Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Ambruticins: Tetrahydropyran Ring Formation and Total Synthesis

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1. General Experimental

All reactions were carried out using standard Schlenk syringe-septa techniques in flame dried glassware under a positive pressure of nitrogen in anhydrous solvents unless otherwise stated. Reagents were purchased from commercial suppliers and used without further purification unless reported. Anhydrous THF, Et_2O, hexane, DCM, toluene and MeCN were dried by passing through a modified Grubbs system of alumina columns and stored under nitrogen and over 3Å molecular sieves. MeOH was dried by distillation from calcium hydride and stored under nitrogen and over 3Å molecular sieves. Degassed solvents were prepared by freeze-pump-thaw cycling under nitrogen or by sparging with nitrogen.

Analytical thin layer chromatography (TLC) was carried out on Merck silica gel 60 F_{254} analytical plates and were developed using UV fluorescence (254 nm) or $KMnO_4$ / Δ. Flash column chromatography was carried out on Sigma Aldrich silica gel 60 Å (43-63 µm) and an organic solvent system as stated.

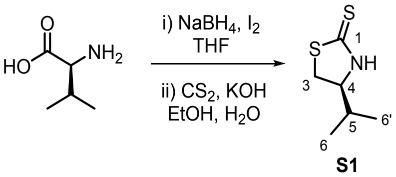
Infrared spectra were recorded on a Perkin-Elmer FT-IR spectrometer spectrum 2 with selected peaks of interested reported as absorption maxima (cm^{-1}). Mass spectrometry (MS) and High-resolution mass spectrometry (HRMS) were performed using electrospray ionisation (ESI) on a Bruker microOTOF II (TOF) or atmospheric pressure chemical ionisation (APCI) on a Thermo Scientific Orbitrap Elite (LC-Orbitrap). Optical rotation was measured on a Bellingham and Stanley Ltd. ADP220 polarimeter and is quoted in (° ml)(g dm)$^{-1}$. Melting points of solid products were recorded on a Stuart MP20.

NMR spectra were recorded on Varian 400-MR (400 MHz), JeolECZ400 (400 MHz), BrukerNano400 (400 MHz) and Bruker Advance III HD 500 Cryo (500 MHz) spectrometers at ambient temperature. Spectra were recorded in deuterochloroform referenced to residual $CHCl_3$ (^1H, 7.26 ppm; ^{13}C, 77.2 ppm), deuterated methanol referenced to residual MeOH (^1H, 3.30 ppm; ^{13}C, 49.0 ppm) or deuterated acetone referenced to residual acetone (^1H, 2.09 ppm; ^{13}C, 30.6 ppm). Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (*J*) are reported in Hertz (Hz). The following abbreviations are used to describe multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), br. (broad), ap. (apparent). COSY, HMBC, and HSQC NMR spectra were routinely used to definitively assign the signals of ^1H and ^{13}C NMR spectra.

2. Total Synthesis of Ambruticin J

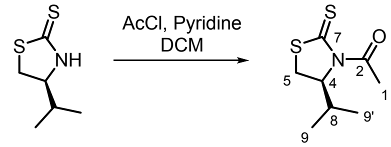
2.1. Synthesis of Vinyl Iodide 13

(*S*)-4-Isopropylthiazolidine-2-thioneacid (S1)



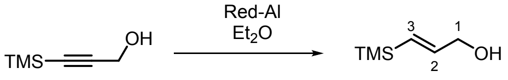
L-Valine (8.03 g, 68.3 mmol) was dissolved in THF (180 mL) under nitrogen and cooled to 0 °C when $NaBH_4$ (6.20 g, 163.9 mmol) was added in one portion. After stirring for 5 minutes, iodine (17.30 g, 68.3 mmol) in THF (20 mL) was added dropwise over 20 minutes. The reaction mixture was warmed slowly to room temperature and then refluxed for 24 hours. The reaction mixture was cooled to room temperature and methanol was added until the solution became clear and the solvent was removed *in vacuo*. The crude material was dissolved in 1 M KOH solution (200 mL) and stirred for 4 hours when the solution was extracted with EtOAc (3 × 200 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and the solvent removed *in vacuo* to afford L-valinol (5.31 g, 75%) as a colourless oil. The crude product was dissolved in ethanol (17 mL) and CS_2 (7.85 mL) was added. KOH (7.64 g, 136.1 mmol) in water/MeOH, 1:1 (50 mL) was added by an addition funnel over 20 minutes. The reaction mixture was refluxed for 3 days before being cooled to room temperature and the solvent removed *in vacuo*. The solution was dissolved in 2 M HCl (30 mL) and extracted with DCM (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo* to afford **S1** (6.50 g, 80%) as a yellow solid; $[\alpha]_D^{23}$ = -41.0 (*c* 1, $CHCl_3$), lit.[1] $[\alpha]_D^{20}$ = -35.9 (*c* 1, $CHCl_3$); ν_{max} (UATR) 3176, 2960, 2869, 1661, 1482, 1268, 1029, 977; δ_H (400 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.8, 6-H_3), 1.03 (3H, d, *J* 6.8, 6′-H_3), 1.92 – 2.02 (1H, m, 5-H), 3.31 (1H, dd, *J* 11.1, 8.4, 3-*H*H), 3.50 (1H, dd, *J* 11.1, 8.2, 3-H*H*), 4.01 – 4.08 (1H, m, 4-H), 8.22 (1H, s, NH); δ_C (101 MHz, $CDCl_3$) 18.4 (C-6), 19.0 (C-6′), 32.2 (C-5), 36.2 (C-3), 70.2 (C-4), 201.3 (C-1); m/z (ESI): $[M+H]^+$ = 175.1. Data consistent with the literature.[1]

(*S*)-1-(4-Isopropyl-2-thioxothiazolidin-3-yl)ethan-1-one (15)



Auxiliary **S1** (1.40 g, 8.70 mmol) was dissolved in DCM (35 mL) under an atmosphere of nitrogen then AcCl (0.92 mL, 13.0 mmol) was added. Pyridine (1.05 mL, 13.0 mmol) was added dropwise and the reaction mixture was stirred for 2 hours. The reaction mixture was filtered, and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (10% EtOAc in petroleum ether 60:40) to afford acylated auxiliary **15** (1.77 g, quant.) as a yellow oil; $[\alpha]^{23}_{D}$ = +412.0 (*c* 1, $CHCl_3$), lit.[1] $[\alpha]^{20}_{D}$ = +442.1 (*c* 1, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 0.97 (3H, d, *J* 6.9, 9-H_3), 1.05 (3H, d, *J* 6.8, 9′-H_3), 2.29 – 2.43 (1H, m, 8-H), 2.76 (3H, s, 1-H_3), 3.02 (1H, dd, *J* 11.5, 1.1, 5-*H*H), 3.50 (1H, dd, *J* 11.5, 8.0, 5-H*H*), 5.11 – 5.17 (1H, m, 4-H); δ_C (101 MHz, $CDCl_3$) 17.9 (C-9), 19.2 (C-9′), 27.1 (C-1), 30.6 (C-8), 30.9 (C-5), 71.4 (C-4), 170.9 (C-2), 203.4 (C-7); m/z (ESI): $[M+H]^+$ = 204.05. Data consistent with the literature.[1]

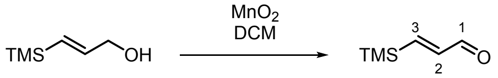
(*E*)-3-(Trimethylsilyl)prop-2-en-1-ol (S3)



S2 **S3**

A 70% solution of Red-Al in toluene (3.48 mL, 14.04 mmol) was dissolved in Et_2O (40 mL) under nitrogen and cooled to 0 °C then propargylic alcohol **S2** (1.01 g, 7.80 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 1 hour then quenched with 1 M H_2SO_4 (20 mL). The layers were separated and the organic layer washed with water (2 × 20 mL) and brine (20 mL). The combined aqueous phases were extracted with Et_2O (2 × 60 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (40% Et_2O in pentane) to afford the volatile allylic alcohol **S3** (0.84 g, 82%) as a colourless oil; ν_{max} (film) 3314, 2955, 2899, 1622, 1247, 861, 832; δ_H (400 MHz, $CDCl_3$) 0.07 (9H, s, $Si(CH_3)_3$), 1.52 (1H, t, *J* 6.0, OH), 4.18 (2H, ddd, *J* 6.0, 4.4, 1.8, 1-H_2), 5.92 (1H, dt, *J* 18.8, 1.8, 3-H), 6.18 (1H, dt, *J* 18.8, 4.4, 2-H); δ_C (101 MHz, $CDCl_3$) -1.2 ($Si(CH_3)_3$), 65.7 (C-1), 129.7 (C-3), 145.0 (C-2). Data consistent with the literature.[2]

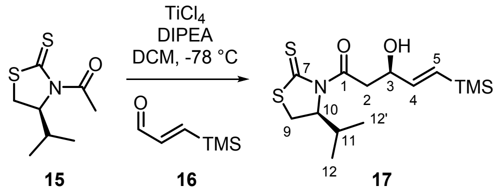
(*E*)-3-(Trimethylsilyl)acrylaldehyde (16)



S3 **16**

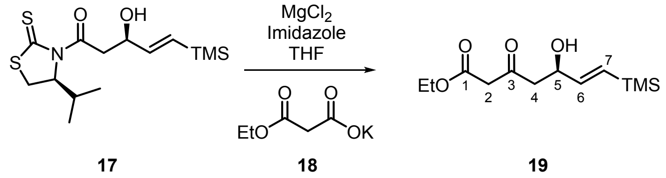
Alcohol **S3** (0.98 g, 7.52 mmol) was dissolved in DCM (38 mL) under nitrogen when activated MnO_2 (13.02 g, 150.01 mmol) was added. The reaction mixture was stirred for 1 hour, filtered over Celite, washed with DCM (100 mL) and the solvent removed *in vacuo* to afford the volatile aldehyde **16** (0.97 g, quant.) as a colourless oil; ν_{max} (film) 2957, 2799, 1692, 1250, 837; δ_H (400 MHz, $CDCl_3$) 0.17 (9H, s, $Si(CH_3)_3$), 6.50 (1H, dd, *J* 18.7, 7.6, 2-H), 7.18 (1H, d, *J* 18.7, 3-H), 9.49 (1H, d, *J* 7.6, 1-H); δ_C (101 MHz, $CDCl_3$) -1.8 ($Si(CH_3)_3$), 144.3 (C-2), 159.0 (C-3), 195.0 (C-1); m/z (APCI): $[M+H]^+$ = 129.10. Data consistent with the literature.[2]

(*R*,*E*)-3-Hydroxy-1-((*S*)-4-isopropyl-2-thioxothiazolidin-3-yl)-5-(trimethylsilyl)pent-4-en-1-one (17)



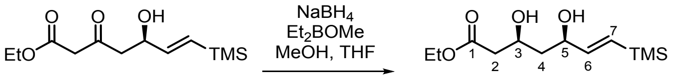
Acylated auxiliary **15** (1.45 g, 7.14 mmol) was dissolved in DCM (70 mL) under nitrogen and cooled to -78 °C when $TiCl_4$ (1 M in DCM, 7.14 mL, 7.14 mmol) was added dropwise over 15 minutes. The reaction mixture was stirred for 20 minutes when DIPEA (1.49 mL, 8.57 mmol) was added dropwise. The reaction mixture was stirred for 1 hour when aldehyde **16** (0.92 g, 7.14 mmol) in DCM (5 mL) was added dropwise. After stirring at -78 °C for 1 hour, aqueous saturated ammonium chloride (25 mL) was added and the reaction mixture was stirred for a further hour at room temperature. The solution was washed with DCM (3 × 50 mL), the combined organic layers dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (22% EtOAc in petroleum ether 60:40) to afford aldol product **17** (1.768 g, 75%) as a yellow oil; $[\alpha]_D^{22}$ = +308.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3436, 2958, 1688, 1246, 1156, 835; δ_H (400 MHz, $CDCl_3$) 0.07 (9H, s, $Si(CH_3)_3$), 0.98 (3H, d, *J* 6.9, 12-H_3), 1.07 (3H, d, *J* 6.8, 12′-H_3), 2.19 – 2.48 (1H, m, 11-H), 2.82 (1H, s, br. s, OH), 3.04 (1H, dd, *J* 11.5, 1.1, 9-*H*H), 3.29 (1H, dd, *J* 17.6, 9.0, 2-*H*H), 3.41 – 3.55 (1H, dd, *J* 11.5, 7.7, 9-H*H*), 3.55 – 3.73 (1H, dd, *J* 17.6, 8.0, 2-H*H*), 4.54 – 4.77 (1H, m, 3-H), 5.15 (1H, ddd, *J* 7.7, 6.3, 1.1, 10-H), 5.96 (1H, dd, *J* 18.8, 1.4, 5-H), 6.08 (1H, dd, *J* 18.8, 4.6, 4-H); δ_C (101 MHz, $CDCl_3$) -1.2 ($Si(CH_3)_3$), 18.0 (C-12), 19.3 (C-12′), 30.9 (C-9), 31.0 (C-11), 45.1 (C-2), 70.4 (C-3), 71.6 (C-10), 130.5 (C-5), 145.8 (C-4), 172.7 (C-1), 203.1 (C-7); HRMS (ESI) calc. for $[C_{14}H_{26}NO_2S_2Si]$ 332.1169 Found 332.1162.

Ethyl (*R*,*E*)-5-hydroxy-3-oxo-7-(trimethylsilyl)hept-6-enoate (19)



Potassium-3-ethoxy-2-methyl-3-oxopropanoate **18** (1243 mg, 7.30 mmol) and $MgCl_2$ (348 mg, 3.65 mmol) were added to a solution of aldol product **17** (1100 mg, 3.32 mmol) in THF (11 mL) under nitrogen and stirred for 45 minutes. Imidazole (248 mg, 3.65 mmol) was added and the reaction mixture was stirred for 72 hours. The mixture was diluted with EtOAc (50 mL) and washed with 1 M HCl (20 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with aqueous saturated sodium hydrogen carbonate (30 mL) and the aqueous layer extracted with EtOAc (2 × 30 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (5% Et_2O in DCM) to afford alcohol **19** (810 mg, 94%) as a yellow oil; $[\alpha]_D^{21}$ = +14.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3464, 2957, 1742, 1714, 1248, 1215, 750; δ_H (400 MHz, $CDCl_3$) 0.06 (9H, s, $Si(CH_3)_3$), 1.28 (3H, t, *J* 7.1, OCH_2CH_3), 2.68 – 2.77 (2H, m, OH and 4-*H*H), 2.80 (1H, dd, *J* 17.3, 4.0, 4-H*H*), 3.48 (2H, s, 2-H_2), 4.20 (2H, q, *J* 7.1, OCH_2CH_3), 4.59 (1H, ap. dtd, *J* 8.6, 4.0, 1.1, 5-H), 5.93 (1H, dd, *J* 18.7, 1.1, 7-H), 6.02 (1H, dd, *J* 18.7, 4.0, 6-H); δ_C (101 MHz, $CDCl_3$) -1.2 ($Si(CH_3)_3$), 14.3 (OCH_2CH_3), 49.4 (C-4), 50.2 (C-2), 61.7 (OCH_2CH_3), 70.0 (C-5), 130.5 (C-7), 145.8 (C-6), 167.1 (C-1), 203.1 (C-3); HRMS (ESI) calc. for [$C_{12}H_{22}O_4SiNa$] 281.1180 Found 281.1191.

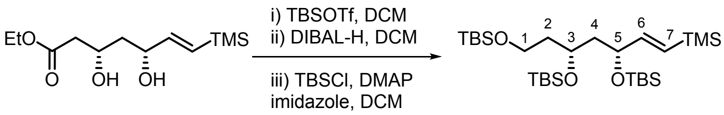
Ethyl (3*S*,5*R*,*E*)-3,5-dihydroxy-7-(trimethylsilyl)hept-6-enoate (20)



19 20

Ketone **19** (680 mg, 2.63 mmol) was dissolved in THF (18 mL) and MeOH (5 mL) under nitrogen and cooled to -78 °C when Et_2BOMe (0.42 mL, 3.16 mmol) was added dropwise and the reaction mixture was stirred for 15 minutes. $NaBH_4$ (114 mg, 3.02 mmol) was added in one portion and the reaction mixture was stirred for 3 hours when AcOH (4 mL) was added and the mixture was warmed to room temperature. The reaction mixture was diluted with EtOAc (25 mL) and the resulting solution was washed with aqueous saturated sodium hydrogen carbonate (20 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was dissolved in methanol (20 mL) and the solvent removed *in vacuo* to afford diol **20** (689 mg, quant.) as a yellow oil; $[\alpha]_D^{21}$ = +12.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3412, 2955, 1733, 1248, 866, 838; δ_H (400 MHz, $CDCl_3$) 0.06 (9H, s, $Si(CH_3)_3$), 1.28 (3H, t, *J* 7.1, OCH_2CH_3), 1.62 – 1.70 (2H, m, 4-H_2), 2.48 – 2.51 (2Hf, m, 2-H_2), 4.18 (2H, q, *J* 7.1, OCH_2CH_3), 4.26 – 4.33 (1H, m, 4-H), 4.35 – 4.41 (1H, m, 5-H), 5.90 (1H, dd, *J* 18.7, 0.9, 7-H), 6.03 (1H, dd, *J* 18.7, 5.0, 6-H); δ_C (101 MHz, $CDCl_3$) -1.2 ($Si(CH_3)_3$), 14.3 (OCH_2CH_3), 41.8 (C-2), 42.4 (C-4), 61.0 (OCH_2CH_3), 68.8 (C-3), 74.6 (C-5), 129.6 (C-7), 147.6 (C-6), 172.7 (C-1); HRMS (ESI) calc. for [$C_{12}H_{24}O_4SiNa$] 283.1336 Found 283.1334.

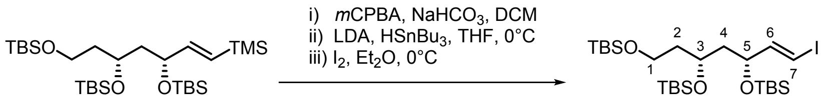
(3*R*,5*R*,*E*)-7-(Trimethylsilyl)hept-6-ene-1,3,5-(*tert*-butyldimethylsilyloxy)-triol (22)



20 22

Diol **20** (0.85 g, 3.26 mmol) was dissolved in DCM (33 mL) under nitrogen and cooled to 0 °C then TBSOTf (4.50 mL, 19.58 mmol) was added dropwise. The reaction mixture was stirred for 20 minutes and quenched with a solution of aqueous saturated sodium hydrogen carbonate (15 mL). The organic layer was separated and the aqueous extracted with DCM (2 × 20 mL). The combined organic layers were washed sequentially with 2 M HCl (20 mL) and brine (30 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was dissolved in DCM (33 mL) under nitrogen and cooled to -78 °C then 1 M DIBAL-H in hexane (7.17 mL, 7.17 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 hours. The reaction mixture was cooled to 0 °C, aqueous saturated potassium sodium tartrate solution (40 mL) was added and the mixture was stirred for 5 hours at room temperature. The layers were separated and the aqueous layer extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The material was dissolved in DCM (33 mL) and imidazole (424 mg, 6.52 mmol), TBSCl (0.98 g, 6.52 mmol) and a spatula tip of DMAP were added. The reaction mixture was stirred for 3 hours then water (20 mL) was added and the solution was acidified with 2 M HCl (15 mL). The organic layer was separated and the aqueous extracted with DCM (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (0-1% Et_2O in petroleum ether 60:40) to afford TBS alcohol **22** (1.34 g, 73%) as a colourless oil; $[\alpha]_D^{21}$ = +14.0 (*c* 1, $CHCl_3$); ν_{max} (film) 1955, 2930, 2887, 1472, 1250, 833; δ_H (400 MHz, $CDCl_3$) 0.00 – 0.06 (27H, m, $Si(CH_3)_3$ and 3 × $Si(CH_3)_2$), 0.86 – 0.90 (27H, m, 3 × $SiC(CH_3)_3$), 1.53 – 1.80 (4H, m, 2-H_2 and 4-H_2), 3.67 (2H, m, 1-H_2), 3.89 (1H, ap. tt, *J* 6.8, 5.1, 3-H), 4.17 (1H, ap. dtd, *J* 7.2, 6.0, 1.1, 5-H), 5.76 (1H, dd, *J* 18.6, 1.1, 7-H), 5.95 (1H, dd, *J* 18.6, 6.0, 1H); δ_C (101 MHz, $CDCl_3$) -5.1 ($Si(CH_3)$, -4.5 ($Si(CH_3)$, -4.2 ($Si(CH_3)$, -4.2 ($Si(CH_3)$, -3.9 ($Si(CH_3)$, -2.8 ($Si(CH_3)$, -1.2 ($Si(CH_3)$, 18.2 ($Si\mathit{C}(CH_3)_3$), 18.4 ($Si\mathit{C}(CH_3)_3$), 18.5 ($Si\mathit{C}(CH_3)_3$), 25.9 ($SiC(\mathit{C}H_3)_3$), 26.1 ($SiC(\mathit{C}H_3)_3$), 26.2 ($SiC(\mathit{C}H_3)_3$), 40.4 (C-2), 46.1 (C-4), 60.1 (C-1), 66.9 (C-3), 73.4 (C-5), 129.2 (C-7), 149.2 (C-6); HRMS (ESI) calc. for $[C_{28}H_{64}NaO_3Si_4]$ 583.3825 Found 583.3831.

(3*R*,5*R*,*E*)-7-Iodo-hept-6-ene-1,3,5-(*tert*-butyldimethylsilyloxy)-triol (13)



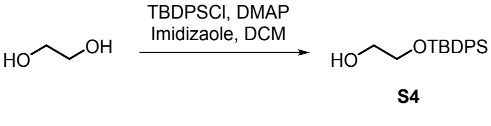
22 **13**

Vinyl silane **22** (542 mg, 0.97 mmol) was dissolved in DCM (10 mL) under nitrogen and cooled to 0 °C when $NaHCO_3$ (180 mg, 2.13 mmol) and *m*CPBA (70 wt%, 476 mg, 1.93 mmol) were added sequentially and the reaction mixture was stirred for 16 hours at room temperature. The reaction mixture was diluted with aqueous saturated sodium thiosulfate solution (30 mL) and DCM (50 mL). The organic layer was separated and the aqueous extracted with further DCM (2 × 30 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (2% Et_2O in petroleum ether 60:40) to afford crude epoxide **23** (410 mg, 73%) as a colourless oil and a 3:1 mixture of diastereoisomers.

DIPA (0.30 mL, 2.13 mmol) was dissolved in THF (10 mL) under nitrogen and cooled to 0 °C then 2.45 M *n*-BuLi in hexanes (0.72 mL, 1.78 mmol) was added dropwise and the reaction mixture was stirred at 0 °C for 30 minutes. $HSnBu_3$ (0.38 mL, 1.42 mmol) was added, and the reaction mixture was stirred for a further 30 minutes. Epoxide **23** (436 mg, 0.71 mmol) in THF (3 mL) was added dropwise and the reaction mixture was stirred at 0 °C for 3 hours then aqueous saturated ammonium chloride (10 mL) was added. The resulting solution was extracted with hexane (3 × 40 mL) and the combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was dissolved in Et_2O (7 mL) and cooled to 0 °C when I_2 (198 mg, 0.78 mmol) in Et_2O (4 mL) was added dropwise. The reaction mixture was stirred for 30 minutes then quenched with aqueous saturated sodium thiosulfate (10 mL). The organic layer was separated and the aqueous extracted with hexane (3 × 20 mL). The combined organic layers were washed with 3 M NaOH (20 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (20% DCM in petroleum ether 60:40) to afford vinyl iodide **13** (389 mg, 65% over two steps) as a colourless oil; $[\alpha]_D^{21}$ = +10.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2954, 2929, 2886, 2857, 1472, 1255, 1093, 835; δ_H (400 MHz, $CDCl_3$) -0.01 – 0.10 (18H, m, 3 × $Si(CH_3)_2$), 0.86 – 0.96 (27H, m, 3 × $SiC(CH_3)_3$), 1.48 – 1.75 (4H, m, 2-H_2 and 4-H_2), 3.66 (2H, m, 1-H_2), 3.89 (1H, ap. p, *J* 6.1, 3-H), 4.21 (1H, ap. qd, *J* 6.5, 1.1, 5-H), 6.23 (1H, dd, *J* 14.4, 1.1, 7-H), 6.54 (1H, dd, *J* 14.4, 6.5, 6-H); δ_C (101 MHz, $CDCl_3$) -5.1 (2 × $SiCH_3$), -4.6 ($SiCH_3$), -4.23 ($SiCH_3$), -4.22 ($SiCH_3$), -4.17 ($SiCH_3$), 18.2 ($Si\mathit{C}(CH_3)_3$), 18.3 ($Si\mathit{C}(CH_3)_3$), 18.5 ($Si\mathit{C}(CH_3)_3$), 26.0 ($SiC(\mathit{C}H_3)_3$), 26.1 ($SiC(\mathit{C}H_3)_3$), 26.2 ($SiC(\mathit{C}H_3)_3$), 40.4 (C-2), 45.7 (C-4), 59.8 (C-1), 66.5 (C-3), 72.7 (C-5), 76.3 (C-7), 149.2 (C-6); HRMS (ESI) calc. for $[C_{25}H_{55}O_3Si_3I]$ 615.2550 Found 615.2568.

2.2. Synthesis of Vinyl Boronic Ester 14

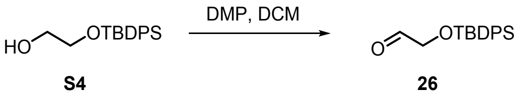
2-(*tert*-Butyldiphenylsilyloxy)ethan-1-ol (S4)



To a solution of ethylene glycol (22.30 mL, 400 mmol) in DCM (100 mL) under nitrogen was added imidazole (3.00 g, 44 mmol) and a spatula tip of DMAP. TBDPSCl (10.50 mL, 40 mmol) was added dropwise and the reaction mixture was stirred for 24 hours. Water (50 mL) was added and the solution was acidified with 2 M HCl (10 mL). The organic layer was separated and the aqueous extracted with DCM (2 × 100 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$

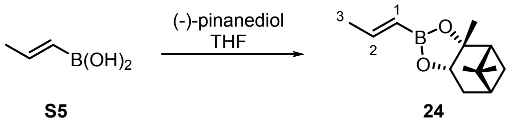
and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (20% EtOAc in petroleum ether 60:40) to afford alcohol **S4** (8.66 g, 76%) as a yellow oil; ν_{max} (film) 3385, 2930, 2857, 1427, 1110, 699; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, ^{t}Bu), 2.13 (1H, t, *J* 6.2, OH), 3.65 – 3.71 (2H, m, CH_2), 3.74 – 3.79 (2H, m, CH_2OH), 7.36 – 7.45 (5H, m, ArH), 7.65 – 7.70 (3H, m, ArH); δ_C (101 MHz, $CDCl_3$) 19.4 (Si*C*(CH_3)$_3$), 27.0 (SiC(*C*H_3)$_3$), 63.9 (CH_2), 65.2 (CH_2OH), 128.0 (ArC), 130.0 (ArC), 133.5 (ArC), 135.7 (ArC). Data consistent with the literature.[3]

2-(*tert*-Butyldiphenylsilyloxy)ethan-1-al (26)



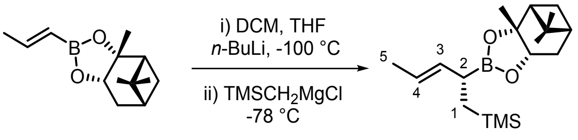
Alcohol **S4** (4.00 g, 14.1 mmol) was dissolved in DCM (70 mL) under nitrogen when DMP (7.17 g, 16.9 mmol) was added and the reaction mixture was stirred for 1 hour. Aqueous saturated sodium hydrogen carbonate (50 mL) was added and the organic phase separated. The aqueous phase was extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine (50 mL) dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was filtered through a pad of silica and washed with Et_2O (200 mL) and the solvent removed *in vacuo* to afford aldehyde **26** (3.77 g, 95%) as a colourless oil which was used directly in the next step without further purification; ν_{max} (film) 2931, 2857, 1738, 1427, 1111, 699; δ_H (400 MHz, $CDCl_3$) 1.10 (9H, s, SiC(CH_3)$_3$), 4.22 (2H, d, *J* 1.0, CH_2), 7.35 – 7.47 (6H, m, ArH), 7.63 – 7.68 (4H, m, ArH), 9.73 (1H, t, *J* 1.0, HCO); δ_C (101 MHz, $CDCl_3$) 19.4 (Si*C*(CH_3)$_3$), 26.9 (SiC(*C*H_3)$_3$), 70.2 (CH_2), 128.1 (ArCH), 130.3 (ArC), 132.7 (ArC), 135.7 (ArCH), 201.9 (CO). Data consistent with the literature.[3]

(-)-Pinanediol (*E*)-1-propen-1-ylboronate (24)



Boronic acid **S5** (922 mg, 10.7 mmol) and (-)-pinanediol (1830 mg, 10.7 mmol) were dissolved in THF (22 mL) and stirred for 30 minutes. The solvent was removed *in vacuo* and the crude product purified by flash column chromatography (8% Et_2O in petroleum ether 60:40) to afford boronate **24** (2316 mg, 98%) as a white crystalline solid; $[\alpha]^{25}_{D}$ = -24.0 (*c* 1, $CHCl_3$) lit. enantiomer[4] $[\alpha]^{23}_{D}$ = +24.2 (*c* 1.3, $CHCl_3$); ν_{max} (UATR) 2942, 2912, 1636, 1358, 986; δ_H (400 MHz, $CDCl_3$) 0.84 (3H, s, pinanyl CH_3), 1.14 (1H, d, *J* 10.9, pinanyl H), 1.28 (3H, s, pinanyl CH_3), 1.39 (3H, s, pinanyl CH_3), 1.85 (3H, dd, *J* 6.4, 1.7, 3-CH_3), 1.87 – 1.93 (2H, m, CH_2), 2.05 (1H, dd, *J* 6.0, 4.9, pinanyl CH), 2.16 – 2.24 (1H, m, pinanyl CH), 2.34 (1H, ddt, *J* 14.0, 8.7, 2.2, pinanyl CH), 4.29 (1H, dd, *J* 8.7, 1.9, CHOB), 5.47 (1H, dq, *J* 17.9, 1.7, 1-H), 6.64 (1H, dq, *J* 17.9, 6.4, 2-H); δ_C (101 MHz, $CDCl_3$) 21.9, 24.2, 26.6, 27.3, 28.8, 35.7, 38.3, 39.7, 51.5, 77.8 (OCH), 85.6 (OC), 120.1 (br, C-1), 149.7 (C-2). Data consistent with the literature.[4]

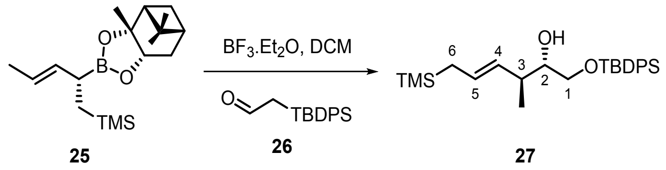
Trimethyl (*S*,*E*)-2-((-)-pinanediol boronate)-pent-3-en-1-yl)silane (25)



24 **25**

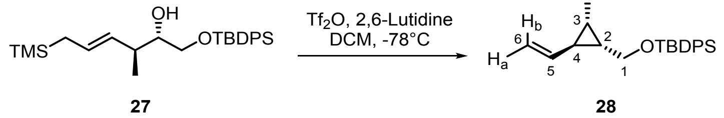
DCM (2.86 mL) and THF (80 mL) were cooled to -100 °C under nitrogen when 2.45 M *n*-BuLi in THF (11.68 mL, 28.62 mmol) was added dropwise over 10 minutes. The reaction mixture was stirred for 20 minutes when boronic ester **24** (6.30 g, 28.62 mmol) in THF (15 mL) was added dropwise over 10 minutes. The reaction mixture was stirred for 2 minutes and warmed to 0 °C. After 40 minutes the reaction mixture was cooled to -78 °C when 1.3 M $TMSCH_2MgCl$ in THF (22.0 mL, 28.62 mmol) was added dropwise. The reaction mixture was stirred at -78 °C for 3 hours, room temperature for 18 hours and quenched with aqueous saturated ammonium chloride (25 mL). The resulting solution was diluted with Et_2O (250 mL) and water (150 mL). The organic layer was separated and the aqueous extracted with Et_2O (2 × 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (3% Et_2O in petroleum ether 60:40) to afford boronic ester **25** (7.66 g, 84%) as a colourless oil; $[\alpha]_D^{25}$ = -22.0 (*c* 1, $CHCl_3$) lit.[4] $[\alpha]_D^{25}$ = -11.75 (*c* 0.45, $CHCl_3$); ν_{max} (film) 2916, 1367, 1246, 1031, 857, 834; δ_H (400 MHz, $CDCl_3$) -0.03 (9H, s, $Si(CH_3)_3$), 0.63 (1H, dd, *J* 14.5, 7.6, 1-*H*H), 0.82 (1H, dd, *J* 14.5, 7.6, 1-H*H*), 0.83 (3H, s, CH_3), 1.11 (1H, d, *J* 10.9, C*H*H), 1.27 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.61 – 1.65 (3H, m, 5-H_3), 1.78 – 1.85 (1H, m, C*H*H), 1.85 – 1.91 (2H, m, 2-H and CH), 2.04 (1H, t, *J* 5.6, CH), 2.13 – 2.22 (1H, m, CH*H*), 2.32 (1H, ddt, *J* 14.4, 8.7, 2.4, C*H*H), 4.25 (1H, dd, *J* 8.7, 2.0, BOCH), 5.33 – 5.47 (2H, m, 3-H and 4-H); δ_C (101 MHz, $CDCl_3$) -0.8 ($Si(CH_3)_3$), 17.9 (C-1), 18.2 (C-5), 24.2 (CH_3), 26.3 (CH_2), 27.3 (CH_3), 28.7 (CH_3), 35.7 (CH_2), 38.4 (C), 39.6 (CH), 51.6 (CH), 77.9 (CH), 85.6 (OC), 123.1 (C-4), 134.6 (C-3); HRMS (ESI) calc. for $[C_{18}H_{34}BO_2Si]$ 321.2419 Found 321.2404. Data consistent with the literature.[4]

(2*S*,3*S*,*E*)-1-(*tert*-Butyldiphenylsilyloxy)-3-methyl-6-(trimethylsilyl)hex-4-en-2-ol (27)



Boronic ester **25** (9.40 g, 29.34 mmol) and aldehyde **26** (9.12 g, 32.27 mmol) were dissolved in DCM (150 mL) under nitrogen and cooled to -78 °C. $BF_3.Et_2O$ (3.62 mL, 29.34 mmol) was added dropwise and the reaction mixture was stirred at -78 °C for 4 hours. Aqueous saturated sodium hydrogen carbonate (50 mL) was added, and the reaction mixture was warmed to room temperature. Et_2O (50 mL) was added, the organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (8% Et_2O in petroleum ether 60:40) to afford alcohol **27** (11.26 g, 87%) as a colourless oil; $[\alpha]_D^{22}$ = -8.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3583, 3473, 2956, 2858, 1428, 1111, 699; δ_H (400 MHz, $CDCl_3$) -0.05 (9H, s, TMS), 0.96 (3H, d, *J* 7.0, 3-CH_3), 1.06 (9H, s, $SiC(CH_3)_3$), 1.41 (2H, dd, *J* 8.0, 1.3, 6-H_2), 2.28 (1H, m, 3-H), 2.36 (1H, d, *J* 3.2, OH), 3.48 – 3.56 (1H, m, 2-H), 3.59 (1H, dd, *J* 10.0, 7.2, 1-*H*H), 3.67 (1H, dd, *J* 10.0, 3.6, 1-H*H*), 5.20 (1H, ap. ddt, *J* 15.5, 8.3, 1.3, 4-H), 5.40 (1H, ap. dt, *J* 15.5, 8.0, 5-H), 7.34 – 7.46 (6H, m, ArH), 7.64 – 7.69 (4H, m, ArH); δ_C (101 MHz, $CDCl_3$) -1.8 (TMS), 17.4 (CH_3-3), 19.4 (Si*C*(CH_3)$_3$), 23.0 (C-6), 27.0 (SiC(*C*H_3)$_3$), 39.8 (C-3), 66.4 (C-1), 75.6 (C-2), 127.8 (C-5), 127.9 (ArCH), 129.9 (ArCH), 130.0 (C-4), 133.5 (ArC), 135.8 (ArCH); HRMS (ESI) calc. for $[C_{26}H_{40}O_2Si_2Na]$ 463.2459 Found 463.2459.

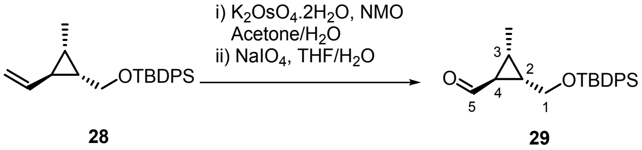
***tert*-Butyl(((1*S*,2*S*,3*S*)-2-methyl-3-vinylcyclopropyl)methoxy)diphenylsilane (28)**



Alcohol **27** (1.158 g, 2.63 mmol) was dissolved in DCM (26 ml) and cooled to -78 °C under nitrogen when 2,6-lutidine (0.40 mL, 3.42 mmol) was added and the reaction mixture was stirred for 5 minutes. Tf_2O (0.53 mL, 3.16 mmol) was added and the reaction mixture was stirred for 3 minutes before quenching with DIPEA (4.5 mL, 24.5 mmol). The mixture was warmed to room temperature and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (2% Et_2O in petroleum ether 60:40) to afford alcohol **28** (0.882 g, 96%) as a colourless oil; $[\alpha]_D^{22}$ = -45.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2959, 2935, 2858, 1428, 1111, 1086, 699; δ_H (500 MHz, $CDCl_3$) 0.92 – 1.00 (2H, m, 3-H and 4-H), 1.07 (9H, s, $SiC(CH_3)_3$), 1.09 (3H, d, *J* 6.1, 3-CH_3), 1.16 – 1.22 (1H, m, 2-H), 3.61 (1H, dd, *J* 11.1, 8.3, 1-H*H*), 3.85 (1H, dd, *J* 11.1, 6.1, 1-*H*H), 4.82 (1H, dd, *J* 10.3, 1.8, 6-H_a), 4.97 (1H, ddd, *J* 17.1, 1.8, 0.6, 6-H_b), 5.42 (1H, ddd, *J* 17.1, 10.3, 8.4, 5-H), 7.35 – 7.44 (6H, m, ArH), 7.66 – 7.73 (4H, m, ArH);

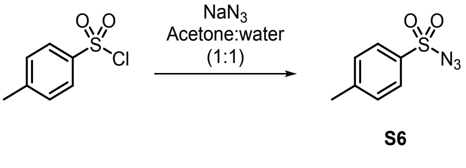
δ_C (101 MHz, $CDCl_3$) 12.7 (CH_3), 19.4 (Si*C*(CH_3)$_3$), 19.6 (C-2/3), 27.0 (SiC(*C*H_3)$_3$, 27.6 (C-2/3), 28.6 (C-4), 63.2 (C-1), 111.5 (C-6), 127.8 (ArCH), 129.7 (ArCH), 134.2 (ArC), 135.8 (ArCH), 141.7 (C-5); HRMS (ESI) calc. for [$C_{23}H_{31}OSi$] 351.2139 Found 351.2142.

(2*S*,3*R*,4*S*)-2-((*tert*-Butyldiphenylsilyloxy)methyl)-3-methylcyclopropane-1-carbaldehyde (29)



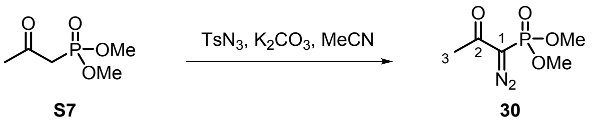
Alkene **28** (500 mg, 1.43 mmol) was dissolved in acetone (6 mL) and water (1 mL) then potassium osmate dihydrate (5 mg, 0.02 mmol) and NMO (251 mg, 2.15 mmol) were added sequentially and the reaction mixture was stirred at room temperature. After 18 hours the reaction mixture was diluted with EtOAc (75 mL) and water (50 mL). The organic layer was separated and the aqueous was extracted with further EtOAc (2 × 50 mL). The combined organics were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude diol was dissolved in THF (5 mL) and water (3.5 mL) and $NaIO_4$ (428 mg, 2.00 mmol) was added. The reaction mixture was stirred at room temperature for 2 hours. The solution was filtered through a pad of Celite and washed with DCM (50 mL). The organic phase was washed with aqueous saturated sodium thiosulfate (20 mL) and the aqueous extracted with DCM (2 × 50 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo* to afford aldehyde **29** (448 mg, 89%) as a light brown oil; $[\alpha]_D^{25}$ = +7.0 (*c* 0.7, $CHCl_3$); ν_{max} (film) 2930, 2857, 1710, 1428, 1111, 702; δ_H (400 MHz, $CDCl_3$) 0.91 (9H, s, SiC(CH_3)$_3$), 0.99 (3H, d, *J* 6.3, 3-CH_3), 1.31 (1H, ap. td, *J* 9.5, 5.0, 4-H), 1.53 (1H, dqd, *J* 9.5, 6.3, 4.5, 3-H), 1.72 (1H, dddd, *J* 9.5, 7.5, 6.3, 4.5, 2-H), 3.55 (1H, dd, *J* 11.2, 7.5, 1-*H*H), 3.65 (1H, dd, *J* 11.2, 6.3, 1-H*H*), 7.18 – 7.33 (6H m, ArH), 7.46 – 7.58 (4H, m, ArH), 8.93 (1H, d, *J* 5.0, 5-H); δ_C (101 MHz, $CDCl_3$) 12.1 (CH_3-3), 19.4 (Si*C*(CH_3)$_3$), 21.5 (C-3), 27.0 (SiC(*C*H_3)$_3$), 29.3 (C-2), 36.4 (C-4), 61.6 (C-1), 127.9 (ArCH), 129.9 (ArCH), 130.0 (ArCH), 133.7 (ArC), 135.8 (ArCH), 135.8 (ArCH), 200.6 (C-5); HRMS (ESI) calc. for [$C_{22}H_{28}O_2SiNa$] 375.1751 Found 375.1764.

4-Methylbenzenesulfonyl azide (S6)



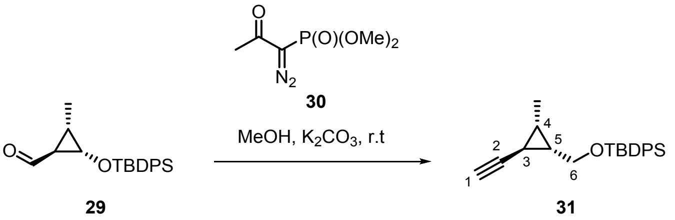
To a stirred solution of 4-toluenesufonyl chloride (5.01 g, 26.29 mmol) in acetone (75 mL) and water (75 mL) at 0 °C was added sodium azide (1.74 g, 26.77 mmol) and the reaction mixture was stirred at 0 °C for 3 hours. The solvent volume was reduced by half *in vacuo* and the resulting solution was extracted with Et_2O (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo* to afford azide **S6** (5.09 g, 99%) as a colourless oil; ν_{max} (film) 2123, 1596, 1368, 1164, 1086; δ_H (400 MHz, $CDCl_3$) 2.48 (3H, s, CH_3), 7.35 – 7.48 (2H, m, ArH), 7.67 – 7.96 (2H, m, ArH); δ_C (101 MHz, $CDCl_3$) 21.9 (CH_3), 127.7 (ArCH), 130.5 (ArCH), 135.7 (ArC), 146.4 (ArC); m/z (ESI): $[M+Na]^+$ = 220.01. Data consistent with the literature.[5]

Dimethyl (1-diazo-2-oxopropyl)phosphonate (30)



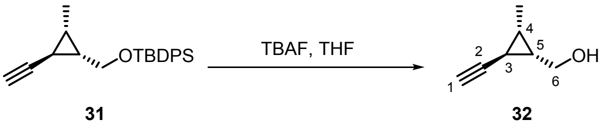
K_2CO_3 (274 mg, 1.98 mmol) and TsN_3 (392 mg, 1.98 mmol) were added to a stirred solution of dimethyl 2-oxopropylphosphonate (300 mg, 1.80 mmol) in MeCN (4 mL) at 0 °C under nitrogen. After stirring for 4 hours at room temperature the solvent was removed *in vacuo*. The crude residue was dissolved in DCM (30 mL) and washed with water (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (90% EtOAc in petroleum ether 60:40) to afford phosphonate **30** (259 mg, 75%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 2.26 (3H, s, 3-H_3), 3.83 (6H, d, *J* 12.0, 2 × OMe); δ_C (101 MHz, $CDCl_3$) 27.3 (C-3), 53.7 (d, *J* 5.4, OMe), 190.1 (d, *J* 13.0, C-2); m/z (ESI): $[M+H]^+$ = 193.04. Data consistent with the literature.[6]

tert-Butyl(((1*S*,2*S*,3*S*)-2-ethynyl-3-methylcyclopropyl)methoxy)diphenylsilane (31)



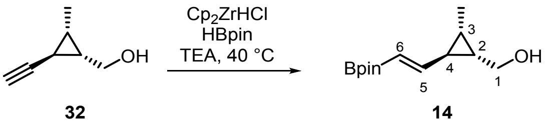
To a stirred solution of aldehyde **29** (4.70 g, 13.33 mmol) in MeOH (123 mL) under nitrogen was added K_2CO_3 (3.68 g, 26.66 mmol) followed by phosphonate **30** (3.84 g, 20.00 mmol) in MeOH (10 mL). After 16 hours the reaction mixture was diluted with Et_2O (500 mL) and washed sequentially with aqueous saturated sodium hydrogen carbonate (250 mL) and brine (250 mL). The organic layer was dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (3% Et_2O in petroleum ether 60:40) to afford alkyne **31** (4.24 g, 91%) as a colourless oil; $[\alpha]_D^{22}$ = +68.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3313, 2931, 2858, 2120, 1428, 1112, 1084; δ_H (400 MHz, $CDCl_3$) 0.77 (1H, ap. td, *J* 5.0, 2.1, 3-H), 1.06 (9H, s, $SiC(CH_3)_3$), 1.08 (3H, d, *J* 6.4, 4-CH_3), 1.27 (1H, dqd, *J* 9.0, 6.4, 5.0, 4-H), 1.47 (1H, dddd, *J* 9.0, 8.1, 6.0, 5.0, 5-H), 1.82 (1H, d, *J* 2.1, 1-H), 3.53 (1H, dd, *J* 11.2, 8.1, 6-*H*H), 3.81 (1H, dd, *J* 11.2, 6.0, 6-H*H*), 7.34 – 7.45 (6H, m, ArH), 7.66 – 7.71 (4H, m, ArH); δ_C (101 MHz, CDCl$_3$) 12.0 (C-3), 12.5 (CH$_3$-4), 19.4 (Si*C*(CH$_3$)$_3$), 21.2 (C-4), 27.0 (SiC(*C*H$_3$)$_3$), 28.6 (C-5), 62.5 (C-6), 64.4 (C-1), 87.0 (C-2), 127.9 (ArCH), 129.8 (ArCH), 133.89 (ArC), 133.91 (ArC), 135.78 (ArCH), 135.80 (ArCH); HRMS (ESI) calc. for [$C_{23}H_{28}OSiNa$] 371.1802 Found 371.1808.

((1*S*,2*S*,3*S*)-2-Ethynyl-3-methylcyclopropyl)methanol (32)



Silyl ether **31** (4.23 g, 12.14 mmol) was dissolved in THF (100 mL) under nitrogen and cooled to 0 °C then 1 M TBAF in THF (36.4 mL, 36.4 mmol) was added dropwise. The reaction mixture was stirred under nitrogen at room temperature for 18 hours and then quenched with aqueous saturated ammonium chloride (100 mL) and diluted with Et$_2$O (300 mL). The organic layer was separated and the aqueous extracted with Et$_2$O (2 × 200 mL). The combined organic layers were dried over MgSO$_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (40% Et$_2$O in petroleum ether 60:40) to afford alcohol **32** (1.26 g, 94%) as a colourless oil; $[\alpha]_D^{22}$ = +57.0 (*c* 1, CHCl$_3$); ν_{max} (film) 3291, 3017, 2960, 2932, 2877, 2116, 1071, 1024; δ_H (400 MHz, CDCl$_3$) 0.88 (1H, ap. td, *J* 4.9, 2.1, 3-H), 1.15 (3H, d, *J* 6.4, 4-CH$_3$), 1.26 – 1.38 (1H, m, 4-H), 1.39 – 1.52 (2H, m, OH and 5-H), 1.85 (1H, d, *J* 2.1, 1-H), 3.54 (1H, dd, *J* 11.6, 8.2, 6-*H*H), 3.76 (1H, dd, *J* 11.6, 6.7, 6-H*H*); δ_C (101 MHz, CDCl$_3$) 12.3 (C-3), 12.4 (CH$_3$-4), 21.0 (C-4), 28.7 (C-5), 61.6 (C-6), 64.9 (C-1), 86.4 (C-2); HRMS (APCI) calc. for [$C_7H_{10}O$] 111.0804 Found 111.0807.

((1*S*,2*S*,3*S*)-2-Methyl-3-((*E*)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)cyclopropyl)methanol (14)

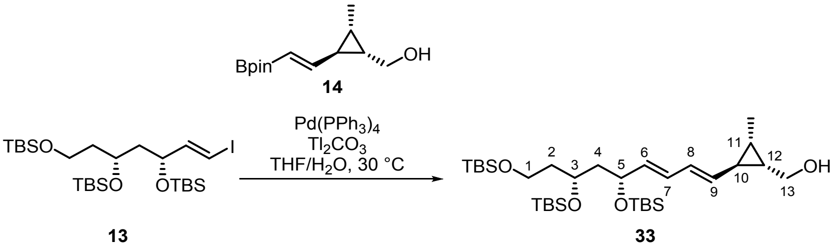


HBpin (0.73 mL, 5.06 mmol), triethylamine (0.04 mL, 0.25 mmoL) and Cp$_2$ZrHCl (16 mg, 0.06 mmol) were added sequentially to a stirred solution of alkyne **32** (279 mg, 2.53 mmol) under nitrogen and the reaction mixture was heated at 40 °C for 18 hours. The reaction mixture was cooled to 0 °C, quenched with water (30 mL) and diluted with DCM (50 mL). The organic layer was separated and the aqueous extracted with further DCM (2 × 30 mL). The combined organic layers were dried over Na$_2$SO$_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (55% Et$_2$O in petroleum ether 60:40 + 0.1% TEA) to afford vinyl boronic ester **14** (587 mg, 97%) as a colourless oil; $[\alpha]_D^{24}$ = +6.0 (*c* 1, CHCl$_3$); ν_{max} (film) 3419, 2977, 2930, 2877, 1630, 1353, 1139; δ_H (400 MHz, CDCl$_3$) 1.13 – 1.20 (5H, m, 3-H, 4-H and 3-CH$_3$), 1.25 (12H, s, Bpin), 1.31 – 1.39 (1H, m, 2-H), 3.58

(1H, ddd, *J* 11.7, 8.2, 4.5, 1-*H*H), 3.78 (1H, ddd, *J* 11.7, 6.7, 5.3, 1-H*H*), 5.43 (1H, d, *J* 17.8, 6-H), 6.17 (1H, dd, *J* 17.8, 8.8, 5-H); δ_C (101 MHz, $CDCl_3$) 12.5 (3-CH_3), 20.8 (C-3), 24.91 (Bpin CH_3), 29.0 (C-2), 31.0 (C-4) , 62.0 (Bpin C), 83.2 (C-1), 156.8 (C-5); HRMS (ESI) calc. for [$C_{13}H_{23}BO_3Na$] 261.1635 Found 261.1646.

2.3. Synthesis of Aldehyde 11

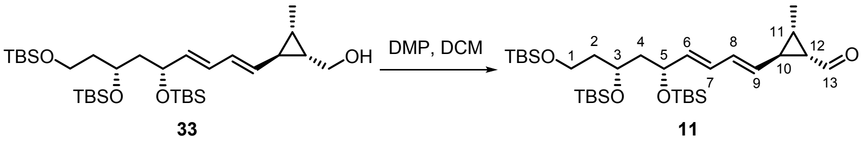
((1*S*,2*S*,3*S*)-2-Methyl-3-((1*E*,3*E*,5*R*,7*R*)-5,7,9-tris((*tert*-butyldimethylsilyl)oxy)nona-1,3-dien-1-yl)cyclopropyl)methanol (33)



To a stirred solution of boronic ester **14** (54 mg, 0.23 mmol) in degassed THF (2 mL) and water (1 mL) under nitrogen was added vinyl iodide **13** (141 mg, 0.23 mmol) in degassed THF (1 mL) followed by $Pd(PPh_3)_4$ (26 mg, 0.02 mmol) and the reaction mixture was stirred at room temperature for 5 minutes. Tl_2CO_3 (216 mg, 0.46 mmol) was added and the reaction mixture was heated at 30 °C for 3 hours. The reaction mixture was filtered over Celite, eluting with ether (50 mL) and water (20 mL). The layers were separated, and the aqueous phase extracted with further Et_2O (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (30 % Et_2O in petroleum ether 60:40) to afford diene **33** (117 mg, 85%) as a colourless oil; $[\alpha]^{24}_{D}$ = +12.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3348, 2954, 2929, 2885, 1655, 1252, 1074, 933, 773; δ_H (400 MHz, $CDCl_3$) 0.00 (3H, s, $SiCH_3$), 0.02 – 0.04 (15H, m, 5 × $SiCH_3$), 0.86 – 0.89 (27H, m, 3 × $SiC(CH_3)_3$), 0.99 – 1.08 (2H, m, 11-H and 12-H), 1.15 (3H, d, *J* 5.8, 11-CH_3), 1.18 – 1.27 (1H, m, 10-H), 1.29 – 1.33 (1H, m, OH), 1.50 – 1.78 (4H, m, 2-CH_2 and 4-CH_2), 3.58 (1H, dd, *J* 11.3, 8.6, 13-*H*H), 3.61 – 3.73 (2H, m, 1-CH_2), 3.79 (1H, dd, *J* 11.3, 6.6, 13-H*H*), 3.82 – 3.92 (1H, m, 3-H), 4.20 (1H, ap. q, *J* 6.7, 5-H), 5.19 – 5.29 (1H, m, 9-H), 5.43 – 5.53 (1H, m, 6-H), 5.97 – 6.07 (2H, m, 7-H and 8-H); δ_C (101 MHz, $CDCl_3$) -5.14 ($SiCH_3$), -5.12 ($SiCH_3$), -4.6 ($SiCH_3$), -4.2 (2 × $SiCH_3$), -3.9 ($SiCH_3$), 12.7 (CH_3-11), 18.2 ($SiC(CH_3)_2$), 18.3 ($SiC(CH_3)_2$), 18.5 ($SiC(CH_3)_2$), 20.0 (12-H), 26.1 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 28.1 (11-H), 28.3 (10-H), 40.4 (C-2), 46.8 (C-4), 60.1 (C-1), 62.3 (C-13), 66.9 (C-3), 70.9 (C-

5), 127.9 (C-7/8), 129.6 (C-7/8), 134.1 (C-6), 136.5 (C-9); HRMS (ESI) calc. for [$C_{32}H_{66}O_4Si_3Na$] 621.4162 Found 621.4158.

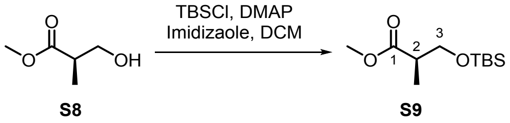
(1*S*,2*S*,3*S*)-2-Methyl-3-((1*E*,3*E*,5*R*,7*R*)-5,7,9-tris(*tert*-butyldimethylsiloxy)nona-1,3-dien-1-yl)cyclopropane-1-carbaldehyde (11)



Alcohol **33** (30 mg, 0.05 mmol) was dissolved in DCM (0.5 mL) under nitrogen and cooled to 0 °C, then DMP (25 mg, 0.06 mmol) was added. The reaction mixture was stirred for 2 hours at room temperature then quenched with aqueous saturated sodium thiosulfate (2 mL) and aqueous saturated sodium hydrogen carbonate (2 mL) and stirred for 10 minutes. The aqueous phase was extracted with DCM (3 × 10 mL) and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (10% Et_2O in petroleum ether 60:40) to afford aldehyde **11** (29 mg, 97%) as a colourless oil; $[\alpha]_D^{22}$ = +27.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2954, 2928, 2856, 1704, 1472, 1214, 835, 751; δ_H (400 MHz, $CDCl_3$) 0.00 (3H, s, $SiCH_3$), 0.02 – 0.04 (15H, m, 5 × $SiCH_3$), 0.84 – 0.91 (27H, m, 3 × $SiC(CH_3)_3$), 1.31 (3H, d, *J* 6.4, 11-CH_3), 1.51 – 1.77 (5H, m, 2-H_2, 4-H_2 and 11-H), 1.97 (1H, ap. dt, *J* 9.1, 4.5, 12-H), 2.17 (1H, ddd, *J* 8.6, 6.3, 4.5, 10-H), 3.60 – 3.71 (2H, m, 1-H_2), 3.86 (1H, ap. p, *J* 6.2, 3-H), 4.22 (1H, ap. q, *J* 6.6, 5-H), 5.22 (1H, dd, *J* 14.8, 8.6, 9-H), 5.57 (1H, dd, *J* 14.9, 6.6, 6-H), 6.04 (1H, dd, *J* 14.9, 10.5, 7-H), 6.13 (1H, dd, *J* 14.8, 10.5, 8-H), 9.48 (1H, d, *J* 4.5, 13-H); δ_C (101 MHz, $CDCl_3$) -5.14 ($SiCH_3$), -5.12 ($SiCH_3$), -4.6 ($SiCH_3$), -4.2 (2 × $SiCH_3$), -4.0 ($SiCH_3$), 12.8 (CH_3-11), 18.2 ($Si\mathit{C}(CH_3)_3$), 18.3 ($Si\mathit{C}(CH_3)_3$), 18.5 ($Si\mathit{C}(CH_3)_3$), 26.1 (2 × $SiC(\mathit{C}H_3)_3$), 26.2 ($SiC(\mathit{C}H_3)_3$), 27.0 (C-11), 33.3 (C-10), 37.6 (C-12), 40.4 (C-2), 46.6 (C-4), 60.0 (C-1), 66.8 (C-3), 70.6 (C-5), 128.9 (C-7), 130.4 (C-8), 132.5 (C-9), 136.0 (C-6), 199.9 (C-13); HRMS (ESI) calc. for [$C_{32}H_{64}O_4Si_3Na$] 619.4005 Found 619.3999.

2.4. Synthesis of Phosphorus Diamide S14

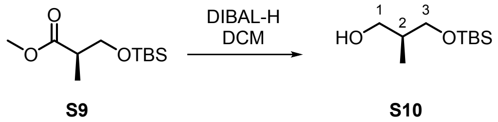
Methyl (*R*)-3-(*tert*-butyldimethylsilyloxy)-2-methylpropanoate (S9)



Alcohol **S8** (5.00 g, 42 mmol) was dissolved in DCM (150 mL) then imidazole (5.76 g, 85 mmol) was added. The reaction mixture was cooled to 0 °C then TBSCl (14.60 g, 97 mmol) and a spatula tip of DMAP were added. The reaction mixture was stirred at room temperature for 24 hours then water

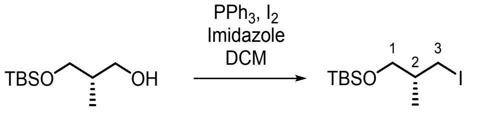
(100 mL) was added and the solution acidified to pH 2 with 2 M HCl. The organic layer was separated and the aqueous extracted with further DCM (2 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and the solvent removed *in vacuo* to afford TBS protected alcohol **S9** (9.70 g, 99%) as a colourless oil; $[\alpha]_D^{22}$ = -16.0 (*c* 1, $CHCl_3$), lit.[7] $[\alpha]_D^{20}$ = -19.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2951, 2928, 2850, 1740, 838; δ_H (400 MHz,$CDCl_3$) 0.03 (3H, s, $SiCH_3$), 0.04 (3H, s, $SiCH_3$), 0.87 (9H, s, $SiC(CH_3)_3$), 1.13 (3H, d, *J* 7.0, 2-CH_3), 2.65 (1H, ap. h, *J* 7.0, 2-H), 3.65 (1H, dd, *J* 9.7, 6.0, 3-*H*H), 3.67 (3H, s, OCH_3), 3.77 (1H, dd, *J* 9.7, 7.0, 3-H*H*); δ_C (101 MHz, $CDCl_3$) -5.3 ($Si(CH_3)_2$), 13.6 (Si*C*$(CH_3)_3$), 18.4 (CH_3-2), 26.0 (SiC(*C*$H_3)_3$), 42.7 (C-2), 51.7 (OCH_3), 65.4 (C-3), 175.7 (C-1). Data consistent with the literature.[7]

(*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpropan-1-ol (S10)



Ester **S9** (9.70 g, 41.74 mmol) was dissolved in DCM (150 mL) under nitrogen and cooled to -78 °C when 1 M DIBAL-H in hexane (94 mL, 94 mmol) was added slowly. The reaction mixture was stirred for 1 hour at room temperature and poured onto a solution of 1 M HCl (100 mL) at 0 °C. The resulting solution was stirred for 30 minutes. The organic layer was separated and the aqueous extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and the solvent removed *in vacuo* to afford alcohol **S10** (6.86 g, 80%) as a colourless oil; $[\alpha]_D^{24}$ = -9.0 (*c* 1, $CHCl_3$), lit.[7] $[\alpha]_D^{24}$ = -11.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3350, 2934, 2854, 770; δ_H (400 MHz, $CDCl_3$) 0.06 (6H, s, $Si(CH_3)_2$), 0.82 (3H, d, *J* 6.9, 2-CH_3), 0.88 (9H, s, $SiC(CH_3)_3$), 1.86 – 1.99 (1H, m, 2-H), 2.84 (1H, br. s, OH), 3.53 (1H, dd, *J* 10.0, 8.0, 1-*H*H), 3.57 – 3.67 (2H, m, 3-H_2), 3.72 (1H, ddd, *J* 10.0, 4.4, 0.8, 1-H*H*); δ_C (101 MHz, $CDCl_3$) -5.43 ($SiCH_3$), -5.37 ($SiCH_3$), 13.3 (CH_3), 18.4 (Si*C*$(CH_3)_3$), 26.0 (SiC(*C*$H_3)_3$, 37.2 (C-2), 68.6 (CH_2), 69.0 (CH_2). Data consistent with the literature.[7]

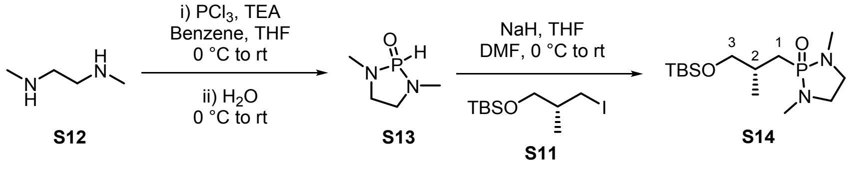
(*R*)-*tert*-Butyl(3-iodo-2-methylpropoxy)dimethylsilane (S11)



S10 **S11**

Alcohol **S10** (6.85 g, 33.51 mmol), PPh_3 (11.43 g, 43.57 mmol) and imidazole (3.42 g, 50.27 mmol) were dissolved in DCM (135 mL) under nitrogen and cooled to 0 °C, then I_2 (11.48 g, 45.24 mmol) was added portion wise. The reaction mixture was warmed to room temperature and stirred in the dark for 16 hours. The reaction mixture was diluted with Et_2O (100 mL) and filtered over celite. The organic layer was washed sequentially with aqueous saturated sodium thiosulfate (75 mL), aqueous saturated sodium hydrogen carbonate (75 mL) and brine (75 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (4% Et_2O in petroleum ether 60:40) to afford iodide **S11** (6.23 g, 78%) as a colourless oil; $[\alpha]_D^{20}$ = -13.0 (*c* 1, $CHCl_3$), lit.[8] $[\alpha]_D^{20}$ = -9.5 (*c* 4.03, $CHCl_3$); ν_{max} (film) 2955, 2929, 2895, 1471, 1098, 834, 774; δ_H (400 MHz, $CDCl_3$) 0.06 (3H, s, $SiCH_3$), 0.06 (3H, s, $SiCH_3$), 0.89 (9H, s, $SiC(CH_3)_3$), 0.95 (3H, d, *J* 6.7, 2-CH_3), 1.56 – 1.71 (1H, m, 2H), 3.25 (1H, dd, *J* 9.5, 5.6, 3-*H*H), 3.30 (1H, dd, *J* 9.5, 5.2, 3-H*H*), 3.39 (1H, dd, *J* 10.0, 6.9, 1-*H*H), 3.52 (1H, dd, *J* 10.0, 5.0, 1-H*H*); δ_C (101 MHz, $CDCl_3$) -5.2 ($SiCH_3$), 14.1 (C-3), 17.4 (CH_3-2), 18.5 (Si*C*(CH_3)$_3$), 26.1 (SiC(*C*H_3)$_3$), 37.6 (C-2), 66.9 (C-1); m/z (APCI): $[M+H]^+$ = 314.10. Data consistent with the literature.[8]

(*R*)-2-(3-(*tert*-Butyldimethylsiloxy)-2-methylpropyl)-1,3-dimethyl-1,3,2-diazaphospholidine 2-oxide (S14)

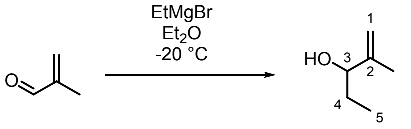


To a vigorously stirred solution of amine **S12** (1.00 mL, 9.29 mmol) and degassed triethylamine (5.18 mL, 37.16 mmol) in degassed THF (11 mL) and degassed benzene (7.45 mL) at 0 °C under nitrogen was added PCl_3 (0.81 mL, 9.29 mmol) in degassed benzene (3.7 mL) dropwise. The reaction mixture was stirred for 1 hour at room temperature then cooled to 0 °C. A solution of water (0.17 mL, 9.29 mmol) in THF (2 mL) was added dropwise and the reaction mixture was stirred at room temperature for 4 hours. The reaction mixture was filtered over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was dissolved in a mixture of benzene (5 mL) and THF (5 mL) and filtered over celite, eluting with a solution of benzene (5 mL) and THF (5 mL). The solvent was removed *in vacuo* to afford phosphorus acid diamide **S13**[8] (629 mg, 51%) as an orange oil which was used in the next step without further purification.

