduction 102310 Bezene D-6

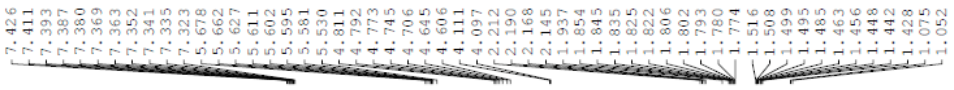


Rearrangement 102410

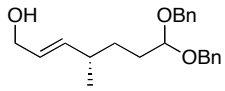


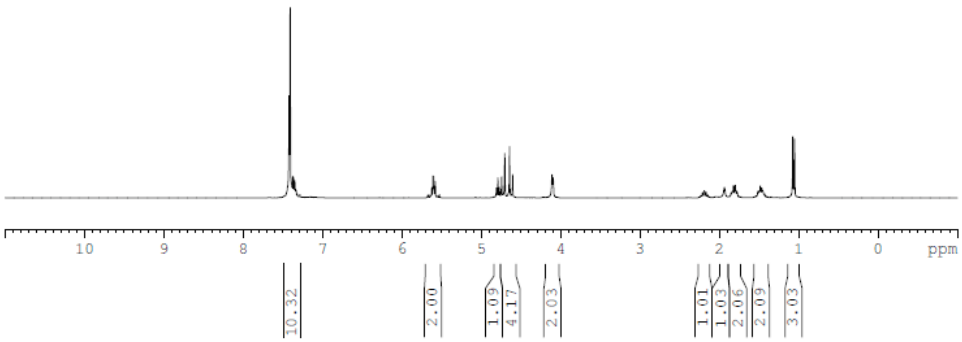


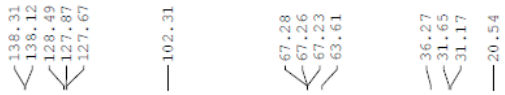




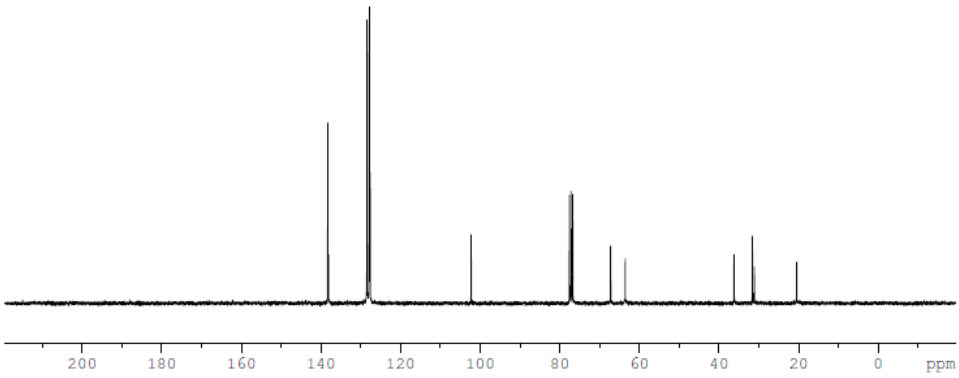
1H Allylic alcohol Benzylic acetal 081110

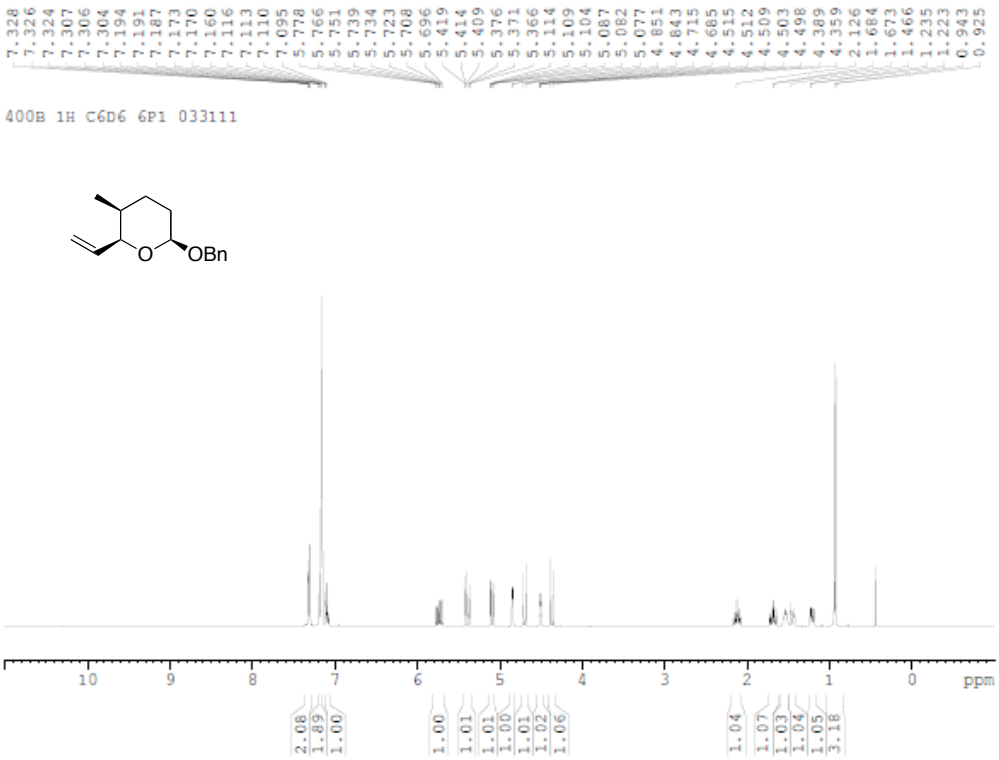


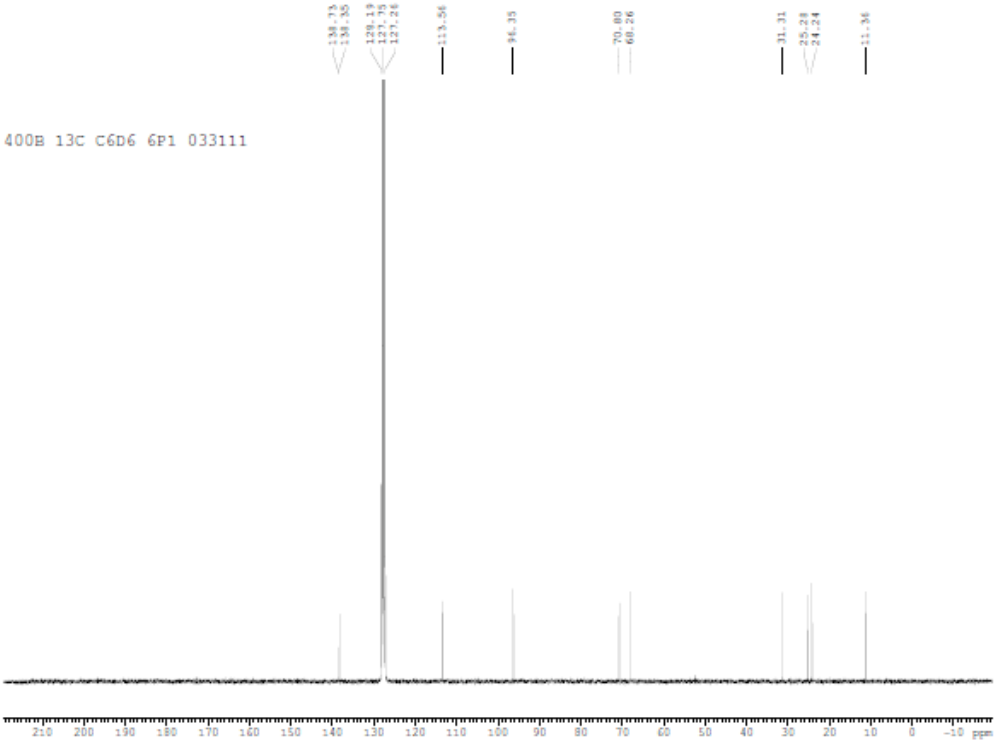


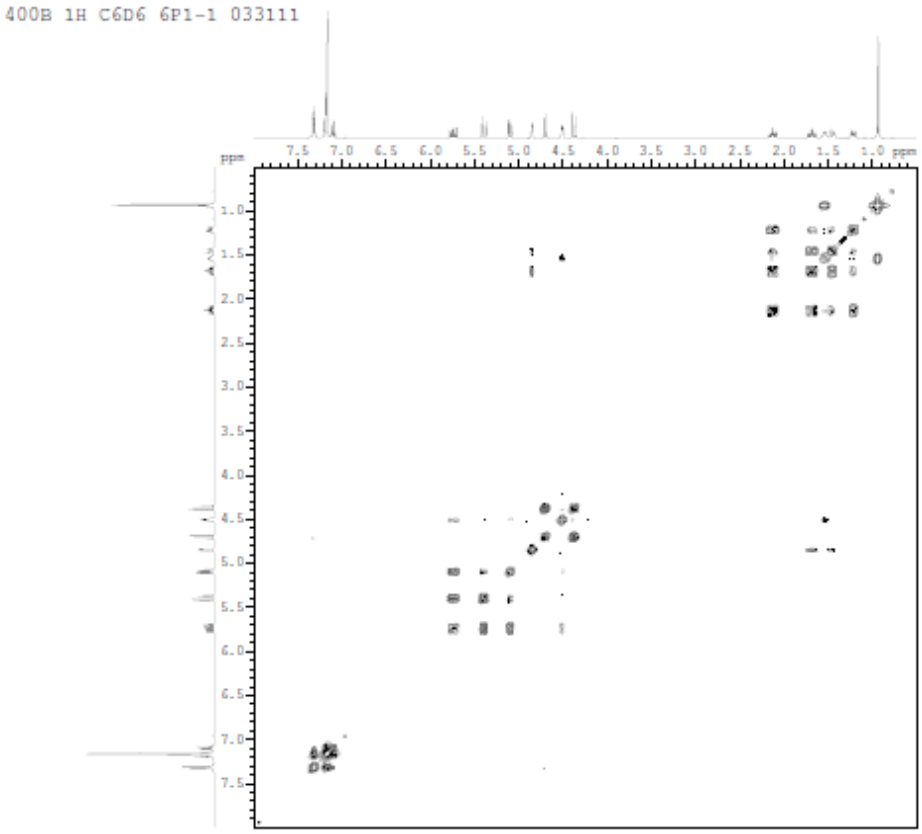


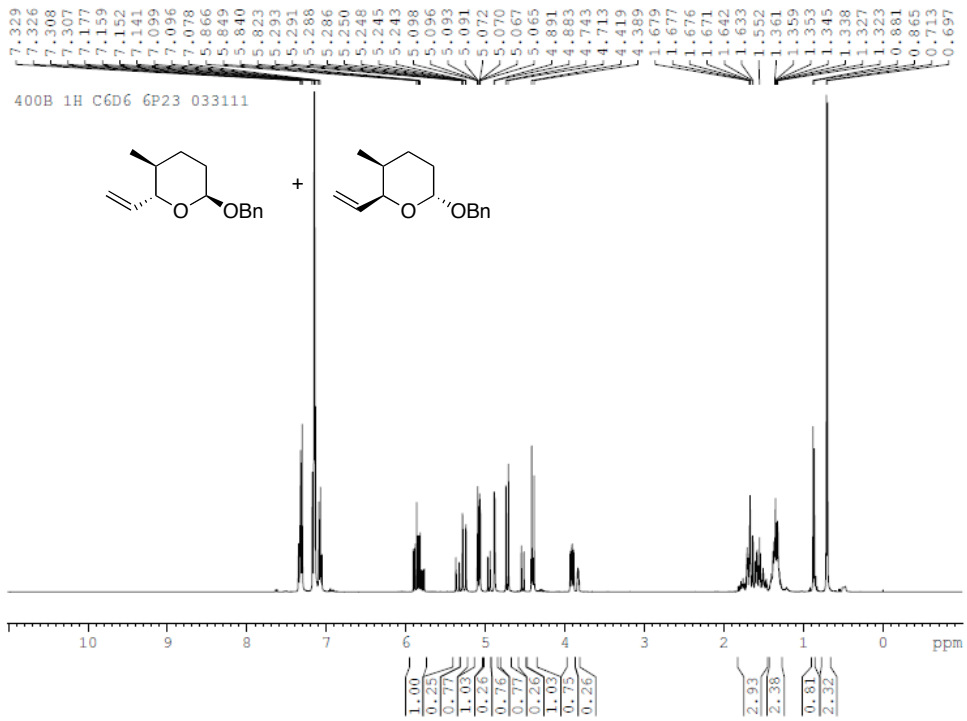
13C Allylic alcohol Benzylic acetal 081110

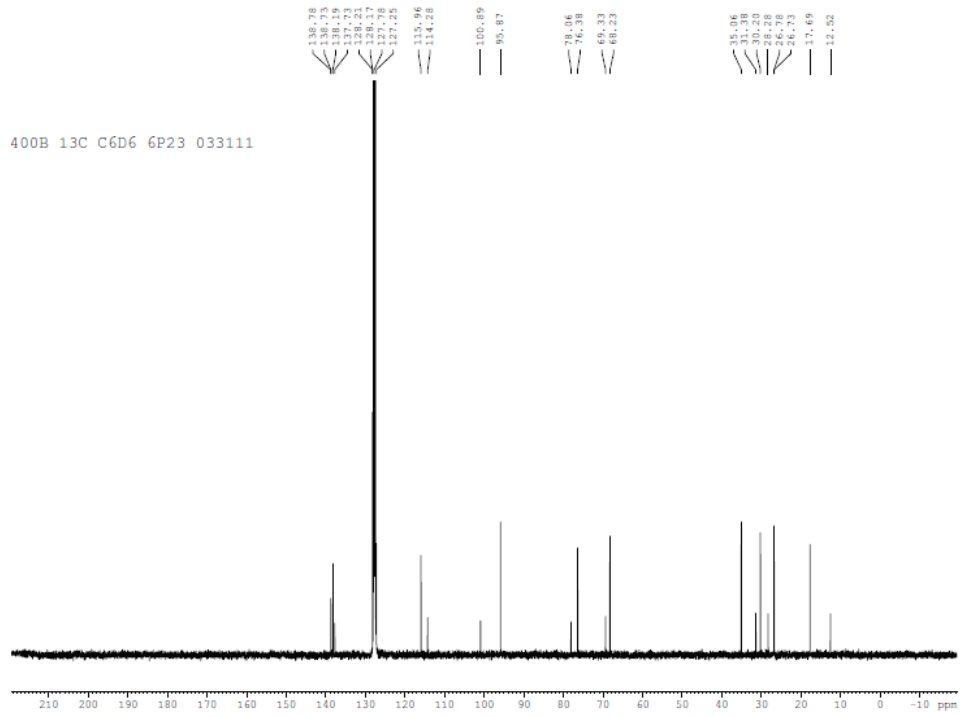


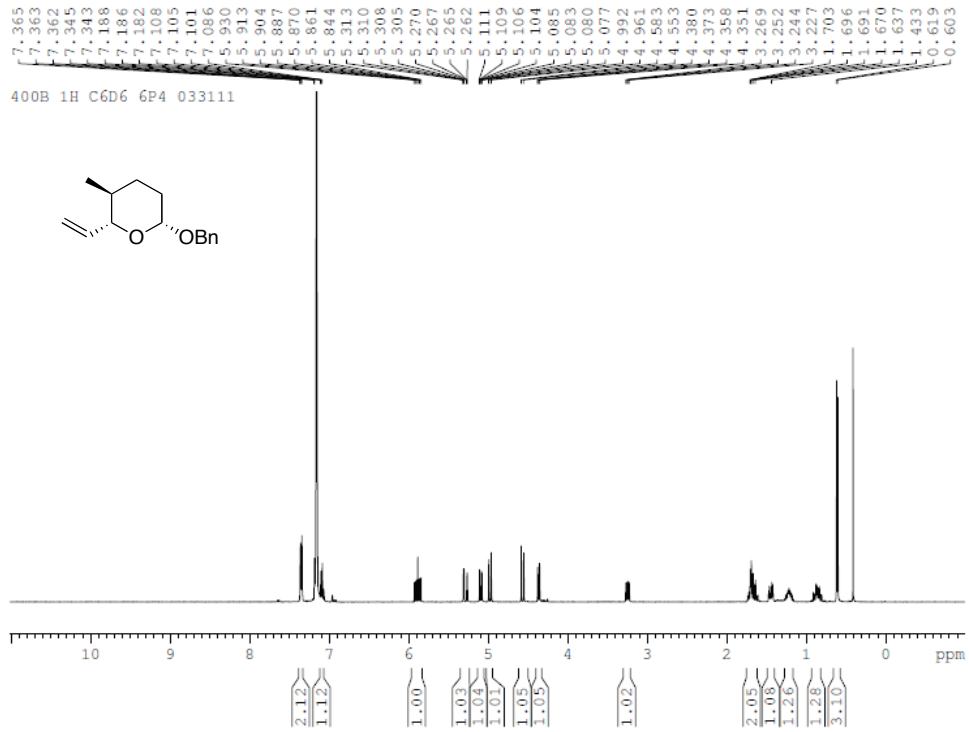

7.328
7.326
7.324
7.307
7.306
7.304
7.194
7.191
7.187
7.173
7.170
7.160
7.116
7.113
7.110
7.095
5.778
5.766
5.751
5.739
5.734
5.723
5.708
5.696
5.419
5.414
5.409
5.376
5.371
5.366
5.114
5.109
5.104
5.087
5.082
5.077
4.851
4.843
4.715
4.685
4.515
4.512
4.509
4.503
4.498
4.389
4.359
2.126
1.684
1.673
1.466
1.235
1.223
0.943
0.925
400B 1H C6D6 6P1 033111
O
OBn
10
9
8
7
6
5
4
3
2
1
0
ppm
2.08
1.89
1.00
1.00
1.01
1.01
1.00
1.01
1.02
1.06
1.04
1.07
1.03
1.04
1.05
3.18

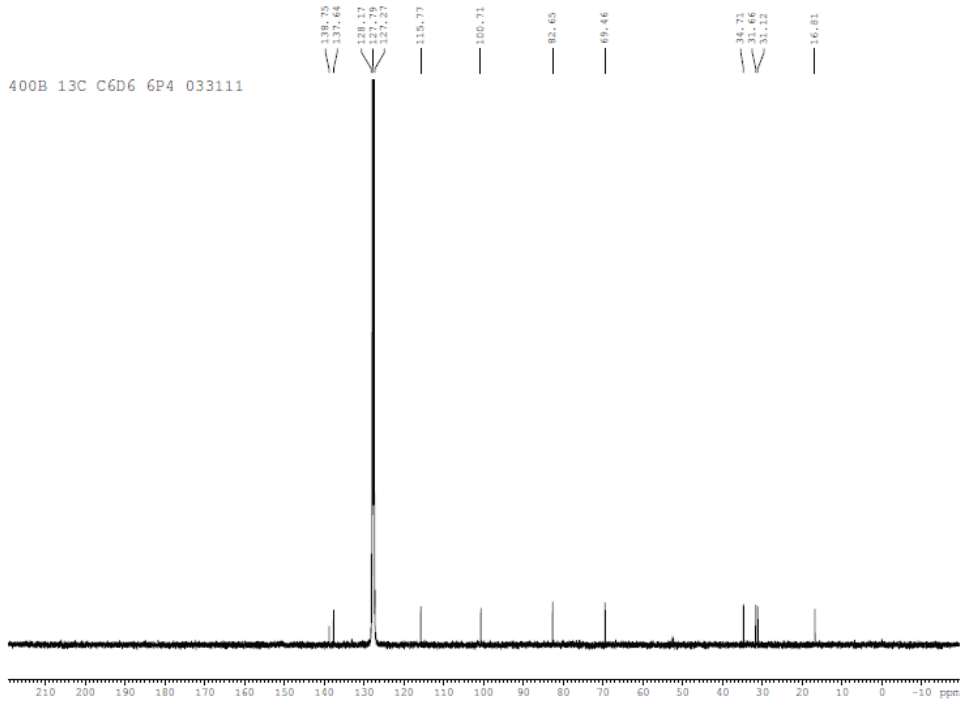

138.73
138.35
129.19
128.75
127.24
113.54
86.35
70.80
68.26
31.31
25.28
24.24
21.36
400B 13C C6D6 6P1 033111
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

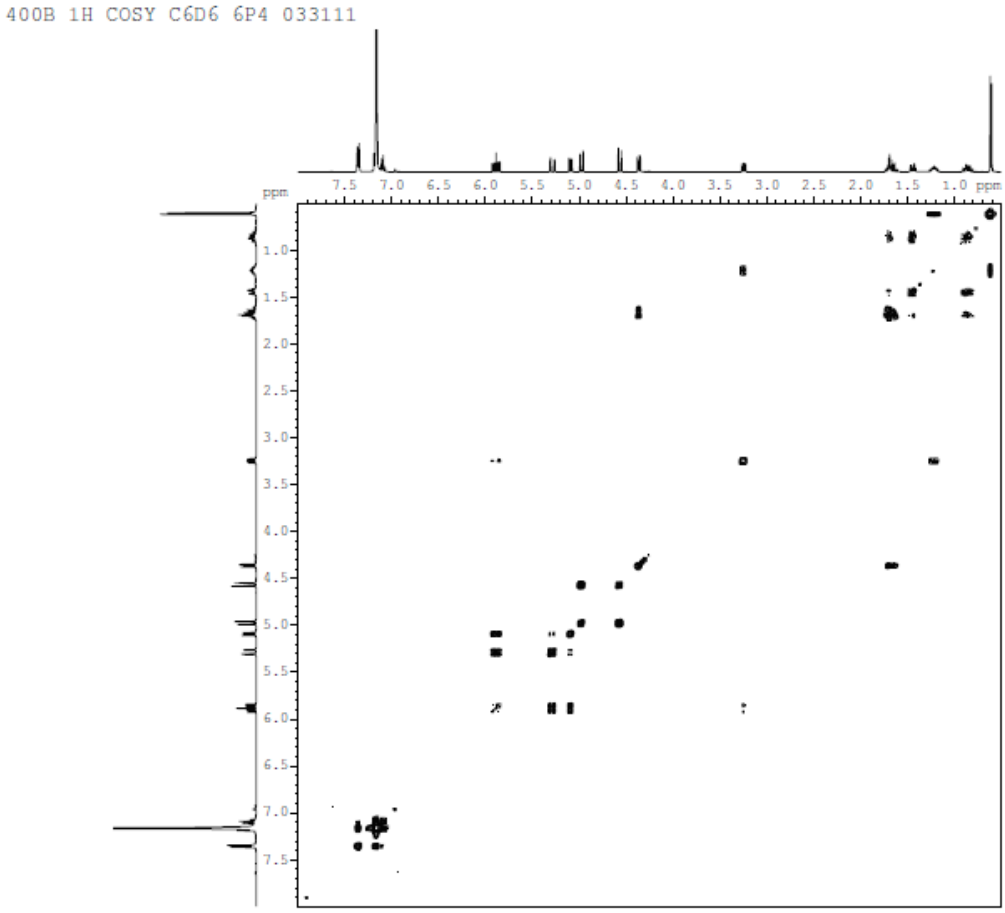

400B 1H C6D6 6P1-1 033111
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

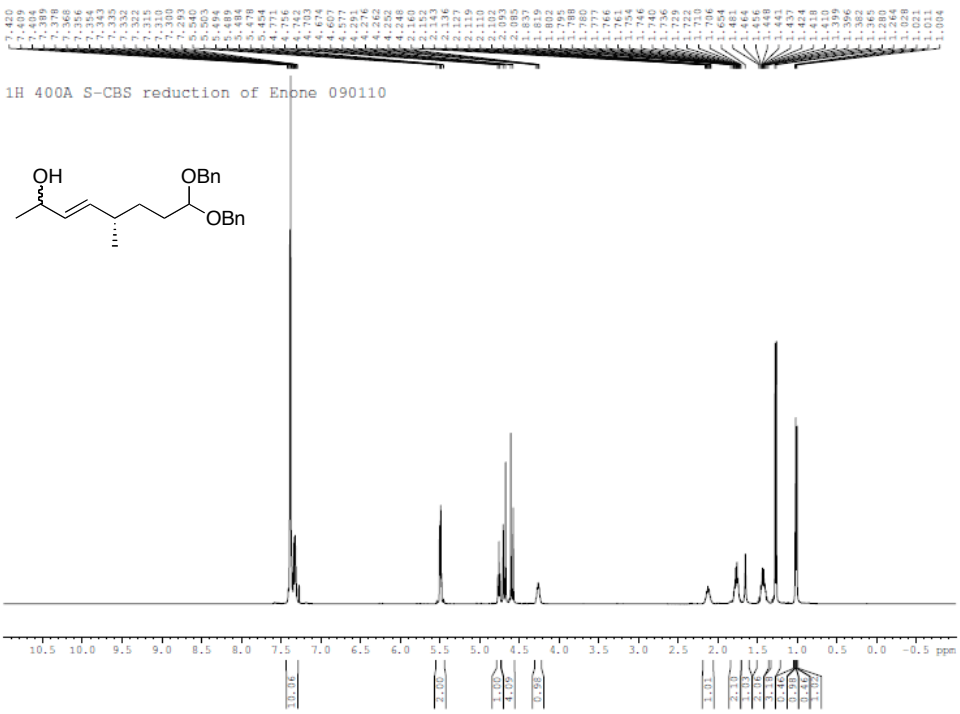

400B 1H C6D6 6P23 033111
OBn
OBn
ppm

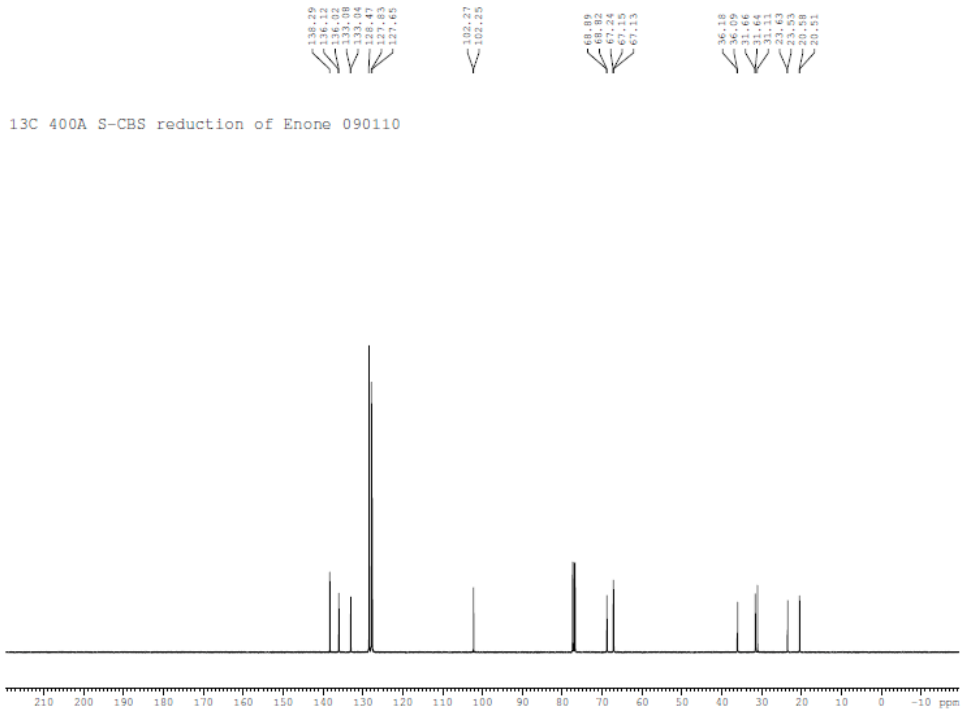

400B 13C C6D6 6P23 033111
ppm

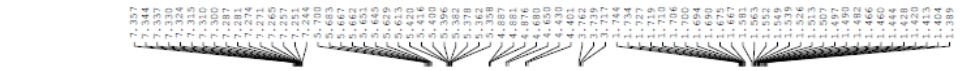

400B 1H C6D6 6P4 033111
OBn
ppm


400B 13C C6D6 6P4 033111
ppm

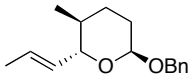

400B 1H COSY C6D6 6P4 033111
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5

