Stereocontrolled Total Synthesis of the Potent Anti-inflammatory and Pro-resolving Lipid Mediator Resolvin D3 and its Aspirin-Triggered 17*R*-Epimer

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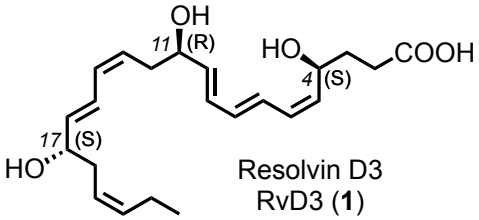

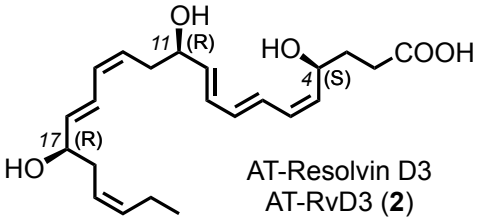

Supporting Information

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General Methods

Unless otherwise noted, all reactions were carried out in a flame-dried flask with stir bar under argon routed through a three-necked valve. Reactions were carried out at room temp using DriSolv solvents purchased commercially from VWR. All reagents used were purchased without further purification from Sigma Aldrich, Strem, and Alfa Aesar.

Progress was monitored and recorded using EMD analytical thin layer chromatography plates, Silica Gel 60 F_{254}. TLC plates were visualized through UV absorbance, (254 nm), or staining such as vanillin, phosphomolybdic acid, potassium-permanganate, or ninhydrin followed by heating. Unless otherwise stated, purification was carried out by flash column chromatography manually using Silica Gel (100-200 mesh) or automatically using the Biotage Isolera One.

Characterization was carried out using LC-MS, NMR and UV-VIS instrumentation. All ^{1}H and ^{13}C spectra were procured on Varian 400, 500 and 600 MHz NMR instruments in the solvent indicated. ^{1}H and ^{13}C chemical shifts, (δ), are recorded in parts per million, (ppm), and referenced to the residual solvent converted by the TMS scale ($CDCl_3$, ^{1}H = 7.26 ppm). Splitting patterns are denoted by s, d, t, dd, td, ddd, and m and refer to the respective multiplicities; singlet, doublet, triplet, doublet of doublets, triplet of doublets, doublet of doublet of doublet and multiplet. Mass spectra were recorded on an Agilent 1260 LC/MS. High resolution mass spectra were recorded on an Agilent LCTOF (2006) using APCI/ESI multimode. UV-Vis spectra were obtained by a Hewlett-Packard 8350 instrument.

Experimental Procedures

***(S)*-O-*t*-Butyldimethylsilyl glycidol (8)**. To a solution of TBS-Cl (15.3 g, 101.5 mmol), imidazole (6.9 g, 101.5 mmol) and DMAP (412 mg, 3.4 mmol) dissolved in 125 mL dry CH_2Cl_2 at 0°C was added *R*-glycidol (5.0 g, 67.5 mmol) at 0°C. The reaction was allowed to stir overnight at room temperature. It was then quenched with saturated aqueous NH_4Cl (125 mL) and extracted with Et_2O (3 x 125 mL). The combined extract was dried with Na_2SO_4 and evaporated to give a crude clear oil which was then chromatographed on silica gel using EtOAc-hexanes mixture of (1:20) as the eluent to afford the *(S)*-protected glycidol **8** as a viscous and colorless oil (12.2 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (dd, *J* = 11.9, 3.2 Hz, 1H), 3.65 (dd, *J* = 11.9, 4.8 Hz, 1H), 3.13 – 3.01 (m, 1H), 2.76 (dd, *J* = 5.2, 4.0 Hz, 1H), 2.63 (dd, *J* = 5.2, 2.7 Hz, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) 63.88, 52.56, 44.60, 26.01, 18.50, -5.17, -5.21. (Ref. Wang, Jian-Chao; *J. Org. Chem.* **1999**, *64*, 8090-9097).

(*S*)-1-(*t*-Butyldiphenylsilyloxy)hept-4-yn-2-ol (16). To a solution of 1-butyne (286 mg, 5.3 mmol) in dry THF (10 mL) was added 2.5 M *n*-BuLi (2.12 mL, 5.3 mmol) at -78°C. After 0.25h $BF_3.Et_2O$ (0.64 mL, 5.3 mmol) was added dropwise at -78°C. To the reaction mixture was added glycidol derivative **8** (0.5 g, 2.65 mmol) and stirred for 3 h at -78°C. The reaction mixture was warmed to room temperature, quenched with saturated aqueous NH_4Cl (15 mL) and extracted with Et_2O (3 x 15 mL). The organic layer was dried with $MgSO_4$, filtered and the solvent removed in vacuo. The crude reaction mixture was purified on silica gel using EtOAc-hexanes (4%) as the eluent to afford compound **16** as a clear colorless oil (600 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 - 3.72 (m, 1H), 3.70 (dd, *J* = 9.9, 4.2 Hz, 1H), 3.60 (dd, *J* = 9.8, 5.8 Hz, 1H), 2.46 (d, *J* = 4.8 Hz, 1H), 2.42 – 2.33 (m, 2H), 2.22 – 2.10 (m, 2H), 1.11 (t, 3H), 0.90 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 84.15, 75.21, 70.63, 65.81, 26.03, 23.55, 18.46, 14.33, 12.55, -5.23, -5.26.

(*S*)-2-(*t*-Butyldiphenylsilyloxy)hept-4-yn-1-ol (17) Part 1: To a flask with imidazole (95 mg, 1.39 mmol) and DMAP (8 mg, 0.06 mmol) in CH_2Cl_2 (5 mL total volume) was added TBDPS-Cl (0.36 mL, 1.39 mmol) dropwise at 0°C. The alcohol **16** (280 mg, 1.15 mmol) was cannulated to the flask and stirred overnight at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl (7 mL) and extracted with Et_2O (3 x 7 mL). The organic layer was dried with $MgSO_4$, filtered and the solvent removed in vacuo. The crude reaction mixture was purified on silica gel using EtOAc-hexanes (1%) as the eluent to afford di-

protected derivative (*S)*-1-(*t*-butyldimethylsilyloxy)-2-(*t*-butyldiphenylsilyloxy)hept-4-yne (525 mg, 89%) as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.65 (m, 4H), 7.55 – 7.29 (m, 6H), 3.83 (p, *J* = 5.5 Hz, 1H), 3.55 (dd, *J* = 5.4, 3.3 Hz, 2H), 2.44 – 2.34 (m, 1H), 2.32 – 2.23 (m, 1H), 2.12 (qt, *J* = 7.5, 2.4 Hz, 2H), 1.10 (t, 3H), 1.07 (s, 9H), 0.84 (s, 9H), -0.03 (s, 3H), -0.06 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 136.10, 136.03, 134.47, 134.34, 129.69, 129.66, 127.62, 83.29, 76.47, 72.78, 65.80, 27.09, 26.05, 24.12, 19.54, 18.46, 14.34, 12.62, -5.34, -5.35. Part 2: To a solution of the product of Part 1 (0.5 g, 1.04 mmol) in CH_2Cl_2 (5 mL) was added camphor sulfonic acid (144 mg, 0.62 mmol) at room temperature and monitored for 1h. The reaction was quenched with Et_3N (0.09 mL, 0.62 mmol) and the solvent was evaporated in vacuo without workup. The crude reaction mixture was purified on silica gel using EtOAc-hexanes (1:10) as the eluent to afford alcohol **17** as a clear colorless oil (370 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 4H), 7.57 – 7.37 (m, 6H), 4.06 – 3.87 (m, 1H), 3.70 (d, *J* = 4.6 Hz, 2H), 2.47 (ddt, *J* = 16.4, 7.7, 2.5 Hz, 1H), 2.36 (ddt, *J* = 16.4, 4.9, 2.4 Hz, 1H), 2.18 – 2.06 (m, 3H), 1.16 (s, 9H), 1.10 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 135.86, 135.71, 133.64, 133.62, 129.89, 129.85, 127.80, 127.68, 83.83, 75.43, 72.62, 65.56, 27.01, 23.91, 19.33, 14.10, 12.4.

***(2S, 4Z)*-2-(*t*-Butyldiphenylsilyloxy)hept-4-en-1-ol (18)**. To a solution of alcohol **17** (3.9 g, 10.2 mmol) in EtOAc (200 mL) was added Lindlar catalyst (200 mg). The reaction mixture was placed under a H_2 atmosphere and stirred for 2 h. The reaction was filtered through celite and the solvent was removed in vacuo. The crude product was purified on silica gel using EtOAc-hexanes (3:22) as an eluent to afford the alcohol **18** as a clear colorless oil (3.5 g, 94%). 1H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.56 (m, 4H), 7.51 – 7.30 (m, 6H), 5.43 – 5.28 (m, 1H), 5.17 (dtt, *J* = 10.7, 7.6, 1.5 Hz, 1H), 3.79 (dtd, *J* = 8.5, 4.8, 3.6 Hz, 1H), 3.63 – 3.43 (m, 2H), 2.36 – 2.23 (m, 1H), 2.22 – 2.10 (m, 1H), 1.91 – 1.73 (m, 2H), 1.09 (s, 9H), 0.84 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 136.03, 135.85, 134.42, 133.97, 133.93, 129.97, 129.93, 127.91, 127.80, 123.7 , 74.00, 65.74, 31.69, 27.19, 20.61, 19.49, 14.24.

***(3S, 1E, 5Z)*-3-(*t*-Butyldiphenylsilyloxy)-1-iodoocta-1,5-diene (19).** Part 1: To a solution of DMSO (0.43 mL, 3.7 mmol) in CH_2Cl_2 (15 mL) was added oxalyl chloride (0.33 mL, 3.7 mmol) at -78°C. To the reaction mixture was cannulated alcohol **18** (0.5 g, 1.87 mmol) and stirred for 1 h. Et_3N was added to the reaction at -78°C and stirred for 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) and extracted with Et_2O (3 x 20 mL).

The Et_2O was washed with brine, dried with $MgSO_4$ and filtered. The solvent was removed in vacuo and the crude product was purified on silica gel using EtOAc-Hexanes (1:4) as the eluent to afford the aldehyde 2*S*, 4Z, 2-(*t*-butyldiphenylsilyloxy)hept-4-enal as a colorless oil (0.44 g, 90%). 1H NMR (400 MHz, $CDCl_3$) δ 9.57 (d, *J* = 1.7 Hz, 2H), 7.71 – 7.61 (m, 4H), 7.49 – 7.33 (m, 6H), 5.52 – 5.41 (m, 1H), 5.40 – 5.27 (m, 1H), 4.06 (td, *J* = 6.5, 1.7 Hz, 1H), 2.44 (dt, *J* = 14.1, 6.7 Hz, 1H), 2.34 (dt, *J* = 13.9, 6.5 Hz, 1H), 1.99 – 1.87 (m, 2H), 1.12 (s, 9H), 0.90 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 203.52, 135.95, 135.95, 135.11, 133.24, 133.12, 130.18, 130.13, 127.95, 127.89, 122.17, 77.94, 31.15, 27.08, 20.74, 19.49, 14.14. Part 2. To a solution of $CrCl_2$ (3.4 g, 27.3 mmol) dissolved in THF (40 mL total volume) was cannulated a mixture of 2*S*, 4Z, 2-(*t*-butyldiphenylsilyloxy)hept-4-enal aldehyde (1.0 g, 2.7 mmol) and CHI_3 (5.4 g, 13.7 mmol) dissolved in anhydrous THF (10 mL) under Argon at 0°C. The reaction was stirred at 0°C for 3 h and an additional 1 h at room temperature. The reaction mixture was quenched with water (50 mL) extracted with Et_2O (3 x 50 mL) rinsed with brine and dried over $MgSO_4$. The organic phase was filtered and the solvent was removed in vacuo to afford a crude oil which was purified on silica gel using first pure pentanes and then EtOAc-hexanes (1:24) as the eluent to afford compound **19** as a clear colorless oil (780 mg, 59%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.54 (m, 4H), 7.51 – 7.32 (m, 6H), 6.49 (dd, *J* = 14.4, 6.5 Hz, 1H), 5.98 (dd, *J* = 14.4, 1.1 Hz, 1H), 5.49 – 5.32 (m, 1H), 5.32 – 5.13 (m, 1H), 4.17 – 3.98 (m, 0H), 2.32 – 2.07 (m, 2H), 1.84 (dtd, *J* = 9.2, 7.4, 5.6 Hz, 2H), 1.07 (s, 9H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.04, 136.03, 136.01, 134.54, 133.97, 133.65, 129.90, 129.87, 127.74, 127.72, 123.18, 76.88, 75.93, 35.31, 27.14, 20.75, 19.48, 14.33.

***(3S, 1E, 5Z)*-3-(*t*-Butyldimethylsilyloxy)-1-iodoocta-1,5-diene (5).** To a solution of the TBDPS-protected vinyl iodide **19** (0.8 g, 1.63 mmol) in THF (5 mL) was added 1.0 M solution of TBAF (1.63 mL, 1.63 mmol) at 0°C and stirred for 2 h. The reaction was quenched with water (10 mL) and extracted with Et_2O (5 x 10 mL), rinsed with brine, dried over $MgSO_4$ and filtered. The crude reaction mixture was purified on silica gel using EtOAc-hexanes (10%) as the eluent to afford the alcohol (3*S*, 1*E*, 5*Z*)-1-iodoocta-1,5-diene-3-ol (0.38 g, 92%) as a clear colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.60 (dd, *J* = 14.4, 5.8 Hz, 1H), 6.37 (dd, *J* = 14.5, 1.3 Hz, 1H), 5.73 – 5.52 (m, 1H), 5.45 – 5.25 (m, 1H), 4.23 – 3.98 (m, 1H), 2.31 (ddd, *J* = 7.7, 6.5, 1.6 Hz, 2H), 2.14 – 1.95 (m, 2H), 0.98 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 147.92, 134.93, 122.82, 77.48, 77.38, 77.16, 76.84, 74.01, 34.68, 20.89, 14.35. The alcohol

(0.38 g, 1.5 mmol) was protected using TBS-OTf (0.54 mL, 3.0 mmol) and 2,6-lutidine (0.52 mL, 4.5 mmol) in anhydrous CH_2Cl_2 (20 mL). The reaction mixture was quenched after 2 h with saturated aqueous NH_4Cl (20 mL) and extracted with Et_2O (3 x 20 mL). The Et_2O was rinsed with brine, dried with $MgSO_4$ and filtered. The solvent was removed in vacuo and the crude product was purified on silica gel using EtOAc-Hexanes (1:49) as the eluent to afford the silylated vinyl iodide **5** as a colorless oil (0.54 g, 98%).^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (dd, *J* = 14.3, 5.7 Hz, 1H), 6.21 (dd, *J* = 14.3, 1.5 Hz, 1H), 5.54 – 5.42 (m, 1H), 5.37 – 5.24 (m, 1H), 4.17 – 4.00 (m, 1H), 2.33 – 2.18 (m, 2H), 2.03 (dt, *J* = 14.9, 7.4 Hz, 1H), 0.96 (t, *J* = 7.5 Hz, 4H), 0.89 (s, 9H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.90, 134.39, 123.75, 75.86, 75.20, 35.70, 25.96, 20.90, 18.37, 14.37, -4.48, -4.68.

***(R)*-1, 2-di-(*t*-Butyldimethylsilyloxy)-5-trimethylsilyl-pent-4-yne (20)**. Part 1: To a solution of TMS acetylene (5.6 mL, 39.8 mmol) in THF (40 mL) was added 2.5 M *n*-BuLi (15.9 mL, 39.8 mmol) at -78°C. After 0.25 h $BF_3.Et_2O$ (5.0 mL, 39.8 mmol) was added drop wise at -78°C. To the reaction mixture was added (*R*)-O-*t*-butyldimethylsilyl glycidol **13** (5.0 g, 26.5 mmol) and stirred for 3 h at -78°C. The reaction mixture was warmed to room temperature, quenched with saturated aqueous NH_4Cl (45 mL) and extracted with Et_2O (3 x 45 mL). The organic layer was dried with $MgSO_4$, filtered and the solvent removed in vacuo. The crude reaction mixture was purified on silica gel using EtOAc-hexanes (4%) as the eluent to afford 2*R*, 1, (*t*-butyldimethyl-silyloxy)-5-trimethylsilyl-pent-4-yn-2-ol (5.5 g, 73%) as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (dt, *J* = 11.1, 5.9 Hz, 1H), 3.72 (dd, *J* = 10.0, 4.1 Hz, 1H), 3.63 (dd, *J* = 10.0, 5.6 Hz, 1H), 2.51 – 2.41 (m, 2H), 1.64 (s, 1H), 0.91 (s, 11H), 0.14 (s, 2H), 0.09 (s, 5H), 0.08 (s, 6H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 102.96, 87.19, 70.32, 65.60, 26.03, 24.67, 18.48, 0.17, -5.24, -5.28. Part 2: To a solution of the product of Part 1 (5.7g, 19.9 mmol) in anhydrous CH_2Cl_2 (30 mL) was added TBS-Cl (3.6 g, 23.9 mmol), imidazole (1.6g, 23.9 mmol), and DMAP (243 mg, 1.99 mmol) at 0°C. The reaction was allowed to stir at room temperature overnight. It was then quenched with saturated aqueous NH_4Cl (30 mL) and extracted with Et_2O (3 x 30 mL). The combined extract was dried with $MgSO_4$, filtered and evaporated to give a crude clear oil which was then chromatographed on silica gel using EtOAc-hexanes mixture of (1:24) as the eluent to afford the product **20** as a viscous and colorless oil (7.5g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 – 3.75 (m, 1H), 3.60 – 3.47 (m, 2H), 2.50 (dd, *J* = 16.8, 5.3 Hz, 1H), 2.30 (dd, *J* = 16.8, 6.5 Hz, 1H), 0.89 (s, 18H), 0.14 (s, 9H), 0.11 (s, 3H),

0.08 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 104.86, 85.95, 72.25, 66.83, 26.13, 26.01, 18.53, 18.29, 0.23, -2.78, -4.29, -4.44, -5.18, -5.24.

***(R)*-2-(*t*-Butyldimethylsilyloxy)-5-trimethylsilyl-pent-4-yn-1-ol (11)**. To a solution of protected diol **20** (3.4 g, 8.5 mmol) in a 1:1 mixture of dry CH_2Cl_2/MeOH (20 mL) was added camphor sulfonic acid (1.0 g, 4.2 mmol) at 0°C. The reaction was allowed to stir for 0.5 h and quenched with Et_3N (1.2 mL, 8.5 mmol). The solvent was removed in vacuo without work-up and purified on silica gel using EtOAc-hexanes mixture (7%) as the eluent to afford the product **11** as a viscous and colorless oil (1.9 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 – 3.84 (m, 1H), 3.67 (ddd, *J* = 11.2, 5.8, 3.8 Hz, 1H), 3.57 (ddd, *J* = 11.2, 5.8, 3.8 Hz, 1H), 2.51 – 2.33 (m, 3H), 1.88 (dd, *J* = 7.1, 6.0 Hz, 2H), 0.90 (s, 9H), 0.14 (s, 9H), 0.13 (s, 4H), 0.11 (s, 4H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 103.47, 86.91, 71.64, 66.04, 25.94, 25.52, 18.20, 0.16, -4.34, -4.59.

***(R)*-2-(*t*-Butyldimethylsilyloxy)-5-trimethylsilyl-pent-4-ynal (21)**. To a -78°C solution of DMSO (1.3 mL, 18.5 mmol) in anhydrous CH_2Cl_2 (40 mL) was added oxalyl chloride (1.1 mL, 12.3 mmol) drop wise. After 0.25 h alcohol **11** (1.58 g, 6.2 mmol) was added and stirred for 1 h at -78°C. To the reaction mixture was added Et_3N (4.3 mL, 30.8 mmol) and stirred for another 3 h at -78°C. The reaction mixture was allowed to warm to room temperature and quenched with saturated aqueous NH_4Cl (45 mL) and extracted with Et_2O (3 x 45 mL). The combined extract was dried with Na_2SO_4 and evaporated to give a crude clear oil which was then chromatographed on silica gel using EtOAc-hexanes mixture of (1:20) as the eluent to afford the aldehyde **21** as a viscous and colorless oil (1.6g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 1.3 Hz, 1H), 4.17 – 4.05 (m, 1H), 2.64 (dd, *J* = 17.0, 5.0 Hz, 1H), 2.48 (dd, *J* = 17.0, 7.8 Hz, 1H), 0.94 (s, 9H), 0.14 (s, 12H), 0.13 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 202.25, 101.99, 87.54, 76.25, 31.08, 25.87, 24.65, 18.39, 0.08, -4.57.

***(2E*, 4*R*)-4-(*t*-Butyldimethylsilyloxy)-7trimethylsilyl-hept-2-en-6-ynal (22)**. To a solution of aldehyde **21** (700 mg, 2.46 mmol) dissolved in Toluene (15 mL) was added (Triphenylphosphoranylidene)acetaldehyde (750 mg, 2.46 mmol) and heated to reflux overnight. The solvent was removed in vacuo without work up and the crude mixture was purified on silica gel using a EtOAc-hexanes mixture of (1:20) as the eluent to afford aldehyde **22** as a clear viscous oil (634 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (d, *J* = 8.0 Hz, 1H), 6.90 (dd, *J* = 15.5, 4.3 Hz, 1H), 6.31 (ddd, *J* = 15.5, 8.0, 1.4 Hz, 1H), 4.54 (ddd, *J* = 11.8, 6.1, 1.4 Hz, 1H), 2.55 (dd, *J* = 16.6, 6.2 Hz, 1H), 2.44 (dd, *J* = 16.6, 7.4 Hz, 1H), 0.91 (s, 9H), 0.15 (s, 9H), 0.11

(s, 3H), 0.07 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 193.56, 157.92, 131.40, 102.21, 70.66, 29.11, 25.87, 18.30, 0.11, -4.63, -4.69.

(3S, 1E, 4E)*-3-(*t*-Butyldimethylsilyloxy)-1-iodoocta-1,5-diene (10)**. To a solution of $CrCl_2$ (2.0 g, 16.1 mmol) dissolved in THF (65 mL total volume) was cannulated a mixture of aldehyde **22** (560 mg, 1.8 mmol) and CHI_3 (3.2 g, 8.05 mmol) dissolved in anhydrous THF (10 mL) under Argon at 0°C. The reaction was stirred at 0°C for 3 h and an additional 1 h at room temperature. The reaction mixture was quenched with water (80 mL) extracted with Et_2O (3 x 80 mL) rinsed with brine and dried over $MgSO_4$. The organic phase was filtered and the solvent was removed in vacuo to afford a crude oil which was purified on silica gel using first pure pentanes and then EtOAc-hexanes (1:24) as the eluent to afford a 9:1 mixture of compound **10** and its ***E, Z stereoisomer (see inset) as a clear colorless oil (660 mg, 84%). The desired product was able to be isolated but not without some loss in the yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (dd, *J* = 14.5, 10.7 Hz, 1H), 6.32 (d, *J* = 14.5 Hz, 1H), 6.15 (ddd, *J* = 15.2, 10.8, 1.2 Hz, 1H), 5.78 (dd, *J* = 15.2, 5.7 Hz, 1H), 4.27 (d, *J* = 6.6 Hz, 1H), 2.49 – 2.29 (m, 2H), 0.90 (s, 9H), 0.14 (s, 9H), 0.09 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 144.72, 136.49, 129.69, 103.74, 86.78, 79.23, 71.48, 29.90, 25.97, 18.39, 0.20, -4.42, -4.60.

***(3S, 1E, 4Z)*-3-(*t*-Butyldimethylsilyloxy)-1-iodoocta-1,5-diene.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (dd, *J* = 10.0, 7.6 Hz, 1H), 6.45 (ddt, *J* = 15.2, 9.9, 1.3 Hz, 1H), 6.27 (d, *J* = 7.6 Hz, 1H), 6.04 (dd, *J* = 15.2, 5.3 Hz, 1H), 4.36 (dt, *J* = 6.9, 5.3 Hz, 1H), 2.45 (d, *J* = 6.6 Hz, 2H), 0.94 (s, 9H), 0.15 (d, *J* = 0.5 Hz, 9H), 0.12 (s, 3H), 0.10 (d, *J* = 0.5 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.18, 137.85, 129.99, 128.48, 86.83, 82.57, 71.65, 29.80, 26.04, 18.39, 0.24, -4.31, -4.42; HRMS (ESI) *m/z* calcd for $C_{17}H_{35}INOSi_2$: $[M+NH4]^+$: 452.1297 found: 452.1302.

Dimethyl (2*S*)-2-hydroxypentanedioate (23). To a solution of (*S)*-γ-carboxy butyrolactone [S-5-oxo-2-tetrahydrofurancarboxylic acid] (5.0g, 38.5 mmol) in dry MeOH (40 mL) was added 4 drops of concentrated HCl and heated to reflux overnight. The reaction was cooled to 0°C and quenched with $NaHCO_3$ and filtered. The solvent was then evaporated with no further workup and the crude was purified on silica gel using EtOAc-hexanes mixture of (1:1) as the eluent to afford the product **23** as a viscous and colorless oil (6.5g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23 (dd, *J* = 7.9, 4.2 Hz, 1H), 3.78 (s, 3H), 3.66 (s, 3H), 2.94 (s, 1H), 2.60 – 2.33 (m, 2H), 2.24 – 2.05 (m, 1H), 1.99 – 1.83 (m, 1H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.14, 173.67, 69.58, 52.76, 51.84, 29.53, 29.39.

