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Supporting Information

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Total Synthesis of Amphidinolide F**

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SUPPORTING INFORMATION

Table of Contents

General: All experiments involving air- and moisture-sensitive compounds were performed under an atmosphere of dry argon in flame-dried glassware. The solvents were purified by distillation over the drying agents indicated, and were transferred under argon: THF, Et_2O (Mg/anthracene), CH_2Cl_2 (P_4O_{10}), Et_3N (CaH_2), MeOH (Mg), DMF (Desmodur®, dibutyltin dilaurate), toluene (Na/K). Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM® SIL/UV254); flash chromatography: Merck silica gel 60N (Spherical, neutral, 230–400 mesh). ^{1}H and ^{13}C NMR spectra were recorded by using a DPX 300 (300 MHz), AV 400 (400 MHz), AV 500 (500 MHz), AV 600 (600 MHz) spectrometer in the solvent indicated; chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to tetramethylsilane scale ($CDCl_3$: δ_C = 77.16 ppm; residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm; CD_2Cl_2: δ_C = 53.84 ppm; residual $CHDCl_2$ in CD_2Cl_2: δ_H = 5.32 ppm; C_6D_6: δ_C = 128.06 ppm; residual C_6H_6 in C_6D_6: δ_H = 7.16 ppm; $(CD_3)_2CO$: δ_C = 205.87 ppm; residual $(CH_3)_2CO$ in $(CD_3)_2CO$: δ_H = 2.09 ppm). Multiplicities are described by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, pent. = pentet, m = multiplet, b = broad. Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectra were recorded with a Perkin-Elmer Spectrum One FT-IR spectrometer equipped with Perkin-Elmer Universal ATR Sampling Accessory, wavenumbers ($\tilde{\nu}$) in cm^{-1}. Optical rotations ($[\alpha]_D^{20}$) were measured with a Perkin-Elmer Model 343 polarimeter. Low resolution mass spectra (MS) were obtained with a Finnigan MAT 8200 (70 eV, EI); high-resolution mass spectra (HRMS) were obtained with a Finnigan MAT 95 (ESI-MS) or a Bruker APEX III FT-ICR-MS (7 T magnet). Unless stated otherwise, all commercially available compounds (Aldrich, Strem, TCI, Alpha-Aesar, Acros) were used as received.

Where indicated, the signal assignments in the NMR spectra are unambiguous; the numbering scheme is arbitrary and shown in the inserts. The assignments are based upon 1D and 2D spectra recorded using the following pulse sequences from the Bruker standard pulse program library: DEPT; COSY (*cosygpqf* and *cosydqtp*); HSQC (*hsqcedetgpsisp2.2*) optimized for $^1J_{C,H}$ = 145 Hz; HMBC (*hmbcetgpl3nd*) for correlations via $^nJ_{C,H}$; HSQC-TOCSY (*invietgsml*) using an MLEV17 mixing time of 120 ms; NOESY (noesygpph).

Preparation of Fragment D

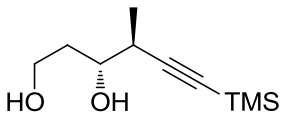
Compound S1. A flame-dried, 1000-mL round-bottomed flask equipped with an argon inlet, a rubber septum and a magnetic stir-bar, was charged with 1,3-propanediol (28.7 mL, 400 mmol, 2.0 equiv), CH_2Cl_2 (400 mL) and triethylamine (33.4 mL, 240 mmol, 1.2 equiv) to give a clear solution. After cooling to 0 °C using an ice bath, a solution of TBSCl (30.1 g, 200 mmol, 1.0 equiv) in CH_2Cl_2 (60 mL) was added via cannula and the resulting mixture stirred at room temperature overnight (15 h). For work up, aq. sat. $NaHCO_3$ (100 mL) was added. The contents were transferred to a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (40 mL). The combined organic phases were washed with H_2O (100 mL) and brine (100 mL). The organic layer was then dried using $MgSO_4$, filtered and evaporated and the remaining yellow oil was purified by flash chromatography (SiO_2, hexanes/EtOAc, 30→50%) to afford **S1** as a colorless oil (32.7 g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (t, *J* = 5.6 Hz, 2H), 3.80 (t, *J* = 5.6 Hz, 2H), 2.31 (bs, 1H), 1.78 (quint, *J* = 5.6 Hz, 2H), 0.90 (s, 9H), 0.08 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.1, 62.6, 34.4, 26.0 (3C), 18.3, –5.4 ppm (2C); IR (film): 3347, 2929, 2857, 1472, 1388, 1361, 1254, 1086, 1006, 961, 833, 773 cm^{-1}.

Compound 6. A 1000-mL round-bottomed flask, equipped with a magnetic stir-bar, was charged with alcohol **S1** (14.0 g, 73.6 mmol, 1.0 equiv). CH_2Cl_2 (360 mL) and pH 8.6 carbonate buffer (365 mL) containing potassium bromide (876 mg, 7.36 mmol, 0.10 equiv) were added and the resulting biphasic mixture was cooled to 0 °C using an ice bath. Once this temperature was reached, 2,2,6,6-tetramethyl-piperidin-1-yl)oxyl (TEMPO, 115 mg, 0.736 mmol, 0.01 equiv) was introduced, causing a color change of the organic layer to bright orange. Next, an aqueous solution of sodium hypochlorite (~ 10%, 95 mL) was diluted with pH 8.6 carbonate buffer (365 mL) in a 1000-mL Erlenmeyer flask. This solution was also cooled to 0 °C before it was added to the biphasic mixture, which was then stirred at this temperature until the reaction was complete, as judged by TLC analysis (~ 1 h; note: when complete conversion is reached, a color change occurs from bright orange to light yellow). The reaction was quenched with aq. sat. $Na_2S_2O_3$ (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 40 mL) and the combined organic extracts were washed with H_2O (100 mL) and brine (100 mL) before being dried over Na_2SO_4. The solvent was evaporated to give the volatile aldehyde **6** (11.9 g, 86%) as a colorless oil, which was used in the next step without further purification. ^{1}H NMR (300 MHz, C_6D_6): δ = 9.40 (t, *J* = 1.9 Hz, 1H), 3.57 (t, *J* = 6.0 Hz, 2H), 2.03 (dt, *J* = 1.9, 6.0 Hz, 2H), 0.90 (s, 9H), –0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, C_6D_6): δ = 200.5, 58.0, 47.2, 26.6 (3C), 18.9, –4.8 ppm (2C); IR (film): 2955, 2930, 2886, 2858, 1727, 1472, 1464, 1389, 1361, 1254, 1212, 1094, 970, 820, 774 cm^{-1}; MS (EI): *m/z* (%): 131 (M^+–57, 68), 101 (100), 75 (51), 59 (27), 45(10); HRMS (CI (FE), *i*-butane) calcd. for $C_9H_{21}O_2Si$ [M + H^+] 189.1311, found 189.1309.

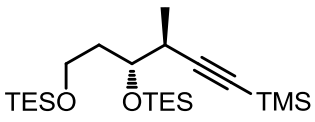
Compound 8. A three-necked, 500-mL jacketed Schlenk flask, equipped with a magnetic stir-bar, argon bubbler and two septa, was charged with $Pd(OAc)_2$ (596 mg, 2.65 mmol, 0.05 equiv), THF (16 mL) and PPh_3 (696 mg, 2.65 mmol, 0.05 equiv). The resulting orange solution was cooled to –78 °C before a solution of (*S*)-methanesulfonate **7** (17.5 g, 79.6 mmol, 1.5 equiv) in THF (20 mL) was added. After stirring for 10 min, a solution of aldehyde **6** (10.0 g, 53.1 mmol, 1.0 equiv) in THF (16 mL) was introduced before diethylzinc (1.0 M in hexane, 159 mL, 159 mmol, 3.0 equiv) was added via cannula (care was taken to add the solution dropwise directly into the mixture). The reaction was stirred for 1 h at this temperature before it was allowed to gradually warm to –20 °C over 4 h and stirred at this temperature for 12 h. At this point, the gray mixture was diluted with *tert*-butyl methyl ether (80 mL) and the reaction was carefully quenched with aqueous sat. NH_4Cl (40 mL). The resulting emulsion was filtered through a pad of Celite that was carefully rinsed with *tert*-butyl methyl ether (160 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 50 mL). The combined extracts were washed with aq. sat. NH_4Cl (70 mL), H_2O (100 mL) and brine (100 mL), dried over $MgSO_4$, filtered and evaporated. The crude product was purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 3→7%) to give product **8** (14.5 g, 87%) as a mixture of diastereomers (90:10, *anti:syn*). $[\alpha]_D^{20} = -6.2°$ (c = 1.07, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.00-3.59 (m, 3H), 3.53 (bs, 1H, *syn*), 2.90 (bs, 1H, *anti*), 2.60 (dq, *J* = 4.5, 7.0 Hz, 1H, *anti*), 2.64-2.48 (m, 1H, *syn*), 1.83-1.61 (m, 2H), 1.21 (d, *J* = 6.6 Hz, 3H, *syn*), 1.20 (d, *J* = 7.1 Hz, 3H, *anti*), 0.90 (s, 9H), 0.14 (s, 9H, *anti*), 0.13 (s, 9H, *syn*), 0.08 (s, 6H, *syn*), 0.07 ppm (s, 6H, *anti*); ^{13}C NMR (75 MHz, $CDCl_3$, only

for major *anti-isomer*): δ = 108.3, 86.9, 73.3, 62.0, 36.3, 34.0, 26.0 (3C), 18.4, 16.6, 0.3 (3C), –5.3 ppm (2C); IR (film): 3509, 2956, 2930, 2858, 2167, 1472, 1388, 1361, 1249, 1081, 833, 774 cm^{-1}; MS (EI): *m/z* (%): 261 (M^+–53, 8), 189 (33), 147 (20), 131 (100), 126 (19), 101 (12), 89 (29), 75 (40), 73 (86), 59 (14); HRMS (ESI-pos) calcd. for $C_{16}H_{34}O_2Si_2Na$ [M + Na^+] 337.1989, found 337.1987.

Compound S2. A 250-mL round-bottomed flask, equipped with a magnetic stir-bar and a glass stopper was charged with alcohol **8** (10.0 g, 31.8 mmol, 1.0 equiv) and HCl (1% in EtOH, *v/v*, 46 mL). The cloudy mixture was stirred at room temperature for 12 h. The resulting clear solution was added to a 500-mL separatory funnel containing aq. sat. $NaHCO_3$ (90 mL) and *tert*-butyl methyl ether (90 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 50 mL), the combined organic phases were washed with H_2O (50 mL) and brine (50 mL), dried over Na_2SO_4, filtered and evaporated. The crude product was triturated with hexane until a white solid had formed. The mother liquor was decanted and the solid crystallized from hot hexane (~ 30 mL). The contents were placed in the freezer overnight to induce crystallization. The small white needles were collected and dried under vacuum to afford diol **S2** (5.8 g, 91%). m.p. = 39-41°C (hexane); $[\alpha]_D^{20} = -9.6°$ (c = 1.67, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 3.96-3.80 (m, 2H), 3.68 (ddd, *J* = 3.9, 5.5, 8.6 Hz, 1H), 2.58 (dq, *J* = 5.8, 7.0 Hz, 1H), 1.88 (bs, 2H), 1.84-1.70 (m, 2H), 1.20 (d, *J* = 7.0 Hz, 3H), 0.16 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 107.3, 88.1, 74.3, 61.5, 36.3, 34.8, 17.1, 0.3 ppm (3C); IR (film): 3343, 2958, 2165, 1408, 1248, 1055, 835, 758 cm^{-1}; MS (EI): *m/z* (%): 126 (M^+–74, 34), 75 (17), 73 (100); HRMS (ESI-pos) calcd. for $C_{10}H_{20}O_2SiNa$ [M + Na^+] 223.1125, found 223.1126.

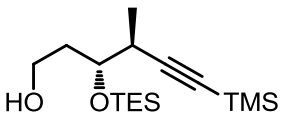


Compound S3. A 250-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with diol **S2** (2.8 g, 13.8 mmol, 1.0 equiv) and CH_2Cl_2 (135 mL). The resulting solution was cooled to 0 °C before 2,6-lutidine (4.8 mL, 41.4 mmol, 3.0 equiv) and TESOTf (6.5 mL, 29.0 mmol, 2.1 equiv) were successively added. The colorless mixture was stirred at this temperature for 1 h. Then a second portion of 2,6-lutidine (2.4 mL, 20.7 mmol, 1.5 equiv) and TESOTf (3.3 mL, 14.5 mmol, 1.05 equiv) was added and stirring continued for 30 min. The reaction was then quenched with aq. sat. NH_4Cl (20 mL) and the aqueous layer extracted with *tert*-butyl methyl ether (3 x 30 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated to a pale yellow oil, which was purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 0.5 → 2%) to give **S3** as a colorless oil (5.9 g, quant.). $[\alpha]_D^{20} = +1.2°$ (c = 1.15, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 3.89 (quint, *J* = 4.1 Hz, 1H), 3.74-3.64 (m, 2H), 2.60 (dq, *J* = 4.4, 7.0 Hz, 1H), 1.89 (ddt, *J* = 3.6, 7.6, 13.5 Hz, 1H), 1.68-1.55 (m, 1H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.61 (q, *J* = 7.9 Hz, 6H), 0.60 (q, *J* = 7.9 Hz, 6H), 0.13 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.4, 85.8, 71.2, 60.1, 36.2, 33.7, 14.9, 7.0 (3C), 6.9 (3C), 5.2 (3C), 4.7 (3C), 0.3 ppm (3C); IR (film): 2955, 2877, 2163, 1458, 1414, 1375, 1248, 1088, 1003, 839, 724 cm^{-1}; MS (EI): *m/z* (%): 399 (M^+–29, 14), 303 (91), 217 (24), 189 (22), 171 (12), 145 (17), 117 (100), 115 (18), 93 (17),

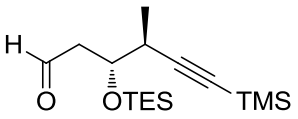


87 (21), 73 (17), 59 (12); HRMS (ESI-pos) calcd. for $C_{22}H_{48}O_2Si_3Na$ [M + Na^+] 451.2854, found 451.2854.

Compound S4. A three-necked, 500-mL jacketed Schlenk flask equipped with a magnetic stir-bar, an argon bubbler and two septa was charged with bissilyl ether **S3** (5.0 g, 11.7 mmol, 1.0 equiv) and CH_2Cl_2 (115 mL). The solution was cooled to −50 °C before MeOH (110 mL) was added and the mixture stirred for 15 min. Next, a solution of PPTS (293 mg, 1.17 mmol, 0.10 equiv) in MeOH (5 mL) was slowly added via syringe and stirring continued at −50 °C for 15 h. The reaction was quenched with aq. sat. $NaHCO_3$ (100 mL) and the mixture allowed to reach ~ 5 °C. H_2O (100 mL) was added and the aqueous phase extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with H_2O (100 mL) and brine (100 mL), dried over Na_2SO_4 and concentrated to a colorless oil, which was purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 1 → 3%) to afford **S4** as a colorless oil (2.9 g, 80%). $[\alpha]_D^{20} = +0.7°$ (c = 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 4.03 (quint, *J* = 4.1 Hz, 1H), 3.66-3.54 (m, 2H), 2.71 (dq, *J* = 4.4, 7.1 Hz, 1H), 1.97 (dddd, *J* = 3.9, 5.6, 7.6, 14.0 Hz, 1H), 1.69 (dddd, *J* = 5.4, 5.7, 8.4, 14.0 Hz, 1H), 1.19 (d, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.57 (q, *J* = 7.9 Hz, 6H), 0.20 ppm (s, 9H); ^{13}C NMR (100 MHz, C_6D_6): δ = 109.7, 86.3, 72.6, 59.9, 36.0, 34.0, 15.2, 7.1 (3C), 5.4 (3C), 0.3 ppm (3C); IR (film): 3343, 2956, 2877, 2165, 1458, 1414, 1375, 1248, 1082, 1005, 837, 724 cm^{-1}; MS (EI): *m/z* (%): 285 (M^+–29, 8), 189 (100), 159 (71), 145 (18), 131 (42), 117 (80), 115 (29), 103 (14), 87 (36), 75 (30), 59 (25); HRMS (ESI-pos) calcd. for $C_{16}H_{34}O_2Si_2Na$ [M + Na^+] 337.1990, found 337.1991.

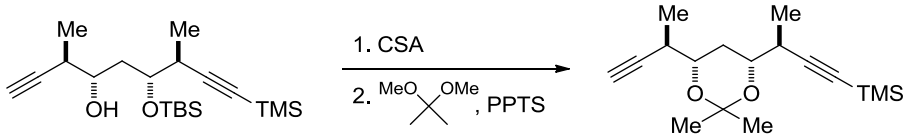


Compound 9. A 250-mL jacketed Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alcohol **S4** (2.0 g, 6.36 mmol, 1.0 equiv) and CH_2Cl_2 (66 mL). The solution was cooled to −30 °C before diisopropylethylamine (4.2 mL, 24.2 mmol, 3.8 equiv) was added followed by DMSO (4.5 mL, 63.6 mmol, 10.0 equiv). The mixture was stirred for 5 min before SO_3·pyridine (6.1 g, 38.1 mmol, 6.0 equiv) was introduced in one portion. The mixture was stirred at −30 °C for 1 h before the reaction was quenched with aq. pH 7.0 buffer (95 mL). The mixture was warmed until two clear layers had formed. The aqueous phase was extracted with Et_2O (2 x 50 mL), the combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, filtered and evaporated. The resulting yellow oil was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 1 → 2%) to afford aldehyde **9** (1.8 g, 93%) as a pale yellow oil (88:12, *anti:syn*). $[\alpha]_D^{20} = -7.1°$ (c = 1.21, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 9.59 (t, *J* = 1.9 Hz, 1H, *syn*), 9.55 (dd, *J* = 1.4, 2.4 Hz, 1 H *anti*), 4.30 (dt, *J* = 4.2, 7.6 Hz, 1H, *anti*), 4.07 (ddd, *J* = 4.4, 6.0, 10.5 Hz, 1H, *syn*), 2.82-2.50 (m, 2H), 2.39 (dd of ABq, *J* = 2.4, 7.6, 16.4 Hz, 1H, *anti*), 2.30 (dd of ABq, *J* = 1.7, 4.3, 16.4 Hz, 1H, *syn*), 1.10 (d, *J* = 7.1 Hz, 3H, *anti*), 1.07 (d, *J* = 7.0 Hz, 3H, *syn*), 0.96 (t, *J* = 8.0 Hz, 9H, *syn*), 0.92 (t, *J* = 7.9 Hz, 9H, *anti*), 1.02-0.90 (m, 6H, *syn*), 0.51 (q, *J* = 7.7 Hz, 6H, *anti*), 0.20 (s, 9H, *syn*), 0.19 ppm (s, 9H, *anti*); ^{13}C NMR (100 MHz, $CDCl_3$, chemical shifts of the major *anti-isomer*): δ = 201.7, 108.1, 87.4, 69.7, 47.5, 33.7, 14.6, 6.9 (3C), 5.1 (3C), 0.2 ppm (3C); IR (film): 2957, 2878, 2168, 1728, 1458, 1413, 1373, 1249, 1084, 1011, 839, 746 cm^{-1}; MS (EI): *m/z* (%): 283 (M^+–29, 5), 187 (56), 157 (100), 147 (12),



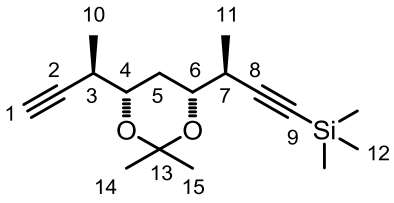
131 (30), 115 (49), 107 (29), 101 (12), 87 (32), 73 (19), 59 (22); HRMS (ESI-pos) calcd. for $C_{16}H_{32}O_2Si_2Na$ [M + Na^+] 335.1833, found 335.1834.

Compound 11. A 50-mL Schlenk flask, equipped with a magnetic stir-bar, and glass stopper was charged with aldehyde **9** (806 mg, 2.58 mmol, 1.0 equiv), (*R*)-methanesulfonate **10** (420 mg, 2.84 mmol, 1.1 equiv), THF (8.3 mL) and HMPA (2.1 mL). $PdCl_2(dppf)\cdot CH_2Cl_2$ (105 mg, 0.129 mmol, 0.05 equiv) was then added, immediately followed by indium(I) iodide (748 mg, 3.10 mmol, 1.2 equiv). The suspension underwent various color changes from a dark red via orange to finally give a cloudy green mixture, which was stirred at room temperature for 2 h. The reaction was quenched with aq. sat. NH_4Cl (10 mL) and Et_2O (6 mL), and the resulting biphasic mixture was stirred for 15 min. The aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and evaporated. The residue was purified without delay by flash chromatography (SiO_2, pentane/Et_2O gradient, 1 → 2%) to give compound **11** as a colorless oil (691 mg, 73%, dr ≥ 92:Σ8,[1] GC/MS). $[\alpha]_D^{20} = +11.7°$ (c = 1.40, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 4.13 (ddd, *J* = 4.0, 5.1, 7.8 Hz, 1H), 3.84-3.77 (m, 1H), 2.75 (dq, *J* = 4.0, 7.0 Hz, 1H), 2.27 (ddq, *J* = 2.5, 4.4, 7.0 Hz, 1H), 2.53 (d, *J* = 4.0 Hz, 1H), 2.27 (ddd, *J* = 2.8, 5.2, 14.0 Hz, 1H), 1.88 (d, *J* = 2.4 Hz, 1H), 1.88 (ddd, *J* = 7.8, 9.4, 14.1 Hz, 1H), 1.24 (d, *J* = 7.0 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.53 (q, *J* = 7.7 Hz, 6H), 0.20 ppm (s, 9H); ^{13}C NMR (100 MHz, C_6D_6): δ = 109.1, 86.7, 85.8, 74.1, 72.7, 71.0, 37.4, 33.6, 33.4, 16.4, 15.2, 7.1 (3C), 5.4 (3C), 0.3 ppm (3C); IR (film): 3533, 3312, 2957, 2878, 2168, 1457, 1412, 1375, 1248, 1086, 1066, 1006, 830, 725 cm^{-1}; MS (EI): *m/z* (%): 337 (M^+–29, 10), 241 (61), 223 (37), 211 (32), 197 (47), 183 (49), 175 (11), 161 (19), 157 (15), 147 (12), 133 (17), 131 (14), 115 (88), 109 (100), 103 (39), 97 (13), 87 (67), 81 (28), 75 (49), 73 (54), 59 (39); HRMS (ESI-pos) calcd. for $C_{20}H_{38}O_2Si_2Na$ [M + Na^+] 389.2302, found 389.2306.



Scheme S1. Determination of the Relative Configuration

Compound S5. A Schlenk flask equipped with a magnetic stir-bar and septum was charged with compound **11** (9.5 mg, 0.0260 mmol, 1.0 equiv), CH_2Cl_2 (300 µL) and MeOH (300 µL). Camphorsulfonic acid (0.60 mg, 0.00260 mmol, 0.10 equiv) was added and the solution stirred for 30 h. For work up, aq. sat. $NaHCO_3$ (2 mL) was introduced and the mixture was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic extracts were washed with brine (1 mL), dried over $MgSO_4$ and evaporated. The resulting white solid was dissolved in CH_2Cl_2 (260 µL) and the solution cooled to 0°C before dimethoxypropane (32



[1] Refers to the sum (Σ) of all other isomers present at this stage.

μL, 0.260 mmol, 10.0 equiv) and camphorsulfonic acid (0.60 mg, 0.00260 mmol, 0.1 equiv) were successively introduced. The mixture was gradually warmed to room temperature and stirred for 15 h. The reaction was quenched with aq. sat. $NaHCO_3$ (2 mL) and the mixture extracted with CH_2Cl_2 (3 x 1 mL). The combined organic extracts were washed with brine (1 mL), dried over $MgSO_4$ and evaporated. The crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 20 → 30%) to afford acetonide **S5** (4.3 mg, 57% over both steps). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.88 (ddd, *J* = 2.5, 4.8, 11.7 Hz, 1H, H-6), 3.86 (ddd, *J* = 2.5, 4.8, 11.7 Hz, 1H, H-4), 2.65 (dq, *J* = 4.8, 7.0 Hz, 1H, H-7), 2.62 (dq, *J* = 4.8, 7.1 Hz, 1H, H-3), 2.09 (d, *J* = 2.5 Hz, 1H, H-1), 1.61 (dt, *J* = 2.5, 12.6 Hz, 1H, H-5a), 1.48 (dt, *J* = 11.7, 12.6 Hz, 1H, H-5b), 1.43 (s, 3H, H-15), 1.41 (s, 3H, H-14), 1.20 (d, *J* = 7.1 Hz, 3H, H-10), 1.17 (d, *J* = 7.1 Hz, 3H, H-11), 0.14 ppm (s, 9H, H-12); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 108.3 (C, C-8), 98.8 (C, C-13), 85.9 (C, C-9), 85.6 (C, C-2), 71.0 (HC, C-4), 71.0 (HC, C-6), 69.7 (HC, C-1), 32.0 (HC, C-7), 31.1 (HC, C-3), 29.9 (H_3C, C-14), 27.9 (H_2C, C-5), 19.8 (H_3C, C-15), 15.3 (H_3C, C-10), 15.0 (H_3C, C-11), 0.1 ppm ($(H_3C)_3Si$, C-12); IR (film): 3312, 2990, 2879, 2169, 1456, 1380, 1275, 1259, 1200, 1171, 1103, 839, 758 cm^{-1}; MS (EI): *m/z* (%): 277 (M^+–15, 41), 181 (19), 167 (71), 109 (44), 95 (72), 81 (40), 79 (17), 73 (100), 59 (45), 53 (14), 43 (26); HRMS (ESI-pos) calcd. for $C_{17}H_{28}O_2SiNa$ [M + Na^+] 315.1751, found 315.1751.

The relative stereochemistry was determined according to Rychnovsky and co-workers by recording the diagnostic ^{13}C-chemical shifts of the *syn* 1,3-diol acetonide (Figure 1).[1] These authors demonstrated that *syn*-1,3 diol acetonides exists in a defined chair confirmation, in which the two alkyl substituents are equatorially disposed. The axial methyl group of the acetonide has a characteristic ^{13}C-chemical shift of ≈ 19 ppm, whereas the chemical shift of the equatorial methyl group is ≈ 30 ppm.

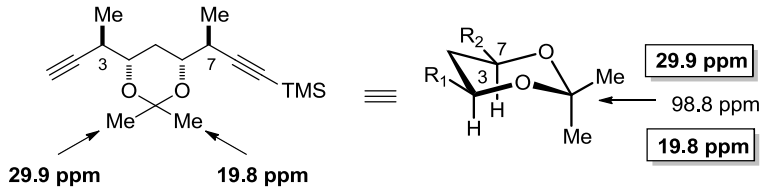
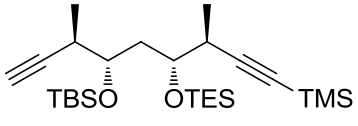


Figure 1: Assignment of the relative stereochemistry of the 1,3-*syn*-hydroxyl groups in compound **S5**

Compound S6. A 50-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper was charged with alcohol **11** (502 mg, 1.37 mmol, 1.0 equiv), and CH_2Cl_2 (4.8 mL). The resulting solution was cooled to 0 °C before 2,6-lutidine (317 μL, 2.74 mmol, 2.0 equiv) was introduced. After ~ 5 min, TBSOTf (327 μL, 1.42 mmol, 1.04 equiv) was added and the solution stirred at 0 °C for 1.5 h. For work up, the reaction was diluted with aq. sat. NH_4Cl (10 mL) and Et_2O (15 mL) and the aqueous layer extracted with Et_2O (3 x 10 mL). The combined organic extracts were washed with H_2O (20 mL) and brine (15 mL), dried over Na_2SO_4, filtered and evaporated, and the crude product was purified by



flash chromatography (SiO_2, pentane) to afford product **S6** as a colorless oil (600 mg, 91%). $[\alpha]_D^{20} = +5.1°$ (c = 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 4.01 (ddd, *J* = 3.6, 5.4, 7.4 Hz, 1H), 3.98 (dt, *J* = 3.5, 6.3 Hz, 1H), 2.82-2.71 (m, 2H), 2.54 (ddd, *J* = 5.5, 6.4, 13.8 Hz, 1H), 1.98 (d, *J* = 2.5 Hz, 1H), 1.90 (ddd, *J* = 6.2, 7.3, 13.7 Hz, 1H), 1.31 (d, *J* = 7.0 Hz, 3H), 1.31 (d, *J* = 7.0 Hz, 3H), 1.02-0.97 (m, 18H), 0.59 (q, *J* = 8.0 Hz, 6H), 0.24 (s, 9H), 0.09 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 108.9, 86.5, 85.8, 72.1, 72.0, 70.7, 38.6, 33.6, 32.3, 26.1 (3C), 18.3, 16.4, 15.8, 7.2 (3C), 5.6 (3C), 0.4 (3C), –4.0, –4.4 ppm; IR (film): 3315, 2957, 2879, 2168, 1462, 1374, 1249, 1063, 1006, 835, 774 cm^{-1}; MS (EI): *m/z* (%): 451 (M^+–29, 7), 269 (44), 223 (11), 197 (100), 147 (12), 115 (20), 87 (18), 73 (55), 59 (11); HRMS (ESI-pos) calcd. for $C_{26}H_{52}O_2Si_3Na$ [M + Na^+] 503.3167, found 503.3165.

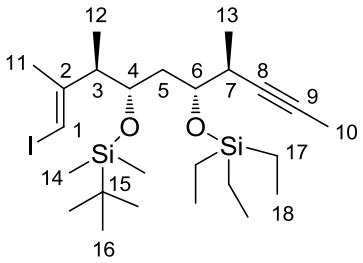
Compound 12. A precooled (0 °C) 50-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper was charged with a solution of phenyldimethylsilyl lithium[2] (0.5 M in THF, 6.2 mL, 3.12 mmol, 3.0 equiv). Copper(I) cyanide (CuCN) (140 mg, 1.56 mmol, 1.5 equiv) was then added in one portion (THF (3.2 mL) was used to rinse the CuCN-containing flask). The resulting blood red solution was stirred at 0 °C for 30 min, causing a color change to dark red/purple, before it was transferred via cannula into a solution of alkyne **S6** (500 mg, 1.04 mmol, 1.0 equiv) in THF (8.4 mL) at 0°C. The flask was sealed with a glass stopper and the mixture stirred at this temperature for 1 h. Next, methyl iodide (647 μL, 10.4 mmol, 10.0 equiv) was introduced and stirring continued at 0 °C for an additional 1 h. For work up, ammonium hydroxyde (30% *v/v* in H_2O, 21 mL) and Et_2O (10 mL) were added under vigorous stirring. The biphasic mixture was transferred into a separatory funnel containing H_2O (40 mL) and Et_2O (20 mL), and the aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with H_2O (3 x 10 mL) and brine (30 mL), dried over Na_2SO_4, filtered and evaporated. The crude material was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 0 → 2%), affording product **12** as a colorless oil (591 mg, 90%). $[\alpha]_D^{20} = -3.6°$ (c = 2.13, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.68-7.64 (m, 2H), 7.31-7.26 (m, 2H), 7.25-7.20 (m, 1H), 5.71 (s, 1H), 4.15-4.10 (m, 1H), 4.07 (dt, *J* = 3.8, 6.3 Hz, 1H), 2.79 (dq, *J* = 3.6, 7.0 Hz, 1H), 2.54 (dq, *J* = 4.5, 6.9 Hz, 1H), 2.09 (ddd, *J* = 5.5, 6.4, 11.9 Hz, 1H), 1.93 (s, 3H), 1.91-1.82 (m, 1H), 1.32 (d, *J* = 7.0 Hz, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.05 (t, *J* = 7.9 Hz, 9H), 1.01 (s, 9H), 0.67 (q, *J* = 7.8 Hz, 6H), 0.48 (s, 3H), 0.47 (s, 3H), 0.21 (s, 9H), 0.17 (s, 3H), 0.12 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.0, 140.2, 134.2 (2C), 129.1, 128.2 (2C), 122.7, 109.6, 86.5, 72.1, 71.9, 50.5, 38.5, 33.8, 26.2 (3C), 22.6, 18.3, 16.7, 14.7, 7.3 (3C), 5.7 (3C), 0.4 (3C), –0.4, –0.5, –3.8, –4.2 ppm; IR (film): 2956, 2878, 2167, 1610, 1461, 1427, 1374, 1248, 1111, 1043, 1005, 825, 772, 726 cm^{-1}; MS (ESI-pos) [M + Na^+] 653 (100); HRMS (ESI-pos) calcd. for $C_{35}H_{66}O_2Si_4Na$ [M + Na^+] 653.4032, found 653.4033.

Compound S7. A 50-mL round-bottomed flask, equipped with a magnetic stir-bar, a reflux condenser and an argon inlet on top of the reflux condenser, was charged with compound **12** (500 mg, 0.792 mmol, 1.0 equiv), MeOH (8.8 mL) and potassium carbonate (328 mg, 2.38 mmol, 3.0 equiv). The mixture was stirred at 40 °C for

3.5 h before it was allowed to cool. Et_2O (6 mL) and H_2O (3 mL) were added and the mixture transferred into a separatory funnel containing H_2O (12 mL). The aqueous layer was extracted with Et_2O (3 x 9 mL). The combined organic phases were washed with brine (18 mL), dried over Na_2SO_4, filtered and evaporated. The crude product was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 0 → 2%) to furnish alkyne **S7** as a pale yellow oil (390 mg, 88%). $[\alpha]_D^{20} = -8.2°$ (c = 2.12, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.66 (dd, *J* = 1.4, 7.9 Hz, 2H), 7.29-7.24 (m, 2H), 7.23-7.17 (m, 1H), 5.72 (s, 1H), 4.07 (ddd, J = 3.8, 5.1, 7.6 Hz, 1H), 4.03 (dt, *J* = 3.3, 6.7 Hz, 1H), 2.71 (ddq, *J* = 2.6, 3.8, 7.0 Hz, 1H), 2.52 (dq, *J* = 3.6, 7.0 Hz, 1H), 2.16 (ddd, *J* = 5.4, 6.7, 12.3 Hz, 1H), 1.90 (s, 3H), 1.88-1.79 (m, 1H), 1.82 (d, *J* = 2.4 Hz, 1H), 1.31 (d, *J* = 7.0 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.02 (t, *J* = 7.9 Hz, 9H), 0.99 (s, 9H), 0.64 (dq, *J* = 1.6, 8.4 Hz, 6H), 0.45 (s, 3H), 0.44 (s, 3H), 0.10 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 158.6, 140.2, 134.3 (2C), 129.1, 128.2 (2C), 123.0, 85.7, 72.0, 71.8, 71.0, 50.0, 37.6, 31.9, 26.2 (3C), 22.5, 18.3, 16.1, 14.1, 7.3 (3C), 5.6 (3C), –0.5, –0.6, –4.1, –4.3 ppm; IR (film): 3312, 2955, 2878, 1609, 1461, 1427, 1374, 1248, 1111, 1043, 1005, 835, 772 cm^{-1}; MS (EI): *m/z* (%): 355 (M^+–203, 5), 223 (10), 197 (100), 135 (25), 115 (15), 73 (12); HRMS (ESI-pos) calcd. for $C_{32}H_{58}O_2Si_3Na$ [M + Na^+] 581.3637, found 581.3638.

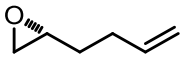
Compound 13. A 50-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alkyne **S7** (319 mg, 0.570 mmol, 1.0 equiv) and THF (6.0 mL). The resulting solution was cooled to –78 °C before *n*-BuLi (1.6 M in hexane, 445 µL, 0.713 mmol, 1.25 equiv) was added dropwise, causing a color change to light red. The solution was stirred at –78 °C for 1 h before methyl iodide (355 µL, 5.70 mmol, 10.0 equiv) was introduced and the cooling bath removed. The mixture was allowed to reach room temperature over the course of 1 h. The reaction was quenched with aq. sat. NH_4Cl (15 mL), the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined extracts were washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 0 → 2%) to afford compound **13** as a colorless oil (317 mg, 97%). $[\alpha]_D^{20} = -1.4°$ (c = 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.69-7.66 (m, 2H), 7.30-7.25 (m, 2H), 7.24-7.18 (m, 1H), 5.75 (s, 1H), 4.17 (ddd, *J* = 4.1, 5.2, 7.4 Hz, 1H), 4.08 (dt, *J* = 3.5, 6.5 Hz, 1H), 2.83-2.74 (m, 1H), 2.54 (dq, *J* = 3.9, 6.8 Hz, 1H), 2.17 (ddd, *J* = 5.4, 6.8, 13.8 Hz, 1H), 1.92 (s, 3H), 1.85 (ddd, *J* = 6.6, 7.3, 13.8 Hz, 1H), 1.53 (d, *J* = 2.4 Hz, 3H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.25 (d, *J* = 7.0 Hz, 3H), 1.05 (t, *J* = 7.9 Hz, 9H), 1.01 (s, 9H), 0.67 (dq, *J* = 1.5, 8.0 Hz, 6H), 0.46 (s, 3H), 0.45 (s, 3H), 0.15 (s, 3H), 0.11 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.0, 140.3, 134.2 (2C), 129.1, 128.2 (2C), 122.5, 81.2, 77.7, 72.2, 72.1, 50.0, 37.6, 32.4, 26.2 (3C), 22.6, 18.3, 16.5, 14.3, 7.3 (3C), 5.6 (3C), 3.7, –0.5 (2 x 1C), –4.1, –4.3 ppm; IR (film): 2955, 2877, 1610, 1461, 1427, 1373, 1247, 1110, 1068, 1041, 1004, 834, 772 cm^{-1}; MS (EI): *m/z* (%): 369 (M^+–203, 15), 237 (89), 211 (100), 135 (50), 115 (28), 87 (18), 73 (19); HRMS (ESI-pos) calcd. for $C_{33}H_{60}O_2Si_3Na$ [M + Na^+] 595.3793, found 595.3796.

Compound 14. *Note: the product is light-sensitive and all manipulations were performed in the dark*. A Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with silane **13** (100 mg, 0.174 mmol, 1.0 equiv), benzene (400 μL) and MeCN (1.0 mL). The resulting solution was cooled to 0 °C before a solution of NIS (196 mg, 0.870 mmol, 5.0 equiv) (the NIS must be white and crystalline) in MeCN (1.0 mL) was added dropwise (~ 3 min). The bright red mixture was kept at 0 °C for 4 h before the reaction was quenched with aq. sat. $Na_2S_2O_3$ (500 μL) under vigorous stirring. The colorless solution was added to a separatory funnel containing Et_2O (10 mL). The aqueous phase was extracted with Et_2O (3 x 10 mL) and the combined extracts were washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and evaporated (in the dark). The remaining pale yellow oil was quickly purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 0 → 1%) to afford alkenyl iodide **14** as a colorless oil (86 mg, 88%). $[\alpha]_D^{20}$ = +6.5° (c = 1.02, C_6H_6); ^{1}H NMR (600 MHz, C_6D_6): δ = 6.10 (s, 1H, H-1), 3.94 (ddd, *J* = 3.8, 4.4, 8.4 Hz, 1H, H-6), 3.89 (ddd, *J* = 3.9, 5.2, 7.2 Hz, 1H, H-4), 2.71 (m, 1H, H-7), 2.55 (m, 1H, H-3), 2.07 (ddd, *J* = 4.5, 7.2, 13.8 Hz, 1H, H-5a), 1.97 (d, *J* = 1.1 Hz, 3H, H-11), 1.72 (d, *J* = 2.5 Hz, 3H, H-10), 1.72 (ddd, *J* = 5.2, 8.4, 13.8 Hz, 1H, H-5b), 1.28 (d, *J* = 7.0 Hz, 3H, H-13), 1.05 (d, *J* = 7.0 Hz, 3H, H-12), 0.98 (t, *J* = 8.0 Hz, 9H, H-18), 0.96 (s, 9H, H-16), 0.58 (q, *J* =8.0 Hz, 6H, H-17), 0.09 (s, 3H, H-14a), 0.06 ppm (s, 3H, H-14b); ^{13}C NMR (150 MHz, C_6D_6): δ = 149.4 (C, C-2), 80.8 (C, C-8), 78.2 (C, C-9), 78.1 (HC, C-1), 72.3 (HC, C-4), 71.9 (HC, C-6), 47.7 (HC, C-3), 37.5 (H_2C, C-5), 32.7 (HC, C-7), 26.1 ($(H_3C)_3$, C-16), 23.6 (H_3C, C-11), 18.2 (CSi, C-15), 15.4 (H_3C, C-12), 15.2 (H_3C, C-13), 7.3 ($(H_3C)_3$, C-18), 5.5 ($(H_2C)_3Si$, C-17), 4.1 (H_3C, C-10), –4.1 (H_3CSi, C-14a), –4.5 ppm (H_3CSi, C-14b); IR (film): 2956, 2930, 2878, 2857, 1607, 1471, 1461, 1412, 1374, 1251, 1152, 1110, 1095, 1066, 1042, 1004, 950, 885, 832, 772 cm^{-1}; MS (EI): *m/z* (%): 507 (M^+–57, 4), 369 (19), 365 (13), 339 (28), 237 (53), 211 (100), 115 (24), 97 (14), 87 (19), 73 (55), 59 (12); HRMS (ESI-pos) calcd. for $C_{25}H_{49}O_2Si_2INa$ [M + Na^+] 587.2208, found 587.2203.



Preparation of Fragment F

Compound 15. A 250-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with (*R,R*)-(-)-N,N'-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (1.3 g, 2.13 mmol, 0.01 equiv), toluene (8.0 mL) and acetic acid (183 μL, 3.20 mmol, 0.015 equiv). The resulting solution was stirred under air for 1 h. During this time the color changed from red to dark brown. The solvent was removed under reduced pressure and the residue dried in high vacuum for 1 h, providing a dark brown solid.



This material was dissolved in (±)-1,2-epoxy-5-hexene (24.0 mL, 213 mmol, 1.0 equiv) and the resulting mixture cooled to 0°C before H_2O (2.1 mL, 115 mmol, 0.54 equiv) was added dropwise. Stirring was continued for 30 min at 0 ºC and at room temperature for 24 h. For work up, the volatile material was isolated by vacuum transfer (50 to 15 mbar, 40°C) into a cooled (0°C) receiving flask. The resulting oil was filtered through a plug of silica to remove residual water, which afforded epoxide **15** as a colorless liquid (7.5 g, 36%, > 99% ee).

$[\alpha]_D^{20}$ = +6.6° (c = 0.39, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85 (ddt, *J* = 6.6, 10.2, 17.1 Hz, 1H), 5.07 (dq, *J* = 1.7, 17.1 Hz, 1H), 5.00 (ddt, *J* = 1.3, 2.5, 10.1 Hz, 1H), 2.94 (ddt, *J* = 2.7, 4.0, 5.4 Hz, 1H), 2.76 (dd, *J* = 4.1, 4.9 Hz, 1H), 2.49 (dd, *J* = 2.7, 5.0 Hz, 1H), 2.30-2.15 (m, 2H), 1.64 ppm (ddt, *J* = 1.5, 5.3, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 115.3, 52.0, 47.3, 31.9, 30.3 ppm; IR (film): 3048, 2980, 2923, 2848, 1641, 1483, 1442, 1410, 1261, 1210, 1132, 1084, 996, 910, 837, 733 cm^{-1}; MS (EI): *m/z* (%): 98 (M^+, 0.5), 83 (11), 79 (11), 67 (77), 65 (10), 57 (32), 55 (52), 54 (77), 53 (33), 41 (100), 39 (89), 31 (72), 29 (77), 27 (64); HRMS (CI (FE), *i*-butane) calcd. for $C_6H_{11}O$ [M + H^+] 99.0810, found 99.0809. The enantiomeric excess was determined by GC using a chiral stationary phase (column. 30 M BGB 174 / BGB 1701 G 513, detector FID, temp. 220 / 50 iso / 320, gas, 0.6 bar H_2, sample 0.2 μL in CH_2Cl_2, t_R = 17.3 min for (*R*)-**15**, 18.0 min for (*S*)-**15**).

Compound 16. Propyne (~ 53 mL) was condensed at –78°C into a 250-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper. THF (51 mL) was then added prior to the dropwise addition of *n*-BuLi (1.6 M in hexane, 32.1 mL, 51.4 mmol, 1.01 equiv). The resulting cloudy white mixture was stirred for 30 min at –78 ºC before BF_3•OEt_2 (6.8 mL, 53.4 mmol, 1.05 equiv) was added dropwise and stirring continued for 30 min at this temperature. Next, a solution of epoxide (*R*)-**15** (5.0 g, 50.9 mmol, 1.0 equiv) in THF (50 mL) was slowly added via cannula. The turbid mixture was stirred for 1 h at –78 ºC before the reaction was quenched with aq. sat. NH_4Cl (20 mL). After reaching room temperature, the biphasic mixture was transferred to a separatory funnel containing Et_2O (20 mL) and H_2O (40 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organic layers were washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4 and evaporated. The crude material was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 0 → 33%) to afford alcohol **16** as a colorless oil (6.1 g, 87%). $[\alpha]_D^{20}$ = –5.8° (c = 0.37, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81 (ddt, *J* = 6.6, 10.1, 17.2 Hz, 1H), 5.03 (ddt, *J* = 1.5, 3.2, 17.2 Hz, 1H), 4.98-4.92 (m, 1H), 3.69 (dt, *J* = 6.3, 11.3 Hz, 1H), 2.36 (ddt, *J* = 2.3, 4.8, 16.4 Hz, 1H), 2.29-2.02 (m, 4H), 1.78 (t, *J* = 2.3 Hz, 3H), 1.63-1.55 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 114.8, 78.4, 75.1, 69.6, 35.2, 29.9, 27.7, 3.5 ppm; IR (film): 3379, 3078, 2977, 2920, 2856, 1641, 1435, 1341, 1211, 1118, 1077, 1024, 994, 910, 848 cm^{-1}; MS (EI): *m/z* (%): 138 (M^+, 0.5), 123 (11), 109 (11), 105 (16), 97(11), 85 (50), 79 (11), 67 (78), 57 (43), 55 (77), 54 (85), 41 (100), 29 (64); HRMS (EI (FE)) calcd. for $C_9H_{14}O$ 138.1045, found 138.1043.

Compound 17. A 500-mL round-bottomed flask, equipped with a magnetic stir-bar and a rubber septum, was charged with alcohol **16** (4.0 g, 29.0 mmol, 1.0 equiv), 2-propanol (250 mL) and $Co(nmp)_2$ (1.6 g, 2.90 mmol, 0.10 equiv).[3] The mixture were purged with O_2 (~ 10 min) before *tert*-butyl hydroperoxide (4.8 M in toluene, 604 μL, 2.90 mmol, 0.10 equiv) was added to the green solution. The mixture was stirred at 55 °C under O_2 (1 atm, balloon) for 17 h before it was cooled to room temperature and purged with argon. The green solution was concentrated to ~ 1/10 of the volume by rotary evaporation (water bath at room temperature, 75 mbar) and transferred into a separatory funnel containing Et_2O (50 mL) and HCl (1.0 M in H_2O, 70 mL). The aqueous layer was extracted with Et_2O (3 x 15 mL). The combined extracts were washed with H_2O (3 x 20 mL) and brine (30 mL), filtered, dried over

Na_2SO_4, and evaporated. The crude product was purified by flash chromatography (SiO_2, pentane/acetone gradient, 0 → 30%) to give product **17** (3.8 g, 84%) as a pale yellow oil. $[\alpha]_D^{20} = -10.0$ ° (c = 0.15, $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6): δ = 3.99-3.92 (m, 1H, H-5), 3.94-3.89 (m, 1H, H-8), 3.41 (ddd, *J* = 3.5, 6.9, 11.4 Hz, 1H, H-9a), 3.24 (dt *J* = 5.7, 11.4 Hz, 1H, H-9b), 2.38 (ddq, *J* = 2.6, 5.1, 16.3 Hz, 1H, H-4a), 2.24 (ddq, *J* = 2.6, 7.0, 16.3 Hz, 1H, H-4b), 1.81-1.77 (bm, 1H, HO), 1.77-1.72 (m, 1H, H-6a), 1.52 (t, *J* = 2.6 Hz, 3H, H-1), 1.54-1.49 (m, 1H, H-7a), 1.51-1.46 (m, 1H, H-6b), 1.39-1.32 ppm (m, 1H, H-7b); ^{13}C NMR (125 MHz, C_6D_6): δ = 80.0 (HC, C-8), 78.1 (HC, C-5), 76.9 (C, C-2), 76.3 (C, C-3), 65.0 (H_2C, C-9), 31.6 (H_2C, C-6), 27.4 (H_2C, C-7), 26.1 (H_2C, C-4), 3.4 ppm (H_3C, C-1); IR (film): 3423, 2919, 2872, 1641, 1444, 1370, 1195, 1099, 1043, 973, 928, 882, 812 cm^{-1}; MS (EI): *m/z* (%): 154 (M^+, 0.1), 101 (100), 95 (13), 83 (12), 79 (14), 57 (77), 55 (28), 53 (12), 43 (18), 41 (10), 39 (10), 27 (11); HRMS (CI (DE), ammonia gas) calcd. for $C_9H_{15}O_2$ [M + H^+] 155.1072, found 155.1071.

Compound 18. A 25-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alcohol **17** (100 mg, 0.650 mmol, 1.0 equiv), CH_2Cl_2 (6.5 mL), diisopropylethylamine (793 μL, 4.55 mmol, 7.0 equiv), and DMSO (231 μL, 3.25 mmol, 5.0 equiv). The resulting mixture was cooled to 0 ºC and stirred at this temperature for 5 min before SO_3·pyridine (310 mg, 1.95 mmol, 3.0 equiv) was introduced in one portion. The pale yellow solution was stirred for 1 h at 0 ºC before the reaction was quenched with aq. HCl (1 M, 10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 1 mL), and the combined extracts were washed with H_2O (1 mL) and brine (1 mL). The crude product was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 70 → 85%) to afford aldehyde **18** (85 mg, 86%) as a pale yellow oil. Aldehyde **18** is quite volatile and care must be taken when removing the solvent to avoid loss of material. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.66 (d, *J* = 1.8 Hz, 1H), 4.39 (ddd, *J* = 1.7, 6.8, 8.3 Hz, 1H), 4.21 (quint, *J* = 6.3 Hz, 1H), 2.50-2-35 (m, 2H), 2.23 (dddd, J = 3.9, 7.4, 7.8, 12.8 Hz, 1H), 2.11-2.00 (m, 1H), 1.98 (ddt, *J* = 6.7, 7.9, 12.4 Hz, 1H), 1.84-1.74 (m, 1H), 1.79 ppm (t, *J* = 2.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.8, 83.4, 79.5, 77.4, 75.1, 30.4, 27.3, 25.5, 3.7 ppm; IR (film): 2920, 2805, 2714, 1730, 1445, 1372, 1293, 1190, 1069, 1002, 883 cm^{-1}; HRMS (CI (FE), *i*-butane) calcd. for $C_9H_{13}O_2$ [M + H^+] 153.0916, found 153.0916.

Compound 19. The preparation of 1-bromo-4-methyl-1,3-pentadiene (**20**) is a modification of the procedure described by Charreau and co-workers:[4]

A flame-dried, 50-mL Schlenk flask, flushed with argon, equipped with a magnetic stir-bar and a septum was charged with a solution of freshly distilled diisopropylamine (703 μL, 5.00 mmol, 1.0 equiv) in Et_2O/THF (7.0 mL/10 mL). The solution was cooled to –78 ºC before *n*-BuLi (1.6 M in hexane, 3.1 mL, 5.00 mmol, 1.0 equiv) was added dropwise. The resulting pale yellow LDA solution was allowed to reach room temperature and stirred for 30 min, before it was cooled to –94 ºC using a pentane/$N_{2(l)}$ bath. Once this temperature had been reached, a pre-cooled (–78°C) solution of dibromomethane (348 μL, 5.00 mmol, 1.0 equiv) in THF (5.0 mL) was carefully added via cannula and the resulting yellow mixture stirred at –90 ºC for 30 min.

