

Supporting information for

Total Synthesis of the Lipid Mediator PD1_{n-3} DPA: Configurational Assignments, Anti-inflammatory and Pro-resolving Actions

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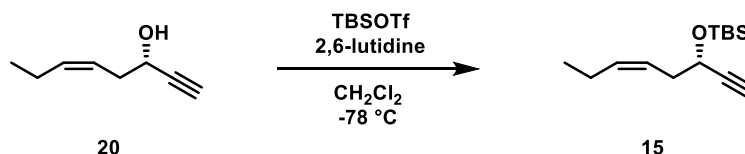
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General Information

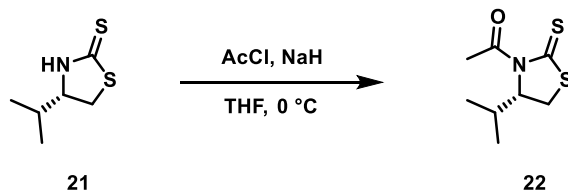
Unless stated otherwise, all commercially available reagents and solvents were used in the form they were supplied without any further purification. The stated yields are based on isolated material. Thin layer chromatography was performed on silica gel 60 F254 aluminum-backed plates fabricated by Merck. Flash column chromatography was performed on silica gel 60 (40-63 μm) produced by Merck. NMR spectra were recorded on a Bruker DRX500, Bruker AVII400 or a Bruker DPX300 spectrometer at 500 MHz, 400 MHz or 300 MHz respectively for ^1H NMR and at 126 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 ^1H NMR ($\text{CDCl}_3 = \delta$ 7.27, $\text{DMSO}-d_6 = \delta$ 2.50 and $\text{MeOH}-d_4 = \delta$ 3.31) and the central carbon solvent resonance in ^{13}C NMR ($\text{CDCl}_3 = \delta$ 77.00 ppm, $\text{DMSO}-d_6 = \delta$ 39.43 and $\text{MeOH}-d_4 = \delta$ 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 C18 stationary phase (Eclipse XDB-C18 $5\mu\text{m}$ 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.

(*S,Z*)-tert-Butyldimethyl(oct-5-en-1-yn-3-yloxy)silane (15).



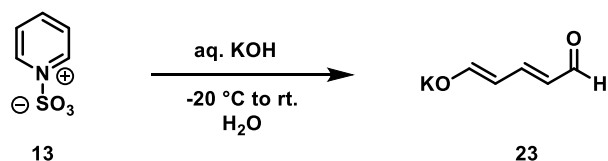
2,6-Lutidine (843 mg, 7.98 mmol, 3.0 equiv.) and TBSOTf (843 mg, 3.19 mmol, 1.2 equiv.) were added to a solution of known¹ (*S*)-oct-5*Z*-en-1-yn-3-ol (**20**) (330 mg, 2.66 mmol, 1 equiv.) in CH₂Cl₂ (26 mL) at -78 °C. The reaction was stirred at that temperature for 4 h before it was quenched with saturated aq. NH₄Cl (15 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were dried (Na₂SO₄), before concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 98:2) to afford the title compound **15** as a colourless oil. Yield: 513 mg (81%); [α]_D²⁰ +21 (c 0.07, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 5.57 – 5.36 (m, 2H), 4.34 (td, *J* = 6.6, 2.1 Hz, 1H), 2.45 (dd, *J* = 7.1, 0.6 Hz, 2H), 2.38 (d, *J* = 2.1 Hz, 1H), 2.07 (p, *J* = 7.1 Hz, 2H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 134.6, 123.8, 85.6, 72.2, 63.0, 36.7, 25.9 (3C), 20.9, 18.4, 14.4, -4.5, -4.9. TLC (hexanes/EtOAc 95:5, CAM stain): *R*_f = 0.66.

(*S*)-1-(4-Isopropyl-2-thioxothiazolidin-3-yl)ethan-1-one (22).



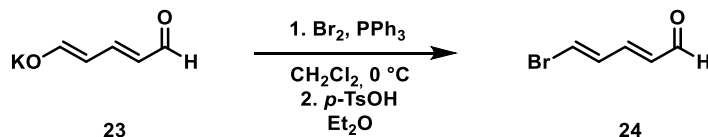
Nagao's chiral auxiliary **22** was prepared from commercially available (*S*)-4-isopropylthiazolidine-2-thione (**21**) by using the procedure of Nagao *et al.*² To thiazolidine (**21**) (7.20 g, 44.6 mmol, 1.0 equiv.) in THF (225 mL), 60% NaH dispersion in mineral oil (1.28 g, 53.4 mmol, 1.2 equiv.) was slowly added at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, and acetyl chloride (4.19 g, 53.4 mmol, 1.2 equiv.) was added dropwise. The reaction mixture was stirred for 30 min at 0 °C, upon which it was warmed to room temperature and allowed to stir for 2 h. The reaction was quenched with saturated NH₄Cl (60 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 60 mL) and the combined organic layers were dried (Na₂SO₄), filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 9:1) to afford the title compound **22** as a yellow oil. All spectroscopic and physical data were in full agreement with those reported in the literature.² Yield: 7.88 g (87%); [α]_D²⁰ +434 (c 0.26, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 5.14 (ddd, *J* = 7.6, 6.2, 1.2 Hz, 1H), 3.50 (dd, *J* = 11.5, 8.0 Hz, 1H), 3.02 (dd, *J* = 11.5, 1.2 Hz, 1H), 2.77 (s, 3H), 2.48 – 2.25 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 203.3, 170.8, 71.4, 30.9, 30.5, 27.0, 19.2, 17.9. TLC (hexanes/EtOAc 4:1, KMnO₄ stain): *R*_f = 0.35.

Potassium (1E,3E)-5-oxopenta-1,3-dien-1-olate (23).



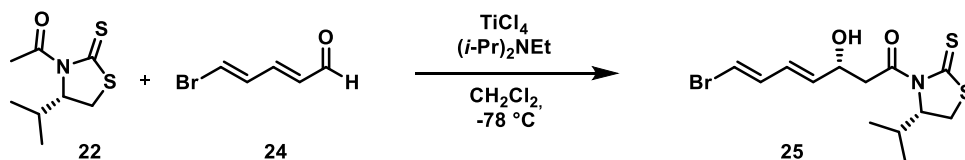
Glutaconaldehyde potassium salt **23** was prepared from commercially available pyridinium-1-sulfonate (**13**) according to the procedure of Becher.³ Pyridinium salt **13** (technical grade, 60.8 g, 0.38 mol, 1.0 equiv.) is added to a solution of KOH (87.5 g, 1.56 mol, 4.1 equiv.) in H₂O (210 mL). The solution is stirred at -20 °C for 1 h before the temperature is slowly raised to 20 °C over 4 h. The mixture is heated to 30-40 °C for 30 min before being cooled down to 5 °C. The crude product is filtered, washed with acetone (2 x 80 mL) and dried. The brown-red solid is dissolved in MeOH (2.2 L), heated to reflux before activated carbon was added. The solution was filtrated, concentrated *in vacuo*. The orange crystals were washed with acetone (2 x 80 mL) and dried to afford the title compound **23** as orange crystals. All spectroscopic and physical data were in full agreement with those reported in the literature.³ Yield: 28.5 g (55%); ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.67 (d, *J* = 9.2 Hz, 2H), 7.04 (t, *J* = 12.9 Hz, 1H), 5.10 (dd, *J* = 13.0, 9.1 Hz, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 184.4 (2C), 159.8, 106.2 (2C). M.p.: 354 – 360 °C, decomp. TLC (EtOAc, KMnO₄ stain): *R*_f = 0.35.

(2E,4E)-5-Bromopenta-2,4-dienal (24).



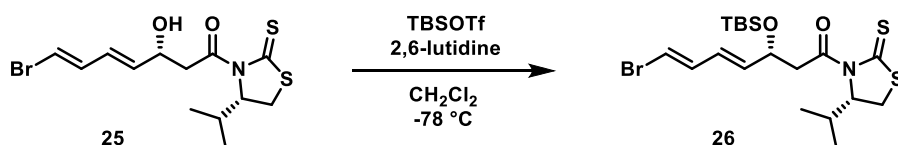
Bromopentadienal **24** was prepared by the bromination of glutaconaldehyde potassium salt **23** according to the protocol reported by Duhamel *et al.*⁴ Bromine (12.6 g, 78.8 mmol, 1.2 equiv.) was added dropwise, at 0 °C, to a solution of triphenylphosphine (21.5 g, 81.9 mmol, 1.2 equiv.) in CH₂Cl₂ (400 mL). Glutaconaldehyde **23** (9.08 g, 66.7 mmol, 1.0 equiv.) was added and the solution was stirred for 4 h at ambient temperature before it was filtered through a pad of silica. The crude product was purified by column chromatography on silica (hexanes/Et₂O 9:1) to afford a mixture of the *E,E*- and the *Z,E*-isomer (3:1). The mixture was dissolved in Et₂O (125 mL), TsOH (600 mg) was added and the solution was stirred for 5 min before being concentrated *in vacuo*. The slurry was dissolved in Et₂O (30 mL), filtered through a pad of silica and concentrated *in vacuo* to afford the title compound **24** as essentially a single isomer. All spectroscopic and physical data were in agreement with those reported in the literature.⁴ Yield: 8.1 g (75%); ¹H NMR (300 MHz, CDCl₃) δ 9.58 (d, *J* = 7.8 Hz, 1H), 7.07 – 6.90 (m, 3H), 6.24 – 6.11 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 193.3, 147.9, 135.7, 132.0, 120.0. TLC (hexanes/Et₂O 9:1, KMnO₄ stain): *R*_f = 0.10.

(R,4E,6E)-7-Bromo-3-hydroxy-1-((S)-4-isopropyl-2-thioxothiazolidin-3-yl)hepta-4,6-dien-1-one (25).



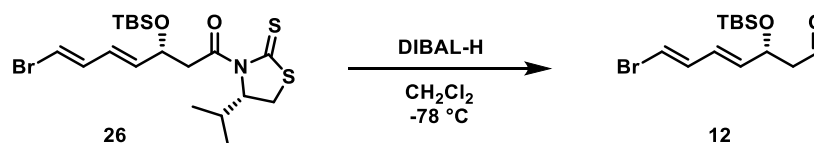
The (*R*)-aldol product **25** was prepared in 92% yield from dienal **24** and the auxiliary **22** according to the procedure of Olivo and coworkers.⁵ To a solution of *N*-acetylthiazolidinethione **22** (5.00 g, 24.6 mmol, 1.0 equiv.) in CH₂Cl₂ (245 mL), TiCl₄ (1M in CH₂Cl₂ 4.66 g, 24.6 mmol, 1.0 equiv.) was added at -78 °C and stirred for 5 min. Diisopropylethylamine (3.81 g, 29.5 mmol, 1.2 equiv.) in CH₂Cl₂ (61 mL) was added and the solution was stirred for 30 min at -78 °C, whereupon the freshly prepared aldehyde **24** (3.56 g, 22.1 mmol, 0.9 equiv.) in CH₂Cl₂ (61 mL) was added dropwise. The mixture was stirred for 1 h at -78 °C, then quenched with half saturated ammonium chloride (100 ml) and warmed to room temperature. The layers were separated and the aq. layer was extracted with CH₂Cl₂ (2 x 80 mL). The combined organic layers were dried (Na₂SO₄) and filtered, before concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 7:3) to afford the title compound **25** as a yellow oil. All spectroscopic and physical data were in full agreement with those reported in the literature.⁵ Yield: 9.0 g (92%). $[\alpha]_D^{20} +271$ (c 0.13, CHCl₃); ¹H NMR (300 MHz, CHCl₃) δ 6.72 (dd, *J* = 13.5, 10.8 Hz, 1H), 6.35 (d, *J* = 13.6 Hz, 1H), 6.26 (ddd, *J* = 15.3, 10.8, 1.5 Hz, 1H), 5.79 (dd, *J* = 15.3, 5.4 Hz, 1H), 5.16 (dd, *J* = 7.8, 6.4 Hz, 1H), 4.76 – 4.65 (m, 1H), 3.70 (dd, *J* = 17.6, 3.1 Hz, 1H), 3.53 (dd, *J* = 11.5, 7.9 Hz, 1H), 3.29 (dd, *J* = 17.6, 8.6 Hz, 1H), 3.04 (dd, *J* = 11.6, 1.1 Hz, 1H), 2.93 (d, *J* = 4.5 Hz, 1H), 2.36 (dq, *J* = 13.6, 6.8 Hz, 1H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 203.1, 172.3, 136.7, 134.8, 128.0, 109.6, 71.5, 68.1, 45.1, 31.0, 30.8, 19.2, 18.0. ⁵ The diastereomeric ratio (15.3:1) on the crude product was determined by HPLC analysis (Eclipse XDB-C18, MeOH/H₂O 70:30, 1.0 mL/min, *t*_r(minor) = 8.65 min and *t*_r(major) = 10.85 min).

(*R*,4*E*,6*E*)-7-Bromo-3-((*tert*-butyldimethylsilyloxy)-1-((*S*)-4-isopropyl-2-thioxothiazolidin-3-yl)hepta-4,6-dien-1-one (26).



According to the procedure of Corey and coworkers,⁶ the alcohol **25** was protected with a TBS-group. 2,6-Lutidine (2.91 g, 27.2 mmol, 3.0 equiv.) and TBSOTf (3.11 g, 11.8 mmol, 1.3 equiv.) were added to a solution of alcohol **25** (3.30 g, 9.1 mmol, 1.0 equiv.) in CH₂Cl₂ (90 mL) at -78 °C. The reaction was stirred at that temperature for 3 h before it was quenched with saturated aq. NH₄Cl (45 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 40 mL). The combined organic layers were dried (Na₂SO₄), before concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 98:2) to afford the title compound **26** as a yellow oil. All spectroscopic and physical data were in full agreement with those reported in the literature.⁵ Yield: 4.2 g (97%); $[\alpha]_D^{20} +263$ (c 0.5, CHCl₃); ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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. TLC (hexanes/EtOAc 95:5, KMnO₄ stain): *R*_f = 0.30.

