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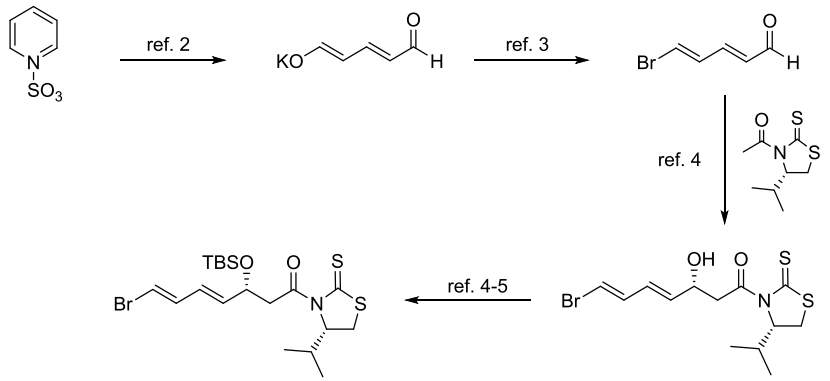
General Information

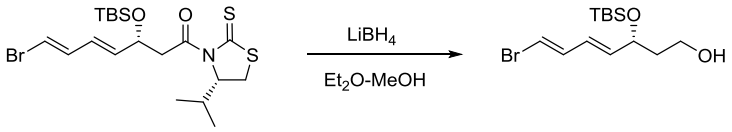
Unless stated otherwise, all commercially available reagents and solvents were used in the form they were supplied without any further purification. The stated yields are based on isolated material. Thin layer chromatography was performed on silica gel 60 F_{254} aluminum-backed plates fabricated by Merck. Flash column chromatography was performed on silica gel 60 (40-63 µm) produced by Merck. NMR spectra were recorded on a Bruker AVI600, Bruker AVII400 or a Bruker DPX300 spectrometer at 600 MHz, 400 MHz or 300 MHz respectively for ^{1}H NMR and at 125 MHz, 100 MHz or 75 MHz respectively for ^{13}C NMR. Coupling constants (*J*) are reported in hertz and chemical shifts are reported in parts per million (δ) relative to the central residual protium solvent resonance in ^{1}H NMR ($CDCl_3$ = δ 7.27, DMSO-d_6 = δ 2.50 and MeOH-d_4 = δ 3.31) and the central carbon solvent resonance in ^{13}C NMR ($CDCl_3$ = δ 77.00 ppm, DMSO-d_6 = δ 39.43 and MeOD-d_4 = δ 49.00). Mass spectra were recorded at 70 eV on Waters Prospec Q spectrometer using EI, ES or CI as the methods of ionization. High resolution mass spectra were recorded on Waters Prospec Q spectrometer using EI or ES as the methods of ionization. Optical rotations were measured using a 1 mL cell with a 1.0 dm path length on a Perkin Elmer 341 polarimeter. HPLC analyses were performed on an Agilent Technologies 1200 Series instrument with diode array detector set at 254 nm and equipped with a C_{18} stationary phase (Eclipse XDB-C18 5µm 4.6 × 150 mm), applying the conditions stated. The UV/Vis spectra from 190-900 nm were recorded using a Biochrom Libra S32PC spectrometer using quartz cuvettes. Diastereomeric ratios reported in this paper have not been validated by calibration, please see reference Wernerova and Hudlicky for discussions and guidelines.[1]

(*R*,4*E*,6*E*)-7-bromo-3-((*tert*-butyldimethylsilyl)oxy)-1-((*S*)-4-isopropyl-2-thioxothiazolidin-3-yl)hepta-4,6-dien-1-one (20).



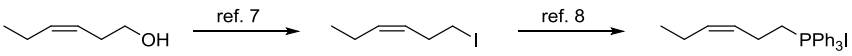
Vinylbromide **20** was prepared in 4 steps from commercially available pyridinium-1-sulfonate (**17**) in 34% overall yield (8.24 g), as previously reported.[2-5] All spectroscopic and physical data were in full agreement with those reported in the literature.[6] $[\alpha]_D^{20}$ = 263 (c = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.69 (dd, *J* = 13.4, 10.7 Hz, 1H), 6.31 (d, *J* = 13.5 Hz, 1H), 6.15 (dd, *J* = 15.5, 11.1 Hz, 1H), 5.79 (dd, *J* = 14.9, 6.6 Hz, 1H), 5.04 (t, *J* = 7.0 Hz, 1H), 4.75 (q, *J* = 6.4 Hz, 1H), 3.64 (dd, *J* = 16.6, 7.8 Hz, 1H), 3.47 (dd, *J* = 10.9, 7.9 Hz, 1H), 3.21 (dd, *J* = 16.4, 4.6 Hz, 1H), 3.03 (d, *J* = 11.6 Hz, 1H), 2.48 – 2.26 (m, 1H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 170.9, 136.8, 127.4, 109.1, 71.8, 69.8, 46.2, 31.0, 30.9, 25.9 (3C), 19.3, 18.2, 17.9, -4.2, -4.8.

(*R*,4*E*,6*E*)-7-bromo-3-((*tert*-butyldimethylsilyl)oxy)hepta-4,6-dien-1-ol (7).



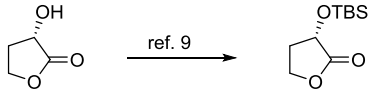
$LiBH_4$ (1.17 mL, 2 M in THF, 2.30 equiv.) was added to a solution of vinylbromid **20** (500 mg, 1.04 mmol, 1.00 equiv.) in Et_2O (8.8 ml) and MeOH (0.59 mL) at 0 °C. More $LiBH_4$ (0.88 mL, 2M in THF, 1.70 equiv.) was added after 5 h and the solution was stirred for another 15 h. Excess $LiBH_4$ was quenched with 0.5 M HCl. The phases were separated and the organic phase was washed with sat. aq. $NaHCO_3$ (5 mL), water (5 mL) and brine (5 mL). The organic layer was dried (Na_2SO_4), before being concentrated *in vacuo.* The crude product was purified by column chromatography on silica (CH_2Cl_2/MeOH 99.5:0.5) to afford the title compound **7** as a yellow oil. Yield: 295 mg (88%); TLC (CH_2Cl_2/MeOH 95:5, CAM stain): R_f = 0.67; $[\alpha]_D^{20}$ = 6.1 (c = 0.1, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (dd, *J* = 13.4, 10.9 Hz, 1H), 6.30 (d, *J* = 13.5 Hz, 1H), 6.12 (dd, *J* = 15.3, 10.8 Hz, 1H), 5.74 (dd, *J* = 15.3, 6.0 Hz, 1H), 4.43 (q, *J* = 5.8 Hz, 1H), 3.85 – 3.74 (m, 1H), 3.73 – 3.66 (m, 1H), 2.05 (bs, 1H), 1.91 – 1.78 (m, 1H), 1.76 – 1.67 (m, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2, 136.9, 127.2, 108.9, 72.1, 60.1, 39.5, 25.0 (3C), 18.3, -4.3, -4.9. HRMS (TOF ES$^+$): Exact mass calculated for $C_{13}H_{25}O_2Si^{79}BrNa$ [*M*+Na]$^+$: 343.0704, found 343.0711.

(*Z*)-hex-3-en-1-yltriphenylphosphonium iodide (9).



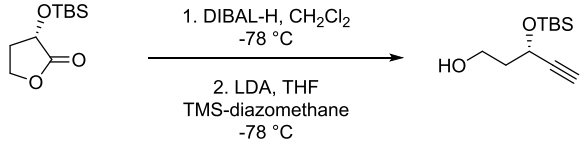
The Wittig salt **9** was prepared in 2 steps from commercially available (Z)-hex-3-en-1-ol (**16**) as previously reported,[7-8] in 90% overall yield (4.20 g). All spectroscopic and physical data were in agreement with those reported in the literature.[8] ^{1}H NMR (400 MHz, DMSO) δ 7.96 – 7.71 (m, 15H), 5.49 – 5.31 (m, 2H), 3.66 (ddd, *J* = 16.1, 8.1, 5.2 Hz, 2H), 2.29 (tt, *J* = 10.2, 5.9 Hz, 2H), 1.85 (p, *J* = 7.4 Hz, 2H), 0.85 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO) δ 134.9 (d, $^{4'}J_{CP}$ = 3.1 Hz, 3C), 133.6 (d, $^{3'}J_{CP}$ = 10.2 Hz, 6C), 133.5 (d, $^{4'}J_{CP}$ = 1.4 Hz), 130.2 (d, $^{3'}J_{CP}$ = 12.4 Hz, 6C), 125.9 (d, $^{3'}J_{CP}$ = 16.6 Hz), 118.4 (d, $^{1'}J_{CP}$ = 85.7 Hz, 3C), 20.4 (d, $^{1'}J_{CP}$ = 48.3 Hz), 20.0, 19.7 (d, $^{2'}J_{CP}$ = 3.4 Hz), 13.8.

(*S*)-3-((*tert*-Butyldimethylsilyl)oxy)dihydrofuran-2(3H)-one (13).



According to the procedure of Corey and coworkers,[9] the alcohol **10** was protected with a TBS-group. All spectroscopic and physical data were in full agreement with those reported in the literature.[10] Yield: g (97%); $[\alpha]_D^{20}$ = -31 (c = 0.15, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 – 4.32 (m, 2H), 4.21 – 4.12 (m, 1H), 2.49 – 2.39 (m, 1H), 2.27 – 2.12 (m, 1H), 0.89 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0, 68.3, 64.8, 32.4, 25.7, 18.3, -4.6, -5.2.

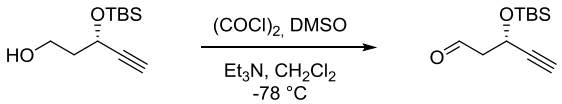
(*S*)-3-((*tert*-Butyldimethylsilyl)oxy)pent-4-yn-1-ol (14).



TBS-protected lactone **13** (1.50 g, 6.90 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (75 mL) and cooled to -78 °C. DIBAL-H (8.3 mL, 1 M in CH_2Cl_2, 8.3 mmol, 1.20 equiv.) was added dropewise and the solution was stirred until deemed complete by TLC (hexanes/EtOAc 6:4) (~2 h). The reaction was stirred for another 30 min before sat. aq. Rochelle-salt (30 mL) was added. The reaction was allowed to reach rt. The phases were separated and the aq. phase was extracted with CH_2Cl_2 (3 x 35 mL) and the combined organic layers were dried ($MgSO_4$), before it was concentrated *in vacuo*. The crude lactol was azetroped twise with 2-Me-THF before being dissolved in THF (18 mL).

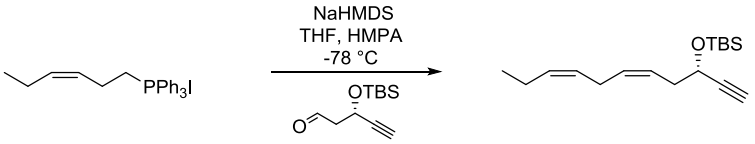
LDA (16.6 mL, 1 M in THF/hexanes) was diluted with THF (20 mL) and cooled to -78 °C. TMS-diazomethane (4.14 mL, 2 M in Et_2O) was added and the reaction was stirred for 30 min. The crude lactol was added as quickly as possible without warming the reaction too much and stirred for another 2 h. The cooling bath was removed and the reaction was slowly allowed to reach rt and then stirred 30 min. The solution was quenched with sat. NH_4Cl (20 mL) (slowly at the beginning!). The phases were separated and the aq. phase was extracted with Et_2O (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$), before being concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 8:2) to afford the title compound **14** as a colourless oil. Yield: 0.63 g (57%); Spectroscopic and physical data were agreement with those reported in the literature.[11] TLC (hexanes/EtOAc 8:2, $KMnO_4$ stain): R_f = 0.21; $[\alpha]_D^{20}$ = -55 (c = 0.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (ddd, *J* = 7.0, 5.1, 2.1 Hz, 1H), 3.89 (ddd, *J* = 11.8, 7.6, 4.2 Hz, 1H), 3.75 (ddd, *J* = 10.9, 6.1, 4.5 Hz, 1H), 2.47 (bs, 1H), 2.42 (d, *J* = 2.1 Hz, 1H), 2.02 – 1.82 (m, 2H), 0.88 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 84.8, 73.2, 61.8, 59.8, 40.2, 25.8 (3C), 18.2, -4.5, -5.1.

(*S*)-3-((*tert*-Butyldimethylsilyl)oxy)pent-4-ynal (15).



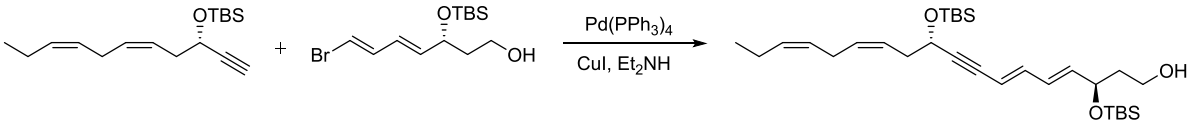
Oxalyl chloride (0.83 mL, 9.68 mmol, 1.10 equiv.) in CH_2Cl_2 (21.0 mL) was added dropwise to a solution of DMSO (1.42 mL, 20.00 mmol, 2.30 equiv.) in CH_2Cl_2 (10.6 mL) at -78 °C. After 15 min, the alcohol **14** (1.87 g, 8.73 mmol, 1.00 equiv.) in CH_2Cl_2 (10.6 mL) was added and the stirring was continued for 20 min at -78 °C before the temperature was raised to -40 °C. After 45 min, the temperature was lowered to -78 °C again, and Et_3N (6.13 mL) was added. The reaction was allowed to reach rt before it was diluted with water (15 mL), extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), before being concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 95:5) to afford the title compound **15** as a yellow oil. Yield: 1.57 g (85%); Spectroscopic and physical data were in full agreement with those reported in the literature.[12] TLC (hexanes/EtOAc 95:5, $KMnO_4$ stain): R_f = 0.17; $[\alpha]_D^{20}$ = -58 (c =0.20, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.82 (t, *J* = 2.1 Hz, 1H), 4.86 (ddd, *J* = 6.9, 5.0, 2.2 Hz, 1H), 2.80 (ddd, *J* = 16.4, 6.8, 2.2 Hz, 1H), 2.69 (ddd, *J* = 16.4, 5.0, 2.0 Hz, 1H), 2.49 (d, *J* = 2.2 Hz, 1H), 0.88 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 83.9, 73.9, 58.2, 51.5, 25.8 (3C), 18.2, -4.5, -5.1.

