Supplementary Material (ESI) for Chemical Communications

Supporting Information

Transforming Terpene Feedstock into Polyketide Architecture

Philipp Winter, Carine Vaxelaire, Christoph Heinz and Mathias Christmann

TU Dortmund University

Otto-Hahn-Straße 6

D-44227 Dortmund

Germany

mathias.christmann@tu-dortmund.de

Content

I. GENERAL PROCEDURE

Solvents of HPLC grade were purchased from Fisher Scientific or VWR (Prolabo). Where dry solvents (diethyl ether, dichloromethane, toluene, DMF or THF) were required they were purified by Solvent Purification Systems M-BRAUN Glovebox Technology SPS-800. Technical quality solvents for column chromatography were used after short path distillation in a rotary evaporator. Unless noted below, all other compounds were reported in literature or were supplied by Aldrich, Acros or AlfaAesar, and used without further purification. *Thin-layer chromatography* (SiO_2, *TLC*) was performed on Merck TLC silica gel 60 F_{254}. *Column chromatography* was performed on Merck silica gel 60 (0.040 – 0.063 nm), using standard flash chromatographic methods. *Melting points* were measured out on a Büchi B-540 block apparatus and are uncorrected. *Optical rotations* were recorded on a Perkin Elmer polarimeter 341 at 589 nm, and were reported as $[\alpha]_D$ (concentration). The *NMR spectra* were recorded on Bruker DRX300 (300 MHz), DRX400 (400 MHz), DRX500 (500 MHz) or DRX600 (600 MHz) spectrometers and were referenced against the residual solvent peaks [$CHCl_3$: δ 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR)]. Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant, and integration. Infrared spectra were recorded on a Nicolet Impact 400D spectrometer on potassium bromide matrix (disk or film). *Low resolution mass spectra* were performed on a Thermo TSQ mass spectrometer, Hewlett Packard 6890 series/Mass selective detector. *High resolution mass spectra* were recorded on a LTQ Orbitrap mass spectrometer coupled to an Accela HPLC-System (HPLC column: Hypersyl GOLD, 50 mm × 1 mm, 1.9 μm). All instruments are from Thermo Electron. *Chiral HPLC analysis* was performed using an Agilent 1200 series HPLC with a diode array detector. Chiral columns include Daicel Chiralpak IA (Chiral Technologies Eur., 25 cm × 4.6 mm I.D.) and Daicel Chiralpak IC (Chiral Technologies Eur., 25 cm × 4.6 mm I.D.). *Chiral GC analysis* was performed using an Agilent 6850 series GC with a FID detector on a Hydrodex-β-6TBDM (Macherey & Nagel, 25 m x 0.25 mm).

[i] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.,* 1997, **62**, 7512.

II. 1,4-Dienes from allylic acetates (conditions and optimisation)

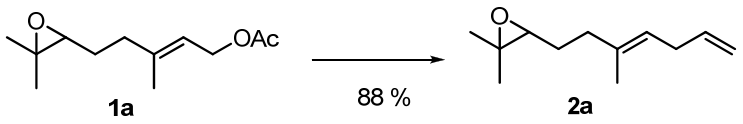
Optimisation of the reaction conditions for the synthesis of 1,4-dienes from allylic acetates (Scheme 1: 1a → 2a)

entry	mol%	catalyst	eq. 	X	T [°C]	solvent	Yield[a] [%]
1	4	Li_2CuCl_4	1.5	Cl	0 → 20	THF	0
2	10	Li_2CuCl_4	1.5	Br	–30	THF	23
3	5	CuI	1.4	Br	–78	THF	53
4	10	CuI	3.0	Br	–78 → –30	THF/DMS= 10:1	70
5	20	$CuBr \cdot SMe_2$	2.0	Br	–30	THF	70
6	20	CuI	1.5	Br	–30	THF/DMS= 10:1	88
7	--	--	1.5	Br	–30	THF/DMS= 10:1	0

[a] isolated yields.

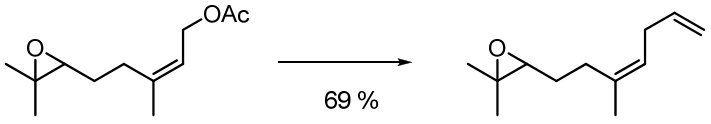
General procedure for the synthesis of 1,4-dienes from allylic acetates (Table 1)

A solution of the allylic acetate (1 mmol) in dry THF (3 mL) was treated at room temperature with copper(I)iodide (38 mg, 0.2 mmol, 20 mol%) and dimethylsulfide (0.3 mL) under argon. The heterogeneous mixture was cooled to –30 °C and became clear after few minutes. Then vinylmagnesium bromide (1.50 mL, 1.5 mmol, 1.5 eq., 1 M in THF) was added over 20 min and stirred for additional 30 min at that temperature. For substrates with a free alcohol, one additional equivalent of vinylmagnesium bromide was used. If the reaction was not completed, additional vinylmagnesium bromide (0.5 mL, 0.5 mmol, 0.5 eq., 1M in THF) could be added slowly. The reaction was quenched with saturated NH_4Cl solution (3 mL) and diluted with water. The aqueous phase was extracted with diethyl ether (3 x 20 mL) and the combined organic layers dried over $MgSO_4$. After evaporation of the solvent the crude residue was subjected to column chromatography (conditions see below) yielding the 1,4-dienes as colourless oils.



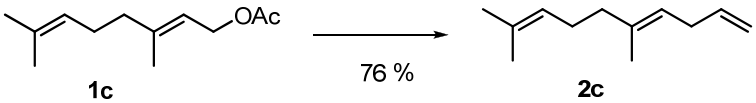
1a **2a**

2a: Eluent: *n*-pentane/ethyl acetate = 50:1, $\mathbf{R_f}$ = 0.62 (*n*-pentane/ethyl acetate = 50:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.27 (s, 3H), 1.31 (s, 3H), 1.60-1.73 (m, 5H), 2.09-2.24 (m, 2H), 2.72 (t, *J* = 6.3 Hz, 1H), 2.75-2.78 (m, 2H), 4.96 (ddt, *J* = 10.0, 3.0, 1.5 Hz ,1H), 5.02 (ddt, *J* = 17.2, 3.6, 1.6 Hz, 1H) 5.20-5.24 (m, 1H), 5.81 (ddt, *J* = 16.3, 10.0, 6.3 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 16.0, 18.7, 24.9, 27.4, 32.3, 36.3, 58.4, 64.2, 114.2, 122.0, 135.5, 137.2; **IR** ($\tilde{\nu}$/cm^{-1}) 680 (w), 875 (w), 909 (m), 994 (w), 1122 (w), 1249 (w), 1378 (m), 1450 (w), 1638 (m), 2925 (m), 2962 (m); **HRMS** (ESI) *m/z* calculated for $C_{12}H_{21}O$ $[M+H]^+$ 181.1587, found 181.1585.



1b **2b**

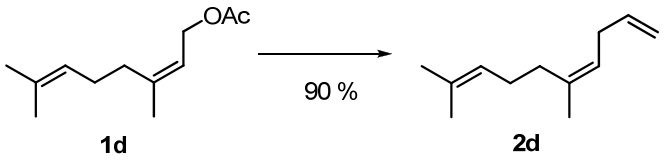
2b: Eluent: *n*-pentane/ethyl acetate = 50:1, $\mathbf{R_f}$ = 0.61 (*n*-pentane/ethyl acetate = 50:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.28 (s, 3H), 1.31 (s, 3H), 1.54-1.71 (m, 2H), 1.74 (d, *J* = 1.0 Hz, 3H), 2.13-2.24 (m, 2H), 2.72 (t, *J* = 6.3 Hz, 1H), 2.76-2.79 (m, 2H), 4.96 (ddt, *J* = 10.4, 3.5, 1.5 Hz, 1H), 5.03 (ddt, *J* = 17.1, 3.5, 1.5 Hz, 1H), 5.22 (t, *J* = 7.3 Hz, 1H), 5.80 (ddt, *J* = 16.6, 10.0, 6.3 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 18.7, 23.4, 24.9, 27.3, 28.4, 32.1, 58.4, 64.0, 114.4, 122.9, 135.5, 137.4; **IR** ($\tilde{\nu}$/cm^{-1}) 680 (m), 793 (w), 864 (m), 908 (s), 995 (m), 1122 (m), 1249 (w), 1323 (w), 1380 (s), 1455 (s), 1638 (m), 2926 (s), 2964 (s), 3079 (w); **HRMS** (ESI) *m/z* calculated for $C_{12}H_{21}O$ $[M+H]^+$ 181.1587, found 181.1584.



1c **2c**

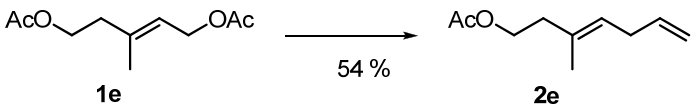
2c: Eluent: cyclohexane, $\mathbf{R_f}$ = 0.73 (cyclohexane); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.62 (s, 3H), 1.63 (s, 3H), 1.70 (d, *J* = 0.9 Hz, 3H), 2.01-2.13 (m, 4H), 2.75-2.78 (m, 2H), 4.96 (ddt, *J* = 10.1, 3.5, 1.5 Hz, 1H), 5.03 (ddt, *J* = 17.1, 3.7, 1.8 Hz, 1H), 5.10-5.14 (m, 1H), 5.16-5.20 (m, 1H), 5.82 (ddt, *J* = 16.3, 10.1, 6.2 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 15.9, 17.7, 25.7, 26.7, 32.2, 39.7, 114.0, 121.3, 124.3, 131.4, 136.4, 137.4; **IR** ($\tilde{\nu}$/cm^{-1}) 831 (w), 909 (s),

992 (m), 1108 (w), 1377 (m), 1441 (m), 1638 (m), 2856 (s), 2916 (s), 2969 (s), 3079 (w); **HRMS** (EI) *m/z* calculated for $C_{12}H_{20}$ $[M]^+$, 164.1560, found 164.1554.



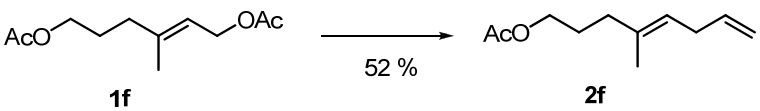
1d **2d**

2d: Eluent: cyclohexane, $\mathbf{R_f}$ = 0.75 (cyclohexane); **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 1.63 (s, 3H), 1.70 (s, 3H), 1.73 (q, *J* = 1.2 Hz, 3H), 2.03-2.12 (m, 4H), 2.74-2.89 (m, 2H), 4.96 (ddt, *J* = 10.1, 3.5, 1.6 Hz, 1H), 5.03 (ddt, *J* = 17.2, 3.7, 1.8 Hz, 1H), 5.10-5.20 (m, 2H), 5.81 (ddt, *J* = 16.5, 10.3, 6.3 Hz, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 17.6, 23.4, 25.7, 26.6, 31.9, 32.2, 114.2, 122.2, 124.2, 131.6, 136.4, 137.7; **IR** ($\tilde{\nu}$/cm^{-1}) 829 (w), 909 (s), 991 (m), 1109 (w), 1378 (m), 1448 (m), 1638 (m), 2857 (s), 2921 (s), 2968 (s), 3079 (w); **HRMS** (EI) *m/z* calculated for $C_{12}H_{20}$ $[M]^+$) 164.1560, found 164.1560.



1e **2e**

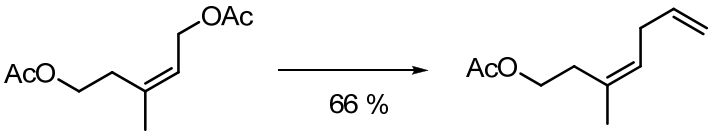
2e: Eluent: *n*-pentane/diethyl ether = 50:1, $\mathbf{R_f}$ = 0.26 (*n*-pentane/diethyl ether = 50:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.65 (s, 3H), 2.04 (s, 3H), 2.33 (t, *J* = 7.0 Hz, 2H), 2.75-2.78 (m, 2H), 4.16 (t, *J* = 7.0 Hz, 2H), 4.97 (ddt, *J* = 10.0, 3.2, 1.5 Hz, 1H), 5.02 (ddt, *J* = 17.2, 3.6, 1.6 Hz, 1H), 5.242-5.26 (m, 1H), 5.80 (ddt, *J* = 16.3, 10.3, 6.1 Hz, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 16.0, 21.0, 32.2, 38.6, 62.9, 114.4, 124.1, 132.3, 136.9, 171.1; **IR** ($\tilde{\nu}$/cm^{-1}) 805 (w), 911 (m), 1042 (s), 1241 (s) 1365 (m), 1384 (m), 1433 (w), 1638 (w), 1743 (s), 2963 (m), 3080 (w); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{17}O_2$ $[M+H]^+$, 169.1223, found 169.1222.



1f **2f**

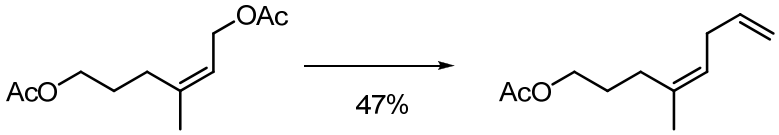
2f: Eluent: *n*-pentane/ethyl acetate = 50:1, $\mathbf{R_f}$ = 0.44 (*n*-pentane/ethyl acetate = 50:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.62 (s, 3H), 1.71-1.78 (m, 2H), 2.05-2.09 (m, 5H), 2.74-2.77 (m, 2H), 4.05 (t, *J* = 6.5 Hz, 2H), 4.96 (ddt, *J* = 10.0, 3.0, 1.5 Hz, 1H), 5.01 (ddt,

J = 17.2, 3.5, 1.9 Hz, 1H), 5.17-5.21(m, 1H), 5.79 (ddt, *J* = 16.3, 10.0, 6.3 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 15.8, 21.0, 26.7, 32.2, 35.7, 64.1, 114.2, 122.1, 135.2, 137.2, 171.2; **IR** ($\tilde{\upsilon}$/cm^{-1}) 606 (w), 910 (m), 994 (w), 1040 (m), 1243 (s), 1366 (m), 1386 (m) 1448 (w), 1638 (w), 1742 (s), 2956 (m), 3079 (w); **HRMS** (ESI) *m/z* calculated for $C_{11}H_{19}O_2$ $[M+H]^+$, 183.1380, found 183.1378.



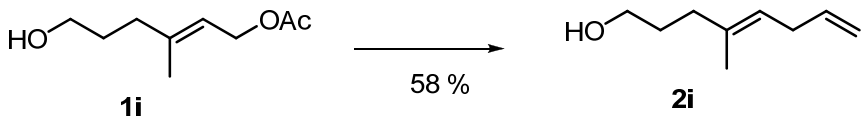
1g **2g**

2g: Eluent: *n*-pentane/ethyl acetate = 10:1, $\mathbf{R_f}$ = 0.56 (*n*-pentane/ethyl acetate = 50:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.76 (d, *J* = 1.0 Hz, 3H), 2.05 (s, 3H), 2.38 (t, *J* = 7.0 Hz, 2H), 2.76-2.79 (m, 2H), 4.12 (t, *J* = 7.0 Hz, 2H), 4.97 (ddt, *J* = 10.0, 3.2, 1.6 Hz, 1H), 5.03 (ddt, *J* = 17.1, 3.5, 2.0 Hz, 1H), 5.31 (t, *J* = 7.3 Hz, 1H), 5.80 (ddt, *J* = 16.3, 10.0, 6.3 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 21.0, 23.6, 31.0, 32.2, 62.6, 114.5, 125.0, 132.1, 137.2, 171.1; **IR** ($\tilde{\upsilon}$/cm^{-1}) 912 (m), 995 (w), 1044 (m), 1236 (s), 1365 (m), 1383 (m), 1448 (w), 1639 (w), 1742 (s), 2970 (m); **HRMS** (ESI) *m/z* calculated for $C_{10}H_{16}O_2Na$ $[M+Na]^+$, 191.1043, found 191.1043.



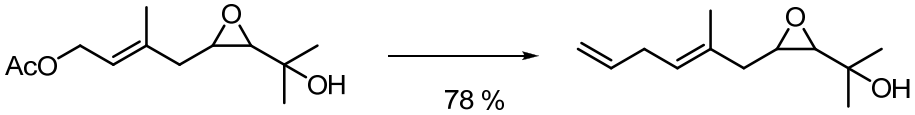
1h **2h**

2h: Eluent: *n*-pentane/diethyl ether = 50:1, $\mathbf{R_f}$ = 0.21 (*n*-pentane/diethyl ether = 50:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.69-1.76 (m, 5H), 2.06 (s, 3H), 2.08-2.12 (m, 2H), 2.72-2.76 (m, 2H), 4.04 (t, *J* = 6.6 Hz, 2H), 4.96 (ddt, *J* = 10.1, 3.3, 1.5 Hz, 1H), 5.02 (ddt, *J* = 17.1, 3.6, 1.8 Hz, 1H), 5.21 (t, *J* = 7.1 Hz, 1H), 5.79 (ddt, *J* = 16.3, 10.1, 6.2 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 21.0, 23.2, 26.7, 27.8, 32.1, 64.1, 114.3, 123.1, 135.2, 137.4, 171.1; **IR** ($\tilde{\upsilon}$/cm^{-1}) 911 (w), 995 (w), 1038 (m), 1242 (s), 1366 (m), 1450 (w), 1638 (w), 1743 (s), 2965 (m); **HRMS** (ESI) *m/z* calculated for $C_{11}H_{19}O_2$ $[M+H]^+$, 183.1380, found 183.1378.



1i **2i**

2i: Eluent: *n*-pentane/ethyl acetate = 5:1, $\mathbf{R_f}$ = 0.35 (*n*-pentane/ethyl acetate = 5:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.50 (s, 1H), 1.63 (s, 3H), 1.66-1.73 (m, 2H), 2.09 (t, *J* = 7.5 Hz, 2H), 2.74-2.78 (m, 2H), 3.64 (t, *J* = 6.5 Hz, 2H), 4.95 (ddt, *J* = 10.0, 3.3, 1.8 Hz, 1H), 5.02 (ddt, *J* = 17.1, 3.5, 1.5 Hz, 1H), 5.20-5.23 (m, 1H), 5.80 (ddt, *J* = 16.6, 10.0, 6.3 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 15.8, 30.7, 32.2, 35.9, 62.7, 114.2, 121.8, 136.0, 137.2; **IR** ($\tilde{\nu}$/cm^{-1}) 909 (m), 993 (w), 1062 (m), 1383 (w), 1434 (w), 1638 (m), 2939 (s), 2976 (m), 3079 (w), 3355 (s); **HRMS** (ESI) *m/z* calculated for $C_9H_{17}O$ $[M+H]^+$, 141.1274, found 141.1272.

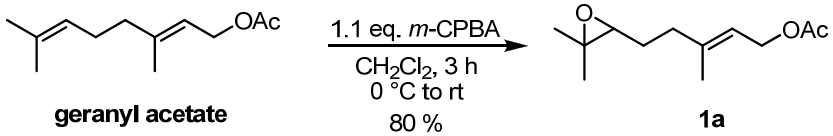


1j **2j**

2j: Eluent: *n*-pentane/diethyl ether = 2:1, $\mathbf{R_f}$= 0.41 (*n*-pentane/diethyl ether = 2:1), **IR** ($\tilde{\nu}$ / cm^{-1}) = 910 (s), 1151 (w), 1181 (w), 1257 (w), 1378 (w), 1638 (m), 2928 (m), 2975(s), 3078 (w), 3446 (s); **^{1}H-NMR** (400 MHz, $CDCl_3$): *δ* 1.25 (s, 3H), 1.31 (s, 3H), 1.70 (s, 3H), 1.78 (bs, 1H), 2.20 (dd, 1H, *J* = 14.6, 5.5 Hz), 2.32 (dd, 1H, *J* = 14.6, 6.5 Hz), 2.73 (d, 1H, *J* = 2.5 Hz), 2.79 (bt, 2H, *J* = 6.8 Hz), 3.10 (ddd, 1H, *J* = 6.5, 5.4, 2.5 Hz), 4.97 (ddt, 1H, *J* = 10.0, 3.0, 1.5 Hz), 5.03 (ddt, 1H, *J* = 17.1, 3.5, 1.5 Hz), 5.30 (tq, 1H, *J* = 7.3, 1.5 Hz), 5.81 (ddt, 1H, *J* = 16.9, 10.2, 6.3 Hz); **^{13}C-NMR** (100 MHz, $CDCl_3$): *δ* 16.6, 24.9, 27.8, 32.2, 41.7, 54.8, 64.8, 67.7, 114.5, 124.1, 132.4, 138.8; **HRMS (ESI)**: *m/z* für $C_{12}H_{21}O_2$ $[M+H]^+$, calculated 197.1536, found 197.1536.

III. Compound characterisation

Epoxide **1a**:

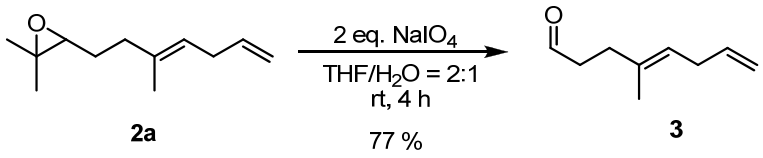


geranyl acetate **1a**

To a solution of geranyl acetate (10.0 g, 51 mmol) in dichloromethane (300 mL) at 0 °C was added *m*-chloroperbenzoic acid (14.0 g, 56 mmol, 1.1 eq., 70 %) portionwise and the white suspension was stirred for 3 h at room temperature. Then a 3N NaOH solution (100 mL) was added and the mixture became a clear solution. The aqueous layer was extracted with dichloromethane (3 x 30 mL) and the combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude compound was purified by flash column chromatography (SiO_2, *n*-pentane/diethyl ether = 20:1 → 10:1 → 5:1) and epoxide **1a** was obtained as a colourless oil (9.14 g, 85 %).

R_f = 0.44 (*n*-pentane/ethyl acetate = 5:1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.25 (s, 3H), 1.29 (s, 3H), 1.62-1.68 (m, 2H), 1.71 (s, 3H), 2.04 (s, 3H), 2.12-2.26 (m, 2H), 2.69 (t, J = 6.0 Hz, 1H), 4.58 (d, J = 7.0 Hz, 2H), 5.38 (tq, J = 7.2, 1.3 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.4, 18.7, 21.0, 24.8, 27.0, 36.1, 58.4, 61.2, 63.9, 118.8, 141.2, 171.0; **HRMS (ESI)**: *m/z* for $C_{12}H_{21}O_3$ $[M+H]^+$, calculated 213.1485, found 213.1485.