Alkyl iodide **S11** (499 mg, 1.59 mmol) and phosphorus acid diamide **S13** (490 mg, 3.65 mmol) were dissolved in THF (6.5 mL) and DMF (1.5 mL) under nitrogen and cooled to 0 °C. NaH (127 mg, 3.18 mmol) was added in one portion and the reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was quenched with aqueous saturated ammonium chloride (5 mL) and diluted with EtOAc (20 mL). The organic layer was separated and the aqueous extracted with EtOAc (3 × 12 mL). The combined organic phases were washed with water (3 × 15 mL), brine (20 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (10% EtOH in EtOAc) to afford phosphorus diamide **S14** (482 mg, 95%) as a colourless oil; $[\alpha]_D^{20}$ = -3.2 (*c* 1, $CHCl_3$), lit.[8] $[\alpha]_D^{20}$ = -6.3 (*c* 3.6, $CHCl_3$); ν_{max} (film) 2954, 2927, 2885, 2855, 1471, 1225, 1083, 834, 774; δ_H (400 MHz, $CDCl_3$) 0.03 (6H, s, $Si(CH_3)_2$), 0.88 (9H, s, $SiC(CH_3)_3$), 0.97 (3H, d, *J* 6.7, 2-CH_3), 1.54 (1H, ap. td, *J* 15.7, 8.8, 1-*H*H), 1.68 – 1.85 (1H, m, 2-H), 2.12 (1H, ddd, *J* 17.3, 15.7, 3.7, 1-H*H*), 2.64 (3H, d, *J* 3.1, NCH_3), 2.66 (3H, d, *J* 3.2, NCH_3), 3.03 – 3.12 (2H, m, NCH_2), 3.16 – 3.25 (2H, m, NCH_2), 3.33 (1H, dd, *J* 9.6, 6.8, 3-*H*H), 3.42 (1H, ddd, *J* 9.6, 5.7, 2.4, 3-H*H*); δ_C (101 MHz, $CDCl_3$) -5.24 ($SiCH_3$), -5.21 ($SiCH_3$), 18.0 (d, *J* 4.7, CH_3-2), 18.5 (Si*C*$(CH_3)_3$), 26.1 (SiC(*C*$H_3)_3$), 30.0 (d, *J* 116.9, C-1)), 31.8 (d, *J* 3.9, C-2), 32.0 (d, *J* 5.3, NCH_3), 32.2 (d, *J* 5.3, NCH_3), 48.3 (d, *J* 7.8, NCH_2), 48.5 (d, *J* 7.8, NCH_2), 68.6 (d, *J* 14.9, C-3); δ_P (162 MHz, $CDCl_3$) 42.03; [$C_{14}H_{33}N_2O_2PSiNa$] 343.1941 Found 343.1931. Data consistent with the literature.[8]

2.5. Synthesis of Ketone S26

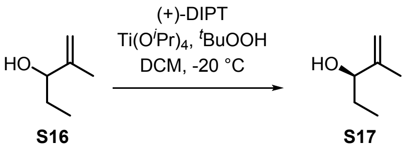
2-Methylpent-1-en-3-ol (S16)



S15 **S16**

Aldehyde **S15** (1.18 mL, 14.28 mmol) was dissolved in Et_2O (30 mL) under nitrogen and cooled to - -20 °C when 1 M EtMgBr in THF (18.56 mL, 18.56 mmol) was added dropwise. The reaction mixture was stirred for 20 minutes then quenched with aqueous saturated ammonium chloride (20 mL). The layers were separated, and the aqueous phase extracted with further Et_2O (2 × 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo.* The crude material was purified by flash column chromatography (DCM) to afford alcohol **S16** (1.23 g, 86%) as a colourless oil; ν_{max} (film) 3367, 2964, 2936, 2877, 1651, 1455, 896; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.5, 5-H_3, 3H), 1.48 – 1.64 (2H, m, 4-H_2), 1.67 – 1.74 (3H, m, 2-CH_3), 3.99 (1H, t, *J* 6.7, 3-H), 4.79 – 4.86 (1H, m, 1-*H*H), 4.89 – 4.95 (1H, m, 1-H*H*); δ_C (101 MHz, $CDCl_3$) 10.0 (C-5), 17.6 (C-4), 27.9 (CH_3-2), 77.5 (C-3), 111.31 (C-1), 147.5 (C-2); HRMS (APCI) calc. for [C_6H_{11}] 83.0855 Found 83.0850. Data consistent with the literature.[9]

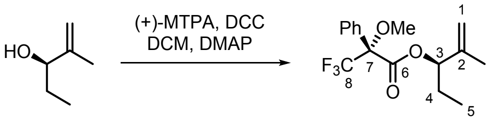
(*R*)-2-Methylpent-1-en-3-ol (S17)



S16 **S17**

Alcohol **S16** (3.13 g, 31.25 mmol) and 4 Å molecular sieves (0.94 g) were dissolved in DCM (156 mL) under nitrogen and cooled to -20 °C, then (+)-DIPT (0.98 mL, 4.69 mmol) and $Ti(O^iPr)_4$ (0.93 mL, 3.13 mmol) were added sequentially. The reaction mixture was stirred for 30 minutes then ^{t}BuOOH (3.13 mL, 17.19 mmol) was added and the reaction mixture was stirred at -20 °C for 48 hours. The reaction mixture was quenched with an aqueous solution of $FeSO_4$/citric acid (16.5 g of $FeSO_4$ and 5.5 g of citric acid in 50 mL of H_2O). The solution was stirred vigorously for 30 minutes at room temperature then extracted with DCM (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (DCM) to afford resolved alcohol **S17** (1.25 g, 80%) as a colourless oil. ^{1}H NMR analysis of the Mosher's ester indicated a 90% ee. $[\alpha]_D^{22}$ = +4.0 (*c* 1, $CHCl_3$) lit.[9] $[\alpha]_D^{20}$ = +4.1 (*c* 1, $CHCl_3$). Data consistent with alcohol **S16** as previously reported.[9]

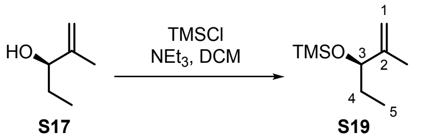
(*R*)-2-Methylpent-1-en-3-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S18)



S17 **S18**

Alcohol **S17** (20 mg, 0.20 mmol) and (+)-MTPA (145 mg, 0.62 mmol) were dissolved in DCM (2 mL) under nitrogen, then DCC (128 mg, 0.62 mmol) and DMAP (76 mg, 0.62 mmol) were added sequentially and the reaction mixture was stirred at room temperature for 5 hours. The reaction mixture was filtered, and the solvent removed *in vacuo*. ^{1}H NMR analysis of the crude material indicated a 90% ee.

(*R*)-Trimethyl((2-methylpent-1-en-3-yl)oxy)silane (S19)

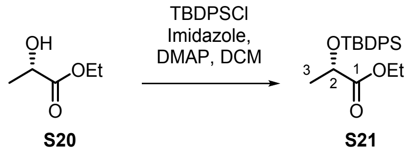


S17 **S19**

Alcohol **S17** (1.20 g, 11.98 mmol) was dissolved in DCM (60 mL) and cooled to 0 °C then NEt_3 (6.68 mL, 47.92 mmol) and TMSCl (3.04 mL, 23.96 mmol) were added sequentially. The reaction mixture was stirred at 0 °C for 30 minutes and quenched with water (30 mL). The organic layer was separated and the aqueous extracted with further DCM (40 mL). The combined organic layers were washed sequentially with ice cold 1 M HCl (25 mL) and aqueous saturated sodium hydrogen carbonate (25 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (1% Et_2O in pentane) to afford to afford volatile silyl ether **S19** (2.01 g, 97%) as a yellow oil; $[\alpha]_D^{22}$ = +14.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2960, 2928, 2873, 1250, 841; δ_H (400 MHz, $CDCl_3$)

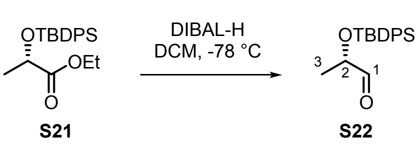
0.09 (9H, s, Si(CH_3)$_3$), 0.84 (3H, t, *J* 7.4, 5-H_3), 1.50 (2H, qd, *J* 7.4, 6.5, 4-H), 1.67 (3H, dd, *J* 1.5, 0.9, 2-CH_3), 3.88 – 3.97 (1H, m, 3-H), 4.73 – 4.78 (1H, m, 1-*H*H), 4.80 – 4.88 (1H, m, 1-H*H*); δ_C (101 MHz, $CDCl_3$) 0.3 (Si(CH_3)$_3$) , 10.4 (5), 17.4 (C-4), 29.1 (CH_3-2), 78.3 (C-3), 110.8 (C-1), 147.8 (C-2); HRMS (ESI) calc. for [$C_9H_{20}OSi$] 173.1356 Found 173.1352.

Ethyl (*S*)-2-(*tert*-butyldiphenylsiloxy)propanoate (S21)



To a solution of alcohol **S20** (2.36 g, 20.00 mmol) in DCM (70 mL) under nitrogen was added imidazole (1.63 g, 24 mmol), TBDPSCl (5.72 mL, 24 mmol) and a spatula tip of DMAP and the reaction mixture was stirred for 24 hours. The reaction was quenched with 2 M HCl (20 mL) and water (50 mL). The organic layer was separated and the aqueous extracted with DCM (2 × 60 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and the solvent removed *in vacuo* to afford silyl alcohol **S21** (7.42 g, quant.) as a colourless oil; $[\alpha]_D^{23}$ = -69.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3072, 2933, 2894, 2858, 1752, 1733, 1428, 1133, 1106; δ_H (400 MHz, $CDCl_3$) 1.10 (9H, s, SiC(CH_3)$_3$), 1.15 (3H, t, *J* 7.0, OCH_2CH_3), 1.37 (3H, d, *J* 6.8, 3-H_3), 4.02 (2H, q, *J* 7.0, OCH_2CH_3), 4.27 (1H, q, *J* 6.8, 2-H), 7.31 – 7.48 (6H, m, ArH), 7.62 – 7.73 (4H, m, ArH); δ_C (101 MHz, $CDCl_3$) 14.2 (OCH_2CH_3), 19.4 (Si*C*(CH_3)$_3$), 21.4 (C-3), 27.0 (SiC(CH_3)$_3$), 66.0 (OCH_2CH_3), 69.1 (C-2), 127.7 (ArCH), 127.8 (ArCH), 129.9 (ArCH), 133.4 (ArC), 133.8 (ArC), 135.9 (ArCH), 136.1 (ArCH), 173.9 (C-1); HRMS (ESI) calc. for [$C_{21}H_{28}NaSiO_3$] 379.1700 Found 379.1689.

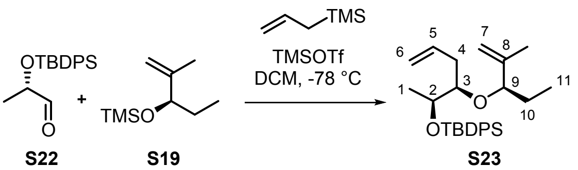
(*S*)-2-(*tert*-Butyldiphenylsiloxy)propanal (S22)



Ester **S21** (2.00 g, 5.60 mmol) was dissolved in DCM (20 mL) under nitrogen and cooled to -78 °C then 1 M DIBAL-H in hexanes (6.20 mL, 6.20 mmol) was added dropwise. The reaction mixture was stirred at -78 °C for 1 hour, then quenched with MeOH (1 mL) dropwise followed by aqueous saturated sodium potassium tartrate solution (50 mL). The reaction mixture was warmed to room temperature and stirred vigorously for 1 hour. The organic layer was separated and the aqueous extracted with DCM (2 × 50 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (3% Et_2O in petroleum ether 60:40) to afford aldehyde **S22** (1.45 g, 83%) as a colourless oil; $[\alpha]_D^{23}$ = -

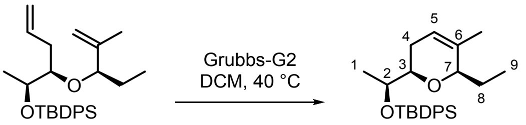
26.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3072, 2959, 2932, 2858, 1738, 1428, 1110, 699; δ_H (400 MHz, $CDCl_3$) 1.11 (9H, s, $SiC(CH_3)_3$), 1.22 (3H, d, *J* 6.8, 3-H_3), 4.09 (1H, qd, *J* 6.8, 1.2, 2-H), 7.34 – 7.47 (6H, m, ArH), 7.62 – 7.68 (4H, m, ArH), 9.64 (1H, d, *J* 1.2, C-1); δ_C (101 MHz, $CDCl_3$) 18.6 (C-3), 19.4 (Si*C*$(CH_3)_3$), 27.0 (SiC(*C*$H_3)_3$), 74.6 (C-2), 127.95 (ArCH), 128.03 (ArCH), 130.16 (ArCH), 130.23 (ArCH), 133.1 (ArC), 133.5 (ArC), 135.89 (ArCH), 135.92 (ArCH), 204.0 (C-1); HRMS (ESI) calc. for $[C_{19}H_{24}NaO_2Si]$ 335.1438 Found 335.1436.

tert-Butyl(((2*S*,3*R*)-3-(((*R*)-2-methylpent-1-en-3-yl)oxy)hex-5-en-2-yl)oxy)diphenylsilane (S23)



Aldehyde **S22** (10.34 g, 33.08 mmol) and silyl ether **S19** (6.10 g, 35.40 mmol) were dissolved in DCM (65 mL) under nitrogen and cooled to -78 °C, then a precooled (-78 °C) mixture of allyltrimethylsilane (5.78 mL, 36.39 mmol) and TMSOTf (0.60 mL, 3.31 mmol) in DCM (1 mL) was added. The reaction mixture was stirred at -78 °C for 5 hours. The reaction mixture was warmed to 0 °C over 1 hour, then quenched with DIPEA (1.15 mL, 6.62 mmol). The reaction mixture was warmed to room temperature and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (75% petroleum ether 60:40 in DCM) to afford ether **S23** (8.90 g, 62%) as a colourless oil; $[\alpha]_D^{23}$ = +20 (*c* 1, $CHCl_3$); ν_{max} (film) 3072, 2962, 2932, 2858, 1642, 1590, 1428, 1104,700; δ_H (400 MHz, $CDCl_3$) 0.83 (3H, t, *J* 7.5, 11-H_3), 1.01 (3H, d, *J* 6.3, 1-H_3), 1.08 (9H, s, $SiC(CH_3)_3$), 1.45 – 1.56 (1H, m, 10-*H*H), 1.63 (3H, s, 8-CH_3), 1.65 – 1.74 (1H, m, 10-H*H*), 1.98 – 2.11 (1H, m, 4-*H*H), 2.16 – 2.27 (1H, m, 4-H*H*), 3.44 (1H, td, *J* 6.6, 2.3, 3-H), 3.88 (1H, qd, *J* 6.3, 2.3, 2-H), 3.97 (1H, dd, *J* 8.1, 6.1, 9-H), 4.76 – 4.78 (1H, m, 7-*H*H), 4.86 – 4.97 (3H, m, 6-H_2 and 7-H*H*), 5.56 – 5.69 (1H, m, 5-H), 7.31 – 7.47 (6H, m, ArH), 7.69 (4H, m, ArH); δ_C (101 MHz, $CDCl_3$) 10.4 (C-11), 16.6 (CH_3-8), 18.0 (C-1), 19.4 (Si*C*$(CH_3)_3$), 26.3 (C-10), 27.2 (SiC(*C*$H_3)_3$), 36.8 (C-4), 71.7 (C-2), 80.2 (C-3), 85.4 (C-9), 114.2 (C-7), 116.4 (C-5), 127.6 (ArCH), 127.7 (ArCH), 129.7 (ArCH), 129.8 (ArCH), 134.1 (ArC), 134.8 (ArC), 136.0 (C-5), 136.2 (ArCH), 145.0 (C-8); HRMS (ESI) calc. for $[C_{28}H_{40}O_2SiNa]$ 459.2690 Found 459.2703.

tert-Butyl((*S*)-1-((2*R*,6*R*)-6-ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)ethoxy)diphenylsilane (S24)



S23 **S24**

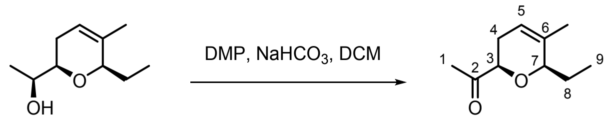
Ether **S23** (150 mg, 0.34 mmol) was dissolved in DCM (6 mL) under nitrogen and heated at 40 °C, then Grubbs Catalyst G2 (6 mg, 0.01 mmol) in DCM (1 mL) was added. The reaction mixture was heated at 40 °C for 16 hours. The solvent was removed *in vacuo* and the crude material was purified by flash column chromatography (15% DCM in petroleum ether 60:40) to afford pyran **S24** (135 mg, 97%) as a colourless oil; $[\alpha]_D^{21}$ = +23.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3071, 2962, 2931, 2856, 1427, 1111, 700; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.3, 9-H_3), 1.03 (3H, d, *J* 6.3, 1-H_3), 1.05 (3H, s, 6-CH_3), 1.44 (1H, m, 8-*H*H), 1.52 – 1.66 (9H, m, $SiC(CH_3)_3$), 1.75 (1H, dqd, *J* 14.7, 7.3, 3.2, 8-H*H*), 1.94 – 2.06 (1H, m, 4-*H*H), 2.06 – 2.17 (1H, m, 4-H*H*), 3.31 (1H, ddd, *J* 10.3, 5.0, 3.4, 3-H), 3.87 (1H, dq, *J* 6.3, 5.0, 2-H), 3.92 – 4.02 (1H, m, 7-H), 5.50 – 5.59 (1H, m, 5-H), 7.31 – 7.44 (6H, m, ArH), 7.65 – 7.80 (4H, m, ArH); δ_C (101 MHz, $CDCl_3$) 9.1 (OCH_2CH_3), 19.1 (CH_3-6), 19.6 ($SiC(CH_3)_3$), 20.3 (C-1), 26.0 (C-8), 27.0 (C-4), 27.2 ($SiC(CH_3)_3$), 72.3 (C-2), 78.2 (C-3), 78.7 (C-7), 120.9 (C-5), 127.6 (ArCH), 129.56 (ArCH), 129.61 (ArCH), 134.3 (ArC), 135.2 (ArC), 135.6 (C-6), 136.2 (ArCH), 136.3 (ArCH); HRMS (ESI) calc. for $[C_{26}H_{36}O_2SiNa]$ 431.2377 Found 431.2378.

(*S*)-1-((2*R*,6*R*)-6-Ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)ethan-1-ol (S25)

S24 **S25**

Silyl ether **S24** (200 mg, 0.5 mmol) was cooled to 0 °C under nitrogen then 1 M TBAF in THF (1.0 mL, 1.0 mmol) was added dropwise. The reaction mixture was stirred under nitrogen at room temperature for 24 hours and then quenched with water (10 mL) and Et_2O (10 mL). The organic layer was separated and the aqueous extracted with Et_2O (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (25% Et_2O in petroleum ether 60:40) to afford alcohol **S25** (83 mg, 98%) as a colourless oil; $[\alpha]_D^{24}$ = +6.0 (*c* 1, $CHCl_3$) lit.[10] $[\alpha]_D^{20}$ = +4.2 (*c* 1.04, $CHCl_3$); ν_{max} (film) 3405, 2966, 2935, 1454, 1265, 1116, 1057, 906, 729; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.2, 9-H_3), 1.14 (3H, d, *J* 6.7, 1-H_3), 1.51 (1H, m, 8-*H*H), 1.57 – 1.61 (3H, m, 6-CH_3), 1.75 (1H, ap. dtd, *J* 14.3, 7.2, 3.0, 8-H*H*), 1.78 – 1.85 (1H, m, 4-*H*H), 2.09 – 2.19 (1H, m, 4-H*H*), 2.22 (1H, d, *J* 3.5, OH), 3.42 (1H, ap. dt, *J* 10.8, 3.5, 3-H), 3.91 (1H, ap. qt, *J* 6.7, 3.5, 2-H), 4.02 – 4.11 (1H, m, 7-H), 5.53 – 5.60 (1H, m, 5-H); δ_C (101 MHz, $CDCl_3$) 8.6 (C-9), 17.6 (C-1), 19.1 (CH_3-6), 24.4 (C-4), 25.8 (C-8), 69.3 (C-2), 76.2 (C-3), 78.3 (C-7), 120.6 (C-5), 135.2 (C-6); HRMS (ESI) calc. for [$C_{10}H_{18}O_2Na$] 193.1199 Found 193.1198. Data consistent with the literature.[10]

1-((2*R*,6*R*)-6-Ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)ethan-1-one (S26)

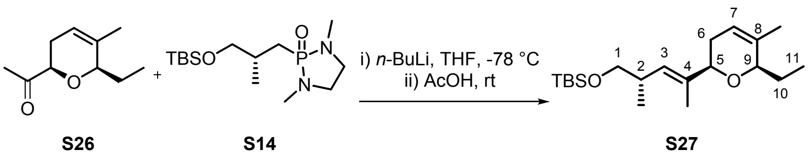


S25 **S26**

Alcohol **S25** (1.20 g, 7.05 mmol) was dissolved in DCM (70 mL) under nitrogen and cooled to 0 °C, then $NaHCO_3$ (2.37 g, 28.20 mmol) and DMP (3.59 g, 8.46 mmol) were added sequentially. The reaction mixture was stirred for 2 hours at room temperature, filtered over celite eluting with Et_2O (100 mL) and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (7% Et_2O in pentane) to afford the volatile ketone **S26** (1.15 g, 97%) as a colourless oil; $[\alpha]^{20}_{D}$ = +166 (*c* 0.25, $CHCl_3$) lit.[10] $[\alpha]^{20}_{D}$ = +181 (*c* 0.257, $CHCl_3$); ν_{max} (film) 2966, 2936, 1720, 1353, 1115, 1057; δ_H (400 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.3, 9-H_3), 1.44 – 1.58 (1H, m, 8-*H*H), 1.56 – 1.62 (3H, m, 6-CH_3), 1.81 (1H, dqd, *J* 14.8, 7.3, 3.5, 8-H*H*), 1.98 – 2.20 (2H, m, 4-H_2), 2.24 (3H, s, 1-H_3), 3.91 (1H, dd, *J* 10.5, 4.2, 3-H), 4.06 – 4.12 (1H, m, 7-H), 5.46 – 5.64 (1H, m, 5-H); δ_C (101 MHz, $CDCl_3$) 8.8 (C-9), 19.1 (CH_3-6), 25.8 (C-8), 25.9 (C-1), 27.5 (C-4), 78.5 (C-7), 78.9 (C-3), 119.7 (C-5), 135.8 (C-6), 210.23 (C-2); HRMS (ESI) calc. for [$C_{10}H_{16}O_2Na$] 191.1043 Found 191.1045. Data consistent with the literature.[10]

2.6. Synthesis of Diene 34

tert-Butyl((*S*, *E*)-4-((2*R*, 6*R*)-6-ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-2-methylpent-3-enyloxy)dimethylsilane (S27)



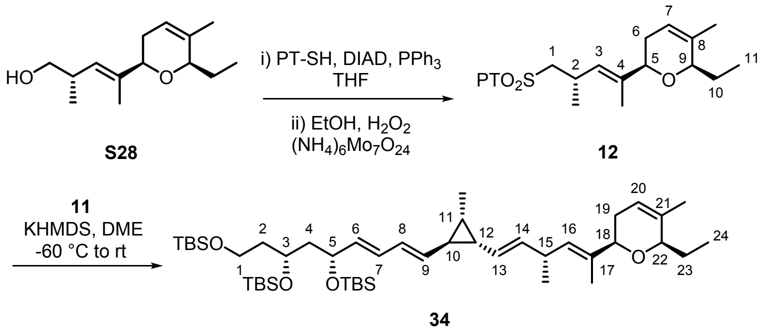
S26 **S14** **S27**

Phosphonamide **S14** (1150 mg, 3.59 mmol) was dissolved in THF (11 mL) under nitrogen and cooled to -78 °C then 2.45 M *n*-BuLi in hexane (1.26 mL, 3.10 mmol) was added dropwise and the reaction mixture was stirred for 2 hours. Neat ketone **S26** (274 mg, 1.63 mmol) was added dropwise and the reaction mixture was stirred at -78 °C for 1 hour. The reaction mixture was warmed to rt and quenched with AcOH (1 mL) and stirred for an additional 20 minutes at room temperature. Aqueous saturated sodium hydrogen carbonate (20 mL) was added and the resulting solution was extracted with DCM (3 × 40 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (5% Et_2O in petroleum ether 60:40) to afford alkene **S27** (278 mg, 50%, E/Z = 7:1) as a colourless oil and ketone **S27** (61 mg, 22%); $[\alpha]_D^{20}$ = +38.0 (*c* 0.5, $CHCl_3$), lit.[8] $[\alpha]_D^{20}$ = +47.7 (*c* 1.37, $CHCl_3$); ν_{max} (film) 2957, 2929, 2857, 1463, 1255, 1090, 836; δ_H (400 MHz, $CDCl_3$) 0.03 (3H, s, $SiCH_3$), 0.03 (3H, s, $SiCH_3$), 0.89 (12H, m, $SiC(CH_3)_3$ and 11-H_3), 0.96 (3H, d, *J* 6.7, 2-CH_3), 1.47 – 1.57 (1H, m, 10-*H*H), 1.53 – 1.62 (3H, m, CH_3-8), 1.67 (3H, d, *J* 1.5, CH_3-4), 1.77 (1H, m, 10-H*H*), 1.83 – 1.90 (1H, m, 6-*H*H), 2.06 – 2.16 (1H, m, 6-H*H*), 2.50 – 2.63 (1H, m, 2-H), 3.35 (1H, dd, *J* 9.7, 7.4, 1-*H*H), 3.45 (1H, dd, *J* 9.7, 5.9, 1-H*H*), 3.83 (1H, dd, *J* 10.6, 3.0, 5-H), 4.03 – 4.15 (1H, m, 9-H), 5.21 (1H, dq, *J* 9.3, 1.5, 3-H), 5.52 – 5.58 (1H, m, 7-H); δ_C (101 MHz, $CDCl_3$) -5.2 ($SiCH_3$), -5.1 ($SiCH_3$), 8.4 (C-11), 12.8 (CH_3-4), 17.4 (Si*C*(CH_3)$_3$), 18.5 (CH_3-8), 19.2 (CH_3-2), 25.8 (C-10), 26.1 (SiC(*C*H_3)), 30.4 (C-6), 35.2 (C-2), 68.1 (C-1), 78.1 (C-5), 78.2 (C-9), 121.2 (C-7), 128.3 (C-3), 135.3 (C-8), 136.5 (C-4); HRMS (ESI) calc. for [$C_{20}H_{38}O_2SiNa$] 361.2533 Found 361.2549. Data consistent with the literature.[8]

(*S*,*E*)-4-((2*R*,6*R*)-6-Ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-2-methylpent-3-en-1-ol (S28)

Silyl ether **S27** (50 mg, 0.15 mmol) was dissolved in THF (1.5 mL) under nitrogen and cooled to 0 °C then 1 M TBAF in THF (0.22 mL, 0.22 mmol) was added dropwise. The reaction mixture was stirred under nitrogen at room temperature for 3 hours and then quenched with aqueous saturated ammonium chloride (5 mL) and the organic solvents removed *in vacuo*. The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (20% EtOAc in petroleum ether 60:40) to afford alcohol **S28** (27 mg, 81%) as a colourless oil; $[\alpha]_D^{21}$ = +41.0 (*c* 1, $CHCl_3$) lit.[8] $[\alpha]_D^{20}$ = +57.1 (*c* 1.52, $CHCl_3$); ν_{max} (film) 3377, 2962, 2930, 2871, 1453, 1028, 733; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.5, 11-H_3), 0.96 (3H, d, *J* 6.5, 2-CH_3), 1.46 – 1.57 (1H, m, 10-*H*H), 1.59 (3H, dd, *J* 2.6, 1.3, 8-CH_3), 1.70 (3H, d, *J* 1.5, 4-CH_3), 1.73 – 1.84 (1H, m, 10-H*H*), 1.87 – 1.98 (1H, m, 6-*H*H), 2.05 – 2.21 (1H, m, 6-H*H*), 2.58 – 2.74 (1H, m, 2-H), 3.36 (1H, m, 1-*H*H), 3.47 (1H, m, 1-H*H*), 3.85 (1H, dd, *J* 10.7, 3.1, 5-H), 4.02 – 4.13 (1H, m, 9-H), 5.21 (1H, m, 3-H), 5.50 – 5.61 (1H, m, 7-H); δ_C (101 MHz, $CDCl_3$) 8.5 (C-11), 13.3 (CH_3-4), 17.1 (CH_3-2), 19.1 (CH_3-8), 25.8 (C-10), 30.5 (C-6), 35.2 (C-2), 68.0 (C-1), 77.7 (C-5), 78.2 (C-9), 120.9 (C-7), 127.2 (C-3), 135.3 (C-8), 138.6 (C-4); HRMS (ESI) calc. for [$C_{14}H_{24}O_2Na$] 247.1669 Found 247.1679. Data consistent with the literature.[8]

(5*R*,7*R*)-7-(*tert*-Butyldimethylsiloxy)-5-((1*E*,3*E*)-4-((1*S*,2*S*,3*S*)-2-((*R*,1*E*,4*E*)-5-((2*R*,6*R*)-6-ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-3-methylhexa-1,4-dien-1-yl)-3-methylcyclopropyl)buta-1,3-dien-1-yl)-2,2,3,3,11,11,12,12-octamethyl-4,10-dioxa-3,11-disilatridecane (34)

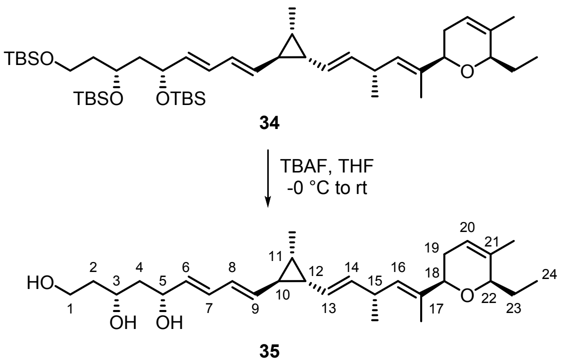


Alcohol **S28** (270 mg, 1.20 mmol), PT-SH (278 mg, 1.56 mmol) and PPh_3 (409 mg, 1.56 mmol) were dissolved in THF (12 mL) under nitrogen and cooled the 0 °C then DIAD (0.31 mL, 1.56 mmol) was added dropwise. The reaction mixture was stirred for 3 hours at room temperature then quenched with aqueous saturated ammonium chloride (20 mL). The resulting solution was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with brine (30 mL), dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was filtered over a small plug of silica eluting with 20% EtOAc in petroleum ether 60:40 and the solvent removed *in vacuo*. The crude material was dissolved in EtOH (40 mL) and cooled to 0 °C then a premixed solution of molybdenate (297 mg, 0.24 mmol) in a 30% aqueous solution of H_2O_2 (1.23 mL, 12.0 mmoL) was added dropwise. The reaction mixture was stirred at room temperature for 17 hours then quenched with water (50 mL). The resulting solution was extracted with DCM (3 × 100 mL) and the combined organic layers dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (10% EtOAc in petroleum ether 60:40) to afford sulfone **12**[8] (303 mg, 61%) as a colourless oil.

Sulfone **12** (76 mg, 0.18 mmol) was dissolved in DME (0.5 mL) under nitrogen and cooled to -60 °C then 1 M KHMDS in THF (0.2 mL, 0.2 mmol) was added dropwise. The reaction mixture was stirred for 15 minutes, then aldehyde **11** (85 mg, 0.14 mmol) in DME (0.5 mL) was added dropwise. The reaction mixture was stirred for 1 hour at -60 °C then 7 hours at room temperature. Water (10 mL) and Et_2O (10 mL) were added, and the organic layer separated. The aqueous was further extracted with Et_2O (3 × 15 mL) and the combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (1% Et_2O in petroleum ether 60:40) to afford alkene **34** (67 mg, 61%) as a yellow oil; $[\alpha]_D^{22}$ = +28.0 (*c* 0.5, $CHCl_3$); ν_{max} (film) 3019, 2958, 2927, 1214, 1080, 746; δ_H (400 MHz, $CDCl_3$) -0.04 – 0.11 (18H, m, 6 × $SiCH_3$), 0.79 – 0.97 (30H, m, 24-H_3 and 3 × $SiC(CH_3)_3$), 1.05 (3H, d, *J* 7.0, 15-CH_3), 1.06 – 1.08 (3H, m, 11-CH_3), 1.09 – 1.14 (2H, m, 10-H and 11-H), 1.47 – 1.54 (3H, m, 4-*H*H, 12-H and 23-*H*H), 1.57 – 1.60 (3H, m, 21-CH_3), 1.62 – 1.67 (3H, m, 17-CH_3), 1.67 – 1.81 (4H, m, 2-H_2, 4-H*H* and 23-H*H*), 1.82 – 1.90 (1H, m, 19-*H*H), 2.07 – 2.16 (1H, m, 19-H*H*), 3.07 (1H, dqd, *J* 8.4, 7.0, 1.5, 15-H), 3.60 – 3.71 (2H, m, 1-H_2), 3.79 – 3.90 (2H, m, 3-H and 18-H), 4.05 – 4.14 (1H, m, 22-H), 4.19 (1H, ap. q, *J* 6.6, 5-H), 5.10 (1H, ddd, *J* 15.3, 8.9, 1.4, 13-H), 5.20 – 5.36 (2H, m, 9-H and 16-H), 5.42 – 5.52 (2H, m, 6-H and 14-H), 5.52 – 5.58 (1H, m, 20-H), 5.93 – 6.08 (2H, m, 7-H and 8-H); δ_C (101 MHz, $CDCl_3$) -5.11 ($SiCH_3$), -5.10 ($SiCH_3$), -4.5 ($SiCH_3$), -4.18 ($SiCH_3$), -4.16 ($SiCH_3$), -3.9 ($SiCH_3$), 8.4 (C-24), 12.5 (CH_3-17), 13.3 (CH_3-11), 18.2 ($Si\mathit{C}(CH_3)_3$), 18.4 ($Si\mathit{C}(CH_3)_3$), 18.5 ($Si\mathit{C}(CH_3)_3$), 19.2 (CH_3-21), 21.3 (CH_3-15), 22.1 (C-11), 25.8 (C-23), 26.10 ($SiC(\mathit{C}H_3)_3$), 26.11 ($SiC(\mathit{C}H_3)_3$), 26.20 ($SiC(\mathit{C}H_3)_3$), 29.7 (C-12), 30.3 (C-19), 31.3 (C-10), 34.4 (C-15), 40.4 (C-2), 46.8 (C-4), 60.1 (C-1), 66.9 (C-3), 71.0 (C-5), 78.1 (C-22), 78.2 (C-18), 121.1 (C-20), 125.6 (C-13), 127.5 (C-7/8), 129.7 (C-9/16), 129.9 (C-7/8), 133.7 (C-6/14), 135.31 (C-21), 135.54 (C-6/14), 135.95 (C-17), 137.0 (C-9/16); HRMS (ESI) calc. for [$C_{46}H_{86}O_4Si_3Na$] 809.5726 Found 809.5700.

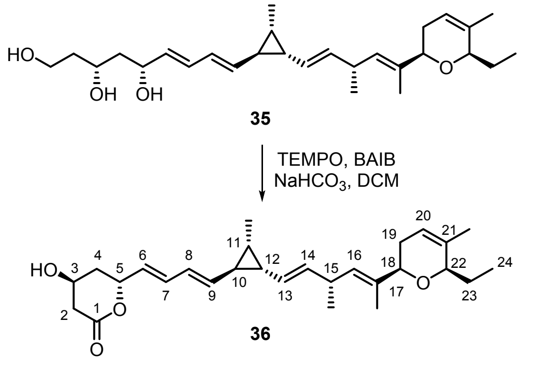
2.7. End-game Synthesis of Ambruticin J (3)

(3*R*,5*R*,6*E*,8*E*)-9-((1*S*,2*S*,3*S*)-2-((*R*,1*E*,4*E*)-5-((2*R*,6*R*)-6-Ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-3-methylhexa-1,4-dien-1-yl)-3-methylcyclopropyl)nona-6,8-diene-1,3,5-triol (35)



Silyl ether **34** (120 mg, 0.15 mmol) was dissolved in THF (1 mL) under nitrogen and cooled to 0 °C then 1 M TBAF in THF (1.35 mL, 1.35 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 16 hours. Aqueous saturated ammonium chloride (10 mL) was added and the resulting solution was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (100% EtOAc) to afford triol **35** (64 mg, 95%) as a yellow oil; $[\alpha]_D^{23}$ = +48.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3361, 2962, 2931, 1655, 1451, 1368, 1115, 1050, 987; δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.3, 24-H_3), 1.05 (3H, d, *J* 6.5, 15-CH_3), 1.06 – 1.09 (4H, m, 11-H and 11-CH_3), 1.12 (1H, ap. dt, *J* 8.8, 4.0, 10-H), 1.46 – 1.57 (2H, m, 12-H and 23-*H*H), 1.57 – 1.61 (3H, m, 21-CH_3), 1.64 (4H, m, 4-*H*H and 17-CH_3), 1.67 – 1.81 (4H, m, 2-H$_2$, 4-H*H* and 23-H*H*), 1.82 – 1.90 (1H, m, 19-*H*H), 2.06 – 2.17 (1H, m, 19-H*H*), 2.67 (2H, s, 2 × OH), 3.07 (1H, ap. dq, *J* 8.5, 6.5, 15-H), 3.72 – 3.90 (3H, m, 1-H$_2$ and 18-H), 3.92 (1H, s, OH), 4.09 (1H, s, 22-H), 4.14 (1H, ap. tdt, *J* 6.9, 4.2, 2.2, 3-H), 4.40 (1H, ddd, *J* 9.9, 6.8, 3.1, 5-H), 5.09 (1H, dd, *J* 15.2, 8.8, 13-H), 5.25 (1H, dt, *J* 8.5, 1.4, 16-H), 5.33 (1H, dd, *J* 15.0, 8.8, 9-H), 5.48 (1H, dd, *J* 15.2, 6.5, 14-H), 5.52 – 5.58 (2H, m, 6-H and 20-H), 6.03 (1H, dd, *J* 15.0, 10.5, 8-H), 6.15 (1H, dd, *J* 15.1, 10.5, 7-H); δ_C (126 MHz, CDCl$_3$) 8.4 (C-24), 12.5 (CH$_3$-17), 13.3 (CH$_3$-11), 19.2 (CH$_3$-21), 21.3 (CH$_3$-15), 22.2 (C-11), 25.8 (C-23), 29.8 (C-12), 30.4 (C-19), 31.2 (C-10), 35.2 (C-15), 38.9 (C-2), 43.5 (C-4), 61.7 (C-1), 72.7 (C-3), 73.8 (C-5), 78.06 (C-22), 78.12 (C-18), 121.1 (C-20), 125.4 (C-13), 126.9 (C-8), 129.7 (C-16), 130.9 (C-7), 132.0 (C-6), 135.30 (C-17/21), 135.31 (C-17/21), 135.7 (C-14), 138.7 (C-9); HRMS (ESI) calc. for [$C_{28}H_{44}O_4Na$] 467.3132 Found 467.3121.

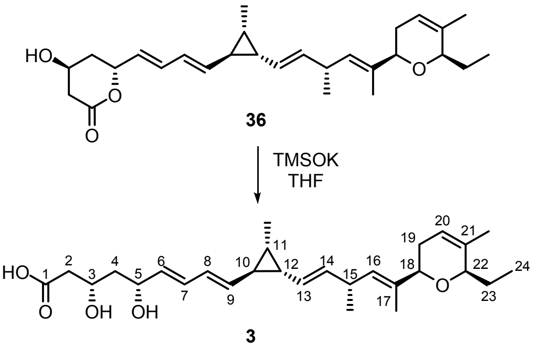
(4*S*,6*R*)-6-((1*E*,3*E*)-4-((1*S*,2*S*,3*S*)-2-((*R*,1*E*,4*E*)-5-((2*R*,6*R*)-6-Ethyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-3-methylhexa-1,4-dien-1-yl)-3-methylcyclopropyl)buta-1,3-dien-1-yl)-4-hydroxytetrahydro-2H-pyran-2-one (36)



Triol **35** (50 mg, 0.11 mmol) was dissolved in DCM (1 mL) under nitrogen then BAIB (116 mg, 0.36 mmol), NaHCO$_3$ (37 mg, 0.44 mmol) and TEMPO (4 mg, 0.02 mmol) were added sequentially. The reaction mixture was stirred at room temperature for 6 hours and then quenched with aqueous saturated sodium thiosulfate (2 mL) and water (10 mL). The solution was extracted with Et$_2$O (2 × 30 mL) and the combined organic layers washed sequentially with aqueous saturated sodium hydrogen carbonate (20 mL) and water (20 mL). The combined aqueous layers were extracted with Et$_2$O (3 × 40 mL). The combined organic layers were washed with brine (30 ml), dried over Na$_2$SO$_4$ and the solvent was removed *in vacuo*. The crude material was purified by flash column chromatography (60% EtOAc in petroleum ether 60:40) to afford lactone **36** (39 mg, 80%) as a yellow oil; $[\alpha]_D^{23}$ = +24.0 (*c* 1, CHCl$_3$); ν_{max} (film) 3416, 2962, 2928, 1727, 1215, 908, 753, 731; δ_H (500 MHz, CDCl$_3$) 0.92 (3H, t, *J* 7.4, 24-H$_3$), 1.07 (3H, d, *J* 6.9, 15-CH$_3$), 1.09 – 1.12 (4H, m, 11-H and 11-CH$_3$), 1.13 – 1.18 (1H, m, 10-H), 1.51 – 1.59 (2H, m, 12-H and 23-*H*H), 1.61 (3H, d, *J* 1.3, 21-CH$_3$), 1.67 (3H, d, *J* 1.4, 17-CH$_3$), 1.76 – 1.82 (1H, m, 23-

H*H*), 1.84 – 1.93 (2H, m, 4-*H*H and 19-*H*H), 1.99 – 2.05 (1H, m, 4-H*H*), 2.11 – 2.17 (1H, m, 19-H*H*), 2.63 (1H, dd, *J* 17.7, 4.0, 2-*H*H), 2.77 (1H, dd, *J* 17.7, 5.0, 2-H*H*), 3.06 – 3.14 (1H, m, 15-H), 3.86 (1H, dd, *J* 10.7, 3.1, 18-H), 4.08 – 4.15 (1H, m, 22-H), 4.37 – 4.43 (1H, m, 3-H), 5.12 (1H, dd, *J* 15.3, 8.8, 13-H), 5.18 – 5.24 (1H, m, 5-H), 5.28 (1H, dq, *J* 8.8, 1.4, 16-H), 5.40 (1H, dd, *J* 15.1, 8.9, 9-H), 5.51 (1H, dd, *J* 15.3, 6.2, 14-H), 5.54 – 5.60 (2H, m, 6-H and 20-H), 6.07 (1H, dd, *J* 15.1, 10.5, 8-H), 6.26 (1H, dd, *J* 15.2, 10.5, 7-H); δ_C (126 MHz, $CDCl_3$) 8.4 (C-24), 12.5 (CH_3-17), 13.3 (CH_3-11), 19.1 (CH_3-21), 21.3 (CH_3-15), 22.3 (C-11), 25.8 (C-23), 30.0 (C-12), 30.3 (C-19), 31.3 (C-10), 35.2 (C-15), 36.6 (C-4), 38.9 (C-2), 62.9 (C-3), 76.2 (C-5), 78.05 (C-22), 78.12 (C-18), 121.1 (C-20), 125.2 (C-13), 126.4 (C-6), 126.5 (C-8), 129.6 (C-16), 133.1 (C-7), 135.3 (C-17/21), 135.3 (C-17/21), 135.8 (C-14), 140.0 (C-9), 170.1 (C-1); HRMS (ESI) calc. for [$C_{28}H_{40}O_4Na$] 463.2819 Found 463.2819.

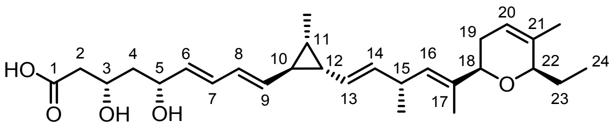
Ambruticin J (3)



Lactone **36** (7.7 mg, 0.02 mmol) was dissolved in THF (0.2 mL) under nitrogen and cooled to 0 °C then TMSOK (11.0 mg, 0.09 mmol) was added. The reaction mixture was stirred for 3 hours at room temperature then quenched with aqueous saturated ammonium chloride (10 mL) and EtOAc (20 mL). The organic layer was separated and the aqueous extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (10% MeOH in DCM + 0.25% AcOH) to afford ambruticin J (8 mg, quant.) as a yellow oil; $[\alpha]_D^{25}$ = +52.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3383, 2962, 2926, 2875, 2857, 1714, 1049; δ_H (500 MHz, $CDCl_3$) δ 0.89 (3H, t, *J* 7.4, 24-H_3), 1.05 (3H, d, *J* 6.8, 15-CH_3), 1.06 – 1.09 (4H, m, 11-H and 11-CH_3), 1.10 – 1.15 (1H, m, 10-H), 1.46 – 1.57 (2H, m, 12-H and 23-*H*H), 1.52 – 1.61 (3H, m, 21-CH_3), 1.63 – 1.68 (4H, m, 4-*H*H and 17-CH_3), 1.70 – 1.80 (2H, m, 4-H*H* and 23-H*H*), 1.81 – 1.88 (1H, m, 19-*H*H), 2.06 – 2.17 (1H, m, 19-H*H*), 2.47 – 2.57 (2H, m, 2-H_2), 3.00 – 3.13 (1H, m, 15-H), 3.84 (1H, dd, *J* 10.7, 3.1, 18-H), 4.03 – 4.12 (1H, m, 22-H), 4.25 – 4.34 (1H, m, 3-H), 4.38 – 4.45 (1H, m, 5-H), 5.09 (1H, ddd, *J* 15.1, 8.9, 1.4, 13-H), 5.25 (1H, d, *J* 8.9, 16-H), 5.34 (1H, dd, *J* 14.9, 8.8, 9-H), 5.45 – 5.58 (3H, m, 6-H, 14-H and 20-H), 6.03 (1H, dd, *J* 14.9, 10.5, 8-H), 6.16 (1H, dd, *J* 15.1, 10.5, 7-H); δ_C (126 MHz, $CDCl_3$) 8.4 (C-24), 12.5 (CH_3-17), 13.3 (CH_3-11), 19.2 (CH_3-21), 21.3 (CH_3-15), 22.2 (C-11), 25.8 (C-23), 29.9 (C-12), 30.4 (C-19), 31.3 (C-10), 35.2 (C-15), 41.4 (C-2), 42.5 (C-4), 68.4 (C-3), 73.2 (C-5), 78.07 (C-22), 78.13 (C-18), 121.1 (C-20), 125.3 (C-13), 126.8 (C-8), 129.7 (C-16), 131.2 (C-6) , 131.4 (C-7), 135.30 (C-17/21), 135.31 (C-17/21), 135.8 (C-14), 139.0 (C-9), 175.1 (C-1); HRMS (ESI) calc. for $[C_{28}H_{42}O_5Na]$ 481.2924 Found 481.2939.

NMR data in CD_3OD: δ_H (500 MHz, (CD_3OD)) 0.88 (3H, t, *J* 7.3, 24-H_3), 1.04 (3H, d, *J* 7.1, 15-CH_3), 1.05 – 1.10 (4H, m, 11-H and 11-CH_3), 1.09 – 1.14 (1H, m, 10-H), 1.45 – 1.56 (2H, m, 12-H and 23-*H*H), 1.59 (3H, s, 21-CH_3), 1.64 (3H, d, *J* 1.5, 17-CH_3), 1.64 – 1.79 (3H, m, 4-H_2 and 23-H*H*), 1.81 – 1.91 (1H, m, 19-*H*H), 2.03 – 2.16 (1H, m, 19-H*H*), 2.40 (1H, dd, *J* 15.4, 8.0, 2-*H*H), 2.47 (1H, dd, *J* 15.4, 4.9, 2-H*H*), 3.04 – 3.14 (1H, m, 15-H), 3.79 – 3.85 (1H, m, 18-H), 4.03 – 4.13 (2H, m, 3-H and 22-H), 4.25 (1H, ap. q, *J* 7.1, 5-H), 5.16 (1H, dd, *J* 15.2, 8.8, 13-H), 5.25 (1H, d, *J* 8.9, 16-H), 5.32 (1H, dd, *J* 14.8, 8.9, 9-H), 5.42 – 5.52 (1H, m, 14-H), 5.53 – 5.62 (2H, m, 6-H and 20-H), 6.05 (1H, dd, *J* 14.8, 10.5, 8-H), 6.16 (1H, dd, *J* 15.2, 10.5, 7-H); δ_C (126 MHz, (CD_3OD)) 8.7 (C-24), 12.7 (CH_3-17), 13.4 (CH_3-11), 19.1 (CH_3-21), 21.6 (CH_3-15), 22.8 (C-11), 26.6 (C-23), 30.6 (C-12), 31.1 (C-19), 32.1 (C-10), 36.3 (C-15), 43.3 (C-2), 45.0 (C-4), 67.5 (C-3), 71.6 (C-5), 79.48 (C-22), 79.54 (C-18), 122.1 (C-20), 126.9 (C-13), 128.4 (C-8), 130.9 (C-16), 132.4 (C-7), 133.1 (C-6), 136.1 (C-21), 136.2 (C-17), 136.3 (C-14), 138.6 (C-9), 175.4 (C-1). ^{1}H and ^{13}C NMR spectra are consistent with those reported in the literature (see Tables 1 and 2).[11,12]

2.8. Comparison of Ambruticin J NMR Data

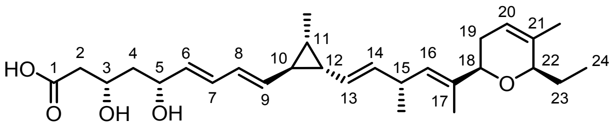


3

Position	Our Synthetic Ambruticin J 500 MHz (CD_3OD): δ_H (multiplet, *J* (Hz))	Taylor's Synthetic Ambruticin J 500 MHz (CD_3OD): δ_H (multiplet, *J* (Hz))[12]
1-H	-	-
2-H_a	2.40 (dd, 15.4, 8.0)	2.38 (dd, 15.3, 8.0)
2-H_b	2.47 (dd, 15.4, 4.9)	2.42 (dd, 15.3, 4.5)
3-H	4.08	4.08
4-H_2	1.72 and 1.65	1.72 and 1.62
5-H	4.25 (ap. q, 7.2)	4.26 (ddd, 7.5, 6.5, 6.5)
6-H	5.53	5.50 (dd, 15.0, 7.5)
7-H	6.16 (dd, 15.2, 10.5)	6.17 (dd, 15.0, 10.5)
8-H	6.05 (dd, 14.8, 10.5)	6.06 (dd, 15.0, 10.5)
9-H	5.32 (dd, 14.8, 8.9)	5.33 (dd, 15.0, 9.0)
10-H	1.12	1.12
11-H	1.10	1.12
12-H	1.49	1.48

13-H	5.16 (dd, 15.2, 8.8)	5.16 (ddd, 15.0, 9.0, 1.0)
14-H	5.46	5.46 (dd, 15.0, 6.5)
15-H	3.09	3.10
16-H	5.25 (d, 8.9)	5.26 (dt, 9.0, 1.0)
18-H	3.82	3.83 (dd, 10.5, 2.5)
19-H$_a$	1.86	1.88
19-H$_b$	2.10	2.11
20-H	5.58	5.58 (dd, 5.5, 1.0)
22-H	4.08	4.08
23-H$_a$	1.52	1.53
23-H$_b$	1.73	1.75
24-H$_3$	0.88 (t, 7.3)	0.89 (t, 7.0)
25-H$_3$	1.06	1.07, (d, 1.0)
26-H$_3$	1.04 (d, 7.1)	1.04 (d, 6.5)
27-H$_3$	1.64 (d, 1.5)	1.65 (d, 1.5)
28-H$_3$	1.59 (s)	1.59 (d, 1)

Table S1. Comparison of ^{1}H-NMR of our synthetic ambruticin J with that reported by Taylor.[12]



3

Position	Our Synthetic Ambruticin J 126 MHz (CD$_3$OD): δ_C	Taylor’s Synthetic Ambruticin J 125 MHz (CD$_3$OD): δ_C[12]
C-1	175.4	177.1
C-2	43.3	44.0
C-3	67.5	67.9
C-4	45.0	44.9
C-5	71.6	71.7
C-6	133.1	133.2
C-7	132.4	132.3
C-8	128.4	128.4
C-9	138.6	138.5
C-10	32.1	32.0
C-11	22.8	22.8
C-12	30.6	30.5
C-13	126.9	126.9
C-14	136.3	136.3
C-15	36.3	36.3
C-16	130.9	130.9
C-17	136.2	136.2
C-18	79.54	79.5
C-19	31.1	31.1
C-20	122.1	122.1
C-21	136.1	136.0
C-22	79.48	79.5
C-23	26.6	26.6
C-24	8.7	8.7

C-25	13.4	13.3
C-26	21.6	21.6
C-27	12.7	12.7
C-28	19.1	19.0

Table S2. Comparison of ^{13}C-NMR of our synthetic ambruticin J and that report by Taylor.[12]

The ^{1}H-NMR and ^{13}C-NMR data for synthetic ambruticin J are in good agreement with the data reported by both Taylor and Reeves.[11,12] The slight deviations in the ^{13}C shifts of C-1 and C-2 are rationalised by considering the exchange/protonation state of the carboxylic acid. Small changes in the exchange/protonation state, caused by differences in pH and/or concentration, are expected to lead to conformational changes in ambruticin J and subsequent changes in chemical shift. Attempts to reconcile the data with that reported by Reeves and Taylor by pH changes were unsuccessful due to decomposition of the sample.

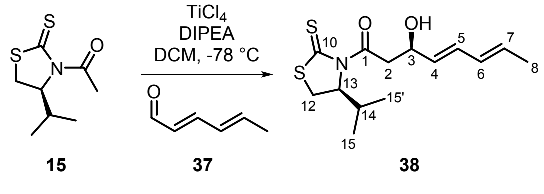
3. Chemical Epoxidation-Cyclisation Studies

3.1. Synthesis of Alkenes 40, 45 and 48

(2*E*,4*E*)-Hexa-2,4-dienal (37)

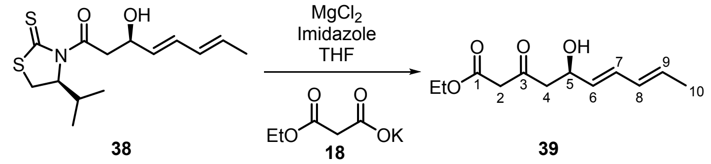
2*E*,4*E*-Hexa-2,4-dienol (0.34 g, 4.4 mmol) was dissolved in DCM (20 mL) under nitrogen when activated MnO$_2$ (11.54 g, 133 mmol) was added and the reaction mixture was stirred for 24 hours. The mixture was filtered over Celite, washed with DCM (50 mL) and the solvent removed *in vacuo* to afford volatile aldehyde **37** (0.42 g, quant.) as a yellow oil; δ_H (400 MHz, CDCl$_3$) 1.87 (3H, d, *J* 5.7, 6-H$_3$), 6.01 (1H, dd, *J* 15.5, 8.0, 2-H), 6.17 – 6.36 (2H, m, 4-H and 5-H), 6.96 – 7.09 (1H, ddd, *J* 15.5, 9.1, 1.1 3-H), 9.49 (1H, dd, *J* 8.0, 1.1, 1-H); δ_C (101 MHz, CDCl$_3$) 19.0 (C-6), 130.0 (C-2), 130.2 (C-4), 142.1 (C-5), 152.8 (C-3), 194.1 (C-1); m/z (ESI): [M+H]$^+$ = 97.06. Data consistent with the literature.[13]

(*R*,4*E*,6*E*)-3-Hydroxy-1-((*S*)-4-isopropyl-2-thioxothiazolidin-3-yl)octa-4,6-dien-1-one (38)



Acylated auxiliary **15** (2.0 g, 9.84 mmol) was dissolved in DCM (100 mL) under nitrogen and cooled to -78 °C when $TiCl_4$ (1 M in DCM, 10 mL, 9.84 mmol) was added dropwise over 15 minutes. The reaction mixture was stirred for 20 minutes then DIPEA (2.1 mL, 11.8 mmol) was added dropwise. The reaction mixture was stirred for 1 hour then aldehyde **37** (1.1 mL, 9.84 mmol) was added dropwise. After stirring at -78 °C for 1 hour, aqueous saturated ammonium chloride (25 mL) was added and the reaction mixture was stirred for a further hour at room temperature. The solution was washed with DCM (3 × 50 mL) dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (18% EtOAc in petroleum ether 60:40) to afford aldol product **38** (1.90 g, 84%) as a yellow oil; $[\alpha]_D^{25}$ = +182.0 (*c* 1, Acetone); ν_{max} (film) 3430, 2962, 1689, 1468, 1162, 725; δ_H (400 MHz, $CDCl_3$) 0.97 (3H, d, *J* 6.9, 15-H_3), 1.05 (3H, d, *J* 6.8, 15'-H_3), 1.75 (3H, d, *J* 6.5, 8-H_3), 2.30 – 2.41 (1H, m, 14-H), 3.02 (1H, d, *J* 11.5, 12-*H*H), 3.33 (1H, dd, *J* 17.5, 8.8, 2-*H*H), 3.51 (1H, dd, *J* 11.5, 7.5, 12-H*H*), 3.61 (1H, dd, *J* 17.5, 3.0, 2-H*H*), 4.64 – 4.78 (1H, m, OH), 5.14 (1H, ap. t, *J* 7.5, 13-H), 5.60 (1H, dd, *J* 15.3, 6.2, 4-H), 5.67 – 5.78 (1H, m, 7-H), 5.98 – 6.09 (1H, m, 6-H), 6.24 (1H, dd, *J* 15.3, 10.5, 5-H); δ_C (101 MHz, $CDCl_3$) 18.0 (C-15), 18.3 (C-8), 19.3 (C-15′), 30.8 (C-12), 31.0 (C-14), 45.5 (C-2), 68.7 (C-3), 71.6 (C-13), 130.7 (C-4), 130.8 (C-6 and C-7), 131.3 (C-5), 172.6 (C-1), 203.2 (C-10); HRMS (ESI) calc. for [$C_{14}H_{21}NO_2S_2Na$] 322.0906 Found 322.0898.

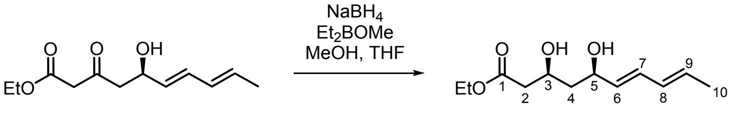
Ethyl (*R*,6*E*,8*E*)-5-hydroxy-3-oxodeca-6,8-dienoate (39)



38 **18** **39**

Potassium-3-ethoxy-2-methyl-3-oxopropanoate (2.82 g, 16.6 mmol) and $MgCl_2$ (0.789 g, 8.29 mmol) were added to a solution of aldol product **38** (2.26 g, 7.54 mmol) in THF (25 mL) under nitrogen and stirred for 45 minutes. Imidazole (0.564 g, 8.29 mmol) was added and the reaction mixture was stirred for 72 hours. The mixture was diluted with EtOAc (30 mL) and washed with 1 M HCl (10 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with aqueous saturated sodium hydrogen carbonate (15 mL) and the aqueous layer extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (15% EtOAc in petroleum ether 60:40) to afford **39** (1.09 g, 64%) as a yellow oil; $[\alpha]_D^{22}$ = +6.0 (*c* 1, Acetone); ν_{max} (film) 3443, 2981, 2914, 1737, 1709, 988; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2, OCH_2CH_3), 1.73 – 1.76 (3H, m, 10-H_3), 2.68 – 2.74 (1H, br. s, OH), 2.74 – 2.80 (2H, m, 4-H_2), 3.47 (2H, s, 2-H_2) , 4.19 (2H, q, *J* 7.2, OCH_2CH_3), 4.61 (1H, ap. q, *J* 6.5, 5-H), 5.53 (1H, ddq, *J* 15.2, 6.4, 0.7, 9-H), 5.71 (1H, dd, *J* 15.0, 6.5, 6-H), 5.97 – 6.04 (1H, m, 8-H), 6.17 – 6.26 (1H, m, 7-H); δ_C (101 MHz, $CDCl_3$) 14.2 (OCH_2CH_3), 18.3 (C-10), 49.8 (C-4), 50.2 (C-2), 61.7 (O*C*H$_2$CH$_3$), 68.4 (C-5), 130.6 (C-9), 130.7 (C-6), 130.9 (C-8), 131.4 (C-7), 167.1 (C-1), 203.0 (C-3); HRMS (ESI) calc. for [C$_{12}$H$_{18}$O$_4$Na] 249.1097 Found 249.1093.

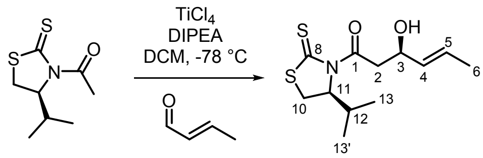
Ethyl (3*S*,5*R*,6*E*,8*E*)-3,5-dihydroxydeca-6,8-dienoate (40)



39 **40**

Ketone **39** (1.01 g, 4.42 mmol) was dissolved in THF (25 mL) and MeOH (7 mL) under nitrogen and cooled to -78 °C when Et$_2$BOMe (0.70 mL, 5.30 mmol) was added dropwise and the reaction mixture was stirred for 15 minutes. NaBH$_4$ (0.19 g, 5.08 mmol) was added in one portion and the reaction mixture was stirred for 3 hours then AcOH (3 mL) was added and the mixture was warmed to room temperature. The reaction mixture was diluted with EtOAc (30 mL) and the resulting solution was washed with aqueous saturated sodium hydrogen carbonate (20 mL). The organic layer was dried over MgSO$_4$ and the solvent removed *in vacuo* to afford diol **40** (1.02 g, quant.) as a yellow oil; $[\alpha]_D^{22}$ = -8.0 (*c* 1, Acetone); ν$_{max}$ (film) 3396, 2981, 2914, 1716, 1164, 987; δ$_H$ (400 MHz, CDCl$_3$) 1.27 (3H, t, *J* 7.1, OCH$_2$*CH$_3$*), 1.57 – 1.72 (2H, m, 4-H$_2$), 1.73 – 1.77 (3H, m, 10-H$_3$), 2.42 – 2.52 (2H, m, 2-H$_2$), 3.07 (1H, br. s, OH), 3.74 (1H, br. s, OH), 4.16 (2H, q, *J* 7.1, O*CH$_2$*CH$_3$), 4.22 – 4.31 (1H, m, 3-H), 4.42 (1H, m, 5-H), 5.54 (1H, dd, *J* 15.2, 6.6, 6-H), 5.71 (1H, dd, *J* 15.0, 6.8, 9-H), 5.97 – 6.08 (1H, m, 8-H), 6.20 (1H, dd, *J* 15.2, 10.4, 7-H); δ$_C$ (101 MHz, CDCl$_3$) 14.3 (OCH$_2$*C*H$_3$), 18.3 (C-10), 41.8 (C-2), 42.9 (C-4), 61.0 (O*C*H$_2$CH$_3$), 68.5 (C-3), 72.6 (C-5), 130.5 (C-9), 130.85 (C-8), 130.93 (C-7), 132.4 (C-6), 172.7 (C-1); HRMS (ESI) calc. for [C$_{12}$H$_{20}$O$_4$Na] 251.1254 Found 251.1252.

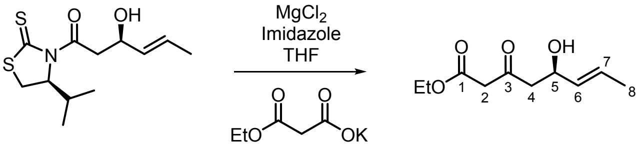
(*R*,*E*)-3-Hydroxy-1-((*S*)-4-isopropyl-2-thioxothiazolidin-3-yl)hex-4-en-1-one (S29)



15 **S29**

Acylated auxiliary **15** (1.69 g, 8.37 mmol) was dissolved in DCM (85 mL) under nitrogen and cooled to -78 °C when TiCl$_4$ (1 M in DCM, 8.37 mL, 8.37 mmol) was added dropwise over 15 minutes. The reaction mixture was stirred for 20 minutes when DIPEA (1.75 mL, 10.04 mmol) was added dropwise. The reaction mixture was stirred for 1 hour then crotonaldehyde (0.69 mL, 8.37 mmol) was added dropwise. After stirring at -78 °C for 1 hour, aqueous saturated ammonium chloride (25 mL) was added and the reaction mixture was stirred for a further hour at room temperature. The solution was washed with DCM (3 × 50 mL) dried over MgSO$_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (30% EtOAc in petroleum ether 60:40) to afford aldol product **S29** (1.73 g, 76%) as a yellow oil; $[\alpha]_D^{22}$ = +251.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3419, 2962, 1688, 1156; δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 7.0, 13-H_3), 1.06 (3H, d, *J* 6.8, 13′-H_3), 1.71 (3H, dd, *J* 6.5, 1.5, 6-H_3), 2.30 – 2.43 (1H, m, 12-H), 2.76 (1H, d, *J* 4.0, OH), 3.03 (1H, dd, *J* 11.5, 1.1, 10-*H*H), 3.29 (1H, dd, *J* 17.5, 9.0, 2-*H*H), 3.52 (1H, dd, *J* 11.5, 8.0, 10-H*H*), 3.61 (1H, dd, *J* 17.5, 2.9, 2-H*H*), 4.61 (1H, m, 3-H), 5.16 (1H, ddd, *J* 8.0, 6.2, 1.1, 11-H), 5.51 – 5.60 (1H, ddq, *J* 15.4, 6.4, 1.5, 4-H), 5.69 – 5.83 (1H, dqd, *J* 15.4, 6.5, 1.1, 5-H); δ_C (101 MHz, $CDCl_3$) 17.9 (C-6), 18.0 (C-13), 19.3 (C-13′), 30.8 (C-10), 31.0 (C-12), 45.6 (C-2), 68.9 (C-3), 71.6 (C-11), 127.6 (C-5), 131.9 (C-4), 172.8 (C-8), 203.16 (C-1); HRMS (ESI) calc. for [$C_{12}H_{19}NO_2S_2Na$] 296.0749 Found 296.0743.

