Supplementary Materials:

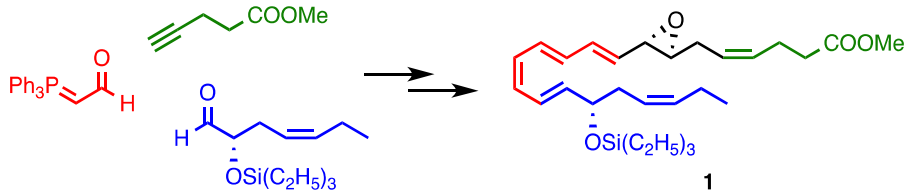
On the total synthesis of 7,8(*S*,*S*)-epoxy-17(*S*)-hydroxy-4(*Z*),9(*E*),11(*E*),13(*Z*),15(*E*),19(*Z*)-docosahexaenoic acid derivative

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General Information

Unless stated otherwise, all reactions were carried out in a flame-dried round-bottom flask equipped with a stirring bar under argon atmosphere. Reactions were carried out using DriSolv solvents purchased from VWR (Radnor, PA, USA). Research-grade reagents were purchased and used without further purification from suppliers including Sigma-Aldrich (St. Louis, MO, USA), Strem Chemicals (Newburyport, MA, USA), Combi-Blocks (San Diego, CA, USA), TCI America (Portland, OR, USA), and Alfa Aesar (Ward Hill, MA, USA).

Reaction progress was monitored using EMD analytical thin-layer chromatography (TLC) plates, Silica Gel 60 F254 (Sigma-Aldrich, St. Louis, MO, USA). TLC plates were visualized through UV absorbance, or staining techniques including vanillin, phosphomolybdic acid, potassium-permanganate, or ninhydrin followed by heating. Purification was carried out by manual flash chromatography or by automated system using Biotage Isolera One (Biotage, Uppsala, Sweden) on Silica Gel (100-200 mesh). The final product was further purified by HPLC on Agilent 1100 Series or 1260 Infinity HPLC system (Agilent, Santa Clara, CA, USA) equipped with a binary pump and diode array detector on a Luna 5 μm Silica (2) 100 Å, 250 × 10 mm column (Phenomenex, Torrance, CA, USA) under straight-phase conditions.

NMR data were procured on Varian NMR spectrometers (Varian Inc, Palo Alto, CA, USA) at 400, 500 or 600 MHz, respectively, for ^{1}H NMR, and at 101, 126 or 151 MHz, for ^{13}C NMR. ^{1}H and ^{13}C chemical shifts (δ) are recorded in parts per million (ppm), relative to the residual protium and carbon solvent resonances in ^{1}H NMR (*e.g.*, Chloroform-*d*, ^{1}H = 7.26 ppm; benzene-d_6, ^{1}H = 7.16 ppm; and methanol-d_4, ^{1}H = 3.31 ppm) and ^{1}C NMR (*e.g.*, Chloroform-*d*, ^{13}C = 77.16 ppm; benzene-d_6, ^{13}C = 128.06 ppm; and methanol-d_4, ^{13}C = 49.00 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.

Liquid chromatography and tandem mass spectrometry (LC-MS/MS) data were procured on a Sciex Triple Quad 7500 (Sciex, Framingham, MA, USA) coupled with an

ExionLC analytical HPLC (Sciex, Framingham, MA, USA) on a Kinetex 2.6 μm PS C18 100 Å, 100 × 3.0 mm column (Phenomenex, Torrance, CA, USA) under reversed phase conditions.

Selected ^{1}H and ^{13}C NMR Spectra

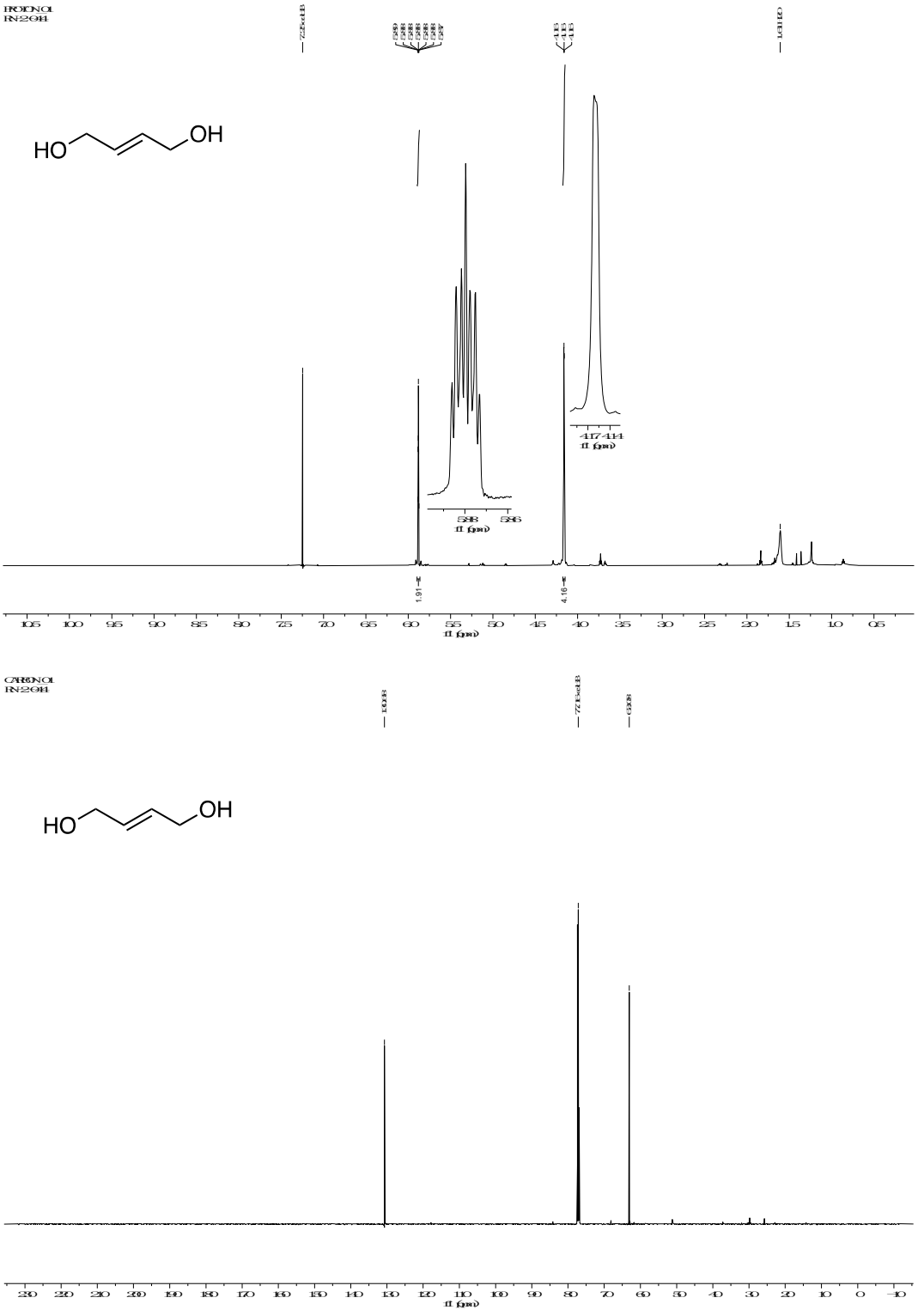


Figure S1. ^{1}H and ^{13}C NMR spectra of *trans*-2-butene-1,4-diol precursor to **4**.