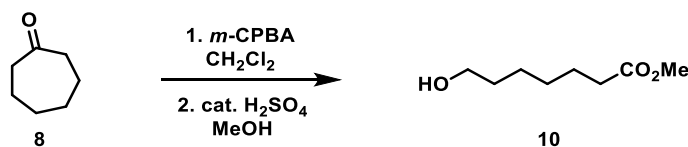
(*R*,4*E*,6*E*)-7-Bromo-3-((*tert*-butyldimethylsilyloxy)hepta-4,6-dienal (12).



Aldehyde **12** was prepared by a DIBAL-H reduction of the protected thiazolidinethione **26** according to the procedure of Olivo *et al.*⁷ DIBAL-H (1.25 mL, 1M in hexanes, 1.2 equiv.) was added to a stirred solution of

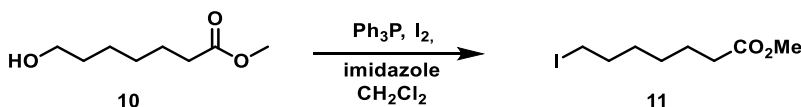
thiazolidinethione **26** (500 mg, 1.04 mmol, 1.0 equiv.) in CH₂Cl₂ (20 mL) at -78 °C. The mixture was stirred for 3 h and then quenched with sat. aq. NaHCO₃ (10 mL). The cooling bath was removed and solid Na-K tartrate (~ 0.7 g) was added and stirring was continued for another 40 min. Et₂O (35 mL) was added. The layers were separated and the aq. layer was extracted with Et₂O (3 x 30 mL). The combined organic layers were dried (Na₂SO₄), before concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 95:5) to afford the title compound **12** as a yellow oil. All spectroscopic and physical data were in full agreement with those reported in the literature.⁷ [α]_D²⁰ +31 (c 0.2, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 9.75 (t, *J* = 2.2 Hz, 1H), 6.69 (dd, *J* = 13.4, 10.8 Hz, 1H), 6.33 (d, *J* = 13.6 Hz, 1H), 6.16 (ddd, *J* = 15.2, 10.6, 1.3 Hz, 1H), 5.75 (ddd, *J* = 15.3, 5.9, 0.8 Hz, 1H), 4.66 (dd, *J* = 6.8, 5.5 Hz, 1H), 2.75 – 2.41 (m, 2H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 201.2, 136.6, 136.1, 127.6, 109.6, 68.5, 51.4, 25.9, 14.3, -4.2, -4.9. TLC (heptane/EtOAc 9:1, CAM stain): *R*_f = 0.22.

Methyl 7-hydroxyheptanoate (**8**).



Utilizing a Baeyer-Villiger reaction followed by an esterification, alcohol ester **10** was prepared from commercially available cycloheptanone **8** according to the procedure of Watanabe and coworkers.⁸ *m*-CPBA (25.00 g, 111.5 mmol, 1.5 equiv.) was dissolved in CH₂Cl₂ (200 mL) and cooled to 0°C. Cycloheptanone **8** (8.30 g, 74.4 mmol, 1.0 equiv.) was then added, and the reaction mixture was stirred at ambient temperature for 5 days. The reaction mixture was cooled to 0 °C, filtered, the filtrate was washed with sat. aq. NaHCO₃ (50 mL), dried (Na₂SO₄) and concentrated *in vacuo*. The crude product was taken up in dry MeOH (150 mL) and added a few drops of conc. H₂SO₄. The reaction mixture was refluxed over night, cooled, added sat. aq. NaHCO₃ (15 mL) and concentrated *in vacuo*. More aq. NaHCO₃ (50 mL) was added to the mixture and the aq. phase was extracted with Et₂O (4 x 100 mL). The organic phases were combined and dried (Na₂SO₄), filtered and concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 4:1) to afford the title compound **10** as a clear oil. All spectroscopic and physical data were in full agreement with those reported in the literature.⁸ Yield: 9.6 g (81%). ¹H NMR (300 MHz, CDCl₃) δ 3.57 (s, 3H), 3.51 (t, *J* = 6.5 Hz, 2H), 2.58 (bs, 1H), 2.22 (t, *J* = 7.5 Hz, 2H), 1.61 – 1.41 (m, 4H), 1.34 – 1.25 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 174.3, 62.5, 51.5, 33.9, 32.4, 28.9, 25.4, 24.8. TLC (hexanes/EtOAc 4:1, KMnO₄ stain): *R*_f = 0.10.

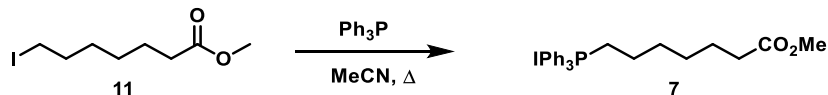
Methyl 7-iodoheptanoate (**11**).



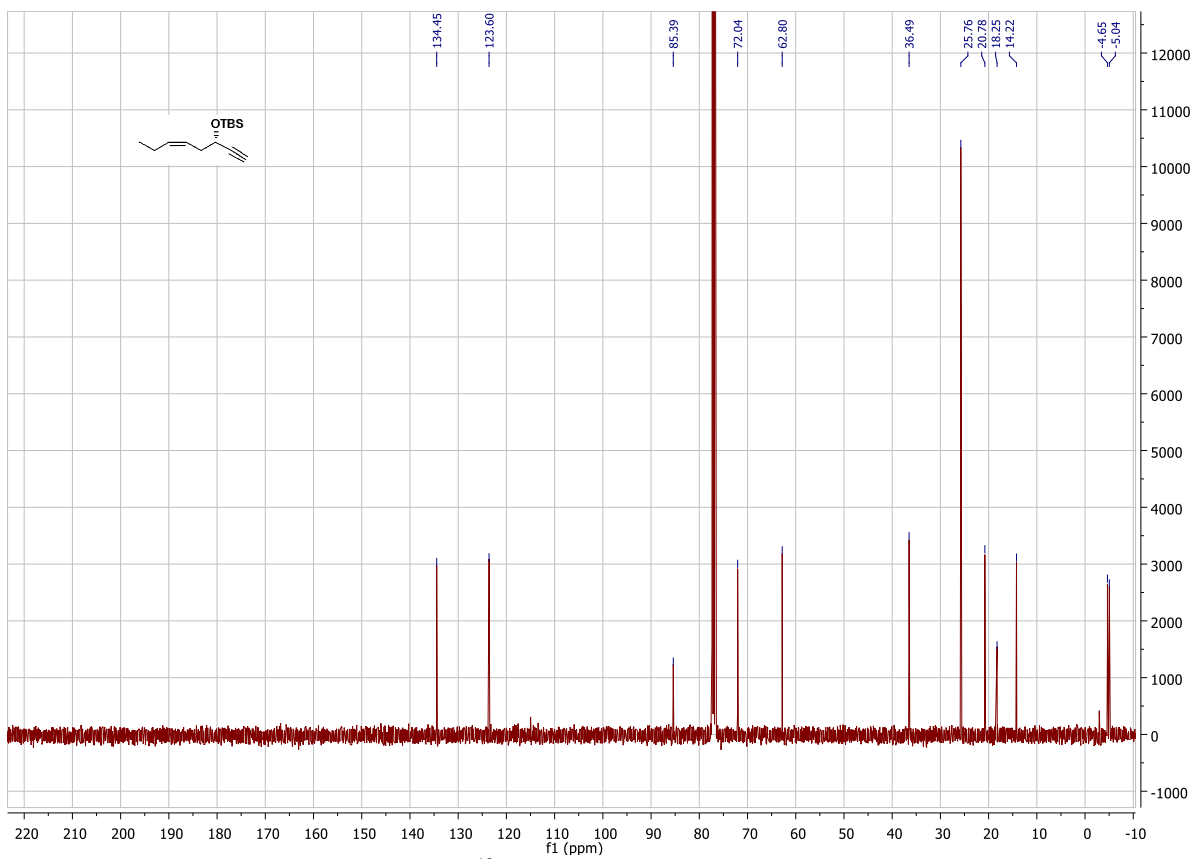
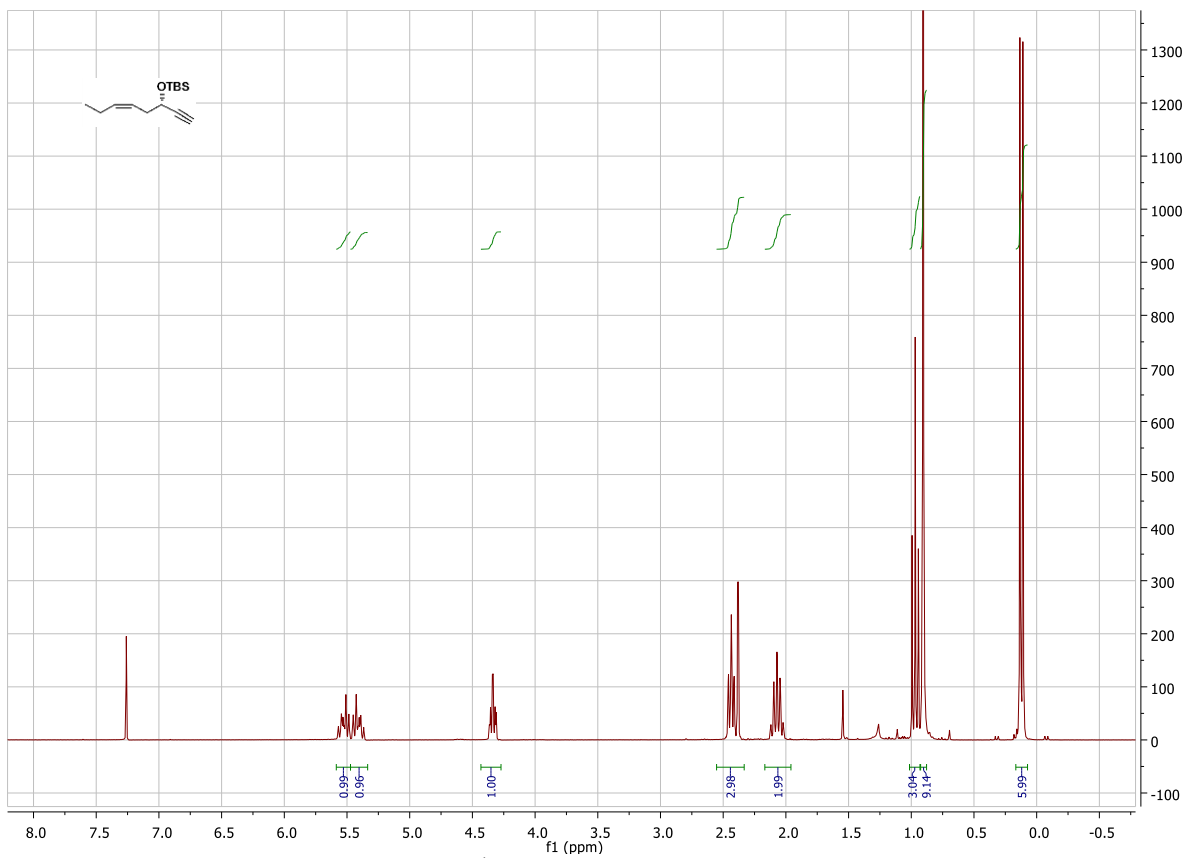
Iodide **11** was prepared from alcohol ester **10** according to the procedure reported by Mioskowski and coworkers.⁹ To a solution of methyl ester **10** (3.10 g, 19.3 mmol) in dry CH₂Cl₂ (200 mL), triphenylphosphine (7.75 g, 29.6 mmol) and imidazole (2.00 g, 29.8 mmol) were added. The reaction flask was placed in a cooling bath (ice, water, salt) for 15 min before iodide (7.60 g, 30.0 mmol) was added in one portion with rapid stirring. The reaction mixture was stirred for 15 min before the cooling bath was removed and the reaction mixture stirred at ambient temperature for another 35 min. A sat. solution of aq. Na₂SO₃ (25 mL) was added, and the aq. phase was extracted with CH₂Cl₂ (2 x 100 mL), dried (Na₂SO₄), filtrated and concentrated *in vacuo*. The crude product was purified by column chromatography on silica (hexanes/EtOAc 92:8) afford the title compound **11** as colourless oil. All spectroscopic and physical data were in full agreement with those reported in the literature.⁹