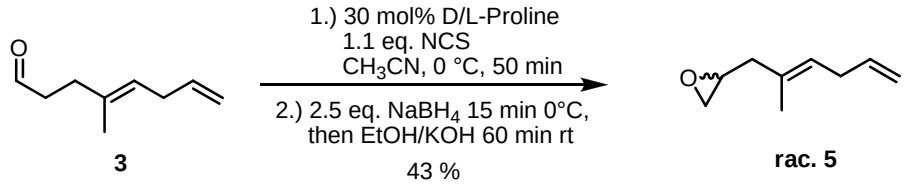
Aldehyde **3**:



To a suspension of epoxide **2a** (2.18 g, 12.1 mmol) in a THF/H_2O mixture (2:1, 60 mL) was added sodium periodate (5.17 g, 24.2 mmol, 2 eq.). The reaction mixture was stirred for 4 h and then the white precipitate was filtered through celite®, rinsed with diethyl ether (50 mL). The aqueous phase was separated and extracted with diethyl ether (2 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude compound was purified by flash column chromatography (SiO_2, *n*-pentane/diethyl ether = 50:1) and compound **3** was obtained as a colourless oil (1.25 g, 77 %).

R_f = 0.28 (cyclohexane/ethyl acetate = 92:8); **IR** ($\tilde{\nu}$ / cm^{-1}) = 910 (w), 996 (w), 1087 (w), 1387 (w), 1639 (w), 1723 (s), 2721 (w), 2918 (m), 2975 (m), 3426 (w); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.64 (s, 3H), 2.36 (t, J = 7.4 Hz, 2H), 2.55 (dt, J = 7.5, 2.1 Hz, 2H), 2.76 (t, J = 6.3 Hz, 2H), 4.95-5.03 (m, 2H), 5.19-5.23 (m, 1H), 5.79 (ddt, J = 16.9, 10.4, 6.2 Hz, 1H); 9.78 (t, J = 2.0 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.1, 31.8, 32.2, 42.1, 114.4, 122.5, 134.4, 136.9; 202.5; **HRMS (ESI)**: *m/z* for $C_9H_{15}O$ $[M+H]^+$, calculated 139.1117, found 139.1115.

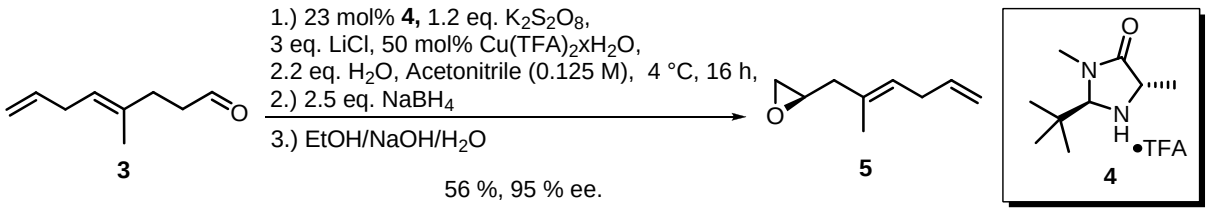
Epoxide **5** (racemic for GC analysis)



A stirred solution of aldehyde **3** (200 mg, 1.45 mmol) and D/L-Proline (51 mg, 0.44 mmol, 30 mol%) in acetonitrile (4 mL) was cooled to 0 °C and treated with *N*-Chlorosuccinimide (212 mg, 1.60 mmol, 1.1 eq.) portionwise. The reaction mixture was warmed to room temperature over 50 min and then recooled to 0 °C, followed by the addition of sodium borohydride (3.63 mmol, 138 mg, 2.5 eq.). After a further 10 min at 0 °C and then 5 min at room temperature, a freshly prepared solution of EtOH/ aqueous KOH (6 mL, solution prepared from: 12 mL EtOH, 12.5 g KOH, 25 mL H_2O) was added and the medium was stirred vigorously for 1 h. The reaction mixture was diluted with water (20 mL) and diethyl ether (10 mL) and the aqueous layer was further extracted with diethyl ether (2 x 25 mL), the organic layers dried over $MgSO_4$ and the solvents removed under reduced pressure. Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 25:1) of the crude product yielded epoxide **5** as a colourless oil (85 mg, 43 %).

R_f= 0.78 (cyclohexane/ethyl acetate = 6:1); **IR** ($\tilde{\nu}$ / cm^{-1}) = 748 (w), 832 (m), 912 (s), 995 (m), 1112 (m), 1406 (m), 1639 (s), 1667 (s), 2921 (s), 2980 (s), 3050 (w), 3410 (w), 3583 (w); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.71 (s, 3H), 2.20 (dd, *J* = 14.6, 5.5 Hz, 1H), 2.28 (dd, *J* = 14.6, 6.0 Hz, 1H), 2.50 (dd, *J* = 5.0, 3.0 Hz, 1H), 2.78-2.81 (m, 3H), 2.98-3.03 (m, 1H), 4.98 (ddt, *J* = 10.0, 5.0, 1.5 Hz, 2H) , 5.03 (ddt, *J* = 17.1, 5.5, 1.8 Hz, 1H), 5.82 (ddt, *J* = 16.9, 10.2, 6.3 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.7, 32.2, 42.5, 46.9, 51.4, 114.5, 123.9, 132.6, 136.9; **HRMS (ESI)**: *m/z* for $C_9H_{15}O$ $[M+H]^+$, calculated 139.1117, found 139.1115.

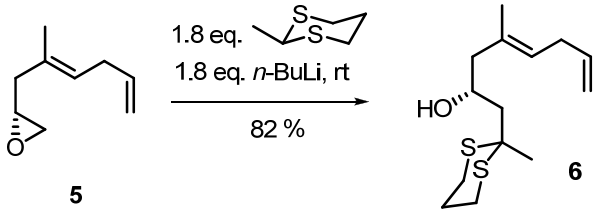
Epoxide **5**:



A single neck, round bottom flask was charged with (2*R*, 5S)-2-*tert*-butyl-3,5-dimethylimidazolidin-4-one trifluoroacetic salt **4** (1.30 g, 4.57 mmol, 23 mol%), lithium chloride (2.58 g, 59.6 mmol, 3.0 eq.), copper trifluoroacetate hydrate (2.88 g, 9.90 mmol, 50 mol%) and potassium persulfate (6.45 g, 23.9 mmol, 1.2 eq.). The solids were dissolved in acetonitrile (159 mL, 0.125 M) and water (0.8 mL, 43.7 mmol, 2.2 eq.) and cooled to 0 °C, before the aldehyde **3** (2.75 g, 19.9 mmol) was added. The green suspension was stirred at 4 °C (fridge) for 16 h, recooled to 0 °C and treated with sodium borohydride (1.88 g, 49.8 mmol, 2.5 eq.) in several portions. After 30 min at 0 °C a freshly prepared NaOH/EtOH solution (74 mL, made from 50 mL water, 24 mL, EtOH and 25 g NaOH) was added to the black suspension and the reaction mixture was stirred vigorously for additional 3 h at room temperature. The reaction mixture was diluted with water (200 mL), extracted with diethyl ether (3 x 150 mL) and the combined organic phases were dried over $MgSO_4$. Careful evaporation (max. 40 °C @ 230 mbar) yielded a crude oil, which was purified by column chromatography (SiO_2, *n*-pentane/diethyl ether = 25:1) to afford epoxide **5** as a colourless liquid (1.54 g, 56 %, 95 % *ee* calculated by chiral GC).

R_f= 0.78 (*cyclohexane*/ethyl acetate = 6:1); **$[\alpha]_D^{20}$**= 4.14 ($CHCl_3$, c = 11.41); **IR** ($\tilde{\nu}$ / cm^{-1}) = 748 (w), 832 (m), 912 (s), 995 (m), 1112 (m), 1406 (m), 1639 (s), 1667 (s), 2921 (s), 2980 (s), 3050 (w), 3410 (w), 3583 (w); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.71 (s, 3H), 2.20 (dd, *J* = 14.6, 5.5 Hz, 1H), 2.28 (dd, *J* = 14.6, 6.0 Hz, 1H), 2.50 (dd, *J* = 5.0, 3.0 Hz, 1H), 2.78-2.81 (m, 3H), 2.98-3.03 (m, 1H), 4.98 (ddt, *J* = 10.0, 5.0, 1.5 Hz, 2H) , 5.03 (ddt, *J* = 17.1, 5.5, 1.8 Hz, 1H), 5.82 (ddt, *J* = 16.9, 10.2, 6.3 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.7, 32.2, 42.5, 46.9, 51.4, 114.5, 123.9, 132.6, 136.9; **HRMS (ESI)**: *m/z* for $C_9H_{15}O$ $[M+H]^+$, calculated 139.1117, found 139.1115.

Dithiane **6**:

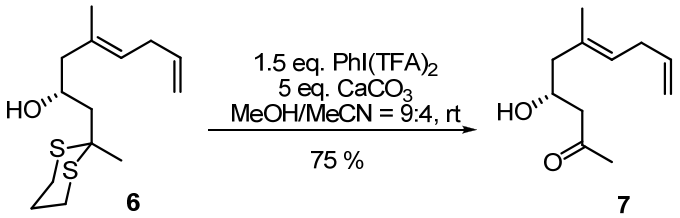


2-Methyl-1,3-dithiane (2.12 g, 15.8 mmol, 1.8 eq.) was dissolved in THF (50 mL) and *n*-BuLi (9.88 mL, 15.8 mmol, 1.8 eq., 1.6 M in hexane) was added dropwise over 20 min. After a

further 10 min at room temperature, epoxide **5** (1.21 g, 8.75 mmol) in THF (10 mL + 2.0 ml rinse) was introduced via cannula over 45 min. After 30 min, the reaction was quenched by addition of a saturated aqueous NH_4Cl solution (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The crude residue was subjected to flash column chromatography (*n*-pentane/diethyl ether = 5:1) yielding dithiane **6** (1.97 g, 82 %) as a yellow oil.

R_f= 0.31 (*cyclohexane*/ethyl acetate = 6:1); **$[\alpha]_D^{20}$**= −36.5 ($CHCl_3$, c = 7.70); **IR** ($\tilde{\nu}$ / cm^{-1}) = 724 (w), 909 (m), 1012 (m), 1085 (m), 1257 (w), 1421 (m), 2925 (s), 3074 (w), 3442 (m), 3818 (w), **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.66 (s, 3H), 1.68 (s, 3H), 1.88-2.07 (m, 3H), 2.13-2.18 (m, 1H), 2.22-2.28 (m, 2H), 2.77-2.83 (m, 4H), 2.92-3.07 (m, 3H), 4.05-4.11 (m, 1H), 4.96-5.06 (m, 2H) , 5.27-5.29 (m, 1H), 5.76-5.86 (m, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.2, 24.8, 26.6, 26.8, 28.5, 32.3, 47.1, 47.9, 48.4, 66.6, 144.5, 125.3, 133.1, 136.9; **HRMS (ESI)**: *m/z* for $C_{14}H_{25}OS_2$ $[M+H]^+$, calculated 273.1341, found 273.1342.

Methylketone **7**

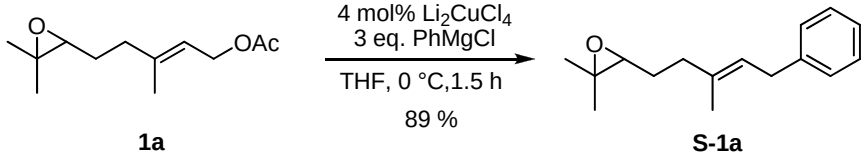


To a suspension of dithiane **6** (95 mg, 0.35 mmol) and calcium carbonate (1.85 mmol, 185 mg, 5 eq.) in a MeOH/acetonitrile solution (9:4) (13 mL) was added $PhI(TFA)_2$ (0.56 mmol, 239 mg, 1.5 eq.) in one portion at room temperature. After 10 min the reaction was quenched with a $Na_2S_2O_3/NaHCO_3$ solution (1:1) (10 mL) and the aqueous phase extracted with dichloromethane (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (*n*-pentane/diethyl ether = 2:1) gave methylketone **7** (48 mg, 75%) as a colourless oil.

R_f= 0.20 (*n*-pentane/diethyl ether = 2:1); **$[\alpha]_D^{20}$**= −25.9 ($CHCl_3$, c = 8.88); **IR** ($\tilde{\nu}$ / cm^{-1}) = 910 (w), 994 (w), 1078 (m), 1359 (m), 1486 (m); 1710 (s), 2388 (w), 2927 (s), 2972 (s), 3457 (s); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.66 (s, 3H), 2.12-2.14 (m, 5H), 2.56-2.59 (m, 2H), 2.74 (bs, 1H), 2.79 (bt, J = 6.6 Hz, 2H), 4.16-4.22 (m, 1H), 4.96-5.05 (m, 2H), 5.27 (dt, J = 7.2, 0.9 Hz, 1H), 5.75-5.85 (m, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.1, 30.9, 32.3, 46.9, 49.5, 65.5,

114.5, 125.4, 132.8, 138.8, 209.4; **HRMS (ESI)**: *m/z* for $C_{11}H_{19}O_2$ $[M+H]^+$, calculated 183.1380, found 183.1379.

(*E*)-2,2-Dimethyl-3-(3-methyl-5-phenylpent-3-enyl)oxirane (Scheme 3, Step a)

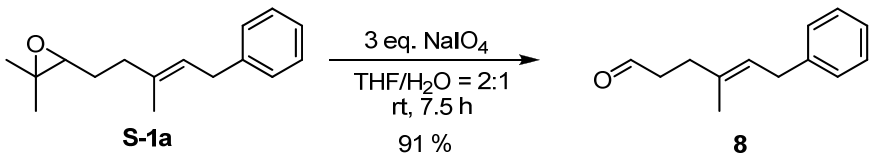


1a **S-1a**

To a solution of epoxide **1a** (406 mg, 1.91 mmol) in THF (10 mL) at 0°C was added dropwise lithium tetrachlorocuprate (0.8 mL, 0.08 mmol, 4 mol%, 0.1 M in THF) and the reaction mixture was stirred for 5 min. Then a solution of phenylmagnesium chloride (2.87 mL, 5.73 mmol, 3 eq., 2M in THF) was slowly added and the reaction mixture was stirred for 1.5 h at 0°C. The reaction was quenched by addition of a saturated NH_4Cl solution (10 mL) and the residues of magnesium salt were dissolved by addition of water. The aqueous phase was separated and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude compound was purified by flash column chromatography (SiO_2, *cyclohexane*/ethyl acetate = 99:1) and epoxide **S-1a** was obtained as an oil (390 mg, 89 %).

$\mathbf{R}_f$ = 0.26 (*cyclohexane*/ethyl acetate = 99:1); **IR** ($\tilde{\nu}$ / cm^{-1}) = 698 (s), 741 (s), 874 (w), 1030 (w), 1122 (m), 1249 (w), 1323 (w), 1377 (s), 1453(s), 1494 (s), 1603 (w), 2923 (s), 2961 (s), 3026 (m), 3061 (w); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.27 (s, 3H), 1.29 (s, 3H), 1.62-1.72 (m, 2H), 1.75 (s, 3H), 2.12-2.27 (m, 2H), 2.72 (t, J = 6.3 Hz, 1H), 3.38 (d, J = 7.5 Hz, 2H), 5.41 (tq, J = 7.3, 1.5 Hz, 1H), 7.17-7.20 (m, 3H), 7.27-7.31 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.2, 18.7, 24.8, 27.4, 34.2, 36.2, 58.4, 64.1, 132.7, 125.7, 128.3 (4 C), 135.2, 141.5; **HRMS (ESI)**: *m/z* for $C_{16}H_{23}O$ $[M+H]^+$, calculated 231.1743, found 231.1743.

Aldehyde **8**

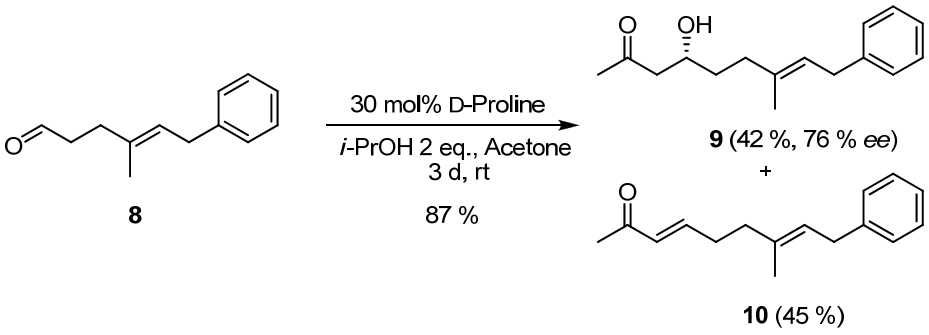


S-1a **8**

To a suspension of sodium periodate (450 mg, 2.1 mmol, 3 eq.) in a THF/H_2O solution (2:1, 5 mL) was added a solution of epoxide **S-1a** (159 mg, 0.7 mmol) dissolved in a THF/H_2O solution (2:1, 1 mL) at room temperature. The reaction mixture was stirred for 7.5 h and then the white precipitate was filtered through celite®, rinsed with diethyl ether (5 mL). The aqueous phase was separated and extracted with diethyl ether (2 x 5 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude compound was purified by flash column chromatography (SiO_2, *n*-pentane/diethyl ether = 50:1 → 25:1) and compound **8** was obtained as an oil (120 mg, 91 %).

R_f = 0.44 (*n*-pentane/diethyl ether = 6:1); **IR** ($\tilde{\nu}$ / cm^{-1}) = 689 (w), 742 (w), 1029 (w), 1074 (w), 1266 (w), 1450 (w), 1602 (w), 1685 (w), 1724 (s), 2721 (w), 2916 (w), 3027 (w), 3061 (w); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.74 (s, 3H), 2.39 (t, 2H, *J* = 7.1 Hz), 2.57 (dt, 2H, *J* = 7.5, 1.0 Hz), 3.37 (d, 2H, *J* = 7.0 Hz), 5.39 (tq, 1H, *J* = 7.4, 1.3 Hz), 7.15-7.21 (m, 3H), 7.27-7.31 (m, 2H), 9.78 (t, 1H, *J* = 1.8 Hz); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.3, 31.8, 34.1, 42.1, 124.1, 125.8, 128.2 (2 C), 128.4 (2 C), 134.1, 141.2, 202.4; HRMS (ESI): *m/z* for $C_{13}H_{17}O$ $[M+H]^+$, calculated 189.1274, found 189.1273.

Hydroxyketone **9** and Enone **10**



8

A solution of aldehyde **8** (522 mg, 2.78 mmol), D-Proline (97 mg, 0.83 mmol) and *iso*-propanol (0.42 mL, 2 equiv.) in acetone (20 mL) was stirred for 3 days at room temperature. The reaction mixture was filtered over celite®, washed with ethyl acetate (20 mL) and the solution was concentrated *in vacuo*. The crude compound was purified by flash column chromatography (SiO_2, *n*-pentane/diethyl ether 7:3 → 1:1) and compound **9** (287 mg, 42 %, 72 % *ee*) and enone **10** (285 mg, 45 %) were obtained as yellow oils.

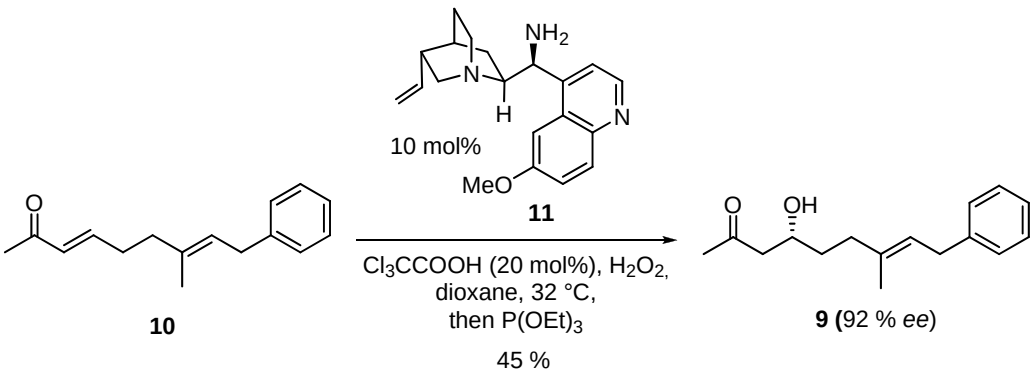
Compound **9**

R_f = 0.23 (*n*-pentane/diethyl ether = 2:1); **$[\alpha]_D^{20}$**= -13.1 ($CHCl_3$, c = 10); **IR** ($\tilde{\nu}$ / cm^{-1}) = 700 (w), 742 (w), 1072 (w), 1097 (m), 1160 (w), 1275 (s), 1361 (s), 1450 (m), 1493 (w), 1711 (s), 2857 (w), 2930 (s), 3026 (w), 3439 (s); **HPLC**: R_t = 8.36 min (major enantiomer), R_t = 7.60 min (minor enantiomer) (Daicel IA, *n*-hexane/*iso*-propanol = 90:10, c = 0.71 mg/mL, 1 mL/min, T = 20°C); **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 1.51-1-58 (m, 1H), 1.62-1.69 (m, 1H), 1.74 (s, 3H), 2.08-2.24 (m, 2H), 2.17 (s, 3H), 2.55 (dd, *J* = 17.6, 9.2 Hz, 1H), 2.63 (dd, *J* = 17.6, 3.1 Hz, 1H), 2.95 (bs, 1H), 3.37 (d, *J* = 7.3 Hz, 2H), 4.02-4.07 (m, 1H), 5.39 (tq, *J* = 7.4, 1.0 Hz, 1H), 7.17-7.20 (m, 3H), 7.27-7.30 (m, 2H); **^{13}C-NMR** (125 MHz, $CDCl_3$): *δ* 16.1, 30.7, 34.2, 34.6, 35.5, 49.9, 67.3, 123.5, 125.7, 128.3 (2 C), 128.3 (2 C), 135.6, 141.6, 209.7; **HRMS (ESI)**: *m/z* for $C_{16}H_{22}O_2$ $[M+H]^+$, calculated 247.1693, found 247.1693.

Compound **10**

R_f = 0.38 (*n*-pentane/diethyl ether = 2:1); **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 1.73 (s, 3H), 2.19-2.23 (m, 2H), 2.19 (s, 3H), 2.37 (dd, *J* = 17.0, 8.5 Hz, 2H), 3.36 (d, *J* = 9.5 Hz, 2H), 5.38 (dt, *J* = 9, 1.5 Hz, 1H), 6.06 (d, *J* = 20 Hz, 1H), 6.06 (td, *J* = 20, 8.5 Hz, 1H), 7.17-7.20 (m, 3H), 7.27-7.30 (m, 2H); **^{13}C-NMR** (125 MHz, $CDCl_3$): *δ* 16.0, 26.7, 30.8, 34.2, 38.0, 124.3, 125.8, 128.3 (2 C), 128.4 (2 C), 131.5, 134.4, 141.3, 148.0, 198.7.