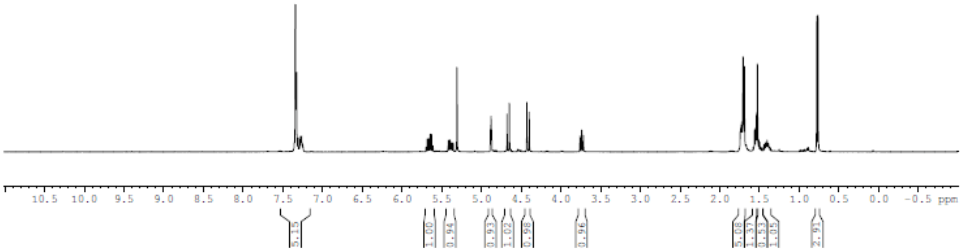

1H 400A S-CBS reduction of Enone 090110
OH
OBn
OBn


13C 400A S-CBS reduction of Enone 090110

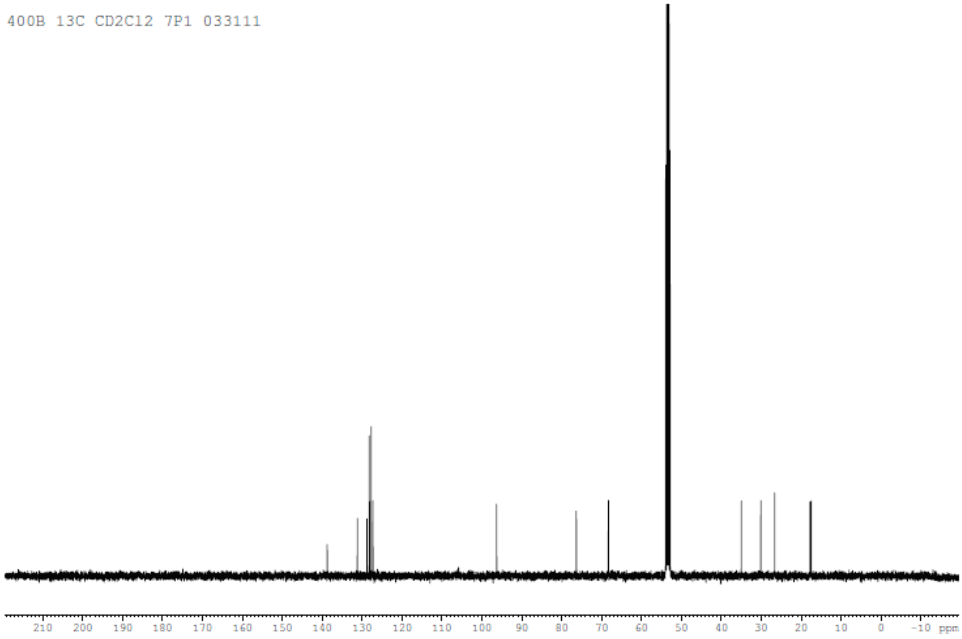


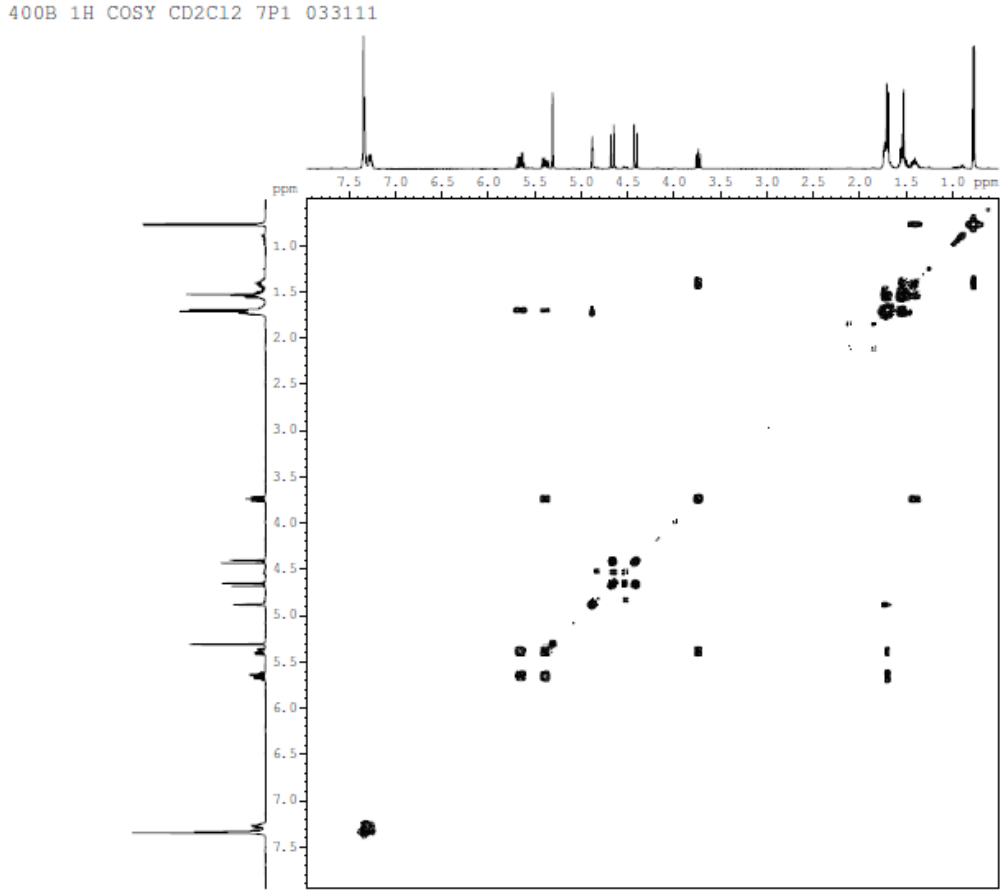
400B 1H CD2C12 7P1 033111

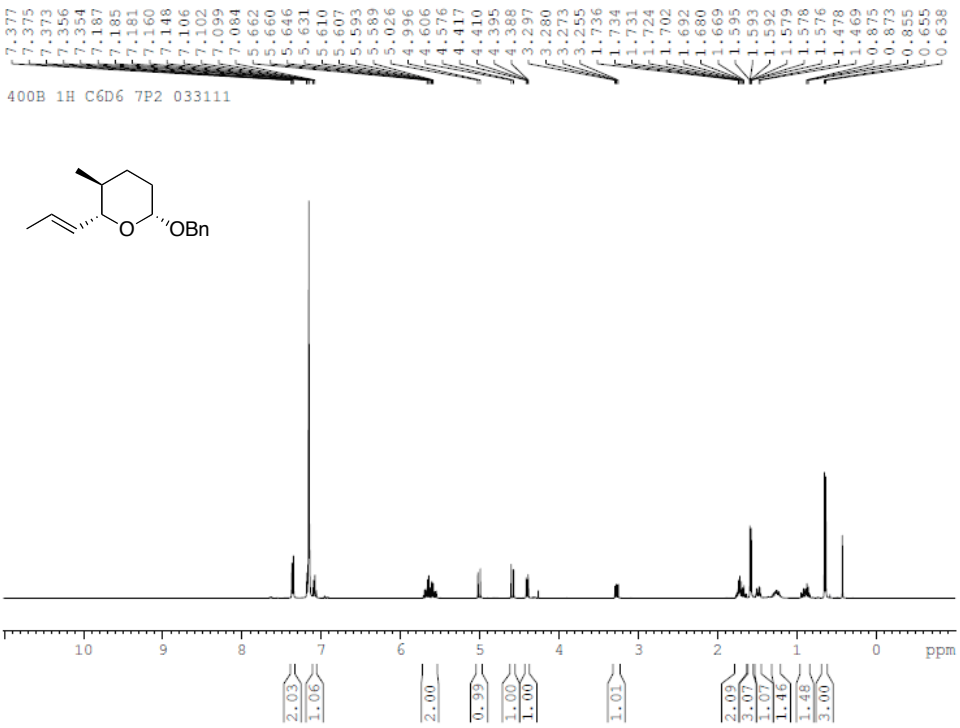


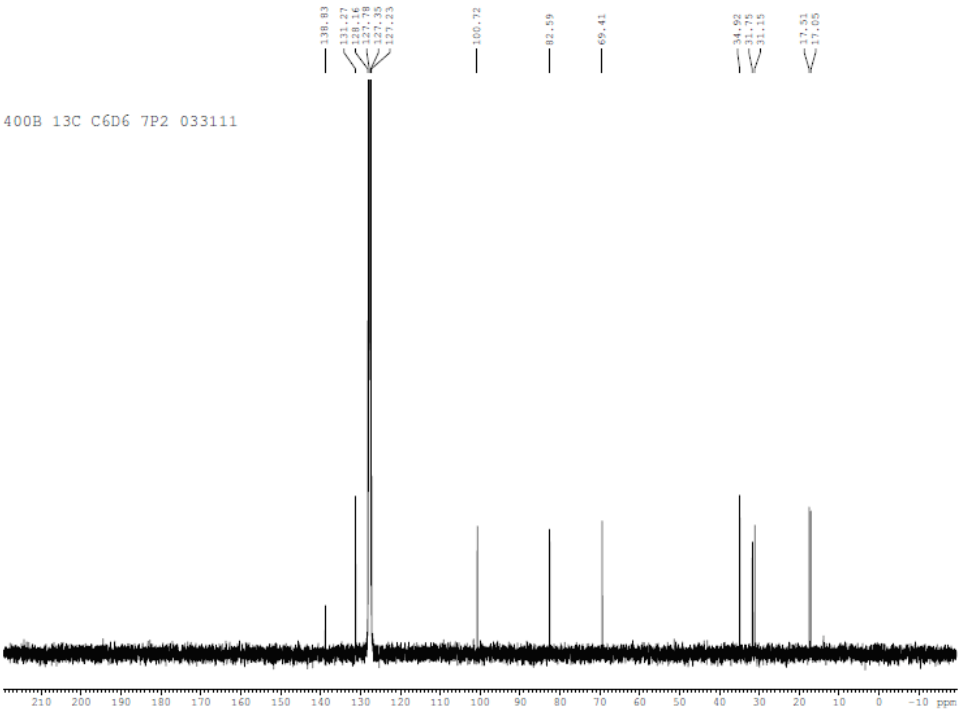


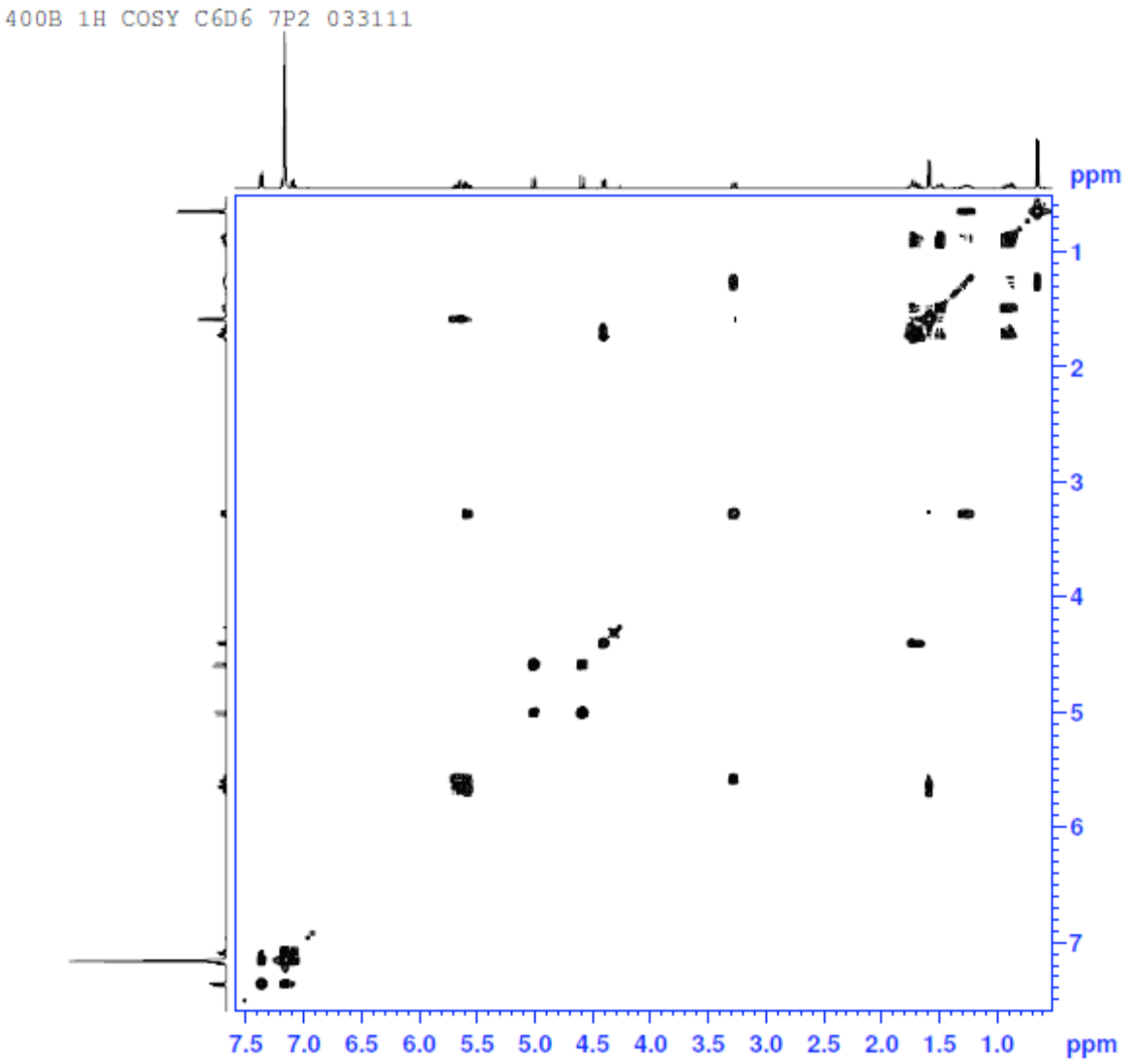
400B 13C CD2C12 7P1 033111

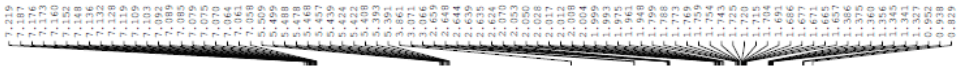



400B 1H COSY CD2Cl2 7P1 033111
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

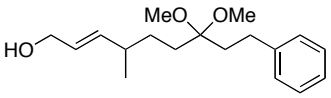


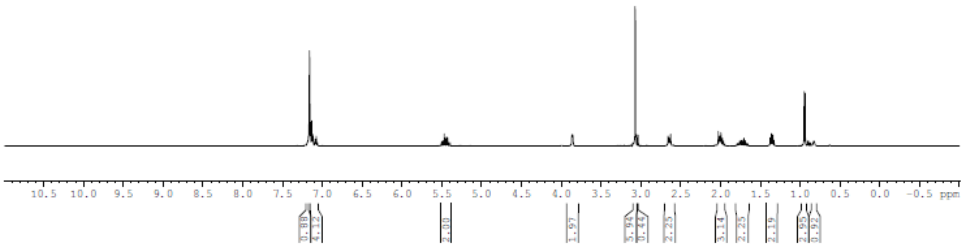


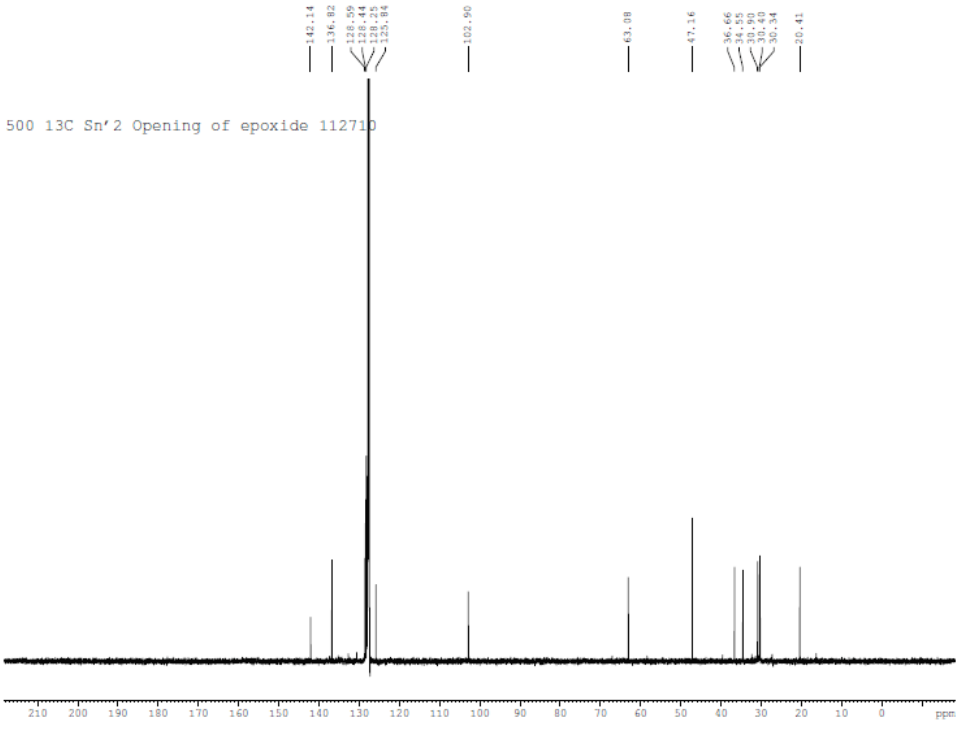

400B 1H COSY C6D6 7P2 033111
ppm
1
2
3
4
5
6
7
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm