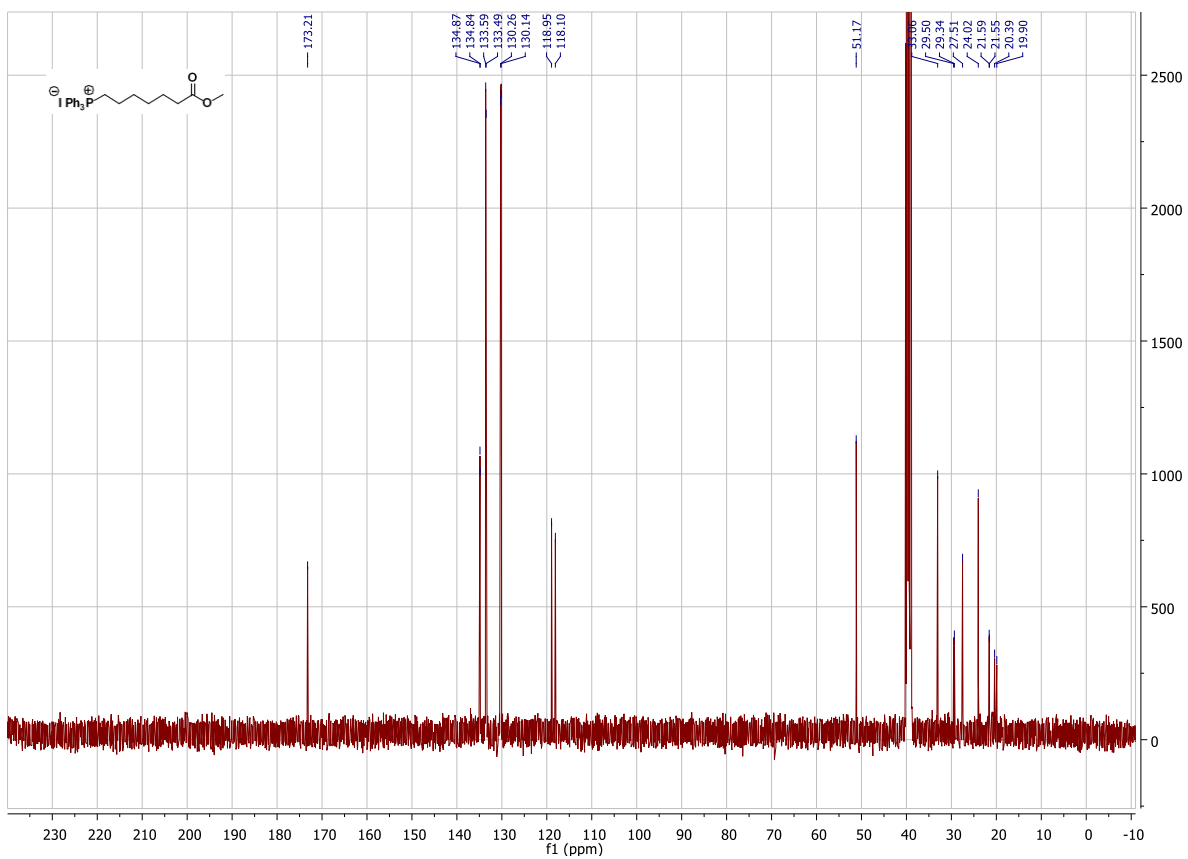
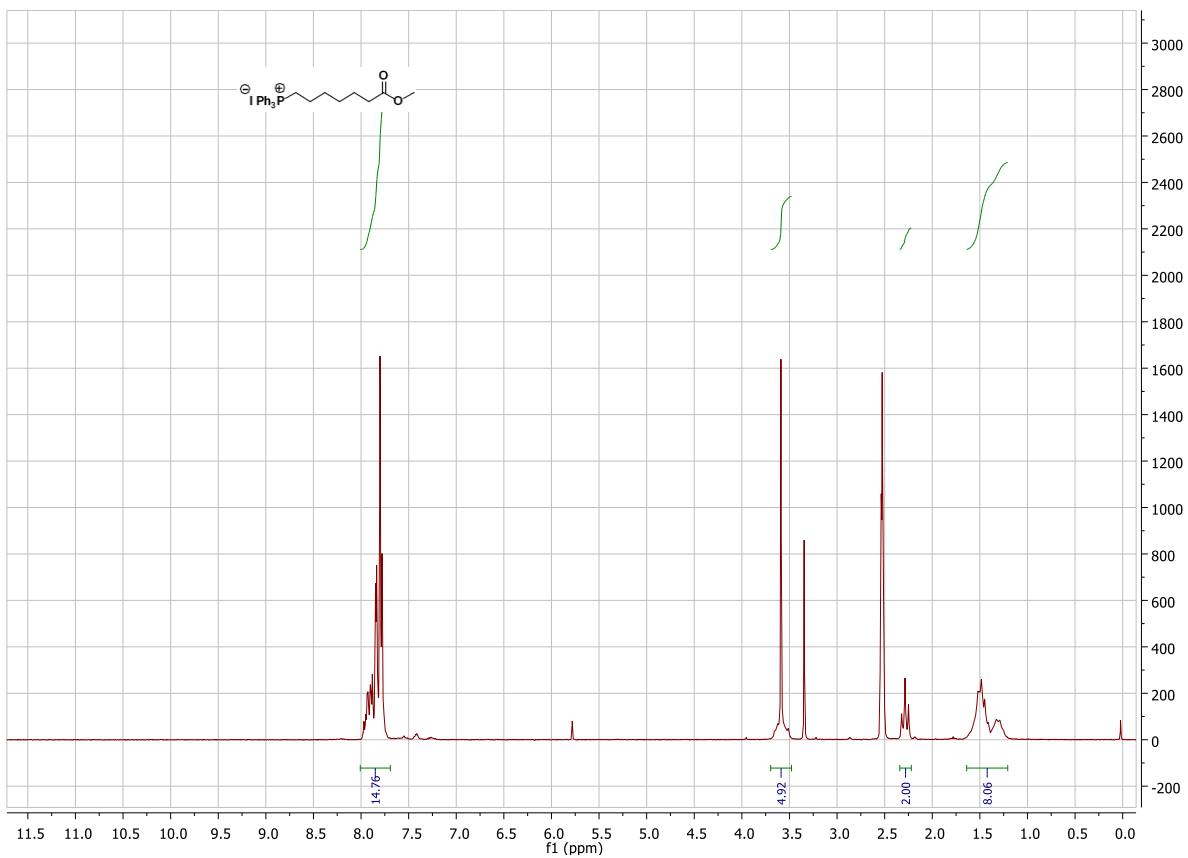
Yield: 4.4 g (85%). ^1H NMR (400 MHz, CDCl_3) δ 3.66 (s, 3H), 3.18 (t, $J = 7.0$ Hz, 2H), 2.31 (t, $J = 7.5$ Hz, 2H), 1.82 (p, $J = 7.0$ Hz, 2H), 1.63 (p, $J = 7.6$ Hz, 2H), 1.46 – 1.29 (m, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 174.0, 51.5, 33.9, 33.2, 30.1, 28.0, 24.7, 6.9.

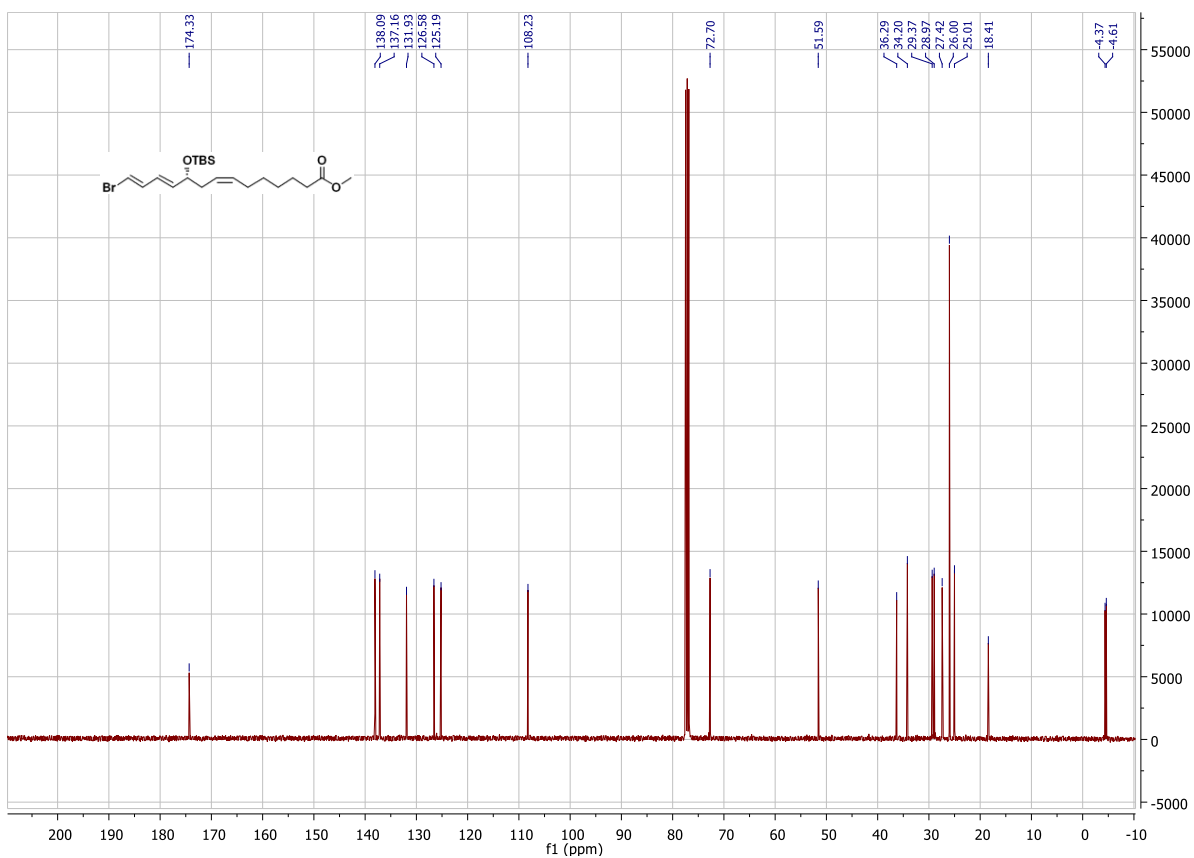
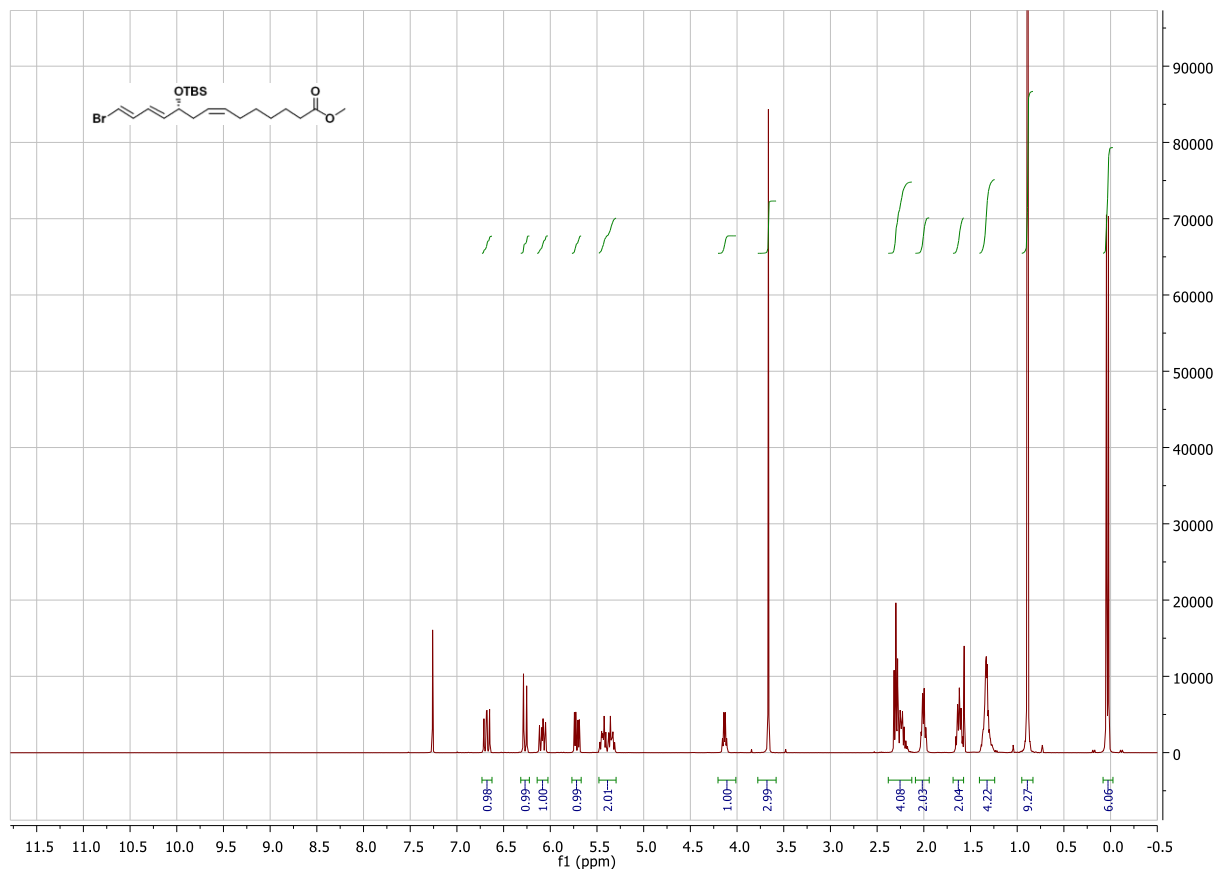
(7-Methoxy-7-oxoheptyl)triphenylphosphonium iodide (7).