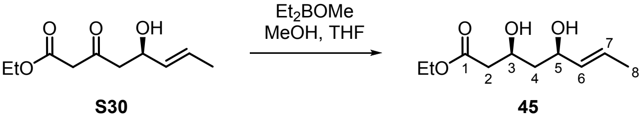
Ethyl (*R*,*E*)-5-hydroxy-3-oxooct-6-enoate (S30)



S29 **S30**

Potassium-3-ethoxy-2-methyl-3-oxopropanoate (1.89 g, 11.1 mmol) and $MgCl_2$ (0.53 g, 5.6 mmol) were added to a solution of aldol product **S29** (1.38 g, 5.05 mmol) in THF (20 mL) under nitrogen and stirred for 45 minutes. Imidazole (0.38 g, 5.55 mmol) was added and the reaction mixture was stirred for 72 hours. The mixture was diluted with EtOAc (30 mL) and washed with 1 M HCl (10 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with aqueous saturated sodium hydrogen carbonate (15 mL) and the aqueous layer extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (30% EtOAc in petroleum ether 60:40) to afford **S30** (0.79 g, 78%) as a yellow oil; $[\alpha]_D^{23}$ = -4.0 (*c* 1, Acetone); ν_{max} (film) 3427, 2982, 2920, 1737, 1709, 1027; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2, OCH_2CH_3), 1.69 (3H, dd, *J* 6.5, 1.7, 8-H_3), 2.65 (1H, br. s, OH), 2.75 (2H, d, *J* 6.5, 4-H_2), 3.47 (1H, s, 2-H_2), 4.19 (2H, q, *J* 7.2, OCH_2CH_3), 4.54 (1H, ap. br. q, *J* 6.5, 5-H), 5.48 (1H, ddq, *J* 15.3, 6.5, 1.7, 6-H), 5.73 (1H, dqd, *J* 15.3, 6.5, 1.0, 7-H); δ_C (101 MHz, $CDCl_3$) 14.3 (OCH_2CH_3), 17.8 (C-8), 49.8 (C-4), 50.2 (C-2), 61.7 (OCH_2CH_3), 68.7 (C-5), 127.7 (C-7), 131.9 (C-6), 167.1 (C-1), 203.2 (C-3); HRMS (ESI) calc. for [$C_{10}H_{16}O_4Na$] 223.0941 Found 223.0948.

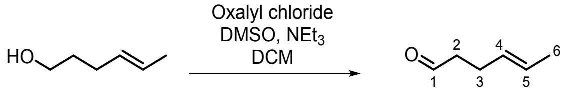
Ethyl (3*S*,5*R*,*E*)-3,5-dihydroxyoct-6-enoate (45)



S30 **45**

Ketone **S30** (750 mg, 3.75 mmol) was dissolved in THF (25 mL) and MeOH (7 mL) under nitrogen and cooled to -78 °C when Et_2BOMe (0.59 mL, 4.49 mmol) was added dropwise and the reaction mixture was stirred for 15 minutes. $NaBH_4$ (163 mg, 4.30 mmol) was added in one portion and the reaction mixture was stirred for 3 hours then AcOH (4 mL) was added and the mixture was warmed to room temperature. The reaction mixture was diluted with EtOAc (25 mL) and the resulting solution was washed with aqueous saturated sodium hydrogen carbonate (20 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (45% EtOAc in petroleum ether 60:40) to afford diol **45** (561 mg, 74%) as a yellow oil; $[\alpha]_D^{23}$ = +56.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3406, 2938, 1731, 1160, 966; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.1, OCH_2CH_3), 1.59 (1H, ap. dt, *J* 14.3, 3.2, 4-*H*H), 1.64 – 1.75 (4H, m, 4-H*H* and 8-H_3), 2.39 – 2.56 (2H, m, 2-H_2), 2.98 (1H, d, *J* 2.1, 5-OH), 3.72 (1H, d, *J* 2.8, 3-OH), 4.17 (2H, q, *J* 7.1, OCH_2CH_3), 4.20 – 4.31 (1H, m, 3-H), 4.31 – 4.38 (1H, m, 5-H), 5.48 (1H, ddq, *J* 15.3, 7.0, 1.6, 6-H), 5.70 (1H, dqd, *J* 15.3, 6.6, 0.9, 7-H); δ_C (101 MHz, $CDCl_3$) 14.3 (OCH_2CH_3), 17.8 (C-8), 41.8 (C-2), 42.9 (C-4), 61.0 (OCH_2CH_3), 68.5 (C-3), 73.0 (C-5), 127.1 (C-7), 133.6 (C-6), 172.7 (C-1); HRMS (ESI) calc. for $[C_{10}H_{19}O_4]$ 203.1278 Found 203.1281.

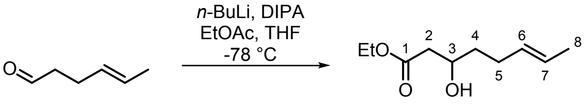
(*E*)-Hex-4-enal (S32)



S31 **S32**

Oxalyl chloride (1.69 mL, 20.0 mmol) was dissolved in DCM (50 mL) and cooled to -78 °C under nitrogen then DMSO (2.13 mL, 30.0 mmol) was added dropwise. The reaction mixture was stirred for 30 minutes then alcohol **S31** (1.18 mL, 10.0 mmol) was added dropwise and the mixture was stirred for an additional hour. Triethyl amine (6.27 mL, 45.0 mmol) was added and the reaction mixture was warmed to room temperature. Water (40 mL) was added and the organic layer separated. The aqueous was extracted with further DCM (2 × 50 mL). The combined organic layers were washed sequentially with 2 M HCl (2 × 30 mL), aqueous saturated sodium hydrogen carbonate (2 × 30 mL) and brine (30 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo* at 0 °C to afford aldehyde **S32** (912 mg, 93%) as an orange oil; ν_{max} (film) 2919, 2856, 2721, 1724, 966; δ_H (400 MHz, $CDCl_3$) 1.63 – 1.66 (3H, m, 6-H_3), 2.28 – 2.36 (2H, m, 3-H_2), 2.45 – 2.53 (2H, m, 2-H_2), 5.37 – 5.55 (2H, m, 4-H and 5-H), 9.76 (1H, t, *J* 1.7, 1-H); δ_C (101 MHz, $CDCl_3$) 18.0 (C-6), 25.3 (C-3), 43.7 (C-2), 126.6 (C-5) , 129.1 (C-4), 202.7 (C-1); m/z (ESI): $[M+H]^+$ = 99.08. Data consistent with the literature.[14]

(±)-Ethyl (*E*)-3-hydroxyoct-6-enoate (49)

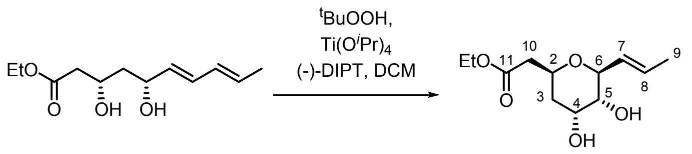


S32 **49**

DIPA (1.41 mL, 10.09 mmol) was dissolved in THF (40 mL) under nitrogen and cooled to 0 °C when 1.5 M *n*-BuLi in hexanes (6.11 mL, 9.17 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 20 minutes and then cooled to -78 °C. EtOAc (2.69 mL, 27.51 mmol) was added dropwise and the reaction mixture was stirred for 20 minutes. Aldehyde **S32** (601 mg, 6.11 mmol) in THF (5 mL) was added dropwise and the reaction mixture was stirred at -78 °C for 2 hours and quenched with aqueous saturated ammonium chloride (10 mL). The reaction mixture was warmed to room temperature and extracted with Et_2O (3 × 75 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (30% Et_2O in petroleum ether 60:40) to afford alcohol **49** (640 mg, 56%) as a yellow oil; ν_{max} (film) 3450, 2920, 1732, 1717, 1157; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.1, OCH_2CH_3), 1.38 – 1.52 (1H, m, 4-*H*H), 1.52 – 1.62 (1H, m, 4-H*H*), 1.62-1.66 (3H, m, 8-H_3) 1.98 – 2.20 (2H, m, 5-H_2), 2.40 (1H, dd, *J* 16.4, 8.9, 2-*H*H), 2.49 (1H, dd, *J* 16.4, 3.3, 2-H*H*), 2.93 (1H, d, *J* 4.0, OH), 3.89 – 4.08 (1H, m, 3-H), 4.17 (1H, q, *J* 7.1, OCH_2CH_3), 5.35 – 5.54 (2H, m, 6-H and 7-H); δ_C (101 MHz, $CDCl_3$) 14.4 (OCH_2CH_3), 18.1 (C-8), 28.7 (C-5), 36.4 (C-4), 41.4 (C-2), 60.9 (OCH_2CH_3), 67.7 (C-3), 125.8 (C-7), 130.7 (C-6), 173.2 (C-1); HRMS (ESI) calc. for [$C_{10}H_{19}O_3$] 187.1329 Found 187.1329.

3.2. Chemical Epoxidation-Cyclisation Studies

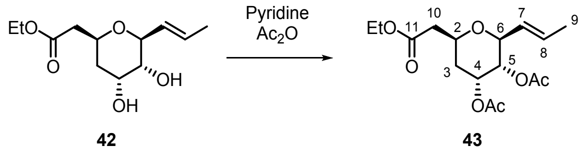
Ethyl 2-((2*S*,4*R*,5*R*,6*S*)-4,5-dihydroxy-6-((*E*)-prop-1-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (42)



40 **42**

In a flame dried flask at -20 °C under nitrogen was added 4 Å molecular sieves (20 mg) and DCM (2 mL) followed by $Ti(O^iPr)_4$ (0.02 mL, 0.03 mmol) and (-)-DIPT (0.01 mL, 0.03 mmol). The reaction mixture was stirred for 5 minutes when allyl alcohol **40** (57 mg, 0.25 mmol) in DCM (1 mL) was added and the solution was stirred for 30 minutes. ^tBuOOH (0.19 mL, 0.5 mmol) was added dropwise and the reaction mixture was stirred at -5 °C for 5 hours. The reaction mixture was quenched with 10 wt.% aqueous tartaric acid (3 mL) and warmed to room temperature. The organic layer was separated and the aqueous extracted with DCM (3 × 15 mL). The combined organic layers were washed with aqueous saturated sodium thiosulfate (10 mL), dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (65% EtOAc in petroleum ether 60:40) to afford tetrahydropyran **42** (32 mg, 52%) as a colourless oil; $[\alpha]^{22}_{D}$ = -34.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3431, 2984, 2920, 1729, 1373, 1071; δ_H (400 MHz, $CDCl_3$) 1.24 (3H, t, *J* 7.1, OCH_2CH_3), 1.61 (1H, ddd, *J* 14.2, 11.7, 2.8, 3-H_{ax}), 1.74 (3H, dd, *J* 6.5, 1.7, 9-H_3), 1.99 (1H, ddd, *J* 14.2, 3.6, 2.1, 3-H_{eq}), 2.16 (1H, br. s, OH), 2.38 (1H, dd, *J* 15.2, 5.9, 10-*H*H), 2.54 (1H, dd, *J* 15.2, 7.3, 10-H*H*), 2.63 (1H, br. s, OH), 3.32 (1H, dd, *J* 9.8, 3.1, 5-H), 3.98 (1H, dd, *J* 9.8, 7.8, 6-H), 4.07 – 4.18 (3H, m, OCH_2CH$_3$ and 4-H), 4.20 – 4.30 (1H, m, 2-H), 5.45 (1H, ddq, *J* 15.4, 7.8, 1.7, 7-H), 5.79 – 5.91 (1H, dq, *J* 15.4, 6.5, 8-H); δ_C (101 MHz, $CDCl_3$) 14.3 (OCH_2CH_3), 18.1 (C-9), 37.1 (C-3), 40.8 (C-10), 60.6 (OCH_2CH_3), 66.6 (C-4), 68.0 (C-2), 71.0 (C-5), 76.9 (C-6), 128.9 (C-7), 132.0 (C-8), 171.0 (C-11); HRMS (ESI) calc. for [$C_{12}H_{21}O_5$] 245.1384 Found 245.1379.

(2*S*,3*R*,4*R*,6*S*)-6-(2-Ethoxy-2-oxoethyl)-2-((*E*)-prop-1-en-1-yl)tetrahydro-2H-pyran-3,4-diyl diacetate (43)



Diol **42** (30 mg, 0.12 mmol) was dissolved in pyridine (0.25 mL, 3.01 mmol) and Ac_2O (0.11 mL, 1.2 mmol) and stirred under nitrogen for 16 hours. The reaction mixture was diluted with water (10 mL) and extracted with DCM (2 × 15 mL). The combined organic layers were washed sequentially with 2 M HCl (2 × 5 mL), sodium hydrogen carbonate (2 × 10 mL) and brine (25 mL). The combined organics were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (40% EtOAc in petroleum ether 60:40) to afford diacetate **43** (32 mg, 82%) as a colourless oil; $[\alpha]_D^{18}$ = -20.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2981, 2938, 1736, 1370, 1243, 1055; δ_H (400 MHz, $CDCl_3$) 1.24 (3H, t, *J* 7.1, OCH_2CH_3), 1.67 (3H, dd, *J* 6.6, 1.7, 9-H_3), 1.70 – 1.77 (1H, m, 3-*H*H), 1.91 – 1.95 (1H, m, 3-H*H*), 1.96 (3H, s, OAc), 2.13 (3H, s, OAc), 2.38 (1H, dd, *J* 15.5, 5.8, 10-*H*H), 2.58 (1H, dd, *J* 15.5, 7.3, 10-H*H*), 4.11 – 4.17 (3H, m, CH_3CH_2O and 6-H), 4.18 – 4.25 (1H, m, 2-H), 4.66 (1H, dd, *J* 10.1, 3.1, 5-H), 5.34 (1H, ddq, *J* 15.3, 7.2, 1.7, 7-H), 5.40 (1H, ap. q, *J* 3.1, 4-H), 5.72 – 5.82 (1H, m, 8-H); δ_C (101 MHz, $CDCl_3$) 14.3 (CH_3CH_2O), 18.1 (C-9), 21.0 (OAc), 21.3 (OAc), 35.6 (C-3), 40.6 (C-10), 60.8 (CH_3CH_2O), 67.4 (C-4), 68.8 (C-2), 70.9 (C-5), 75.0 (C-6), 127.8 (C-7), 131.1 (C-8), 170.1 (OAc), 170.4 (OAc), 170.9 (C-11); HRMS (ESI) calc. for [$C_{16}H_{24}O_7Na$] 315.1414 Found 315.1402.

Upon acetylation of diol **42**, protons 4-H and 5-H exhibited significant downfield shifts, whilst 6-H showed little change in chemical shift (Figure **S1**). This is consistent with the assigned structure of THP **42**.

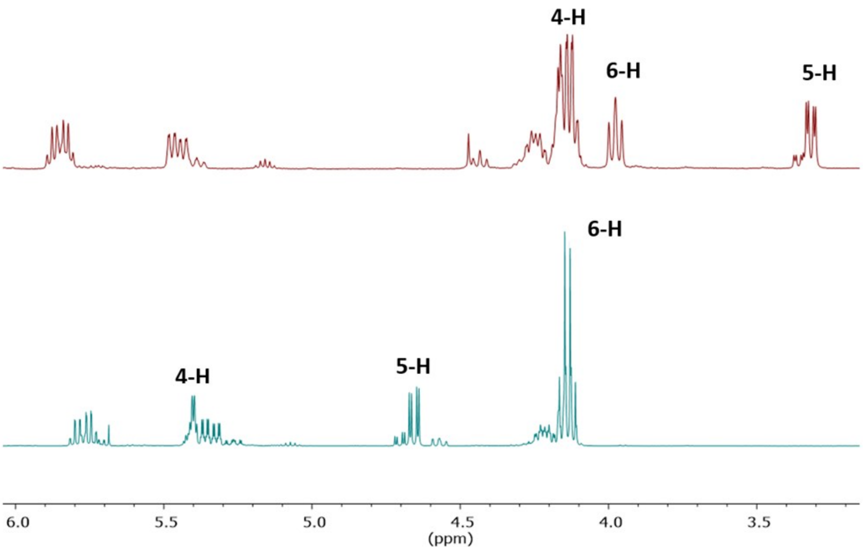
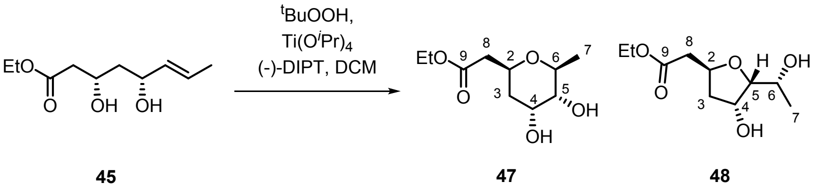


Figure S1. Comparison of key ^{1}H-NMR shifts of diol **42** (Red) and acetylated diol **43** (Blue) used to confirm product.

Ethyl 2-((2*S*,4*R*,5*R*,6*S*)-4,5-dihydroxy-6-methyltetrahydro-2H-pyran-2-yl)acetate (47) and ethyl 2-((2*S*,4*R*,5*R*)-4-hydroxy-5-((*R*)-1-hydroxyethyl)tetrahydrofuran-2-yl)acetate (48)



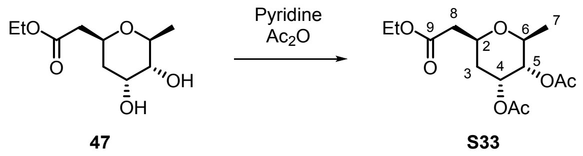
In a flame dried flask at -20 °C under nitrogen was added 4 Å molecular sieves (30 mg) and DCM (2.5 mL) followed by Ti(O^{i}Pr)$_4$ (0.03 mL, 0.10 mmol) and (-)-DIPT (0.03 mL, 0.12 mmol). The reaction mixture was stirred for 5 minutes then allyl alcohol **45** (100 mg, 0.49 mmol) in DCM (0.5 mL) was added and the solution was stirred for 30 minutes. ^{t}BuOOH (0.18 mL, 0.99 mmol) was added dropwise and the reaction mixture was stirred at -5 °C for 5 hours. The reaction mixture was quenched with 10 wt.% aqueous tartaric acid (5 mL) and warmed to room temperature. The organic layer was separated and the aqueous extracted with DCM (3 × 15 mL). The combined organic layers were washed with aqueous saturated sodium thiosulfate (10 mL), dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (70% EtOAc in petroleum ether 60:40) to afford tetrahydropyran **47** (47 mg, 44%) and tetrahydrofuran **48** (20 mg, 19%) as colourless oils.

47: $[\alpha]_D^{22}$ = -85.0 (*c* 1, $CHCl_3$); ν_{max} (film) 3436, 2983, 2923, 1731, 1372, 1180, 1061; δ_H (400 MHz, $CDCl_3$) 1.21 (3H, d, *J* 6.2, 7-H_3), 1.23 (3H, t, *J* 7.1, OCH_2CH_3). 1.58 (1H, ddd, *J* 14.0, 11.6, 2.6, 3-H_{ax}), 1.94 (1H, ddd, *J* 14.0, 3.5, 2.0, 3-H_{eq}), 2.34 (1H, dd, *J* 15.2, 5.6, 8-*H*H), 2.49 (1H, dd, *J* 15.2, 7.7, 8-H*H*), 2.82 (1H, br. s, 5-OH), 3.00 (1H, br. s, 4-OH), 3.20 (1H, m, 5-H), 3.64 (1H, dq, *J* 9.5, 6.2, 6-H), 4.07 (1H, m, 4-H), 4.12 (2H, q, *J* 7.1, OCH_2CH_3), 4.18 (1H, ddd, *J* 7.7, 5.6, 2.0, 2-H); δ_C (101 MHz, $CDCl_3$) 14.3 (C-7), 18.4

(OCH_2CH_3), 38.0 (C-3), 40.9 (C-8), 60.8 (OCH_2CH_3), 67.4 (C-4), 68.1 (C-2), 71.8 (C-6), 73.4 (C-5), 171.6 (C-9); HRMS (ESI) calc. for [$C_{10}H_{19}O_5$] 219.1227 Found 219.1223.

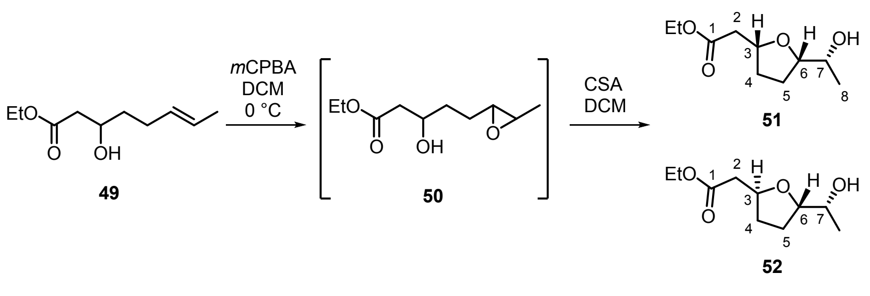
48: $[\alpha]_D^{23}$ = +3.0 (*c* = 0.67, $CHCl_3$); ν_{max} (film) 3419, 2981, 2925, 1732, 1062; δ_H (400 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.1, OCH_2CH_3), 1.34 (3H, d, *J* 6.6, 7-H_3), 1.71 – 1.81 (1H, m, 3-*H*H), 2.21 (1H, ddd, *J* 13.2, 5.6, 1.1, 3-H*H*), 2.53 (1H, dd, *J* 15.5, 5.5, 8-*H*H), 2.61 (1H, dd, *J* 15.5, 7.3, 8-H*H*), 3.08 (1H, s, 6-OH), 3.68 (1H, dd, *J* 4.9, 3.3, 5-H), 4.00 (1H, s, 4-OH), 4.12 – 4.20 (3H, m, OCH_2CH_3 and 6-H), 4.48 – 4.61 (1H, m, 4-H), 4.62 – 4.76 (1H, m, 2-H); δ_C (101 MHz, $CDCl_3$) 14.4 (OCH_2CH_3), 18.9 (C-7), 40.9 (C-8), 41.8 (C-3), 60.8 (OCH_2CH_3), 67.9 (C-6), 73.3 (C-4), 74.8 (C-2), 84.4 (C-5), 171.5 (C-9); HRMS (ESI) calc. for [$C_{10}H_{19}O_5$] 219.1227 Found 219.1230.

(2*S*,3*R*,4*S*,6*S*)-2-(2-Ethoxy-2-oxoethyl)-6-methyltetrahydro-2H-pyran-4,5-diyl diacetate (S33)



Diol **47** (40 mg, 0.18 mmol) was dissolved in pyridine (0.37 mL, 4.57 mmol) and Ac_2O (0.17 mL, 1.8 mmol) and stirred under nitrogen for 16 hours. The reaction mixture was diluted with water (10 mL) and extracted with DCM (2 × 15 mL). The combined organic layers were washed with 2 M HCl (2 × 5 mL), sodium hydrogen carbonate (2 × 10 mL) and brine (25 mL). The combined organics were dried over $MgSO_4$ and the solvent removed *in vacuo* to afford diacetate **S33** (51 mg, 94%) as a yellow oil; $[\alpha]_D^{23}$ = -115.0 (*c* 1, $CHCl_3$); ν_{max} (film) 2988, 2928, 1736, 1370, 1245, 1053; δ_H (400 MHz, $CDCl_3$) 1.13 (3H, d, *J* 6.2, 7-H_3), 1.25 (3H, t, *J* 7.1, OCH_2CH_3), 1.71 (1H, ddd, *J* 14.4, 11.6, 2.6, 3-H_{ax}), 1.92 (1H, ddd, *J* 14.4, 3.7, 2.2, 3-H_{eq}), 1.99 (3H, s, OAc), 2.10 (3H, s, OAc), 2.35 (1H, dd, *J* 15.4, 5.3, 8-*H*H), 2.52 (1H, dd, *J* 15.4, 7.8, 8-H*H*), 3.87 (1H, dq, *J* 10.0, 6.2, 6-H), 4.15 (2H, q, *J* 7.1, OCH_2CH_3), 4.18 – 4.22 (1H, m, 2-H), 4.52 (1H, dd, *J* 10.0, 3.0, 5-H), 5.39 (1H, m, 4-H); δ_C (101 MHz, $CDCl_3$) 14.4 (OCH_2CH_3), 18.1 (C-7), 21.0 (OAc), 21.20 (OAc), 35.8 (C-3), 40.7 (C-8), 60.8 (OCH_2CH_3), 67.3 (C-4), 69.0 (C-2), 70.2 (C-6), 73.1 (C-5), 170.2 (OAc), 170.3 (OAc), 171.0 (C-9); HRMS (ESI) calc. for [$C_{14}H_{23}O_7$] 303.1438 Found 303.1427.

(±)-Ethyl 2-(5-(1-hydroxyethyl)tetrahydrofuran-2-yl)acetate (51 and 52)

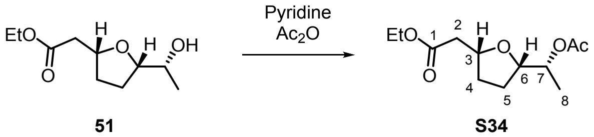


Alkene **49** (300 mg, 1.61 mmol) was dissolved in DCM (10 mL) under nitrogen and cooled to 0 °C when *m*CPBA (70 wt%, 596 mg, 2.42 mmol) was added and the reaction mixture was stirred for 3 hours. The reaction mixture was diluted with aqueous saturated sodium thiosulfate solution (15 mL) and DCM (10 mL). The organic layer was separated and the aqueous extracted with further DCM (2 × 50 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (70% Et_2O in petroleum ether 60:40) to afford a complex mixture. The crude mixture was dissolved in DCM (10 mL) and CSA (32 mg, 0.14 mmol) was added. The reaction mixture was stirred for 18 hours and quenched with aqueous saturated sodium hydrogen carbonate (5 mL). The organic layer was separated and the aqueous extracted with further DCM (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (50% EtOAc in petroleum ether 60:40) to afford tetrahydrofuran **51** (112 mg, 34%) and tetrahydrofuran **52** (98 mg, 30%) as colourless oils. The diastereoisomers were determined by nOe analysis showing enhancements between 3-H and 6-H for **51** (see NMR appendix).

51: (Syn) ν_{max} (film) 3453, 2977, 2880, 1733, 1067; δ_H (400 MHz, $CDCl_3$) 1.09 (3H, d, *J* 6.6, 8-H_3), 1.26 (3H, t, *J* 7.2, OCH$_2$*CH*$_3$), 1.61 – 1.71 (1H, m, 4-*H*H), 1.71 – 1.83 (1H, m, 5-*H*H), 1.94 1H, (ap. dq, *J* 12.4, 8.0, 5-H*H*), 2.06 (1H, ap. dtd, *J* 12.0, 8.0, 7.0, 4-H*H*), 2.45 – 2.57 (2H, m, 2-H_2), 2.67 – 2.75 (1H, m, OH), 3.85 (1H, ddd, *J* 8.0, 7.0, 3.0, 6-H), 3.93 – 4.04 (1H, m, 7-H), 4.07 – 4.26 (2H, m, O*CH*$_2$CH$_3$), 4.33 (1H, ap. tt, *J* 7.0, 5.6, 3-H); δ_C (101 MHz, $CDCl_3$) 14.3 (OCH$_2$*C*H$_3$), 18.0 (C-8), 23.3 (C-5), 31.2 (C-4), 41.0 (C-2), 60.9 (O*C*H$_2$CH$_3$), 67.3 (C-7), 75.7 (C-3), 84.0 (C-6), 171.7 (C-1); HRMS (ESI) calc. for [$C_{10}H_{18}NaO_4$] 225.1097 Found 225.1100.

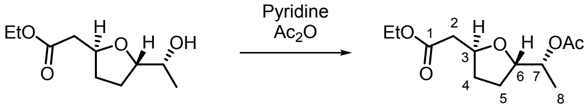
52: (Anti) ν_{max} (film) 3453, 2976, 2876, 1733, 1064; δ_H (400 MHz, $CDCl_3$) 1.10 (3H, d, *J* 6.5, 8-H_3), 1.26 (3H, t, *J* 7.1, OCH$_2$*CH*$_3$), 1.57 – 1.70 (1H, m, 4-*H*H), 1.83 – 1.96 (2H, m, 5-H_2), 2.08 – 2.20 (2H, m, OH and 4-H*H*), 2.45 (1H, dd, *J* 15.2, 6.0, 2-*H*H), 2.59 (1H, dd, *J* 15.2, 7.5, 2-H*H*), 3.84 – 4.02 (2H, m, 6-H and 7-H), 4.15 (2H, q, *J* 7.1, O*CH*$_2$CH$_3$), 4.40 (1H, ap. tt, *J* 7.5, 6.0, 3-H); δ_C (101 MHz, $CDCl_3$) 14.4 (OCH$_2$*C*H$_3$), 18.1 (C-8), 24.9 (C-5), 32.2 (C-4), 41.0 (C-2), 60.7 (O*C*H$_2$CH$_3$), 68.0 (C-7), 76.3 (C-3), 82.9 (C-6), 171.4 (C-1); HRMS (ESI) calc. for [$C_{10}H_{18}NaO_4$] 225.1097 Found 225.1105.

(±)-Ethyl 2-((2*R*,5*S*)-5-((*R*)-1-acetoxyethyl)tetrahydrofuran-2-yl)acetate (S34)



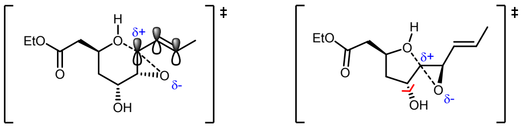
Alcohol **51** (50 mg, 0.25 mmol) was dissolved in pyridine (0.34 mL, 4.20 mmol) and Ac_2O (0.24 mL, 2.50 mmol) and stirred under nitrogen for 16 hours. The reaction mixture was diluted with water (10 mL) and extracted with DCM (2 × 15 mL). The combined organic layers were washed with 2 M HCl (2 × 5 mL), aqueous saturated sodium hydrogen carbonate (2 × 10 mL) and brine (25 mL). The combined organics were dried over MgSO$_4$ and the solvent removed *in vacuo* to afford acetate **S34** (63 mg, quant.) as a yellow oil; ν_{max} (film) 2981, 2878, 1732, 1238, 1033; δ_H (400 MHz, CDCl$_3$) 1.19 (3H, d, *J* 6.4, 8-H$_3$), 1.24 (3H, t, *J* 7.1, OCH$_2$*CH$_3$*), 1.60 (1H, ap. ddt, *J* 11.9, 8.5, 6.7, 4-*H*H), 1.77 (1H, ap. ddt, *J* 12.5, 8.5, 7.0, 5-*H*H), 1.94 (1H, ap. dq, *J* 12.5, 7.0, 5-H*H*), 2.00 – 2.11 (4H, m, 4-H*H* and OAc), 2.41 (1H, dd, *J* 15.1, 6.6, 2-*H*H), 2.60 (1H, dd, *J* 15.1, 6.7, 2-H*H*), 3.91 (1H, ap. td, *J* 7.0, 4.7, 6-H), 4.07 – 4.19 (2H, m, O*CH$_2$*CH$_3$), 4.30 (1H, m, 3-H), 4.90 (1H, ap. qd, *J* 6.4, 4.7, 7-H); δ_C (101 MHz, CDCl$_3$) 14.7 (OCH$_2$*C*H$_3$), 16.5 (C-8), 21.9 (OAc), 27.3 (C-5), 31.3 (C-4), 41.5 (C-2), 61.0 (O*C*H$_2$CH$_3$), 72.2 (C-7), 76.6 (C-3), 81.6 (C-6), 171.0 (OAc), 171.7 (C-1); HRMS (ESI) calc. for [C$_{12}$H$_{20}$NaO$_5$] 267.1203 Found 267.1192.

(±)-Ethyl 2-((2S,5*S*)-5-((*R*)-1-acetoxyethyl)tetrahydrofuran-2-yl)acetate (S35)



52 **S35**

Alcohol **52** (25 mg, 0.13 mmol) was dissolved in pyridine (0.17 mL, 2.10 mmol) and Ac$_2$O (0.12 mL, 1.25 mmol) and stirred under nitrogen for 16 hours. The reaction mixture was diluted with water (10 mL) and extracted with DCM (2 × 15 mL). The combined organic layers were washed with 2 M HCl (2 × 5 mL), aqueous saturated sodium hydrogen carbonate (2 × 10 mL) and brine (25 mL). The combined organics were dried over MgSO$_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography (20% EtOAc in petroleum ether 60:40) to afford acetate **S35** (26 mg, 83%) as a colourless oil; ν_{max} (film) 2981, 2939, 1731, 1371, 1238; δ_H (400 MHz, CDCl$_3$) 1.19 (3H, d, *J* 6.5, 8-H$_3$), 1.24 (3H, t, *J* 7.1, OCH$_2$*CH$_3$*), 1.49 – 1.67 (1H, m, 4-*H*H), 1.67 – 1.86 (1H, m, 5-*H*H), 1.94 – 2.08 (4H, m, 5-H*H* and OAc), 2.08 – 2.21 (1H, m, 4-H*H*), 2.41 (1H, dd, *J* 15.2, 6.8, 2-*H*H), 2.62 (1H, dd, *J* 15.2, 6.5, 2-H*H*), 4.00 (1H, ap. td, *J* 7.2, 4.8, 6-H), 4.13 (2H, q, *J* 7.1, O*CH$_2$*CH$_3$), 4.26 – 4.38 (1H, m, 3-H), 4.90 (1H, ap. qd, *J* 6.5, 4.8, 7-H); δ_C (101 MHz, CDCl$_3$) 14.3 (OCH$_2$*C*H$_3$), 15.9 (C-8), 21.5 (OAc), 27.5 (C-5), 31.8 (C-4), 40.8 (C-2), 60.6 (O*C*H$_2$CH$_3$), 72.3 (C-7), 76.3 (C-3), 80.7 (C-6), 170.7 (OAc), 171.2 (C-1); HRMS (ESI) calc. for [C$_{12}$H$_{20}$NaO$_5$] 267.1203 Found 267.1196.



Stabilised 6-*endo* Transition State

Detabilised 5-*exo* Transition State

Figure S2. Proposed role of 8,9-alkene and C-5 alcohol in directing cyclisation of 4,5-epoxy alcohol **40**.

4. References

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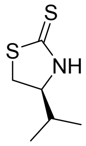
5. NMR Appendix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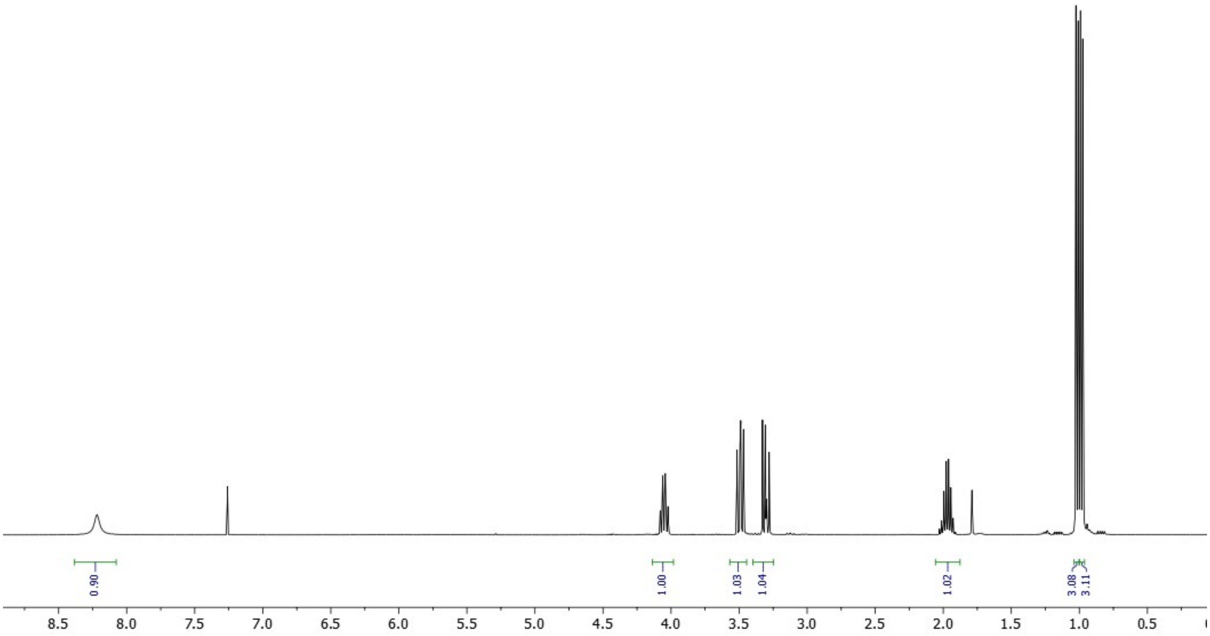
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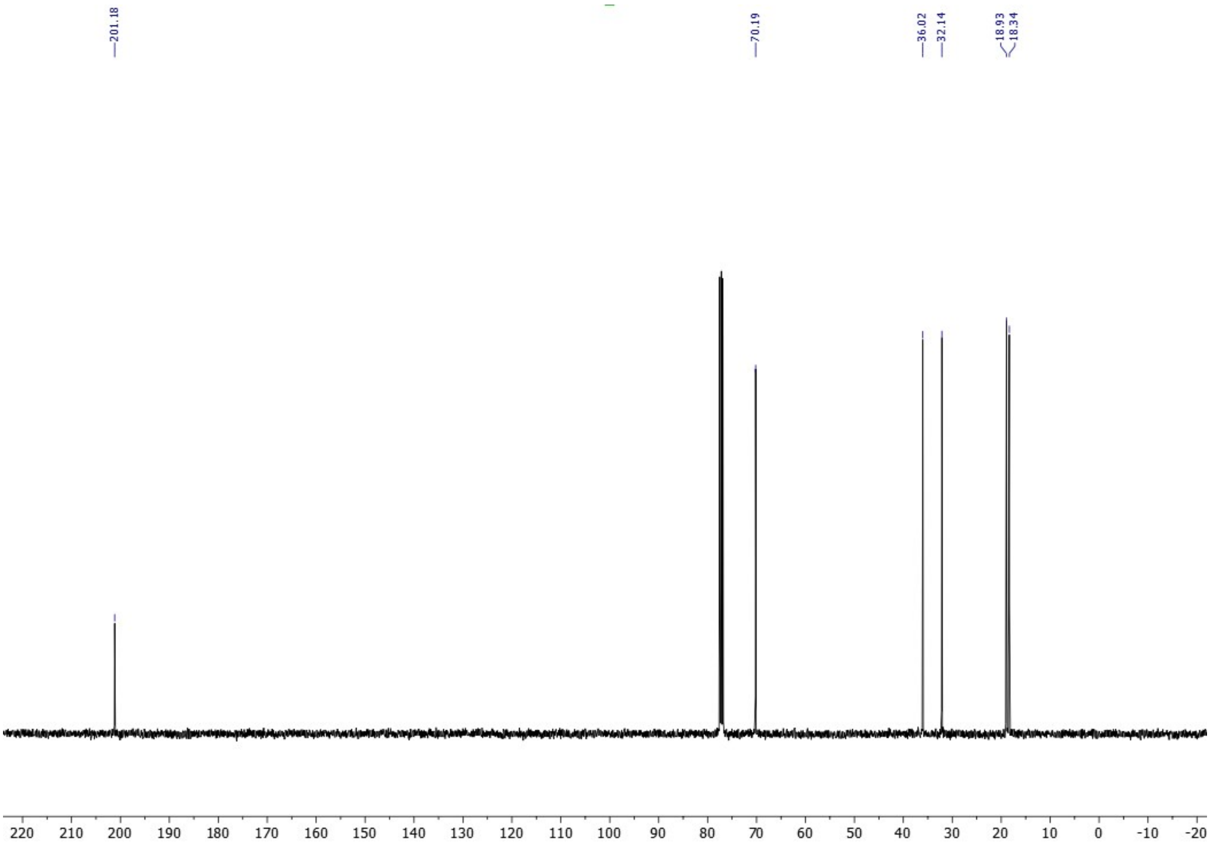
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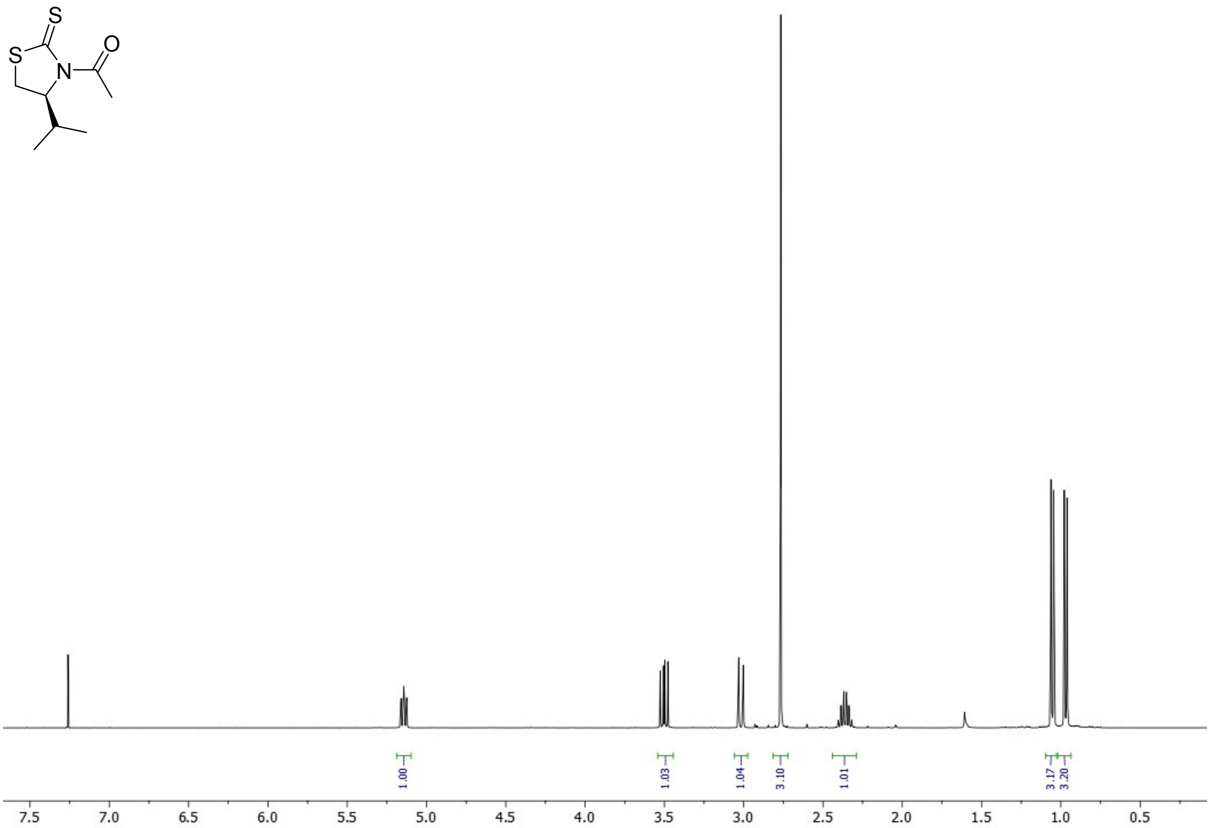
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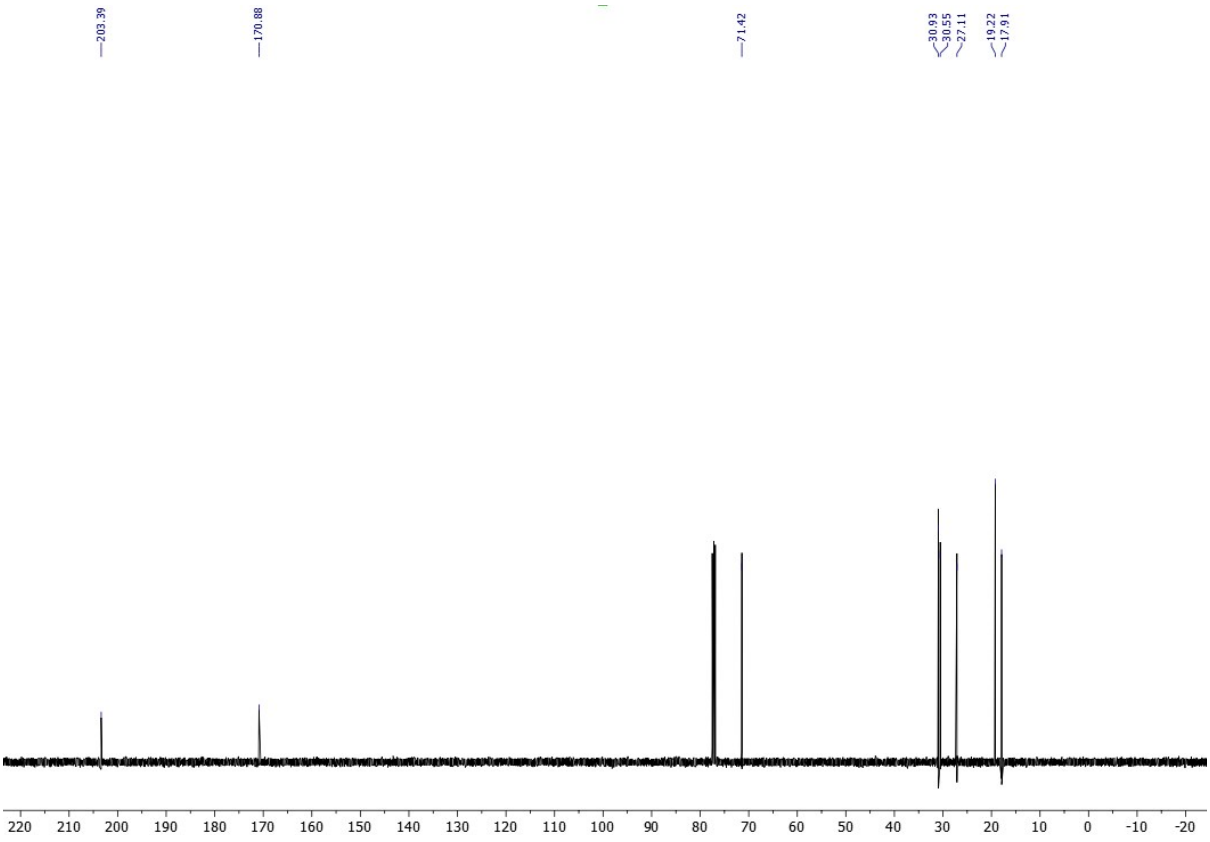
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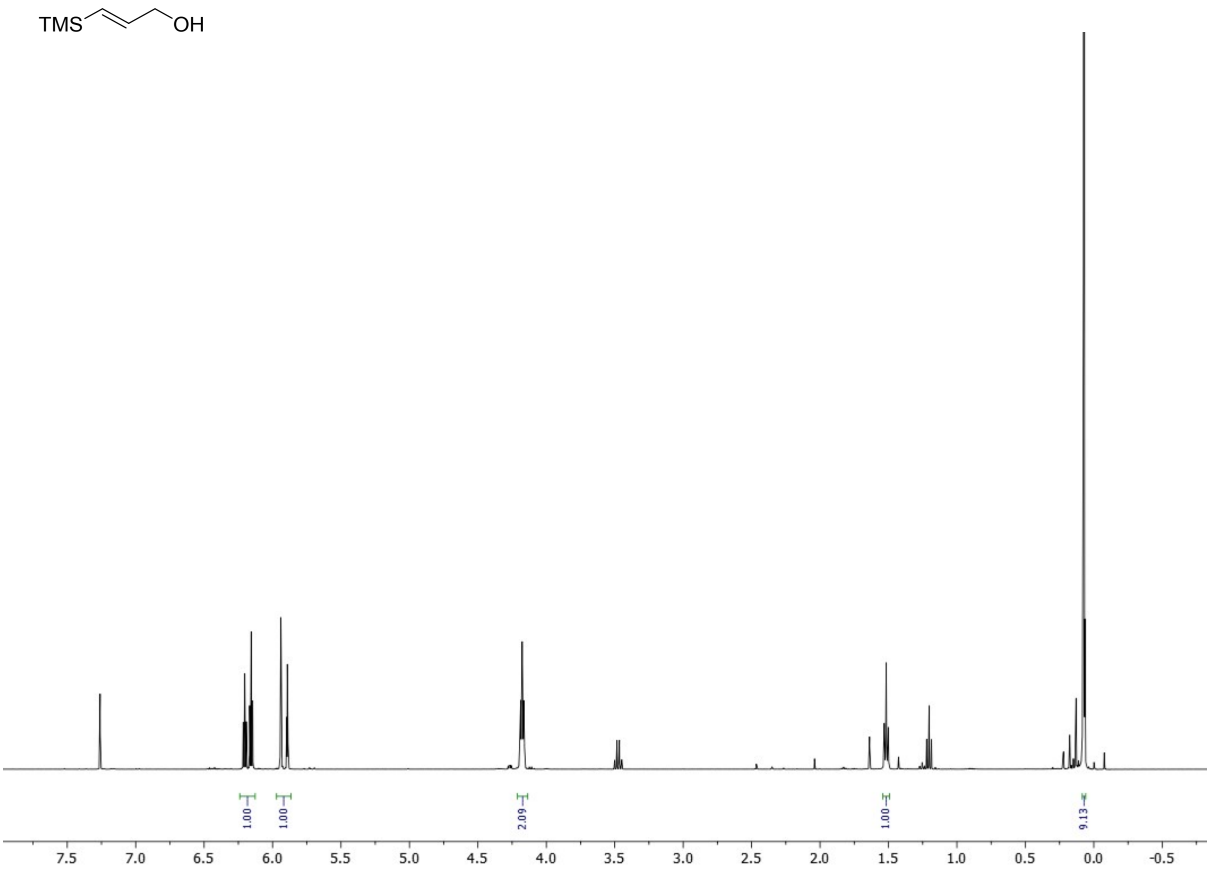
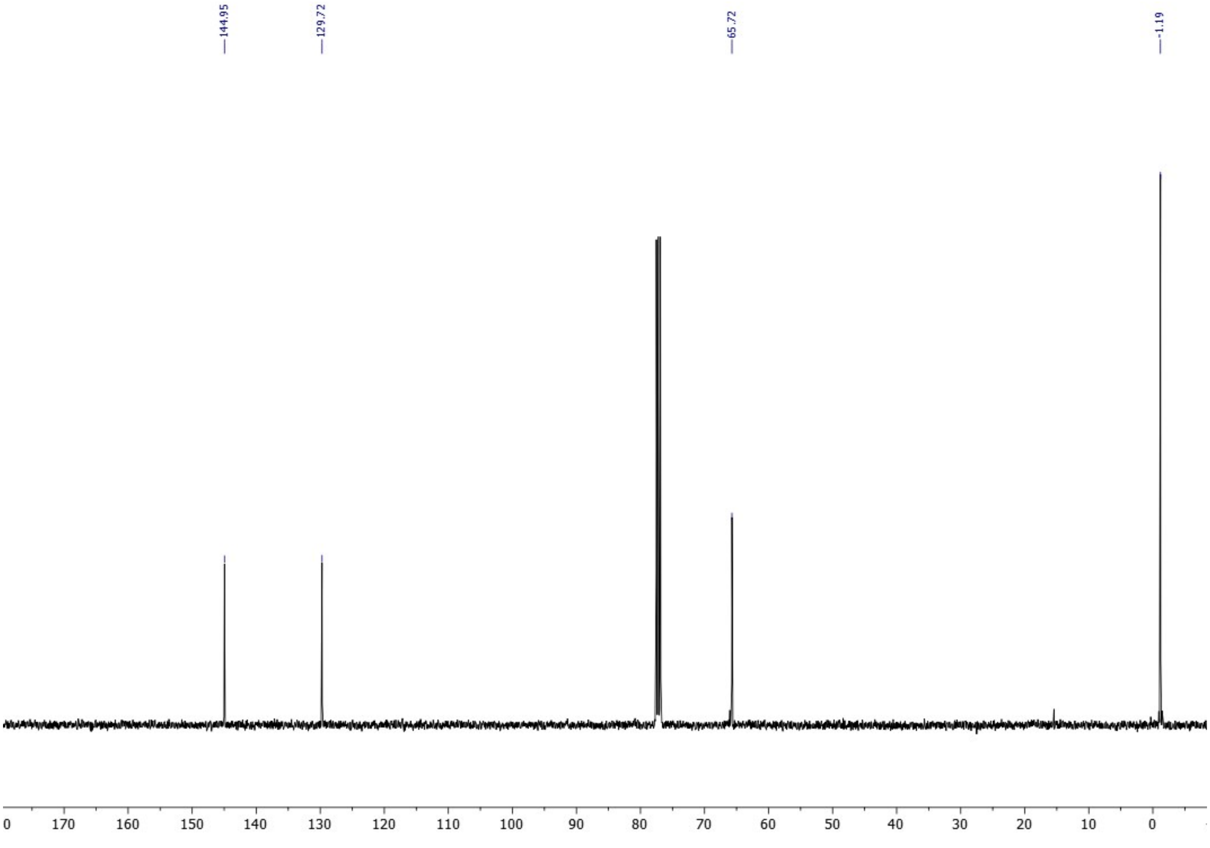

TMS
OH
1.00
1.00
2.09
1.00
9.13
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


144.95
129.72
65.72
-1.19
0
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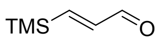
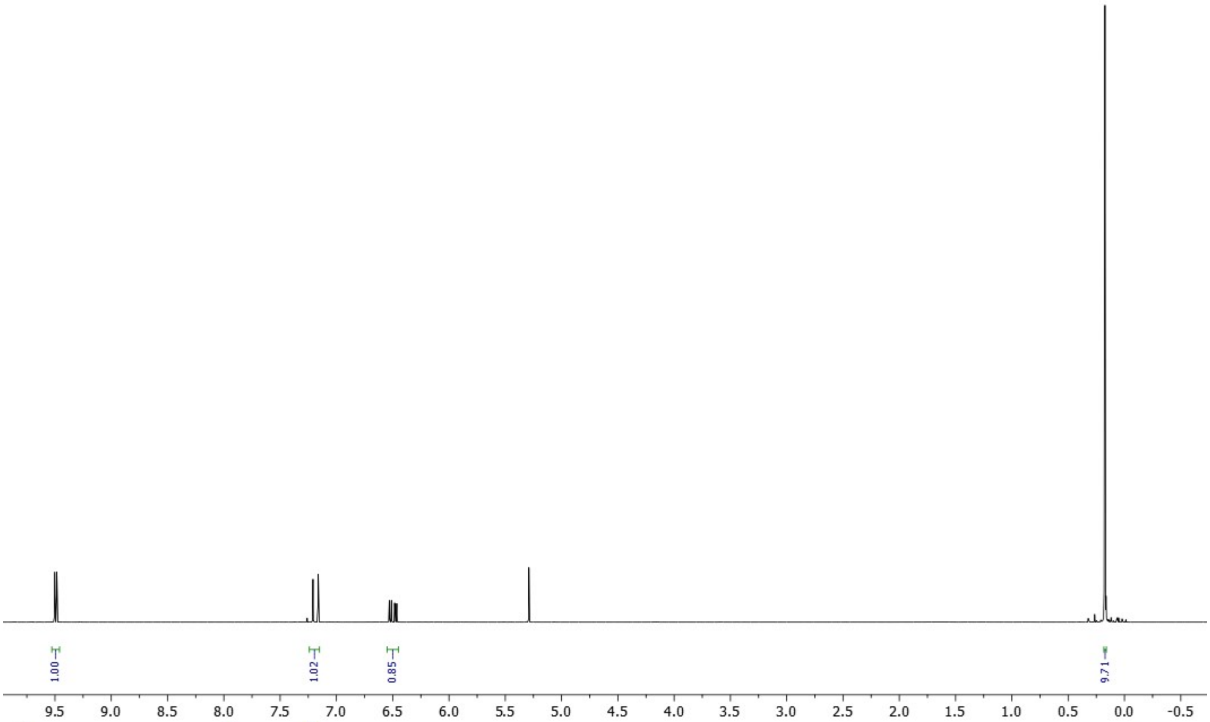
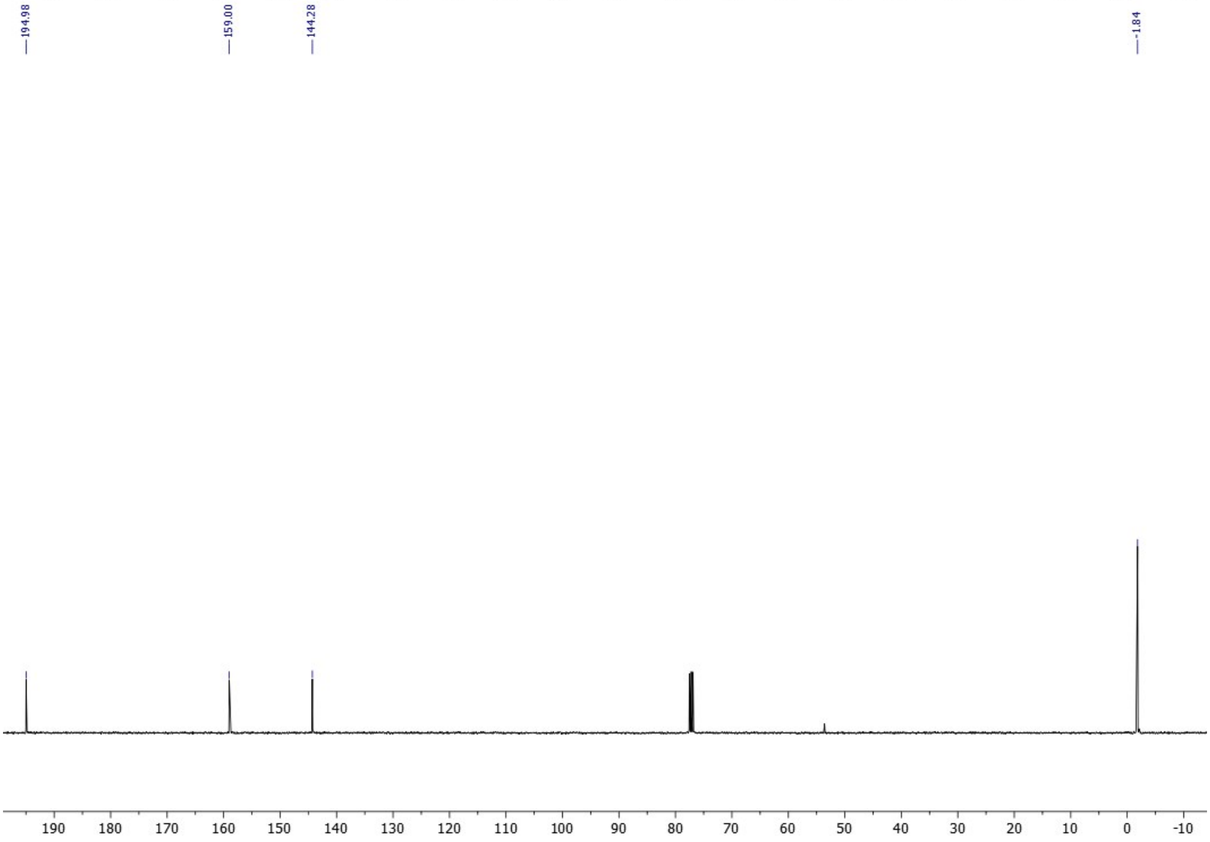
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


TMS
O


1.00
1.02
0.85
9.71
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


194.98
159.00
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190
180
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140
130
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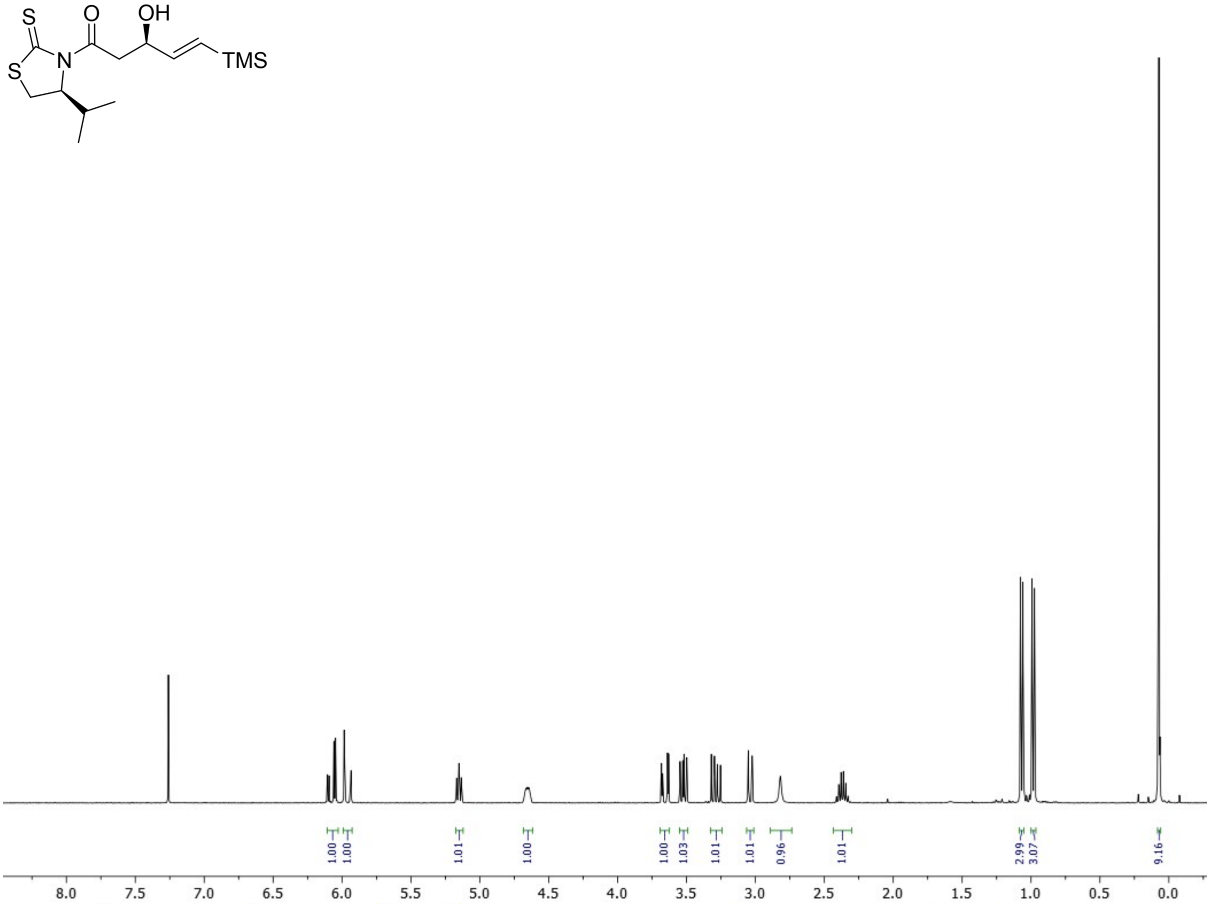
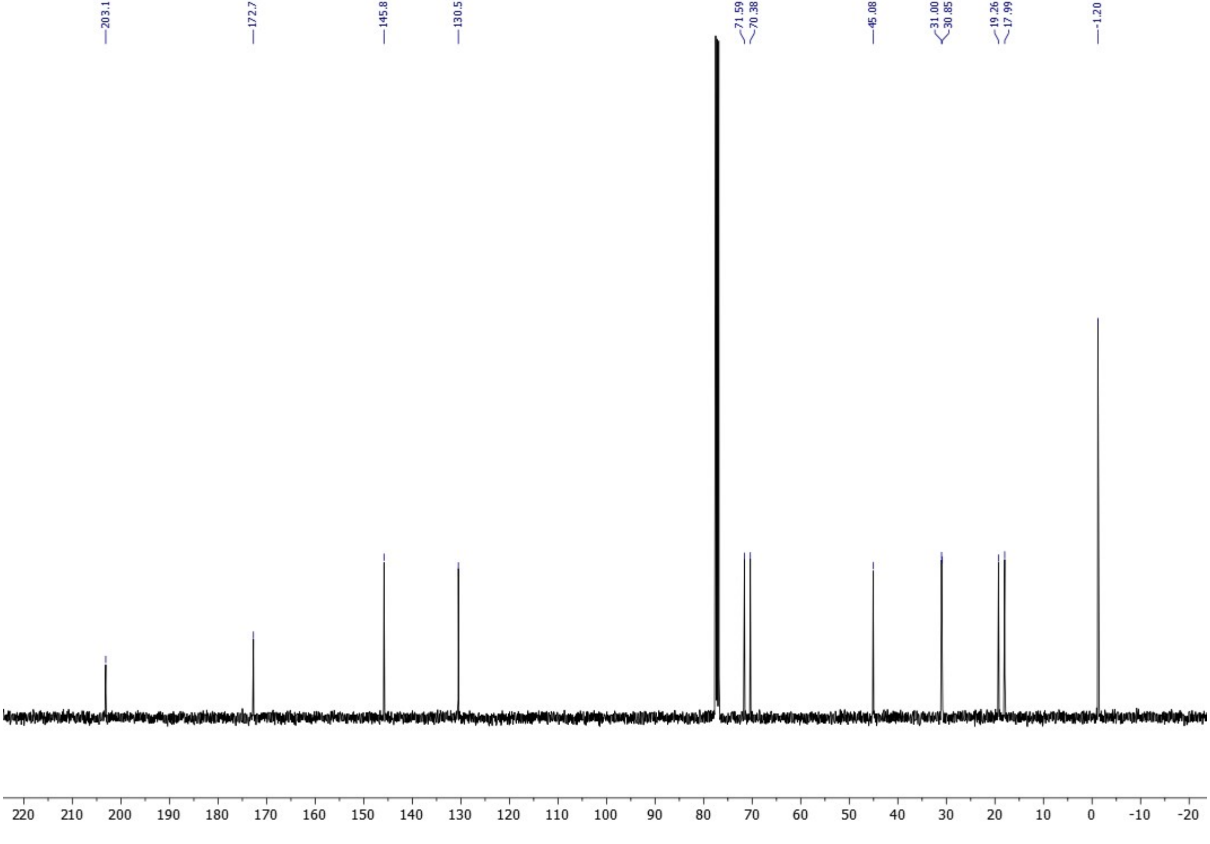
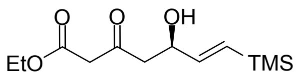
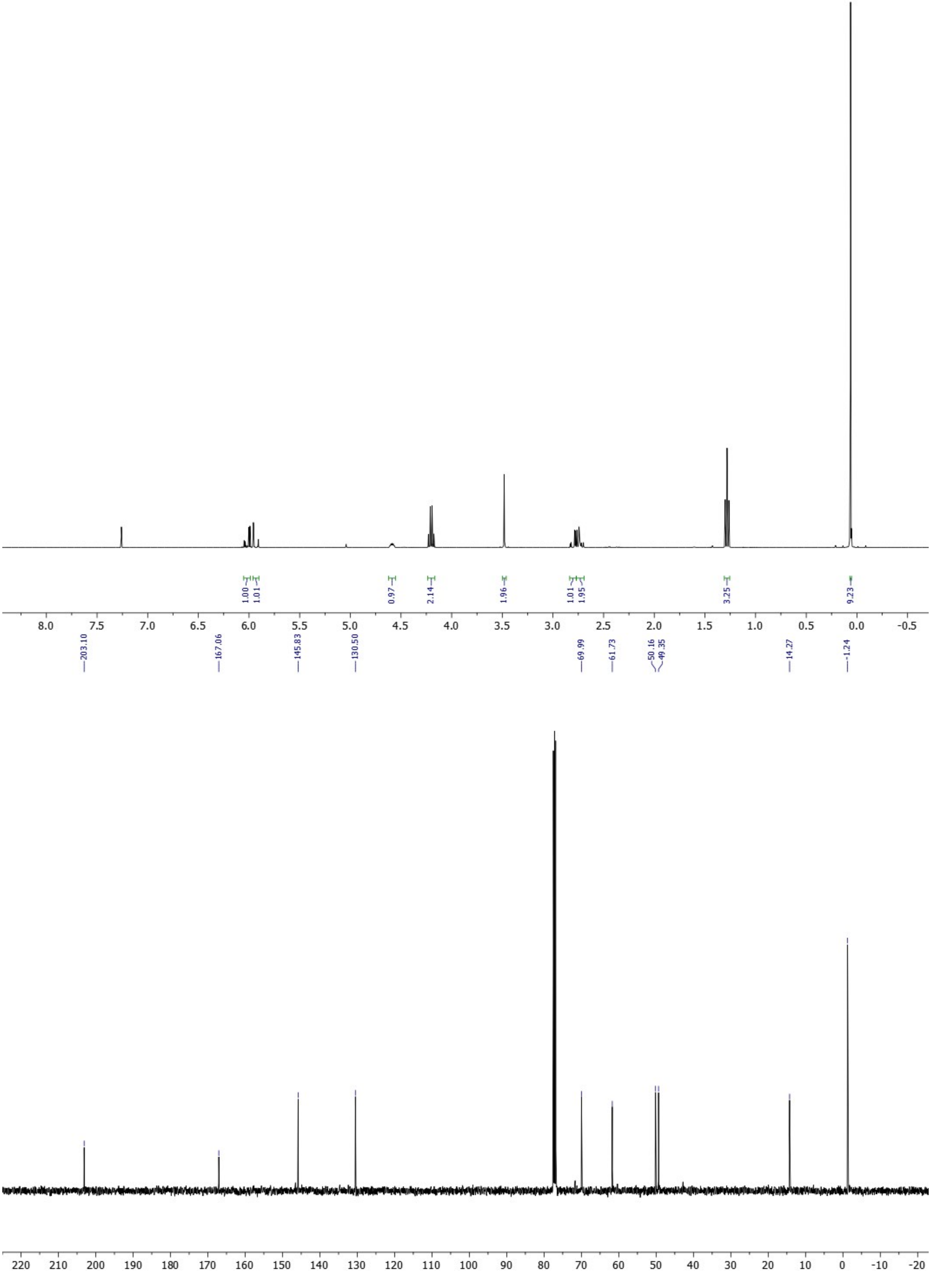
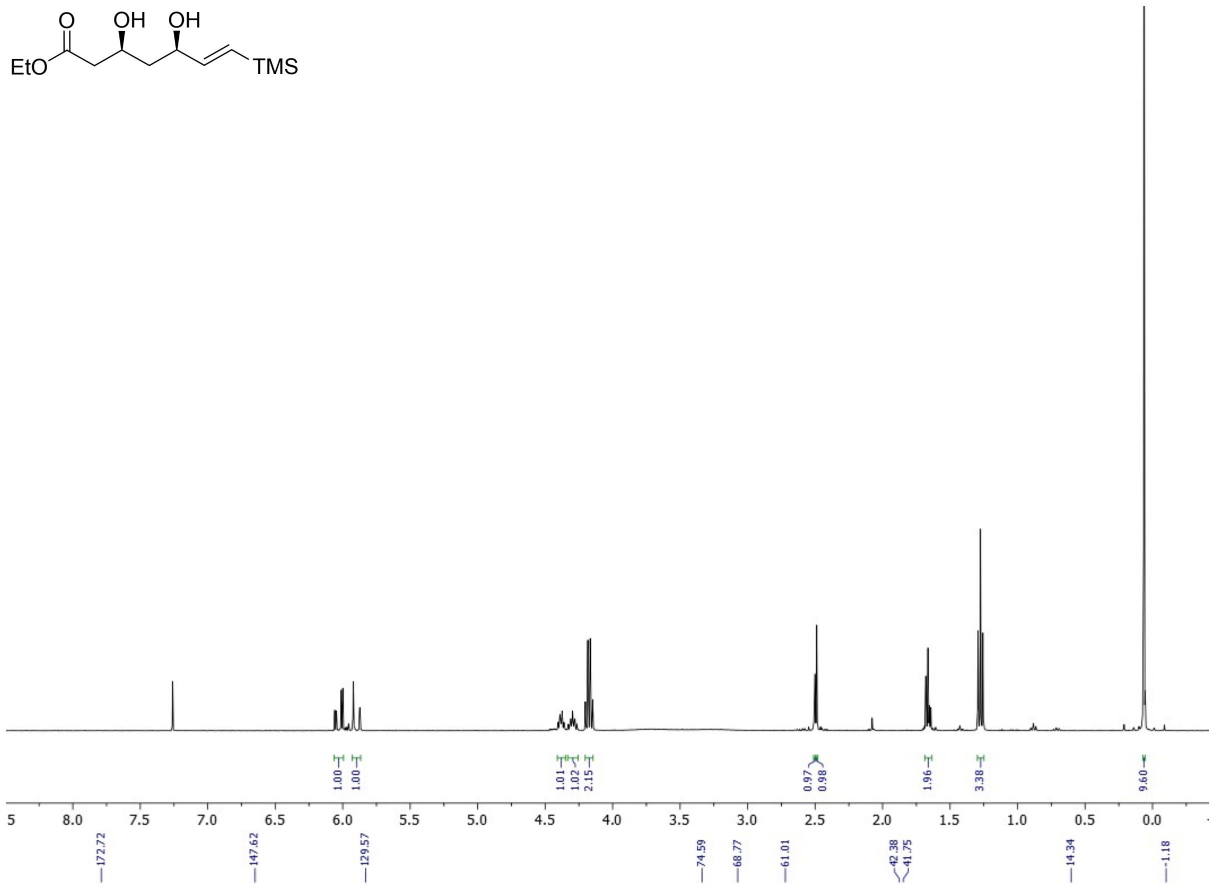
100
90
80
70
60
50
40
30
20
10
0
-10