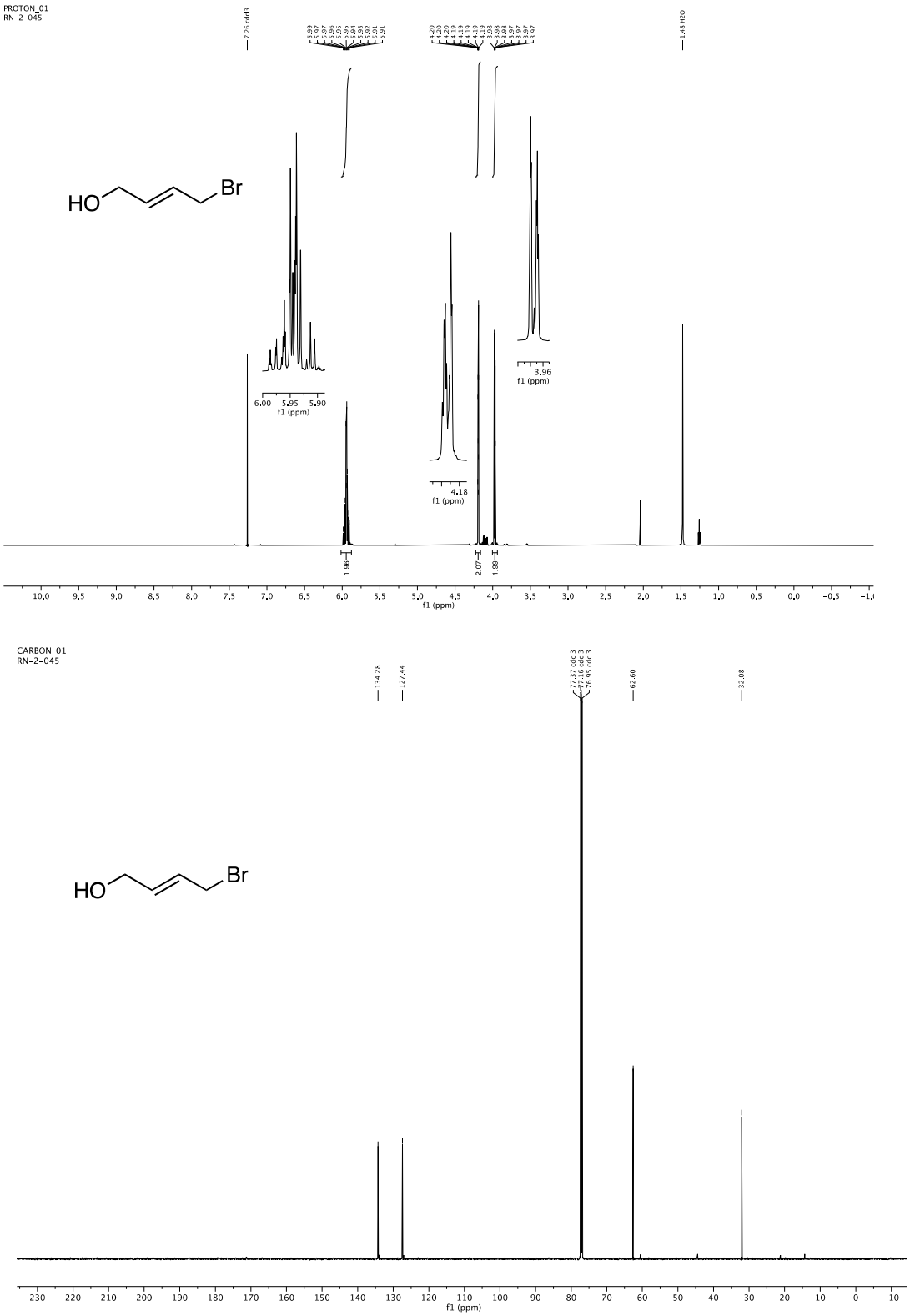


Figure S2. ^{1}H and ^{13}C NMR spectra of compound **4**.