Iodide **11** (4.40 g, 16.29 mmol) was dissolved in dry MeCN (145 mL) and stirred under argon. Triphenylphosphine (10.90 g, 41.56 mmol) was added and the reaction mixture was heated to reflux for 12 h. The reaction mixture was concentrated *in vacuo*. The crude product was purified by column chromatography on silica ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 95:5) to afford the title compound **7** as a clear oil. Yield: 7.90 g (91%); ^1H NMR (400 MHz, CDCl_3) δ 7.91 – 7.64 (m, 15H), 3.78 – 3.63 (m, 2H), 3.62 (s, 3H), 2.26 (t, $J = 7.2$ Hz, 2H), 1.73 – 1.46 (m, 6H), 1.43 – 1.22 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 173.2, 134.9 (d, $^4J_{\text{CP}} = 3.0$ Hz, 3C), 133.5 (d, $^3J_{\text{CP}} = 10.1$ Hz, 6C), 130.2 (d, $^2J_{\text{CP}} = 12.4$ Hz, 6C), 118.5 (d, $^1J_{\text{CP}} = 85.7$ Hz, 3C), 51.17, 33.06, 29.4 (d, $^2J_{\text{CP}} = 16.8$ Hz), 27.51, 24.02, 21.6 (d, $^3J_{\text{CP}} = 4.3$ Hz), 20.1 (d, $^1J_{\text{CP}} = 49.8$ Hz); HRESIMS m/z 405.1975 [$M\text{-I}$] $^+$ (calcd for $\text{C}_{26}\text{H}_{30}\text{O}_2\text{P}$, 405.1983). TLC ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 95:5, KMnO_4 stain): $R_f = 0.32$.







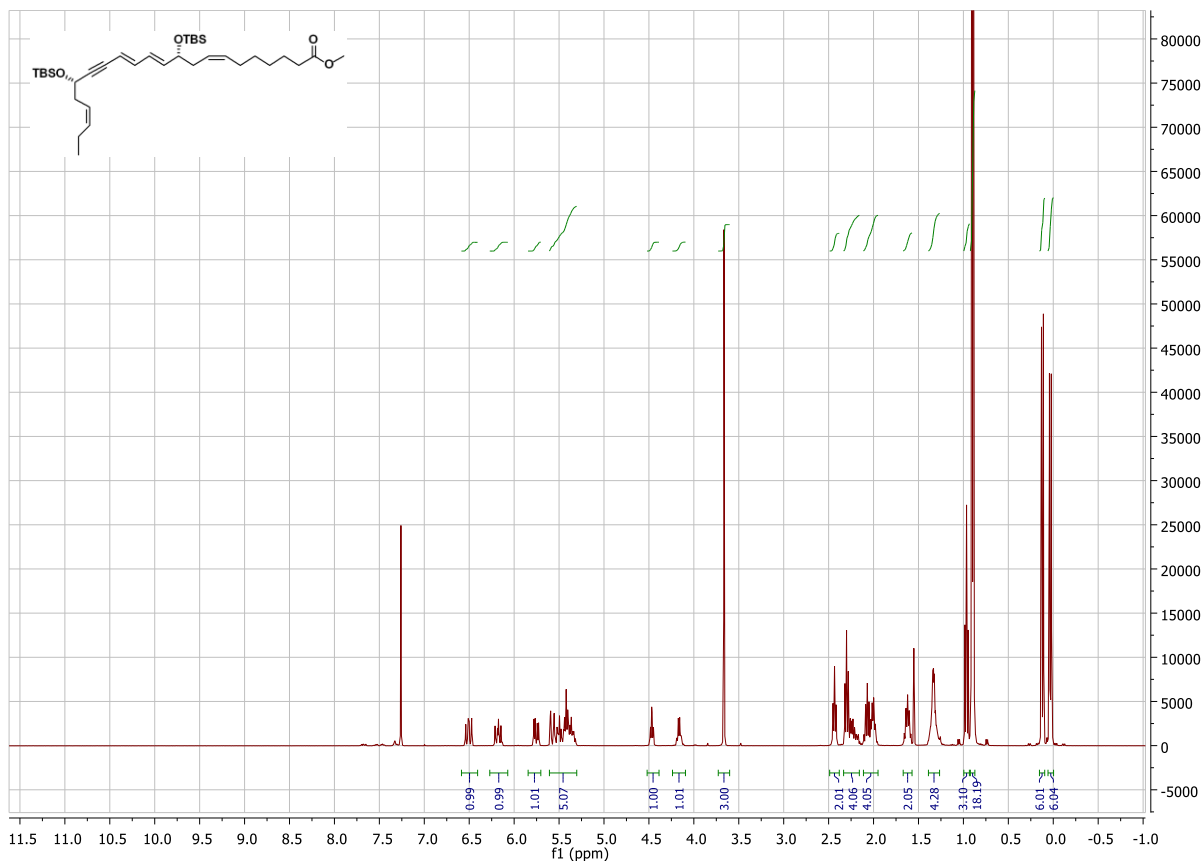


Figure S-7 $^1\text{H-NMR}$ spectrum of compound 18.

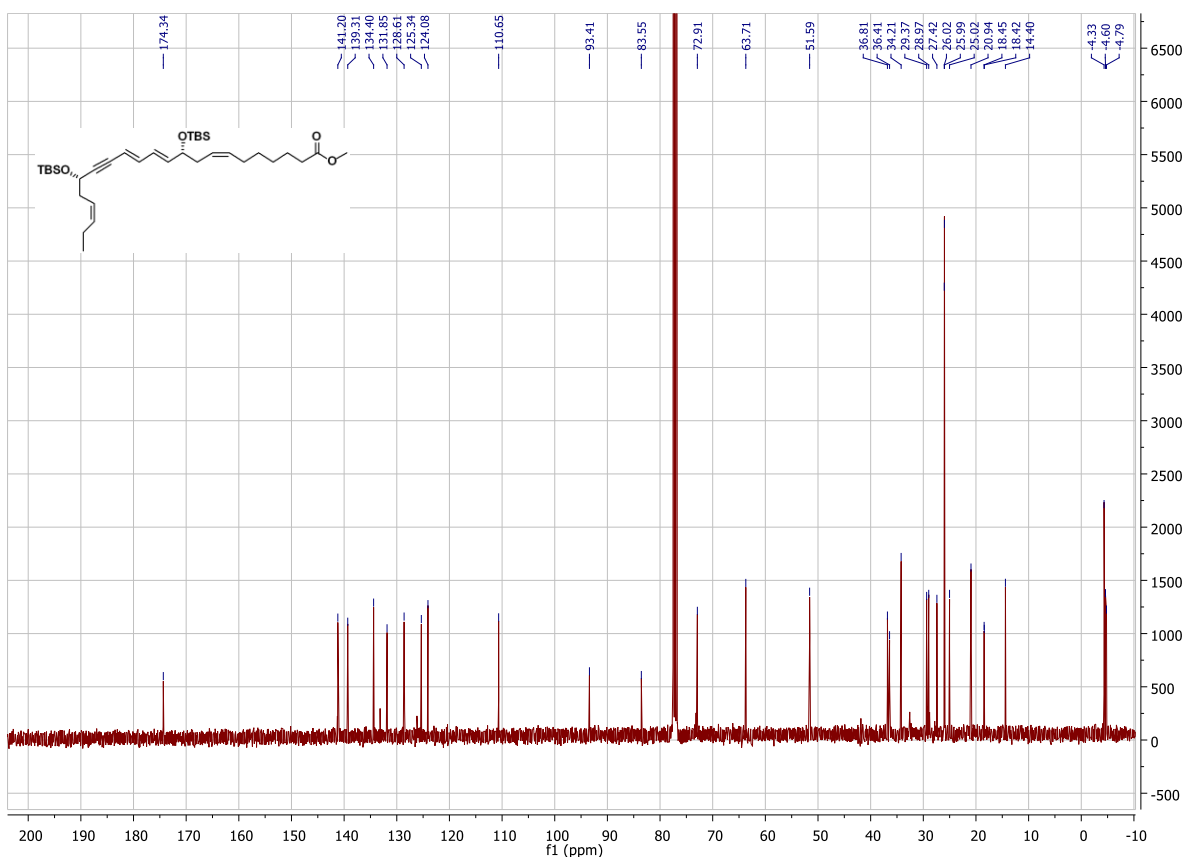


Figure S-8 $^{13}\text{C-NMR}$ spectrum of compound 18.

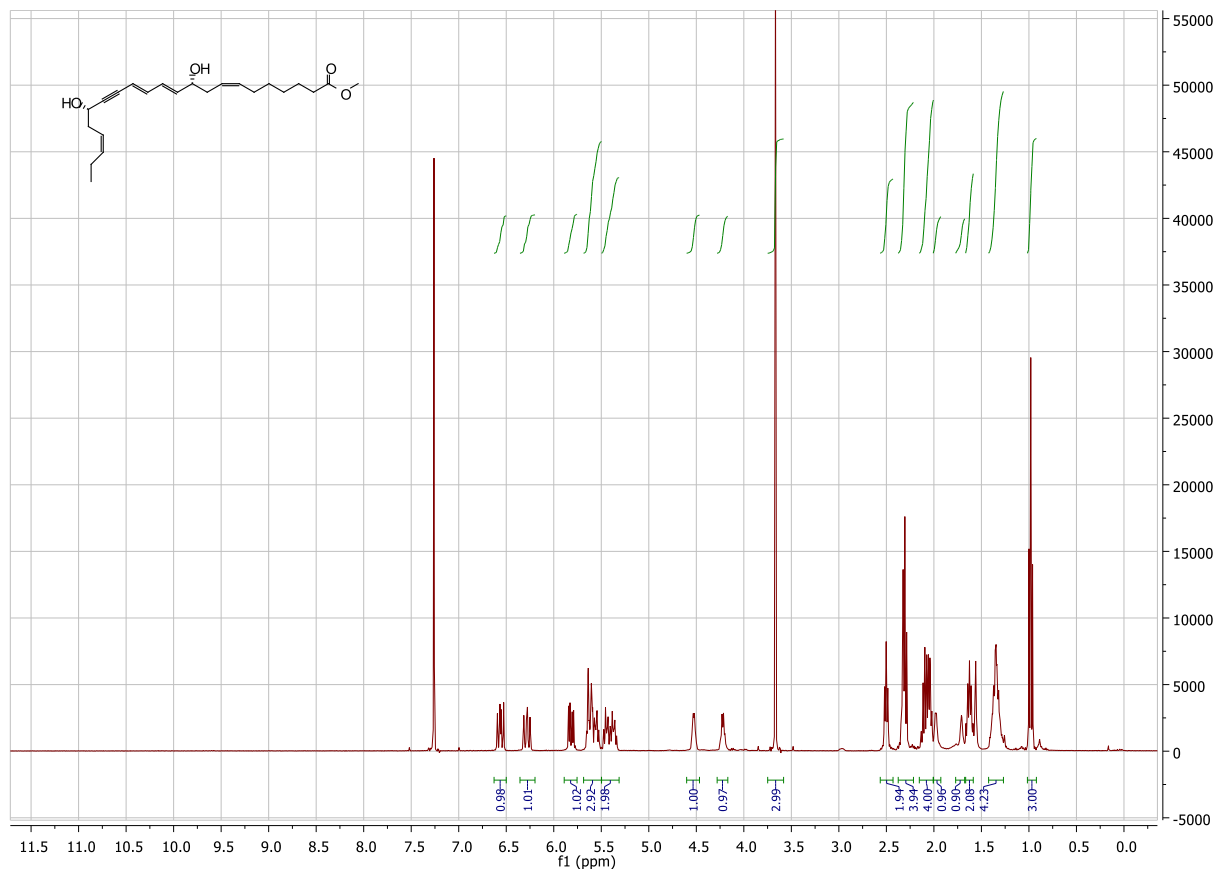


Figure S-9 ¹H-NMR spectrum of compound 19.

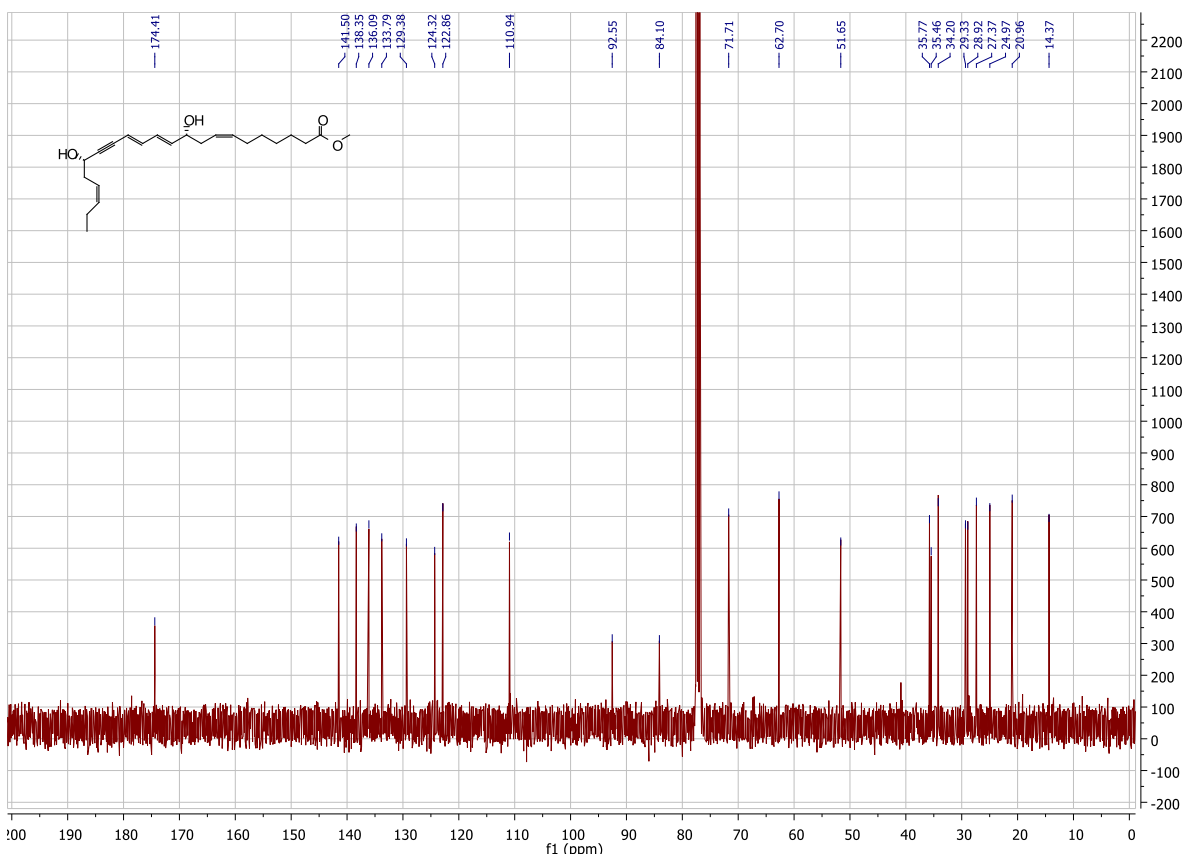


Figure S-10 ¹³C-NMR spectrum of compound 19.