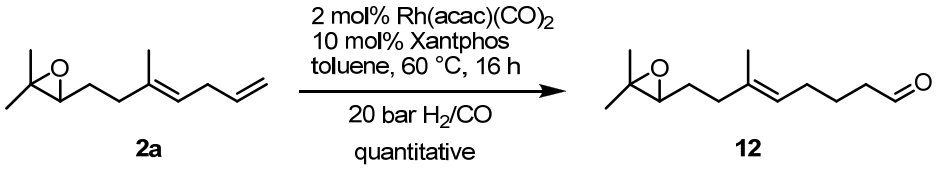
Oxa-Michael conditions for the conversion of **10** to **9**



Amine **11** (52 mg, 0.16 mmol, 0.1 eq.) was added to a solution of trichloroacetic acid (52.1 mg, 0.32 mmol, 0.3 eq) in 1,4-dioxane (6.4 mL). Then enone **10** (365 mg, 1.6 mmol, 1 eq.) was added followed by the addition of aqueous hydrogen peroxide (486 μL, 3 eq., 4.8 mmol, 30% w/w) after 20 min at ambient temperature. After 48 h at 32°C, triethylphosphite

(3 equiv., 830 mL, 3.0 mmol) was added dropwise at 0°C and the reaction mixture was stirred for 15 h at 32°C. Additional triethylphosphite (2 equiv., 554 mL, 3.2 mmol) was added and the reaction further stirred for 6 h. The reaction mixture was extracted with diethyl ether (2 x 35 mL) and the combined organic phases were washed with brine, dried over Na_2SO_4 and filtered. The resulting solution was concentrated *in vacuo*. The crude compound was purified by flash column chromatography (SiO_2, *n*-pentane/diethyl ether = 1:1) and compound **9** (177 mg, 45 %, 92 % *ee*) was obtained as a yellow oil.

Aldehyde **12**

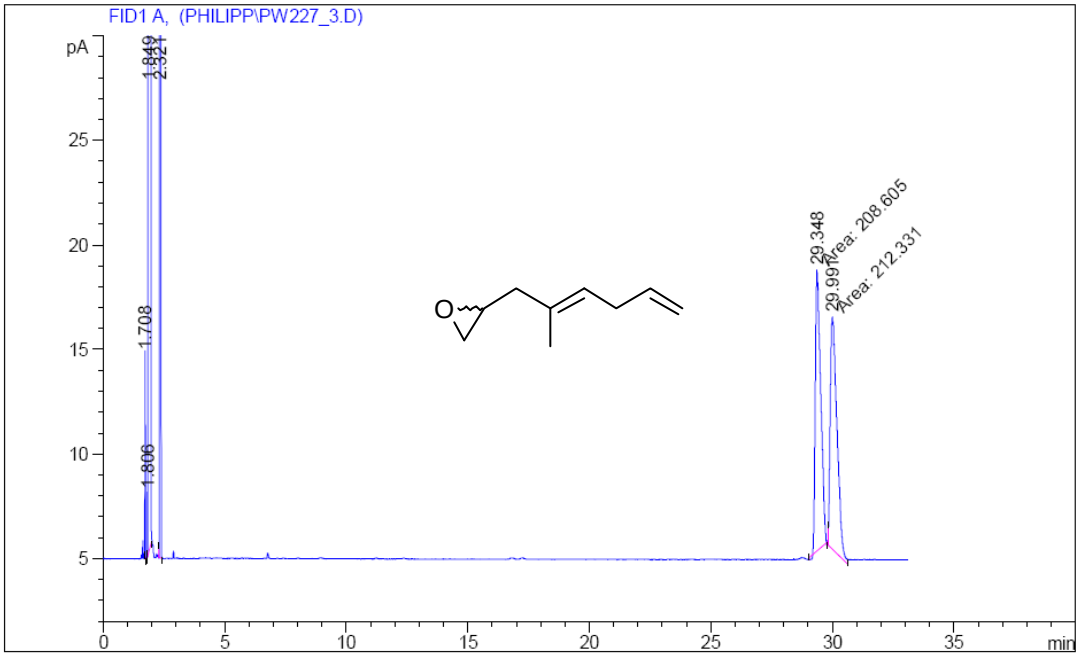


2a **12**

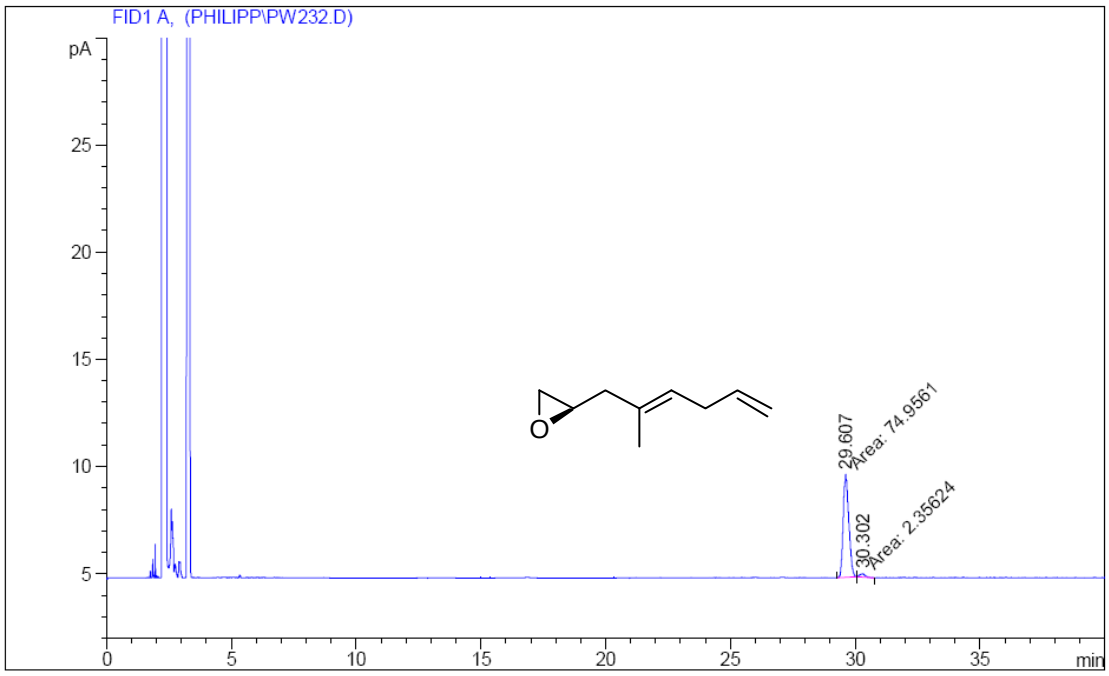
A reaction vial was charged with epoxide **2a** (90 mg, 0.5 mmol), $Rh(acac)(CO)_2$ (2.6 mg, 0.01 mmol, 2 mol%), Xantphos (4,5-Bis(diphenyl-phosphino)-9,9-dimethylxanthene) (30 mg, 0.05 mmol, 10 mol%) and toluene (2 mL). The yellow solution was stirred at 60 °C for 16 h under an H_2/CO atmosphere (20 bar) and subjected directly to column chromatography (SiO_2, *n*-pentane/diethyl ether = 6:1). The aldehyde **12** was obtained as a colourless oil (104 mg, 99 %).

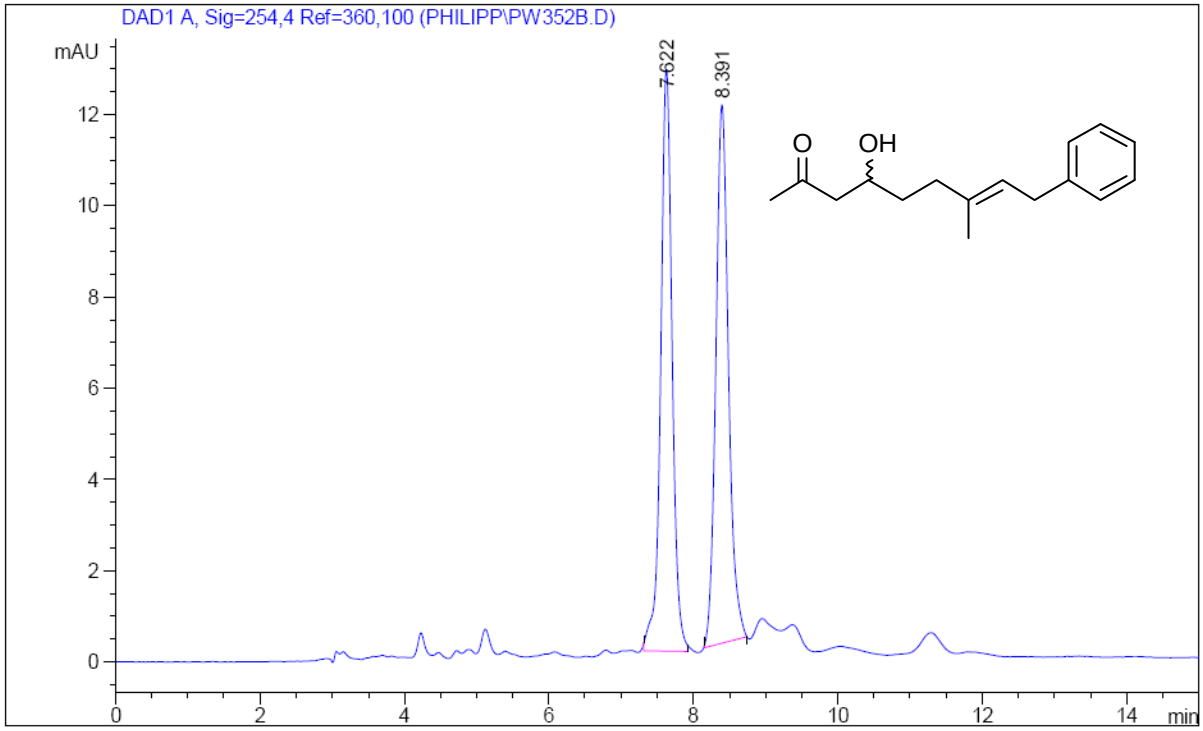
$\mathbf{R_f}$= 0.20 (*n*-pentane/diethyl ether = 6:1); **IR** ($\tilde{\nu}$ / cm^{-1}) = 680 (w), 872 (w), 1120 (m), 1380 (m), 1453 (m), 1724 (s), 2959 (s), 3494 (s), 3650 (w), 3673 (w); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 1.27 (s, 3H), 1.30 (s, 3H), 1.61 (s, 3H), 1.64-1.73 (m, 4H), 2.02-2.41 (m, 4H), 2.42 (dt, J = 7.3, 1.6 Hz, 2H), 2.70 (t, J = 6.3 Hz, 1H), 5.15 (tq, J = 7.2, 1.3 Hz, 1H), 9.77 (t, J = 1.8 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 16.0, 18.7, 22.2, 24.9, 27.2, 27.4, 36.3, 43.3, 58.3, 64.1, 123.8, 135.5, 202.7; **HRMS (ESI)**: *m/z* for $C_{15}H_{26}O_2N$ $[M+NH_4]^+$, calculated 252.1958, found 252.1952.

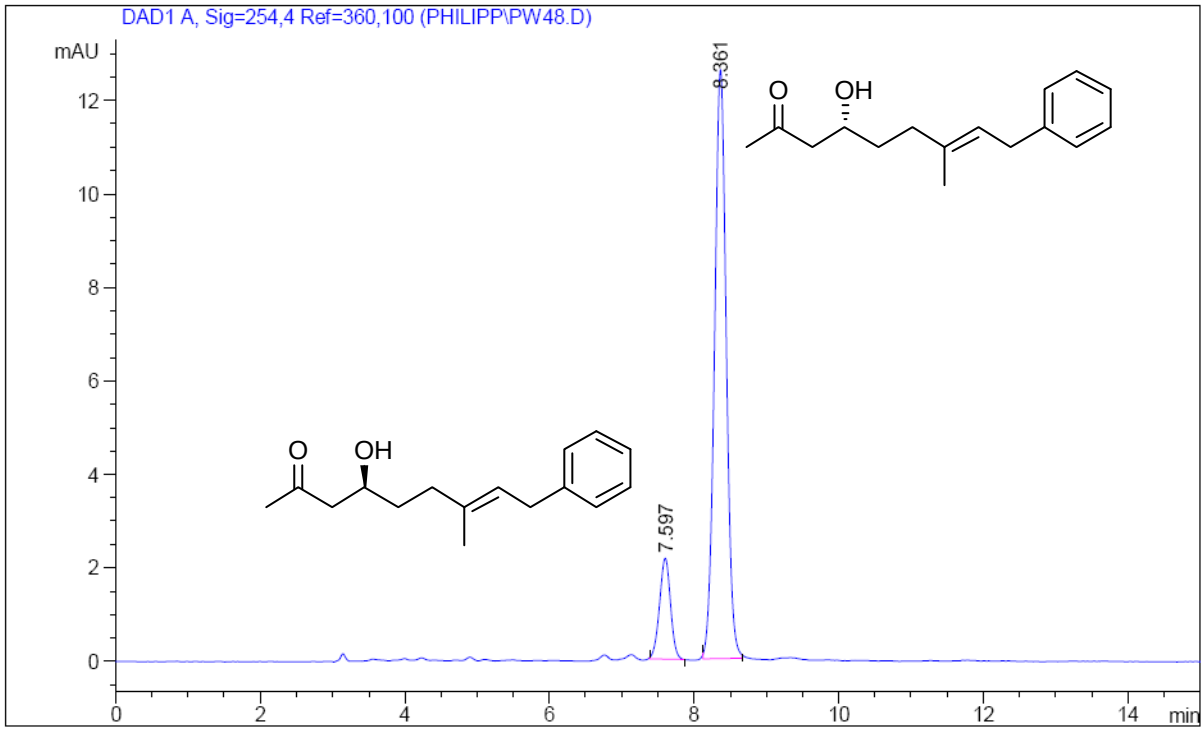
```
Data File C:\CHEM32\2\DATA\PHILIPP\PW227_3.D
Sample Name: PW 227

    ========================================================================
    Acq. Operator   : Bokelmann
    Acq. Instrument : GC 6850                          Location : Vial 2
    Injection Date  : 16-Feb-10, 13:27:38                   Inj :   1
                                                      Inj Volume : 1 µl
    Acq. Method     : C:\CHEM32\2\METHODS\PHILIPP.M
    Last changed    : 2/16/2010 1:23:29 PM by Bokelmann
                      (modified after loading)
    Analysis Method : C:\CHEM32\2\METHODS\AT_MERKS.M
    Last changed    : 6/30/2010 10:41:54 AM by Bokelmann
                      (modified after loading)
    Sample Info     : MN Hydrodex-ß-6TDBM
                      80°C
                      0.9ml/min He
                      100:1 split
```

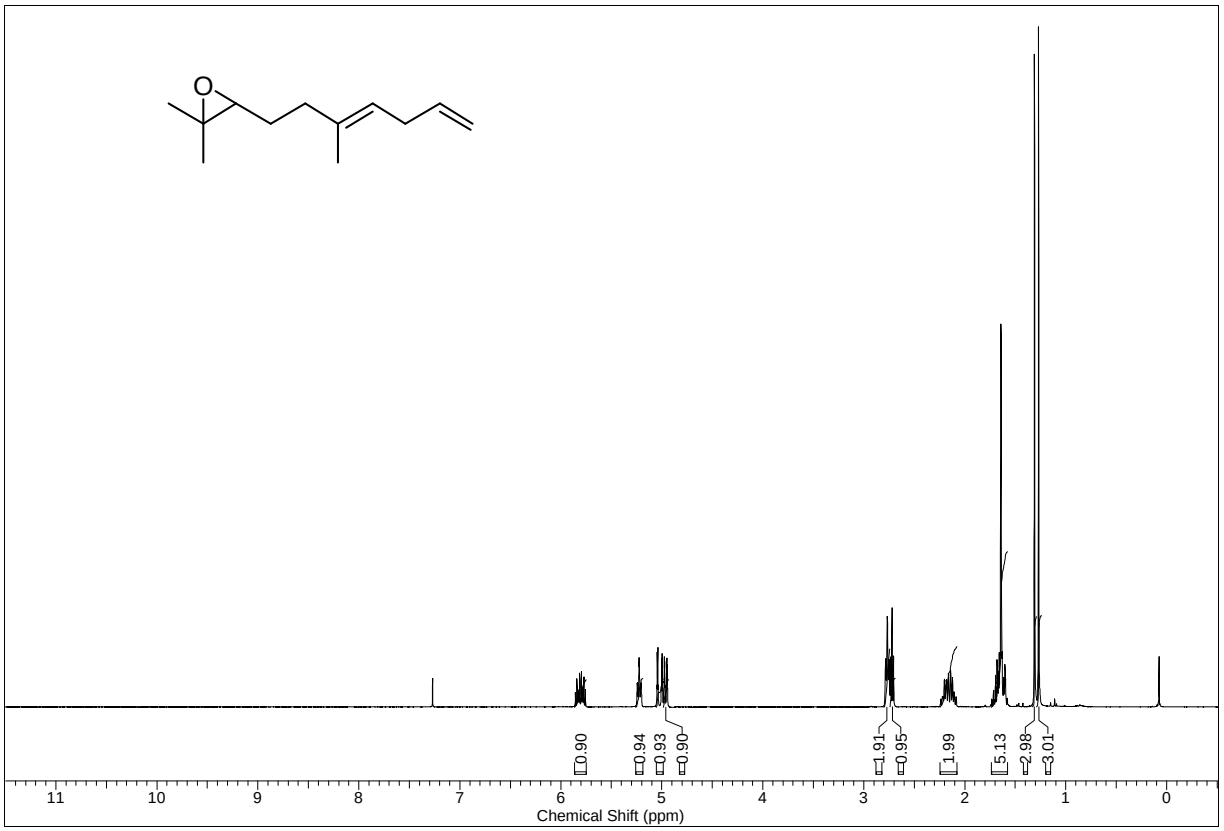


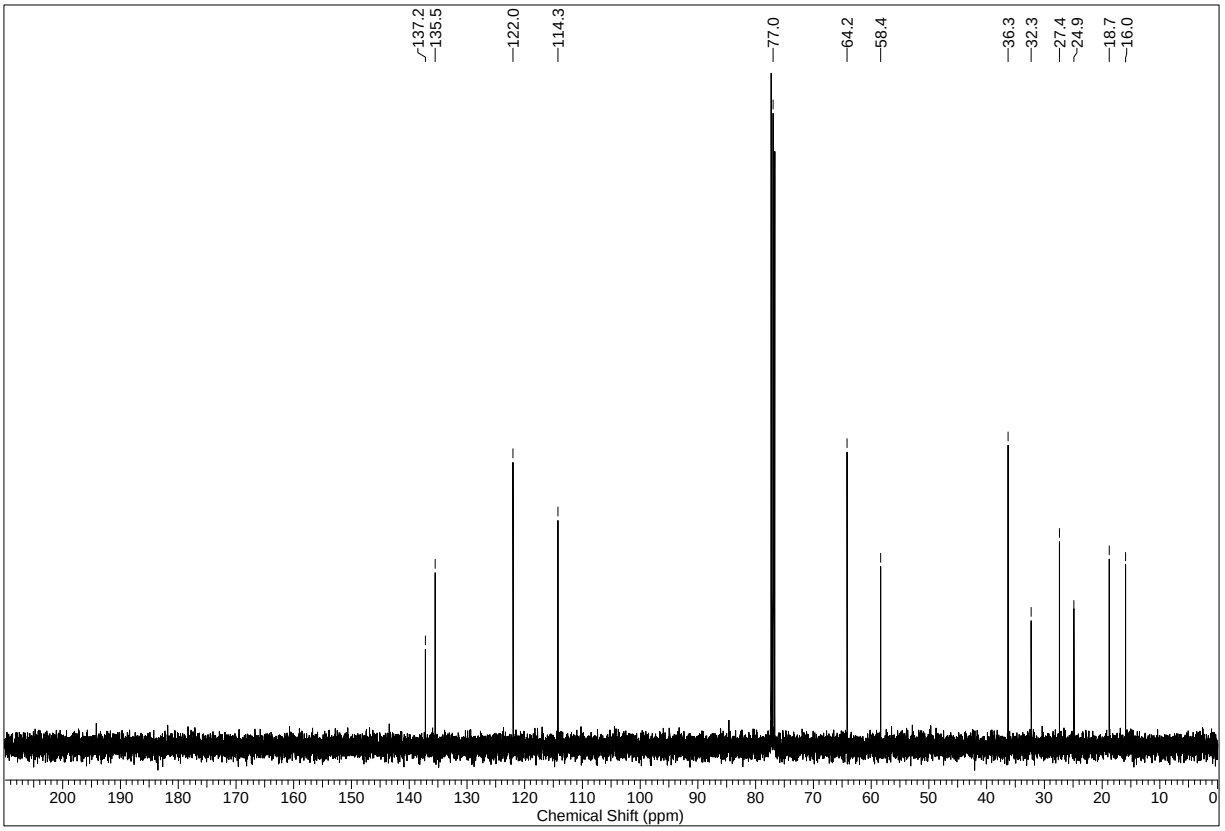
```
Data File C:\CHEM32\2\DATA\PHILIPP\PW232.D
Sample Name: PW232

    ========================================================================
    Acq. Operator   : Bokelmann
    Acq. Instrument : GC 6850                          Location : Vial 1
    Injection Date  : 17-Feb-10, 09:51:10                   Inj :   1
                                                      Inj Volume : 1 µl
    Acq. Method     : C:\CHEM32\2\METHODS\PHILIPP.M
    Last changed    : 2/16/2010 2:09:55 PM by Bokelmann
    Analysis Method : C:\CHEM32\2\METHODS\AT_MERKS.M
    Last changed    : 6/30/2010 11:13:43 AM by Bokelmann
                      (modified after loading)
    Sample Info     : MN Hydrodex-ß-6TDBM
                      80°C
                      0.9ml/min He
                      100:1 split
```