During this time a separate flame-dried, 25-mL Schlenk flask, equipped with a magnetic stir-bar and a septum, was flushed with argon and charged with phenyl prenyl sulfone (1.0 g, 5.00 mmol, 1.0 equiv). The solid was dissolved in THF (8.0 mL) and the resulting solution cooled to –78 ºC before *n*-BuLi (1.6 M in hexane, 3.1 mL, 5.00 mmol, 1.0 equiv) was added, causing a color change to bright orange. Once the addition was complete, the cooling bath was removed and the solution of the lithiated sulfone allowed to reach room temperature. After stirring for 30 min, the solution was cooled again to –78 ºC and was then slowly added via cannula to the carbene solution stirred at –95 ºC. When the addition was complete, the resulting yellow/brown mixture was warmed over the course of 2.5 h to –20 ºC. The reaction was quenched with EtOH (500 µL) and aq. sat. NH_4Cl (10 mL). The contents were immediately transferred to a separatory funnel and diluted with H_2O (ca. 30 mL) until two clear layers were observed. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were washed with H_2O (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and evaporated. The remaining pale yellow oil was subjected, without delay, to flash chromatography (SiO_2, pentane). The resulting 1-bromo-4-methyl-1,3-pentadiene **20** (502 mg, 62%, *E:Z* ~ 95:5, ^{1}H NMR) was immediately used in the next step (Note: *bromide* **20** *is very sensitive to temperature and light and should be freshly prepared and manipulated within 1h; otherwise, isomerization may lead to unusable isomer mixtures*).

A flame-dried 50-mL Schlenk flask, equipped with a magnetic stir-bar and a septum, was charged with bromide **20** (502 mg, 3.12 mmol, 5.7 equiv). After immersing the flask into a dry ice/acetone bath, Et_2O (6.2 mL) was added at –78 ºC followed by *t*BuLi (1.7 M in pentane, 4.0 mL, 6.87 mmol, 12.5 equiv). The resulting yellow lithiodiene solution was stirred at this temperature for 1 h.

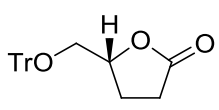
An argon flushed 100-mL jacketed Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with freshly sublimed zinc bromide (1.1 g, 4.73 mmol, 8.6 equiv) and Et_2O (7.8 mL), and the resulting mixture was stirred at room temperature until a colorless solution had formed. This solution was then cooled to –35 ºC before the solution of the lithiodiene was added drop-wise over 10 min. The mixture was warmed to 0 ºC and stirred for 1 h at this temperature before a solution of lithio (–)-N-methyl-ephedrine [prepared from (–)-N-methyl-ephedrine (559 mg, 3.12 mmol, 5.7 equiv) and *n*-BuLi (1.6 M in hexane, 1.9 mL, 3.12 mmol, 5.7 equiv) in toluene (5.2 mL) at 0 ºC] was added and stirring continued at 0 ºC for 1 h. The mixture was then cooled to –20 ºC before a solution of aldehyde **18** (84 mg, 0.550 mmol, 1.0 equiv) in Et_2O (2.0 mL) was introduced (the flask containing the aldehyde was rinsed with Et_2O (500 µL) and this wash was also added to the Schlenk flask). The resulting mixture was stirred at –20 ºC for 18 h before the reaction was quenched with aq. sat. NH_4Cl (10 mL) and diluted with H_2O (10 mL). The aqueous phase was extracted with Et_2O (3 x 20 mL), and the combined extracts were washed with H_2O (30 mL) and brine (30 mL), dried over Na_2SO_4, filtered and evaporated. The remaining pale yellow oil was purified by flash chromatography (SiO_2, pentane/Et_2O gradient, 12.5 → 50%) to afford product **19** as a colorless oil (110 mg, 85%, dr ~ 93:7, ^{1}H NMR). $[\alpha]_D^{20} = +19.3$ ° (c = 0.67, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6): δ = 6.71 (ddd, *J* = 1.2, 11.0, 15.1 Hz, 1H, H-11), 5.87 (bd, *J* = 11.0 Hz, 1H, H-12), 5.58 (dd, *J* = 6.2, 15.1 Hz, 1H, H-10), 4.02-3.96 (m, 1H, H-5), 3.99-3.94 (m, 1H, H-9), 3.92-3.87 (m, 1H, H-8), 2.82 (bs, 1H, HO), 2.41 (ddq, *J* = 2.6, 5.1, 16.3 Hz, 1H, H-4a), 2.25

(ddq, J = 2.6, 7.3, 16.3 Hz, 1H, H-4b), 1.84-1.78 (m, 1H, H-6a), 1.66-1.61 (m, 1H, H-7a), 1.61 (s, 3H, H-14), 1.59 (s, 3H, H-15), 1.53 (t, J = 2.6 Hz, 3H, H-1), 1.55-1.49 (m, 1H, H-6b), 1.50-1.43 ppm (m, 1H, H-7b); ^{13}C NMR (150 MHz, C_6D_6): δ = 134.9 (C, C-13), 129.8 (HC, C-10), 128.5 (HC, C-11), 125. 5 (HC, C-12), 83.2 (HC, C-8), 78.1 (HC, C-5), 77.0 (C, C-2), 76.2 (C, C-3), 75.4 (HC, C-9), 31.7 (H_2C, C-6), 28.0 (H_2C, C-7), 25.9 (H_2C, C-4 and H_3C, C-14), 18.2 (H_3C, C-15), 3.4 ppm (H_3C, C-1); IR (film): 3434, 2968, 2919, 1659, 1443, 1376, 1280, 1220, 1055, 986, 960, 871, 812 cm^{-1}; MS (EI): *m/z* (%): 234 (M^+, 5), 123 (55), 111 (21), 105 (12), 95 (100), 93 (18), 81 (18), 79 (33), 77 (15), 67 (23), 55 (21), 53 (12), 43 (42), 41 (16); HRMS (EI (DE)) calcd. for $C_{15}H_{22}O_2$ 234.1620, found 234.1618.

Preparation of Fragment E

Compound 22.[5] A 1000-mL, round-bottomed flask, equipped with a magnetic stir-bar, additional funnel and a gas outlet, was successively charged with D-glutamic acid (25.0 g, 170 mmol, 1.0 equiv), H_2O (60 mL) and conc. HCl (25 mL). The resulting solution was cooled to 0 ^oC before a solution of $NaNO_2$ (15.2 g, 221 mmol, 1.3 equiv) in H_2O (80 mL) was added dropwise (~ 40 min), causing a gentle evolution of N_2 gas. Once the addition was complete, the colorless solution was warmed to room temperature and stirred for 72 h. All volatile materials were then evaporated (bath temperature 50 ^oC, 75 mbar) to leave a white solid that was washed with EtOAc (100 mL) and filtered off. The filter cake was washed again with EtOAc (2 x 100 mL), the combined filtrates were dried with $MgSO_4$, and evaporated and the residue dried for 13 h at 2.3x10^{-2} mbar. The remaining pale yellow solid (20.1 g, 91%) was used in the next step without further purification. Its spectral data matched those reported in the literature.[5a-b]

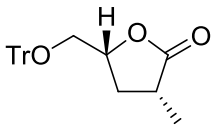
This crude material (20.1 g, 154 mmol, 1.0 equiv) was further dried by azeotropic distillation of toluene (50 mL) followed by drying in high vacuum, before it was dissolved in THF (320 mL). After cooling to 0 ^oC, borane dimethylsulfide complex (18.3 mL, 193 mmol, 1.25 equiv) was added dropwise (~ 15 min). Once the addition was complete, the mixture was stirred at room temperature overnight (16 h). For work up, the mixture was cooled to 0 ^{o} C and the reaction carefully quenched with MeOH (81 mL). The solvents were evaported (18 mbar) and the remaining yellow oil was passed through a silica gel plug (SiO_2, hexanes/EtOAc, 50%) to afford alcohol **21** as a pale yellow oil (11.8 g, 66%), the spectral data of which match those reported in the literature.[5a-b]



A 500-mL round-bottomed flask, equipped with a large magnetic stir-bar, an argon adaptor and a glass stopper, was charged with alcohol **21** (11.8 g, 102 mmol, 1.0 equiv). Pyridine (55 mL) was then added, followed by trityl chloride (28.9 g, 104 mmol, 1.02 equiv), and the resulting yellow mixture was stirred overnight (~ 14 h), during which time a thick suspension was formed. The mixture was diluted with H_2O (500 mL) and extracted with EtOAc (3 x 100 mL). The combined extracts were washed with H_2O (100 mL) and brine (100 mL), dried over $MgSO_4$, and evaporated. The remaining orange syrup was purified by flash chromatography (SiO_2, hexanes/EtOAc, 10%) and the collected product recrystallised from hexane to afford compound **22** as colorless needles (33.1 g, 91%). The spectral data match those reported in the literature.[5a] M.p. 148-150

°C; $[\alpha]_D^{20} = -7.9°$ (c = 0.09, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.46-7.40 (m, 6H), 7.34-7.28 (m, 7H), 7.27-7.22 (m, 2H), 4.65 (dddd, *J* = 3.5, 4.3, 10.1, 11.6 Hz, 1H), 3.42 (dd, *J* = 3.5, 10.4 Hz, 1H), 3.16 (dd, *J* = 4.3, 10.4 Hz, 1H), 2.69 (ddd, *J* = 6.6, 10.1, 17.8 Hz, 1H), 2.51 (ddd, J = 7.0, 10.1, 17.8 Hz, 1H), 2.25 (dddd, *J* = 6.6, 7.9, 10.1, 17.9 Hz, 1H), 2.04 ppm (dddd, *J* = 5.8, 6.8, 10.1, 17.6 Hz, 1H); IR (film): 3062, 3001, 2961, 2919, 2872, 1771, 1594, 1488, 1449, 1342, 1218, 1183, 1082, 1043, 950, 751, 697 cm^{-1}; MS (EI): *m/z* (%): 358 (M^+, 26), 281 (24), 258 (21), 243 (100), 183 (11), 165 (55), 105 (25), 99 (17), 77 (11), 43 (13); HRMS (ESI-pos) calcd. for $C_{24}H_{22}O_3Na$ [M + Na^+] 381.1461, found 381.1460.

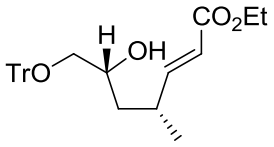
Compound S8. This compound was prepared by adapting a procedure of Nishida and co-workers:[6] A 500-mL round-bottomed flask, equipped with a magnetic stir-bar, an argon inlet and a septum, was charged with diisopropylamine (6.3 mL, 44.9 mmol, 1.4 equiv) and THF (220 mL). The solution was cooled to −78 °C before *n*-BuLi (1.6 M in hexane, 24.1 mL, 38.5 mmol, 1.2 equiv) was added dropwise to afford a light yellow solution, which was allowed to warm to 0 °C and stirred at this temperature for 15 min. Next, the mixture was cooled to −78 °C before a solution of lactone **22** (11.5 g, 32.1 mmol, 1.0 equiv) in THF (80 mL) was slowly added. Stirring was continued for 15 min at this temperature before a solution of methyl iodide (2.4 mL, 38.5 mmol, 1.2 equiv) in THF (40 mL) was introduced and the mixture gradually warmed to −30 °C over 4 h. The reaction was quenched with aq. sat. Na_2SO_4 (100 mL) and the mixture diluted with *tert*-butyl methyl ether (100 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 50 mL), the combined extracts were washed with H_2O (100 mL) and brine (100 mL), dried over $MgSO_4$ and evaporated. The resulting material was used in the next step without further purification.



A second 500-mL round-bottomed flask, equipped with a magnetic stir-bar, an argon inlet and a septum, was charged with diisopropylamine (6.3 mL, 44.9 mmol, 1.4 equiv) and THF (200 mL). The solution was cooled to −78 °C before *n*-BuLi (1.6 M in hexane, 24.1 mL, 38.5 mmol, 1.2 equiv) was slowly added. The resulting light yellow solution was warmed to 0 °C and stirred for 15 min before it was cooled back to −78 °C. A solution of the crude material of the previous step in THF (119 mL) was added over the course of ~ 25 min and stirring was continued at this temperature for 20 min. The reaction was quenched with aq. sat. Na_2SO_4 (100 mL) and the aqueous layer extracted with *tert*-butyl methyl ether (3 x 70 mL). The combined organic extracts were washed with H_2O (100 mL) and brine (100 mL), dried over $MgSO_4$ and evaporated. The residue was dried in high vacuum to afford lactone **S8** as a white solid (11.1 g, 93% over two steps). The crude material was of sufficient purity to be used in the next step. M.p. 111-113 °C (*tert*-butyl methyl ether); $[\alpha]_D^{20} = -6.0°$ (c = 0.025, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.40 (m. 6H), 7.34-7.28 (m, 6H), 7.27-7.22 (m, 3H), 4.52 (dddd, *J* = 4.0, 5.2, 6.0, 10.4 Hz, 1H), 3.29 (dd, *J* = 3.9, 10.4 Hz, 1H), 3.26 (dd, *J* = 5.3, 10.4 Hz, 1H), 2.68 (ddq, *J* = 7.1, 8.9, 11.7 Hz, 1H), 2.37 (ddd, *J* = 6.1, 8.9, 12.6 Hz, 1H), 1.69 (ddd, *J* = 10.3, 11.7, 12.5 Hz, 1H), 1.28 ppm (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5, 143.7 (3C), 128.8 (6C), 128.1 (6C), 127.3 (3C), 86.9, 77.3, 65.2 35.5, 33.2, 15.5 ppm; IR (film): 3058, 2973, 2935, 2873, 1768, 1595, 1489, 1449, 1375, 1356, 1346, 1319, 1294, 1207, 1175, 1158, 1105, 1035, 1025, 996, 958, 930, 901, 785, 769, 748,

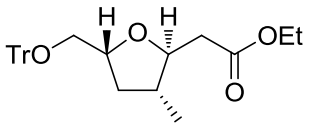
697 cm^{-1}; MS (EI): *m/z* (%): 372 (M^+, 18), 295 (24), 258 (26), 243 (100), 165 (31), 113 (13), 105 (14); HRMS (EI (DE)) calcd. for $C_{25}H_{24}O_3$ 372.1725, found 372.1722.

Compound 23. A 500-mL round-bottomed flask, equipped with a magnetic stir-bar, an argon inlet and a septum, was charged with lactone **S8** (8.3 g, 22.4 mmol, 1.0 equiv) and CH_2Cl_2 (90 mL). The resulting solution was cooled to −78 °C before DIBAL-H (1.0 M in hexane, 24.6 mL, 24.6 mmol, 1.1 equiv) was added dropwise over ~ 15 min. The mixture was stirred at this temperature for 1.25 h before the reaction was quenched by the dropwise addition of MeOH (17 mL). The mixture was transferred into a 1000-mL Erlenmeyer flask containing aq. sat. sodium potassium tartrate (Rochelle salt, 50 mL). The contents were allowed to warm to room temperature and vigorously stirred for 1 h. The resulting biphasic mixture was diluted with H_2O (100 mL) and the aqueous layer extracted with CH_2Cl_2 (3 x 50 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried over $MgSO_4$ and evaporated to give a pale yellow oil.



The crude lactol was azeotropically dried with toluene before it was dissolved in toluene (112 mL). After addition of (carbethoxymethylene)-triphenylphosphorane (11.7 g, 33.6 mmol, 1.5 equiv), the mixture was stirred at 80 °C for 16 h. The solvent was evaporated and the remaining syrup purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 0 → 30%) to give alkene **23** as a pale yellow oil (8.5 g, 85% over two steps). $[\alpha]_D^{20} = -22.8°$ (c = 0.87, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45-7.40 (m, 6H), 7.34-7-28 (m, 6H), 7.28-7.22 (m, 3H), 6.86 (dd, *J* = 7.7, 15.7 Hz, 1H), 5.69 (dd, *J* = 1.2, 15.7 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.85-3.77 (m, 1H), 3.19 (dd, *J* = 3.2, 9.4 Hz, 1H), 3.02 (dd, *J* = 7.4, 9.4 Hz, 1H), 2.49-2.38 (m, 1H), 1.58 (ddd, *J* = 6.5, 8.6, 13.9 Hz, 1H), 1.35-1.28 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.03 ppm (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 154.2, 143.9 (3C), 128.8 (6C), 128.0 (6C), 127.3 (3C), 119.7, 86.9, 68.7, 67.8, 60.3, 39.3, 32.9, 19.0, 14.4 ppm; IR (film): 3479, 3059, 2931, 2872, 1775, 1716, 1651, 1597, 1490, 1448, 1368, 1277, 1181, 1074, 1034, 986, 900, 765, 747, 706 cm^{-1}; HRMS (ESI-pos) calcd. for $C_{29}H_{32}O_4Na$ [M + Na^+] 467.2193, found 467.2191.

Compound S9. A 250-mL, round-bottomed flask, equipped with a magnetic stir-bar, an argon inlet and a septum, was charged with alkene **23** (6.1 g, 13.7 mmol, 1.0 equiv) and THF (70 mL). After cooling to 0 °C, a solution of TBAF·$3H_2O$ (1.0 M in THF, 20.6 mL, 20.6 mmol, 1.5 equiv) was added and the mixture stirred at this temperature for 2.5 h. After the reaction was judged complete by TLC analysis, the solvent was evaporated and the residue purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 3 → 5%) to afford compound **S9** as a white solid (5.3 g, 87%). Crystals suitable for X-ray analysis were obtained from acetone. M.p. 112-113 °C (acetone); $[\alpha]_D^{20} = -6.9°$ (c = 3.05, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49-7.42 (m, 6H), 7.32-7.18 (m, 9H), 4.27-4.12 (m, 1H), 4.18 (dq, *J* = 1.8, 7.1 Hz, 2H), 3.90 (td, *J* = 4.2, 8.5 Hz, 1H), 3.16 (dd, *J* = 5.3, 9.4 Hz, 1H), 3.02 (dd, *J* = 4.8, 9.4 Hz, 1H), 2.57 (dd, *J* = 4.2, 14.8 Hz, 1H), 2.49 (dd, *J* = 8.1, 14.8 Hz, 1H), 2.23-2.15 (m, 1H), 2.00-1.87 (m, 1H), 1.43 (ddd, *J* = 8.9, 10.8, 12.3 Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.03 ppm (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 144.3 (3C), 128.9 (6C), 127.9 (6C), 127.0 (3C), 86.5, 81.6, 77.4, 66.8, 60.6, 40.0, 39.5, 37.9, 16.3 14.4 ppm; IR



(film): 3058, 3032, 2959, 2929, 2872, 1734, 1596, 1490, 1448, 1383, 1367, 1321, 1275, 1251, 1196, 1153, 1092, 1075, 1032, 992, 945, 899, 836, 776, 765, 747, 701 cm^{-1}; MS (EI): *m/z* (%): 444 (M^+, 0.3), 243 (100); HRMS (ESI-pos) calcd. for $C_{29}H_{32}O_4Na$ [M + Na^+] 467.2193, found 467.2195.

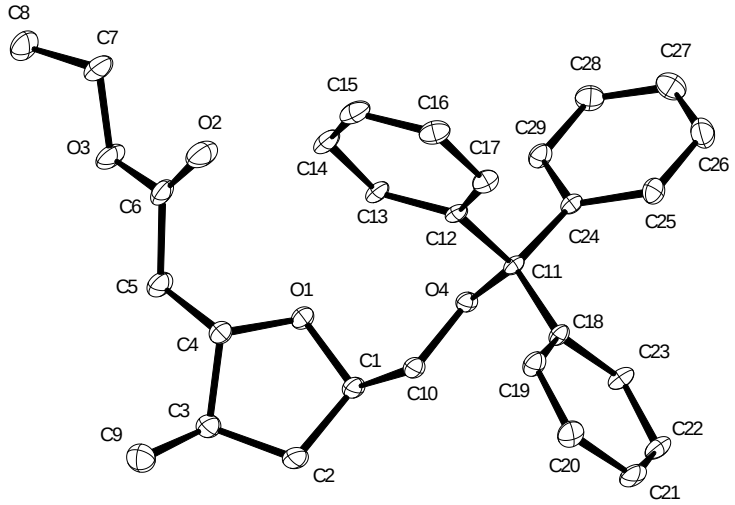
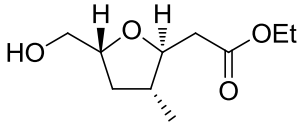


Figure S2. Structure of compound **S9** in the solid state; anisotropic displacement parameters are drawn at the 50% probability level, hydrogen atoms are omitted for clarity.

X-ray Crystal Structure Analysis of Compound S9: C_{29} H_{32} O_4, M_r = 444.55 g · mol^{-1}, colorless plate, crystal size 0.081 x 0.075 x 0.022 mm, monoclinic, space group $P2_1$, a = 8.5248(11) Å, b = 16.366(2) Å, c = 8.5436(11) Å, β = 97.619(2)°, V = 1181.4(3) $Å^3$, T = 100 K, Z = 2, D_{calc} = 1.250 g·cm^3, λ = 0.71073 Å, μ(*Mo-K*$_\alpha$) = 0.082 mm^{-1}, Gaussian absorption correction (T_{min} = 0.99, T_{max} = 1.00), Bruker-AXS Smart APEX-II diffractometer, 2.41 < θ < 31.39°, 27387 measured reflections, 4007 independent reflections, 3764 reflections with $I > 2\sigma(I)$, Structure solved by direct methods and refined by full-matrix least-squares against F^2 to R_1 = 0.051 [$I > 2\sigma(I)$], wR_2 = 0.142, 300 parameters, absolute structure parameter = 0(10), H atoms riding, S = 1.078, residual electron density +0.5 / -0.4 e $Å^{-3}$.

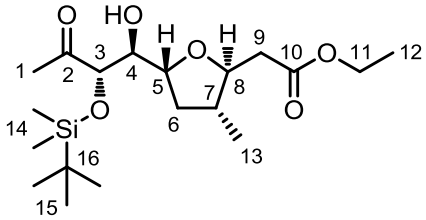
CCDC 815411 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Compound 24. A 250-mL, round-bottomed flask, equipped with a magnetic stir-bar, an argon inlet and a septum, was charged with compound **S9** (2.9 g, 6.58 mmol, 1.0 equiv), CH_2Cl_2 (131 mL) and EtOH (7.4 mL). The mixture was cooled to 0 °C before trifluoroacetic acid (14 mL) was slowly added. The mixture was stirred at 0 °C for 1 h before the reaction was quenched at 0 °C by the slow addition of aq. sat. $NaHCO_3$ (150 mL) (Note: once the biphasic mixture has a pH ~ 7-8, it become colorless). The mixture was transferred to a separatory funnel and the aqueous layer extracted with EtOAc (3 x 50 mL). The combined extracts were washed with brine (100 mL) and the solvents evaporated. The remaining crude



oil was dissolved in EtOAc (150 mL), aq. sat. K_2CO_3 (50 mL) was added, and the resulting mixture stirred for 15 min. The aqueous layer was extracted with EtOAc (50 mL), the combined organic phases were washed with H_2O (50 mL) and brine (100 mL), dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 25 → 75%) to give alcohol **24** as a pale yellow oil (1.1 g, 86%). $[\alpha]_D^{20} = -28.0°$ (c = 1.95, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.06 (q, *J* = 7.2 Hz, 2H), 4.01 (ddt, *J* = 3.5, 5.9, 9.5 Hz, 1H), 3.76 (dt, *J* = 4.4, 8.3 Hz, 1H), 3.54 (dd, *J* = 3.4, 11.7 Hz, 1H), 3.42 (dd, *J* = 5.6, 11.7 Hz, 1H), 2.97 (bs, 1H), 2.45 (dd, *J* = 4.5, 15.3 Hz, 1H), 2.38 (dd, *J* = 7.9, 15.3 Hz, 1H), 2.01 (dt, *J* = 6.4, 12.2 Hz, 1H), 1.95-1.83 (m, 1H), 1.39-1.35 (ddd, *J* = 9.5, 10.5, 12.0 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.95 ppm (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.5, 81.4, 78.9, 64.7, 60.5, 39.8, 39.2, 36.3, 16.2, 14.1 ppm; IR (film): 3457, 2956, 2930, 2870, 1783, 1732, 1462, 1369, 1327, 1276, 1254, 1191, 1093, 1027, 939, 836, 779, 673, 662 cm^{-1}; MS (EI): *m/z* (%): 171 (M^+–31, 100), 157 (10), 144 (17), 129 (11), 125 (82), 115 (48), 99 (34), 97 (69), 83 (31), 71 (27), 69 (76), 68 (12), 57 (29), 55 (39), 45 (15), 43 (54), 41 (56), 31 (20), 29 (72), 27 (31); HRMS (ESI-pos) calcd. for $C_{10}H_{18}O_4Na$ [M + Na^+] 225.1097, found 225.1097.

Compound 27. A 100-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alcohol **24** (848 mg, 4.19 mmol, 1.0 equiv), which was azeotropically dried with benzene. CH_2Cl_2 (42 mL) was added and the resulting solution cooled to 0 °C before DMSO (1.5 mL, 21.0 mmol, 5.0 equiv) and diisopropylethylamine (5.1 mL, 29.3 mmol, 7.0 equiv) were successively introduced. The mixture was stirred at 0 °C for ~ 5 min prior to the addition of SO_3·pyridine (2.0 g, 12.6 mmol, 3.0 equiv) and stirring continued at 0 °C for 1 h. The reaction was then quenched with aq. sat. $NaHCO_3$ (5 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic phases were dried over $MgSO_4$ and evaporated to give crude aldehyde **25**, which was immediately used in the next step without further purification. Its spectral data matched those reported in the literature.[7]



The crude aldehyde **25** was azeotropically dried with benzene before it was dissolved in DMF (3.1 mL). 1-(*tert*-Butyldimethylsiloxy)-2-propanone **26** (17.8 mL, 92.2 mmol, 22.0 equiv) and L-proline (241 mg, 2.10 mmol, 0.50 equiv) were added and the mixture was stirred for 18 h. For work up, the DMF was distilled off under reduced pressure and the residue purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 8 → 12%) to afford compound **27** as a colorless oil (1.1 g, 66% over two steps). $[\alpha]_D^{20} = -4.3$ ° (c = 0.49, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.13 (q, *J* = 7.1 Hz, 2H, H-11), 4.12-4.07 (m, 1H, H-5), 3.89 (d, *J* = 7.1 Hz, 1H, H-3), 3.85 (ddd, *J* = 4.1, 8.1, 8.7 Hz, 1H, H-8), 3.52 (ddd, *J* = 3.4, 7.1, 8.1 Hz, 1H, H-4), 2.49 (dd, *J* = 4.1, 15.1 Hz, 1H, H-9a), 2.41 (dd, *J* = 8.1, 15.1 Hz, 1H, H-9b), 2.34 (d, *J* = 8.1 Hz, 1H, HO), 2.19 (s, 3H, H-1), 2.07 (ddd, *J* = 5.7, 6.8, 12.1 Hz, 1H, H-6a), 2.02-1.96 (m, 1H, H-7), 1.58 (ddd, *J* = 10.2, 11.0, 12.1 Hz, 1H, H-6b), 1.24 (t, *J* = 7.2 Hz, 3H, H-12), 1.03 (d, *J* = 6.5 Hz, 3H, H-13), 0.88 (s, 9H, H-15), 0.05 (s, 3H, H-14a), 0.01 ppm (s, 3H, H-14b); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 210.4 (C, C-2), 171.3 (C, C-10), 82.1 (HC, C-8), 79.3 (HC, C-3), 76.4 (HC, C-5), 74.3 (HC, C-4), 60.5 (H_2C, C-11), 40.1 (HC, C-7), 39.5 (H_2C, C-9),

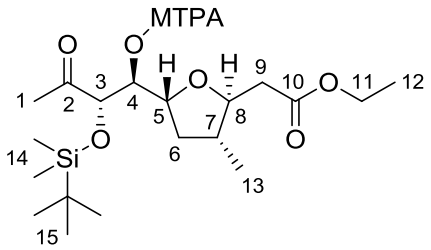
36.8 (H_2C, C-6), 25.7 (H_3C, C-1 and $(H_3C)_3$,C-15), 18.0 (CSi, C-16), 16.1 (H_3C, C-13), 14.2 (H_3C, C-12), −5.1 (H_3CSi, C-14a), −5.2 ppm (H_3C, C-14b); IR (film): 3456, 2957, 2931, 2859, 1737, 1667, 1463, 1419, 1251, 1208, 1142, 1095, 1033, 945, 897, 836, 778, 713, 675 cm^{-1}; MS (EI): *m/z* (%): 313 (M^+−75, 71), 201 (16), 188 (21), 171 (100), 143 (12), 131 (33), 129 (10), 125 (62), 113 (19), 109 (18), 97 (25), 83 (15), 75 (44), 73 (30), 69 (14), 55 (10), 43 (19), 29 (11); HRMS (ESI-pos) calcd. for $C_{19}H_{36}O_6SiNa$ [M + Na^+] 411.2173, found 411.2173.

Mosher Ester Analysis of Alcohol 27. To a solution of alcohol **27** (3.0 mg, 0.00772 mmol, 1.0 equiv) in CH_2Cl_2 (150 μL) was added pyridine (3.9 μL, 0.0479 mmol, 6.2 equiv) followed by (*R*)-α-methoxy−α-trifluoromethyl-phenylacetyl chloride ((*R*)-MTPA-Cl) (8.1 μL, 0.0432 mmol, 5.6 equiv) and DMAP (19 mg, 0.154 mmol, 20.0 equiv). The reaction was stirred overnight before a second portion of pyridine (9.7 μL, 0.120 mmol, 15.6 equiv), (*R*)-MTPA-Cl (14 μL, 0.0726 mmol, 9.4 equiv) and DMAP (50 mg, 0.406 mmol, 52.6 equiv) was added. The reaction was stirred until TLC analysis showed complete consumption of the substrate. Standard aqueous workup followed by flash chromatography (SiO_2, hexanes/EtOAc, 10%) gave the corresponding (*S*)-Mosher ester **(*S*)-MTPA-27**, which analyzed as follows: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63-7.57 (m, 2H), 7.43-7.36 (m, 3H), 5.23 (dd, *J* = 4.6, 6.7 Hz, 1H), 4.13-4.05 (m, 4H), 3.78 (ddd, *J* = 4.3, 8.0, 9.1 Hz, 1H), 3.55 (d, *J* = 1.0 Hz, 3H), 2.46 (dd, *J* = 4.3, 14.8 Hz, 1H), 2.36 (dd, *J* = 7.9, 14.8 Hz, 1H), 2.22-2.17 (m, 1H), 2.17 (s, 3H), 1.97-1.89 (m, 1H),1.27-1.13 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.93-0.88 (m, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.7, 171.1, 166.3, 132.4, 129.7, 128.4, 128.0, 81.5, 79.1, 77.7, 77.4, 75.4, 60.6, 55.8, 40.1, 39.4, 37.3, 26.5, 25.7 (3C), 18.2, 15.8, 14.3, −5.0, −5.1 ppm (6C overlapping between 129.7 and 128.0 ppm).

The same procedure was followed for the preparation of **(*R*)-MTPA-27** ester, which analyzed as follows: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64-7.56 (m, 2H), 7.43-7.33 (m, 3H), 5.26 (dd, *J* = 3.4, 8.2 Hz, 1H), 4.14-4.06 (m, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.97 (d, *J* = 3.4 Hz, 1H), 3.88 (td, *J* = 4.1, 8.6 Hz, 1H), 3.59 (d, *J* = 1.2 Hz, 3H), 2.51 (dd, *J* = 4.0, 14.7 Hz, 1H), 2.36 (dd, *J* = 8.1, 14.7 Hz, 1H), 2.30 (dt, *J* = 6.5, 12.0 Hz, 1H), 2.04-1.96 (m, 1H), 1.78 (s, 3H), 1.31-1.21 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.1, 171.0, 166.1, 132.8, 129.5, 128.3, 127.6, 81.5, 79.6, 77.7, 77.4, 75.7, 60.6, 56.1, 40.2, 39.5, 37.9, 26.6, 25.8 (3C), 18.3, 16.1, 14.3, −5.0, −5.2 ppm (6C overlapping between 129.5 and 127.6 ppm).

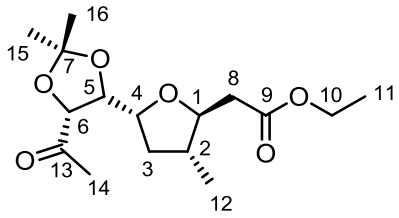
Both products were analyzed according to Hoye and co-workers:[8]

Table S1. Mosher Ester Analysis for the Assignment of the C(4) Stereocenter; arbitrary numbering as shown in the Insert



Assignment	**27** (δ), ppm	**δ (S-ester)**, ppm	**δ (R-ester)**, ppm	**Δ (δ-(S–R))**, ppm
1	2.19	2.17	1.783	0.388
3	3.89	4.100	3.973	0.127
4	3.52	5.233	5.261	–0.028
5	4.09	~ 4.10	~ 4.10	0.000
6	2.07	2.203	2.302	–0.099
	1.58	1.190	1.260	–0.070
7	2.00	1.931	1.999	–0.068
8	3.85	3.783	3.878	–0.095
9	2.41	2.358	2.364	–0.006
	2.49	2.466	2.511	–0.045
11	4.13	~ 4.10	4.078	0.022
12	1.24	1.221	1.229	–0.008
13	1.03	0.904	1.046	–0.142
14	0.05	0.096	0.046	0.050
15	0.01	0.917	0.905	0.012

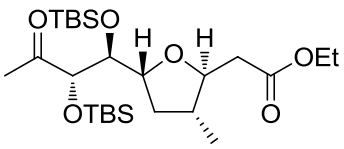
Compound S10. A Teflon screw-capped vial was charged with alcohol **27** (69 mg, 0.178 mmol, 1.0 equiv) and THF (2.6 mL). The solution was cooled to 0 °C before pyridine (588 μL, 7.30 mmol, 41.0 equiv), HF·pyridine (401 μL, 4.45 mmol, 25.0 equiv) and EtOH (39 μL, 0.676 mmol, 3.8 equiv) were added. The vial was placed in the refrigerator for 48 h. Since TLC analysis showed that the reaction was incomplete, a second portion of HF·pyridine (99 μL, 1.10 mmol, 6.2 equiv) was added. After additional 7 h, the reaction was quenched with aq. sat. $NaHCO_3$ (3 mL) and the aqueous layer was extracted with EtOAc (3 x 2 mL). The combined extracts were dried over $MgSO_4$ and concentrated to give the desired diol (44 mg, 90%) as an oil, which was directly used in the next step.



The crude diol (13 mg, 0.0474 mmol, 1.0 equiv) was dissolved in 2,2-dimethoxypropane (474 μL, 3.87 mmol, 81.6 equiv). TsOH (0.82 mg, 0.00474 mmol, 0.1 equiv) was added and the mixture stirred overnight. The reaction was quenched with aq. sat. $NaHCO_3$ (1 mL) and the aqueous layer extracted with EtOAc (3 x 1 mL). The combined extracts were dried over $MgSO_4$ and evaporated and the residue was purified by flash chromatography (SiO_2, hexanes/EtOAc, 50%) to afford acetal **S10** (10 mg, 67% over two steps). It should be noted that this compound was found rather unstable on silica gel as well as upon long-term storage

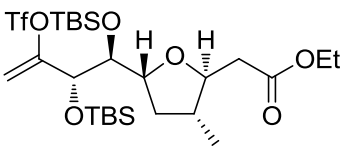
in the freezer. ^{1}H NMR (400 MHz, [D_6]-acetone): δ = 4.40 (d, *J* = 8.6 Hz, 1H, H-6), 4.33 (dd, *J* = 1.6, 8.7 Hz, 1H, H-5), 4.05 (q, *J* = 7.0 Hz, 2H, H-10), 4.01 (ddd, *J* = 1.6, 6.9, 9.0 Hz, 1H, H-4), 3.86 (dt, *J* = 3.0, 9.4 Hz, 1H, H-1), 2.52 (dd, *J* = 3.0, 15.0 Hz, 1H, H-8a), 2.19 (dd, *J* = 9.4, 15.0 Hz, 1H, H-8b), 2.12 (s, 3H, H-14), 2.09 (dt, *J* = 7.0, 12.0 Hz, 1H, H-3a), 1.89-1.77 (m, 1H, H-2), 1.66 (ddd, *J* = 9.0, 11.0, 11.8 Hz, 1H, H-3b), 1.57-1.54 (m, 3H, H-15), 1.33-1.31 (m, 3H, H-16), 1.21 (t, *J* = 7.1 Hz, 3H, H-11), 1.00 ppm (d, *J* = 6.4 Hz, 3H, H-12); ^{13}C NMR (100 MHz, [D_6]-acetone): δ = 210.1 (C, C-13), 171.7 (C, C-9), 110.3 (C, C-7), 83.5 (HC, C-1), 82.0 (HC, C-6), 81.3 (HC, C-5), 75.8 (HC, C-4), 60.6 (H_2C, C-10), 40.7 (HC, C-2), 39.8 (H_2C, C-8), 37.0 (H_2C, C-3), 27.9 (H_3C, C-14), 26.8 (H_3C, C-15), 24.9 (H_3C, C-16), 15.7 (H_3C, C-12), 14.5 ppm (H_3C, C-11).

Compound 28. A 100-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alcohol **27** (870 mg, 2.24 mmol, 1.0 equiv) and CH_2Cl_2 (22 mL). The resulting solution was cooled to 0 °C before pyridine (902 μL, 11.2 mmol, 5.0 equiv) and TBSOTf (2.1 mL, 8.96 mmol, 4.0 equiv) were sequentially added. The mixture was stirred at room temperature until TLC analysis showed complete consumption of starting material (~ 2.5 to 3 h). For work up, aq. sat. NH_4Cl (20 mL) was added and stirring continued for 15 min. The biphasic mixture was transferred into a separatory funnel and the aqueous layer extracted with CH_2Cl_2 (3 x 10 mL). The combined extracts were washed with H_2O (20 mL) and brine (20 mL).



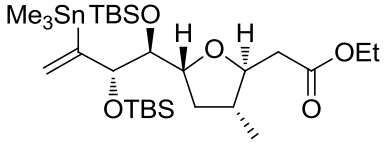
HCl (1% *v/v* in EtOH, 10 mL) was added and the resulting mixture stirred for 30 min to complete the hydrolysis of the silyl enol ether, which is a by-product of the reaction. A standard extractive work up with Et_2O (50 mL) and H_2O (100 mL) furnished a light yellow syrup which was purified by flash chromatography (SiO_2, hexanes/EtOAc gradient, 2 → 4%) to afford product **28** as a colorless oil (1.0 g, 91%). $[\alpha]_D^{20} = -14.4°$ (c = 1.35, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.11 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 2.0 Hz, 1H), 3.87 (ddd, *J* = 5.8, 8.2, 10.2 Hz, 1H), 3.81 (dt, *J* = 3.8, 8.8 Hz, 1H), 3.67 (dd, *J* = 2.0, 8.1 Hz, 1H), 2.48 (dd, *J* = 3.8, 14.9 Hz, 1H), 2.39 (dd, *J* = 8.6, 14.9 Hz, 1H), 2.27-2.15 (m, 1H), 2.20 (s, 3H), 1.98-1.85 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.28-1.16 (m, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 9H), 0.87 (s, 9H), 0.09 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.2, 171.8, 81.2, 80.5 (2C), 79.4, 60.7, 40.3, 39.7, 38.2, 28.2, 26.2 (3C), 26.0 (3C), 18.6, 18.4, 16.1, 14.3, –4.5 (2C), –4.7, –4.9 ppm; IR (film): 2955, 2930, 2888, 2857, 1738, 1714, 1472, 1463, 1388, 1350, 1252, 1193, 1131, 1079, 1039, 963, 938, 856, 834, 806, 777, 679 cm^{-1}; MS (EI): *m/z* (%): 445 (M^+–57, 42), 313 (71), 245 (36), 183 (18), 171 (100), 147 (10), 143 (13), 129 (21), 125 (36), 115 (14), 109 (34), 97 (12), 75 (21), 73 (79); HRMS (ESI-pos) calcd. for $C_{25}H_{50}O_6Si_2Na$ [M + Na^+] 525.3038, found 525.3033.

Compound 29. A 100-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with ketone **28** (500 mg, 0.994 mmol, 1.0 equiv), which was azeotropically dried with benzene under reduced pressure. The compound was then dissolved in THF (5.0 mL) and the solution cooled to –78 °C. Next, a cold (–78°C) solution of KHMDS (214 mg, 1.07 mmol, 1.08 equiv) in THF (5.4 mL) was added dropwise via cannula. The resulting yellow solution was stirred for 1 h at



–78 °C before a pre-cooled (–78°C) solution of phenyl triflimide (888 mg, 2.49 mmol, 2.5 equiv, azeotropically dried with benzene prior to use) in THF (4.5 mL) was added (note that at –78°C, the triflimide solution in THF becomes cloudy). The resulting pale yellow mixture was stirred at –78 °C for 3 h before the reaction was quenched at this temperature with aq. sat. NH_4Cl (10 mL). After reaching ambient temperature, the mixture was added to a separatory funnel containing *tert*-butyl methyl ether (20 mL) and H_2O (20 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 10 mL). The combined extracts were washed with H_2O (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 0 → 1%) to afford enol triflate **29** as a colorless oil (461 mg, 73%). $[\alpha]_D^{20}$ =–8.3° (c = 1.35, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.30 (dd, *J* = 0.9, 3.4 Hz, 1H), 5.25 (d, *J* = 3.4 Hz, 1H), 4.26 (d, *J* = 2.9 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 4.04 (dt, *J* = 6.2, 10.2 Hz, 1H), 3.80 (dt, *J* = 4.1, 8.6 Hz, 1H), 3.63 (dd, *J* = 3.1, 6.7 Hz, 1H), 2.50 (dd, *J* = 4.0, 14.8 Hz, 1H), 2.42 (dd, *J* = 8.2, 14.8 Hz, 1H), 2.06 (dt, *J* = 6.2, 11.8 Hz, 1H), 1.99-1.86 (m, 1H), 1.34 (q, *J* = 11.1 Hz, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 155.2, 120.2, 106.2, 81.1, 78.8, 77.6, 74.9, 60.6, 40.5, 39.7, 37.6, 26.2 (3C), 25.9 (3C), 18.5, 18.3, 16.0, 14.3, –4.2, –4.8 ppm (3C); IR (film): 2957, 2931, 2888, 2859, 1737, 1668, 1473, 1463, 1419, 1325, 1251, 1208, 1142, 1096, 1032, 945, 897, 835, 813, 777, 713, 676, 665 cm^{-1}; MS (EI): *m/z* (%): 577 (M^+–57, 100), 319 (30), 315 (41), 183 (30), 171 (64), 147 (14), 125 (26), 115 (18), 109 (34), 75 (13), 73 (56); HRMS (ESI-pos) calcd. for $C_{26}H_{49}O_8Si_2SF_3Na$ [M + Na^+] 657.2531, found 657.2532.

Compound 30. A 50-mL Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with anhydrous LiCl (188 mg, 4.44 mmol, 10.0 equiv) and triflate **29** (282 mg, 0.444 mmol, 1.0 equiv). The contents were azeotropically dried with benzene before tri(2-furyl)phosphine (62 mg, 0.266 mmol, 0.60 equiv) was added, followed by THF (4.4 mL). The resulting solution was subjected to three freeze/pump/thaw degassing cycles. Once the contents reached room temperature, $Pd_2(dba)_3$ (61 mg, 0.0666 mmol, 0.15 equiv) and hexamethylditin (276 μL, 1.33 mmol, 3.0 equiv) were added and the dark mixture was stirred for 1.5 h. At this time, a second portion of hexamethylditin (276 μL, 1.33 mmol, 3.0 equiv) was introduced and stirring continued for 1.75 h before a third portion of hexamethylditin (276 μL, 1.33 mmol, 3.0 equiv) was introduced. After an additional 1 h, the mixture was diluted with Et_2O (20 mL) and the suspension filtered through a pad of Celite (30 x 10 mm), which was carefully rinsed with Et_2O (40 mL). The combined filtrates were evaporated and the residue was purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 1 → 2%) to afford stannane **30** as a colorless oil (234 mg, 81%). $[\alpha]_D^{20}$ =–23.7° (c = 0.33, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.98 (dd, *J* = 1.5, 2.7 Hz, $J_{Sn\text{-}H}$ = 72.6 Hz, 1H), 5.36 (dd, *J* = 1.5, 2.7 Hz, $J_{Sn\text{-}H}$ = 35.4 Hz, 1H), 4.49-4.45 (m, $J_{Sn\text{-}H}$ = 24.3 Hz, 1H), 4.10 (ddd, *J* = 5.6, 7.2, 10.2 Hz, 1H), 4.03 (dq, *J* = 1.5, 7.2 Hz, 2H), 3.89 (ddd, *J* = 4.0, 8.1, 8.9 Hz, 1H), 3.79 (dd, *J* = 3.1, 7.3 Hz, 1H), 2.36 (dd, *J* = 8.0, 14.9 Hz, 1H), 2.28 (dd, *J* = 4.0, 14.9 Hz, 1H), 1.97 (quint, *J* = 6.1 Hz, 1H), 1.67-1.54 (m, 1H), 1.29-1.18 (m, 1H), 1.12 (s, 9H), 1.03 (s, 9H), 1.06-1.01 (m, 3H), 0.75 (d, *J* = 6.5 Hz, 3H), 0.36 (s, 3H), 0.32 (s, 3H), 0.29 (s, $J_{Sn\text{-}H}$ = 26.0 Hz, 9H), 0.22 (s, 3H), 0.13 ppm



(s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 170.9, 155.3, 126.4, 83.0, 81.1, 80.2, 80.1, 60.3, 40.4, 39.6, 38.8, 26.9 (3C), 26.5 (3C), 19.1, 18.9, 16.1, 14.3, –3.3, –3.4, –3.9, –4.0, –7.7 ppm (3C); IR (film): 2954, 2929, 2888, 2856, 1739, 1472, 1462, 1388, 1361, 1326, 1250, 1194, 1131, 1068, 1038, 1004, 956, 928, 912, 890, 871, 830, 773, 716, 675 cm^{-1}; MS (EI): *m/z* (%): 639 (12), 635 (68), 593 (13), 503 (14), 411 (51), 337 (16), 315 (36), 297 (12), 279 (22), 251 (11), 239 (22), 213 (24), 183 (60), 171 (71), 165 (61), 125 (35), 109 (100), 95 (28), 73 (96); HRMS (ESI-pos) calcd. for $C_{28}H_{58}O_5Si_2SnNa$ [M + Na$^+$] 673.2736, found 673.2742.

Compound 31. A 25-mL round-bottomed flask, equipped with a magnetic stir-bar, a water condenser and argon bubbler was charged with ester **30** (201 mg, 0.310 mmol, 1.0 equiv), THF (1.5 mL), EtOH (1.5 mL) and potassium hydroxyde (3.0 M in H_2O, 1.6 mL, 4.96 mmol, 16.0 equiv). The mixture was stirred at 45 °C for 5 h before it was cooled to room temperature. The reaction was quenched with HCl (1.0 M in H_2O) until a pH ~ 2 was reached and the aqueous phase extracted with Et_2O (5 x 15 mL). The combined organic layers were washed with H_2O (2 x 20 mL), dried over Na_2SO_4, filtered and evaporated. The remaining colorless oil was azeotropically dried three times with benzene to give acid **31** as a colorless wax (189 mg, 98%). $[\alpha]_D^{20} = -17.8°$ (c = 2.60, CH_2Cl_2); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.99 (dd, *J* = 1.5, 2.7 Hz, J_{Sn-H} = 72.6 Hz, 1H), 5.36 (dd, *J* = 1.5, 2.7 Hz, J_{Sn-H} = 35.4 Hz, 1H), 4.50-4.46 (m, J_{Sn-H} = 23.6 Hz, 1H), 4.12 (ddd, *J* = 5.8, 7.1, 10.2 Hz, 1H), 3.81-3.73 (m, 2H), 2.33-2.22 (m, 2H), 1.92 (quint, *J* = 6.1 Hz, 1H), 1.59-1.46 (m, 1H), 1.29-1.18 (m, 1H), 1.13 (s, 9H), 1.04 (s, 9H), 0.70 (d, *J* = 6.5 Hz, 3H), 0.37 (s, 3H), 0.32 (s, 3H), 0.29 (s, J_{Sn-H} = 26.5 Hz, 9H), 0.23 (s, 3H), 0.14 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 177.1, 155.2, 126.4, 82.9, 80.6, 80.2, 79.9, 40.3, 39.1, 38.7, 26.8 (3C), 26.4 (3C), 19.0, 18.8, 15.8, –3.3, –3.5, –3.9, –4.1, –7.8 ppm (3C); IR (film): 2978, 2667, 2589, 1781, 1712, 1465, 1435, 1420, 1351, 1328, 1294, 1270, 1236, 1210, 1147, 1061, 1012, 963, 854, 803, 777, 708 cm^{-1}; MS (EI): *m/z* (%): 607 (M$^+$–15, 41), 345 (12), 335 (11), 325 (11), 287 (43), 239 (21), 209 (18), 185 (13), 171 (45), 165 (79), 163 (60), 155 (86), 143 (34), 125 (24), 109 (21), 95 (12), 75 (39), 73 (100); HRMS (ESI-neg) calcd. for $C_{26}H_{53}O_5Si_2Sn$ [M–H$^-$]: 621.2464, found 621.2465.

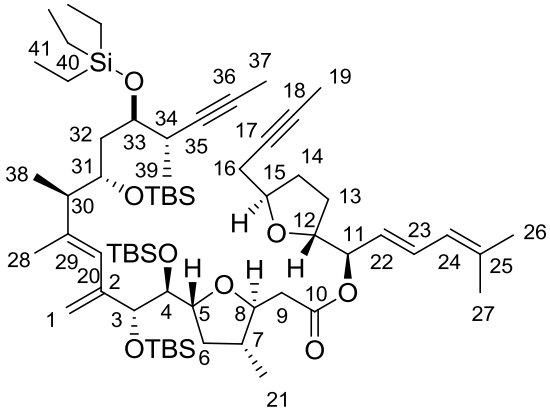
Fragment Coupling and Completion of the Total Synthesis

Compound 32. A Schlenk flask equipped with a magnetic stir-bar and a glass stopper was charged with acid **31** (150 mg, 0.241 mmol, 1.0 equiv). The acid was dried again by azeotropic distillation of benzene (1 mL) and drying in vacuum, before toluene (3.5 mL), triethylamine (296 µL, 2.12 mmol, 8.8 equiv) and 2,4,6-trichlorobenzoyl chloride (79 µL, 0.507 mmol, 2.1 equiv) were sequentially added. The resulting mixture was stirred for 1 h, during which time it became turbid and pale yellow.