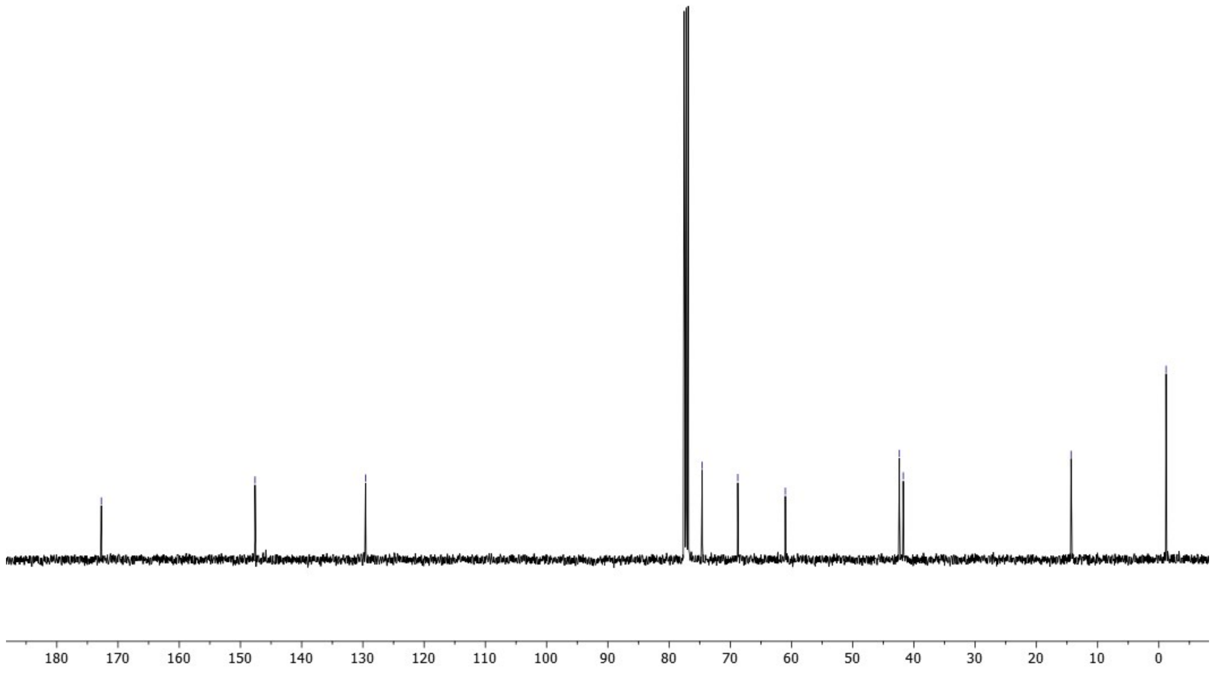

S
O
OH
N
S
TMS
1.00
1.00
1.01
1.00
1.00
1.03
1.01
1.01
0.96
1.01
2.99
3.07
9.16
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

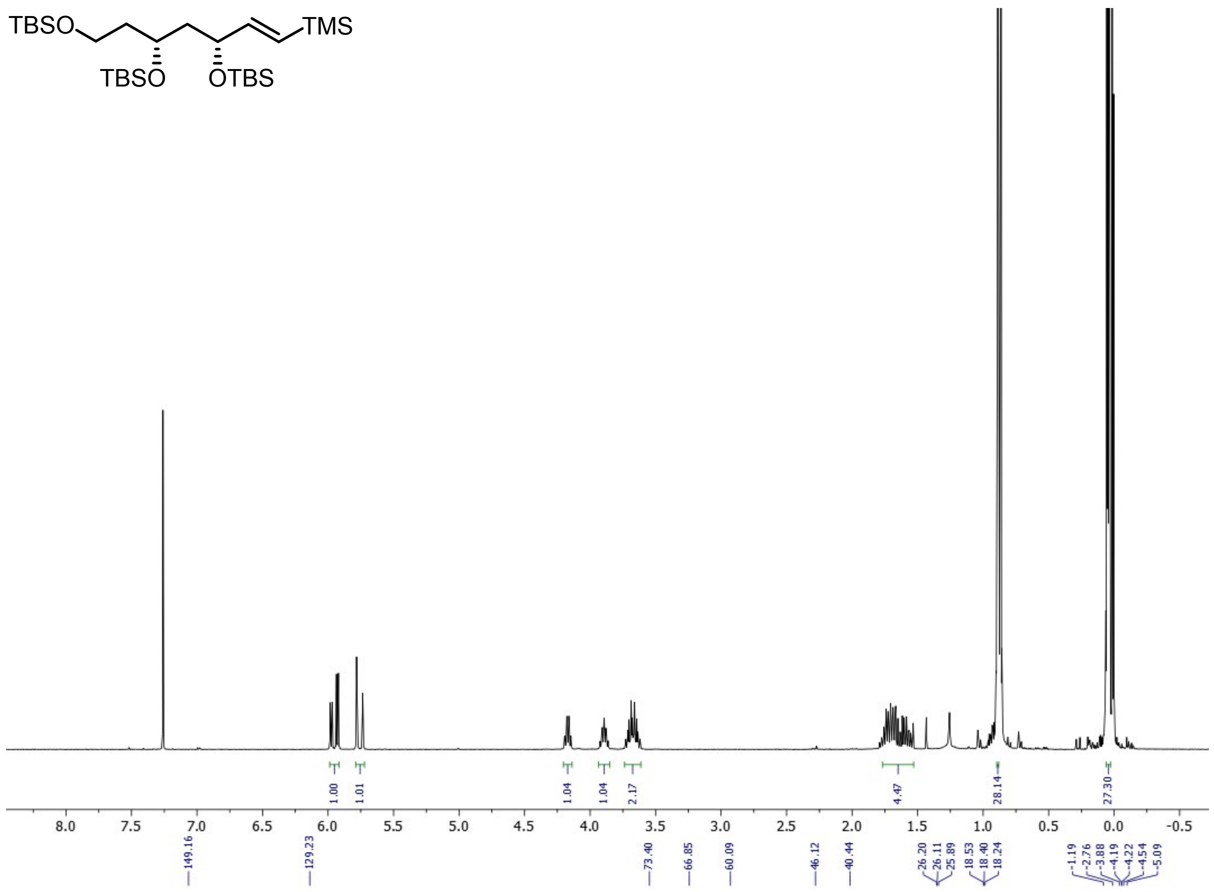

203.14
172.73
145.83
130.52
71.59
70.38
45.08
31.00
30.85
19.26
17.99
-1.20
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

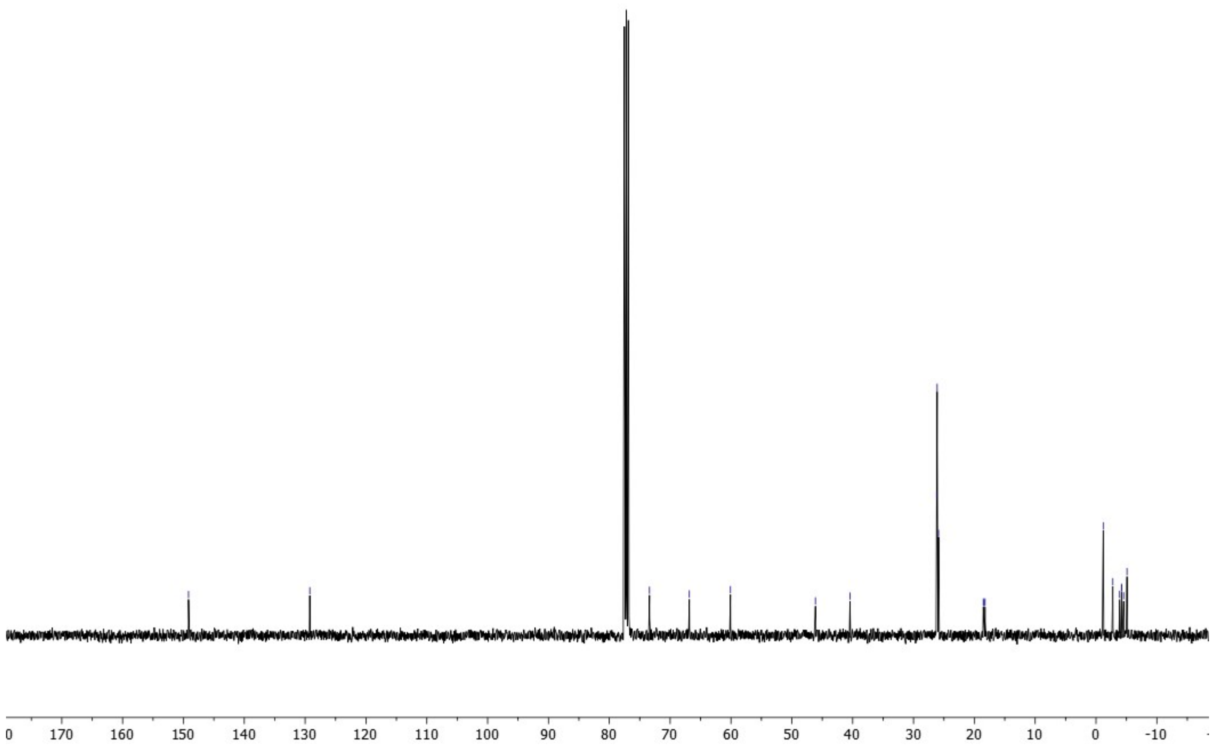

O
O
OH
EtO
TMS

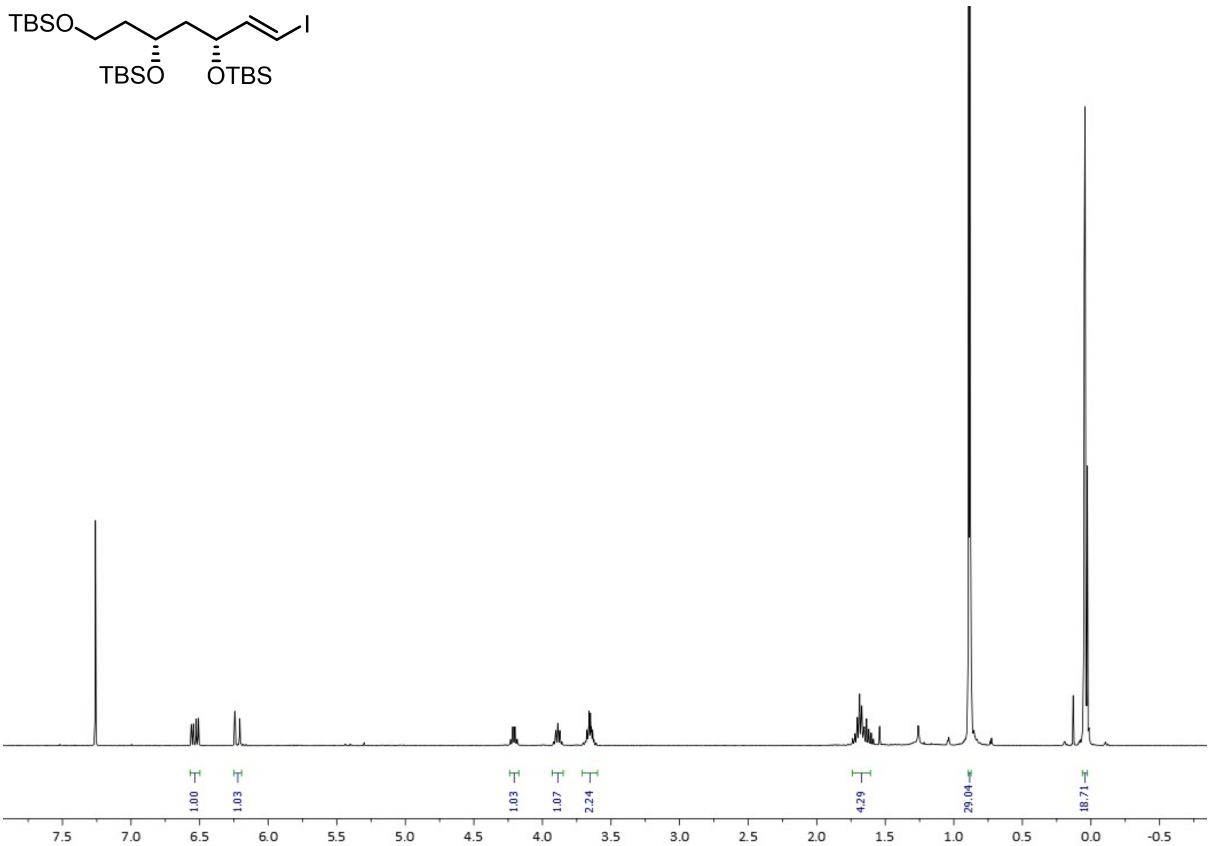

1.00
1.01
0.97
2.14
1.96
1.01
1.95
3.25
9.23
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
203.10
167.06
145.83
130.50
69.99
61.73
50.16
49.35
14.27
-1.24
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

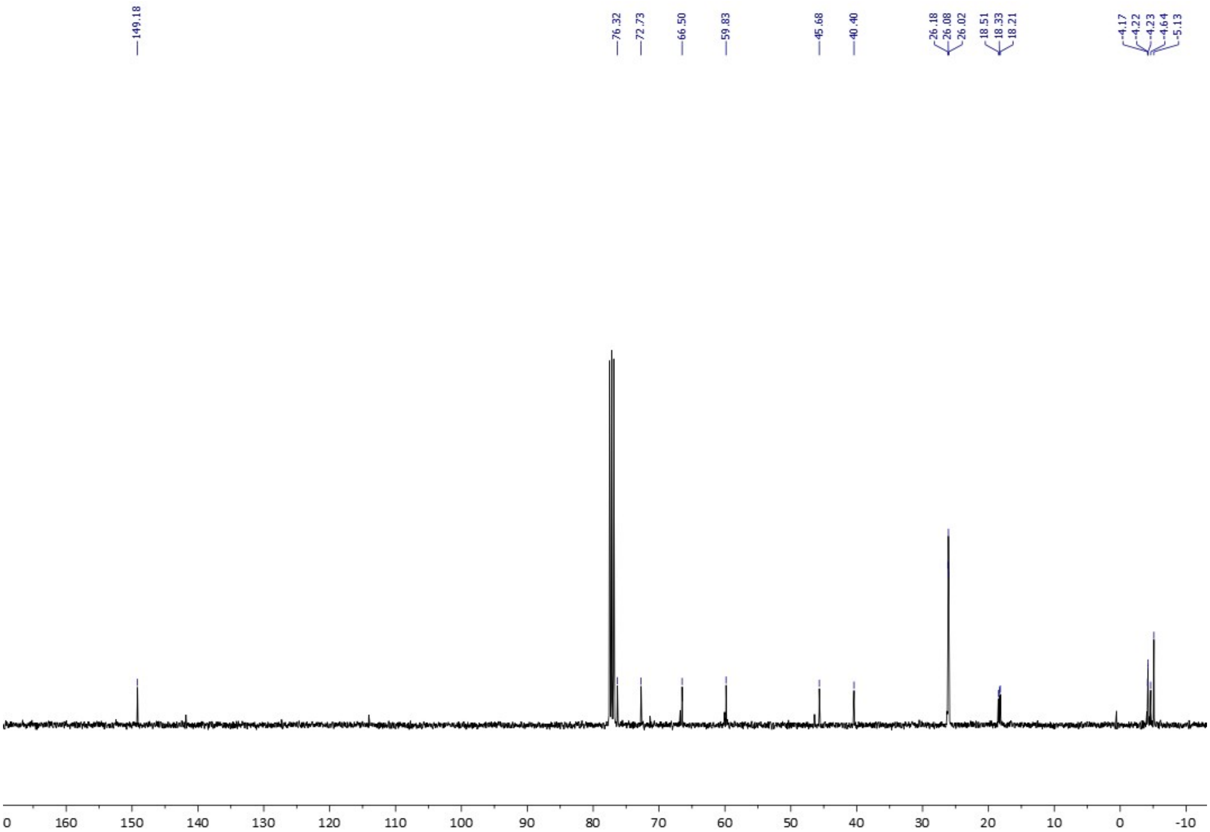

O
OH
OH
EtO
TMS
1.00
1.00
1.01
1.02
2.15
0.97
0.98
1.96
3.38
9.60
5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
172.72
147.62
129.57
74.59
68.77
61.01
42.38
41.75
14.34
-1.18

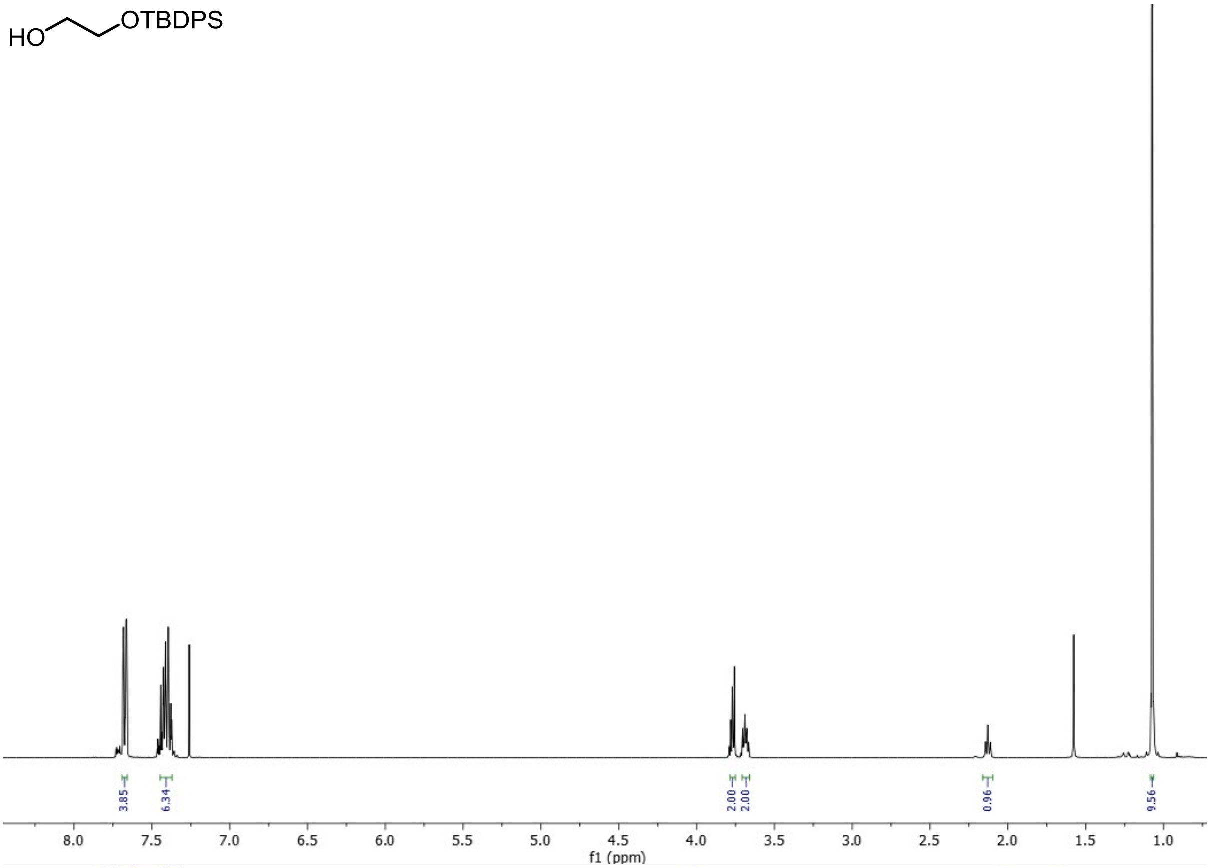

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

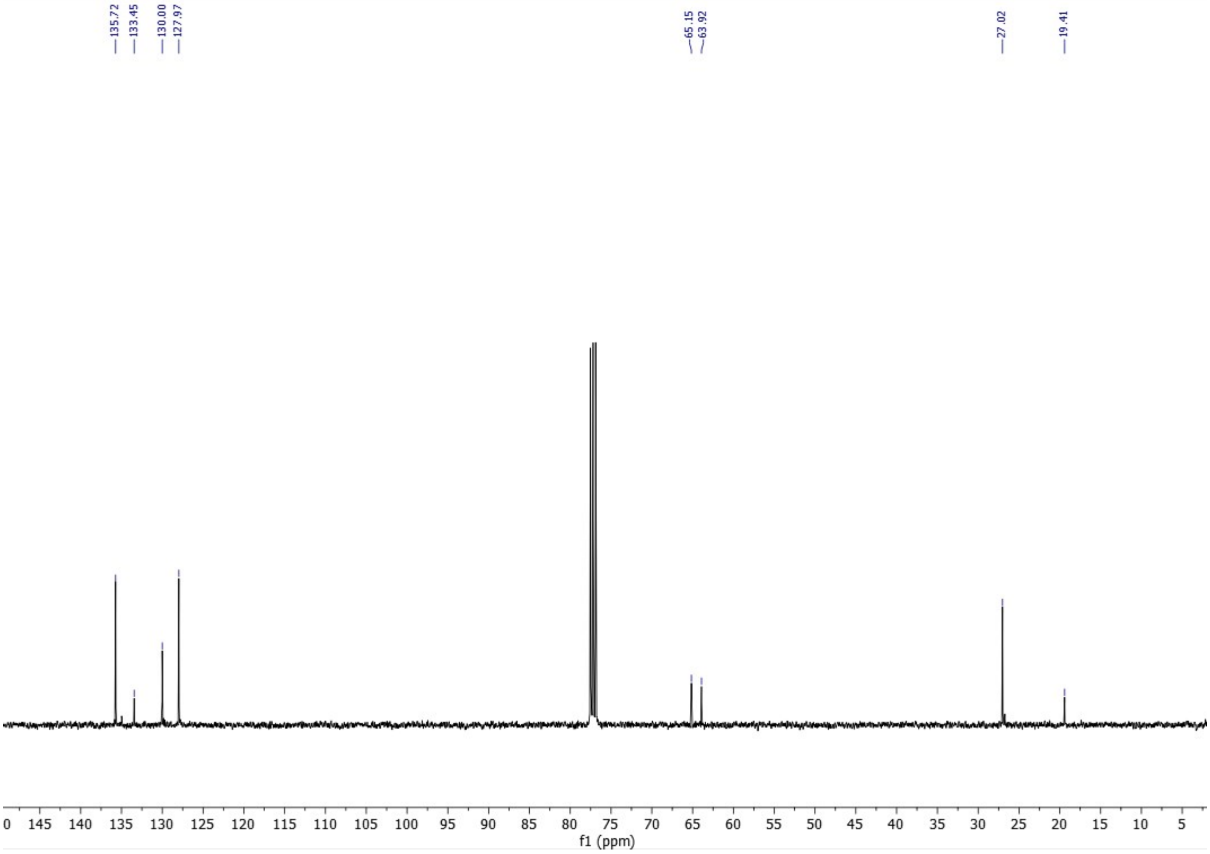

TBSO
TMS
TBSO
OTBS
1.00
1.01
1.04
1.04
2.17
4.47
28.14
27.30
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
149.16
129.23
73.40
66.85
60.09
46.12
40.44
26.20
26.11
25.89
18.53
18.40
18.24
-1.19
-2.76
-3.88
-4.19
-4.22
-4.54
-5.09

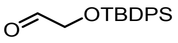

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

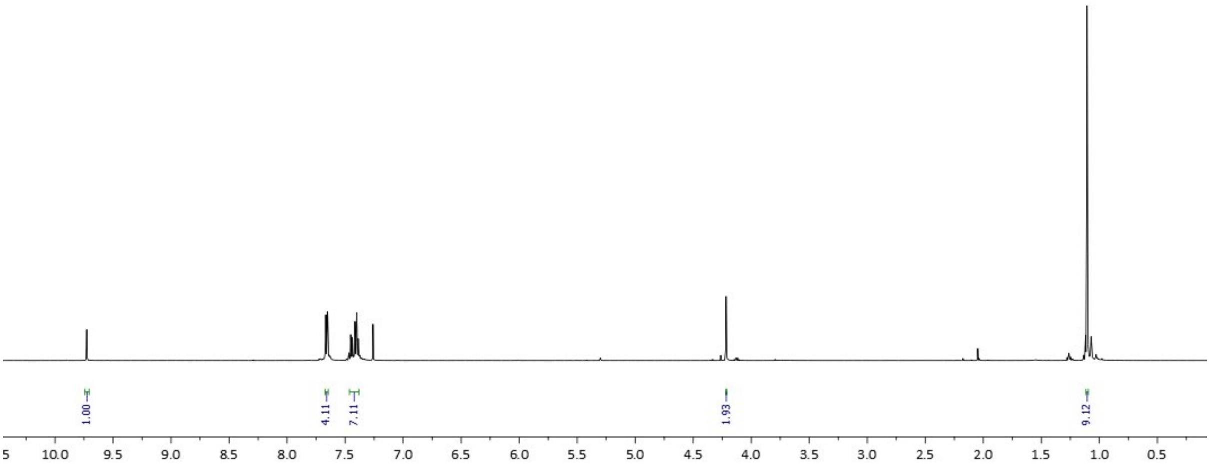

TBSO
TBSO
OTBS
I
1.00
1.03
1.03
1.07
2.24
4.29
29.04
18.71
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

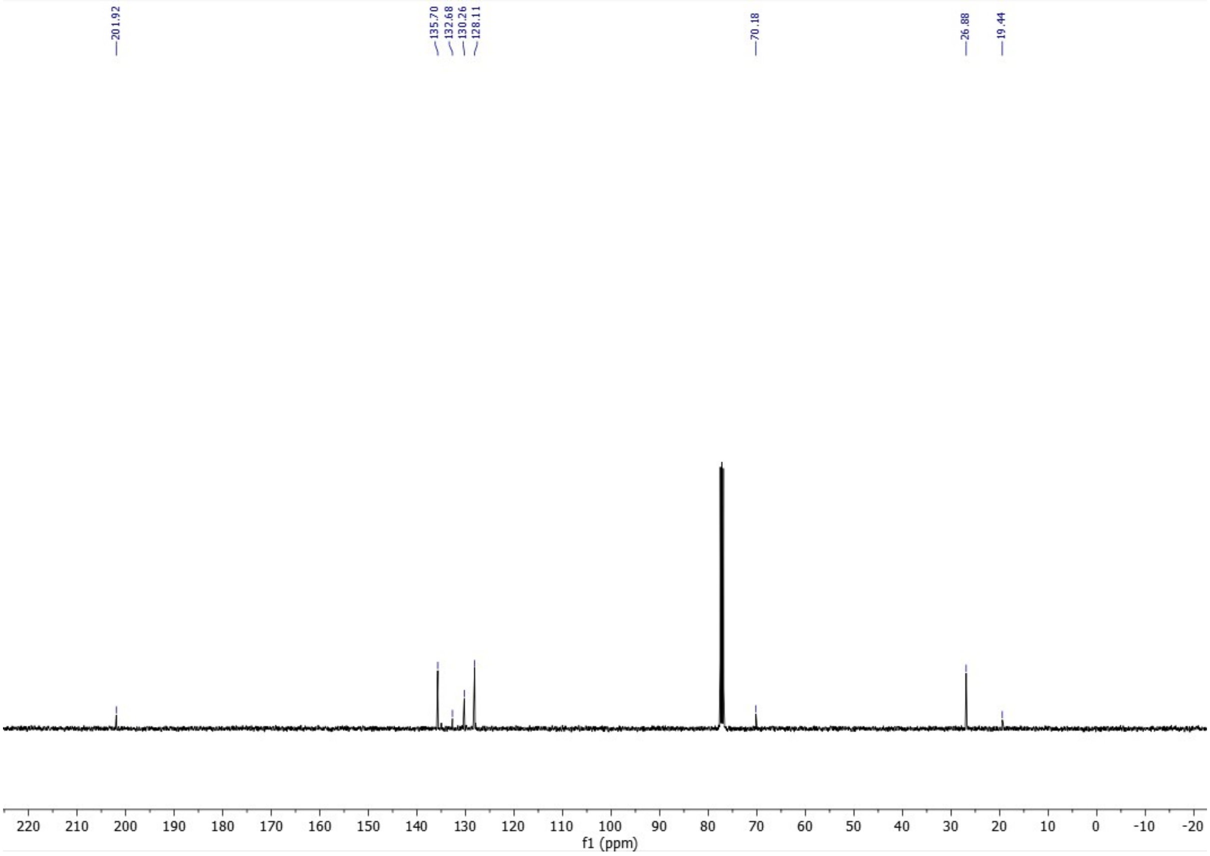

149.18
76.32
72.73
66.50
59.83
45.68
40.40
26.18
26.08
26.02
18.51
18.33
18.21
-4.17
-4.22
-4.23
-4.64
-5.13
0
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

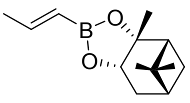

HO
OTBDPS
3.85
6.34
2.00
2.00
0.96
9.56
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


135.72
133.45
130.00
127.97
65.15
63.92
27.02
19.41
0
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
f1 (ppm)

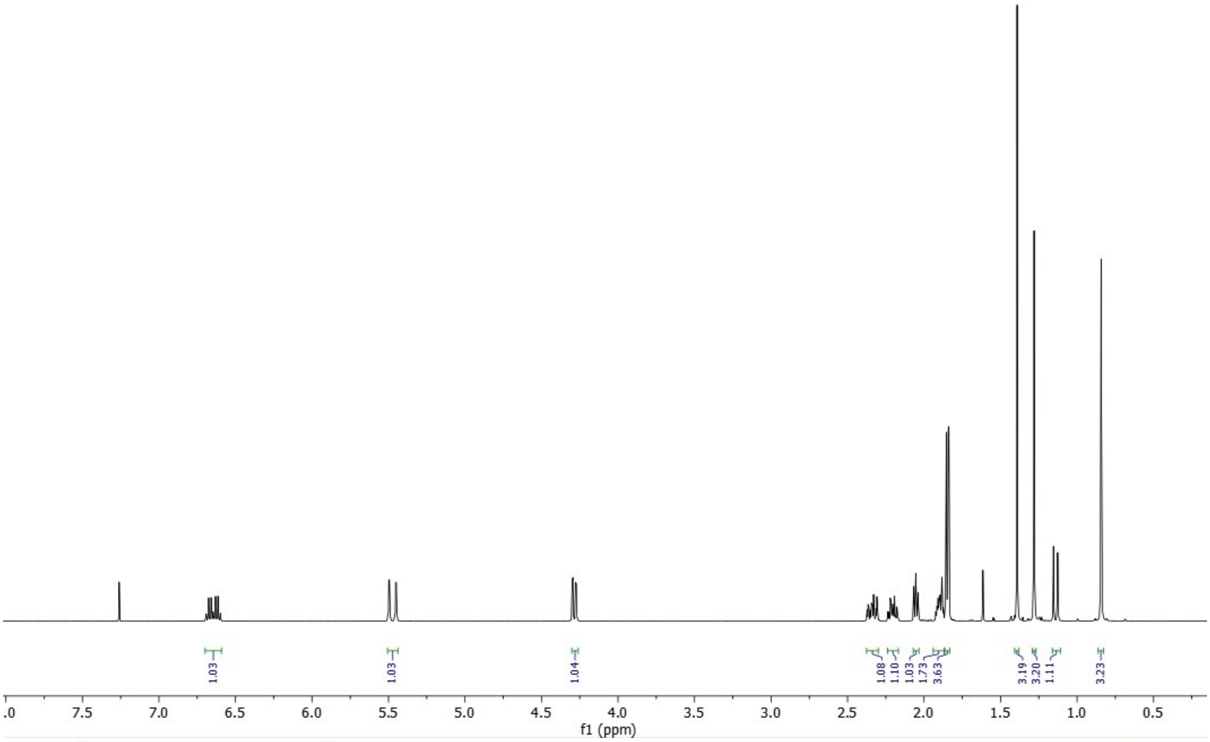

O
OTBDPS


1.00
4.11
7.11
1.93
9.12
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

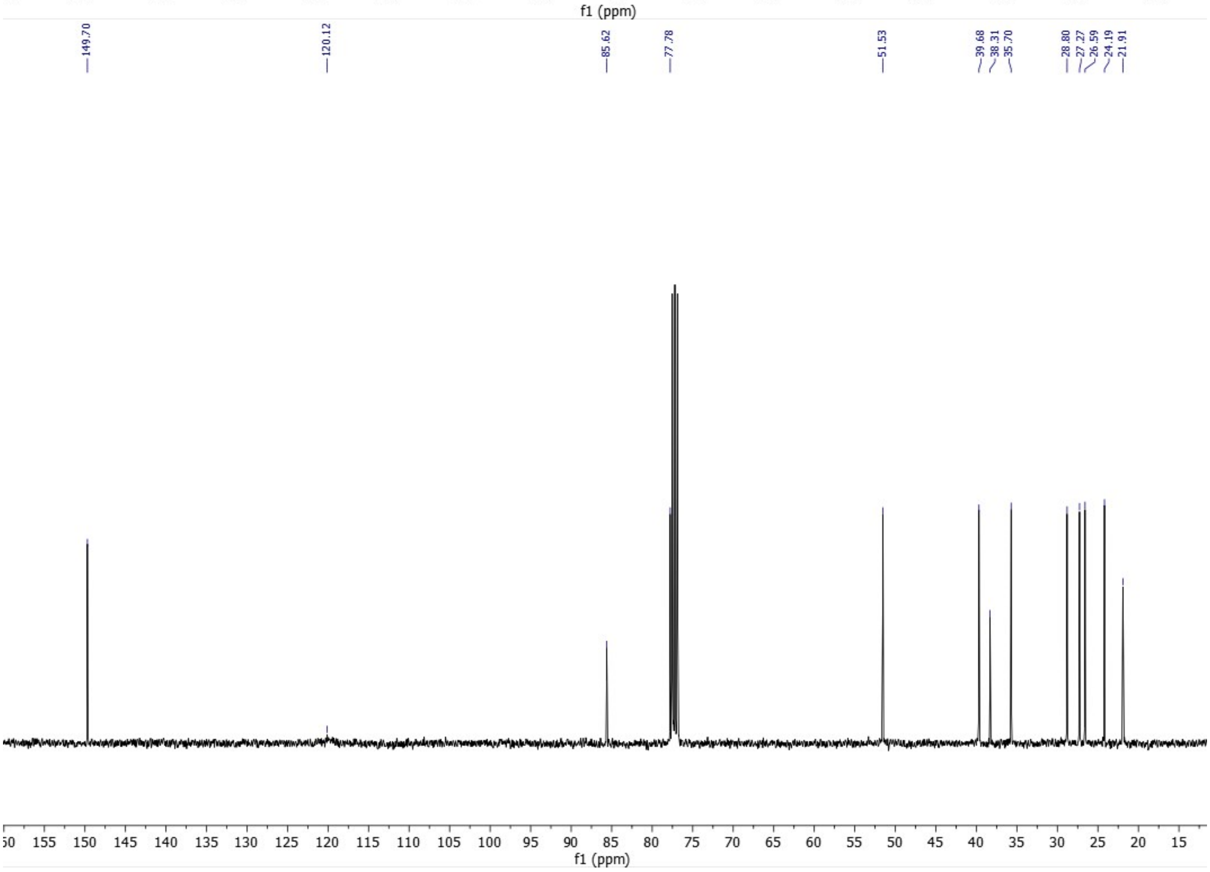

201.92
135.70
132.68
130.26
128.11
70.18
26.88
19.44
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)



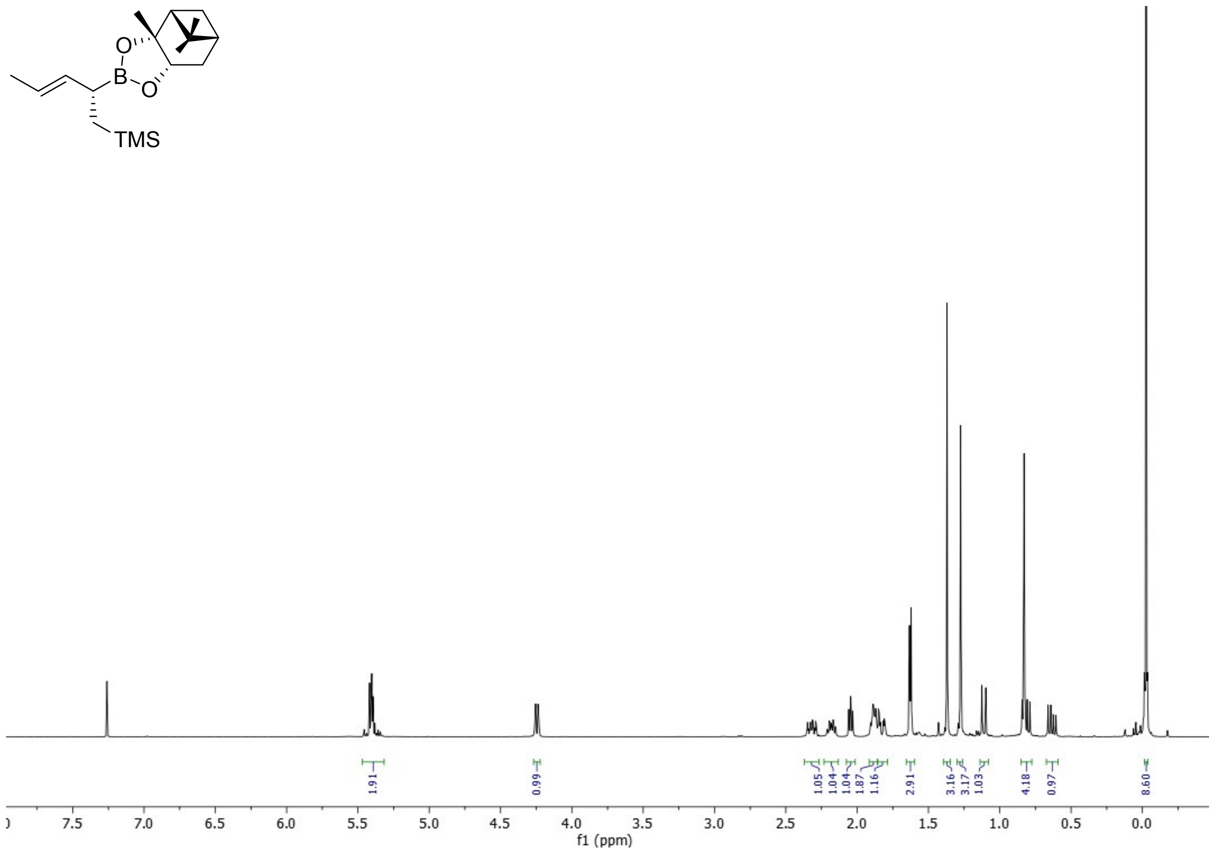
B
O
O

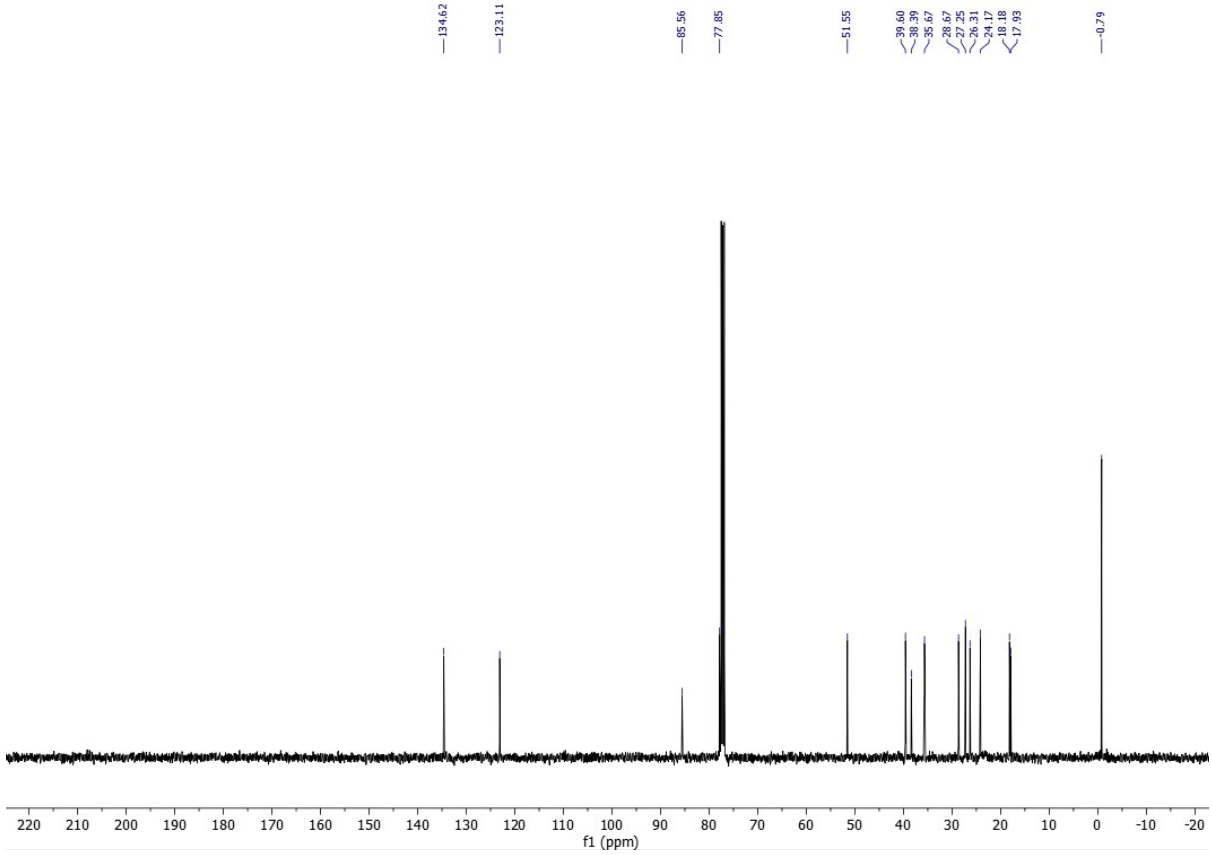


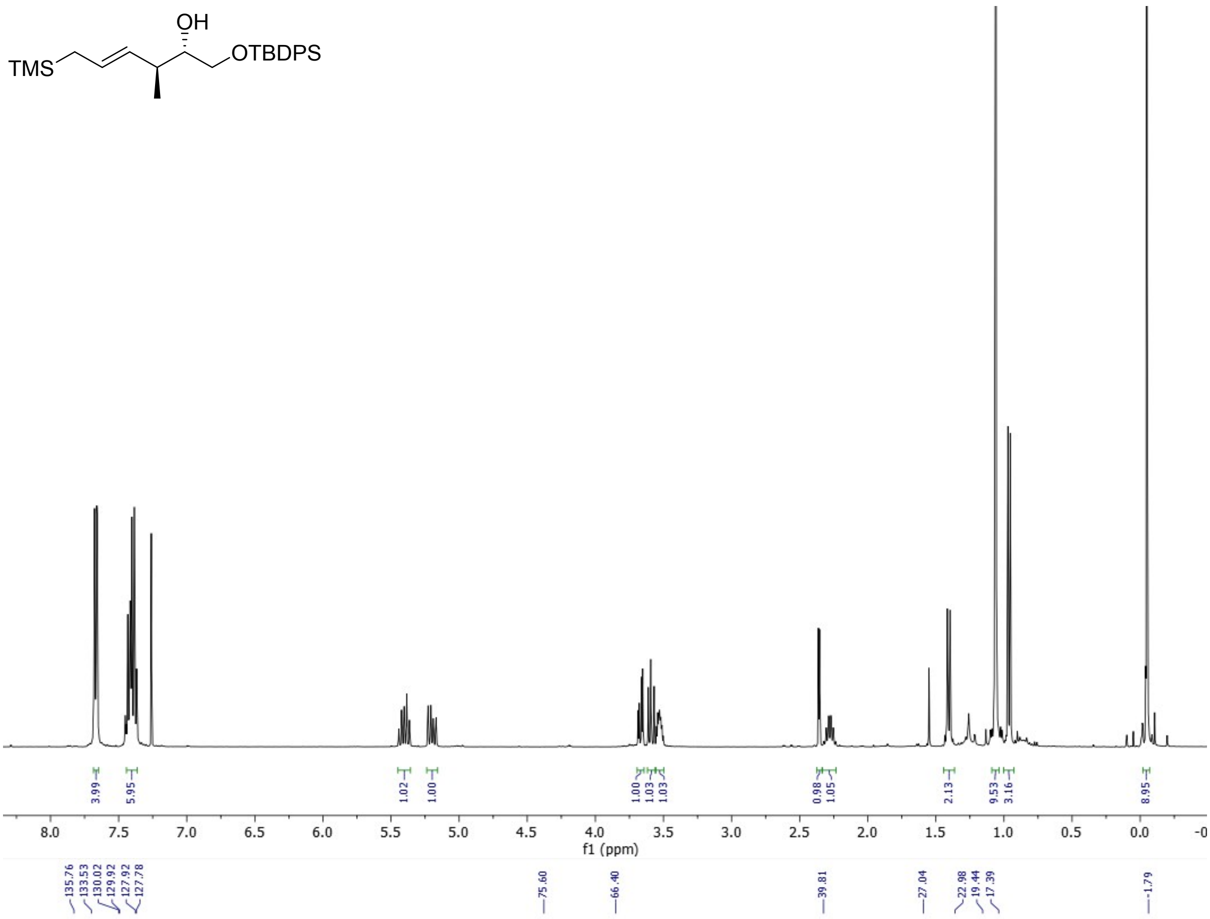
1.03
1.03
1.04
1.08
1.10
1.03
1.73
3.63
3.19
3.20
1.11
3.23
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

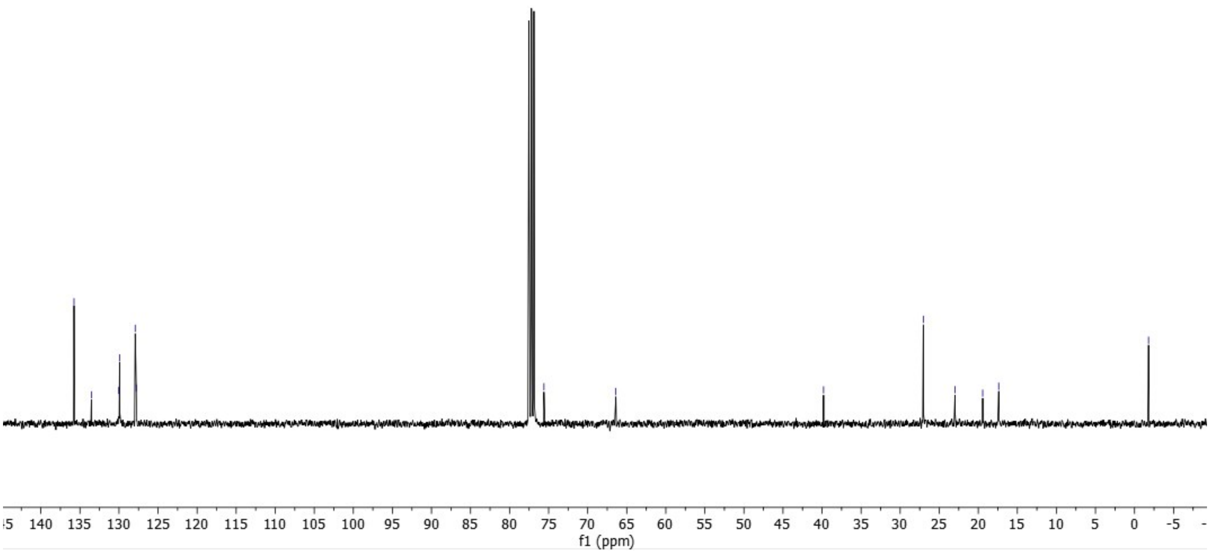


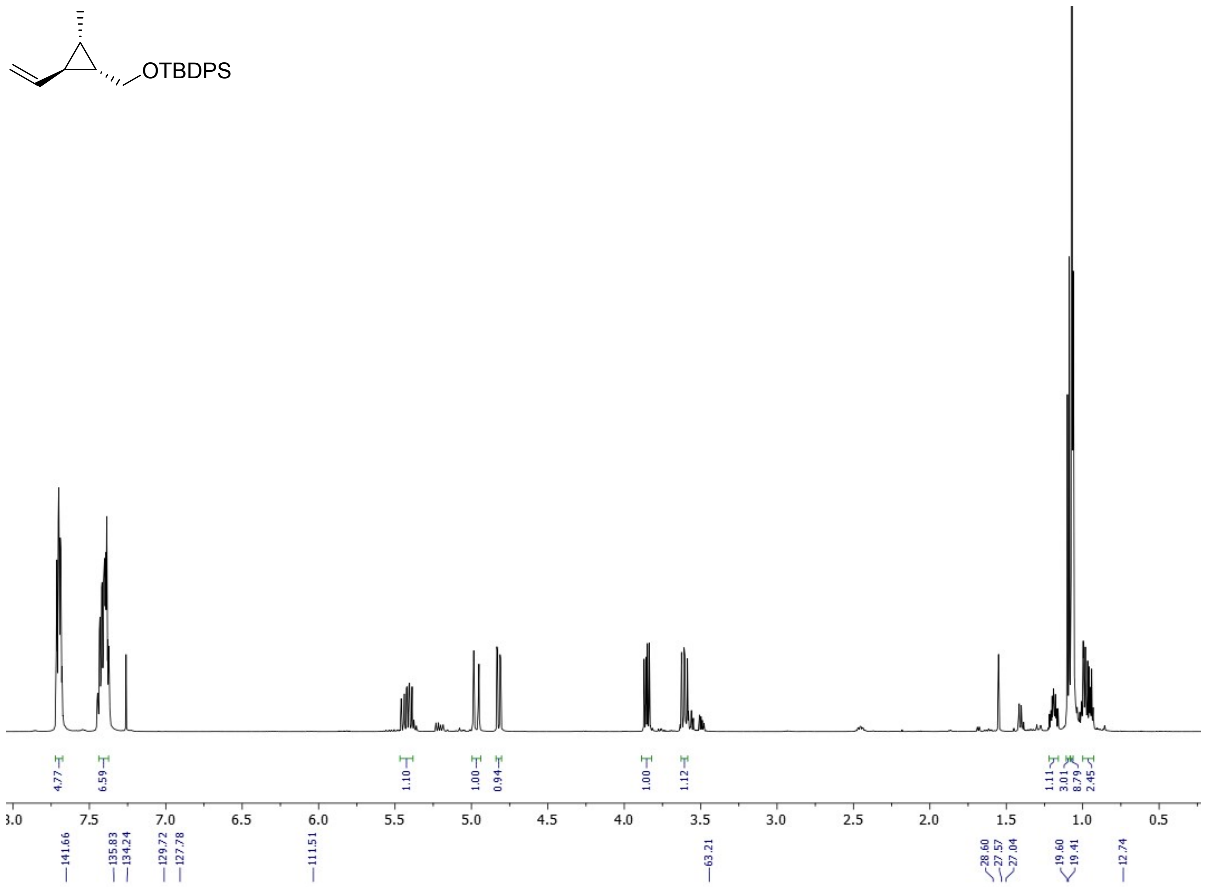
149.70
120.12
85.62
77.78
51.53
39.68
38.31
35.70
28.80
27.27
26.59
24.19
21.91
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
f1 (ppm)

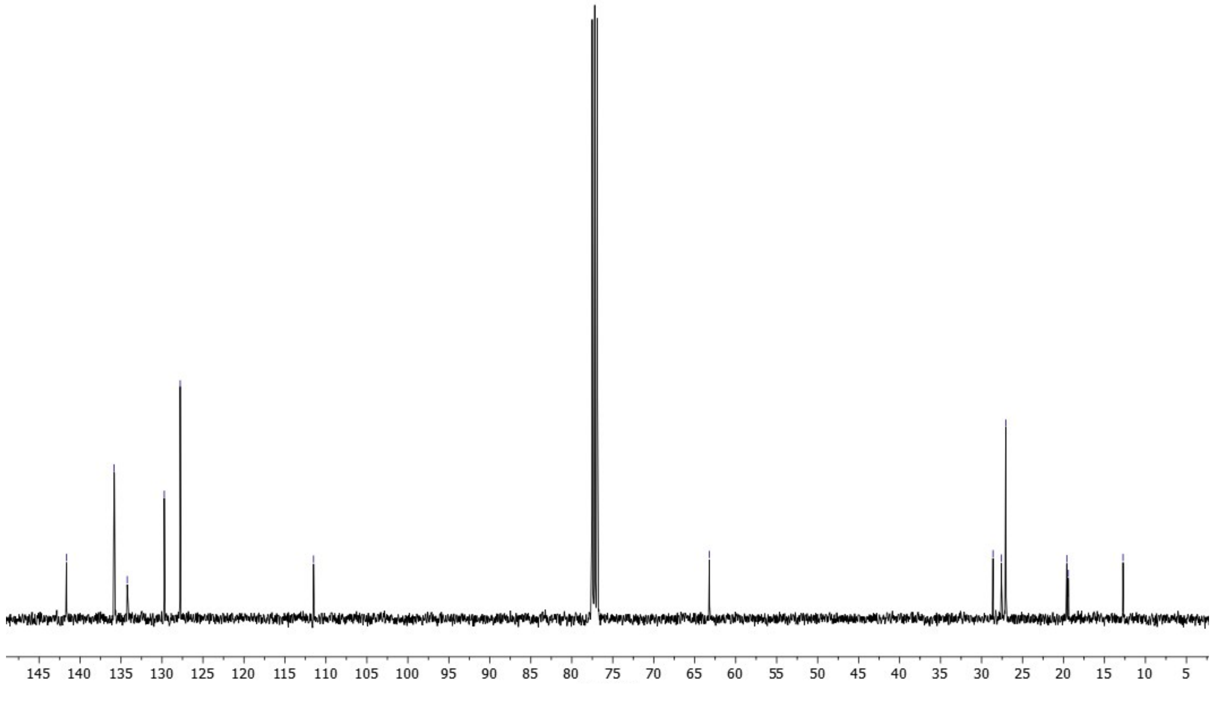

O
B
O
TMS
1.91
0.99
1.05
1.04
1.04
1.87
1.16
2.91
3.16
3.17
1.03
4.18
0.97
8.60
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

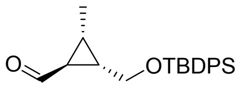

134.62
123.11
85.56
77.85
51.55
39.60
38.39
35.67
28.67
27.25
26.31
24.17
18.18
17.93
-0.79
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

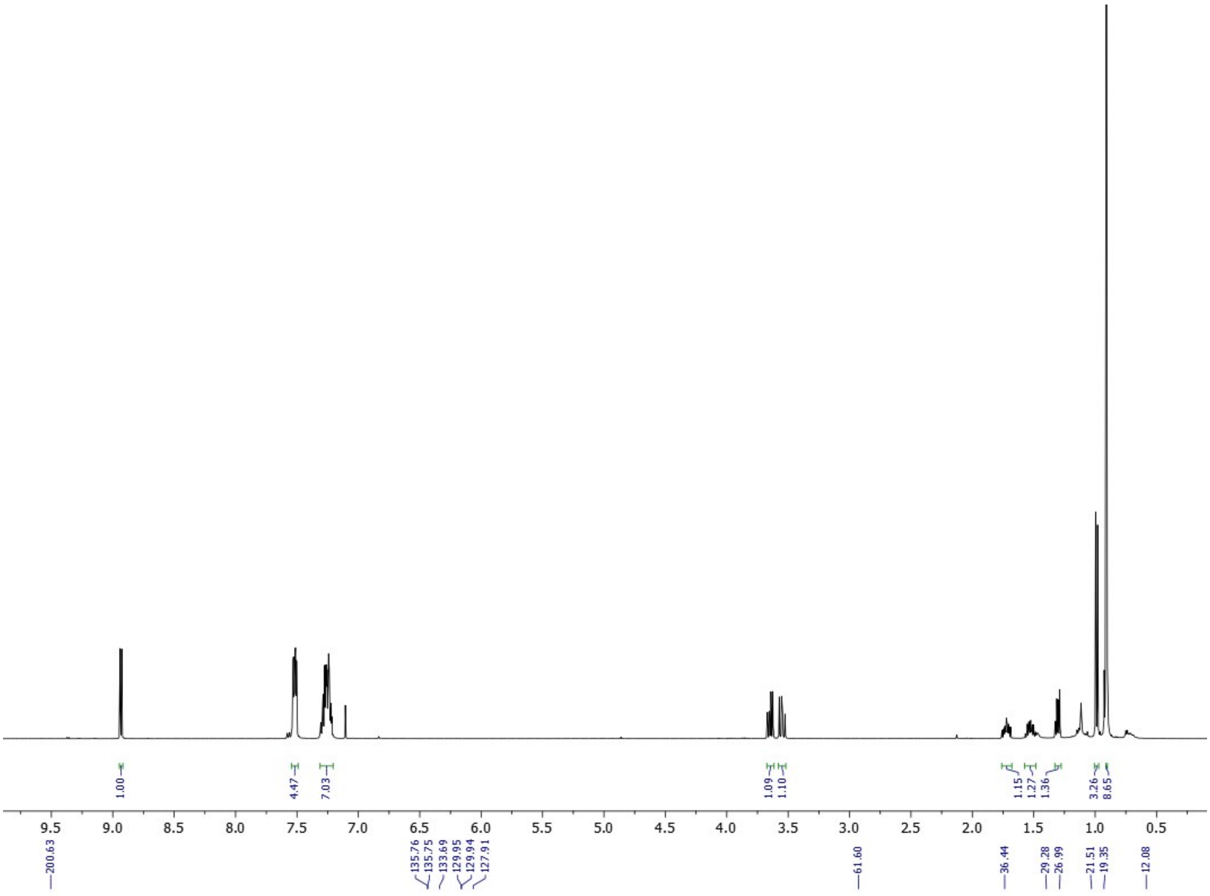

OH
TMS
OTBDPS
3.99
5.95
1.02
1.00
1.00
1.03
1.03
0.98
1.05
2.13
9.53
3.16
8.95
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)
135.76
133.53
130.02
129.92
127.92
127.78
75.60
66.40
39.81
27.04
22.98
19.44
17.39
-1.79

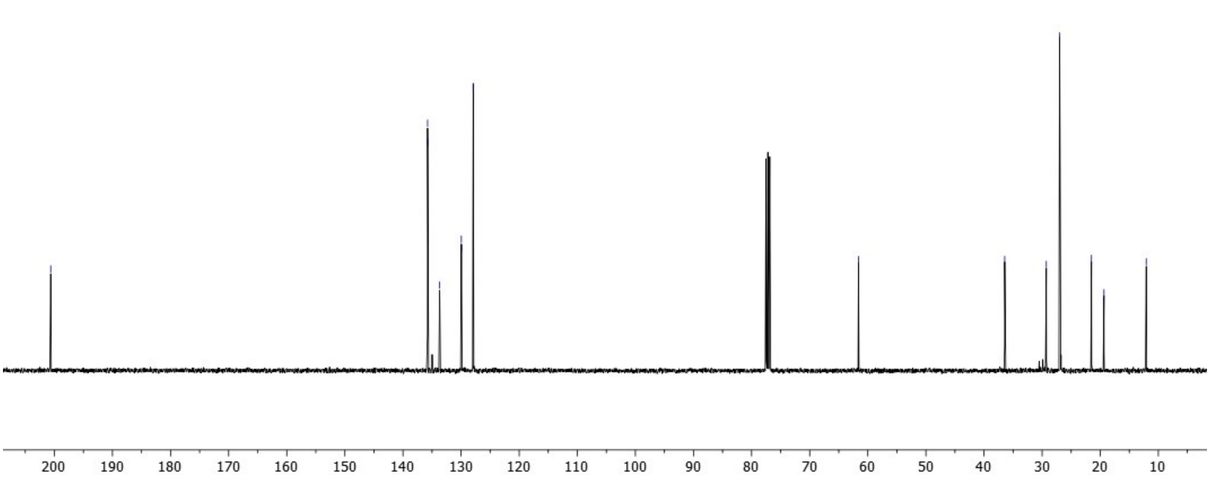

5 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -
f1 (ppm)

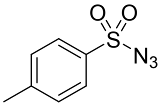

OTBDPS
4.77
6.59
1.10
1.00
0.94
1.00
1.12
1.11
3.01
8.79
2.45
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
141.66
135.83
134.24
129.72
127.78
111.51
63.21
28.60
27.57
27.04
19.60
19.41
12.74