***tert*-Butyldimethyl(((*S*,5*Z*,8*Z*)-undeca-5,8-dien-1-yn-3-yl)oxy)silane (6).**



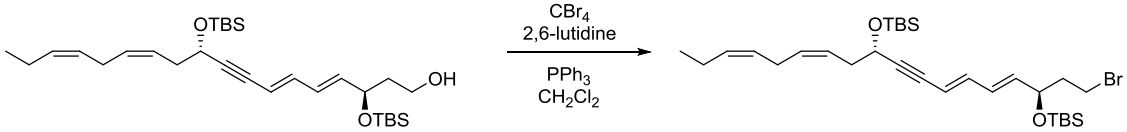
To the Wittig salt **9** (2.80 g, 5.93 mmol, 1.05 equiv.) in THF (53 mL) was added HMPA (8 mL) before NaHMDS (9.9 mL, 0.6 M in toluene, 1.05 equiv.) was slowly added at -78 °C, and then stirred for 5 min at 0 °C. Aldehyde **15** (1.20 g, 5.65 mmol, 1.00 equiv.) was added at -78 °C. The solution was allowed to slowly warm up to room temperature in the dry ice/aceton bath over 20 h before it was quenched with phosphate buffer (20 mL, pH = 7.2). Et_2O (25 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 25 mL) and the combined organic layers were dried (Na_2SO_4), before being concentrated *in vacuo.* The crude product was purified by column chromatography on silica (hexanes/EtOAc 95:5) to afford the title compound **6** as a yellow oil. Less then 5% of the undesired *E*-isomer was obtained as determeined by GLC. Yield: 1.30 g (83%); TLC (hexanes/EtOAc 95:5, $KMnO_4$ stain): R_f = 0.64; $[\alpha]_D^{20}$ = -22 (c =0.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 – 5.43 (m, 2H), 5.42 – 5.26 (m, 2H), 4.40 – 4.31 (m, 1H), 2.81 (t, *J* = 6.5 Hz, 2H), 2.47 (t, *J* = 6.3 Hz, 2H), 2.39 (d, *J* = 1.3 Hz, 1H), 2.07 (p, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.2, 131.1, 127.2, 124.7, 85.5, 72.3, 62.9, 36.8, 26.0, 25.9 (3C), 20.7, 18.4, 14.4, -4.5, -4.9. HRMS (TOF ES$^+$): Exact mass calculated for $C_{17}H_{30}O_1SiNa$ [*M*+Na]$^+$: 301.1963, found 301.1967.

(3*R*,4*E*,6*E*,10*S*,12*Z*,15*Z*)-3,10-*bis*((*tert*-Butyldimethylsilyl)oxy)octadeca-4,6,12,15-tetraen-8-yn-1-ol (21).



To a solution of vinyl bromide **7** (241 mg, 0.75 mmol, 1.00 equiv.) in Et_2NH (3.3 mL) and benzene (0.6 mL), $Pd(PPh_3)_4$ (26 mg, 0,02 mmol, 3 mol%) was added and the reaction was stirred for 45 min in the dark. CuI (7 mg, 0.04 mmol, 5 mol%) in a minimum amount of Et_2NH was added followed by dropwise addition of alkyne **6** (208 mg, 0,75 mmol, 1.00 equiv.) in Et_2NH (1.5 mL). After 20 h of stirring at ambient temperature, the reaction was quenched by addition of saturated NH_4Cl (20 mL). Et_2O (15 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 20 mL) and the combined organic layers were dried (Na_2SO_4), before being concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 8:2) to afford the title compound **21** as a yellow oil. Yield: 276 mg (71%); TLC (hexanes/EtOAc 8:2, $KMnO_4$ stain): R_f = 0.32; $[\alpha]_D^{20}$ = +12 (c =0.10, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.55 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.24 (dd, *J* = 15.2, 10.9 Hz, 1H), 5.80 (dd, *J* = 15.2, 6.1 Hz, 1H), 5.62 (dd, *J* = 15.5, 1.2 Hz, 1H), 5.55 – 5.46 (m, 2H), 5.46 – 5.28 (m, 2H), 4.55 – 4.44 (m, 2H), 3.89 – 3.75 (m, 1H), 3.79 – 3.67 (m, 1H), 2.83 (t, *J* = 5.9 Hz, 2H), 2.49 (t, *J* = 6.2 Hz, 2H), 2.09 (p, *J* = 7.0 Hz, 2H), 1.92 – 1.81 (m, 1H), 1.80 – 1.68 (m, 1H), 0.93 (s, 3H), 0.92 (s, 18H), 0.16 (s, 3H), 0.14 (s, 3H), 0.11 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 138.4, 132.2, 131.0, 129.2, 127.2, 124.9, 111.2, 93.7, 83.5, 72.4, 63.6, 60.2, 39.6, 36.9, 26.0 (7C), 20.7, 18.4, 18.3, 14.4, -4.2, -4.3, -4.8, -4.8. HRMS (TOF ES$^+$): Exact mass calculated for $C_{30}H_{54}O_3Si_2Na$ [*M*+Na]$^+$: 541.3509, found 541.3516.

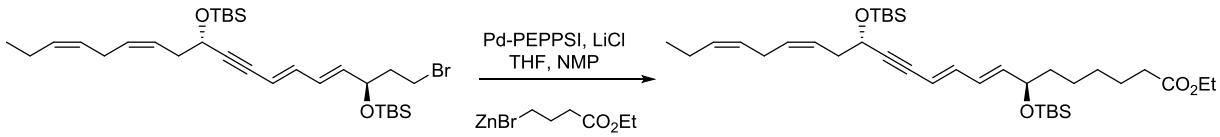
(5*R*,6*E*,8*E*,12*S*)-5-(2-Bromoethyl)-2,2,3,3,14,14,15,15-octamethyl-12-((2*Z*,5*Z*)-octa-2,5-dien-1-yl)-4,13-dioxa-3,14-disilahexadeca-6,8-dien-10-yne (22).



Alchohol **21** (140 mg, 0.27 mmol, 1.00 equiv.) and CBr_4 (134 mg, 0.40 mmol, 1.5 equiv.) was dissolved in CH_2Cl_2 (8 mL) and the reaction was cooled to -10 °C. 2,6-Lutidine (0.3 mL, 0.27 mmol, 1.00 equiv.) was added. Next, PPh_3 (106 mg, 0,40 mmol, 1.50 equiv.) was dissolved in CH_2Cl_2 (1.5 mL) and this solution was added dropwise to the reaction mixture over 15 min. The solution was stirred for another 4 h before it was washed through a plug of silica. Further purification by column chromatography on silica (first pure hexane to get rid of any remaing CBr_4, then hexanes/EtOAc 95:5) afforded the title

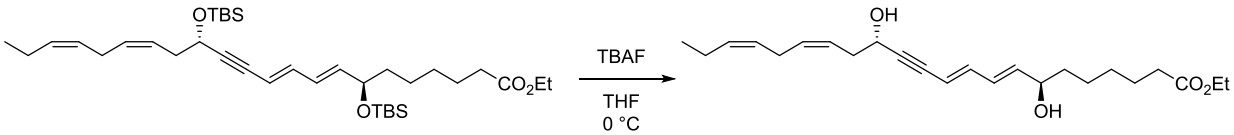
compound **22** as a yellow oil. Yield: 152 mg (97%); TLC (hexanes/EtOAc 9:1, $KMnO_4$ stain): R_f = 0.80; $[\alpha]_D^{20}$ = -19 (c =0.10, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.51 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.21 (dd, *J* = 15.2, 11.0 Hz, 1H), 5.71 (dd, *J* = 15.2, 6.5 Hz, 1H), 5.61 (dd, *J* = 15.7, 1.5 Hz, 1H), 5.54 – 5.42 (m, 2H), 5.41 – 5.25 (m, 2H), 4.49 (td, *J* = 6.5, 1.8 Hz, 1H), 4.40 – 4.30 (m, 2H), 3.52 – 3.35 (m, 2H), 2.81 (t, *J* = 6.0 Hz, 2H), 2.47 (t, *J* = 6.1 Hz, 2H), 2.12 – 1.89 (m, 3H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.91 (s, 7H), 0.89 (s, 8H), 0.14 (s, 3H), 0.11 (s, 2H), 0.08 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 138.1, 132.2, 131.0, 129.5, 127.2, 124.9, 111.4, 93.7, 83.4, 71.0, 63.6, 41.1, 36.9, 30.0, 26.0 (3C), 26.0 (3C), 26.0, 20.7, 18.4, 18.3, 14.4, -4.1, -4.3, -4.7, -4.8. HRMS (TOF ES$^+$): Exact mass calculated for $C_{30}H_{54}O_3Si_2Na$ $[M+Na]^+$: 541.3509, found 541.3516.

Ethyl (7*R*,8*E*,10*E*,14*S*,16*Z*,19*Z*)-7,14-*bis*((*tert*-butyldimethylsilyl)oxy)docosa-8,10,16,19-tetraen-12-ynoate (23).



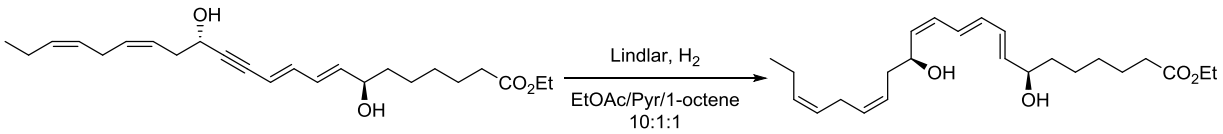
A solution of LiCl (1.75 mL, 0.5 M in THF, 0.88 mmol) and NMP (0.6 mL) was added to Pd-PEPPSI^{TM}-IPr (**24**) (14.8 mg, 0.02 mmol, 8 mol%) and stirred for 10 min. 4-Ethoxy-4-oxobutylzinc bromide (**8**) (0.88 mL, 0.5 M in THF, 0.44 mmol, 1.6 equiv.) was added, followed by alkyl bromide **22** (159 mg, 0.27 mmol, 1.0 equiv.) in NMP (0.71 mL), and the solution was stirred for another 2 h at rt. The mixture was diluted with Et_2O (15 mL) and washed successively with 1 M Na_3EDTA (15 ml) and brine (10 mL). The organic layer was dried (Na_2SO_4), before it was concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 95:5) to afford the title compound **23** as a yellow oil. Yield: 115 mg (68%); TLC (hexanes/EtOAc 9:1, CAM stain): R_f = 0.36; $[\alpha]_D^{20}$ = +10 (c =0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.51 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.15 (dd, *J* = 15.4, 11.0 Hz, 1H), 5.73 (dd, *J* = 15.2, 6.2 Hz, 1H), 5.57 (dd, *J* = 15.7, 1.5 Hz, 1H), 5.51 – 5.44 (m, 2H), 5.44 – 5.25 (m, 2H), 4.48 (td, *J* = 6.6, 1.8 Hz, 1H), 4.19 – 4.05 (m, 3H), 2.86 – 2.76 (m, 2H), 2.50 – 2.43 (m, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.07 (p, *J* = 7.1 Hz, 2H), 1.67 – 1.57 (m, 2H), 1.53 – 1.40 (m, 2H), 1.36 – 1.28 (m, 4H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 6H), 0.13 (s, 3H), 0.11 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 141.3, 139.9, 132.2, 130.9, 128.5, 127.3, 125.0, 110.5, 93.3, 83.6, 72.9, 63.6, 60.3, 38.2, 36.9, 34.5, 29.3, 26.0 (3C), 26.0 (3C), 25.1, 24.9, 20.7, 18.4, 18.4, 14.4, -4.2, -4.3, -4.6, -4.8. HRMS (TOF ES$^+$): Exact mass calculated for $C_{36}H_{64}O_4Si_2Na$ $[M+Na]^+$: 639.4240, found 639.4237.

Ethyl (7*R*,8*E*,10*E*,14*S*,16*Z*,19*Z*)-7,14-dihydroxydocosa-8,10,16,19-tetraen-12-ynoate (25).



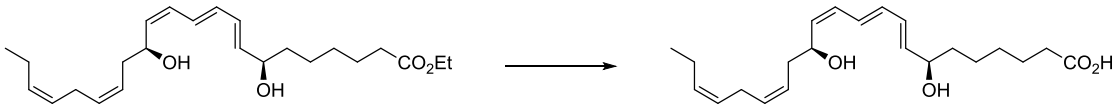
TBAF (0.93 mL 1.0 M in THF, 0.93 mmol, 5.0 equiv.) was added to a solution of TBS-protected alcohol **23** (115 mg, 0.19 mmol, 1.0 equiv.) in THF (5.0 mL) at 0 °C. The reaction was stirred for 20 h before it was quenched with phosphate buffer (pH = 7.2, 3.0 mL). Brine (5 ml) and CH_2Cl_2 (10 ml) were added and the phases were separated. The aq. phase was extracted with CH_2Cl_2 (2 x 10 ml) and the combined organic layer was dried (Na_2SO_4) before being concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 1:1) to afford the title compound **25** as a pale yellow oil. Yield: 70 mg (97%); TLC (hexanes/EtOAc 1:1, $KMnO_4$ stain): R_f = 0.30; $[\alpha]_D^{20}$ = -39 (c = 0.14, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.24 (dd, *J* = 15.4, 10.8 Hz, 1H), 5.78 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.65 – 5.25 (m, 5H), 4.61 – 4.46 (m, 1H), 4.23 – 4.05 (m, 3H), 2.83 (t, *J* = 7.0 Hz, 2H), 2.53 (t, *J* = 6.5 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.07 (p, *J* = 7.4 Hz, 2H), 2.00 (s, 1H), 1.98 (s, 1H), 1.69 – 1.47 (m, 4H), 1.46 – 1.28 (m, 4H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 141.4, 138.9, 132.4, 132.3, 129.2, 126.7, 123.6, 110.7, 92.3, 84.0, 72.2, 62.5, 60.2, 37.0, 35.7, 34.2, 29.0, 25.8, 25.0, 24.8, 20.6, 14.2, 14.2. HRMS (TOF ES$^+$): Exact mass calculated for $C_{24}H_{36}O_4Na$ $[M+Na]^+$: 411.2511, found 411.2520.

Ethyl (7*R*,8*E*,10*E*,12*Z*,14*S*,16*Z*,19*Z*)-7,14-dihydroxydocosa-8,10,12,16,19-pentaenoate (26).