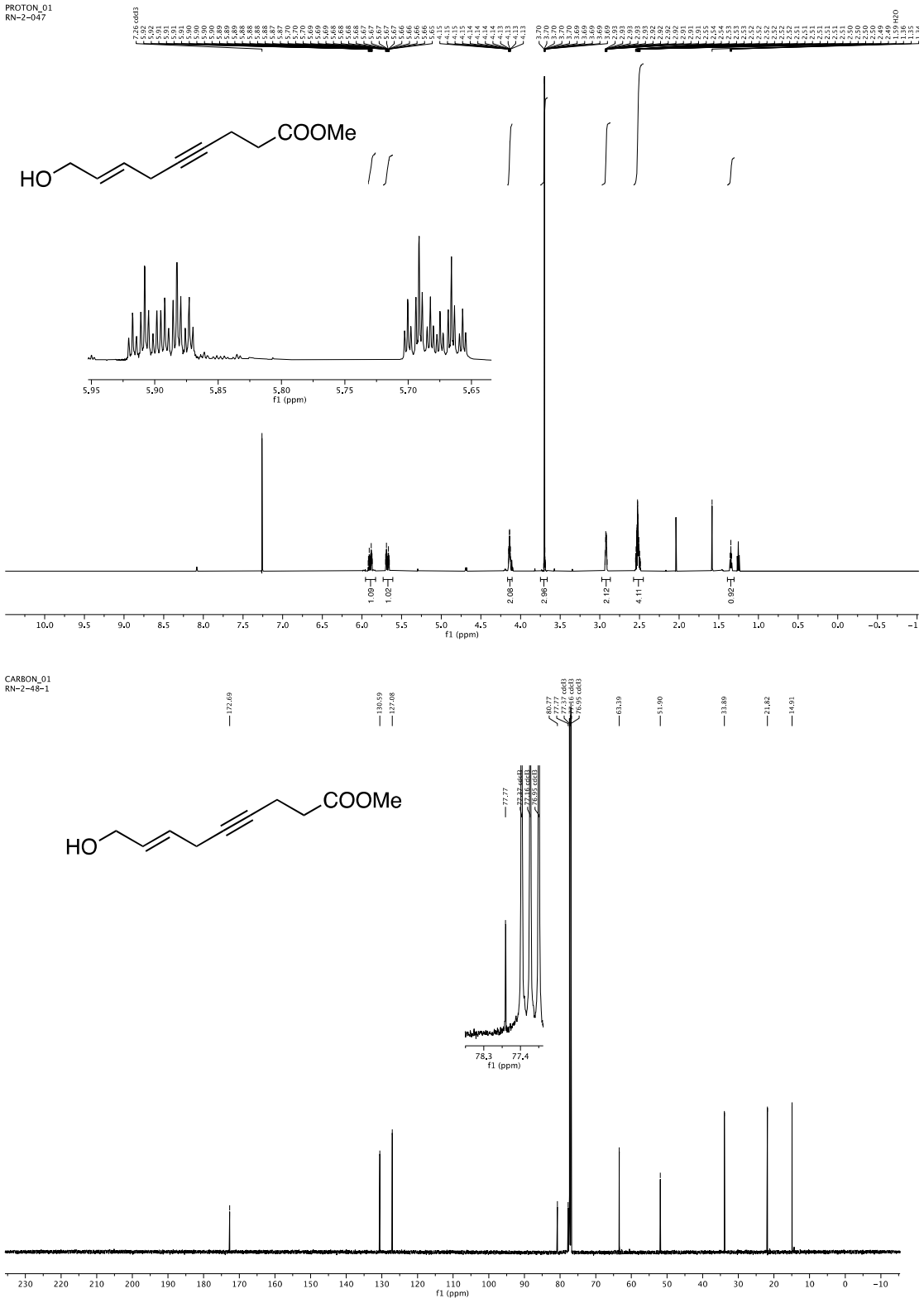


Figure S3. ^{1}H and ^{13}C NMR spectra of skipped enyne precursor to **5**.

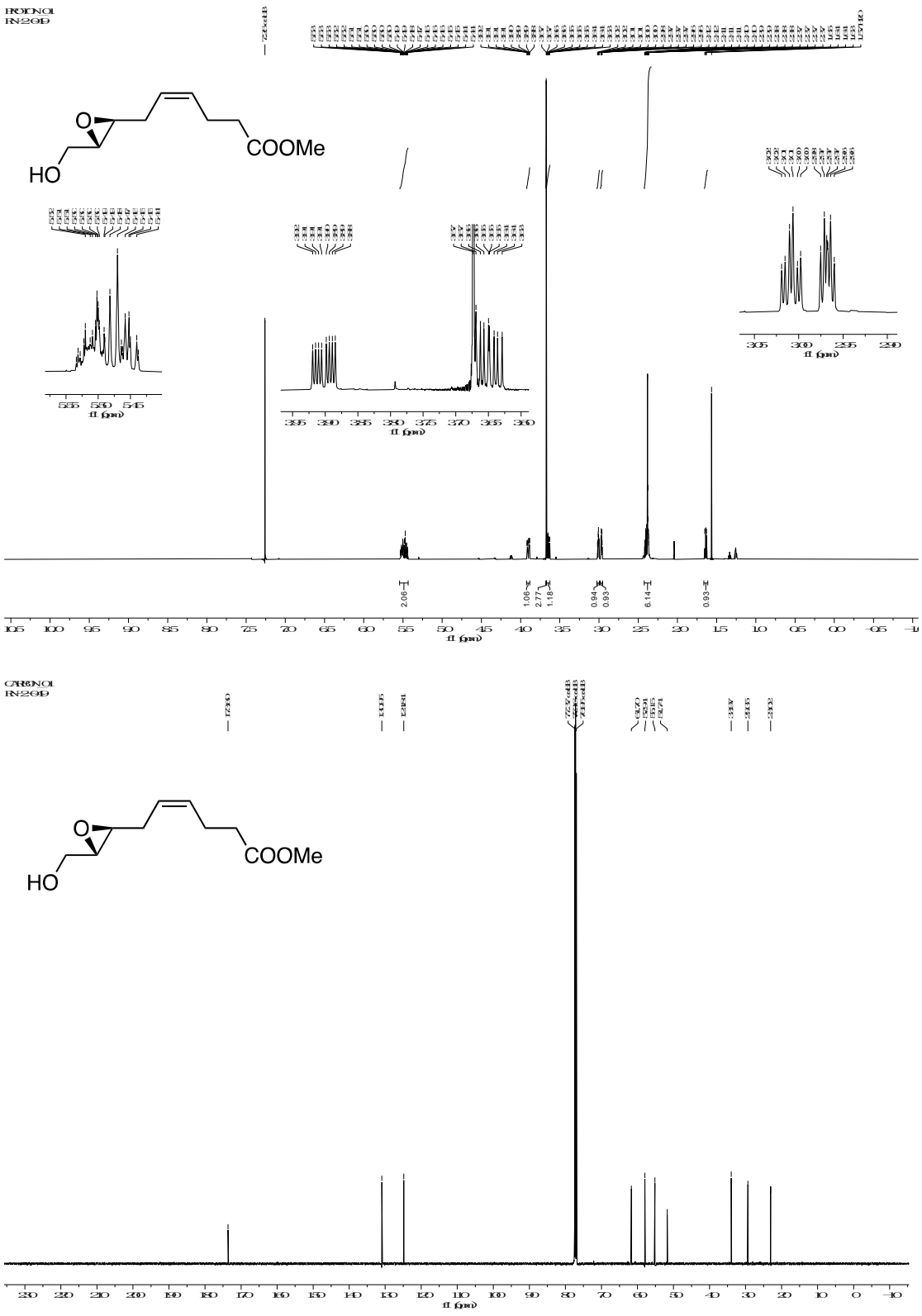


Figure S4. ^{1}H and ^{13}C NMR spectra of epoxyalcohol precursor to **6**.