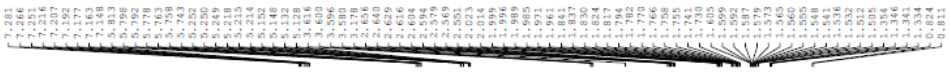
500 1H Sn'2 Opening of epoxide 112710



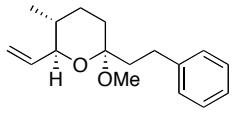


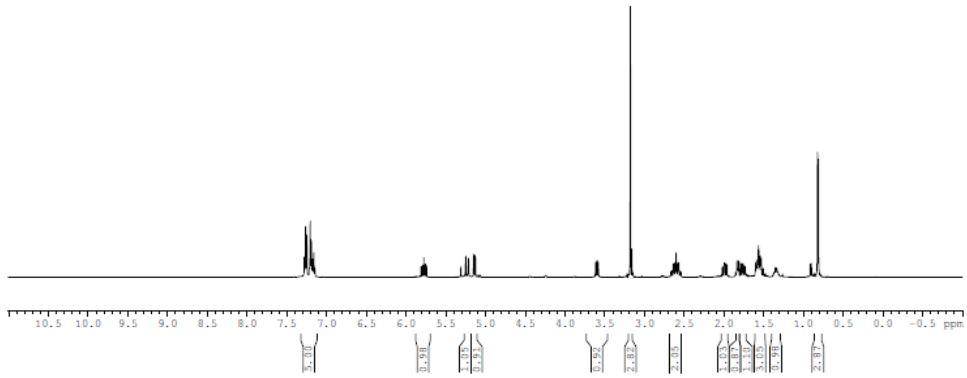


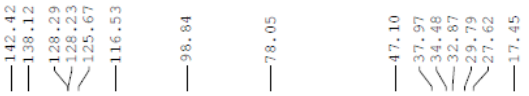
500 13C Sn'2 Opening of epoxide 112710



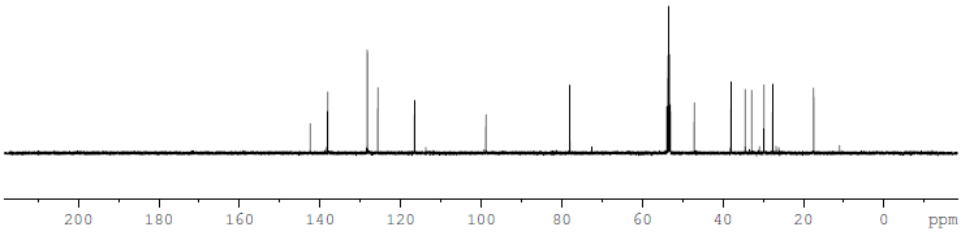
500 1H rearrangement 112810

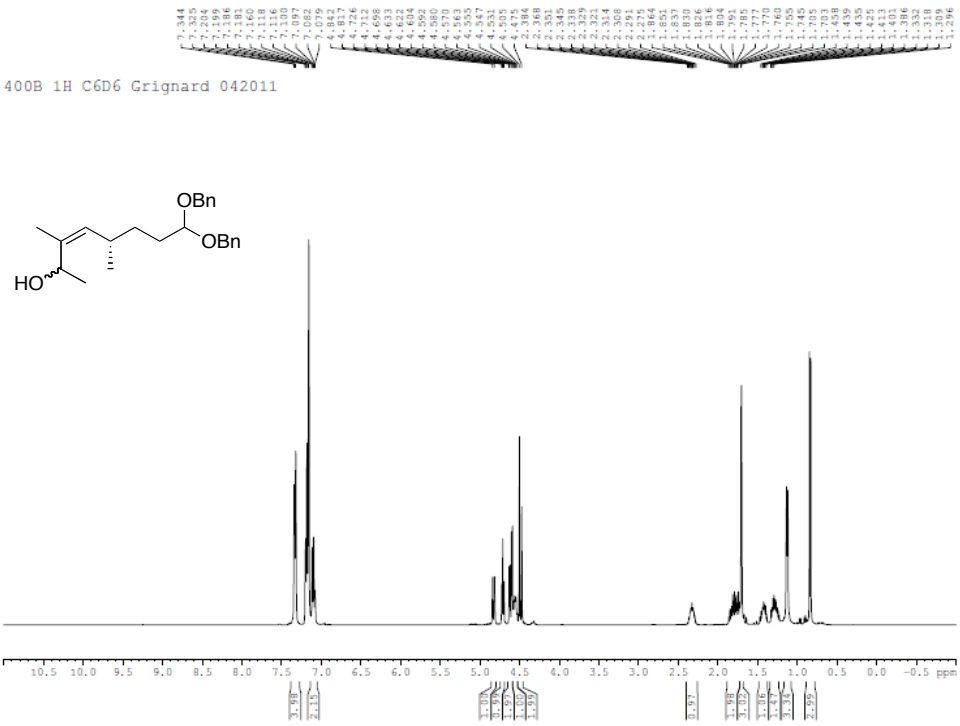


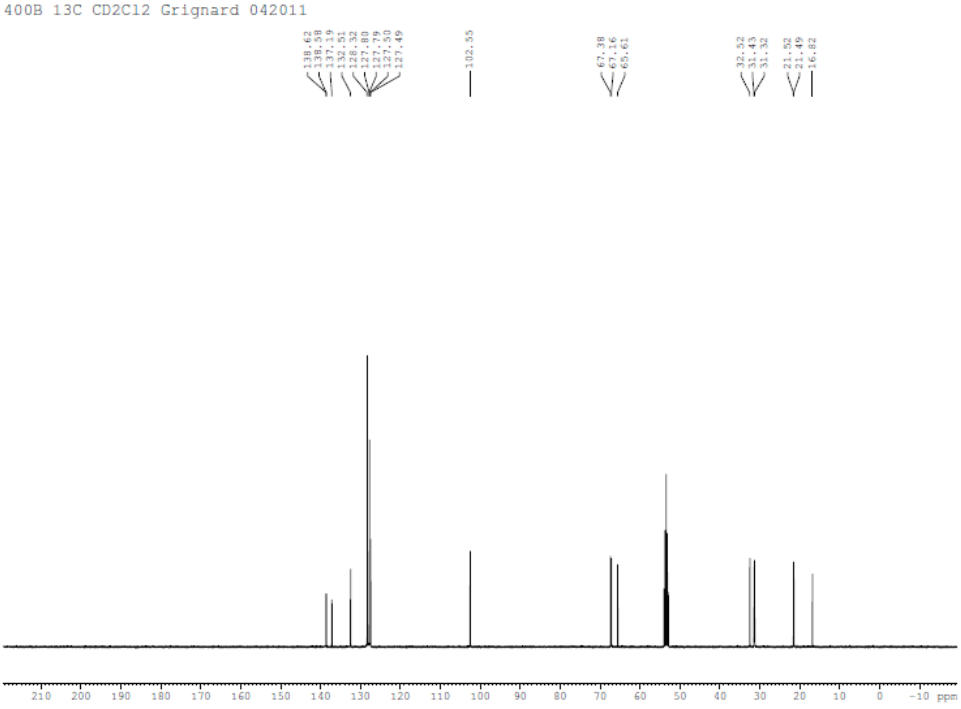


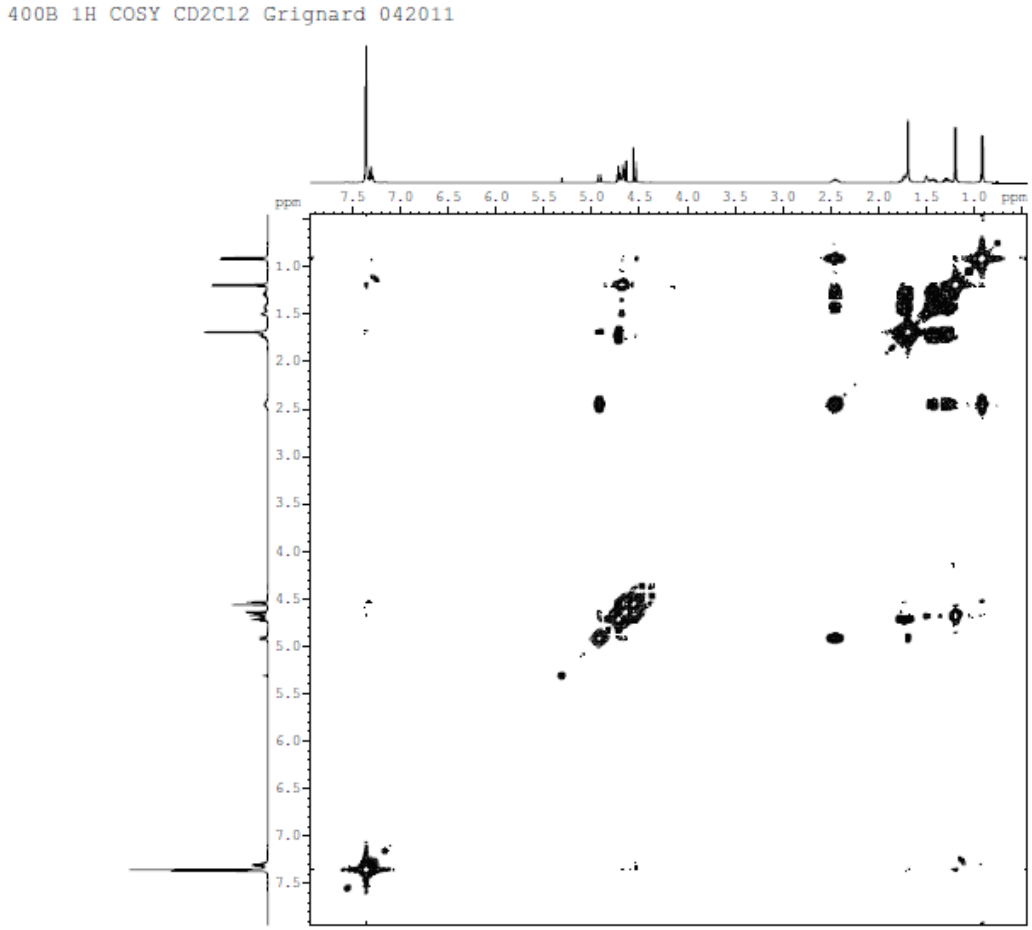


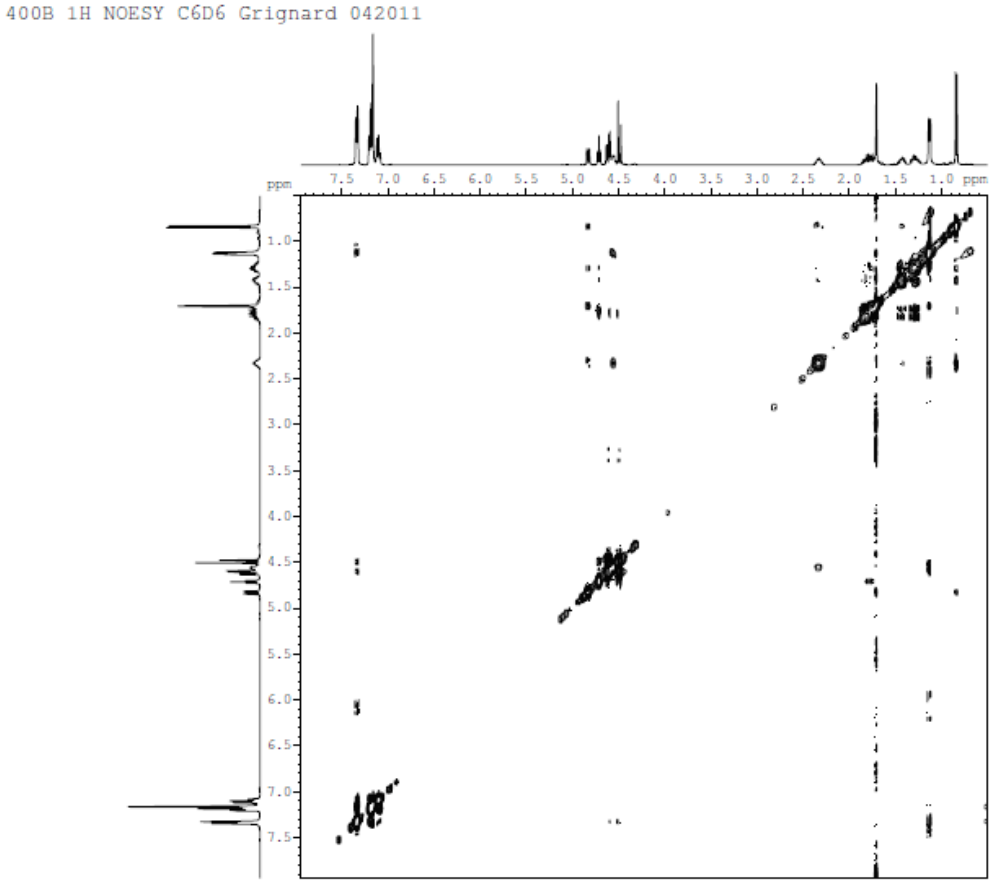
500 13C rearrangement 112810-1



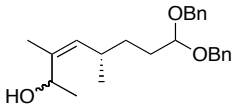

400B 1H C6D6 Grignard 042011
OBn
OBn
HO

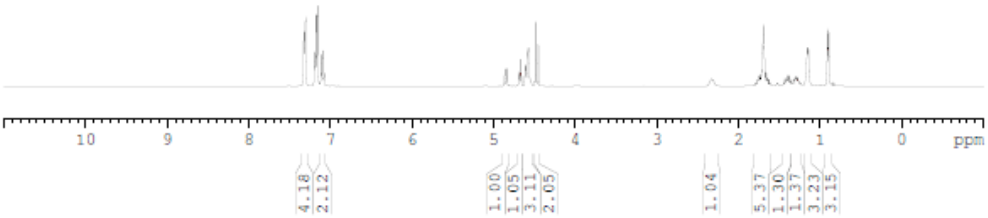

400B 13C CD2Cl2 Grignard 042011

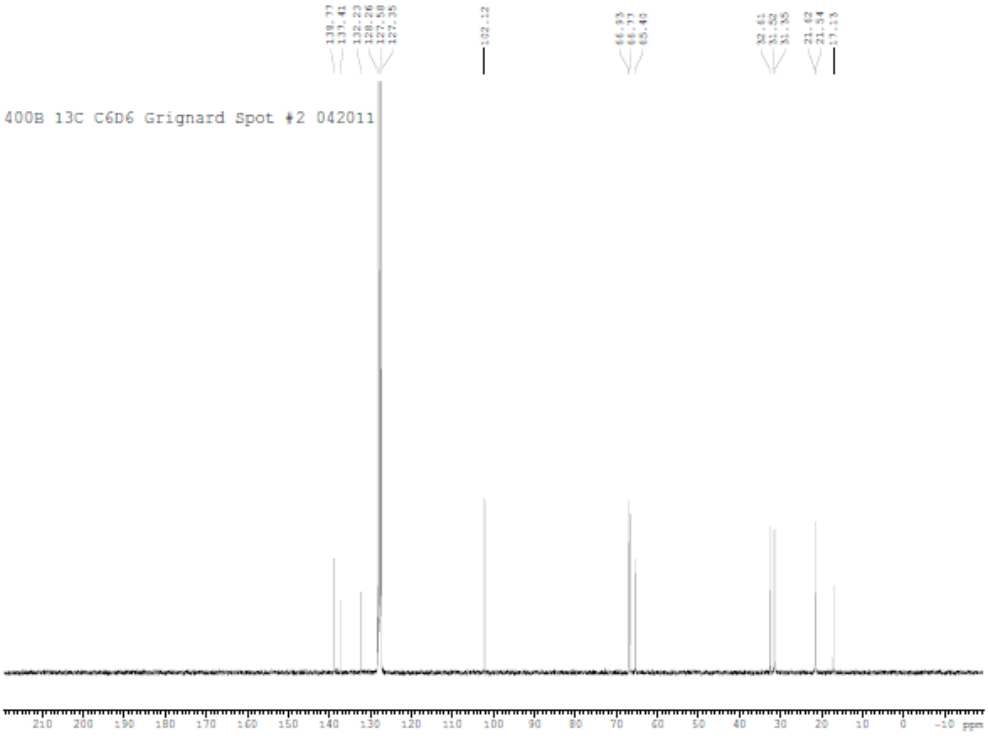

400B 1H COSY CD2Cl2 Grignard 042011
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5

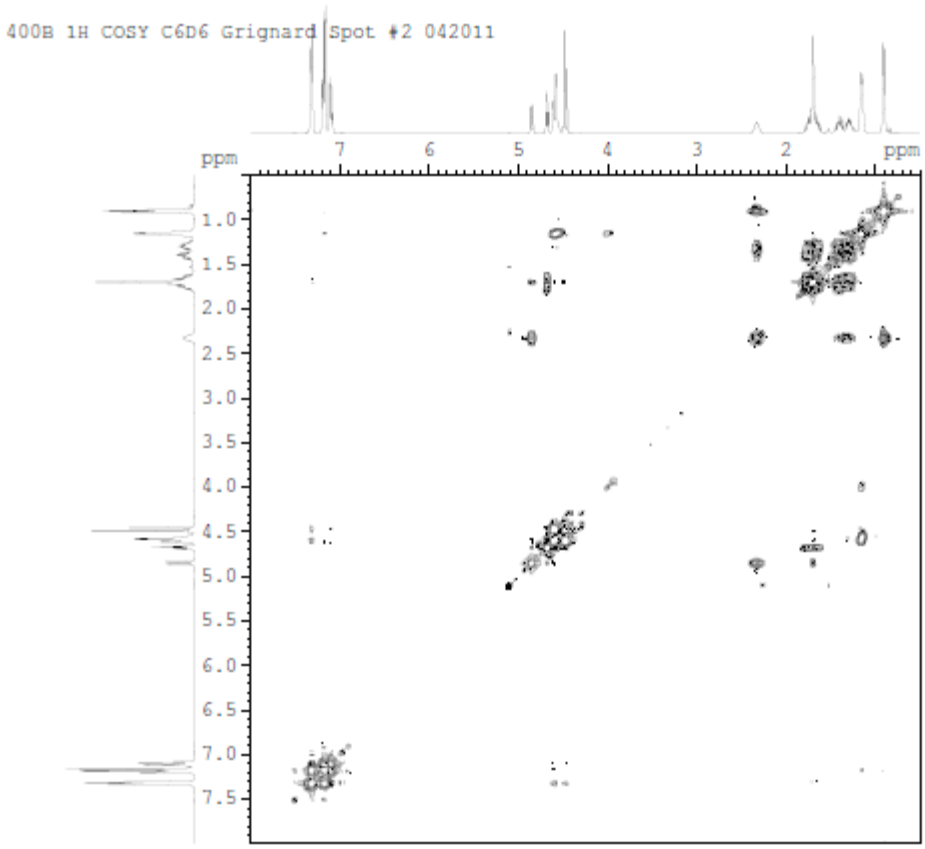

400B 1H NOESY C6D6 Grignard 042011
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

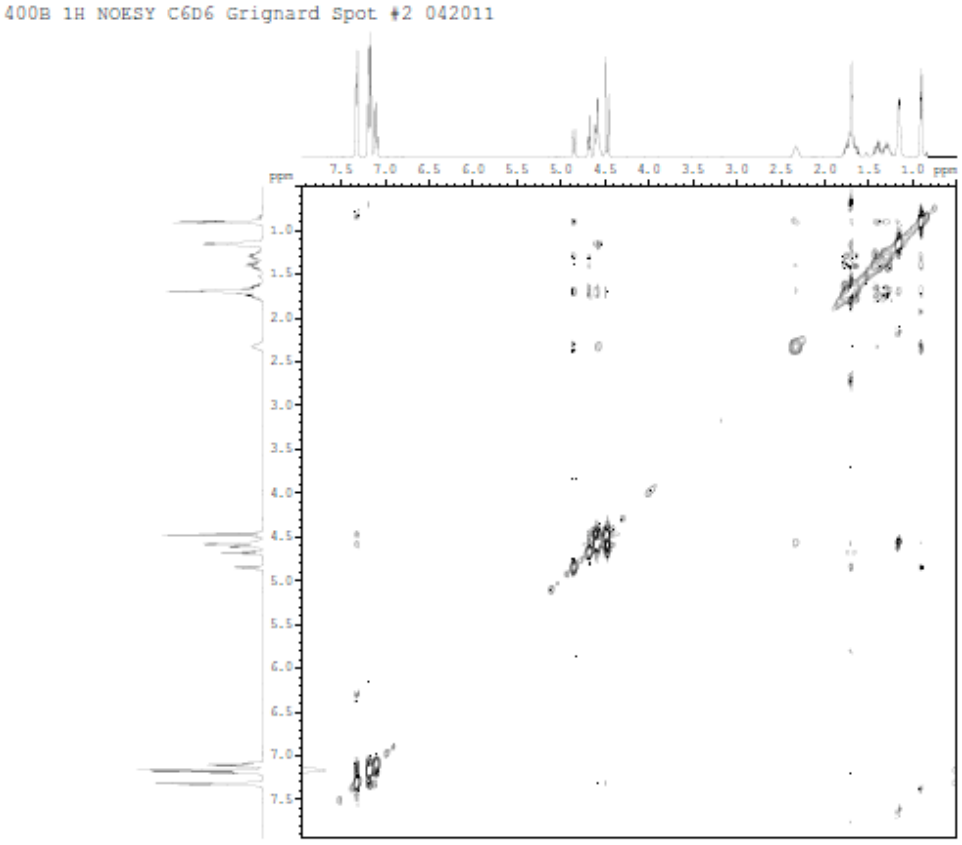
400B 1H C6D6 Grignard Spot #2 042011



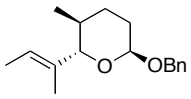


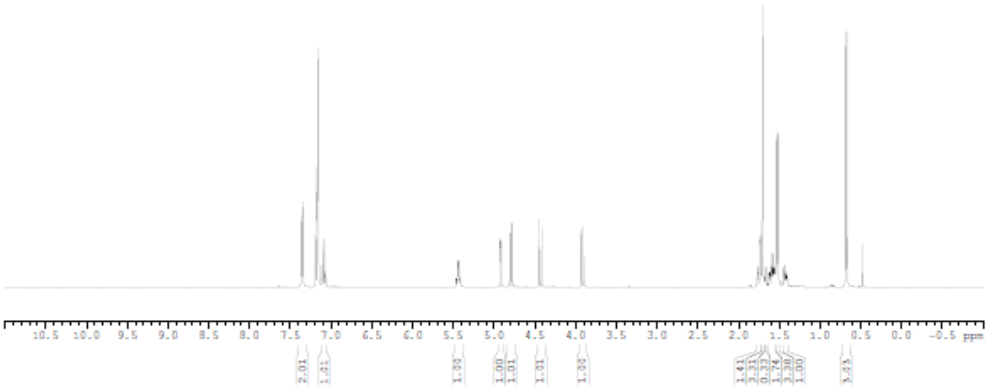


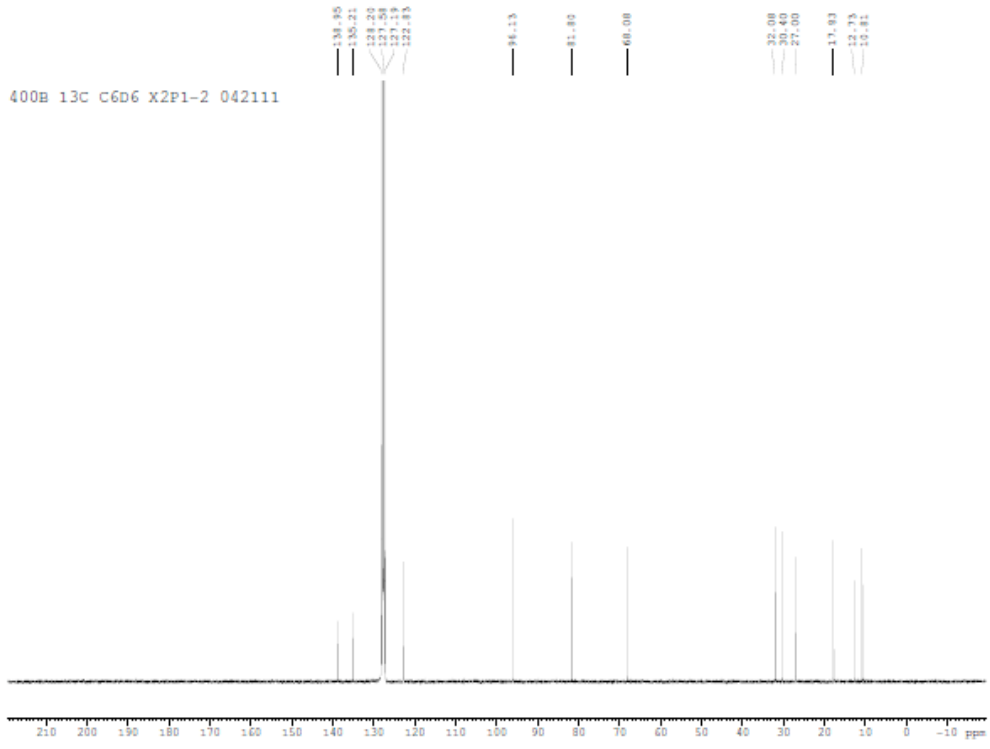



400B 1H NOESY C6D6 Grignard Spot #2 042011
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