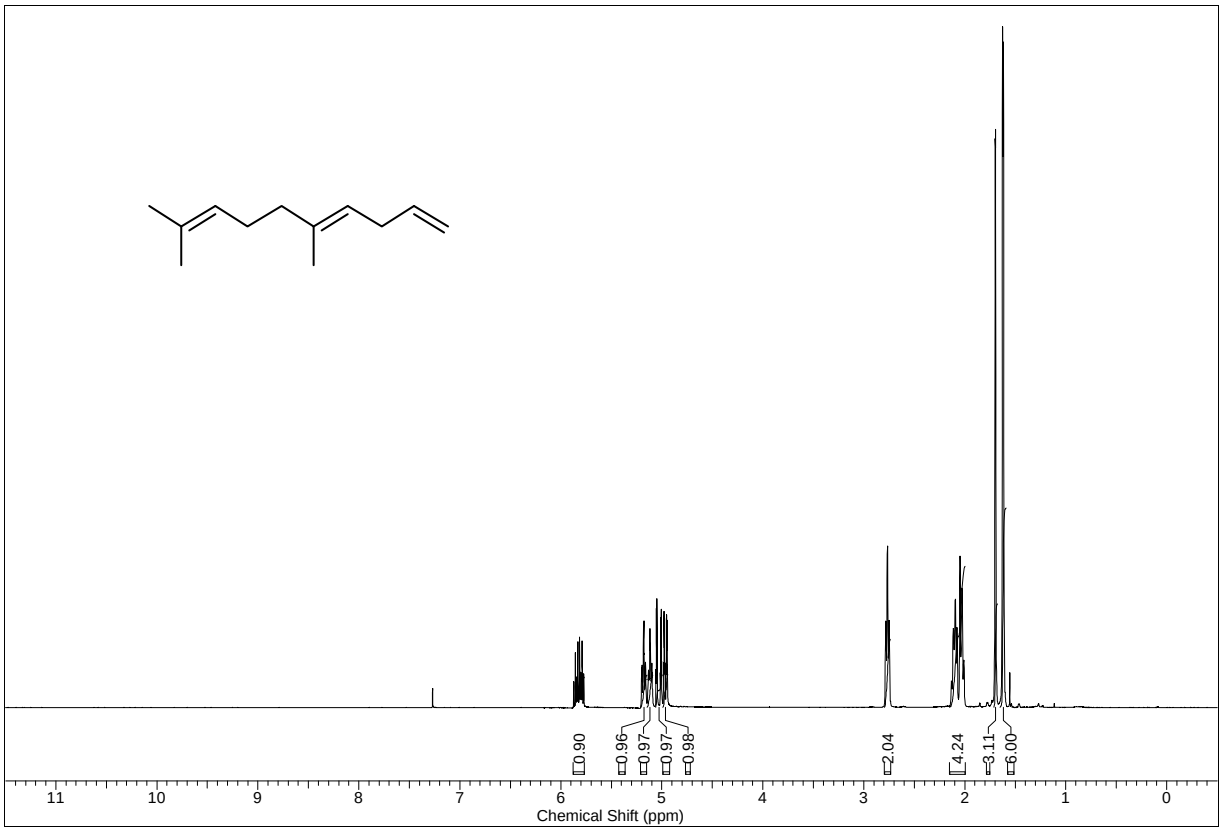


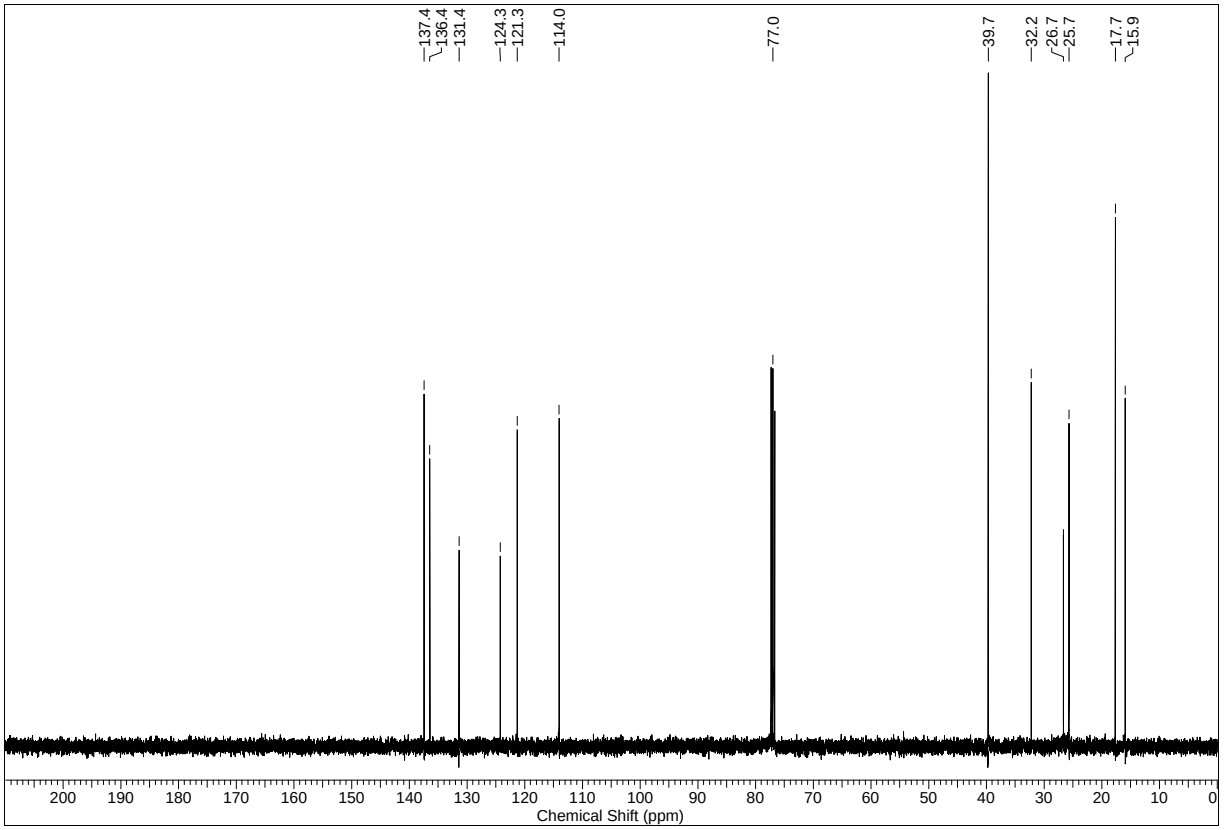

DAD1 A, Sig=254,4 Ref=360,100 (PHILIPP\PW352B.D)
mAU
12
10
8
6
4
2
0
7.622
8.391
O
OH
0
2
4
6
8
10
12
14
min

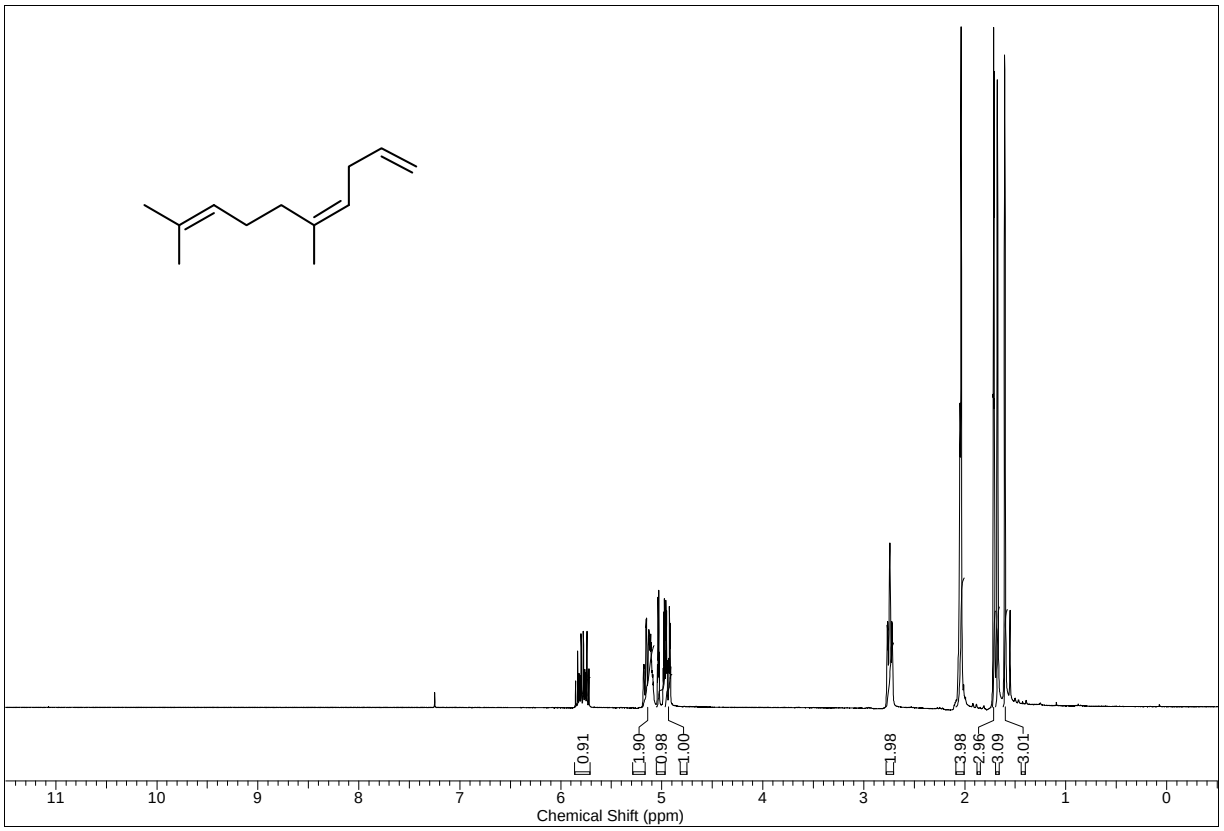

DAD1 A, Sig=254,4 Ref=360,100 (PHILIPP\PW48.D)
mAU
12
10
8
6
4
2
0
8.361
O
OH
7.597
O
OH
0
2
4
6
8
10
12
14
min

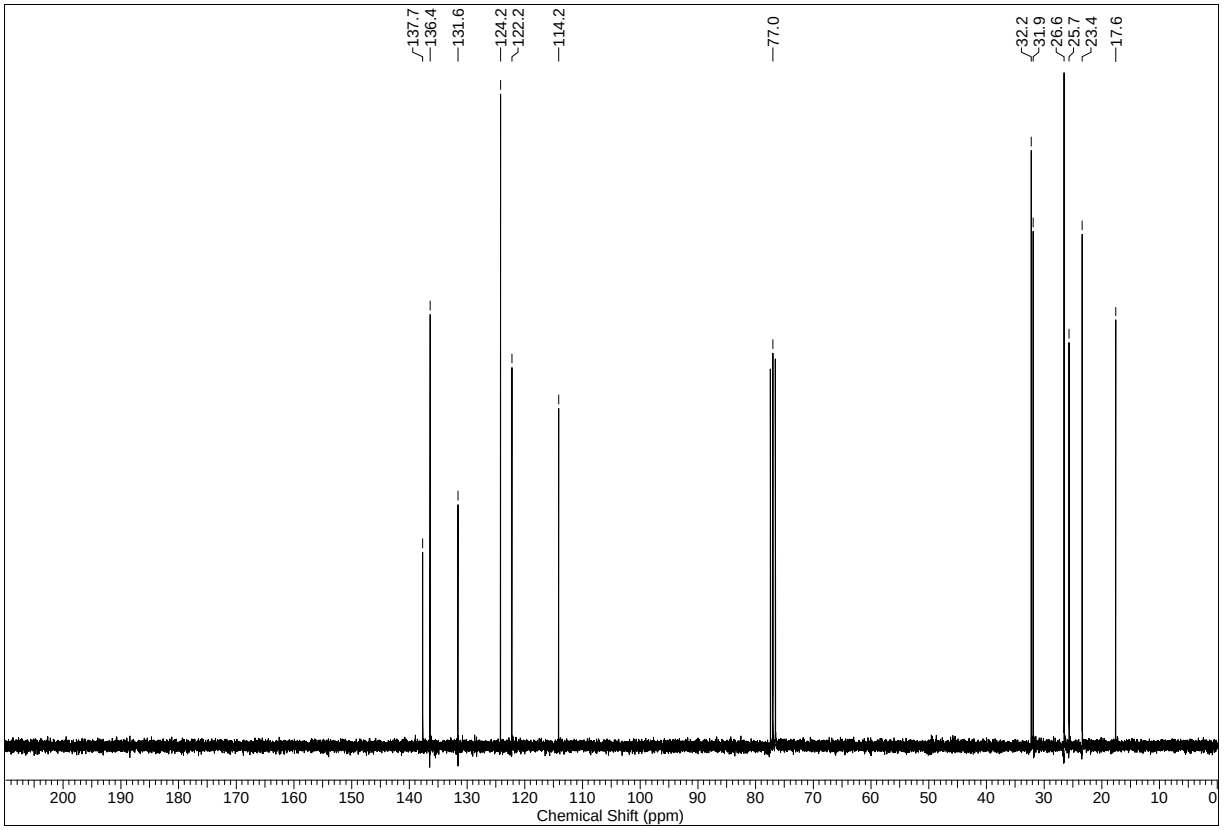

O
0.90
0.94
0.93
0.90
1.91
0.95
1.99
5.13
2.98
3.01
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

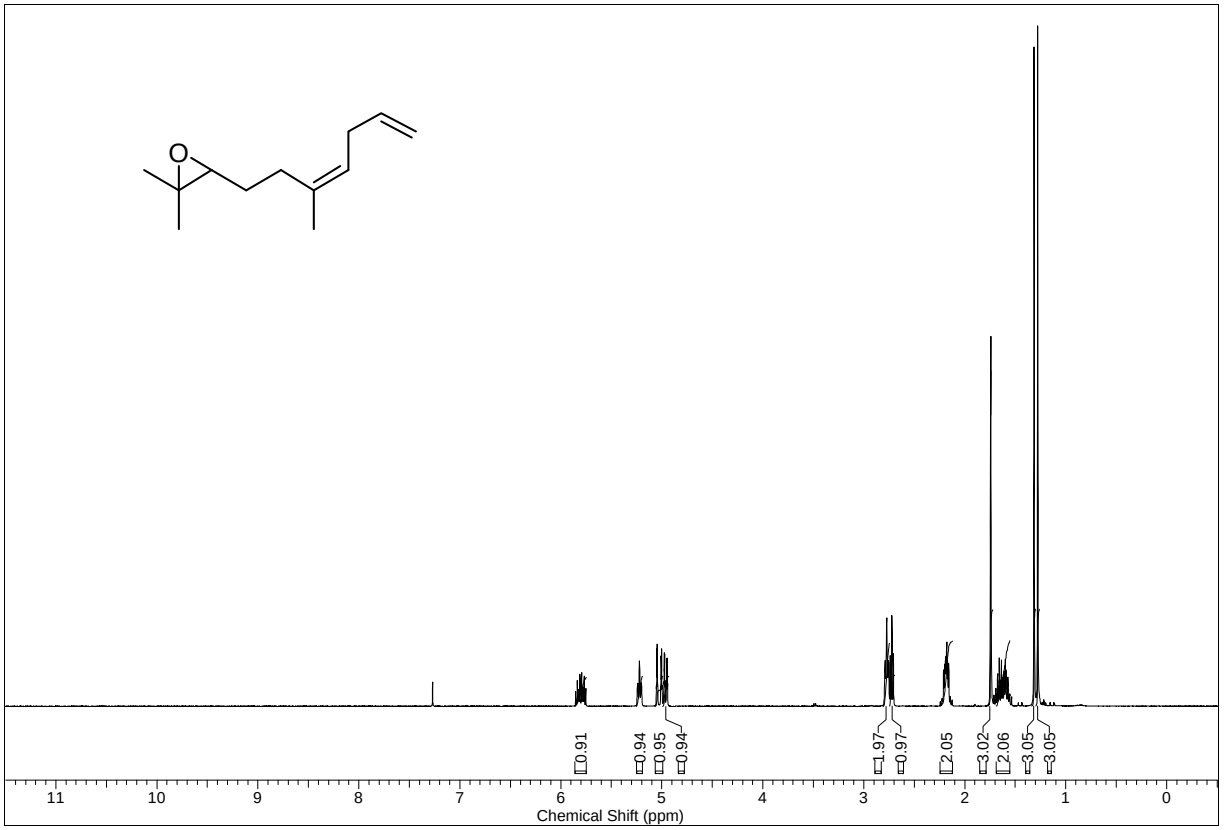

137.2
135.5
122.0
114.3
77.0
64.2
58.4
36.3
32.3
27.4
24.9
18.7
16.0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

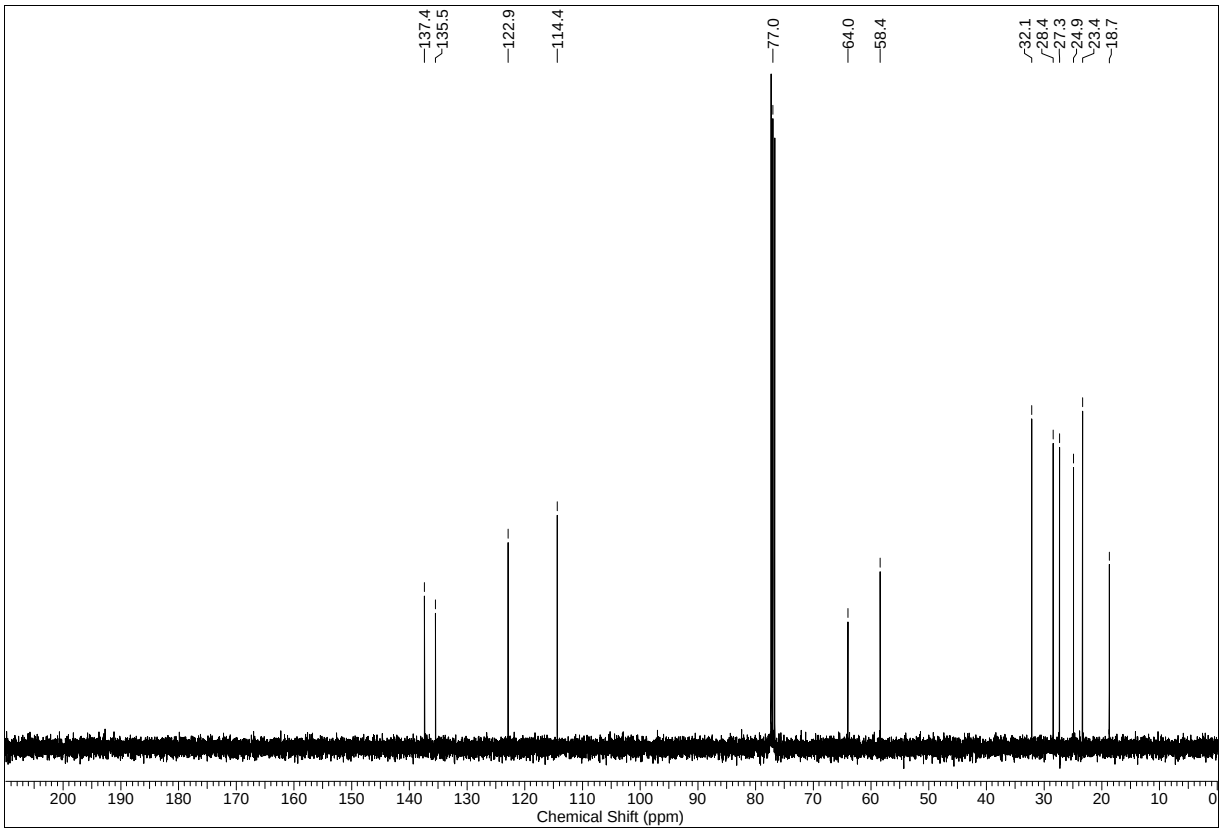

0.90
0.96
0.97
0.97
0.98
2.04
4.24
3.11
6.00
Chemical Shift (ppm)

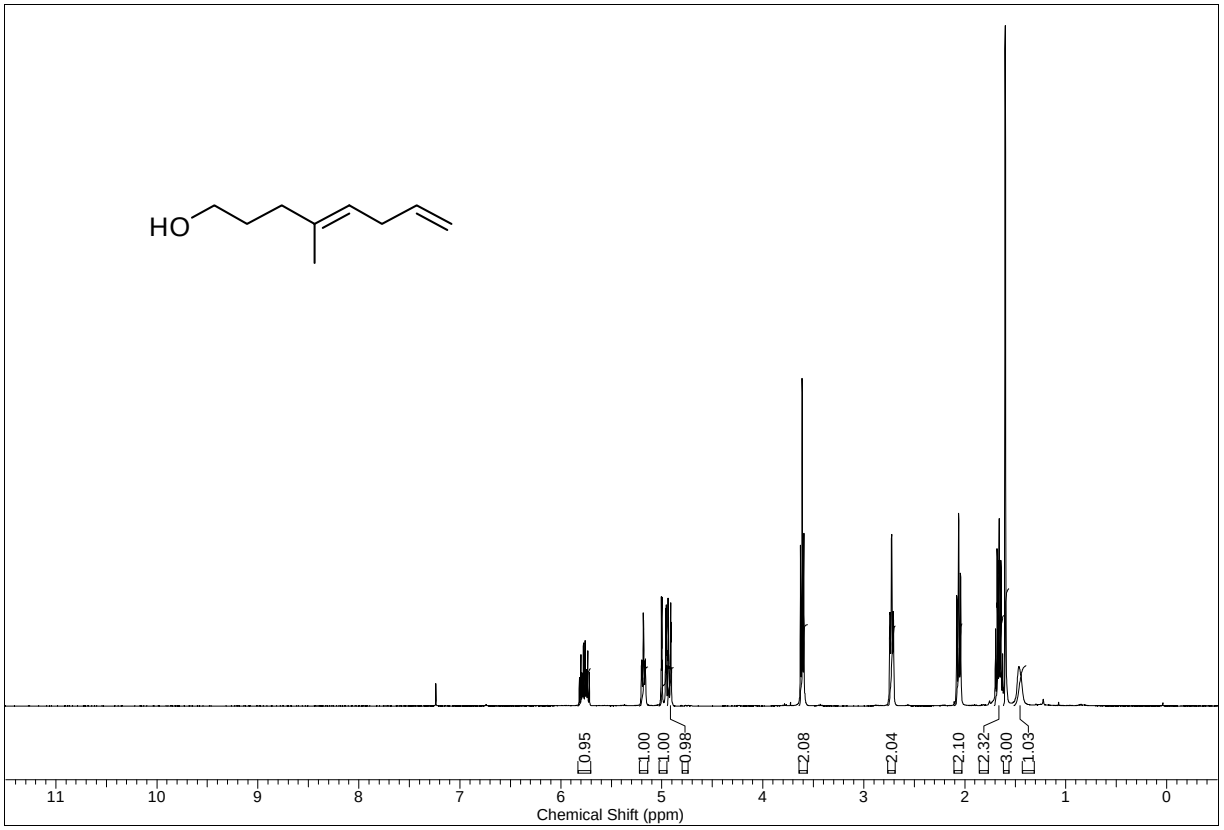

137.4
136.4
131.4
124.3
121.3
114.0
77.0
39.7
32.2
26.7
25.7
17.7
15.9
Chemical Shift (ppm)