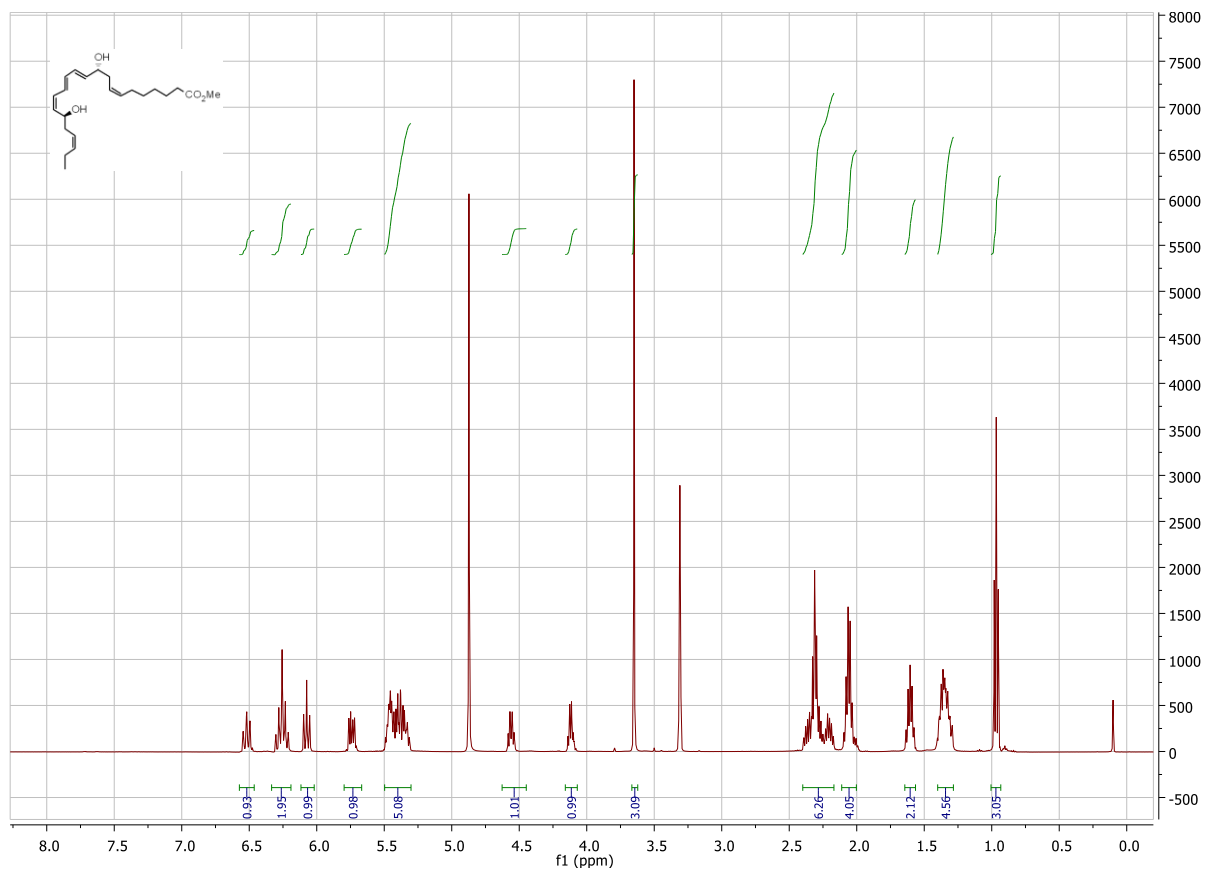


Figure S-11 $^1\text{H-NMR}$ spectrum of compound 6.

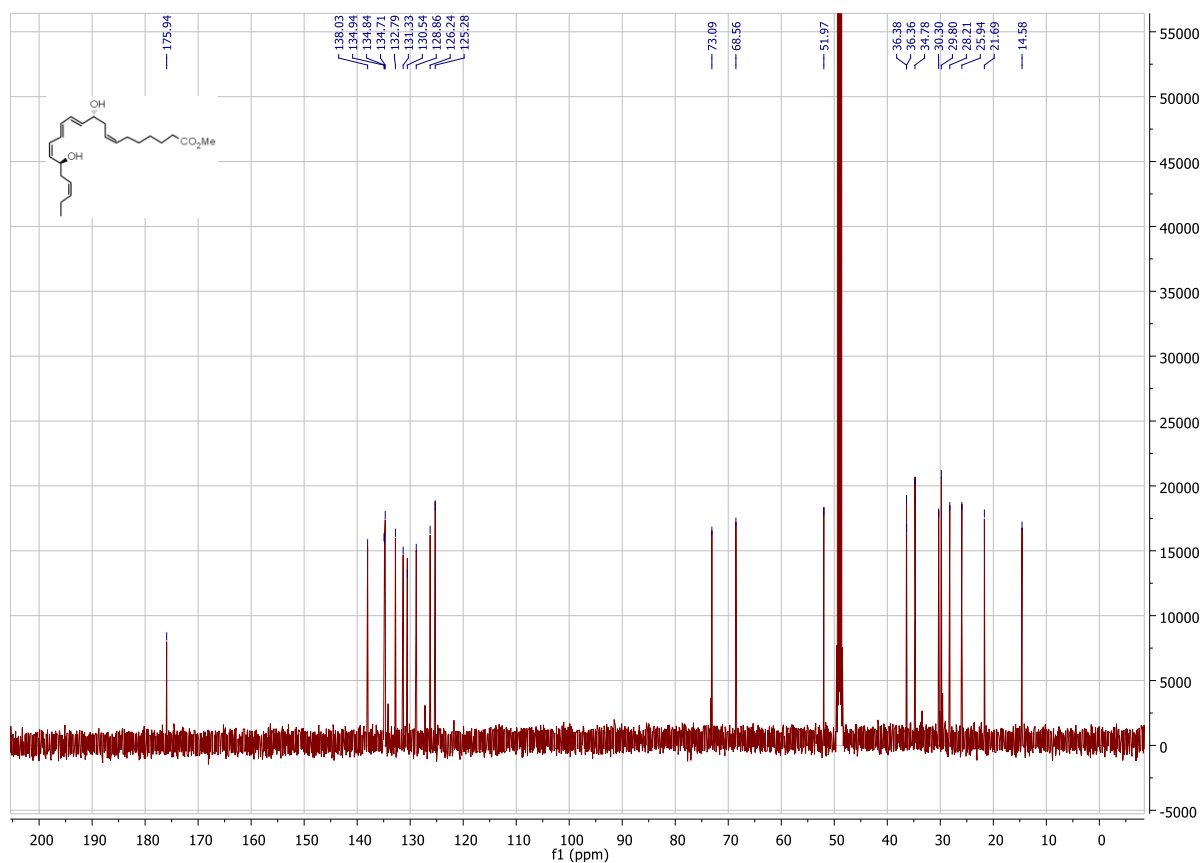


Figure S-12 $^{13}\text{C-NMR}$ spectrum of compound 6.

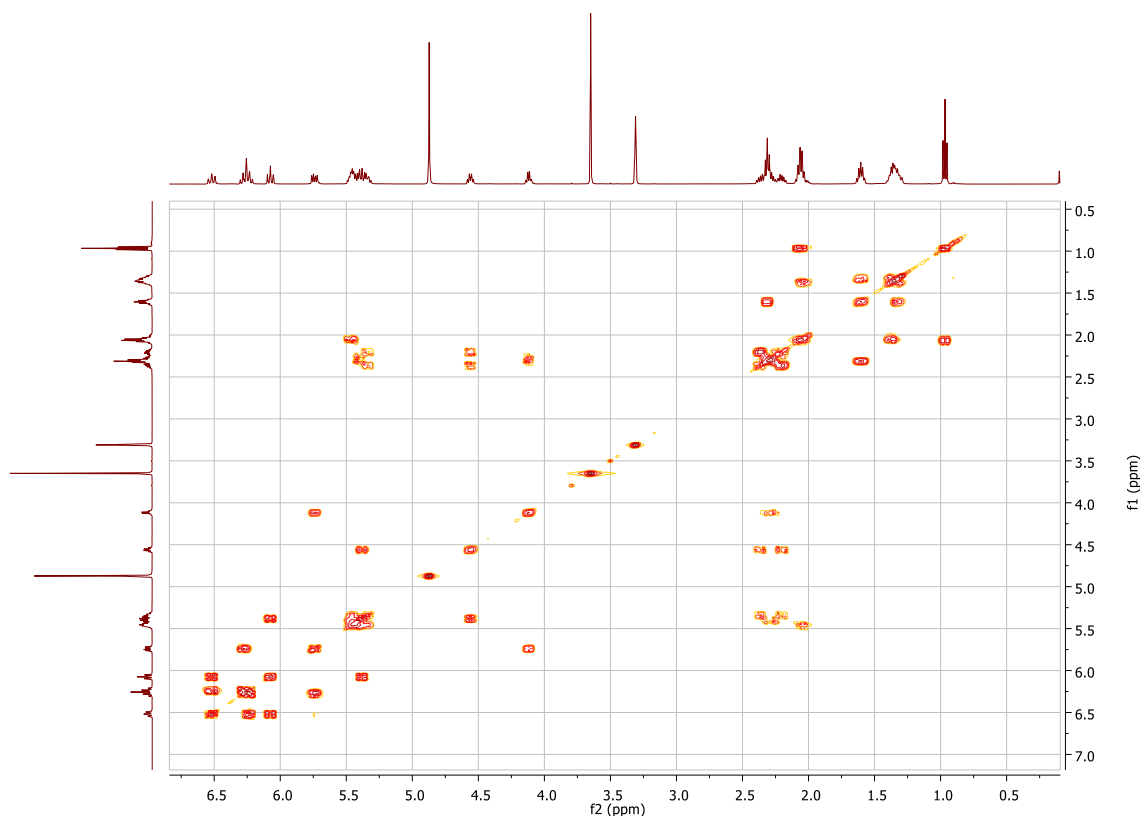


Figure S-13 COSYGP spectrum of compound **6**.

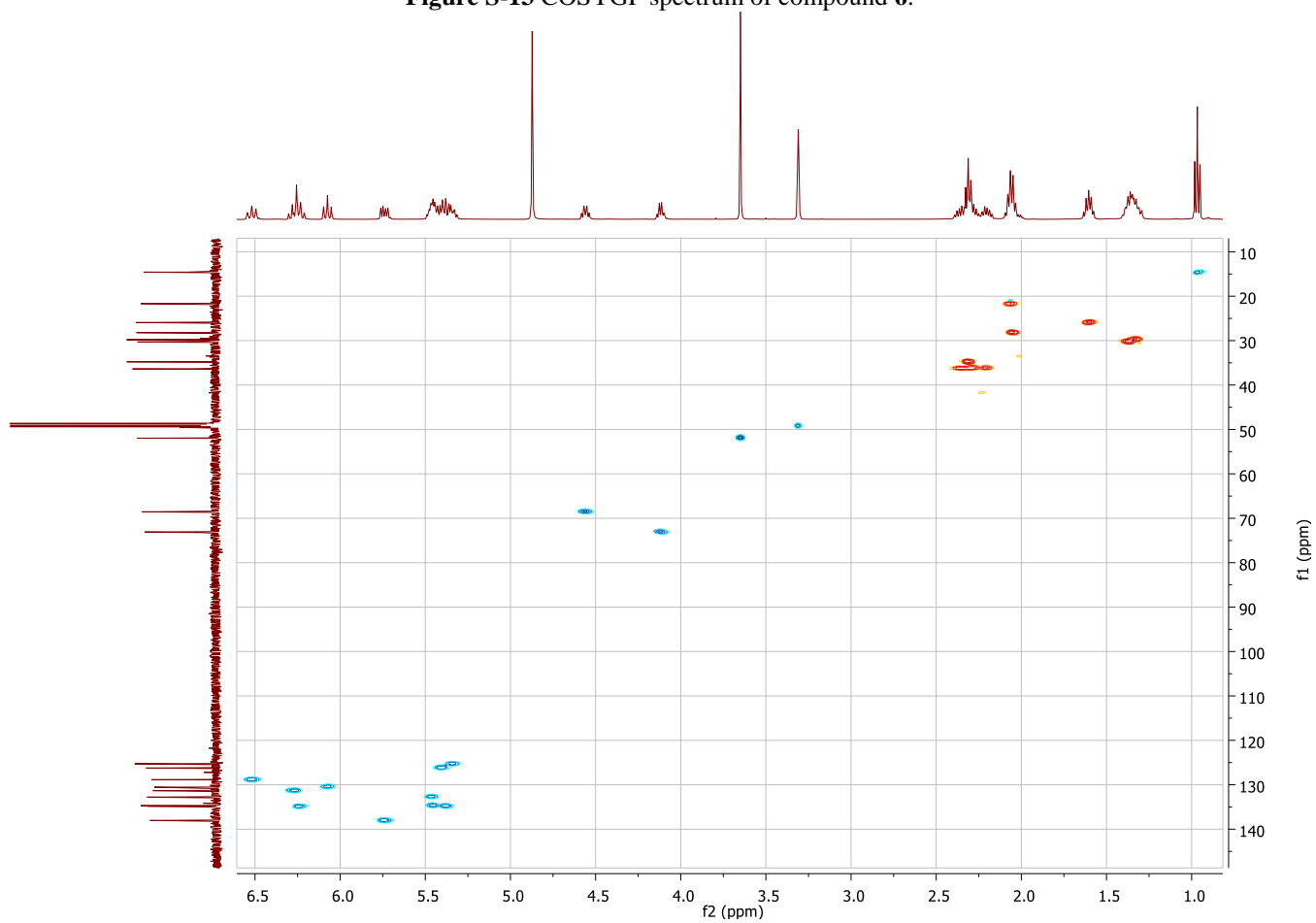


Figure S-14 HSQCETGP spectrum of compound **6**.