A separate 5-mL conical flask, equipped with a magnetic stir-bar, an argon inlet and a septum, was charged with alcohol **19** (73 mg, 0.314 mmol, 1.3 equiv), DMAP (100 mg, 0.820 mmol, 3.4 equiv) and toluene (2.6 mL). The mixture was stirred until all the DMAP had dissolved (~ 5 min). The resulting solution was transferred via cannula into the Schlenk flask containing the Yamaguchi anhydride, washing the conical flask with toluene (220 μL). The resulting reaction mixture was stirred for 3 h before it was diluted with toluene (11 mL). The reaction was quenched with aq. sat. $NaHCO_3$ (7 mL), the aqueous phase diluted with H_2O (20 mL) and extracted with toluene (3 x 20 mL). The combined extracts were washed with H_2O (30 mL) and brine (30 mL), dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash chromatography (SiO_2, hexanes/acetone gradient, 0 → 2%) to give ester **32** as a viscous, colorless oil (162 mg, 80%). $[\alpha]_D^{20} = -13.6°$ (c = 0.63, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6): δ = 6.71 (dd, *J* = 11.0, 14.9 Hz, 1H, H-23), 5.97 (dd, *J* = 1.4, 2.5 Hz, $^3J_{Sn,H}$ = ~ 146 Hz, 1H, H-1a), 5.83 (dm, *J* = 11.2 Hz, 1H, H-24), 5.64 (dd, *J* = 8.4, 14.9 Hz, 1H, H-22), 5.57 (dd, *J* = 6.2, 8.4 Hz, 1H, H-11), 5.35 (dd, *J* = 1.3, 2.6 Hz, $^3J_{119Sn,H}$ = 72.4 Hz, $^3J_{117Sn,H}$ = 70.8 Hz, 1H, H-1b), 4.47 (m, $^3J_{Sn,H}$ = ~ 50 Hz, 1H, H-3), 4.19 (m, 2H, H-12 and H-15), 4.10 (ddd, *J* = 5.9, 7.2, 12.9 Hz, 1H, H-5), 3.93 (ddd, *J* = 4.4, 7.4, 9.0 Hz, 1H, H-8), 3.79 (dd, *J* = 3.3, 7.2 Hz, 1H, H-4), 2.50 (dd, *J* = 4.4, 15.4 Hz, 1H, H-9a), 2.50 (m, 1H, H-16a), 2.38 (dd, *J* = 7.5, 15.4 Hz, 1H, H-9b), 2.32 (m, 1H, H-16b), 1.92 (m, 1H, H-6a), 1.91 (m, 1H, H-14a), 1.72 (m, 1H, H-13a), 1.64 (m, 1H, H-7), 1.59 (m, 1H, H-14b), 1.57 (m, 1H, H-13b), 1.57 (s, 3H, H-26), 1.54 (s, 3H, H-27), 1.52 (t, *J* = 2.5 Hz, 3H, H-19), 1.24 (m, 1H, H-6b), 1.14 (s, 9H, H-33), 1.03 (s, 9H, H-30), 0.76 (d, *J* = 6.5 Hz, 3H, H-21), 0.39 (s, 3H, H-31a), 0.34 (s, 3H, H-31b), 0.30 (s, $^3J_{117Sn,H}$ = 51.6 Hz, $^3J_{119Sn,H}$ = 54.1 Hz, 9H, H-20), 0.22 (s, 3H, H-28a), 0.13 ppm (s, 3H, H-28b); ^{13}C NMR (150 MHz, C_6D_6): δ = 170.2 (C, C-10), 155.3 ($^1J_{119Sn,C}$ = –440.3 Hz, $^1J_{117Sn,C}$ = –421.8 Hz, C, C-2), 136.8 (C, C-25), 131.7 (HC, C-23), 126.4 ($^2J_{119Sn,C}$ = –26.3 Hz, $^2J_{117Sn,C}$ = –25.1 Hz, H_2C, C-1), 125.9 (HC, C-22), 125.1 (HC, C-24), 82.9 ($^2J_{119Sn,C}$ = –50.4 Hz, $^2J_{117Sn,C}$ = –49.0 Hz, HC, C-3), 80.7 (HC, C-8), 80.5 (HC, C-12), 80.0 (HC, C-5), 79.9 (HC, C-4), 78.3 (HC, C-15), 77.2 (HC, C-11), 77.0 (C, C-18), 76.2 (C, C-17), 40.4 (HC, C-7), 40.0 (H_2C, C-9), 38.8 (H_2C, C-6), 31.4 (H_2C, C-14), 28.3 (H_2C, C-13), 26.9 ((H_3C)$_3$, C-33), 26.4 ((H_3C)$_3$, C-30), 26.0 (H_2C, C-16), 25.9 (H_3C, C-26), 19.0 (CSi, C-32), 18.8 (CSi, C-29), 18.2 (H_3C, C-27), 16.1 (H_3C, C-21), 3.4 (H_3C, C-19), –3.2 (H_3CSi, C-31a), –3.3 (H_3CSi, C-31b), –3.9 (H_3CSi, C-28a), –4.1 (H_3CSi, C-28b), –7.7 ppm ($^1J_{119Sn,C}$ = –347.5 Hz, $^1J_{117Sn,C}$ = –332.1 Hz, (H_3C)$_3$Sn, C-20); IR (film): 2956, 2930, 2855, 1739, 1471, 1464, 1421, 1257, 1212, 1143, 1110, 1039, 1026, 950, 837, 779, 748, 703 cm^{-1}; MS (EI): *m/z* (%): 607 (M^+–231, 34), 217 (100), 171 (15), 165 (32), 163 (31), 133 (58), 123 (14), 105 (11), 95 (74), 85 (13), 79 (20), 73 (27); HRMS (ESI-pos) calcd. for $C_{41}H_{74}O_6Si_2SnNa$ [M + Na^+] 861.3937, found 861.3934.

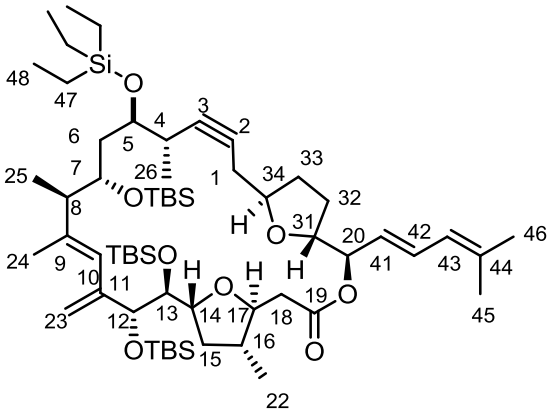
Compound 33. A Schlenk flask equipped with a magnetic stir-bar and a glass stopper, was charged with tetrabutylammonium diphenylphosphinate (215 mg, 0.469 mmol, 4.0 equiv). The compound was dried by azeotropic distillation of benzene (1 mL) and drying in vacuum. Next, DMF (544 μL) was added, followed by a solution of stannane **32** (98 mg, 0.117 mmol, 1.0 equiv.) in DMF (544 μL). The flask containing the stannane was rinsed with DMF (544 μL) and this washing was also added to the Schlenk flask. A solution of iodide **14** (86 mg, 0.152 mmol, 1.3 equiv) in DMF (544 μL) was then added and the flask rinsed with DMF (544 μL), which was also added to the Schlenk flask. Finally, $Pd(PPh_3)_4$ (41 mg, 0.0351

mmol, 0.30 equiv) and copper(I) thiophene-2-carboxylate (CuTC) (67 mg, 0.351 mmol, 3.0 equiv) were quickly introduced in solid form each. The Schlenk flask was sealed with a glass stopper and the orange/brown mixture was stirred at room temperature for 2 h. For work up, the mixture was diluted with Et_2O (14 mL) and 2-(dimethylamino)ethanethiol hydrochloride (0.1 M in H_2O, 8 mL) was added. The aqueous phase was extracted with Et_2O (3 x 14 mL). The combined extracts were washed with H_2O (14 mL) and brine (14 mL), dried over Na_2SO_4, filtered and evaporated. The remaining viscous orange oil was purified by flash chromatography (SiO_2, hexanes/acetone gradient, 3 → 10%) to afford product **33** as a colorless oil (73 mg, 56%). $[\alpha]_D^{20} = -22.4^o$ (c = 1.40, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6): δ =



6.71 (dd, *J* = 11.0, 14.9 Hz, 1H, H-23), 6.08 (s, 1H, H-20), 5.83 (dm, *J* = 11.0 Hz, 1H, H-24), 5.64 (dd, *J* = 8.3, 14.9 Hz, 1H, H-22), 5.59 (dd, *J* = 6.1, 8.3 Hz, 1H, H-11), 5.55 (s, 1H, H-1a), 5.19 (s, 1H, H-1b), 4.36 (s, 1H, H-3), 4.22-4.14 (m, 3H, H-5, H-12, H-15), 4.13 (m, 1H, H-31), 4.05 (m, 1H, H-33), 3.97 (ddd, *J* = 4.2, 8.1, 8.9 Hz, 1H, H-8), 3.87 (dd, *J* = 2.2, 7.7 Hz, 1H, H-4), 2.77 (m, 1H, H-34), 2.60 (m, 1H, H-30), 2.56 (dd, *J* = 8.1, 15.5 Hz, 1H, H-9a), 2.49 (dm, *J* = 16.3 Hz, 1H, H-16a), 2.42 (dd, *J* = 4.2, 15.5 Hz, 1H, H-9b), 2.31 (dm, *J* = 16.3 Hz, 1H, H-16b), 2.15 (m, 1H, H-32a), 2.14 (m, 1H, H-6a), 2.08 (d, *J* = 1.1 Hz, 3H, H-28), 1.90 (m, 1H, H-14a), 1.84 (m, 1H, H-32b), 1.76 (m, 1H, H-7), 1.72 (m, 1H, H-13a), 1.68 (d, *J* = 2.4 Hz, 3H, H-37), 1.59 (m, 2H, H-13b and H-14b), 1.58 (s, 3H, H-26), 1.54 (s, 3H, H-27), 1.53 (m, 3H, H-19), 1.36-1.28 (m, 7H, H-38, H-39 and H-6b), 1.18 (s, 9H, TBS), 1.04 (s, 9H, TBS), 1.04 (m, 9H, TBS), 1.03 (s, 9H, TBS), 0.81 (d, *J* = 6.5 Hz, 3H, H-21), 0.65 (m, 6H, H-40), 0.40 (s, 3H, TBS), 0.39 (s, 3H, TBS), 0.25 (s, 3H, TBS), 0.17 (s, 3H, TBS), 0.16 (s, 3H, TBS), 0.16 ppm (s, 3H, TBS); ^{13}C NMR (150 MHz, C_6D_6): δ = 170.3 (C, C-10), 146.0 (C, C-2), 141.3 (C, C-29), 136.7 (C, C-25), 131.7 (HC, C-23), 126.3 (HC, C-20), 126.0 (HC, C-22), 125.1 (HC, C-24), 115.1 (H_2C, C-1), 80.9 (C, C-35), 80.6 (HC, C-8), 80.5 (HC, C-12), 80.2 (HC, C-4), 80.0 (HC, C-5), 79.1 (HC, C-3), 78.3 (HC, C-15), 77.9 (C, C-36), 77.1 (HC, C-11), 76.9 (C, C-18), 76.2 (C, C-17), 72.9 (HC, C-31), 72.1 (HC, C-33), 47.8 (HC, C-30), 40.5 (HC, C-7), 40.0 (H_2C, C-9), 38.6 (H_2C, C-6), 38.0 (H_2C, C-32), 32.5 (HC, C-34), 31.4 (H_2C, C-14), 28.3 (H_2C, C-13), 26.6 (($H_3C)_3$, TBS), 26.2 (($H_3C)_3$, TBS), 26.2 (($H_3C)_3$, TBS), 26.0 (H_2C, C-16), 25.9 (H_3C, C-26), 18.9 (CSi, TBS), 18.7 (CSi, TBS), 18.3 (CSi, TBS), 18.2 (H_3C, C-27), 17.9 (H_3C, C-28), 16.2 (H_3C, C-21), 15.8 (H_3C, C-39), 15.5 (H_3C, C-38), 7.3 (H_3CSi, C-41), 5.5 (($H_2C)_3Si$, C-40), 3.8 (H_3C, C-37), 3.4 (H_3C, C-19), –3.7 (H_3CSi, TBS), –4.0 (H_3CSi, TBS), –4.2 (H_3CSi, TBS), –4.4 (H_3CSi, TBS), –4.4 (H_3CSi, TBS), –4.6 ppm (H_3CSi, TBS); IR (film): 2961, 2930, 2859, 2313, 1735, 1474, 1463, 1426, 1391, 1258, 1209, 1143, 1107, 1090, 1030, 836, 778, 767, 751, 702 cm^{-1}; MS (ESI-pos) [M + Na^+] 1133 (100); HRMS (ESI-pos) calcd. for $C_{63}H_{114}O_8Si_4Na$ [M + Na^+] 1133.7483, found 1133.7481.

Compound 34. A Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with diyne **33** (70 mg, 0.0629 mmol, 1.0 equiv), which was dried azeotropically by evaporation of degassed toluene (three times). The residue was then dissolved in degassed toluene (11 mL). After this the glass stopper was replaced with an argon bubbler.



In parallel, a stock solution of the catalyst was prepared as follows: a Schlenk flask equipped with a magnetic stir-bar and a glass stopper was charged with complex **39** (21 mg, 0.0336 mmol). Degassed toluene (2.1 mL) was added, followed by degassed CH_2Cl_2 (63 μL), and the resulting mixture stirred for 15 min to provide a 0.015 M stock solution of the activated catalyst.

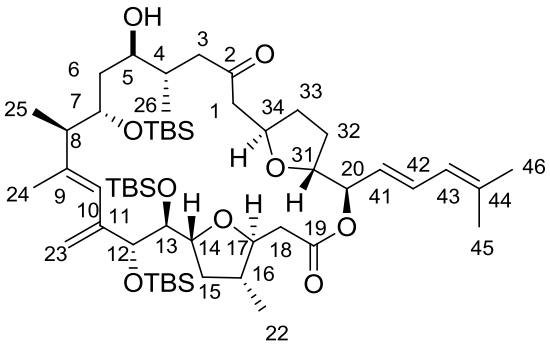
An aliquot of the catalyst solution (812 μL, 0.0126 mmol, 0.20 equiv) was added to the Schlenk flask containing the diyne to give a pale brown mixture. The flask was immersed into a preheated oil bath (60 ^{o}C) and the mixture stirred for 6 h before a second aliquot of the catalyst solution (406 μL, 0.00629 mmol, 0.10 equiv) was introduced. The dark-brown mixture was stirred overnight (~ 14 h) before it was cooled to room temperature, diluted with Et_2O (8 mL) and washed with aq. sat. NH_4Cl (2 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over Na_2SO_4, filtered and evaporated, and the remaining pale brown oil purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 10 → 15%) to give product **34** as a colorless syrup (49 mg, 73%). $[\alpha]_D^{20} = +40.2°$ (c = 0.38, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6, significant line broadening): δ = 6.65 (dd, *J* = ~ 11, ~ 15 Hz, 1H, H-42), 6.48 (s, 1H, H-10), 5.77 (d, *J* = ~ 11 Hz, 1H, H-43), 5.48 (t, *J* = 8.2 Hz, 1H, H-20), 5.43 (dd, *J* = 15.8 Hz, 1H, H-41), 5.10 (s, 1H, H-23a), 5.04 (s, 1H, H-23b), 4.26 (bs, 1H, H-34), 4.15 (s, 1H, H-12), 4.12 (m, 1H, H-7), 4.10 (m, 1H, H-14), 4.03 (m, 1H, H-5), 4.00 (m, 1H, H-31), 3.80 (d, *J* = ~ 7 Hz, 1H, H-13), 3.58 (bs, 1H, H-17), 2.86 (d, *J* = ~ 15 Hz, 1H, H-1a), 2.82 (m, 1H, H-4), 2.73 (bs, 1H, H-8), 2.57 (dd, *J* = ~ 4, ~ 13 Hz, 1H, H-18a), 2.53 (m, 1H, H-16), 2.40 (dd, *J* = 8.0, 13.5 Hz, 1H, H-6a), 2.33 (d, *J* = ~ 13 Hz, 1H, H-18b), 2.18 (dd, *J* = 9.0, 15.0 Hz, 1H, H-1b), 2.13 (d, *J* = 1.0 Hz, 3H, H-24), 2.07 (m, 1H, H-33a), 2.06 (m, 1H, H-15a), 1.83 (ddd, *J* = 3.2, 10.0, 13.6 Hz, 1H, H-6b), 1.60 (m, 1H, H-32a), 1.57 (m, 1H, H-33b), 1.54 (s, 3H, H-45), 1.48 (s, 3H, H-46), 1.45 (m, 3H, H-25), 1.43 (m, 1H, H-32b), 1.34 (m, 3H, H-26), 1.29 (s, 9H, TBS), 1.13 (m, 1H, H-15b), 1.07 (t, *J* = 8.0 Hz, 9H, H-48), 1.05 (s, 9H, TBS), 1.01 (s, 9H, TBS), 0.82 (d, *J* = ~ 6 Hz, 3H, H-22), 0.70 (q, *J* = ~ 8 Hz, 6H, H-47), 0.49 (s, 3H, TBS), 0.43 (s, 3H, TBS), 0.25 (s, 3H, TBS), 0.22 (s, 3H, TBS), 0.13 (s, 3H, TBS), 0.12 ppm (s, 3H, TBS); ^{13}C NMR (150 MHz, C_6D_6): δ = 169.1 (C, C-19), 147.2 (C, C-11), 140.4 (C, C-9), 137.2 (C, C-44), 132.0 (HC, C-42), 129.4 (HC, C-10), 125.9 (HC, C-41), 124.9 (HC, C-43), 114.9 (H_2C, C-23), 83.7 (HC, C-13), 83.0 (C, C-2 or C-3), 81.2 (HC, C-17), 80.1 (HC, C-31), 79.8 (HC, C-14), 79.3 (C, C-2 or C-3), 77.7 (HC, C-34 and C-12), 76.2 (HC, C-20), 73.8 (HC, C-7), 72.4 (HC, C-5), 47.6 (HC, C-8), 38.7 (H_2C, C-6 and C-15), 37.7 (HC, C-16), 37.6 (H_2C, C-18), 32.9 (HC, C-4), 31.2 (H_2C, C-33), 27.8 (H_2C, C-32), 27.0 (($H_3C)_3$, TBS), 26.8 (H_2C, C-1), 26.2 (2 x $(H_3C)_3$, TBS), 25.9 (H_3C, C-45), 19.2 (CSi, TBS),

18.6 (CSi, TBS), 18.3 (CSi, TBS), 18.2 (H_3C, C-46), 17.5 (H_3C, C-25), 16.3 (H_3C, C-24), 16.1 (H_3C, C-22), 14.4 (H_3C, C-26), 7.3 ($(H_3C)_3$, C-48), 5.5 ($(H_2C)_3Si$, C-47), –3.9 (H_3CSi, TBS), –4.1 (2 x H_3CSi, TBS), –4.4 (H_3CSi, TBS), –4.5 (H_3CSi, TBS), –4.8 ppm (H_3CSi, TBS); IR (film): 2953, 2929, 2859, 1740, 1473, 1463, 1428, 1391, 1380, 1361, 1257, 1211, 1141, 1093, 1067, 1043, 836, 778, 746, 702 cm^{-1}; MS (ESI-pos) [M + Na^+] 1079 (100); HRMS (ESI-pos) calcd. for $C_{59}H_{108}O_8Si_4Na$ [M + Na^+] 1079.7014, found 1079.7013.

Compound 36. A Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alkyne **34** (40 mg, 0.0378 mmol, 1.0 equiv), CH_2Cl_2 (3.6 mL) and MeOH (405 μL). The resulting solution was cooled to 0°C before a solution of pyridinium *p*-toluenesulfonate (PPTS, 0.026 M in 9/1 mixture of CH_2Cl_2/MeOH, 291 μL, 0.00756 mmol, 0.20 equiv) was added. The flask was sealed and the mixture stirred at 0°C for 8 h before a second portion of PPTS (0.026 M in 9/1 mixture of CH_2Cl_2/MeOH, 145 μL, 0.00378 mmol, 0.10 equiv) was added. After stirring for additional 12 h, the reaction was quenched with aq. sat. $NaHCO_3$ (3 mL), the mixture was diluted with H_2O (2 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined extracts were washed with aq. sat. $NaHCO_3$ (3 mL) and H_2O (2 x 3 mL), dried over Na_2SO_4, filtered, and evaporated. The resulting yellow oil was purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 10 → 15%) to afford alcohol **36** as a pale yellow oil (31 mg, 87%). $[\alpha]_D^{20}$ = +16.5° (c = 1.00, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_2Cl_2, 253 K): δ = 6.50 (dd, *J* = 11.2, 15.2 Hz, 1H, H-42), 6.28 (s, 1H, H-10), 5.75 (d, *J* = 11.2 Hz, 1H, H-43), 5.32 (dd, *J* = 8.0, 15.2 Hz, 1H, H-41), 4.95 (s, 1H, H-23a), 4.90 (t, *J* = 8.0 Hz, 1H, H-20), 4.81 (s, 1H, H-23b), 4.06-3.99 (m, 2H, H-31 and H-34), 3.90 (dt, *J* = 2.8, 10.4 Hz, 1H, H-7), 3.87 (d, *J* = 2.4 Hz, 1H, H-12), 3.82 (ddd, *J* = 1.6, 8.4, 10.0 Hz, 1H, H-17), 3.59-3.51 (m, 2H, H-14 and H-13), 3.28 (t, *J* = 9.2 Hz, 1H, H-5), 2.49 (dd, *J* = 1.6, 15.6 Hz, 1H, H-18a), 2.43 (dq, *J* = 2.4, 7.2 Hz, 1H, H-8), 2.36 (d, *J* > 16 Hz, 1H, H-1a), 2.31 (dd, *J* = 10.0, 15.6 Hz, 1H, H-18b), 2.30-2.25 (m, 1H, H-4), 2.24 (ddd, *J* = 2.4, 8.8, ~ 16 Hz, 1H, H-1b), 2.05-1.96 (m, 2H, H-15a; H-33a), 1.96-1.88 (m, 1H, H-32a), 1.89-1.82 (m, 1H, H-16), 1.75 (s, 6H, H-45 and H-46), 1.72 (s, 3H, H-24), 1.67 (dd, *J* = 10.4, 13.6 Hz, 1H, H-6a), 1.61-1.52 (m, 1H, H-32b), 1.47-1.37 (m, 1H, H-33b), 1.30-1.22 (m, 1H, H-6b), 1.17-1.13 (m, 1H, H-15b), 1.04 (d, *J* = 6.8 Hz, 3H, H-25), 1.00 (d, *J* = 6.4 Hz, 3H, H-26), 0.99 (d, *J* = 6.4 Hz, 3H, H-22), 0.89 (s, 9H, TBS), 0.86 (s, 9H, TBS), 0.81 (s, 9H, TBS), 0.08 (s, 3H, TBS), 0.05 (s, 3H, TBS), 0.04 (s, 3H, TBS), 0.03 (s, 3H, TBS), –0.02 (s, 3H, TBS),–0.06 ppm (s, 3H, TBS); ^{13}C NMR (125 MHz, CD_2Cl_2, 253 K): δ = 170.8 (C, C-19), 145.9 (C, C-11), 140.4 (C, C-9), 137.9 (C, C-44), 131.1 (HC, C-42), 128.5 (HC, C-10), 125.0 (HC, C-41), 124.0 (HC, C-43), 114.7 (H_2C, C-23), 82.0 (HC, C-13), 81.5 (C, C-3), 81.2 (C, C-2), 80.3 (HC, C-17), 79.4 (HC, C-31), 79.1 (HC, C-14), 77.9 (HC, C-20), 77.6 (HC, C-12), 77.5 (HC, C-34), 73.0 (HC, C-7), 71.5 (HC, C-5), 46.4 (HC, C-8), 40.4 (H_2C, C-6), 40.1 (HC, C-16), 39.6 (H_2C, C-18), 38.5 (H_2C, C-15), 34.8 (HC, C-4), 32.1 (H_2C, C-33), 29.1 (H_2C, C-32), 26.33 ($(H_3C)_3$, TBS), 26.27 (H_2C, C-1), 26.0 (H_3C, C-45), 25.74 ($(H_3C)_3$, TBS), 25.66 ($(H_3C)_3$, TBS), 18.8 (CSi, TBS), 18.4 (CSi, TBS), 18.4 (H_3C, 46), 17.9 (CSi, TBS), 17.6 (H_3C, C-26), 16.1 (H_3C, C-22),

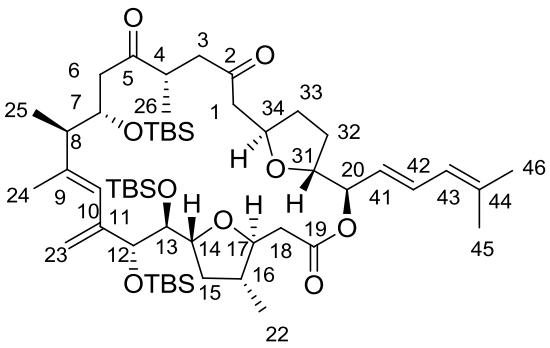
15.6 (H_3C, C-25), 15.4 (H_3C, C-24), –4.1 (H_3CSi, TBS), –4.7 (H_3CSi, TBS), –4.9 (H_3CSi, TBS), –5.0 (H_3CSi, TBS), –5.0 (H_3CSi, TBS), –5.5 ppm (H_3CSi, TBS); IR (film): 2955, 2928, 2856, 2892, 1740, 1470, 1462, 1387, 1361, 1252, 1192, 1145, 1123, 1082, 1073, 1036, 1005, 958, 902, 835, 776 cm^{-1}; MS (ESI-pos) [M + Na^+] 965 (100); HRMS (ESI-pos) calcd. for $C_{53}H_{94}O_8Si_3Na$ [M + Na^+] 965.6149, found 965.6145.

Compound 37. A Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with alcohol **36** (10 mg, 0.0106 mmol, 1.0 equiv) (azeotropically dried from toluene three times) and degassed Et_2O (668 µL). A solution of ($[Cl_2Pt(CH_2{=}CH_2)]_2$) (0.00128 M in Et_2O, 16.5 µL, 0.0212 µmol, 0.002 equiv) was added and the resulting solution stirred at room temperature for 20 min. The mixture was then filtered through a pad of Florisil and the filtrate evaporated to give a colorless oil (9.7 mg, 97%), which was used in the next step without further purification.



The crude enol ether (9.7 mg, 0.0103 mmol, 1.0 equiv) was dissolved in a solution of pyridinium *p*-toluenesulfonate (PPTS, 0.00477 M in wet benzene, 1.9 mL, 0.00925 mmol, 0.90 equiv) and the resulting mixture stirred for 20 min at room temperature. Aq. sat. $NaHCO_3$ (3 mL) and H_2O (3 mL) were added and the aqueous layer extracted with EtOAc (3 x 1 mL). The combined extracts were washed with aq. sat. $NaHCO_3$ (2 mL) and brine (2 mL), dried over Na_2SO_4, filtered, and evaporated to give a colorless oil that was purified by flash chromatography (SiO_2, hexanes/*tert*-butyl methyl ether gradient, 5 → 12%) to give product **37** as a colorless oil (9.7 mg, 98%). As the product is a mixture of three compounds (hydroxyl-ketone and two hemi-ketals), full characterization was delayed until after the next step. IR (film): 3495, 2954, 2927, 2855, 1735, 1462, 1378, 1360, 1250, 1079, 1005, 984, 958, 902, 832, 774, 669 cm^{-1}; MS (ESI-pos) [M + Na^+] 983 (100); MS (ESI-neg) [M – H^-] 959 (100); HRMS (ESI-pos) calcd. for $C_{53}H_{96}O_9Si_3Na$ [M + Na^+] 983.6254, found 983.6260.

Compound 38. A Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with compound **37** (9.0 mg, 0.00936 mmol, 1.0 equiv). CH_2Cl_2 (488 µL) and tetrapropylammonium perruthenate (TPAP) (9.9 mg, 0.0281 mmol, 3.0 equiv) were then introduced and the resulting solution was stirred at room temperature for 2 h. The mixture was filtered through a pad of silica that was carefully rinsed with CH_2Cl_2 (4 mL). The combined filtrates were evaporated and the remaining colorless oil was purified by thin-layer-chromatography (20 x 20 cm, TLC aluminium oxide 60 F_{254} basic, hexanes/CH_2Cl_2, 50%) to provide diketone **38** as a colorless oil (6.3 mg, 70%). $[\alpha]_D^{23} = +9.2°$ (c = 0.55, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 253 K, signals of the major conformer): δ = 6.50 (dd, *J* = 11.3, 14.7 Hz, 1H, H-42), 5.99 (s, 1H, H-10), 5.71 (d, *J* = 11.2



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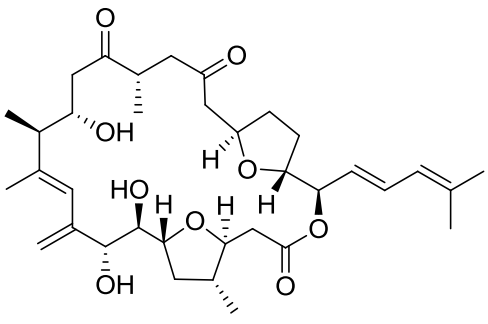

Amphidinolide F (1). A Schlenk flask, equipped with a magnetic stir-bar and a glass stopper, was charged with diketone **38** (15.0 mg, 0.0156 mmol, 1.0 equiv), acetonitrile (2.3 mL), $Et_3N{\cdot}3HF$ (1.84 mL) and triethylamine (1.6 mL). The resulting solution was stirred at 40°C for 3 days before it was allowed to reach ambient temperature. The mixture was diluted with EtOAc (3 mL) and aq. sat. $NaHCO_3$ (6 mL), and the aqueous layer was extracted with EtOAc

(3 x 3 mL). The combined organic phases were washed with aq. sat. $NaHCO_3$ (2 x 3 mL) and brine (3 mL), dried over Na_2SO_4, filtered, and evaporated. The remaining yellow oil was purified by thin-layer-chromatography (20 x 20 cm, TLC silicagel 60 F_{254} basic, hexanes/acetone, 50%) to provide amphidinolide F (5.7 mg, 60%) as a colorless oil. $[\alpha]_D^{23} = -49.0°$ (c = 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 1.4 mg in 180 μL): δ = 6.52 (dd, *J* = 11.0, 15.0 Hz, 1H), 5.99 (s, 1H), 5.76 (d, *J* = 11.0 Hz, 1H), 5.33 (dd, *J* = 8.4, 15.0 Hz, 1H), 5.19 (t, *J* = 8.2 Hz, 1H), 5.16 (d, *J* = 1.4 Hz, 1H), 4.95 (s, 1H), 4.39-4.32 (m, 1H), 4.13-4.05 (m, 3H), 3.95 (t, *J* = 9.0 Hz, 1H), 3.89-3.77 (m, 3H), 3.54 (bs, 2H), 3.18-3.10 (m, 1H), 3.05 (dd, *J* = 8.9, 17.4 Hz, 1H), 2.74 (dd, *J* = 9.3, 15.2 Hz, 1H), 2.72 (dd, *J* = 8.4, 16.0 Hz, 1H), 2.56-2.45 (m, 4H), 2.32 (dd, *J* = 4.2, 17.4 Hz, 1H), 2.27 (dd, *J* = 7.1, 8.9 Hz, 1H), 2.13-2.05 (m, 2H), 1.97-1.89 (m, 1H), 1.85-1.78 (m, 1H), 1.76 (s, 3H), 1.75 (s, 3H), 1.71 (bs, 3H), 1.65-1.55 (m, 1H), 1.53-1.40 (m, 2H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.99 ppm (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 1.4 mg in 180 μL): δ = 213.8, 207.7, 171.3, 144.5, 140.0, 138.3, 132.1, 124.6, 124.2, 124.1, 116.2, 81.5, 80.0, 79.0, 77.9, 76.7 (2C), 75.1, 70.7, 49.5, 48.6, 46.0, 45.7, 42.9, 39.8, 38.8, 36.9, 32.0, 28.5, 26.1, 18.6, 16.3, 15.6, 15.5, 14.2 ppm; IR (film): 2924, 1740, 1365, 1217 cm^{-1}; MS (ESI-pos) [M + Na^+] 639 (100); HRMS (ESI-pos) calcd. for $C_{35}H_{52}O_9Na$ [M + Na^+] 639.3504, found 639.3503.

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(1) (a) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945–948. (b) Rychnovsky, S. D.; Rogers, B. N.; Richardson, T. I. *Acc. Chem. Res.* **1998**, *31*, 9–17.

(2) Best results were obtained when the silyl lithium reagent was prepared and titrated prior to use.

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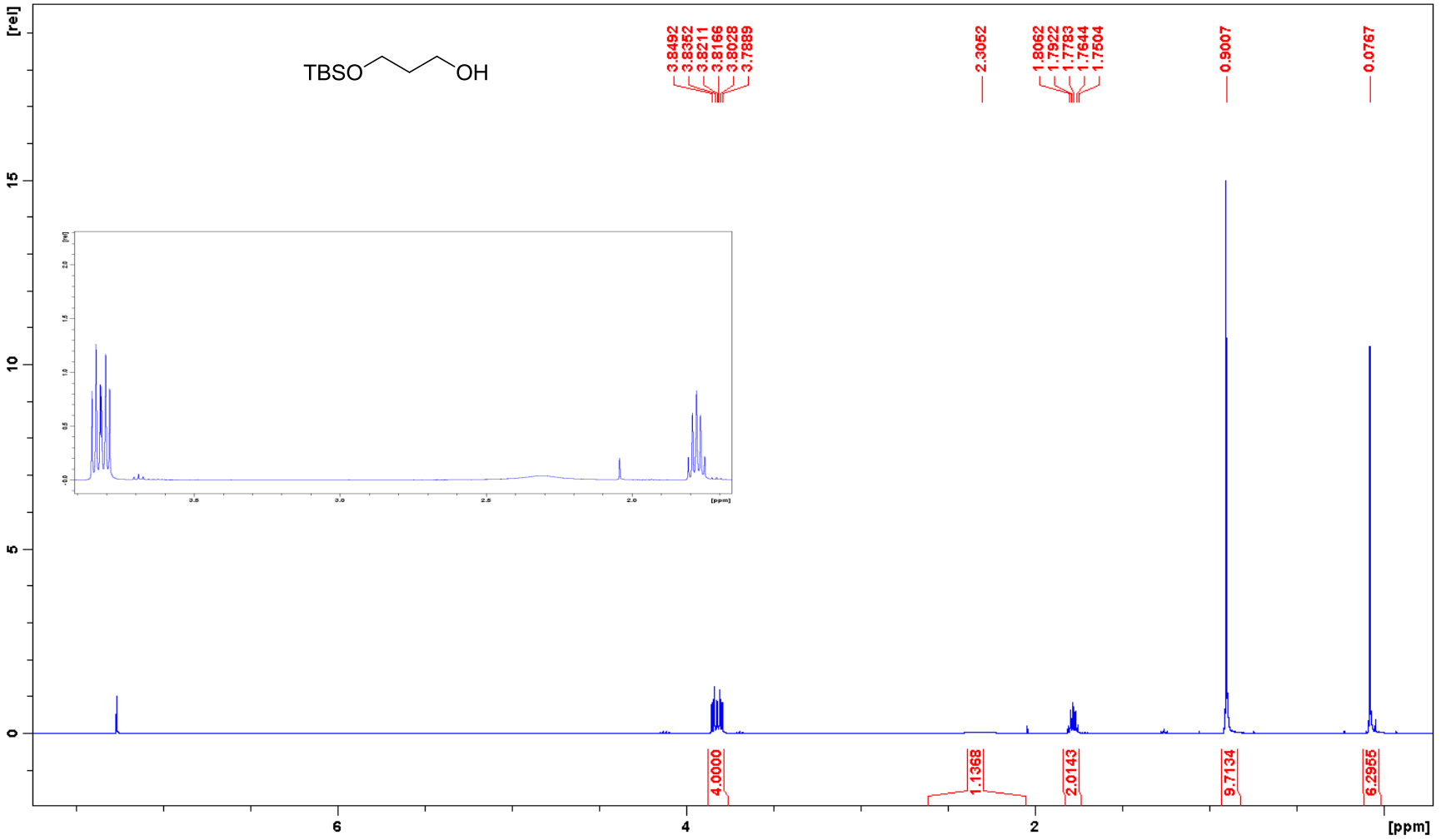
(6) Nishida, Y.; Konno, M.; Fukushima, Y.; Ohrui, H.; Meguro, H. *Agric. Biol. Chem.* **1986**, *50*, 191–193.

(7) Bates, R. H.; Shotwell, J. B.; Roush, W. R. *Org. Lett.* **2008**, *10*, 4343–4346.