To a solution of alkyne **25** (30 mg, 0.077 mmol) in EtOAc/pyridine/1-octene (0.90 mL, 10:1:1) under argon, Lindlar's catalyst (35 mg) was added and the flask was evacuated and filled with argon. The reaction was stirred for 5.5 h at ambient temperature under a balloon of hydrogen gas until completion. The reaction mixture was loaded directly onto a silica gel column and purified by chromatography (toluene/Et_2O/EtOAc 60:35:5) to afford the title compound **26** as a pale oil. Yield: 23 mg (77%); HPLC analysis (Eclipse XDB-C18, MeOH/H_2O 78:22, 1.3 mL/min, t_r = 9.56 min. TLC (Hexane/EtOAc/CH_2Cl_2/MeOH 57.5:30:10:2.5, CAM stain): R_f = 0.24; $[\alpha]_D^{20}$ = -34 (c = 0.05, MeOH); UV (MeOH) λ_{max} 262, 272, 282 nm. ^{1}H NMR (400 MHz, MeOD) δ 6.58 – 6.46 (m, 1H), 6.34 – 6.19 (m, 2H), 6.08 (t, *J* = 11.1 Hz, 1H), 5.72 (dd, *J* = 14.0, 6.7 Hz, 1H), 5.51 – 5.26 (m, 5H), 4.63 – 4.53 (m, 1H), 4.14 – 4.05 (m, 3H), 2.80 (t, *J* = 6.5 Hz, 2H), 2.44 – 2.33 (m, 1H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.27 – 2.19 (m, 1H), 2.08 (p, *J* = 7.4 Hz, 2H), 1.66 – 1.28 (m, 8H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, MeOD) δ 175.5, 138.6, 135.0, 134.8, 132.8, 131.3, 131.3, 130.6, 128.8, 128.2, 126.1, 73.1, 68.5, 61.4, 38.2, 36.5, 35.0, 30.1, 26.6, 26.2, 26.0, 21.5, 14.7, 14.6. HRMS (TOF ES$^+$): Exact mass calculated for $C_{24}H_{38}O_4Na$ [*M*+Na]$^+$: 413.2667, found 413.2677.

MaR1$_{n\text{-}3\ DPA}$ (5).



To a solution of ethyl ester **26** (10 mg, 0.03 mmol, 1.0 equiv.) in THF/MeOH/H_2O (2/2/1, 3.5 mL), solid LiOH (21.5 mg, 0.90 mmol, 35 equiv.) was added at 0 °C. The mixture was stirred at 0 °C for 3 h and then allowed to warm up to room temperature. The solution was acidified with aq. sat. NaH_2PO_4 (4 mL) and then EtOAc (4 mL) was added. The layers were separated and the water phase was extracted with EtOAc (2 x 4 mL). The combined organic layer was dried (Na_2SO_4) before being concentrated *in vacuo.* The crude product was purified by column chromatography on silica (CH_2Cl_2/MeOH 95:5) to afford the title compound **5** as a colorless oil. The chemical purity (>98%) was determined by HPLC analysis (Eclipse XDB-C18, MeOH/10.0 mM HCO_2H/H_2O 70:10:20, 1.0 mL/min): t_r = 9.28 min. Yield: 8 mg (86%); TLC (CH_2Cl_2/MeOH 95:5, CAM stain): R_f = 0.11; $[\alpha]_D^{20}$ = -87 (c = 0,14 MeOH); UV (MeOH) λ_{max} 261, 270, 281 nm. IR (neat) υ = cm^{-1}. ^{1}H NMR (400 MHz, MeOD) δ 6.60 – 6.42 (m, 1H), 6.32 – 6.21 (m, 2H), 6.08 (t, *J* = 10.9 Hz, 1H), 5.73 (dd, *J* = 13.9, 6.7 Hz, 1H), 5.48 – 5.26 (m, 5H), 4.63 – 4.49 (m, 1H), 4.08 (q, *J* = 6.5 Hz, 1H), 2.80 (t, *J* = 6.5 Hz, 2H), 2.44 – 2.35 (m, 1H), 2.31 – 2.18 (m, 3H), 2.08 (p, *J* = 7.3 Hz, 2H), 1.66 – 1.32 (m, 8H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, MeOD) δ 178.1, 138.6, 135.1, 134.7, 132.8, 131.3, 131.2, 130.6, 128.7, 128.2, 126.1, 73.1, 68.5, 38.2, 36.5, 35.3, 30.2, 26.6, 26.3, 26.2, 21.5, 14.7. HRMS (TOF ES$^+$): Exact mass calculated for $C_{22}H_{34}O_4Na$ [*M*+Na]$^+$: 385.2354, found 385.2363.

Human macrophage efferocytosis *in vitro*

Human apoptotic PMN were obtained by density-gradient Ficoll-Histopaque from human peripheral blood. Blood was obtained from healthy human volunteers giving informed consent (protocol #199-P-001297 approved by the Partners Human Research Committee). PMN were labeled with Bisbenzimide H 33342 (Sigma-Aldrich), a fluorescent nuclear dye (10 µg/mL, 30 min, 37 °C) and cultured overnight (5x10^6 cells/mL in PBS$^{+/+}$). Human macrophages were seeded in 96 well plates (5 x 104 cells/well) and incubated with vehicle (PBS containing 0.1% ethanol) or indicated concentrations (10^{-12} to 10^{-8} M) of MaR1 (**4**), MaR1$_{n\text{-}3\ DPA}$ (**5**) or MaR1$_{n\text{-}3\ DPA}$ ethyl ester (**25**) (PBS+/+, 37 °C, 15 min). Fluorescently labeled apoptotic PMN (1.5 x 105 cells/well) were added and cells incubated for additional 45 min at 37 °C. Non-phagocytosed apoptotic PMN were then washed, extracellular florescence quenched and phagocytosis quantified. Results are percent increase over vehicle and expressed as mean ± s.e.m. n = 4 with 3 – 4 determinations for each. *P <0.05, **P <0.01,***P <0.001 and ****P <0.0001 vs. vehicle; #P<0.05, ##P<0.01, ###P <0.001 vs. MaR1 (**4**). Extracellular florescence was quenched and phagocytosis assessed using SpectraMax M3 plate reader (Molecular Devices).

Matching

Human macrophage MaR1$_{n\text{-}3\ DPA}$ (**5**) matches synthetic material **5**. Representative MRM chromatograms of selected ion chromatograms (*m/*z 361-223) depicting (A) MaR1$_{n\text{-}3\ DPA}$ (**5**) obtained from human macrophages (5 x 107/mL) incubated with 0.1 mg opsonized zymosan A and n-3 DPA (1 µM, 37 °C, 30 min, DPBS+/+, pH = 7.45). n = 3 human macrophage preparations. (B) Synthetic material (inset: characteristic UV-absorption spectrum, spectrometer cutoff ~1 nm). (C) Co-injection of human macrophage MaR1$_{n\text{-}3\ DPA}$ (**5**) with synthetic material **5**. n = 3

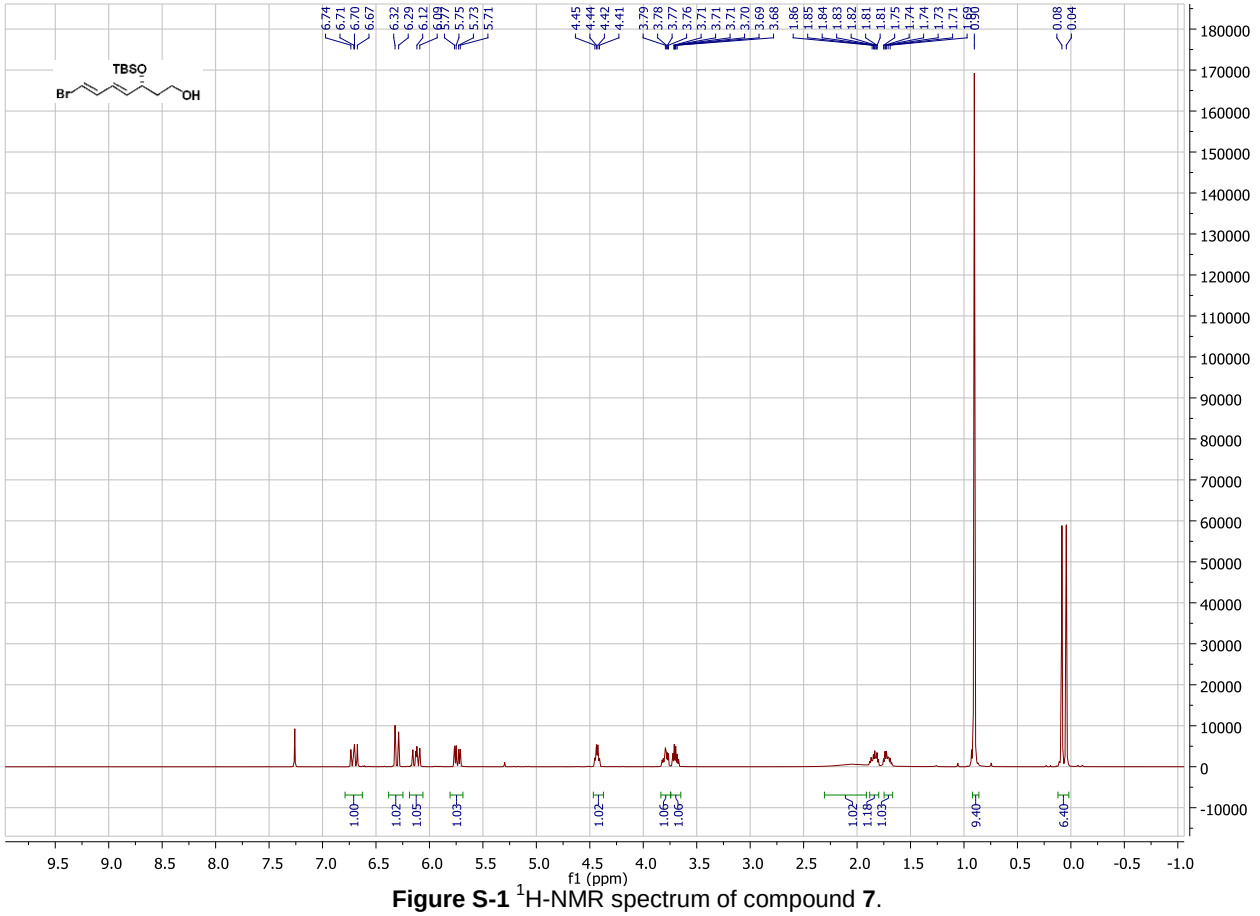


Figure S-1 ^{1}H-NMR spectrum of compound **7**.

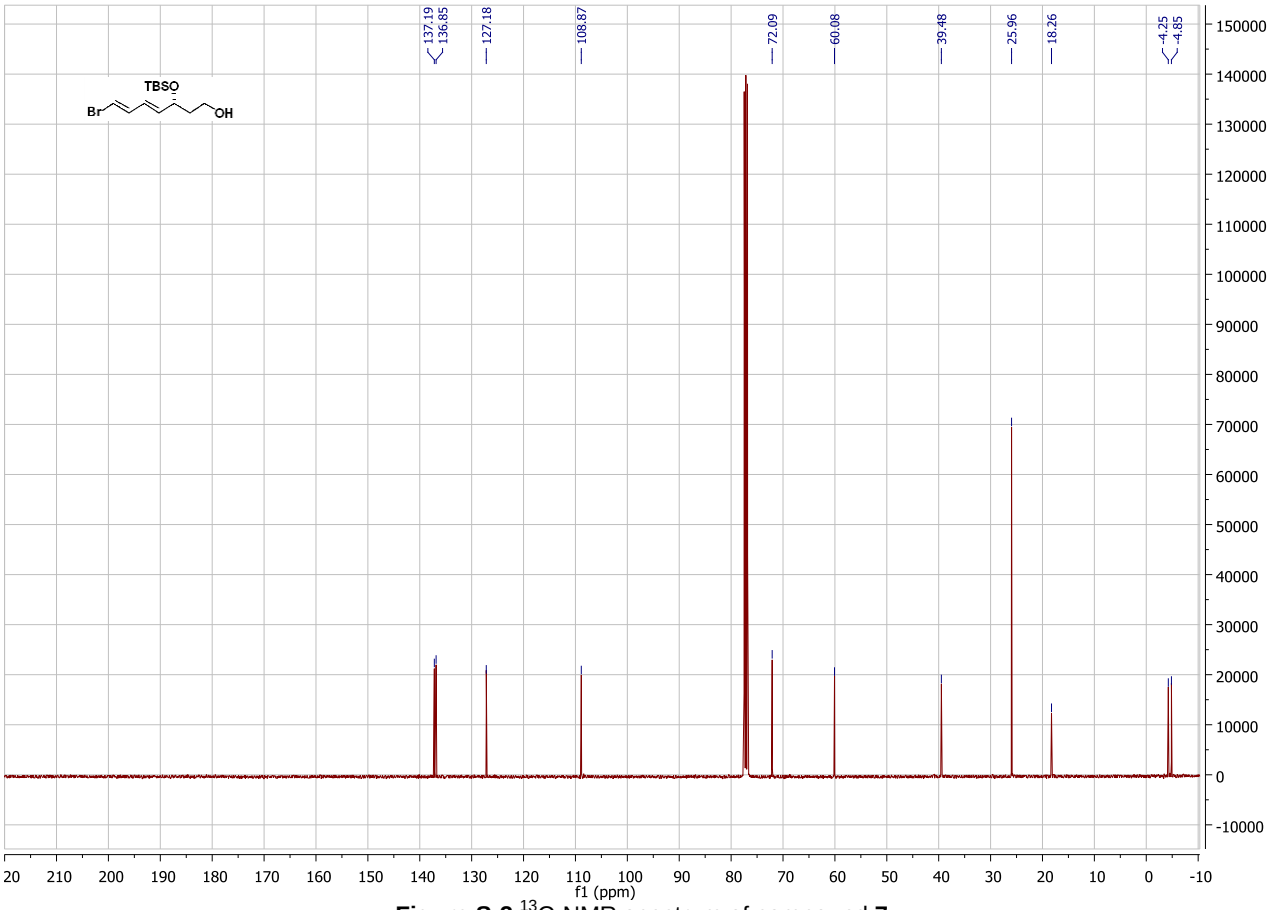


Figure S-2 ^{13}C-NMR spectrum of compound **7**.