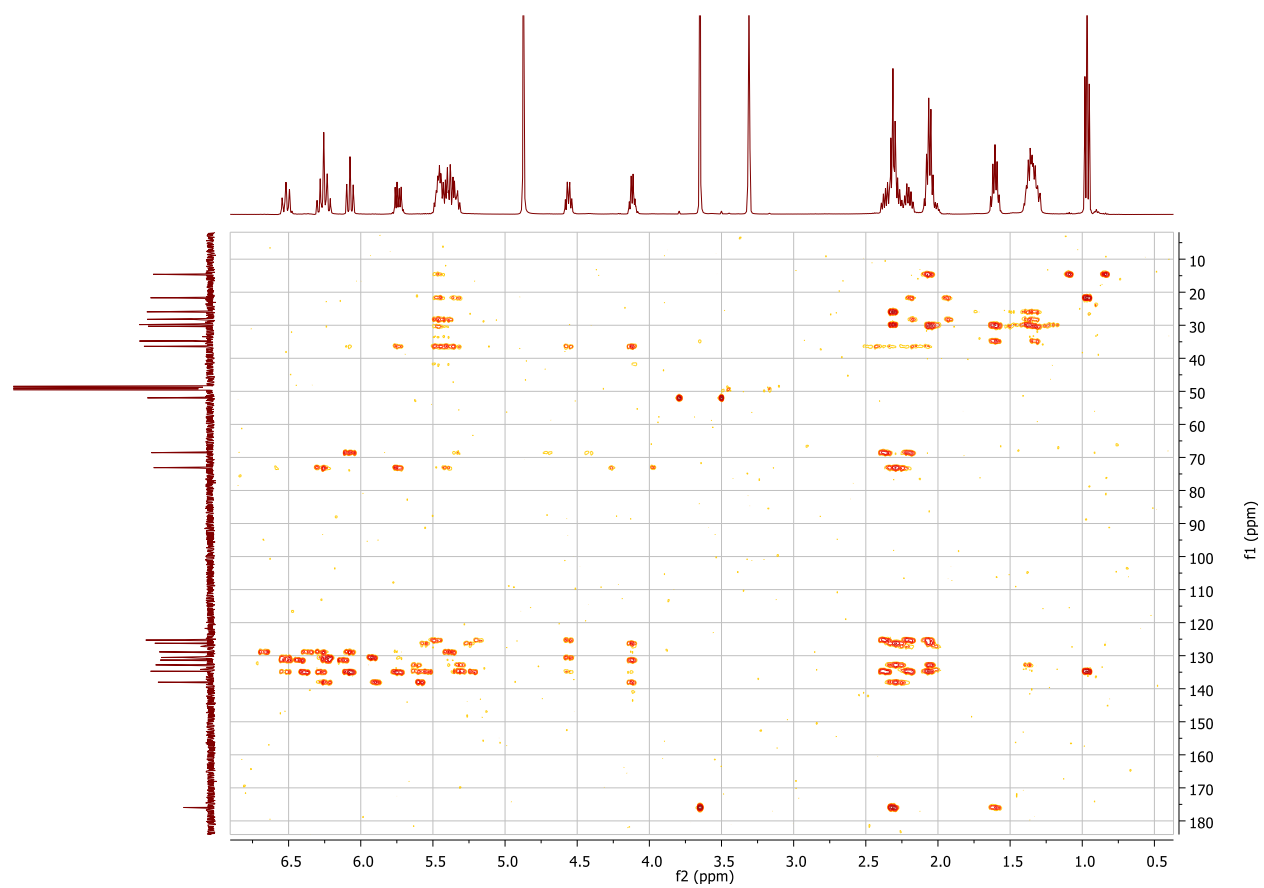
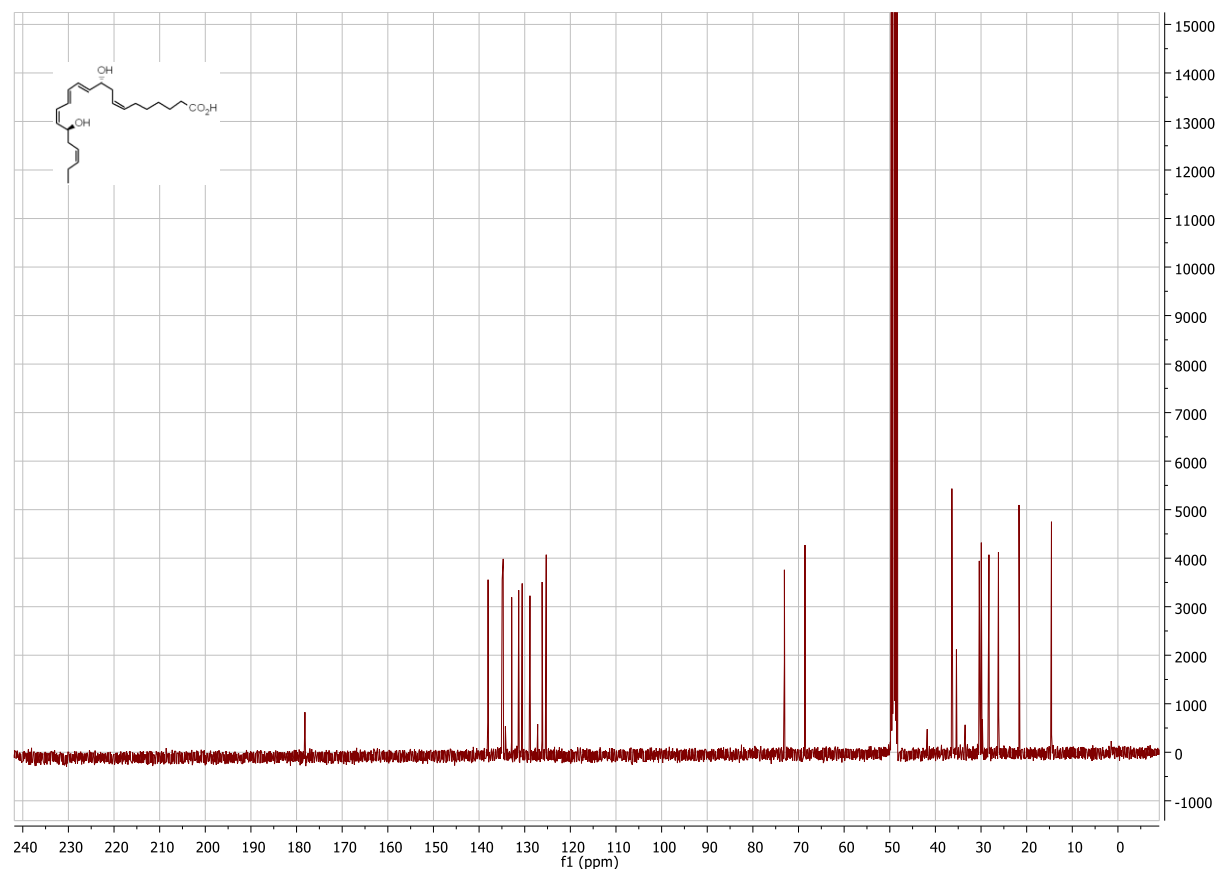
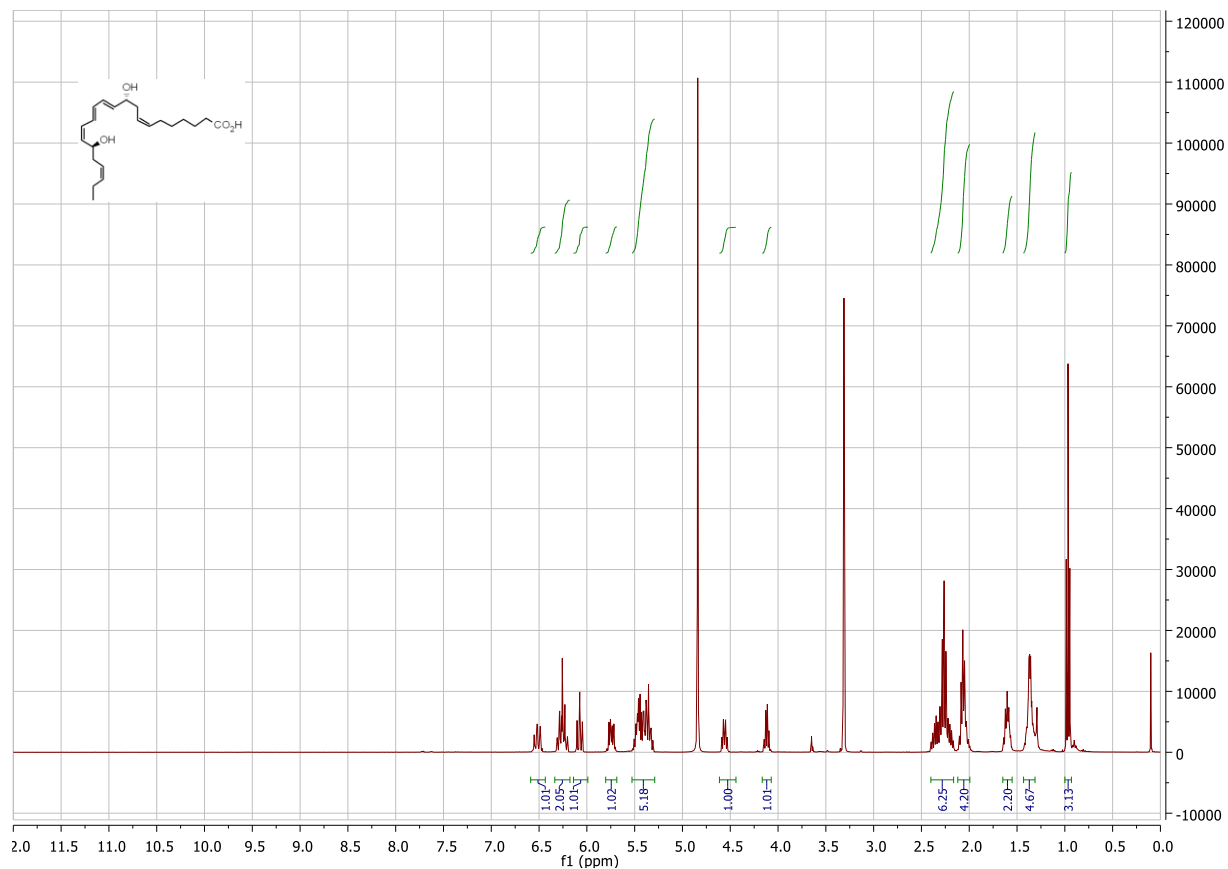
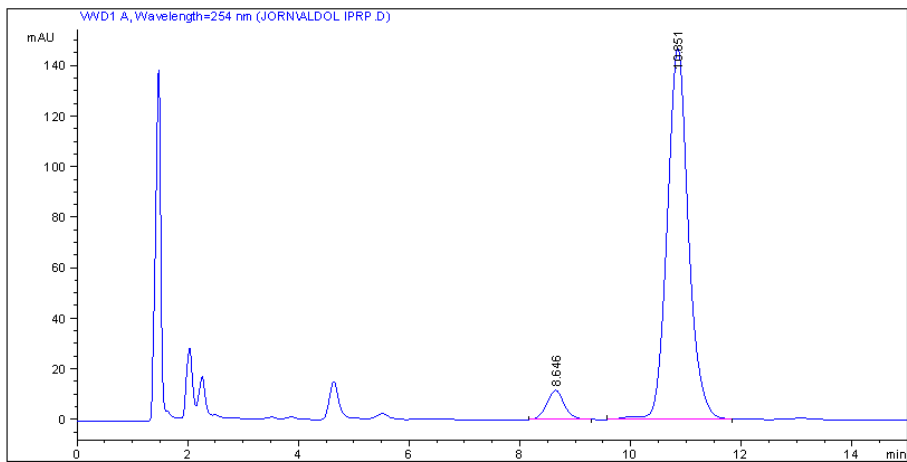


Figure S-15 HMBCGPND spectrum of compound **6**.