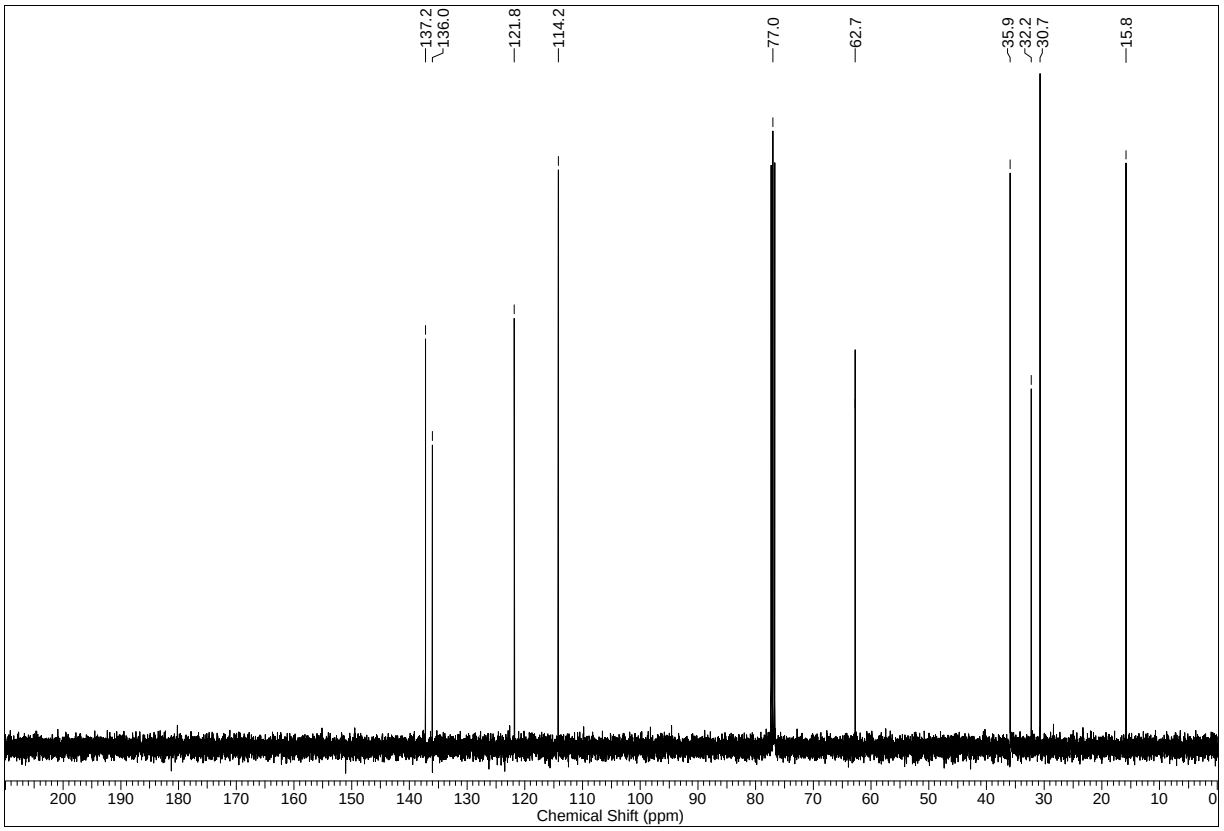

0.91
1.90
0.98
1.00
1.98
3.98
2.96
3.09
3.01
11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

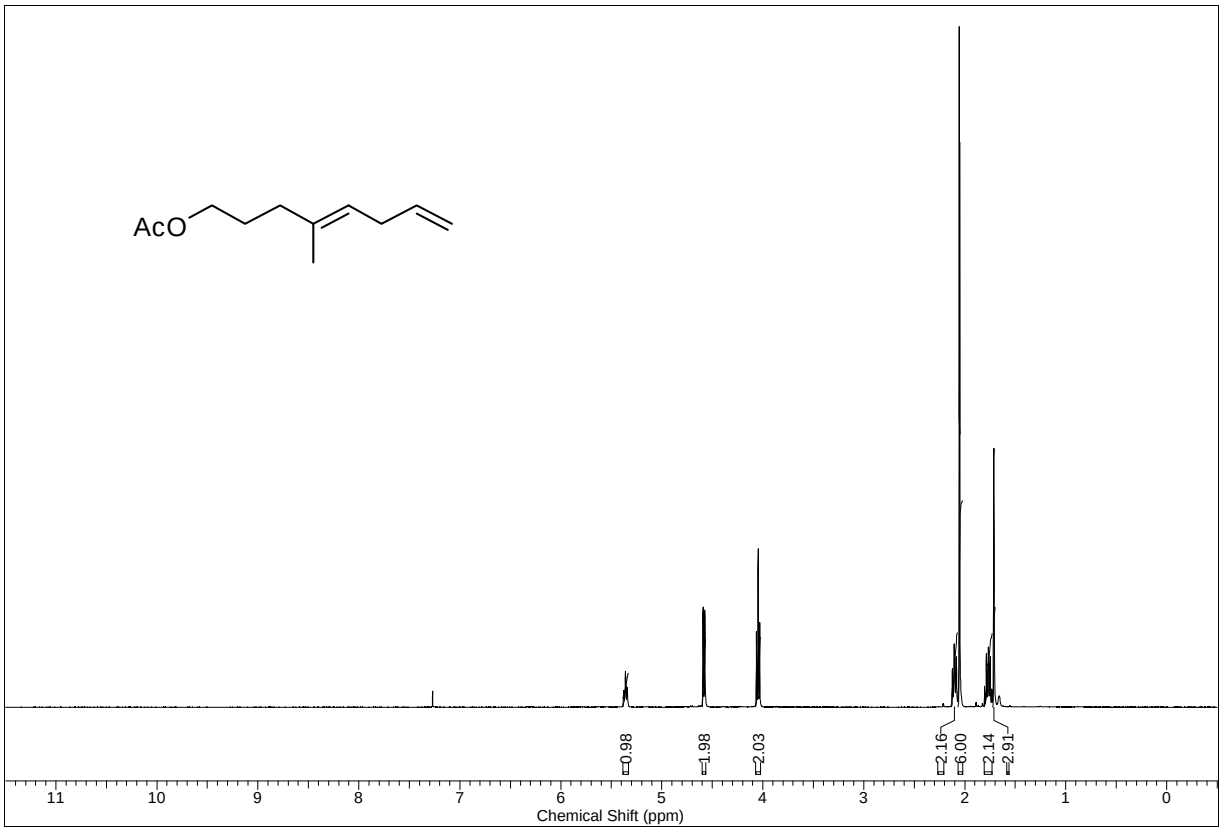

137.7
136.4
131.6
124.2
122.2
114.2
77.0
32.2
31.9
26.6
25.7
23.4
17.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

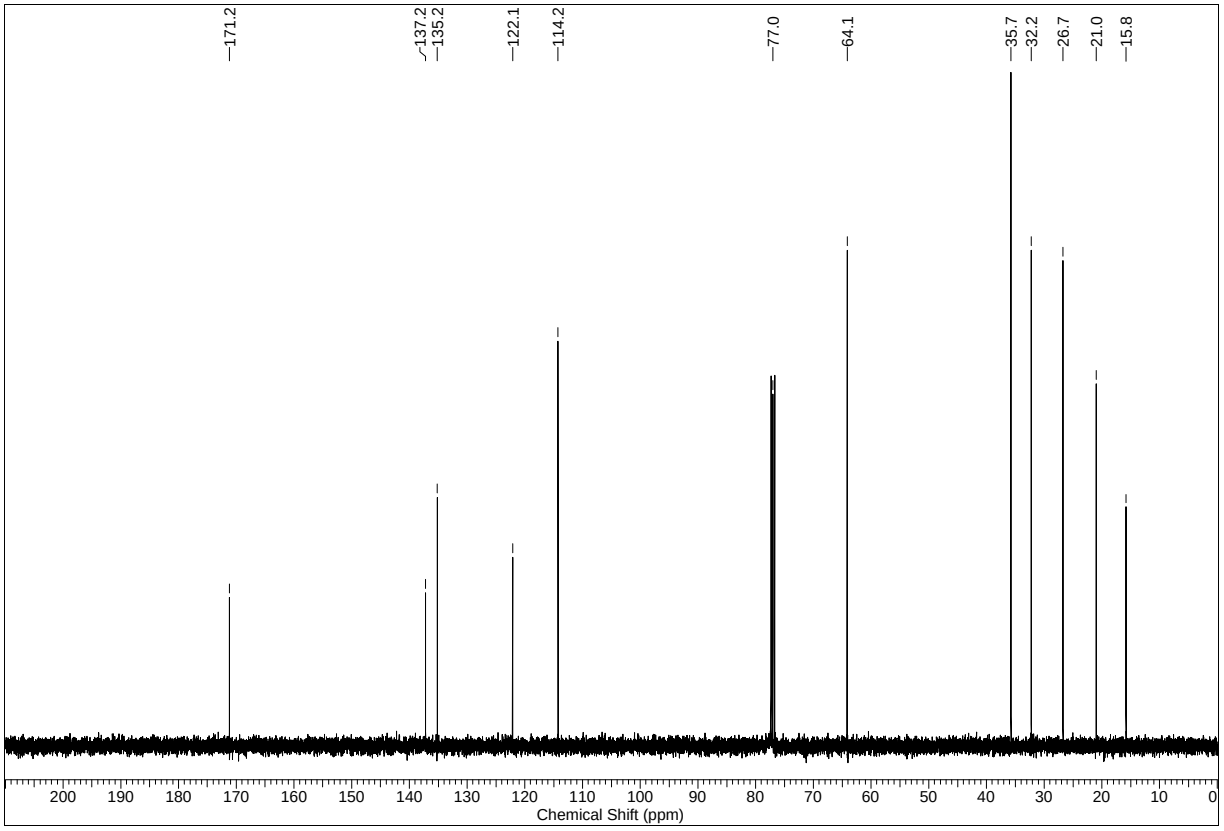

O
0.91
0.94
0.95
0.94
1.97
0.97
2.05
3.02
2.06
3.05
3.05
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

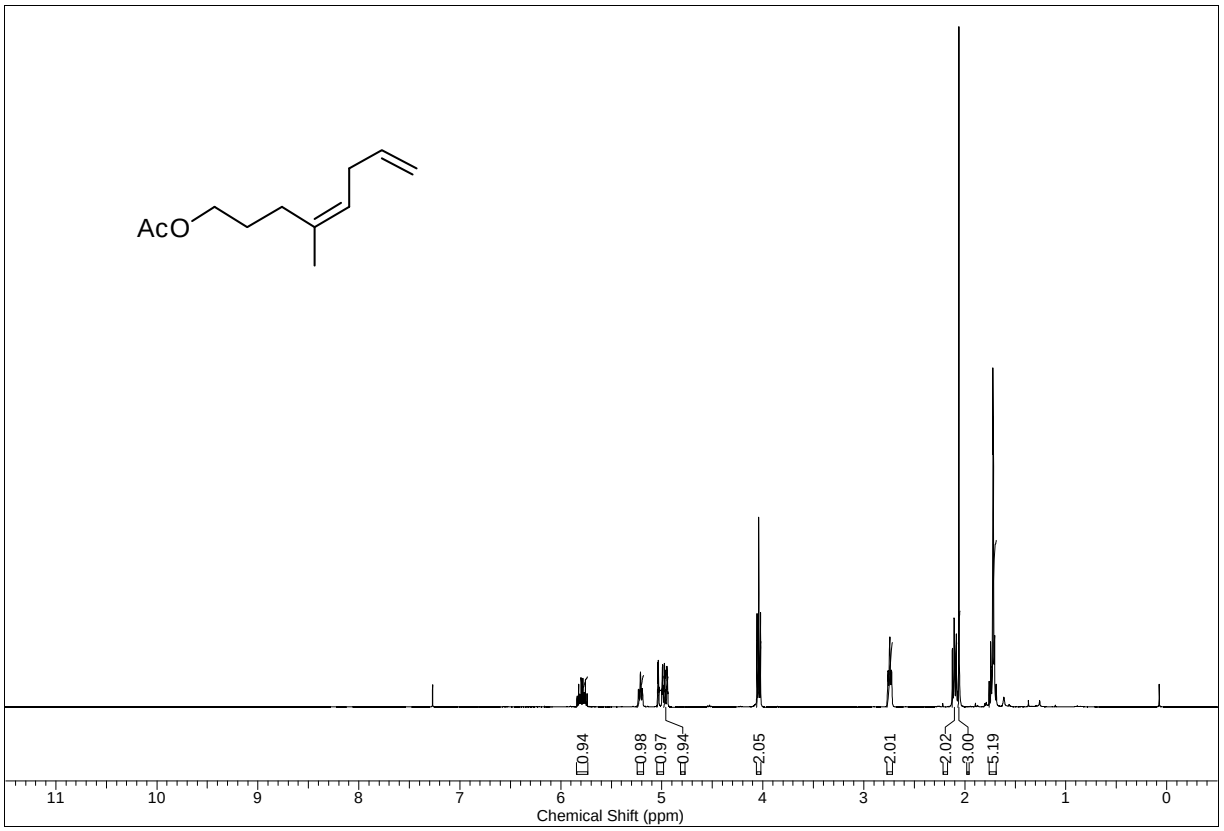

137.4
135.5
122.9
114.4
77.0
64.0
58.4
32.1
28.4
27.3
24.9
23.4
18.7
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

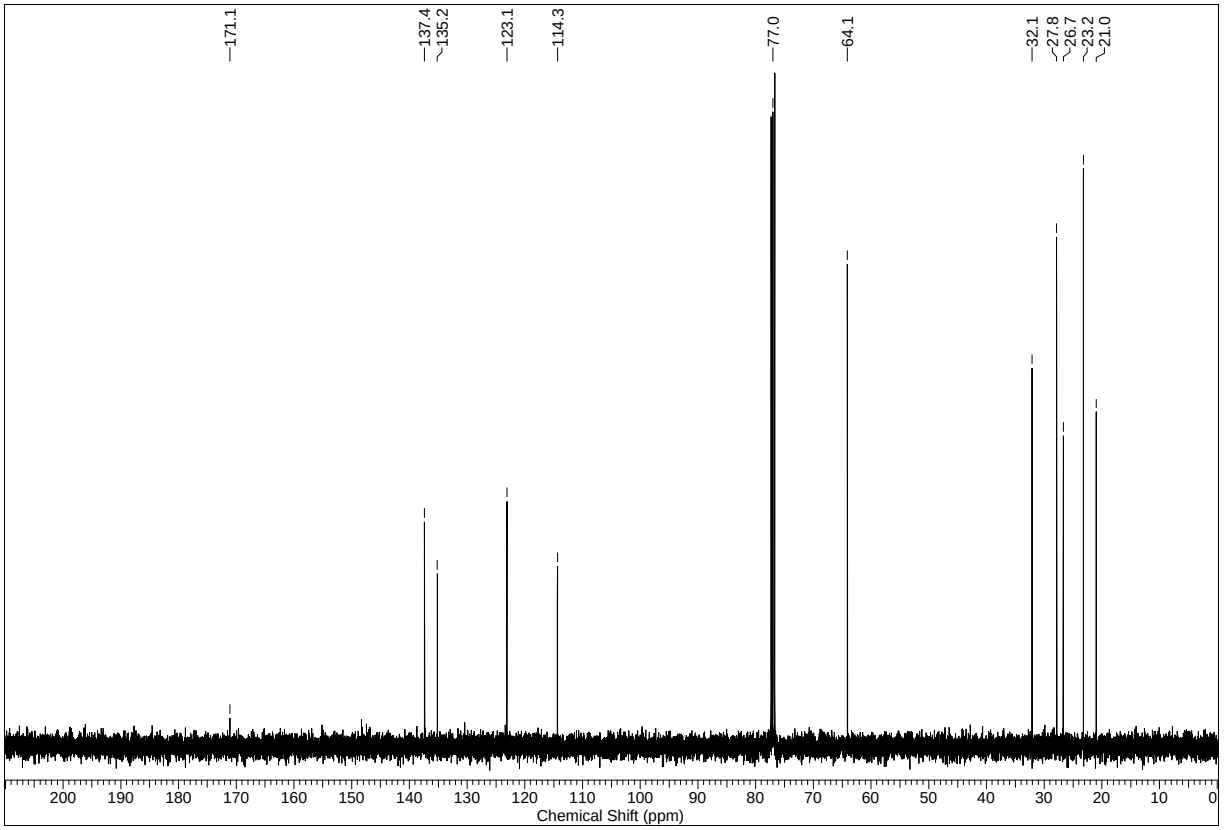

HO
0.95
1.00
1.00
0.98
2.08
2.04
2.10
2.32
3.00
1.03
11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

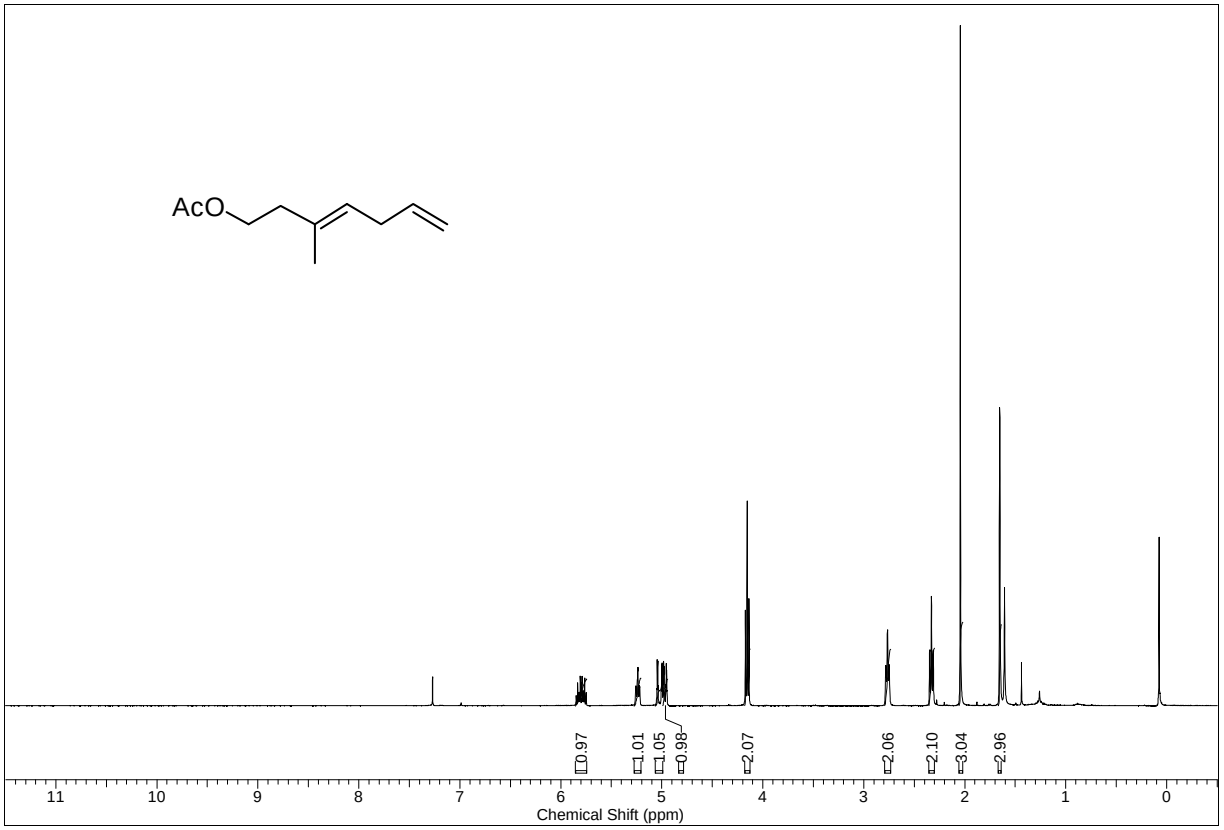

137.2
136.0
121.8
114.2
77.0
62.7
35.9
32.2
30.7
15.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

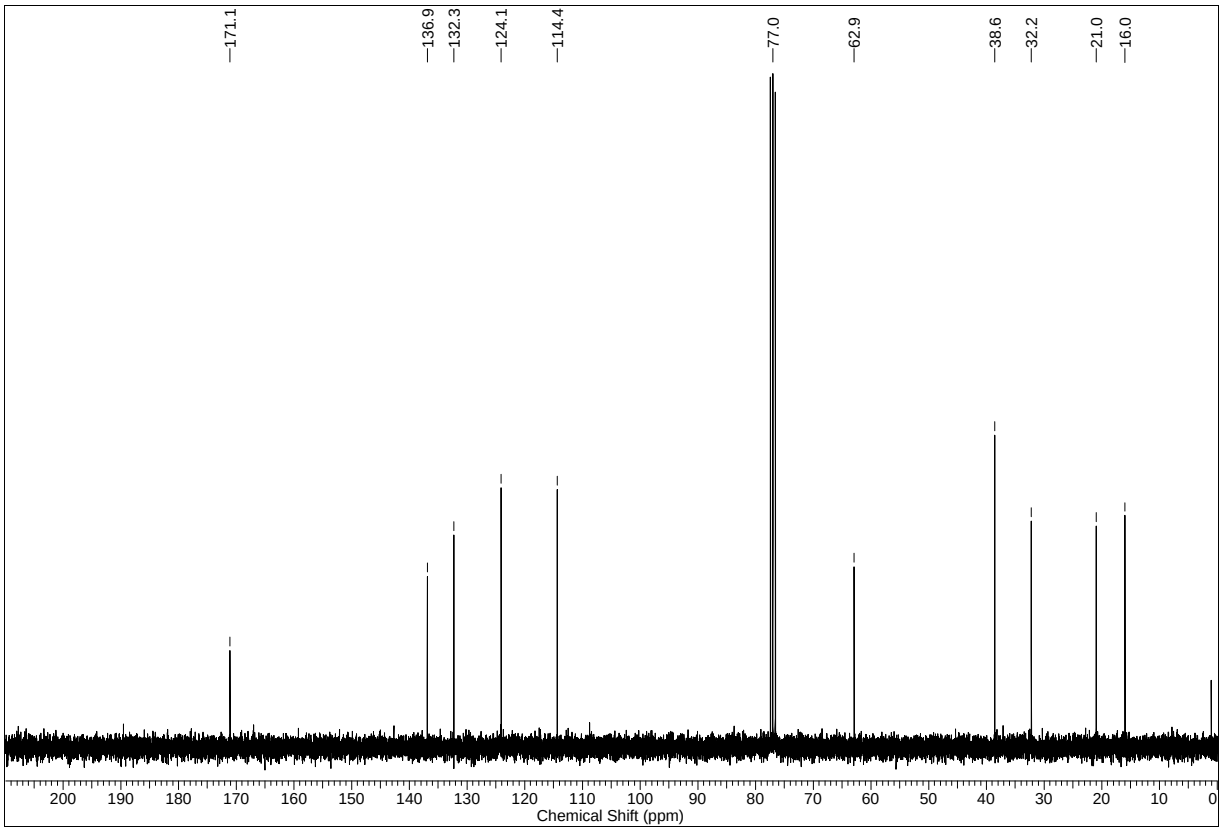

AcO
0.98
1.98
2.03
2.16
6.00
2.14
2.91
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