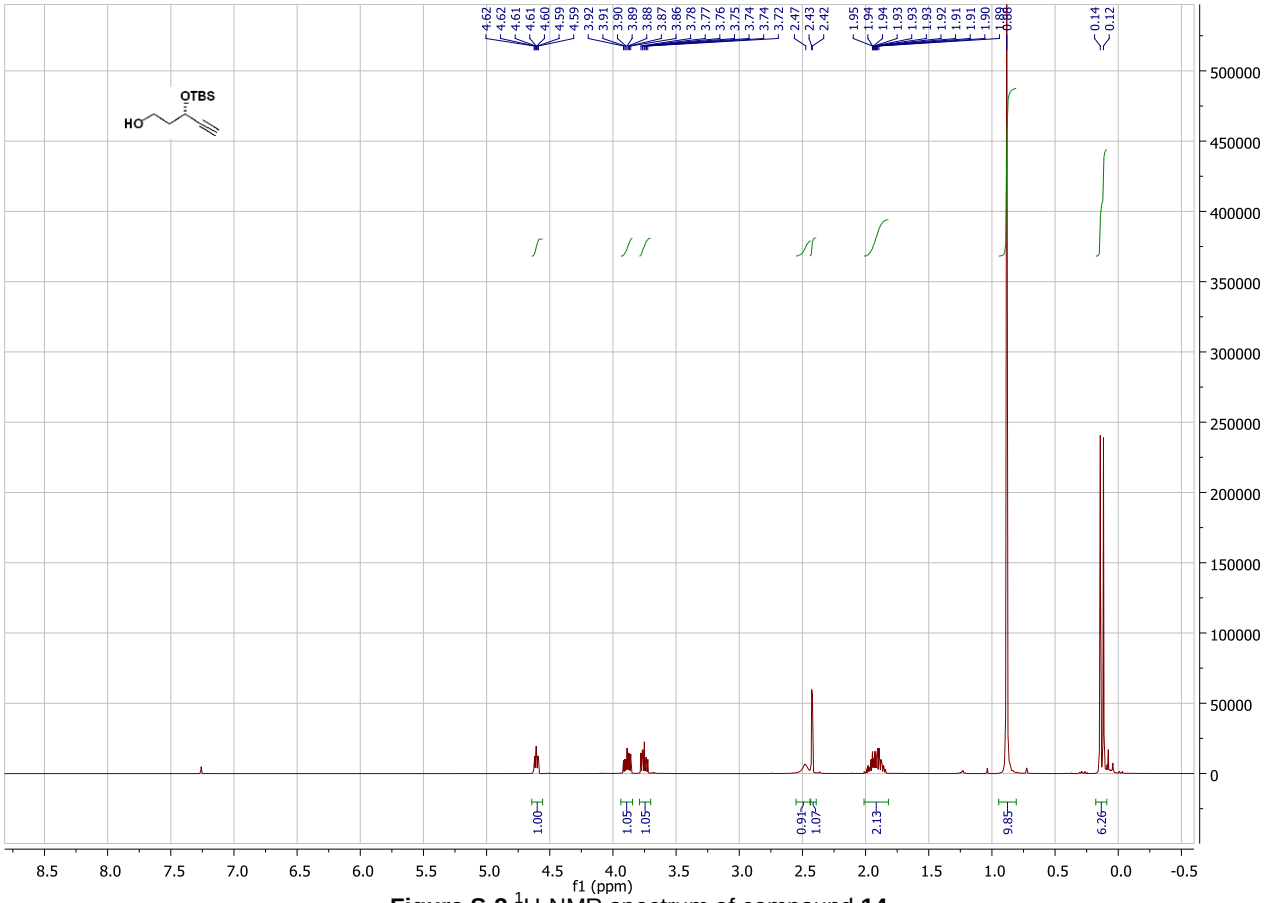


Figure S-3 ^{1}H-NMR spectrum of compound **14**.

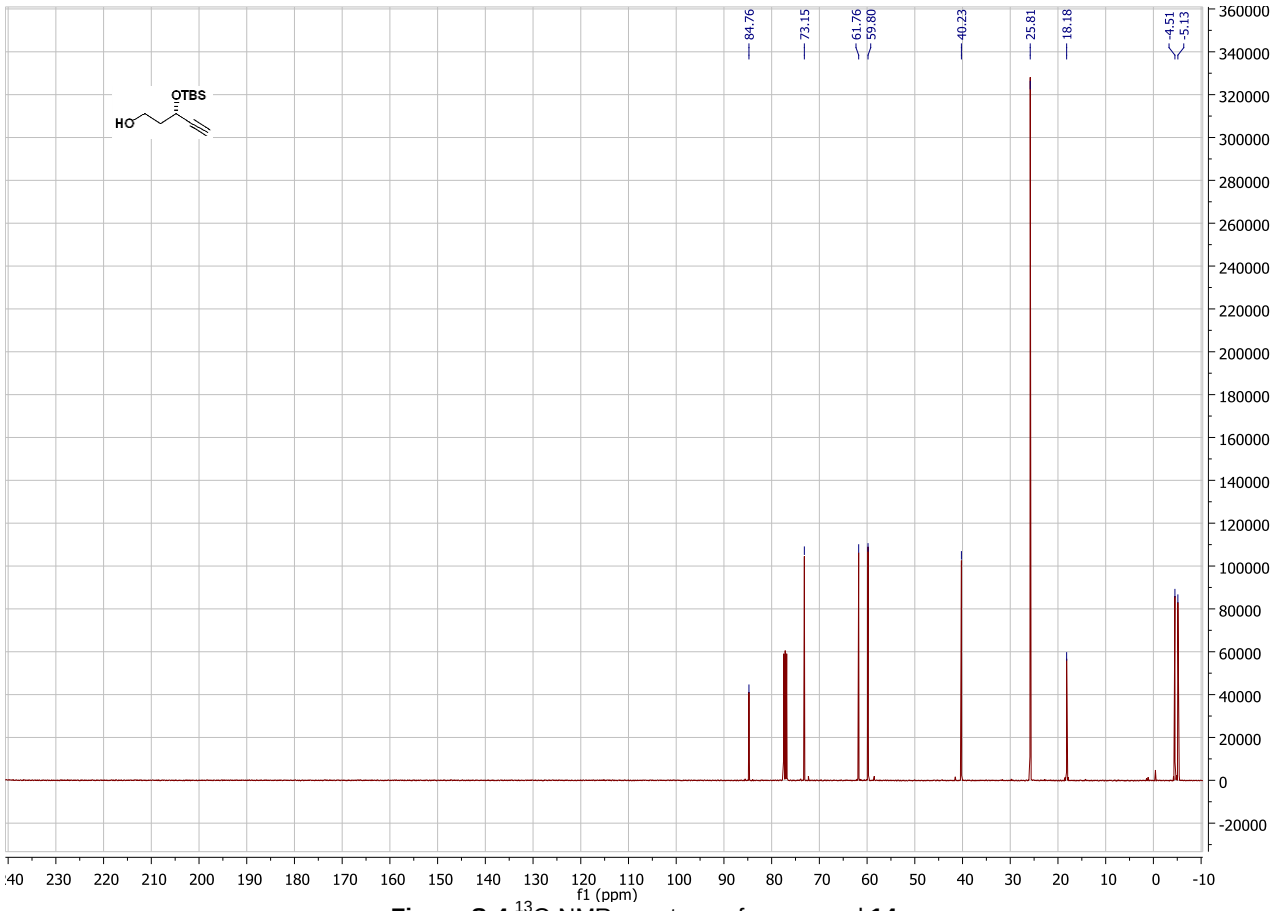


Figure S-4 ^{13}C-NMR spectrum of compound **14**.

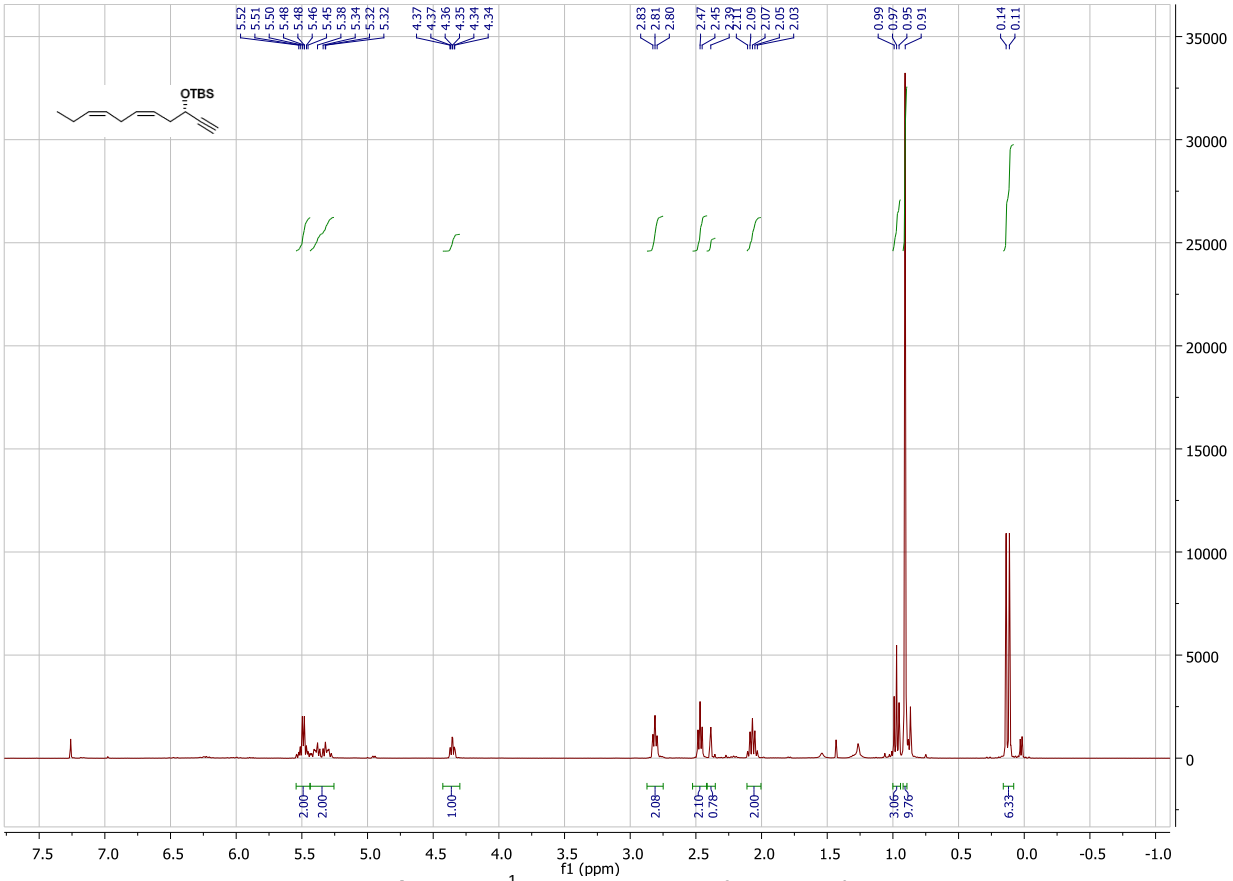


Figure S-5 ^{1}H-NMR spectrum of compound **6**.

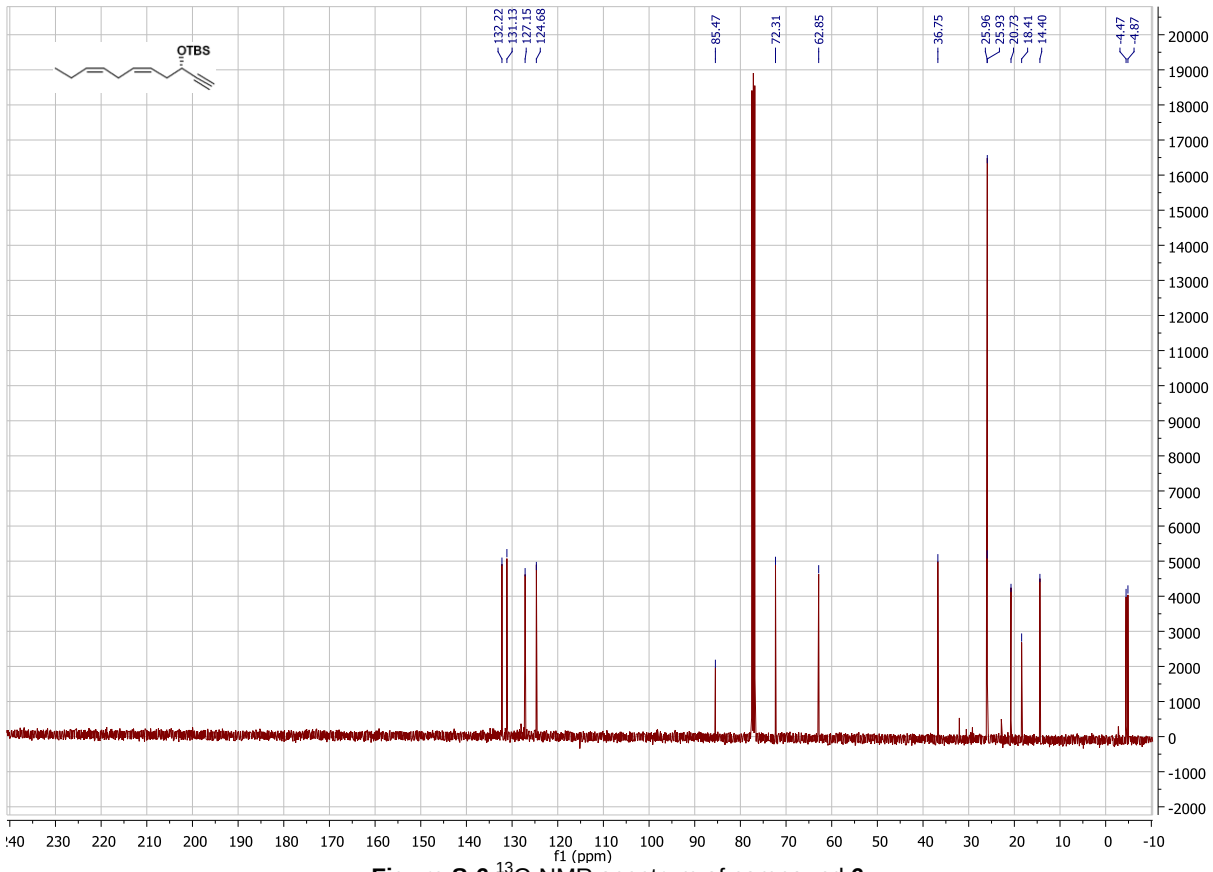


Figure S-6 ^{13}C-NMR spectrum of compound **6**.