Methyl (4*S*)-4,5-dihydroxypentanoate (24). To a solution of compound **23** (6.5g, 37 mmol) in dry THF (55 mL) was added BH_3.DMS dropwise maintaining a temperature of 10-15°C. After stirring at this temperature for 1 h, a catalytic amount of $NaBH_4$ (70mg, 1.9 mmol) was added and stirred for an additional 1 h maintaining the temperature around 10°C. The reaction mixture was quenched with dry MeOH (20 mL) and stirred for an additional .5 h. The solvent was removed in vacuo with no further workup and the crude was purified on silica gel using EtOAc as the eluent to afford the diol **24** as viscous colorless oil (4.7g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 – 3.68 (m, 1H), 3.67 (s, 3H), 3.62 (dd, *J* = 11.1, 3.1 Hz, 1H), 3.44 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.20 (s, 1H), 2.88 (s, 1H), 2.47 (td, *J* = 7.2, 2.9 Hz, 2H), 1.84 – 1.67 (m, 2H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.74, 71.53, 66.61, 51.92, 30.38, 28.06.

Methyl (4*S*)-4-(*t*-butyldimethylsilyloxy)-5-hydroxypentanoate (14). Part 1: To a flask with stir bar was added TBS-Cl (8.2g, 54.5 mmol), imidazole (3.7g, 54.5 mmol) and DMAP (110 mg, 0.9 mmol) and dissolved in 10 mL dry DMF at 0°C. Diol **24** (2.5g, 18 mmol) was suspended in 5 mL dry DMF and cannulated into the reaction flask at 0°C. The reaction was allowed to stir overnight at room temperature. It was then quenched with saturated aqueous NH_4Cl (20 mL) and extracted with Et_2O (3 x 20 mL). The combined extract was dried with Na_2SO_4 and evaporated to give a crude clear oil which was then chromatographed on silica gel using EtOAc-hexanes mixture of (1:24) as the eluent to afford methyl (4*S*)-4,5-*bis*(*t*-butyldimethylsilyloxy)pentanoate as a viscous and colorless oil (6.3g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74 – 3.68 (m, 1H), 3.66 (s, 3H), 3.53 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.39 (dd, *J* = 10.0, 6.8 Hz, 1H), 2.52 – 2.28 (m, 2H), 2.00 – 1.86 (m, 1H), 1.79 – 1.64 (m, 1H), 0.89 (s, 9H), 0.88 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.47, 72.05, 67.14, 51.61, 29.75, 29.47, 26.10, 26.01, 18.50, 18.25, -4.18, -4.70, -5.20, -5.24. Part 2: To a solution of the product from Part 1 (7.7g, 20.5mmol) in a 1:1 mixture of dry CH_2Cl_2/MeOH (50 mL) was added camphor sulfonic acid (3.8g, 16.38 mmol) at 0°C. The reaction was allowed to stir for 0.5 h and quenched with Et_3N (2.85mL, 20.5 mmol). Avoiding workup, the solvent was removed in vacuo and purified on silica gel using EtOAc-hexanes mixture (3:7) as the eluent to afford the alcohol **14** as a viscous and colorless oil (3.1g, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 – 3.77 (m, 1H), 3.67 (s, 3H), 3.59 – 3.48 (m, 1H), 3.52 – 3.41 (m, 1H), 2.47 – 2.29 (m, 2H), 1.94 (t, *J* = 6.3 Hz, 1H), 1.92 – 1.77 (m, 2H), 0.90 (s, 9H), 0.08 (s,

6H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.25, 71.59, 66.01, 51.78, 29.56, 28.70, 25.95, 18.20, -4.44, -4.55; HRMS (ESI) *m/z* calcd for $C_{12}H_{27}O_4Si$: $[M+H]^+$: 263.1673 found: 263.1673.

Methyl (4*S*)-4-(*t*-butyldimethylsilyloxy)-5-oxopentanoate (25). To a -78°C solution of DMSO (1.32 mL, 17.1 mmol) in anhydrous CH_2Cl_2 (30 mL) was added oxalyl chloride (1.01 mL, 11.4 mmol) dropwise. After 0.25 h alcohol **14** (1.5g, 5.7 mmol) was added and stirred for 1 h at -78°C. To the reaction mixture was added Et_3N (3.9 mL, 28.5 mmol) and stirred for another 3 h at -78°C. The reaction mixture was allowed to warm to room temperature and quenched with saturated aqueous NH_4Cl (35 mL) and extracted with Et_2O (3 x 35 mL). The combined extract was dried with Na_2SO_4 and evaporated to give a crude clear oil which was then chromatographed on silica gel using EtOAc-hexanes mixture of (1:5) as the eluent to afford the aldehyde **25** as viscous colorless oil (1.4g, 98%). 1H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, *J* = 1.3 Hz, 1H), 4.11 – 4.02 (m, 1H), 3.67 (s, 3H), 2.47 – 2.38 (m, 2H), 2.09 – 1.96 (m, 1H), 1.91 (td, *J* = 14.1, 7.6 Hz, 1H), 0.92 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 203.46, 173.42, 76.48, 51.81, 28.91, 27.58, 25.85, 18.30, -4.53, -4.93.

***(4S)*-Methyl-4-(*t*-butyldimethylsilyloxy)-hex-5-ynoate (9)**. Part 1: To a solution of CBr_4 (385 mg, 1.16 mmol) at 0°C in anhydrous CH_2Cl_2 (25 mL total volume) was cannulated PPh_3 (607 mg, 2.32 mmol) to give a clear yellow solution. To the reaction mixture at 0°C was added aldehyde 15 (150 mg, 0.58 mmol). The reaction was run for 1 h to assure completion. Without workup the solvent was evaporated in vacuo and the crude mixture was purified on silica gel using EtOAc-hexanes mixture of (1:9) as the eluent to afford the dibromo ester [methyl (4*S*)-4-(*t*-butyldimethylsilyloxy)-6,6-dibromohex-5-enoate] as a viscous and colorless oil (193 mg, 80%). 1H NMR (400 MHz, $CDCl_3$) δ 6.37 (d, *J* = 8.0 Hz, 1H), 4.36 (dt, *J* = 8.0, 6.4 Hz, 1H), 3.68 (s, 3H), 2.44 – 2.35 (m, 2H), 1.90 – 1.80 (m, 2H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.70, 141.43, 89.11, 72.62, 51.79, 31.70, 29.57, 25.89, 18.18, -4.39, -4.91. Part 2: To a solution of dibromo ester from Part 1 (548 mg, 1.32 mmol) at -78°C in anhydrous THF (25 mL) was added 2.0 M solution of LDA (1.98 mL, 4.0 mmol) drop wise and stirred for 0.5 h. The reaction was quenched with water (30 mL) and extracted with Et_2O (3 x 30 mL), dried using $MgSO_4$, filtered and concentrated. The crude was then purified using silica gel with a EtOAc-hexanes eluent of (3:47) to afford the alkyne product **9** (233 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (td, *J* = 6.1, 2.1 Hz, 1H), 3.67 (s, 3H), 2.58 – 2.45 (m, 2H), 2.39 (d, *J* = 2.1 Hz, 1H), 2.05 – 1.94 (m, 2H), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (400 MHz,

$CDCl_3$) δ 173.83, 84.78, 72.74, 61.71, 51.73, 33.50, 29.55, 25.87, 18.31, -4.52, -5.02; HRMS (ESI) *m/z* calcd for $C_{13}H_{25}O_3Si$: $[M+H]^+$: 257.1568 found: 257.1566.

Methyl *(4S, 11R, 7E, 9E)*-4,11-bis(t-butyldimethylsilyloxy)-14-(trimethylsilyl)-tetradeca-7,9-dien-5,13-diynoate (26). To the arm of a three-necked flask was charged $Pd(PPh_3)_4$ (45 mg, .039 mmol) and CuI (10 mg, .078 mmol) under Argon. A solution of alkyne **9** (100 mg, 0.39 mmol), and the dienyl iodide **10** mixture (191mg, 0.43 mmol) and Et_3N (0.64 mL, 3.9 mmol) in C_6H_6 (3 mL) was cannulated into the reaction vessel. The reaction flask was then freeze-thawed with liquid nitrogen three times to remove oxygen. After removing any oxygen from the reaction flask the $Pd(PPh_3)_4$ and CuI was added and the reaction mixture was stirred overnight at room temperature. The reaction was worked up with aqueous saturated NH_4Cl (5 mL) and extracted with Et_2O (3 x 5 mL). The solvent was evaporated and the mixture was purified on silica gel using EtOAc-hexanes (1:24) as the eluent to afford compound **26** as a clear oil (202 mg, 92%). The ***E, Z*** stereoisomer could be isolated during the separation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (dd, *J* = 15.6, 10.9 Hz, 1H), 6.23 (dd, *J* = 15.2, 10.9 Hz, 1H), 5.83 (dd, *J* = 15.3, 5.9 Hz, 1H), 5.58 (d, *J* = 15.5 Hz, 1H), 4.58 (td, *J* = 6.2, 1.8 Hz, 1H), 4.32 (q, *J* = 6.5 Hz, 1H), 3.67 (s, 3H), 2.49 (td, *J* = 7.6, 1.4 Hz, 2H), 2.48 – 2.29 (m, 2H), 2.07 – 1.94 (m, 2H), 0.90 (s, 18H), 0.14 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.94, 141.17, 138.13, 129.15, 110.92, 103.84, 92.70, 86.72, 83.92, 71.78, 62.50, 51.70, 33.65, 30.04, 29.75, 25.97, 25.95, 18.39, 18.36, 0.20, -4.37, -4.40, -4.60, -4.92.

Methyl *(4S, 11R, 7E, 9E)*-4,11-bis(t-butyldimethylsilyloxy)tetradeca-7,9-dien-5,13-diynoate (4). To a solution of compound **26** (80 mg, 0.14 mmol) in MeOH (3 mL) was added Na_2CO_3 (20 mg) and stirred overnight at room temperature. The solvent was removed in vacuo and the crude was dissolved in water (5 mL) and extracted with Et_2O (3 x 5 mL). The oil was purified on silica gel using EtOAc-hexanes (1:49) as the eluent to afford alkyne **4** as a colorless oil (63 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (dd, *J* = 15.4, 11.0 Hz, 1H), 6.26 (dd, *J* = 15.1, 11.1 Hz, 1H), 5.86 (dd, *J* = 15.3, 5.7 Hz, 1H), 5.60 (dd, *J* = 15.6, 1.6 Hz, 1H), 4.58 (td, *J* = 6.0, 1.6 Hz, 1H), 4.42 – 4.30 (m, 1H), 3.67 (s, 3H), 2.49 (td, *J* = 7.2, 1.8 Hz, 2H), 2.48 – 2.38 (m, 1H), 2.33 (ddd, *J* = 16.4, 7.1, 2.7 Hz, 1H), 2.06 – 1.94 (m, 2H), 1.99 (t, *J* = 2.7 Hz, 1H), 0.90 (s, 18H), 0.13 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 173.93, 141.08, 137.75, 129.35, 111.12, 92.78, 83.87, 81.04, 71.49, 70.37, 62.48, 51.72, 33.66,

29.75, 28.59, 25.95, 25.94, 18.39, 18.36, -4.35, -4.44, -4.68, -4.92; HRMS (ESI) *m/z* calcd for $C_{27}H_{46}NaO_4Si_2$: $[M+Na]^+$: 513.2827 found: 513.2838.

Methyl *(4S, 11R, 17S, 7E, 9E, 15E, 19Z)-tris*-(t-butyldimethylsilyloxy)-docosa-7,9,15,19-tetraen-5,13-diynoate (27). To the arm of a three-necked flask was charged $Pd(PPh_3)_4$ (5 mg, .0039 mmol) and CuI (1 mg, .078 mmol) under Argon. A solution of alkyne **4** (19 mg, 0.039 mmol), vinyl iodide **5** (21 mg, 0.058 mmol) and Et_3N (0.05 mL, .39 mmol) in C_6H_6 (1 mL) was cannulated into the reaction vessel. The reaction flask was then freeze-thawed with liquid nitrogen three times to remove oxygen. After removing any oxygen from the reaction flask the $Pd(PPh_3)_4$ and CuI was added and the reaction mixture was stirred overnight at room temperature. The reaction was worked up with aqueous saturated NH_4Cl (3 mL) and extracted with Et_2O (3 x 3 mL). The solvent was evaporated and the mixture was purified on silica gel using EtOAc-hexanes (3:97) as the eluent to afford compound **27** as a clear oil (202 mg, 92%). ^1H NMR (500 MHz, $CDCl_3$) δ 6.54 (dd, *J* = 15.5, 10.9 Hz, 1H), 6.25 (dd, *J* = 15.3, 10.9 Hz, 1H), 6.04 (dd, *J* = 15.7, 5.4 Hz, 1H), 5.86 (dd, *J* = 15.3, 5.7 Hz, 1H), 5.73 – 5.55 (m, 2H), 5.51 – 5.40 (m, 1H), 5.40 – 5.26 (m, 1H), 4.58 (td, *J* = 6.0, 1.6 Hz, 1H), 4.33 (q, *J* = 5.5 Hz, 1H), 4.24 – 4.11 (m, 1H), 3.67 (s, 3H), 2.61 – 2.35 (m, 4H), 2.23 (dp, *J* = 20.8, 7.0 Hz, 2H), 2.11 – 1.95 (m, 4H), 0.95 (t, *J* = 7.6 Hz, 3H), 0.90 (s, 18H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 173.92, 145.23, 141.21, 138.25, 133.99, 129.05, 124.28, 110.89, 109.15, 92.68, 87.10, 83.92, 80.71, 72.75, 71.83, 62.49, 51.71, 36.07, 33.67, 29.77, 29.75, 29.62, 26.00, 25.95, 25.94, 20.89, 18.41, 18.39, 14.34, -4.35, -4.41, -4.46, -4.65, -4.65, -4.92.

***(4S, 11R, 17S)*-Trihydroxydocosa-*(7E, 9E, 15E, 19Z)*-tetraene-5,13-diynoic acid (3)**. To a solution of compound **27** (10 mg, 0.014 mmol) in THF (2 mL) was added 1.0 M solution of TBAF (0.084 mL, 0.084 mmol) at 0°C and stirred for 2 h. The reaction was quenched with water (3 mL) and extracted with Et_2O (5 x 3 mL), rinsed with brine, dried over $MgSO_4$ and filtered. The solvent was the concentrated and freshly prepared CH_2N_2 was added to convert any acid to the ester. The solvent was completely removed in vacuo and the compound was purified on silica gel using MeOH-CH_2Cl_2 (3%) as the eluent to afford an ester/lactone mixture (3:1 ratio see HPLC and NMR data attached). The product was then suspended in a H_2O-MeOH mixture (1:1, 1 mL) and NaOH (1 mg, 2.5 x 10^{-2} mmol) was added. After 3 h the reaction mixture was dried and purified via C-18 reversed Phase HPLC using H_2O-MeOH mixture (41%) to afford

compound **3** as colorless oil (1.5 mg, 27%). ^{1}H NMR (400 MHz, CD_3OD) δ 6.59 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.36 (dd, *J* = 15.4, 10.9 Hz, 1H), 6.03 (dd, *J* = 15.8, 6.1 Hz, 1H), 5.89 (dd, *J* = 15.1, 6.1 Hz, 1H), 5.68 (t, *J* = 14.9 Hz, 2H), 5.55 – 5.45 (m, 1H), 5.42 – 5.33 (m, 1H), 4.52 (dd, *J* = 6.7, 5.0 Hz, 1H), 4.30 – 4.21 (m, 1H), 4.08 (q, *J* = 5.9 Hz, 1H), 2.57 – 2.48 (m, 1H), 2.39 (td, *J* = 15.6, 7.5 Hz, 3H), 2.28 (q, *J* = 7.5 Hz, 2H), 2.06 (dq, *J* = 12.3, 6.8, 6.0 Hz, 2H), 1.97 (q, *J* = 7.2 Hz, 2H), 0.98 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (400 MHz, CD_3OD) δ 180.57, 144.28, 139.62, 136.98, 133.44, 123.68, 110.86, 109.50, 92.69, 85.94, 82.80, 79.96, 71.34, 70.10, 61.98, 61.94, 34.44, 34.20, 33.56, 27.53, 20.22, 13.08; HRMS (ESI) *m/z* calcd for $C_{22}H_{27}O_5^-$: [M^-]: 371.1864 found: 371.1881.

***(4S, 11R, 17S)*-Trihydroxydocosa-*(5Z, 7E, 9E, 13Z, 15E, 19Z)*-hexaenoic acid, or Resolvin D3 (1)**. A flame-dried flask was charged with a freshly prepared Zn/Cu/Ag amalgam (300 mg, excess) and suspended in H_2O-MeOH mixture (1:1, 1 mL). To the reaction slurry was added compound **3** (1.5 mg, 3.8 x 10^{-3} mmol) and stirred for 13 h while monitoring. The reaction was filtered dried and purified via HPLC at H_2O-MeOH mixture (41%) to afford a mixture of the ester and gamma-butyrolactone. This was hydrolyzed in H_2O-MeOH mixture using 3 eq of NaOH. Upon completion the mixture was dried and purified via HPLC to afford Resolvin D3 (**1**) (0.33 mg, 22%). ^{1}H NMR (600 MHz, CD_3OD) δ 6.60 (dd, *J* = 14.6, 11.5 Hz, 1H), 6.52 (dd, *J* = 15.4, 11.1 Hz, 1H), 6.34 (dd, *J* = 14.9, 10.8 Hz, 1H), 6.24 (dd, *J* = 14.6, 10.7 Hz, 1H), 6.13 – 6.02 (m, 2H), 5.75 (dd, *J* = 15.2, 6.7 Hz, 1H), 5.70 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.55 – 5.31 (m, 4H), 4.92 (s, 24H), 4.23 – 4.08 (m, 2H), 2.45 (q, *J* = 7.9 Hz, 2H), 2.38 – 2.22 (m, 4H), 2.07 (q, *J* = 7.3 Hz, 2H), 1.88 (dd, *J* = 14.1, 7.2 Hz, 1H), 1.82 – 1.71 (m, 1H), 0.98 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (600 MHz, CD_3OD) δ 182.46, 137.54, 137.49, 135.48, 134.75, 134.58, 131.75, 131.04, 130.31, 129.15, 128.17, 126.58, 125.52, 73.20, 73.07, 68.86, 36.68, 36.23, 35.43, 35.28, 21.68, 14.54. ; HRMS (ESI) *m/z* calcd for $C_{22}H_{31}O_5^-$: [M^-]: 375.2177 found: 375.2182.

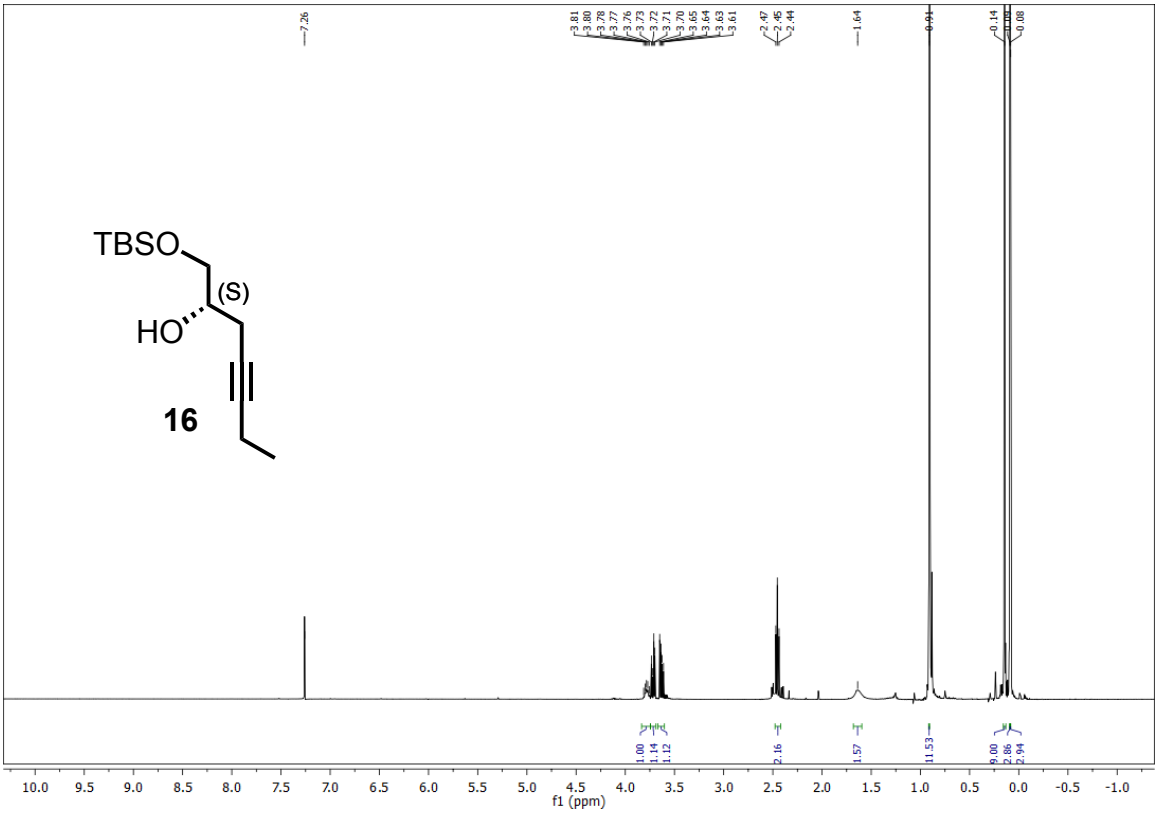
(*R*)-1-(*t*-Butyldiphenylsilyloxy)hept-4-yn-2-ol (30). This compound was prepared from protected *S*-Glycidol similarly to its enantiomer, compound **16**. ^{1}H NMR (400 MHz $CDCl_3$) δ 3.79 – 3.70 (m, 1H), 3.70 (dd, *J* = 9.8, 4.2 Hz, 1H), 3.60 (dd, *J* = 9.8, 5.8 Hz, 1H), 2.46 (s, 1H), 2.42 – 2.32 (m, 2H), 2.16 (dt, *J* = 7.5, 2.4 Hz, 2H), 1.11 (t, *J* = 7.5 Hz, 3H), 0.90 (s, 8H), 0.08 (s, 6H). ^{13}C NMR (400 MHz $CDCl_3$) δ 84.11, 75.17, 70.59, 65.77, 25.98, 23.51, 18.42, 14.29, 12.51, -5.28, -5.31.

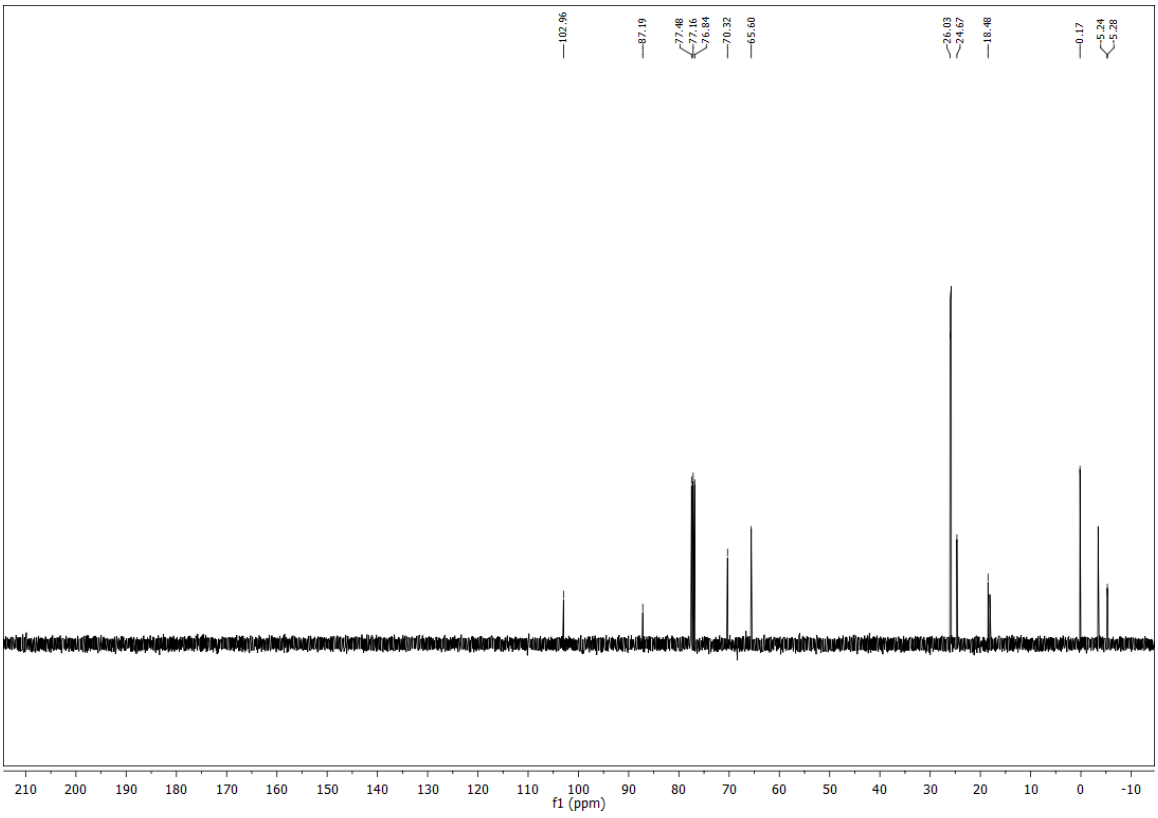
***(3R, 1E, 5Z)*-3-(*t*-Butyldimethylsilyloxy)-1-iodoocta-1,5-diene (31).** This compound was prepared similarly to its enantiomer, compound **5**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (dd, *J* = 14.3, 5.7 Hz, 1H), 6.21 (dd, *J* = 14.3, 1.3 Hz, 1H), 5.54 – 5.41 (m, 1H), 5.38 – 5.25 (m, 1H), 4.14 – 4.04 (m, 1H), 2.29 – 2.19 (m, 2H), 2.09 – 1.96 (m, 2H), 0.89 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.87, 134.40, 123.73, 77.48, 77.16, 76.84, 75.88, 75.18, 35.67, 25.95, 20.89, 18.37, 14.39, -4.49, -4.69.