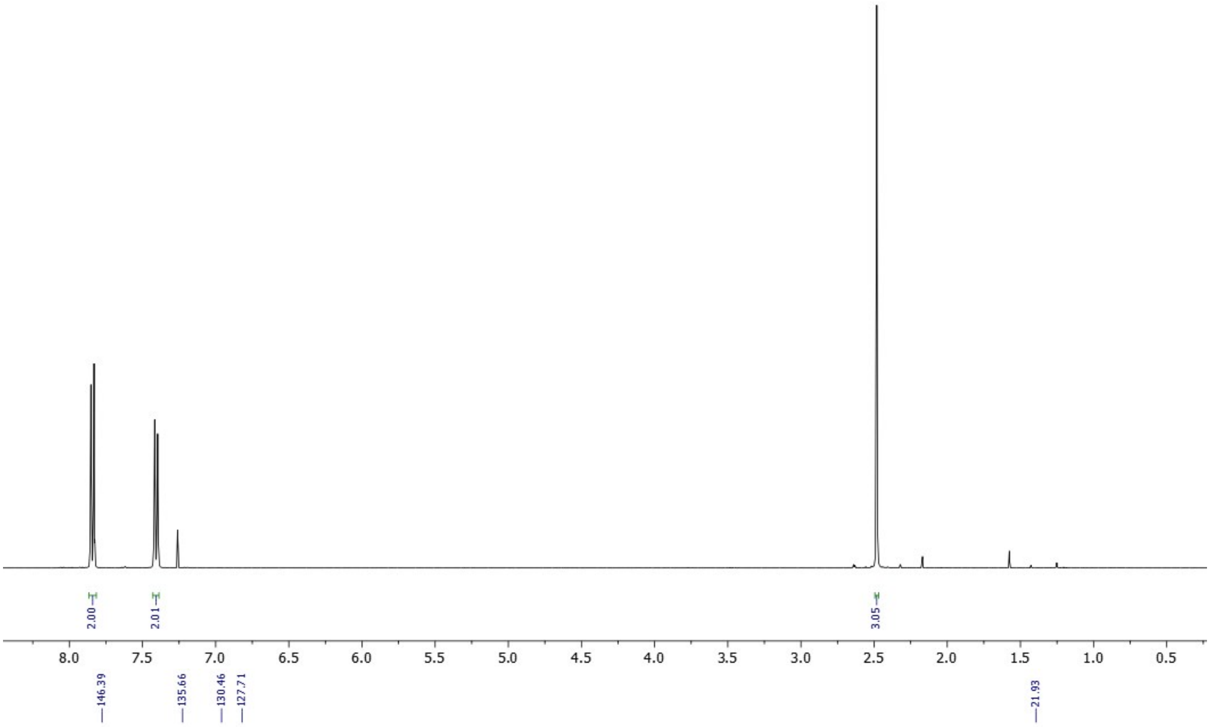

145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5

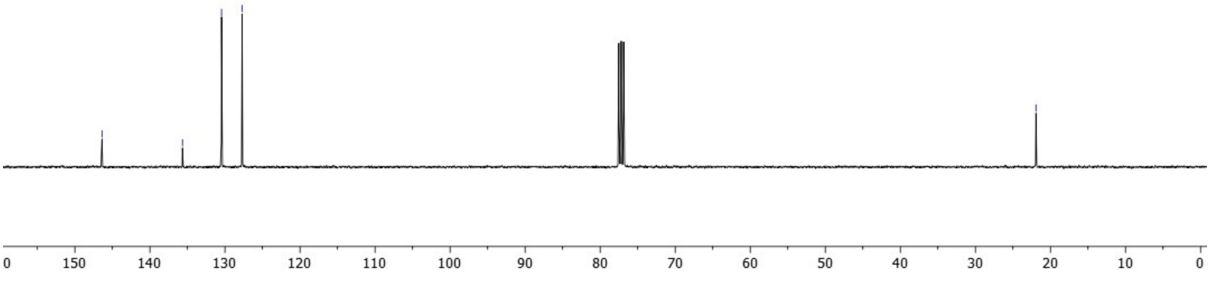

O
OTBDPS

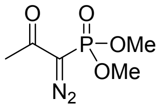

1.00
4.47
7.03
1.09
1.10
1.15
1.27
1.36
3.26
8.65
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
200.63
135.76
135.75
133.69
129.95
129.94
127.91
61.60
36.44
29.28
26.99
21.51
19.35
12.08

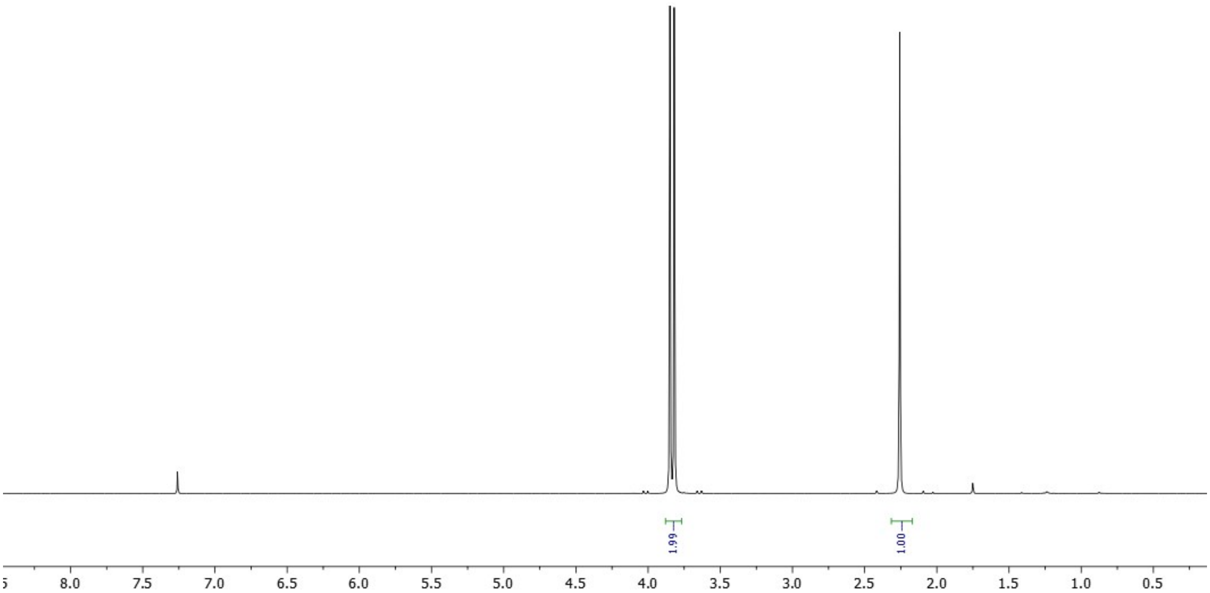

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

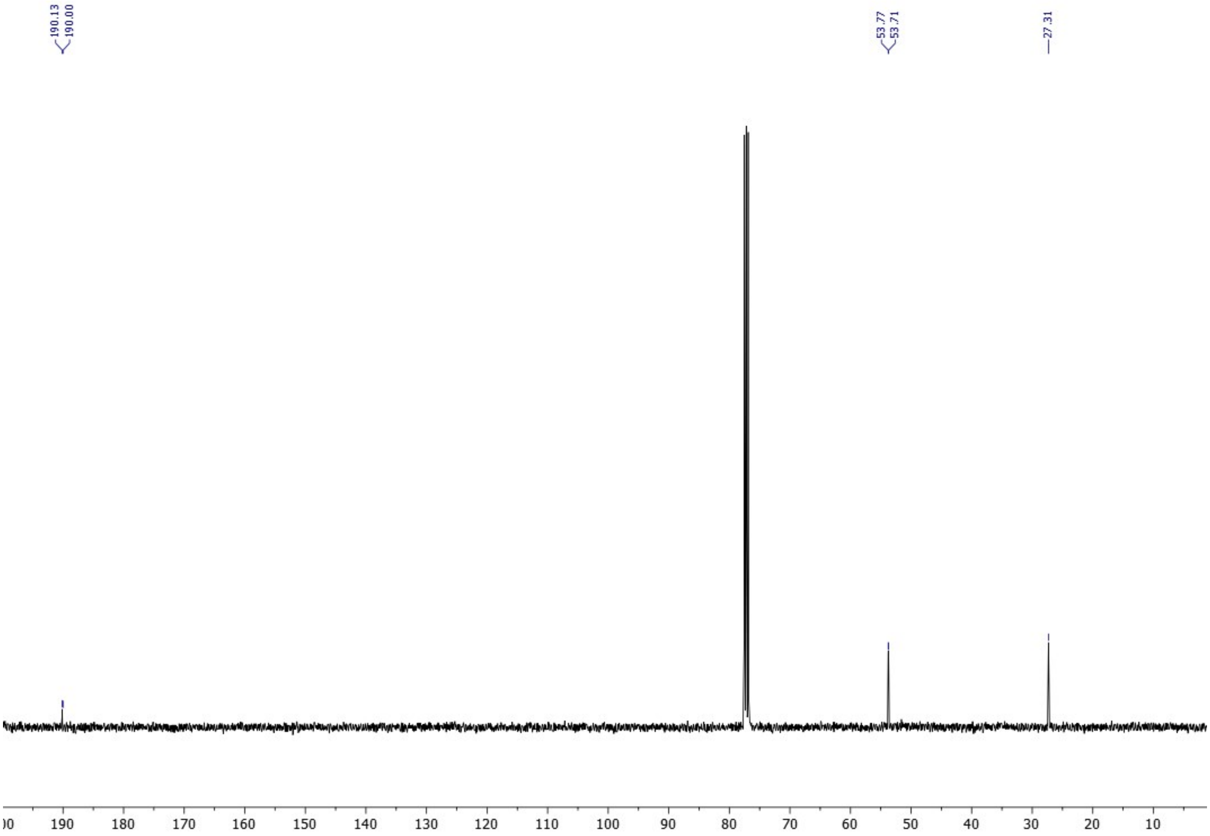

O
O
S
N3


2.00
2.01
3.05
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
146.39
135.66
130.46
127.71
21.93


0
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


O
O
P
OMe
OMe
N2


1.99
1.00
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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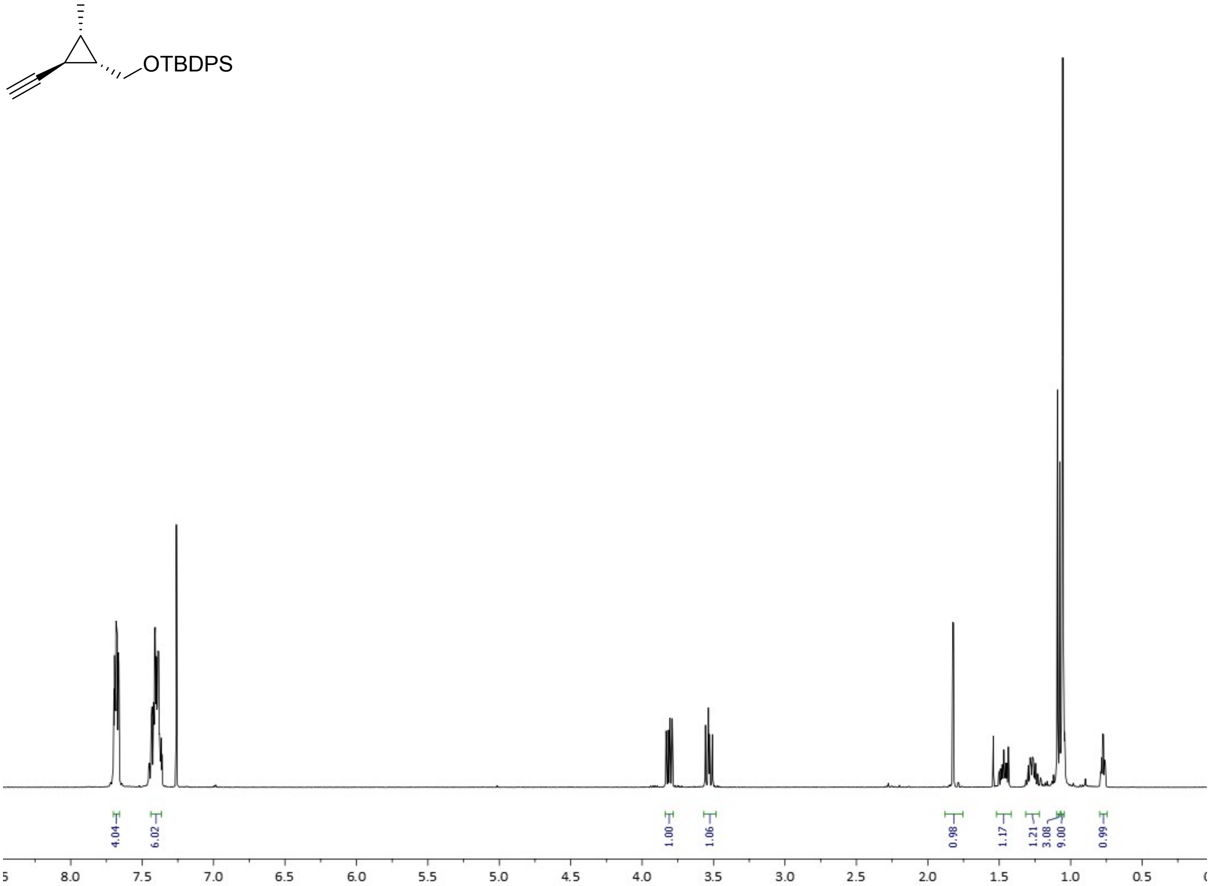
OTBDPS
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1.17
1.21
3.08
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7.5
7.0
6.5
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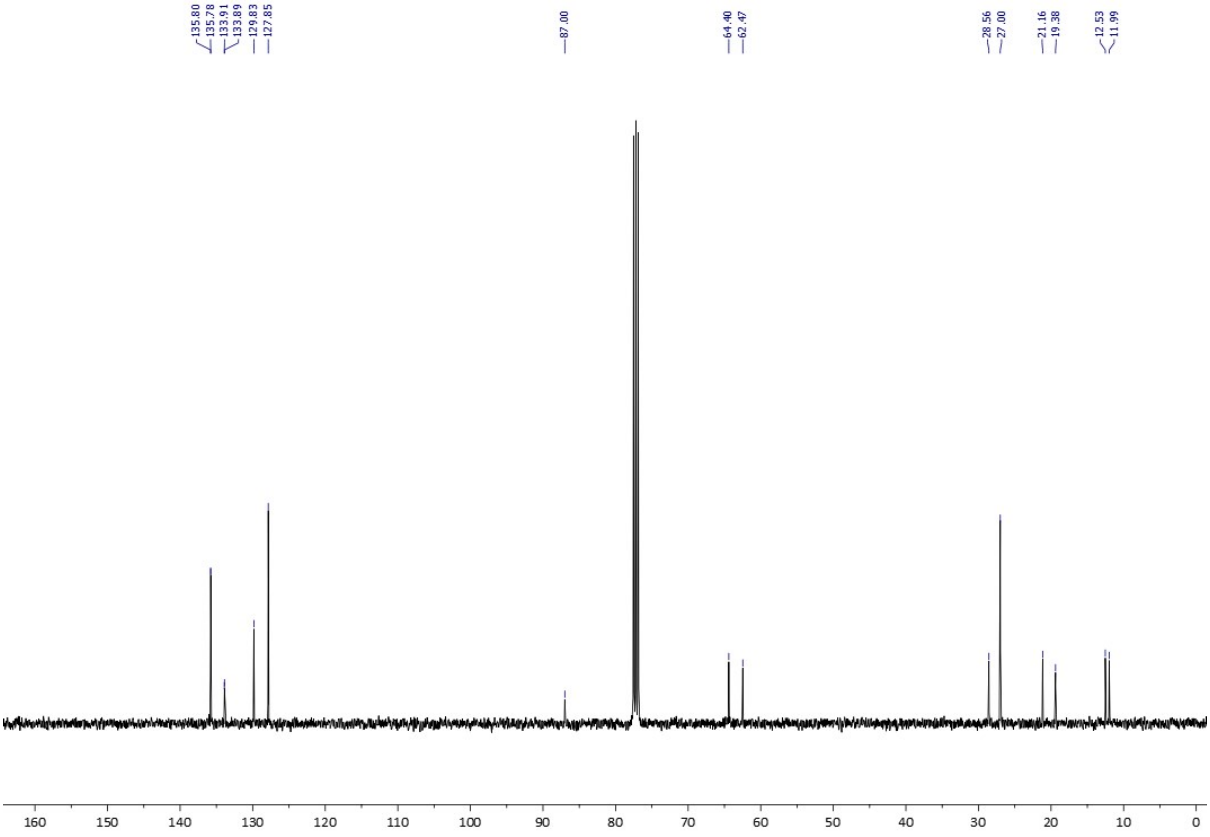
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64.40
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21.16
19.38
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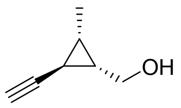
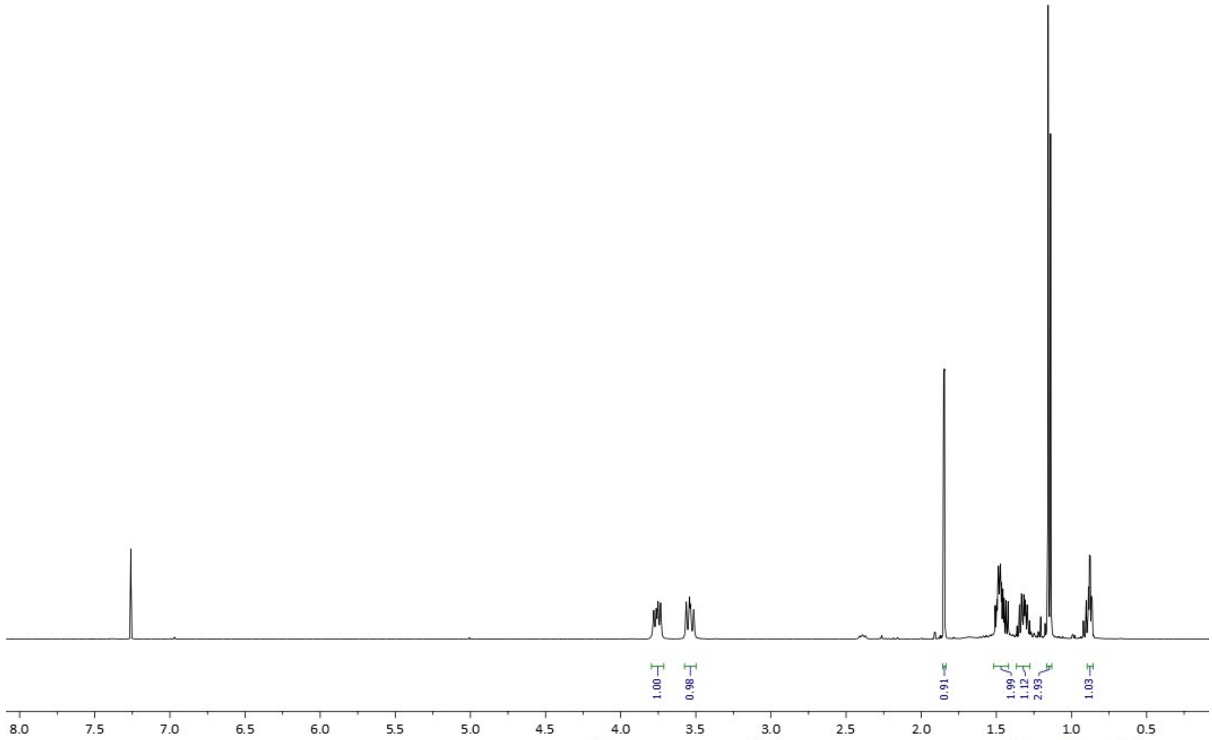

OH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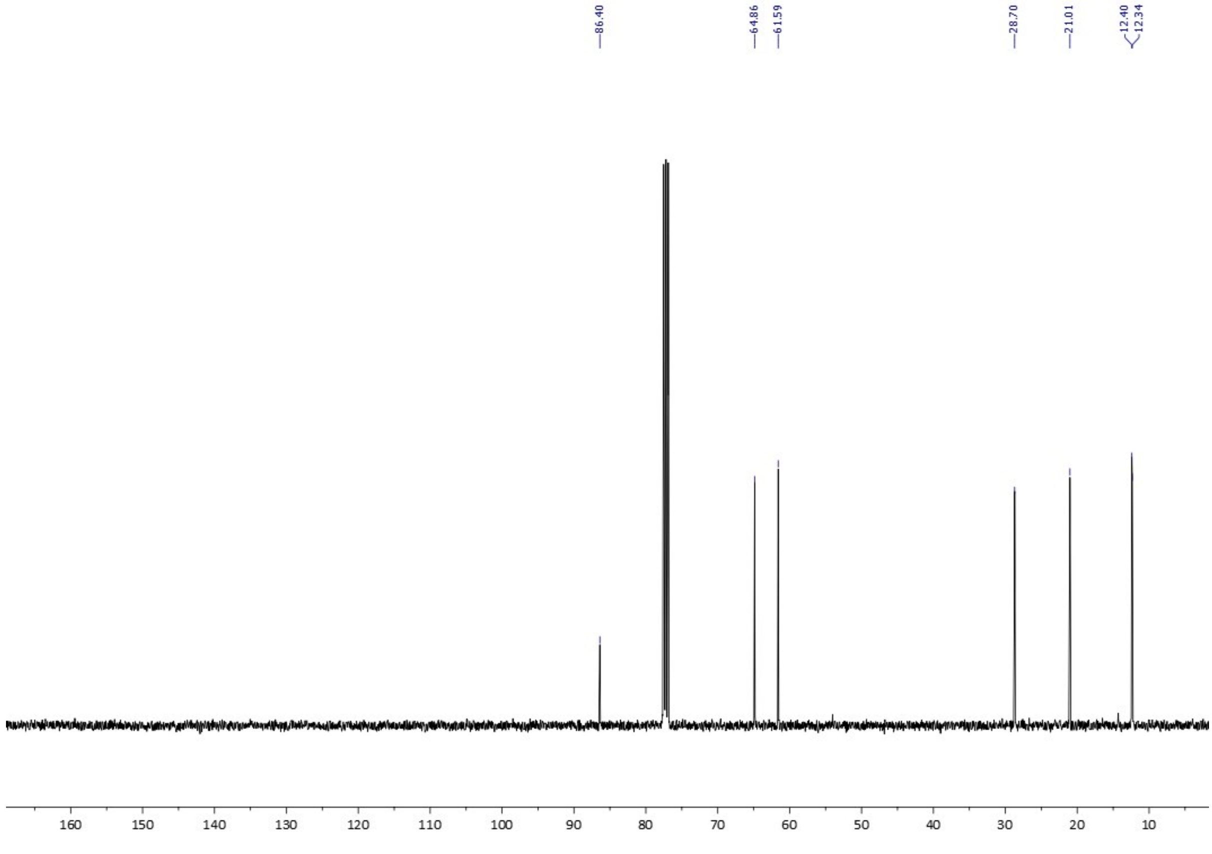
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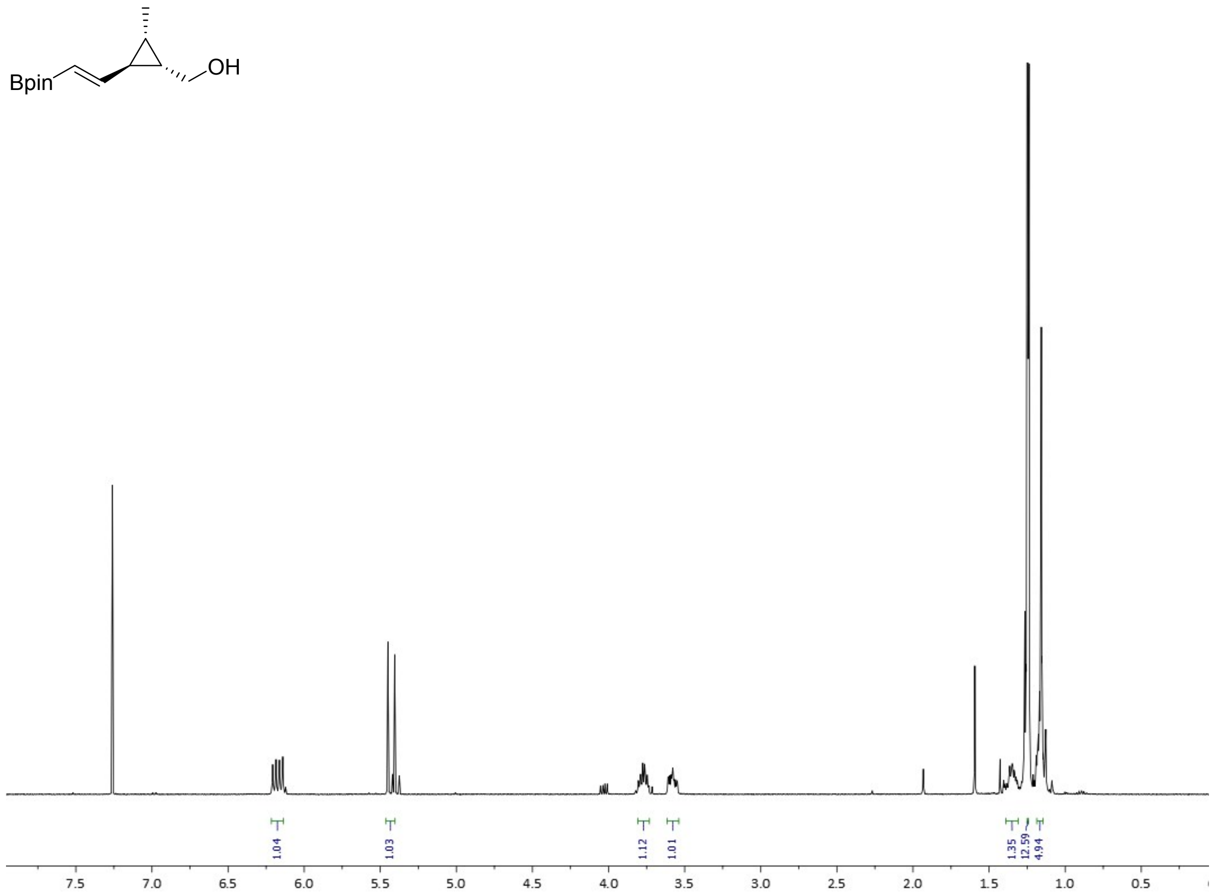
Bpin
OH
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1.01
1.35
12.59
4.94
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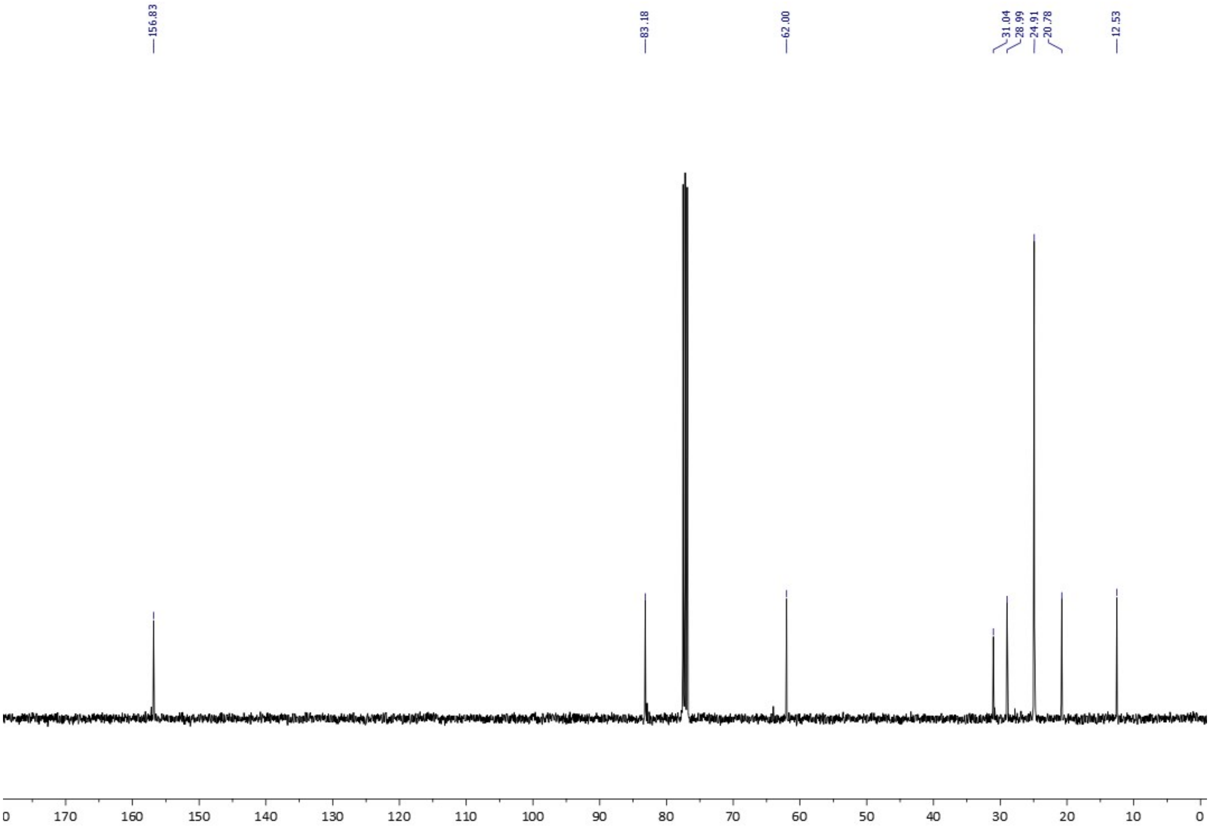
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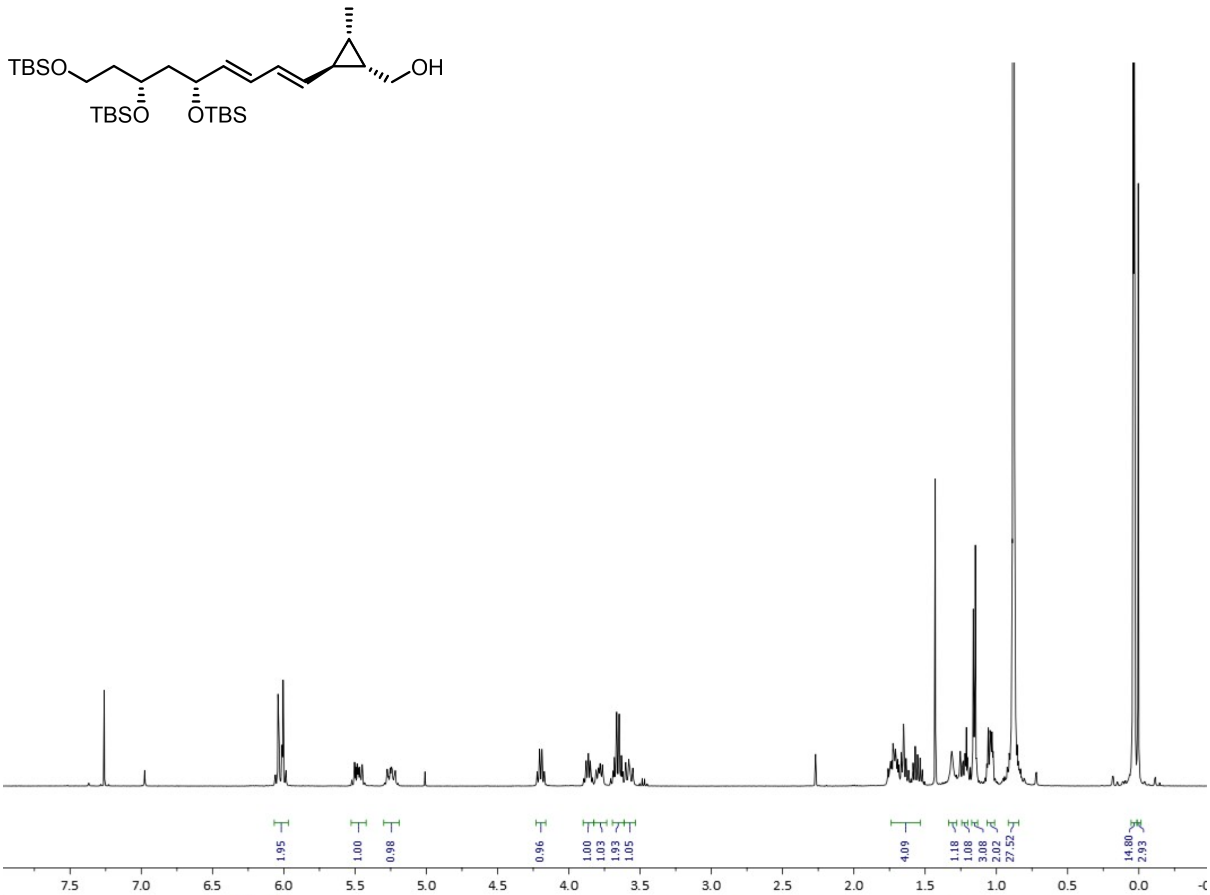
0

TBSO
TBSO
OTBS
OH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3.08
2.02
27.52
14.80
2.93
7.5
7.0
6.5
6.0
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2.0
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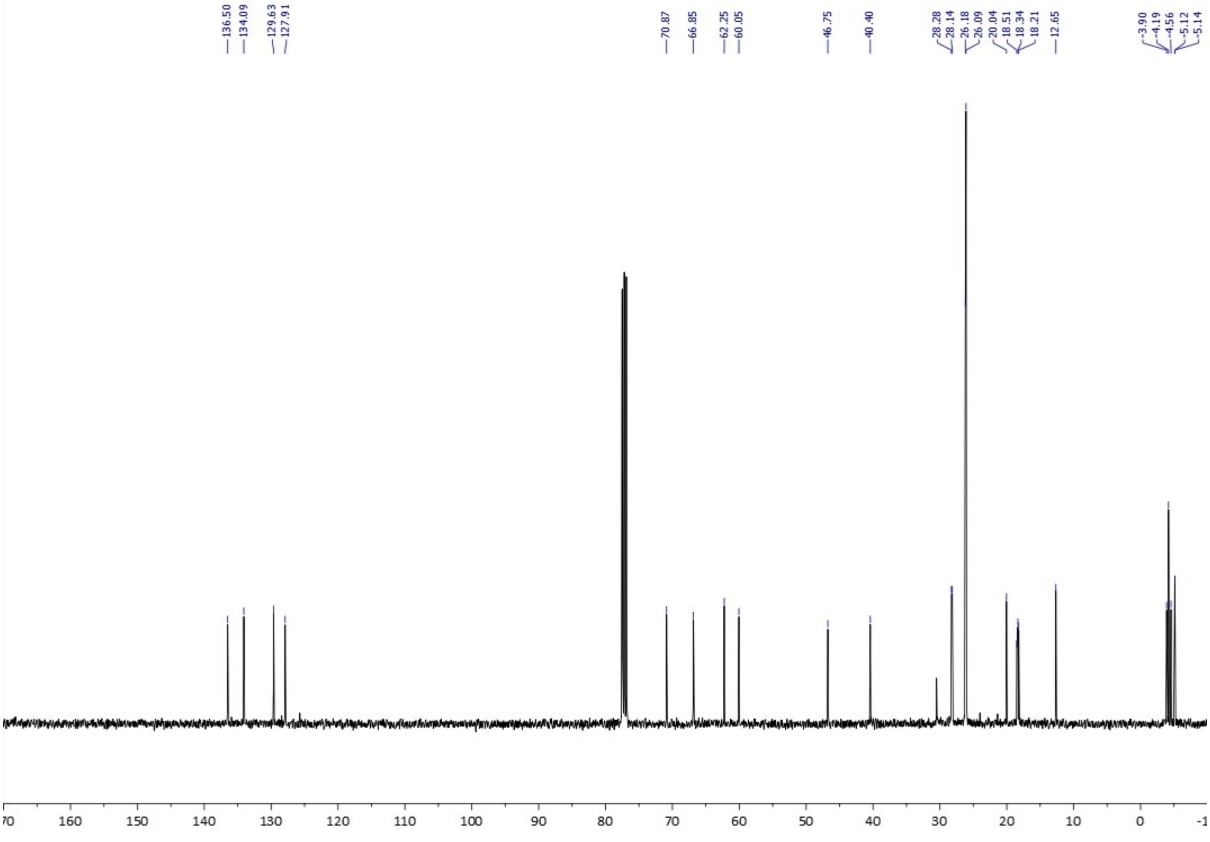
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66.85
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40.40
28.28
28.14
26.18
26.09
20.04
18.51
18.34
18.21
12.65
-3.90
-4.19
-4.56
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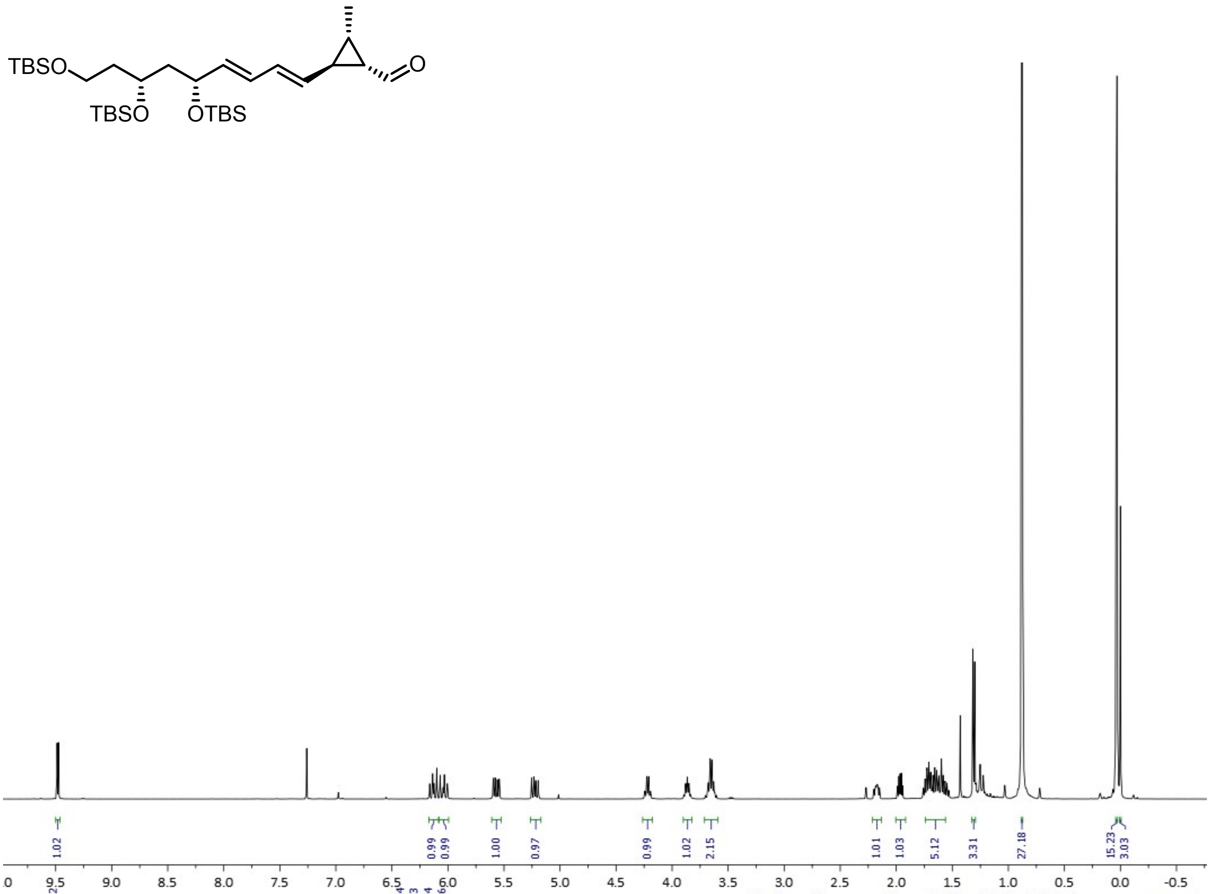
TBSO
TBSO
OTBS
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1.02
0.99
0.99
1.00
0.97
0.99
1.02
2.15
1.01
1.03
5.12
3.31
27.18
15.23
3.03
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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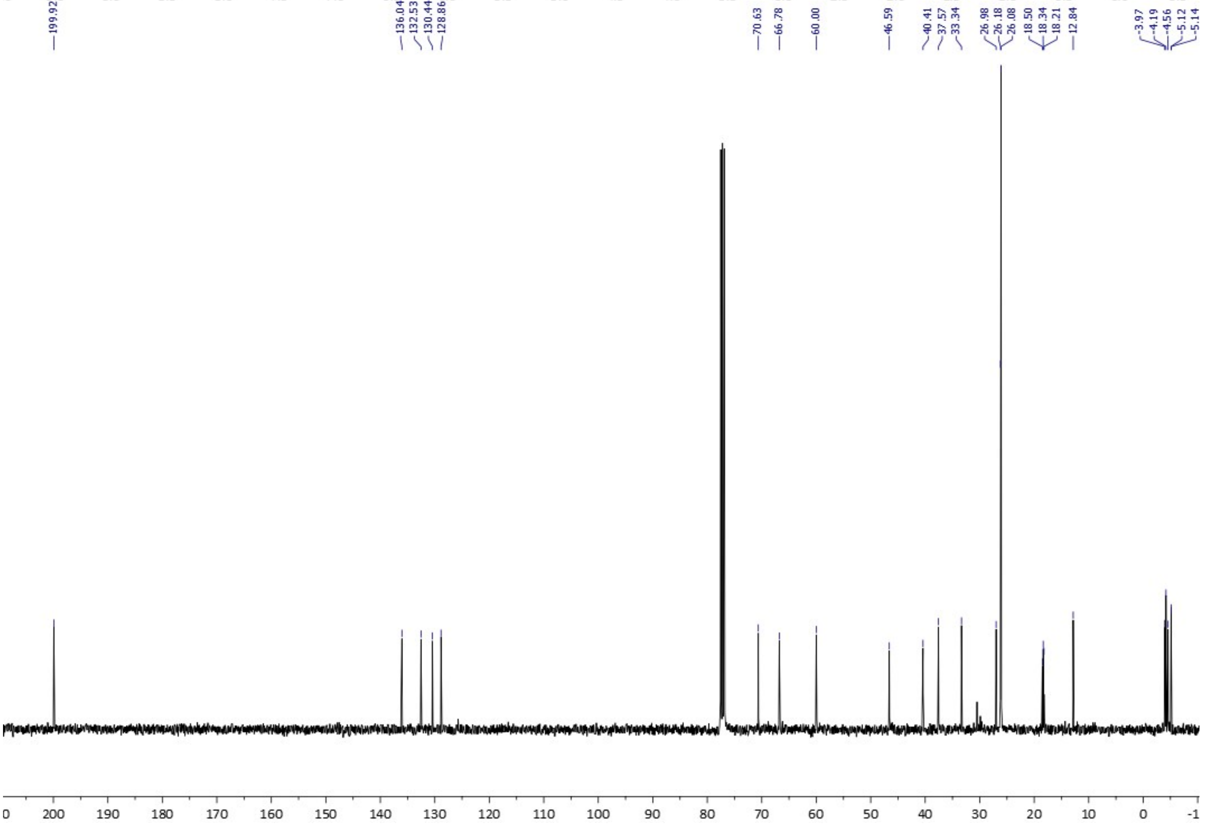
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5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33.34
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26.18
26.08
18.50
18.34
18.21
12.84
-3.97
-4.19
-4.56
-5.12
-5.14
0
200
190
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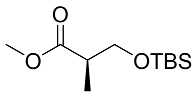
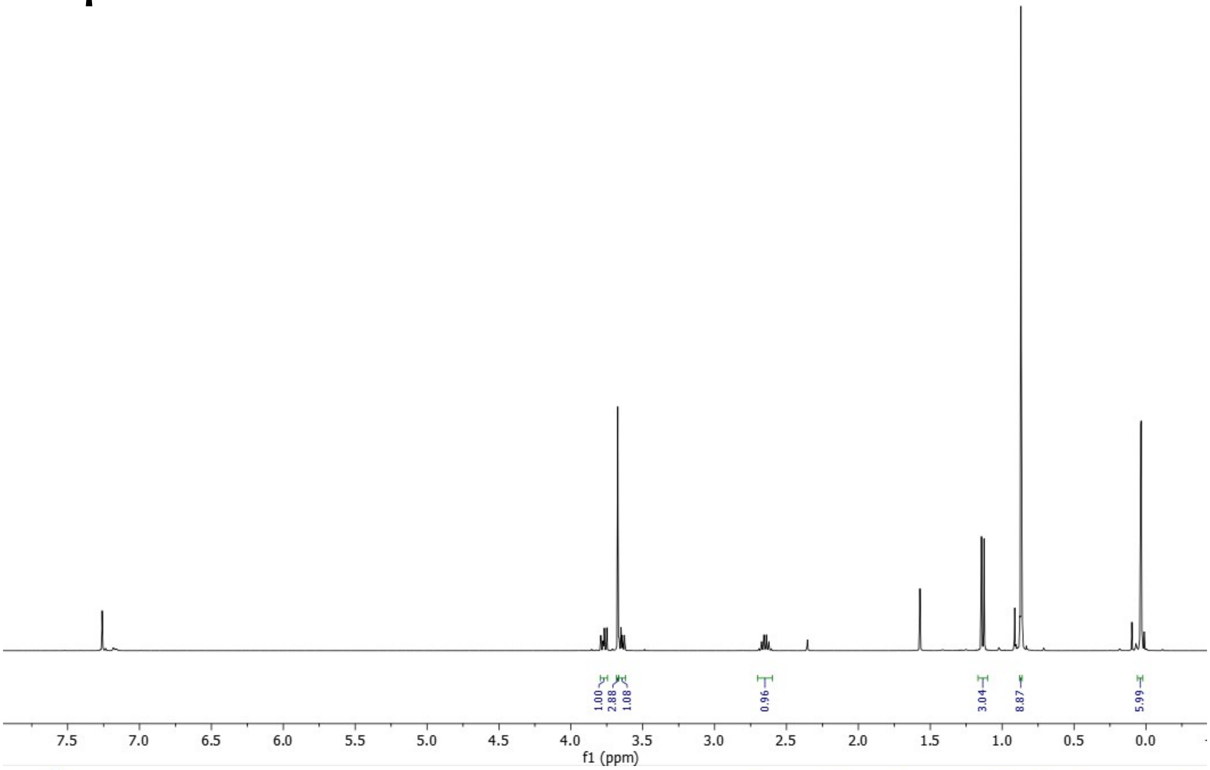
0
-1


O
O
OTBS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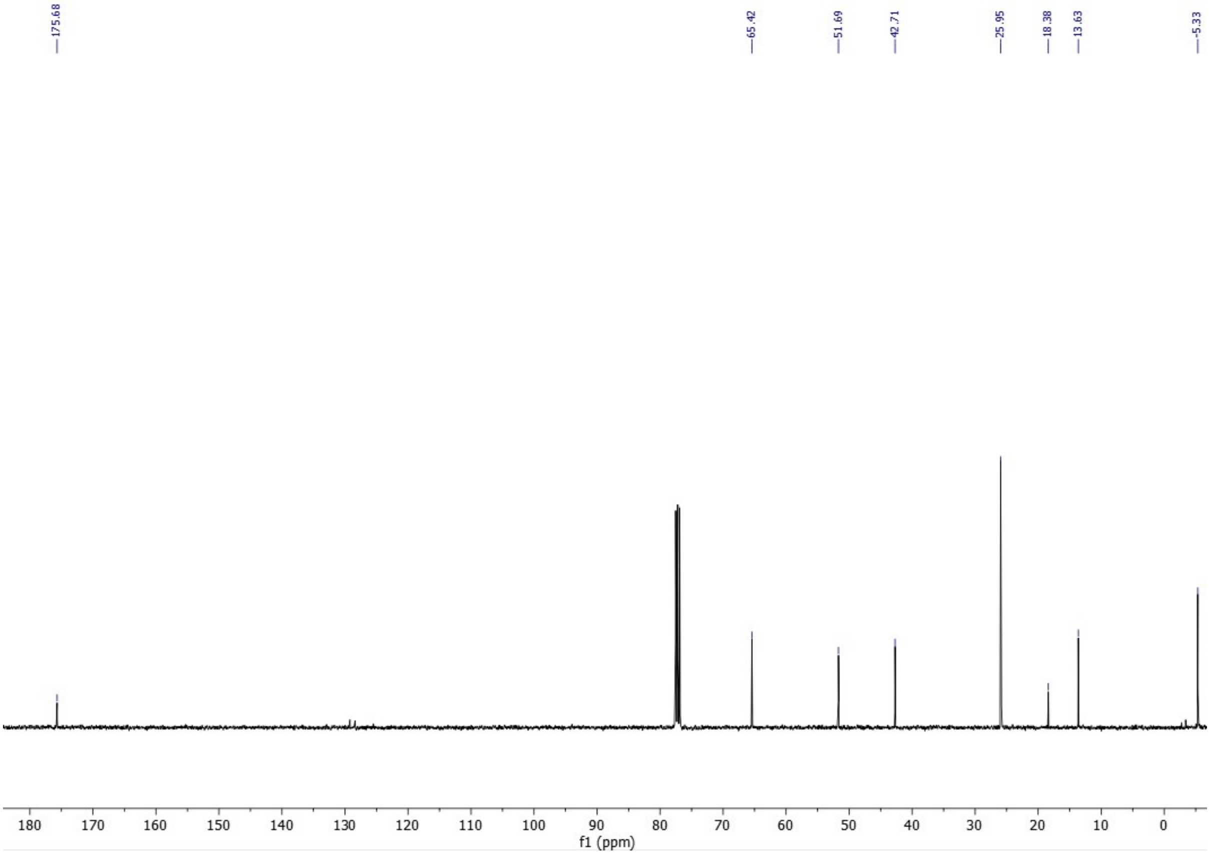
1.08
0.96
3.04
8.87
5.99
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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65.42
51.69
42.71
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18.38
13.63
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180
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90
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70
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50
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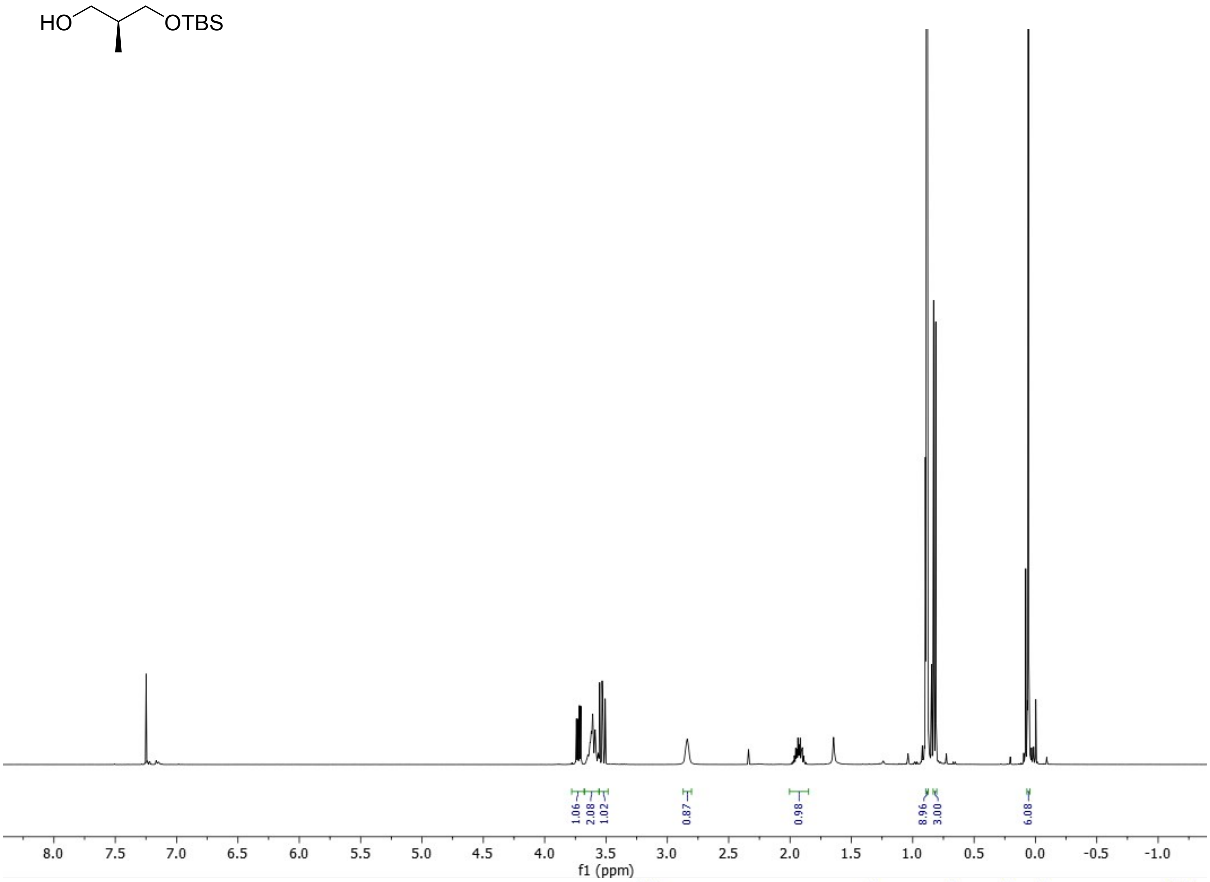
f1 (ppm)


HO
OTBS
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2.08
1.02
0.87
0.98
8.96
3.00
6.08
8.0
7.5
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6.5
6.0
5.5
5.0
4.5
4.0
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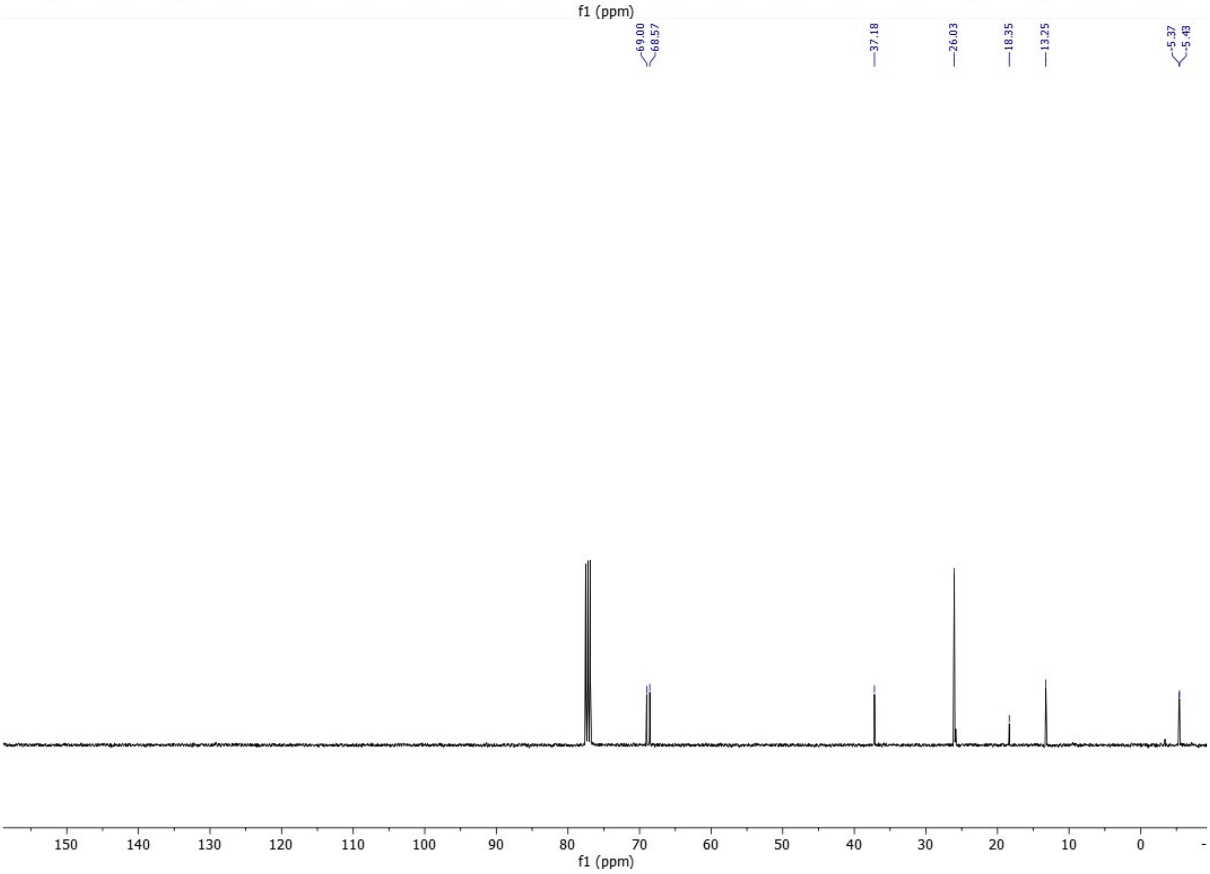
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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26.03
18.35
13.25
-5.37
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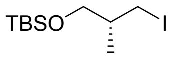
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


TBSO
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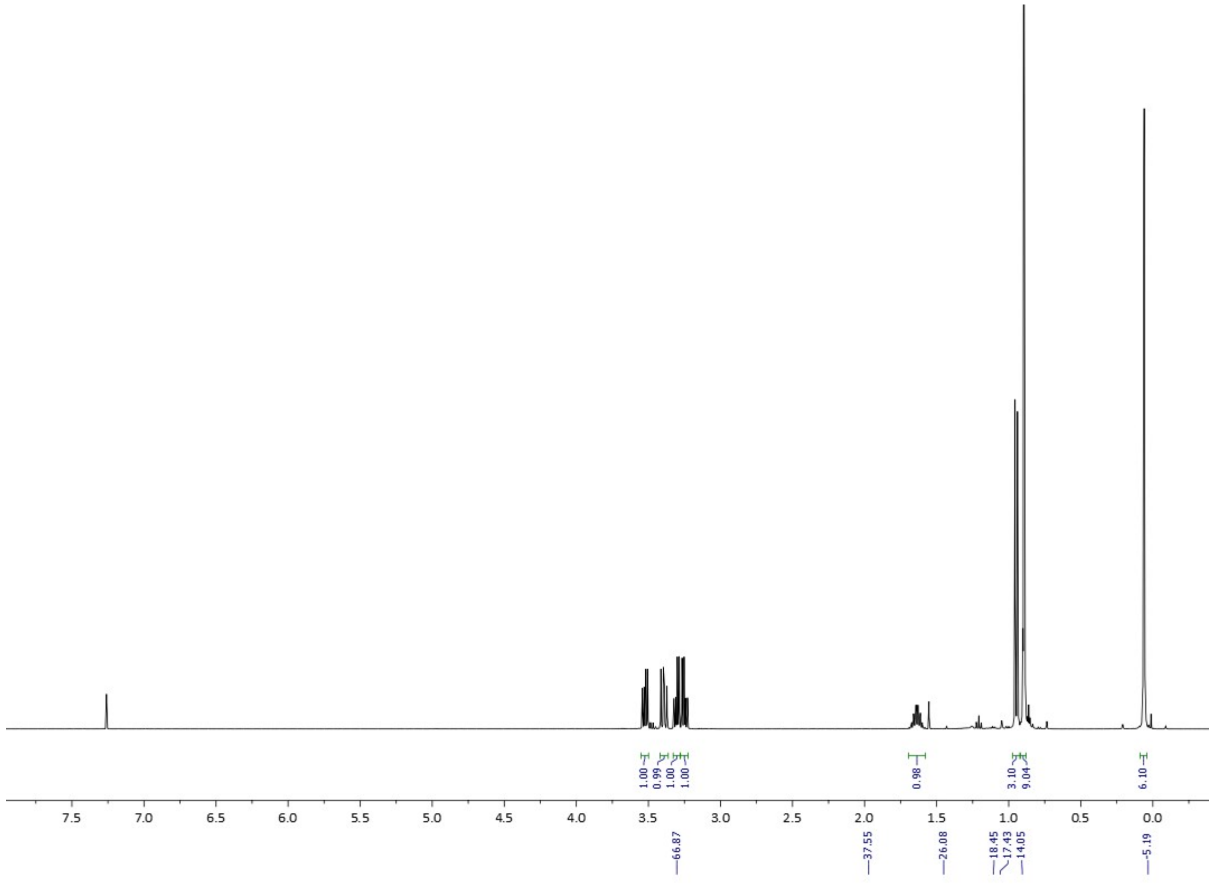
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1.00
1.00
0.98
3.10
9.04
6.10
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
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0.5
0.0
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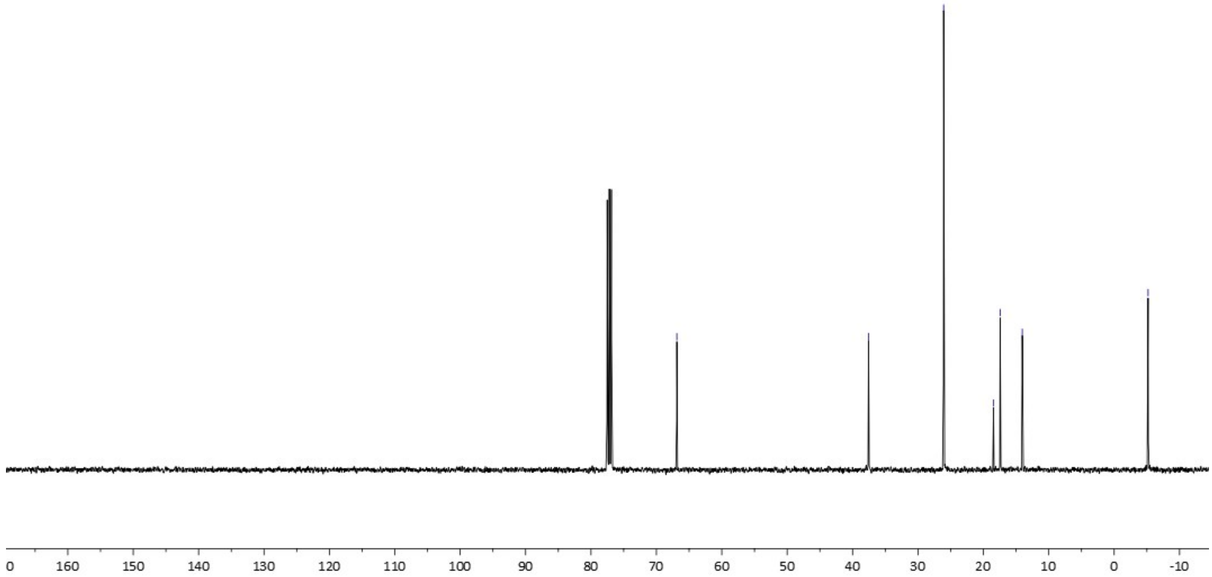
17.43
14.05
-5.19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100
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60
50
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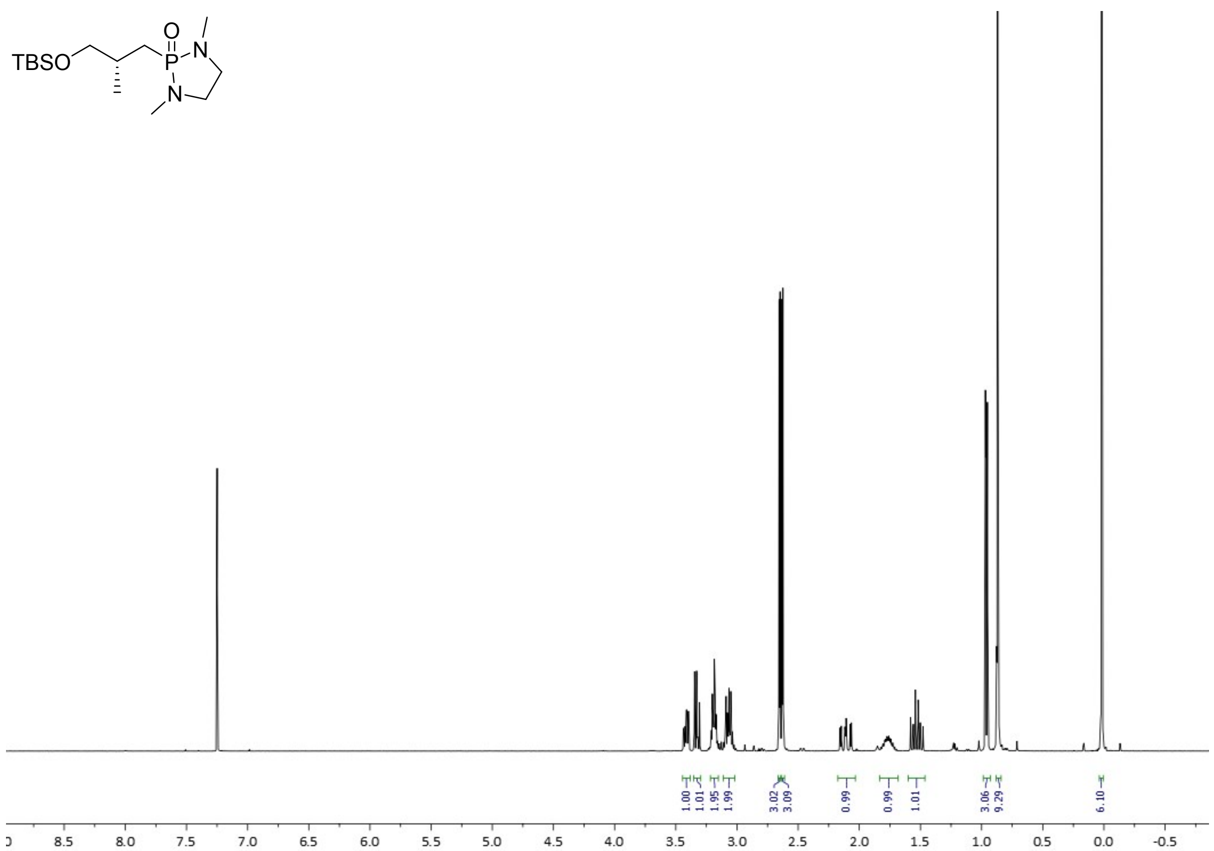
10
0
-10