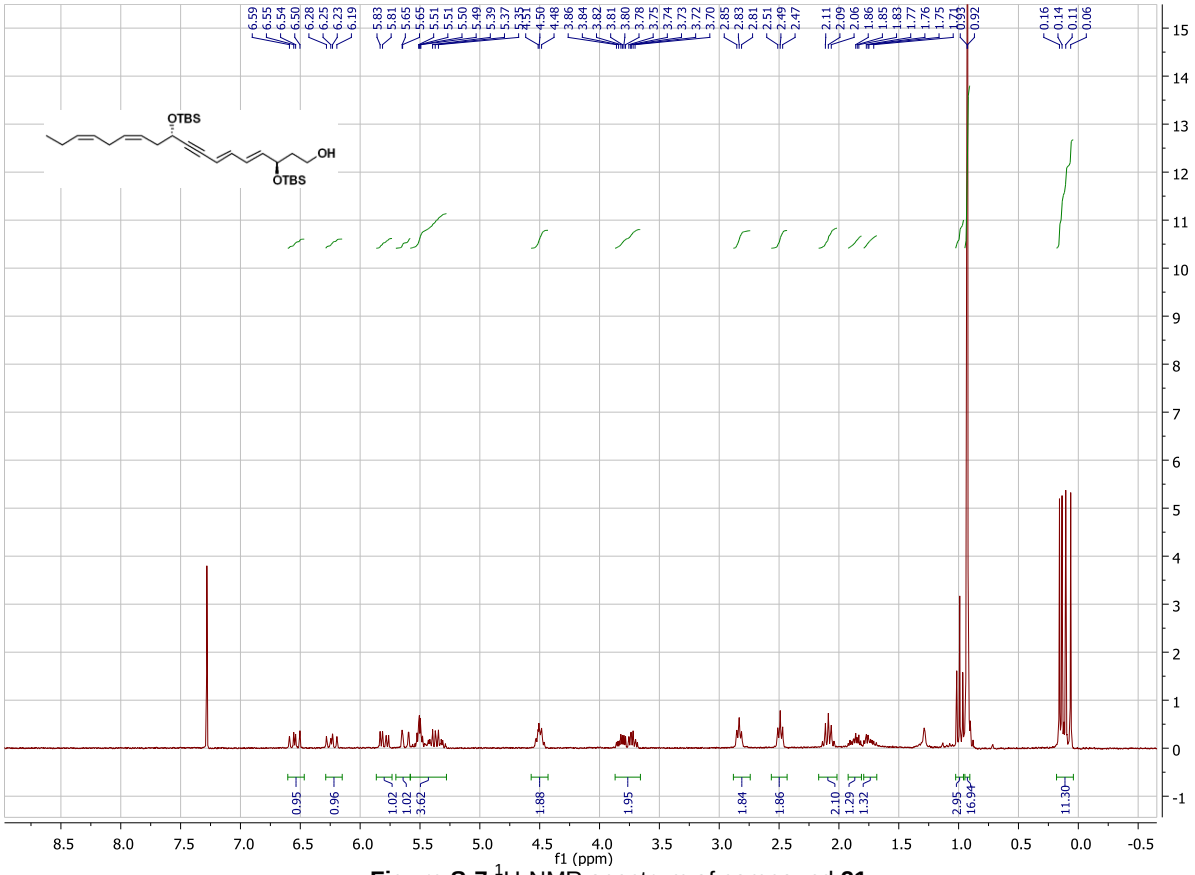


Figure S-7 ^{1}H-NMR spectrum of compound **21**.

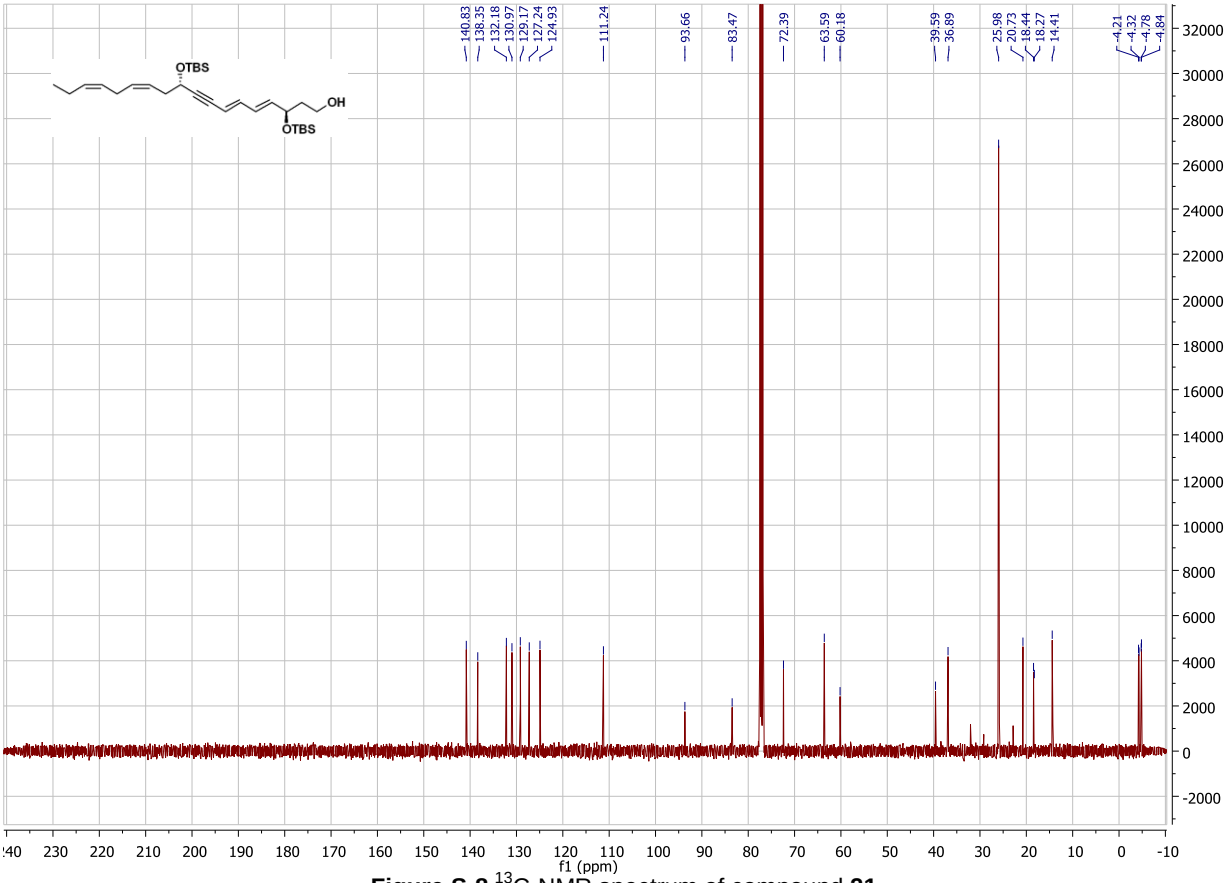


Figure S-8 ^{13}C-NMR spectrum of compound **21**.

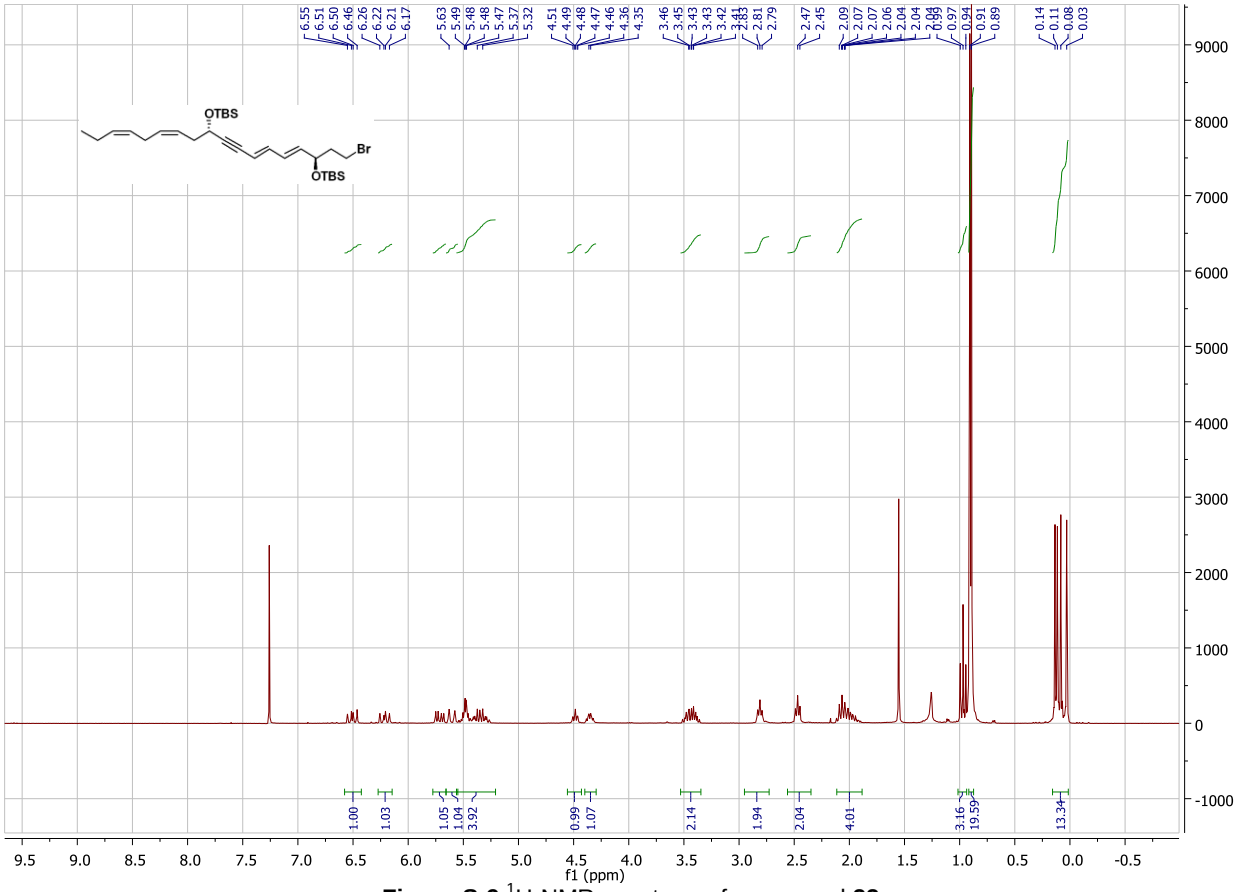


Figure S-9 ^{1}H-NMR spectrum of compound **22**.

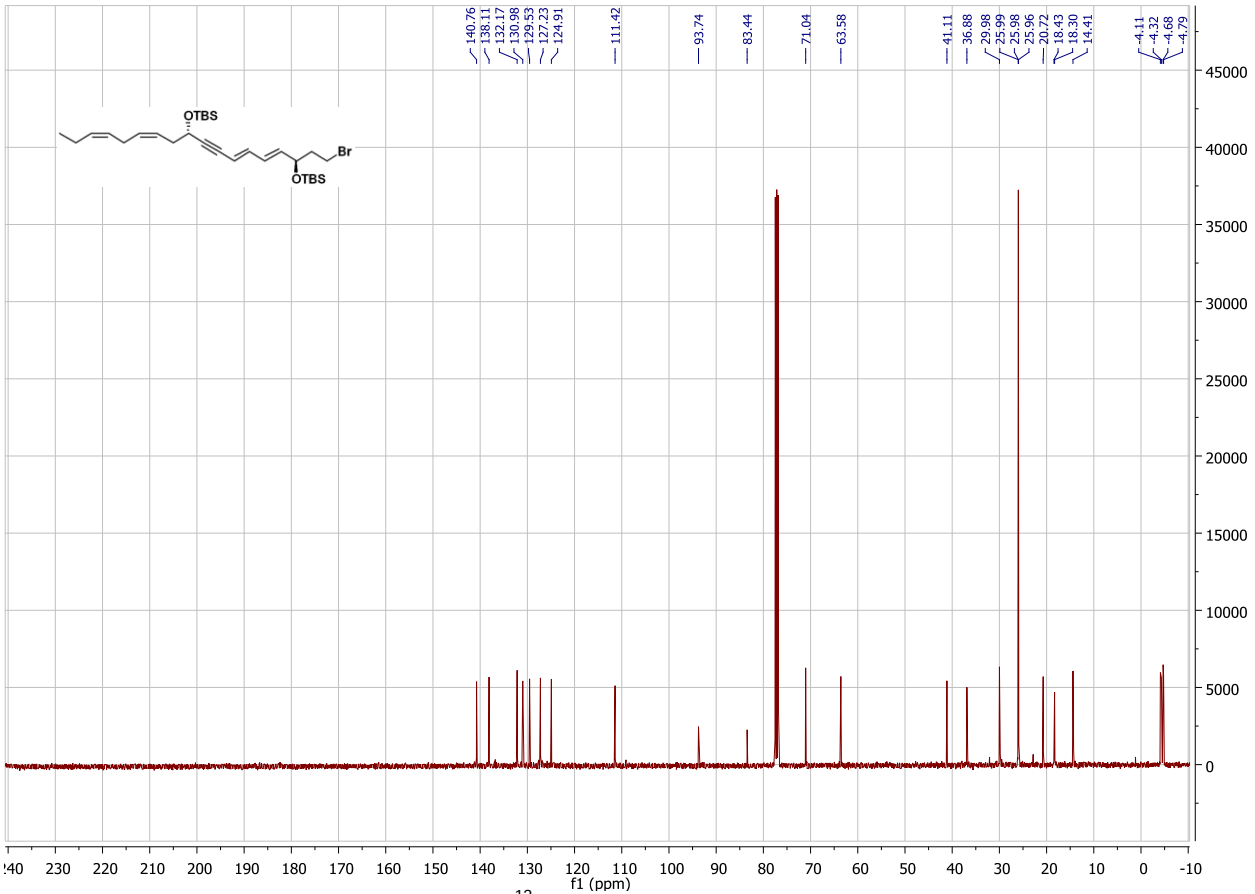


Figure S-10 ^{13}C-NMR spectrum of compound **22**.