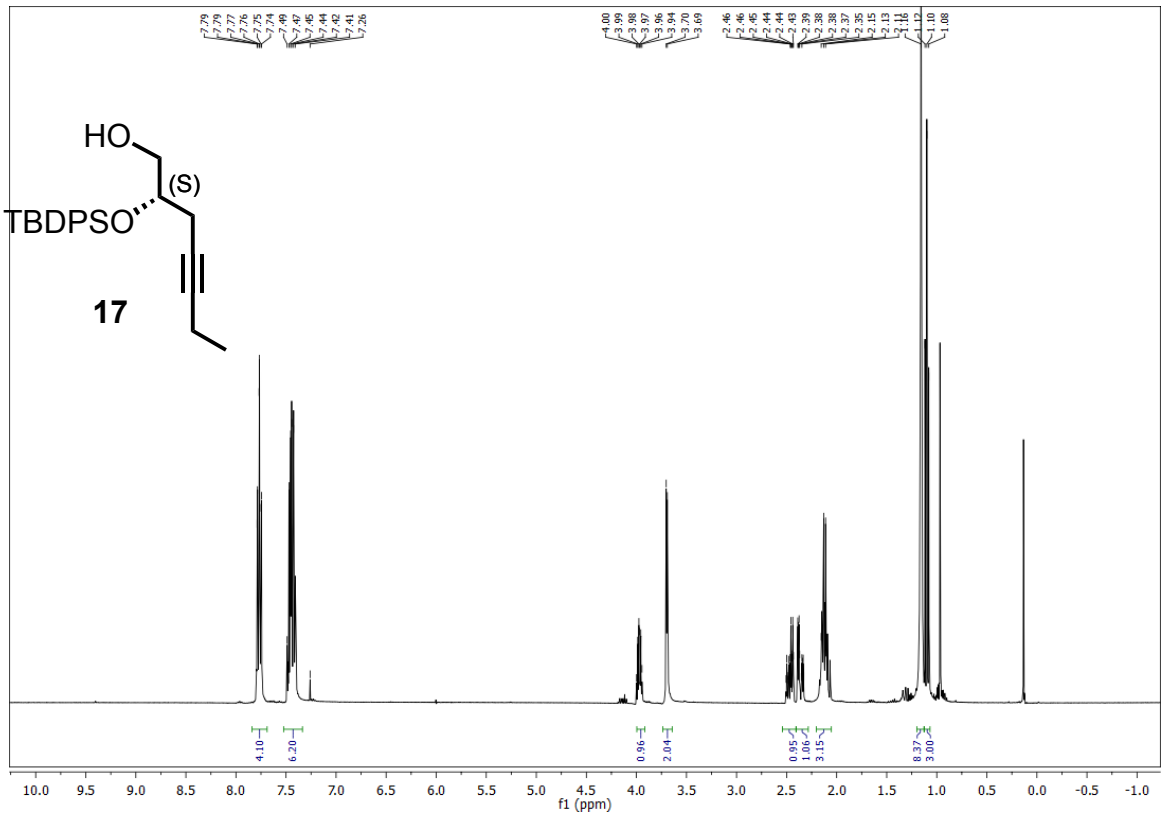
Methyl *(4S, 11R, 17R, 7E, 9E, 15E, 19Z)-tris*-(t-butyldimethylsilyloxy)-docosa-7,9,15,19-tetraen-5,13-diynoate (32). This compound was prepared from alkyne **4** and vinyl iodide **31**, similarly to its 17*S*-epimer, compound **27**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.25 (dd, *J* = 15.3, 10.9 Hz, 1H), 6.04 (dd, *J* = 15.7, 5.4 Hz, 1H), 5.86 (dd, *J* = 15.0, 5.7 Hz, 1H), 5.70 – 5.54 (m, 2H), 5.52 – 5.40 (m, 1H), 5.37 – 5.26 (m, 1H), 4.58 (td, *J* = 6.1, 1.9 Hz, 1H), 4.33 (q, *J* = 6.1 Hz, 1H), 4.15 (q, *J* = 6.3 Hz, 1H), 3.67 (s, 3H), 2.55 – 2.37 (m, 4H), 2.30 – 2.18 (m, 2H), 2.09 – 1.94 (m, 4H), 0.95 (t, 3H), 0.90 (s, 18H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.94, 145.23, 141.22, 138.26, 133.99, 129.06, 124.29, 110.90, 109.16, 92.69, 87.11, 83.93, 80.71, 72.76, 71.84, 62.49, 51.71, 36.08, 33.67, 29.87, 29.75, 29.62, 26.01, 25.96, 25.94, 20.89, 18.41, 18.39, 14.28, -4.35, -4.41, -4.46, -4.65, -4.65, -4.92.

***(4S, 11R, 17R)*-Trihydroxydocosa-*(5Z, 7E, 9E, 13Z, 15E, 19Z)*-hexaenoic acid, or AT-Resolvin D3 (2)**. This compound was prepared from compound **32** similarly to its 17*S*-epimer, Resolvin D3 (**1**). The removal of the silyl protective groups led to a similar mixture of hydrolysis products, which were similarly converted to **2**. ^{1}H NMR (600 MHz, CD_3OD) δ 6.59 (dd, *J* = 14.7, 11.5 Hz, 1H), 6.52 (dd, *J* = 15.2, 11.2 Hz, 1H), 6.33 (dd, *J* = 15.1, 10.7 Hz, 1H), 6.24 (dd, *J* = 14.7, 10.9 Hz, 1H), 6.08 (td, *J* = 11.1, 4.3 Hz, 2H), 5.75 (dd, *J* = 15.1, 6.6 Hz, 1H), 5.70 (dd, *J* = 15.1, 6.6 Hz, 1H), 5.48 (td, *J* = 11.1, 5.8 Hz, 2H), 5.45 – 5.37 (m, 2H), 4.61 (q, *J* = 7.2 Hz, 1H), 4.19 – 4.16 (m, 1H), 4.14 (q, *J* = 6.7 Hz, 1H), 2.52 – 2.38 (m, 2H), 2.30 (dq, *J* = 29.2, 7.3 Hz, 4H), 2.08 (dt, *J* = 14.4, 7.1 Hz, 2H), 1.87 (dt, *J* = 15.0, 7.3 Hz, 1H), 1.77 (dt, *J* = 13.7, 6.7 Hz, 1H), 0.98 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (600 MHz, CD_3OD) δ 182.45, 137.54, 137.49, 135.48, 134.75, 134.58, 131.76, 131.04, 130.31, 129.15, 128.17, 126.58, 125.52, 73.20, 73.07, 68.86, 49.51, 49.34, 49.17, 49.00, 48.83, 48.66, 48.49, 36.68, 36.23, 35.43, 35.28, 21.68, 14.54; HRMS (ESI) *m/z* calcd for $C_{22}H_{31}O_5$: [M^-]: 375.2177 found: 375.2185.