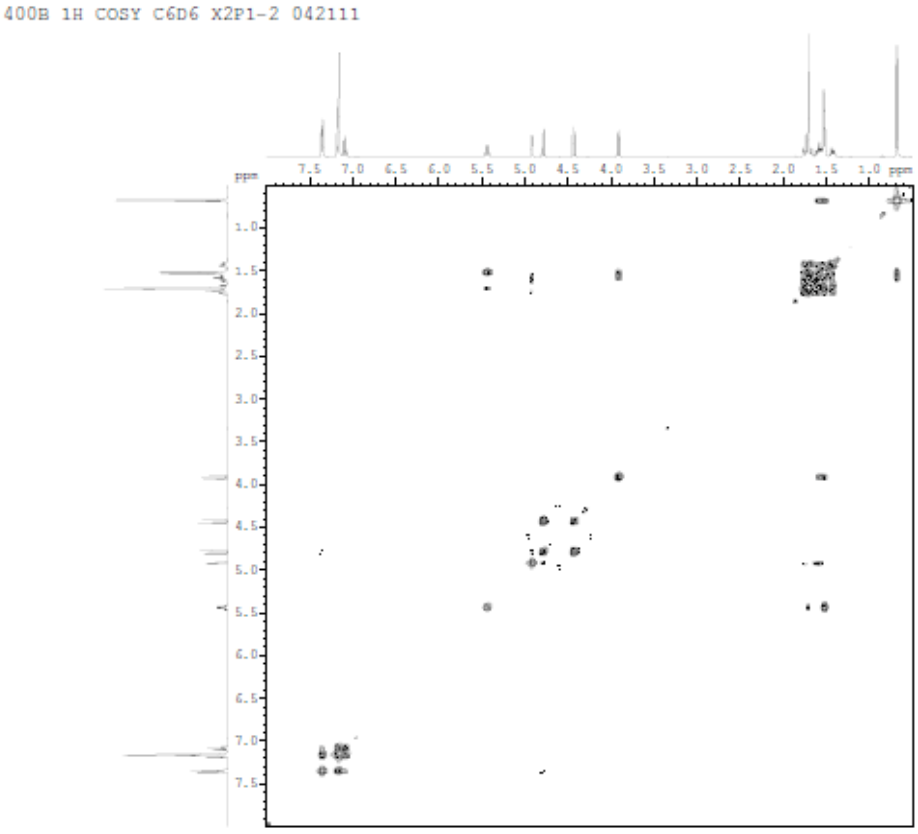
400B 1H C6D6 X2P1-2 042111

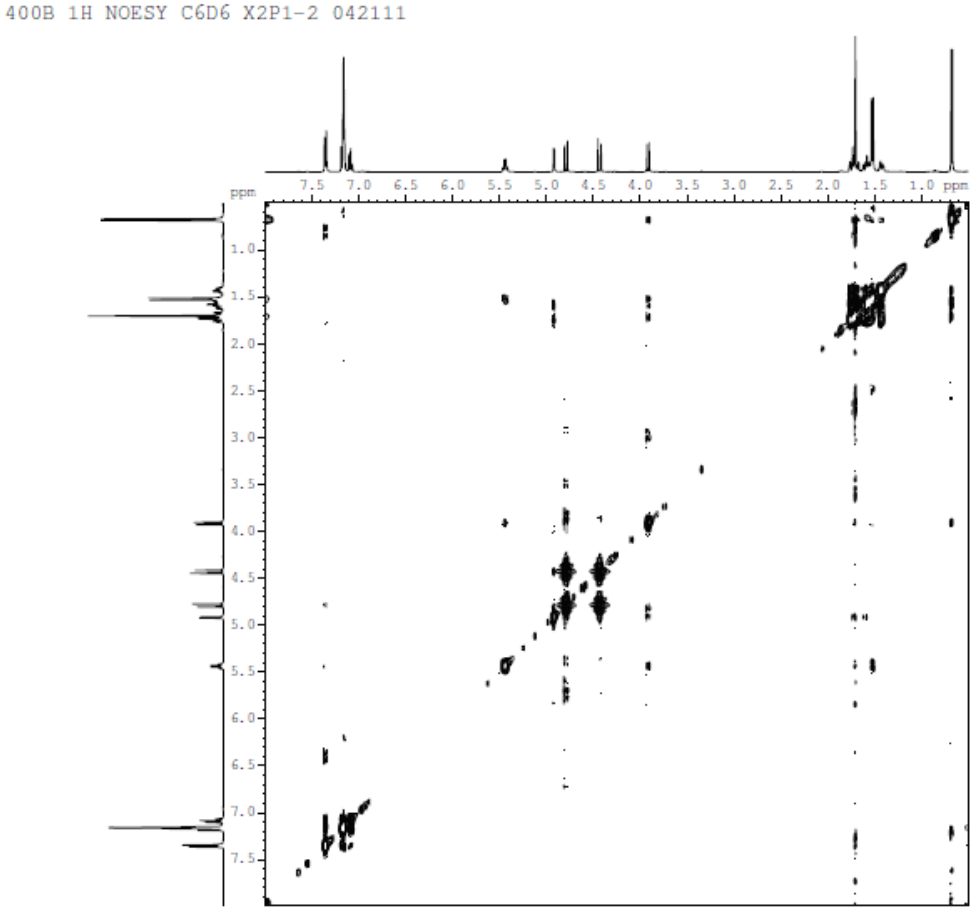


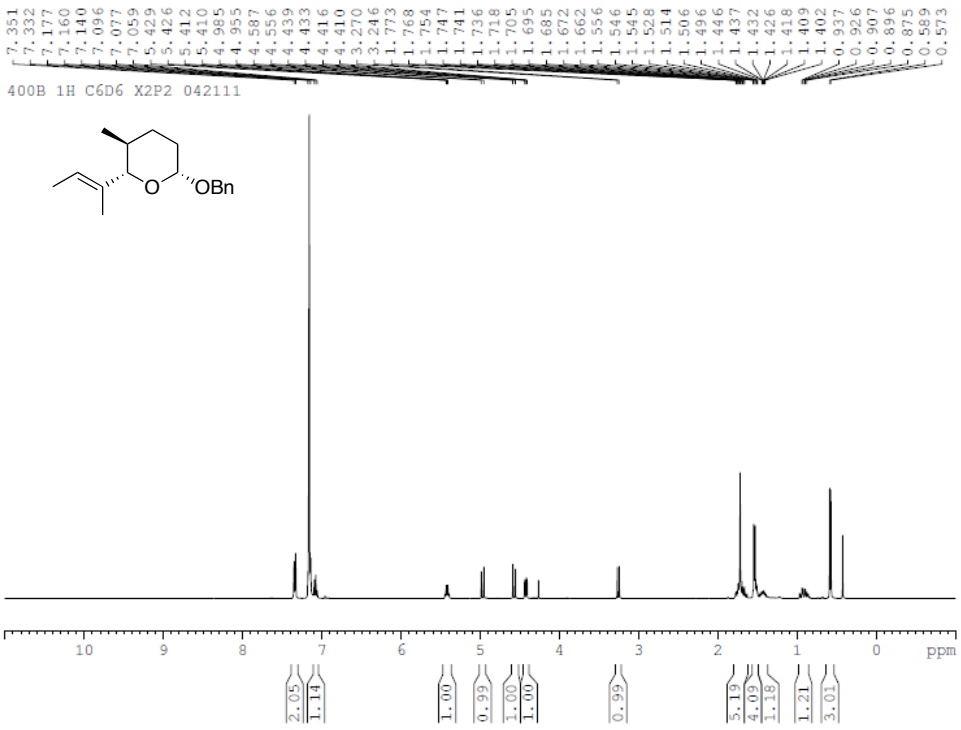




400B 13C C6D6 X2P1-2 042111




400B 1H NOESY C6D6 X2P1-2 042111
ppm
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
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5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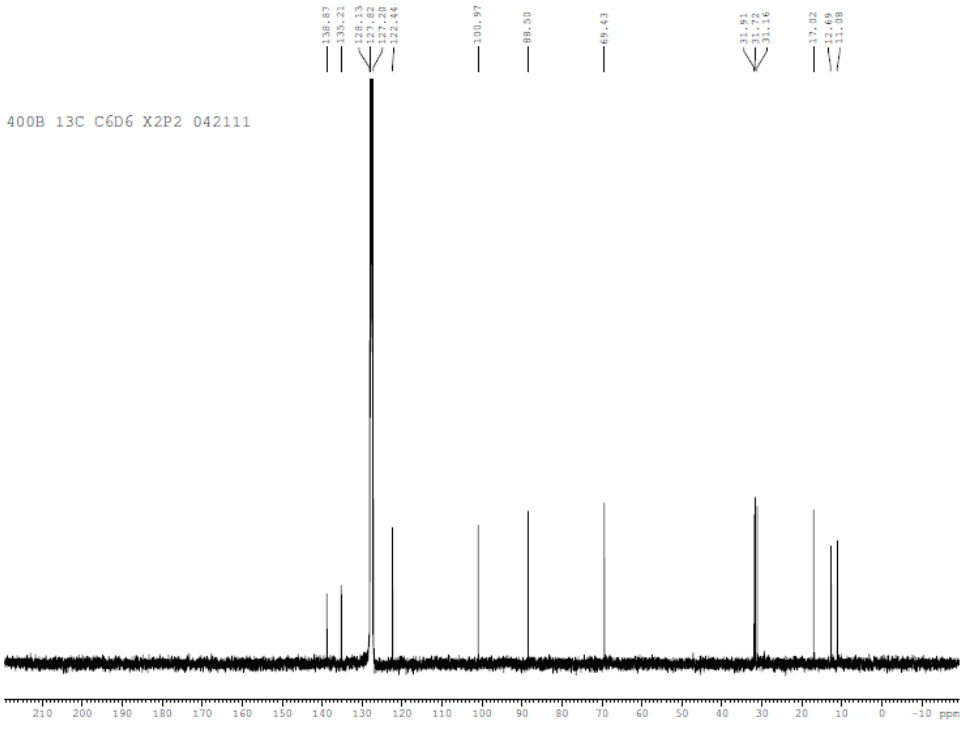
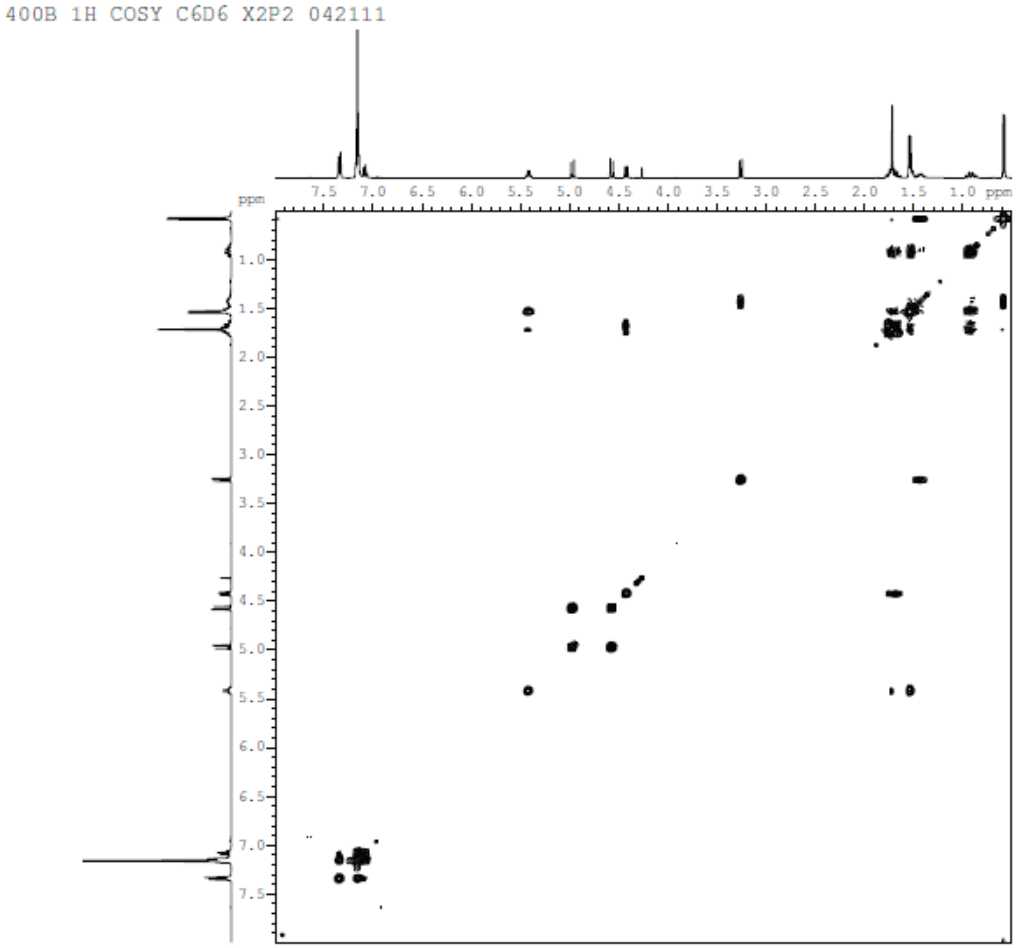
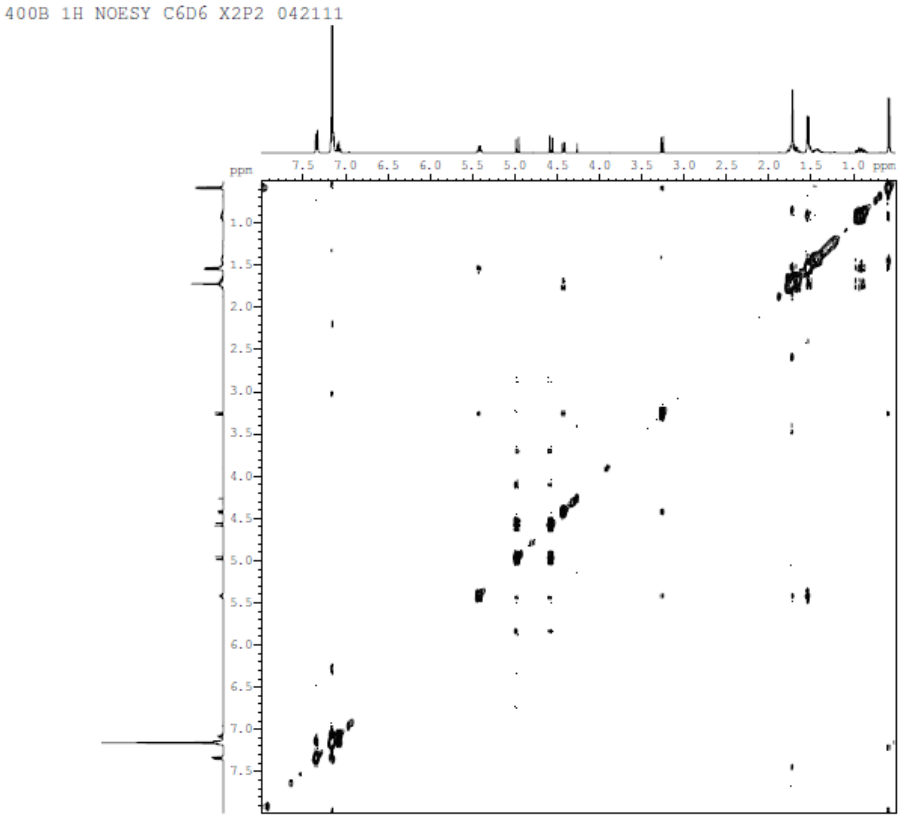
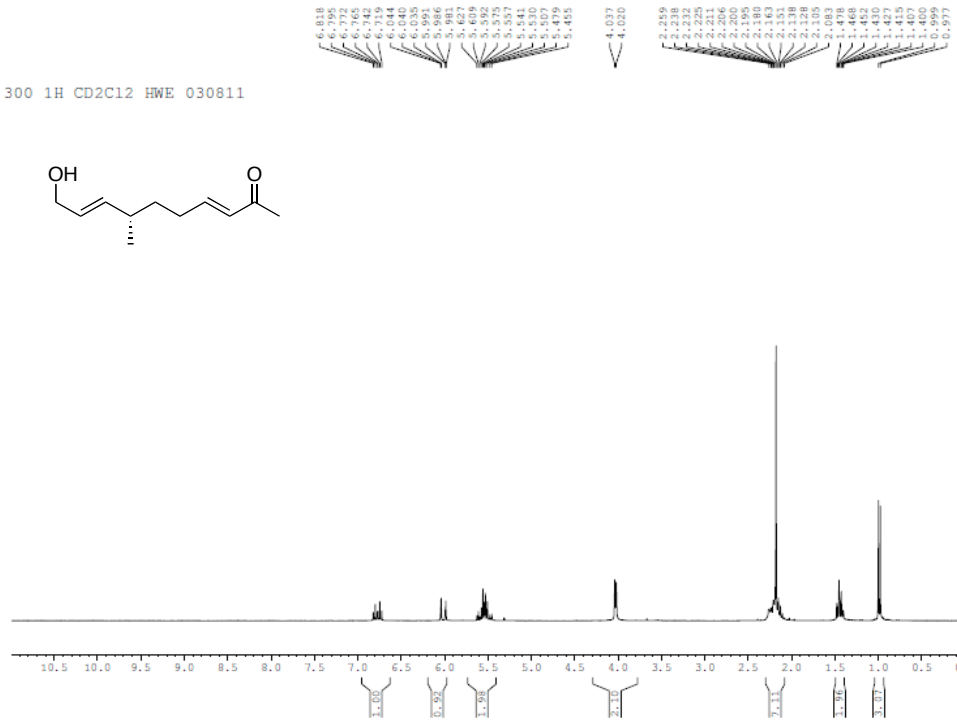
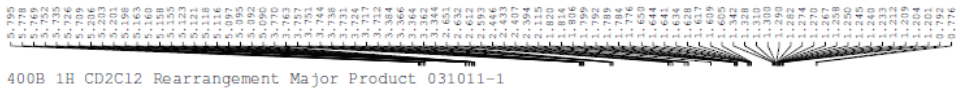
7.332
7.177
7.160
7.140
7.096
7.077
7.059
5.429
5.426
5.412
5.410
4.985
4.955
4.587
4.556
4.439
4.433
4.416
4.410
3.270
3.246
1.773
1.768
1.754
1.747
1.741
1.736
1.718
1.705
1.695
1.685
1.672
1.662
1.556
1.546
1.545
1.528
1.514
1.506
1.496
1.446
1.437
1.432
1.426
1.418
1.409
1.402
0.937
0.926
0.907
0.896
0.875
0.589
0.573
400B 1H C6D6 X2P2 042111
O
OBn
10
9
8
7
6
5
4
3
2
1
0
ppm
2.05
1.14
1.00
0.99
1.00
1.00
0.99
5.19
4.09
1.18
1.21
3.01


138.87
135.21
128.13
127.82
127.20
122.44
100.97
88.50
69.43
31.91
31.72
31.16
17.02
12.69
11.08
400B 13C C6D6 X2P2 042111
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

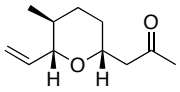

400B 1H COSY C6D6 X2P2 042111
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

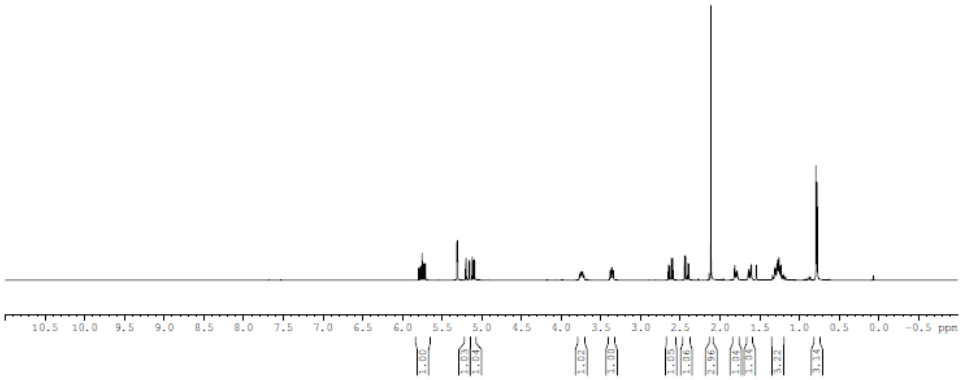

400B 1H NOESY C6D6 X2P2 042111
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

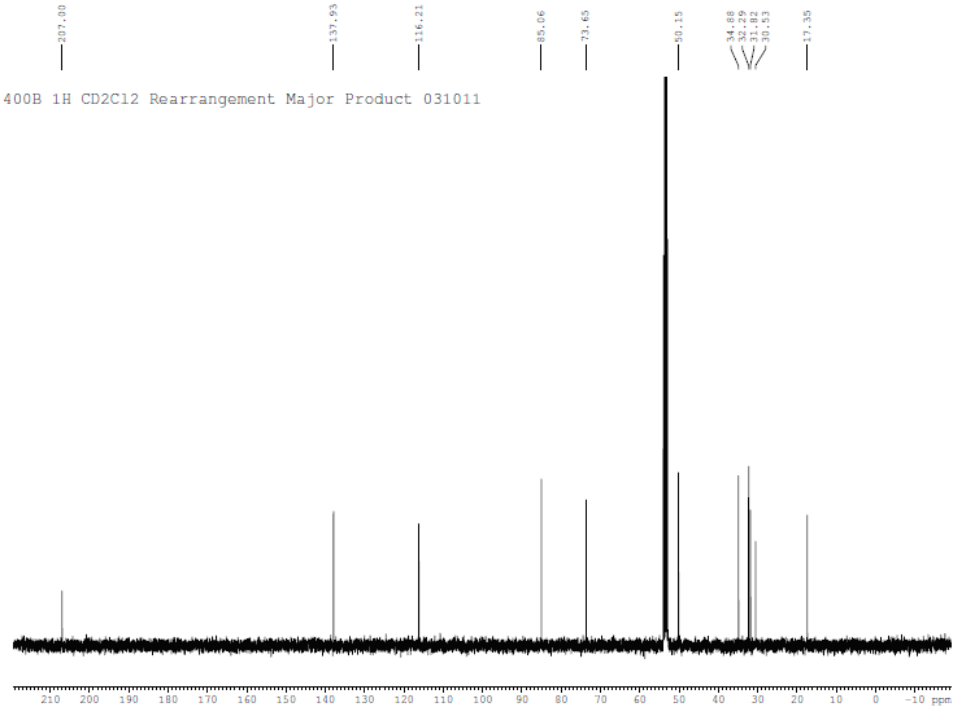

6.818
6.795
6.772
6.765
6.742
6.719
6.644
6.640
6.635
6.591
6.586
5.981
5.627
5.609
5.592
5.575
5.557
5.541
5.530
5.507
5.479
5.455
4.037
4.020
2.259
2.238
2.232
2.225
2.211
2.206
2.200
2.195
2.180
2.163
2.151
2.138
2.128
2.105
2.083
1.478
1.468
1.452
1.430
1.427
1.415
1.407
1.400
0.999
0.977
OH
O
300 1H CD2C12 HWE 030811
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
1.00
0.90
1.98
2.10
7.11
2.96
3.07
198.56
148.50
137.10
131.15
128.54
63.20
36.01
35.03
30.23
26.55
20.21
300 13C CD2C12 HWE 030811
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm

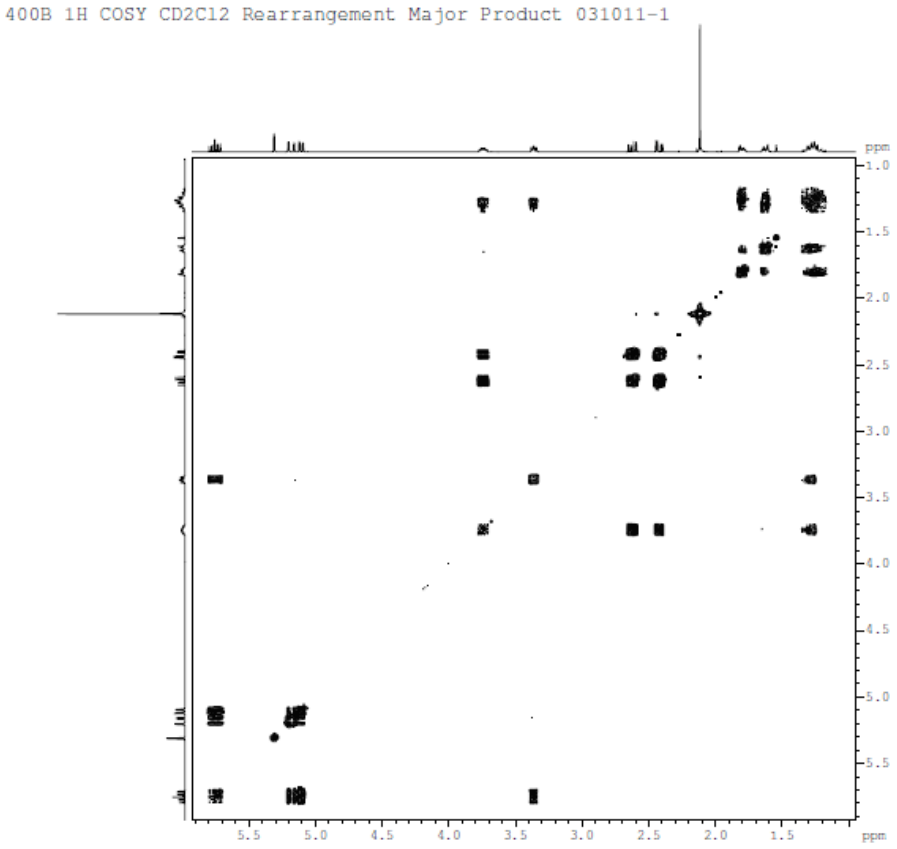


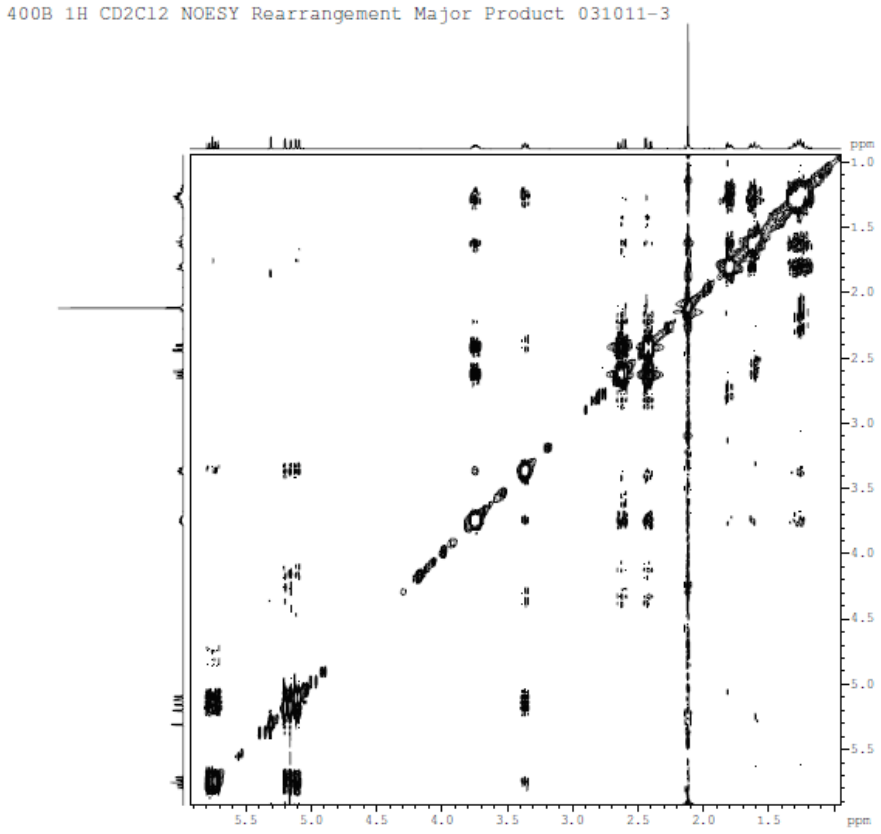
400B 1H CD2Cl2 Rearrangement Major Product 031011-1



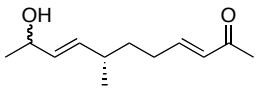


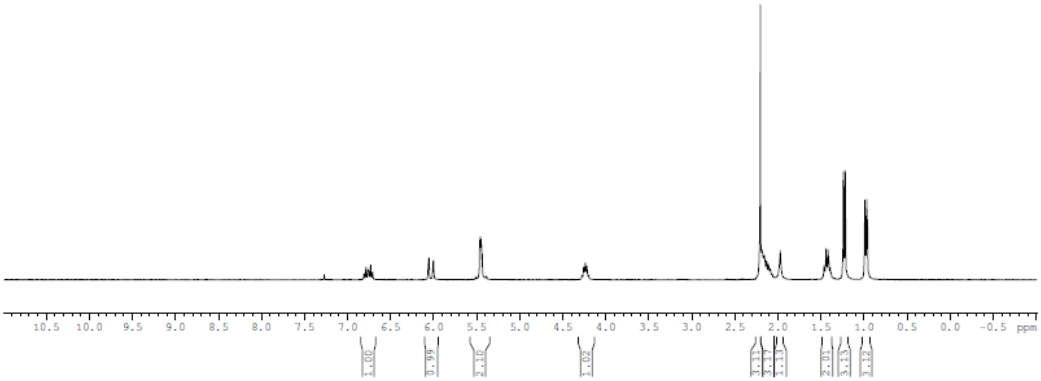



400B 1H COSY CD2Cl2 Rearrangement Major Product 031011-1
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

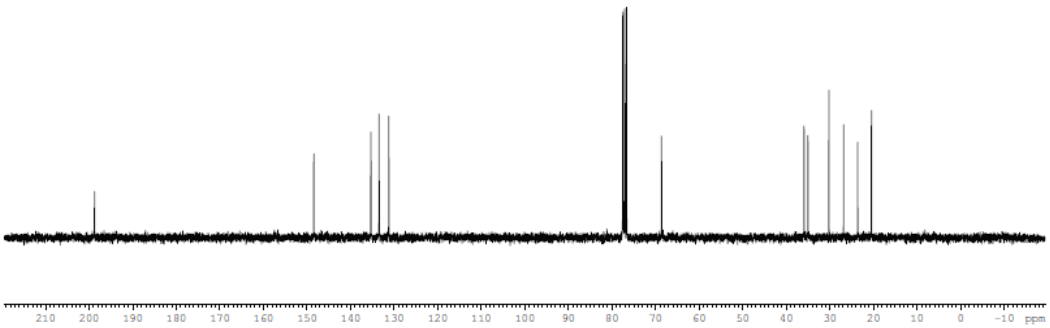

400B 1H CD2C12 NOESY Rearrangement Major Product 031011-3
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

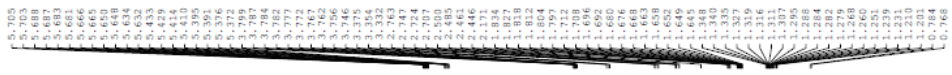
300 1H CDCl3 HWE 031711



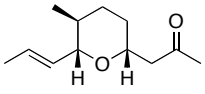


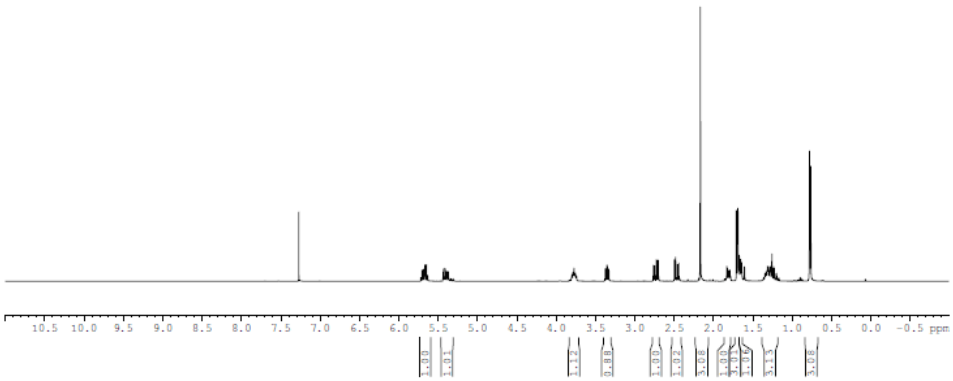
300 13C CDCl3 HWE 031711

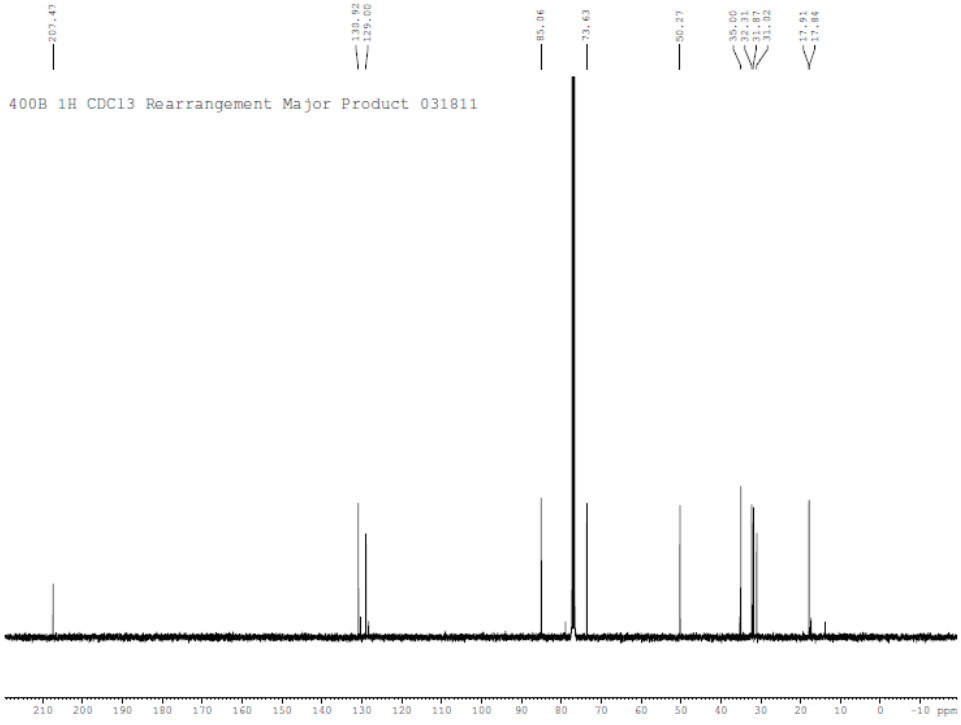


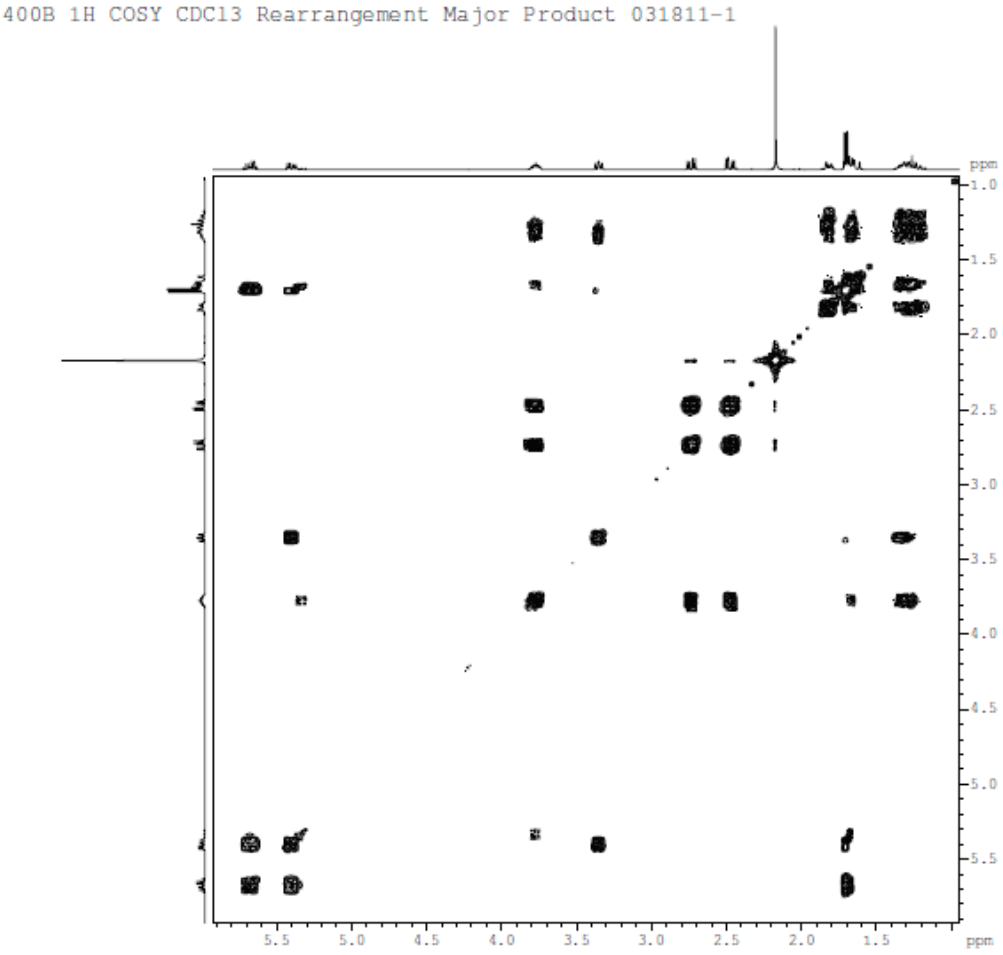


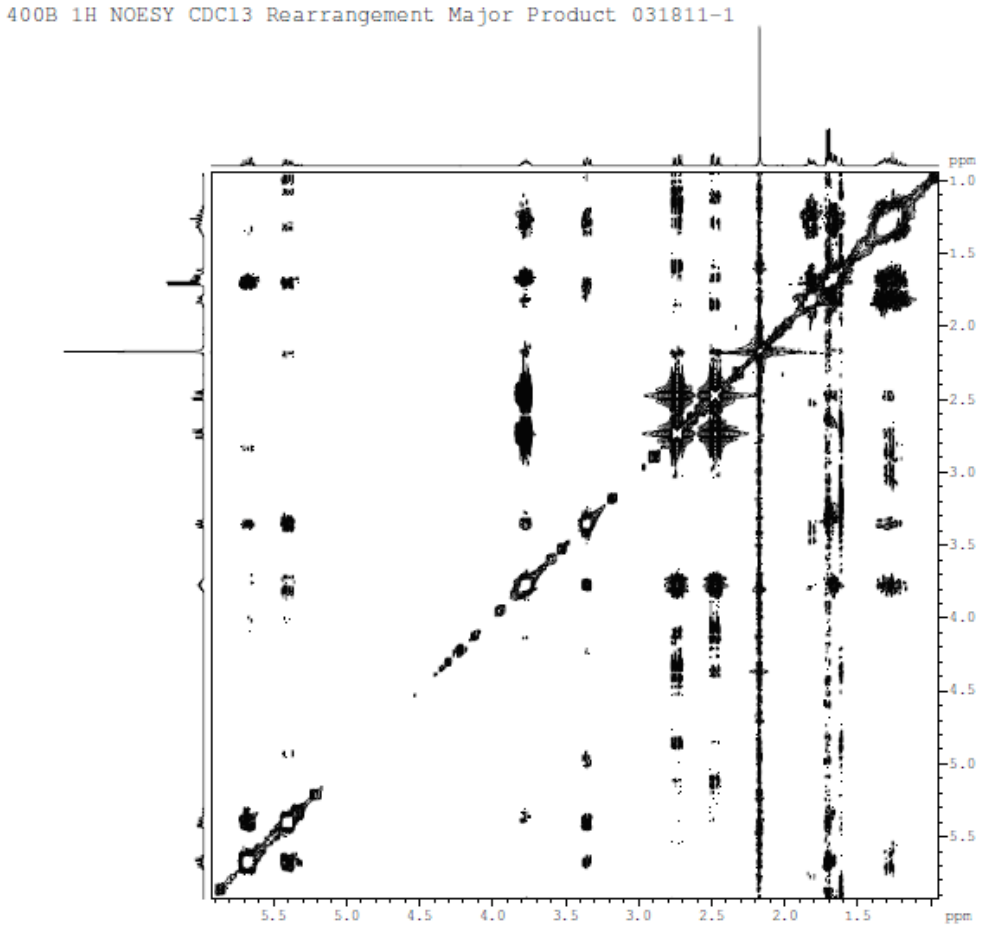
400B 1H CDCl3 Rearrangement Major Product 031811-1