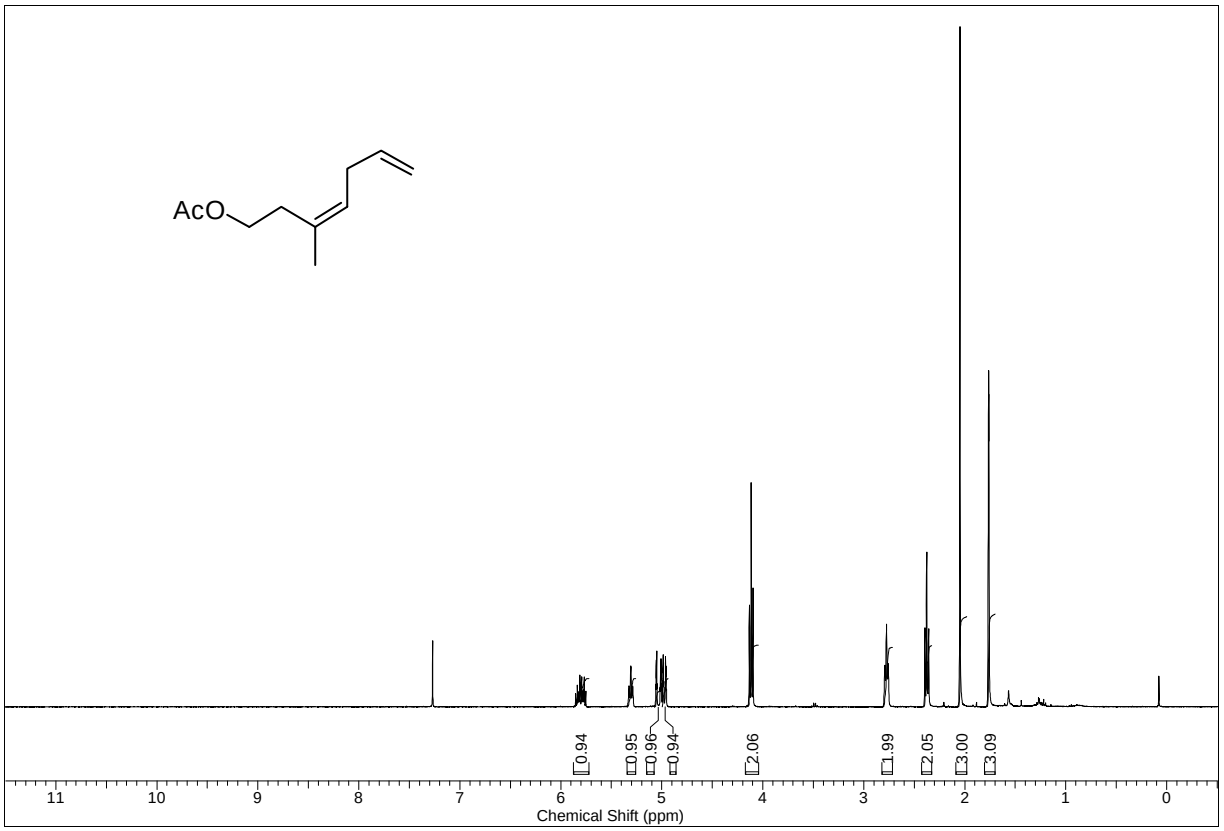

171.2
137.2
135.2
122.1
114.2
77.0
64.1
35.7
32.2
26.7
21.0
15.8
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

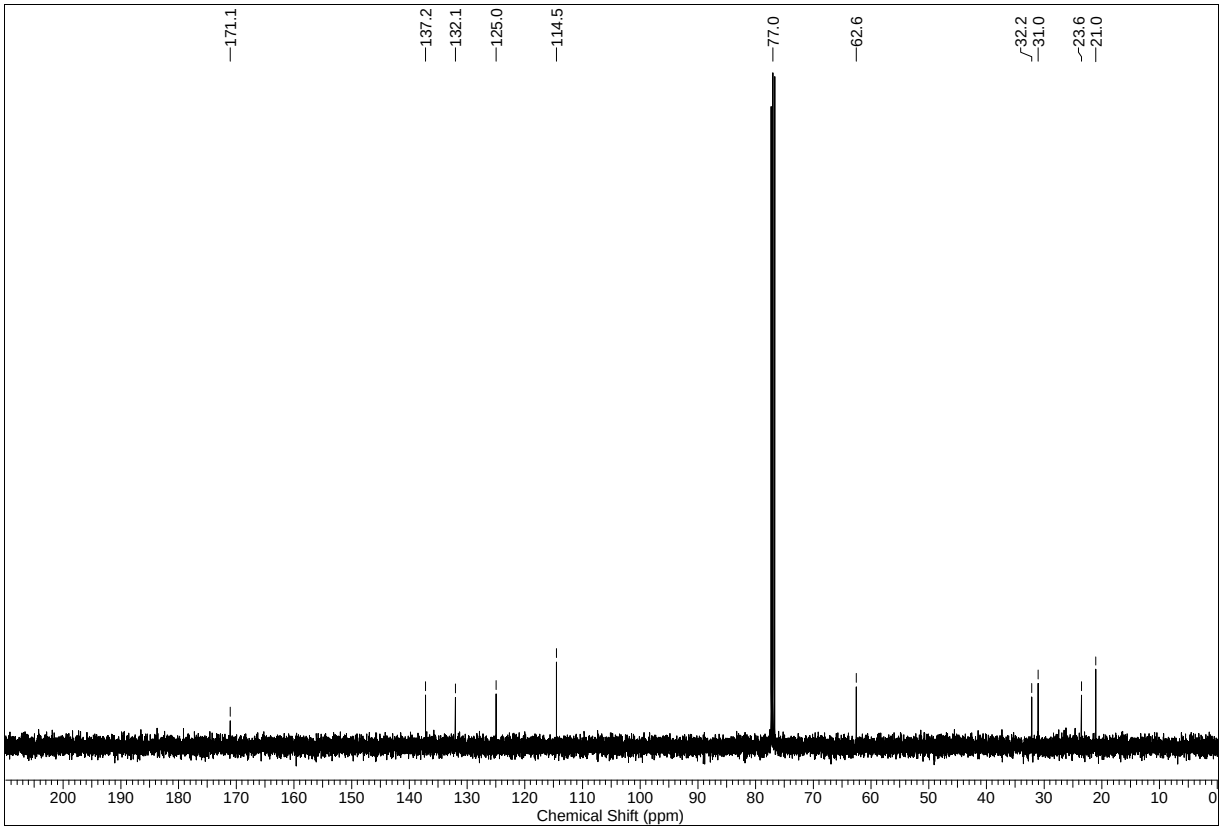

AcO
0.94
0.98
0.97
0.94
2.05
2.01
2.02
3.00
5.19
Chemical Shift (ppm)

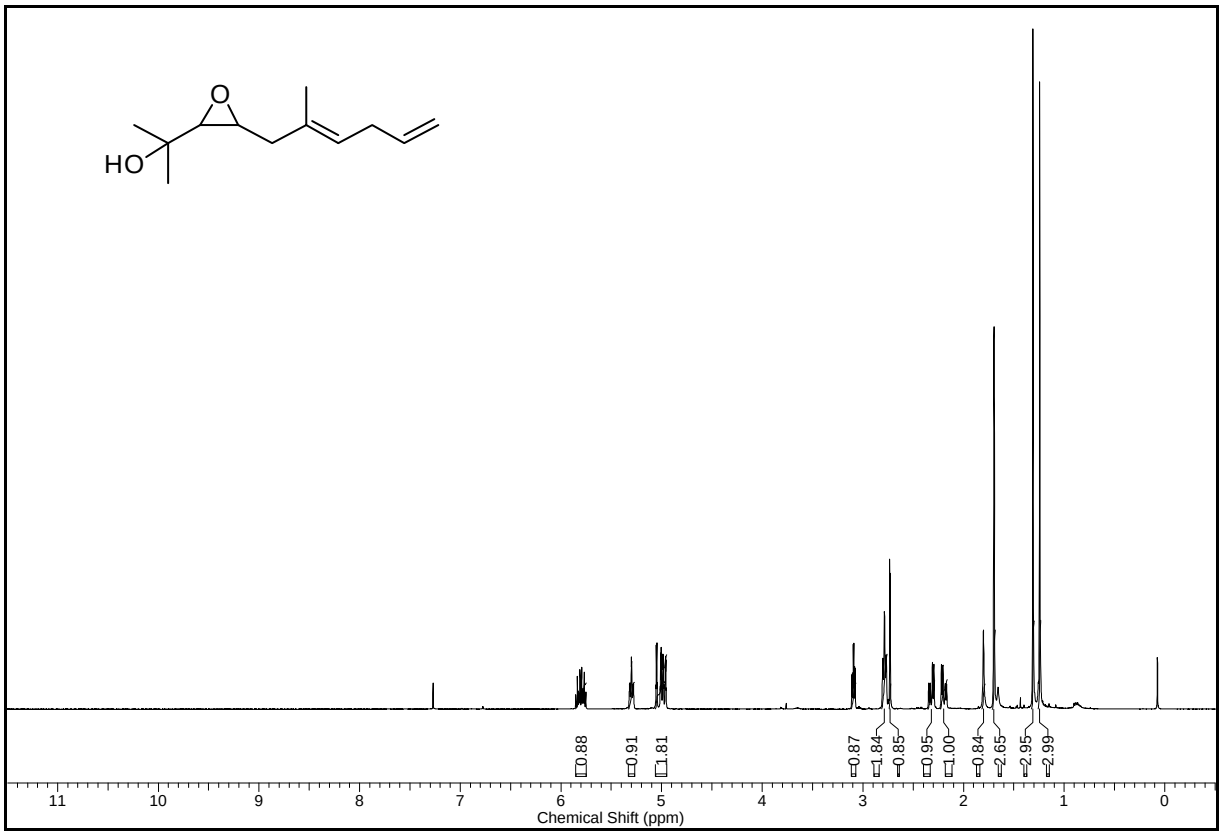

171.1
137.4
135.2
123.1
114.3
77.0
64.1
32.1
27.8
26.7
23.2
21.0
Chemical Shift (ppm)

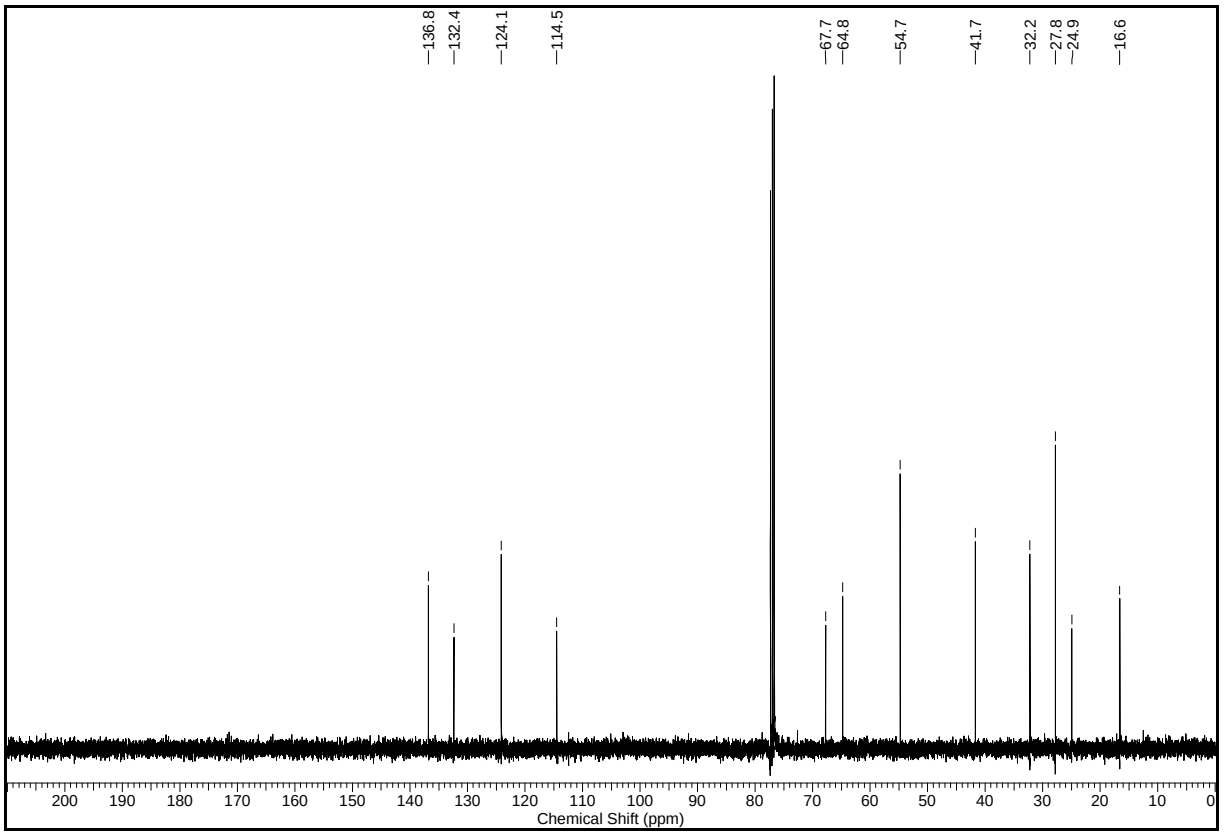

AcO
0.97
1.01
1.05
0.98
2.07
2.06
2.10
3.04
2.96
Chemical Shift (ppm)

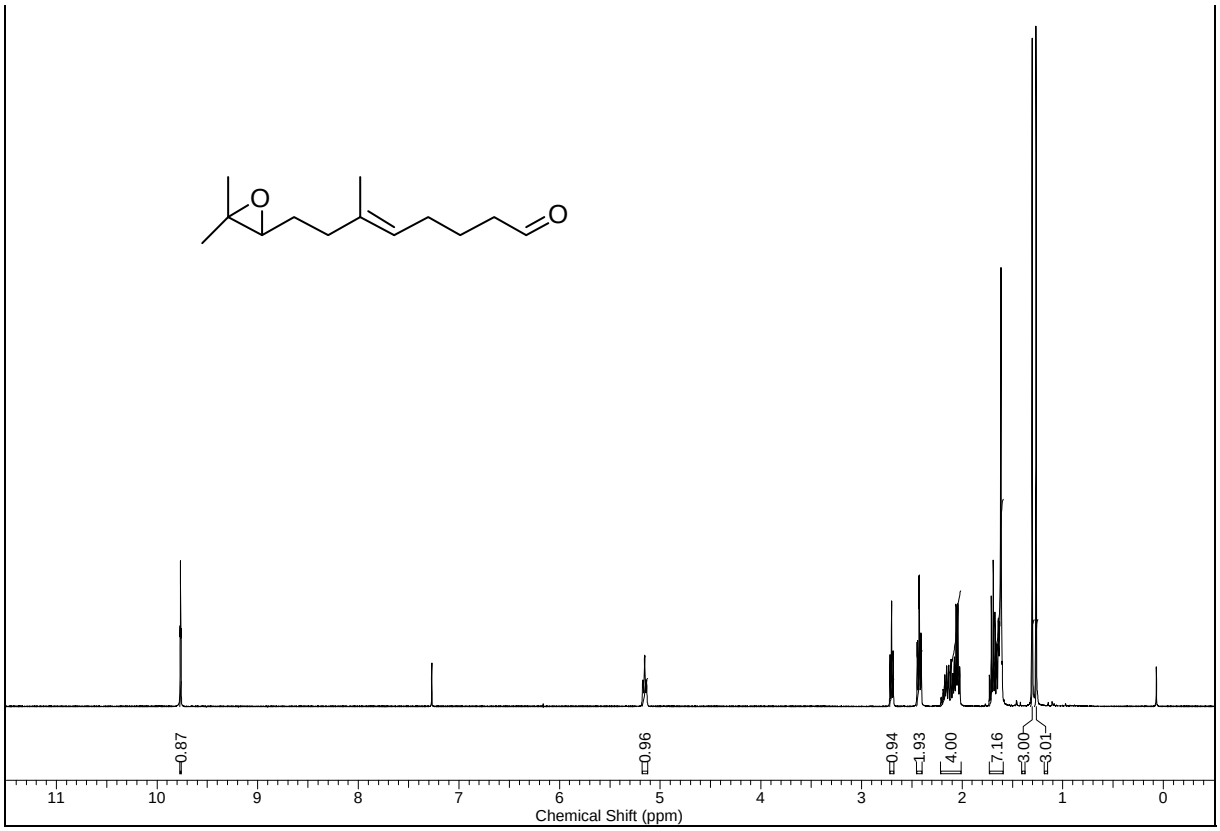

171.1
136.9
132.3
124.1
114.4
77.0
62.9
38.6
32.2
21.0
16.0
Chemical Shift (ppm)

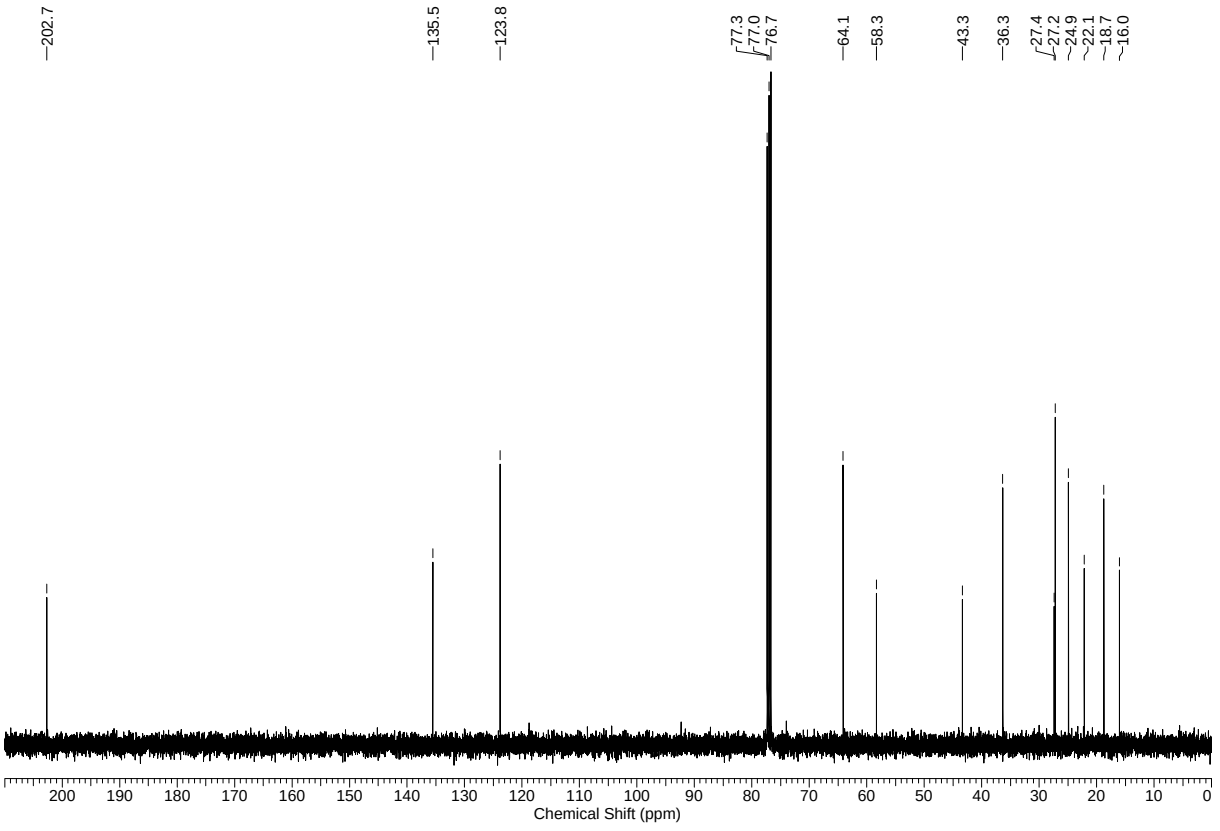

AcO
0.94
0.95
0.96
0.94
2.06
1.99
2.05
3.00
3.09
Chemical Shift (ppm)

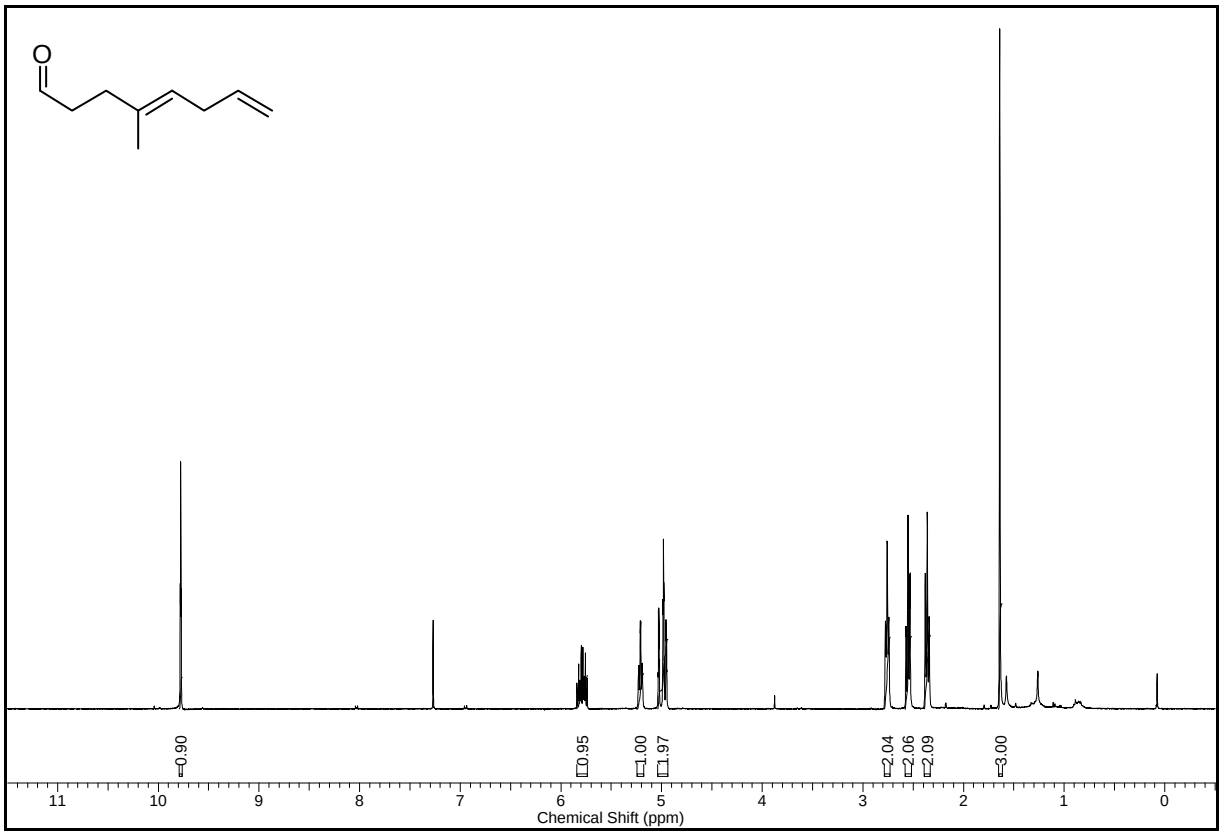

171.1
137.2
132.1
125.0
114.5
77.0
62.6
32.2
31.0
23.6
21.0
Chemical Shift (ppm)