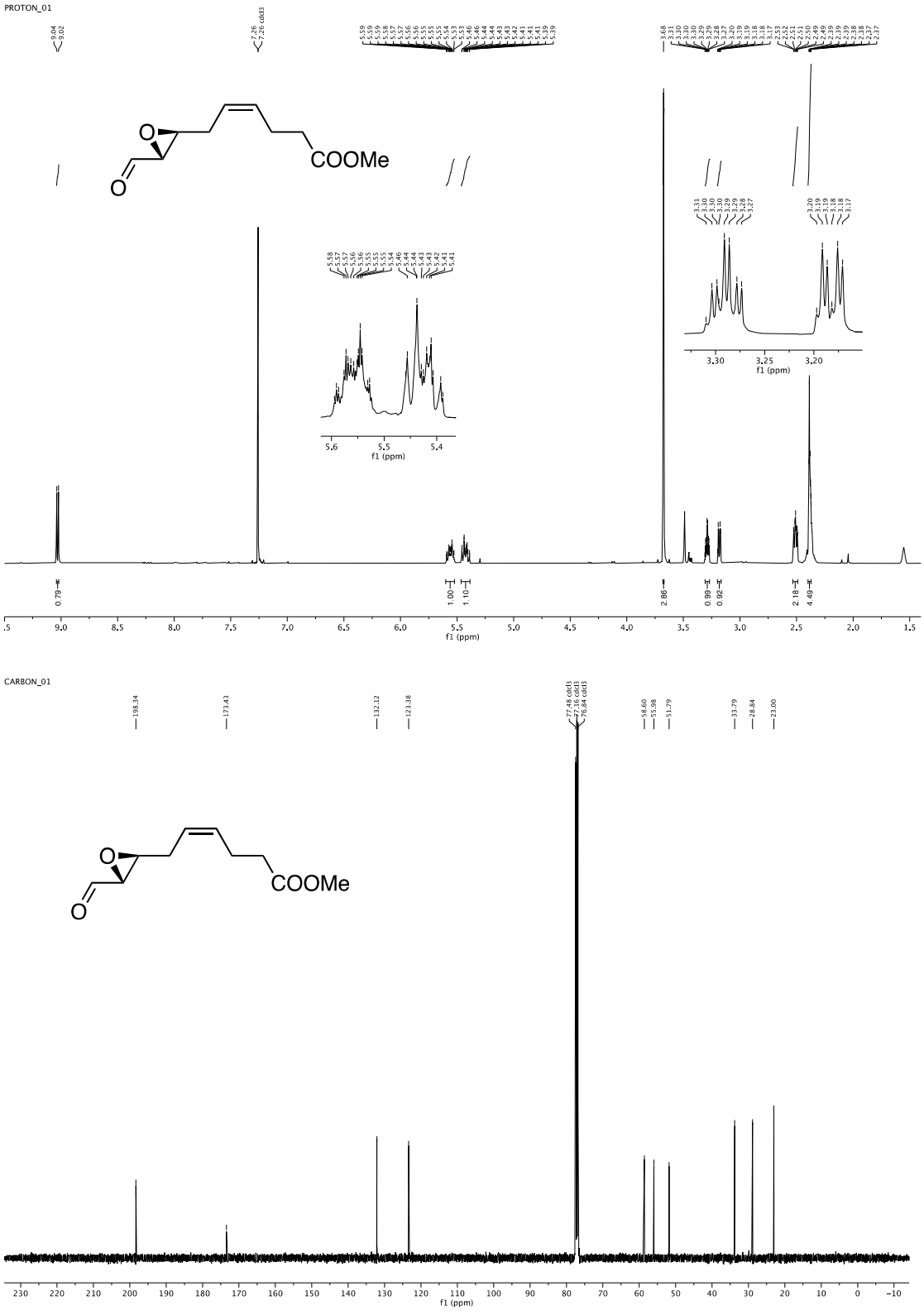


Figure S5. ^{1}H and ^{13}C NMR spectra of epoxyaldehyde **6**.

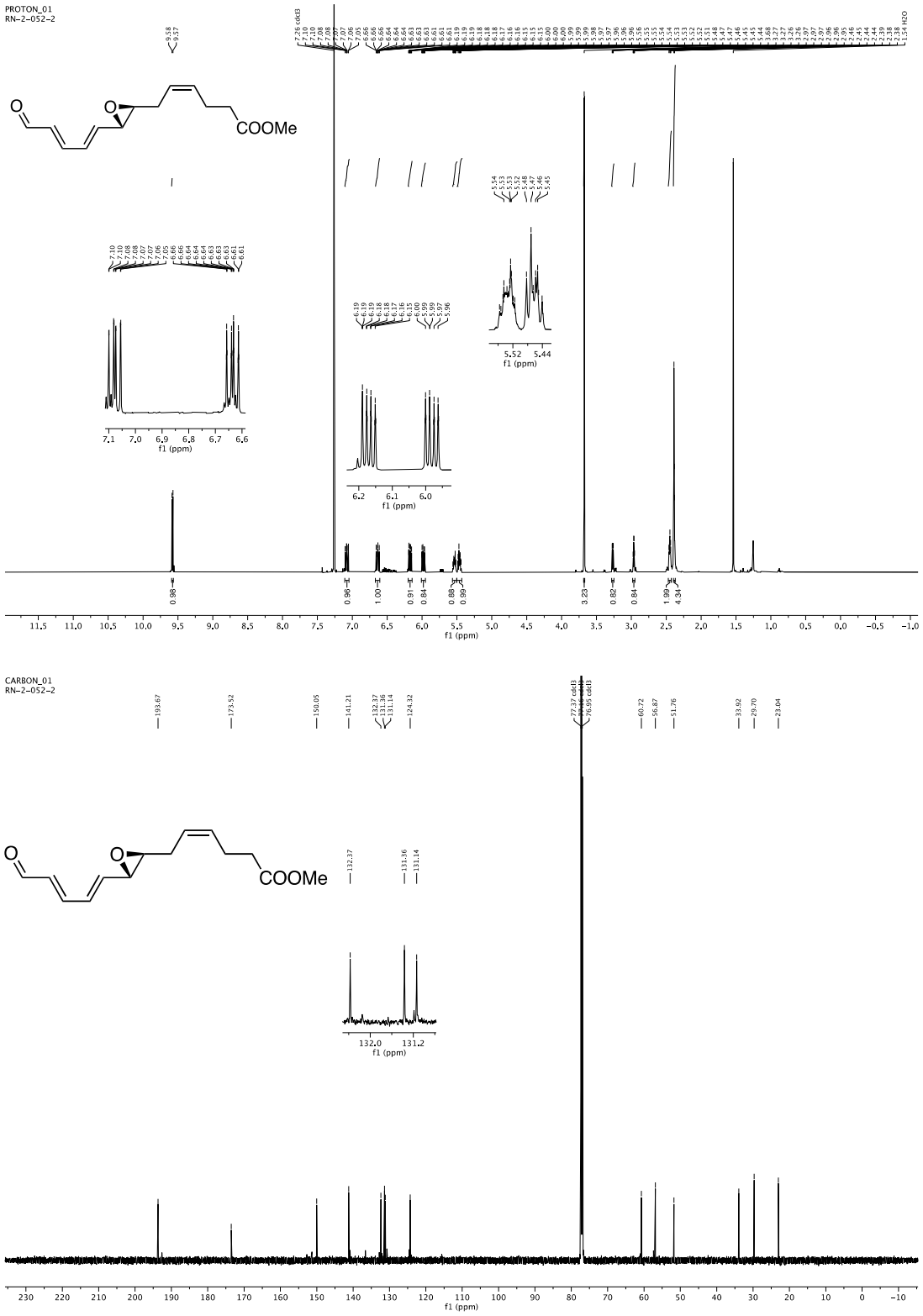


Figure S6. ^{1}H and ^{13}C NMR spectra of C_1–C_{13} epoxydienal **2**.