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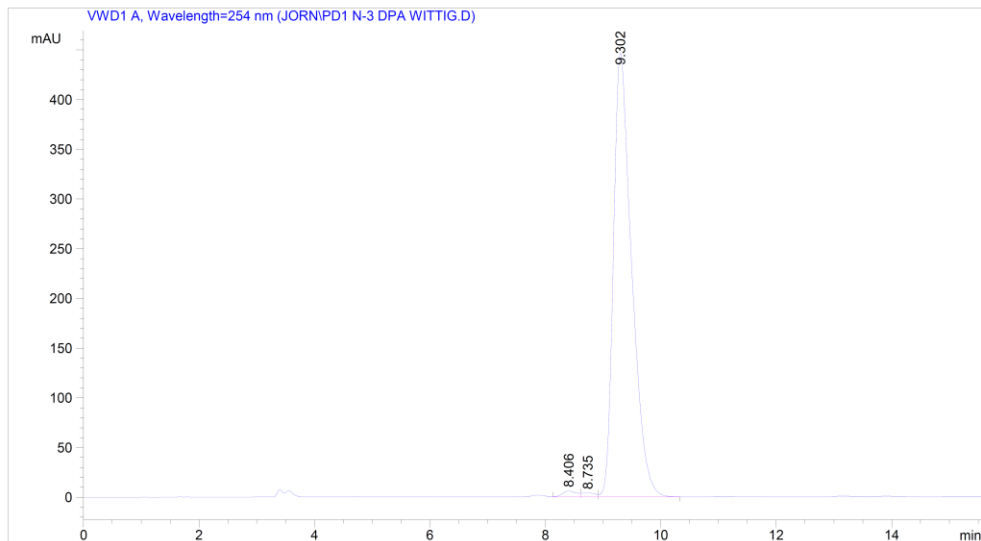
Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Sample Amount : 1.00000 [ng/ul] (not used in calc.)
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.646	BB	0.3304	255.66954	11.57739	6.1309
2	10.851	BB	0.4029	3914.47632	146.75571	93.8691

Totals : 4170.14586 158.33310

Figure S-18 HPLC chromatogram of aldol product 25.



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 Area Percent Report
 =====

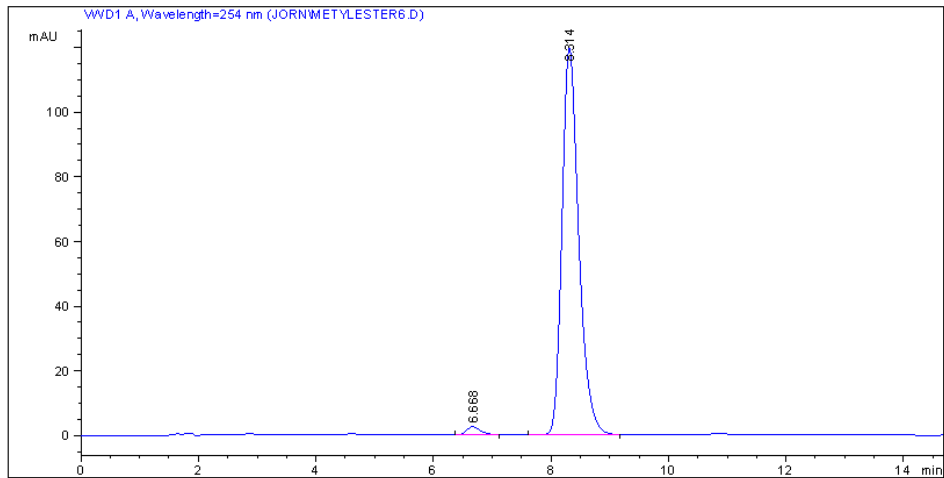
Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Sample Amount : 1.00000 [ng/ul] (not used in calc.)
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.406	VV	0.2556	104.40636	6.03794	1.0492
2	8.735	VV	0.2419	63.90968	3.93536	0.6423
3	9.302	VB	0.3212	9782.51172	446.45831	98.3085

Totals : 9950.82775 456.43160

Figure S-19 HPLC chromatogram of compound 14.



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

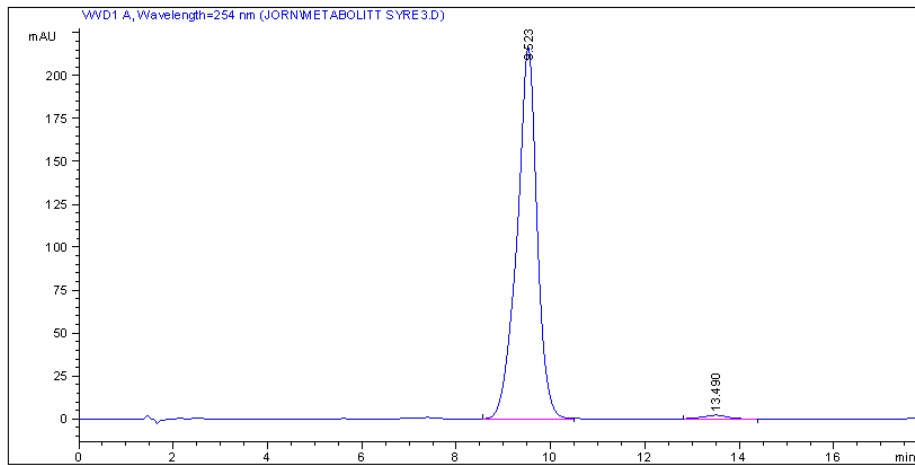
Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type Width Area Height Area
# [min] [min] mAU *s [mAU ] %
-----|-----|-----|-----|-----|-----
1  6.668 BB  0.2502  42.36370  2.53597  1.7535
2  8.314 BB  0.3014 2373.62427 119.61662 98.2465

Totals :                          2415.98797 122.15259

```

Figure S-20 HPLC chromatogram of methyl ester 6.



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                          Area Percent Report
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Sorted By      :      Signal
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  9.523 BB  0.4282 6400.36182 216.30191 98.8673
2 13.490 BB  0.4940  73.32443  2.11902  1.1327

Totals :                          6473.68625 218.42093

```

Figure S-21 HPLC chromatogram of PD1_{n-3} DPA (5).

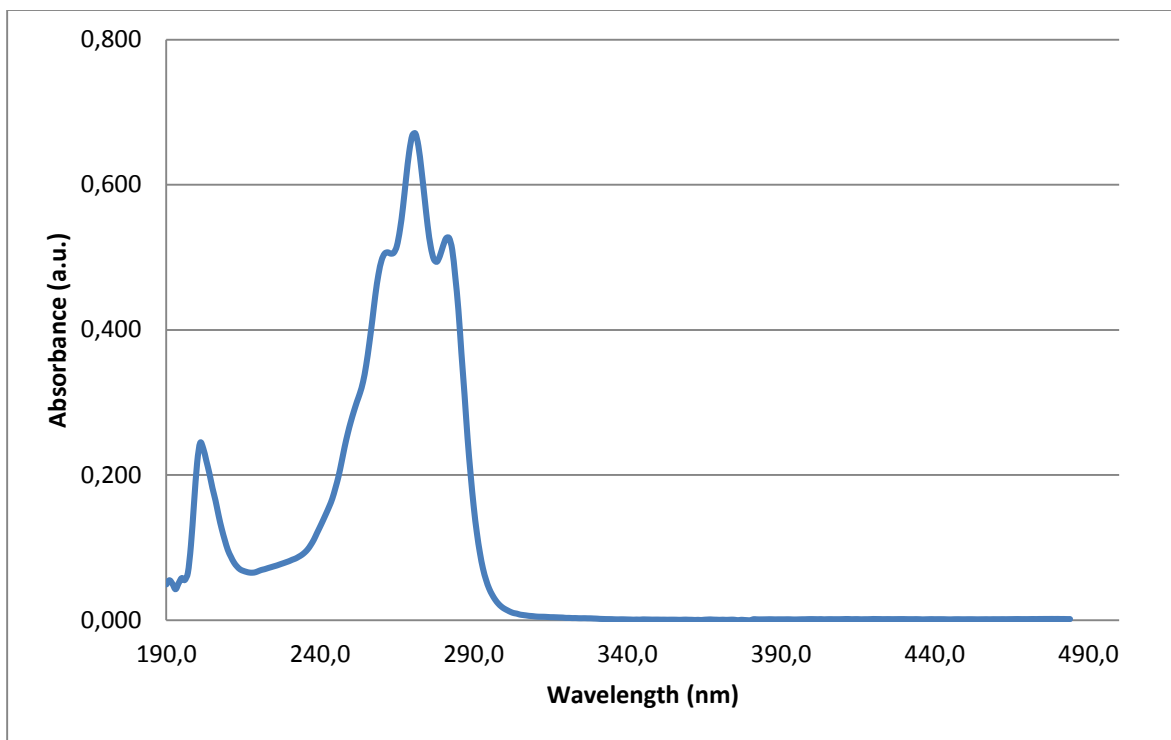


Figure S-22 UV-Vis chromatogram of methyl ester **6**.

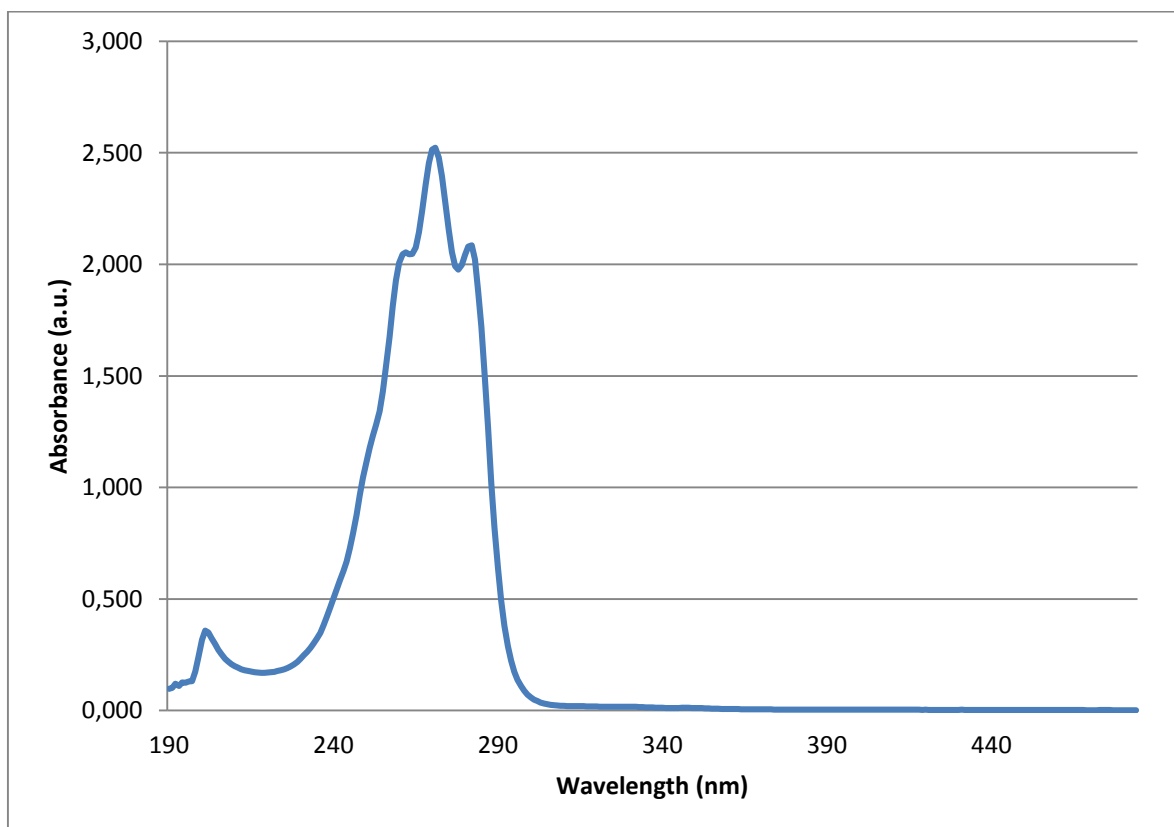


Figure S-23 UV-Vis chromatogram of PD_{1n-3}DPA (**5**).