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



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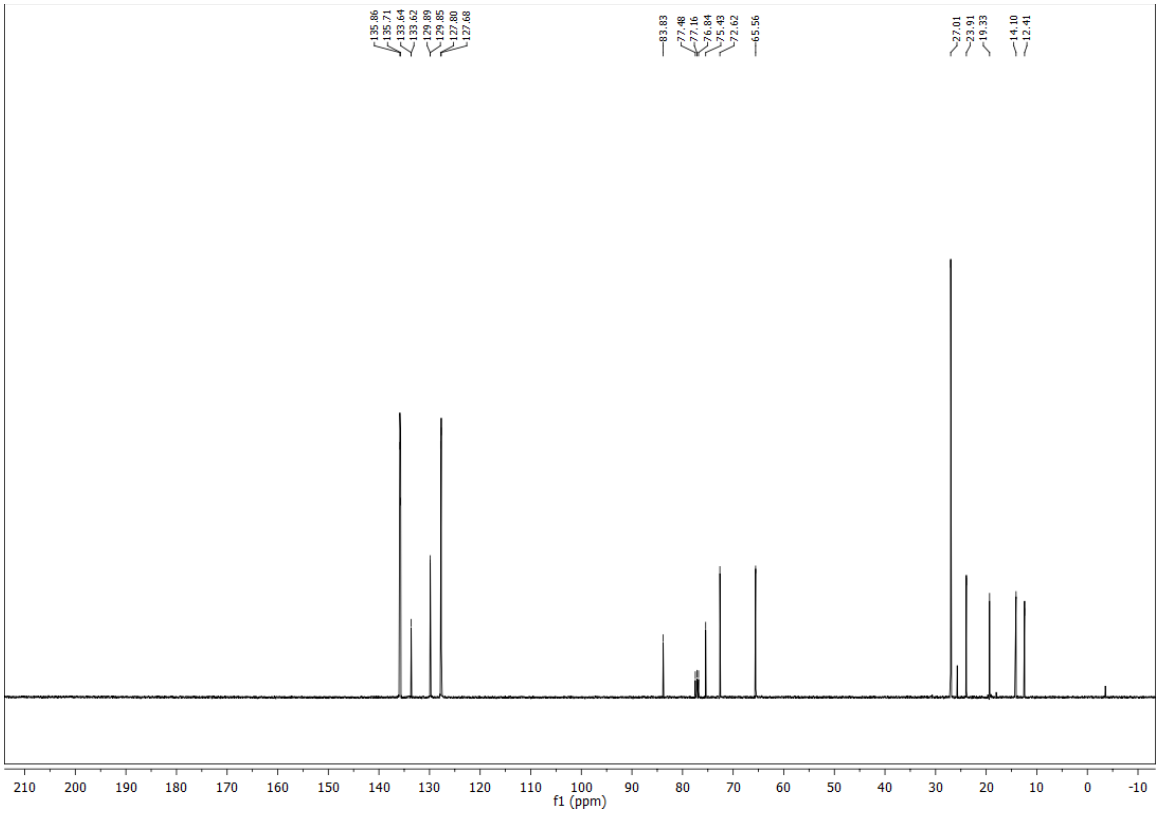
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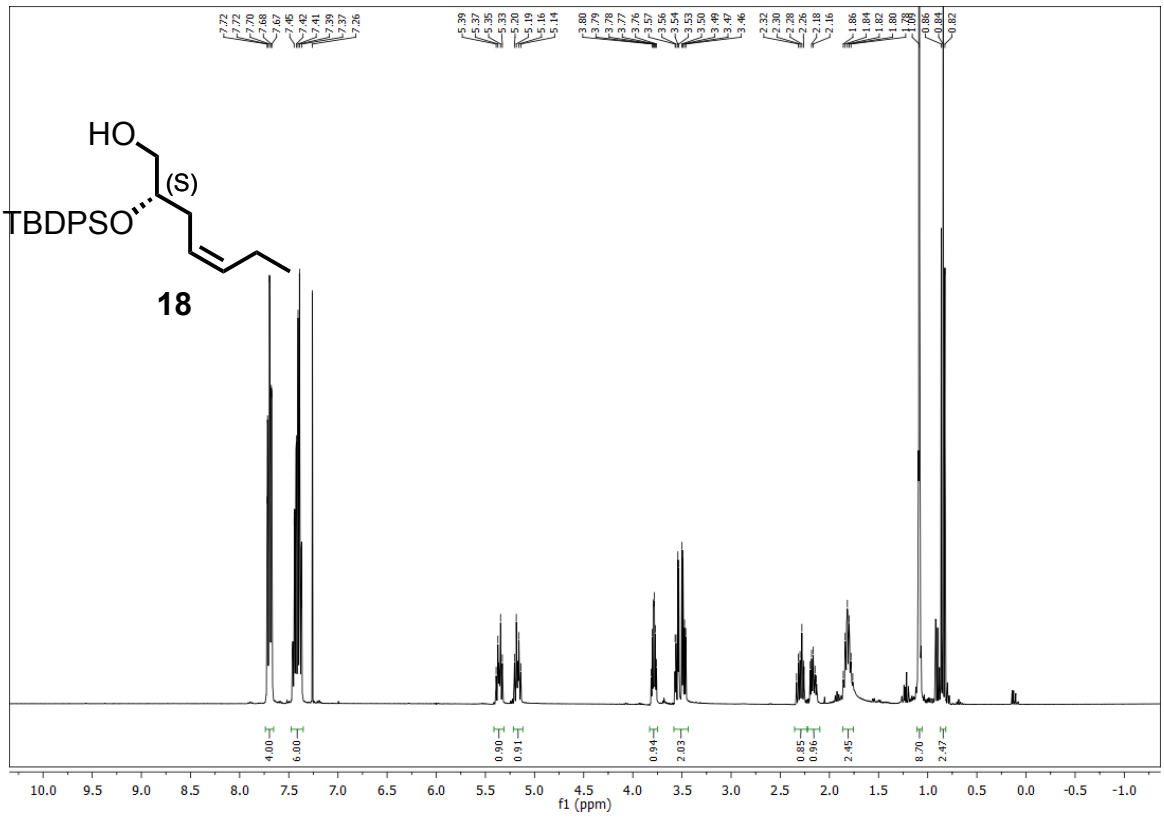
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(S)
TBDPSO
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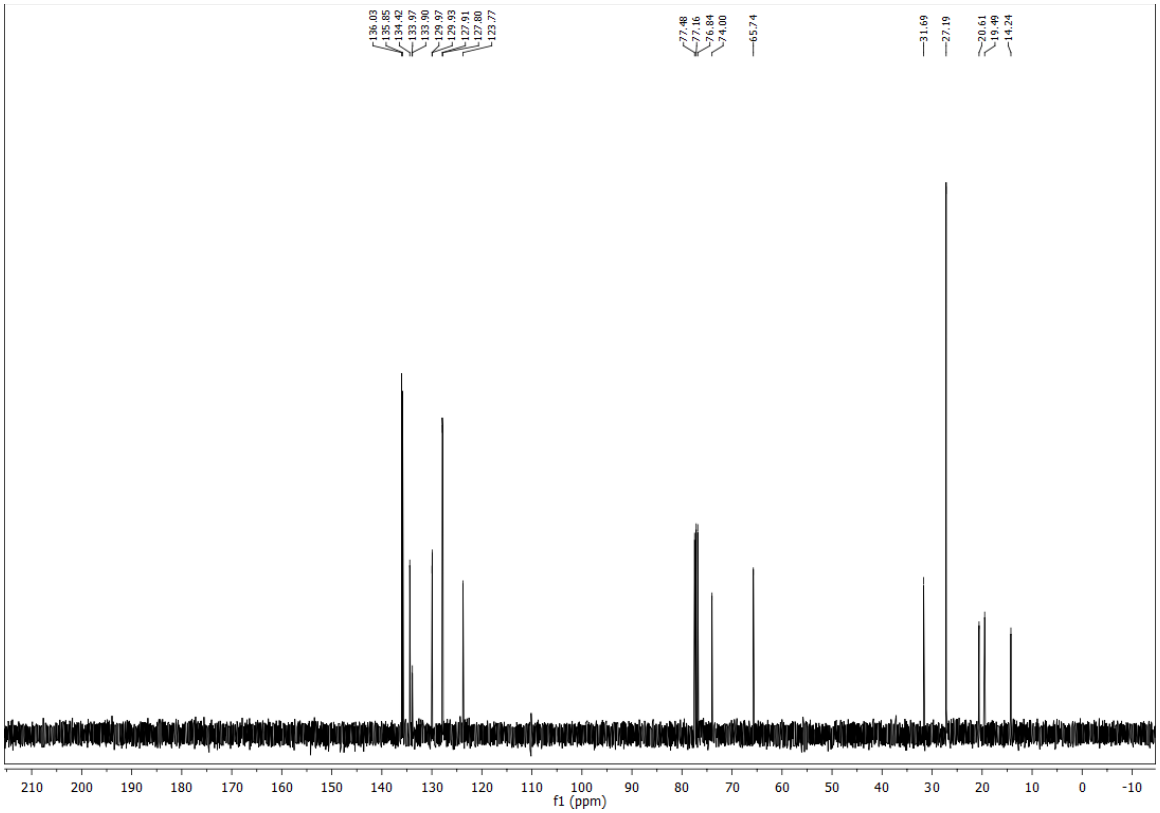
f1 (ppm)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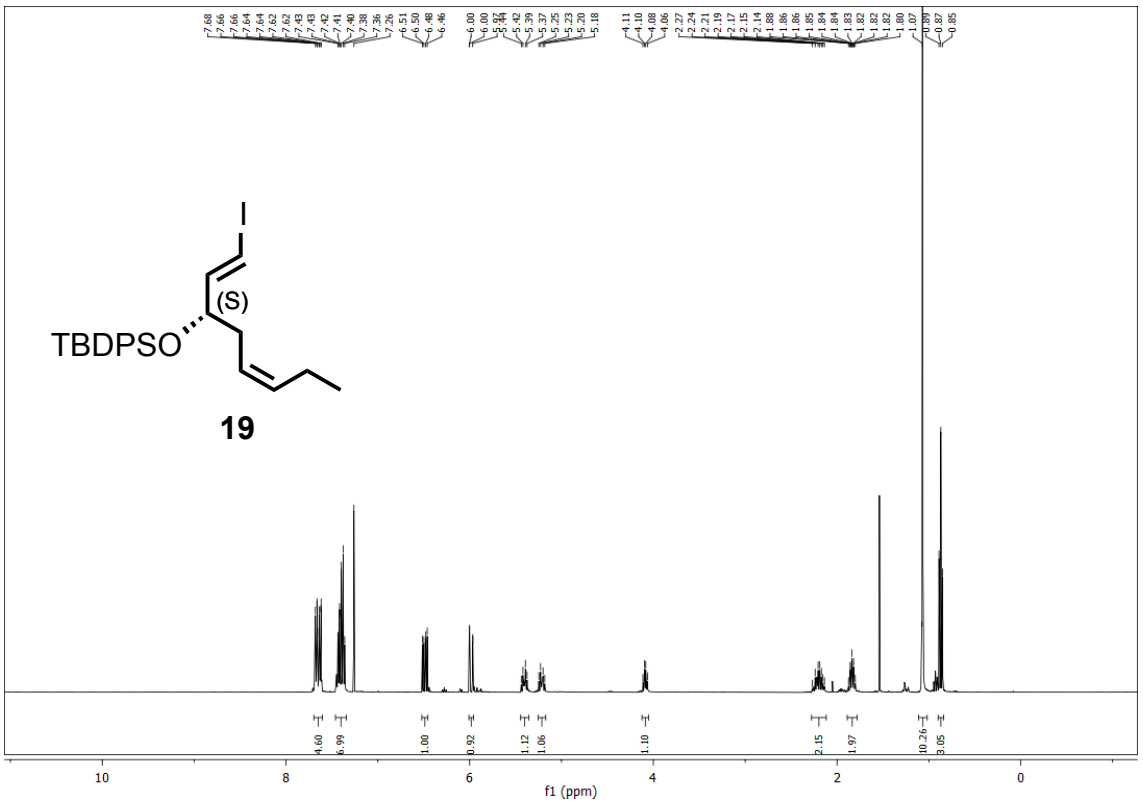
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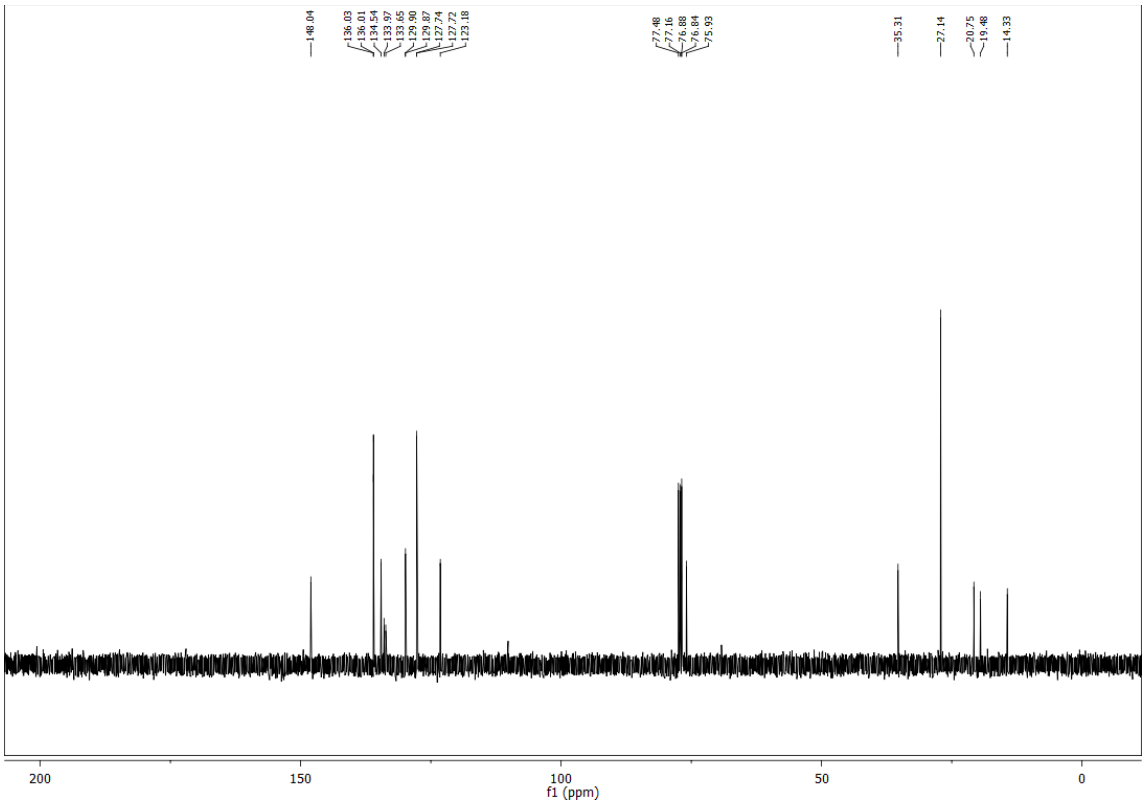
f1 (ppm)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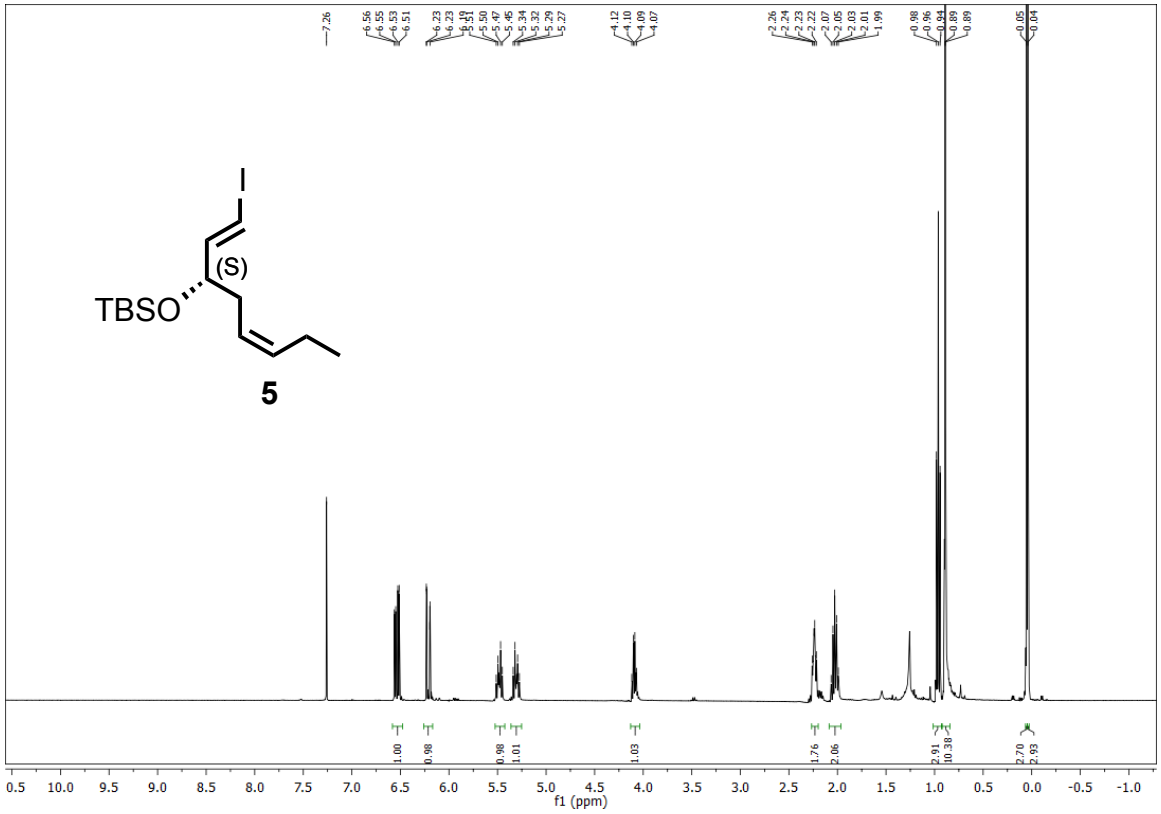
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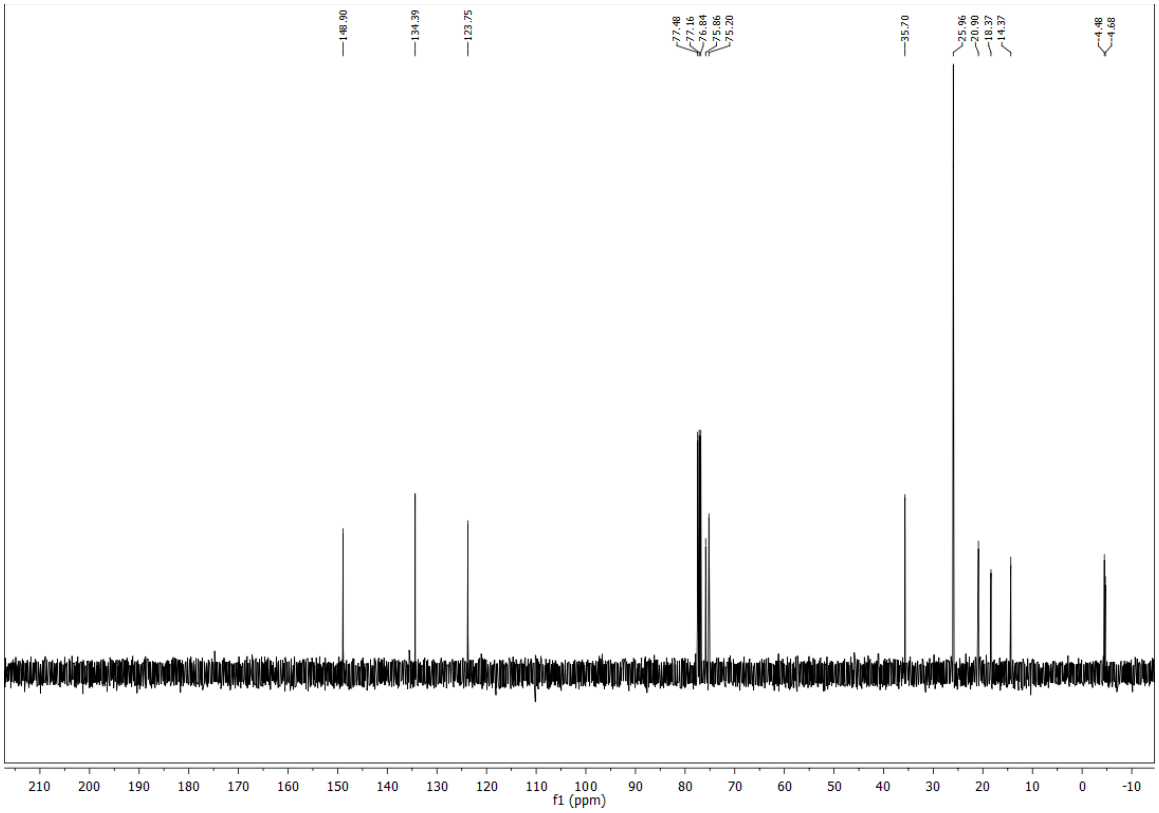
f1 (ppm)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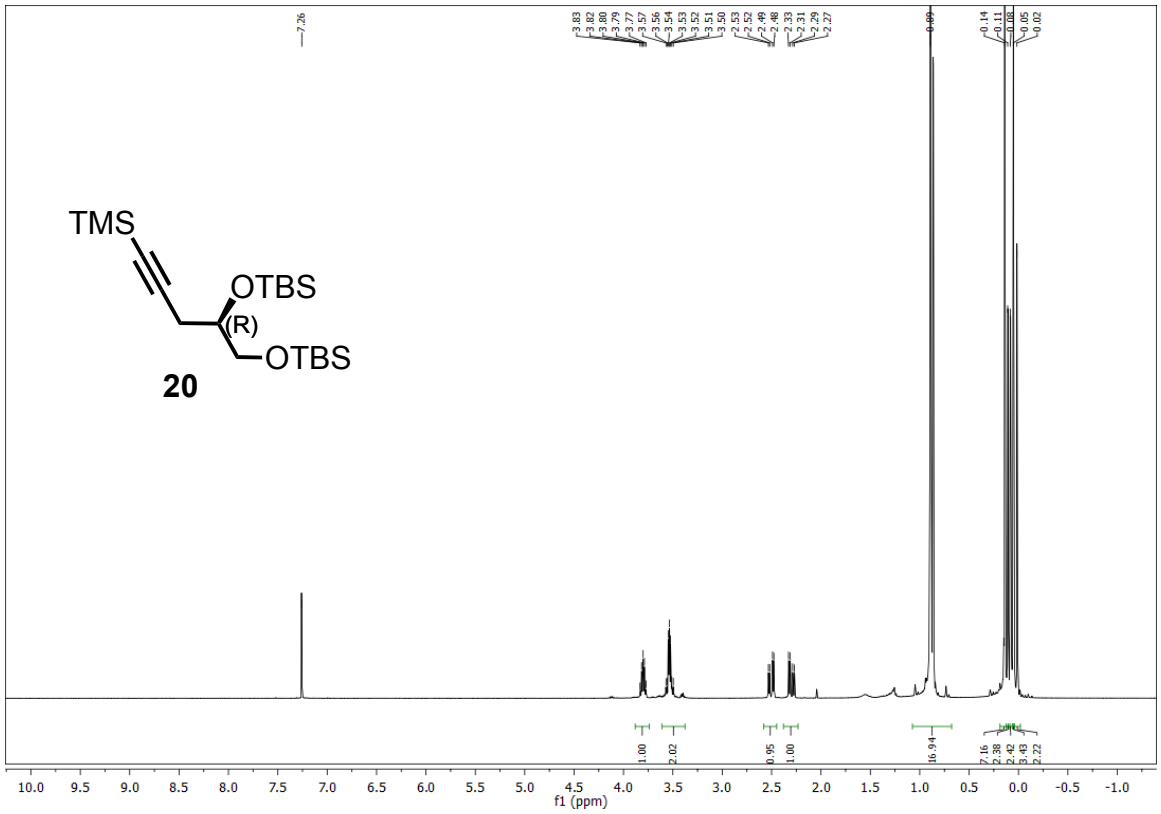
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(R)
OTBS
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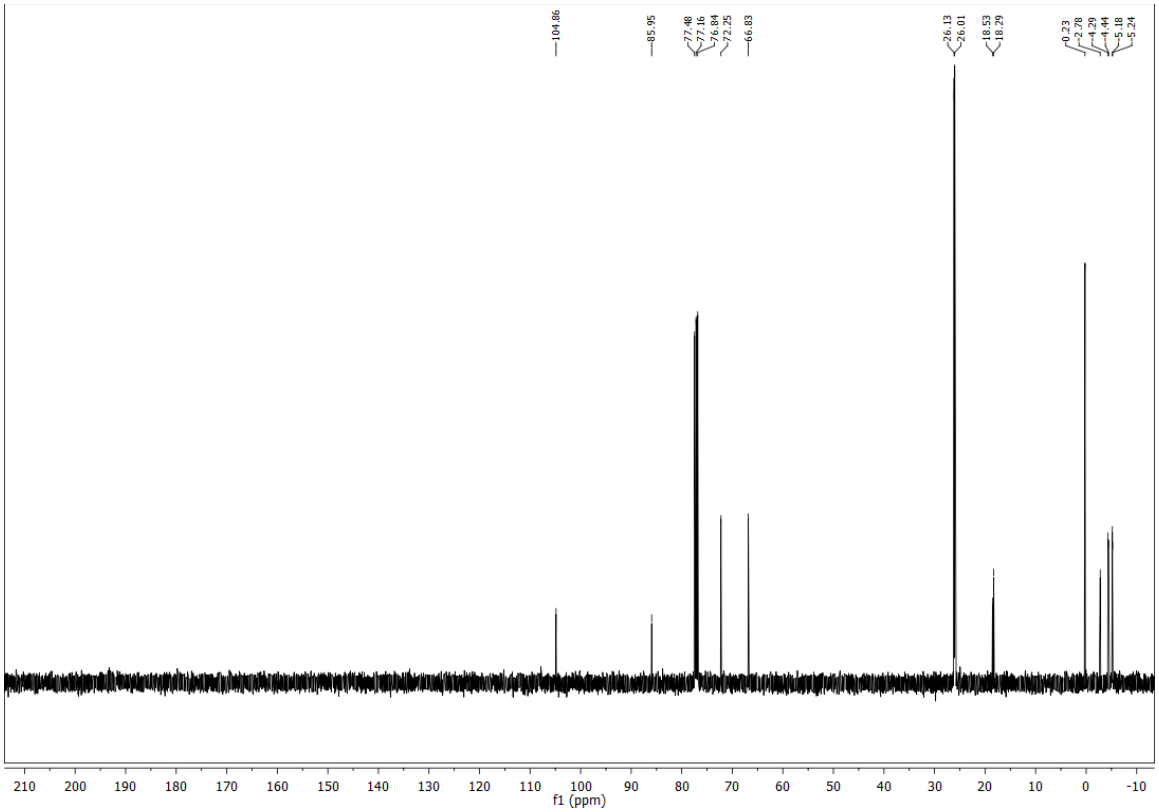
f1 (ppm)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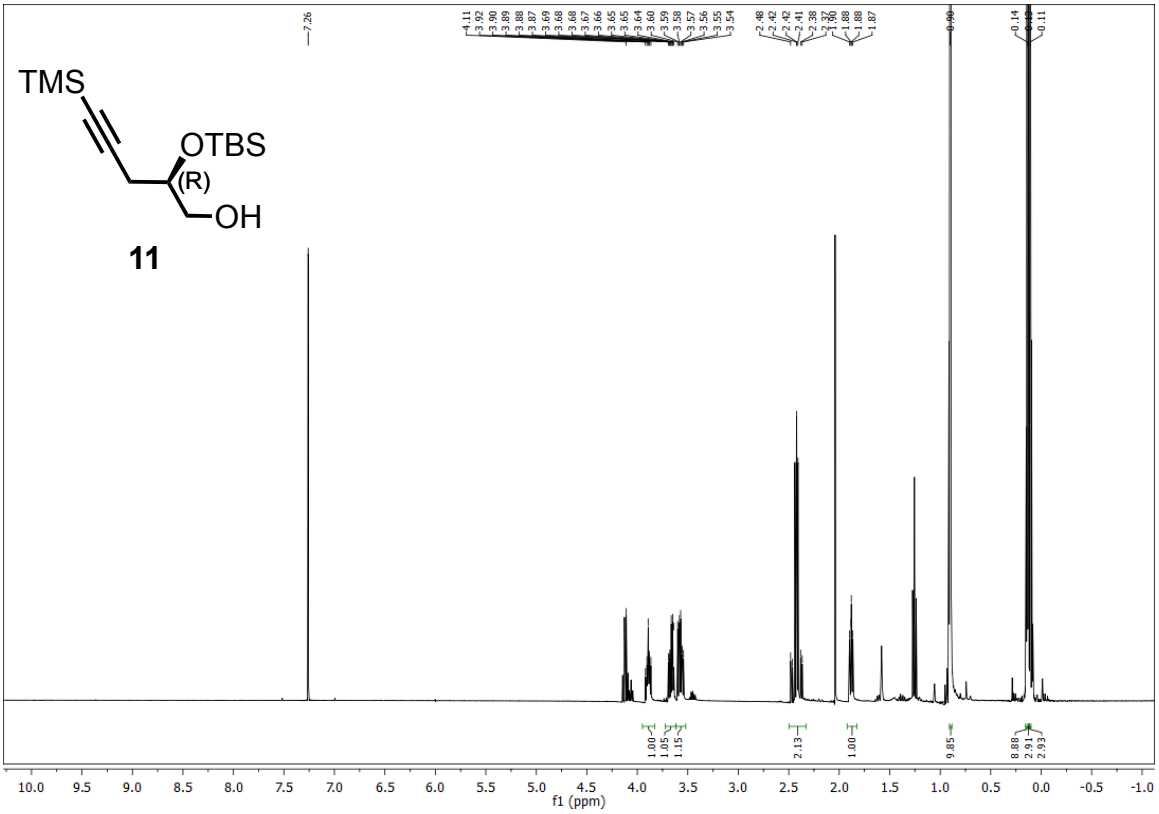
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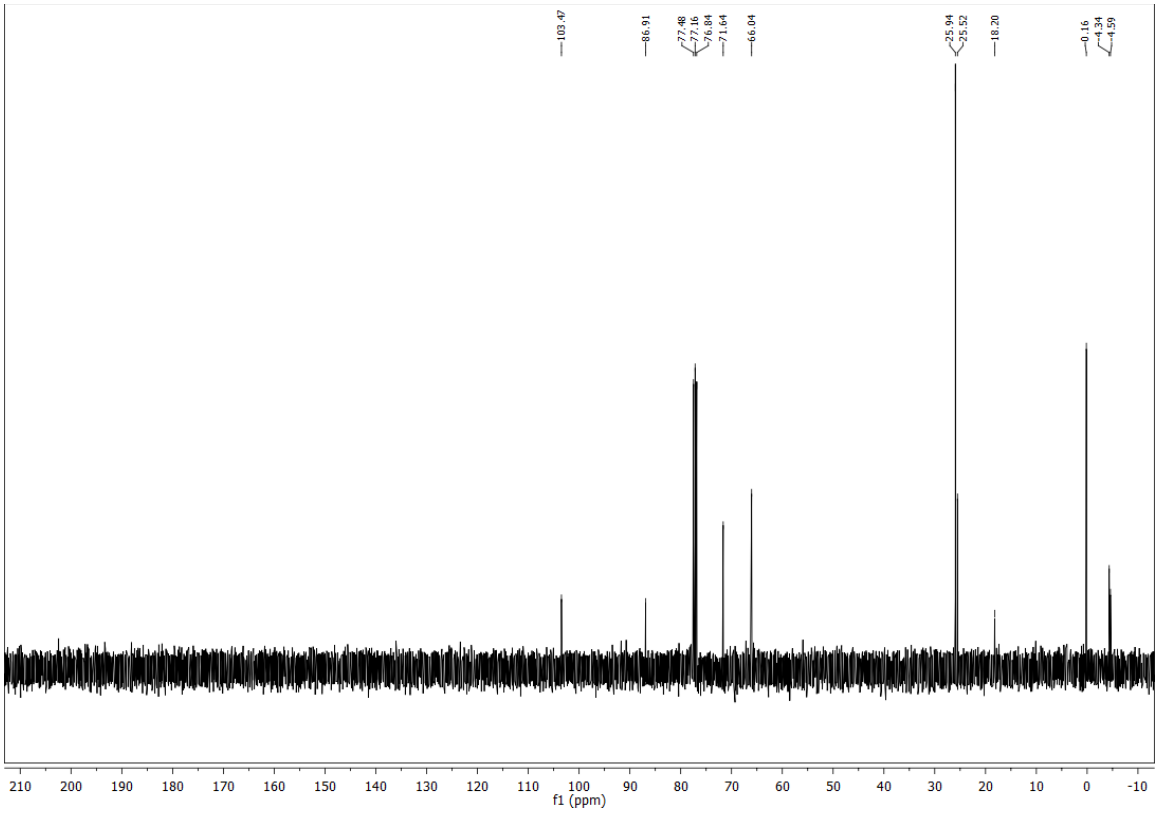