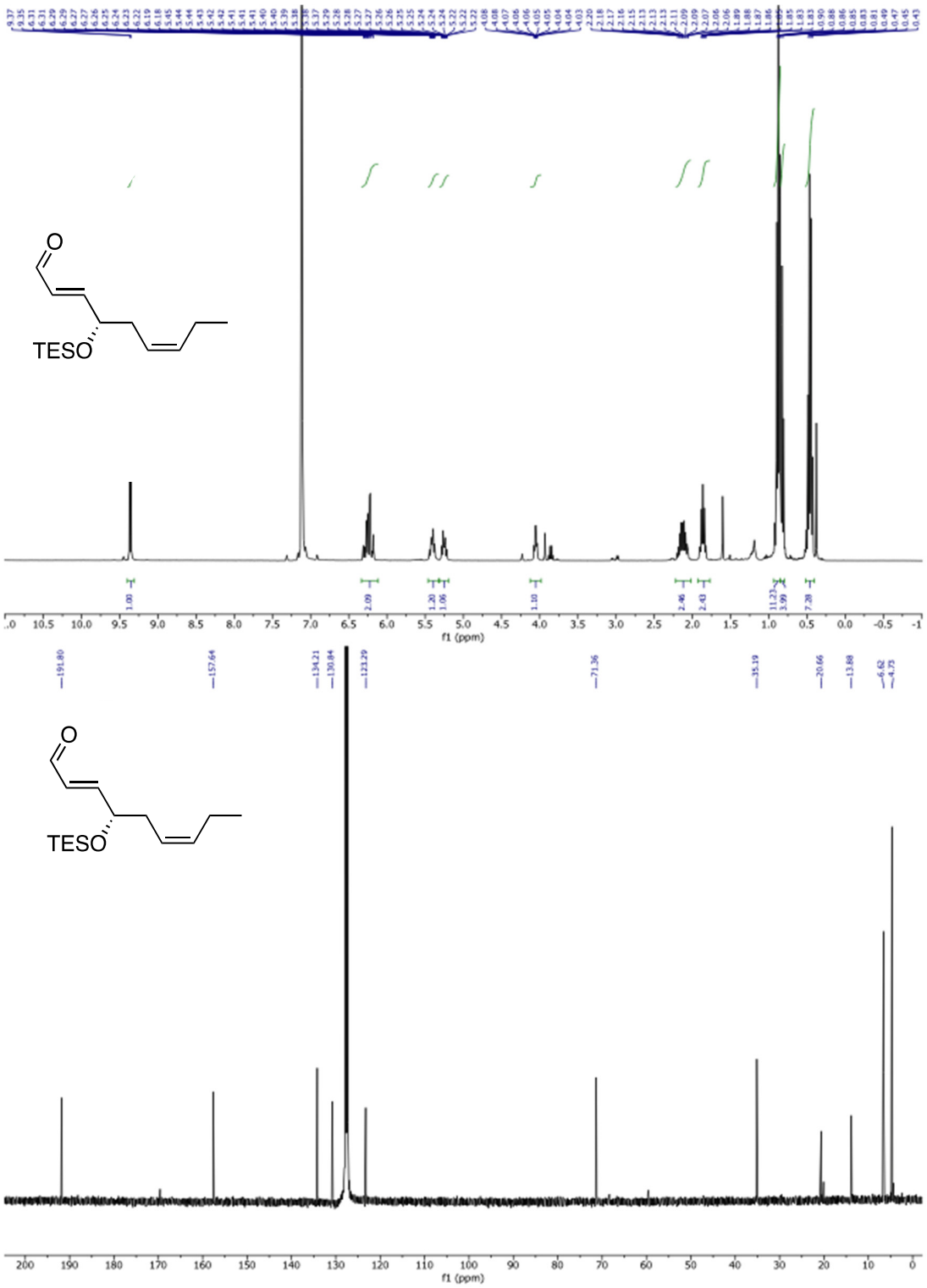


Figure S7. ^{1}H and ^{13}C NMR spectra of compound **8**.

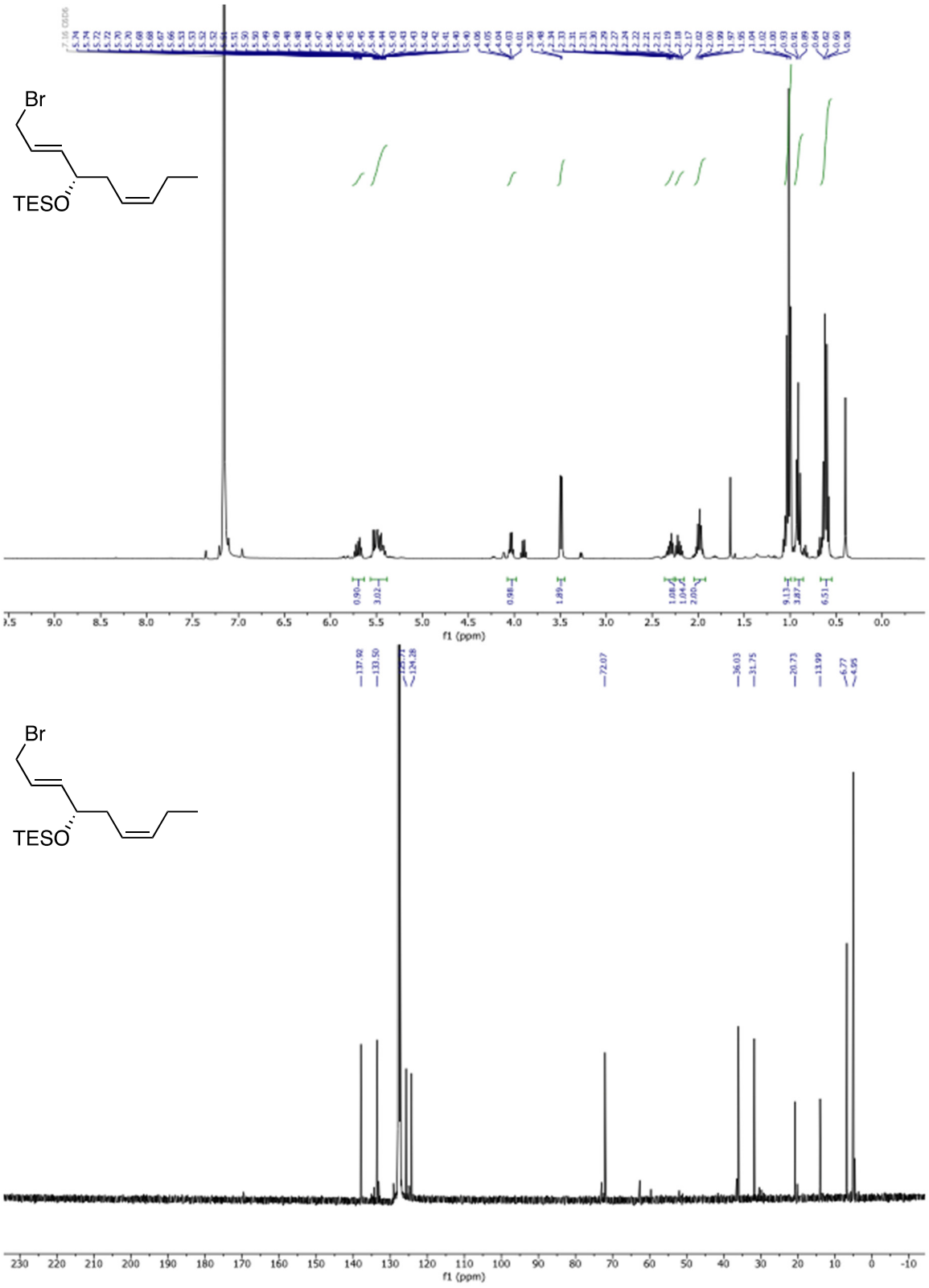


Figure S8. ^{1}H and ^{13}C NMR spectra of allylic bromide **9**.