(8) Hoye, T. R., Jeffrey, C. S., Shao, F. *Nature Protocols* **2007**, *2*, 2451 – 2458.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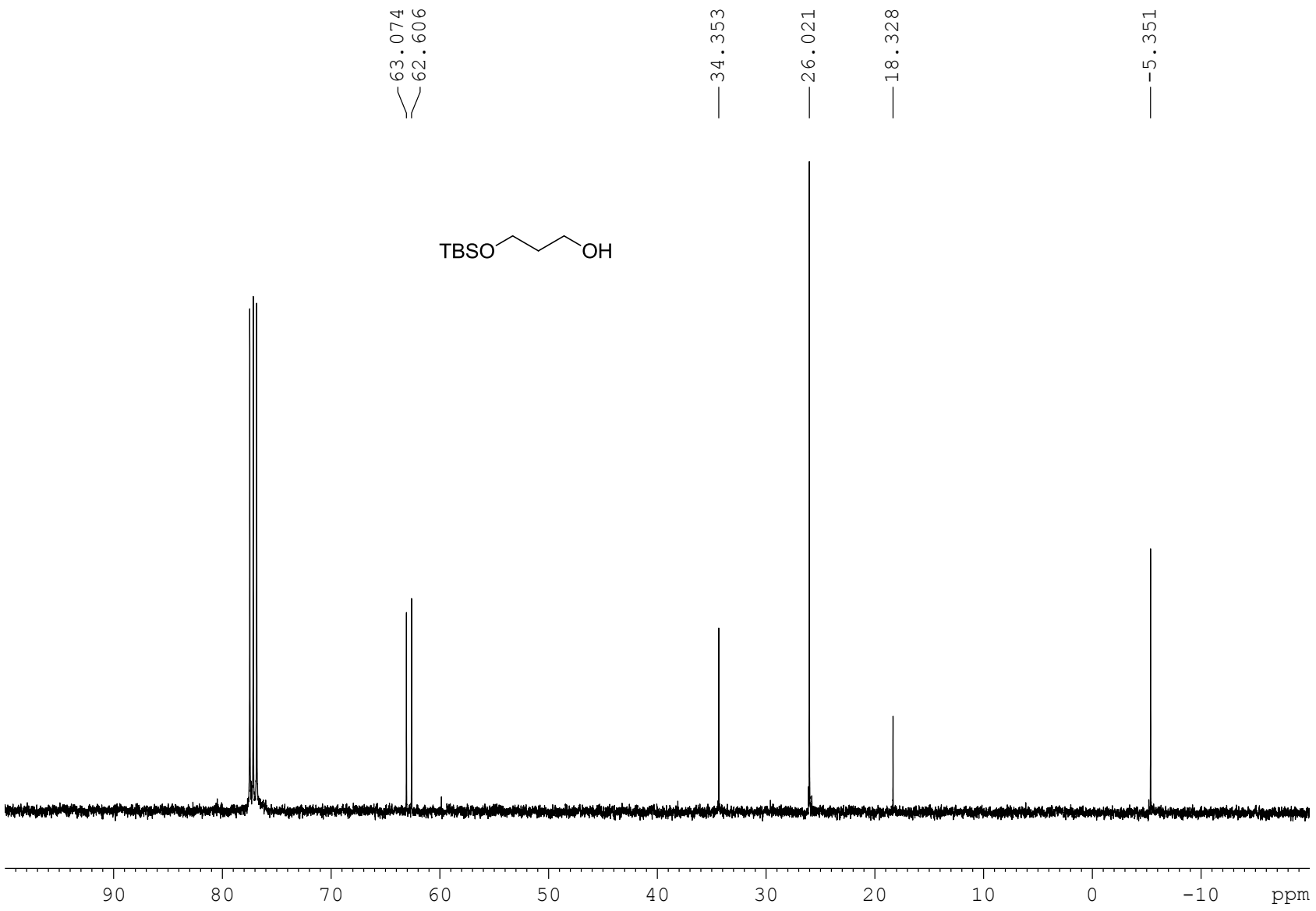
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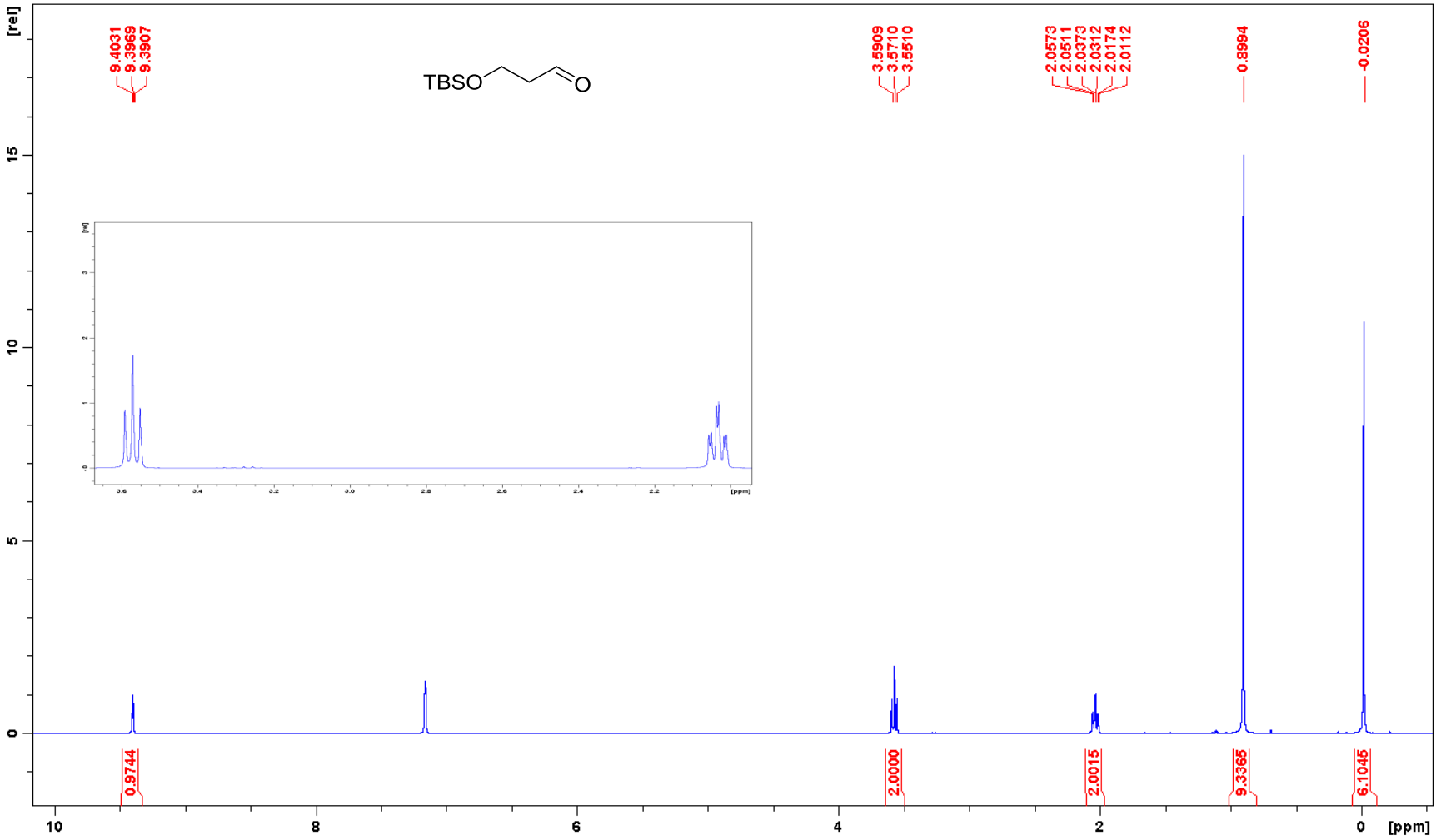
ppm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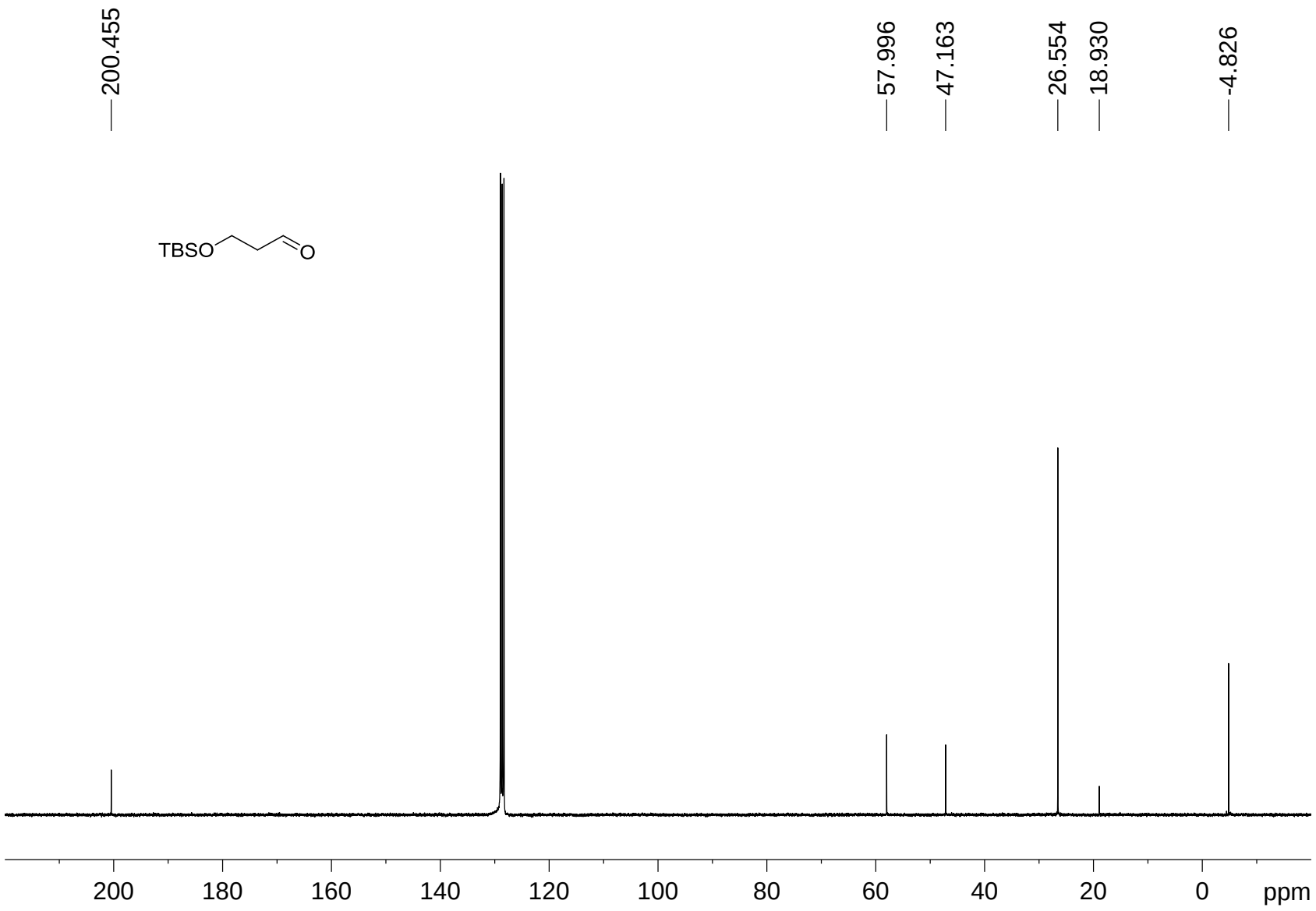
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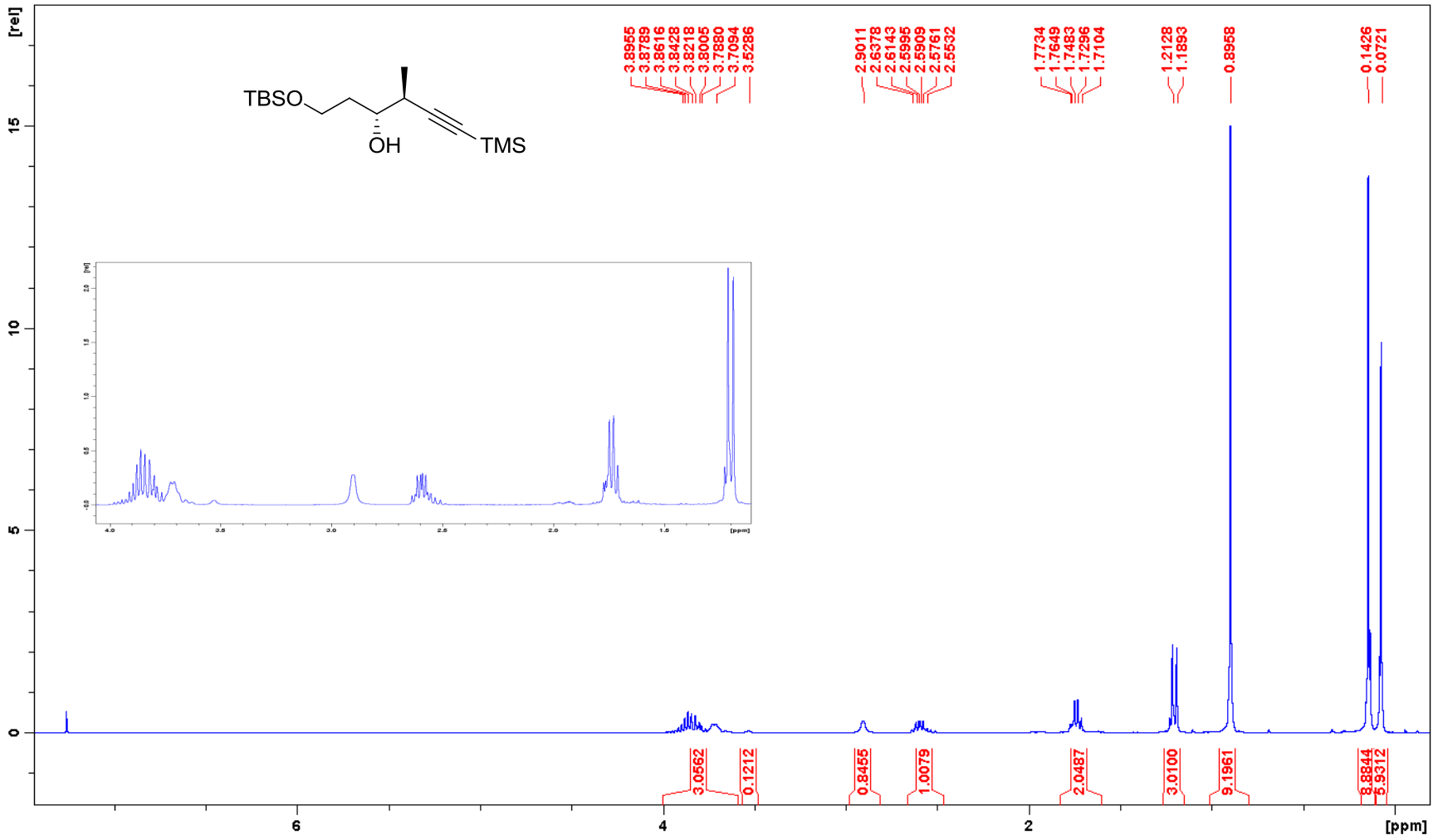
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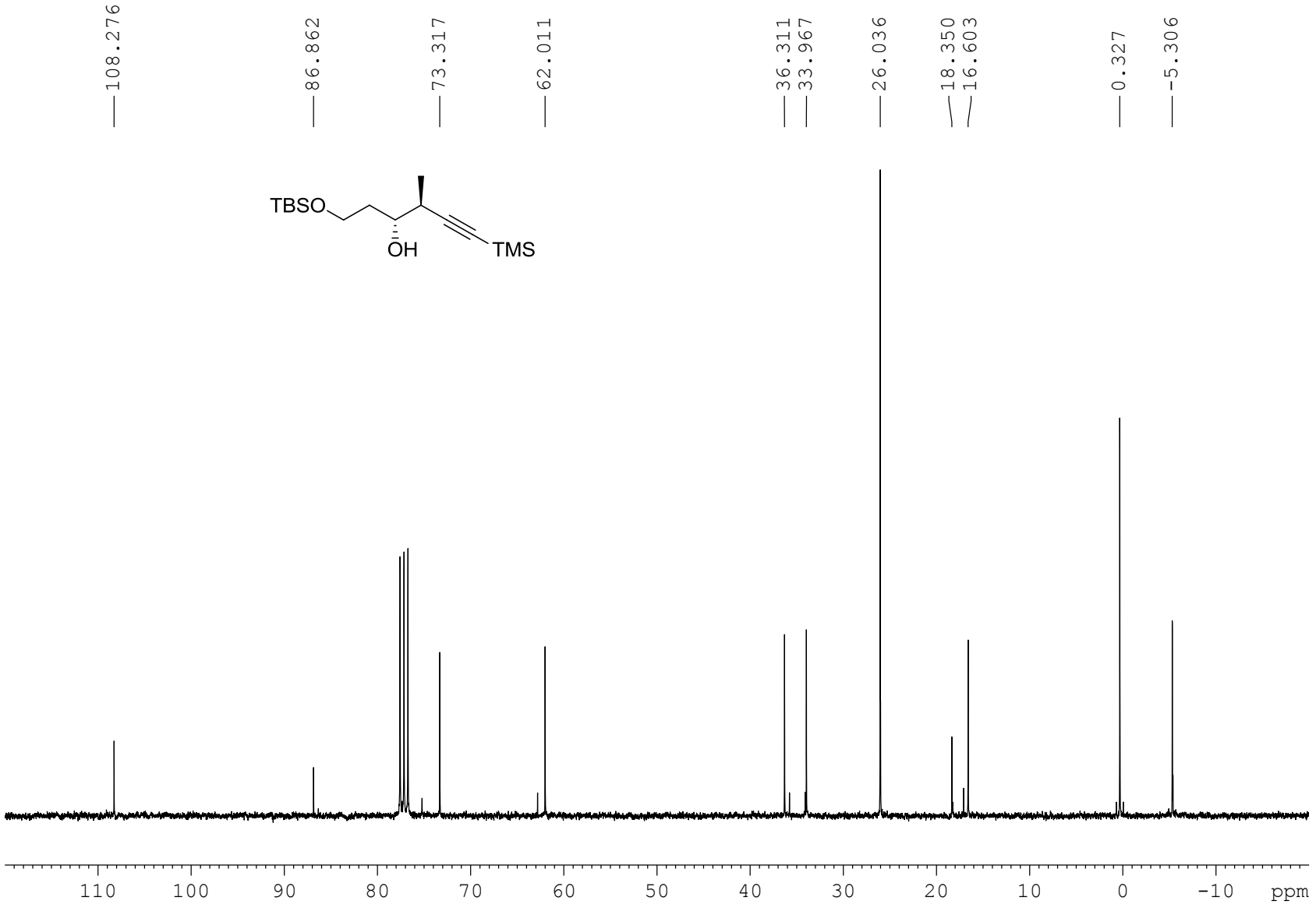
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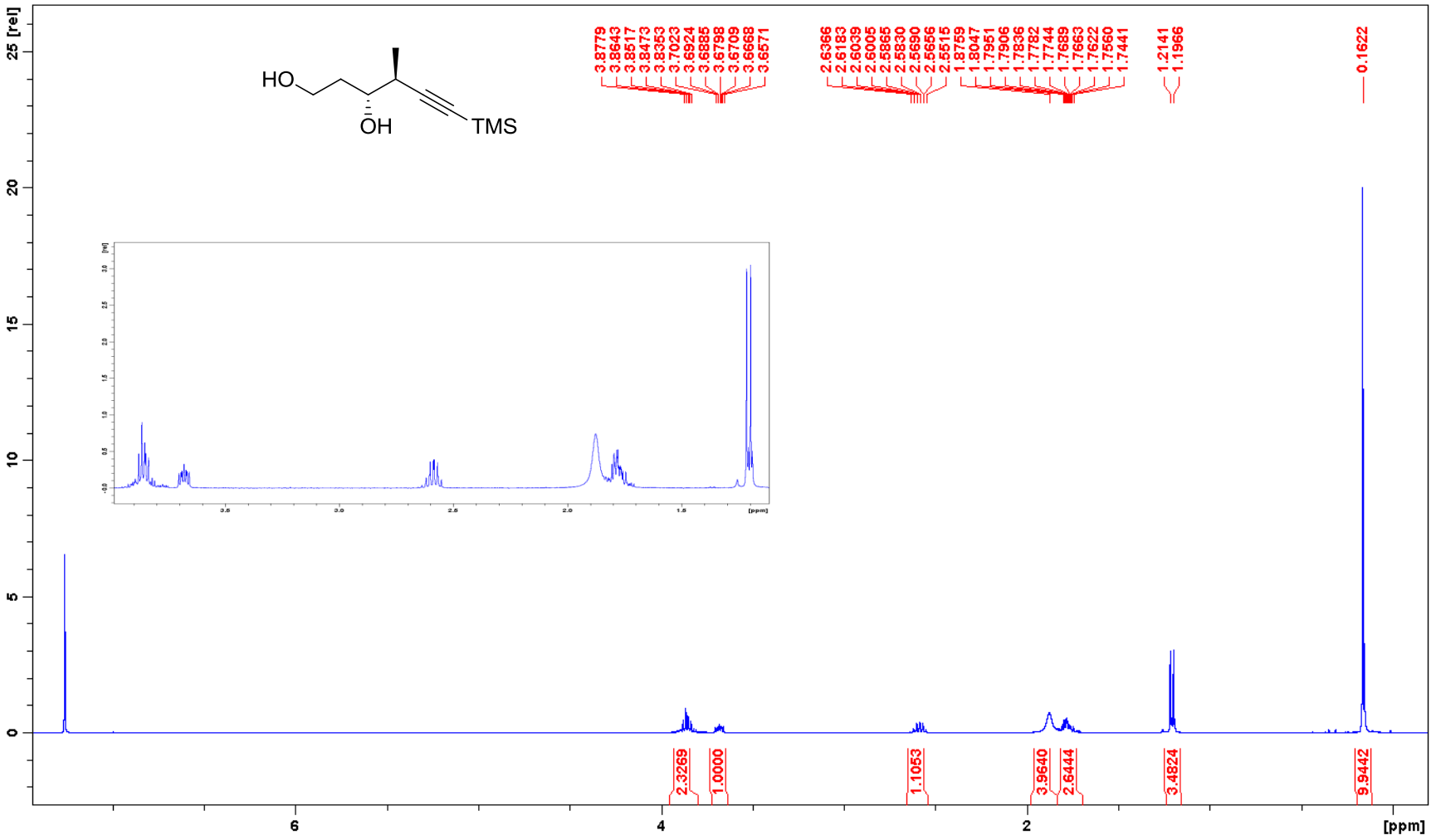
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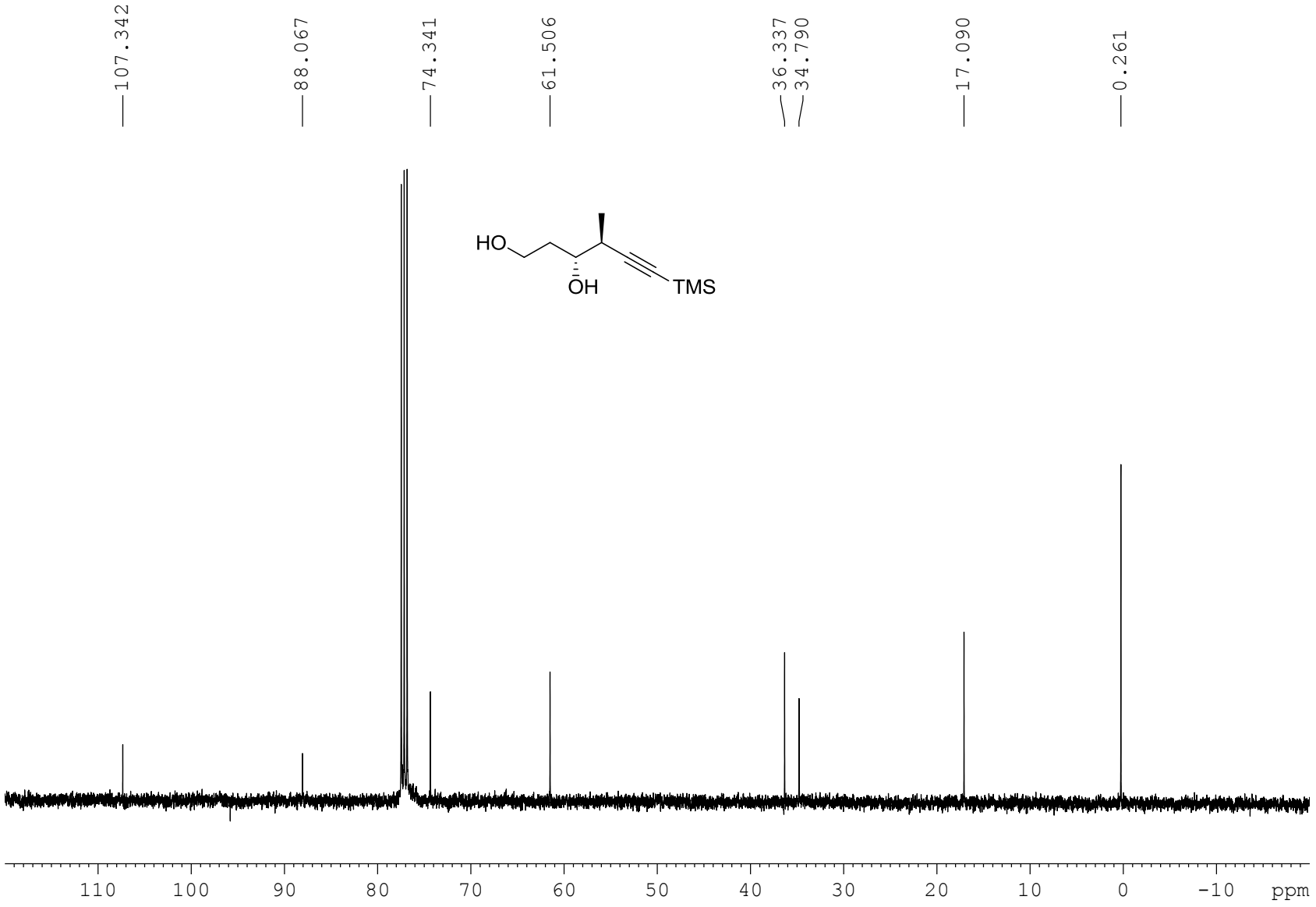
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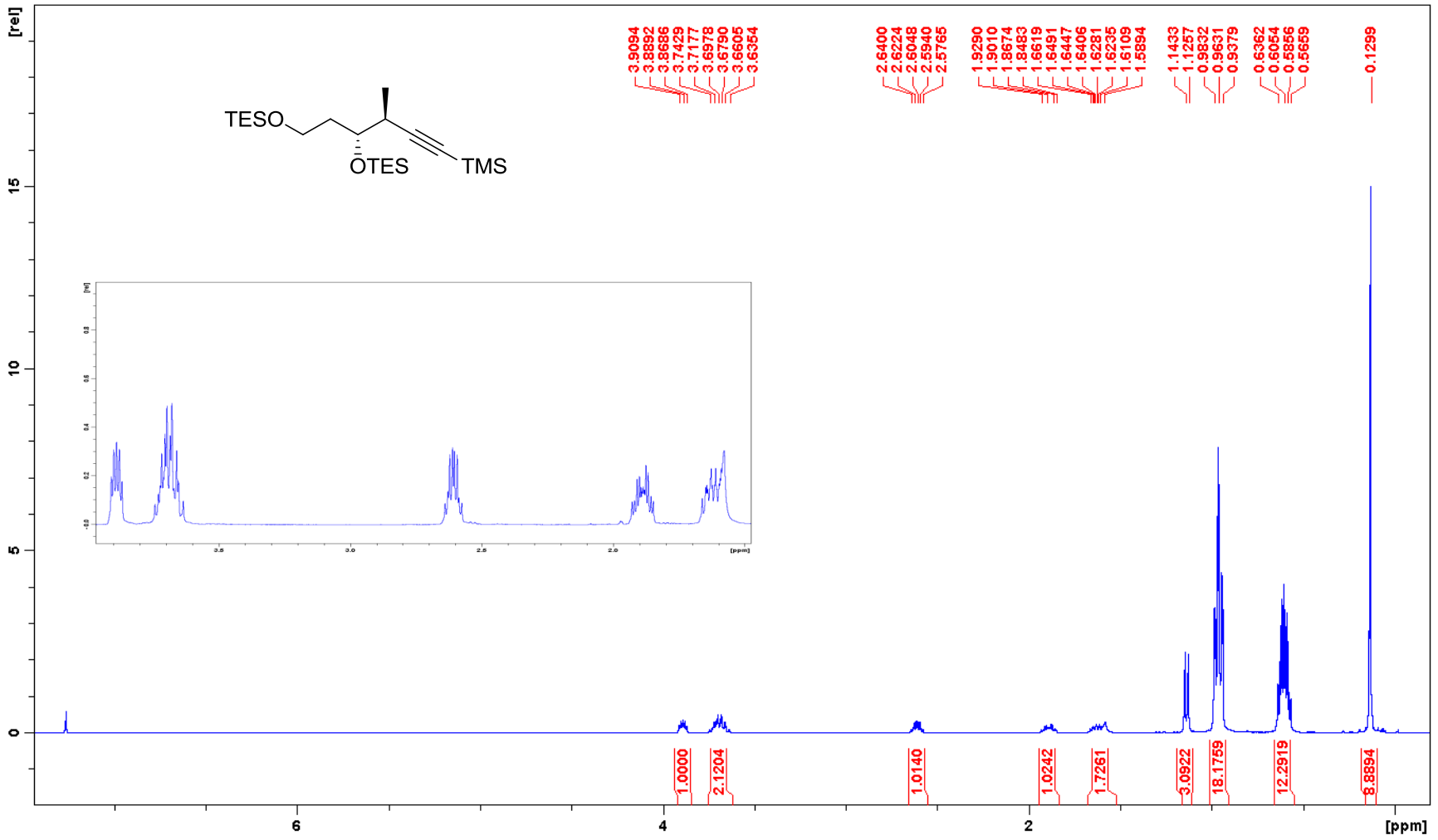
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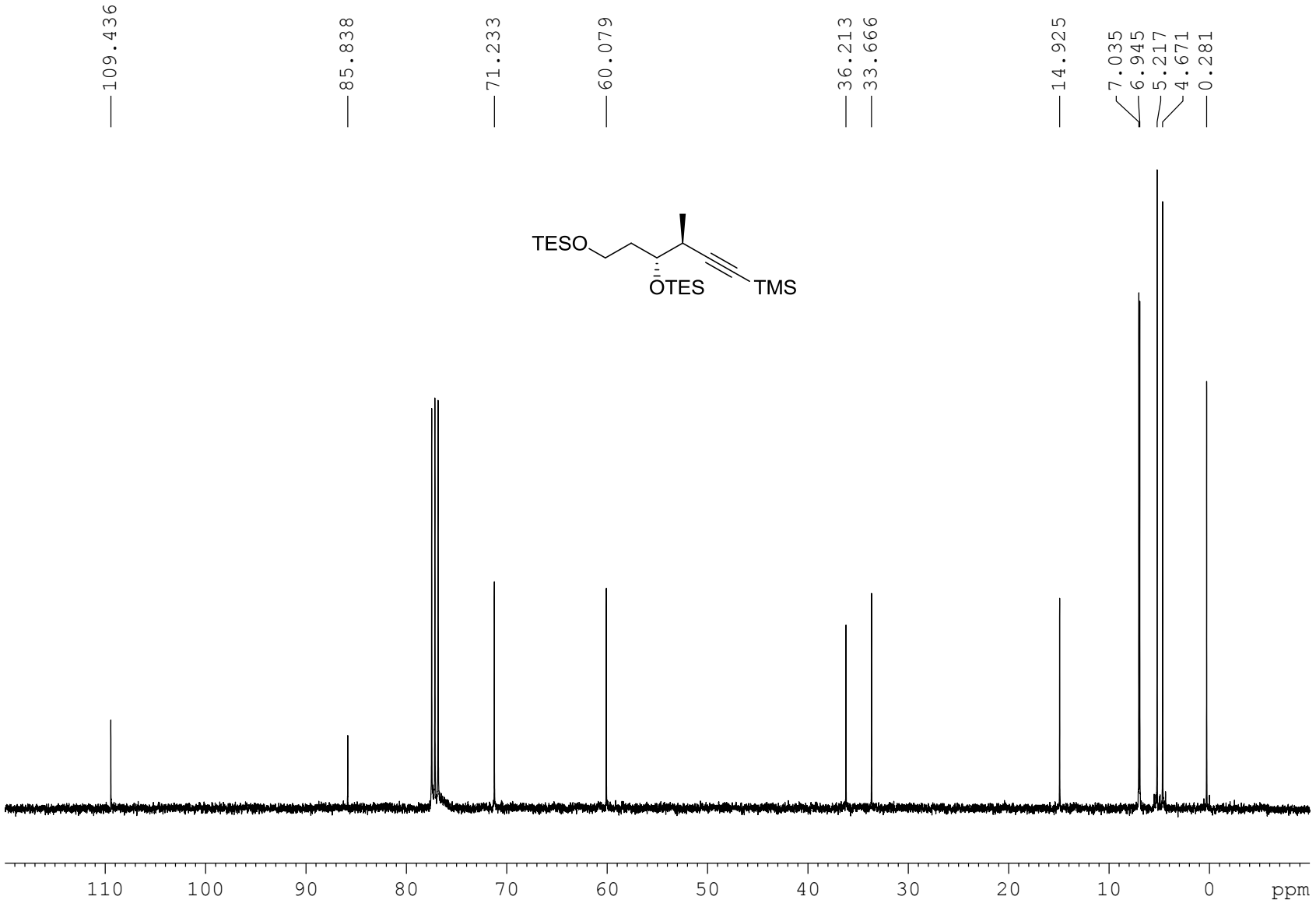
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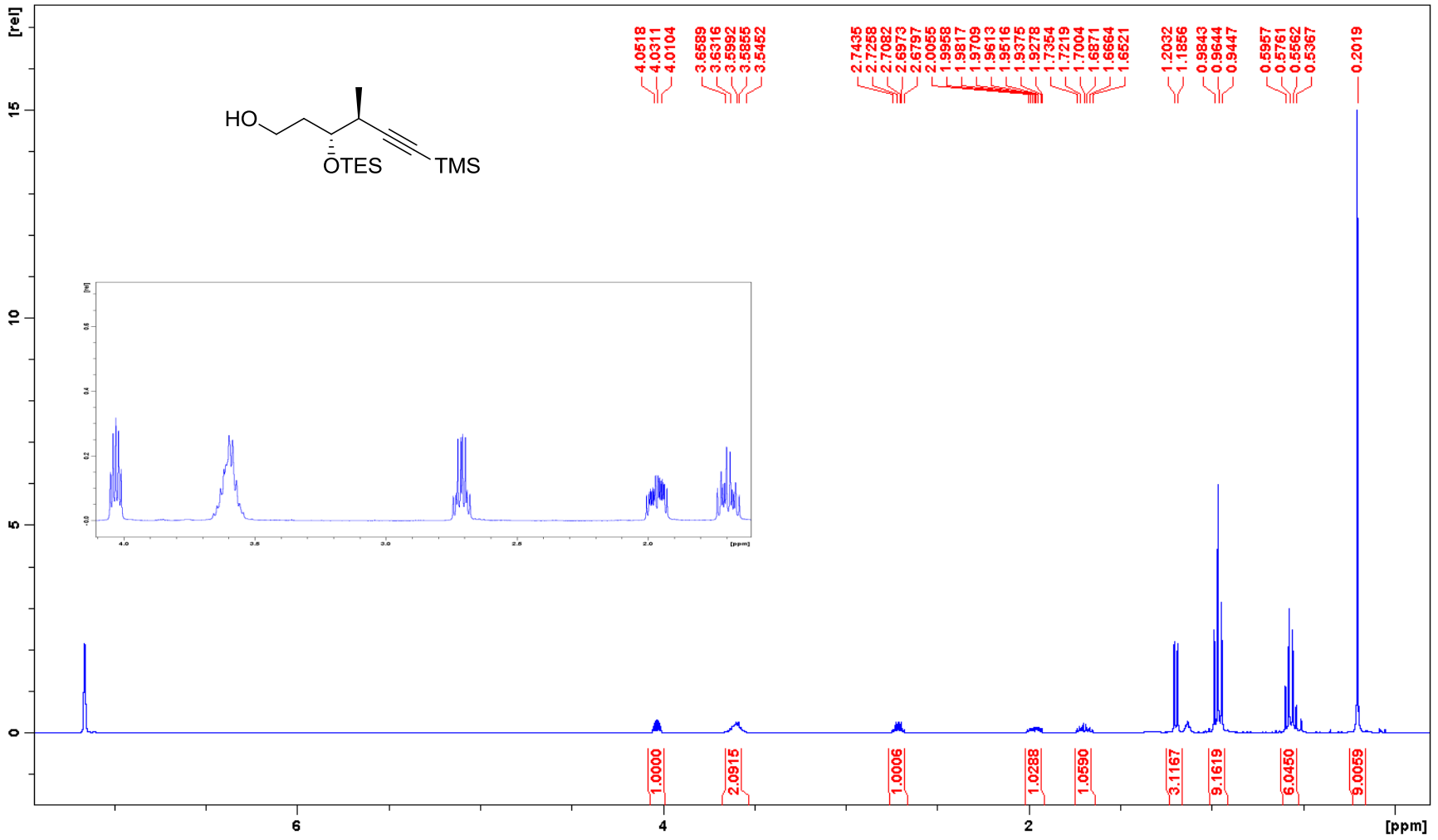
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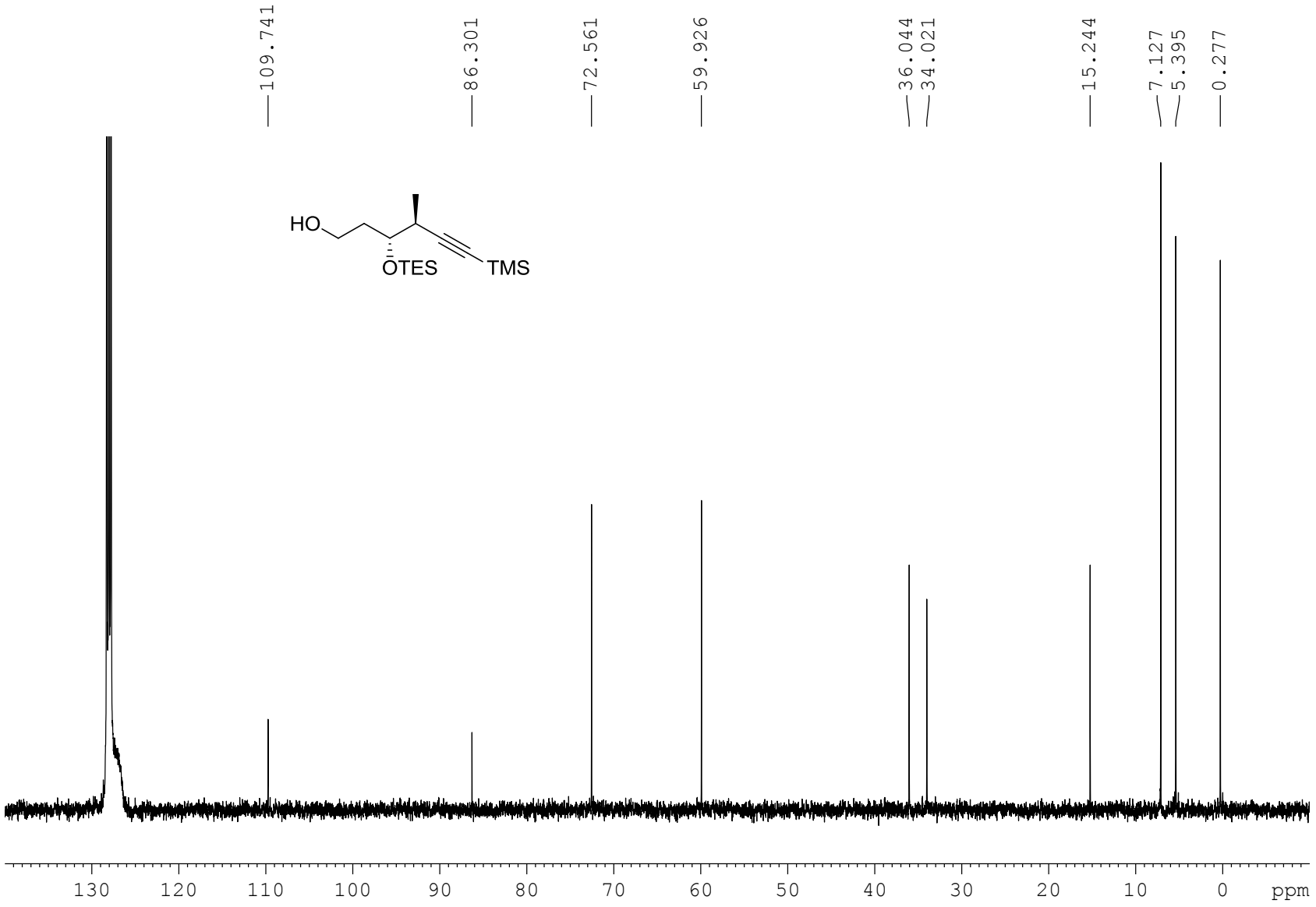
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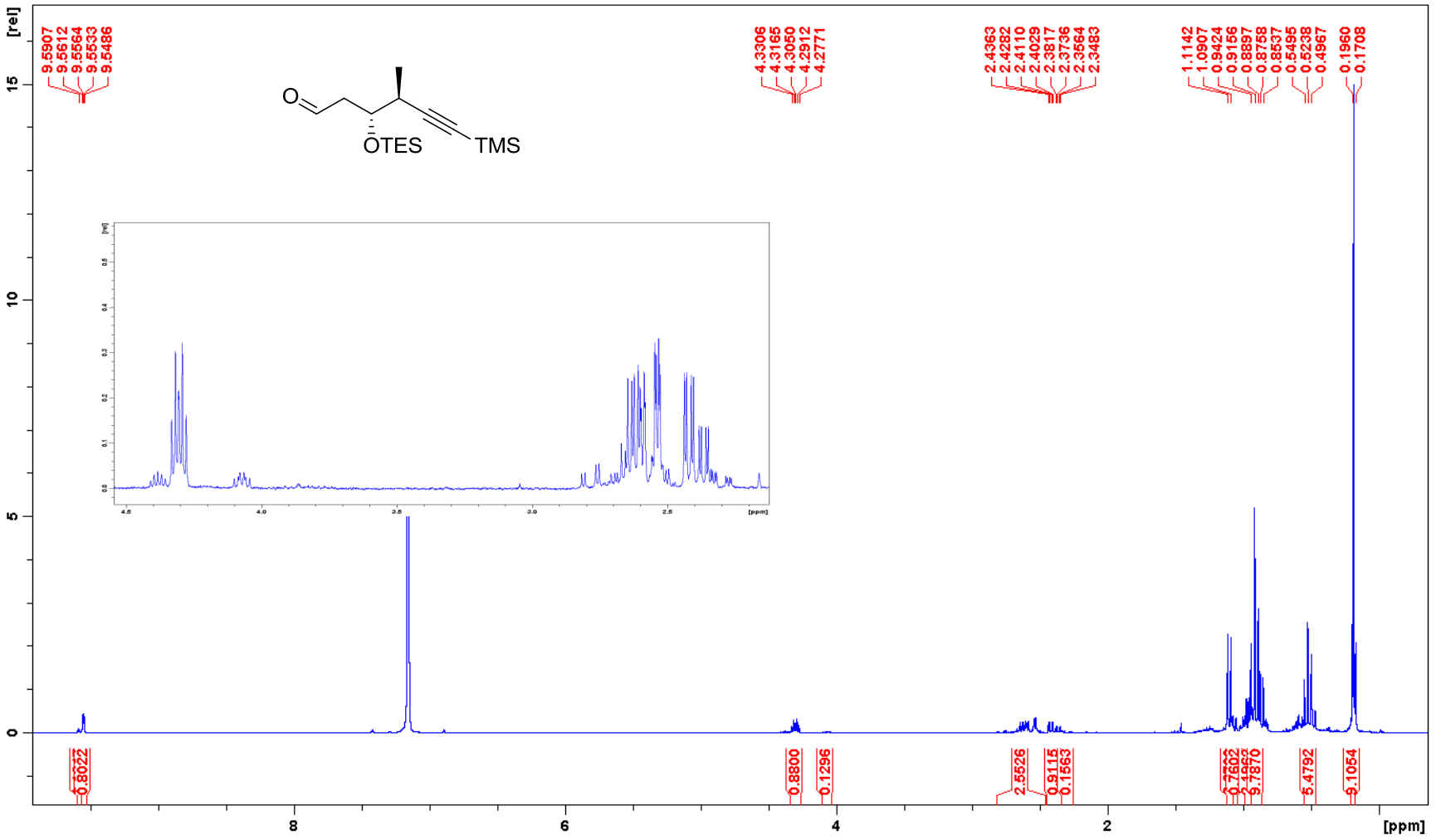
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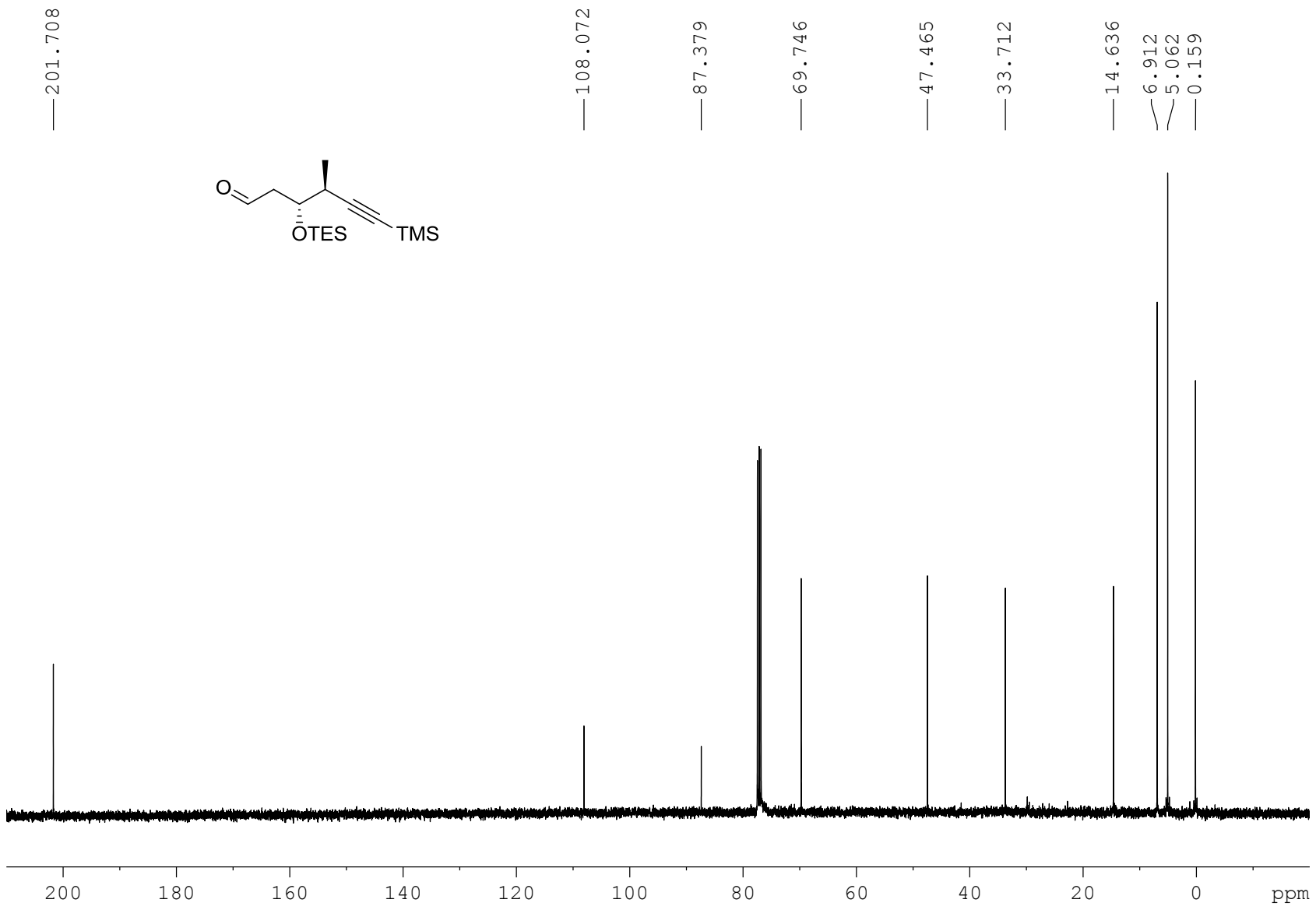
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69.746
47.465
33.712
14.636
6.912
5.062
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O
OTES
TMS
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0
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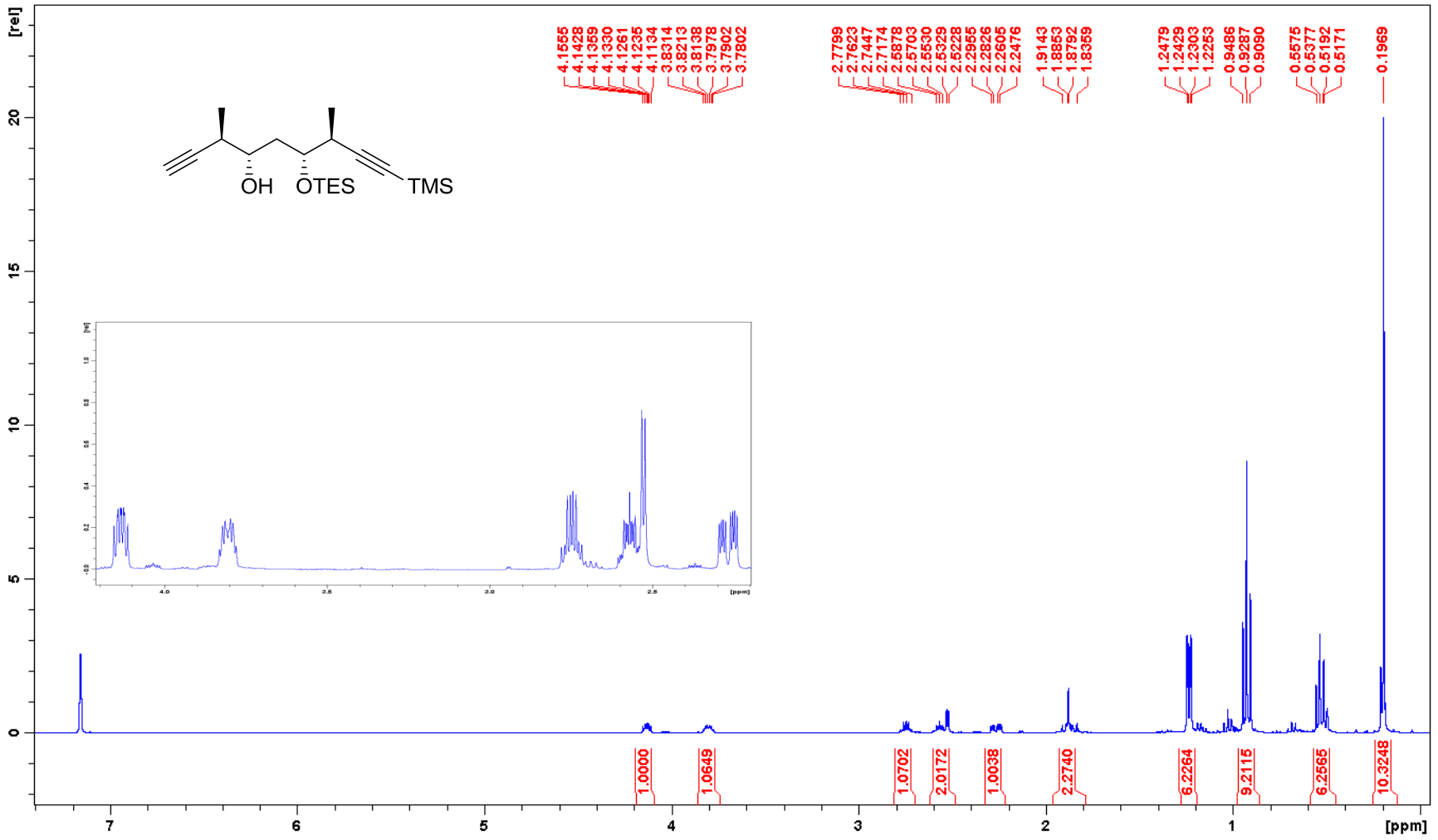
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OTES
TMS
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4.1330
4.1261
4.1235
4.1134
3.8314
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3.8138
3.7978
3.7902
3.7802
2.7799
2.7623
2.7447
2.7174
2.5878
2.5703
2.5530
2.5329
2.5228
2.2955
2.2826
2.2605
2.2476
1.9143
1.8853
1.8792
1.8359
1.2479
1.2429
1.2303
1.2253
0.9486
0.9287
0.9090
0.5575
0.5377
0.5192
0.5171
0.1969
1.0000
1.0649
1.0702
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7
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3
2
1
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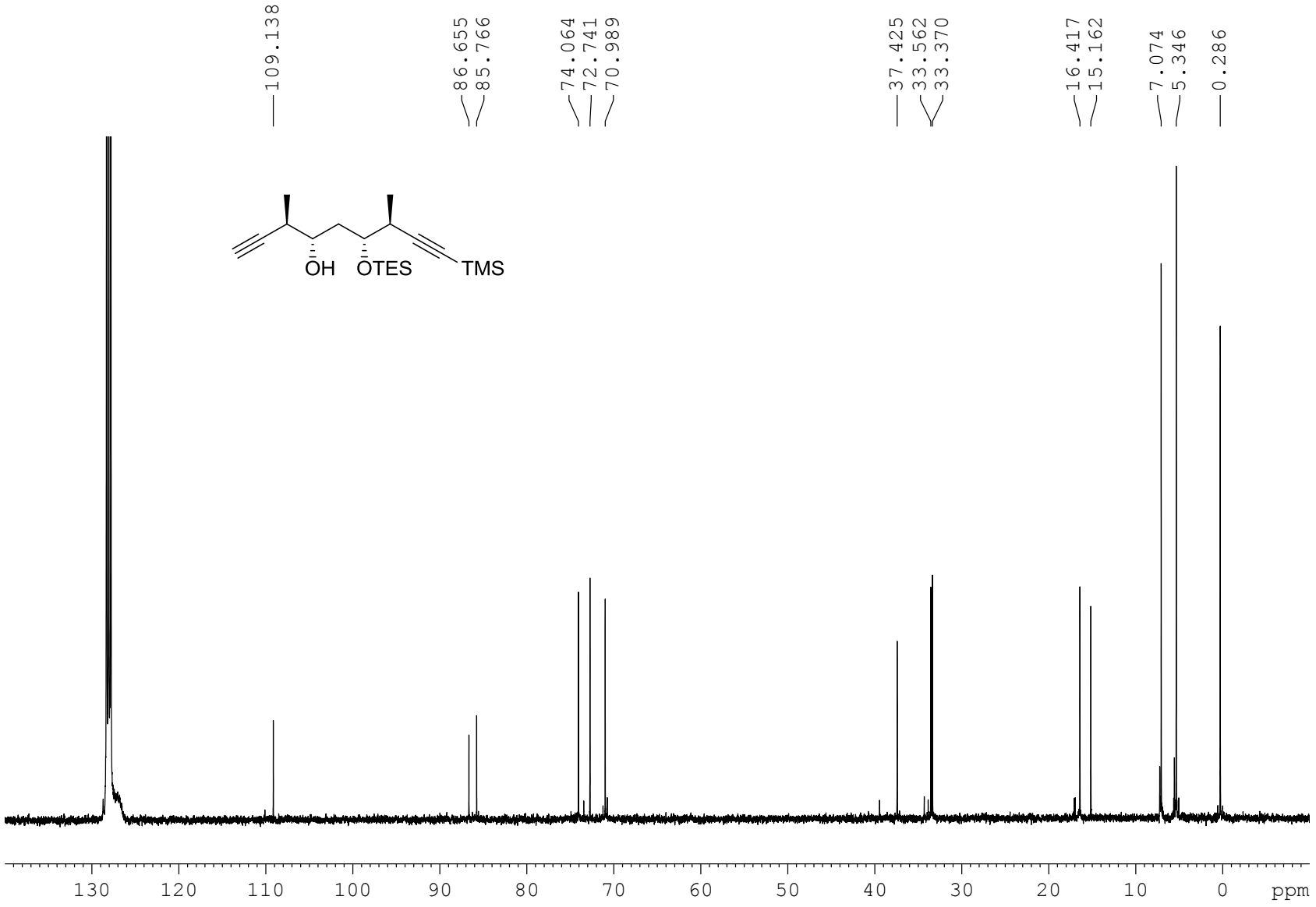
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5.346
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TMS
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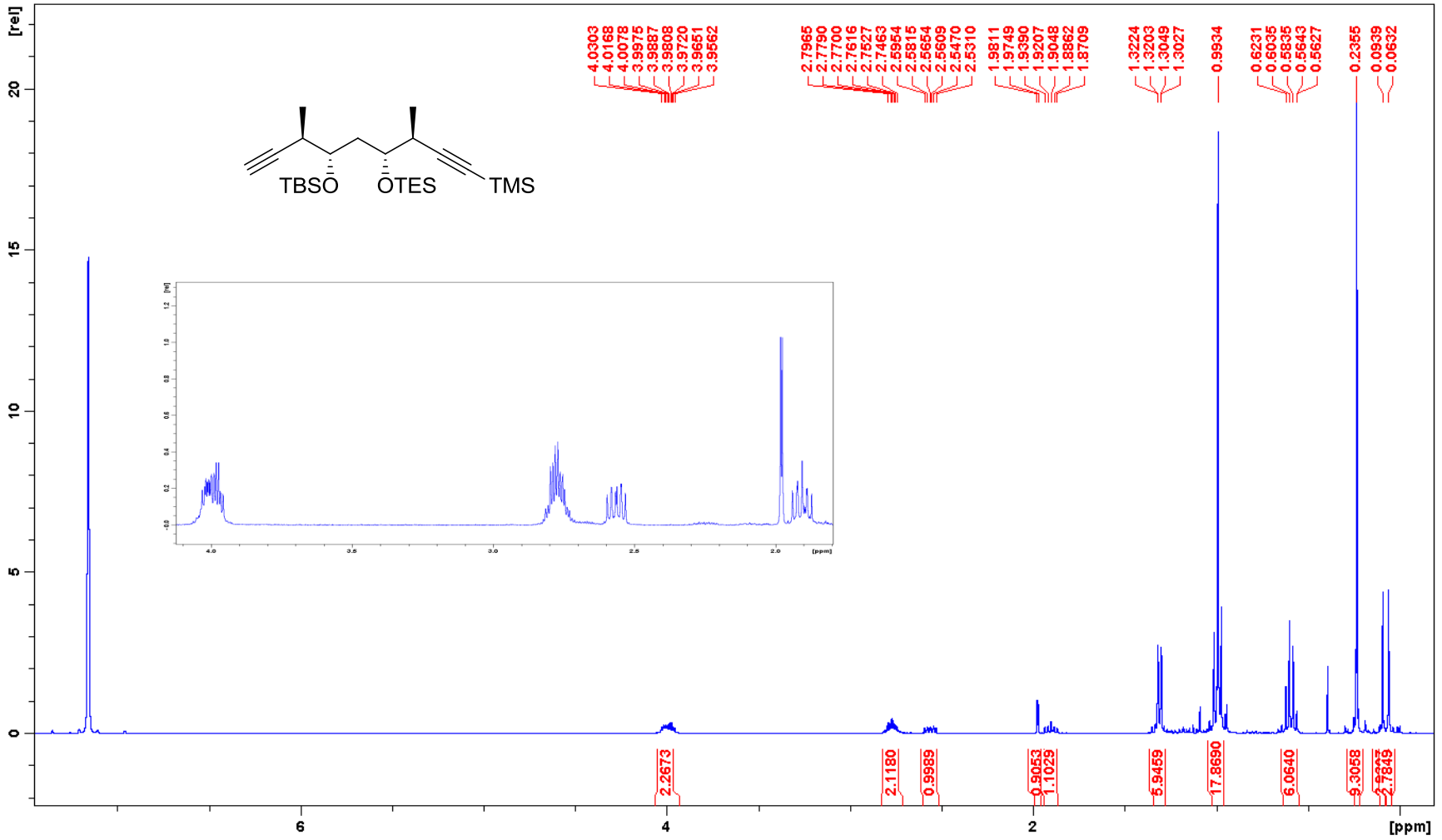
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3.9562
2.7965
2.7790
2.7700
2.7616
2.7527
2.7463
2.5954
2.5815
2.5654
2.5609
2.5470
2.5310
1.9811
1.9749
1.9390
1.9207
1.9048
1.8862
1.8709
1.3224
1.3203
1.3049
1.3027
0.9934
0.6231
0.6035
0.5835
0.5643
0.5627
0.2355
0.0939
0.0632
TBSO
OTES
TMS
2.2673
2.1180
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5.9459
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4
2
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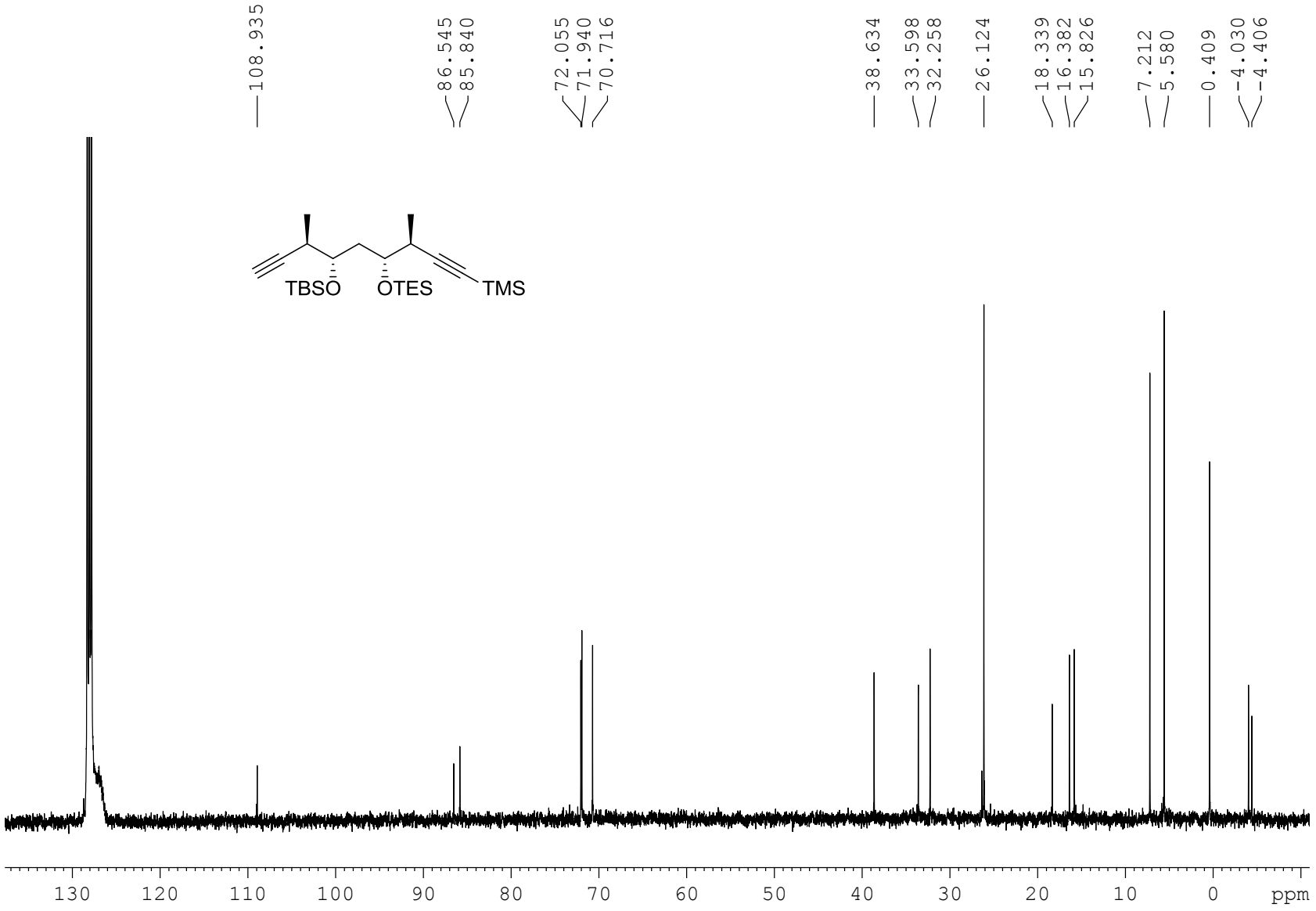
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33.598
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26.124
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15.826
7.212
5.580
0.409
-4.030
-4.406
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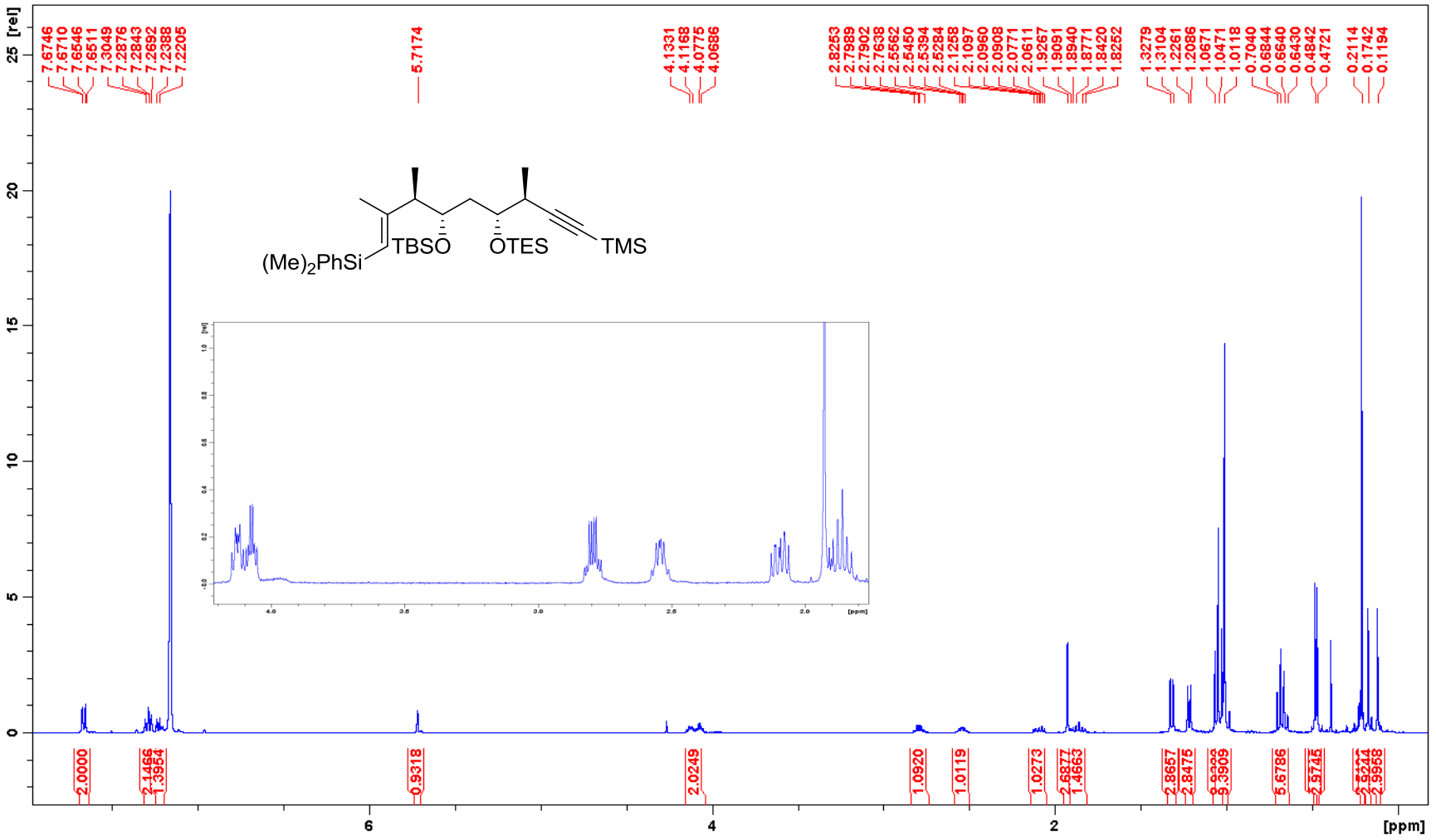
OTES
TMS
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.2388
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4.1331
4.1168
4.0775
4.0686
2.8253
2.7989
2.7902
2.7638
2.5562
2.5450
2.5394
2.5284
2.1258
2.1097
2.0960
2.0908
2.0771
2.0611
1.9267
1.9091
1.8940
1.8771
1.8420
1.8252
1.3279
1.3104
1.2261
1.2086
1.0671
1.0471
1.0118
0.7040
0.6844
0.6640
0.6430
0.4842
0.4721
0.2114
0.1742
0.1194
(Me)2PhSi
TBSO
OTES
TMS
2.0000
2.1466
1.3954
0.9318
2.0249
1.0920
1.0119
1.0273
2.6877
1.4663
2.8657
2.8475
3.3909
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2.9244
2.9958
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15
10
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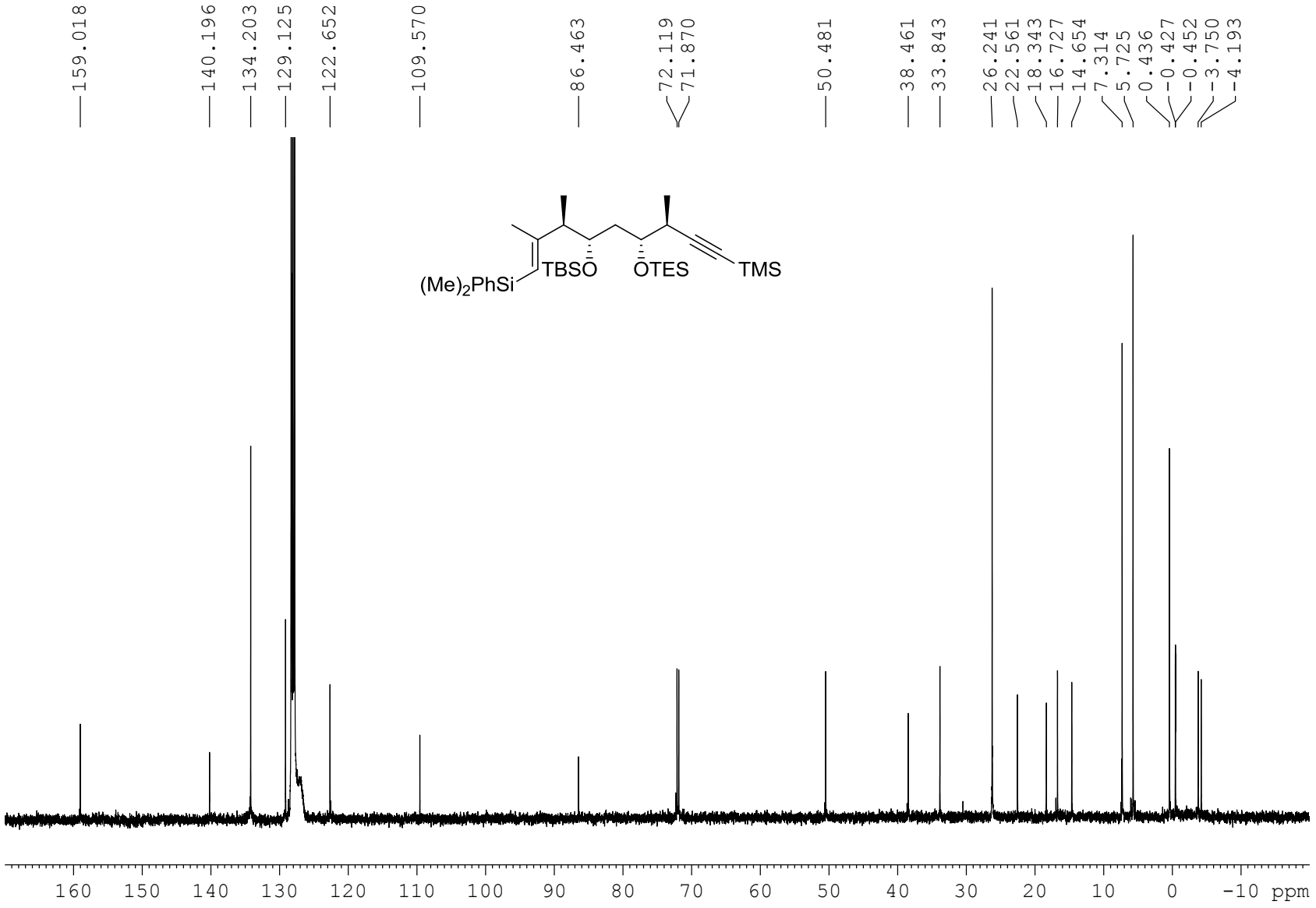
4
2
[ppm]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134.203
129.125
122.652
109.570
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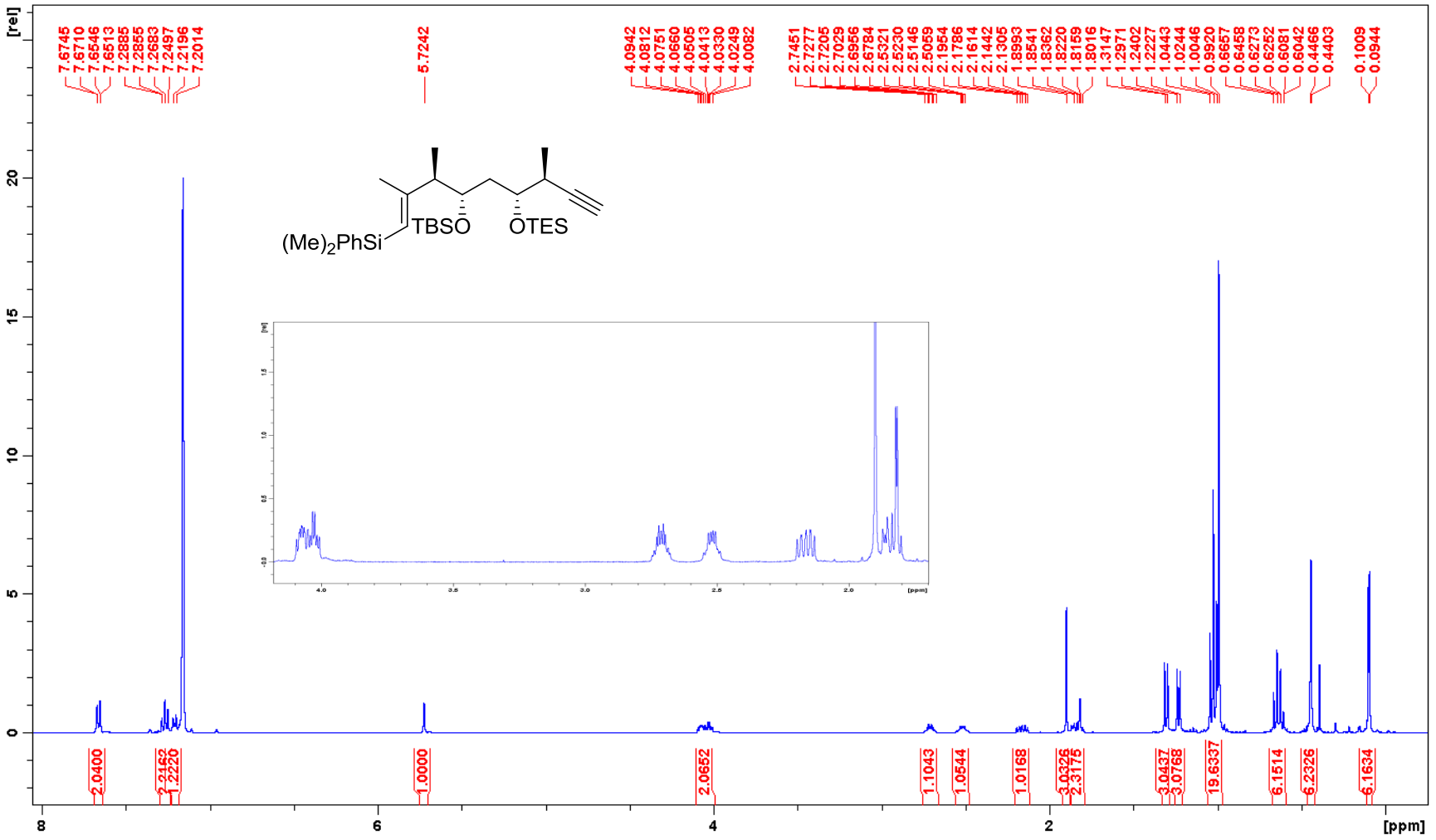
72.119
71.870
50.481
38.461
33.843
26.241
22.561
18.343
16.727
14.654
7.314
5.725
0.436
-0.427
-0.452
-3.750
-4.193
(Me)2PhSi
TBSO
OTES
TMS
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm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7.2855
7.2683
7.2497
7.2196
7.2014
5.7242
4.0942
4.0812
4.0751
4.0660
4.0505
4.0413
4.0330
4.0249
4.0082
2.7451
2.7277
2.7205
2.7029
2.6956
2.6784
2.5321
2.5230
2.5146
2.5059
2.1954
2.1786
2.1614
2.1442
2.1305
1.8993
1.8541
1.8362
1.8220
1.8159
1.8016
1.3147
1.2971
1.2402
1.2227
1.0443
1.0244
1.0046
0.9920
0.6857
0.6458
0.6273
0.6252
0.6081
0.6042
0.4466
0.4403
0.1009
0.0944
(Me)2PhSi
TBSO
OTES
2.0400
2.2162
1.2220
1.0000
2.0652
1.1043
1.0544
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2.3175
3.0437
3.0768
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6.1514
6.2326
6.1634
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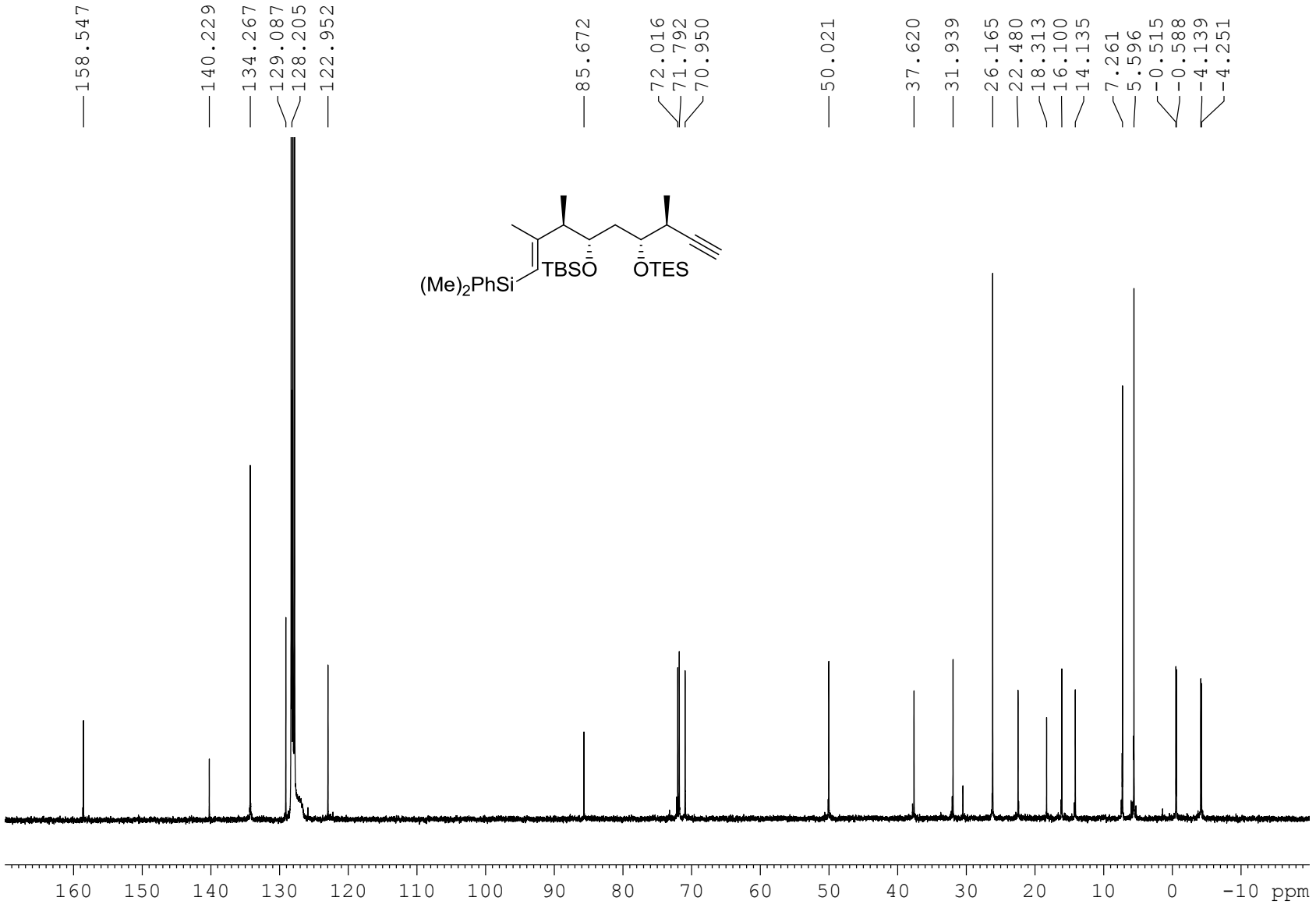
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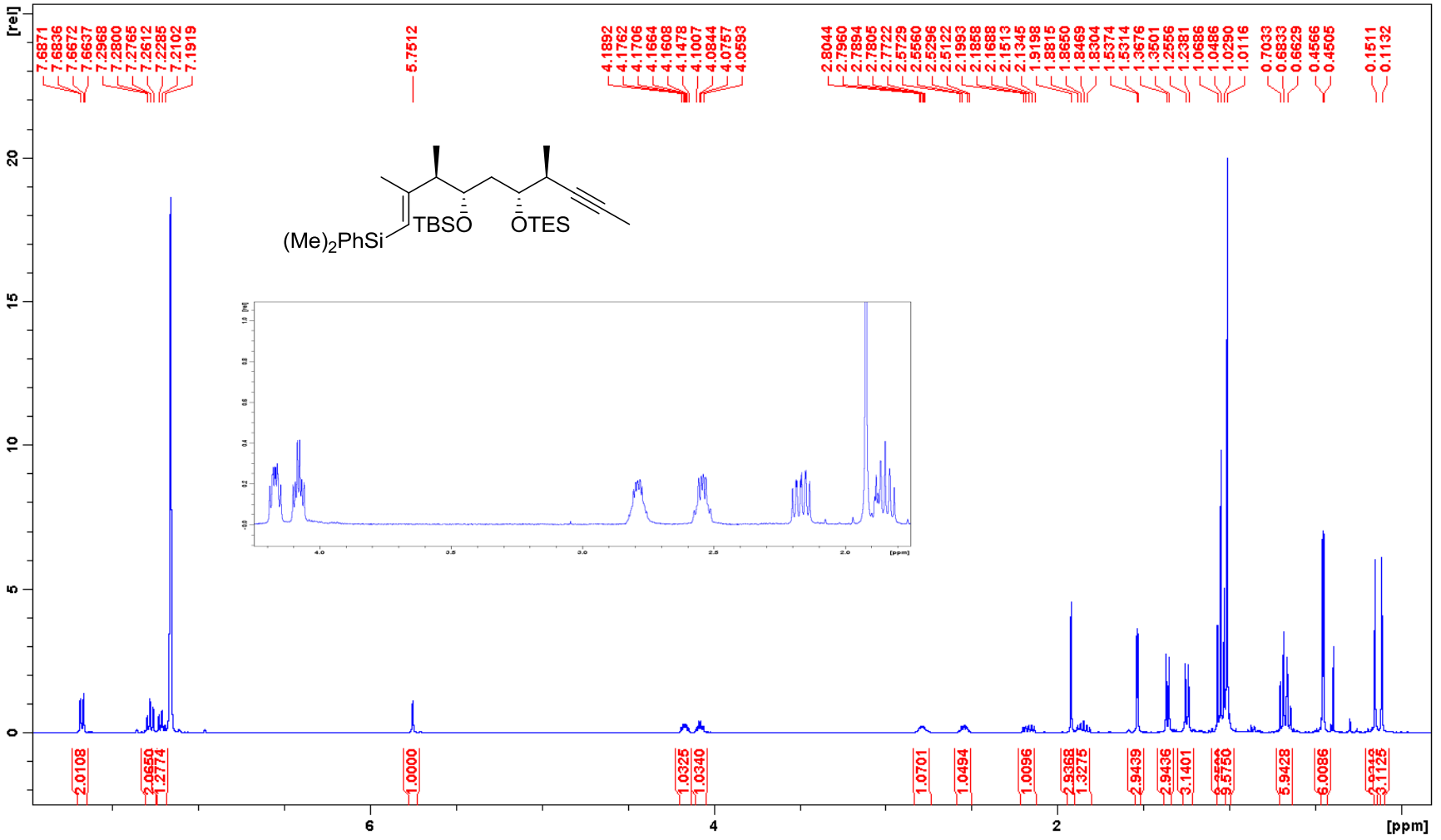
128.205
122.952
85.672
72.016
71.792
70.950
50.021
37.620
31.939
26.165
22.480
18.313
16.100
14.135
7.261
5.596
-0.515
-0.588
-4.139
-4.251
TBSO
OTES
(Me)2PhSi
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10 ppm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7.2102
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4.1892
4.1762
4.1706
4.1664
4.1608
4.1478
4.1007
4.0844
4.0757
4.0693
2.8044
2.7960
2.7894
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2.7722
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2.1993
2.1858
2.1688
2.1513
2.1345
1.9198
1.8815
1.8650
1.8469
1.8304
1.5374
1.5314
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1.3501
1.2556
1.2381
1.0686
1.0486
1.0290
1.0116
0.7033
0.6833
0.6629
0.4566
0.4505
0.1511
0.1132
TBSO
OTES
(Me)2PhSi
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2.0650
1.2774
1.0000
1.0325
1.0340
1.0701
1.0494
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2.9436
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5.9428
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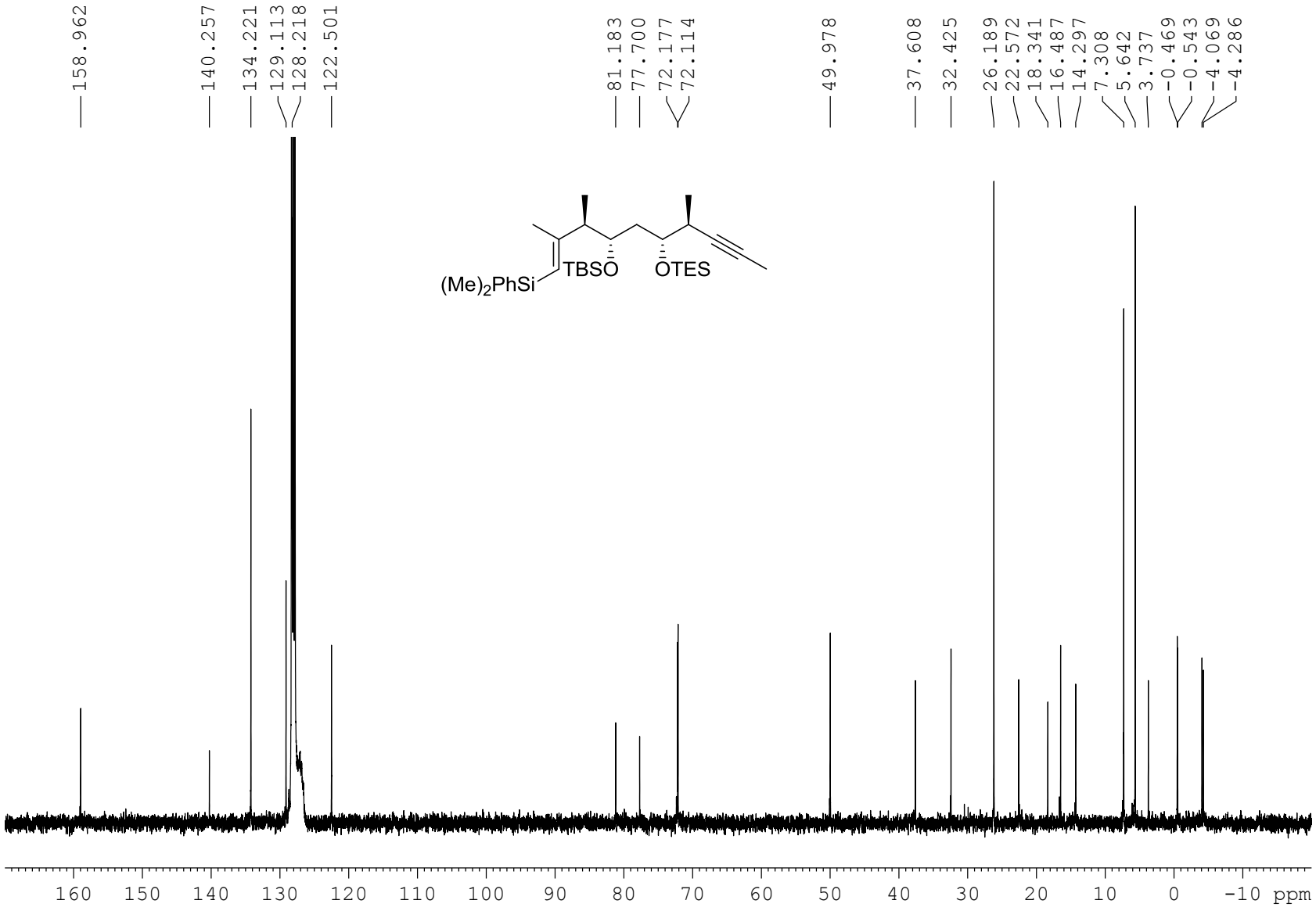
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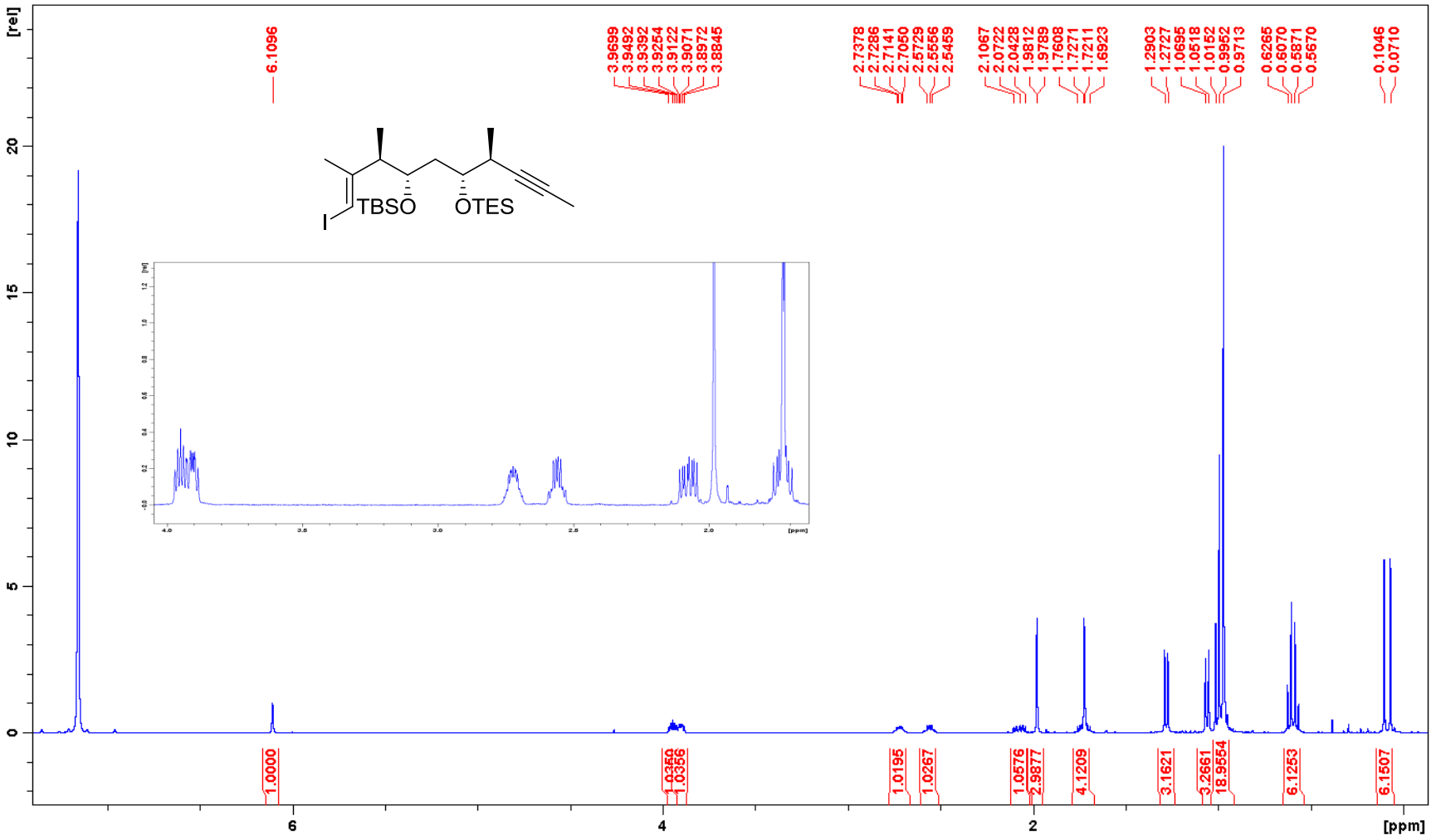
37.608
32.425
26.189
22.572
18.341
16.487
14.297
7.308
5.642