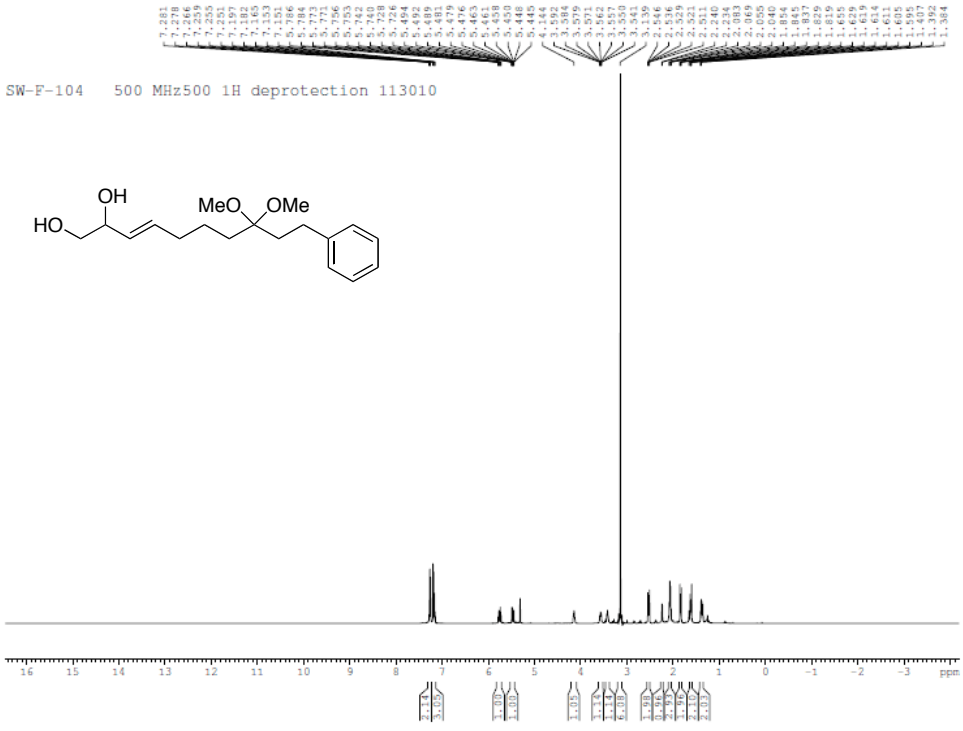


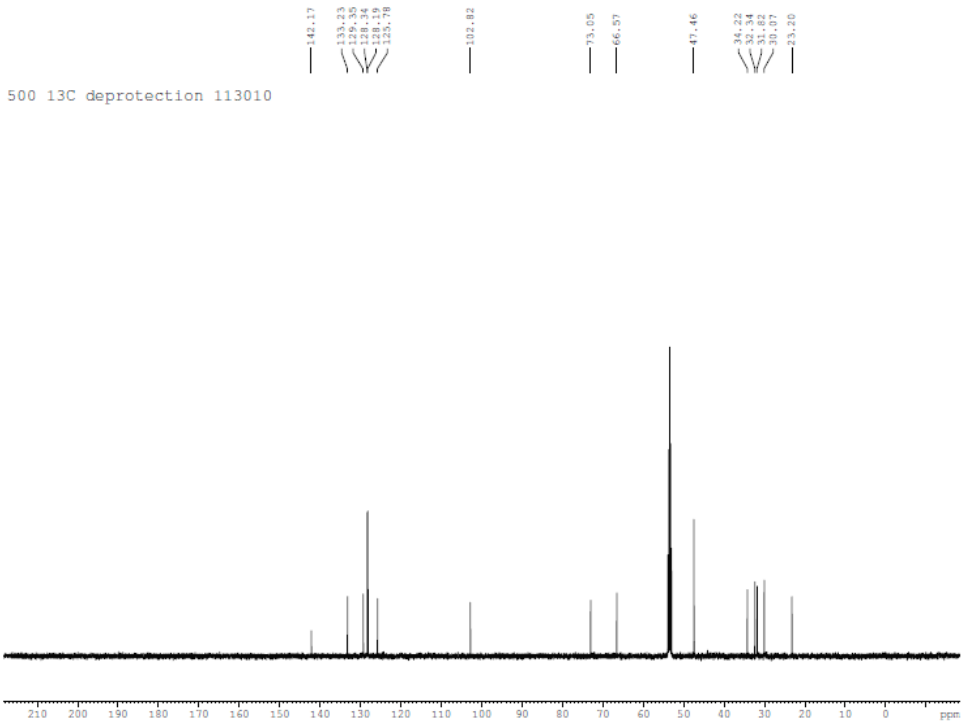


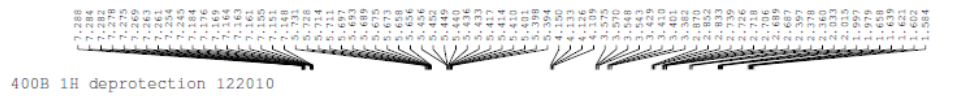


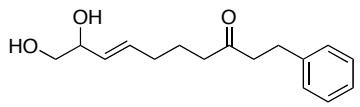

400B 1H COSY CDCl3 Rearrangement Major Product 031811-1
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

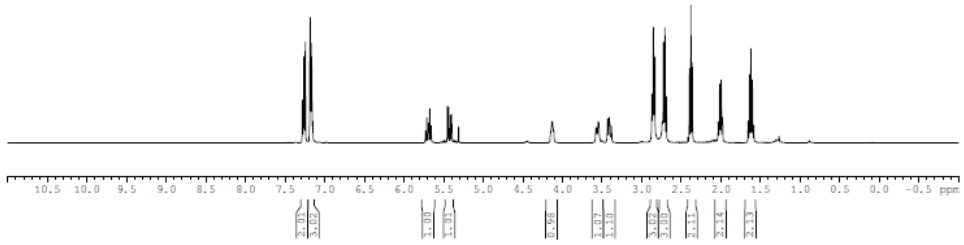

400B 1H NOESY CDCl3 Rearrangement Major Product 031811-1
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm

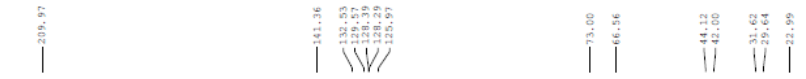

SW-F-104 500 MHz500 1H deprotection 113010
OH
HO
MeO
OMe
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2 −3 ppm


142.17
133.23
129.35
128.34
128.19
125.78
102.82
73.05
66.57
47.46
34.22
32.34
31.82
30.07
23.20
500 13C deprotection 113010
ppm

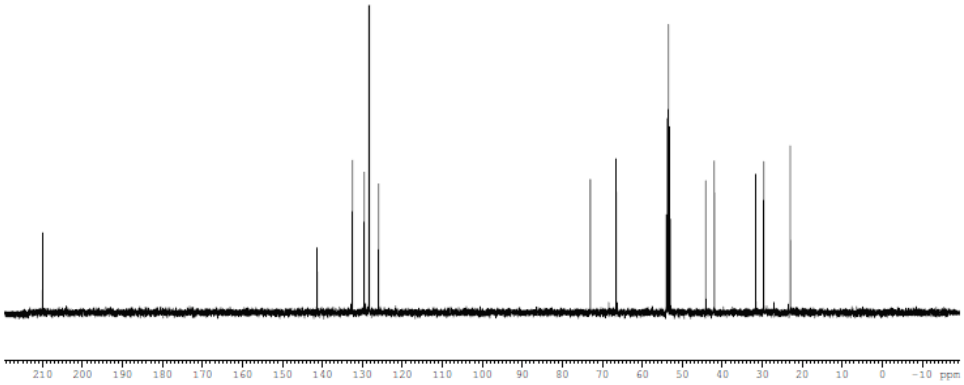

400B 1H deprotection 122010


OH
HO
O

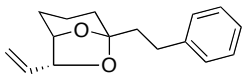

ppm

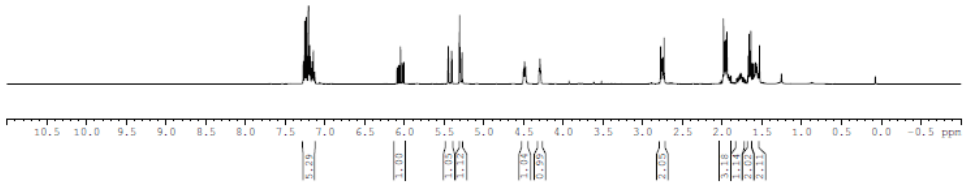


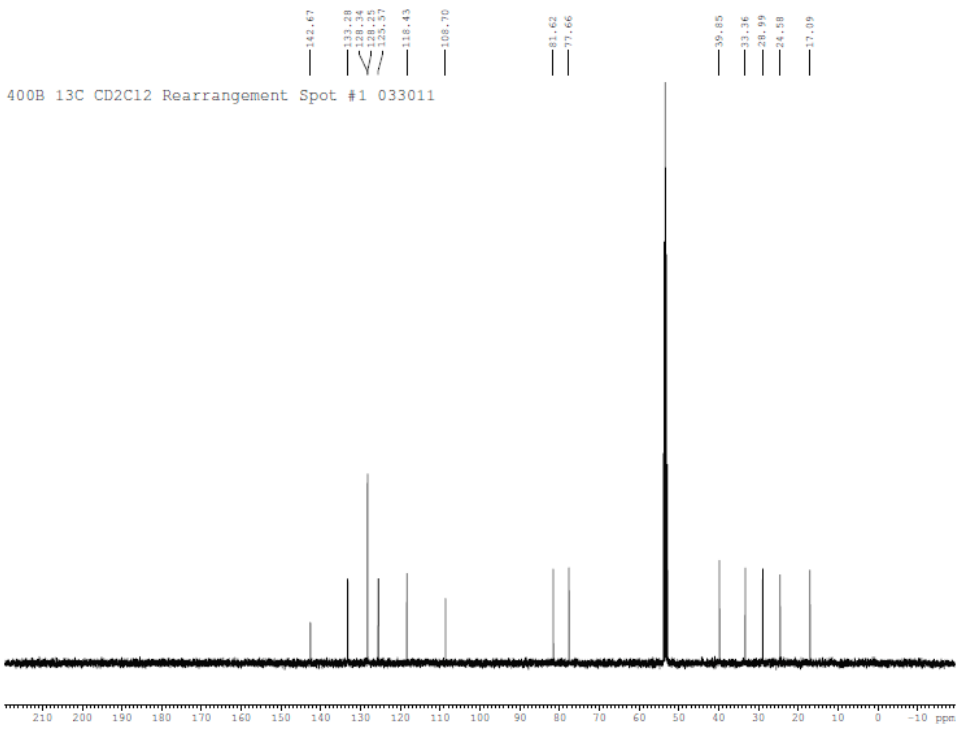
400B 13C deprotection 122010

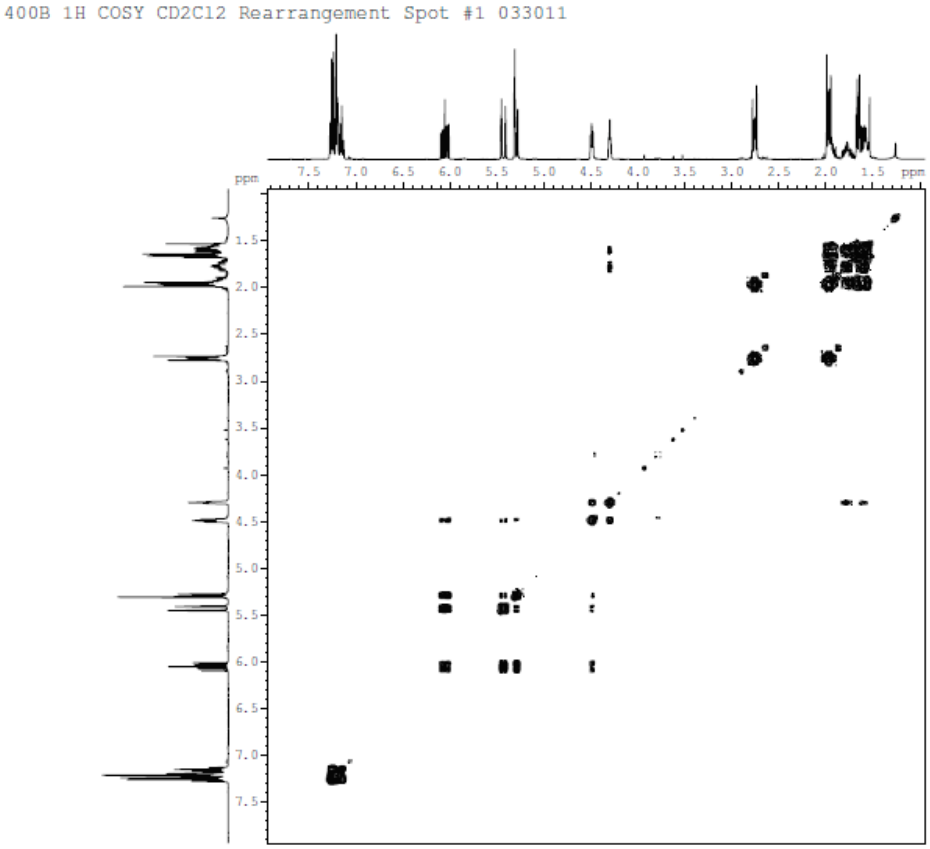


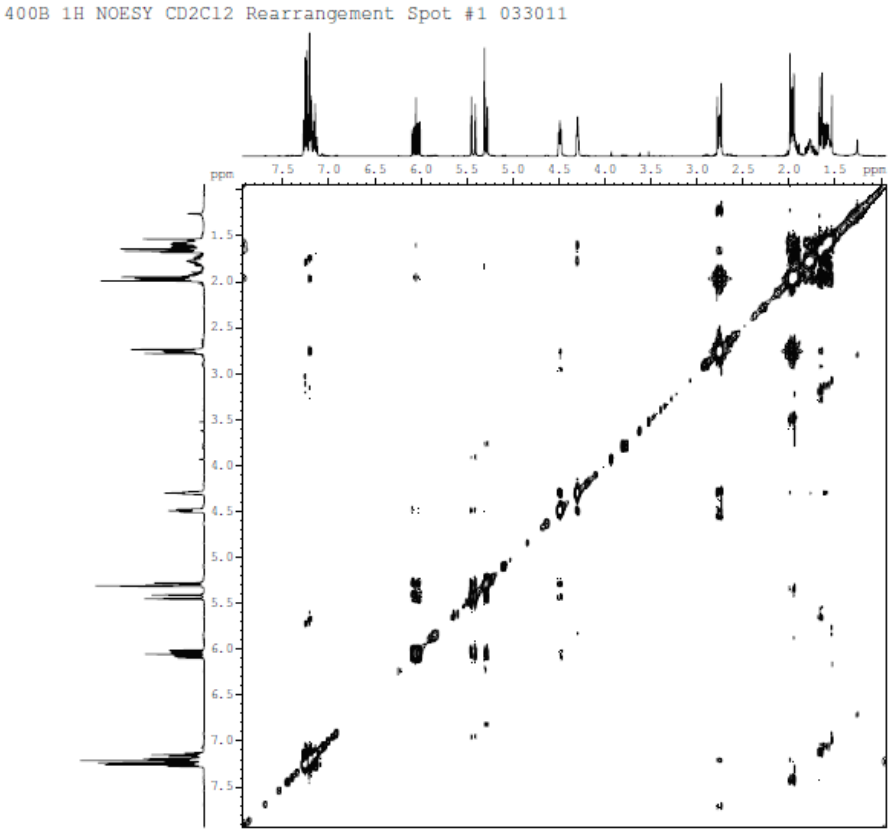
400B 1H CD2C12 Rearrangement Spot #1 033011



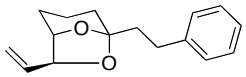


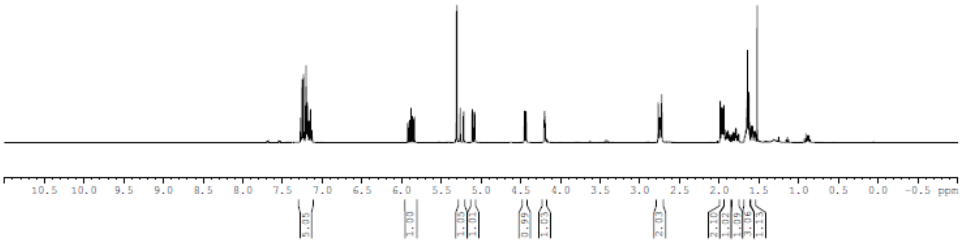

142.67
133.28
129.34
128.25
125.57
118.43
108.70
81.62
77.66
39.85
33.36
28.99
24.58
17.09
400B 13C CD2Cl2 Rearrangement Spot #1 033011
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm

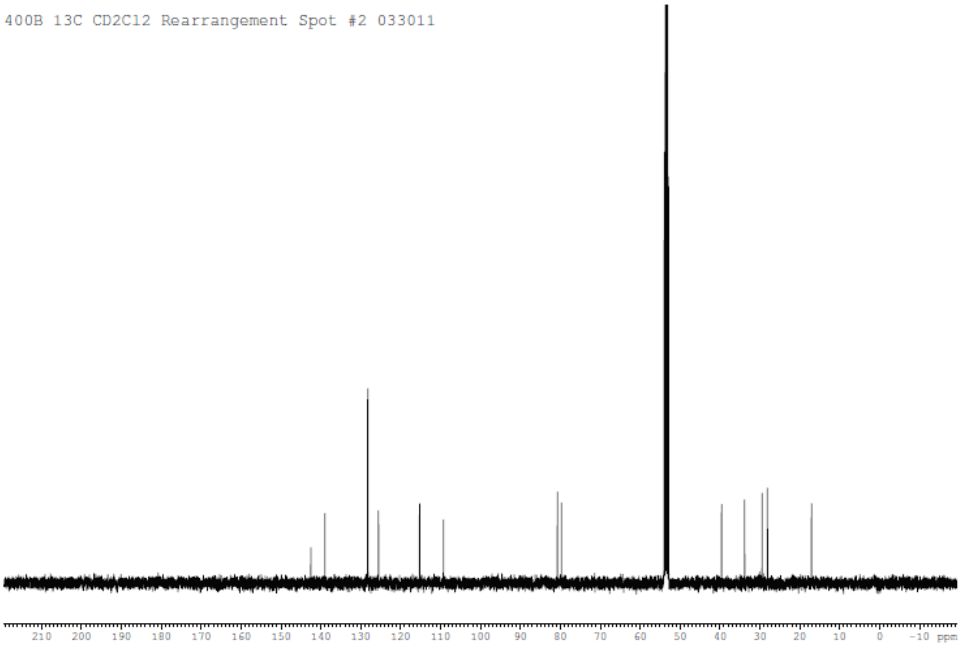

400B 1H COSY CD2C12 Rearrangement Spot #1 033011
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5


400B 1H NOESY CD2Cl2 Rearrangement Spot #1 033011
ppm
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 ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5

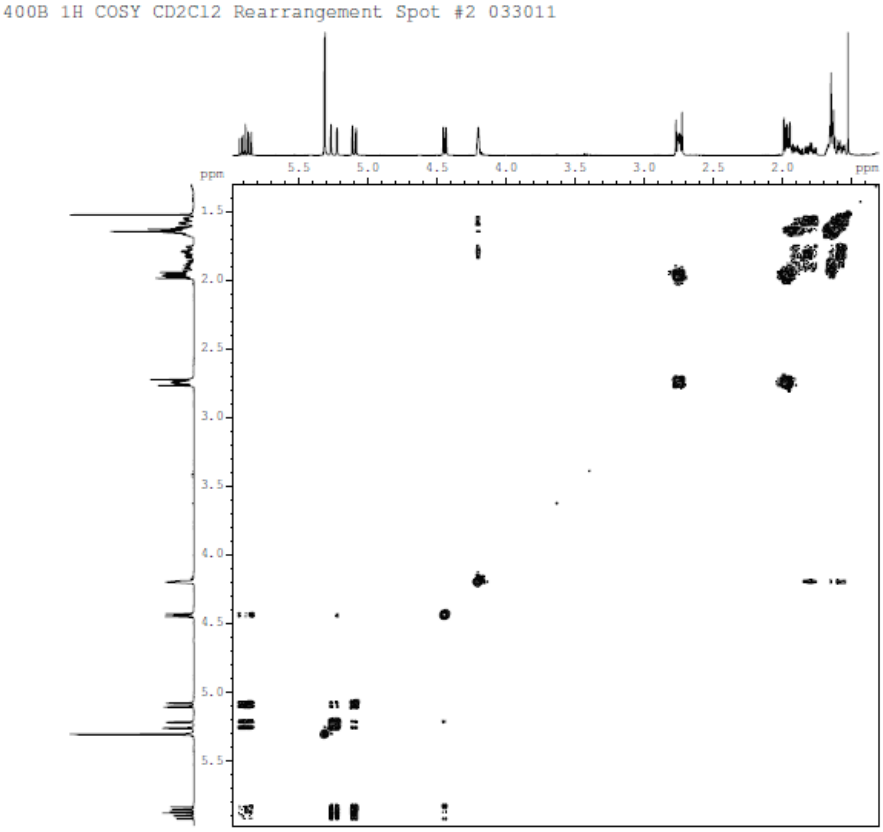
400B 1H CD2Cl2 Rearrangement Spot #2 033011

