SUPPORTING INFORMATION

Total Synthesis of (–)-Sinulariadiolide. A Transannular Approach

Zhanchao Meng and Alois Fürstner*

Max-Planck-Institut für Kohlenforschung, D-45470 Mülheim /Ruhr, Germany

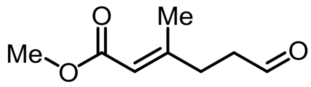
email: fuerstner@kofo.mpg.de

Table of Contents

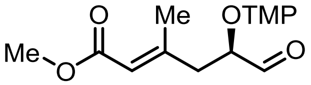
Experimental Details and Characterization Data

General. Unless stated otherwise, all reactions were carried out in flame-dried glassware using anhydrous solvents under argon. The solvents were purified by distillation over the following drying agents and were transferred under argon: THF, Et_2O (Mg/anthracene), toluene (Na/K), CH_2Cl_2 (CaH_2), MeOH (Mg, stored over MS 3 Å); DMF, MeCN, Et_3N, pentane and pyridine were dried by an adsorption solvent purification system based on molecular sieves. Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM®SIL/UV254); Flash chromatography: Merck silica gel 60 (40–63 µm) with predistilled or HPLC grade solvents; Celite® was dried at 170°C for 48 h under high vacuum (1×10^{-3} mbar) and stored under argon. NMR: Spectra were recorded on Bruker DPX 300, AV 400, AV 500 or AVIII 600 spectrometers in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δ_C = 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm). IR: Spectrum One (Perkin-Elmer) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FTMS (7 T magnet) or Mat 95 (Finnigan). Optical rotations ($[\alpha]_{\boldsymbol{D}}^{\boldsymbol{20}}$) were measured with a Perkin-Elmer Model 343 polarimeter. LC-MS analyses were conducted on a Shimadzu LC/MS 2020 instrument (pumps LC-20AD, autosampler SIL-20AC, column oven CTO-20AC, diode array detector SPD-M20A, controller CBM-20A, ESI detector and software Labsolutions) with an ZORBAX Eclipse Plus C18 1.8 µm, 3.0 or 4.6 mm ID × 50 mm (Agilent). A binary gradient of MeCN or MeOH in water or aq. triethylammonium acetate buffer (pH 8) was used at a flow rate of 0.5 (3.0 mm ID) or 0.8 (4.6 mm ID) mL/min. The oven temperature was kept at 35 °C and the detection wave length at 254 nm. Preparative LC was performed with a Shimadzu LC-20A prominence system (pumps LC-20AP, column oven CTO-20AC, diode array detector SPD-M20A, fraction collector FRC-10A, controller CBM-20A and software LC-solution); conditions for each compound are specified below. ee-Determinations were performed by HPLC or GC using the chiral stationary phases under the conditions specified below. Unless stated otherwise, all commercially available compounds (Alfa Aesar, Aldrich, TCI, Strem Chemicals) were used as received.

Methyl (*E*)-3-methyl-6-oxohex-2-enoate (4). Dimethyl sulfate (3.0 mL, 31.7 mmol) was added to a solution of the geranic acid **3** (85% pure, 5.0 g, 29.7 mmol) and diisopropylethylamine (5.7 mL, 32.7 mmol) in MeCN (6 mL) at 0 °C. After stirring for 6 h, the mixture was diluted with CH_2Cl_2 (200 mL) and cooled to –78 °C. Ozone gas was bubbled through this solution at –78 °C for 3 h. At this point, excess ozone was removed by bubbling argon through the solution for 30 min. Triphenylphosphine (1.03 g, 3.93 mmol) was then added and stirring continued at −78 °C for 30 min and for 1 h at ambient temperature. The mixture was then washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/EtOAc, 15:1 to 4:1) to afford the title compound as a yellow oil (2.71 g, 58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (t, *J* = 1.3 Hz, 1H), 5.66 (q, *J* = 1.3 Hz, 1H), 3.67 (s, 3H), 2.69–2.57 (m, 2H), 2.48–2.44 (m, 2H), 2.16 (d, *J* = 1.3 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.5, 166.8, 157.5, 115.9, 50.9, 41.3, 32.60, 18.8 ppm; IR (film) ν = 2951, 1713, 1435, 1149, 1081 cm^{-1}; MS (EI): *m/z* (%) 41 (100%), 67 (62%), 95 (44%); HRMS (ESI): *m/z* calcd. for $C_8H_{12}O_3Na$ $[M+Na]^+$: 179.06786, found: 179.06787.