3.737
-0.469
-0.543
-4.069
-4.286
TBSO
OTES
(Me)2PhSi
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm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2.5459
2.1067
2.0722
2.0428
1.9812
1.9789
1.7608
1.7271
1.7211
1.6923
1.2903
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1.0695
1.0518
1.0152
0.9952
0.9713
0.6265
0.6070
0.5871
0.5670
0.1046
0.0710
TBSO
OTES
1.0000
1.0350
1.0356
1.0195
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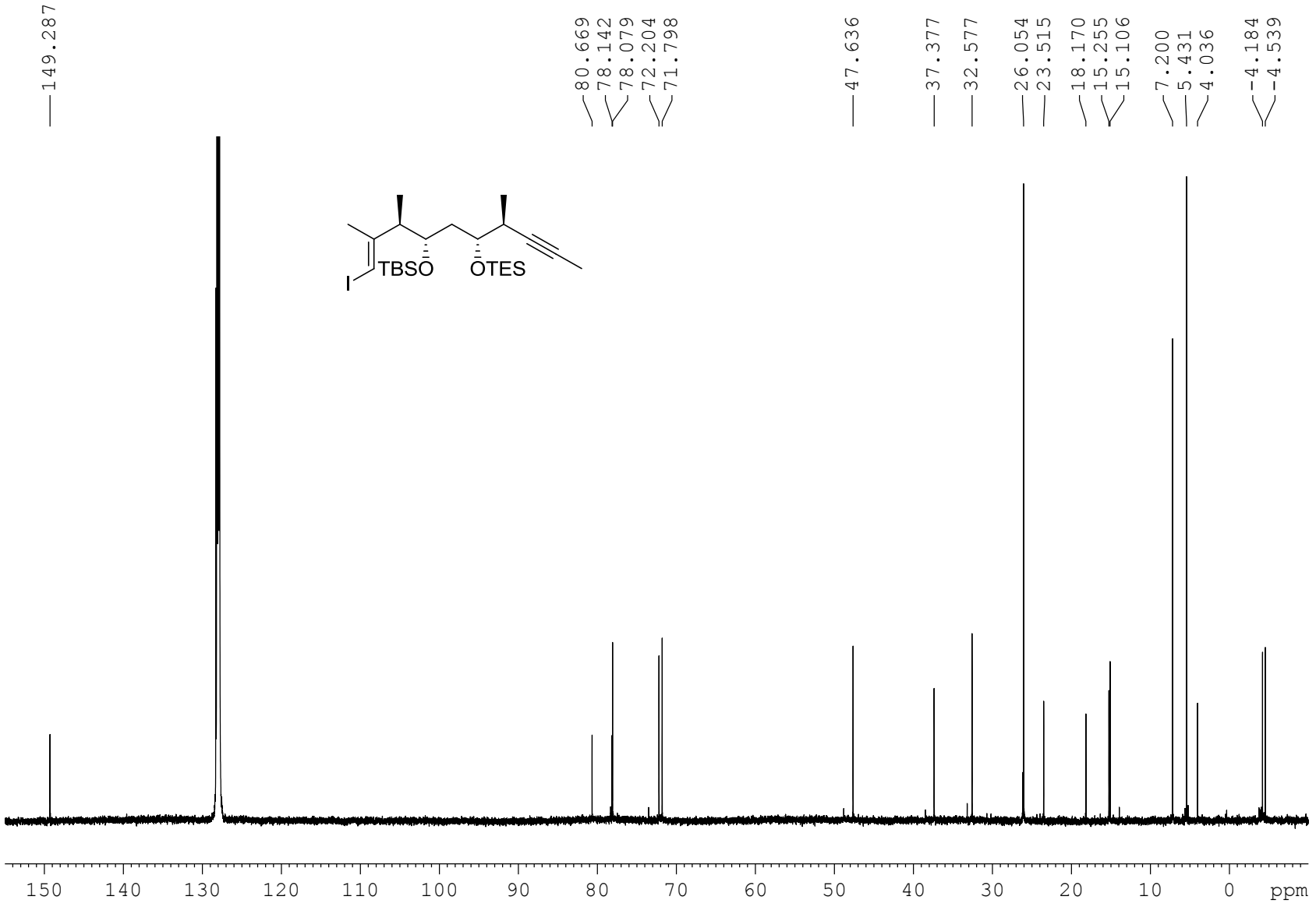
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18.170
15.255
15.106
7.200
5.431
4.036
-4.184
-4.539
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OTES
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140
130
120
110
100
90
80
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60
50
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20
10
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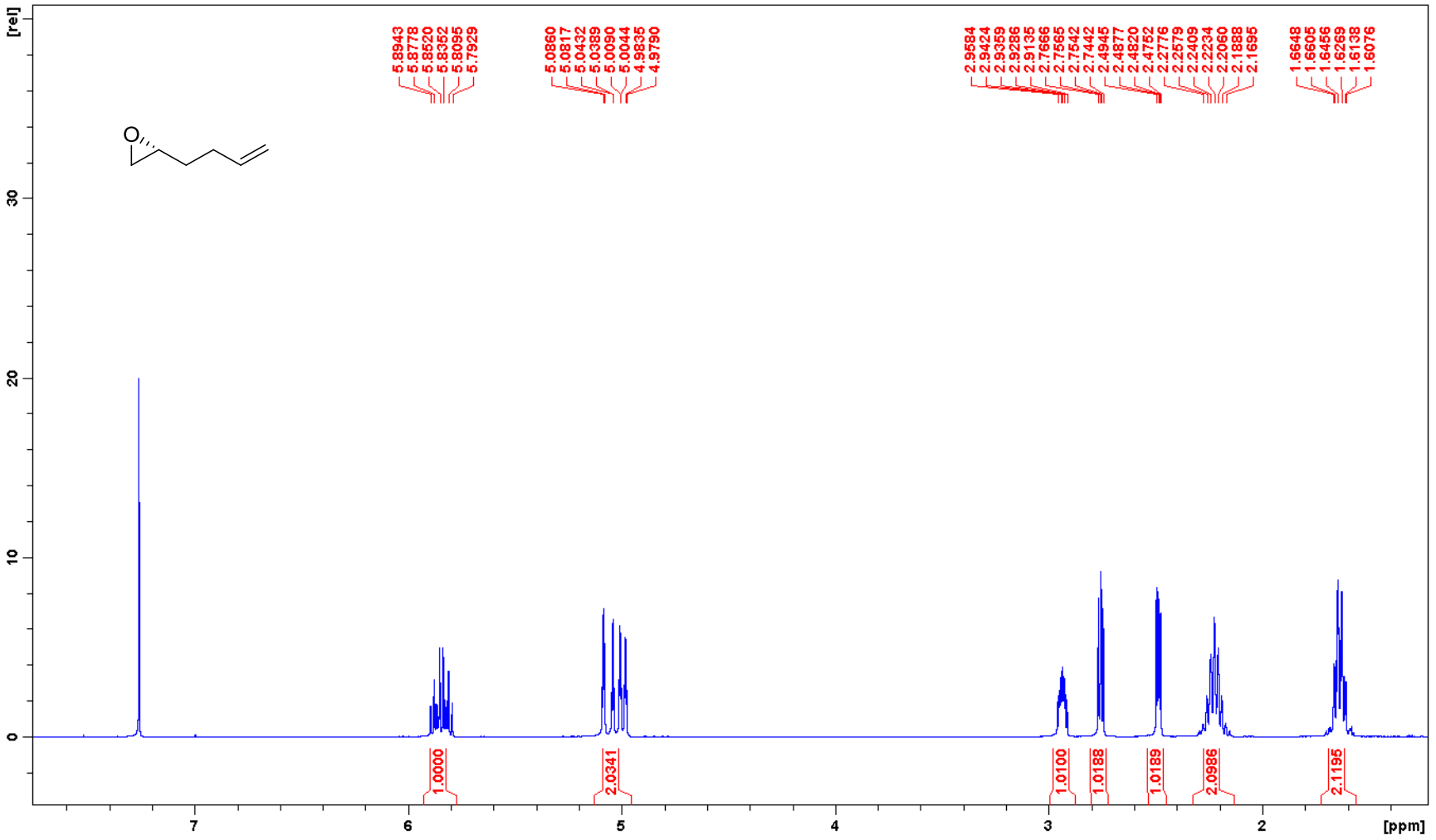
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5.0817
5.0432
5.0389
5.0090
5.0044
4.9835
4.9790
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2.9424
2.9359
2.9286
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2.7442
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2.4820
2.4752
2.2776
2.2579
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2.2234
2.2060
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1.6138
1.6076
O
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1.0189
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2.1195
7
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4
3
2
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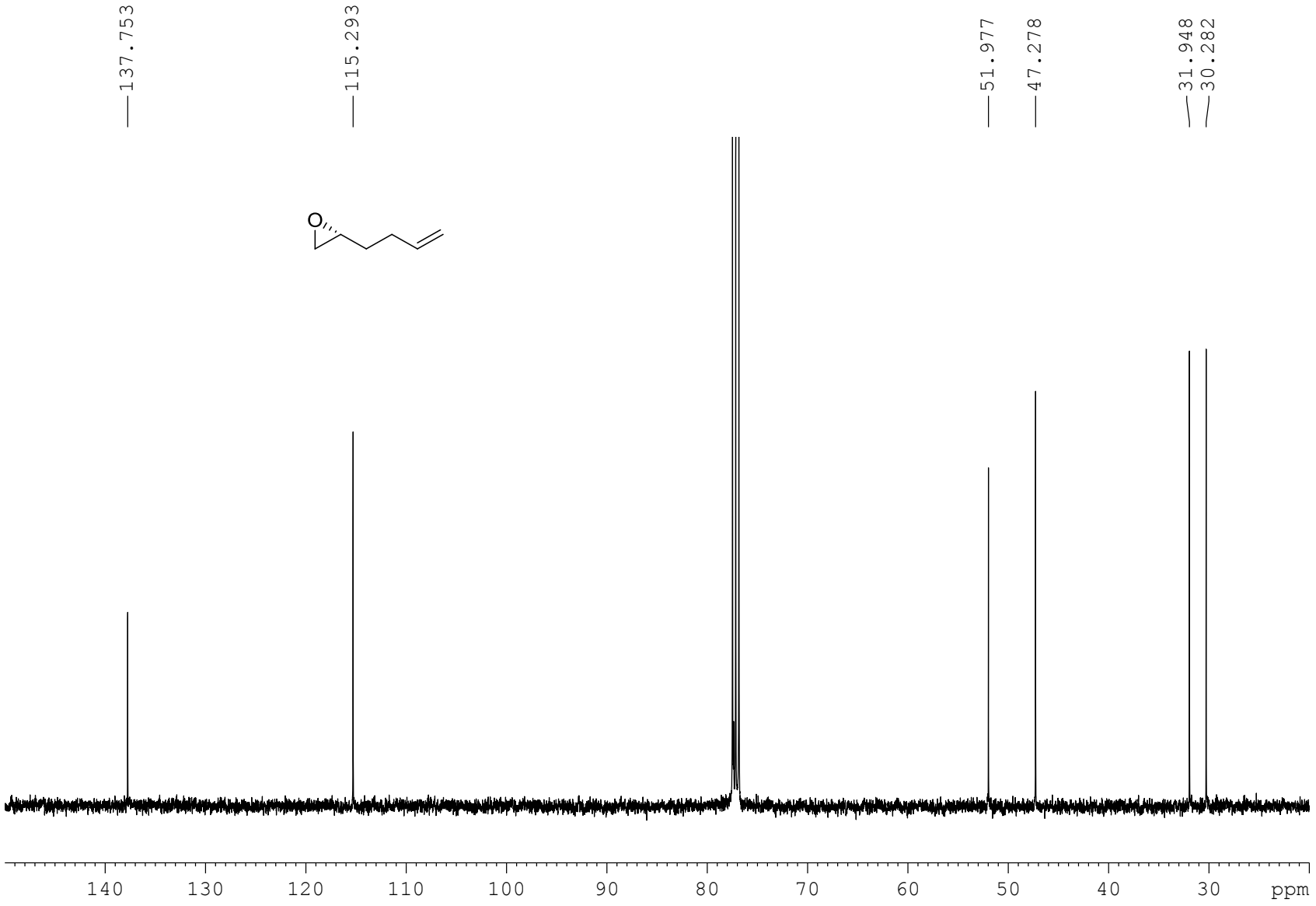
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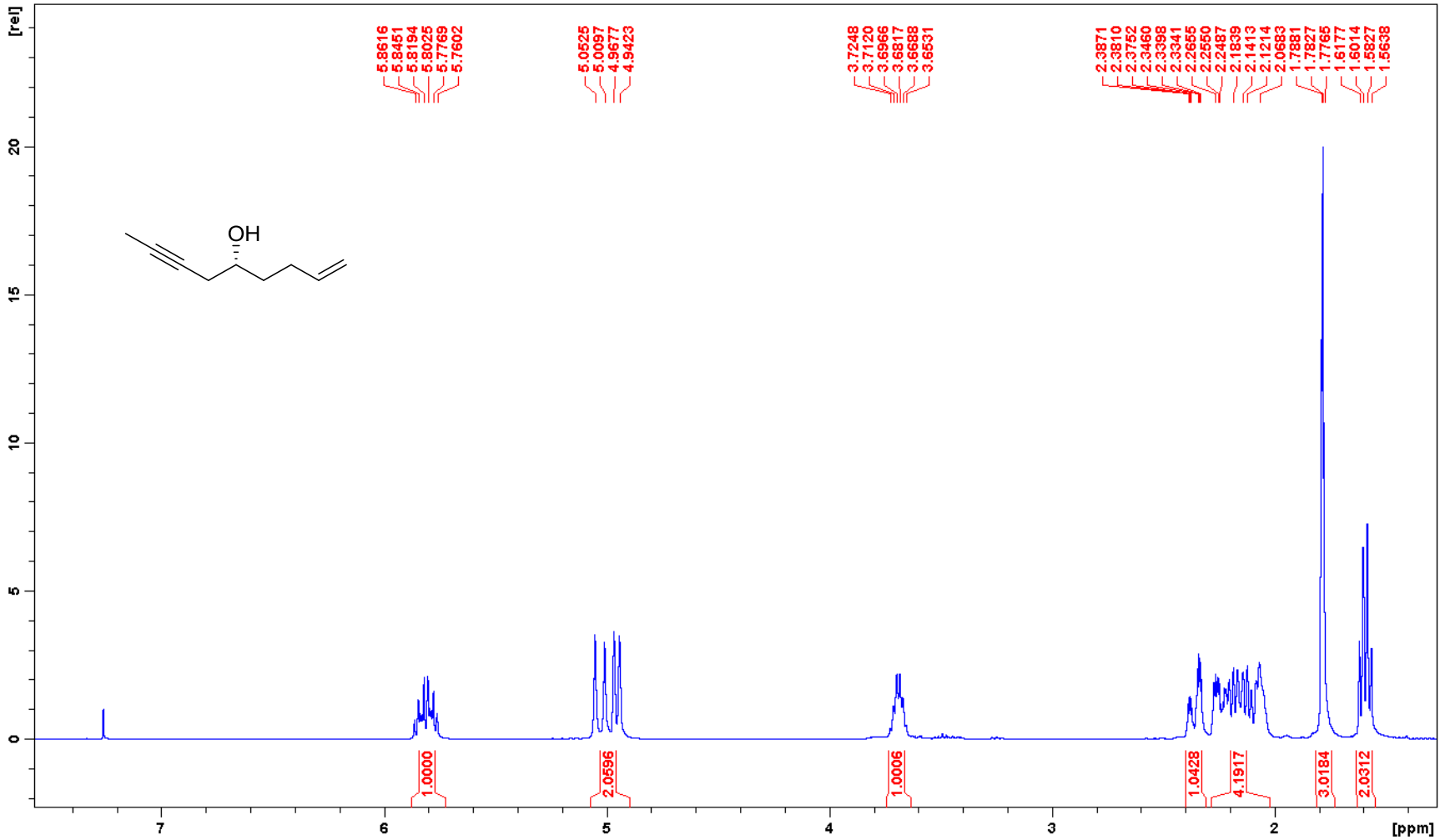
O
140
130
120
110
100
90
80
70
60
50
40
30
ppm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10
5
0
OH
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5.0525
5.0097
4.9677
4.9423
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3.7120
3.6966
3.6817
3.6688
3.6531
2.3871
2.3810
2.3752
2.3460
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2.2655
2.2550
2.2487
2.1839
2.1413
2.1214
2.0683
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1.7827
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1.6177
1.6014
1.5827
1.5638
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7
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4
3
2
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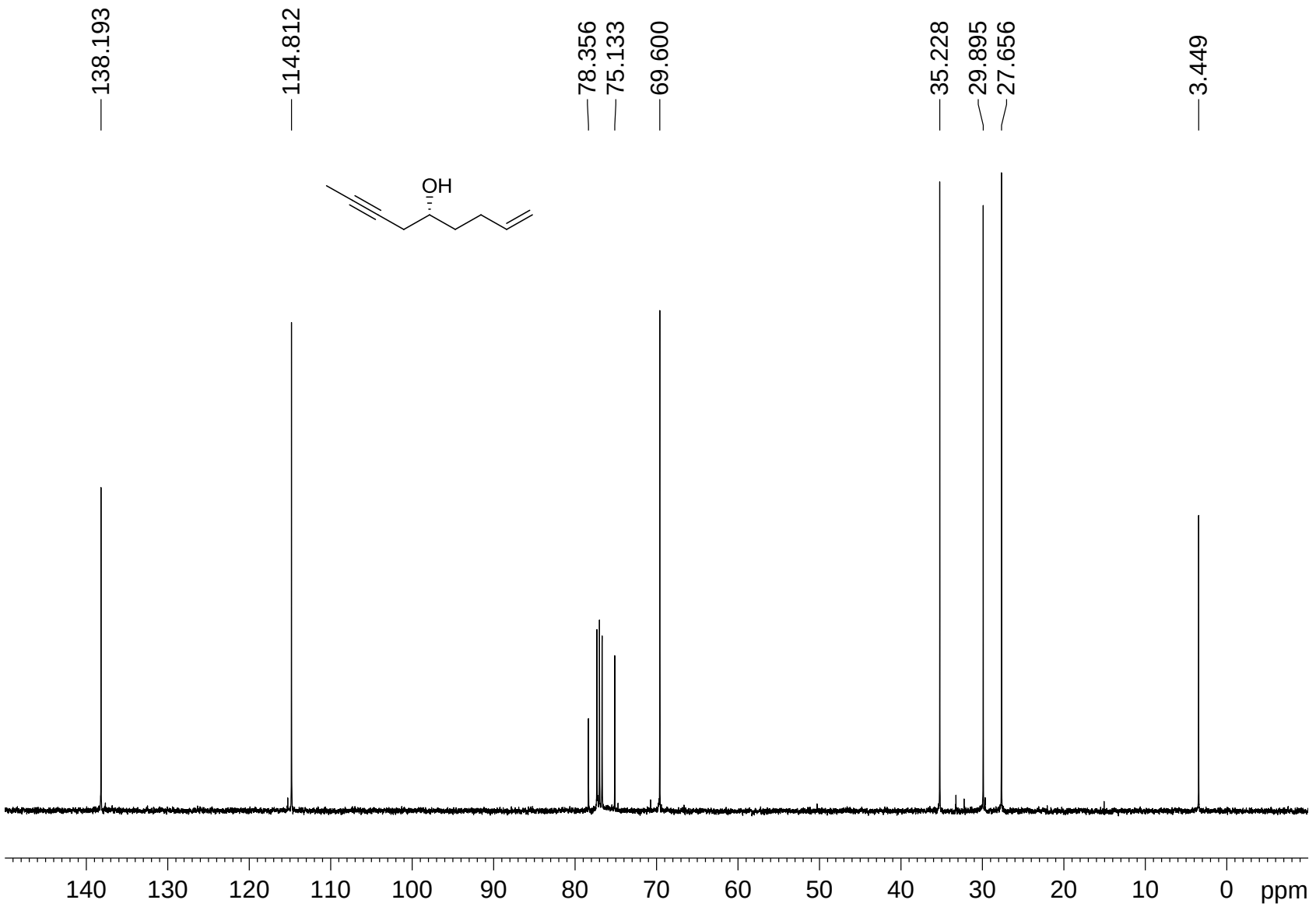
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OH
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130
120
110
100
90
80
70
60
50
40
30
20
10
0
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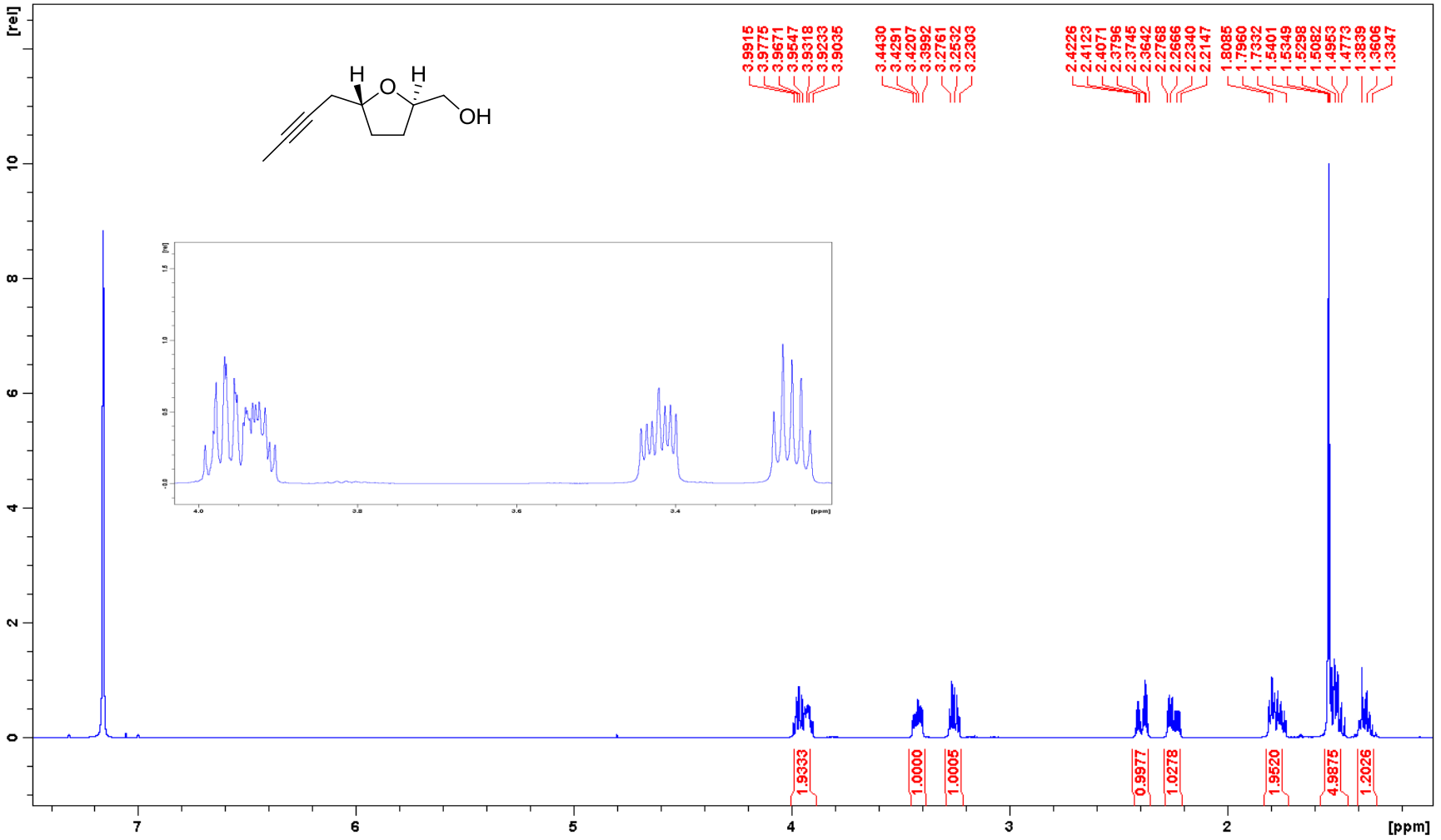
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H
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3.9035
3.4430
3.4291
3.4207
3.3992
3.2761
3.2532
3.2303
2.4226
2.4123
2.4071
2.3796
2.3745
2.3642
2.2768
2.2666
2.2340
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1.5298
1.5082
1.4953
1.4773
1.3839
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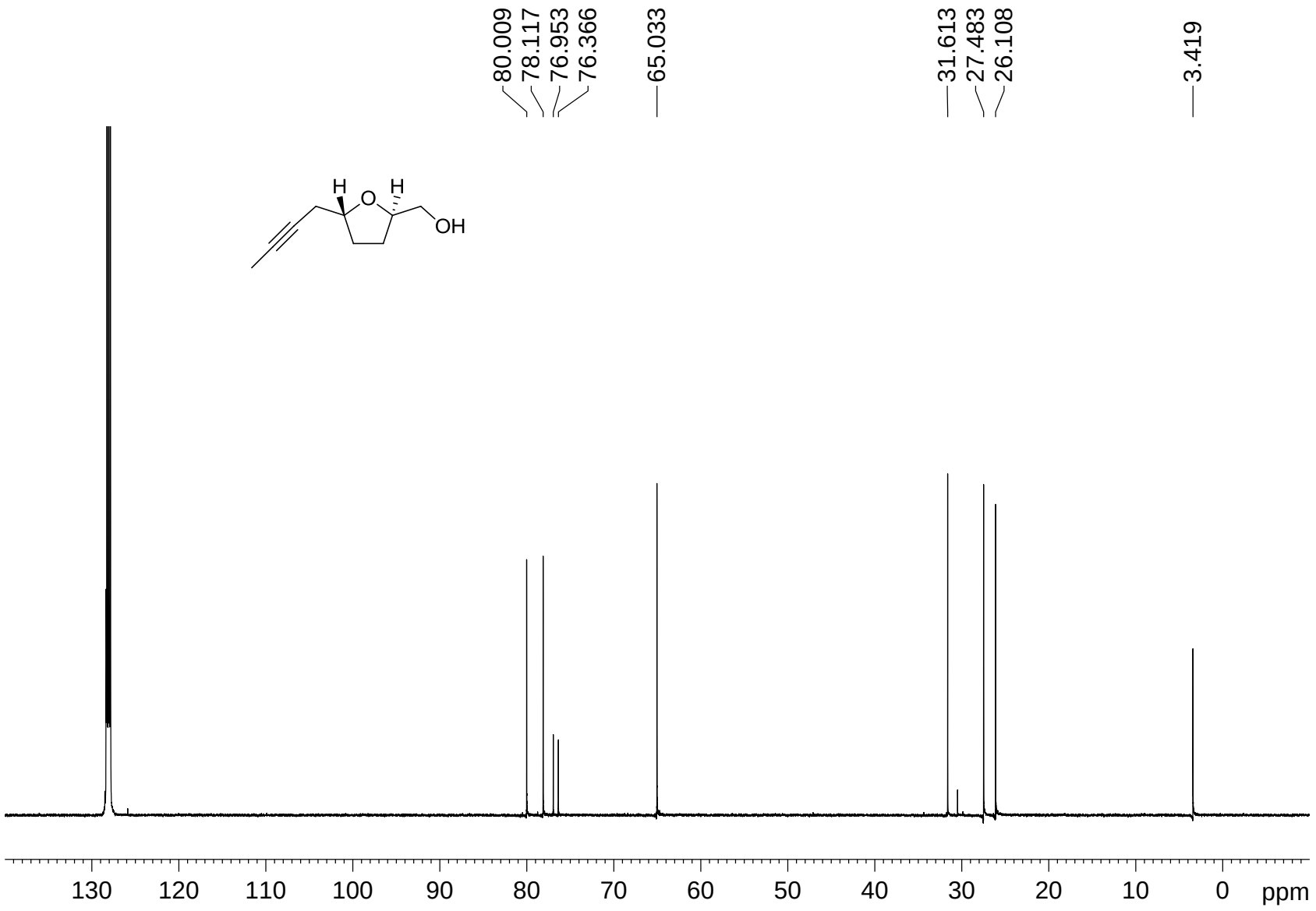
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O
H
OH
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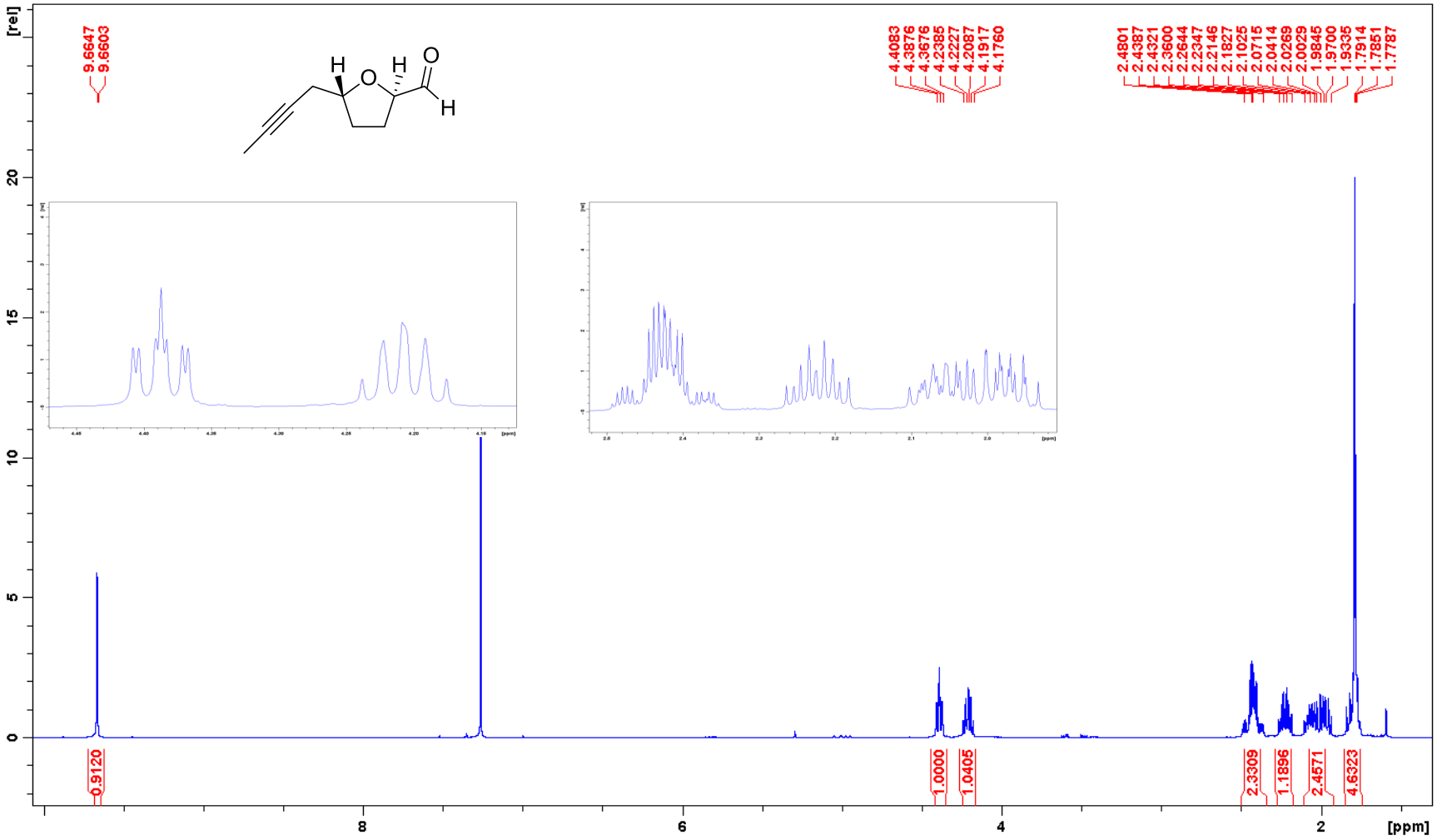
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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2.4387
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2.2644
2.2347
2.2146
2.1827
2.1025
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2.0414
2.0269
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1.9700
1.9335
1.7914
1.7851
1.7787
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O
H
O
H
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1.1896
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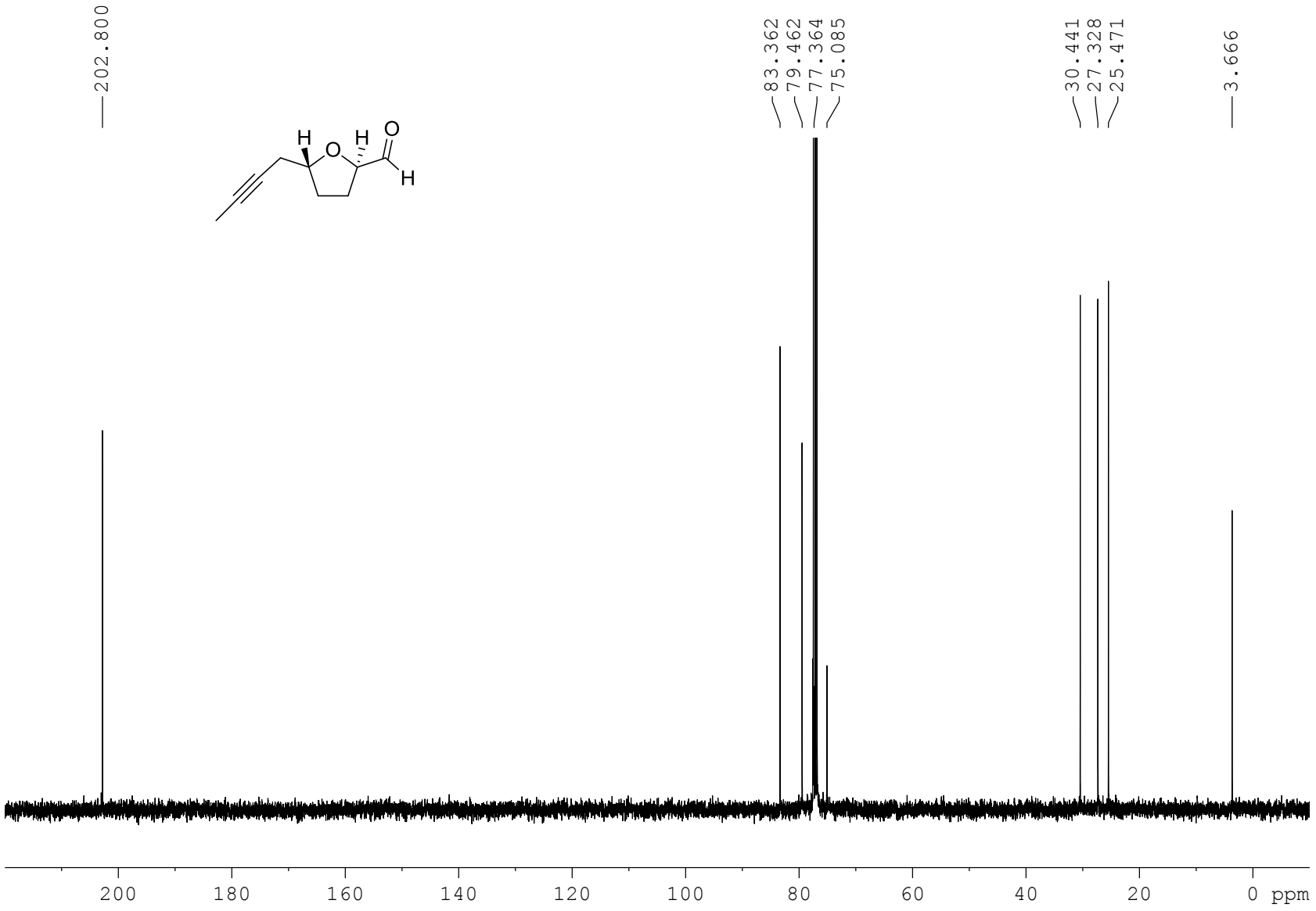
[ppm]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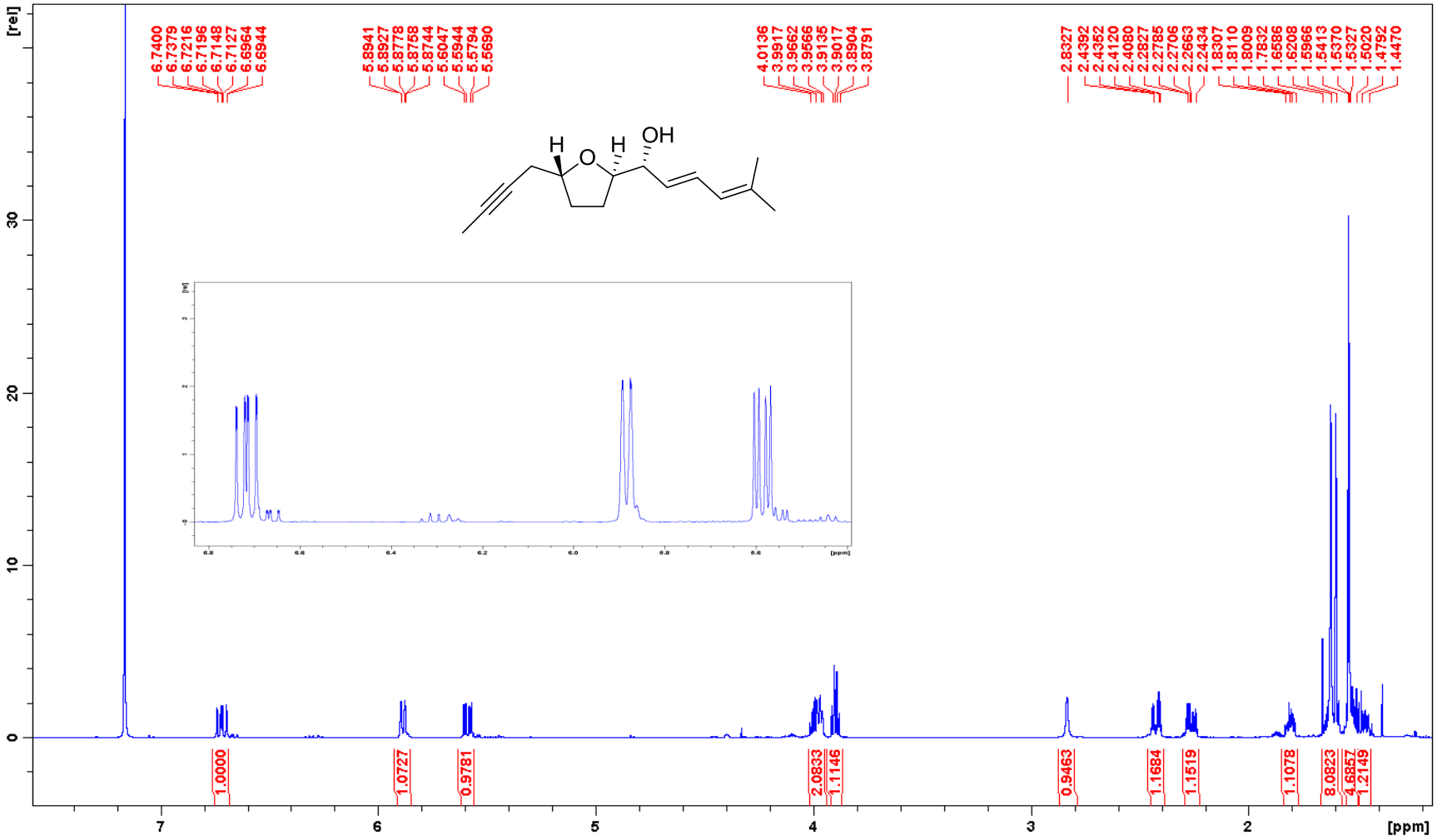
H
O
H
O
H
200
180
160
140
120
100
80
60
40
20
0 ppm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5.8758
5.8744
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5.5944
5.5794
5.5690
4.0136
3.9917
3.9662
3.9566
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3.9017
3.8904
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1.5020
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O
H
OH
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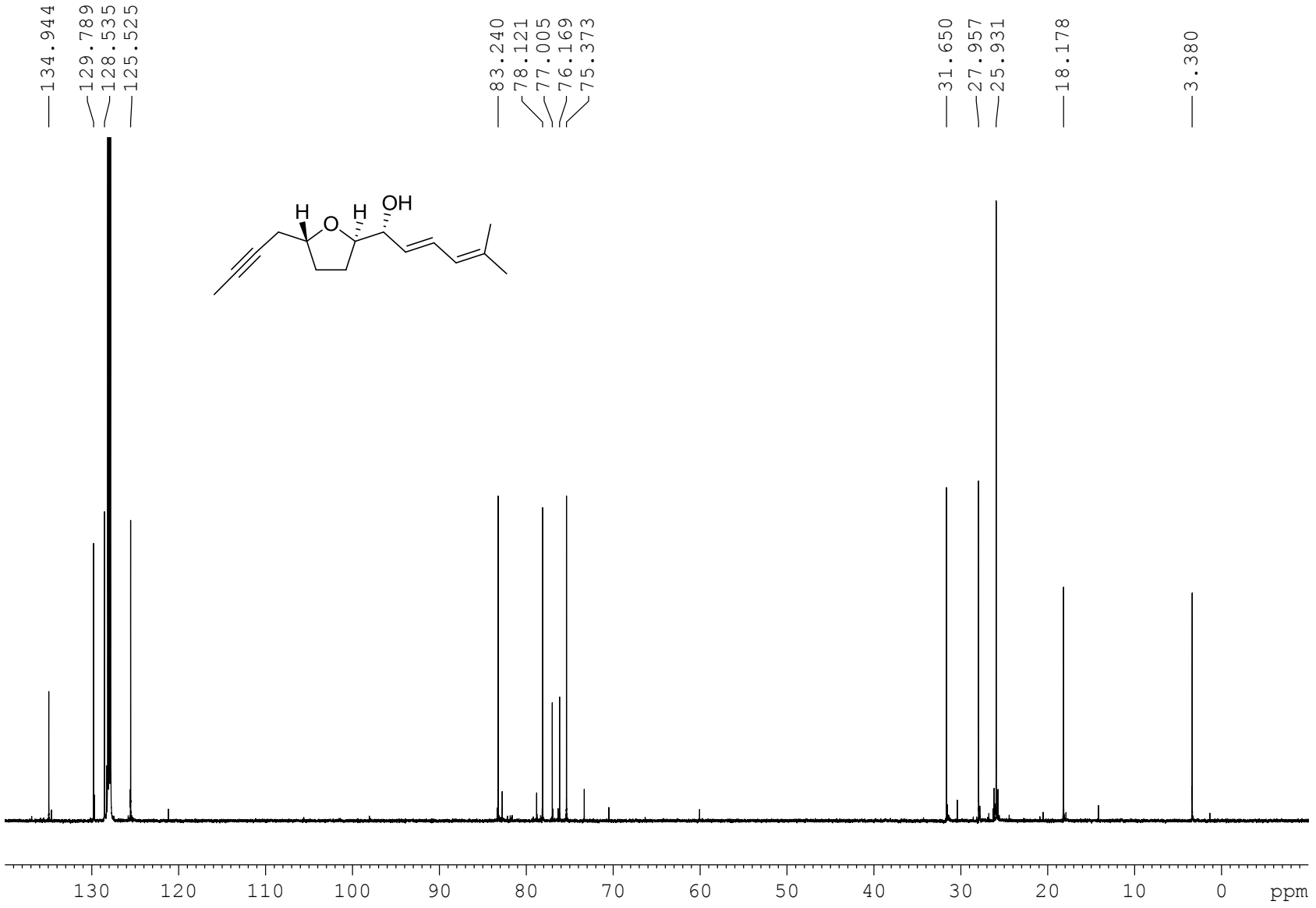
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OH
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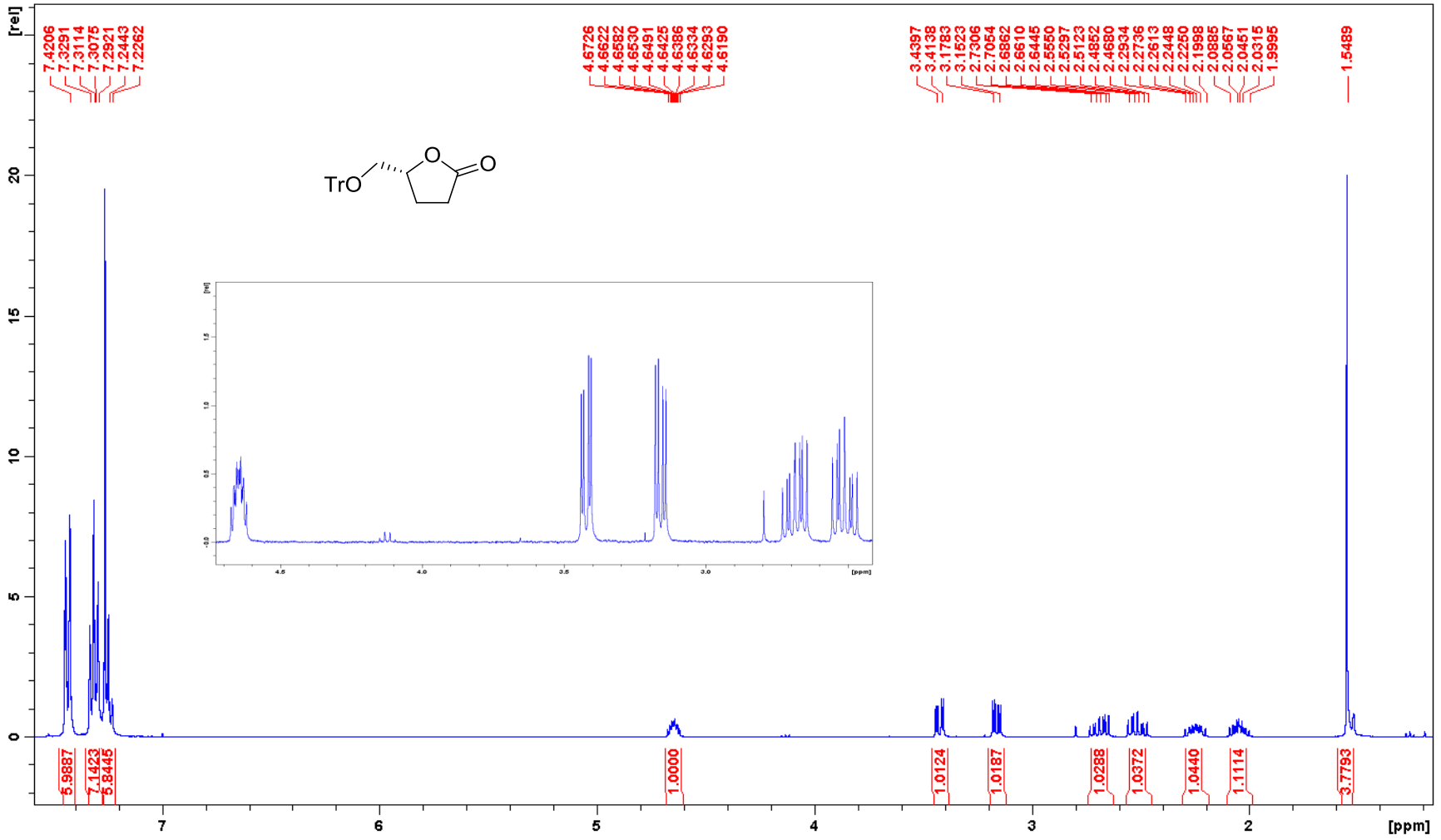
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3.4138
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2.7054
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2.6610
2.6445
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2.4852
2.4680
2.2934
2.2736
2.2613
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2.0451
2.0315
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1.5489
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O
O
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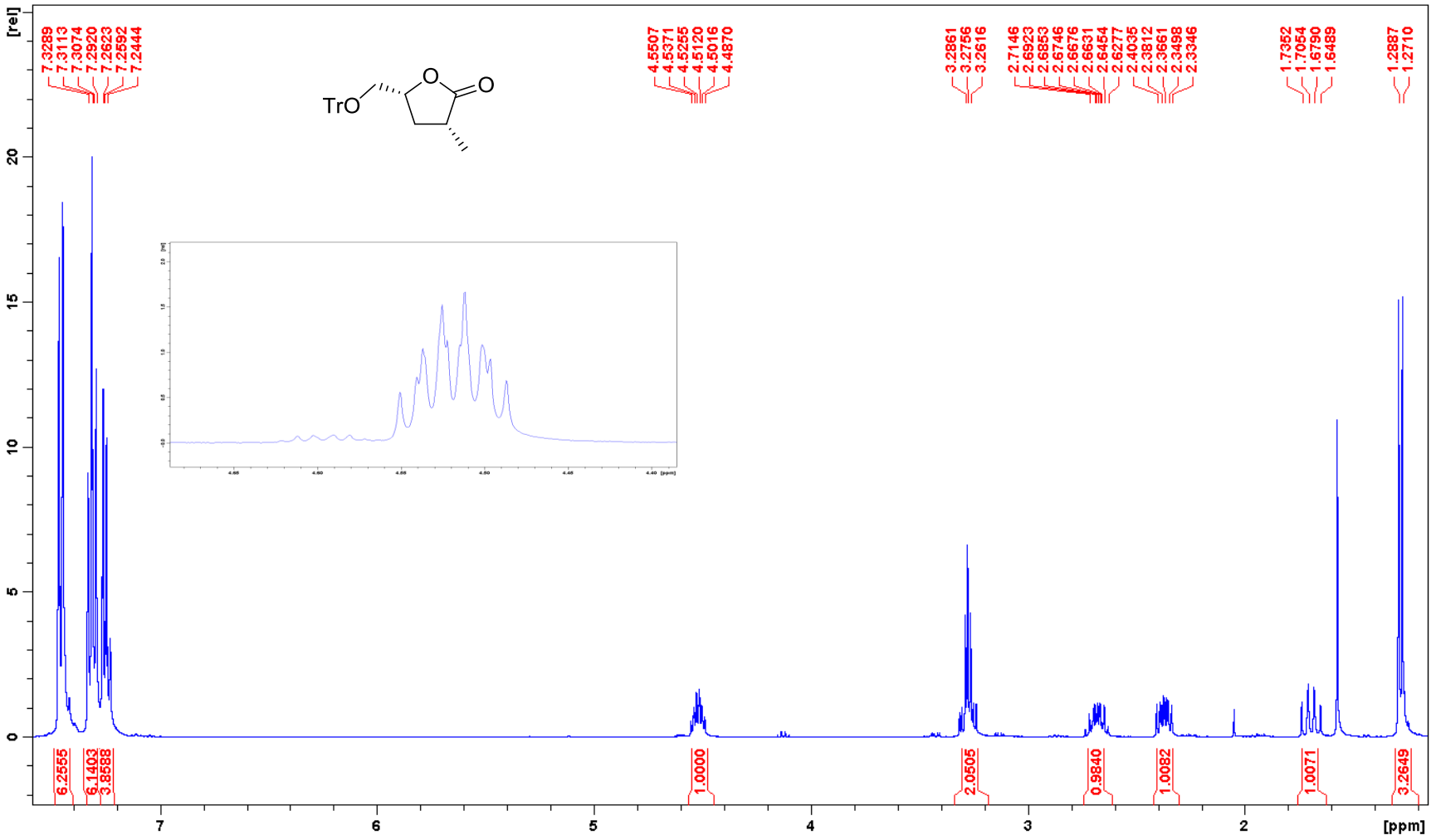
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2.3346
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1.2887
1.2710
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O
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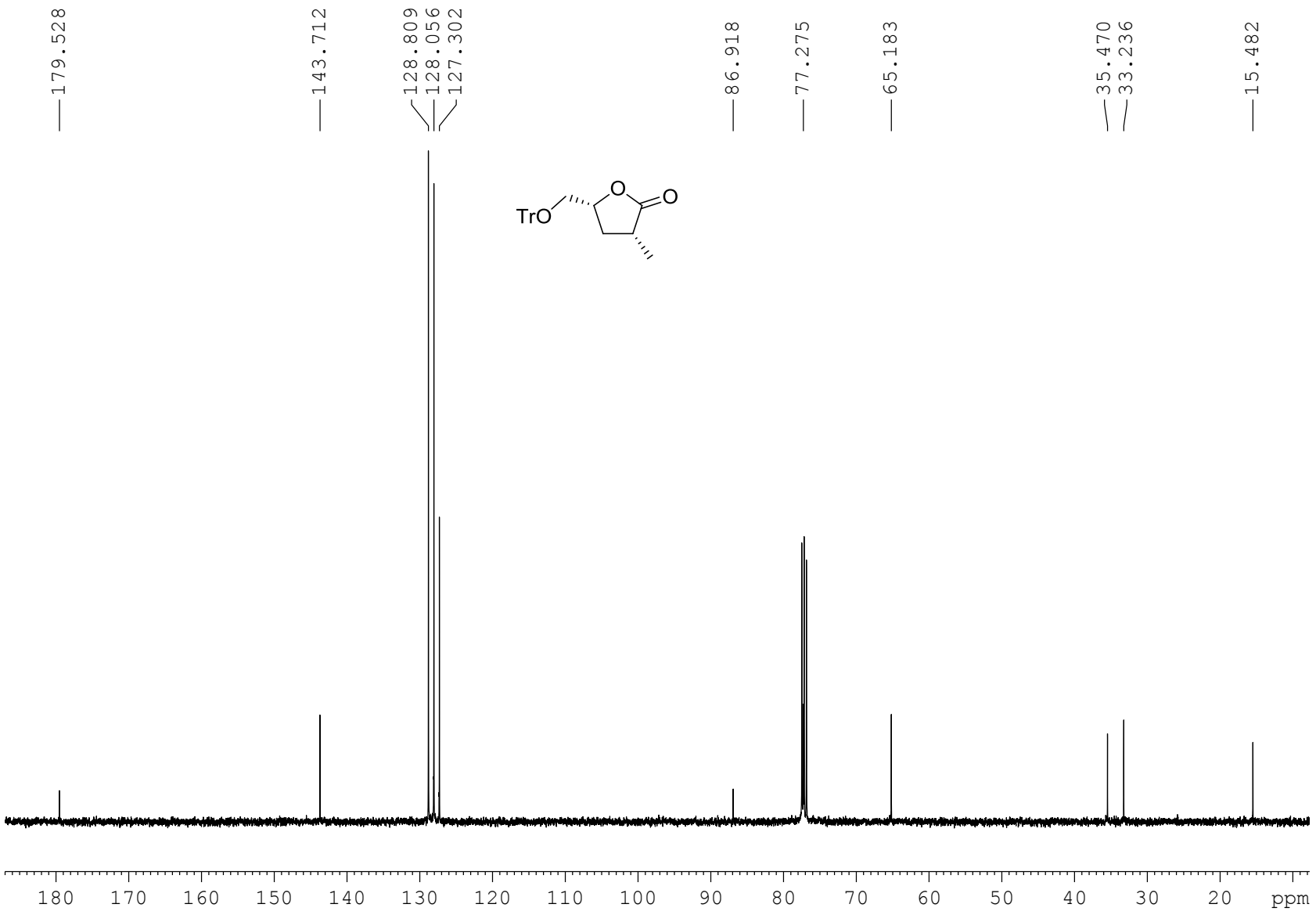
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160
150
140
130
120
110
100
90
80
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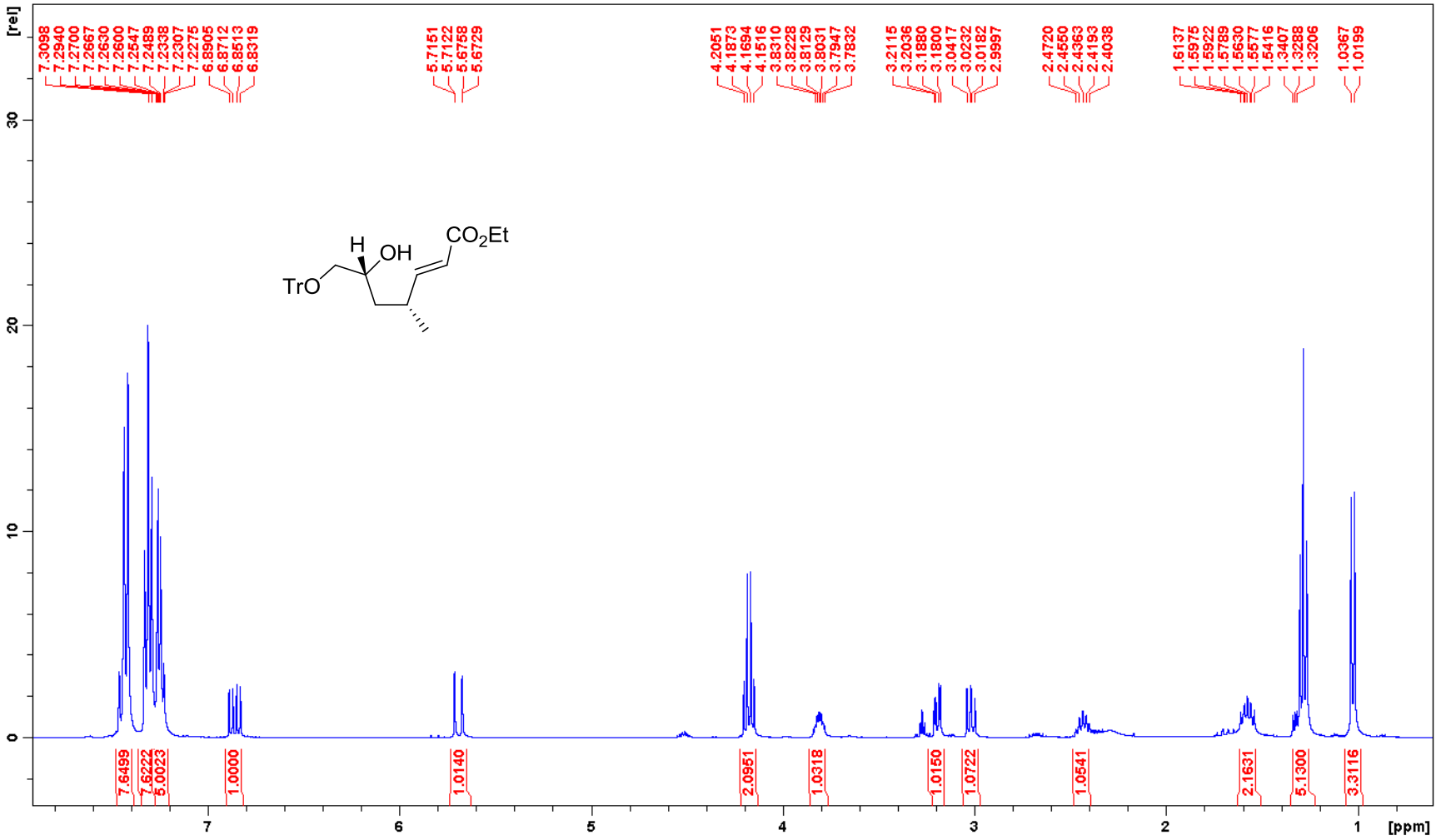
50
40
30
20
ppm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6.8712
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5.6729
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4.1873
4.1694
4.1516
3.8310
3.8228
3.8129
3.8031
3.7947
3.7832
3.2115
3.2036
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OH
CO2Et
TrO
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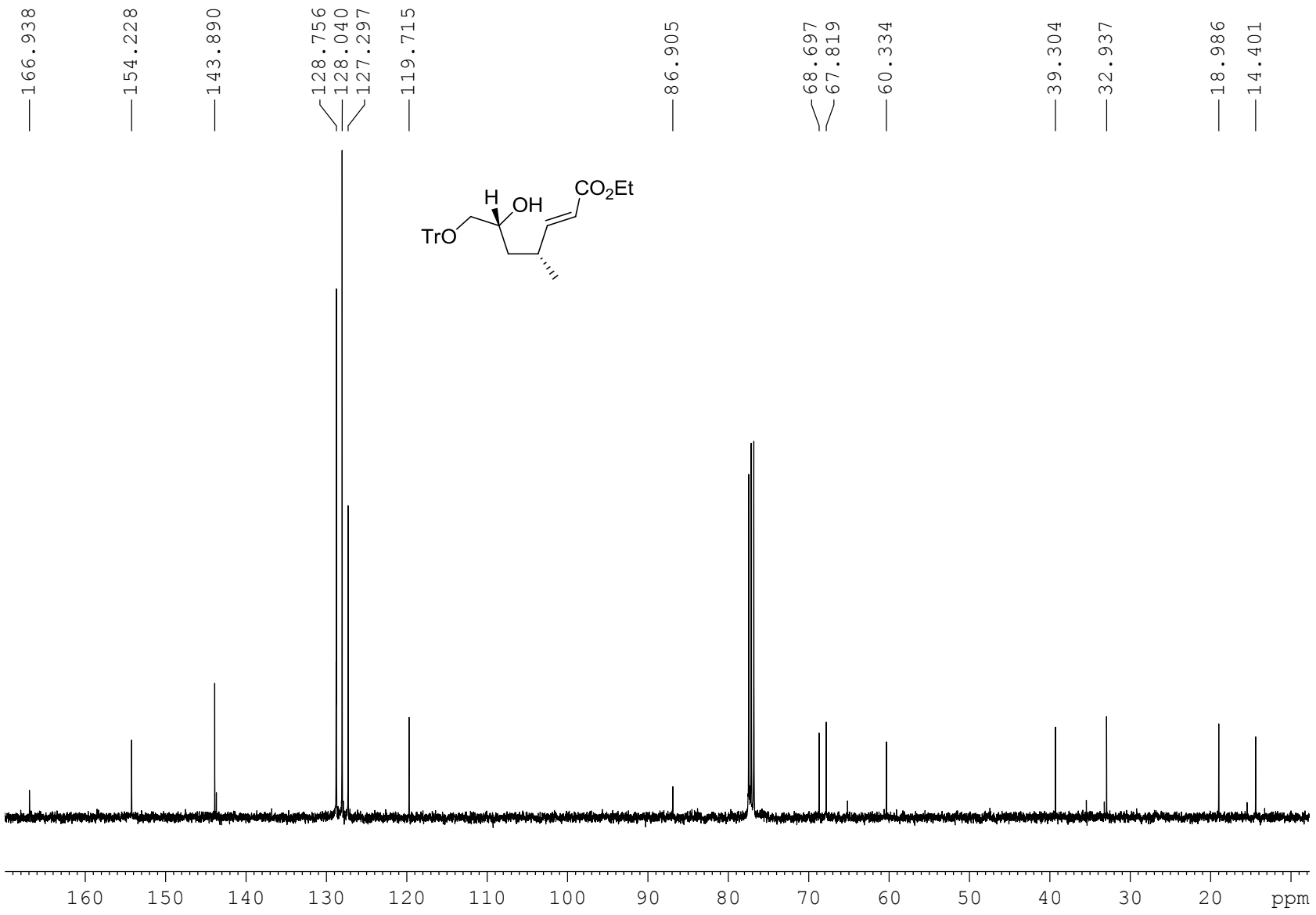
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32.937
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14.401
H
OH
CO2Et
TrO
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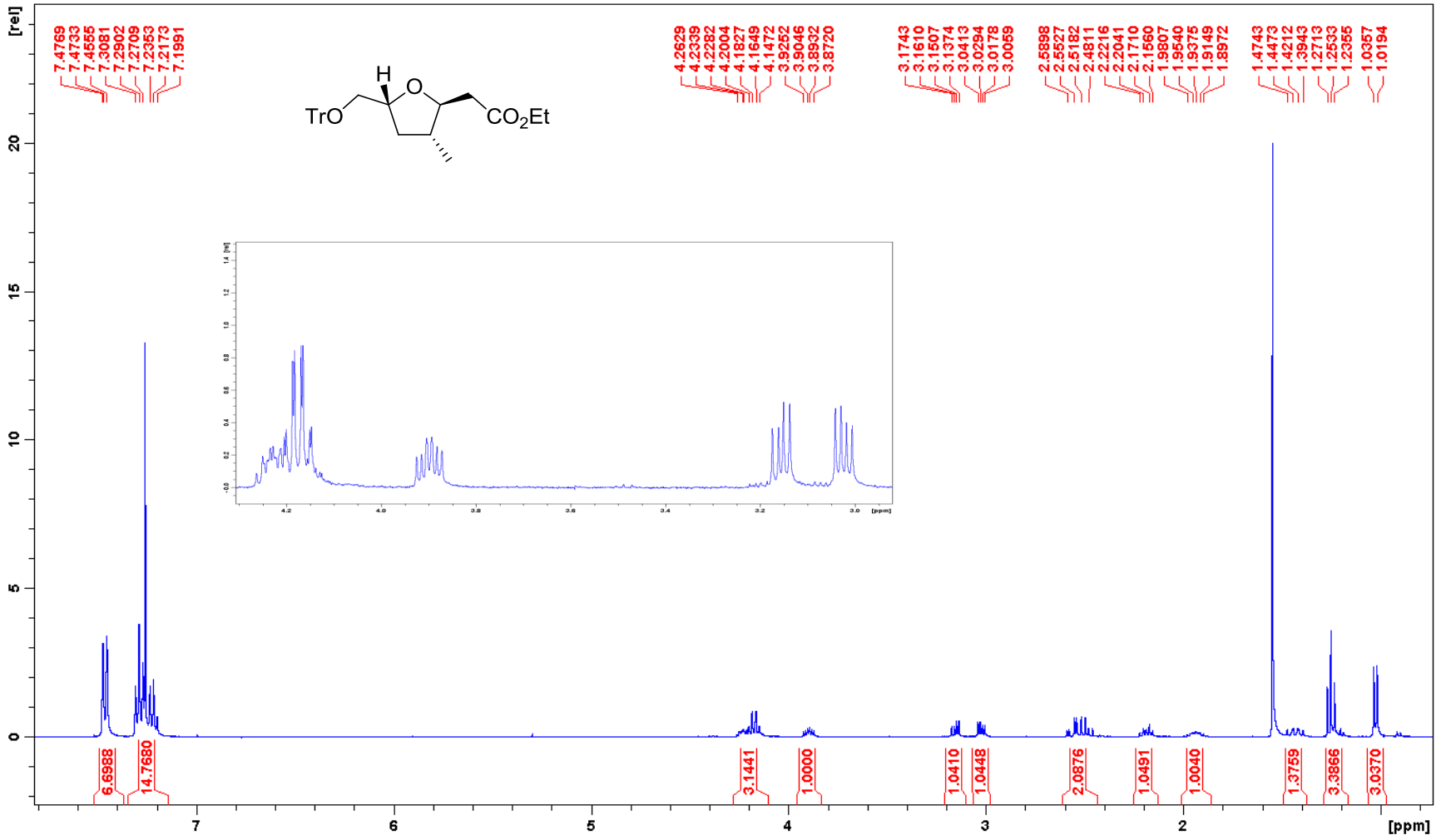
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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4.2004
4.1827
4.1649
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3.1743
3.1610
3.1507
3.1374