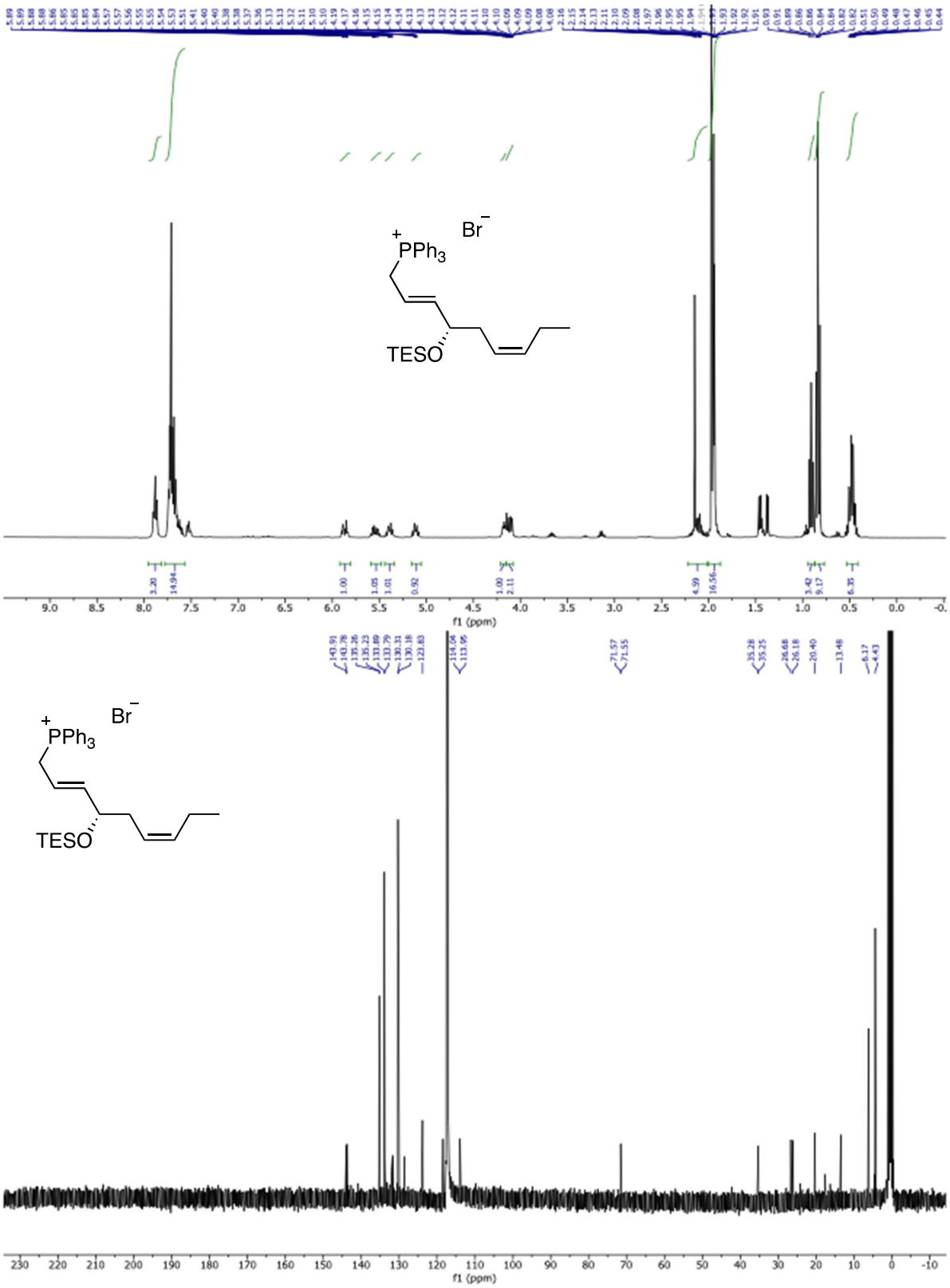


Figure S9.[1]H and [13]C NMR spectra of phosphonium bromide **3**.

UV, HPLC, and LC-MS/MS Chromatograms and Spectra

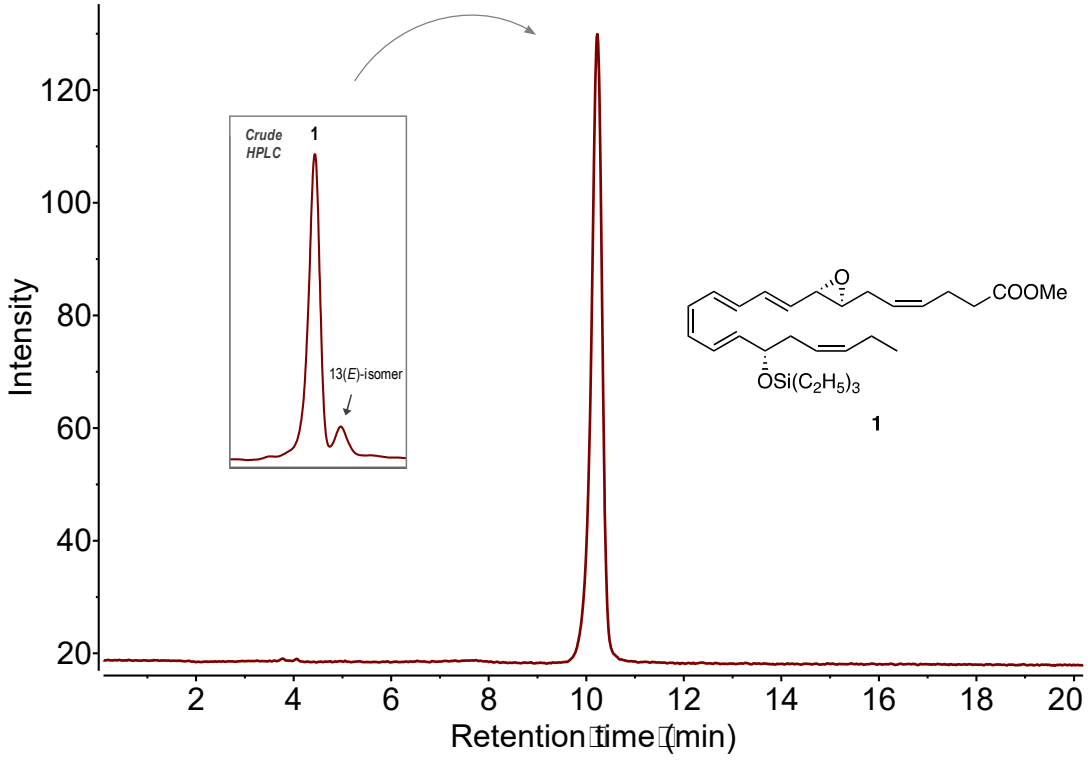


Figure S10. HPLC chromatogram of purified target compound **1**. *Inset,* chromatographic trace of crude mixture showing the presence of the 13(*E*)-geometric isomer (~1:9 *E*/*Z* ratio).