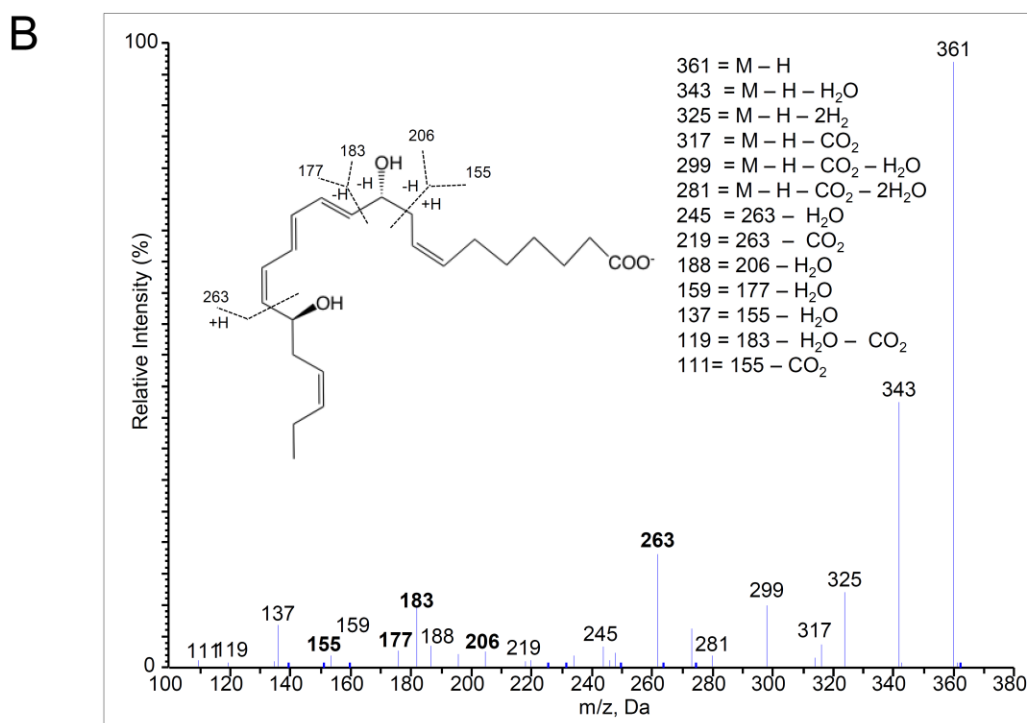
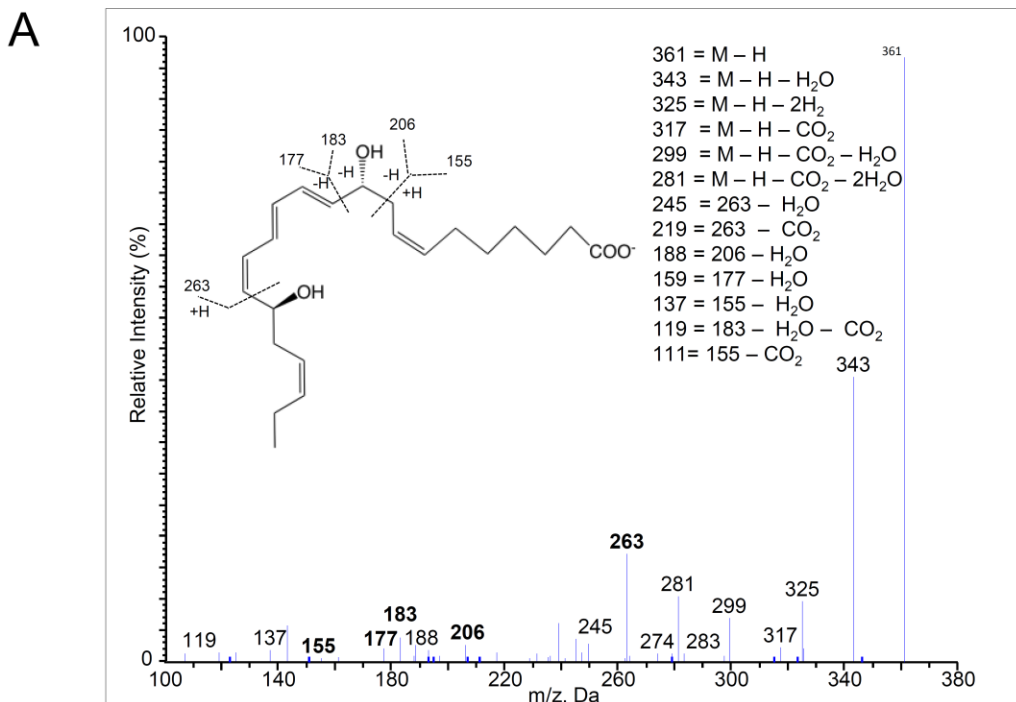


Figure S-24 Matching MS-MS spectra for exudate PD1_{n-3}DPA (**5**) and synthetic material **5**. Representative MS-MS spectra. A) Endogenous PD1_{n-3}DPA (**5**) obtained from mice injected with zymosan (1 mg/mouse) and exudates collected at 4 h. MS-MS spectrum for peak at T_R = 12.4 min. n = 4 mice exudates. B) MS-MS spectrum of synthetic material **5** (T_R = 12.4 min). d = 4.

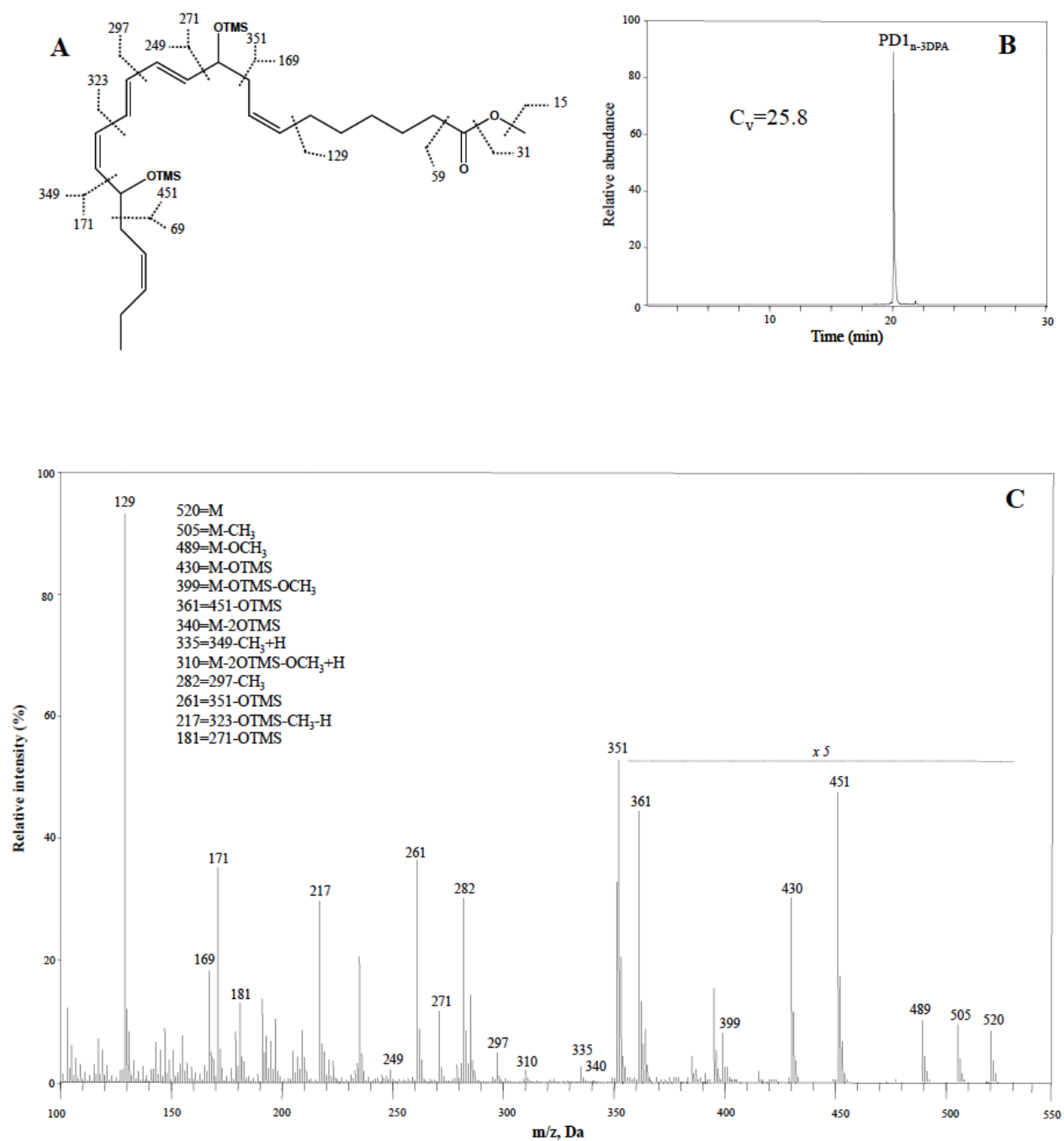


Figure S-25 Physical properties of synthetic PD1_{n-3} DPA (**5**) determined by GC-MS. A) Selected ion chromatogram (*m/z* 351) of PD1_{n-3} DPA (**5**) (*T_R* = 20.1 min and *C_v* = 25.8). B) GC-MS spectrum of the derivatized PD1_{n-3} DPA (**5**). MS-spectra were obtained following treatment with diazomethane and BSTFA. See experimental procedures for further details.

Table S1. Assigned fragments of *bis*-OTMS-methyl ester of **6** obtained from GC/MS analyses.

Fragment (m/z, Da)	Mass of Lost Fragment (m/z, Da)	Fragment Assignment
520		M
505	15	M-CH ₃
489	31	M-OCH ₃
451	69	M-CH ₂ (CH) ₂ CH ₂ CH ₃
430	90	M-OTMS
399	121	M-OTMS-OCH ₃
361	159	M-CH ₂ (CH) ₂ CH ₂ CH ₃ -OTMS
351	169	M-(CH) ₂ (CH ₂) ₅ COOCH ₃
340	180	M-(OTMS) ₂
335	185	M-CHOTMSCH ₂ (CH) ₂ CH ₂ CH ₃ -CH ₂ ⁻
310	210	M-(OTMS) ₂ -OCH ₂ -
297		(CH) ₂ CHOTMSCH ₂ (CH) ₂ (CH ₂) ₅ COOCH ₃
282		(CH) ₂ CHOTMSCH ₂ (CH) ₂ (CH ₂) ₅ COO
271		CHOTMSCH ₂ (CH) ₂ (CH ₂) ₅ COOCH ₃
261		CHOTMS(CH) ₆ CHCH ₂ (CH) ₂ CH ₂ CH ₃
249	271	M-CHOTMSCH ₂ (CH) ₂ (CH ₂) ₅ COOCH ₃
217	303	M-(CH) ₂ CHOTMSCH ₂ (CH) ₂ CH ₂ CH ₃ -OTMS-CH ₄ ⁺
181		CHCH ₂ (CH) ₂ (CH ₂) ₅ COOCH ₃
171		CHOTMSCH ₂ (CH) ₂ CH ₂ CH ₃
169		CH ₂ (CH) ₂ (CH ₂) ₅ COOCH ₃
129		(CH ₂) ₅ COOCH ₃
81		CHCH ₂ (CH) ₂ CH ₂ CH ₃
73		TMS
69		CH ₂ (CH) ₂ CH ₂ CH ₃
59		COOCH ₃

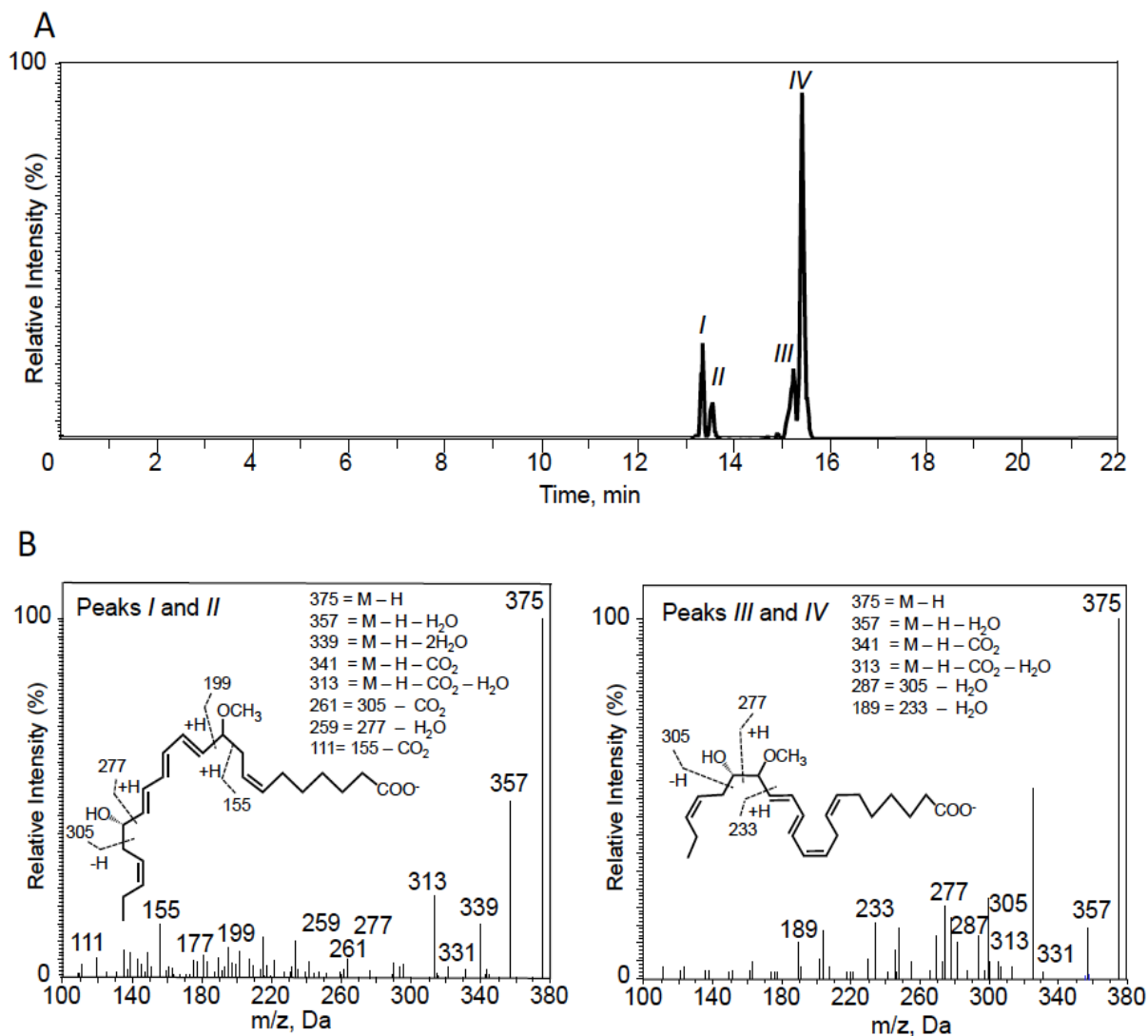


Figure S26. Methanol trapping products of the 16,17-epoxy-PD1_{n-3} DPA. Soybean lipoxygenase (50U/100 μ l) was incubated with n-3 DPA (0.2 μ M, borate buffer, pH = 8.0, r.t.). The reaction was quenched with eight volumes acidified methanol (apparent pH \sim 3.5) and products assessed by lipid mediator metabololipidomics. (A) Multiple Reaction Monitoring Chromatogram (375 > 277). (B) MS-MS fragmentation patterns for products under peaks I-IV. Results are representative of n = 3 incubations.

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