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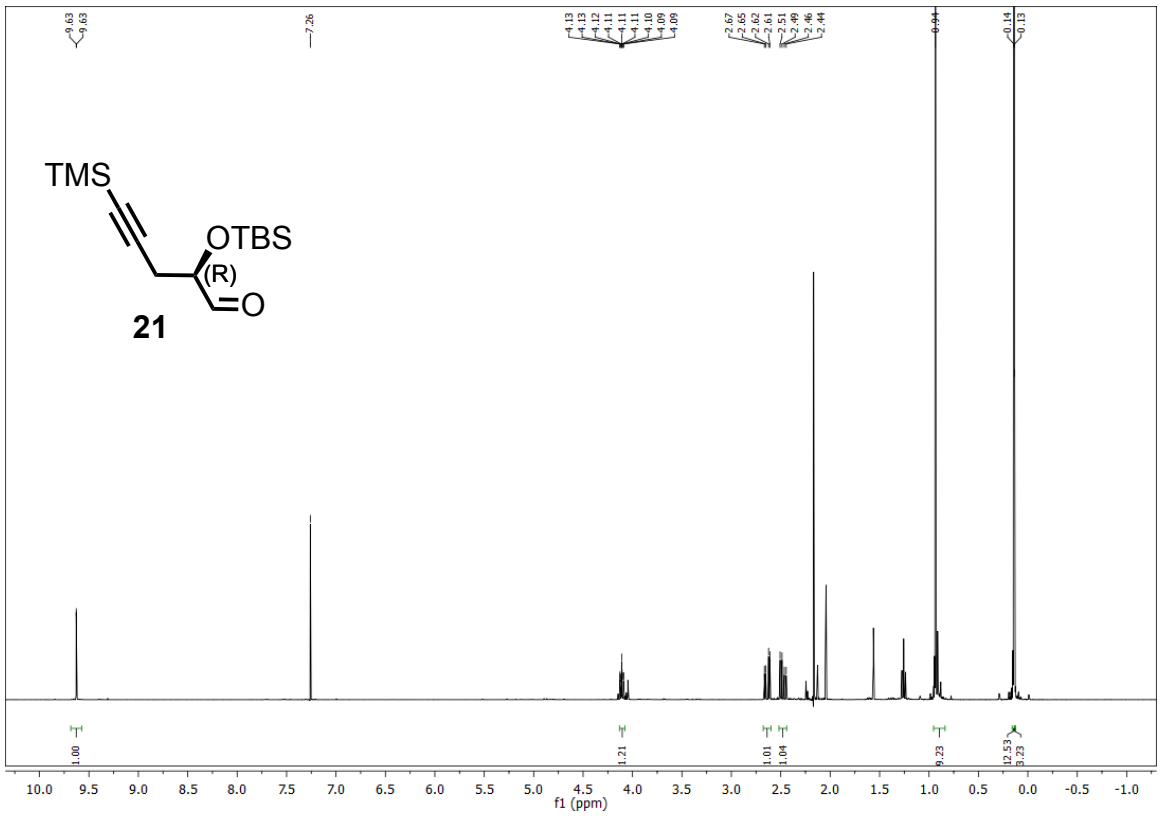
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(R)
O
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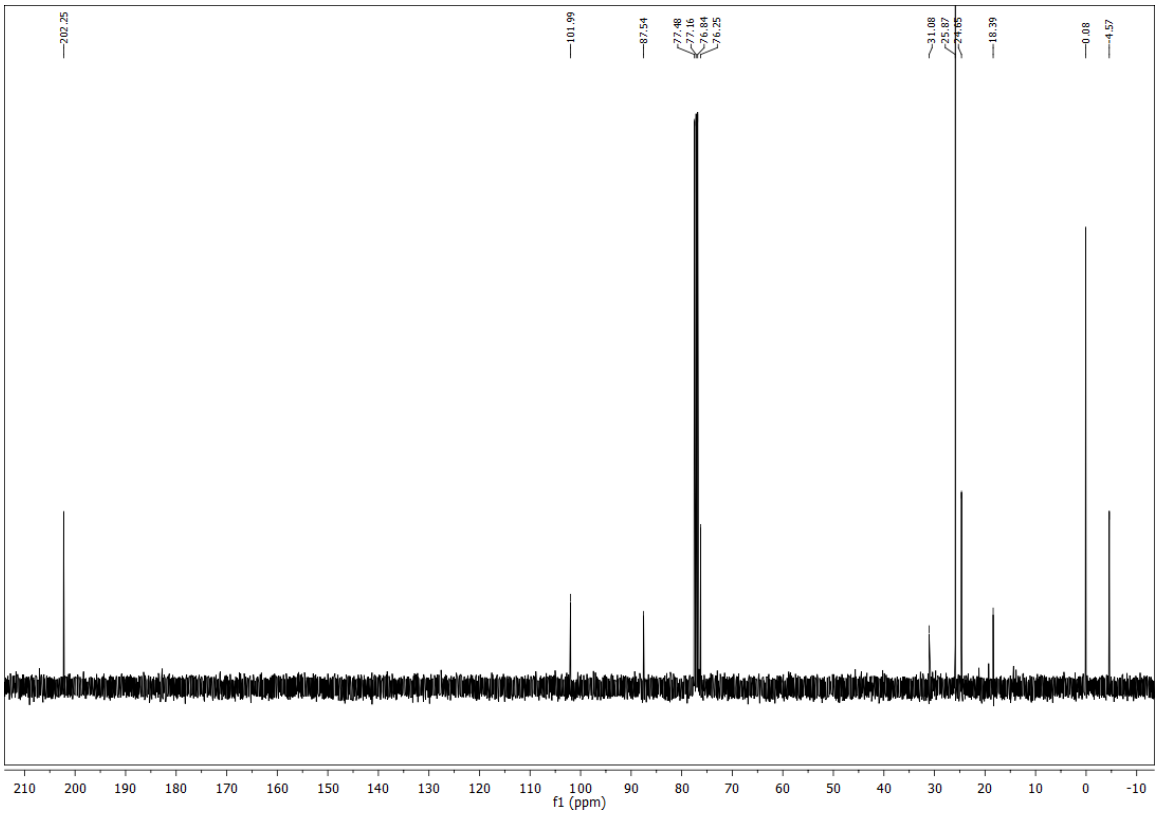
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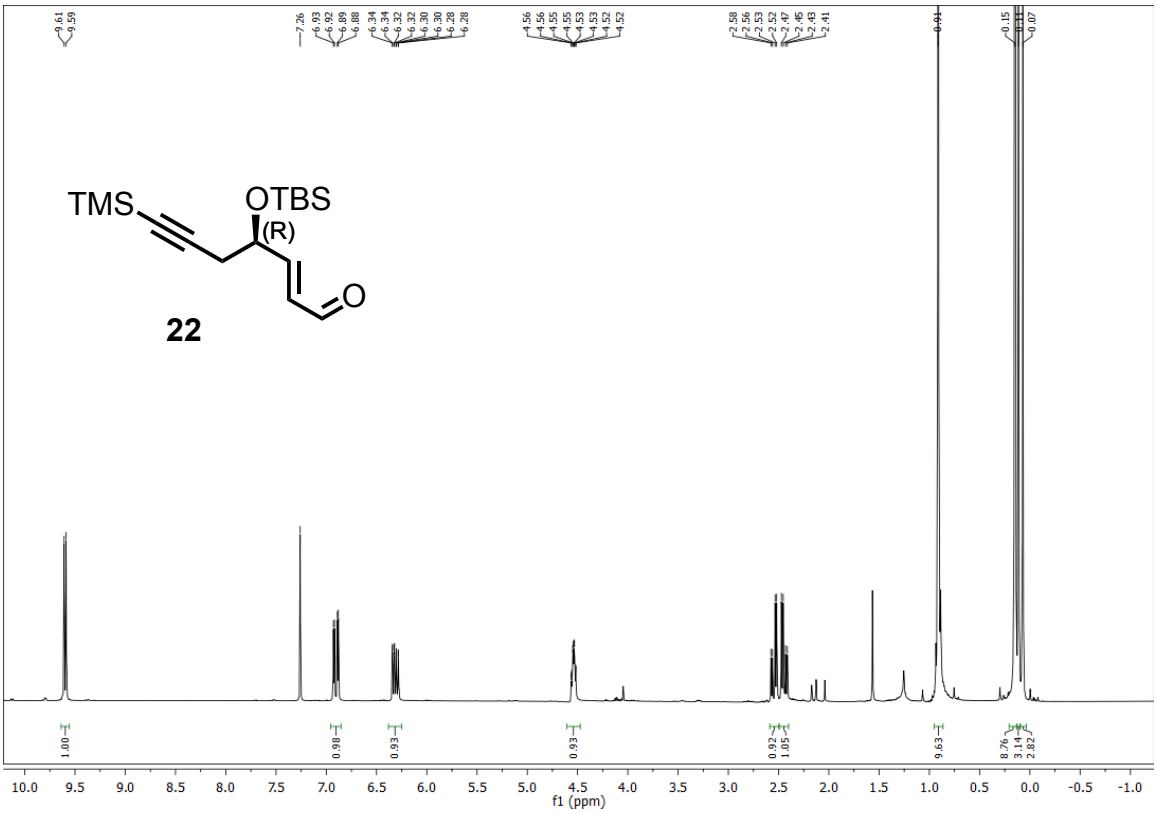
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(R)
O
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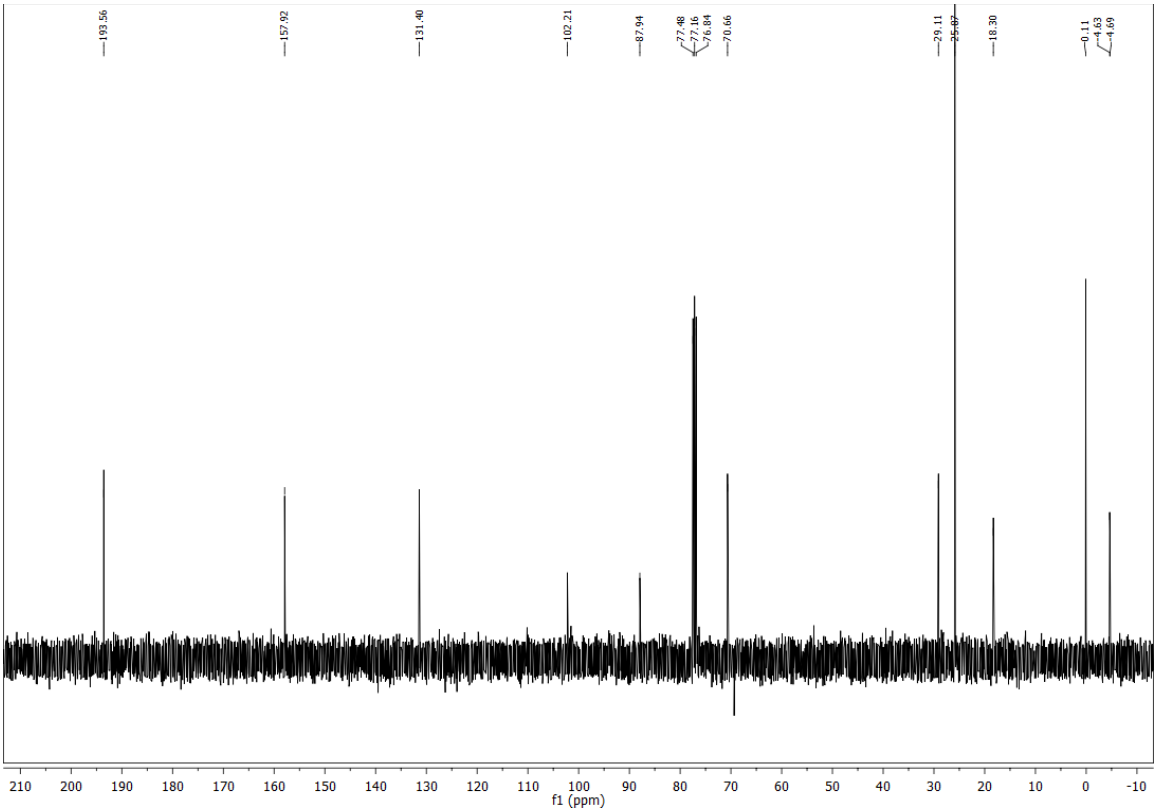
f1 (ppm)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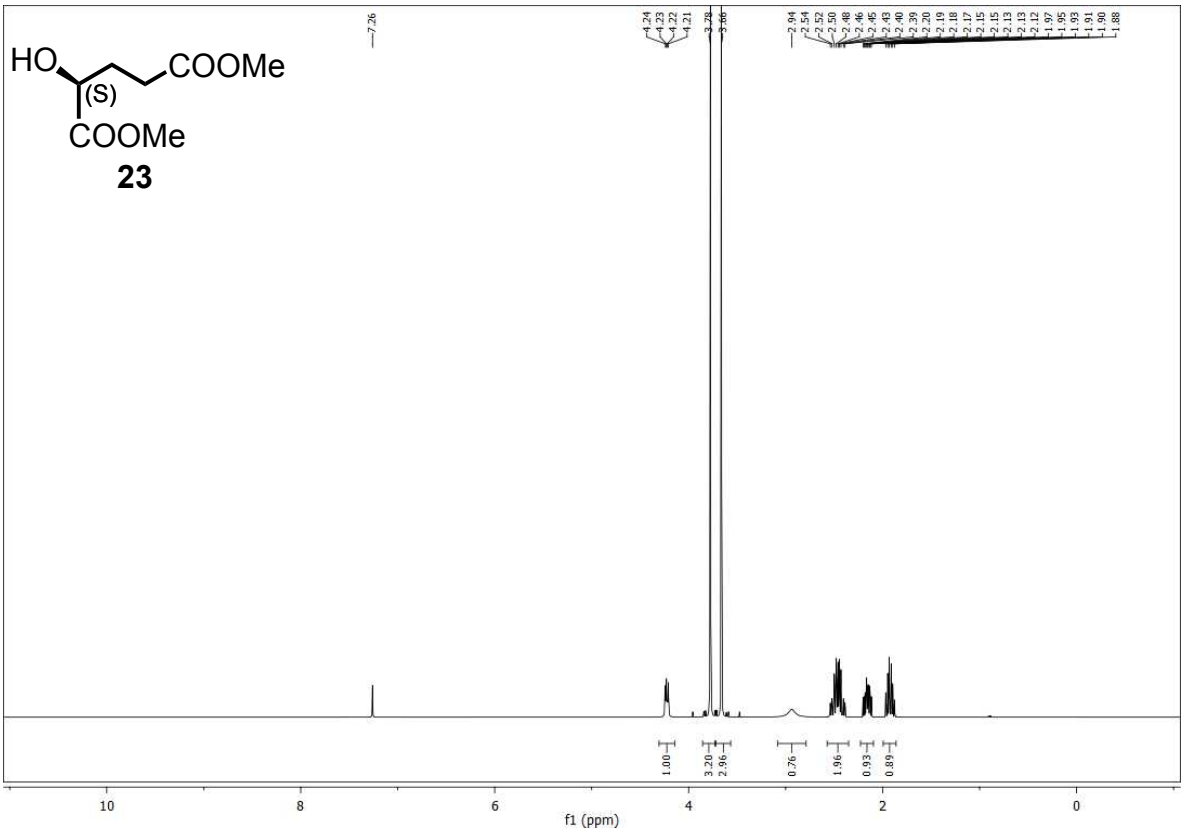
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COOMe
COOMe
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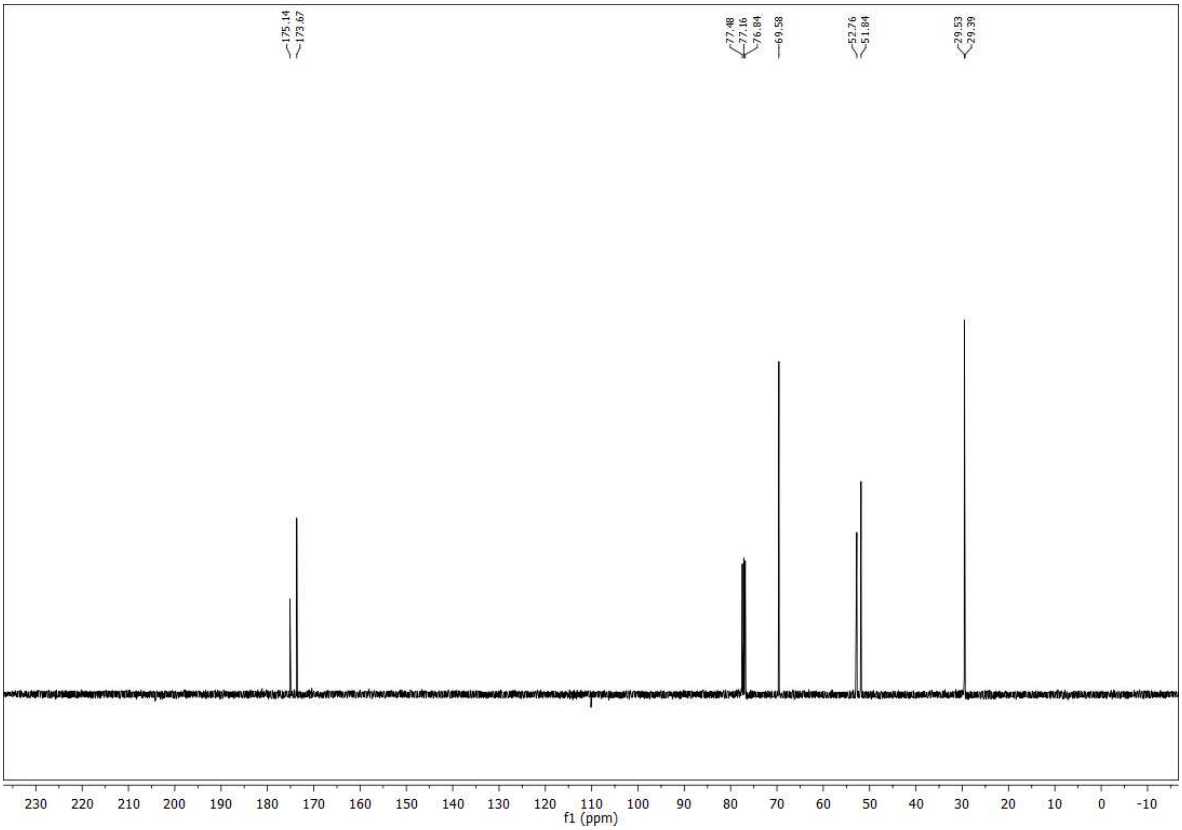
f1 (ppm)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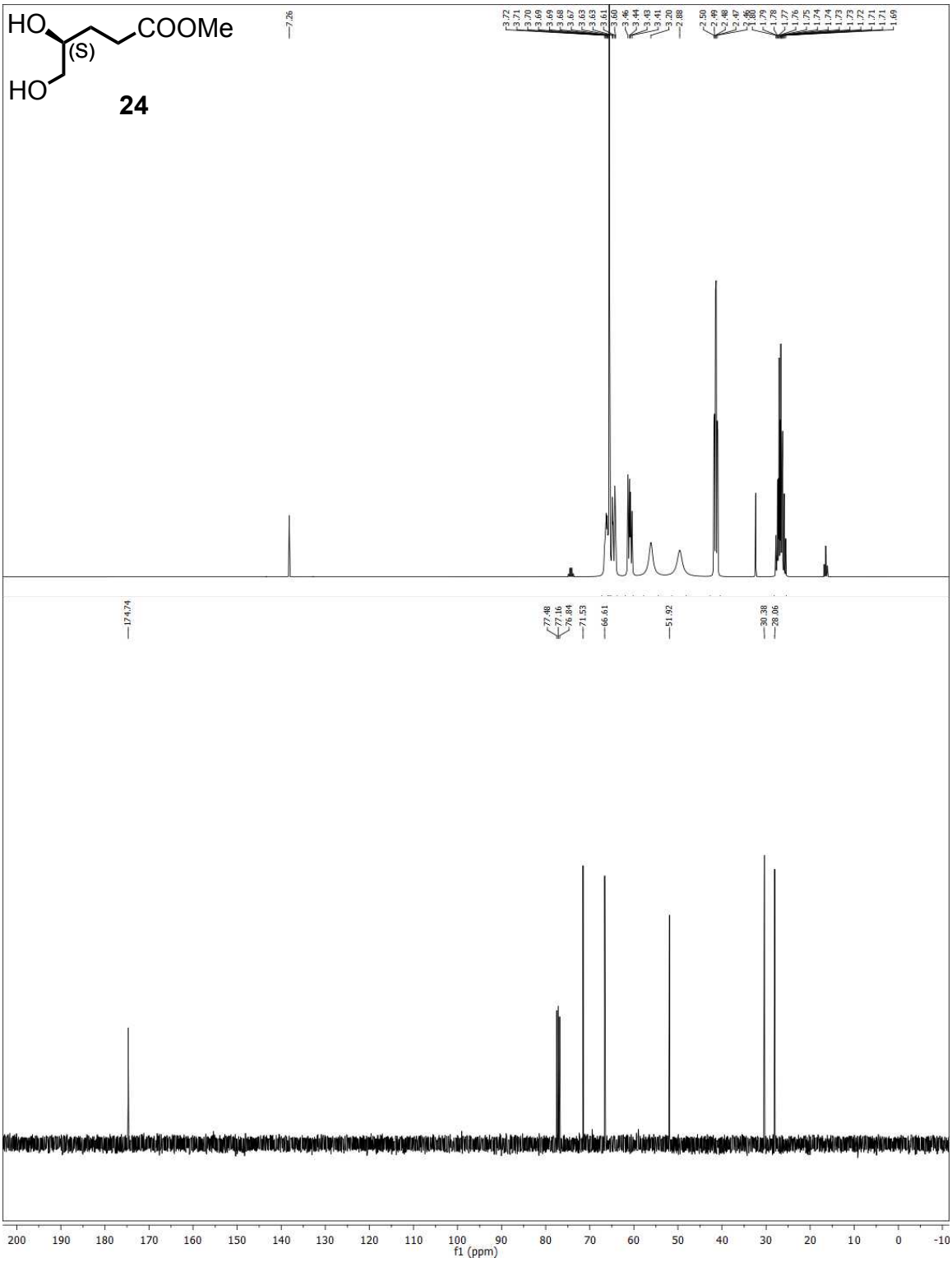
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COOMe
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3.69
3.68
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3.63
3.63
3.61
3.60
3.46
3.44
3.43
3.41
3.20
2.88
2.50
2.49
2.48
2.47
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1.78
1.77
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1.75