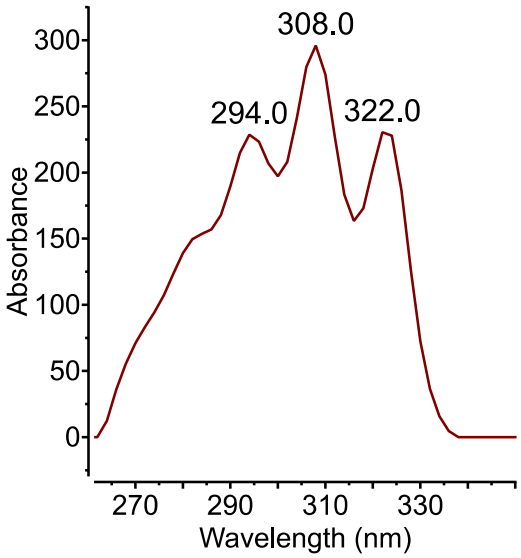


Figure S11. UV absorbance spectrum of compound **1**.

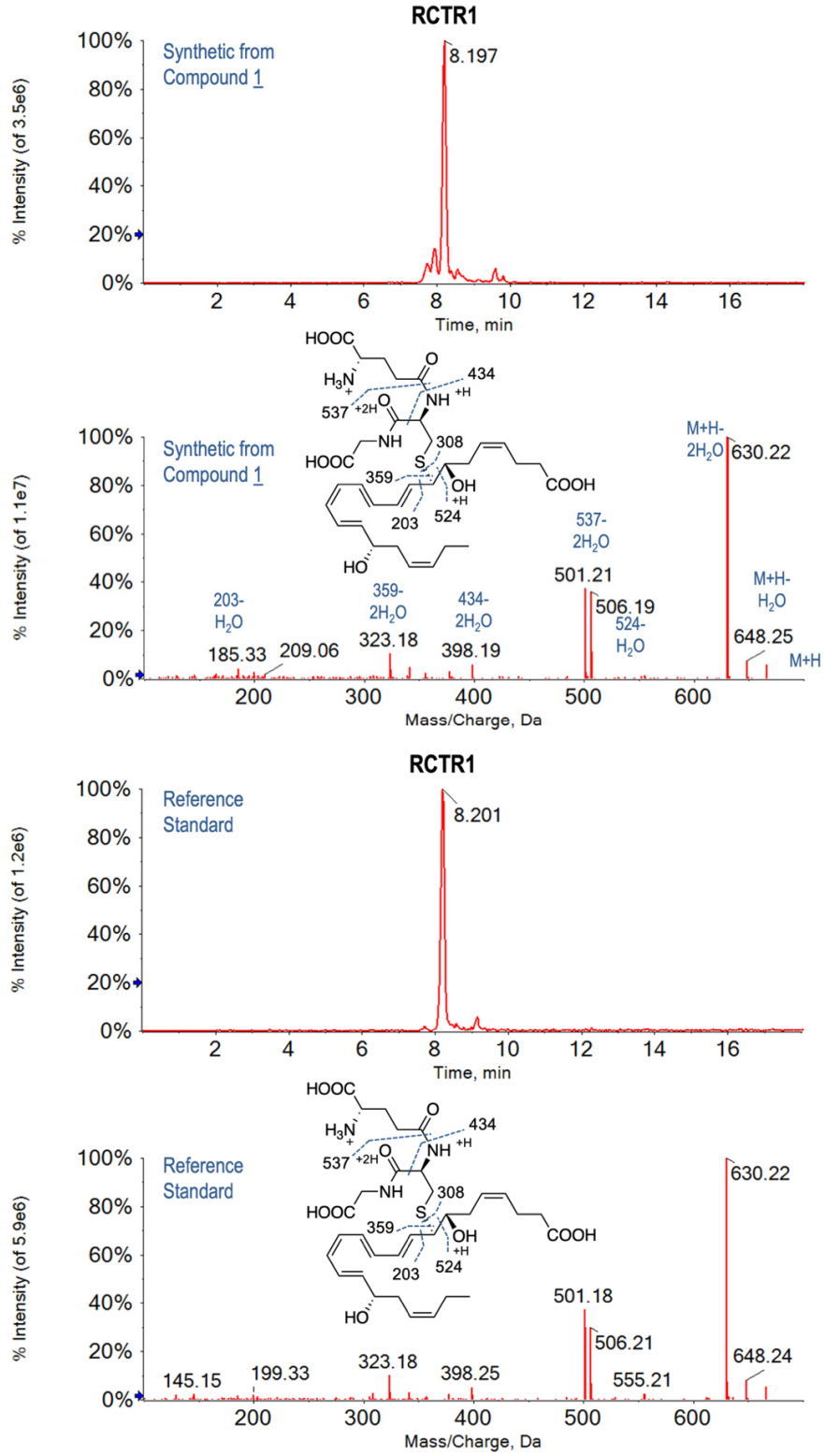


Figure S12. Retention time and MS² fragmentation spectrum of RCTR1, synthesized from compound **1**, and matching of these physical properties to the reference standard.