3.0413
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3.0178
3.0059
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2.5527
2.5182
2.4811
2.2216
2.2041
2.1710
2.1560
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1.9540
1.9375
1.9149
1.8972
1.4743
1.4473
1.4212
1.3943
1.2713
1.2533
1.2355
1.0357
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O
TrO
CO2Et
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1.0040
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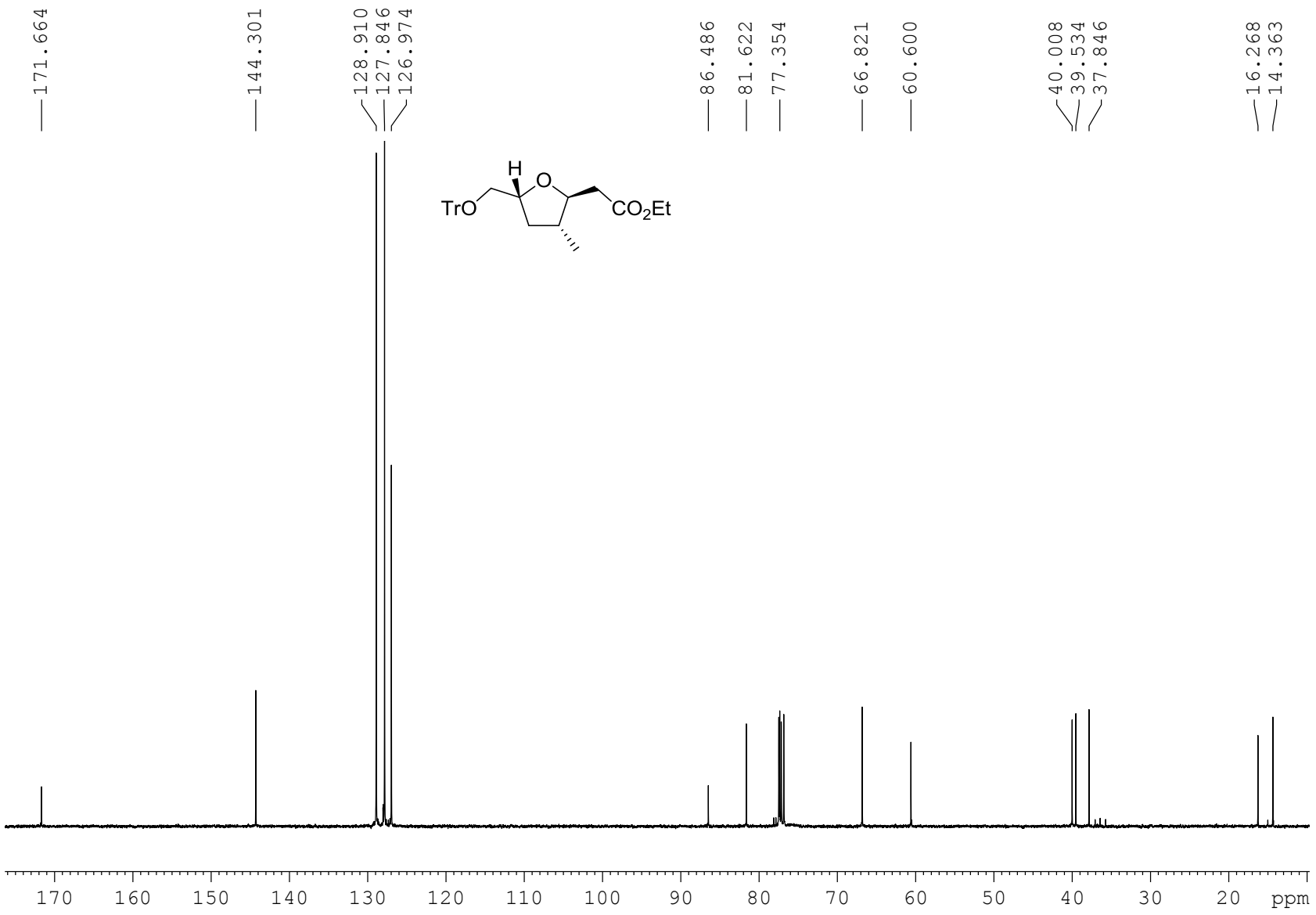
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39.534
37.846
16.268
14.363
H
O
TrO
CO2Et
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160
150
140
130
120
110
100
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80
70
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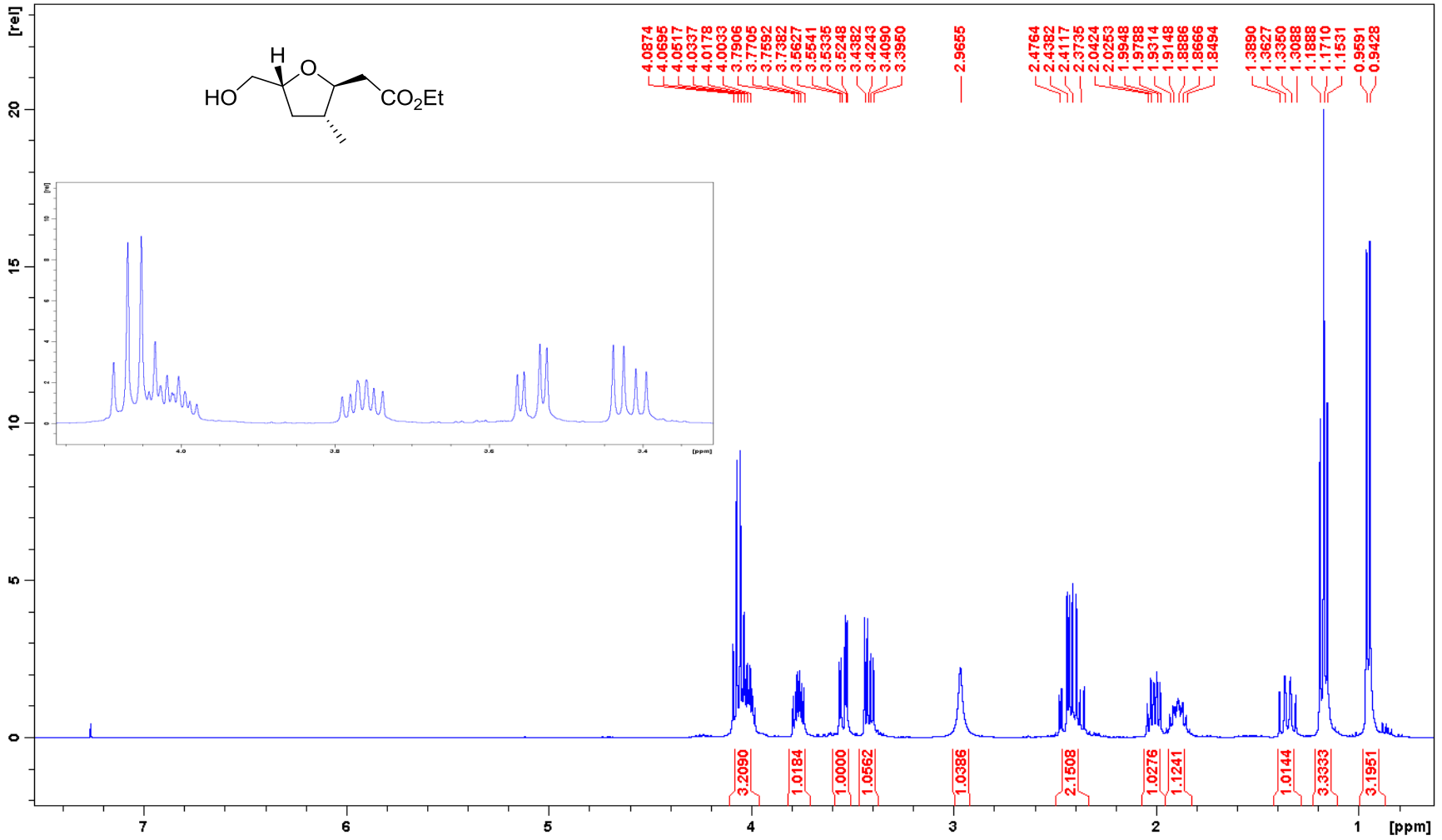
50
40
30
20
ppm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3.7382
3.5627
3.5541
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3.3950
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1.1710
1.1531
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0.9428
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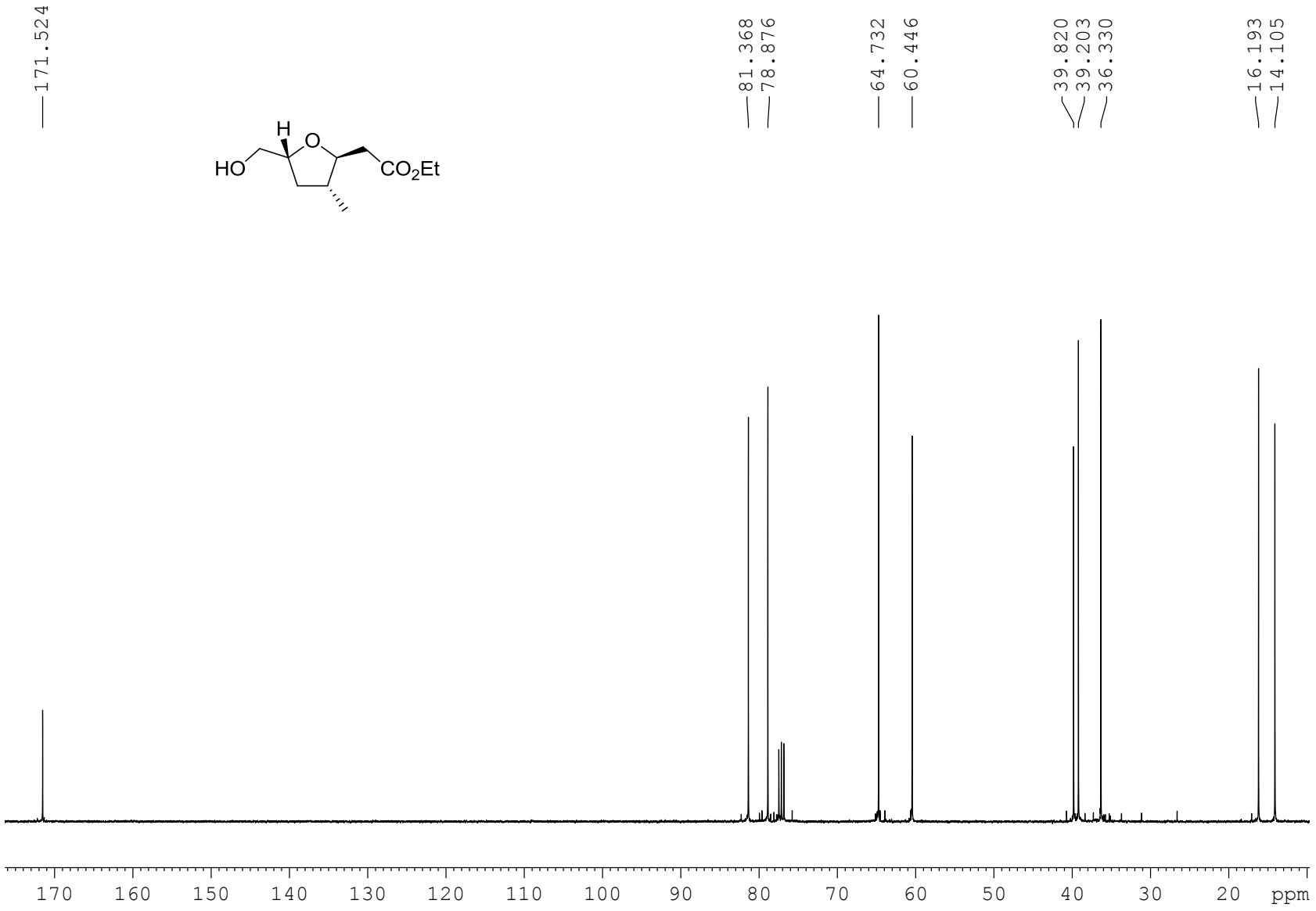
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H
O
HO
CO2Et
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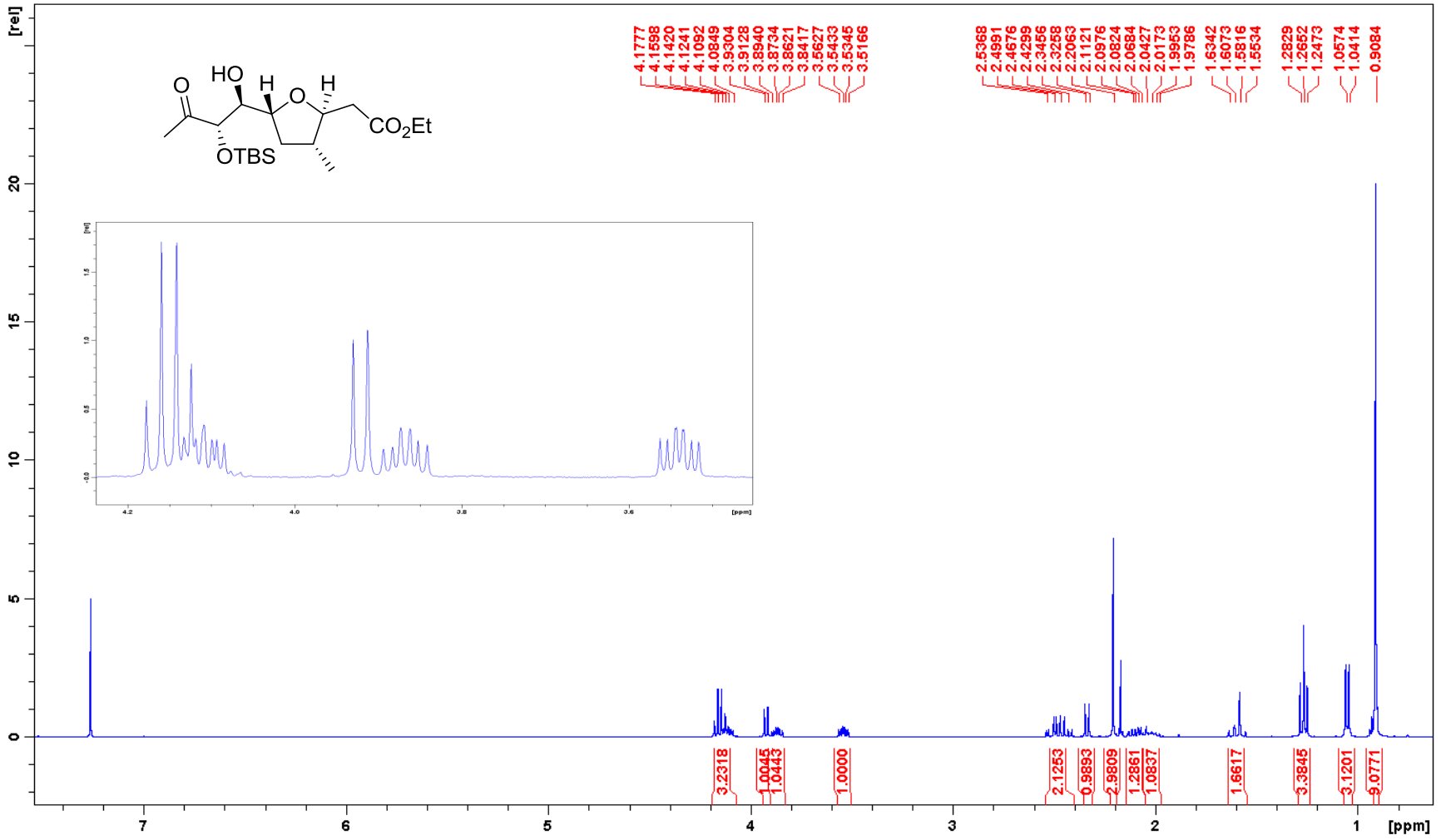
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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H
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OTBS
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3.9128
3.8940
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3.8621
3.8417
3.5627
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2.4299
2.3456
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2.2063
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2.0824
2.0684
2.0427
2.0173
1.9953
1.9786
1.6342
1.6073
1.5816
1.5534
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1.2652
1.2473
1.0574
1.0414
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1.0443
1.0000
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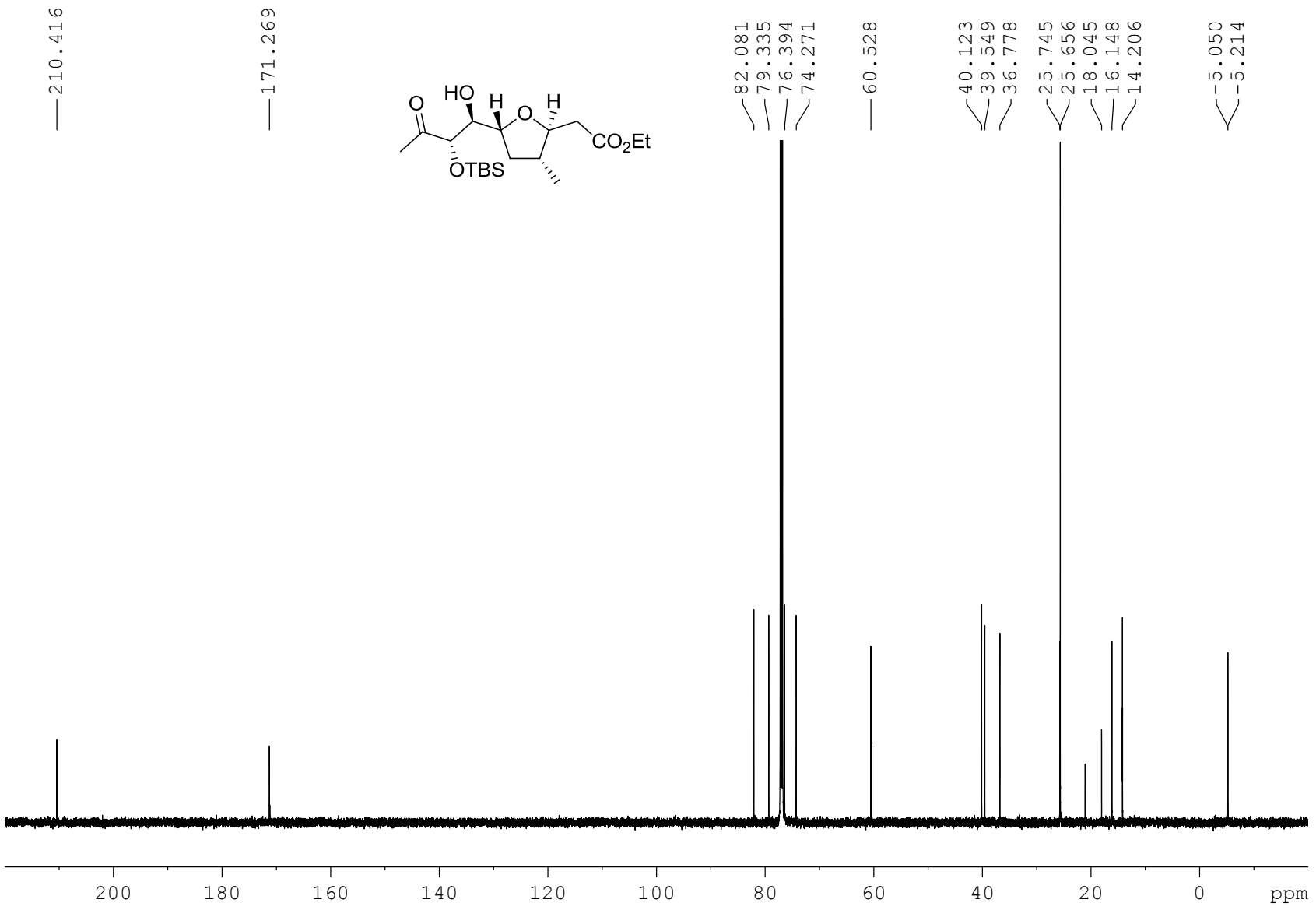
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-5.214
O
HO
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O
H
CO2Et
OTBS
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120
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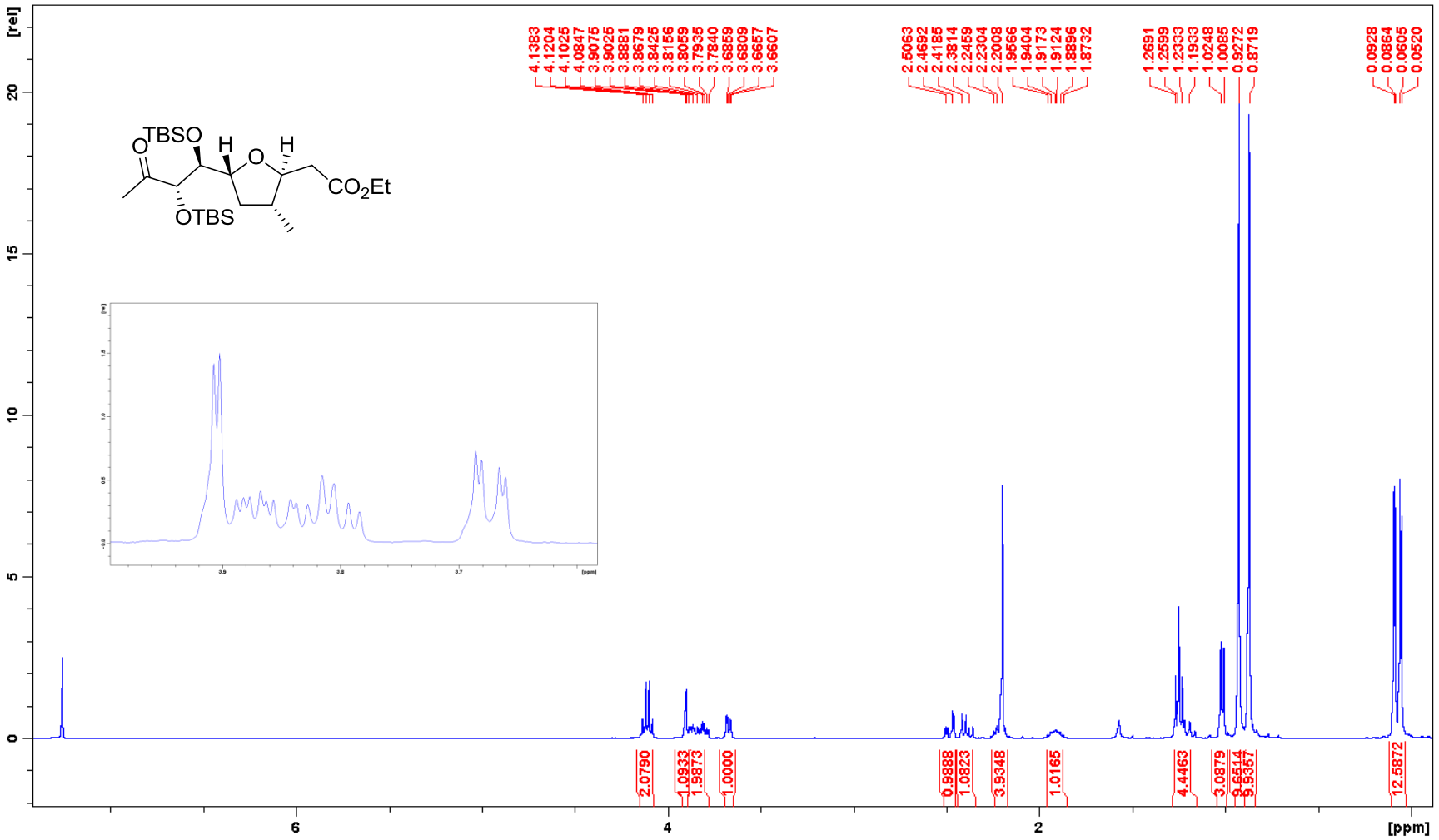
60
40
20
0
ppm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3.6607
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2.2304
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1.9173
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1.8732
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1.1933
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0.8719
0.0928
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1.0933
1.9873
1.0000
0.9888
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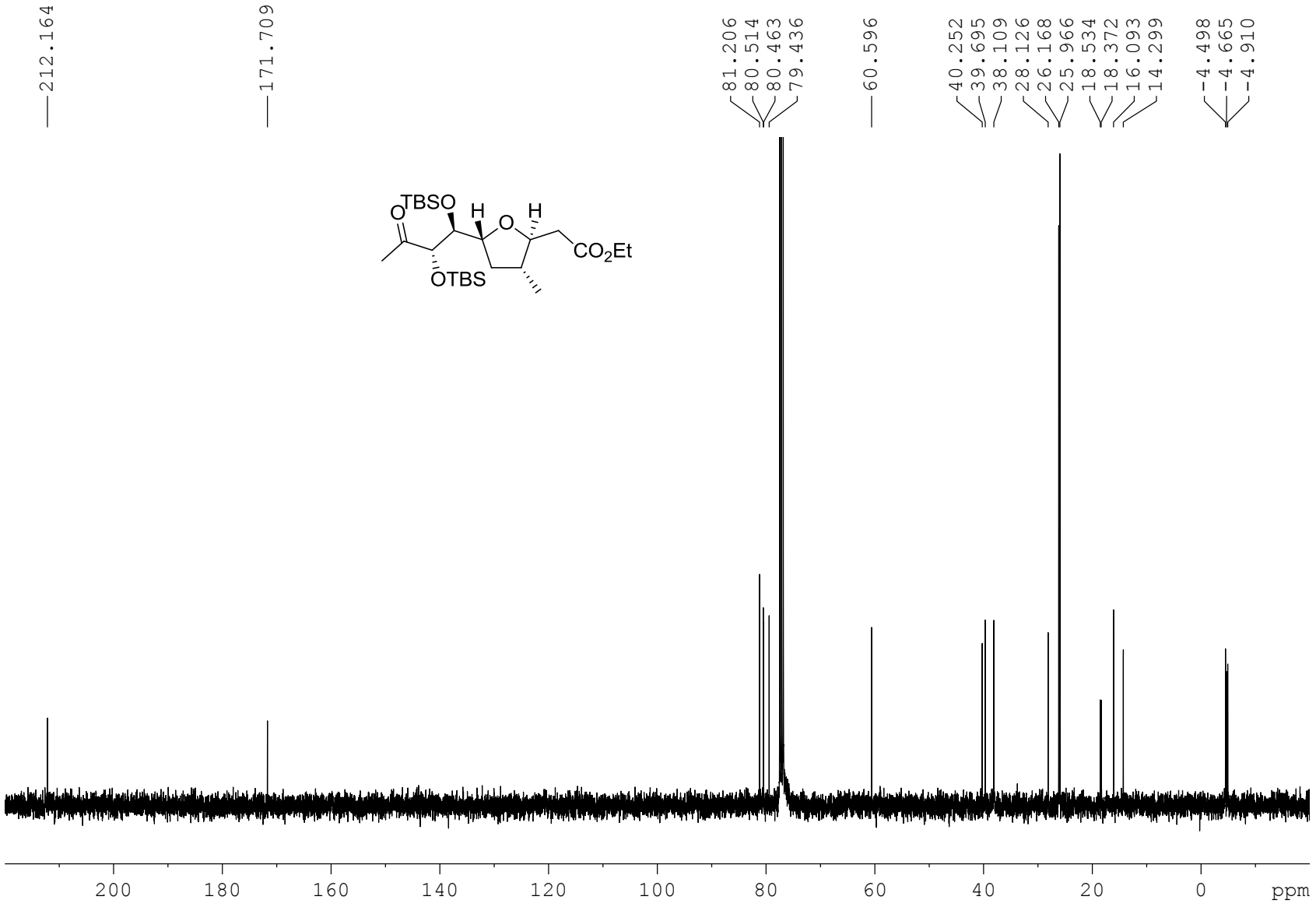
O
H
CO2Et
OTBS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18.372
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O
H
CO2Et
OTBS
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160
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120
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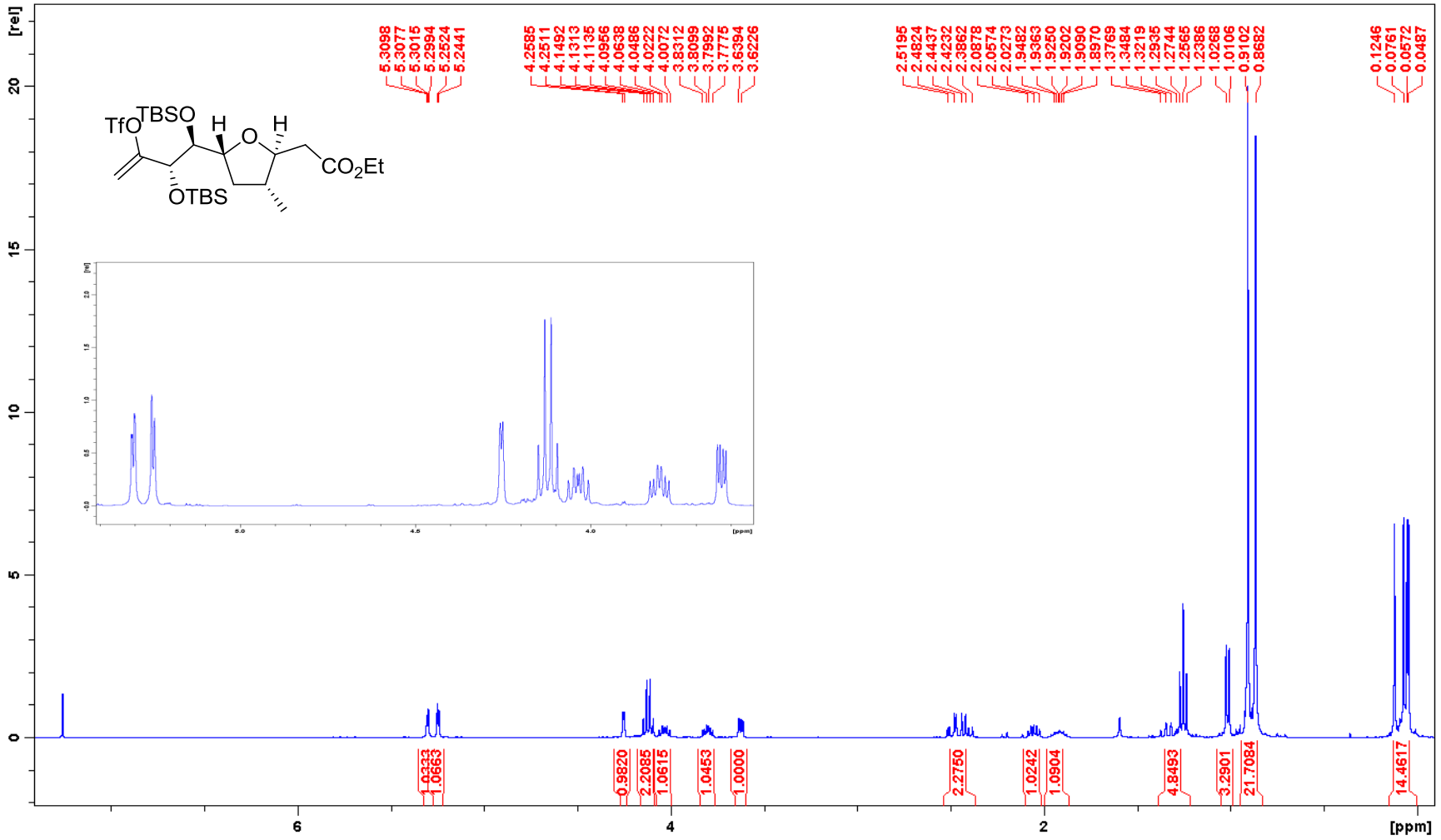
60
40
20
0
ppm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5.2441
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2.4437
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1.9202
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1.2744
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2
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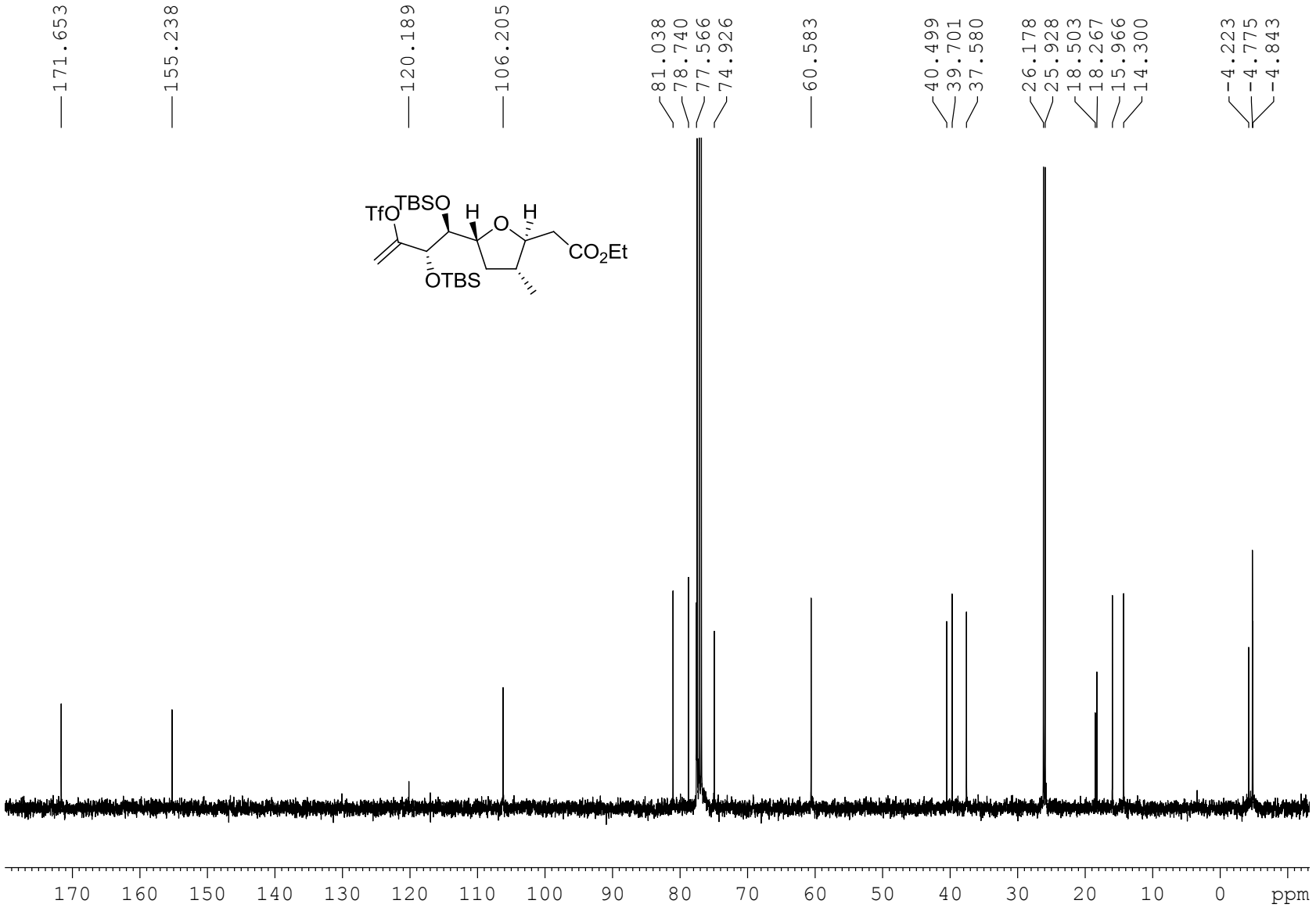
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26.178
25.928
18.503
18.267
15.966
14.300
-4.223
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-4.843
TfO
TBSO
H
O
H
CO2Et
OTBS
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140
130
120
110
100
90
80
70
60
50
40
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20
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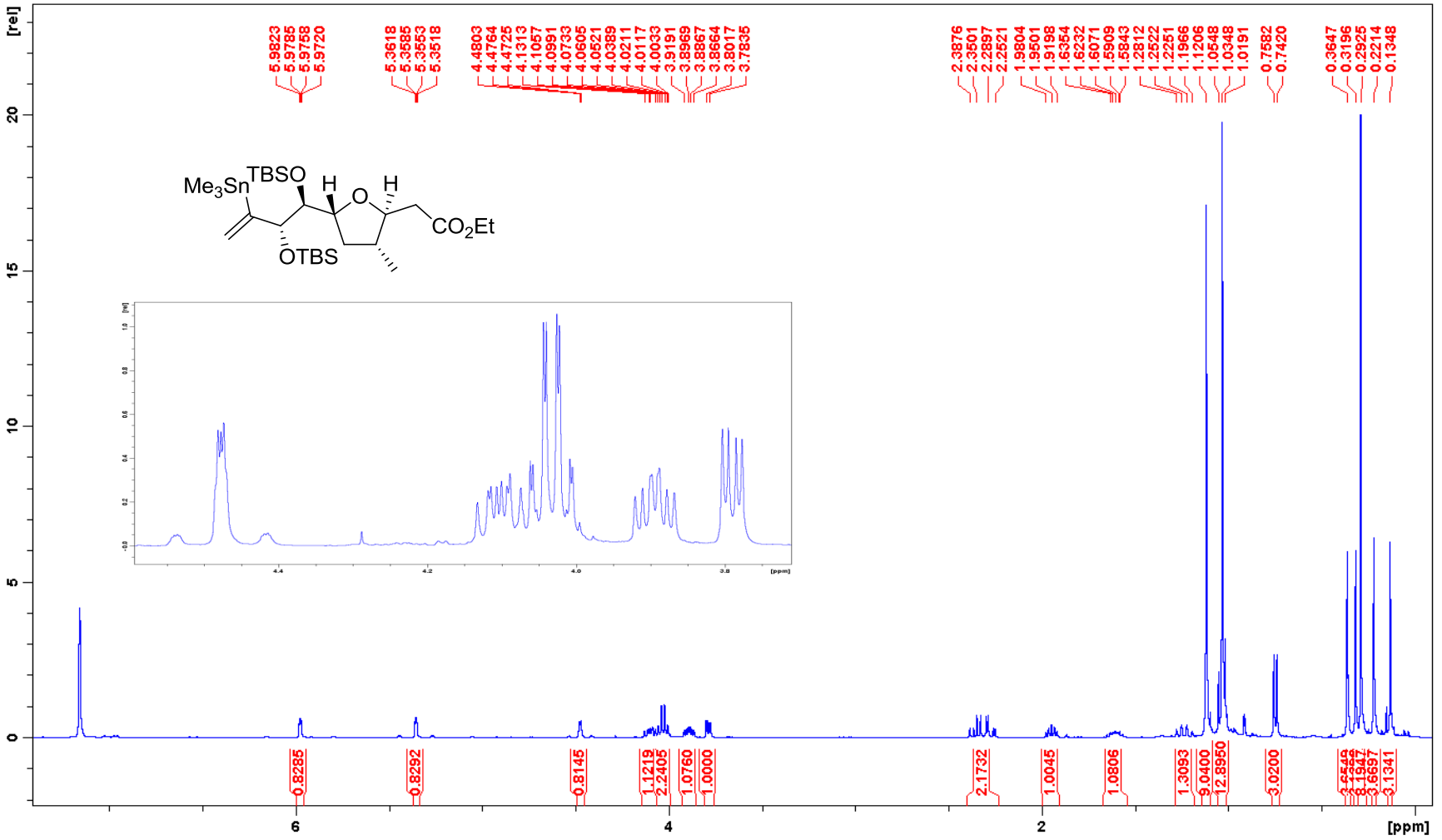
0
ppm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0.7420
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0.2925
0.2214
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Me3Sn
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O
H
CO2Et
OTBS
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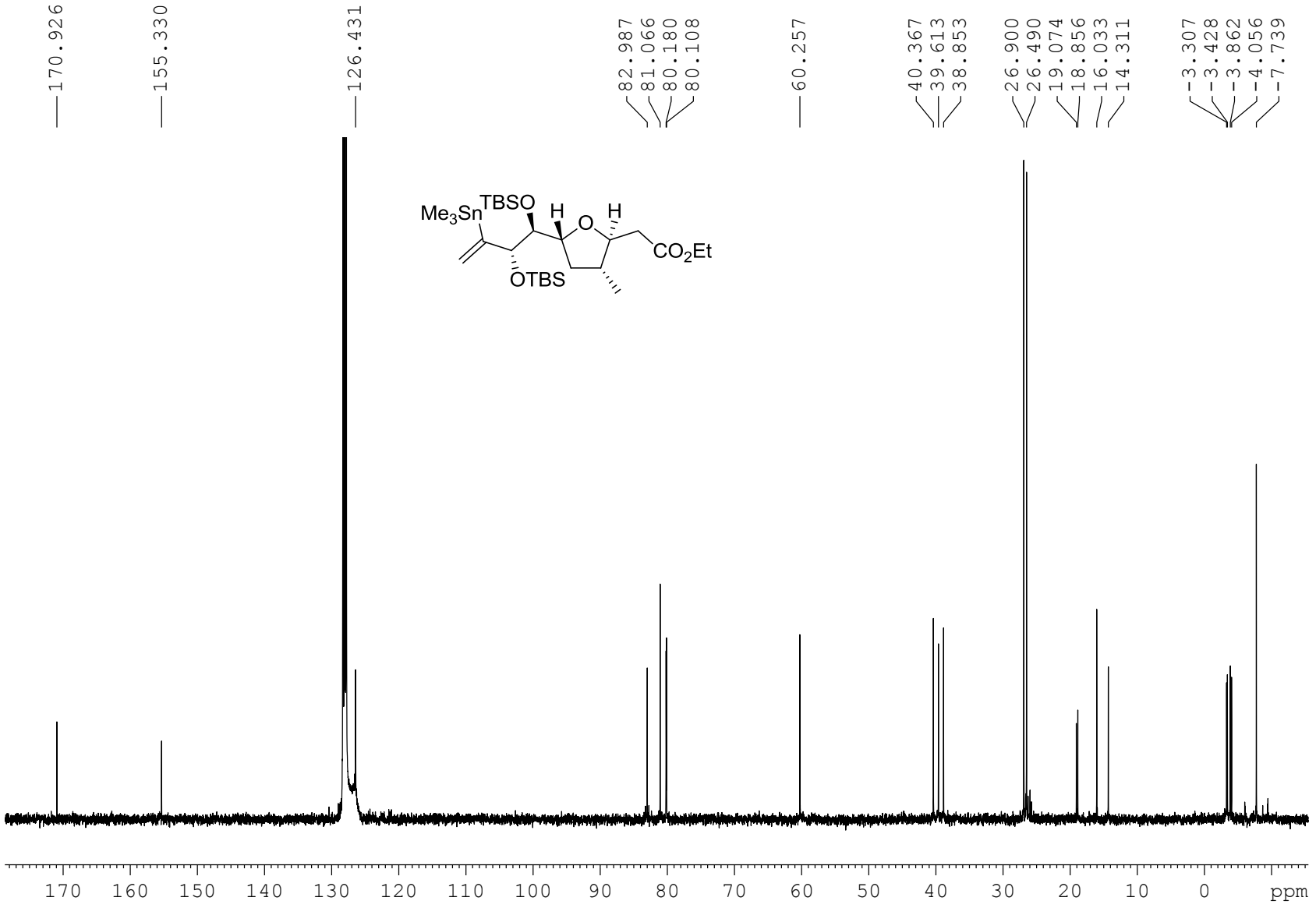
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Me3Sn
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H
O
H
CO2Et
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60
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0
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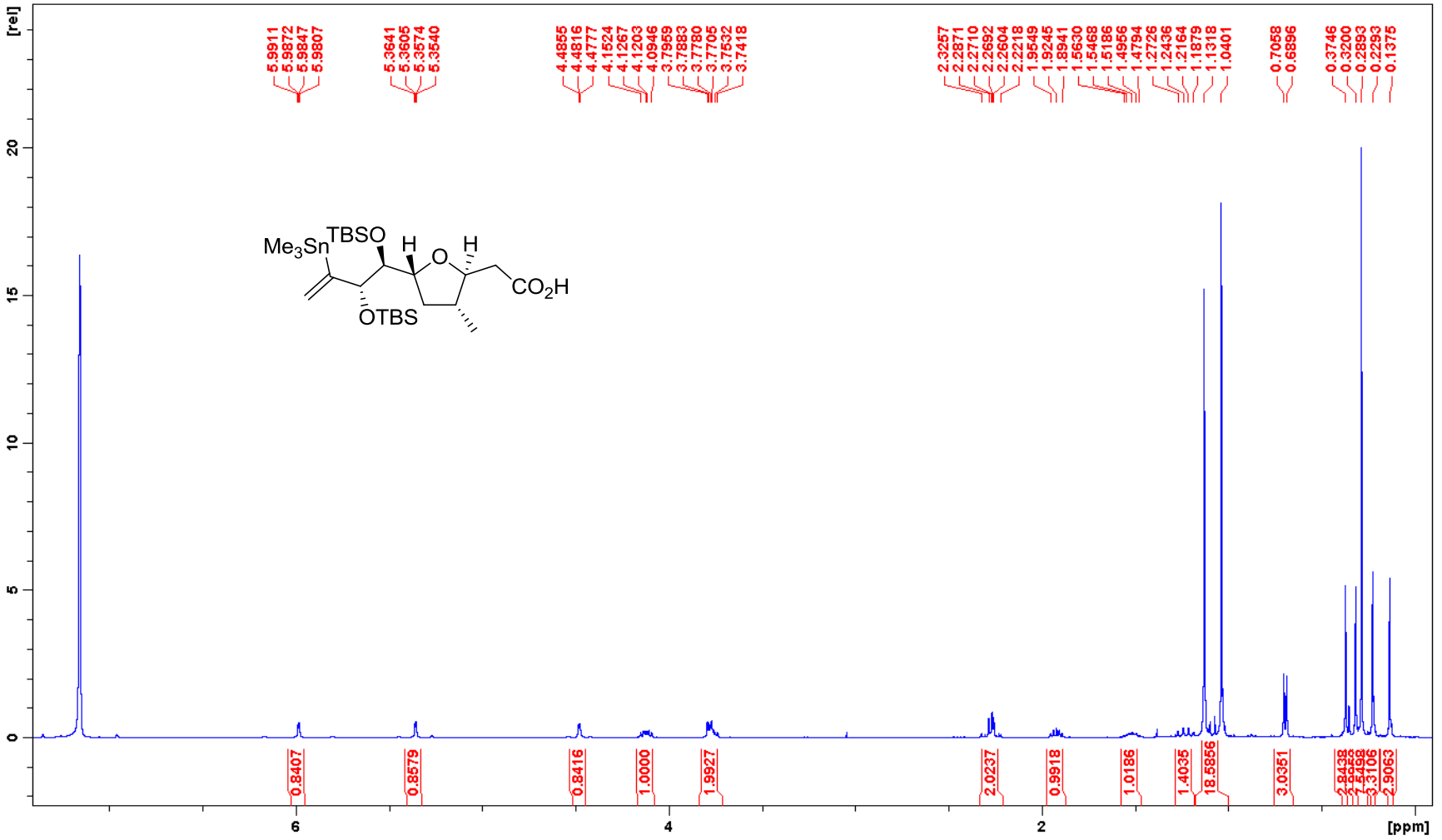
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O
H
CO2H
OTBS
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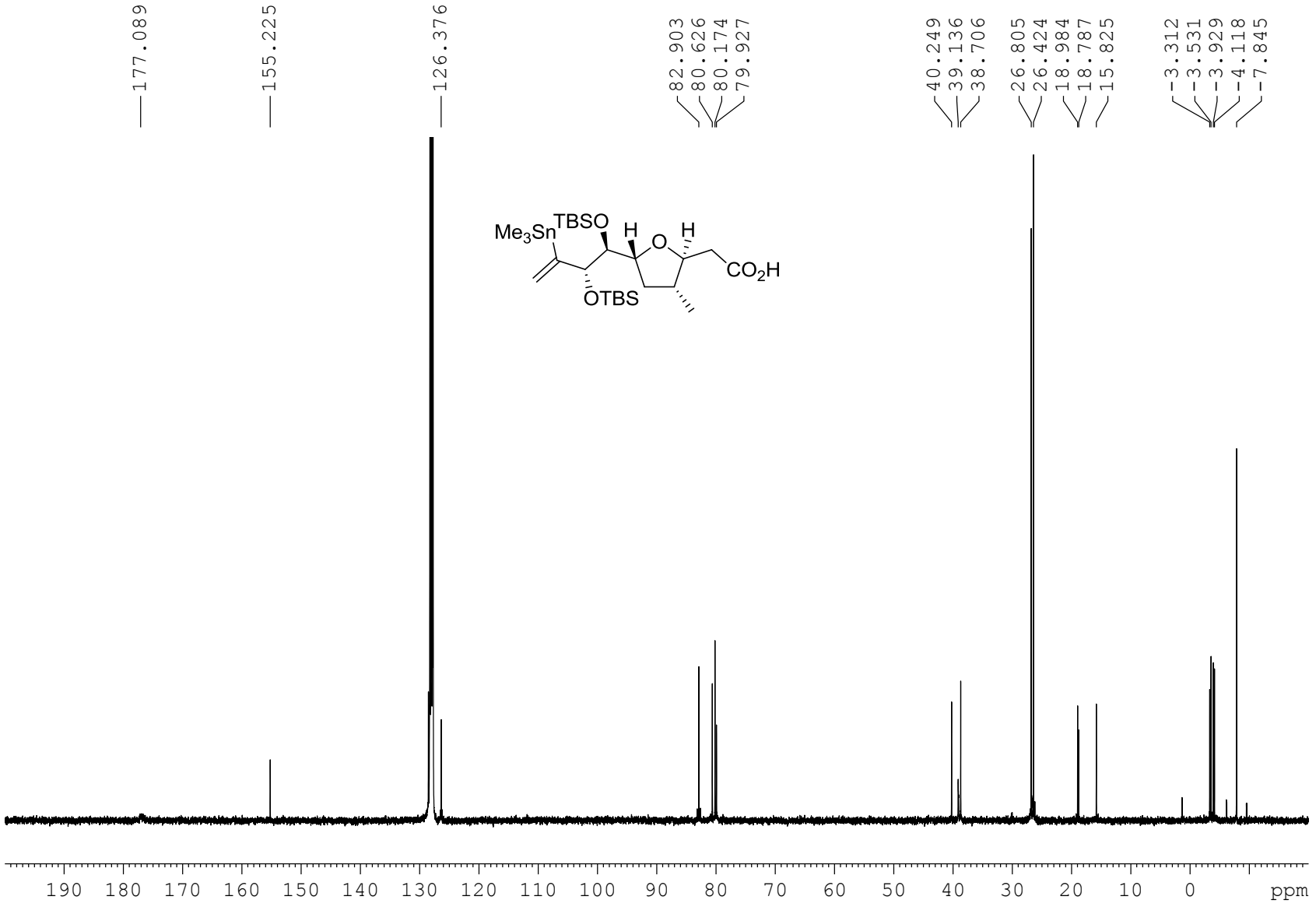
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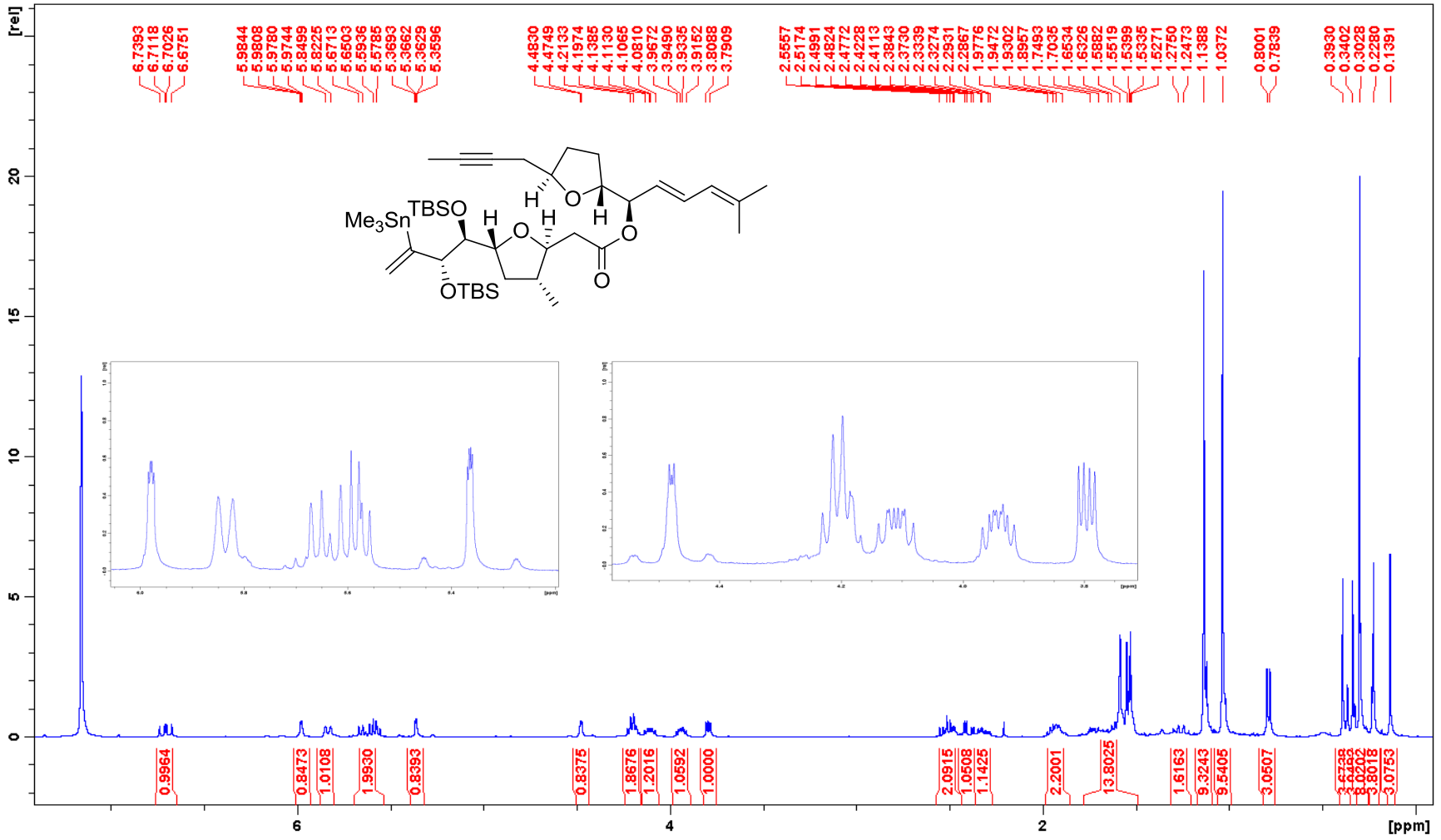
26.424
18.984
18.787
15.825
-3.312
-3.531
-3.929
-4.118
-7.845
Me3Sn
TBSO
H
O
H
CO2H
OTBS
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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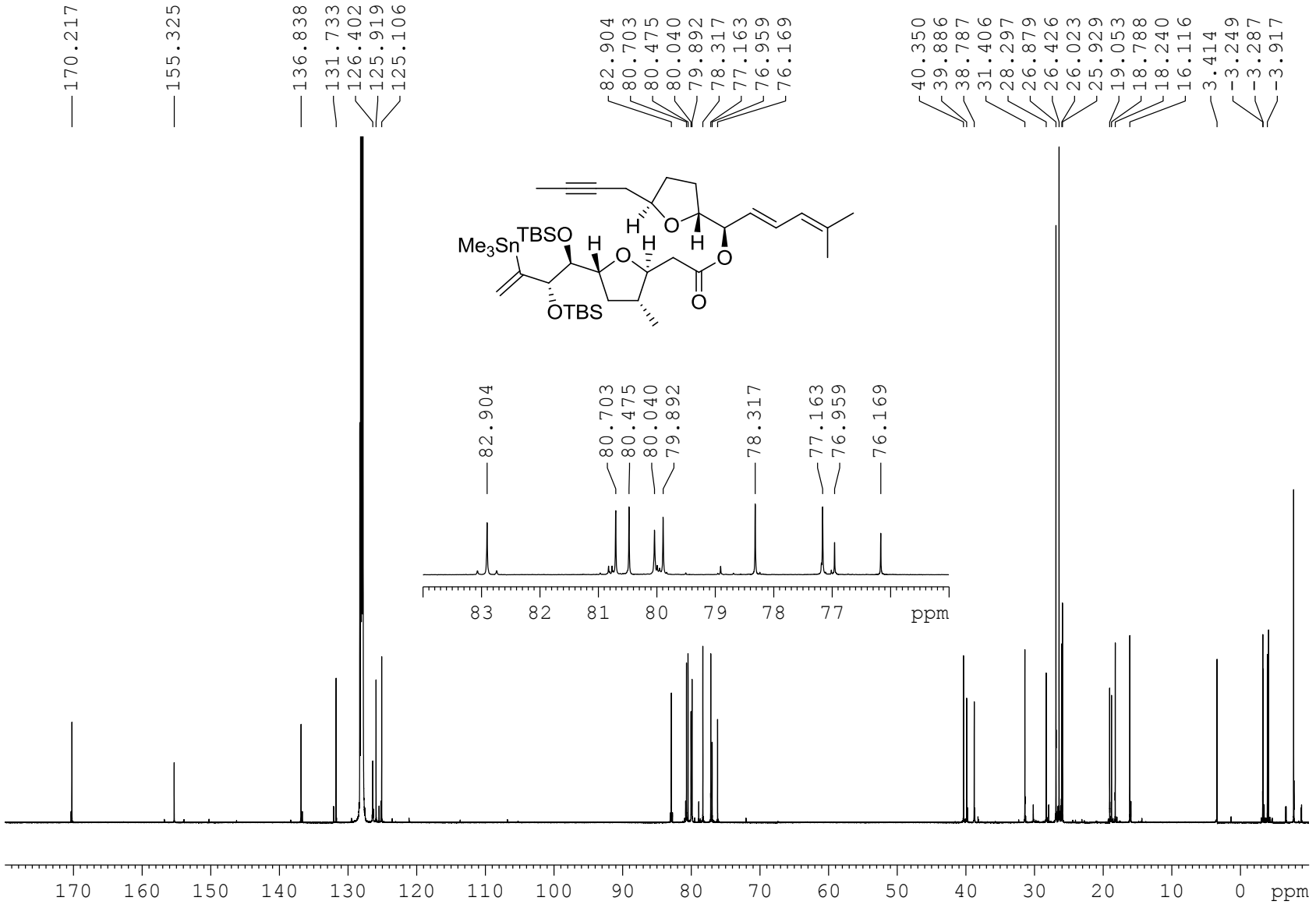
6.7393 6.7118 6.7026 6.6751
5.9844 5.9808 5.9780 5.9744 5.8499 5.8225 5.6713 5.6603 5.5936 5.5785 5.3693 5.3662 5.3629 5.3596
4.4830 4.4749 4.2133 4.1974 4.1385 4.1130 4.1065 4.0810 3.9672 3.9490 3.9335 3.9152 3.8088 3.7909
2.5557 2.5174 2.4991 2.4824 2.4772 2.4228 2.4113 2.3843 2.3730 2.3339 2.3274 2.2931 2.2867 1.9776 1.9472 1.9302 1.8957 1.7493 1.7035 1.6534 1.6326 1.5882 1.5519 1.5399 1.5335 1.5271 1.2750 1.2473 1.1388 1.0372
0.8001 0.7839
0.3930 0.3402 0.3028 0.2280 0.1391
Me3Sn
TBSO
OTBS
H
O
0.9564 0.8473 1.0108 1.9930 0.8393 0.8375 1.8676 1.2016 1.0592 1.0000 2.0915 1.0508 1.1425 2.2001 13.8025 1.6163 9.3243 9.5405 3.0507 2.6238 3.6483 8.0202 3.8018 3.0753
6
4
2
[ppm]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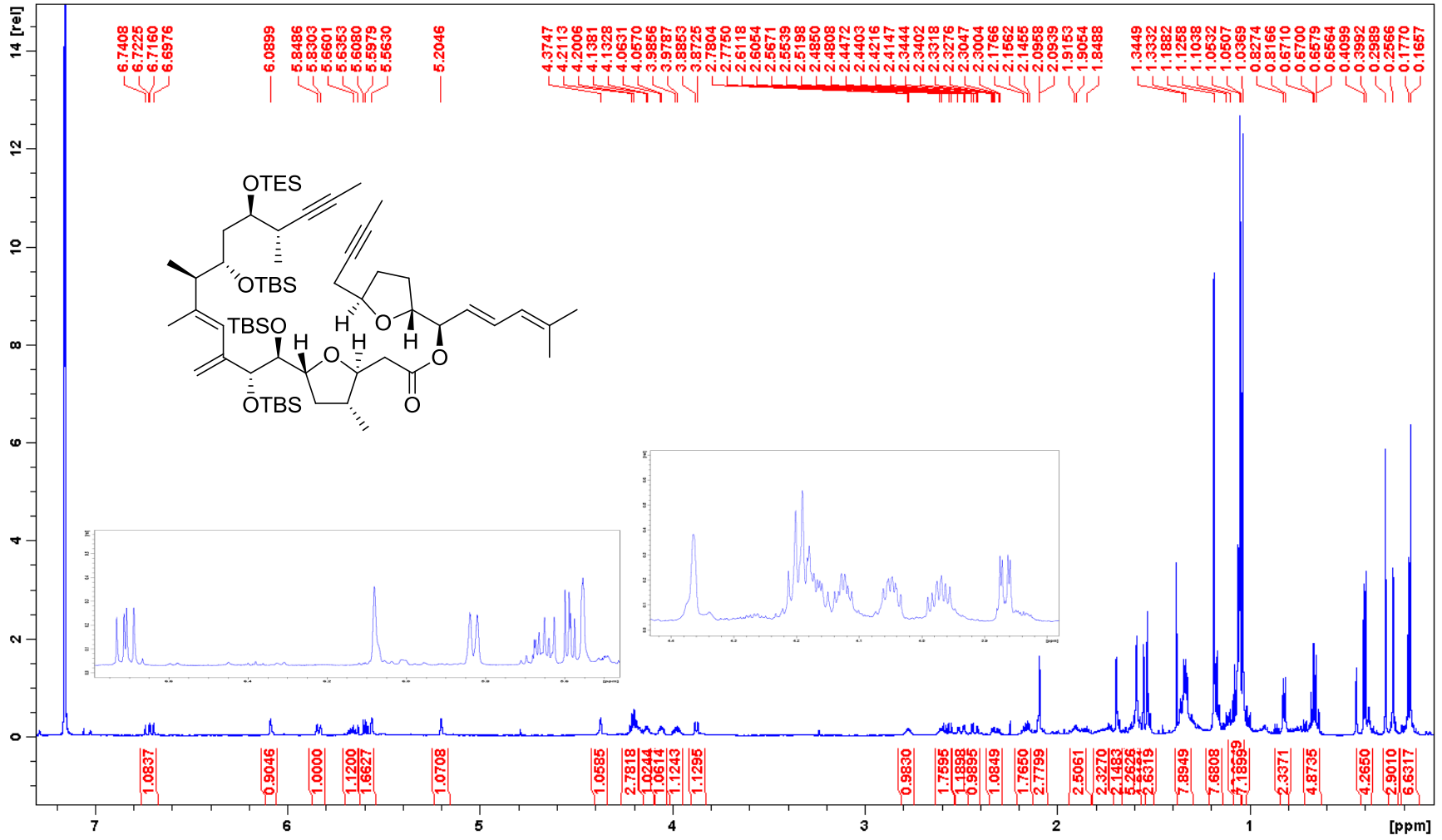
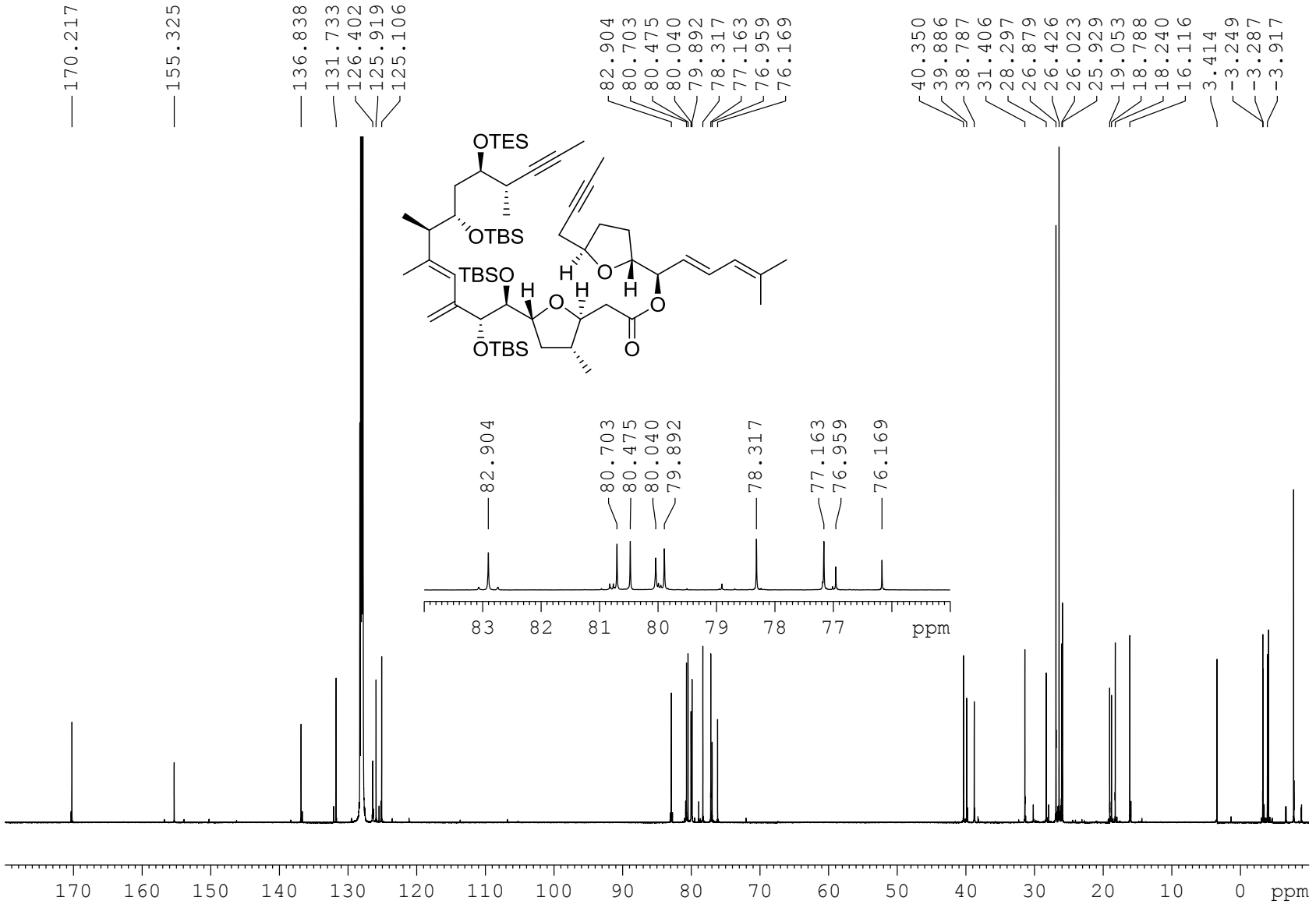
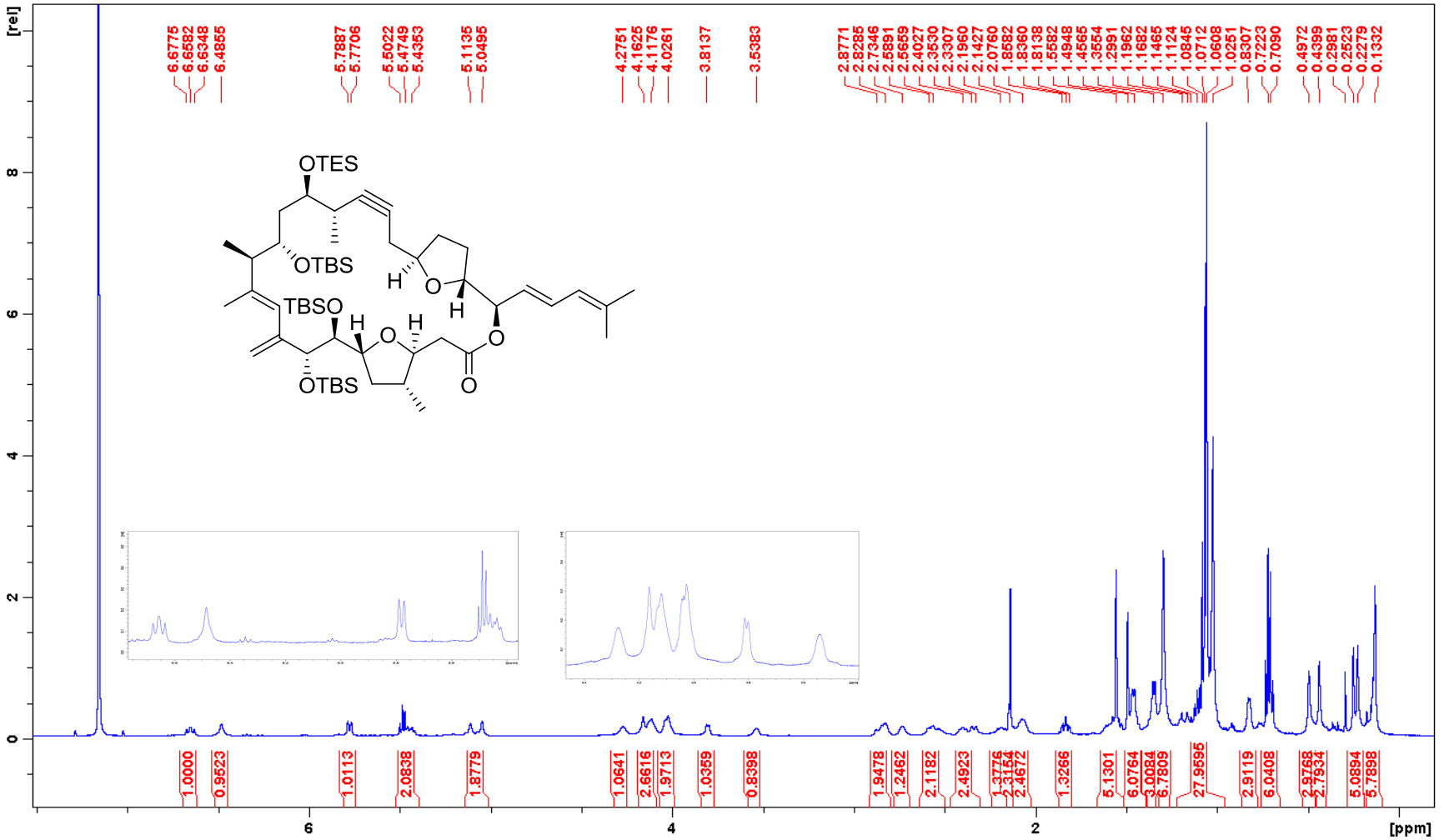
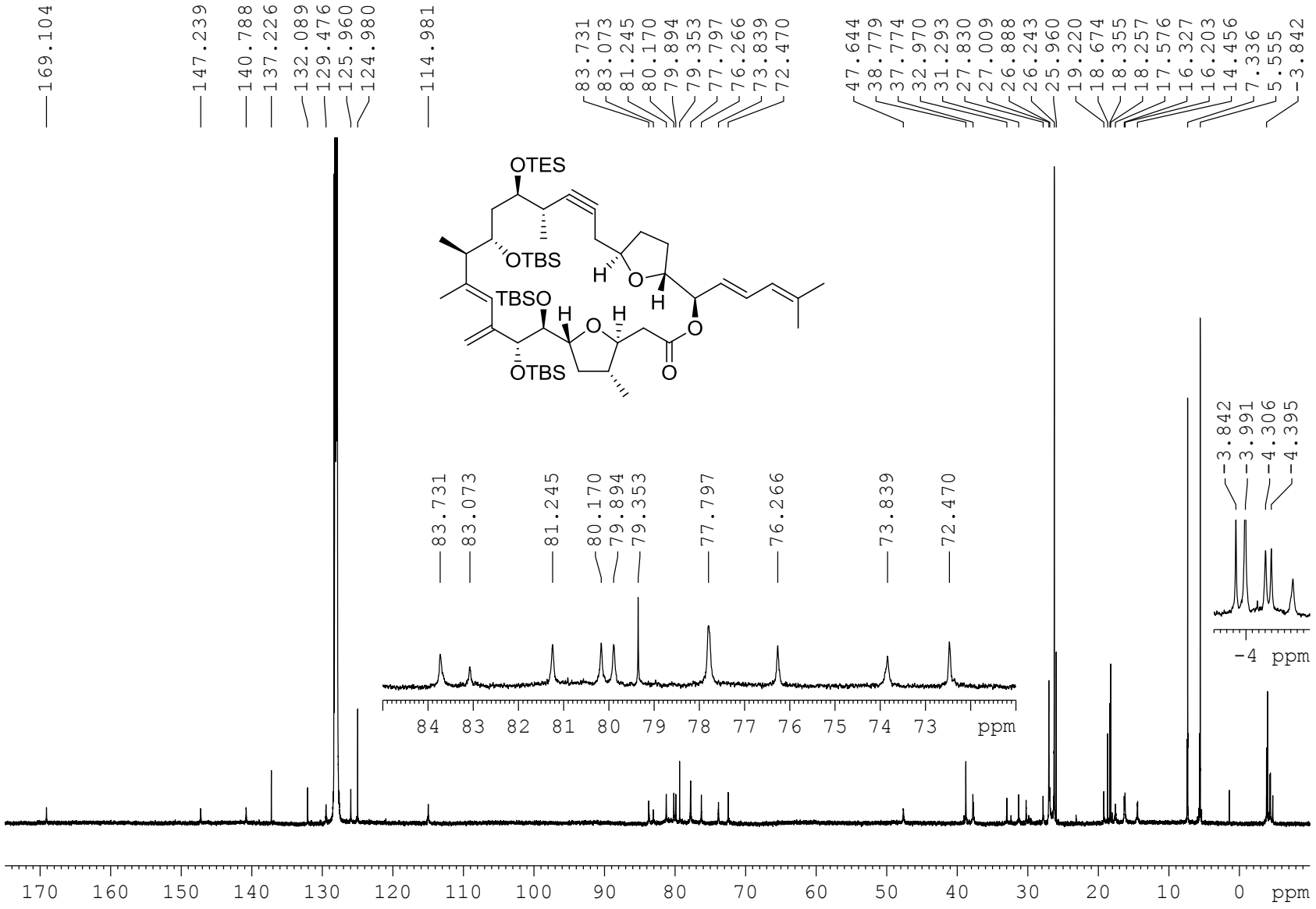
155.325
136.838
131.733
126.402
125.919
125.106
82.904
80.703
80.475
80.040
79.892
78.317
77.163
76.959
76.169
40.350
39.886
38.787
31.406
28.297
26.879
26.426
26.023
25.929
19.053
18.788
18.240
16.116
3.414
-3.249
-3.287
-3.917
Me3Sn
TBSO
OTBS
H
O
ppm