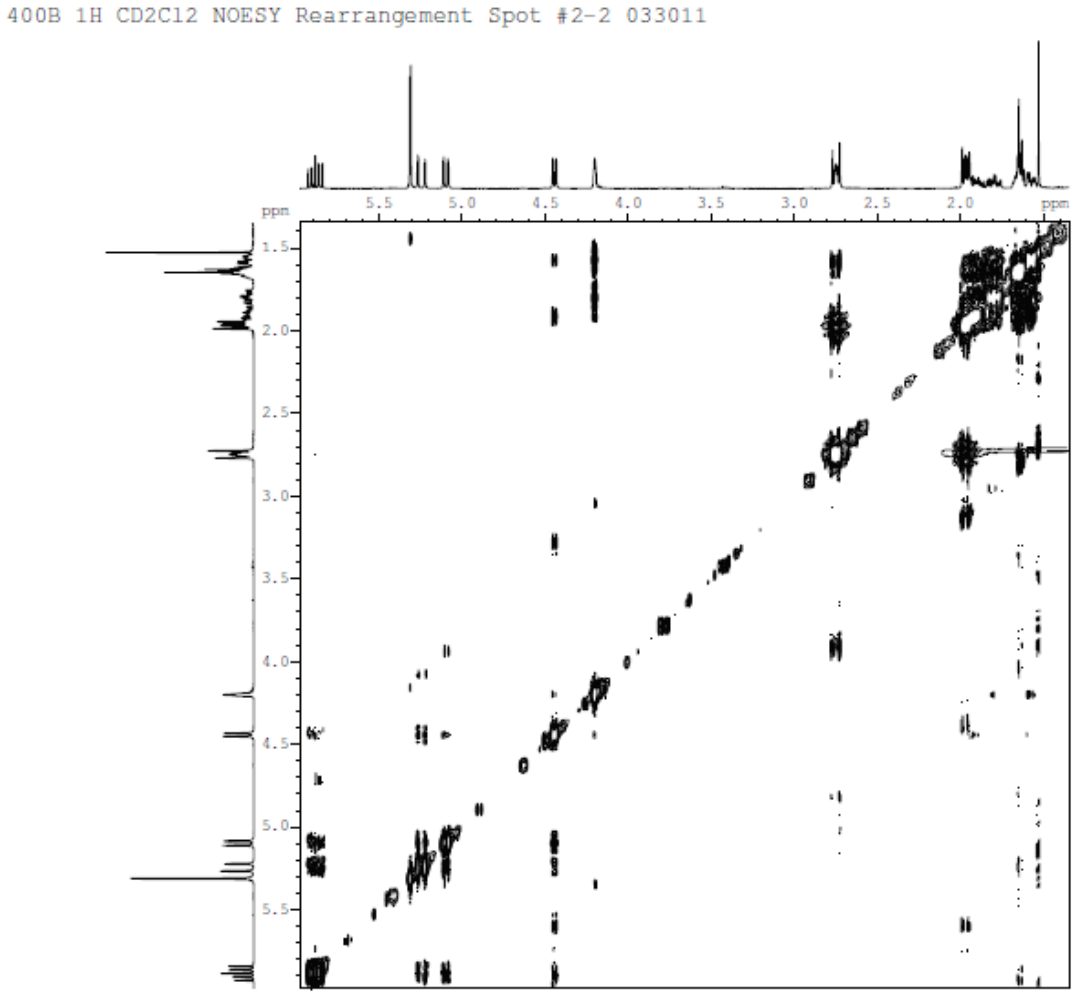


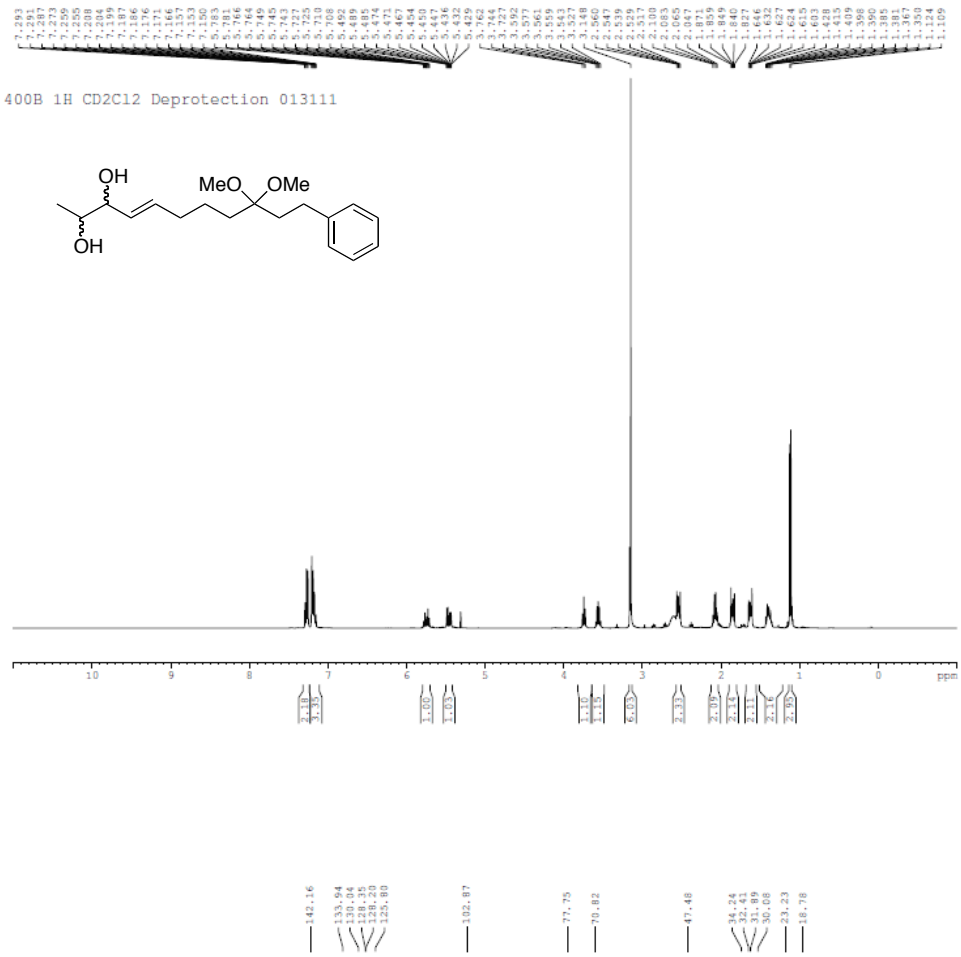


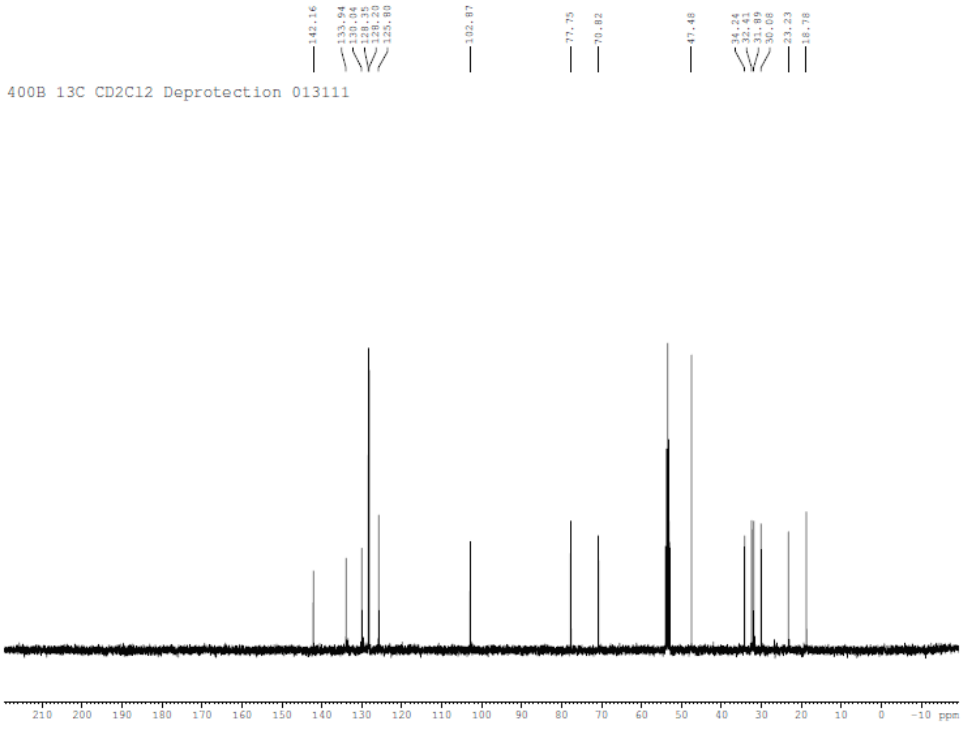


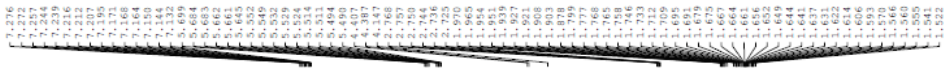
400B 13C CD2Cl2 Rearrangement Spot #2 033011


400B 1H COSY CD2Cl2 Rearrangement Spot #2 033011
ppm
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5

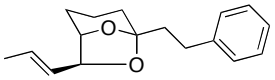

400B 1H CD2C12 NOESY Rearrangement Spot #2-2 033011
ppm
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5

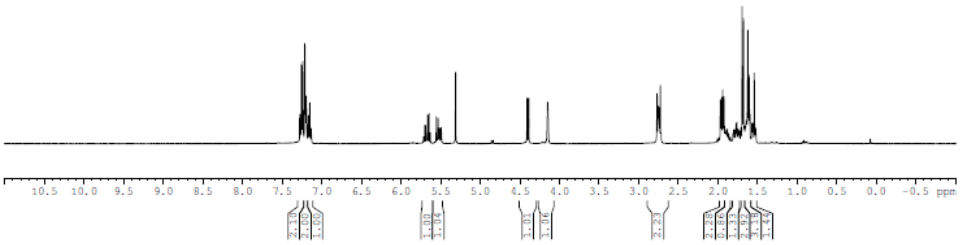

400B 1H CD2Cl2 Deprotection 013111
OH
MeO
OMe
OH

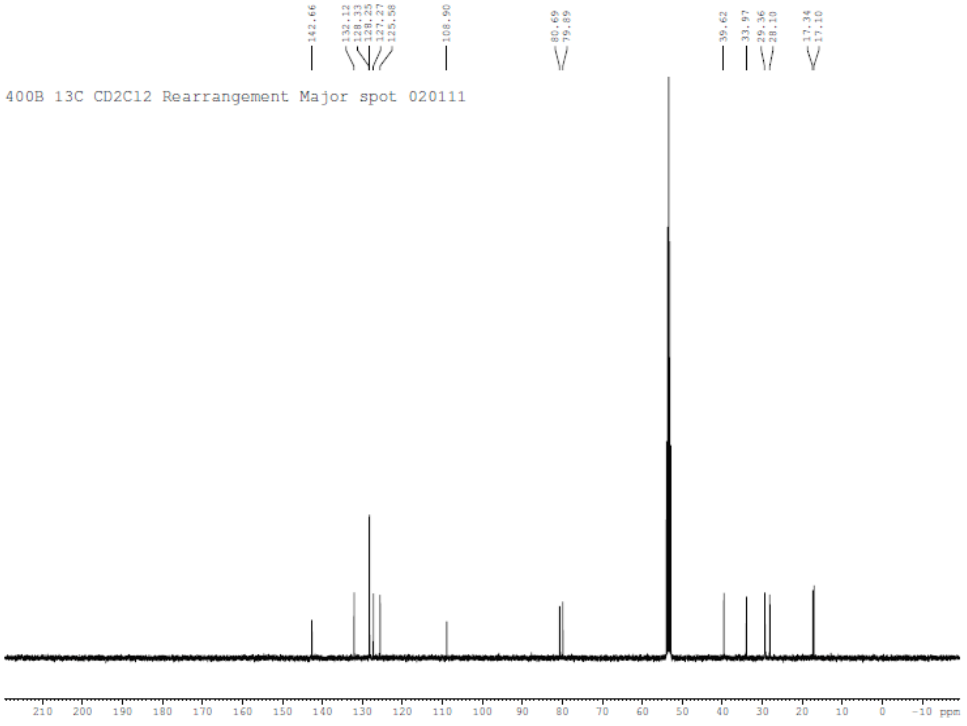

400B 13C CD2Cl2 Deprotection 013111



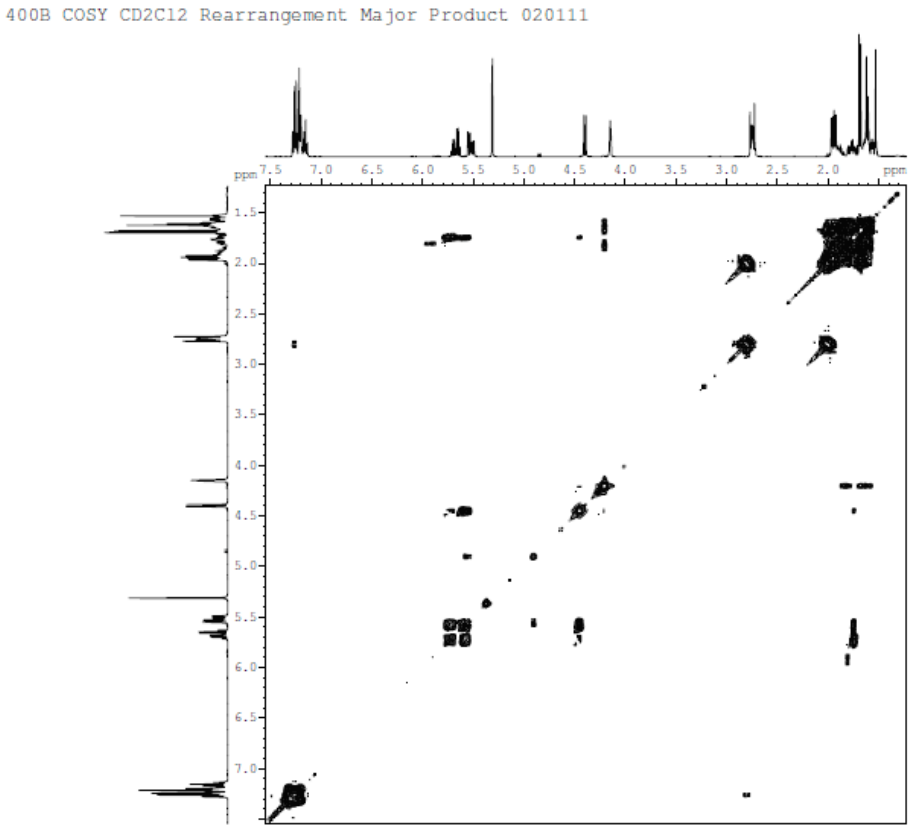
400B 1H CD2Cl2 Rearrangement Major Product 020111

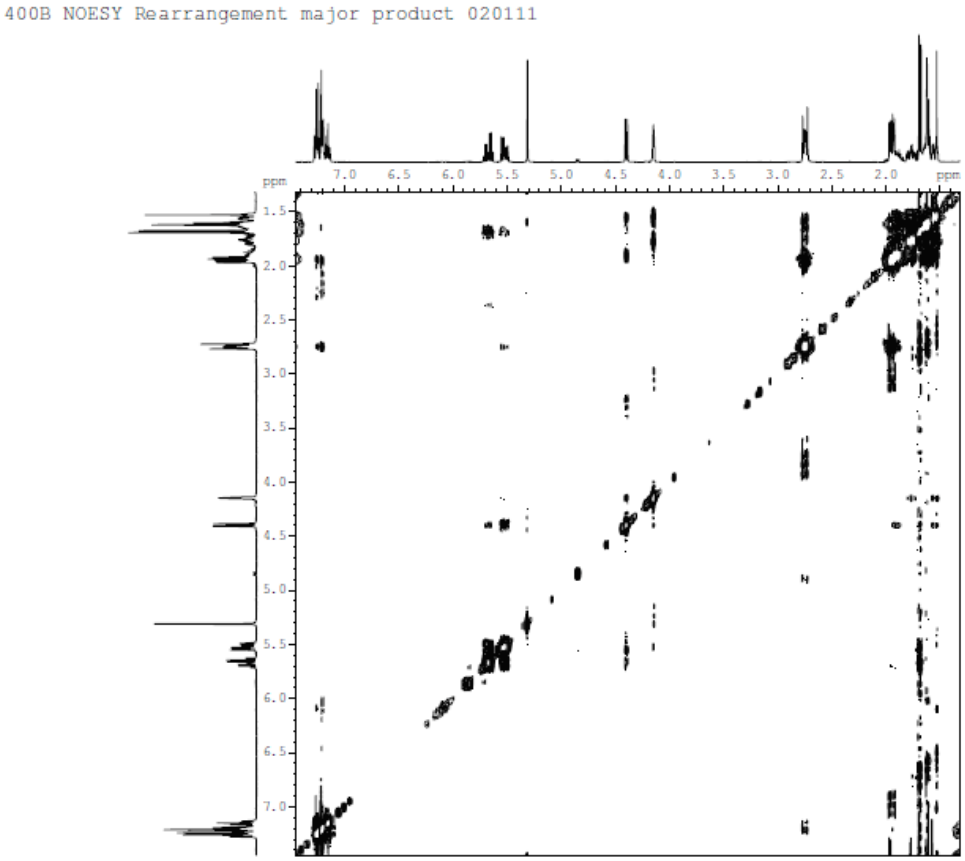




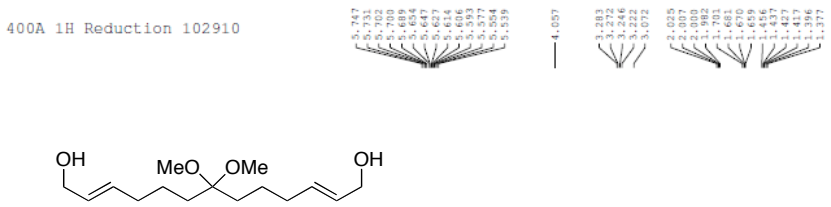


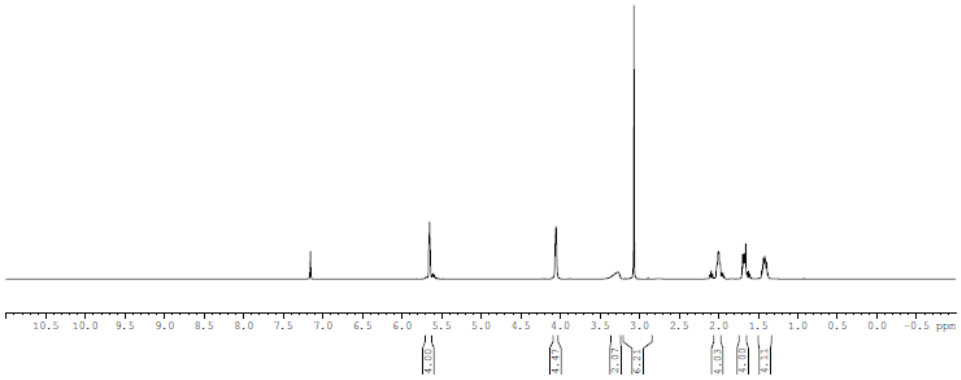
400B 13C CD2Cl2 Rearrangement Major spot 020111


400B COSY CD2Cl2 Rearrangement Major Product 020111
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0

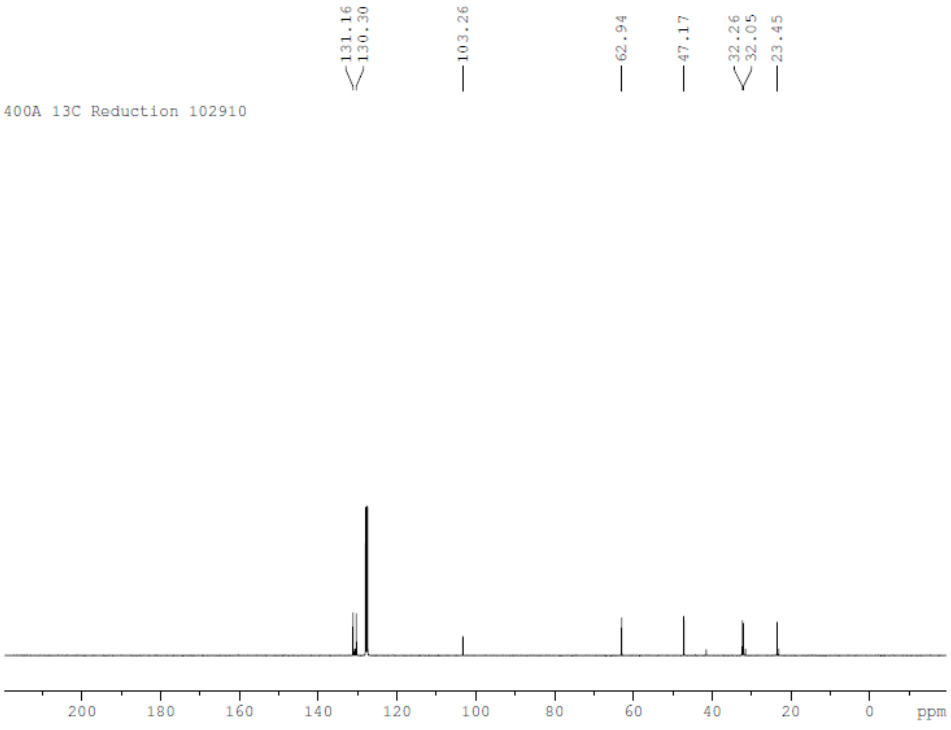


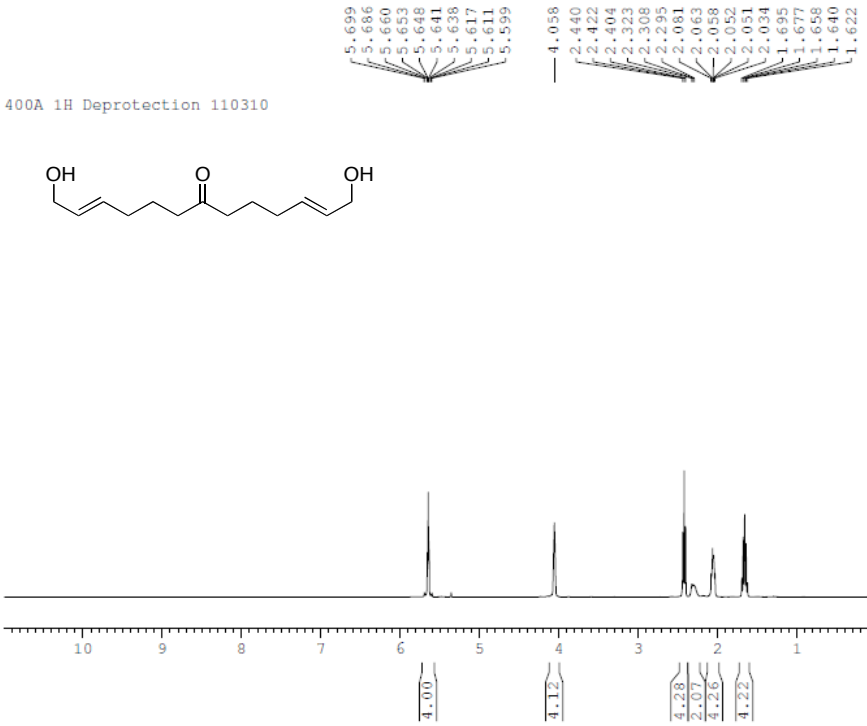
400A 1H Reduction 102910

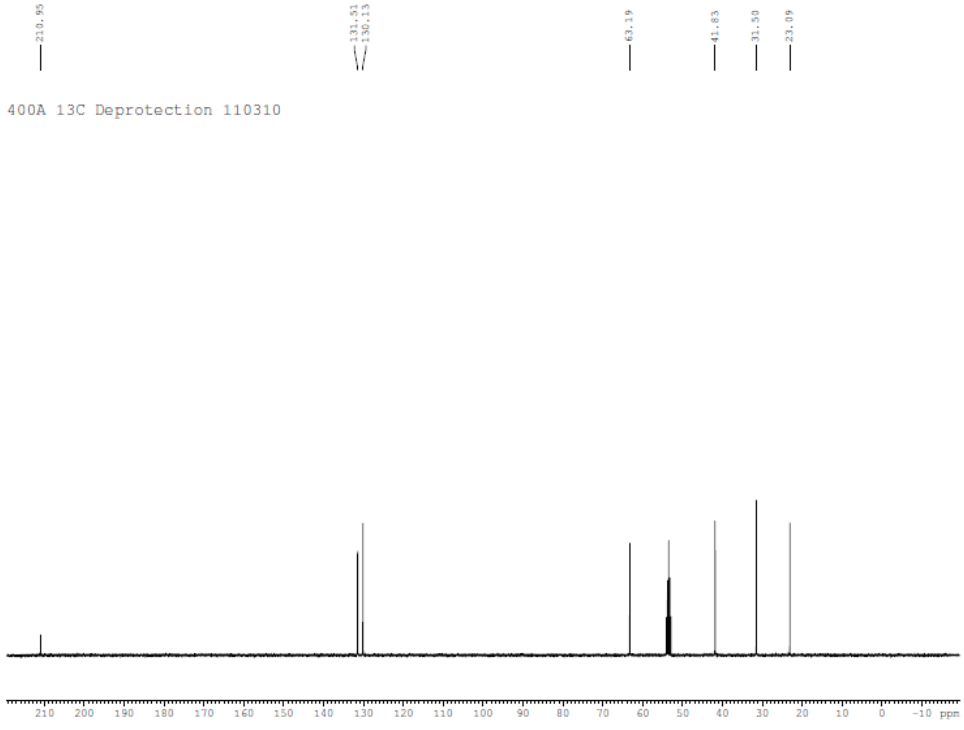


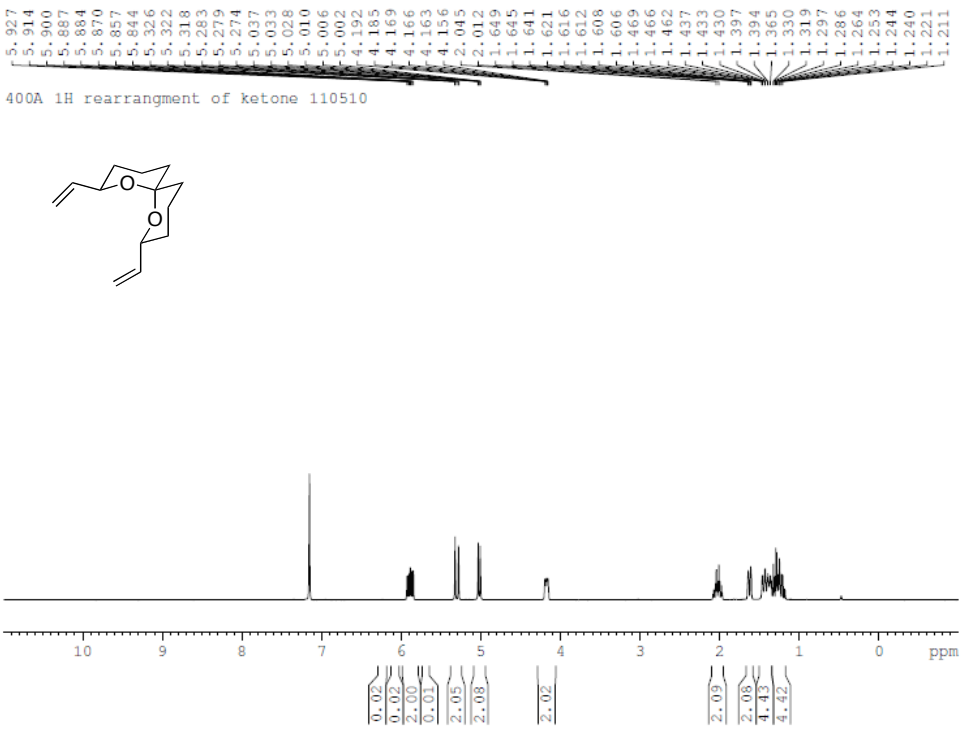


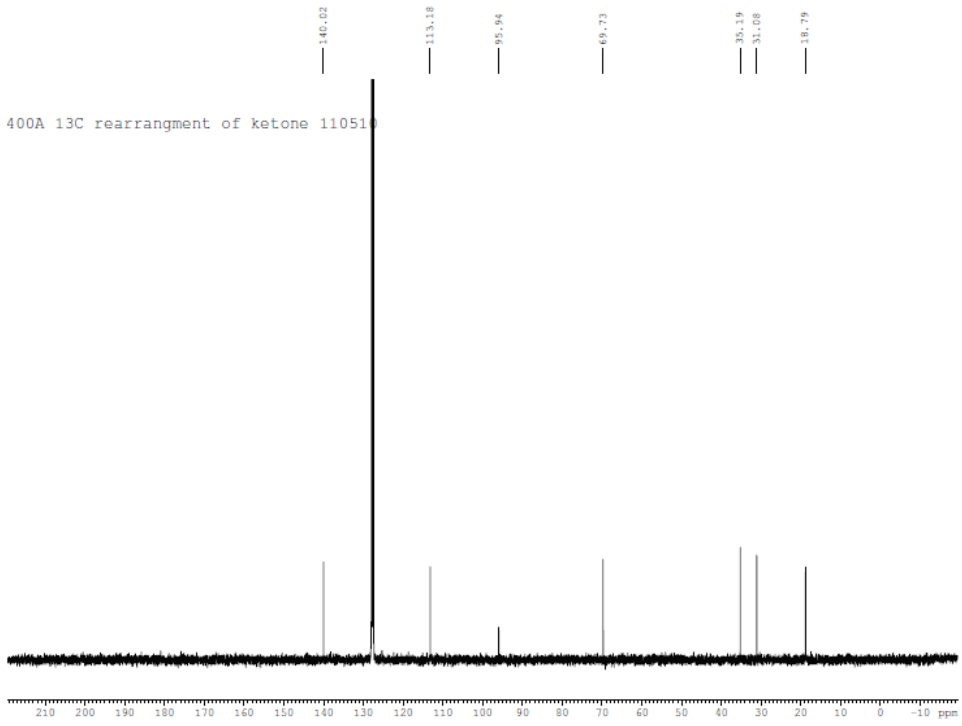
400A 13C Reduction 102910

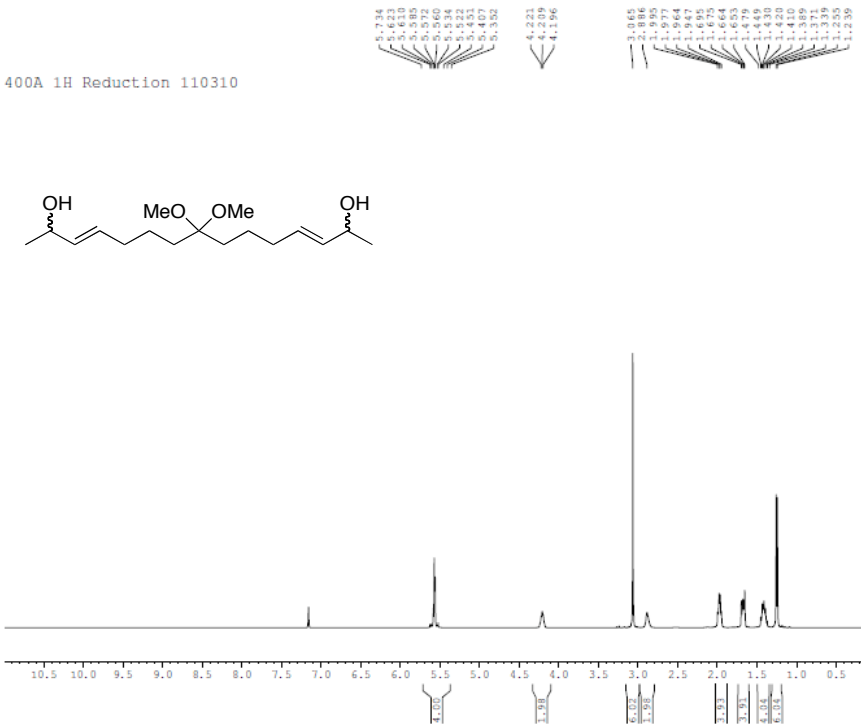


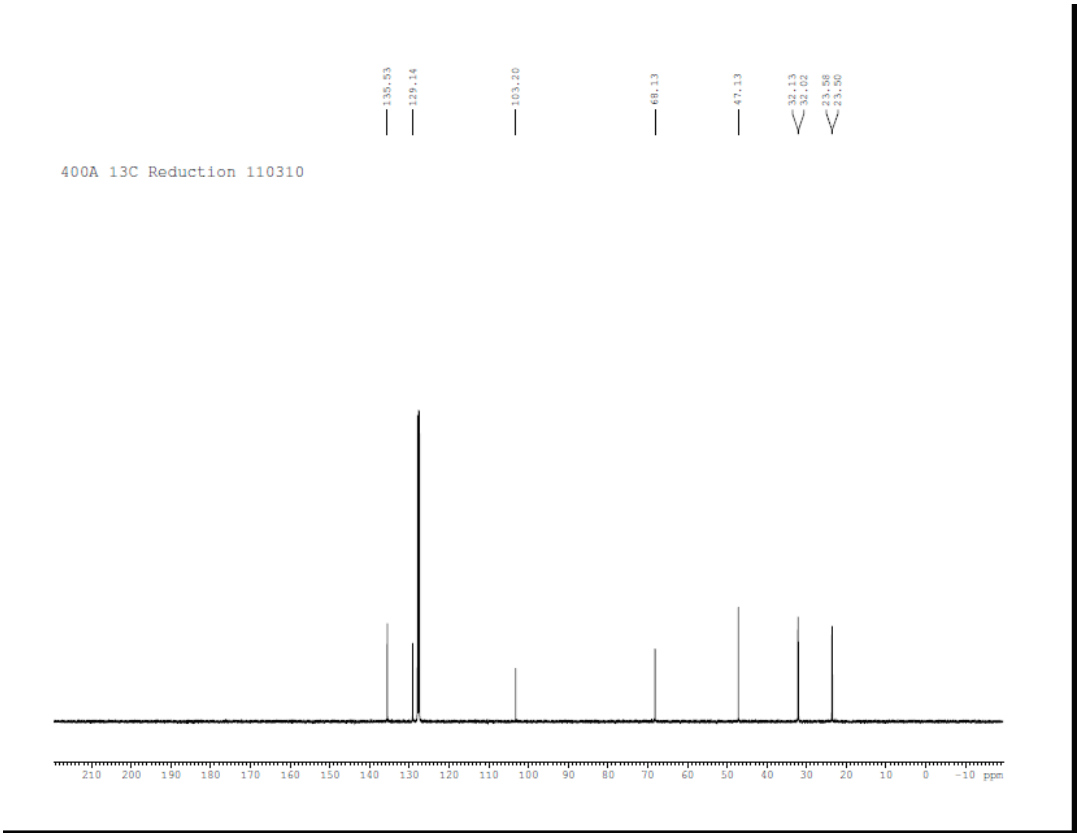

5.699
5.686
5.660
5.653
5.648
5.641
5.638
5.617
5.611
5.599
4.058
2.440
2.422
2.404
2.323
2.308
2.295
2.081
2.063
2.058
2.052
2.051
2.034
1.695
1.677
1.658
1.640
1.622
400A 1H Deprotection 110310
OH
O
OH
10
9
8
7
6
5
4
3
2
1
0
ppm
4.00
4.12
4.28
2.07
4.26
4.22