TBSO
O
P
N
N
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1.99
3.02
3.09
0.99
0.99
1.01
3.06
9.29
6.10
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
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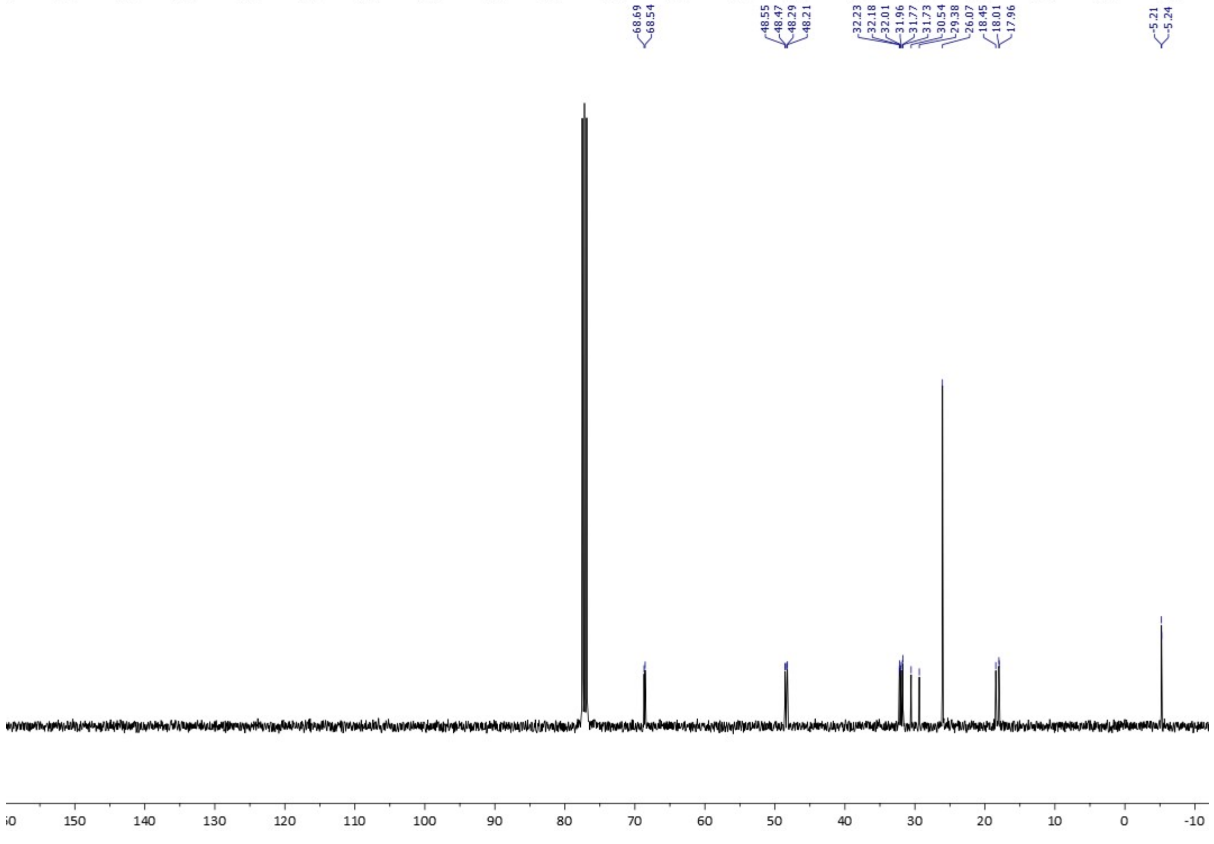
0.0
-0.5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32.18
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31.96
31.77
31.73
30.54
29.38
26.07
18.45
18.01
17.96
-5.21
-5.24
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100
90
80
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60
50
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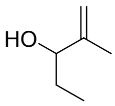
20
10
0
-10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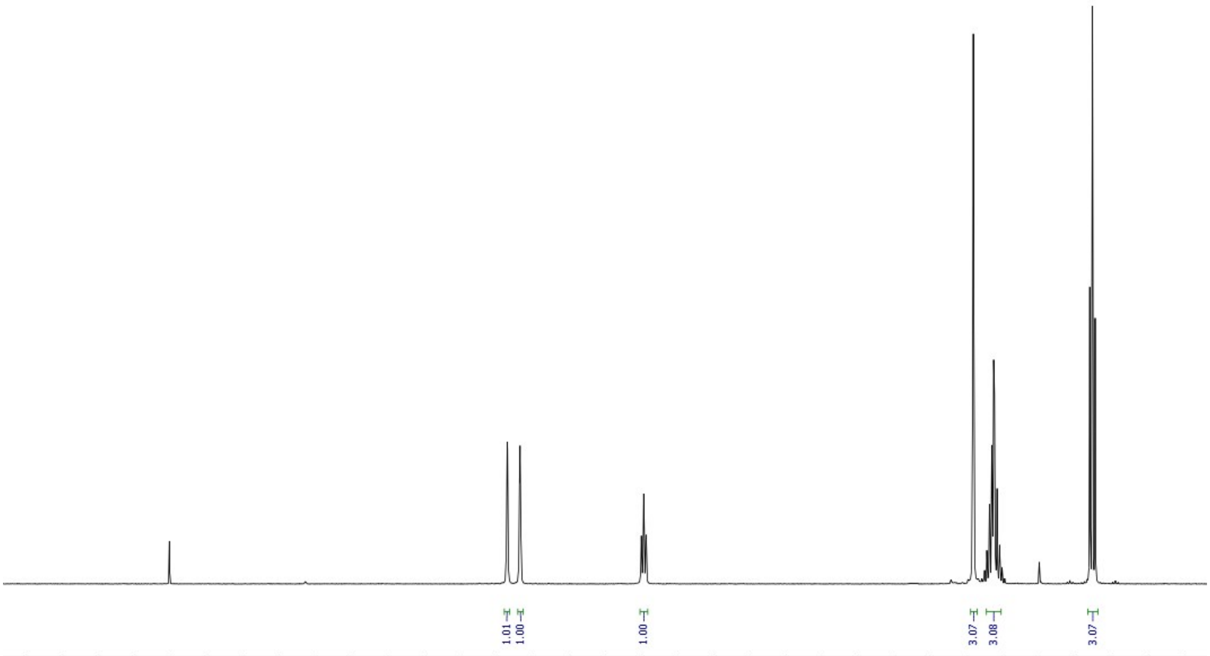
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1.00
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3.08
3.07
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7.5
7.0
6.5
6.0
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4.5
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3.0
2.5
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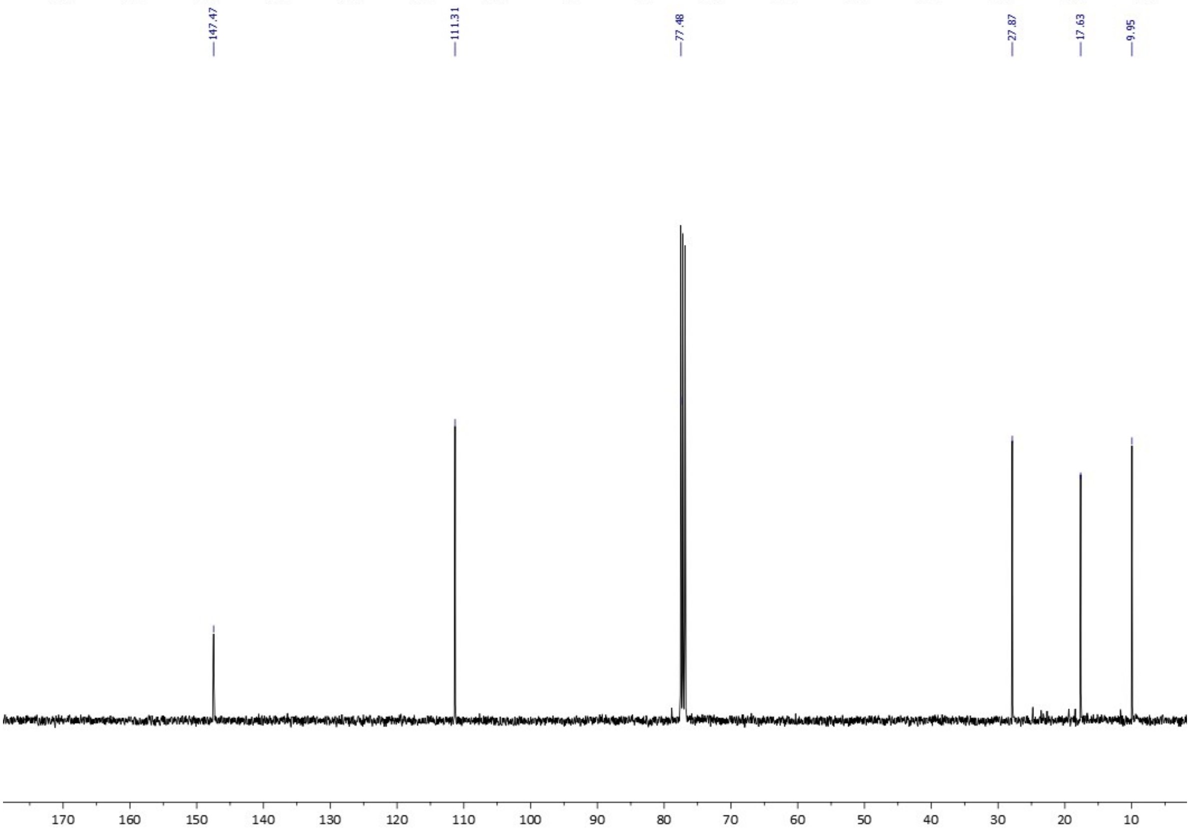
1.0
0.5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140
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120
110
100
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80
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20
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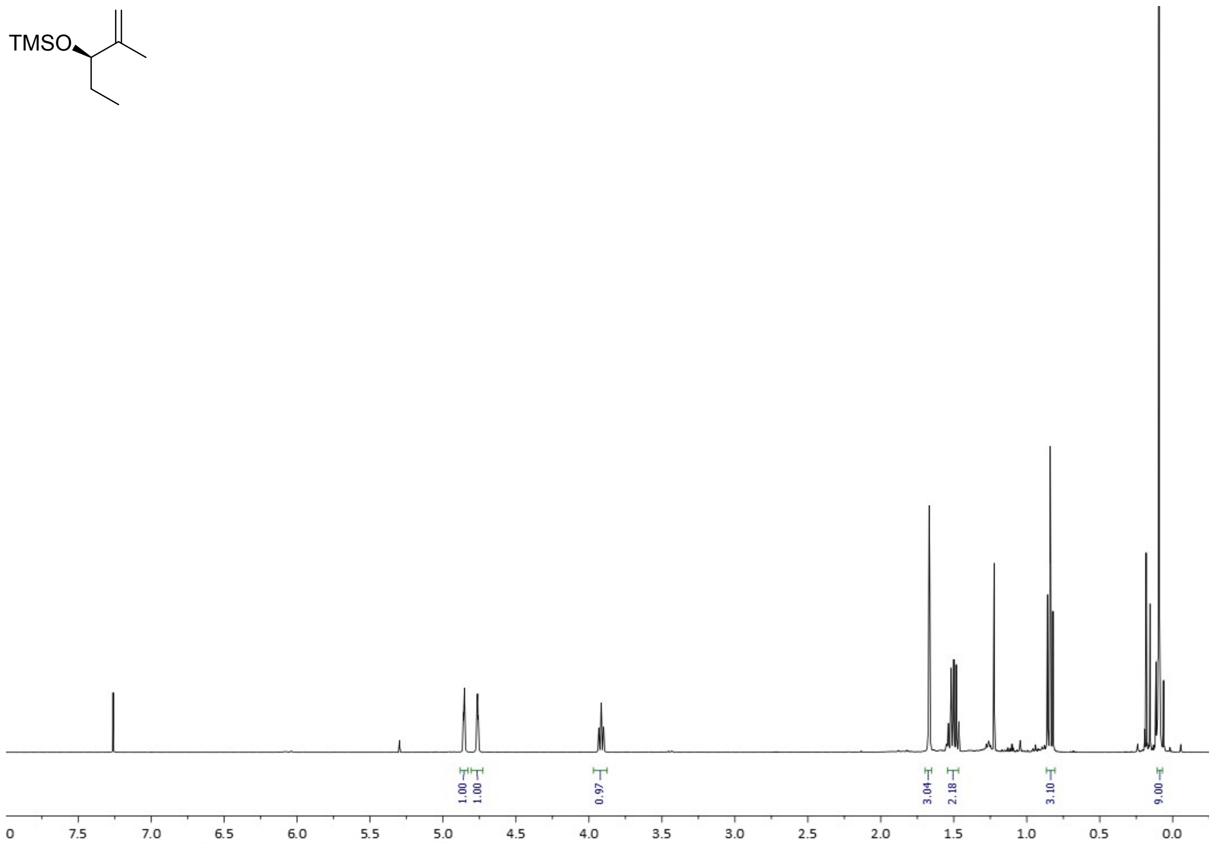
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0
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5.0
4.5
4.0
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3.0
2.5
2.0
1.5
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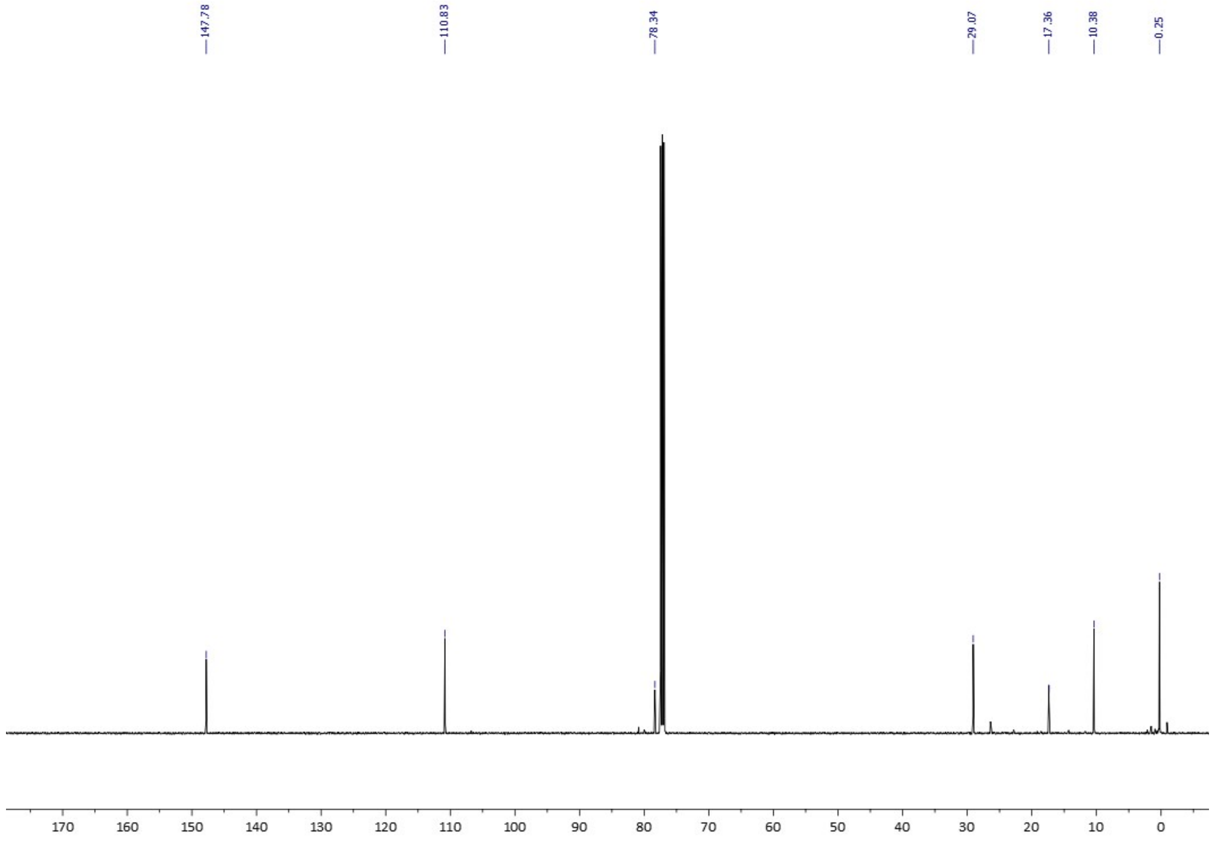
0.5
0.0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70
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30
20
10
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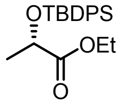
OTBDPS
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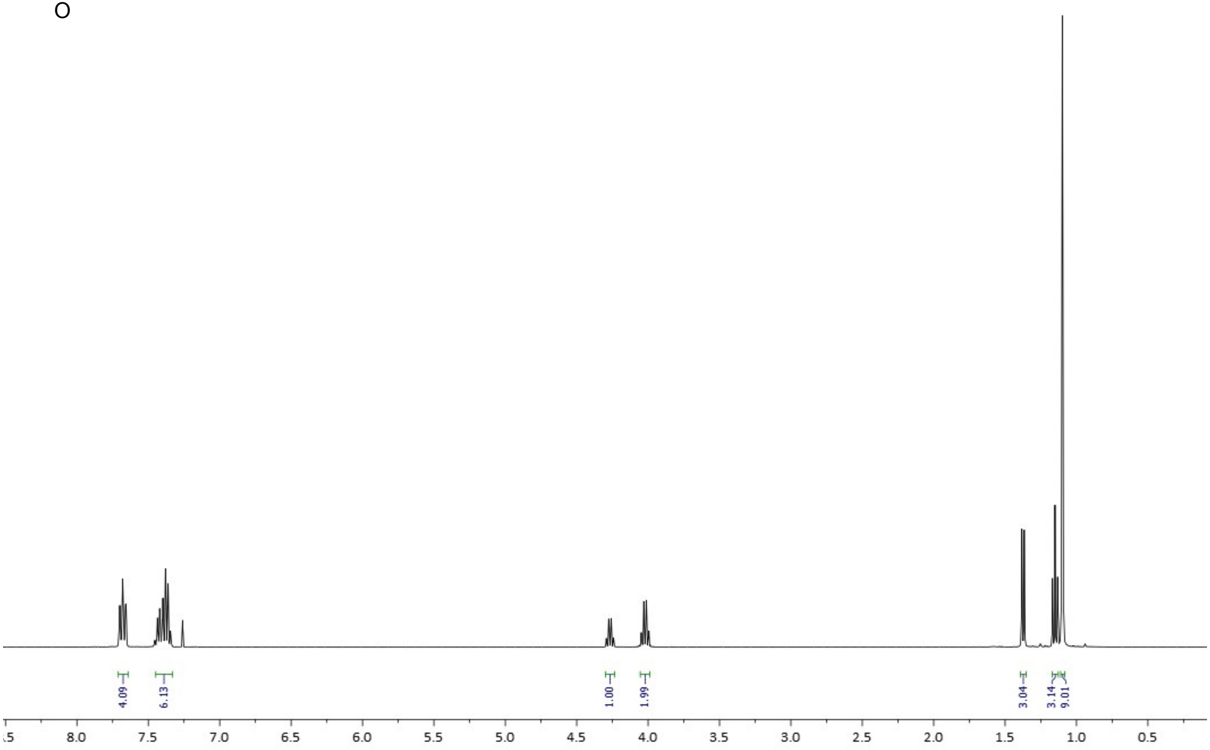
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6.13
1.00
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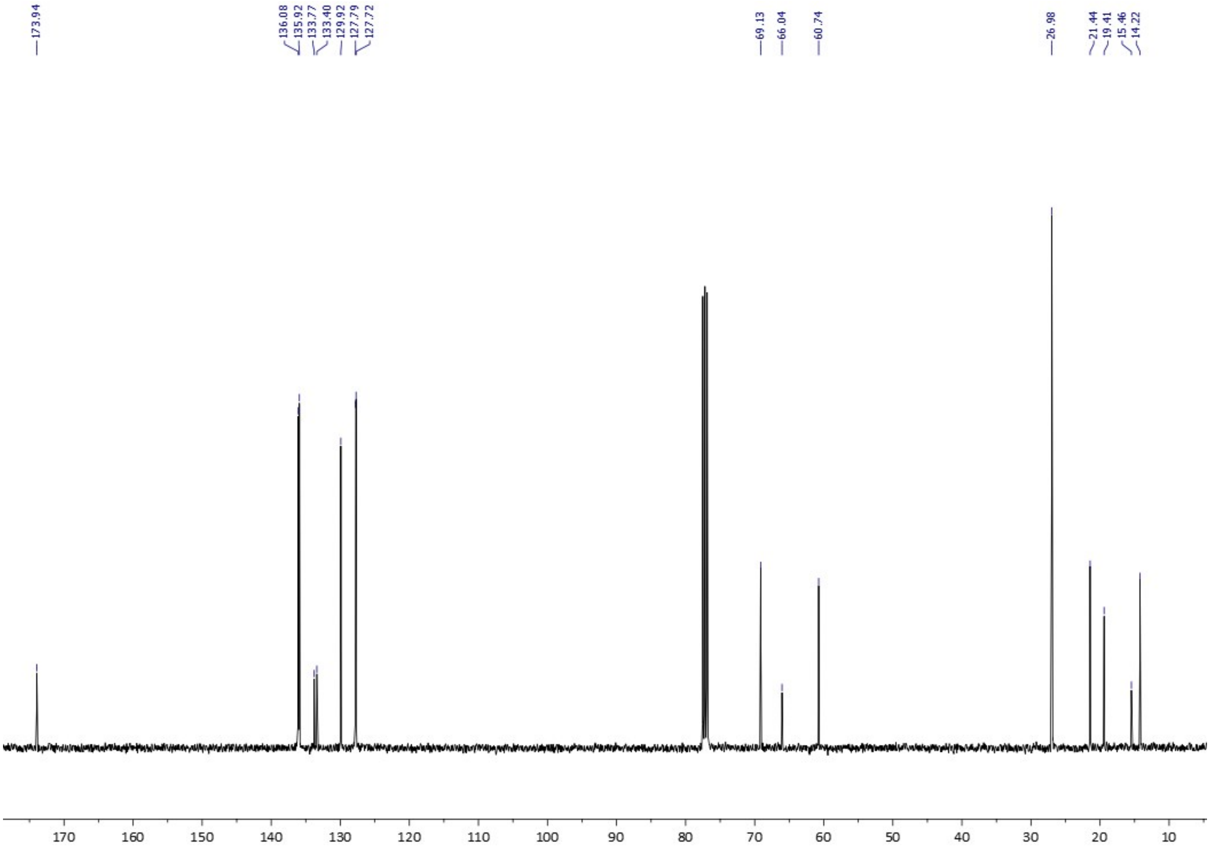
3.14
9.01
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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129.92
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127.72
69.13
66.04
60.74
26.98
21.44
19.41
15.46
14.22
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


OTBDPS
O
1.00
4.39
6.64
1.03
3.25
9.30
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
4.5
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3.5
3.0
2.5
2.0
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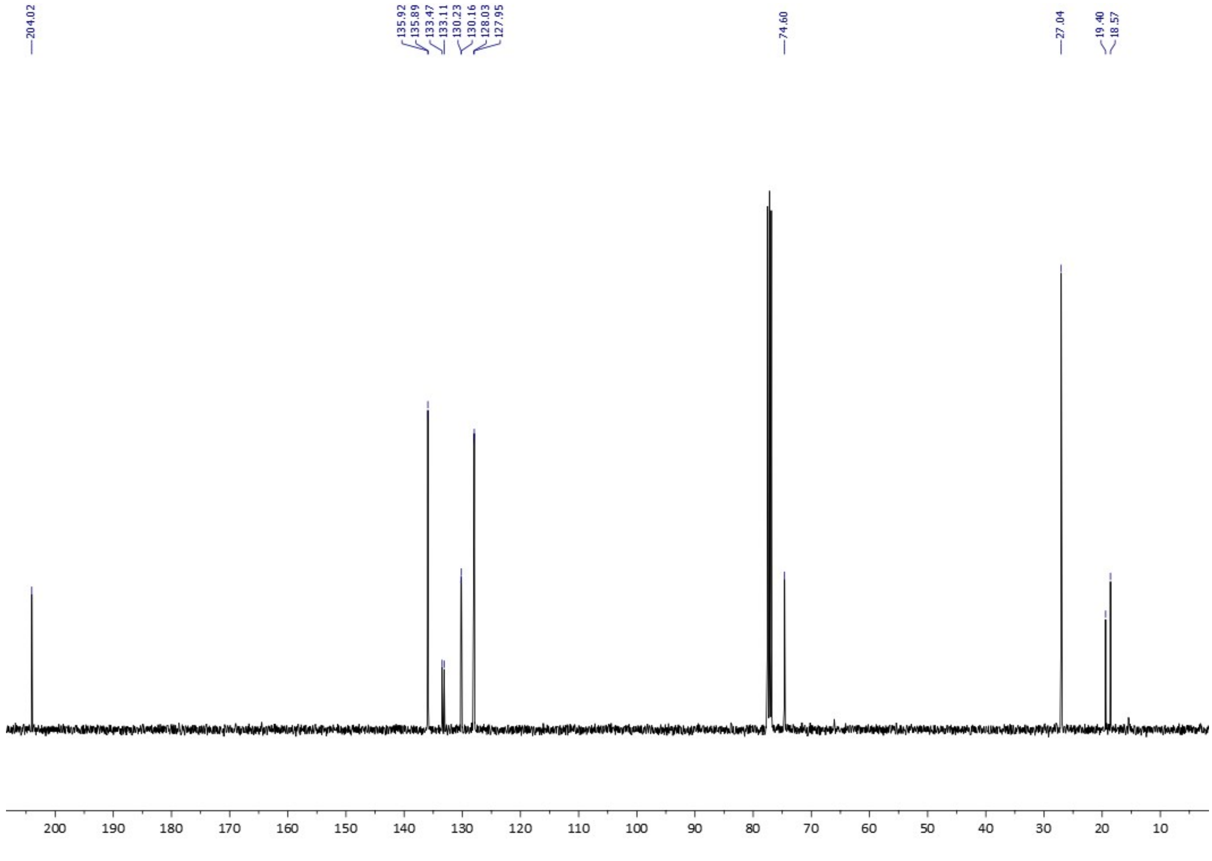
1.0
0.5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74.60
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18.57
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190
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120
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100
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80
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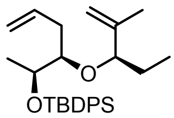
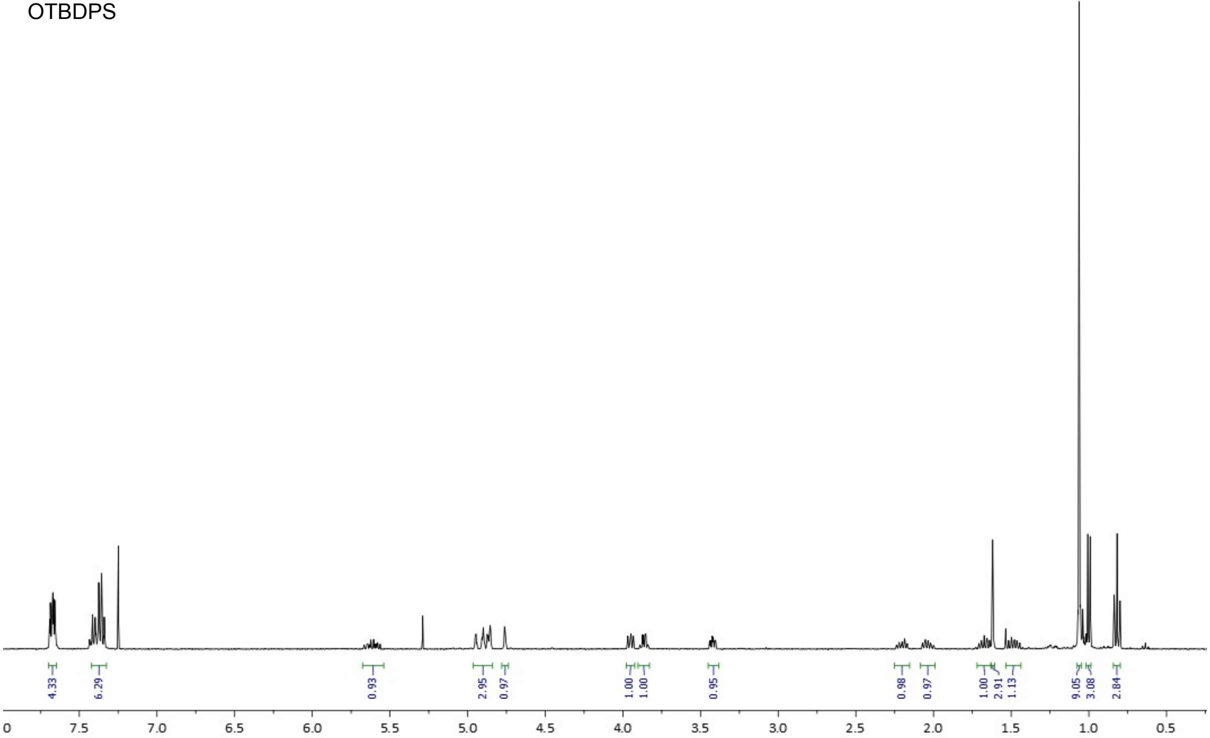

O
OTBDPS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6.29
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1.00
0.95
0.98
0.97
1.00
2.91
1.13
9.05
3.08
2.84
0
7.5
7.0
6.5
6.0
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4.5
4.0
3.5
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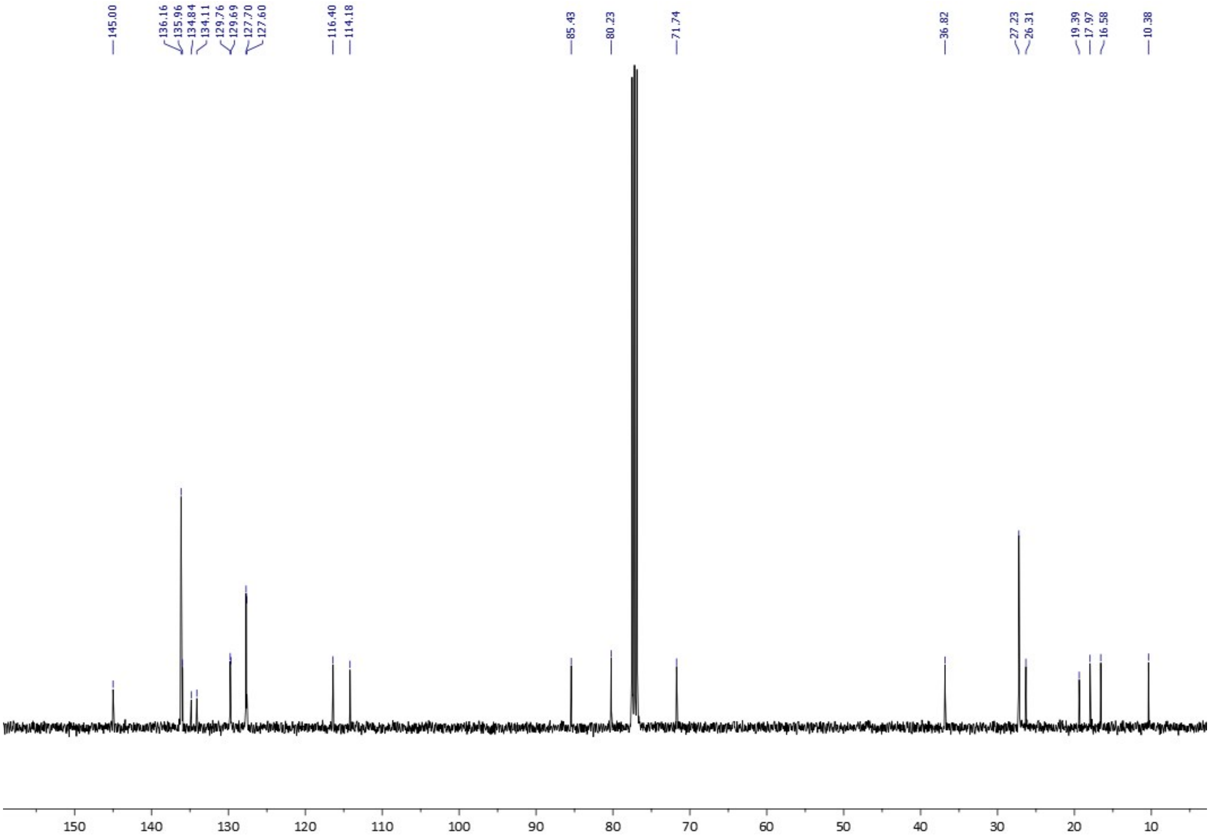
2.5
2.0
1.5
1.0
0.5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127.70
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116.40
114.18
85.43
80.23
71.74
36.82
27.23
26.31
19.39
17.97
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10.38
150
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120
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100
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80
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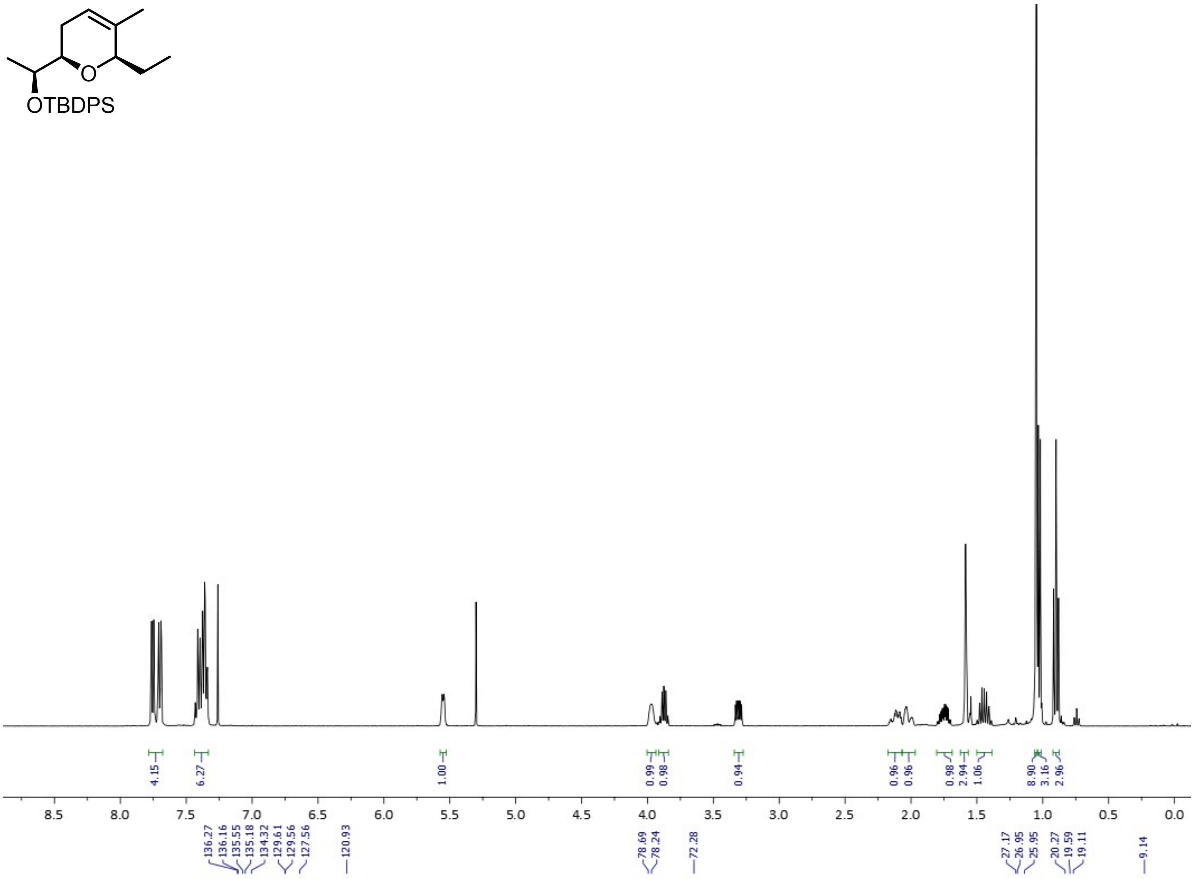
O
OTBDPS
4.15
6.27
1.00
0.99
0.98
0.94
0.96
0.96
0.98
2.94
1.06
8.90
3.16
2.96
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
136.27
136.16
135.55
135.18
134.32
129.61
129.56
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78.24
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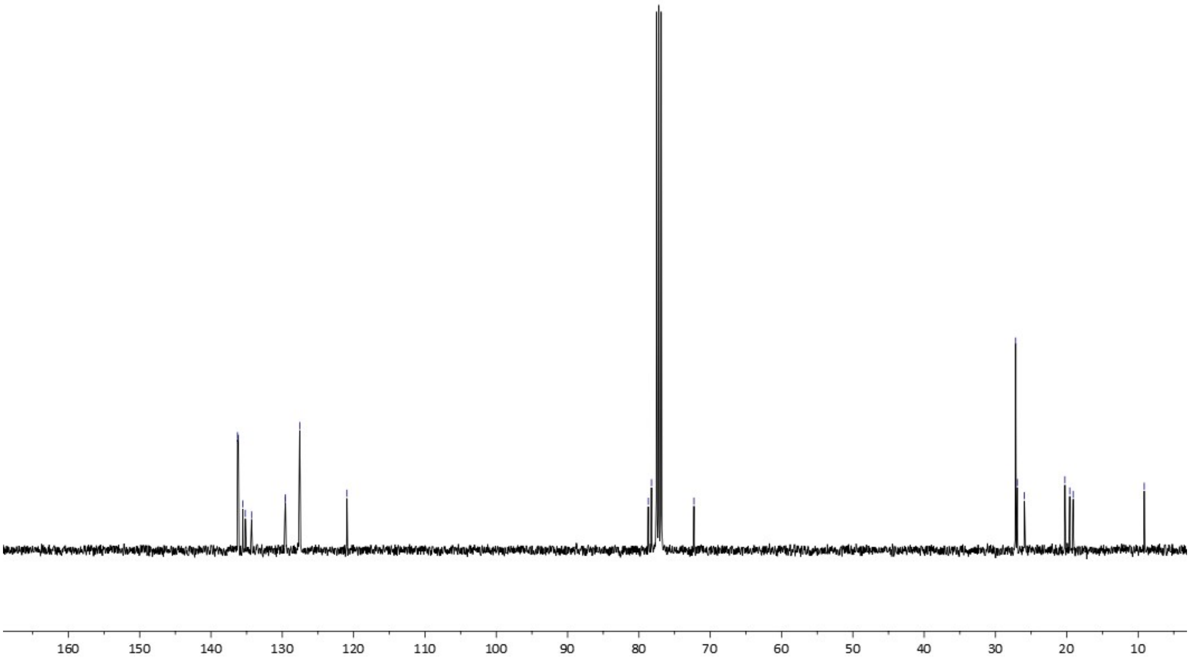
20.27
19.59
19.11
9.14