OTES
OTBS
TBSO
H
O
H
H
O
H
O
OTBS
O
14 [rel]
12
10
8
6
4
2
0
7
6
5
4
3
2
1
[ppm]


170.217
155.325
136.838
131.733
126.402
125.919
125.106
82.904
80.703
80.475
80.040
79.892
78.317
77.163
76.959
76.169
40.350
39.886
38.787
31.406
28.297
26.879
26.426
26.023
25.929
19.053
18.788
18.240
16.116
3.414
-3.249
-3.287
-3.917
OTES
OTBS
TBSO
OTBS
H
O
H
H
O
H
O
O
83
82
81
80
79
78
77
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


[rel]
[ppm]
OTES
OTBS
TBSO
OTBS
H
O
H
H
O
H
O
O
6.6775
6.6582
6.6348
6.4855
5.7887
5.7706
5.5022
5.4749
5.4353
5.1135
5.0495
4.2751
4.1625
4.1176
4.0261
3.8137
3.5383
2.8771
2.8285
2.7346
2.5891
2.5659
2.4027
2.3530
2.3307
2.1960
2.1427
2.0760
1.8582
1.8360
1.8138
1.5582
1.4948
1.4565
1.3554
1.2991
1.1962
1.1682
1.1465
1.1124
1.0845
1.0712
1.0608
1.0251
0.8307
0.7223
0.7090
0.4972
0.4399
0.2981
0.2523
0.2279
0.1332
1.0000
0.9523
1.0113
2.0838
1.8779
1.0641
2.6616
1.9713
1.0359
0.8398
1.9478
1.2462
2.1182
2.4923
1.3776
2.3154
2.4672
1.3266
5.1301
6.0764
3.0084
6.7809
27.9595
2.9119
6.0408
2.9768
2.7934
5.0894
5.7898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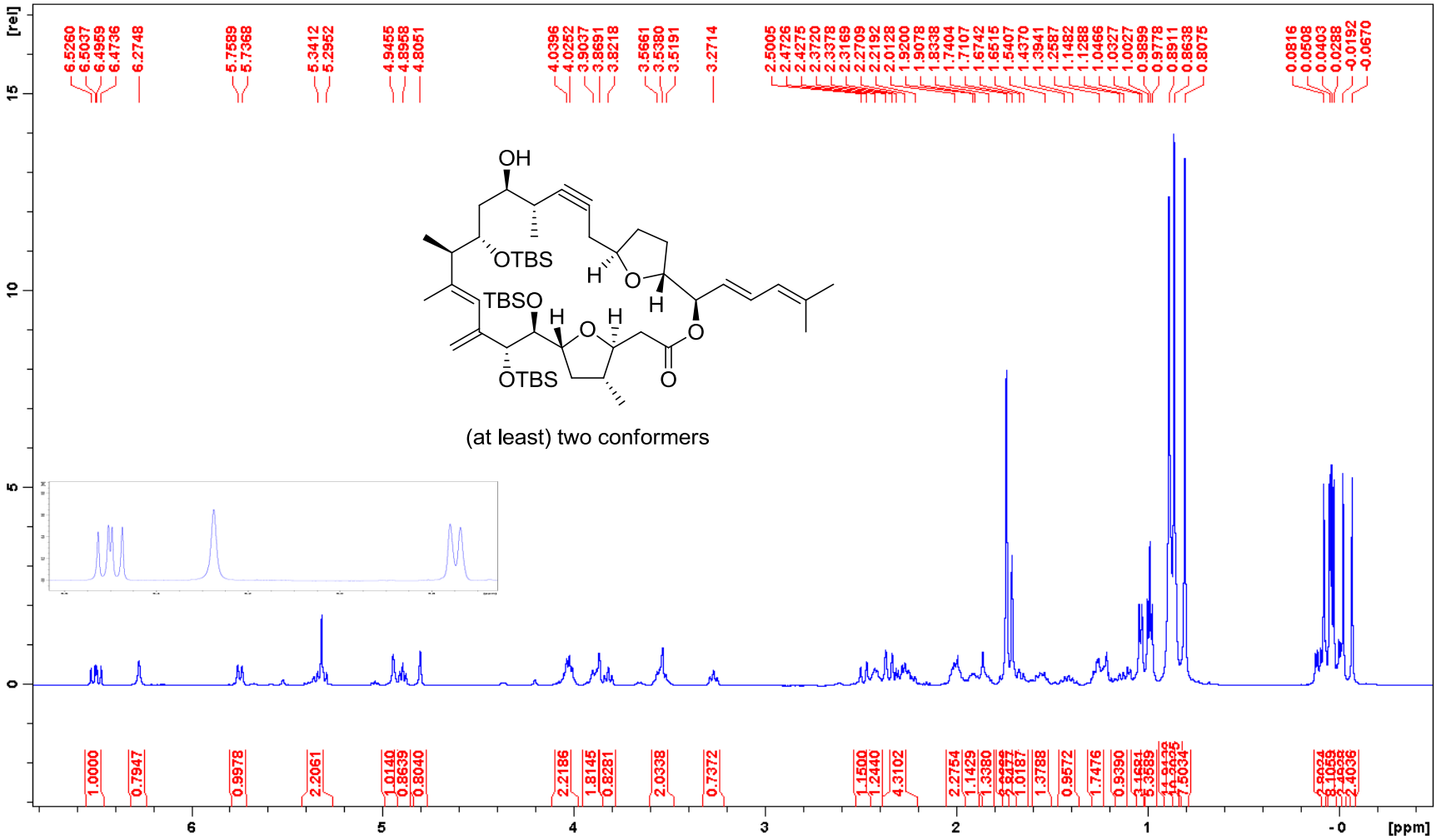
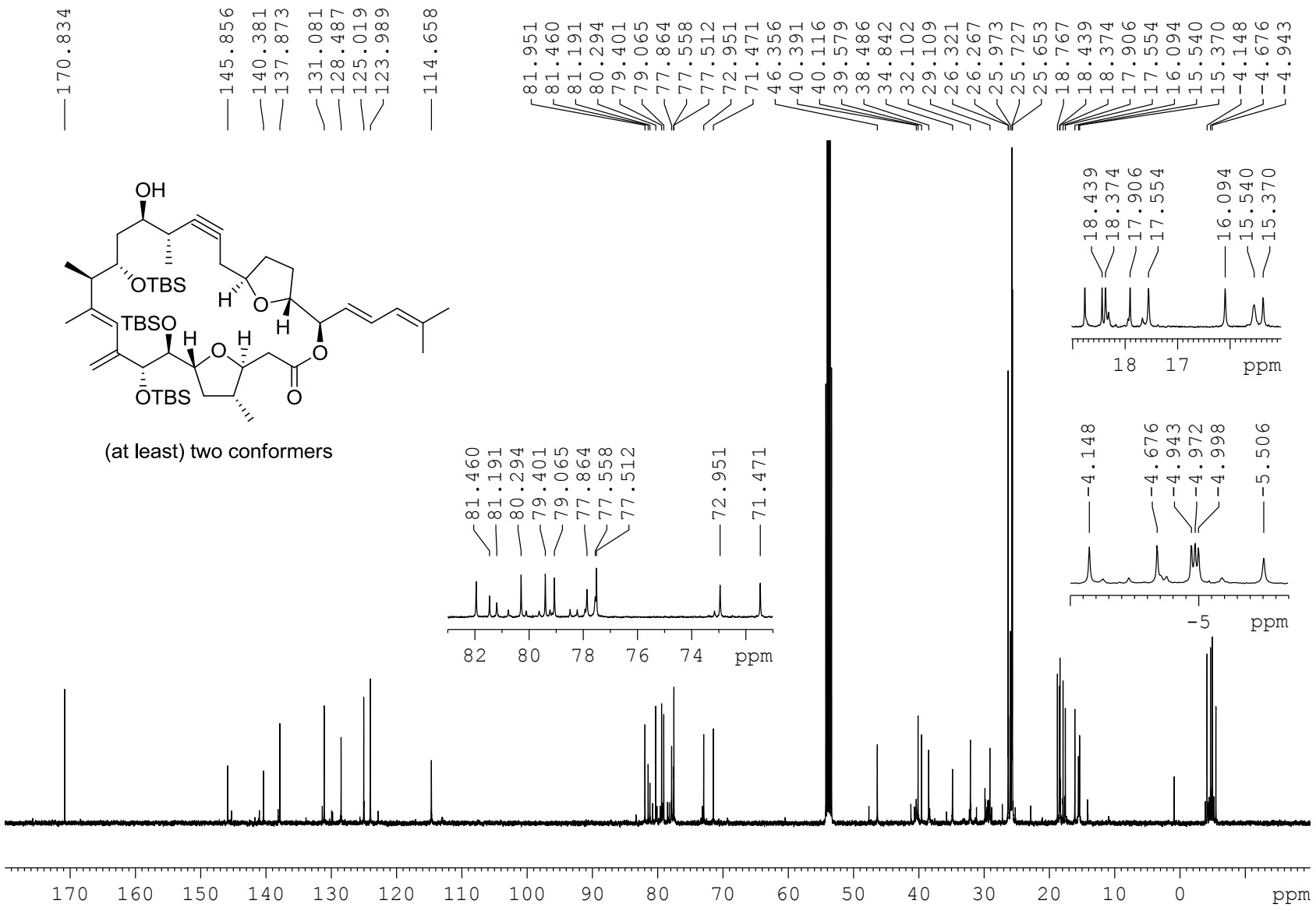
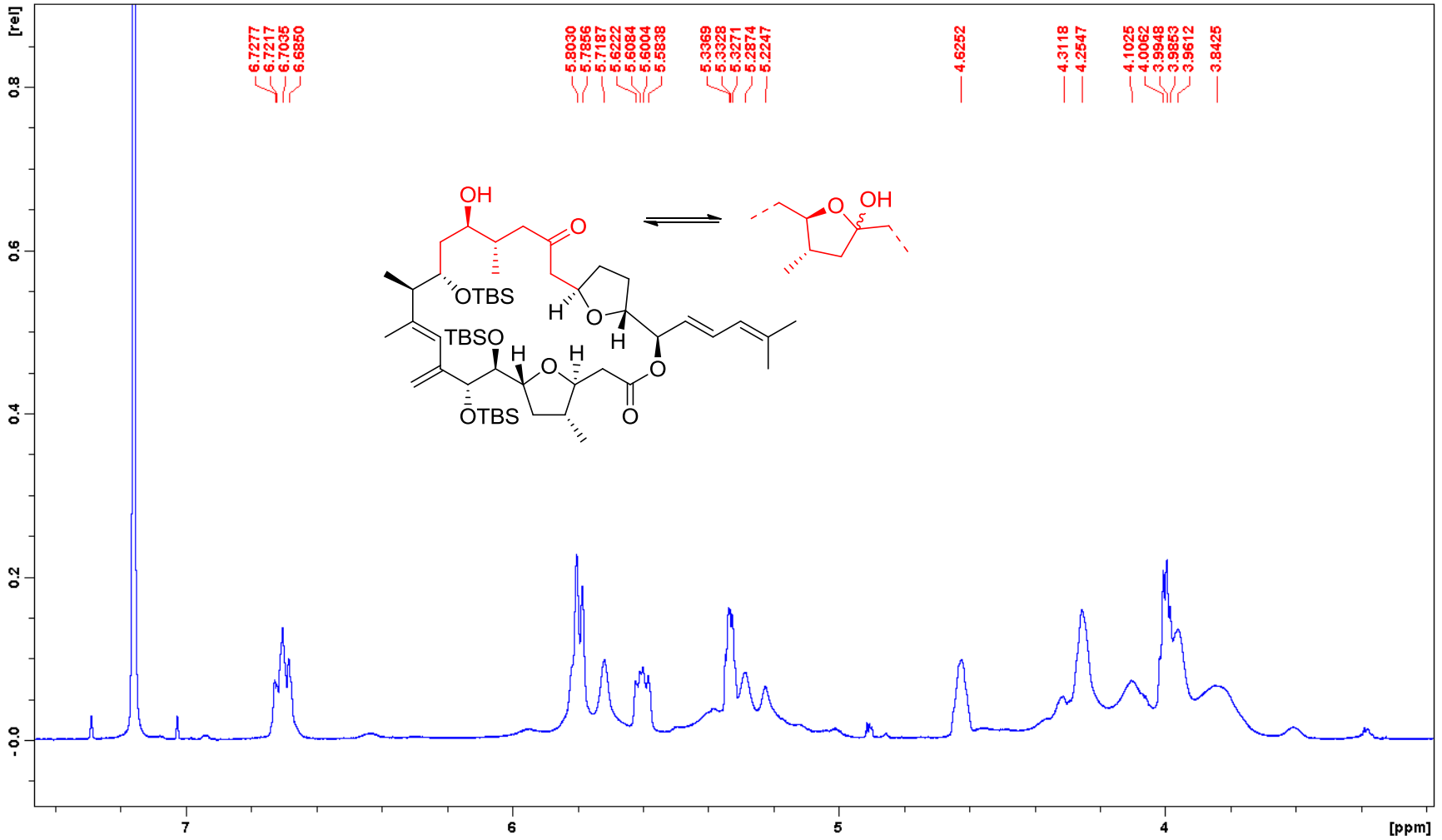
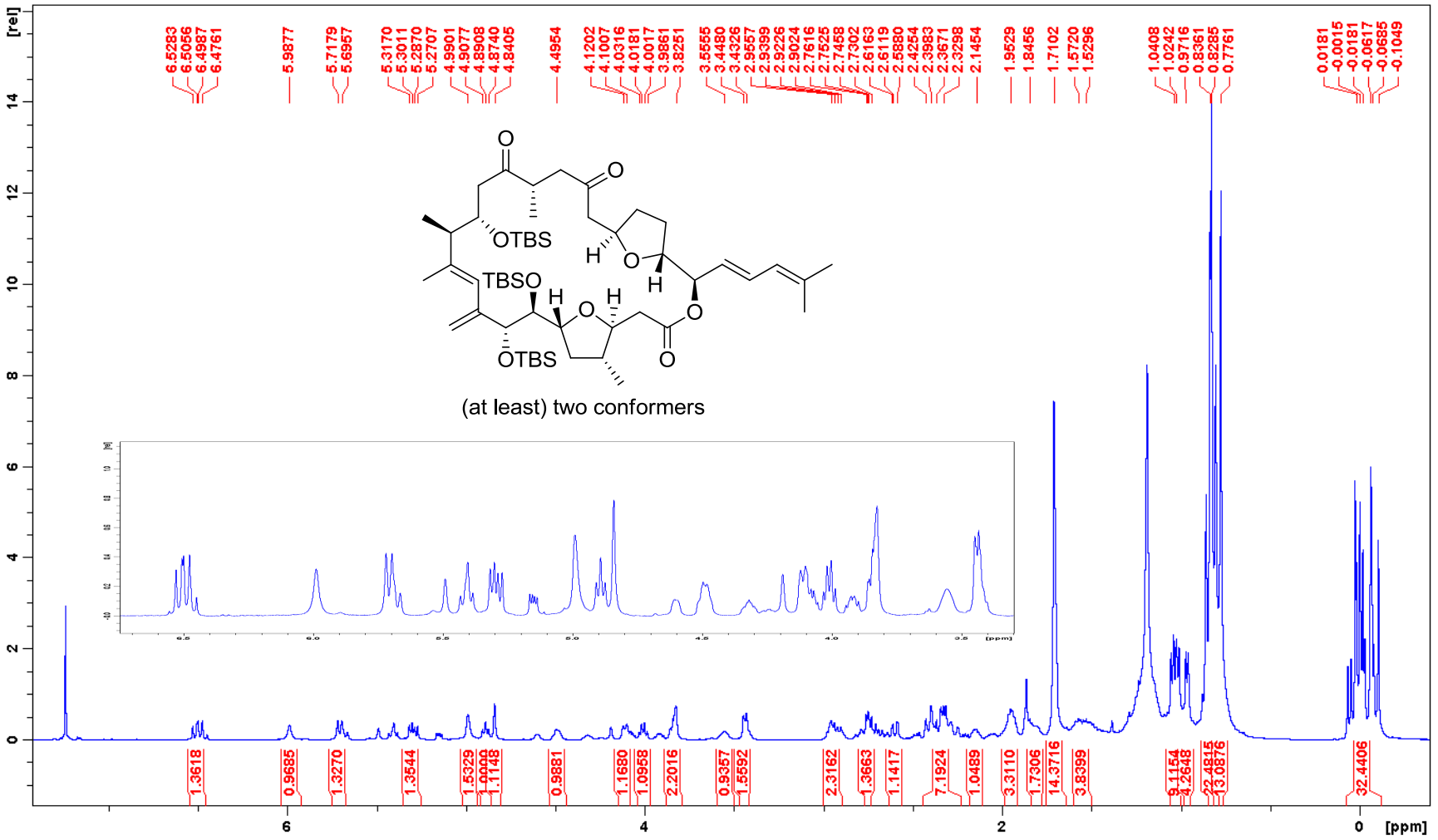
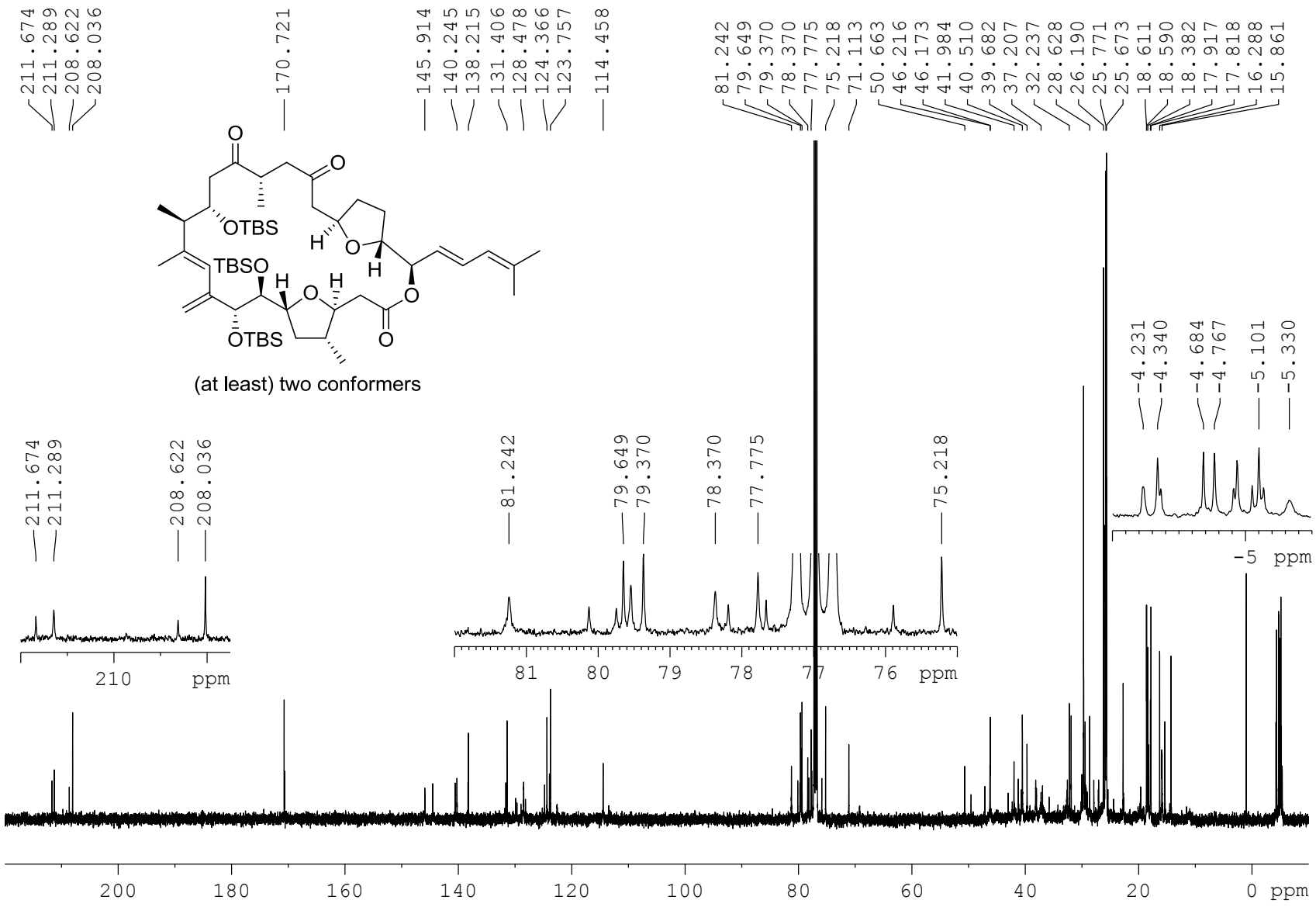
140.788
137.226
132.089
129.476
125.960
124.980
114.981
83.731
83.073
81.245
80.170
79.894
79.353
77.797
76.266
73.839
72.470
47.644
38.779
37.774
32.970
31.293
27.830
27.009
26.888
26.243
25.960
19.220
18.674
18.355
18.257
17.576
16.327
16.203
14.456
7.336
5.555
-3.842
OTES
OTBS
TBSO
OTBS
H
O
H
H
O
H
O
O
-3.842
-3.991
-4.306
-4.395
-4 ppm
84 83 82 81 80 79 78 77 76 75 74 73 ppm
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