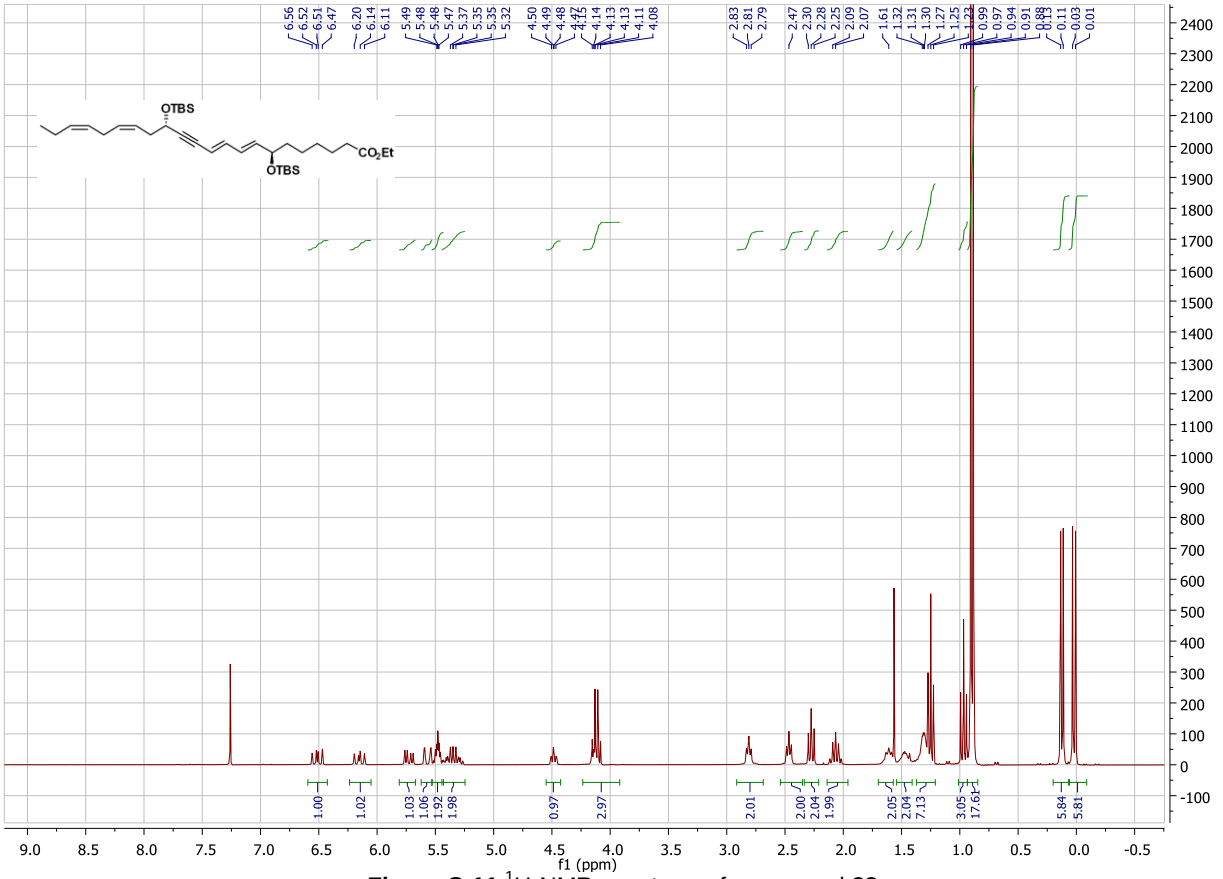


Figure S-11 ^{1}H-NMR spectrum of compound **23**.

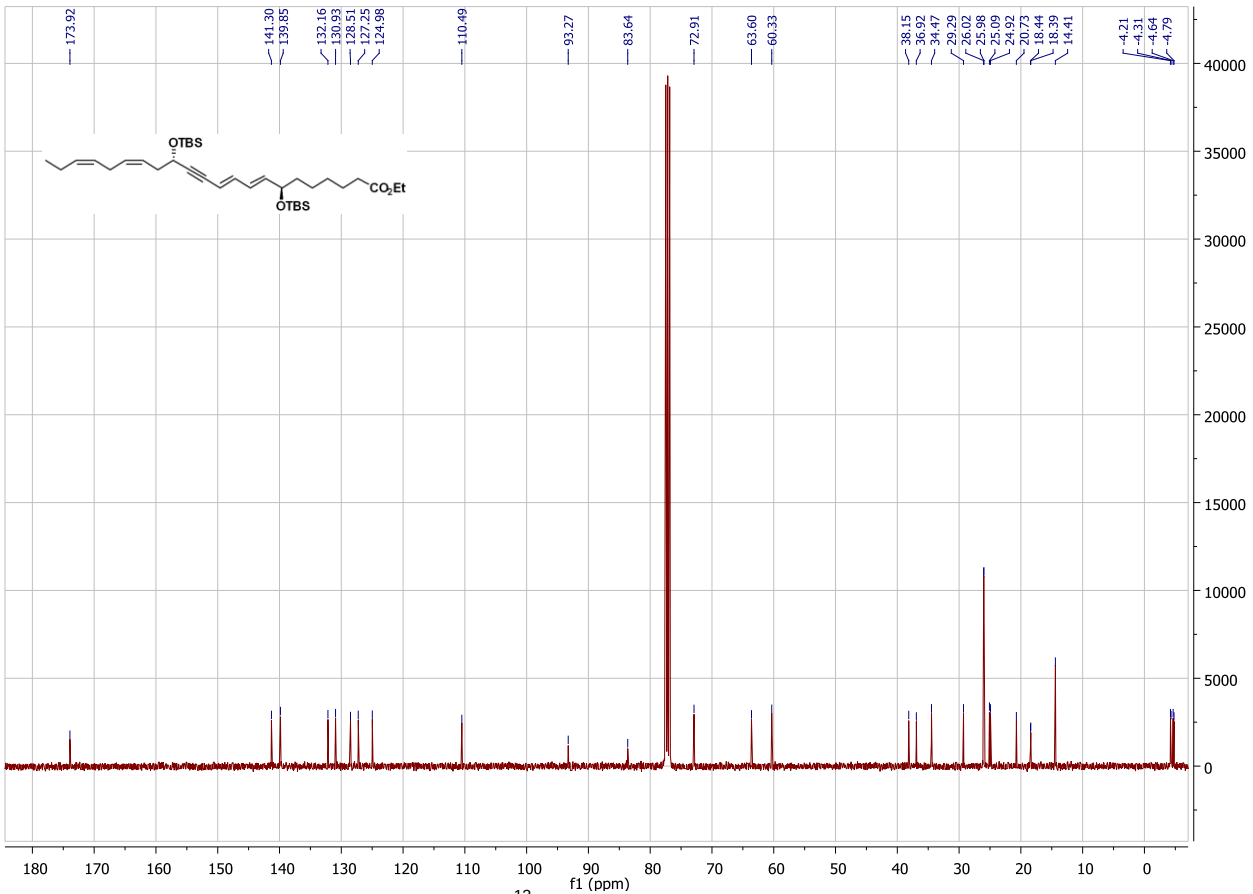


Figure S-12 ^{13}C-NMR spectrum of compound **23**.

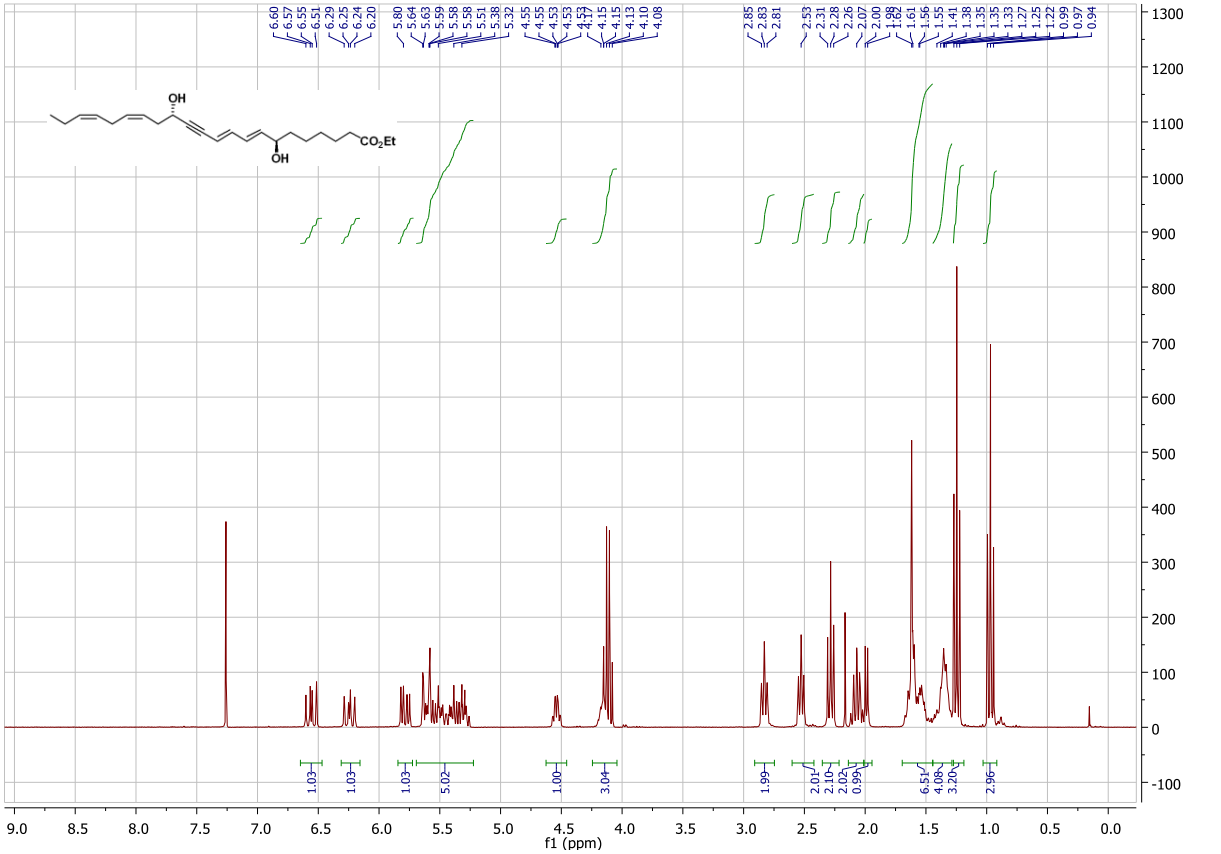


Figure S-13 ^{1}H-NMR spectrum of compound **25**.

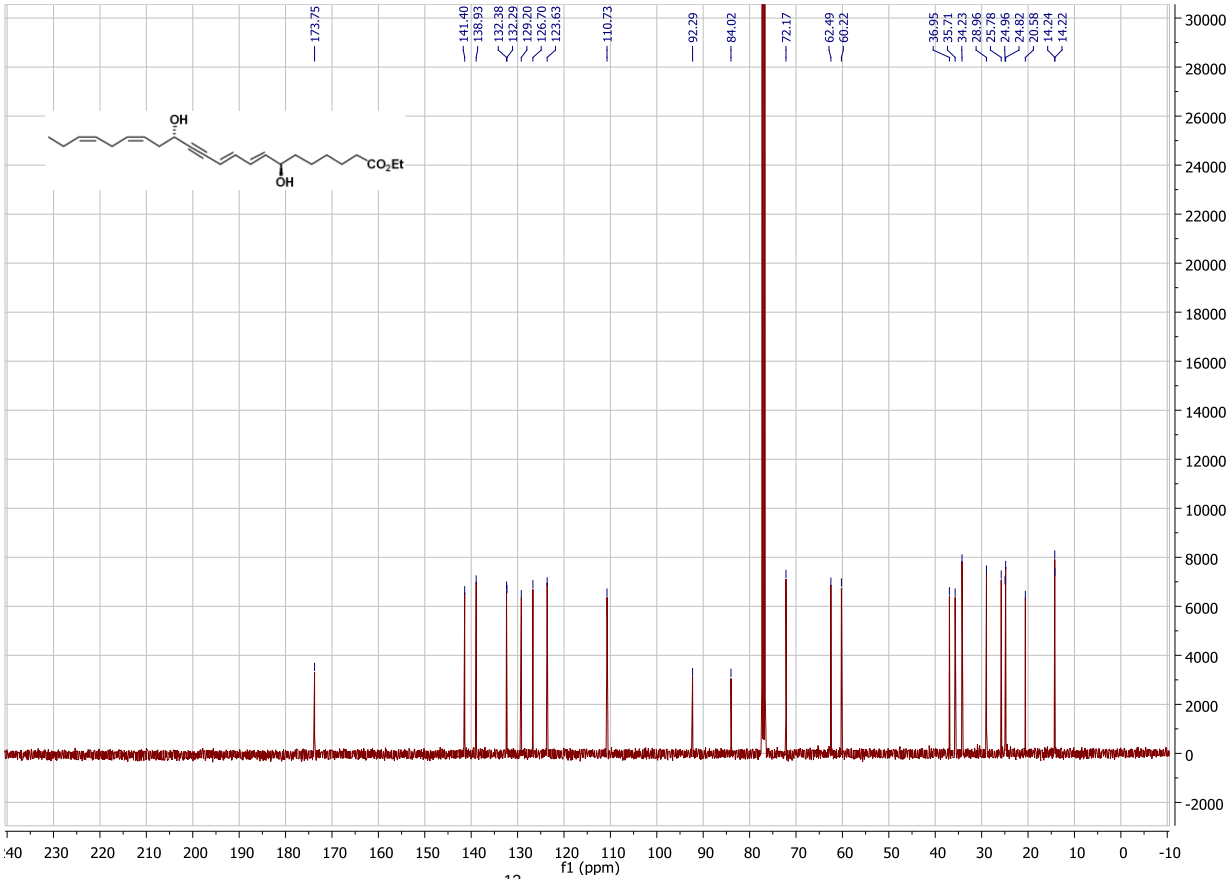


Figure S-14 ^{13}C-NMR spectrum of compound **25**.