160
150
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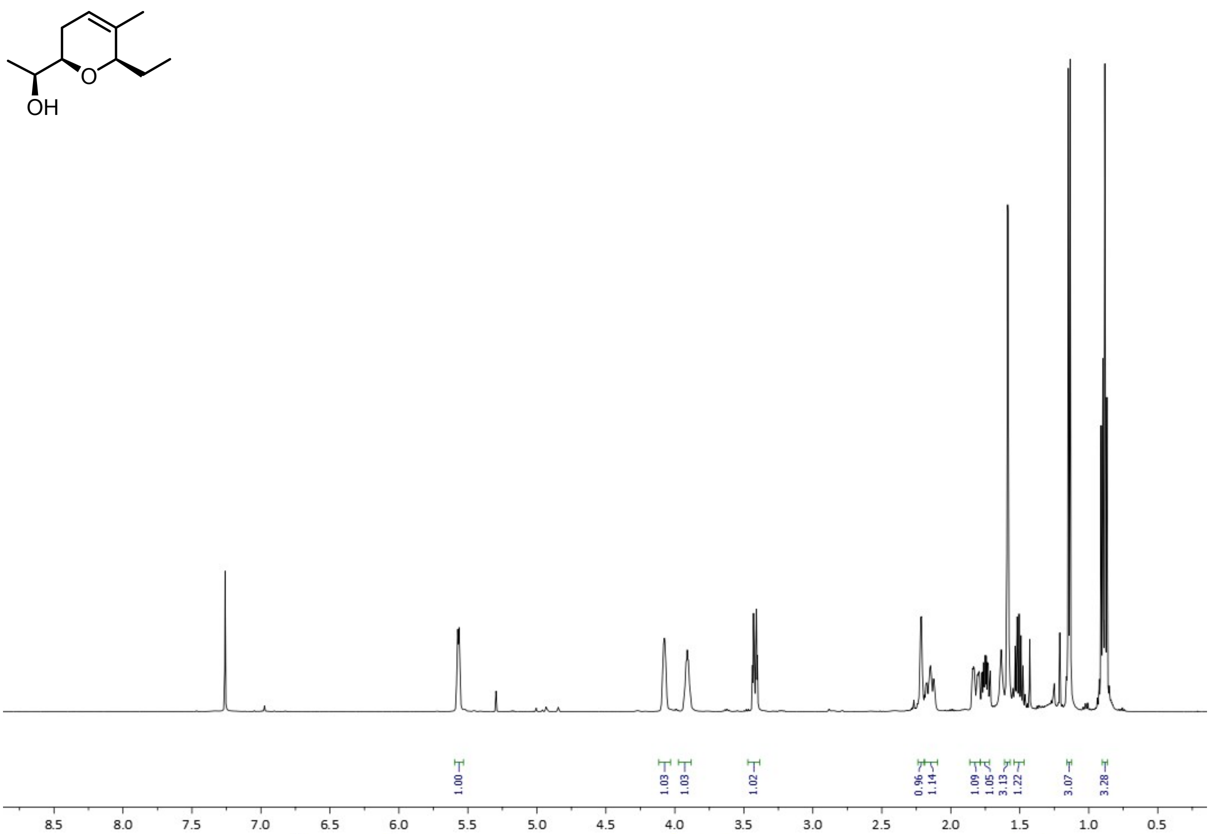
OH
O
1.00
1.03
1.03
1.02
0.96
1.14
1.09
1.05
3.13
1.22
3.07
3.28
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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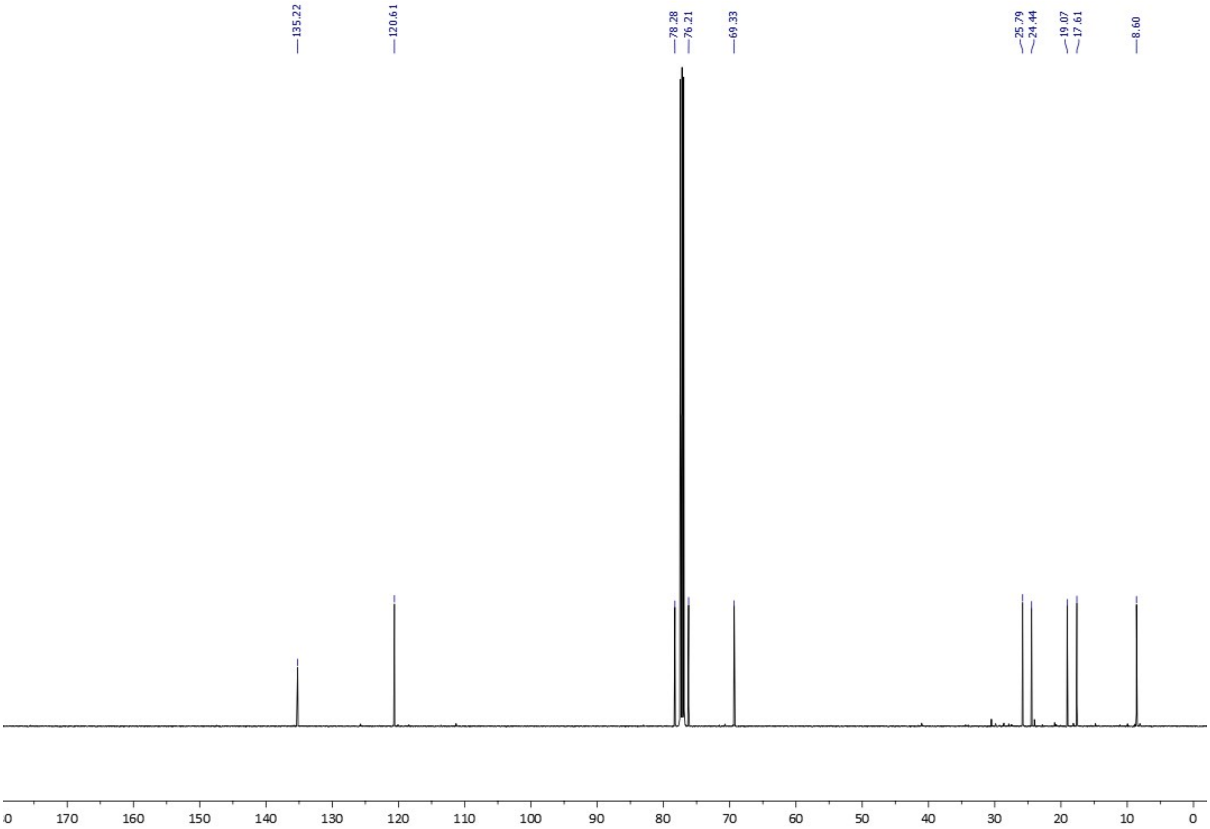
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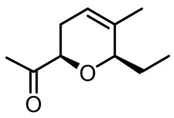
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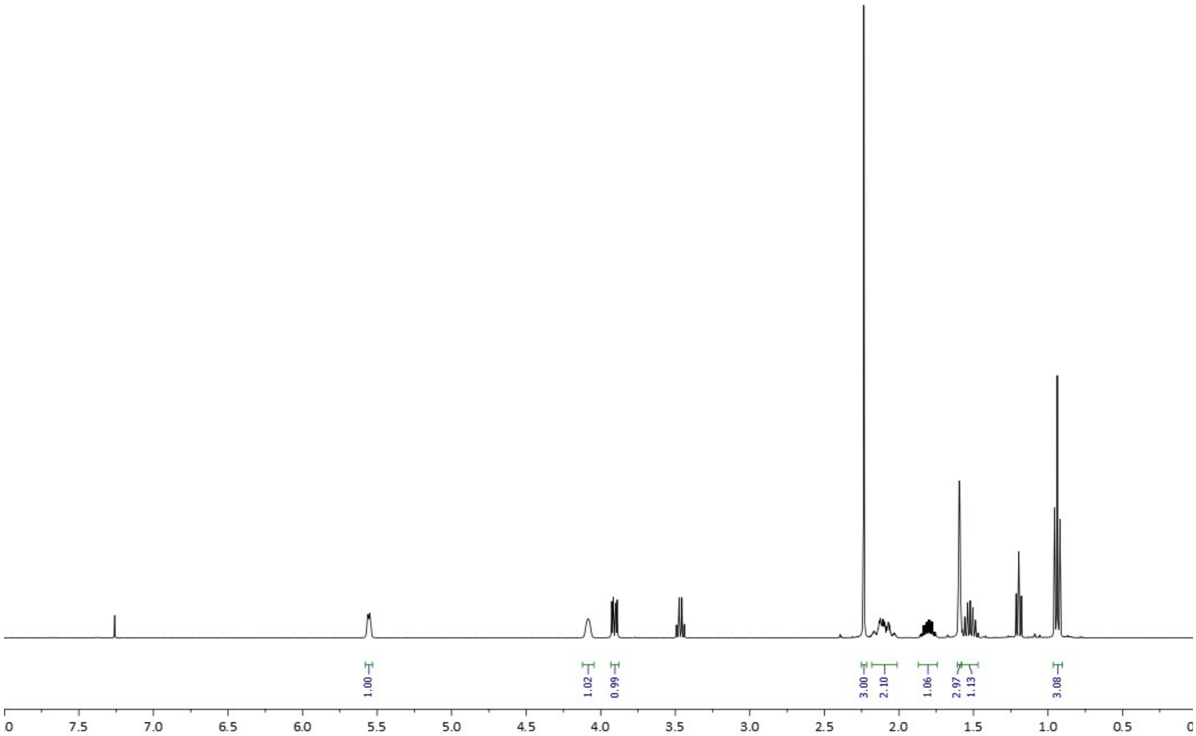
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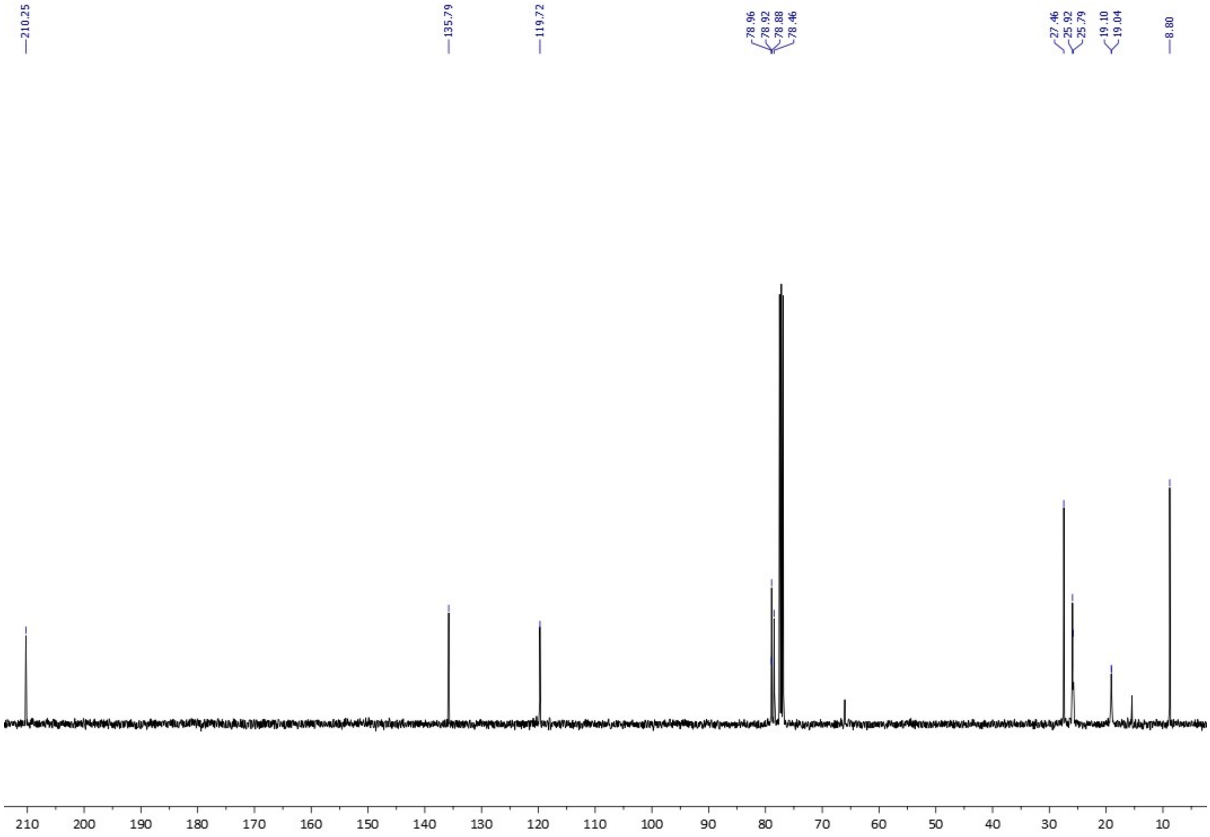
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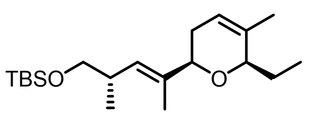
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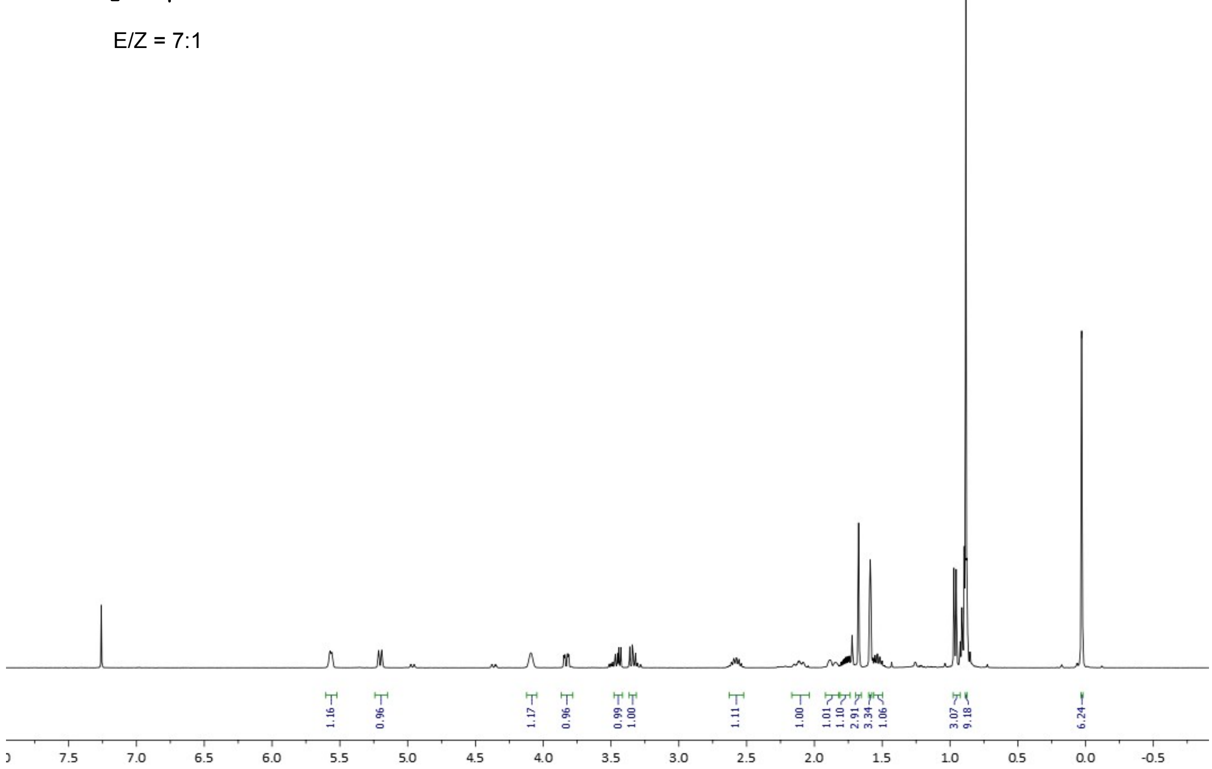
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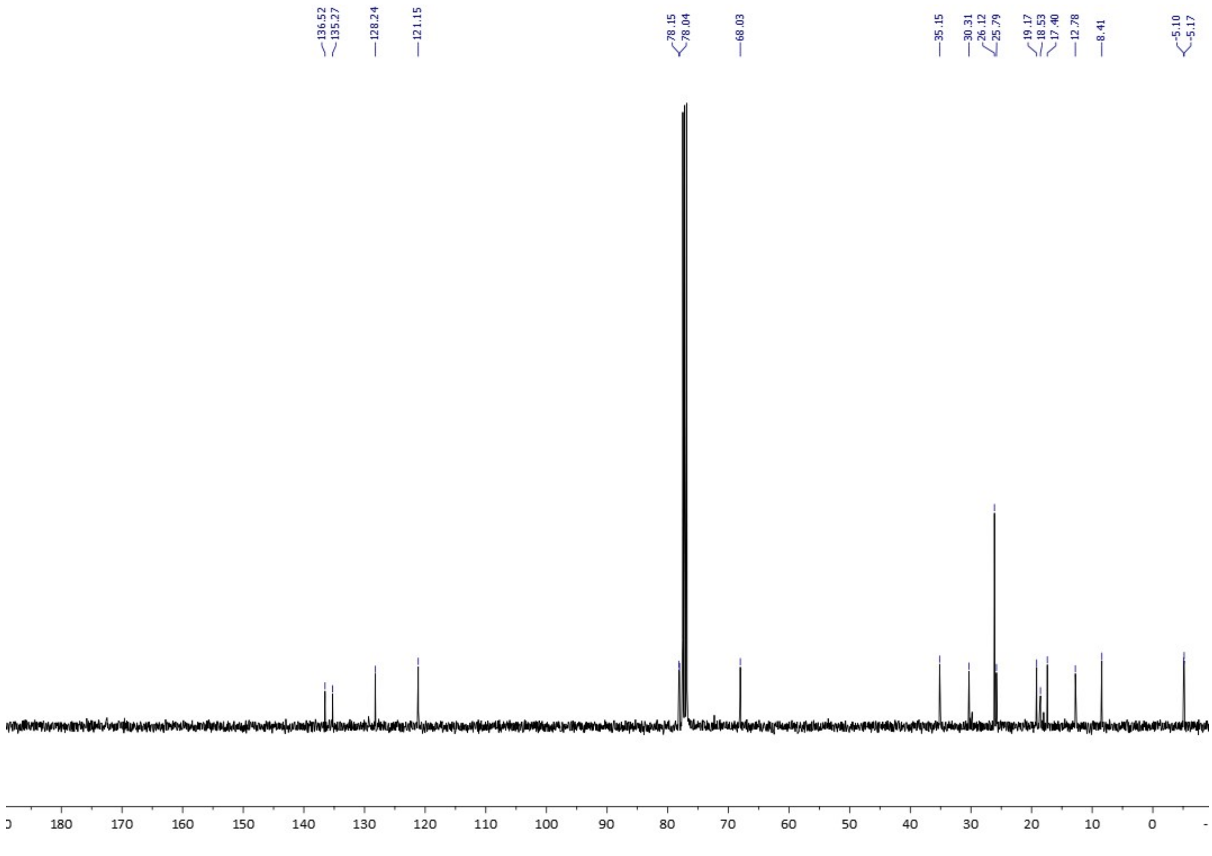
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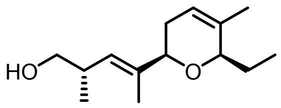
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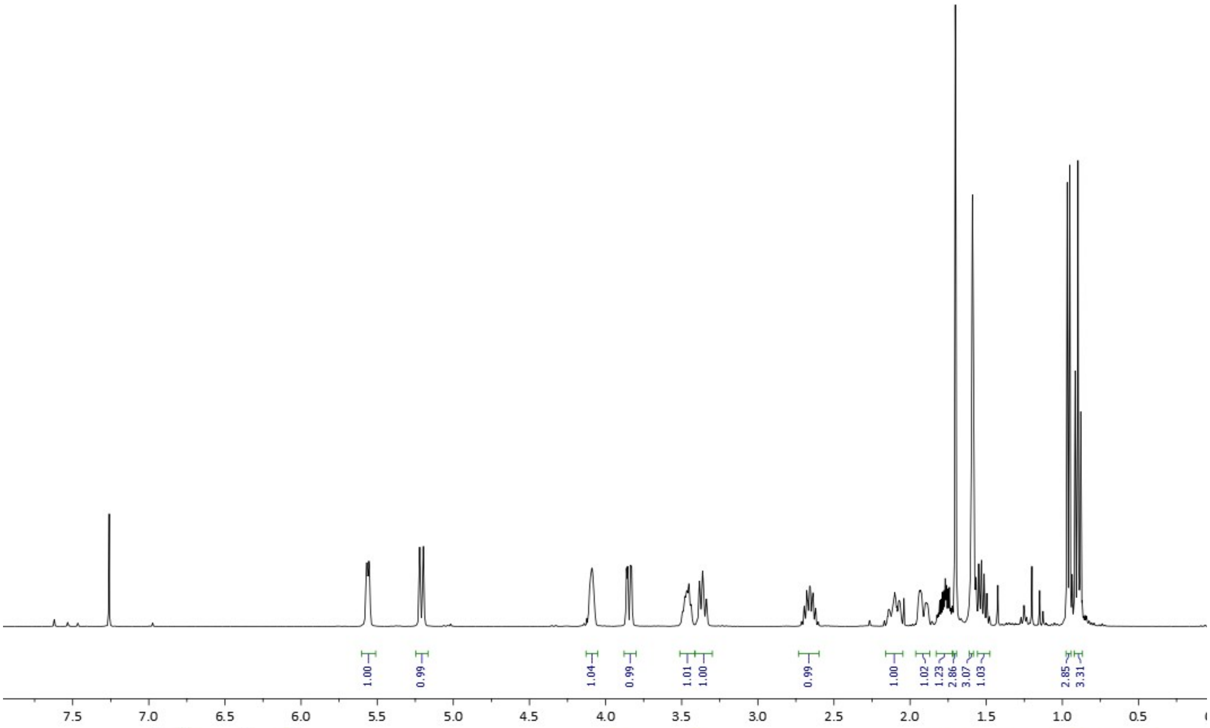
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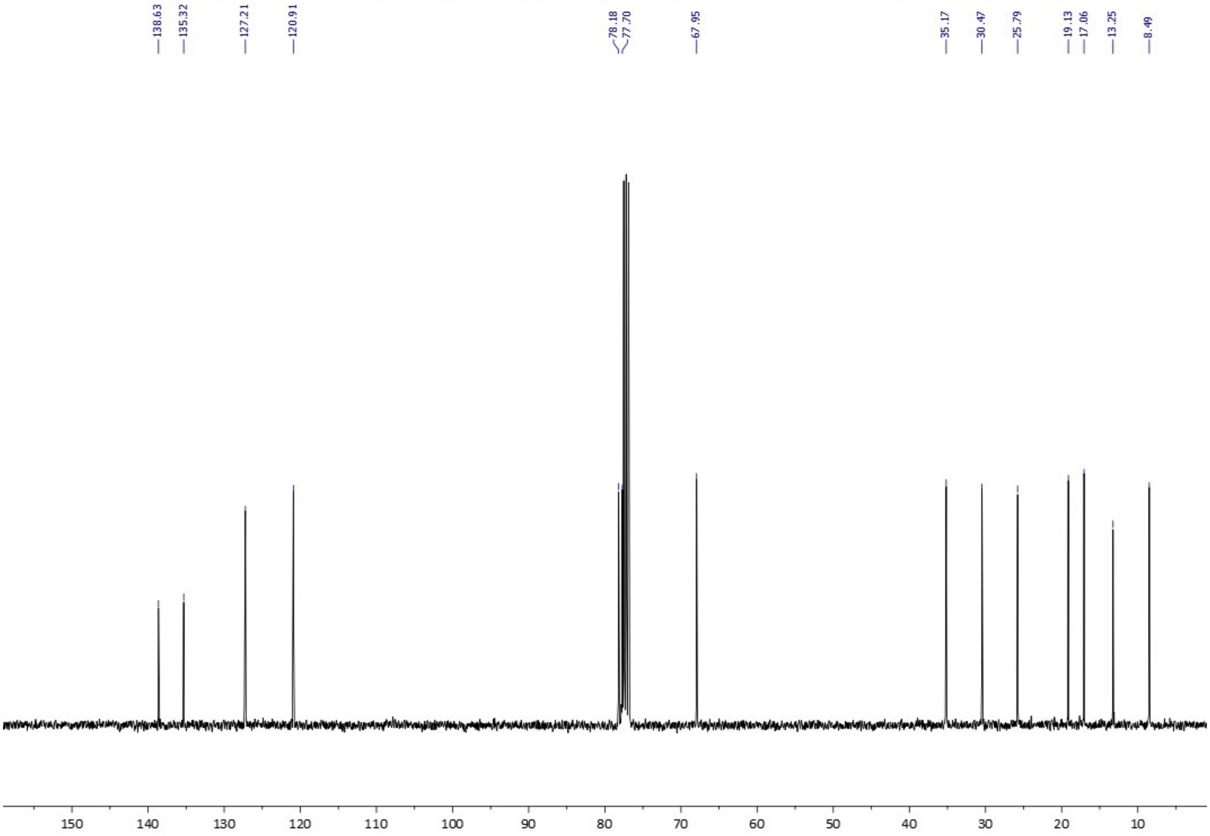
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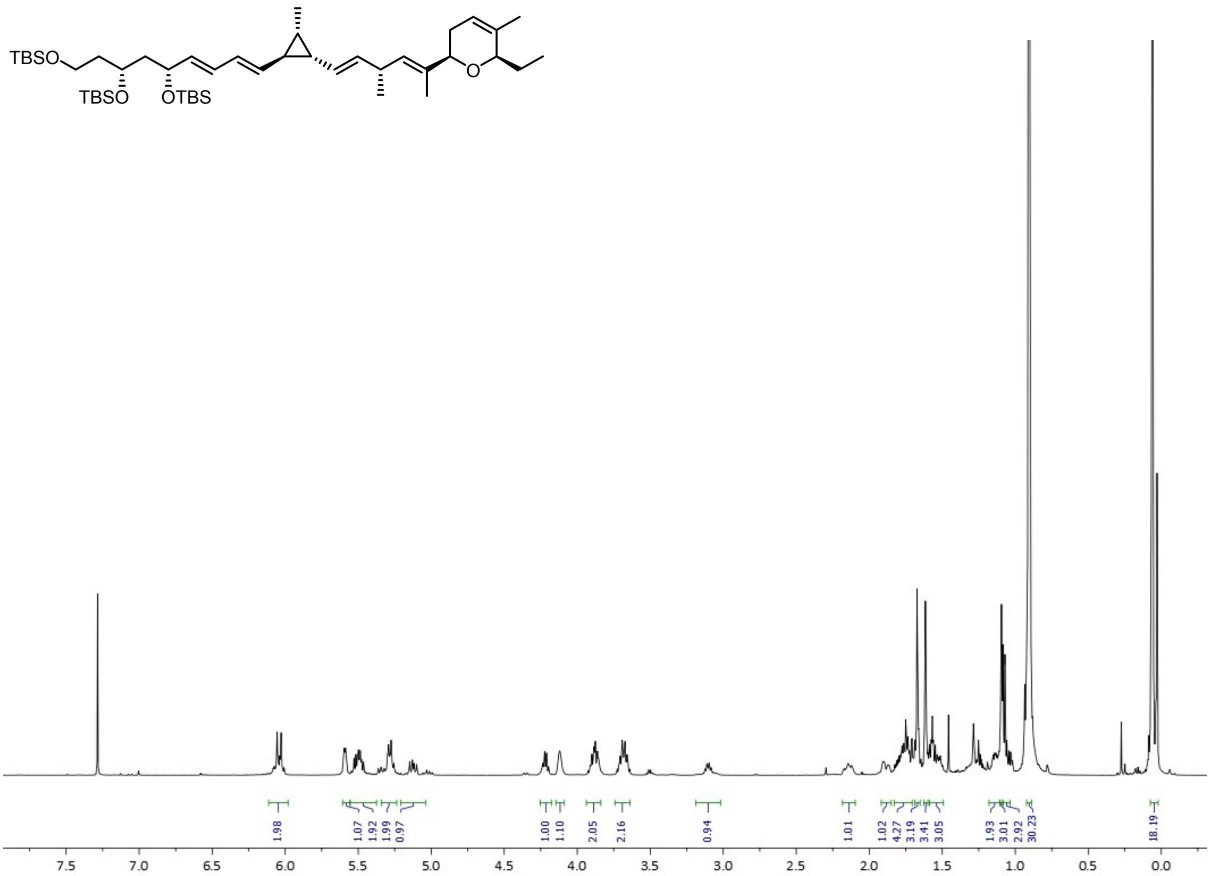
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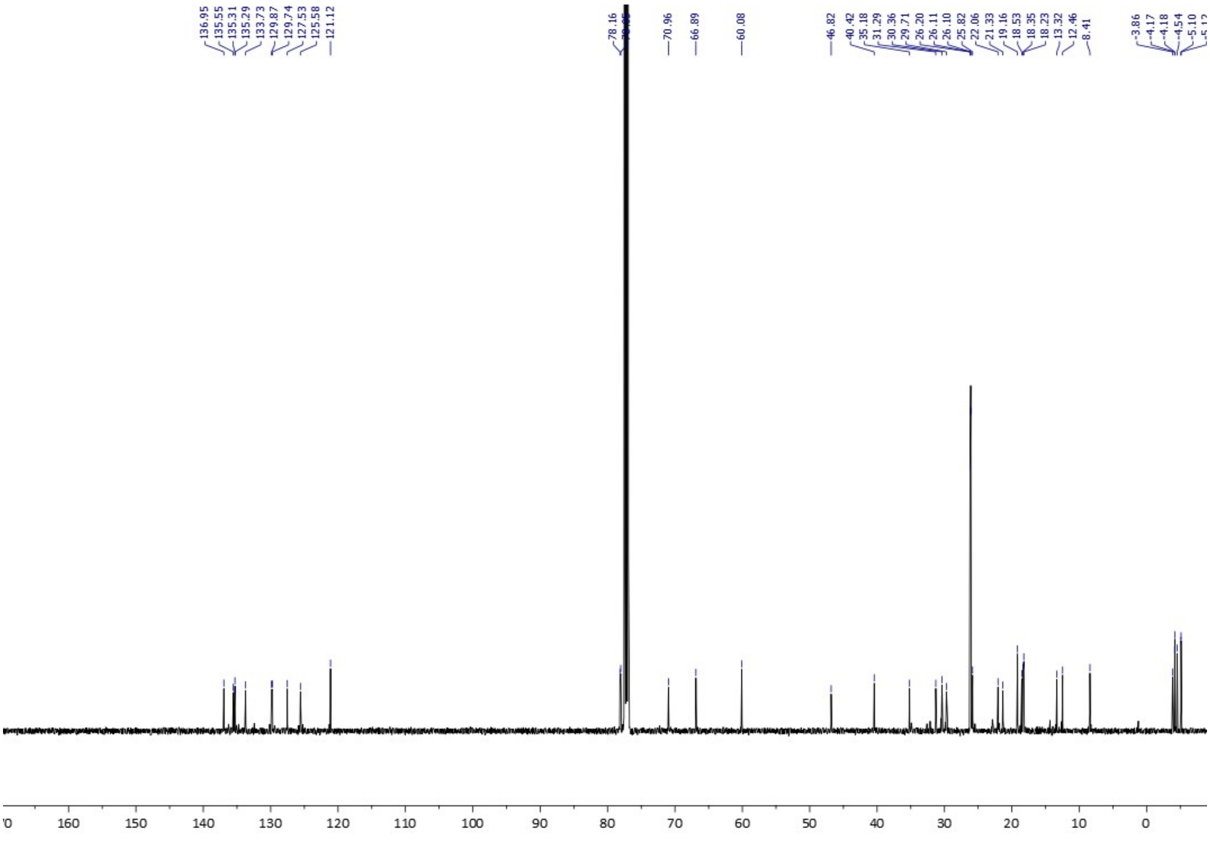
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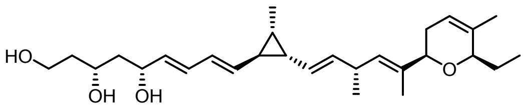
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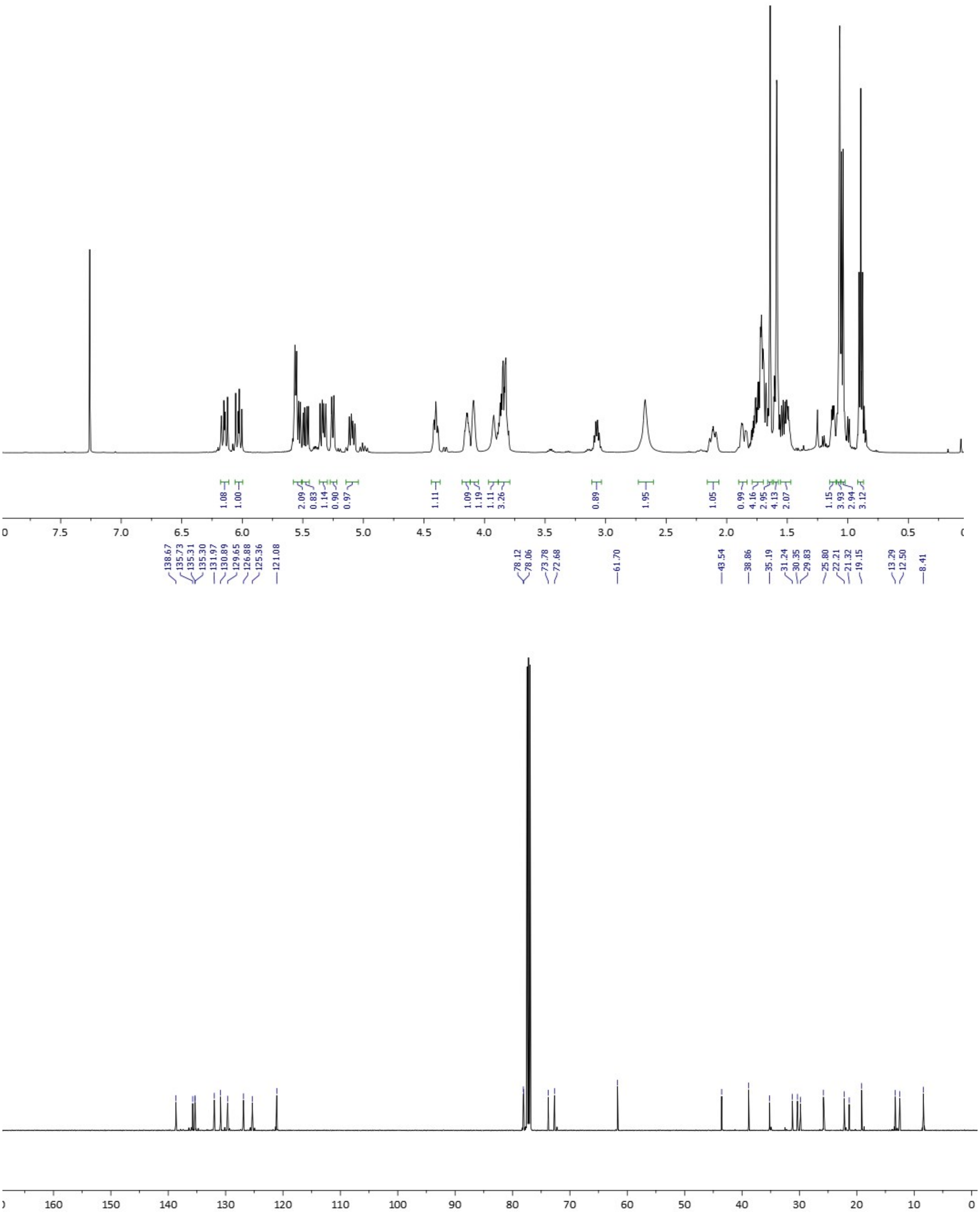
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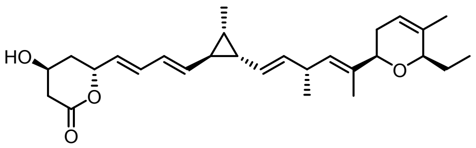
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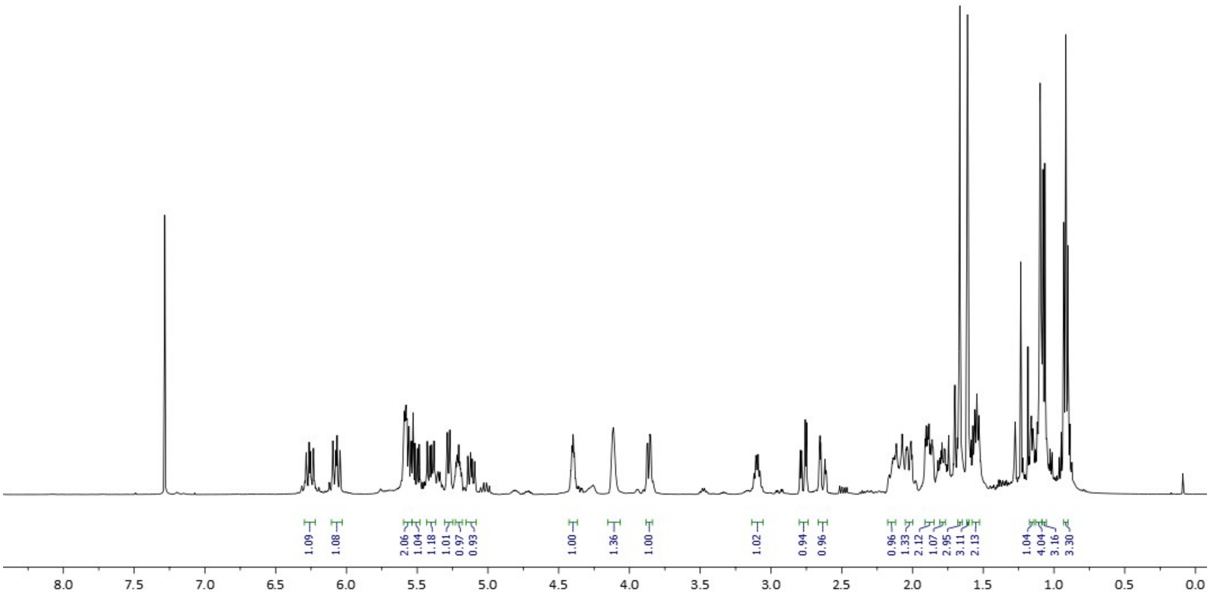
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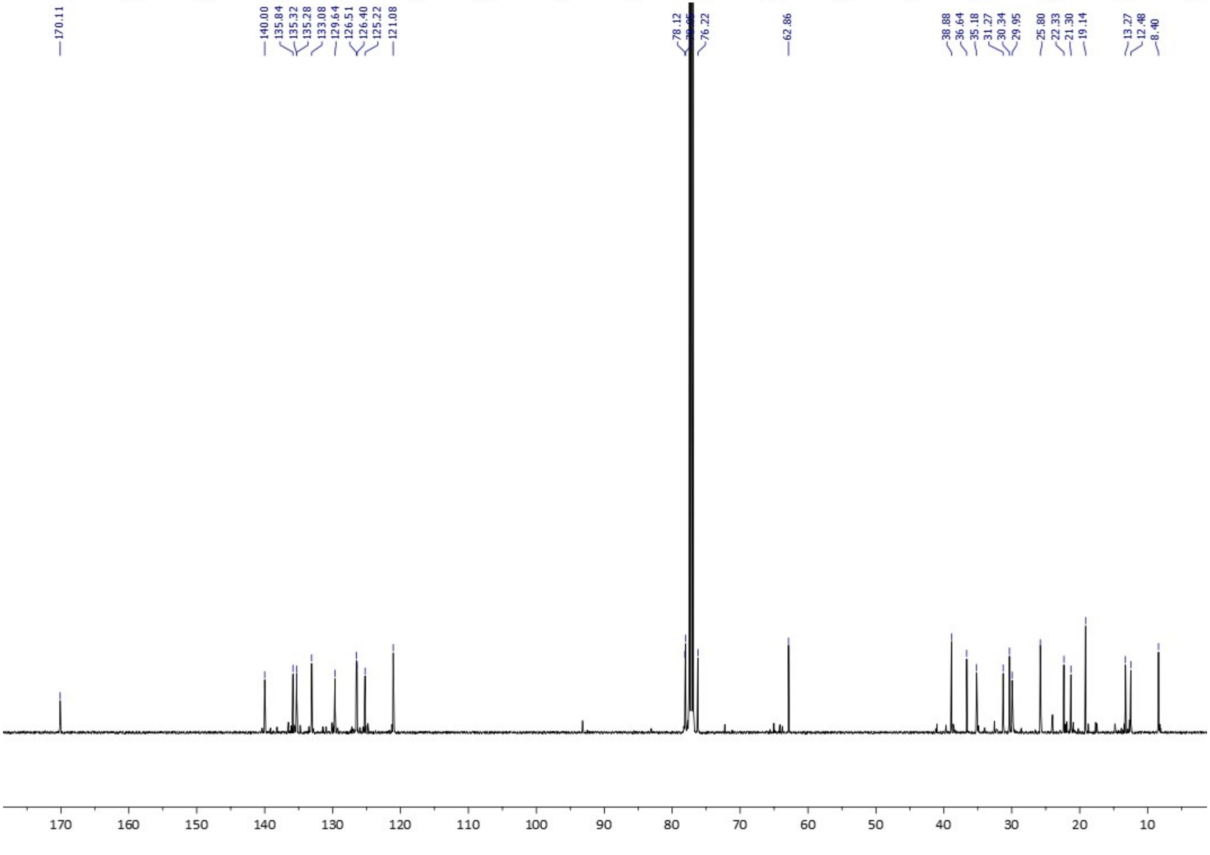
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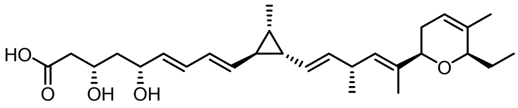
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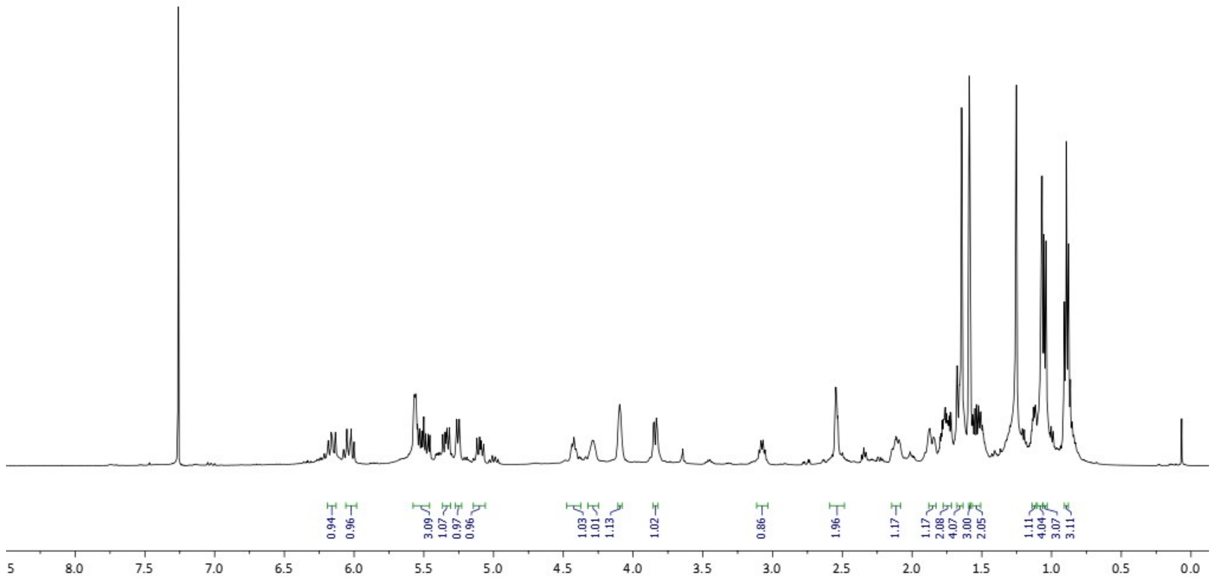
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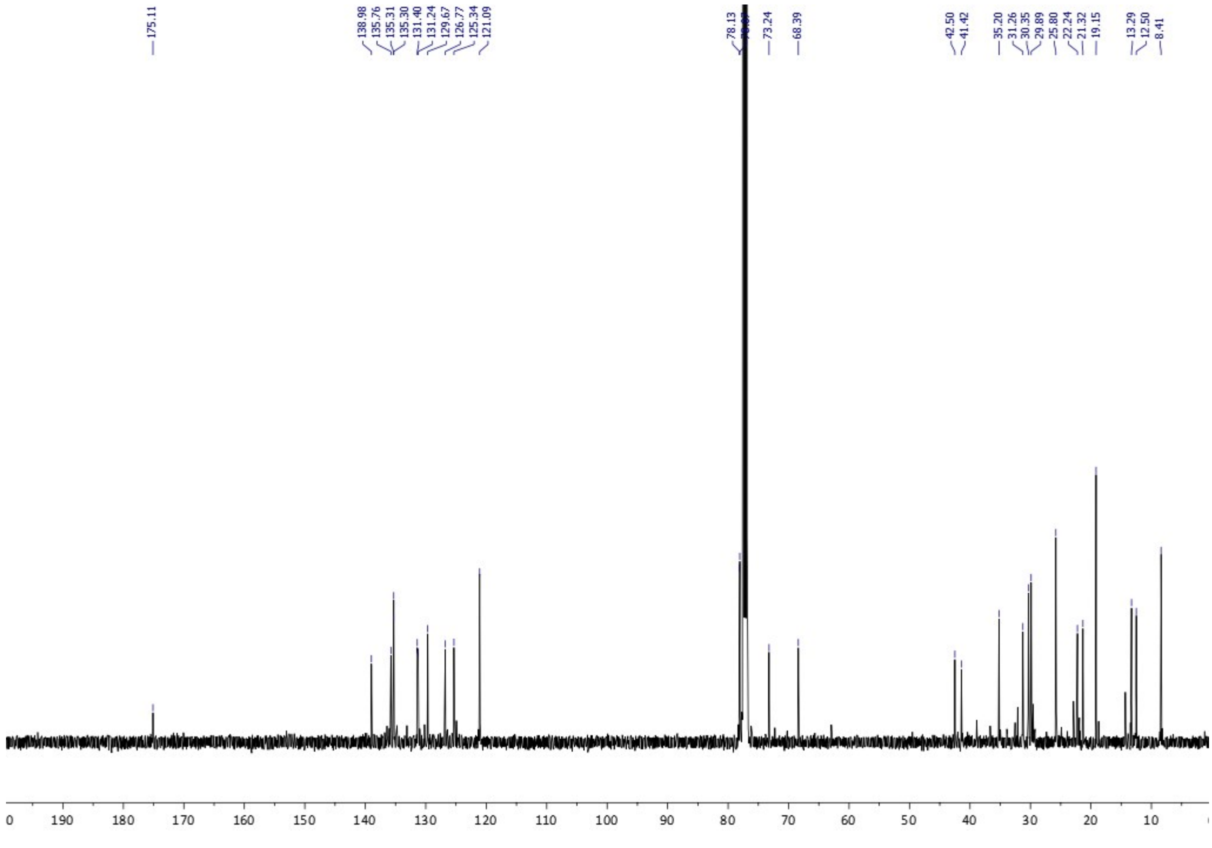
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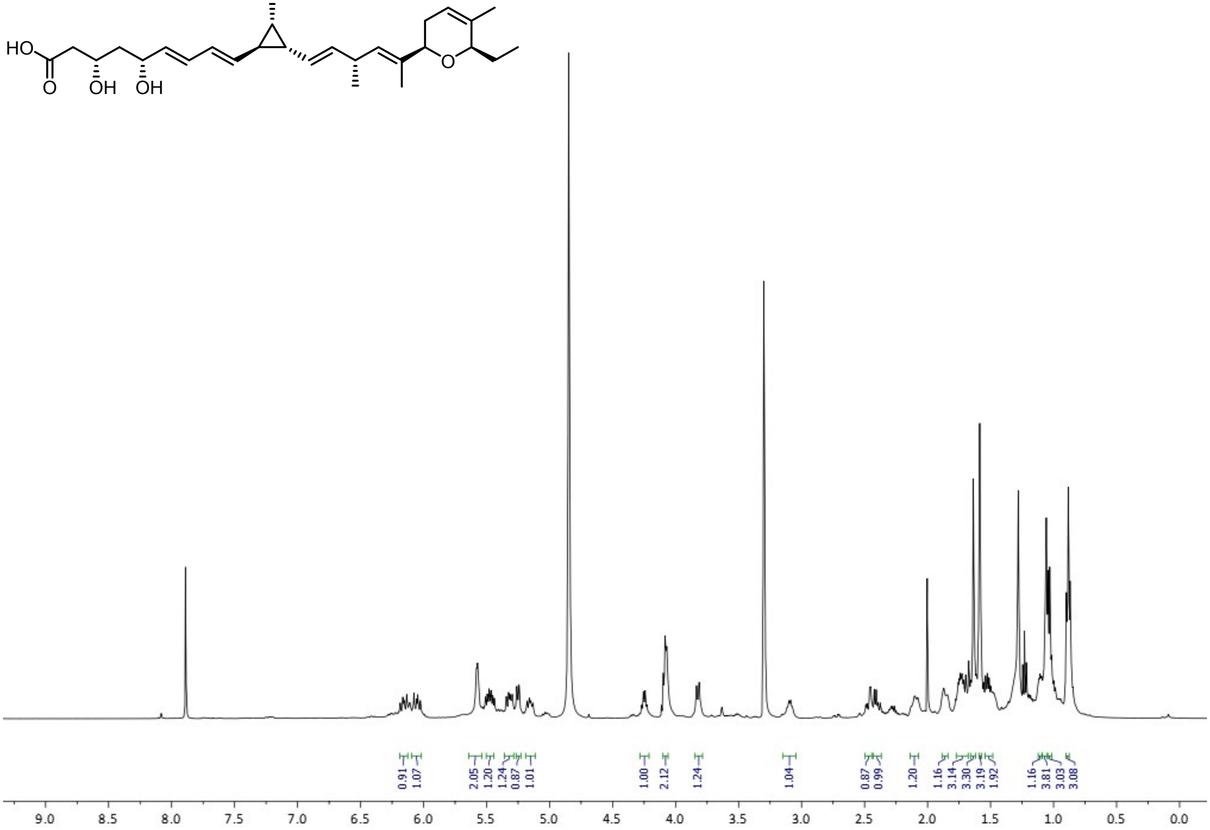
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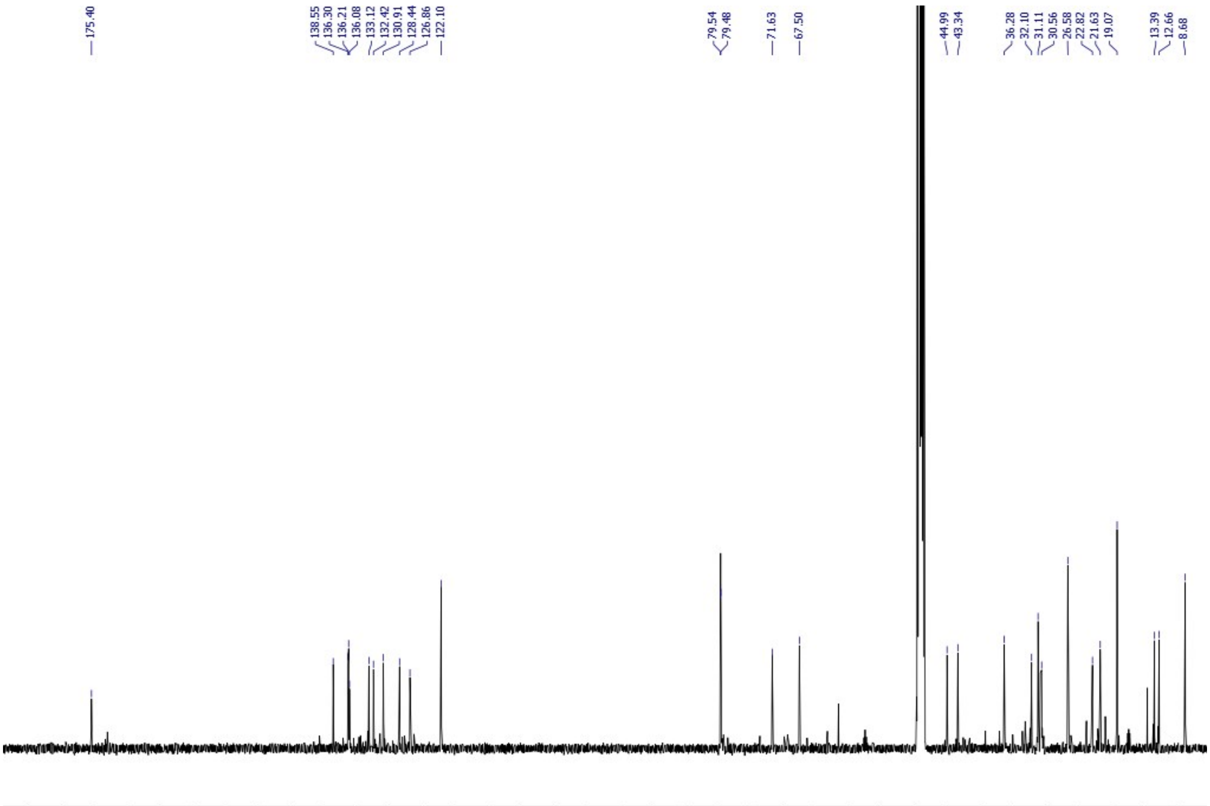
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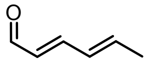
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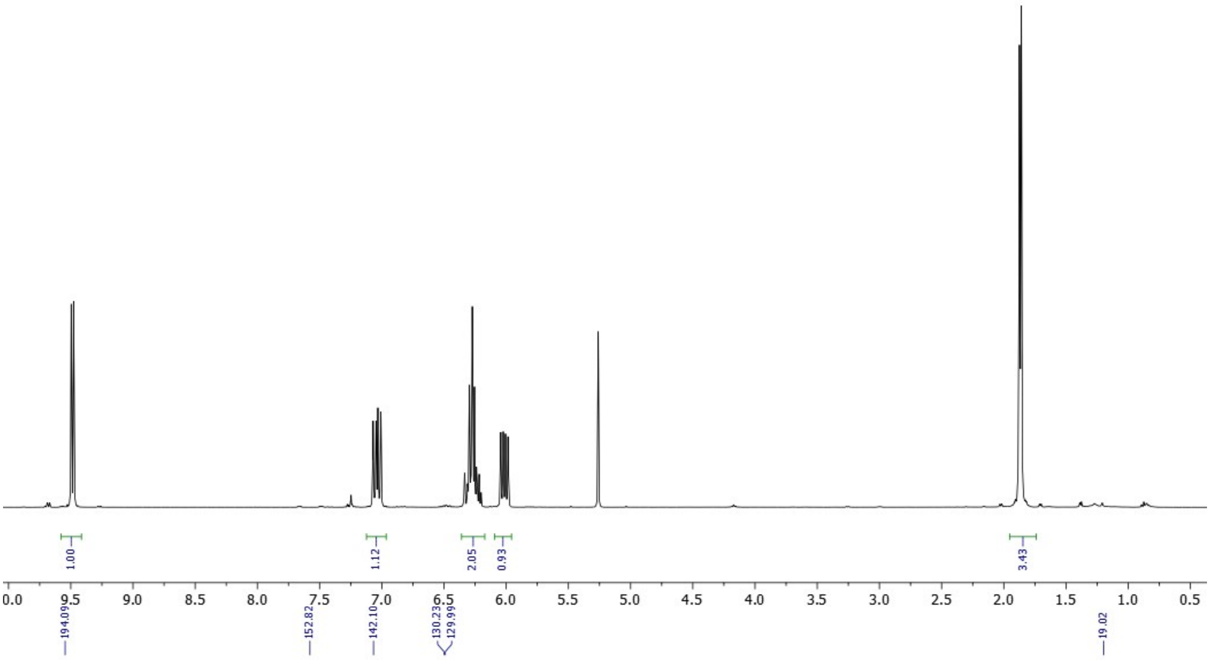
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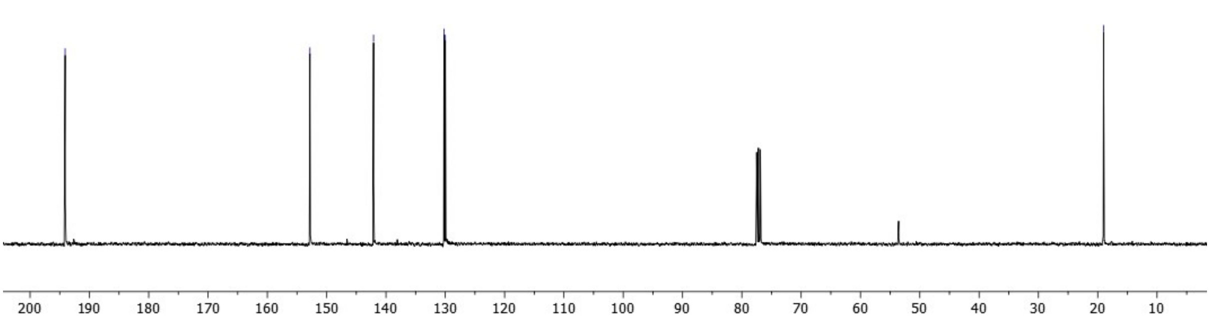
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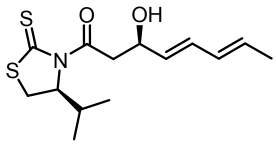
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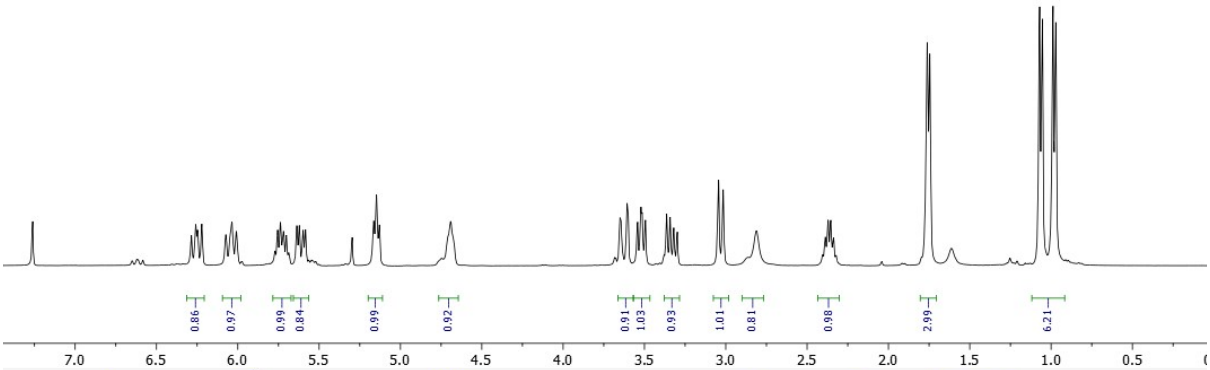
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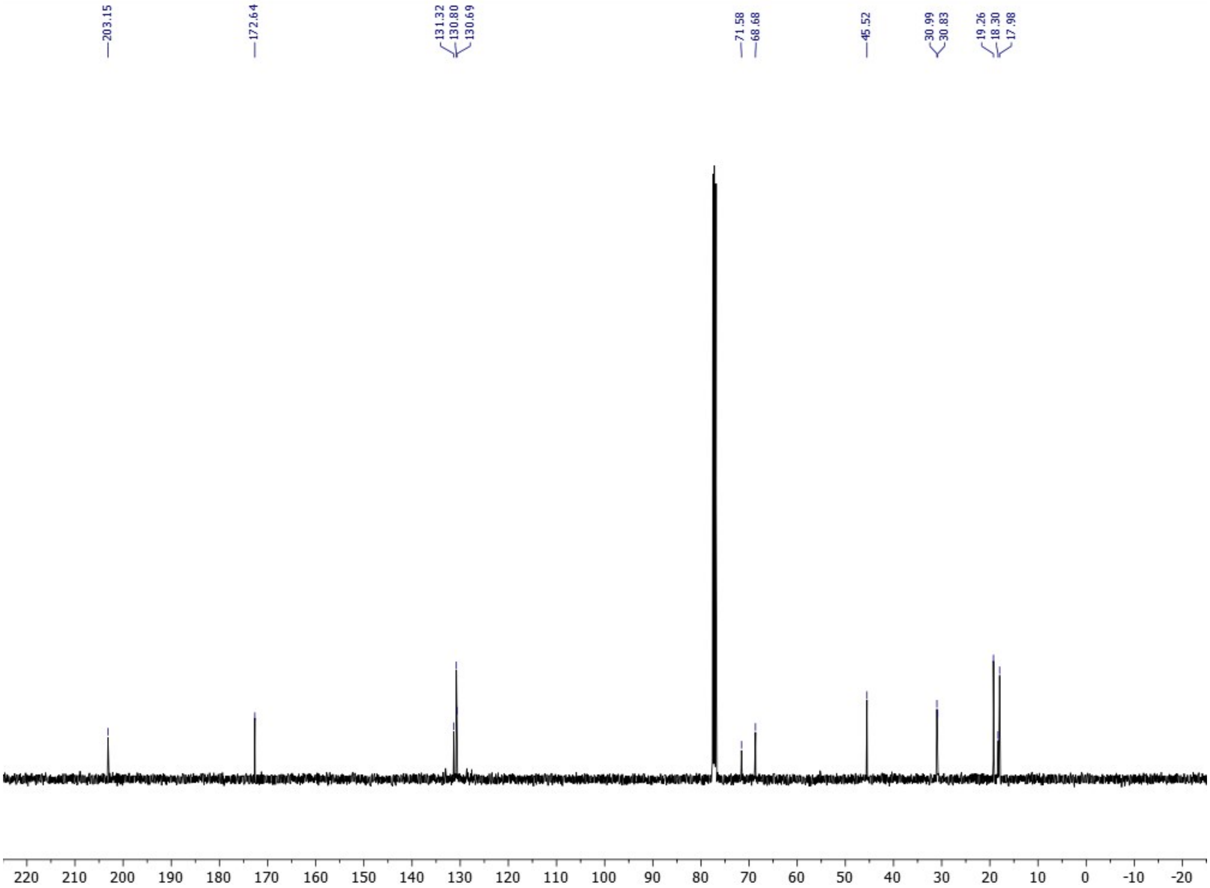
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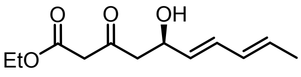
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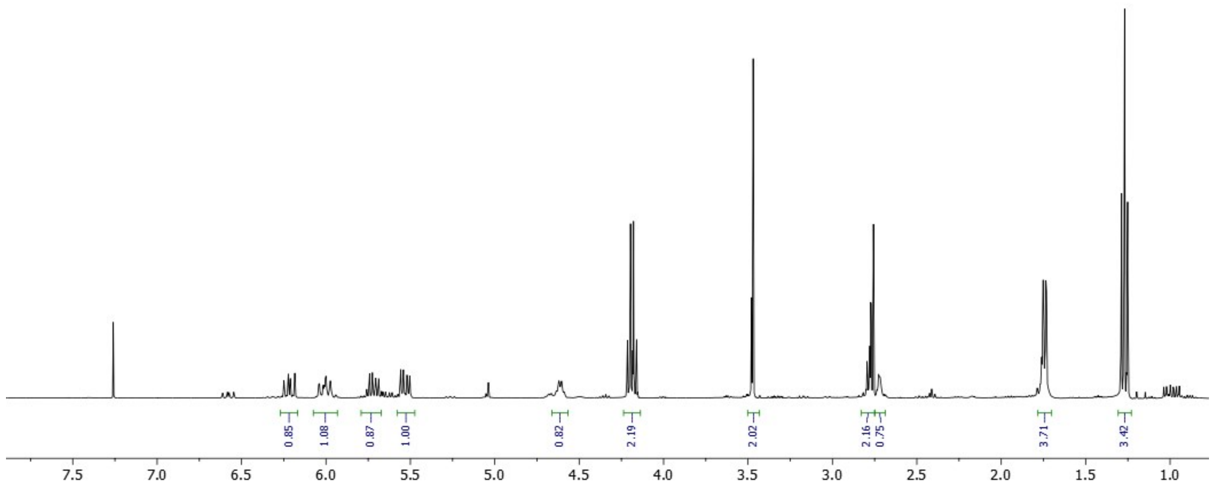
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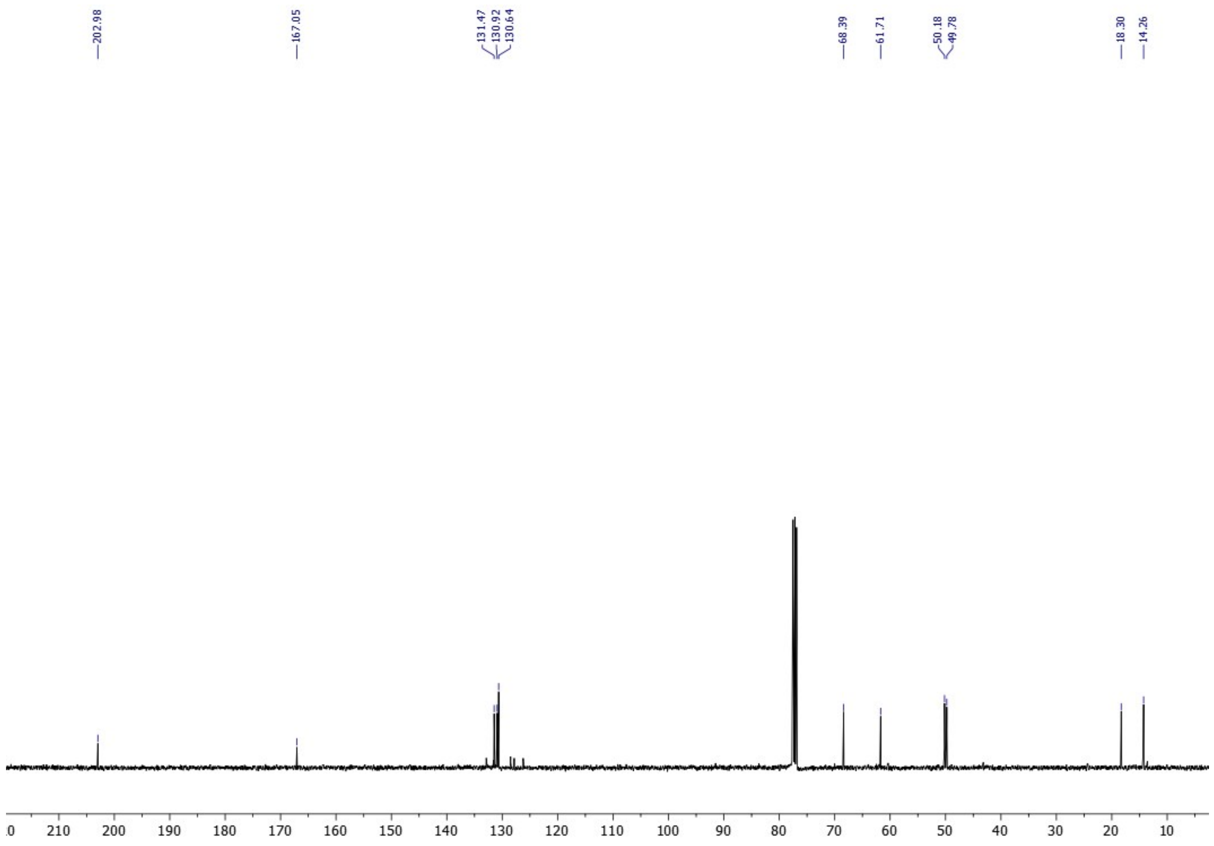
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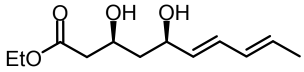
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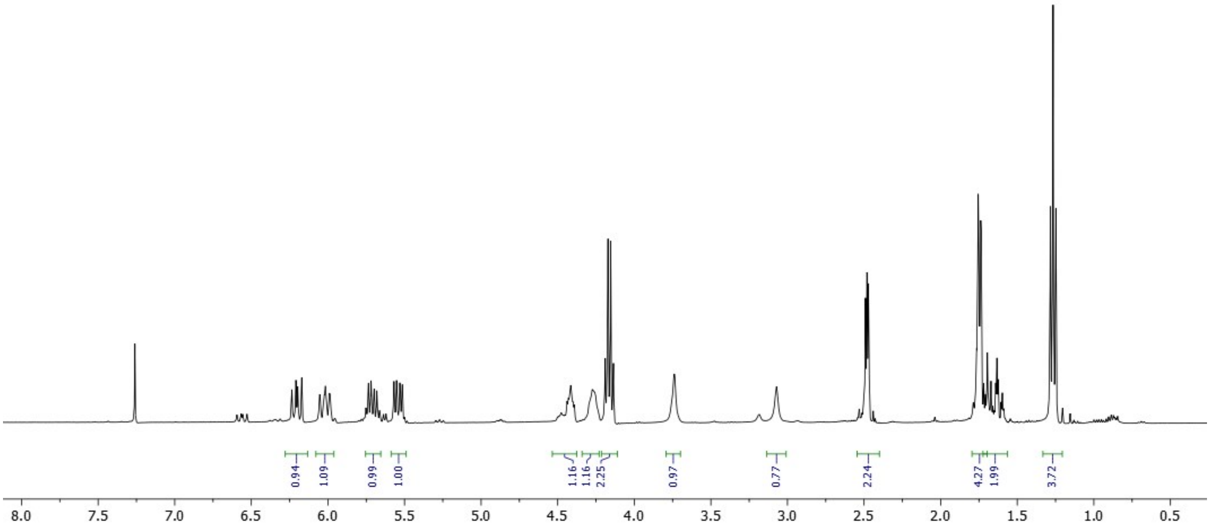
EtO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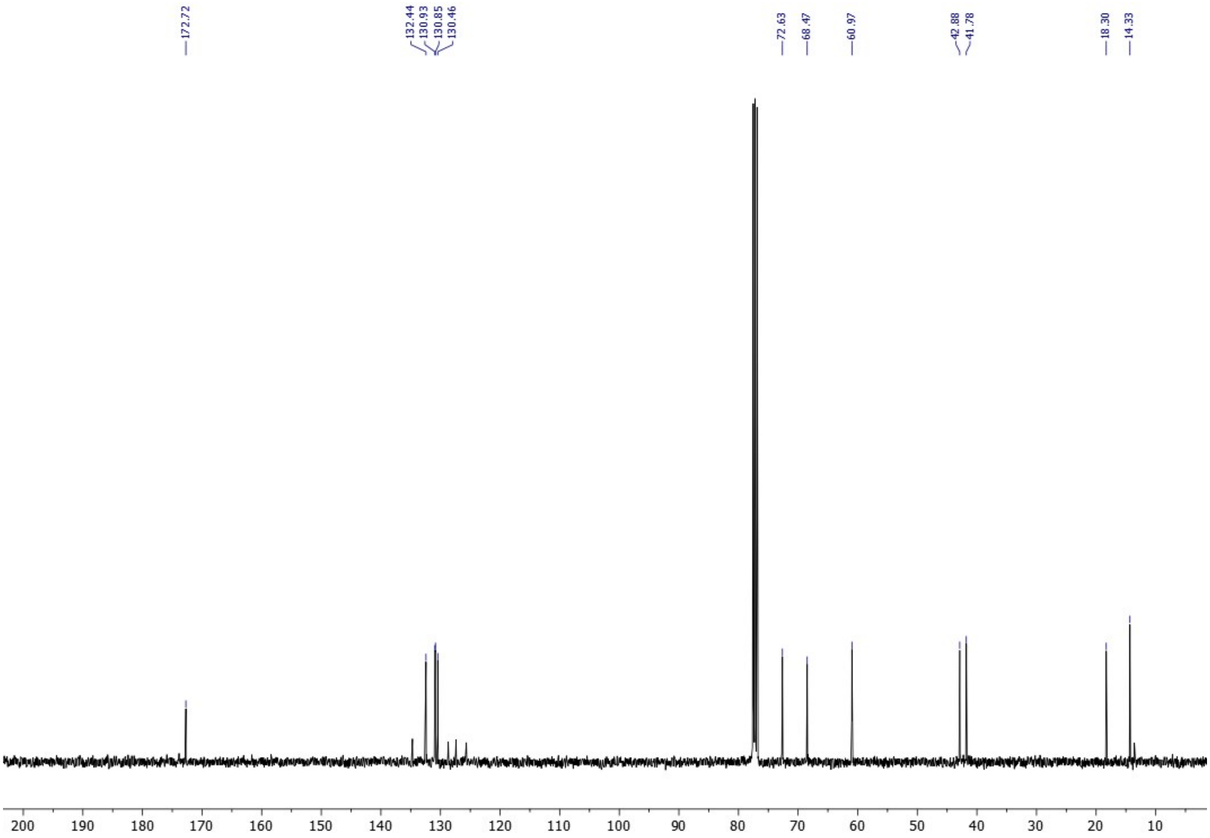
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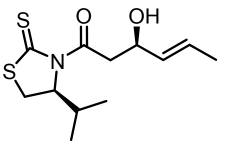
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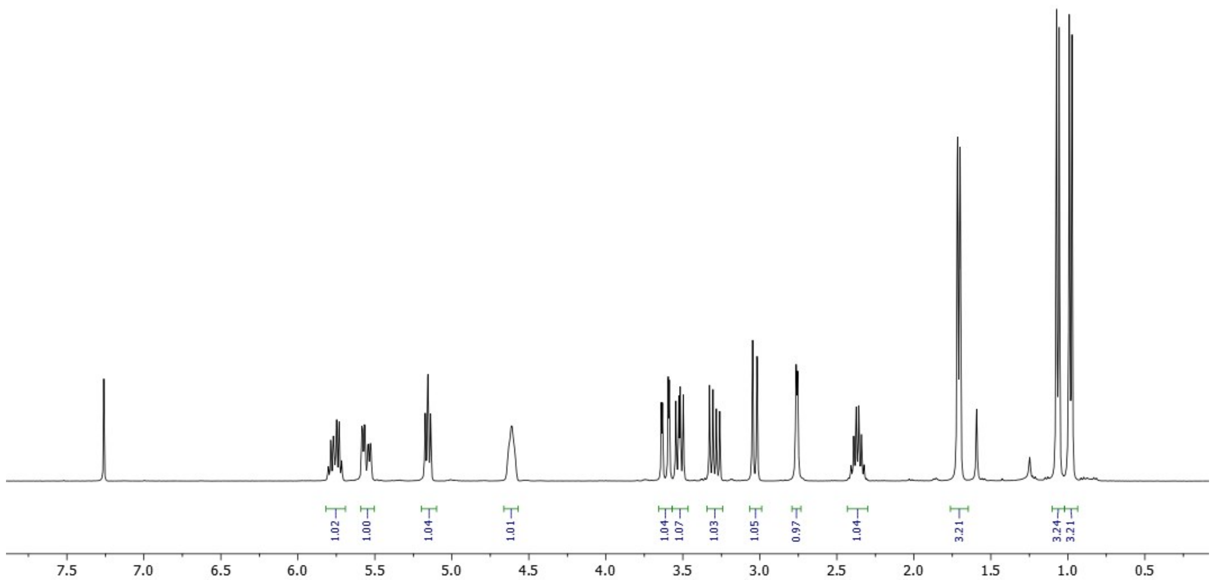
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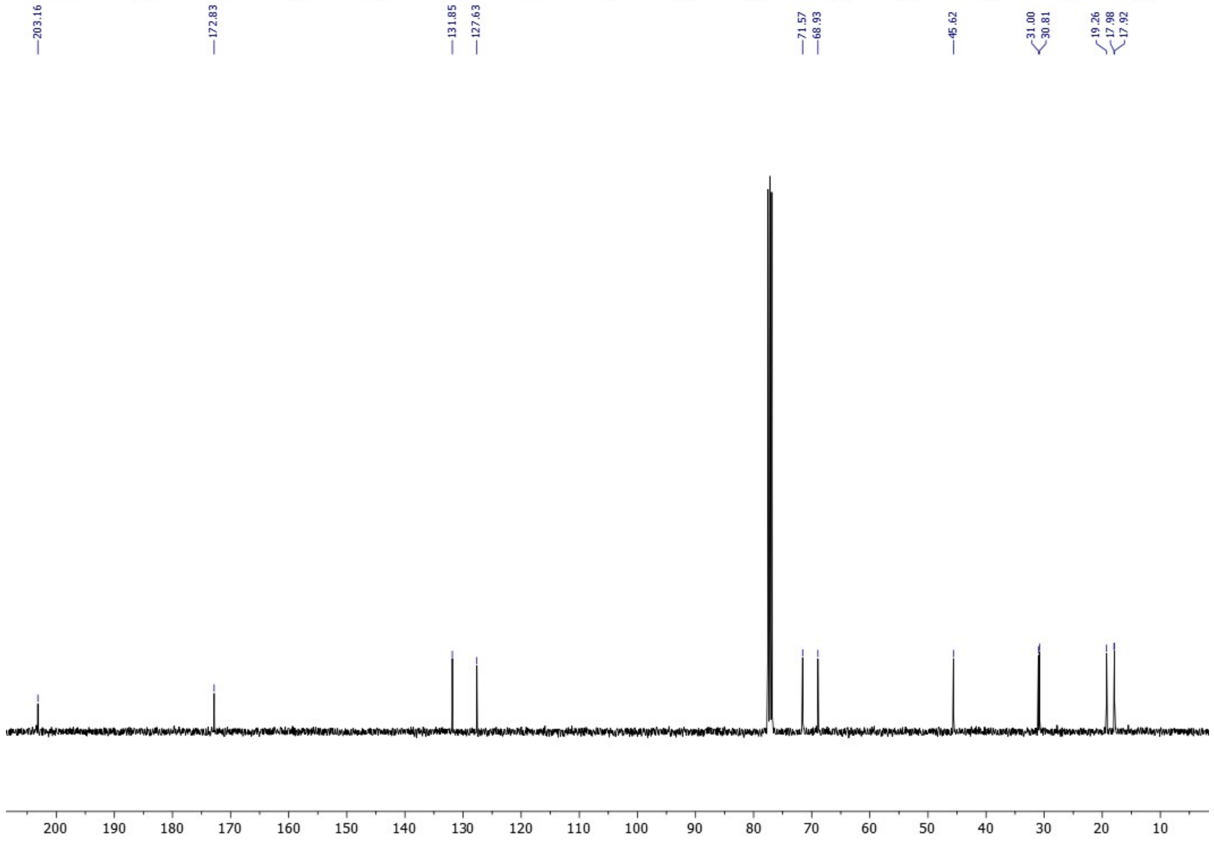
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127.63
71.57
68.93
45.62
31.00
30.81
19.26
17.98
17.92
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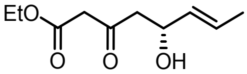
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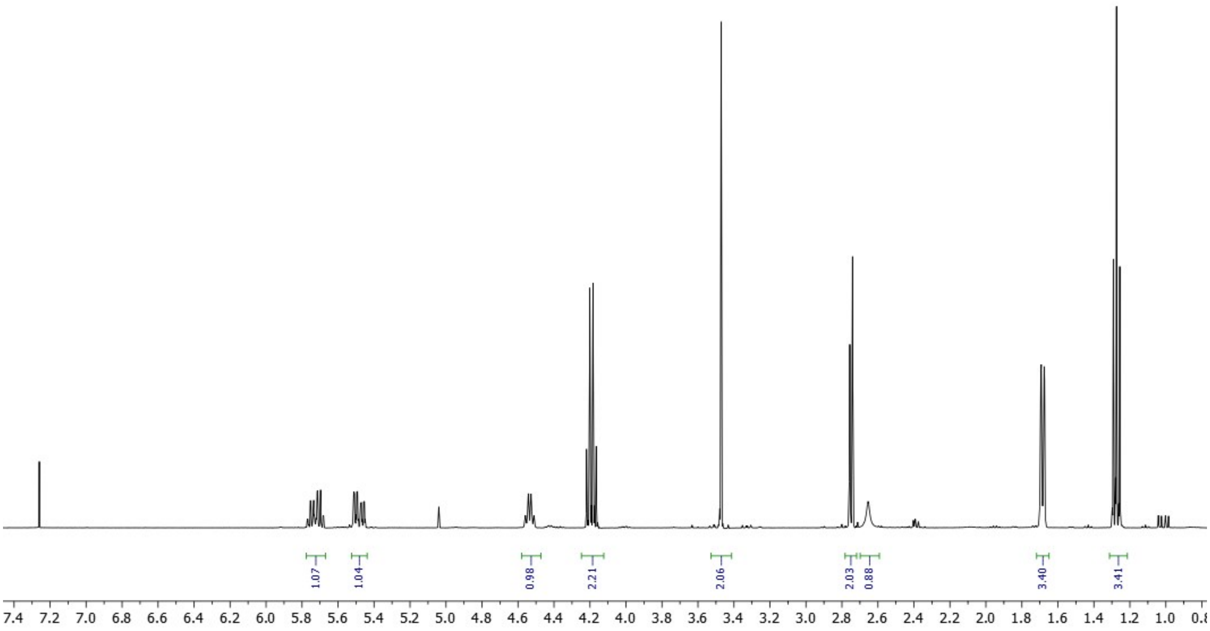
O
OH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3.40
3.41
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
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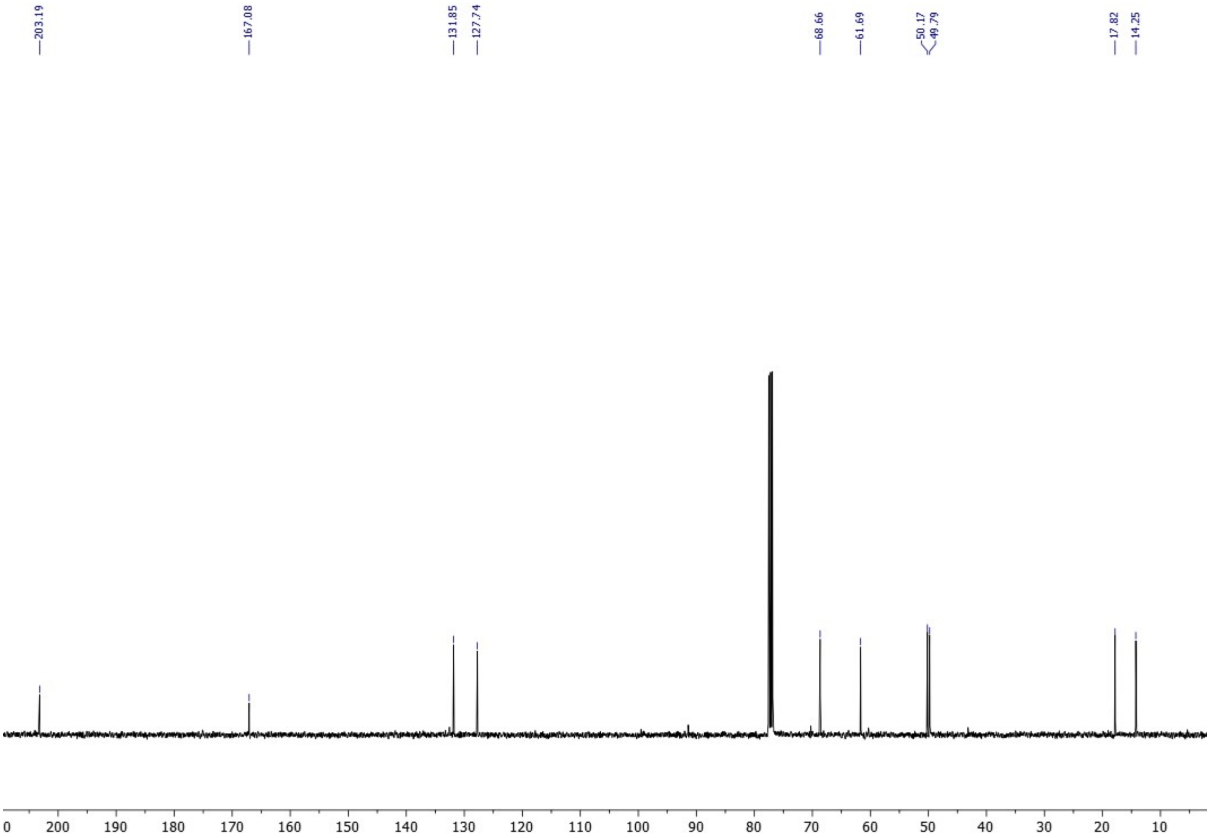
0.8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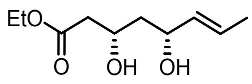
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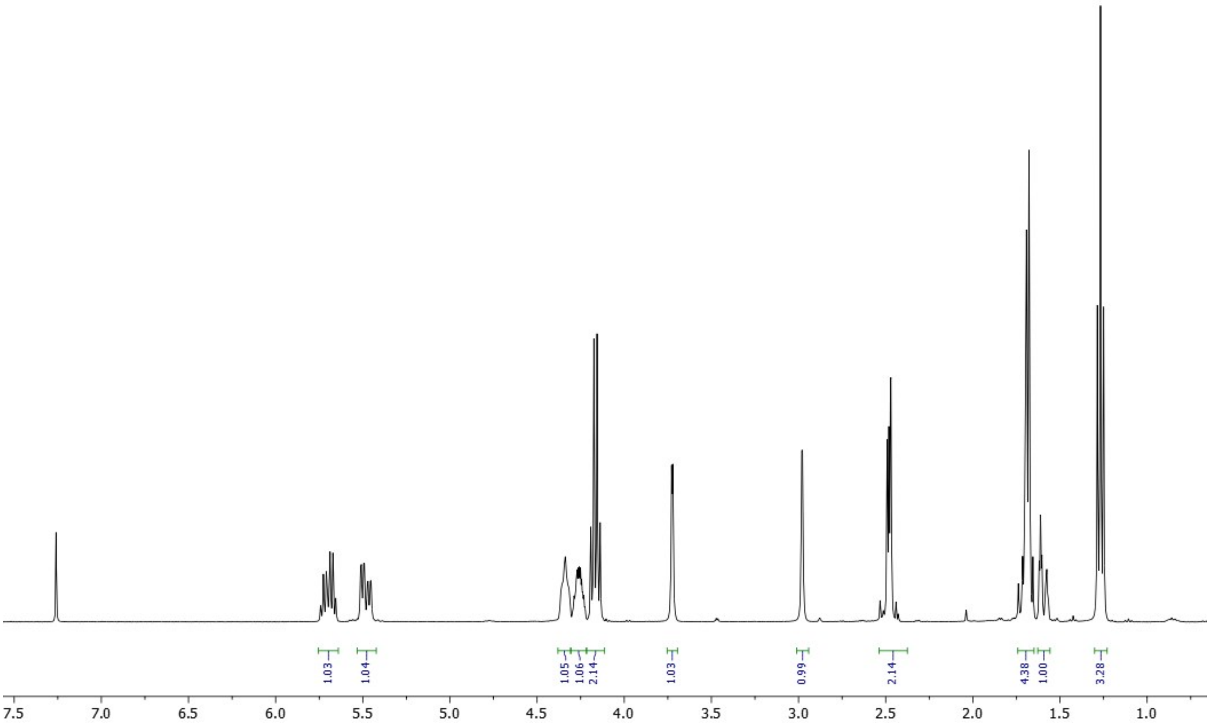
OH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1.03
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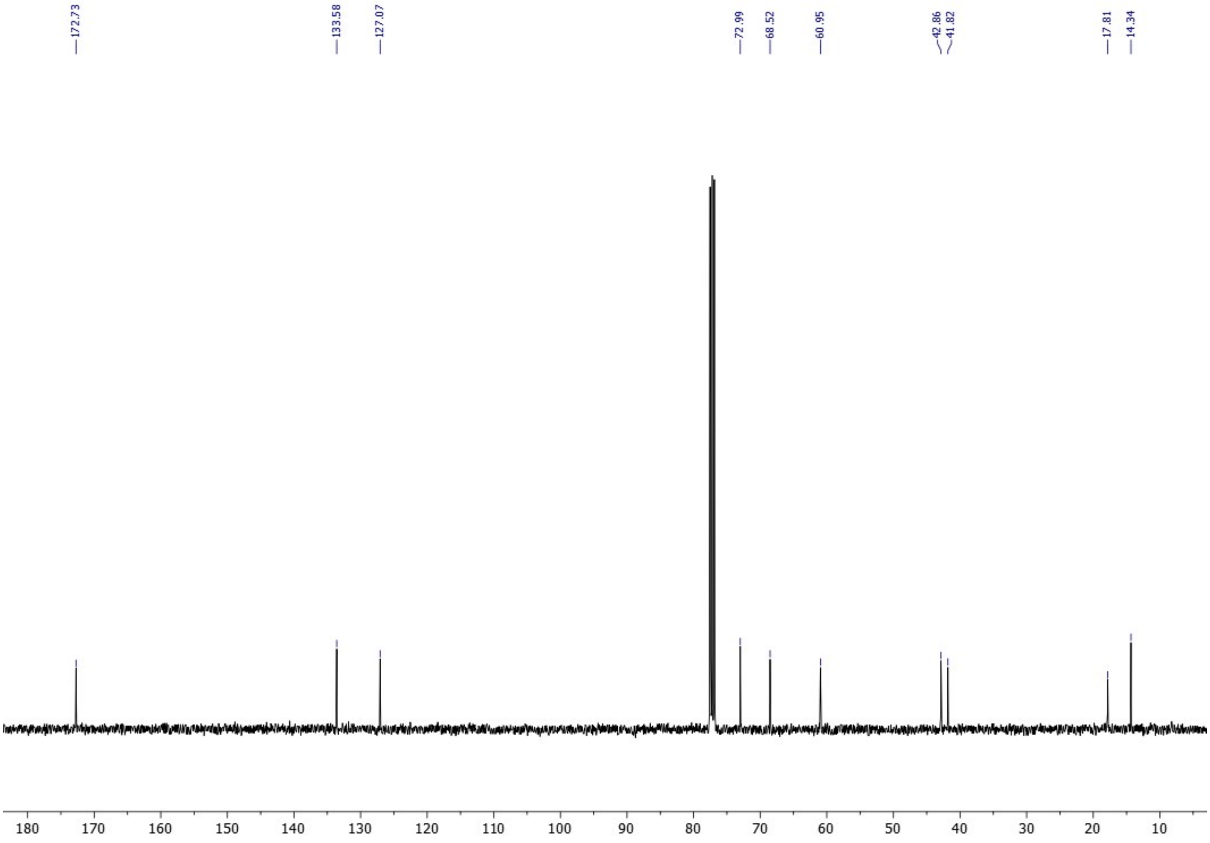
1.0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20
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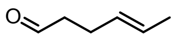
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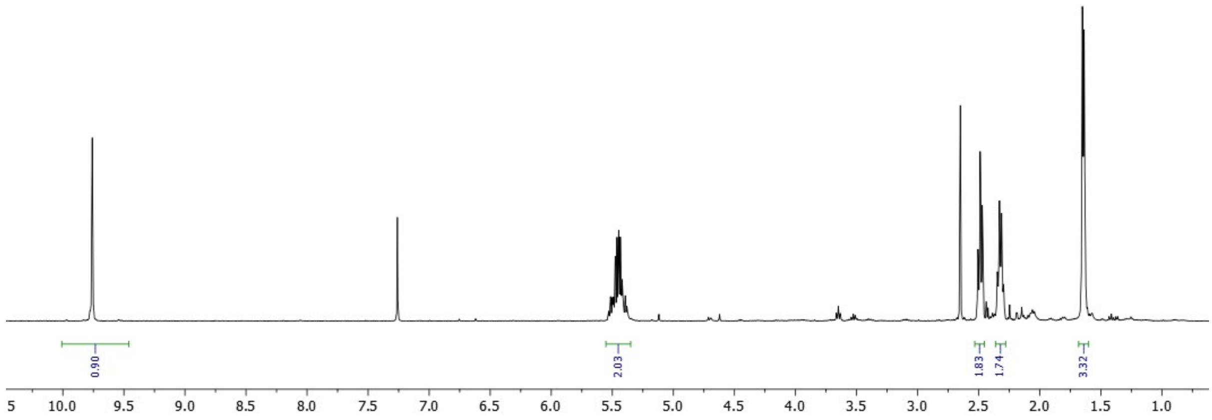
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8.5
8.0
7.5
7.0
6.5
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5.0
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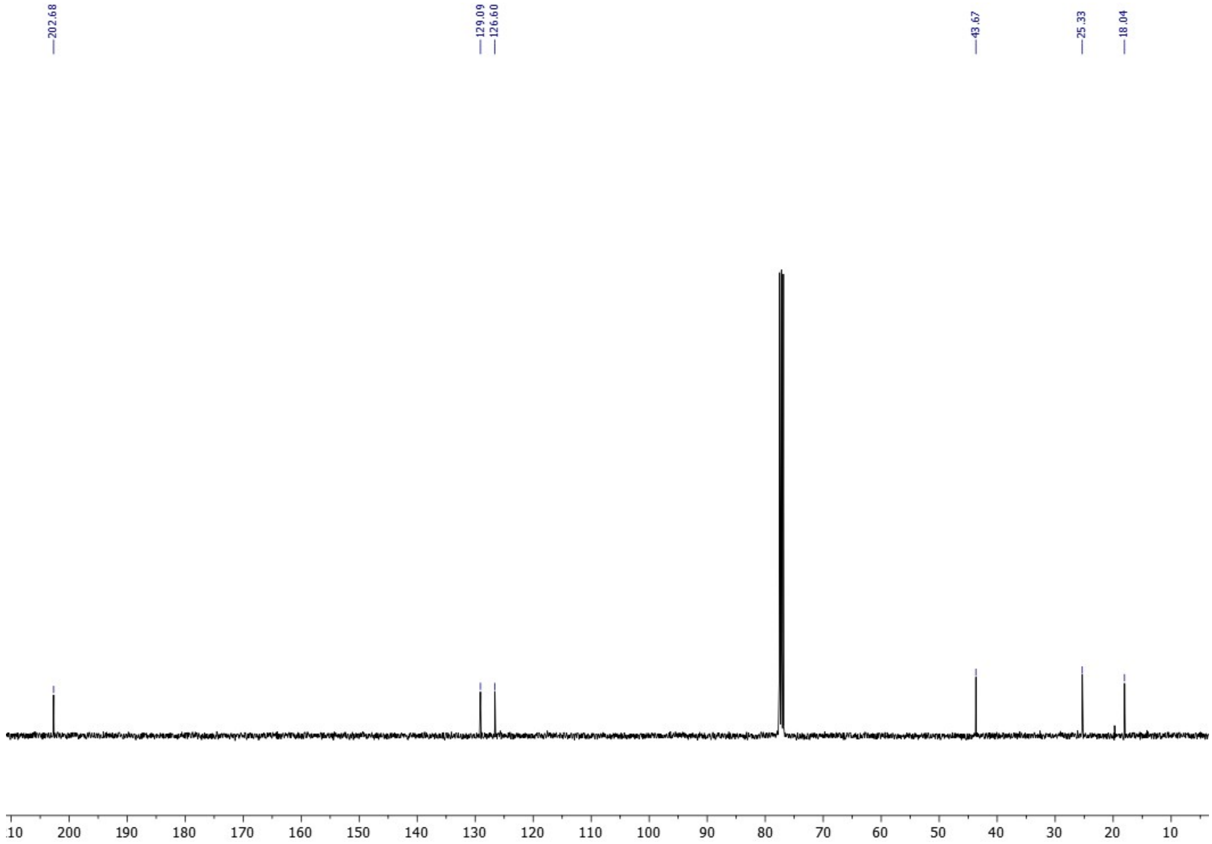
3.0
2.5
2.0
1.5
1.0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43.67
25.33
18.04
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100
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80
70
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40
30
20
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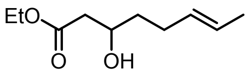
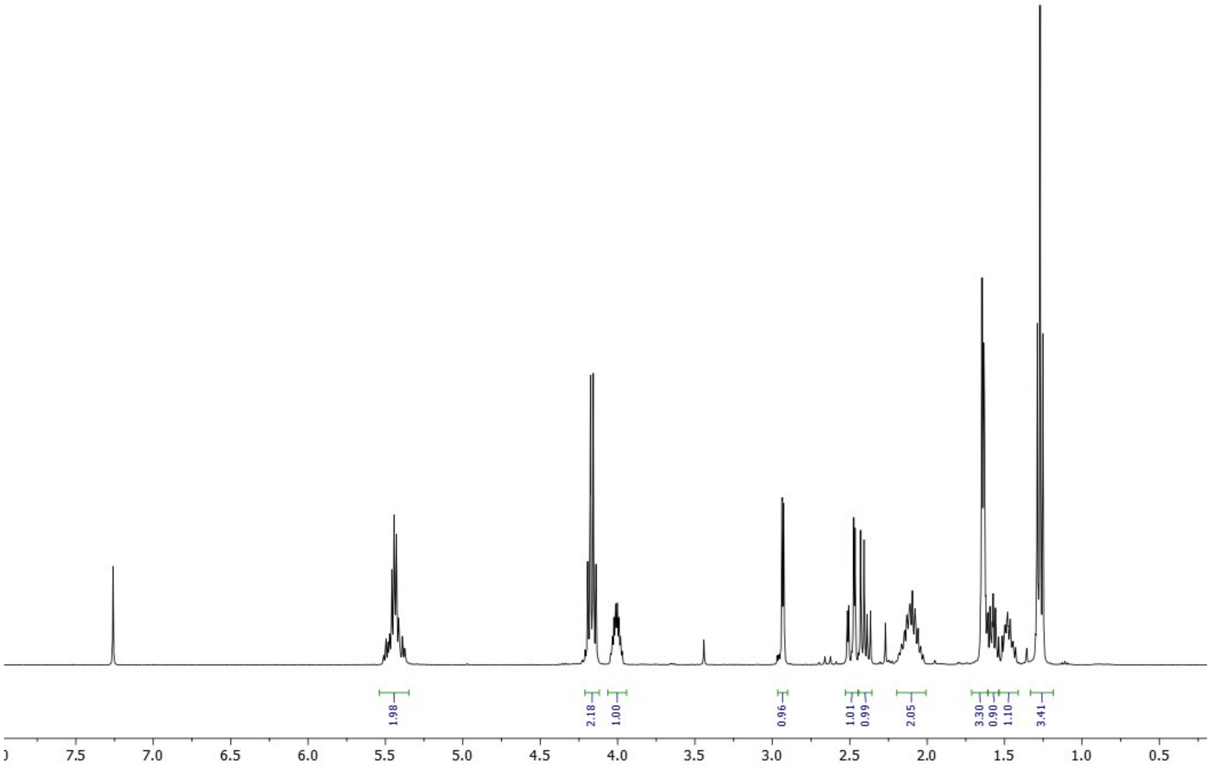