[rel]
15
10
5
0
6.5260
6.5037
6.4959
6.4736
6.2748
5.7589
5.7368
5.3412
5.2952
4.9455
4.8958
4.8051
4.0396
4.0252
3.9037
3.8691
3.8218
3.5661
3.5380
3.5191
3.2714
2.5005
2.4726
2.4275
2.3720
2.3378
2.3169
2.2709
2.2192
2.0128
1.9200
1.9078
1.8338
1.7404
1.7107
1.6742
1.6515
1.5407
1.4370
1.3941
1.2587
1.1482
1.1288
1.0466
1.0327
1.0027
0.9899
0.9778
0.8911
0.8638
0.8075
0.0816
0.0508
0.0403
0.0288
-0.0192
-0.0670
OH
OTBS
TBSO
OTBS
H
O
H
H
O
H
O
O
(at least) two conformers
1.0000
0.7947
0.9978
2.2061
1.0140
0.8639
0.8040
2.2186
1.8145
0.8281
2.0338
0.7372
1.1500
1.2440
4.3102
2.2754
1.1429
1.3380
1.0187
1.3788
0.9572
1.7476
0.9390
3.1681
5.3589
7.5034
6
5
4
3
2
1
-0
[ppm]

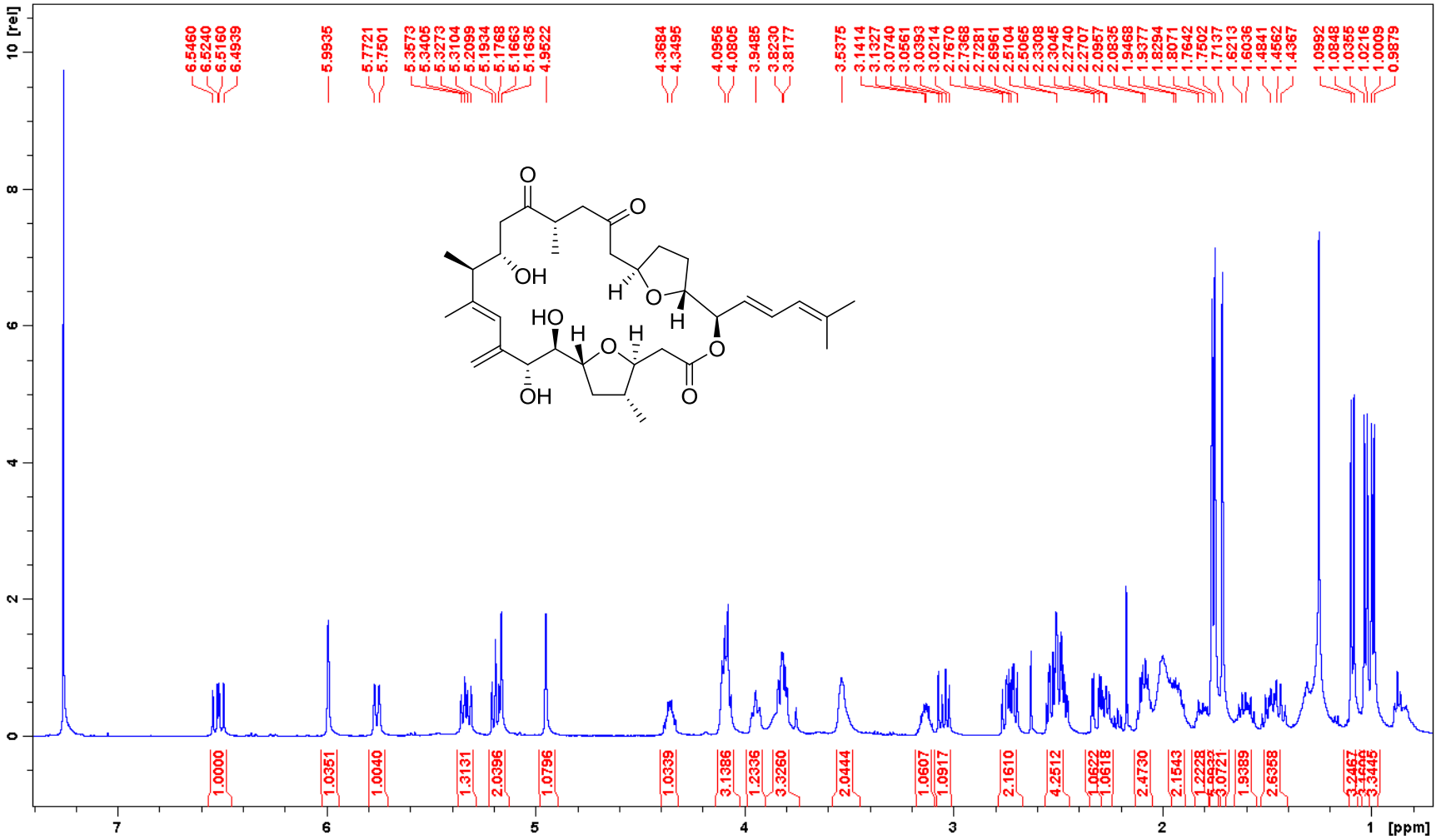

170.834
145.856
140.381
137.873
131.081
128.487
125.019
123.989
114.658
81.951
81.460
81.191
80.294
79.401
79.065
77.864
77.558
77.512
72.951
71.471
46.356
40.391
40.116
39.579
38.486
34.842
32.102
29.109
26.321
26.267
25.973
25.727
25.653
18.767
18.439
18.374
17.906
17.554
16.094
15.540
15.370
-4.148
-4.676
-4.943
-4.943
OH
OTBS
TBSO
OTBS
H
O
O
(at least) two conformers
ppm
ppm
ppm
ppm


6.7277
6.7217
6.7035
6.6850
5.8030
5.7856
5.7187
5.6222
5.6084
5.6004
5.5838
5.3369
5.3328
5.3271
5.2874
5.2247
4.6252
4.3118
4.2547
4.1025
4.0062
3.9948
3.9853
3.9612
3.8425
[rel]
0.8
0.6
0.4
0.2
-0.0
7
6
5
4
[ppm]
OH
O
OTBS
TBSO
OTBS
H
O
H
O
H
O
O
O
OH

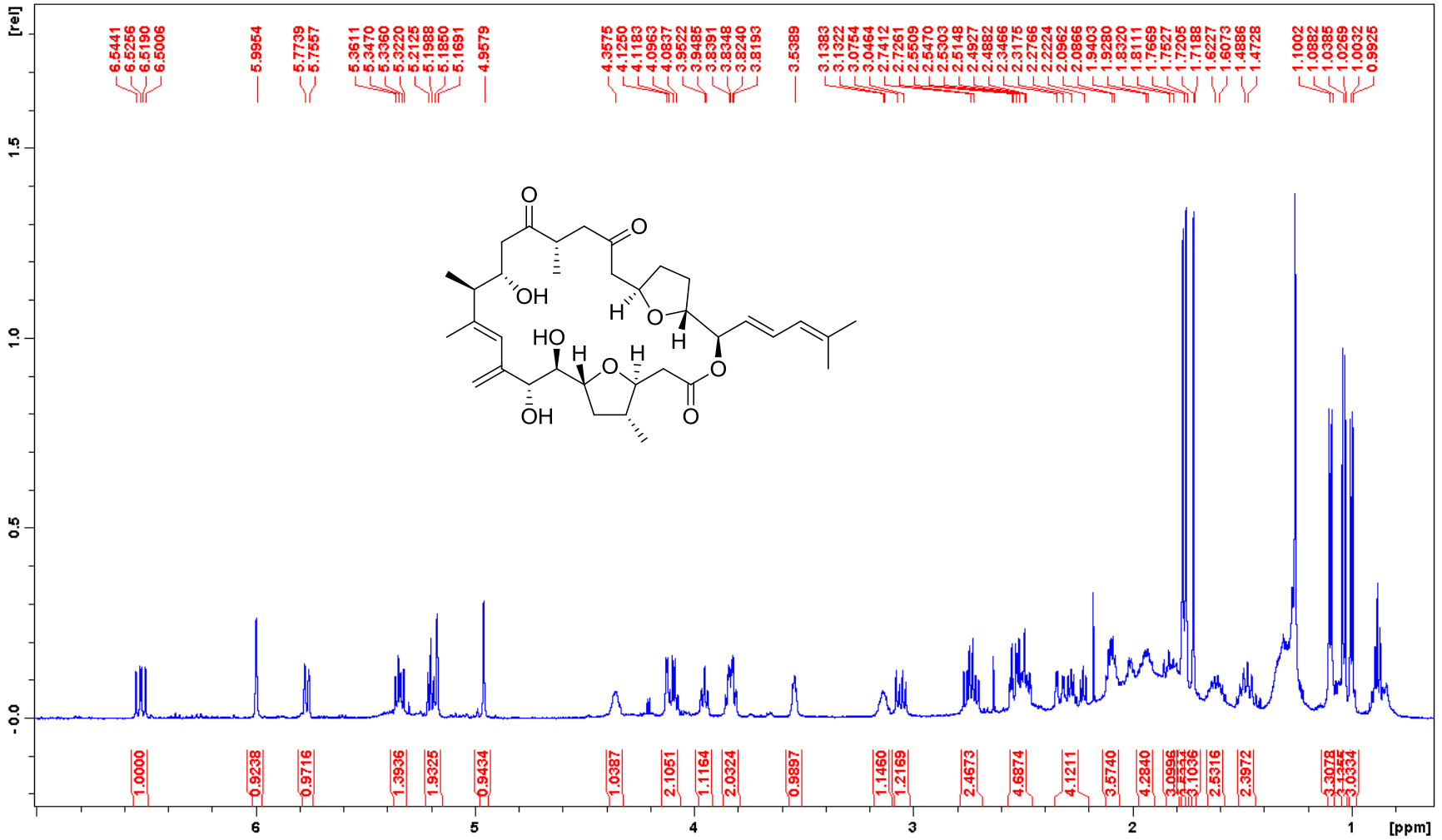

[rel]
6.5283
6.5056
6.4987
6.4761
5.9877
5.7179
5.6957
5.3170
5.3011
5.2870
5.2707
4.9901
4.9077
4.8908
4.8740
4.8405
4.4954
4.1202
4.1007
4.0316
4.0181
4.0017
3.9861
3.8251
3.5555
3.4480
3.4326
2.9557
2.9399
2.9226
2.9024
2.7616
2.7525
2.7458
2.7302
2.6163
2.6119
2.5880
2.4254
2.3983
2.3671
2.3298
2.1454
1.9529
1.8456
1.7102
1.5720
1.5296
1.0408
1.0242
0.9716
0.8361
0.8285
0.7761
0.0181
-0.0015
-0.0181
-0.0617
-0.0685
-0.1049
OTBS
TBSO
OTBS
(at least) two conformers
1.3618
0.9685
1.3270
1.3544
1.5329
1.0000
1.1148
0.9881
1.1680
1.0958
2.2016
0.9357
1.5592
2.3162
1.3663
1.1417
7.1924
1.0489
3.3110
1.7306
14.3716
3.8399
9.1154
4.2648
22.4815
13.0876
32.4406
[ppm]

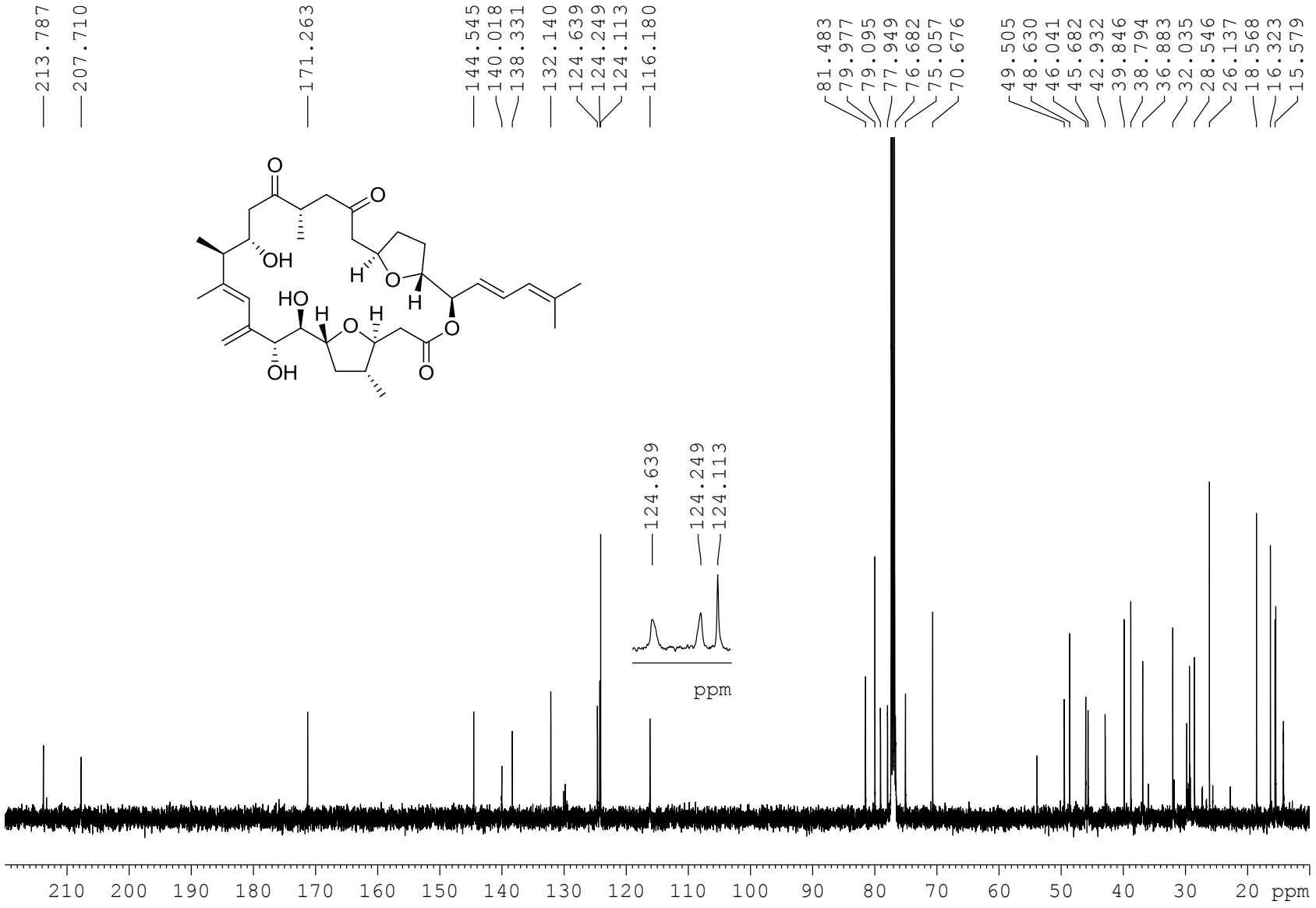

211.674
211.289
208.622
208.036
170.721
145.914
140.245
138.215
131.406
128.478
124.366
123.757
114.458
81.242
79.649
79.370
78.370
77.775
75.218
71.113
50.663
46.216
46.173
41.984
40.510
39.682
37.207
32.237
28.628
26.190
25.771
25.673
18.611
18.590
18.382
17.917
17.818
16.288
15.861
-4.231
-4.340
-4.684
-4.767
-5.101
-5.330
OTBS
TBSO
OTBS
(at least) two conformers
210 ppm
81 80 79 78 77 76 ppm
-5 ppm
200 180 160 140 120 100 80 60 40 20 0 ppm

1.4 mg in 180 µL – 500 MHz

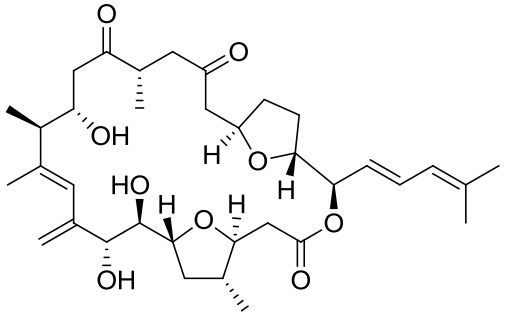


0.4 mg in 180 µL – 600 MHz



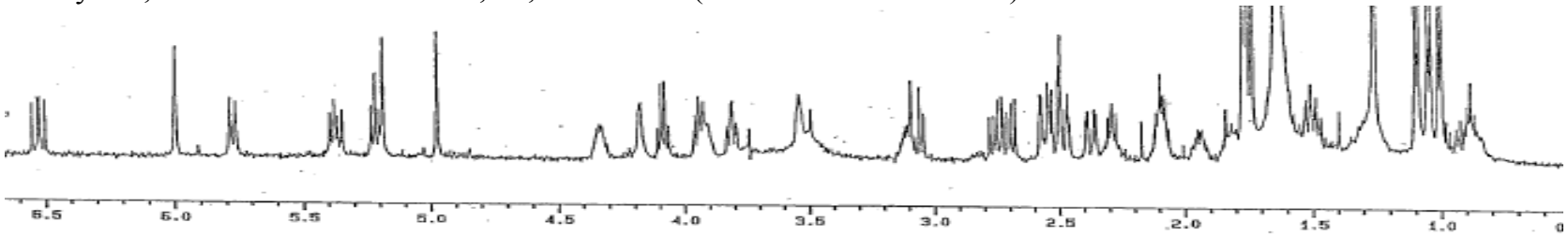

213.787
207.710
171.263
144.545
140.018
138.331
132.140
124.639
124.249
124.113
116.180
81.483
79.977
79.095
77.949
76.682
75.057
70.676
49.505
48.630
46.041
45.682
42.932
39.846
38.794
36.883
32.035
28.546
26.137
18.568
16.323
15.579
O
O
OH
H
O
H
HO
H
H
O
O
OH
O
124.639
124.249
124.113
ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

Comparison of ^{1}H spectra of amphidinolide F:



Fürstner *et al.* (1.4 mg in 180 μL).

Kobayashi, J. *et al. J. Antibiot.* **1991**, *44*, 1259-1261 (unknown concentration).



Carter, R. G. *et al. Angew. Chem. Int. Ed.* **2012**, *51*, 7948-7951 (1.4 mg in 180 μL).