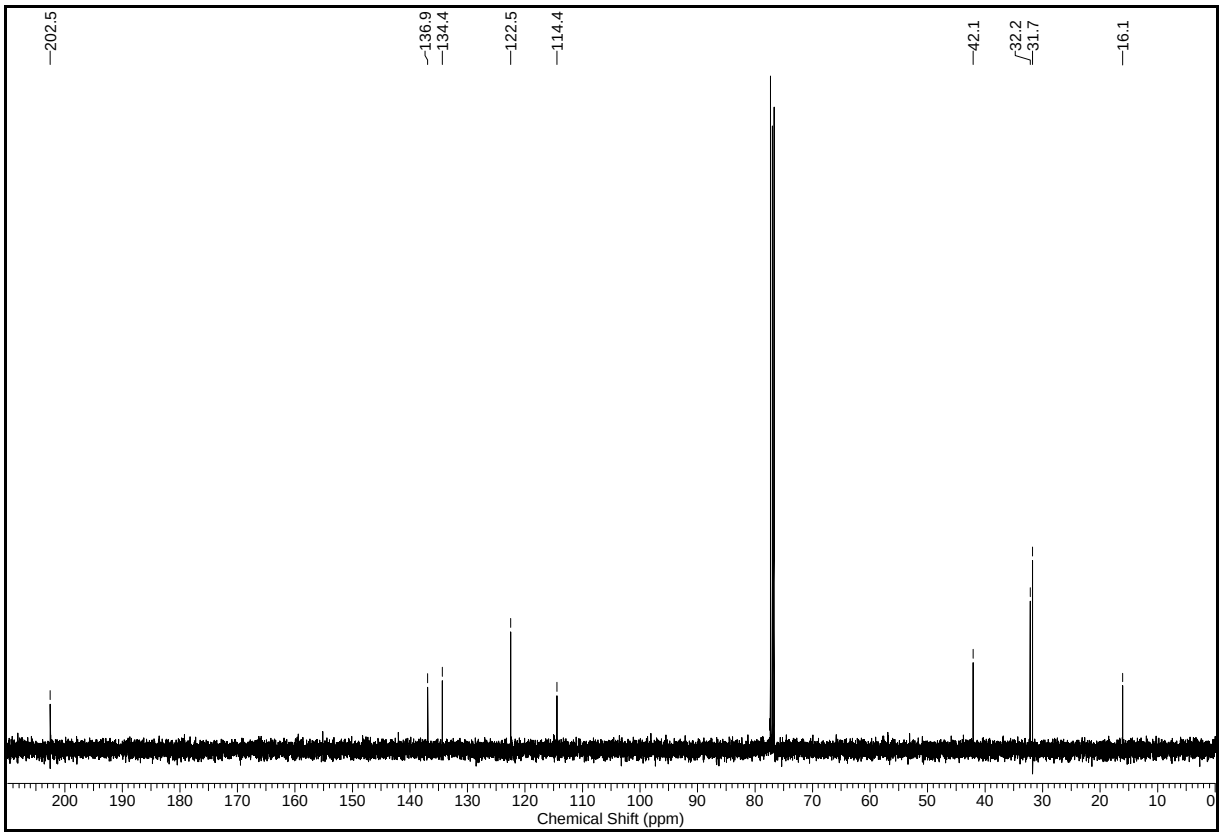

O
HO
0.88
0.91
1.81
0.87
1.84
0.85
0.95
1.00
0.84
2.65
2.95
2.99
11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

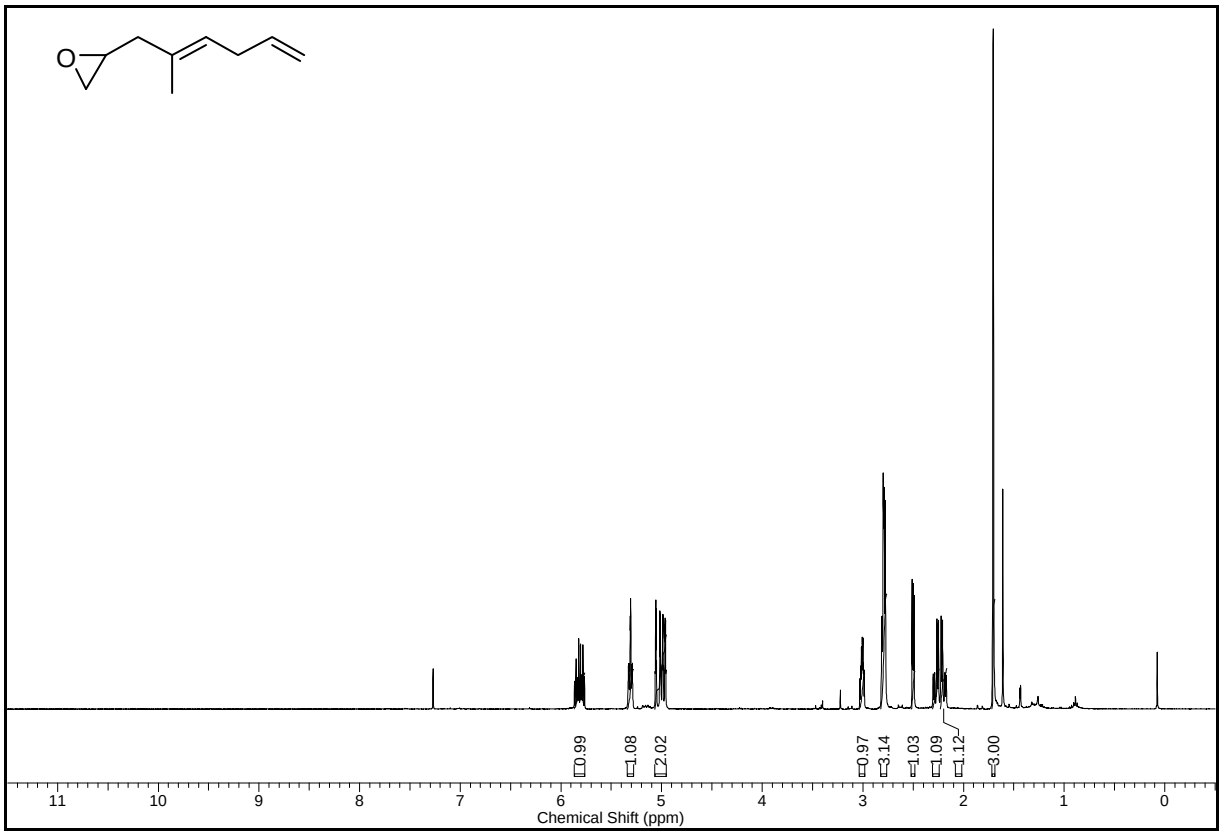

136.8
132.4
124.1
114.5
67.7
64.8
54.7
41.7
32.2
27.8
24.9
16.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

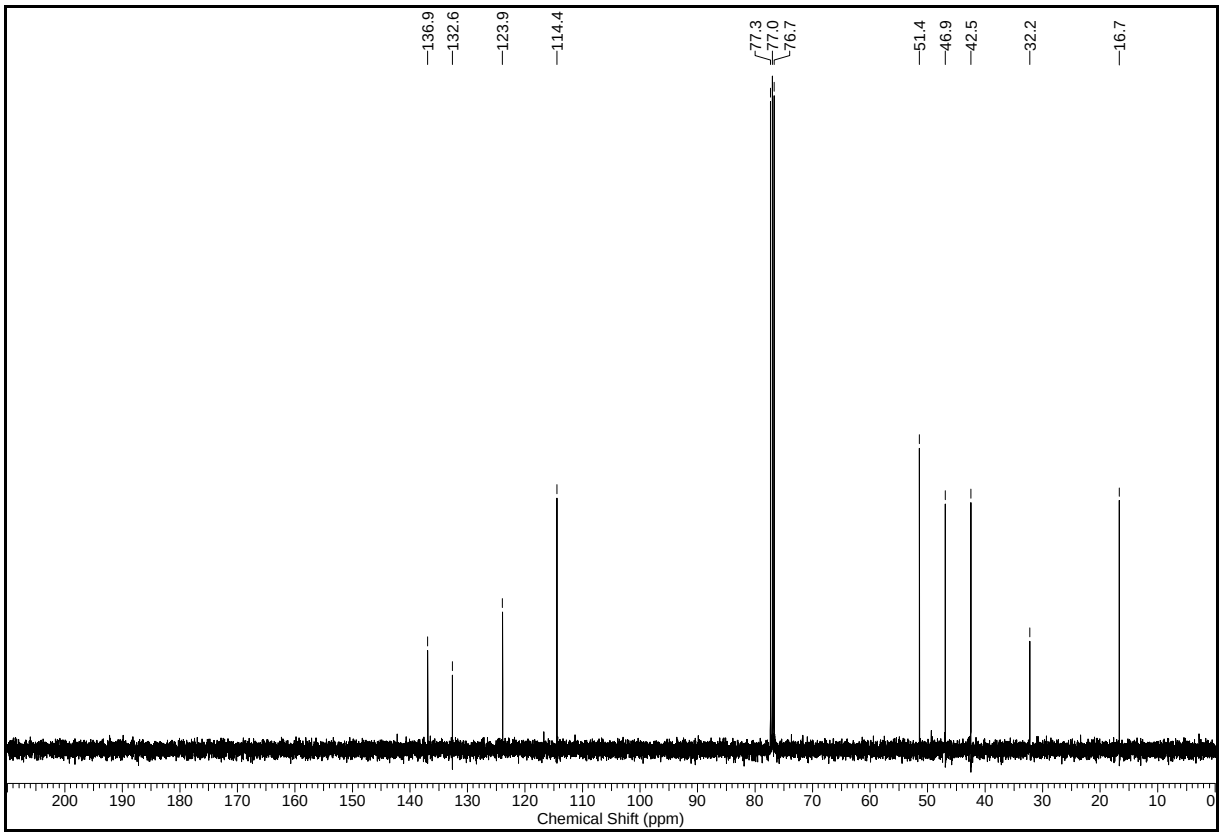

O
O
0.87
0.96
0.94
1.93
4.00
7.16
3.00
3.01
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

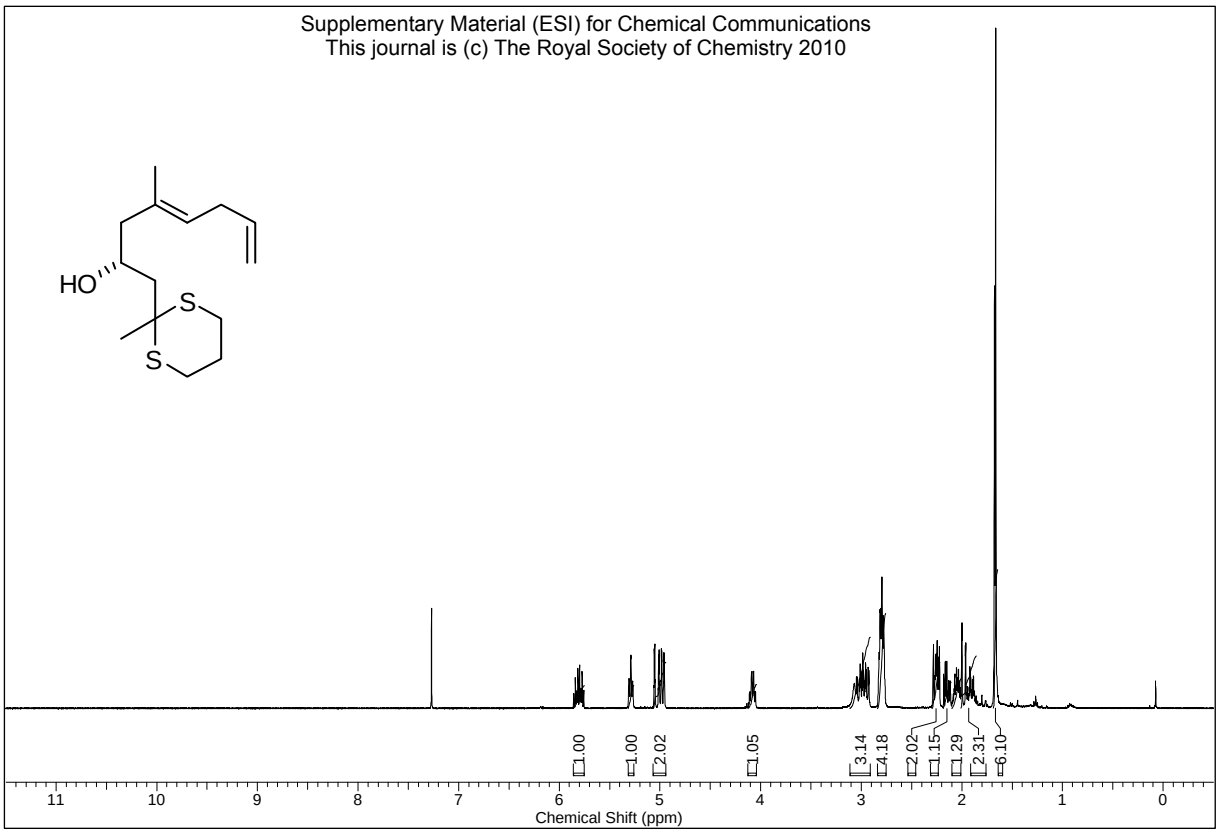

202.7
135.5
123.8
77.3
77.0
76.7
64.1
58.3
43.3
36.3
27.4
27.2
24.9
22.1
18.7
16.0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

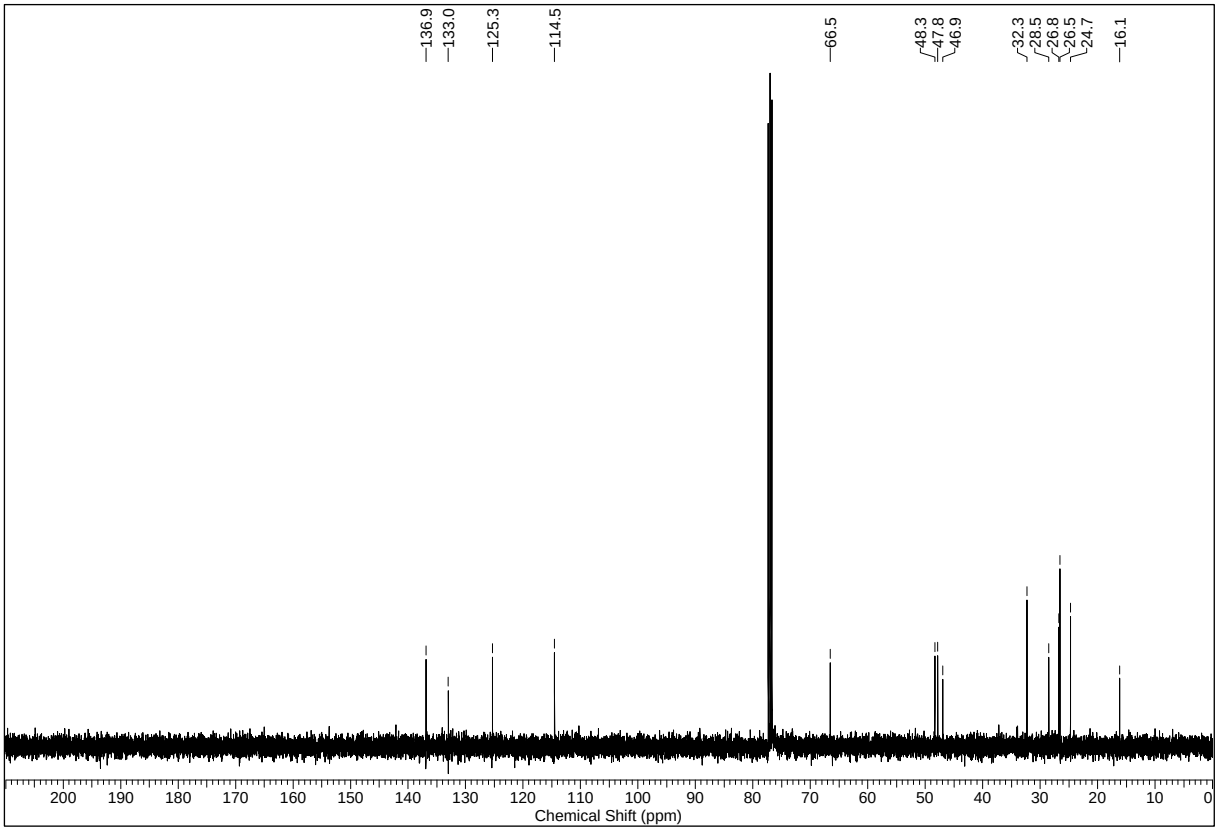

O
0.90
0.95
1.00
1.97
2.04
2.06
2.09
3.00
11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

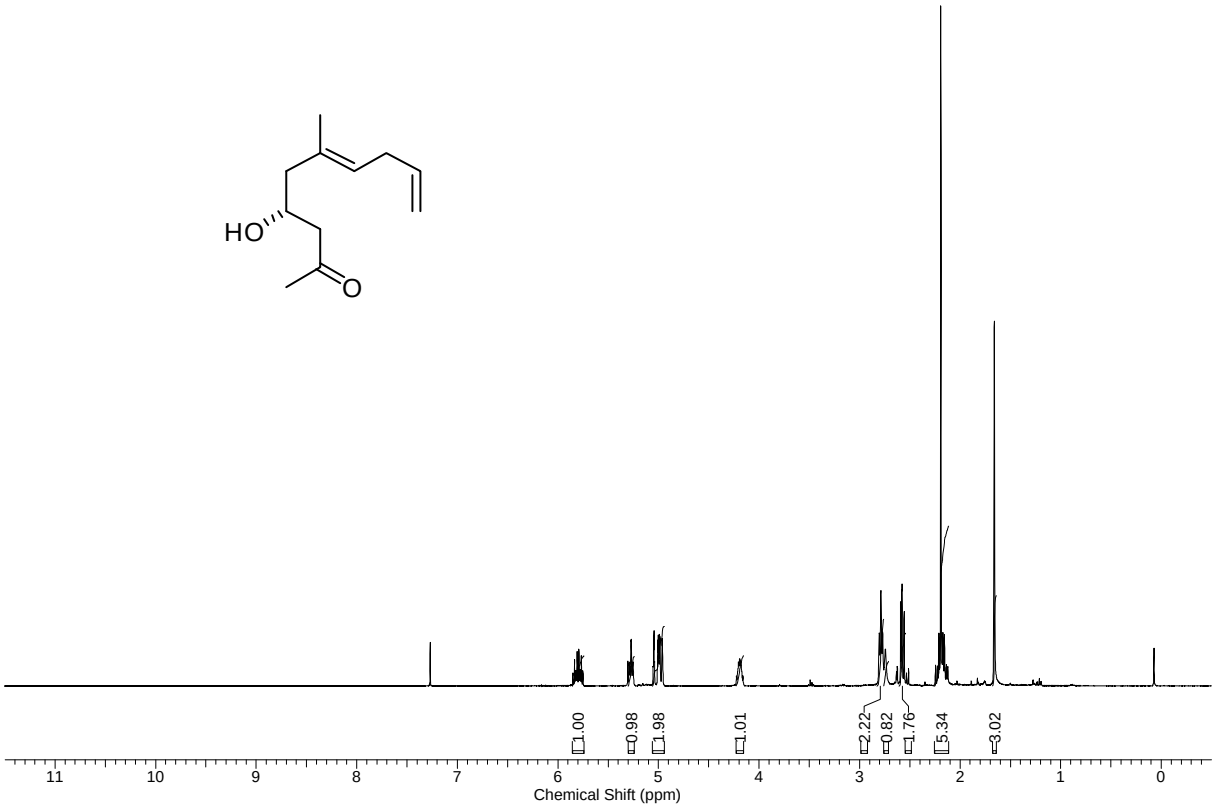

202.5
136.9
134.4
122.5
114.4
42.1
32.2
31.7
16.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

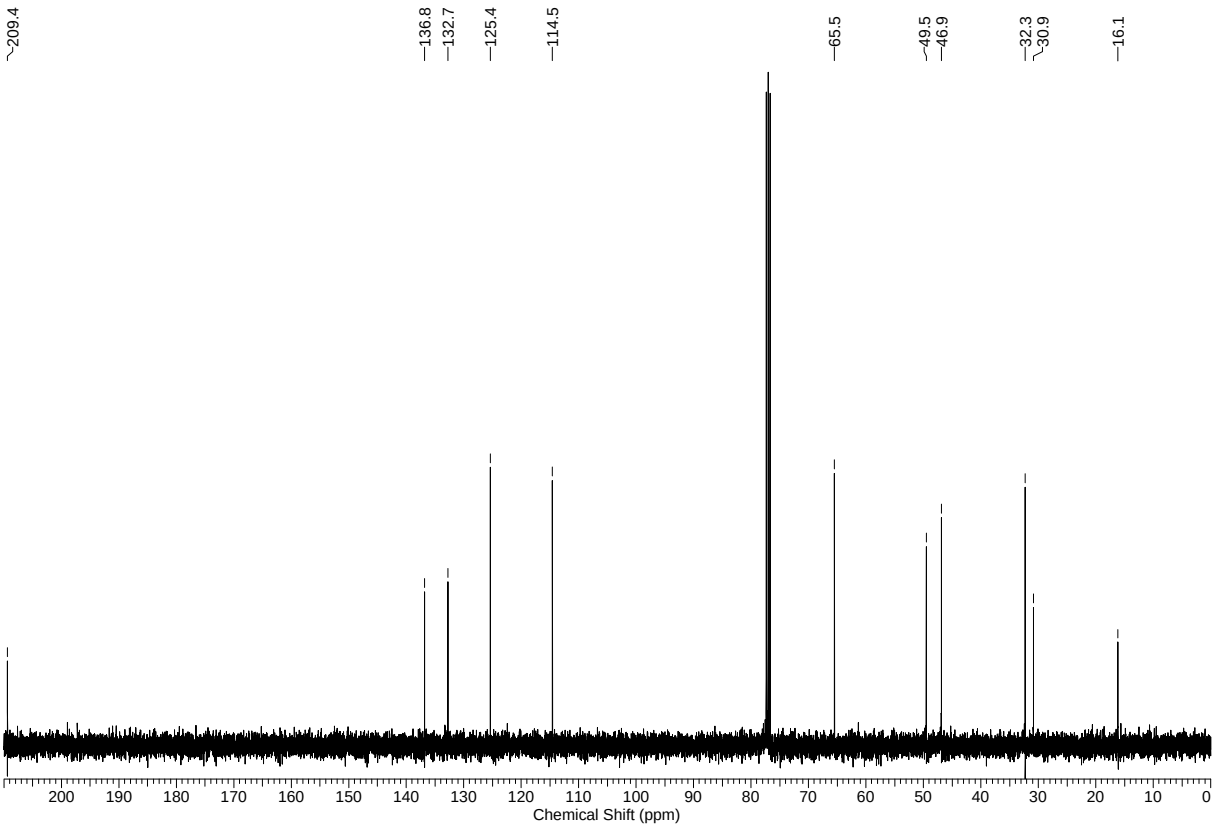

O
0.99
1.08
2.02
0.97
3.14
1.03
1.09
1.12
3.00
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