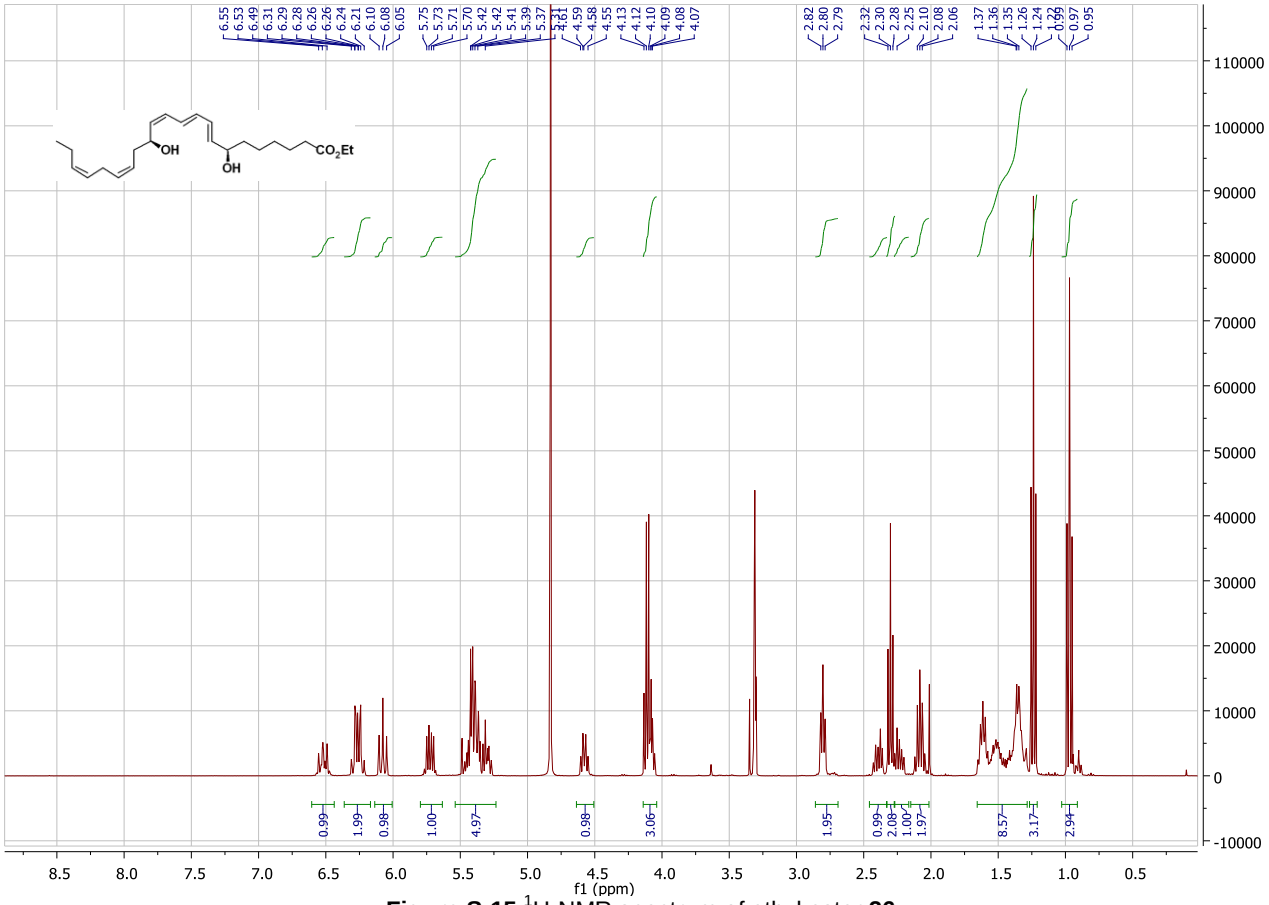


Figure S-15 ^{1}H-NMR spectrum of ethyl ester **26**.

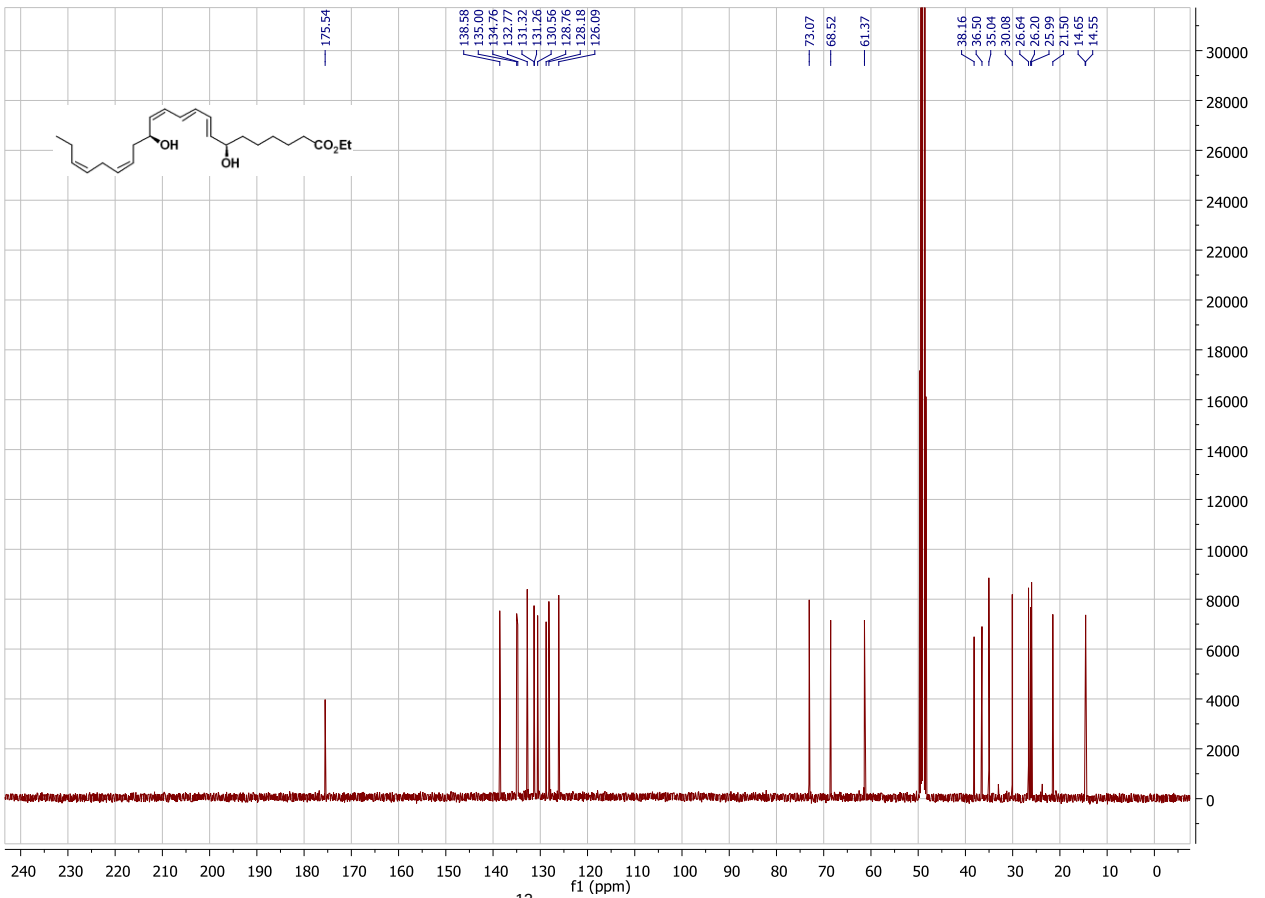


Figure S-16 ^{13}C-NMR spectrum of ethyl ester **26**.

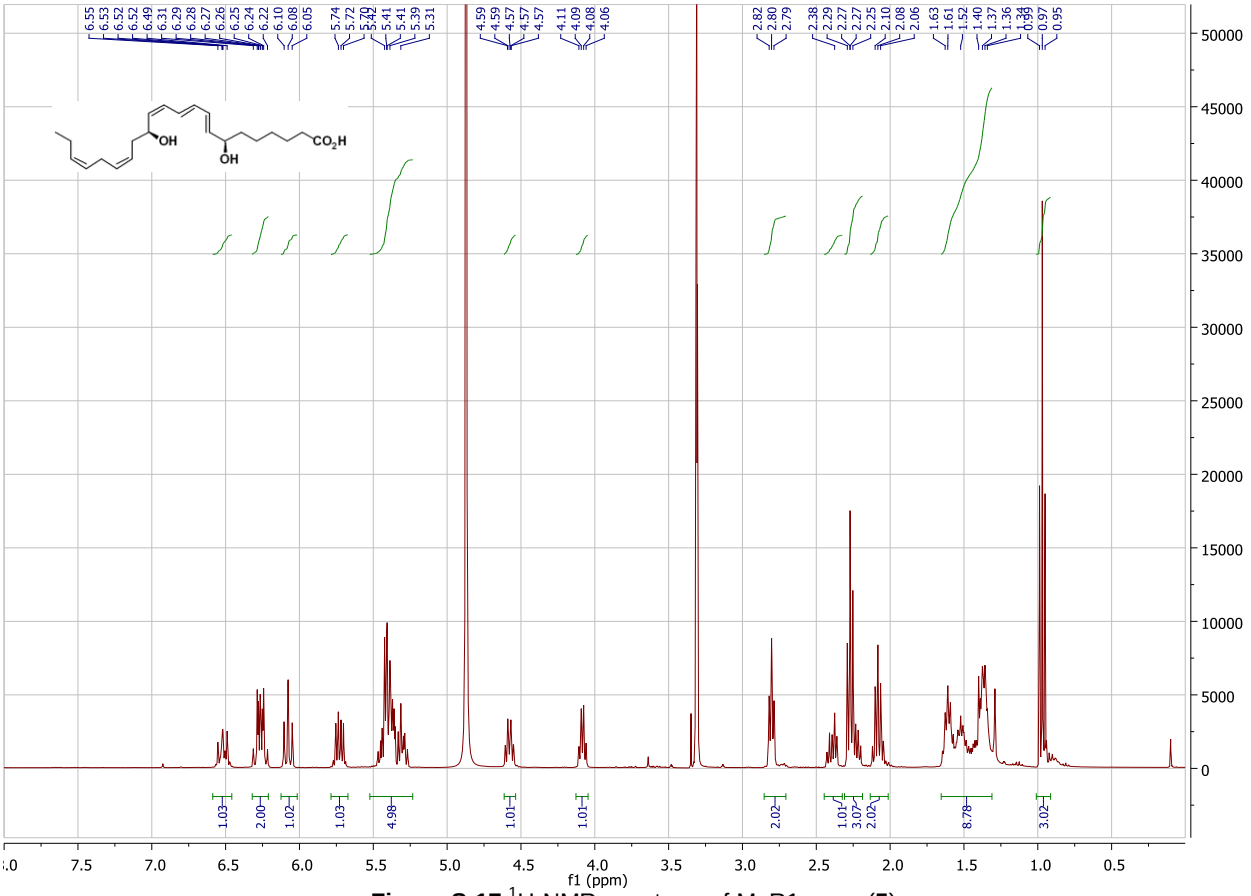


Figure S-17 ^{1}H-NMR spectrum of MaR1$_{n\text{-}3\ DPA}$ (**5**).

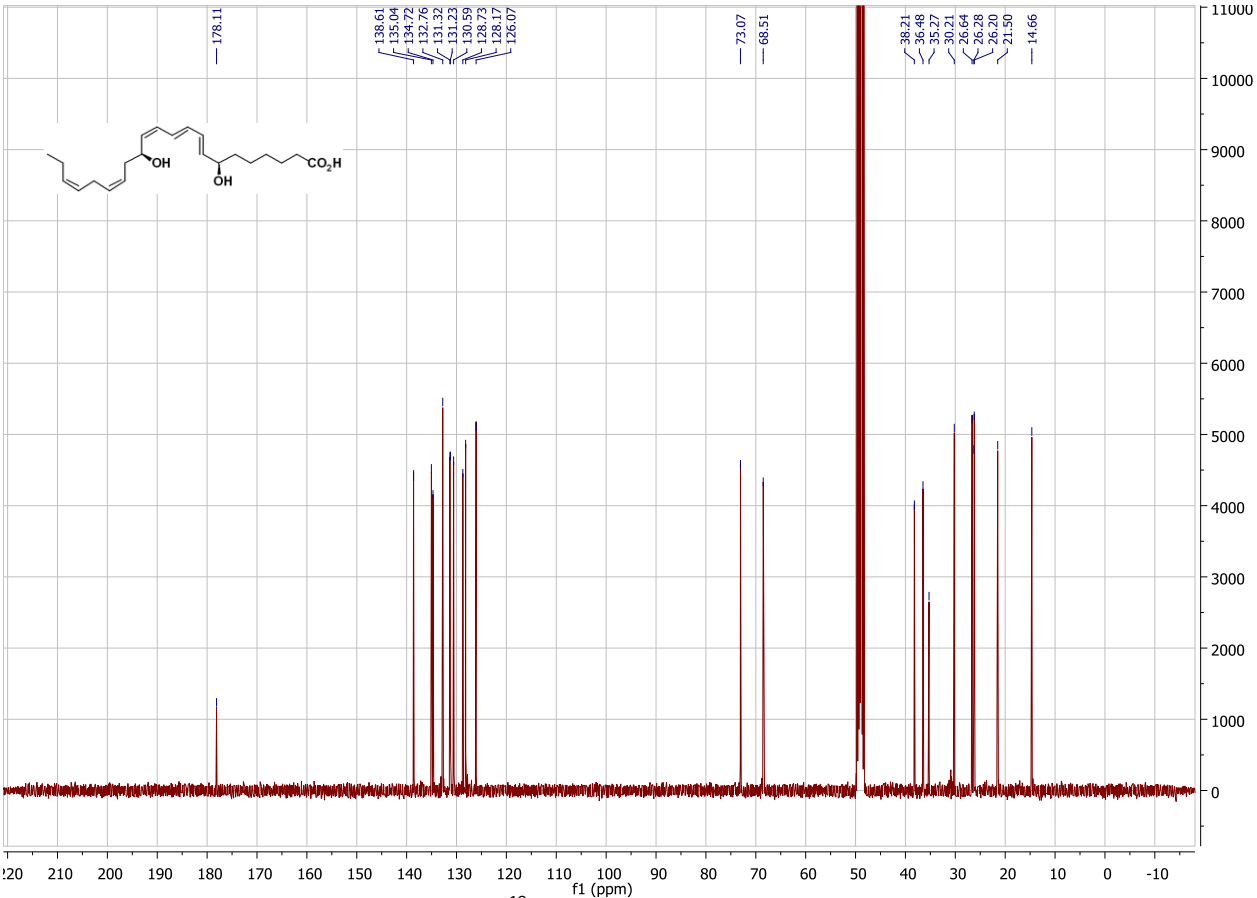


Figure S-18 ^{13}C-NMR spectrum of MaR1$_{n\text{-}3\ DPA}$ (**5**).