EtO
O
OH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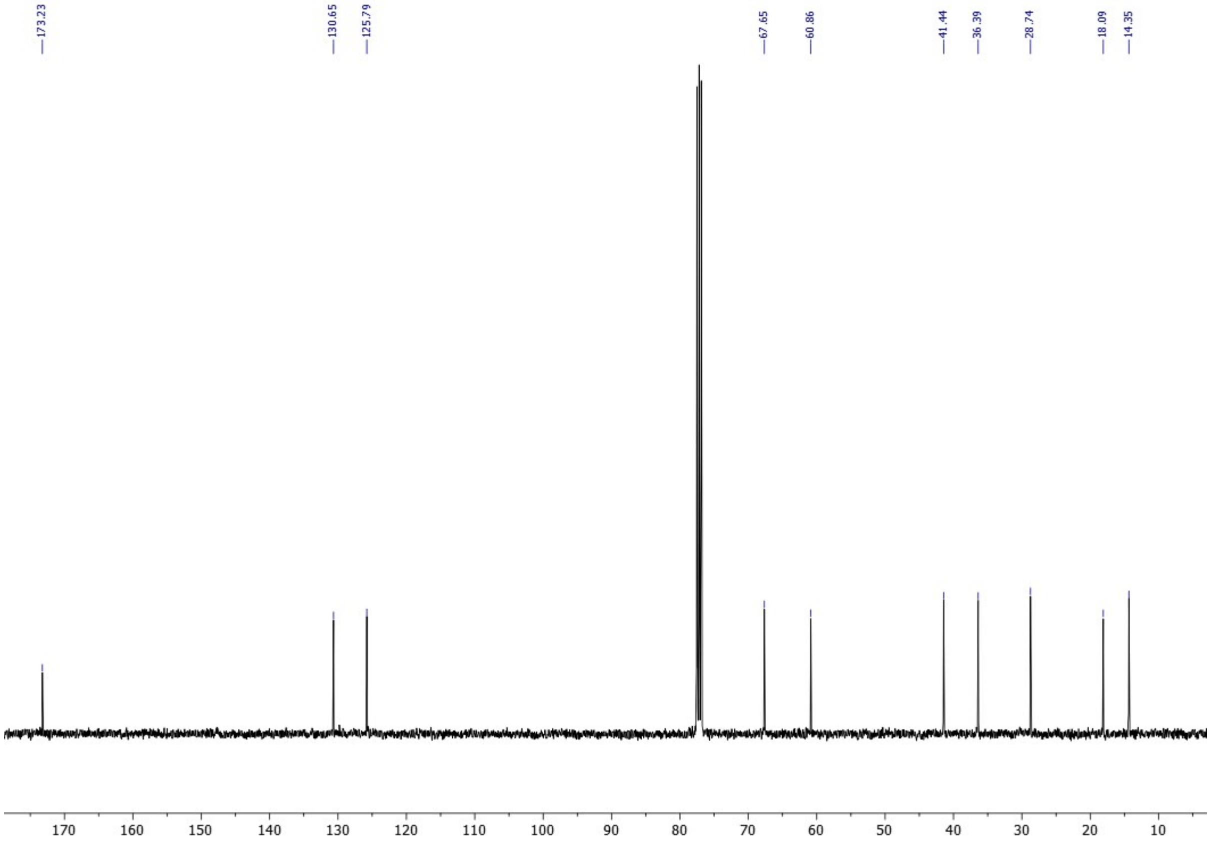
0.99
2.05
3.30
0.90
1.10
3.41
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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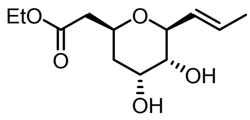
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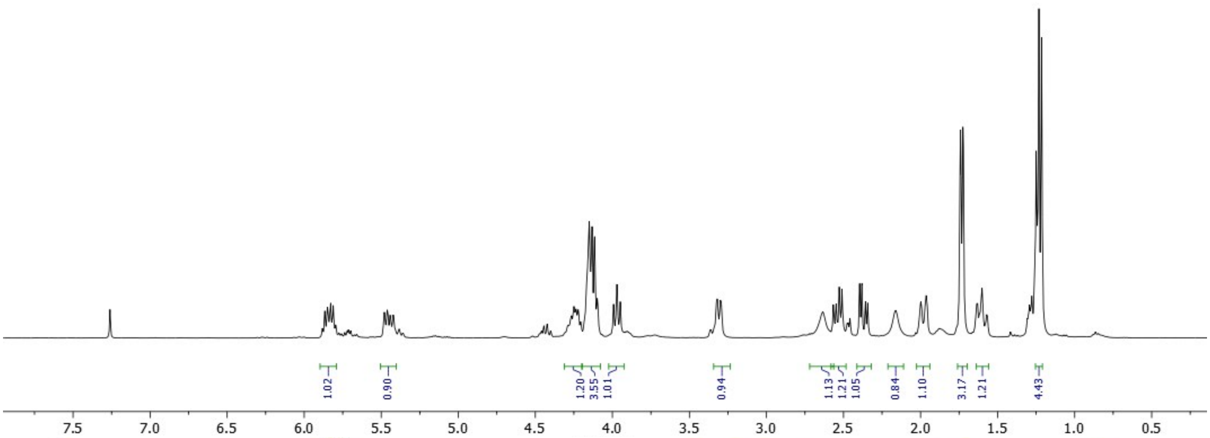
O
O
OH
OH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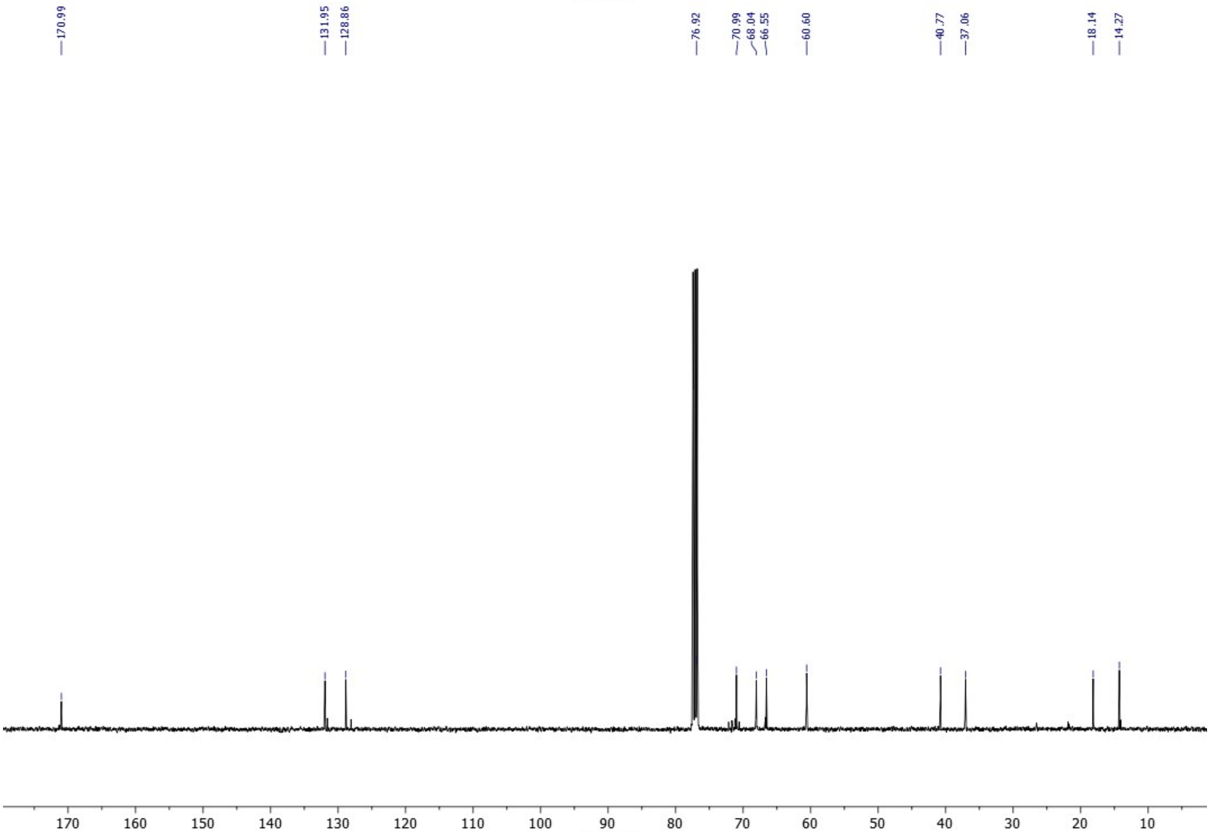
0.90
1.20
3.55
1.01
0.94
1.13
1.21
1.05
0.84
1.10
3.17
1.21
4.43
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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76.92
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40.77
37.06
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120
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100
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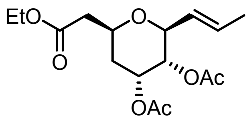
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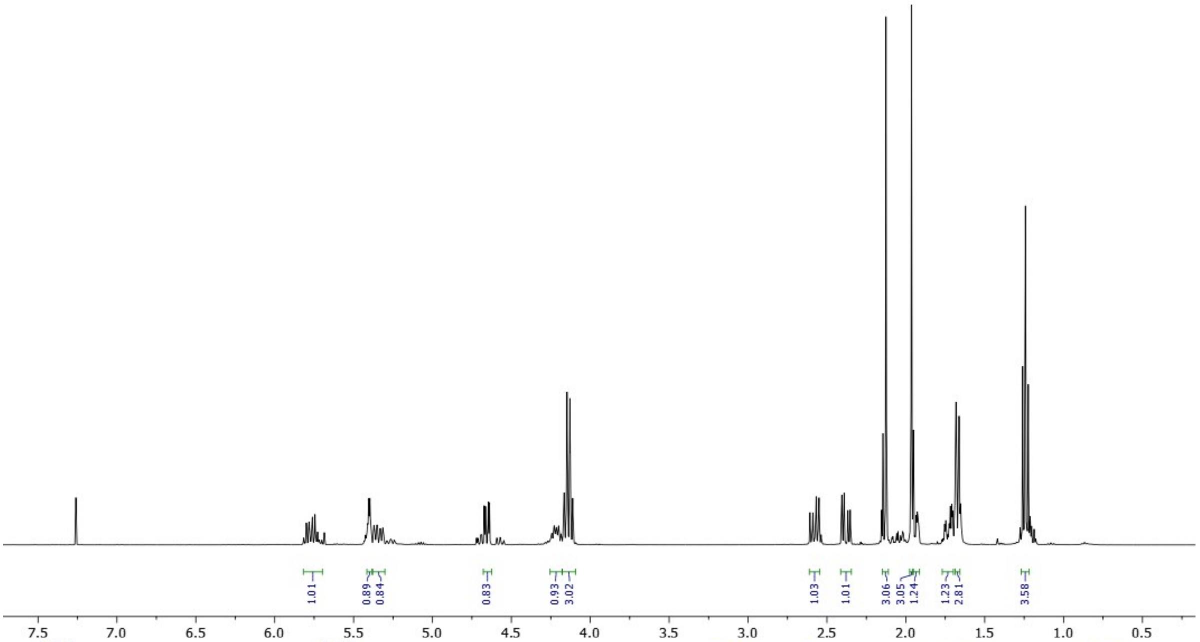
O
OAc
OAc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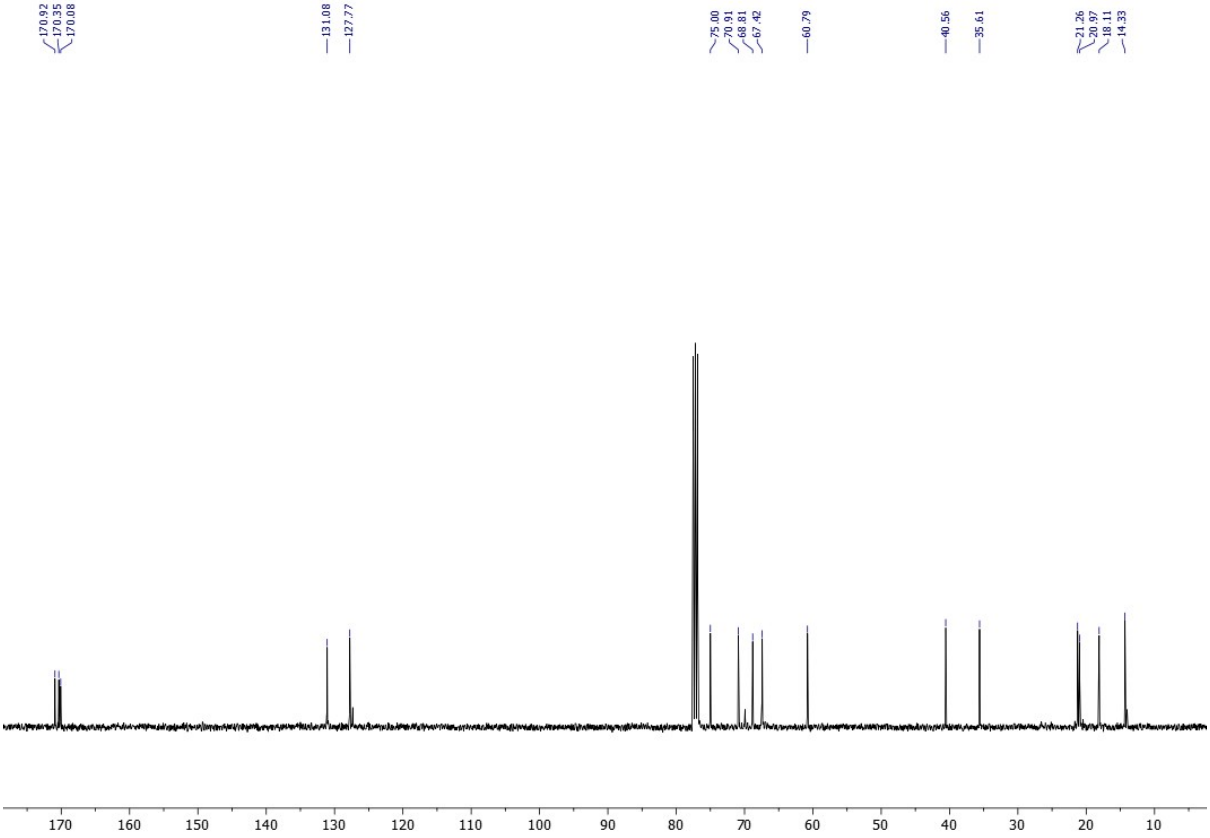
0.89
0.84
0.83
0.93
3.02
1.03
1.01
3.06
3.05
1.24
1.23
2.81
3.58
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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170.08
131.08
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75.00
70.91
68.81
67.42
60.79
40.56
35.61
21.26
20.97
18.11
14.33
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160
150
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130
120
110
100
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80
70
60
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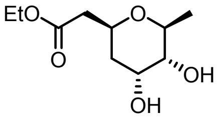
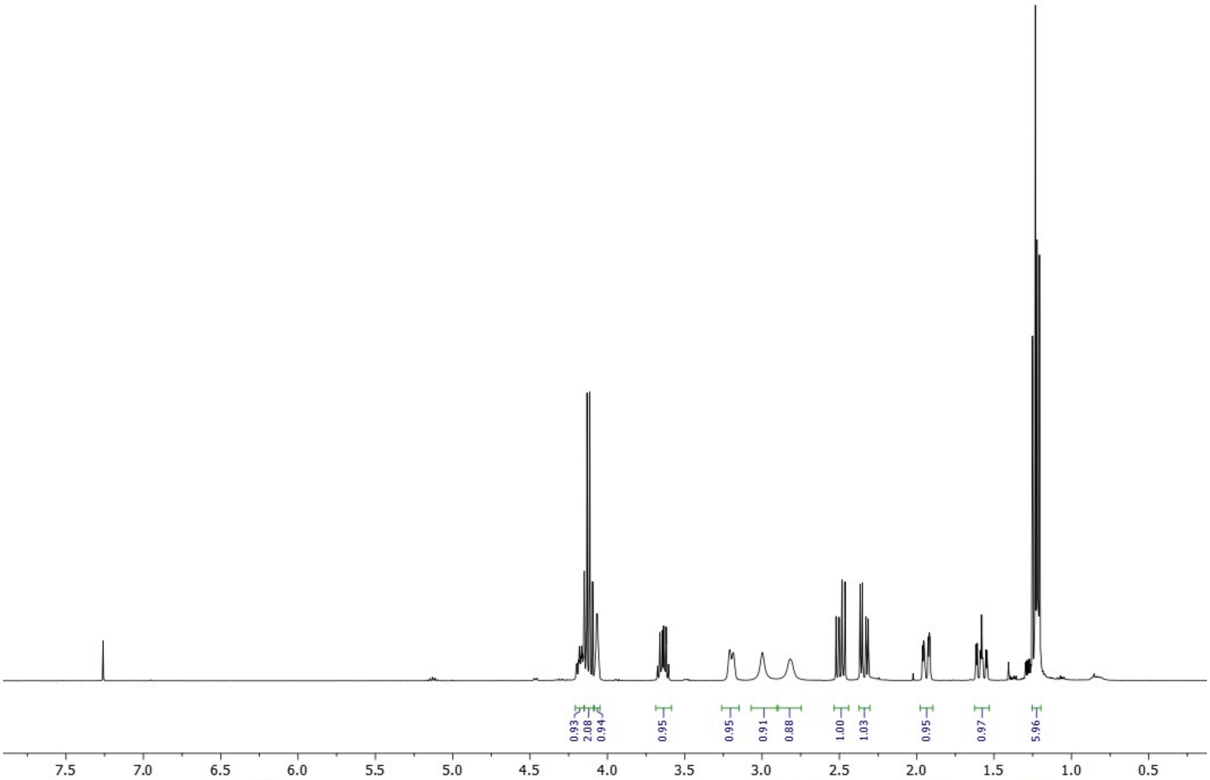
40
30
20
10


EtO
O
O
OH
OH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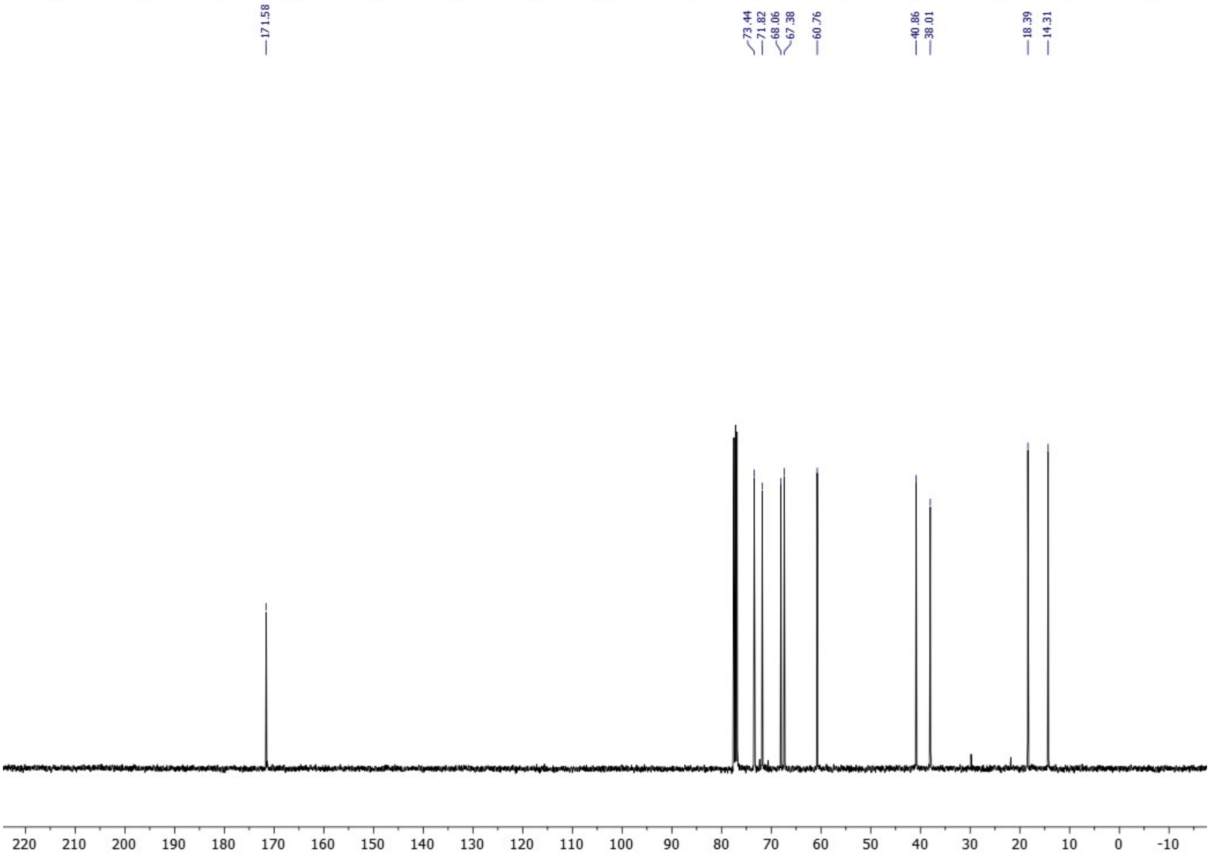
0.94
0.95
0.95
0.91
0.88
1.00
1.03
0.95
0.97
5.96
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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68.06
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60.76
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38.01
18.39
14.31
220
210
200
190
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100
90
80
70
60
50
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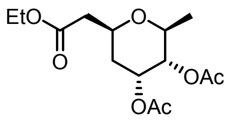
0
-10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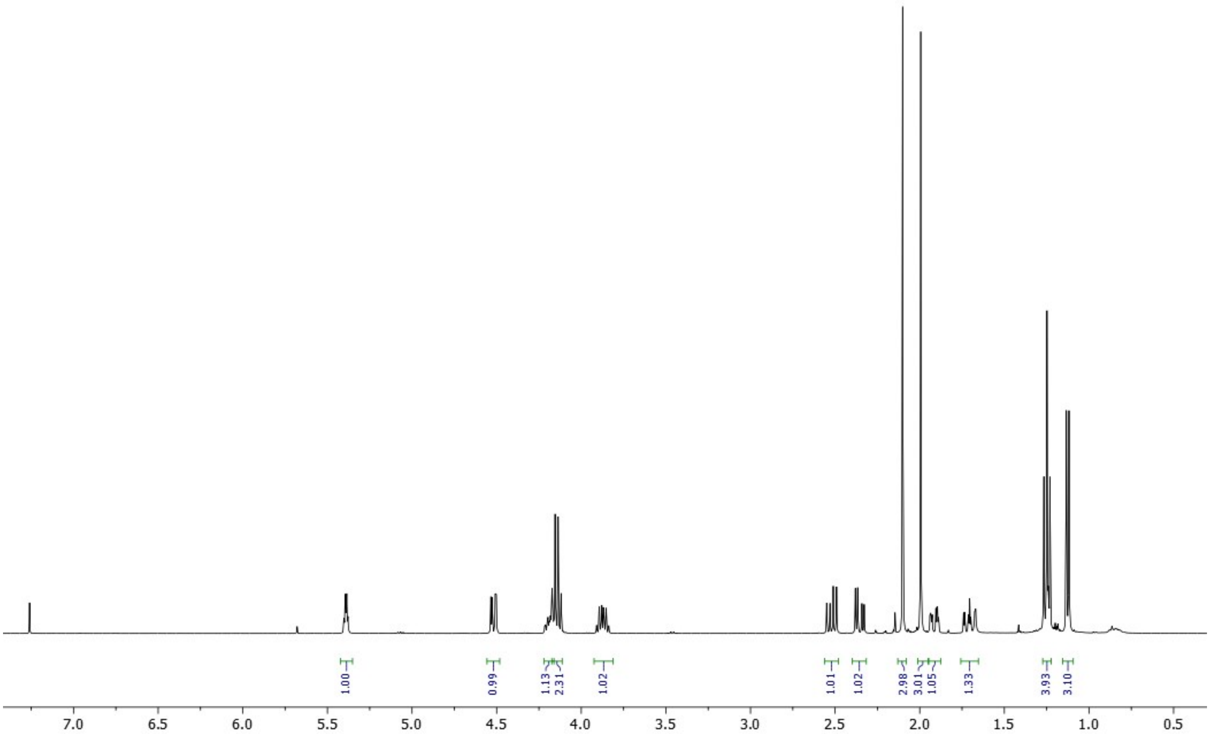
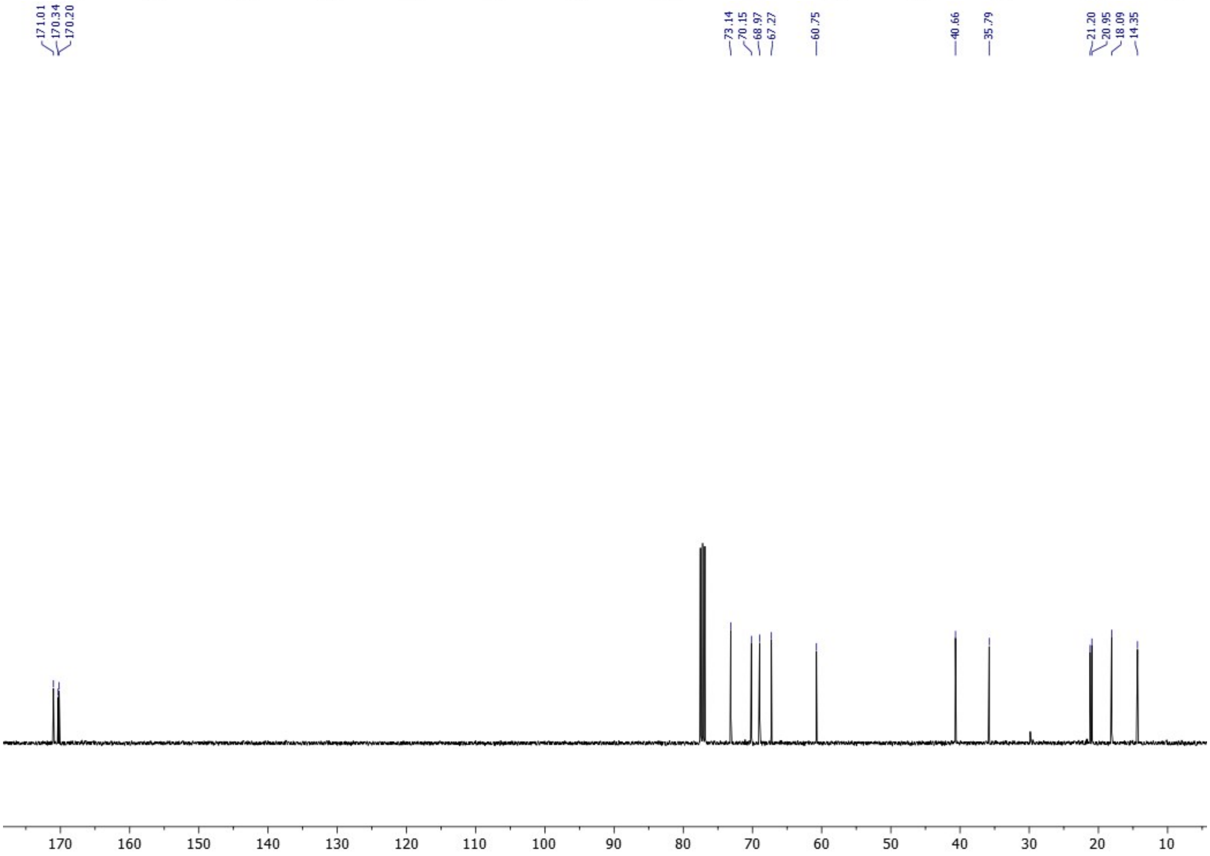
O
O
OAc
OAc


1.00
0.99
1.13
2.31
1.02
1.01
1.02
2.98
3.01
1.05
1.33
3.93
3.10
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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170.20
73.14
70.15
68.97
67.27
60.75
40.66
35.79
21.20
20.95
18.09
14.35
170
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150
140
130
120
110
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80
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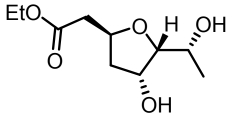
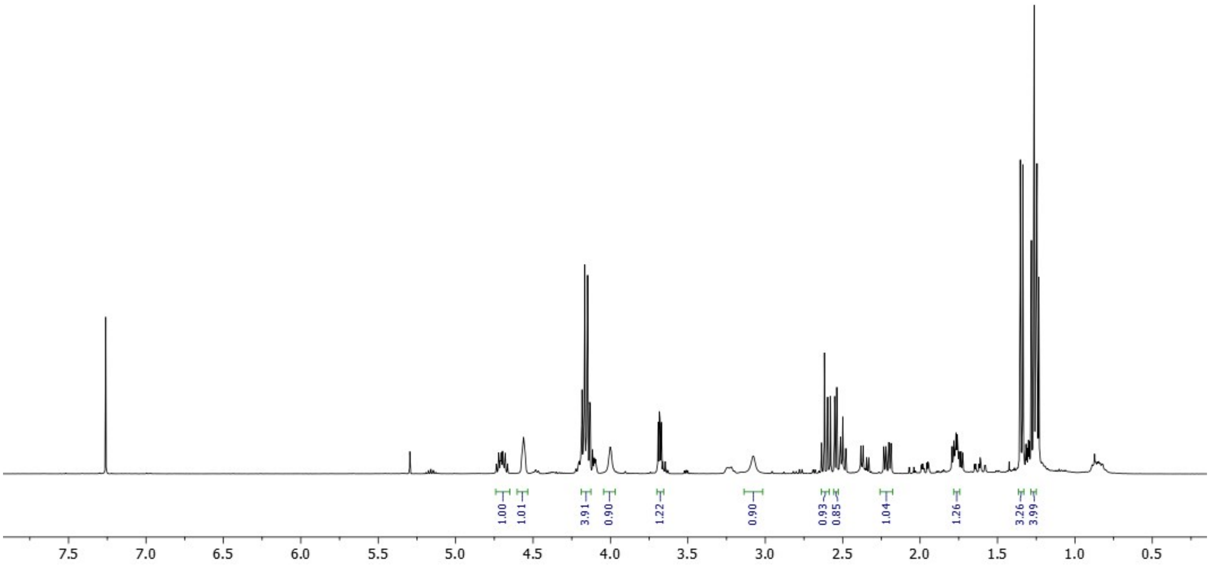
40
30
20
10


EtO
O
O
H
OH
OH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1.01
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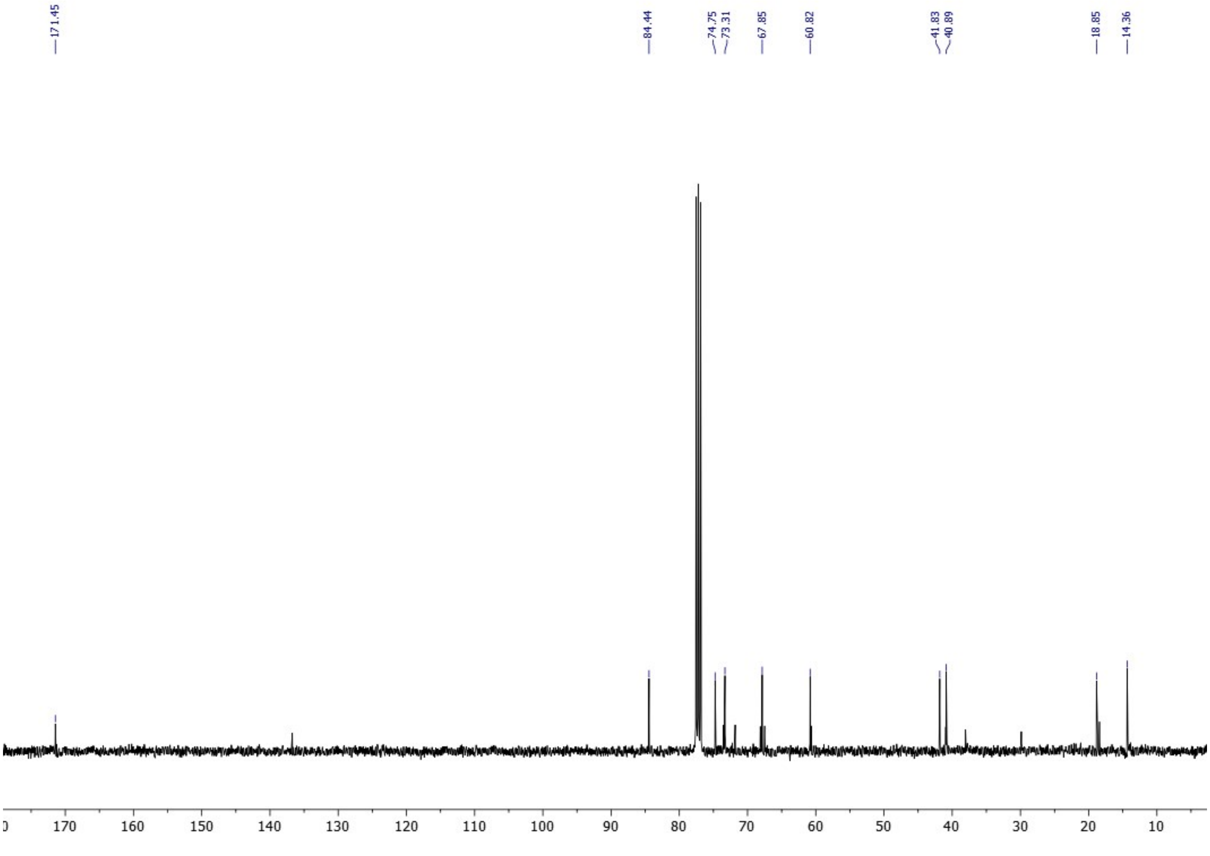
0.90
1.22
0.90
0.93
0.85
1.04
1.26
3.26
3.99
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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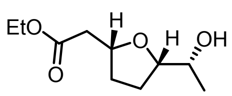
74.75
73.31
67.85
60.82
41.83
40.89
18.85
14.36
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


EtO
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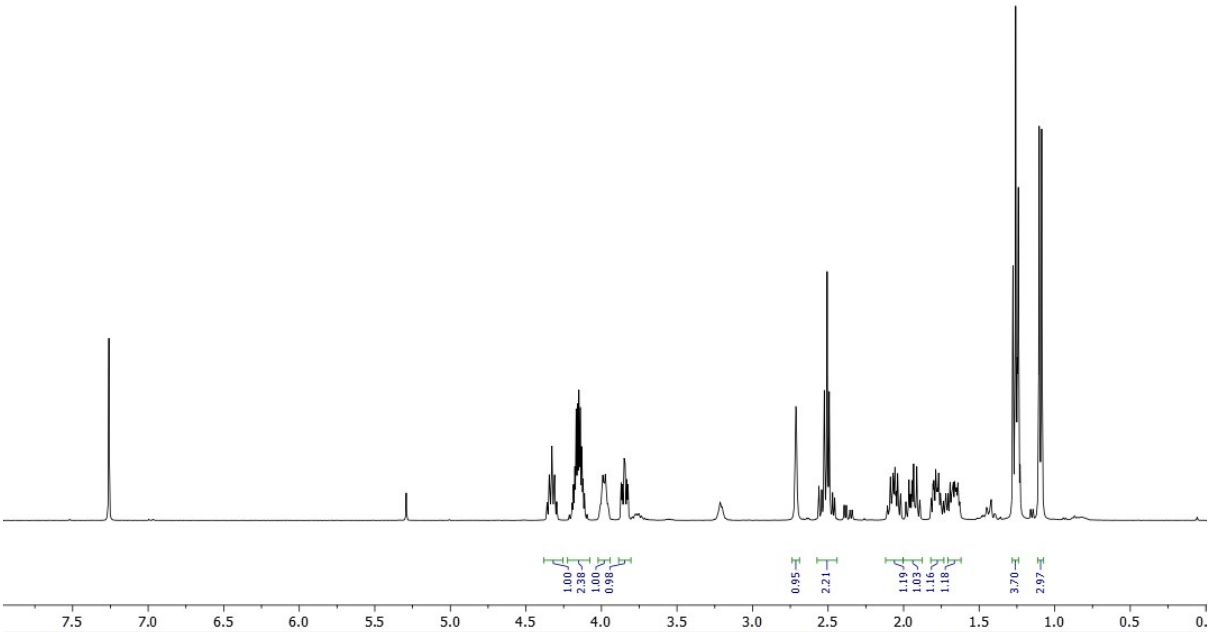
H
O
H
OH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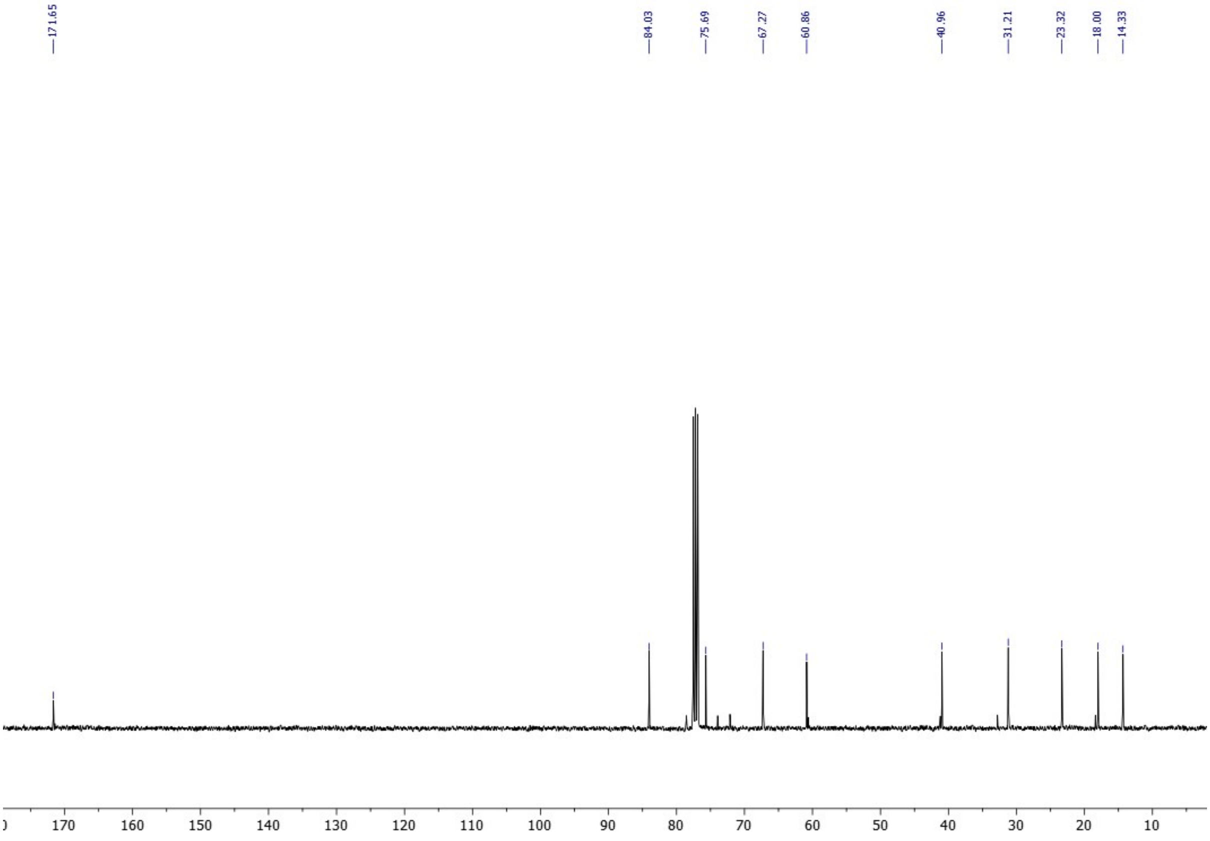
2.38
1.00
0.98
0.95
2.21
1.19
1.03
1.16
1.18
3.70
2.97
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.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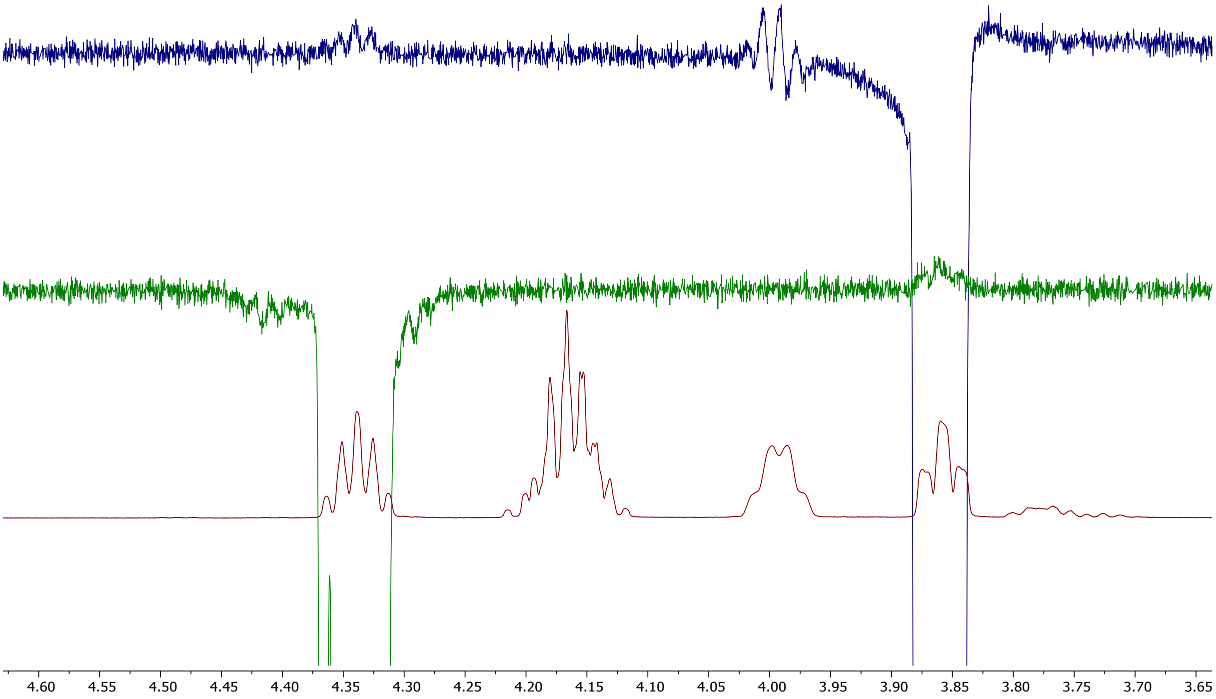
84.03
75.69
67.27
60.86
40.96
31.21
23.32
18.00
14.33
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

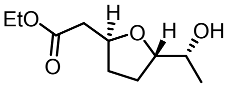


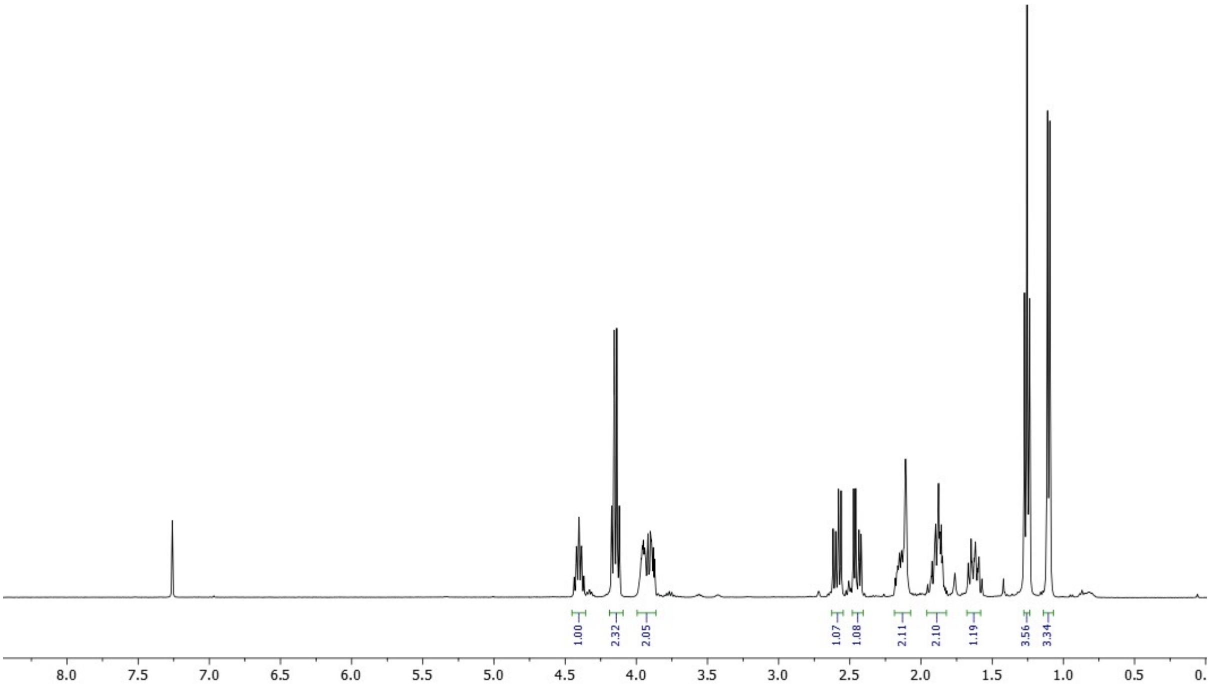
<u>nOe Experiment on THF 49</u>

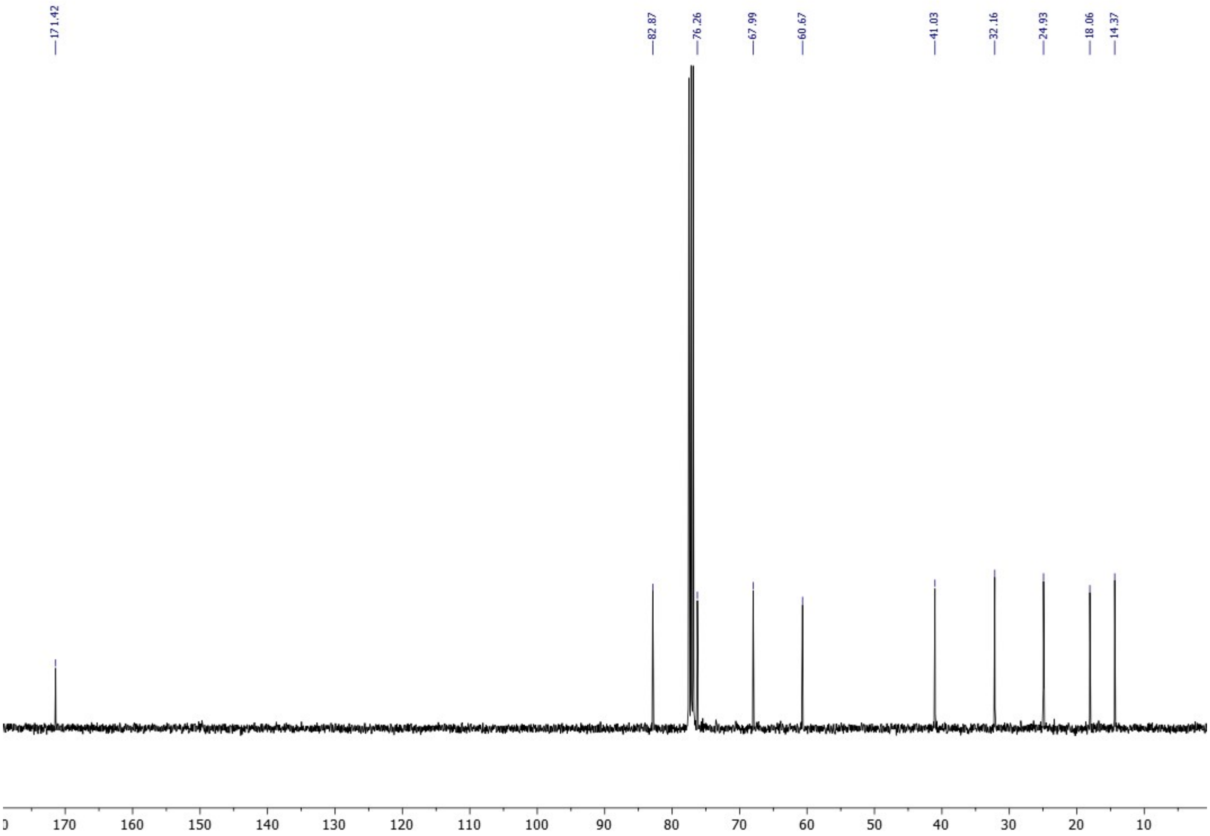
Blue – Irradiation of 6-H (3.85 ppm) and corresponding nOe enhancement of 3-H (4.33 ppm).

Green – Irradiation of 3-H (4.33 ppm) and corresponding nOe enhancement of 6-H (3.85 ppm).

Red – ^{1}H-NMR of THF **49**.


EtO
O
H
O
H
OH


1.00
2.32
2.05
1.07
1.08
2.11
2.10
1.19
3.56
3.34
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.


171.42
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76.26
67.99
60.67
41.03
32.16
24.93
18.06
14.37
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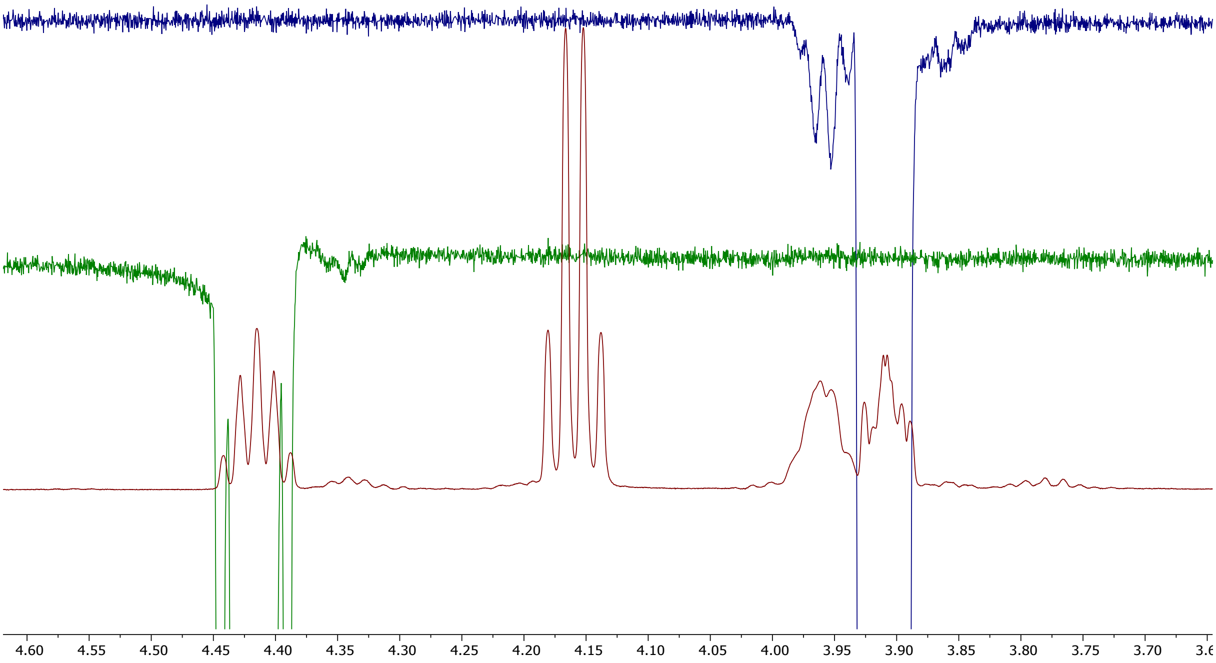
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

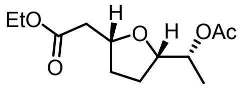


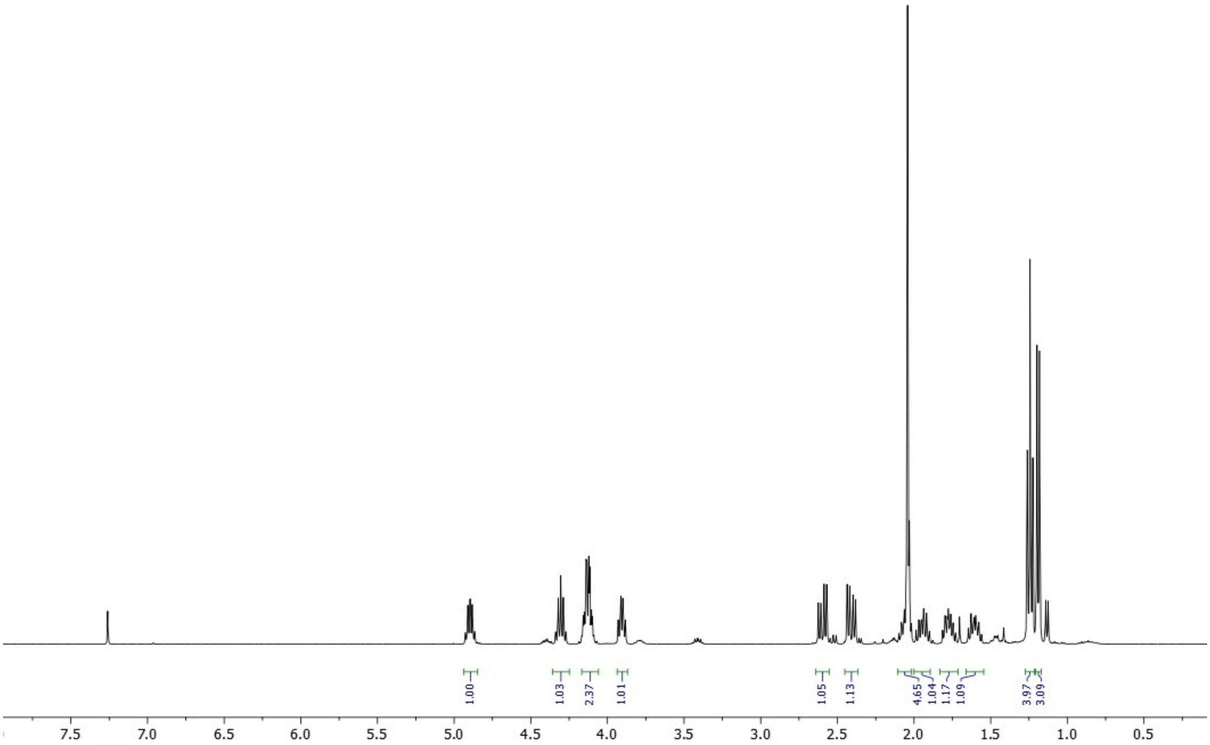
nOe Experiment on THF 50

Blue – Irradiation of 6-H (3.90 ppm) and no nOe enhancement of 3-H (4.40 ppm)

Green – Irradiation of 3-H (4.33 ppm) and no nOe enhancement of 6-H (3.90 ppm).

Red – ^{1}H-NMR of THF **50**.


EtO
O
H
O
H
OAc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1.03
2.37
1.01
1.05
1.13
4.65
1.04
1.17
1.09
3.97
3.09
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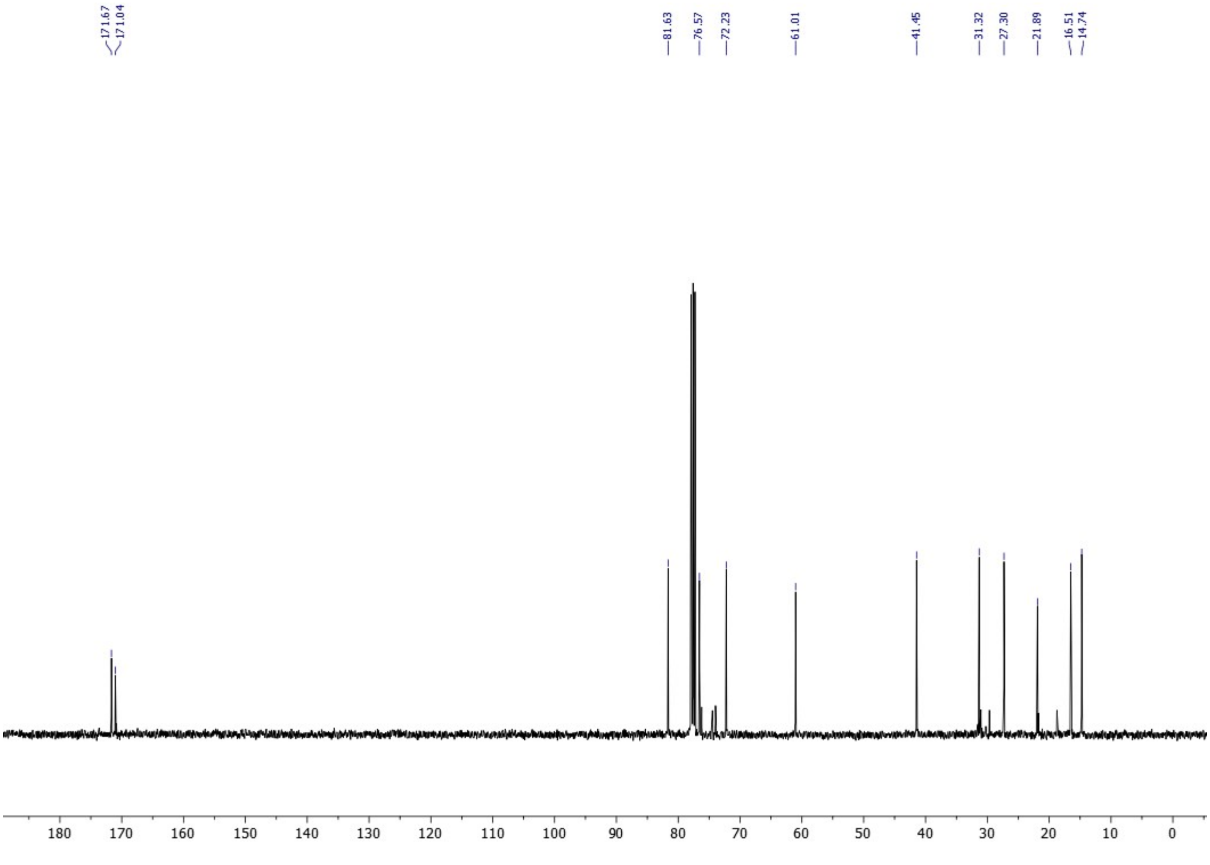
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


171.67
171.04
81.63
76.57
72.23
61.01
41.45
31.32
27.30
21.89
16.51
14.74
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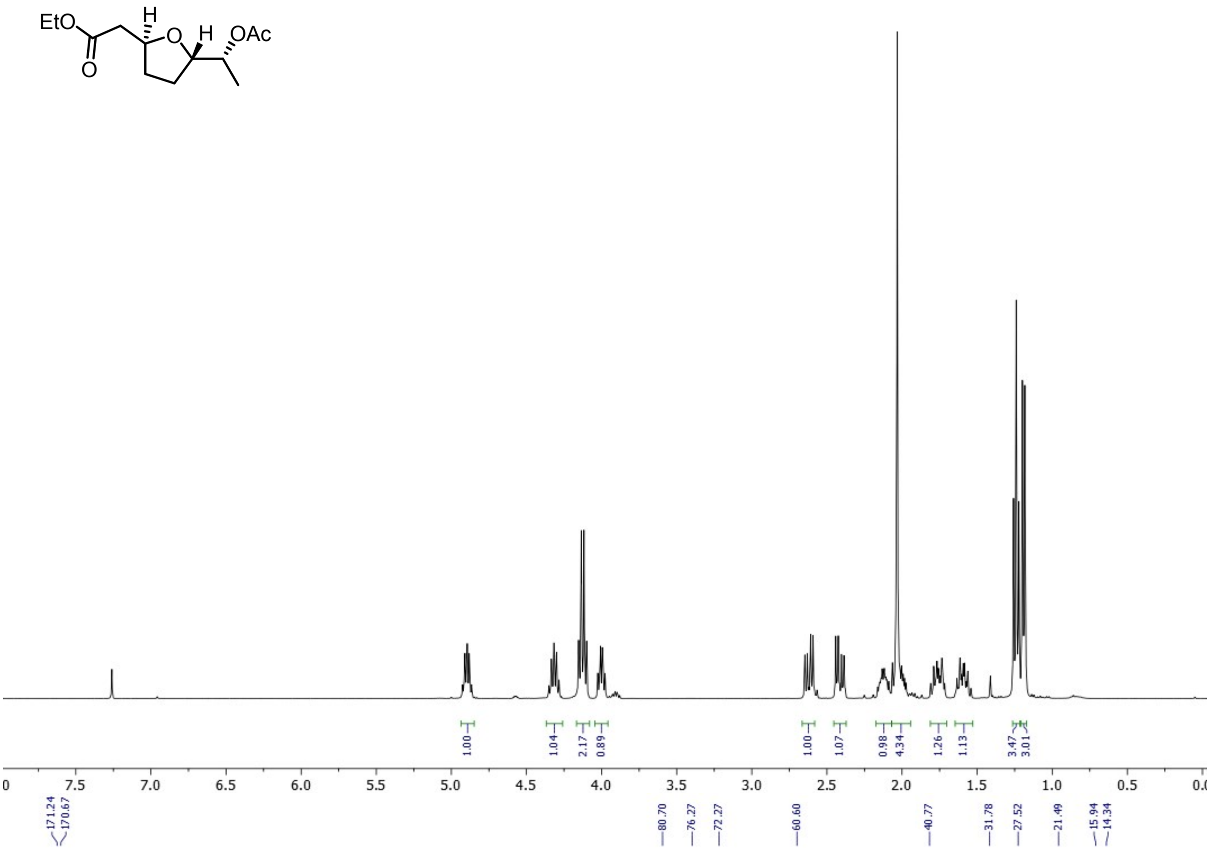
50
40
30
20
10
0


EtO
O
H
O
H
OAc
1.00
1.04
2.17
0.89
1.00
1.07
0.98
4.34
1.26
1.13
3.47
3.01
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
171.24
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80.70
76.27
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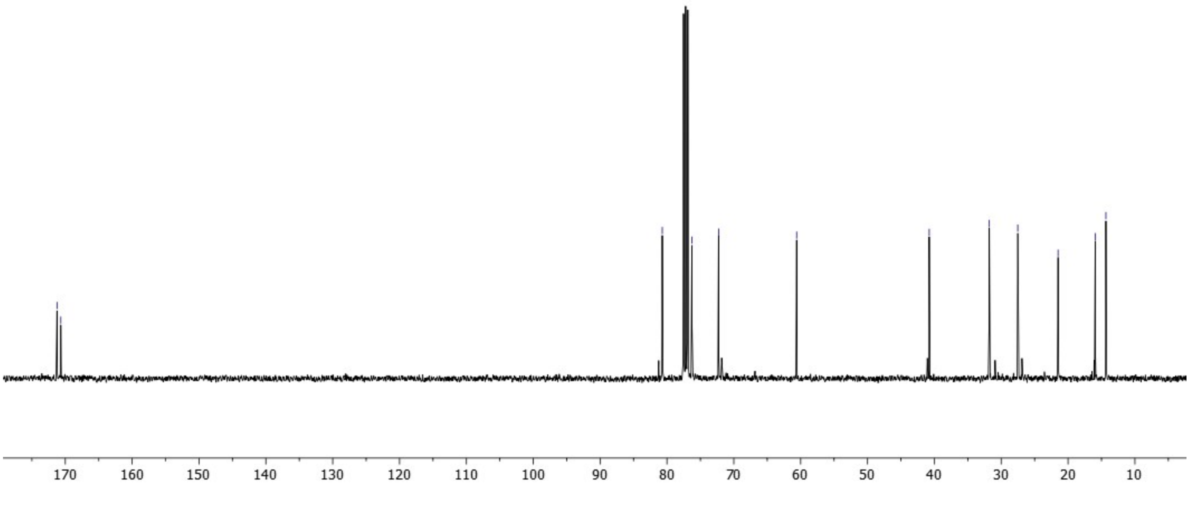
60.60
40.77
31.78
27.52
21.49
15.94
14.34


170
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10