1.74
1.74
1.73
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190
180
170
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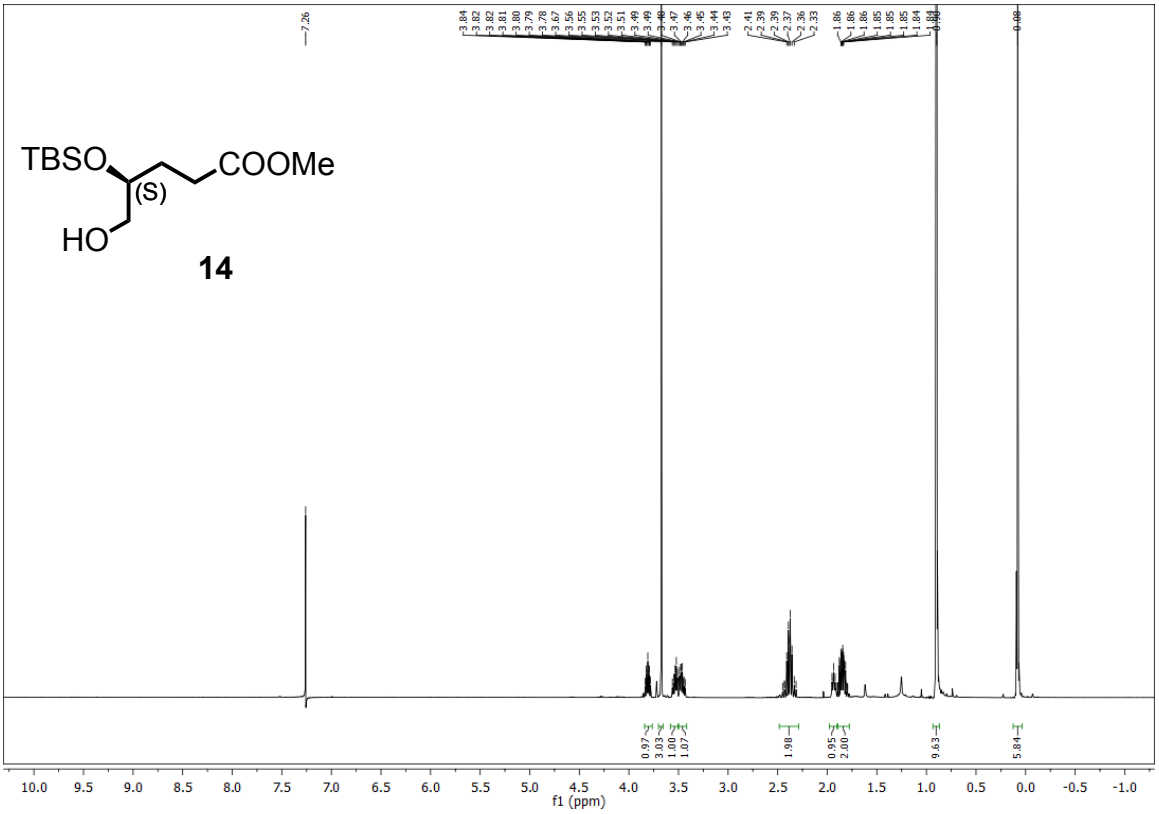
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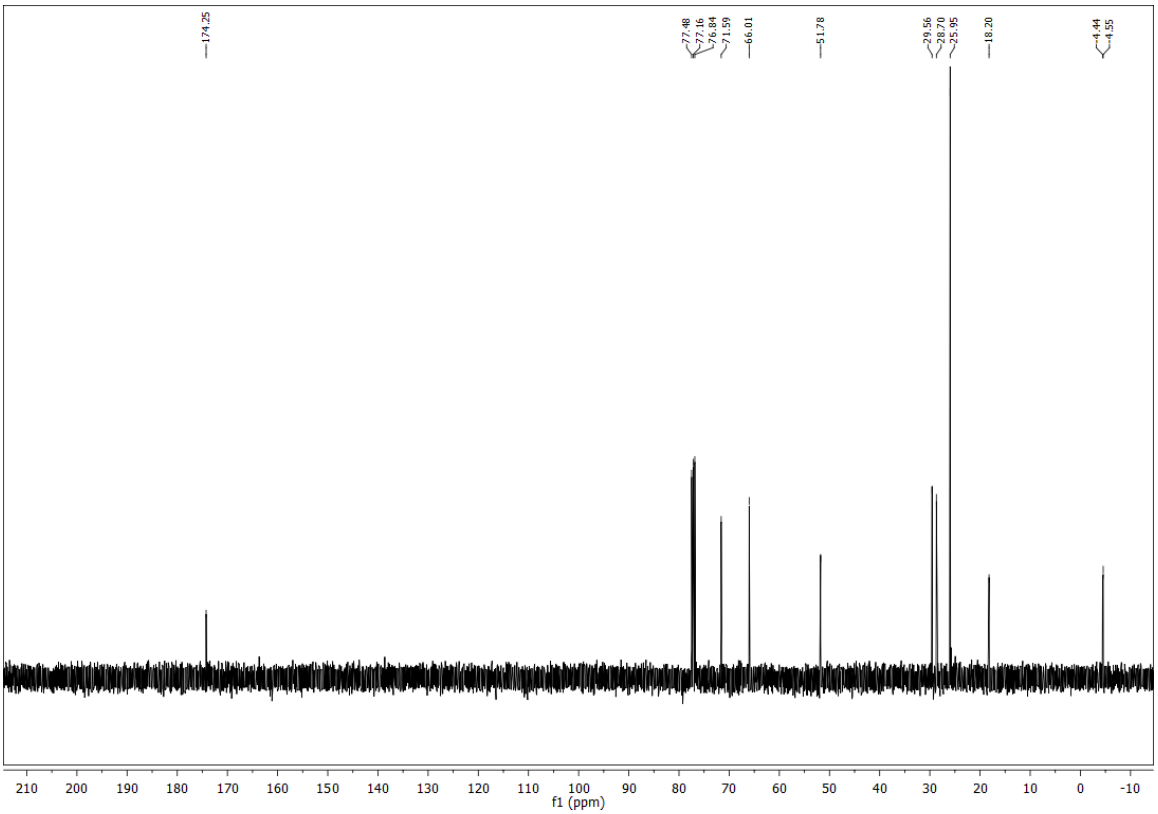
(S)
COOMe
HO
14
f1 (ppm)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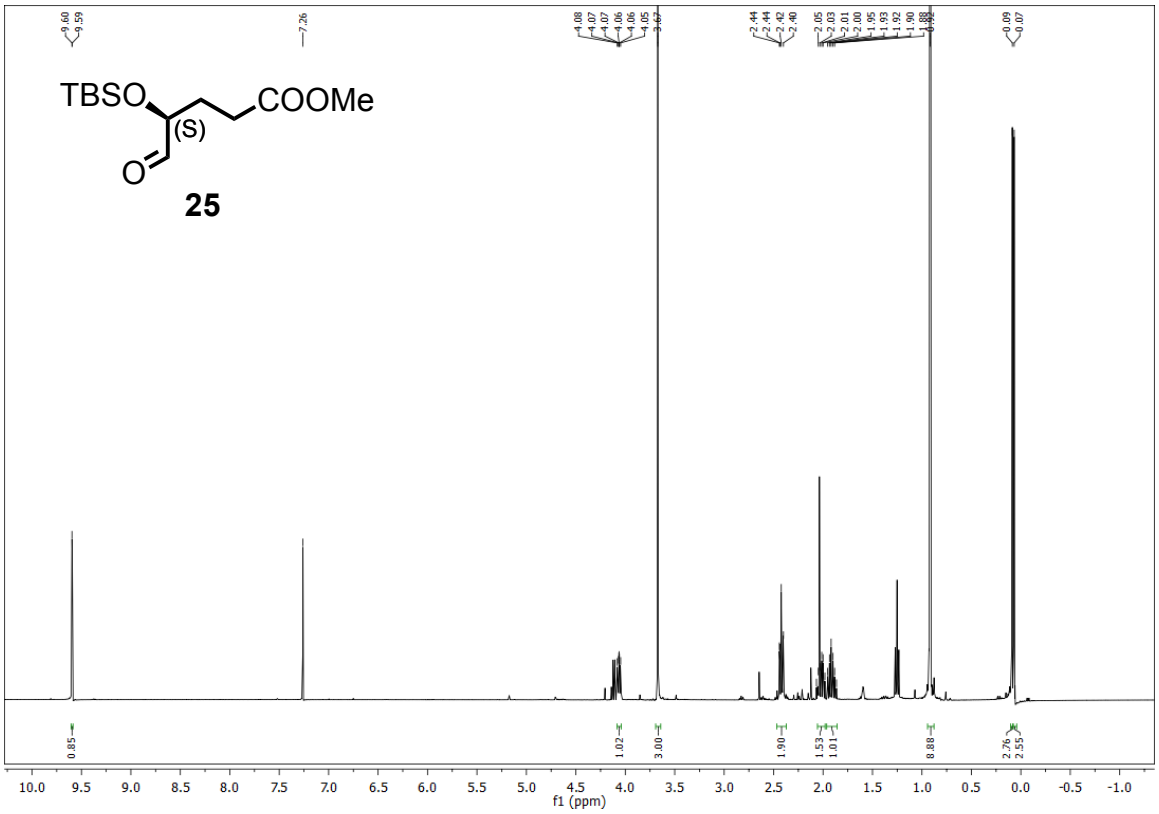
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COOMe
O
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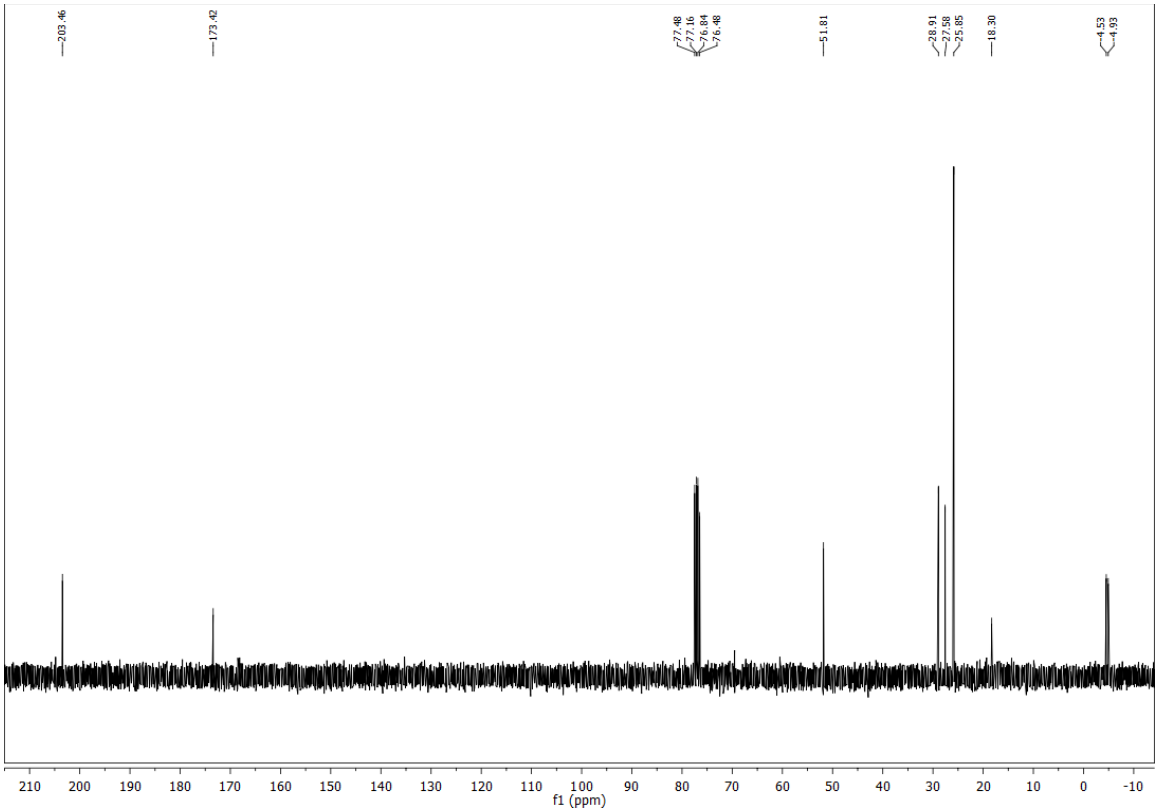
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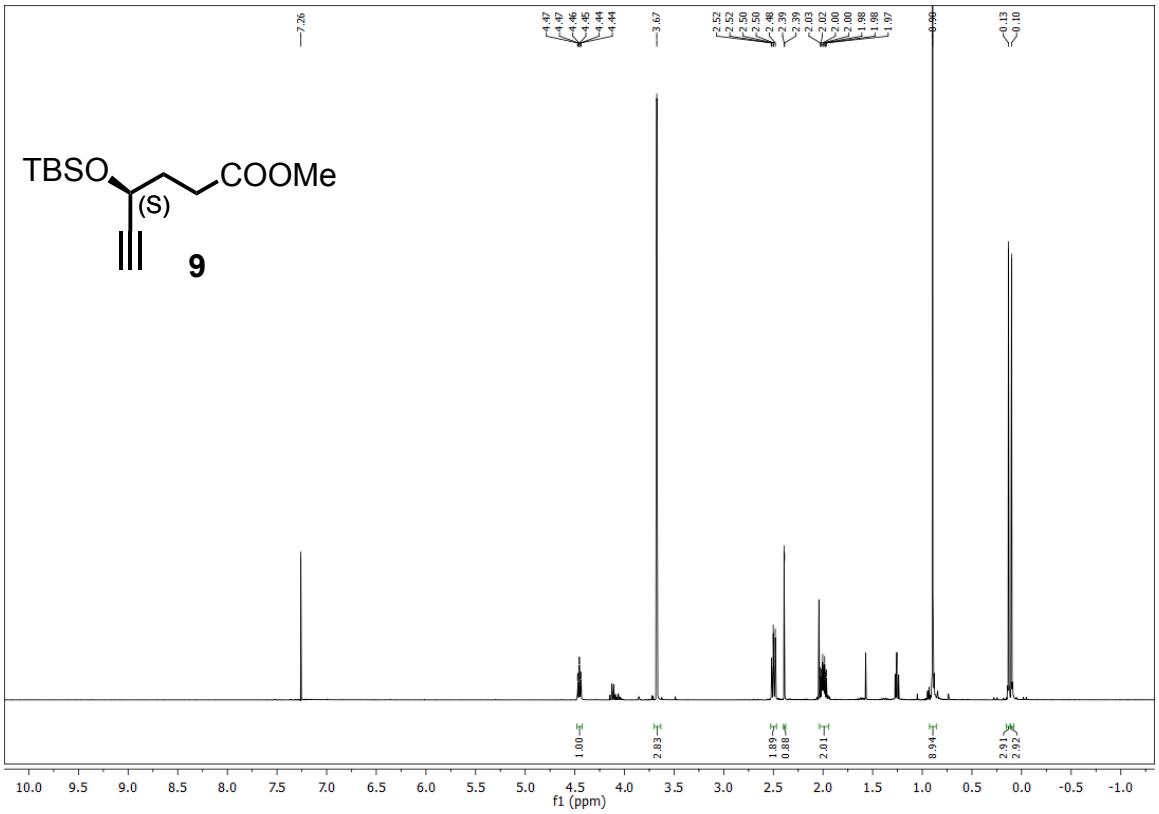
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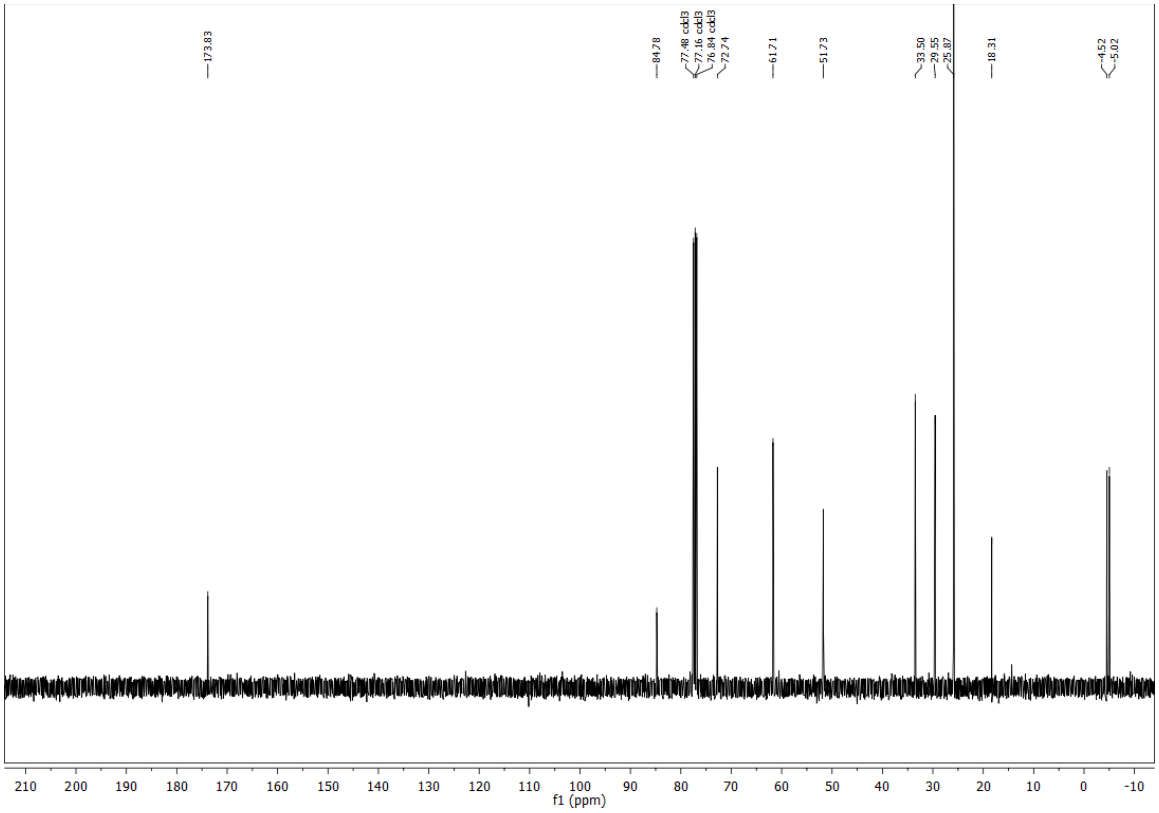
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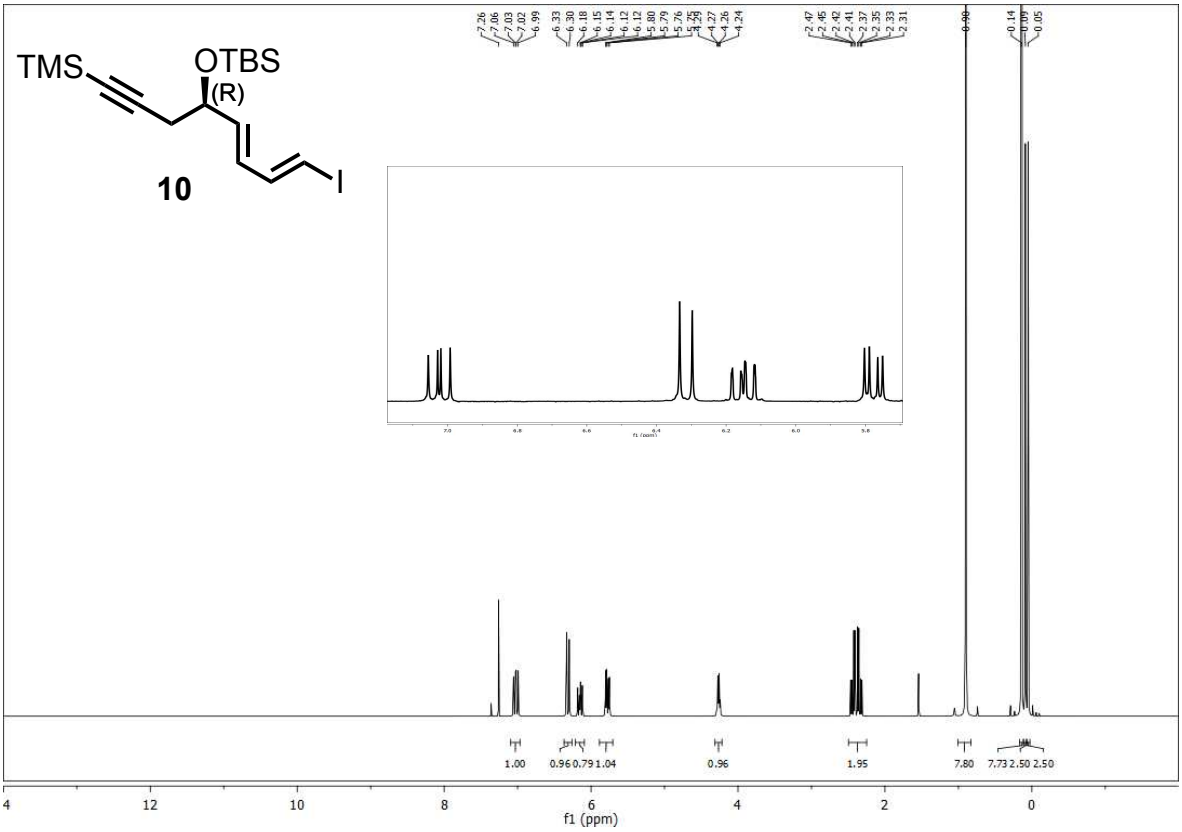
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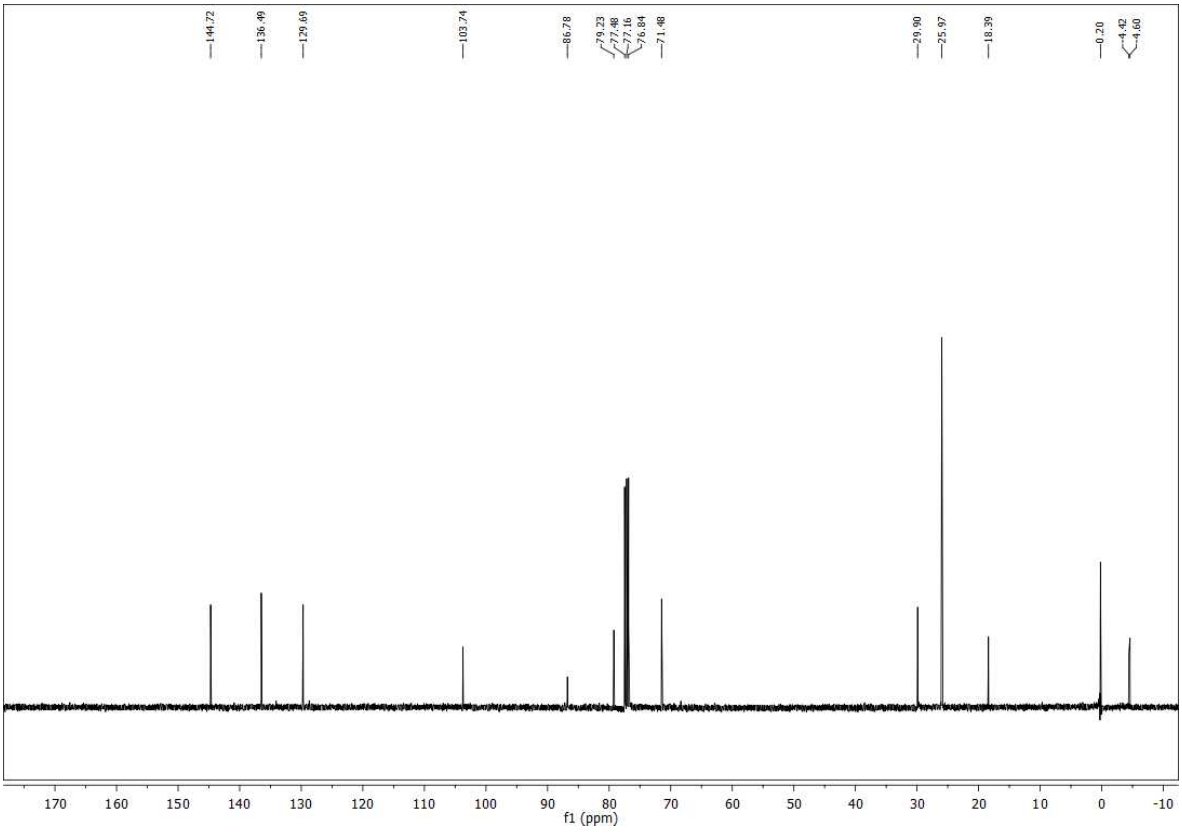
I
f1 (ppm)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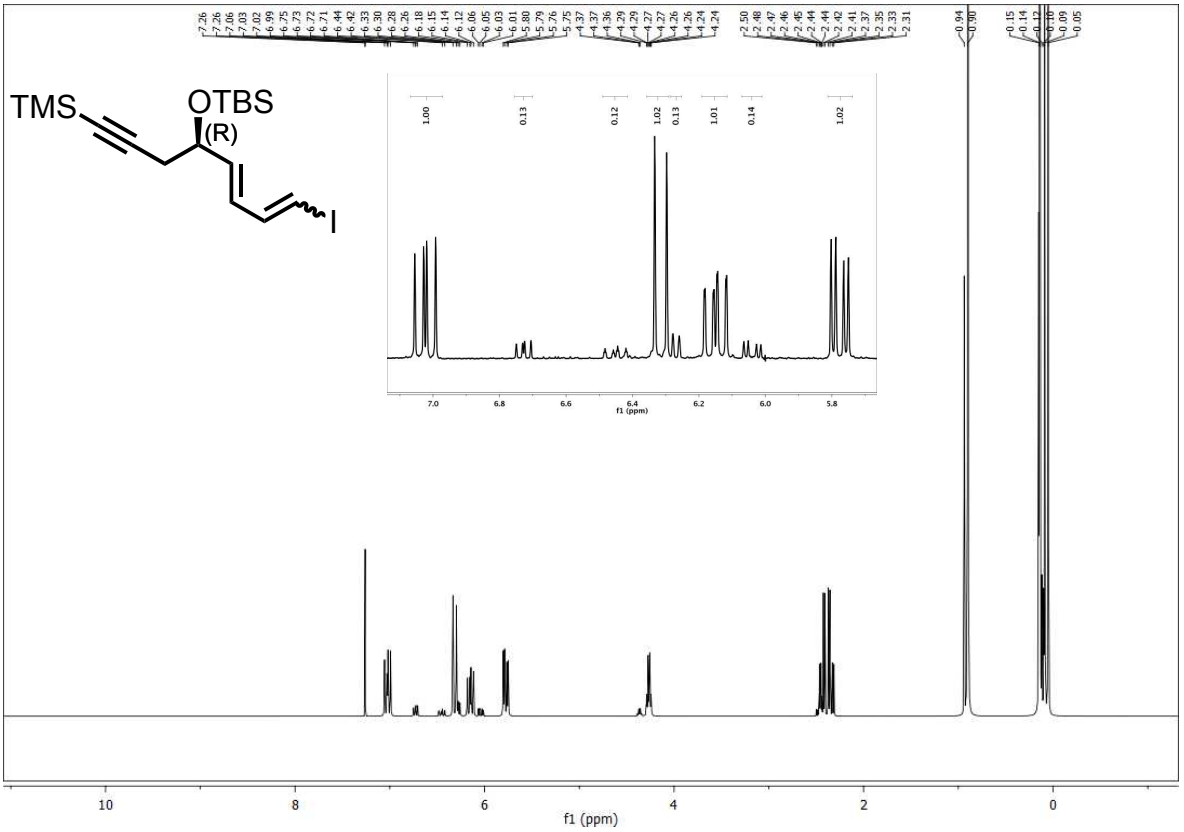
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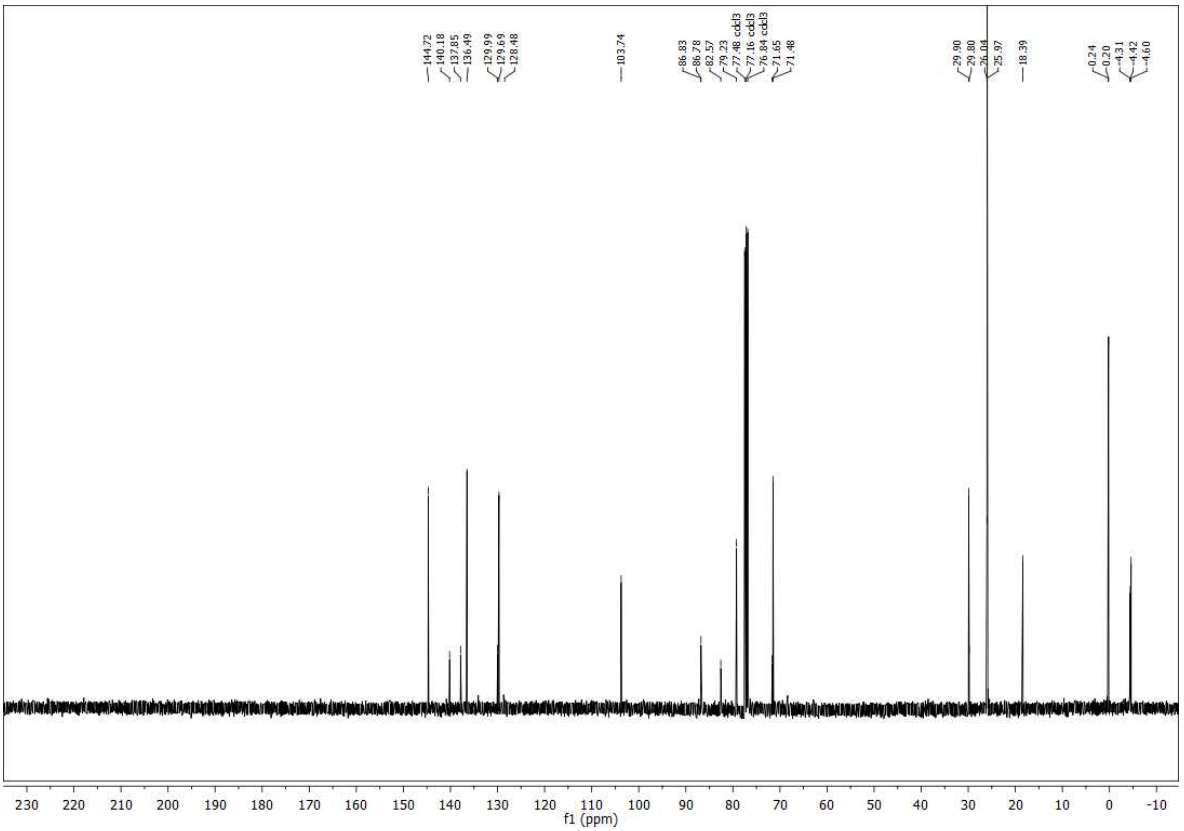
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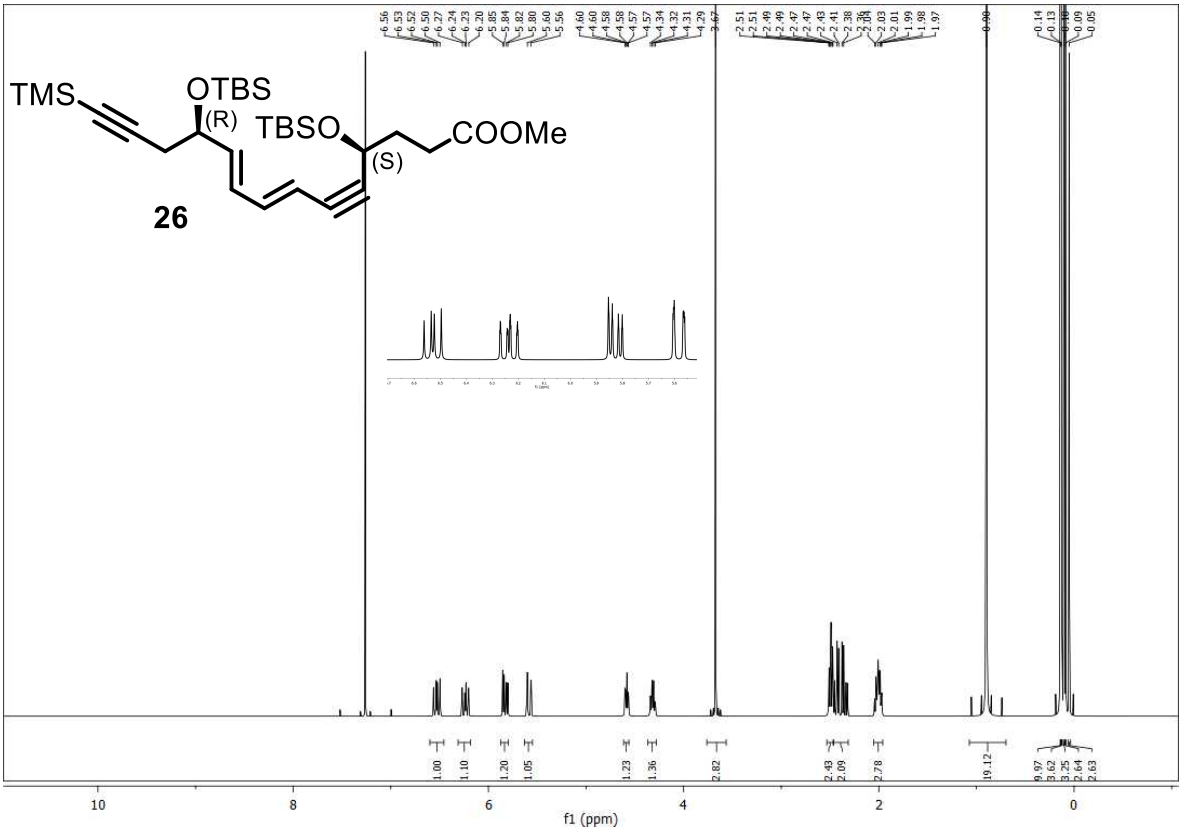