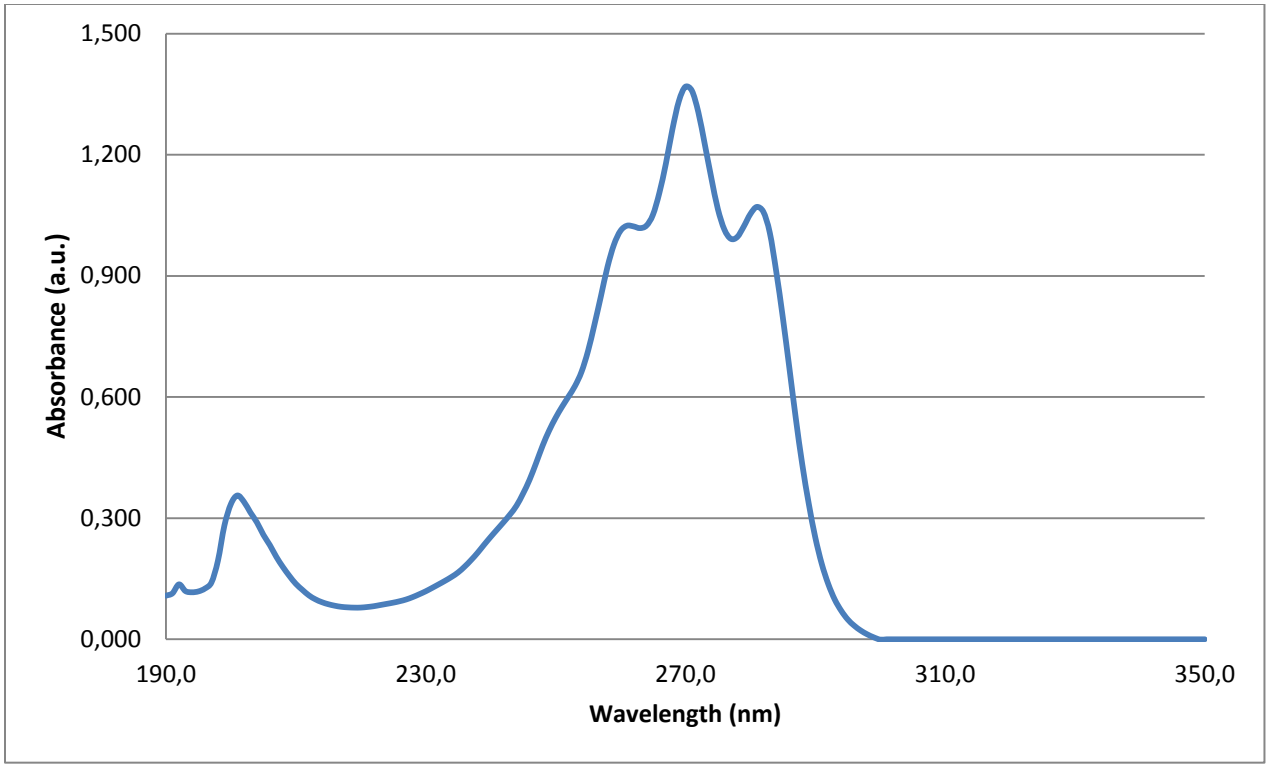


Figure S-19 UV-Vis chromatogram of ethyl ester **26**.

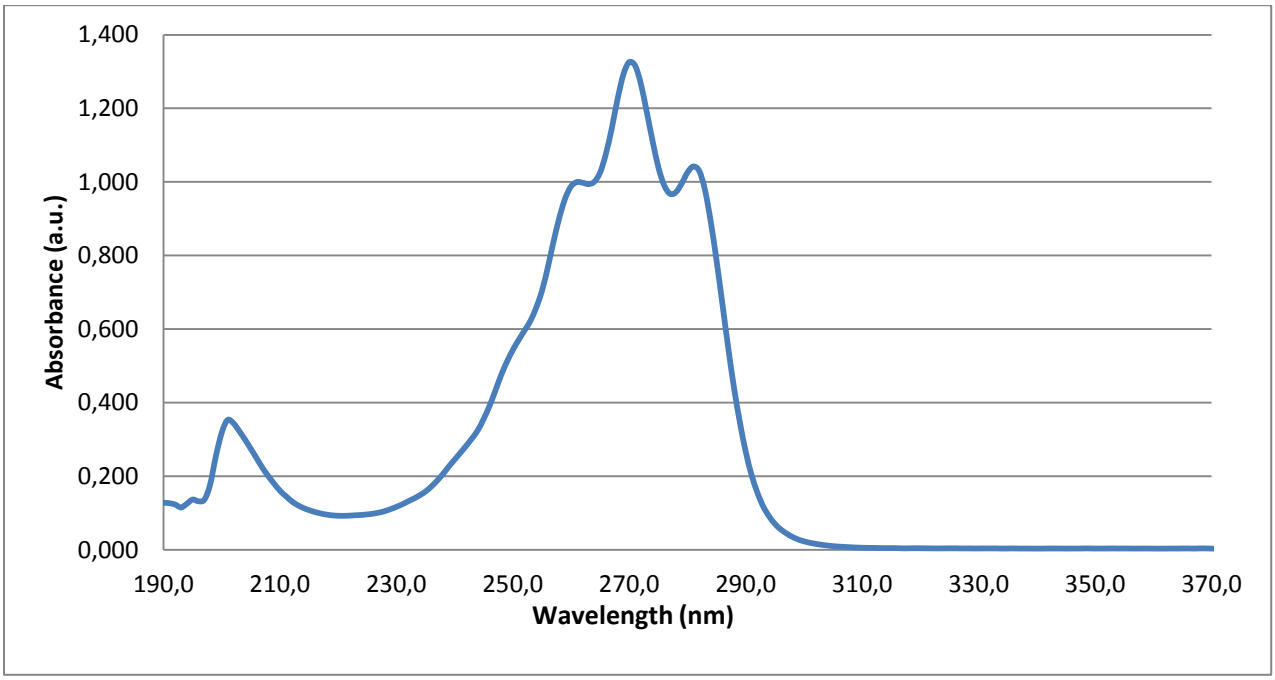
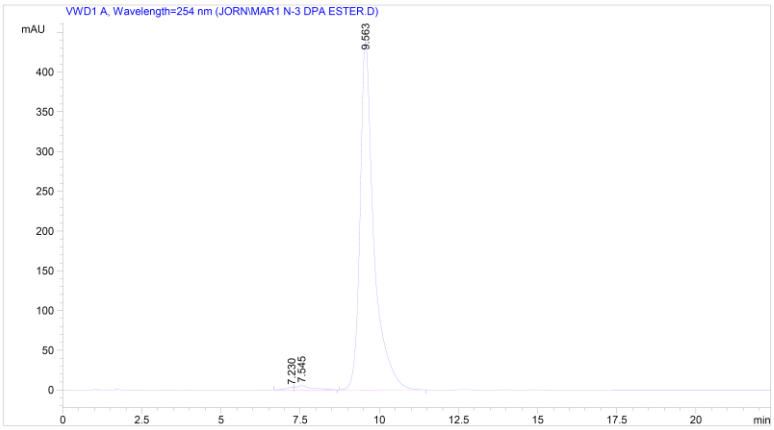


Figure S-20 UV-Vis chromatogram of MaR1$_{n\text{-}3\ DPA}$ (**5**).

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================================================================================
                            Area Percent Report
================================================================================

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Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.230 BV    0.2577   51.84959    2.96812   0.3843
   2   7.545 VB    0.4849  189.92511    5.37709   1.4076
   3   9.563 BB    0.4348 1.32514e4   439.50296  98.2082

Totals :                  1.34932e4   447.84816

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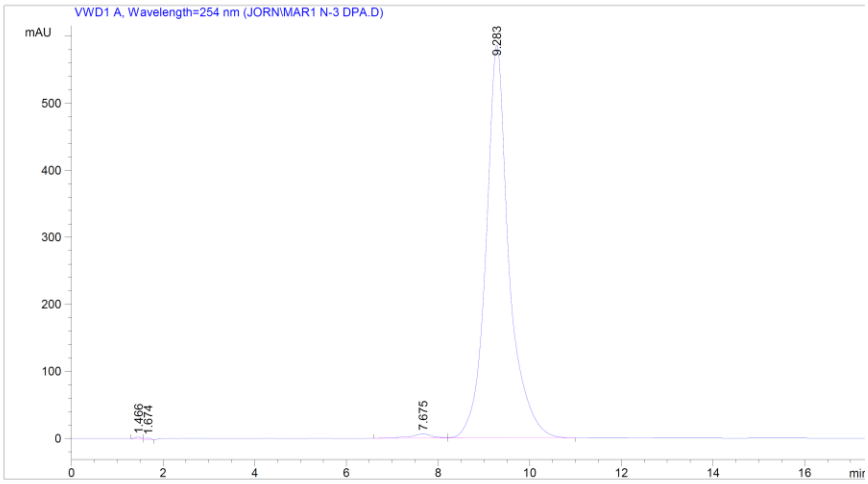
Figure S-21 HPLC chromatogram of ethyl ester **26**.

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   1.466 BV    0.1512   27.86030    2.94407   0.1350
   2   1.674 VV    0.1485   18.57285    1.81574   0.0900
   3   7.675 BV    0.4743  219.81453    6.48084   1.0650
   4   9.283 VB    0.4987 2.03737e4   586.10352  98.7100

Totals :                  2.06399e4   597.34417

================================================================================
                            *** End of Report ***
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Figure S-22 HPLC chromatogram of MaR1$_{n\text{-}3\ DPA}$ (**5**)

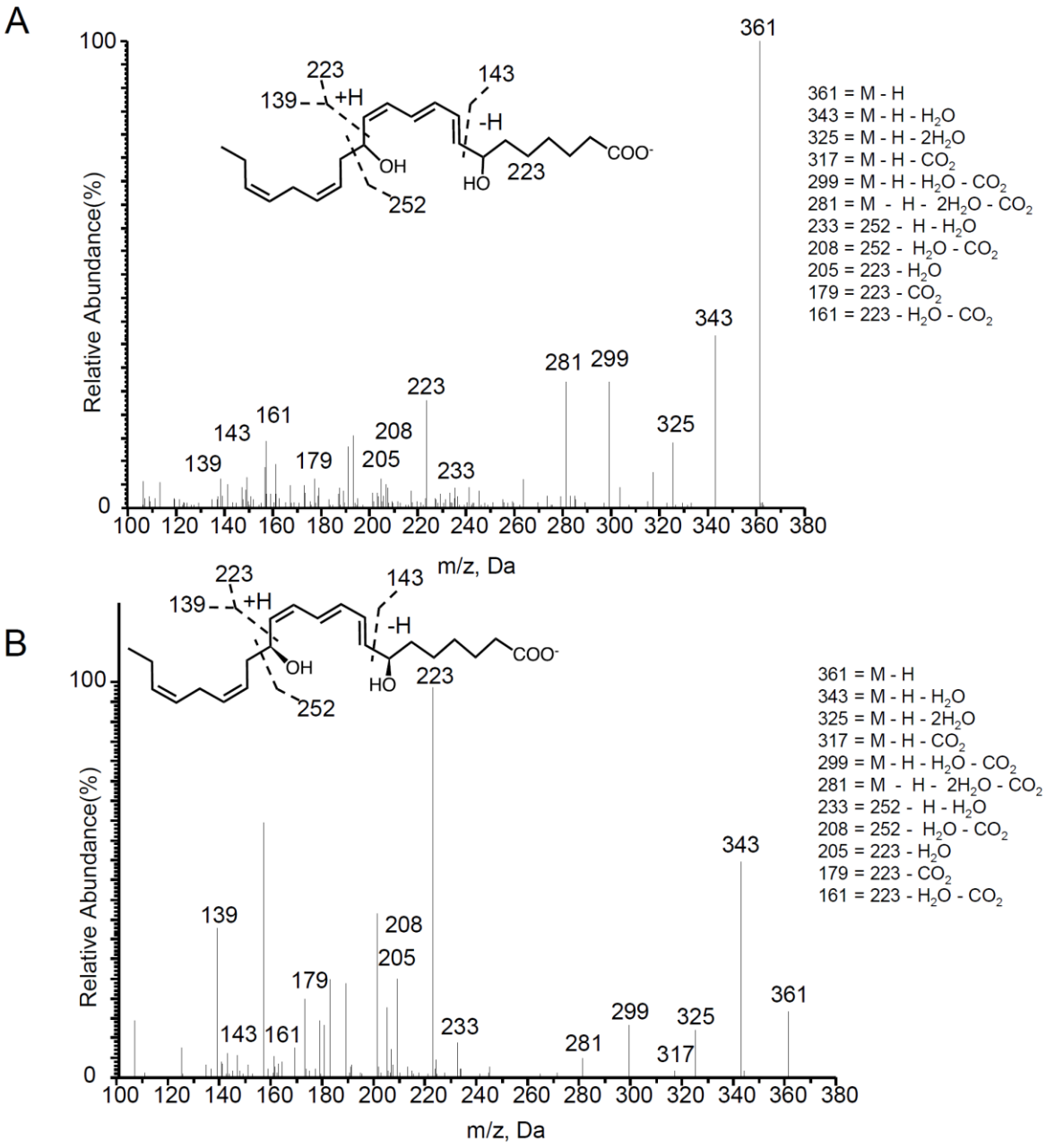

Figure S-23: Matching MS-MS spectra for human macrophage MaR1$_{n\text{-}3\ DPA}$ and synthetic material. Representative MS-MS spectra. A) human macrophage MaR1$_{n\text{-}3\ DPA}$. MS-MS spectrum for peak at T_R = ~14.1 min). n = 3 human macrophage preparations. B) MS-MS spectrum of synthetic material (T_R = ~14.1 min). d = 4.

References

1. Wernerova, M.; Hudlicky, T. *Synlett* **2010**, *18*, 2701
2. Becher, B. *Org. Synth.* **1980**, *59*, 79
3. Soullez, D; Ple, G; Duhamel, L; Duhamel, P. *J. Chem. Soc.***1997**, *11*, 1639
4. Romero-Ortega, M; Colby, D. A; Olivo, H. F. *Tetrahedron Lett.* **2002**, *43*, 6439
5. E. J. Corey, H. Cho, C. Rucker, D. H. Hua. *Tetrahedron Lett.* **1981**, *22*, 3455
6. Tello-Aburto, R; Ochoa-Teran, A; Olivo, H. F. *Tetrahedron. Lett.* **2006**, *47*, 5915
7. Detterbeck, R.; Guggisberg, A.; Popaj, K.; Hesse, M. *Helv. Chim. Acta*, **2002**, *85*, 1742
8. Kojima, K.; Koyama, K.; Amemiya, S. *Tetrahedron* **1985**, *41*, 4449
9. Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
10. Schinzer, D.; Bauer, A.; Schieber, J. *Chem. Eur. J.* **1999,** *5*, 2492
11. Takano, S.; Sugihara, T.; Ogasawara, K. *Tetrahedron Lett.* **1991**, *32*, 2797.
12. Smith, A. B. III; Ott, G. R. *J. Am. Chem. Soc*. **1998**, *120*, 3935