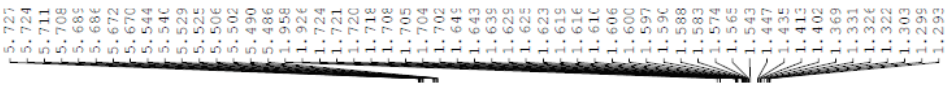

210.95
131.51
130.13
63.19
41.83
31.50
23.09
400A 13C Deprotection 110310
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10 ppm


5.927
5.914
5.900
5.887
5.884
5.870
5.857
5.844
5.326
5.322
5.318
5.283
5.279
5.274
5.037
5.033
5.028
5.010
5.006
5.002
4.192
4.185
4.169
4.166
4.163
4.156
2.045
2.012
1.649
1.645
1.641
1.621
1.616
1.612
1.608
1.606
1.469
1.466
1.462
1.437
1.433
1.430
1.397
1.394
1.365
1.330
1.319
1.297
1.286
1.264
1.253
1.244
1.240
1.221
1.211
400A 1H rearrangment of ketone 110510
O
O
10
9
8
7
6
5
4
3
2
1
0
ppm
0.02
0.02
2.00
0.01
2.05
2.08
2.02
2.09
2.08
4.43
4.42

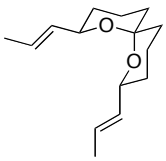

140.02
113.18
95.94
69.73
35.19
31.08
18.79
400A 13C rearrangment of ketone 110510
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

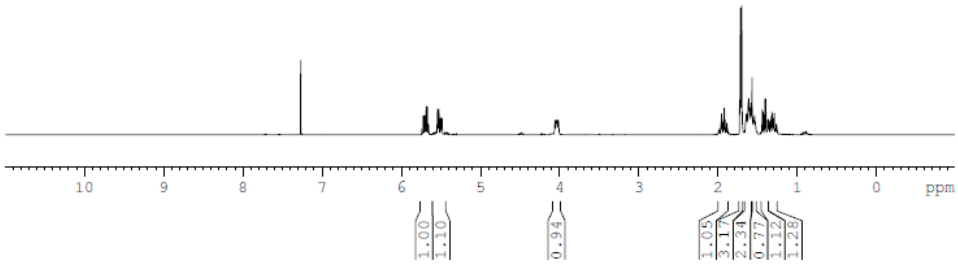

400A 1H Reduction 110310
OH
MeO
OMe
OH
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm


400A 13C Reduction 110310
135.53
129.14
103.20
68.13
47.13
32.13
32.02
23.58
23.50
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm

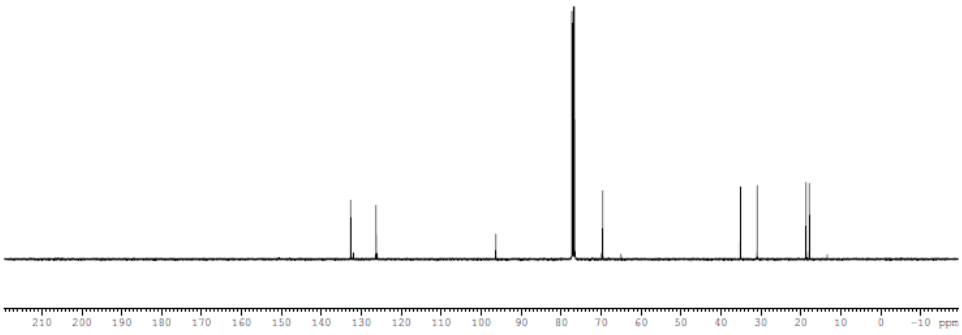


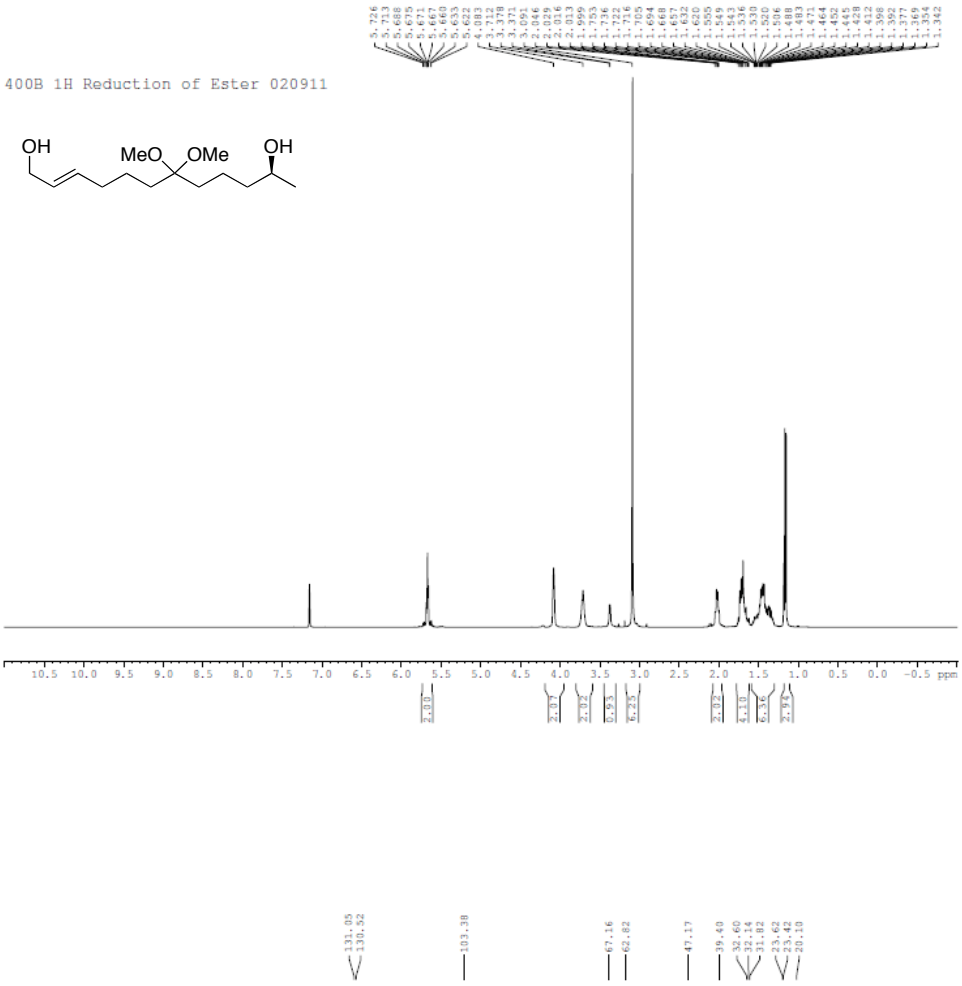
400B 1H CDCl3 Rearrangement Product Top SPT 011811

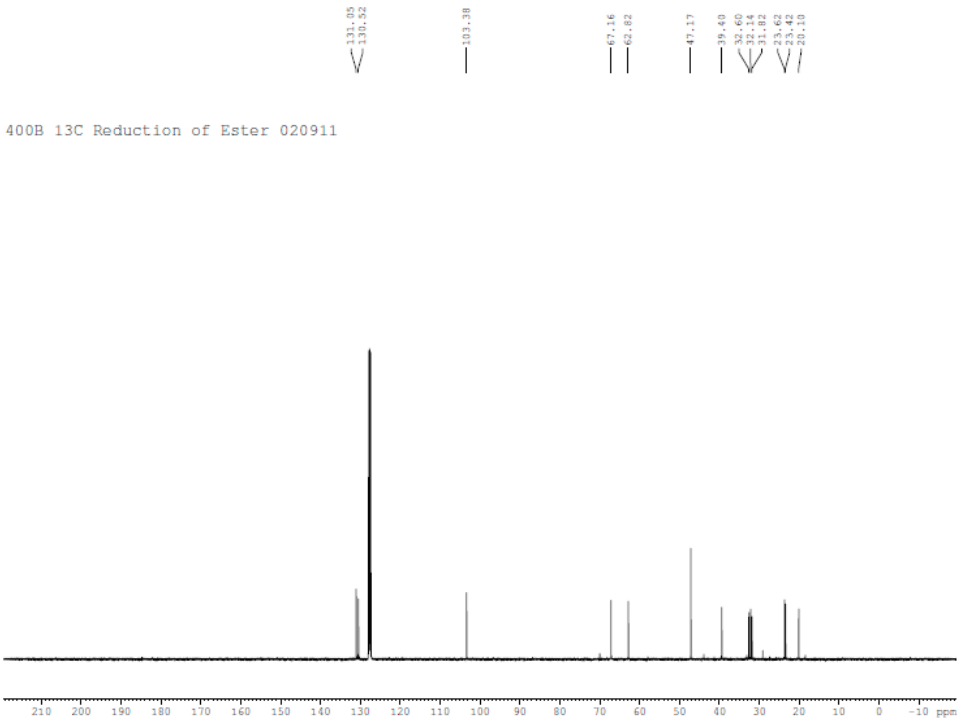


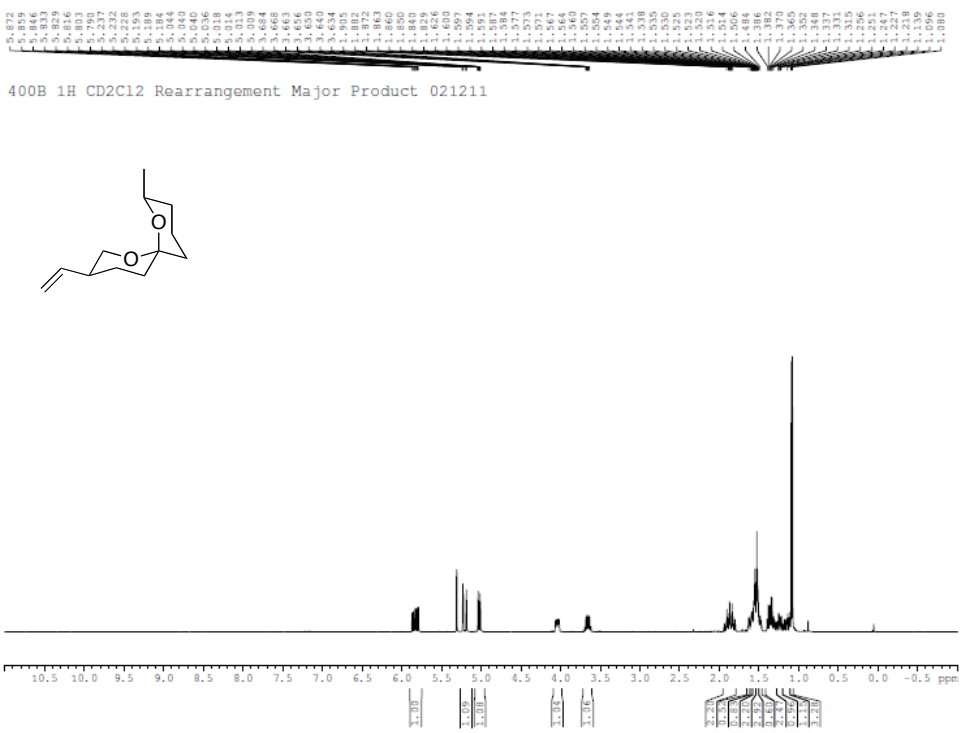


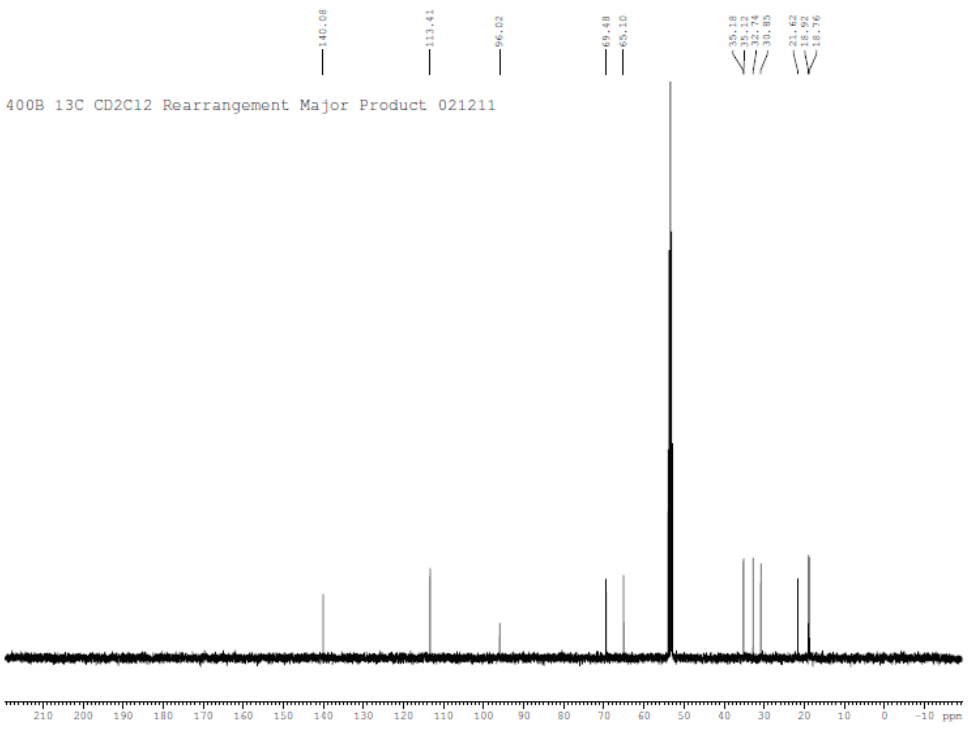
400B 13C CDCl3 Rearrangement Product Top SPT 011811

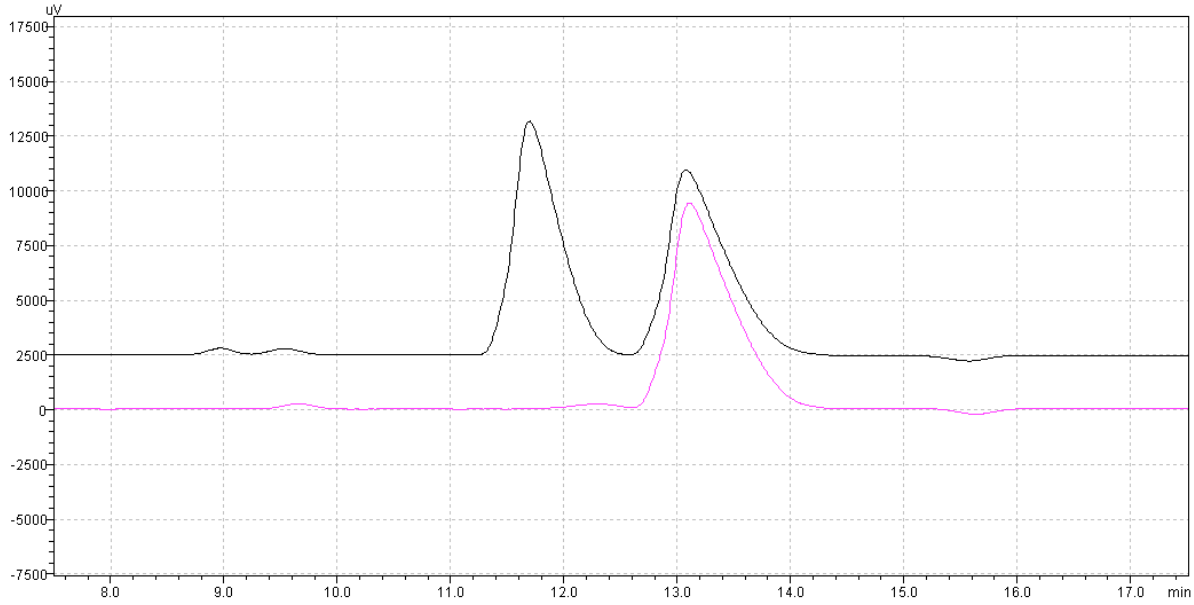



400B 1H Reduction of Ester 020911
OH
MeO
OMe
OH

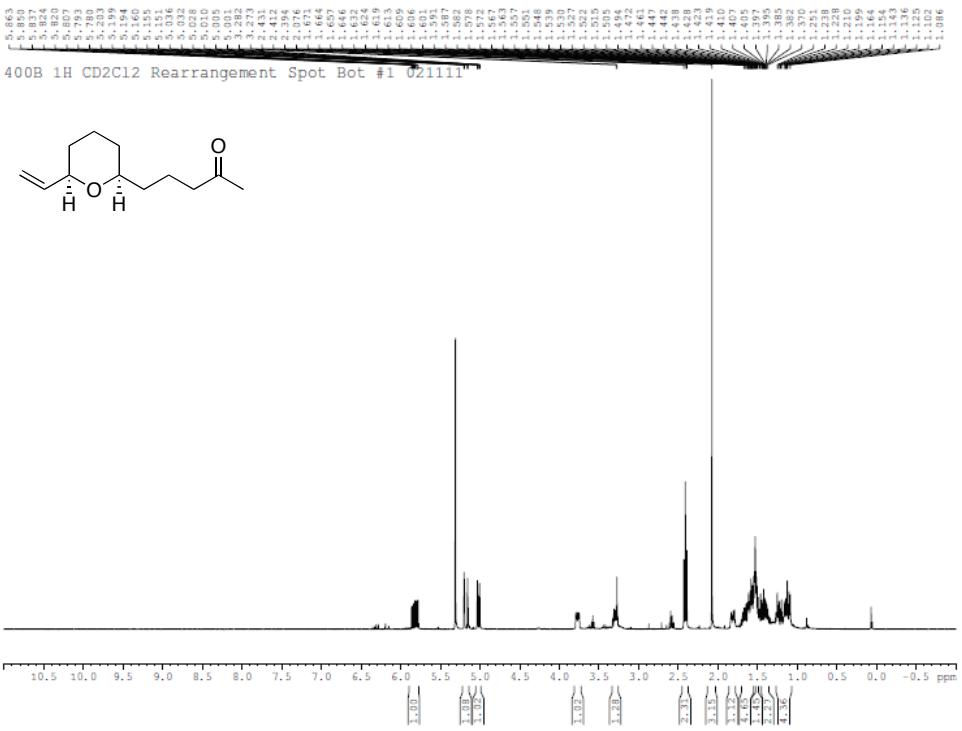

400B 13C Reduction of Ester 020911

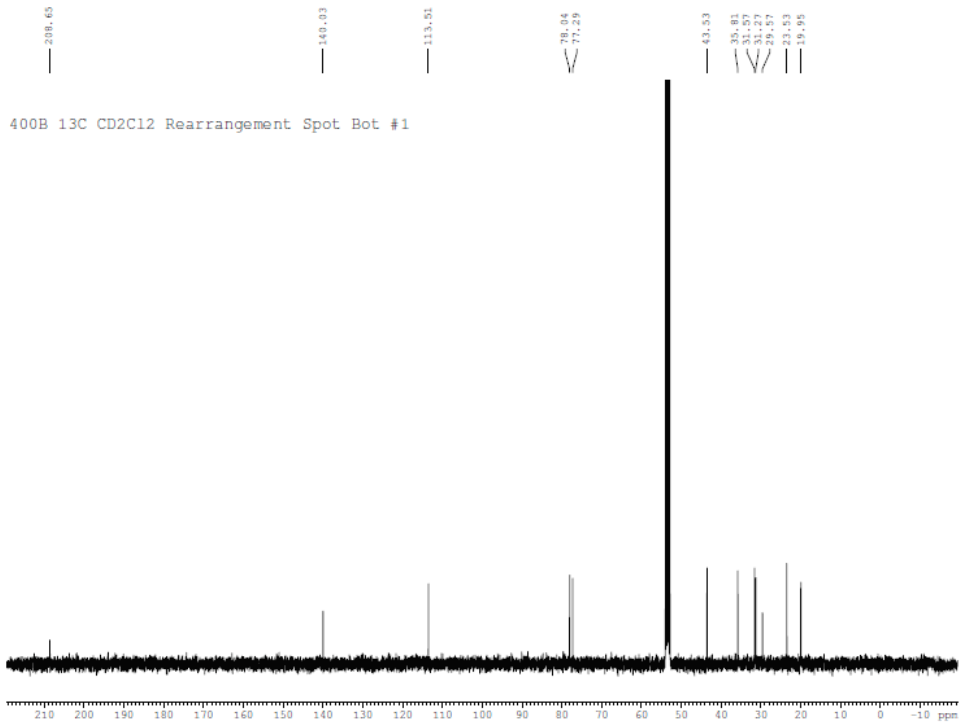

400B 1H CD2Cl2 Rearrangement Major Product 021211

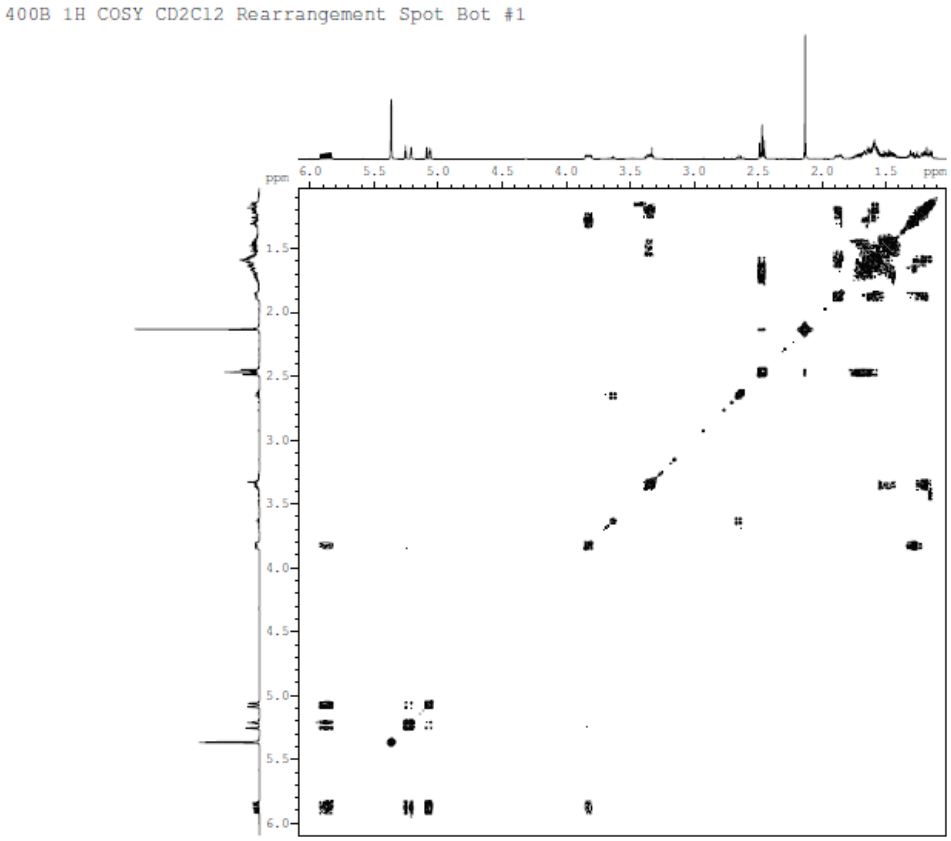

400B 13C CD2Cl2 Rearrangement Major Product 021211

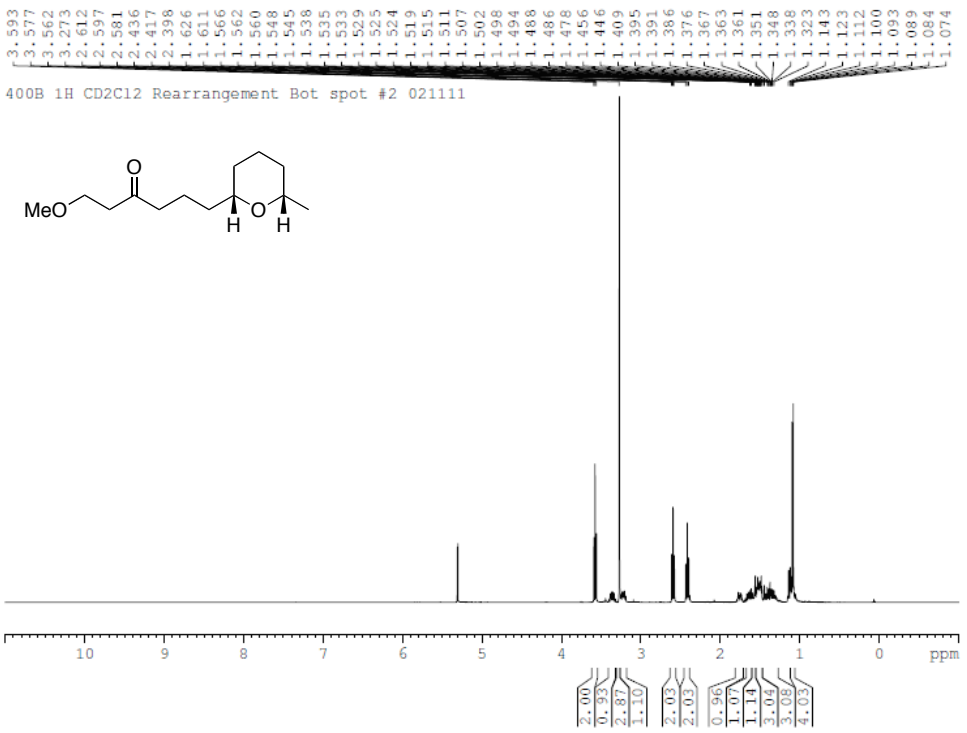


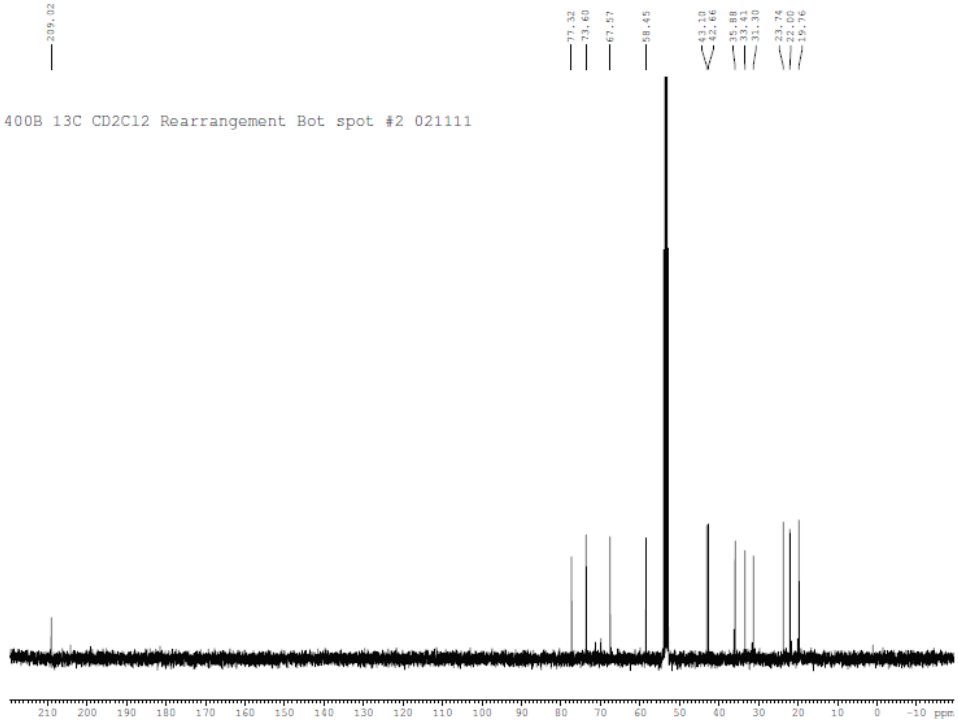
	Ret. T	Area	Area %	ee
Racemic ketal	11.695	308218.4	49.74	
	13.075	311457.1	50.26	0.52
Enantio-Enriched	12.29	7190.9	2	
	13.105	349449.5	98	96