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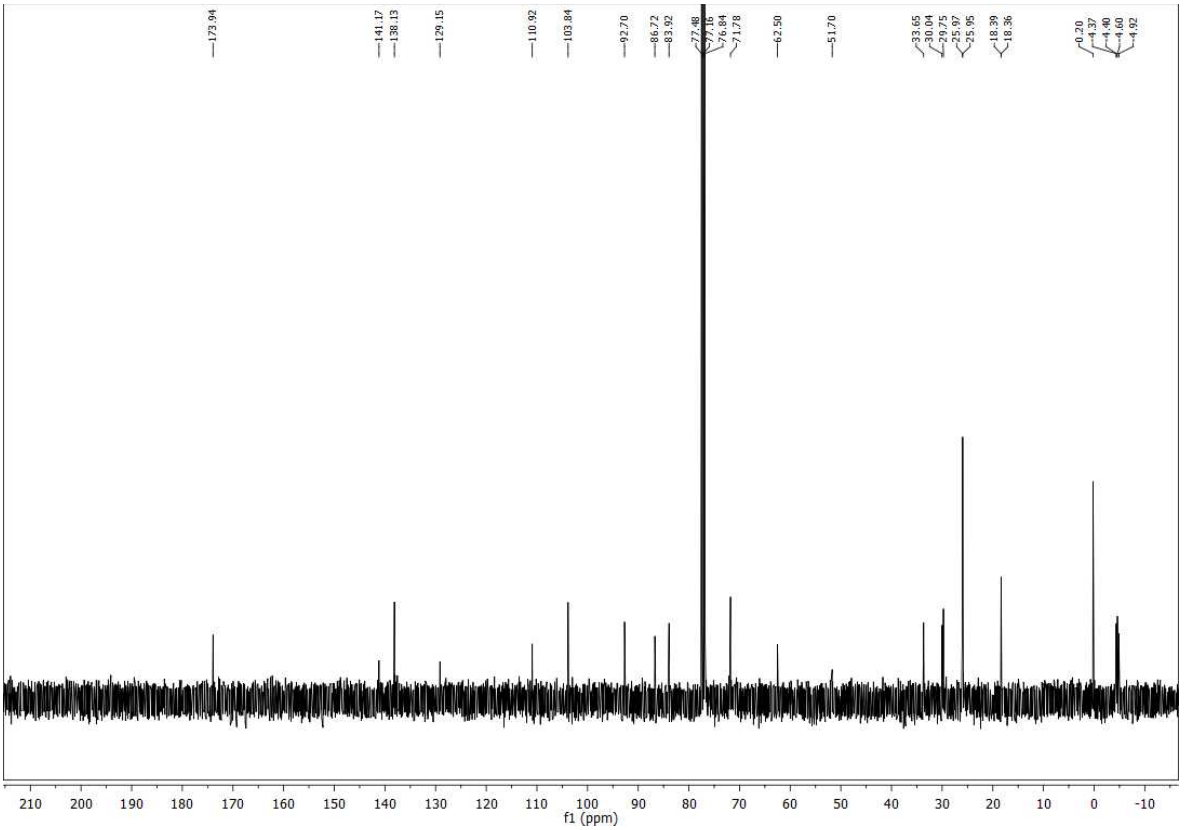
(R)
TBSO
(S)
COOMe
26
f1 (ppm)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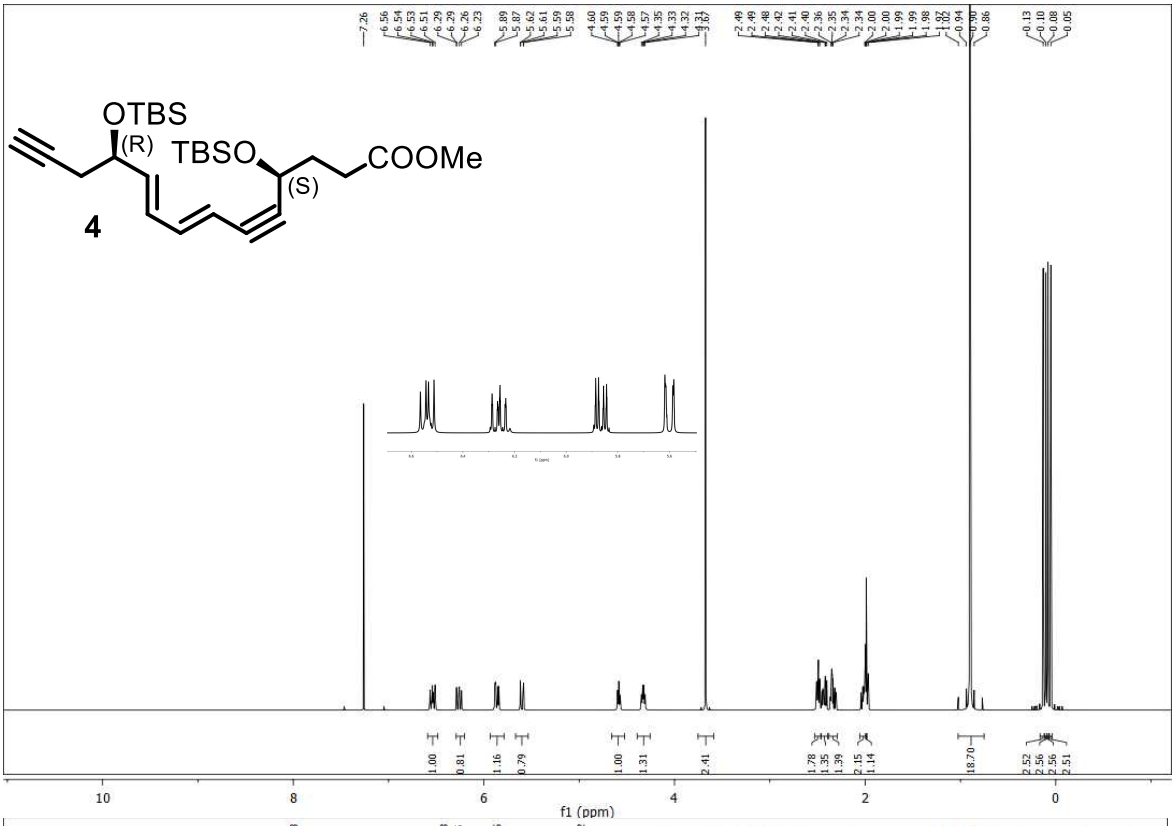
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TBSO
(S)
COOMe
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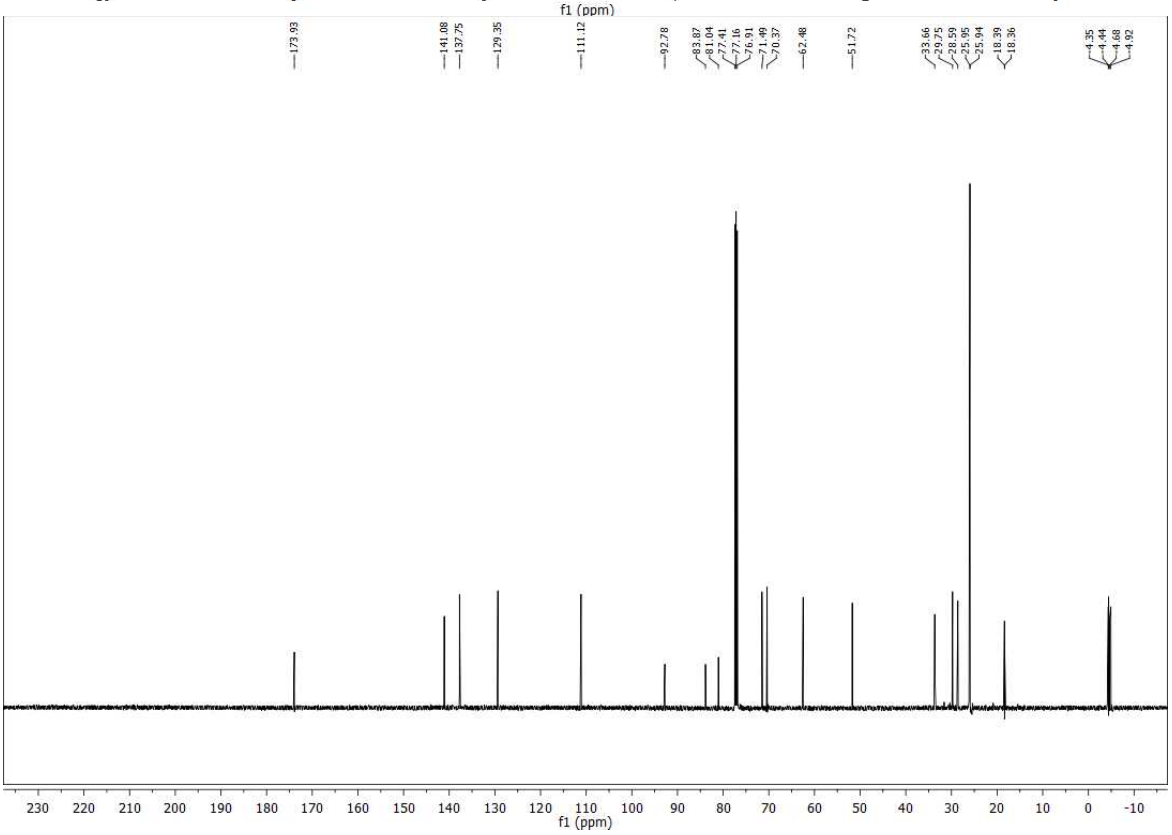
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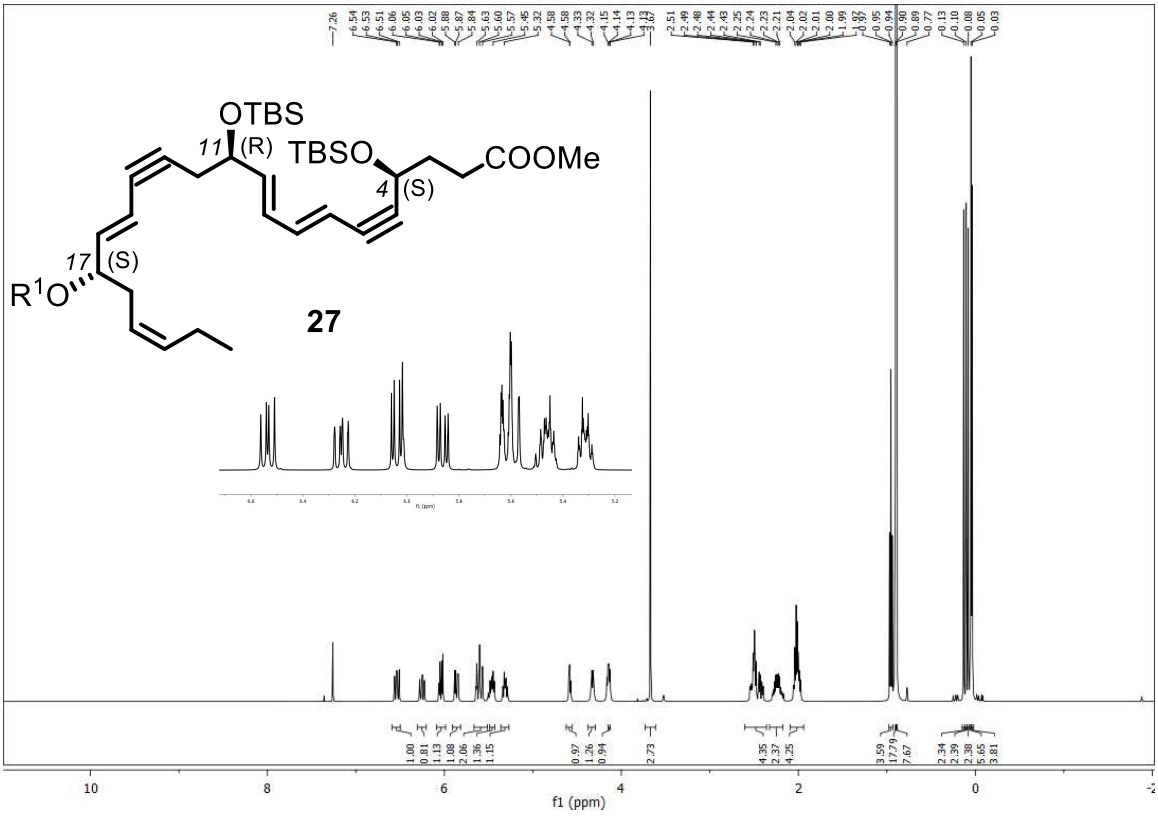
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COOMe
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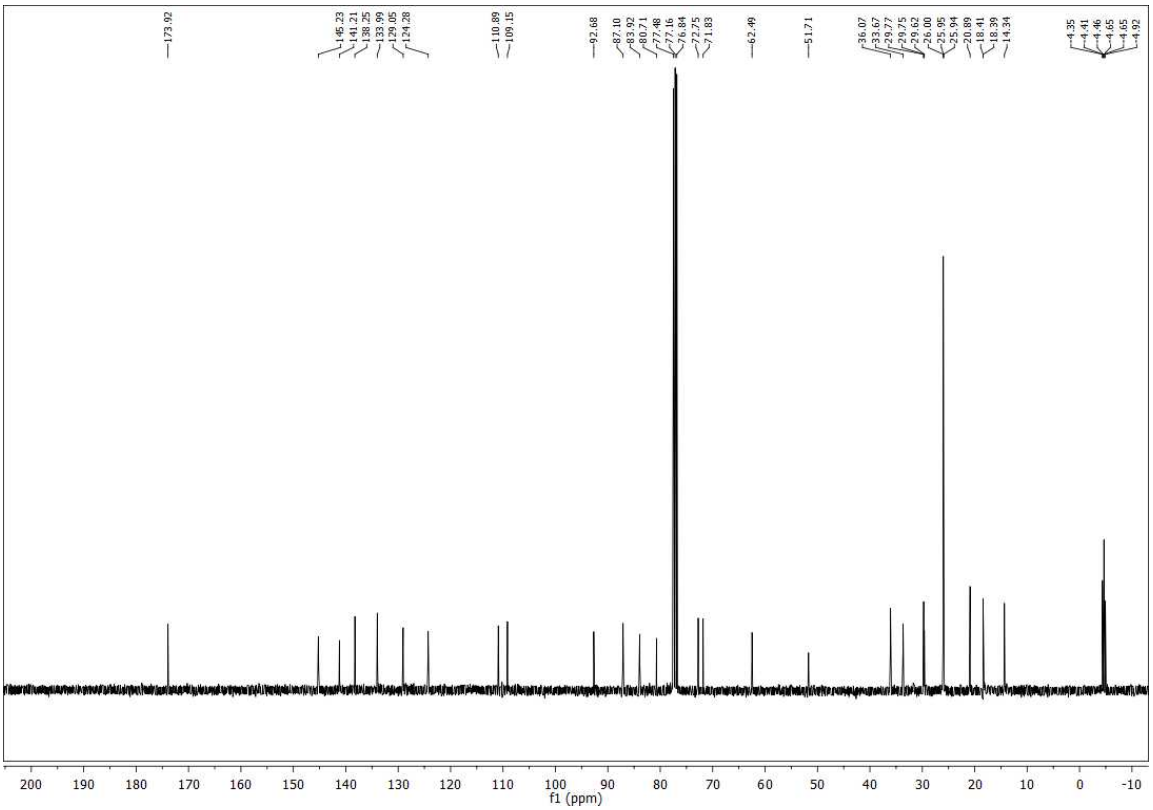
17 (S)
R1O
27
f1 (ppm)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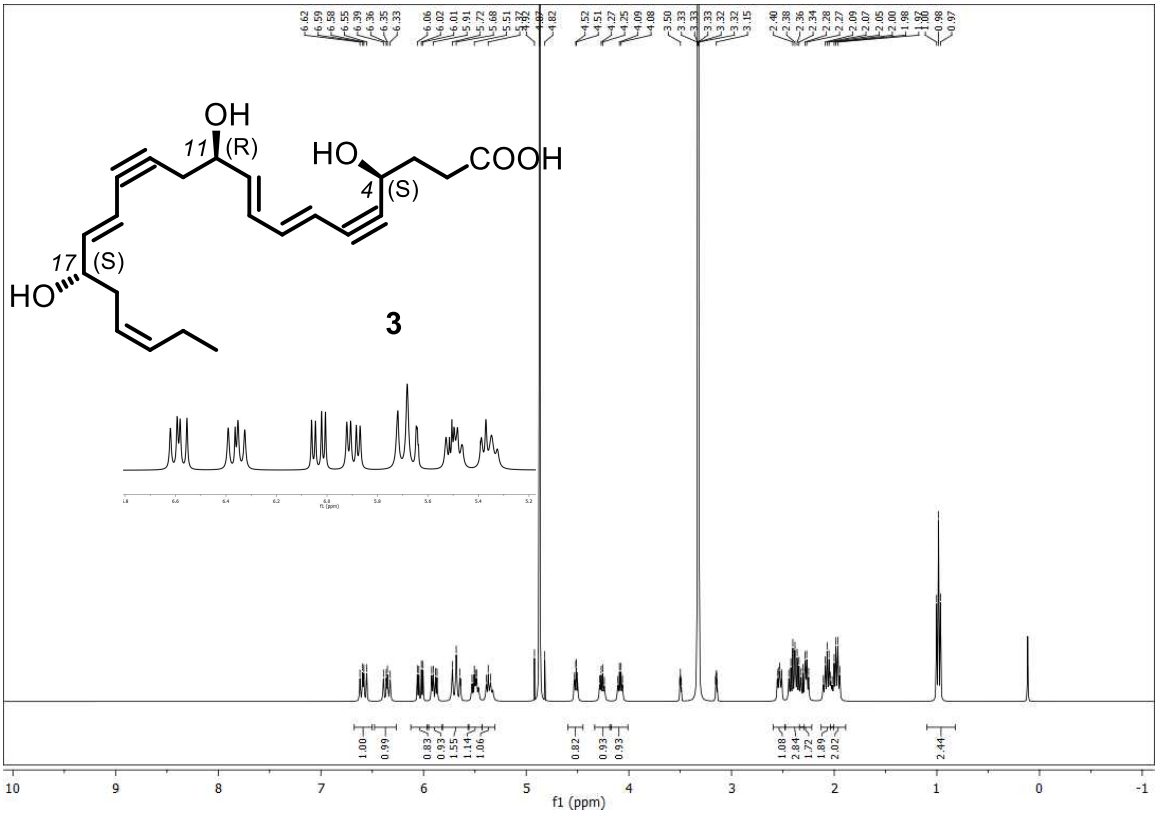
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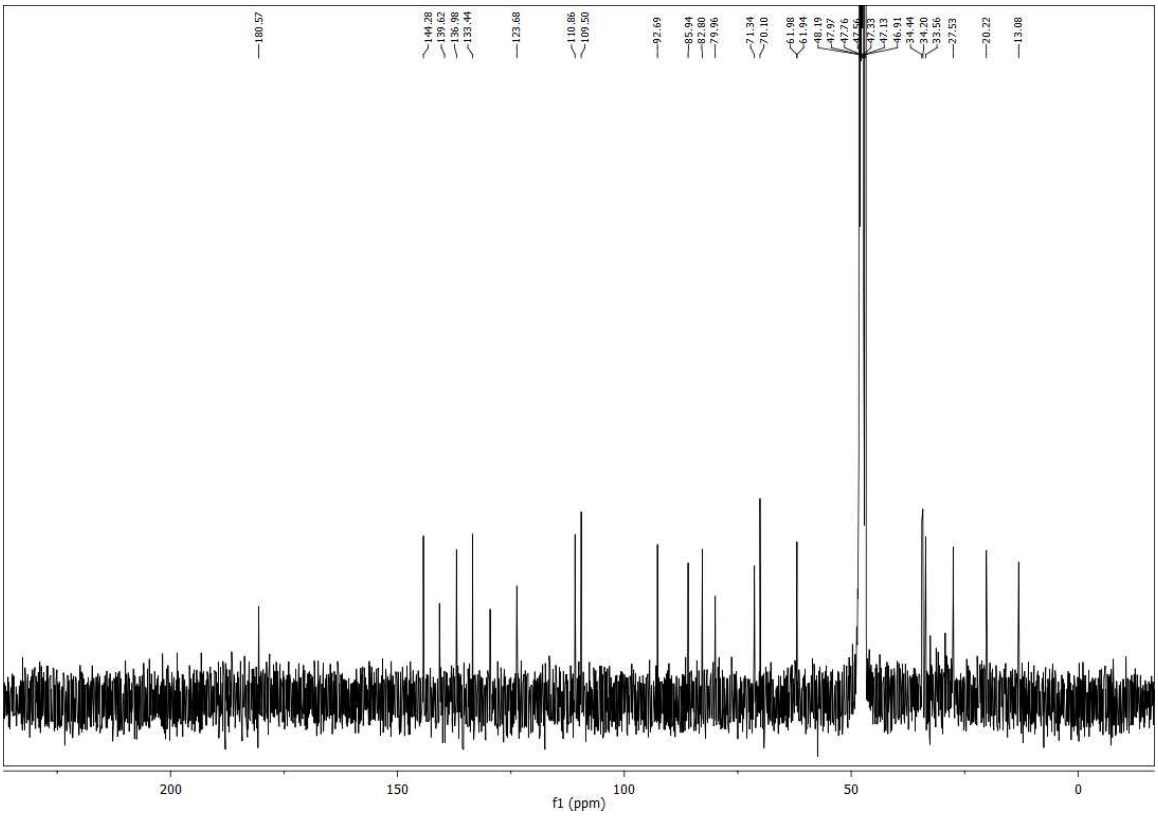
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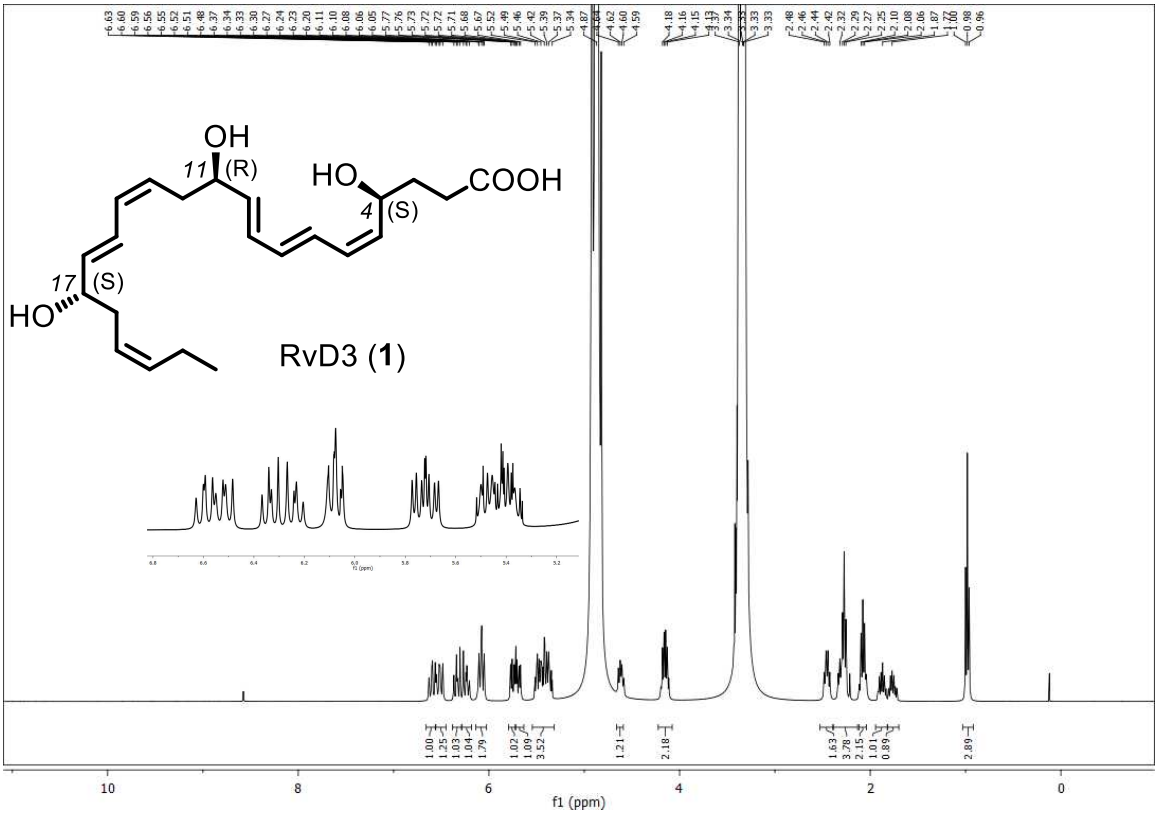
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4 (S)
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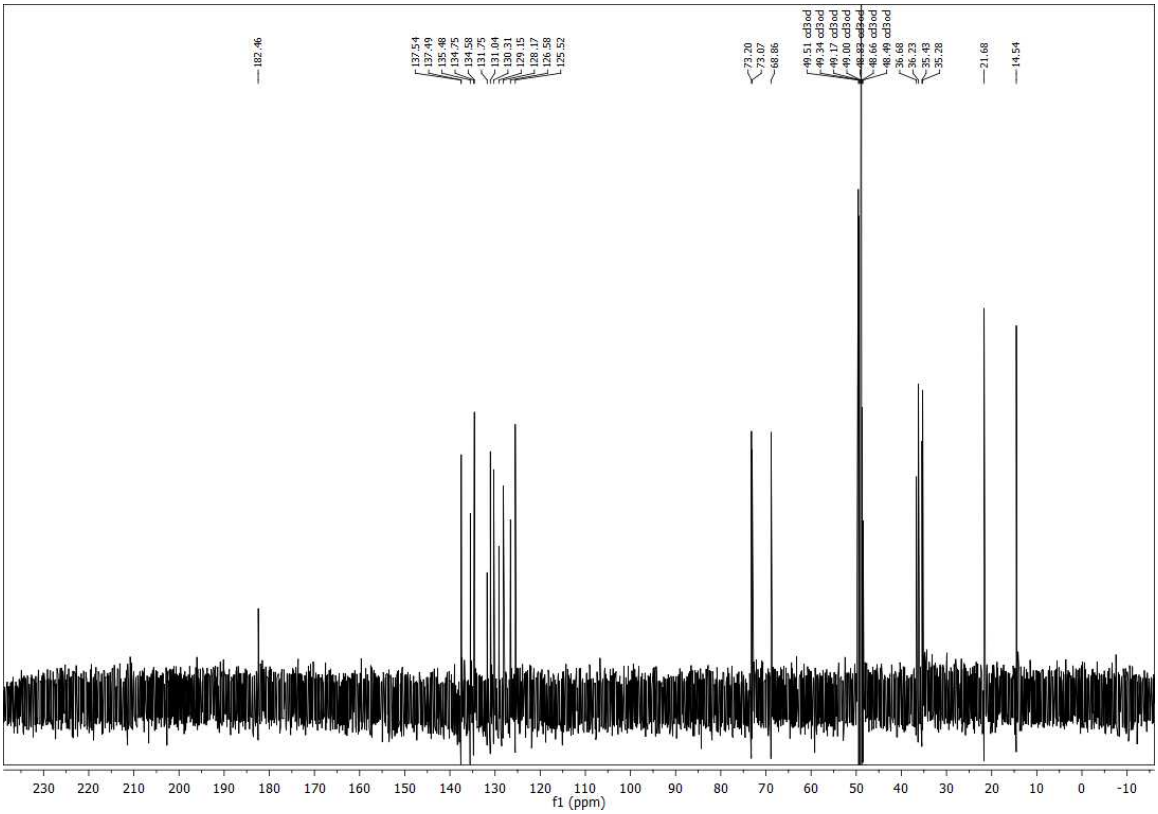
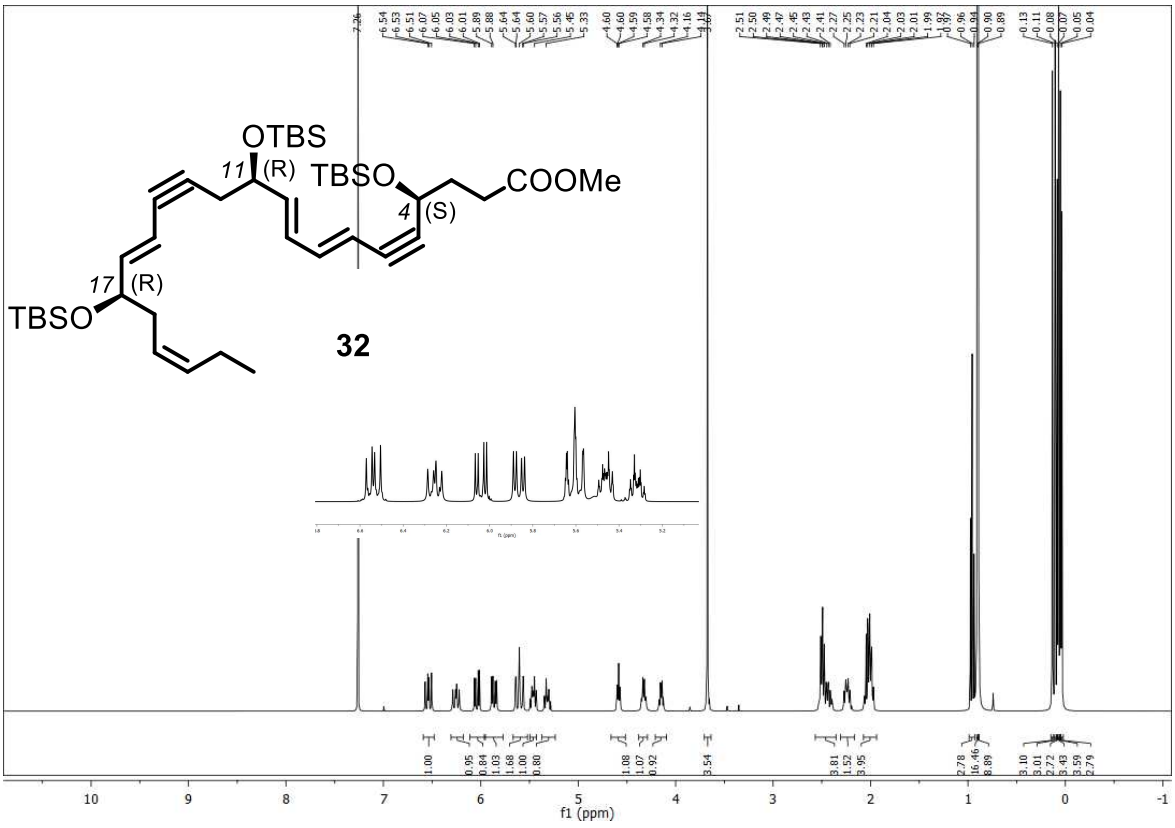
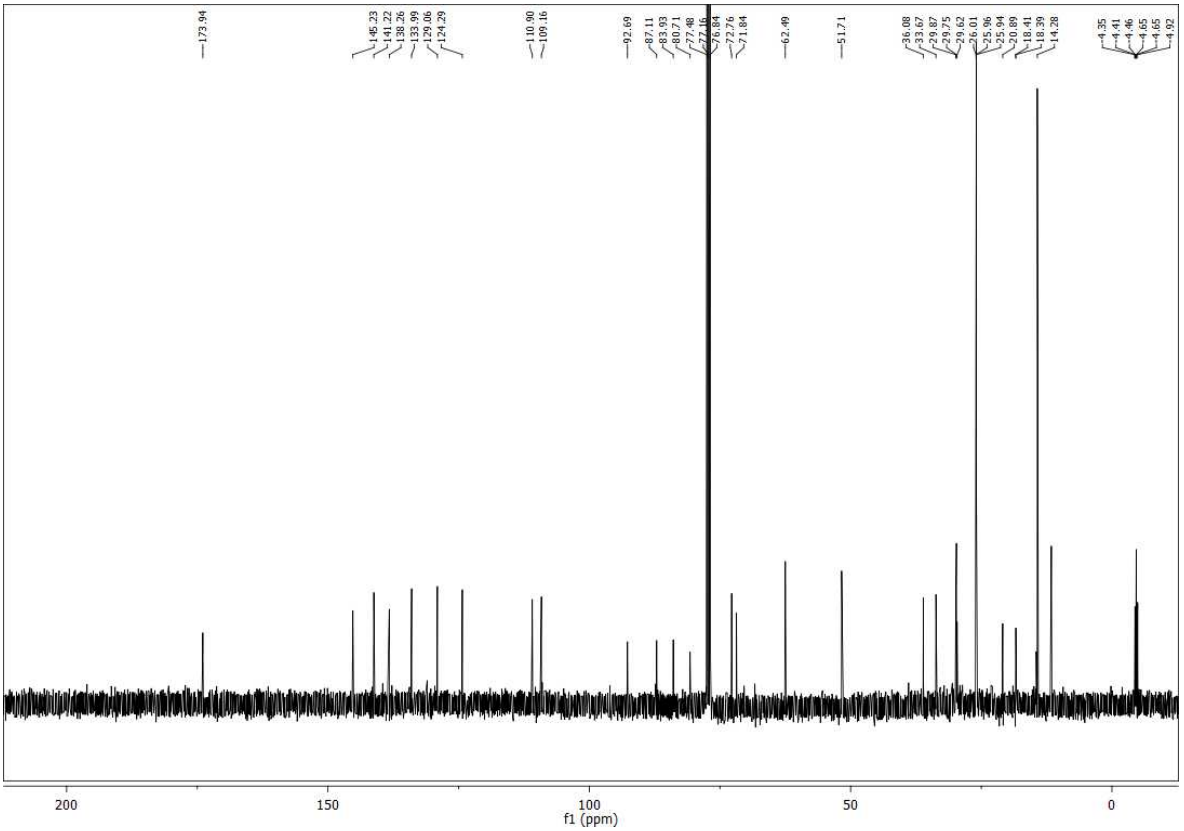
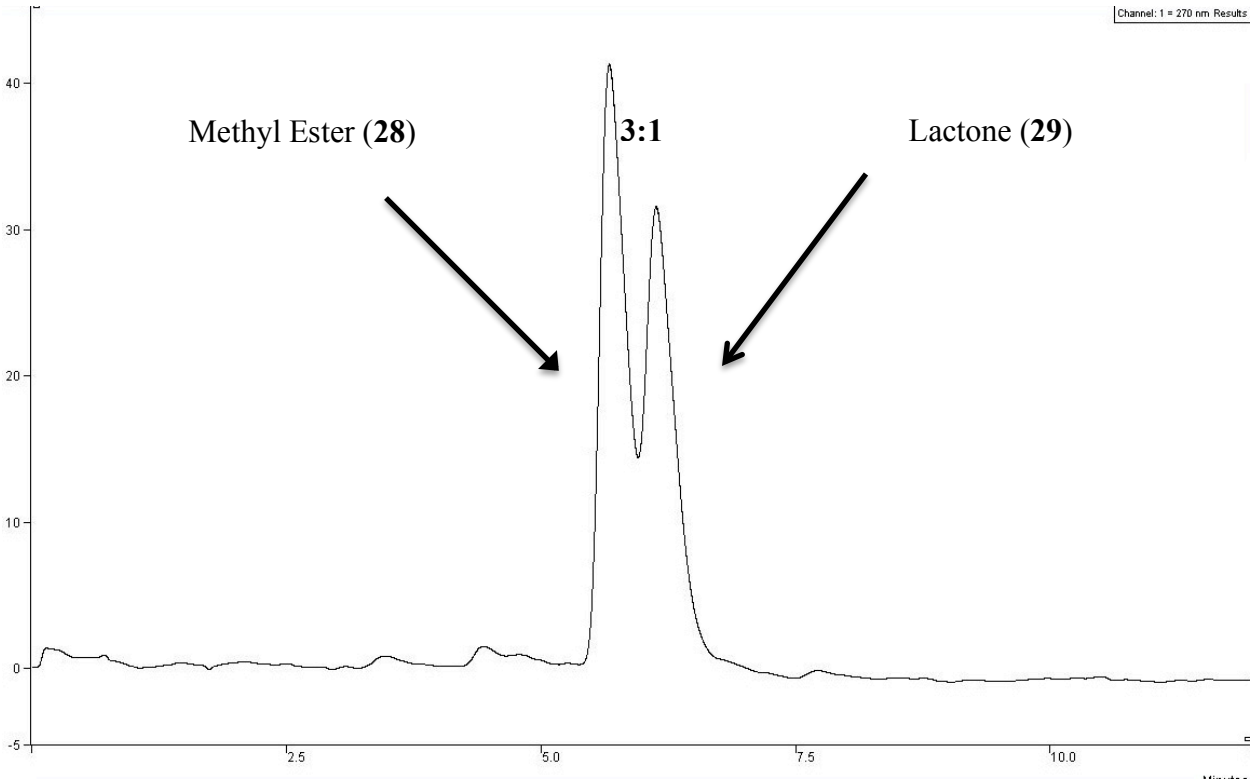
RvD3 (1)
f1 (ppm)