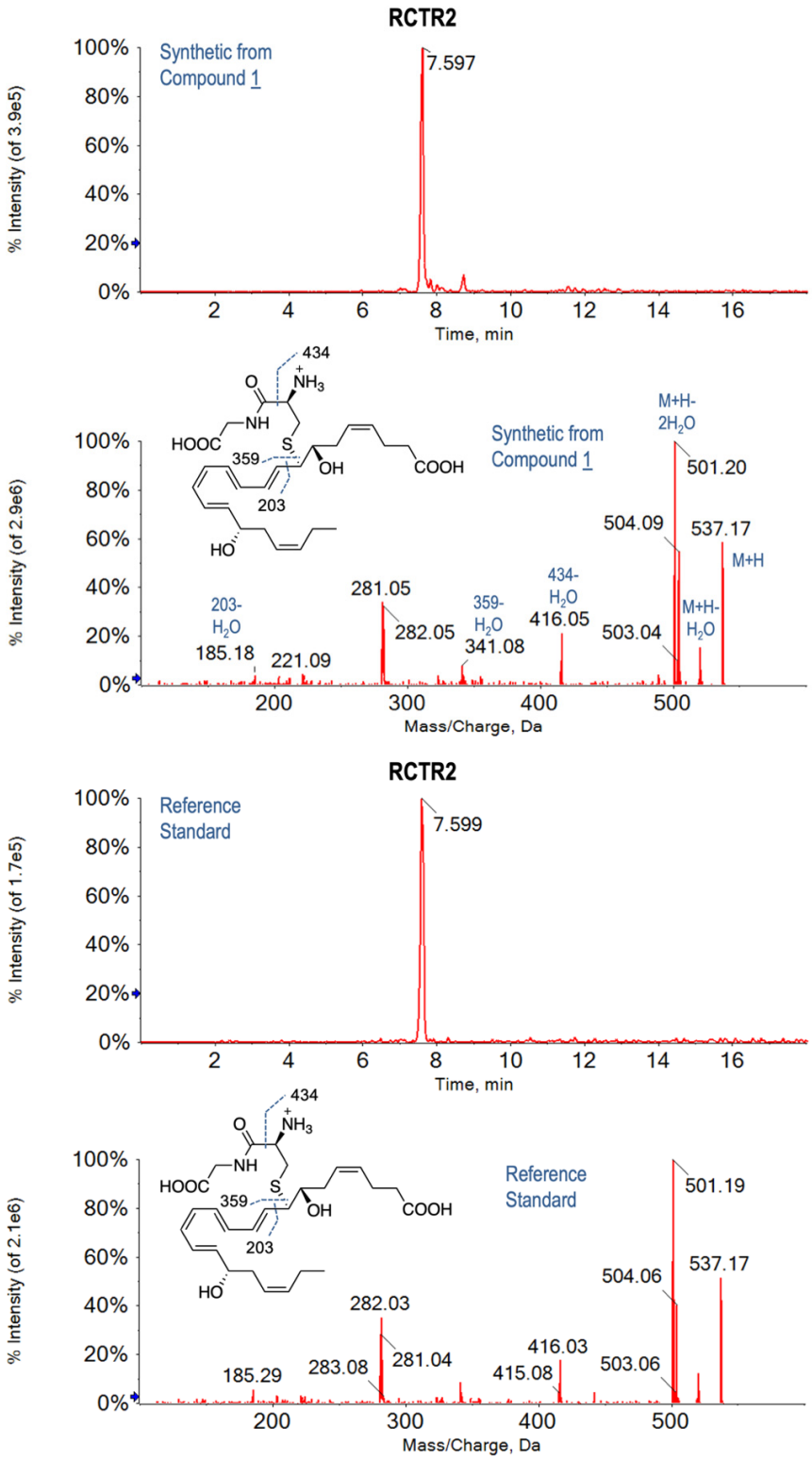


Figure S13. Retention time and MS² fragmentation spectrum of RCTR2, synthesized from compound **1**, and matching of these physical properties to the reference standard.

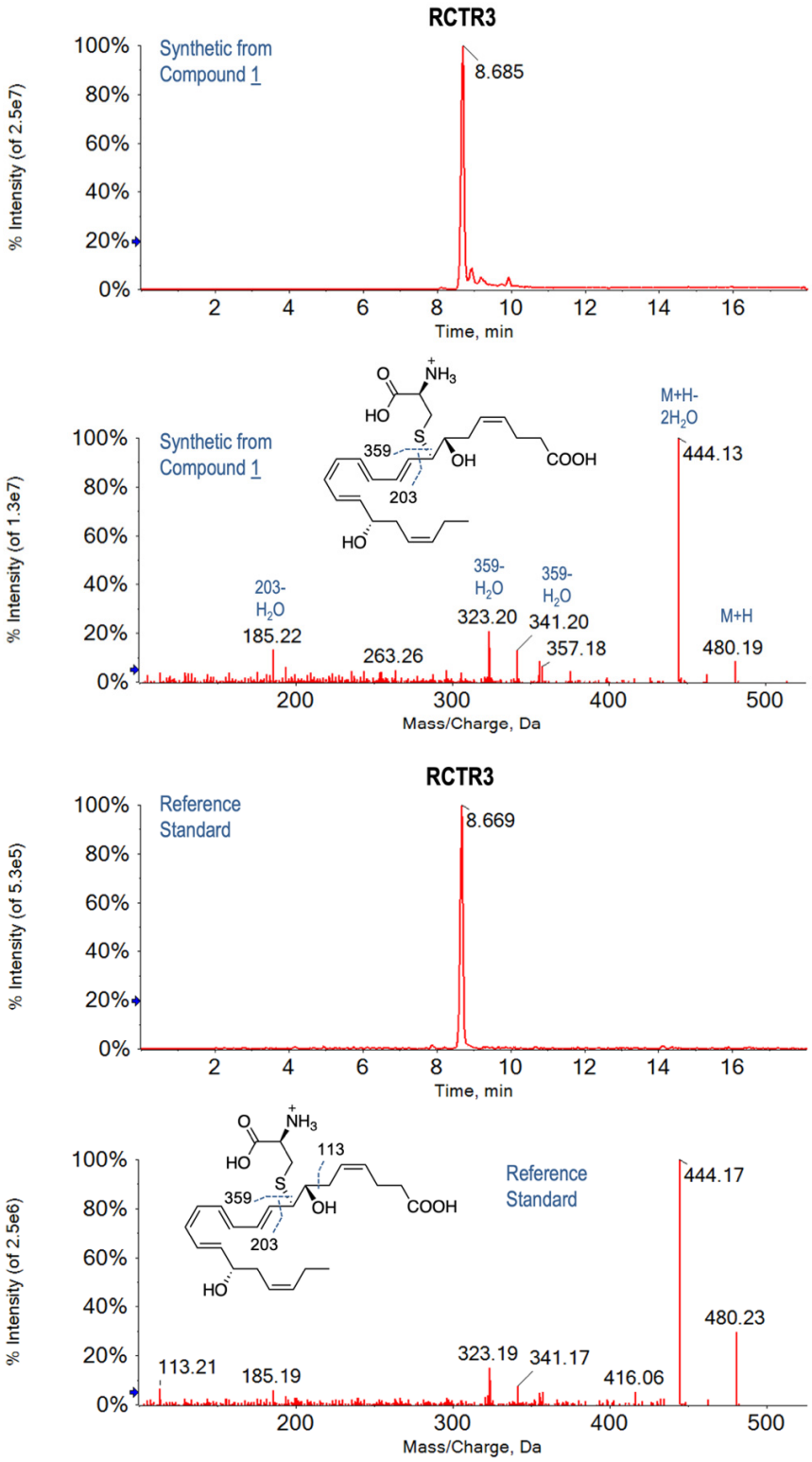


Figure S14. Retention time and MS² fragmentation spectrum of RCTR3, synthesized from compound **1**, and matching of these physical properties to the reference standard.