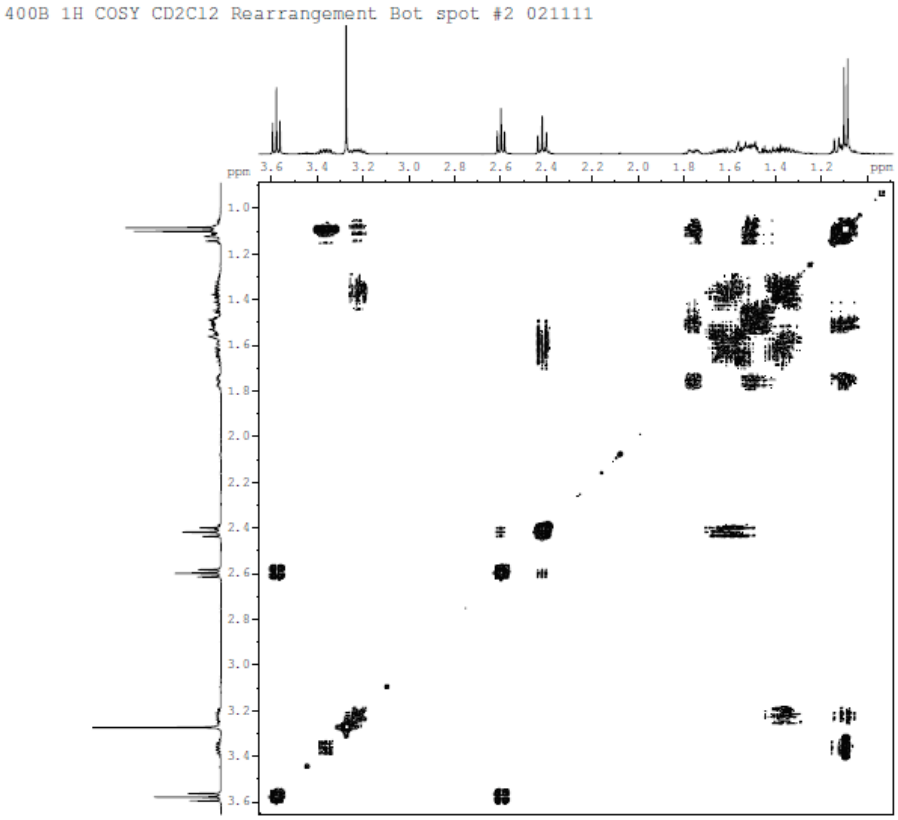

400B 1H CD2Cl2 Rearrangement Spot Bot #1 021111"
O
H
O
H

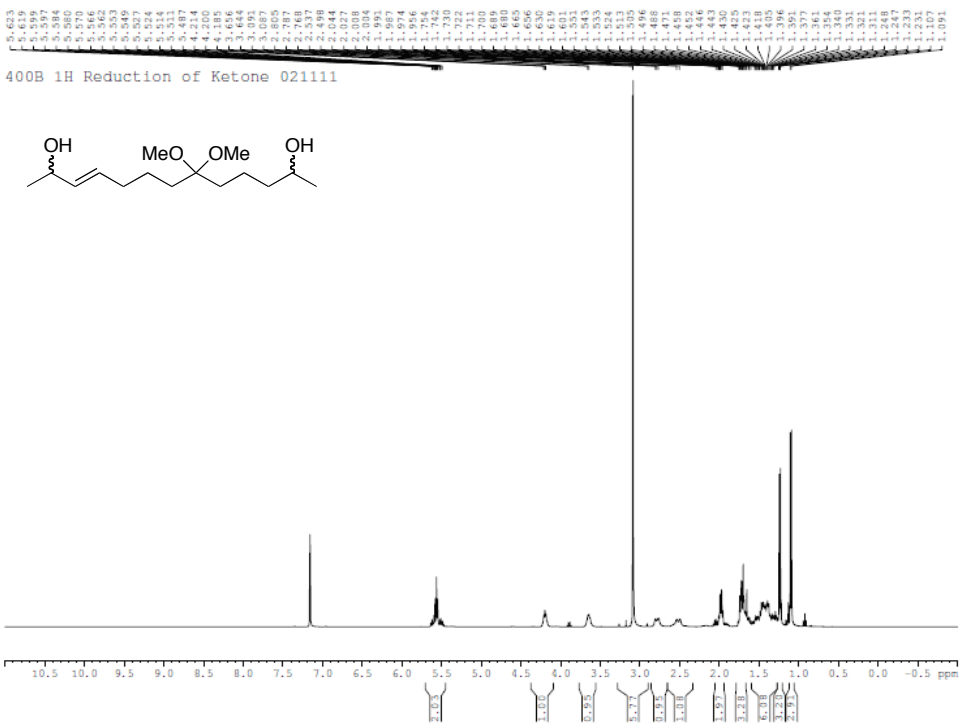

208.65
140.03
113.51
78.04
77.29
63.53
35.81
31.57
31.27
29.57
23.53
19.95
400B 13C CD2Cl2 Rearrangement Spot Bot #1

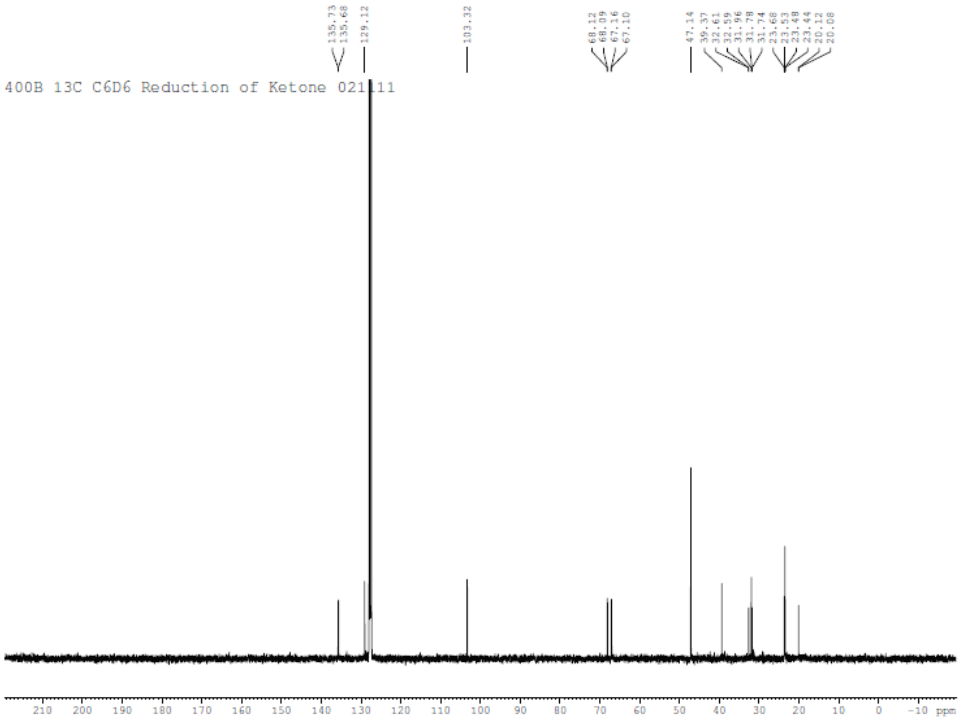

400B 1H COSY CD2C12 Rearrangement Spot Bot #1
ppm
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0

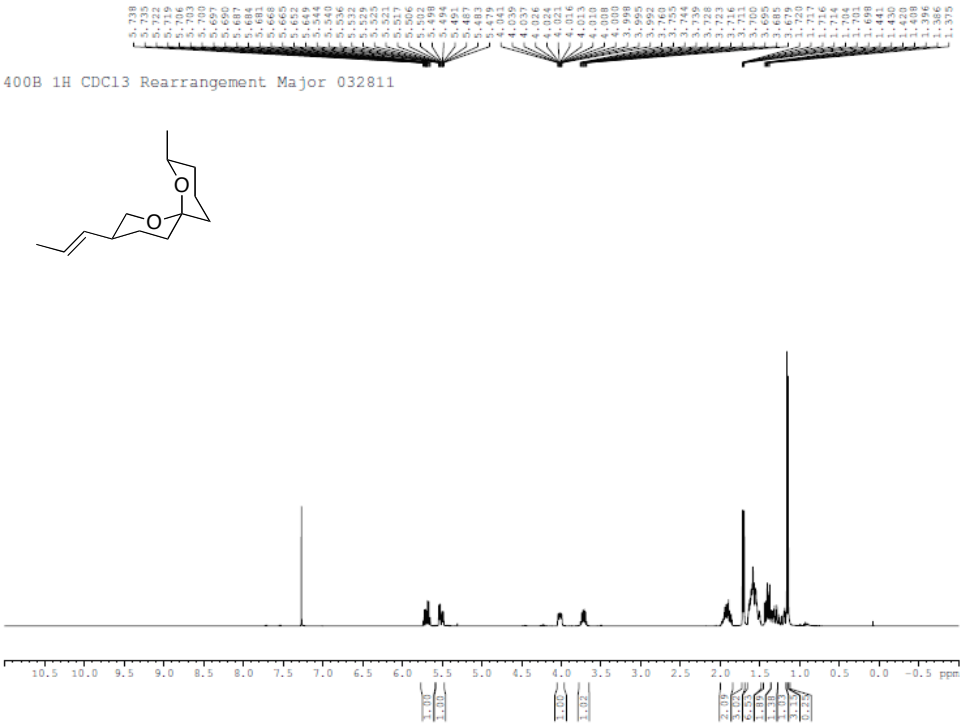

400B 1H CD2Cl2 Rearrangement Bot spot #2 021111
MeO
O
H
O
H
ppm

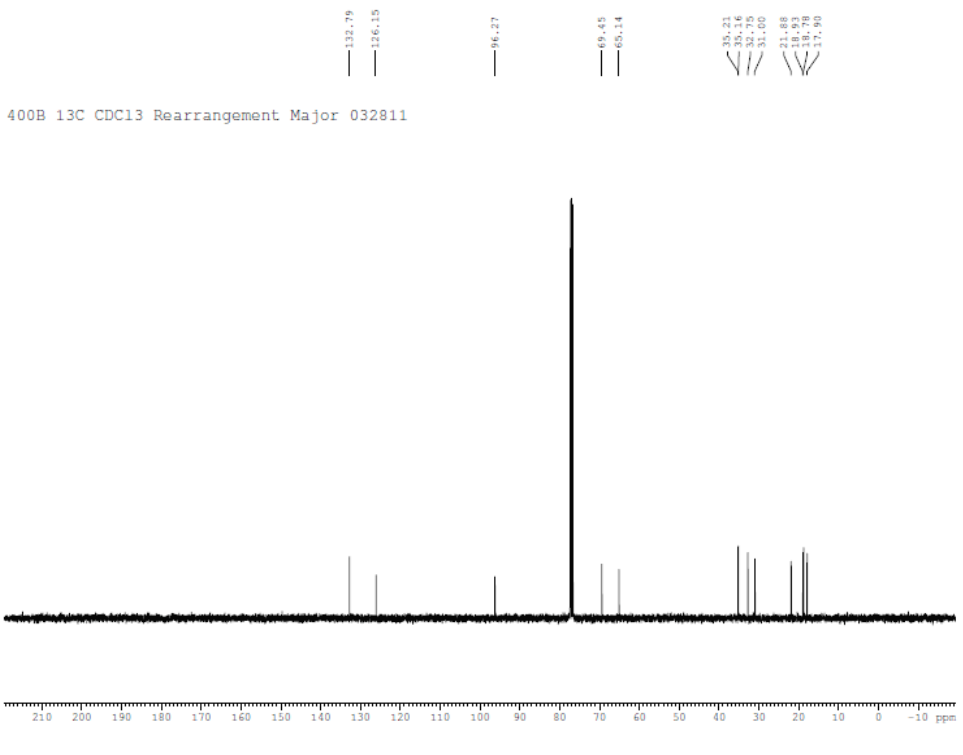

400B 13C CD2Cl2 Rearrangement Bot spot #2 021111
ppm

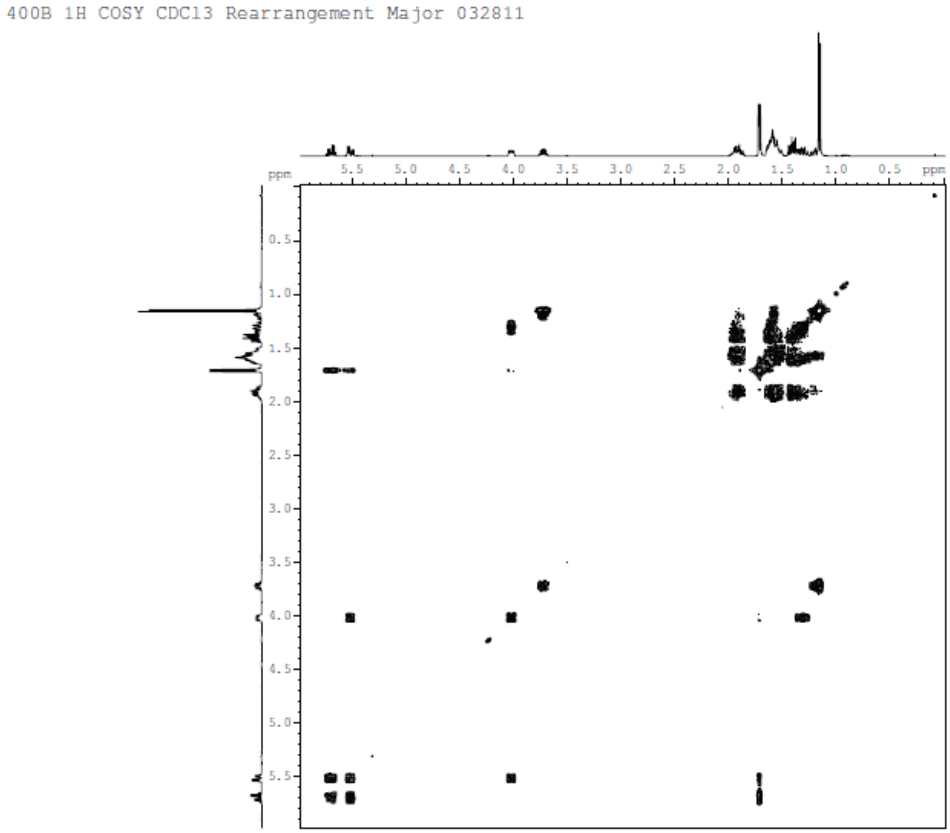

400B 1H COSY CD2Cl2 Rearrangement Bot spot #2 021111
ppm
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
ppm
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6


400B 1H Reduction of Ketone 021111
OH
MeO
OMe
OH

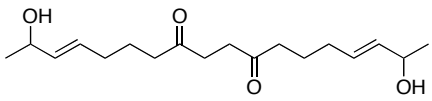

400B 13C C6D6 Reduction of Ketone 021111

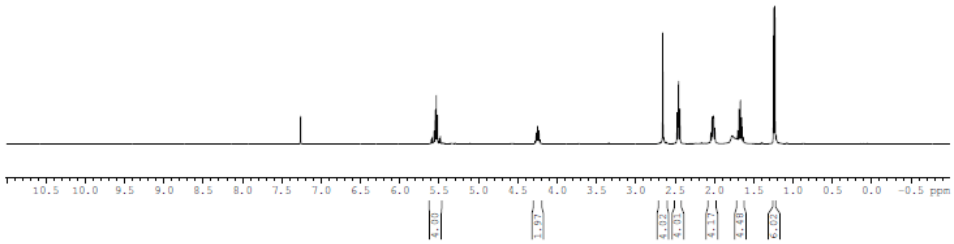

400B 1H CDCl3 Rearrangement Major 032811


400B 13C CDCl3 Rearrangement Major 032811

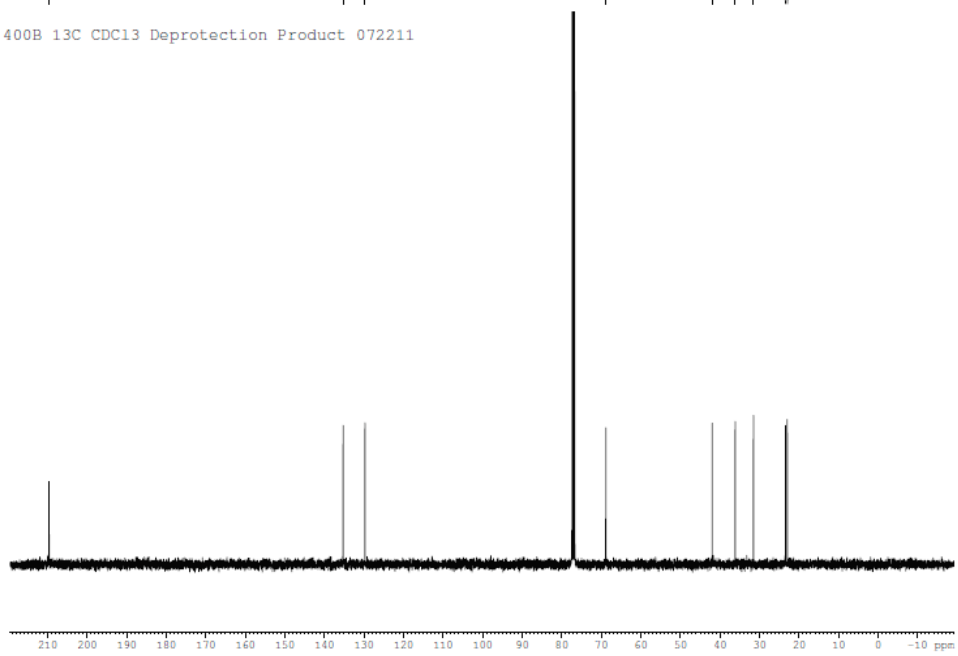

400B 1H COSY CDCl3 Rearrangement Major 032811
ppm
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5

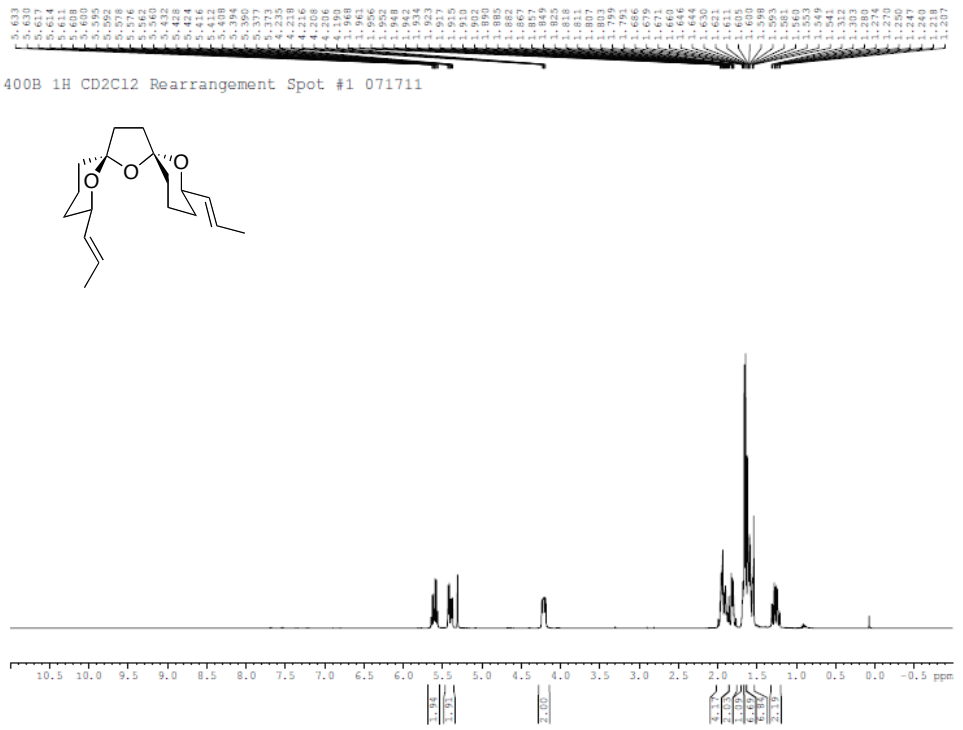
400B 1H CDCl3 Deprotection Product 072211

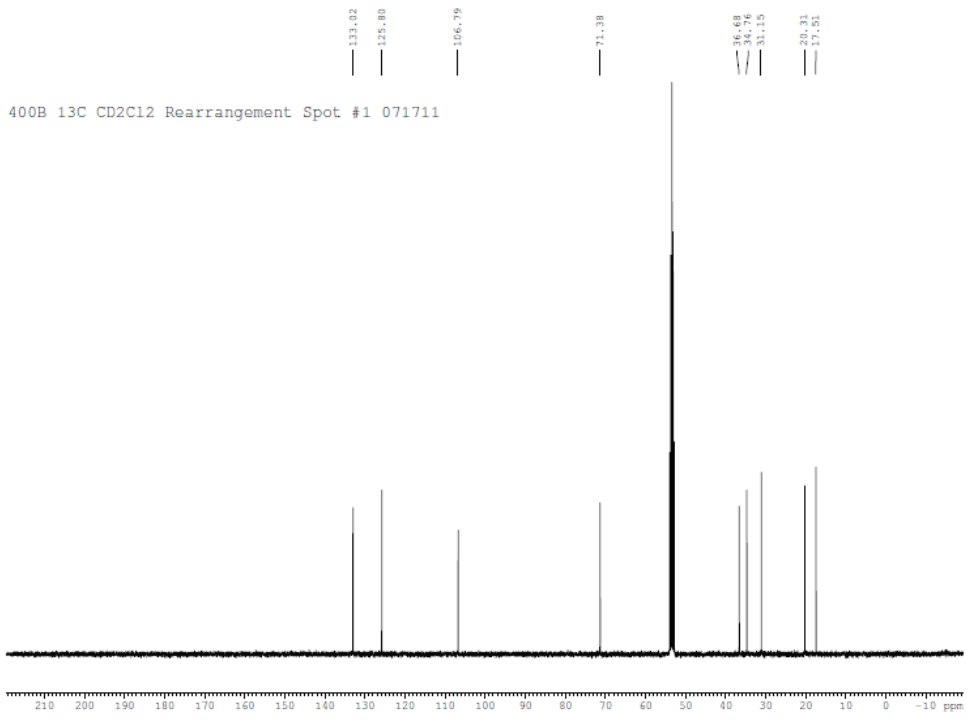


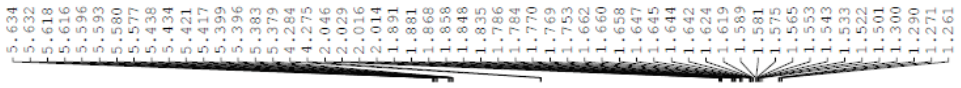


400B 13C CDCl3 Deprotection Product 072211

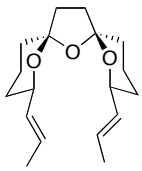


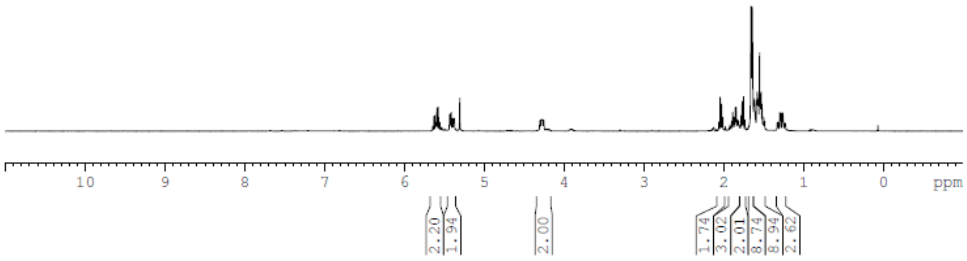

400B 1H CD2Cl2 Rearrangement Spot #1 071711

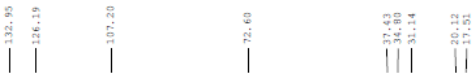

400B 13C CD2Cl2 Rearrangement Spot #1 071711



400B 1H CD2C12 Rearrangement Spot #2 071711







400B 13C CD2C12 Rearrangement Spot #2 071711