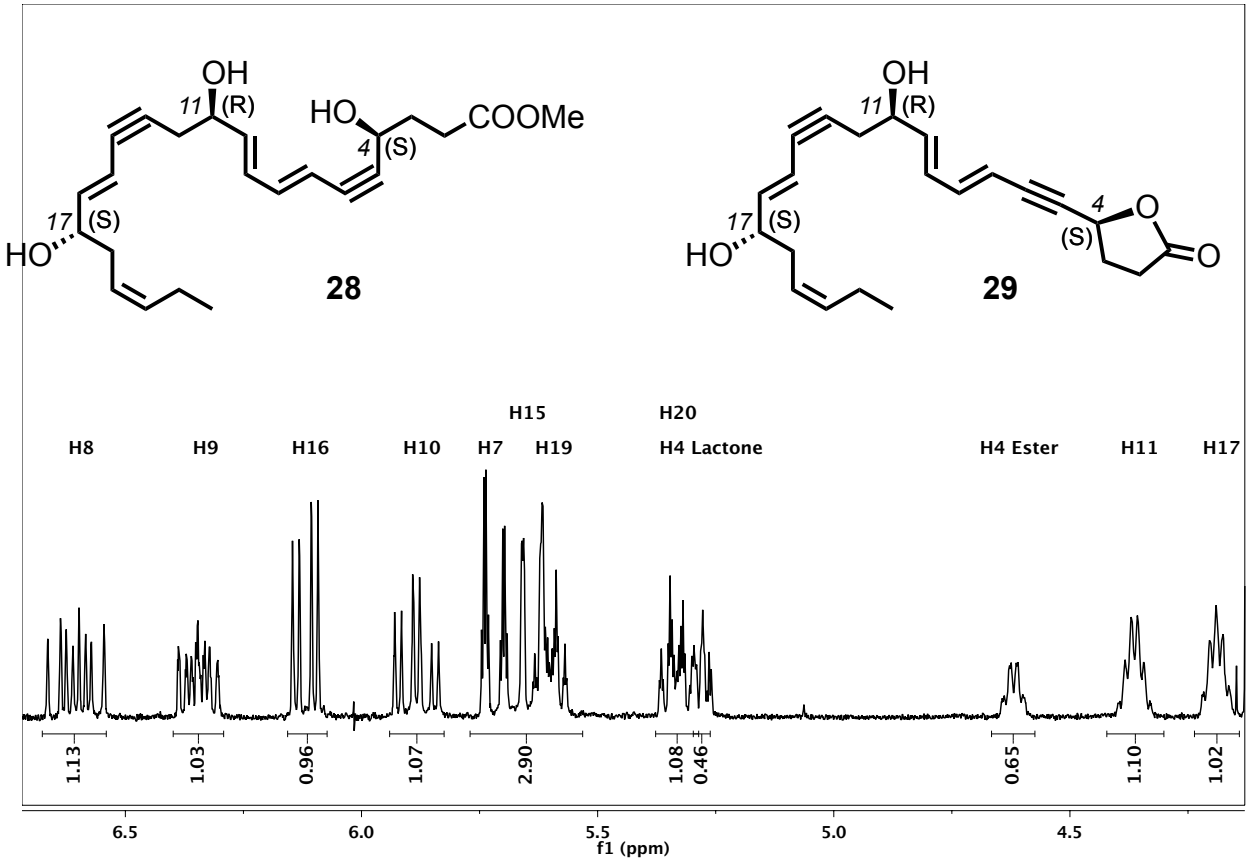

f1 (ppm)

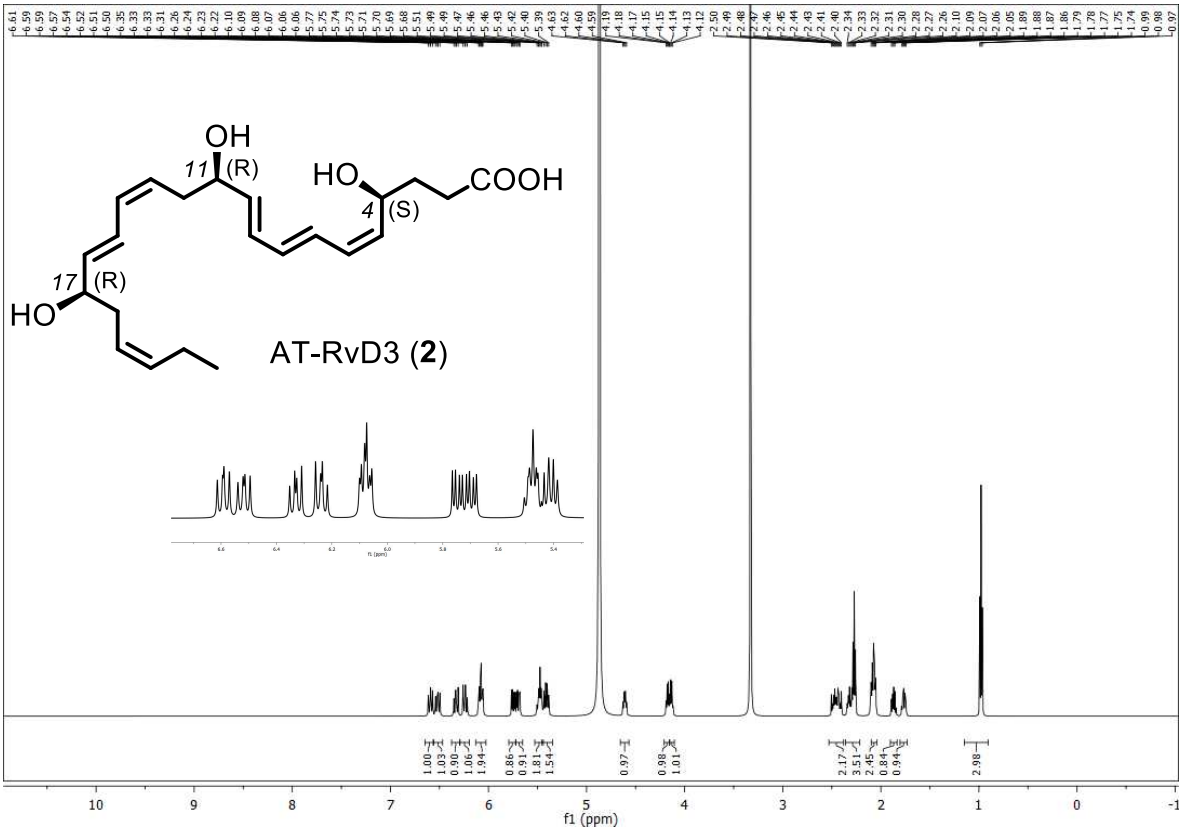

OTBS
11 (R)
TBSO
4 (S)
COOMe
17 (R)
TBSO
32
f1 (ppm)

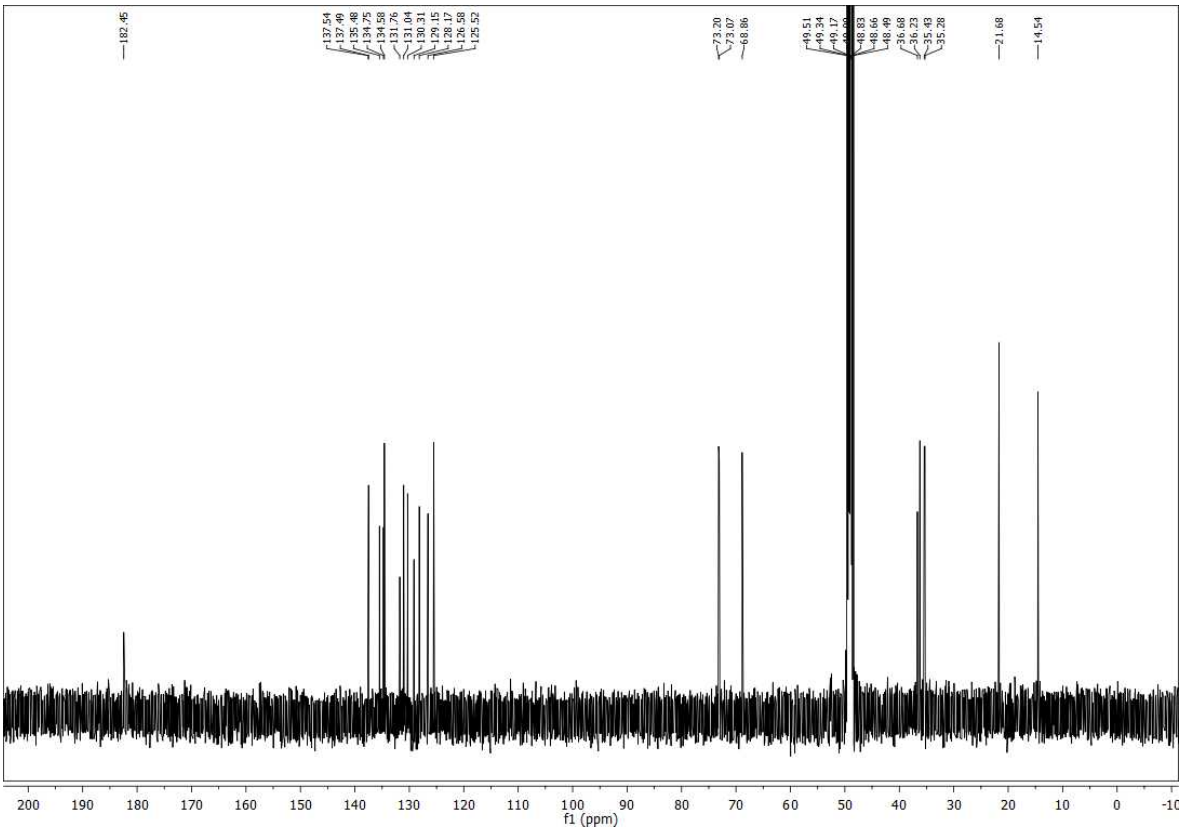

f1 (ppm)

HPLC and ^{1}H and ^{13}C NMR spectra of Ester Lactone Mix

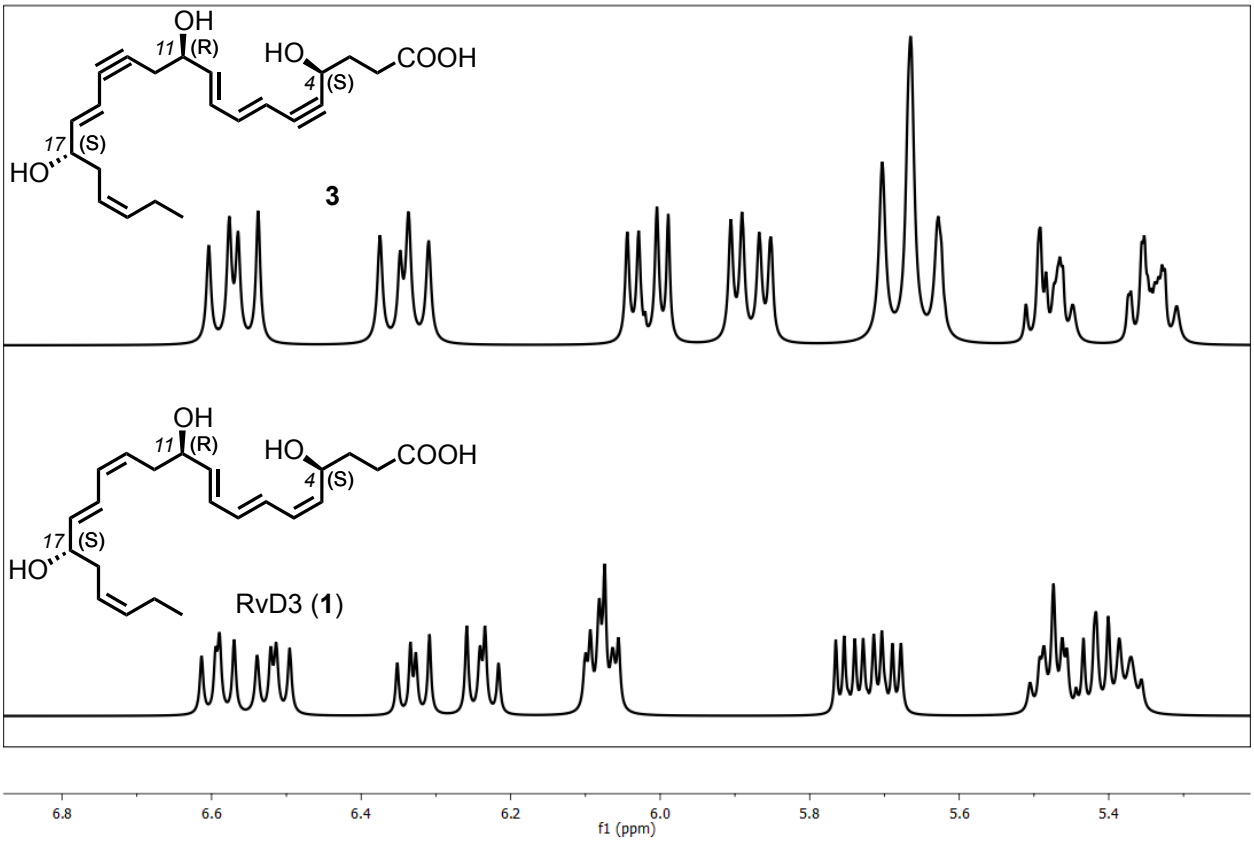




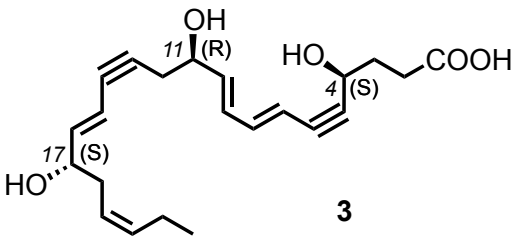

OH
11 (R)
HO
COOH
4 (S)
17 (R)
HO
AT-RvD3 (2)
f1 (ppm)


f1 (ppm)

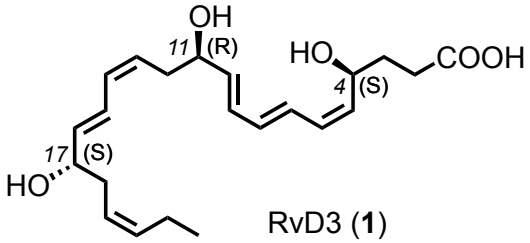
Comparison of the olefinic region of the ^{1}H-NMR spectra of the bis-acetylenic compound **3** and its hydrogenation product RvD3 (**1**)



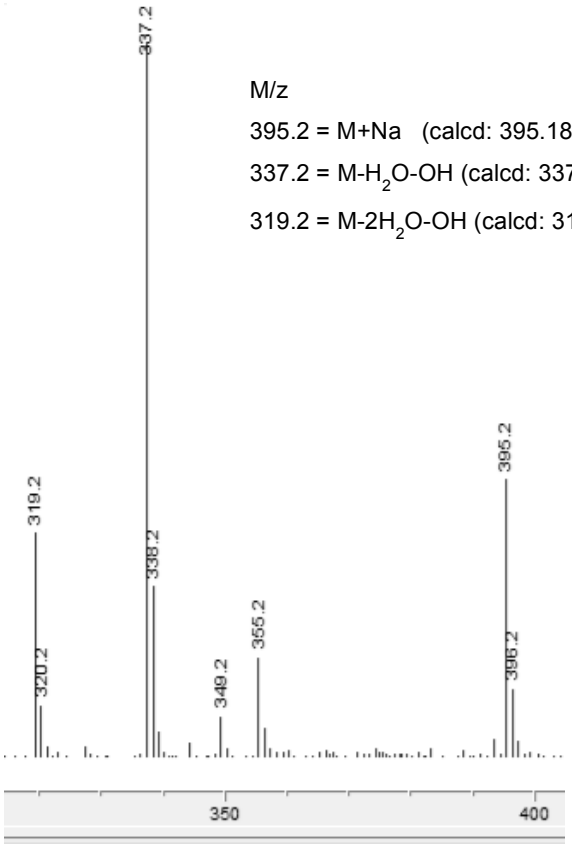
Comparison of the bis-acetylenic compound **3** and its hydrogenation product RvD3 (**1**) with Mass spectrometry



3



RvD3 (**1**)

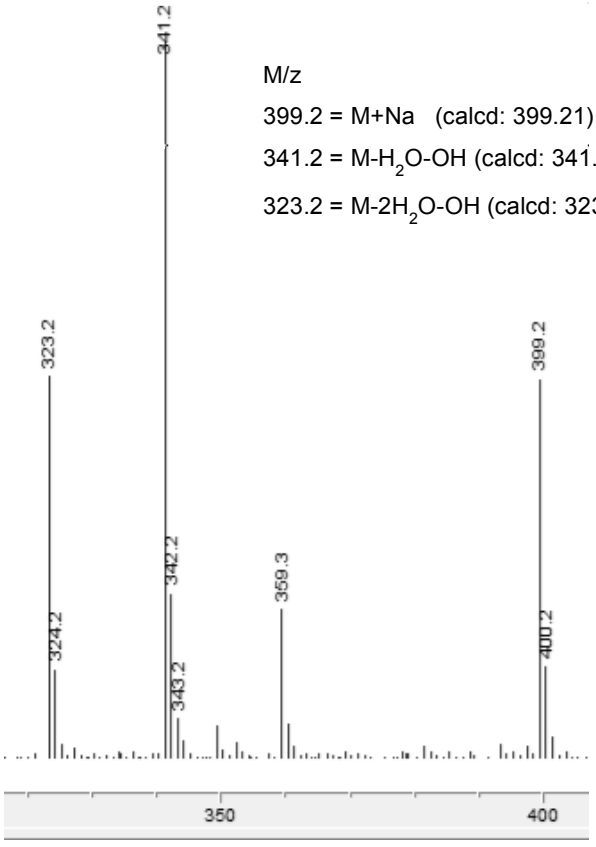


M/z

395.2 = M+Na (calcd: 395.18)

337.2 = M-H_2O-OH (calcd: 337.18)

319.2 = M-2H_2O-OH (calcd: 319.17)



M/z

399.2 = M+Na (calcd: 399.21)

341.2 = M-H_2O-OH (calcd: 341.21)

323.2 = M-2H_2O-OH (calcd: 323.20)

Comparison of the olefinic region of the ^{1}H-NMR spectra of RvD3 (**1**) and AT-RvD3 (**2**)