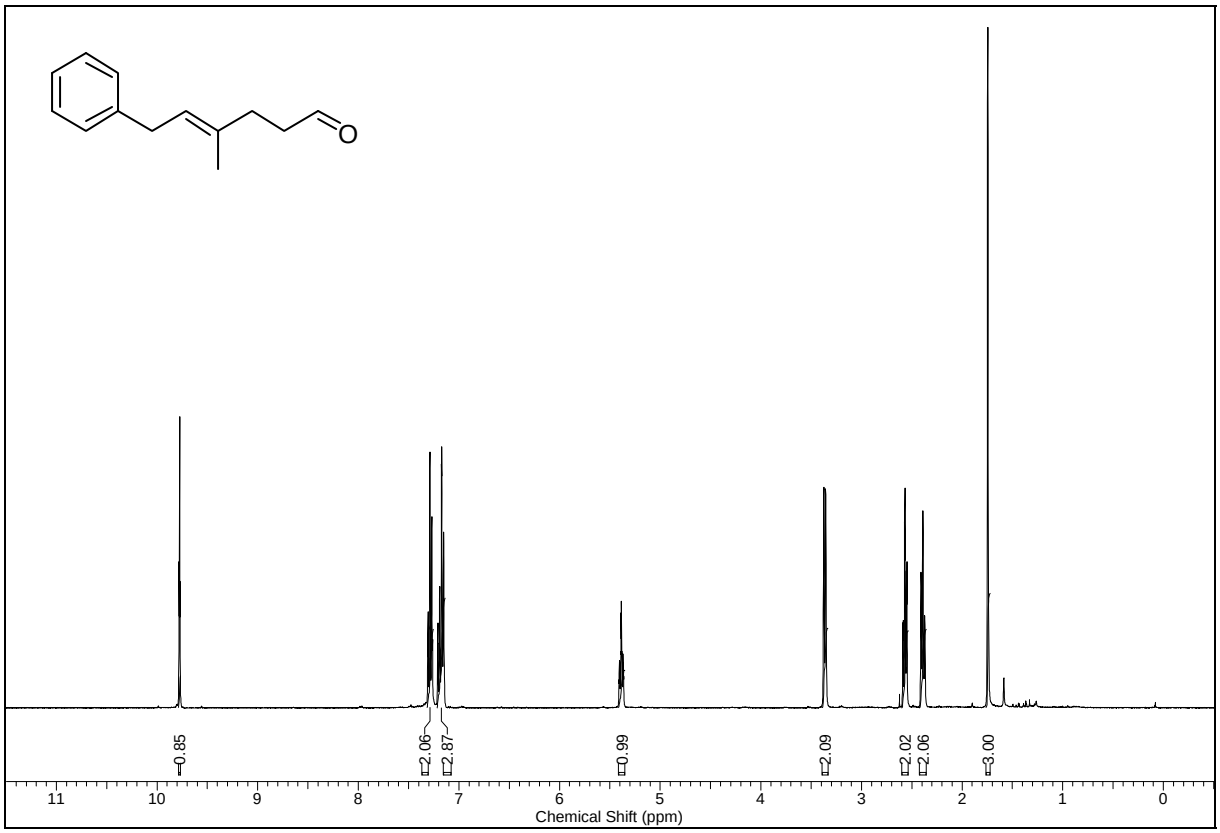

136.9
132.6
123.9
114.4
77.3
77.0
76.7
51.4
46.9
42.5
32.2
16.7
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

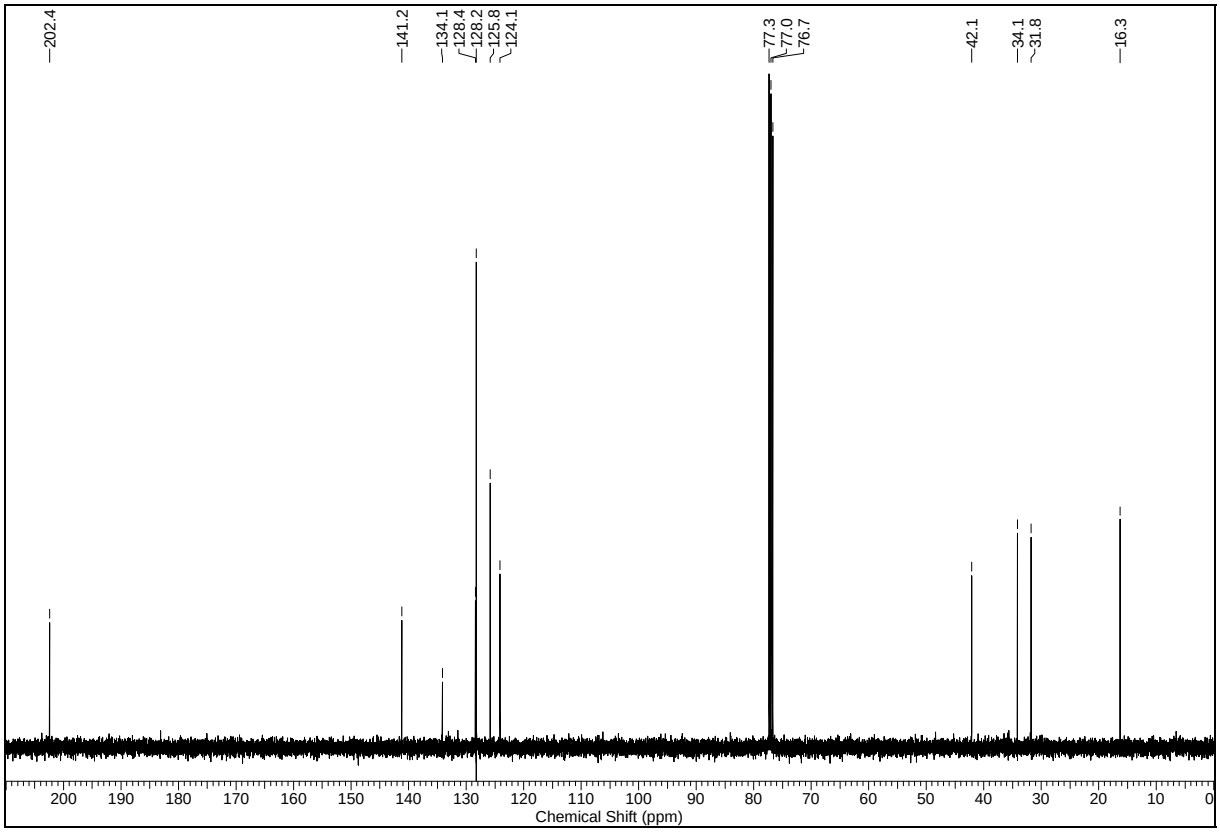

HO
S
S
1.00
1.00
2.02
1.05
3.14
4.18
2.02
1.15
1.29
2.31
6.10
Chemical Shift (ppm)

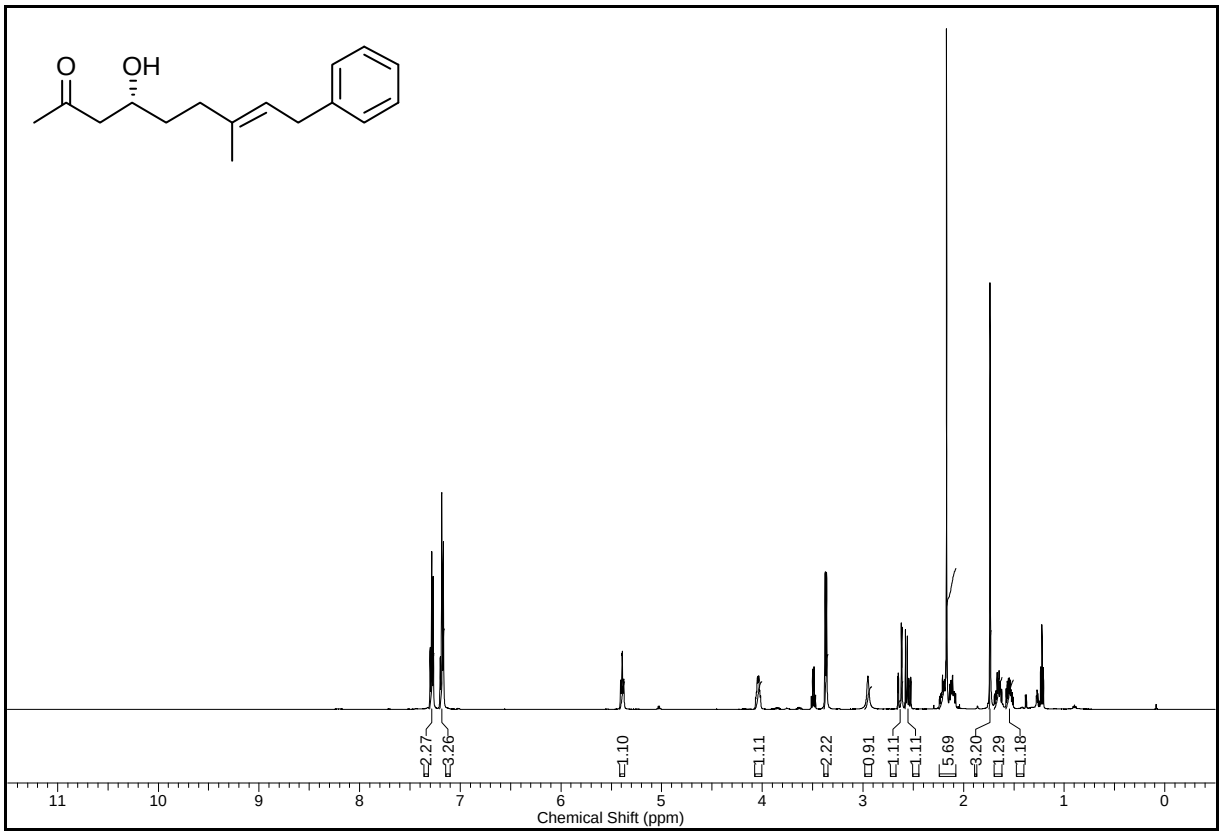

136.9
133.0
125.3
114.5
66.5
48.3
47.8
46.9
32.3
28.5
26.8
26.5
24.7
16.1
Chemical Shift (ppm)

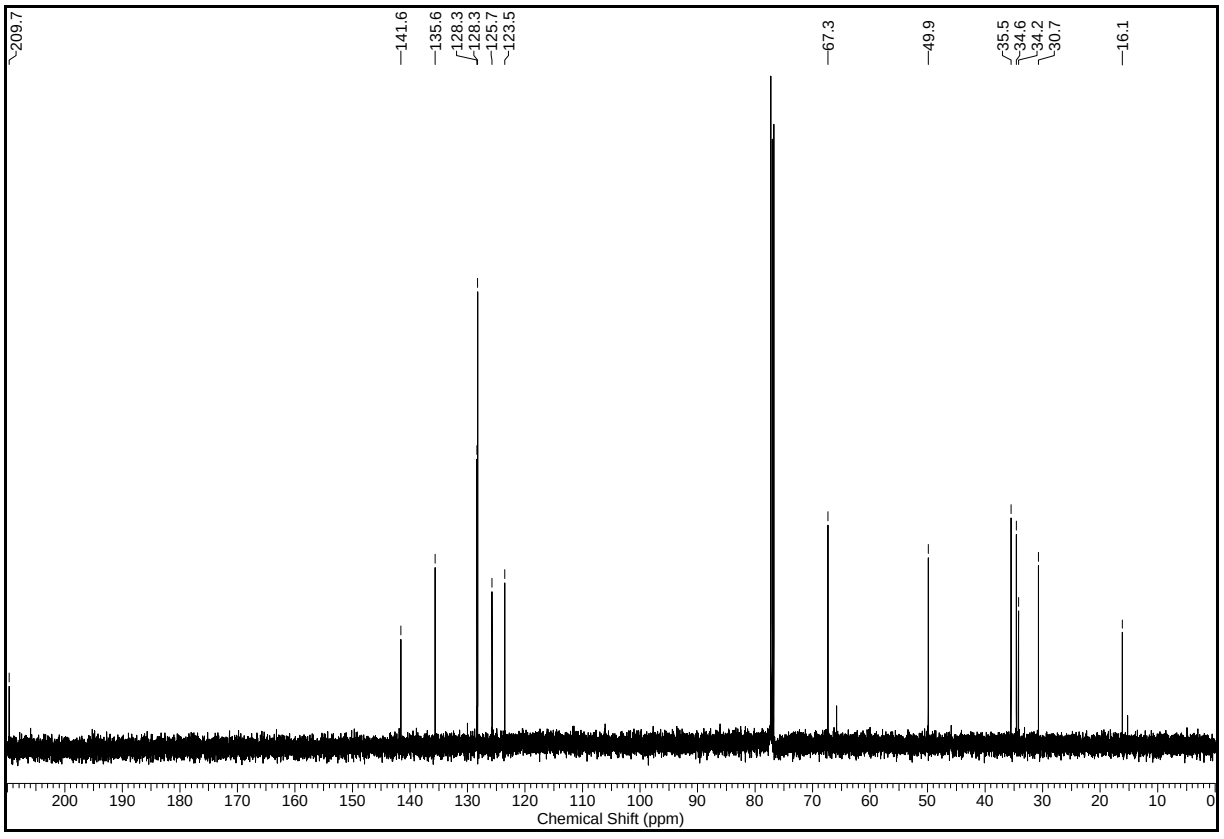

HO
O
1.00
0.98
1.98
1.01
2.22
0.82
1.76
5.34
3.02
Chemical Shift (ppm)

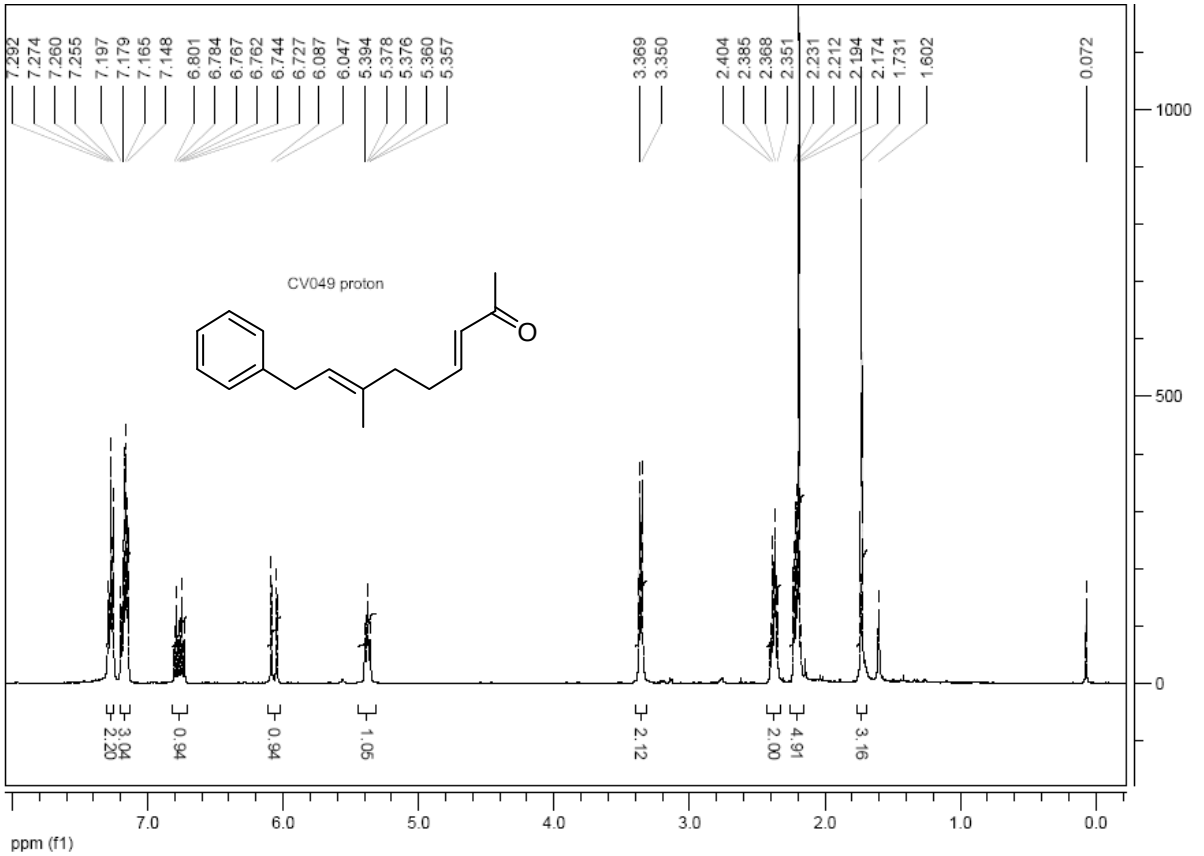

209.4
136.8
132.7
125.4
114.5
65.5
49.5
46.9
32.3
30.9
16.1
Chemical Shift (ppm)

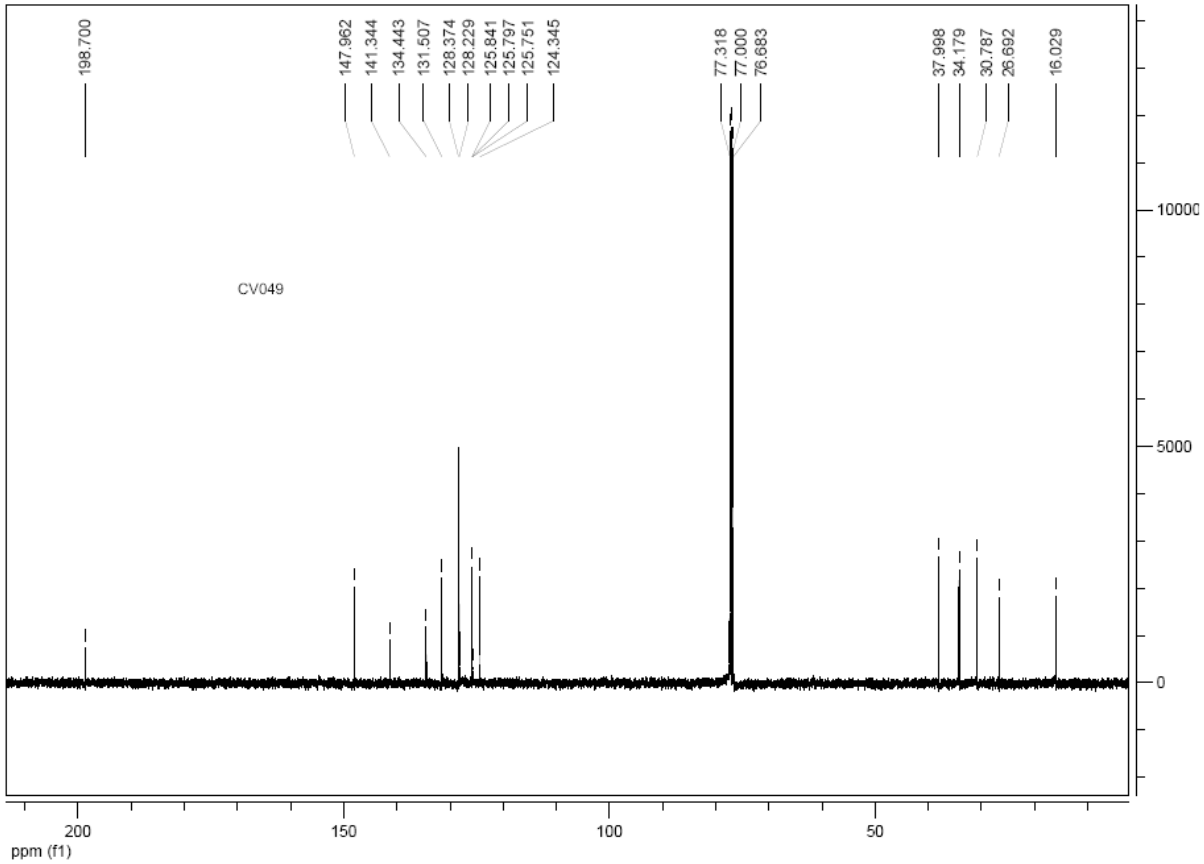

O
0.85
2.06
2.87
0.99
2.09
2.02
2.06
3.00
11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)


202.4
141.2
134.1
128.4
128.2
125.8
124.1
77.3
77.0
76.7
42.1
34.1
31.8
16.3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


O
OH
2.27
3.26
1.10
1.11
2.22
0.91
1.11
1.11
5.69
3.20
1.29
1.18
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


209.7
141.6
135.6
128.3
128.3
125.7
123.5
67.3
49.9
35.5
34.6
34.2
30.7
16.1
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)


7.292
7.274
7.260
7.255
7.197
7.179
7.165
7.148
6.801
6.784
6.767
6.762
6.744
6.727
6.087
6.047
5.394
5.378
5.376
5.360
5.357
3.369
3.350
2.404
2.385
2.368
2.351
2.231
2.212
2.194
2.174
1.731
1.602
0.072
CV049 proton
O
2.20
2.04
0.94
0.94
1.05
2.12
2.00
4.61
3.16
1000
500
0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


198.700
147.962
141.344
134.443
131.507
128.374
128.229
125.841
125.797
125.751
124.345
77.318
77.000
76.683
37.998
34.179
30.787
26.692
16.029
CV049
10000
5000
0
200
150
100
50
ppm (f1)