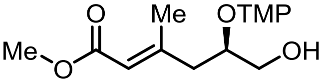


Methyl (*R*,*E*)-3-methyl-6-oxo-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hex-2-enoate (5). Catalyst **8**·HBF_4 (979 mg, 3.20 mmol)[1] and $CuCl_2$ (206 mg, 1.53 mmol) were added to a stirred solution of compound **4** (2.0 g, 12.8 mmol) and oven-dried molecular sieves (4 Å, ca. 500 mg) in DMF (12 mL) at –10 °C under air. After stirring at this temperature for 10 min, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (2.0 g, 12.8 mmol) was added in portions to the resulting green solution. Stirring was continued at –10 °C for 24 h before the mixture was diluted with *tert*-butyl methyl ether (10 mL) and the reaction quenched with sat. aq. NH_4Cl (2 mL) and water (5 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 50 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 10:1 to 8:1) to afford the title compound as a colorless oil (3.24 g, 81%). $[\alpha]_D^{20}$ = 74.0 (c = 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.81 (d, *J* = 4.2 Hz, 1H), 5.71 (q, *J* = 1.2, 1.2, 1.2 Hz, 1H), 4.31 (td, *J* = 6.7, 6.7, 4.2 Hz, 1H), 3.670 (s, 3H), 2.58 (ddd, *J* = 14.1, 6.5, 1.1 Hz, 1H), 2.48 (ddd, *J* = 14.1, 6.9, 1.1 Hz, 1H), 2.20 (d, *J* = 1.3 Hz, 3H), 1.60–1.51 (m, 1H), 1.46–1.41 (m, 4H), 1.34–1.25 (m, 1H), 1.170 (s, 3H), 1.12 (s, 9H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.9, 166.5, 153.8, 118.6, 86.1, 50.9, 41.3, 40.1, 34.3, 33.9, 20.5,

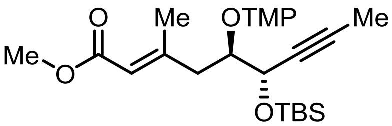


20.3, 19.3, 17.0 ppm; IR (film) ν = 2935, 1722, 1650, 1436, 1361, 1224, 1152 cm^{-1}; MS (ESI): *m*/*z*: 312 [*M*+H$^+$]; 334 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{17}H_{30}NO_4$ [*M*+H$^+$]: 312.21693, found: 312.21681.

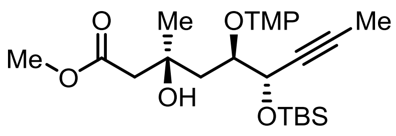
ee-Determination: Methyl (*R,E*)-6-hydroxy-3-methyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)-oxy)hex-2-enoate (S1). Sodium borohydride (64.2 mg, 1.70 mmol) was added to a solution compound **5** (132 mg, 0.429 mmol) in THF/MeOH (4 mL, 1:1) at 0 °C. The mixture was stirred for 30 min at this temperature before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The aqueous layer was extracted with EtOAc (3 x 30 mL), the combined extracts were washed with brine (50 mL), dried over $MgSO_4$ and evaporated. The crude material was purified by flash chromatography on silica (hexanes/EtOAc, 3:1) to afford the title compound as a colorless oil (124 mg, 93%, 65.3% ee). [The ee was determined by HPLC analysis: Daicel 150 mm Chiralcel OZ-3R, 4.6 mm i.D. acetonitrile/water = 60/40, v = 1.0mL·min^{-1}, λ = 220 nm, t (major) = 6.21 min, t (minor) = 6.56 min.]. $[\alpha]_D^{20}$ = 29.0 (c = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (d, *J* = 7.2 Hz, 1H), 5.72 (q, *J* = 1.5, 1.5, 1.0 Hz, 1H), 4.50–4.43 (m, 1H), 3.97 (dd, *J* = 12.0, 9.5 Hz, 1H), 3.69 (s, 3H), 3.62–3.56 (m, 1H), 2.26–2.20 (m, 1H), 2.24 (s, 3H), 2.09 (ddd, *J* = 13.6, 4.9, 1.1 Hz, 1H), 1.56– 1.52 (m, 1H), 1.49– 1.45 (m, 3H), 1.40–1.34 (m, 1H), 1.32 (s, 3H), 1.30 (s, 3H), 1.12 (s, 3H), 1.10 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.0, 156.3, 117.4, 78.3, 68.1, 61.6, 60.0, 50.9, 42.4, 40.3, 39.9, 34.5, 32.5, 20.6, 20.4, 19.3, 17.1 ppm; IR (film) ν = 3305, 2932, 2873, 1719, 1647, 1435, 1224, 1150, 1045 cm^{-1}; MS (ESI): *m*/*z*: 314 [*M*+H$^+$]; 336 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{17}H_{32}NO_4$ [*M*+H$^+$]: 314.23258, found: 314.23274.



Methyl (*5R,6S,E*)-6-((*tert*-butyldimethylsilyl)oxy)-3-methyl-5-((2,2,6,6 tetramethylpiperidin-1-yl)oxy)non-2-en-7-ynoate (6). A solution of 1-propynylmagnesium bromide (0.5 M in THF, 50.0 mL, 25.0 mmol) was added to a solution of compound **5** (6.89 g, 22.1 mmol) in pentane (100 mL) at –78 °C. The mixture was stirred at this temperature for 30 min and at –20 °C for 1 h. For work up, the mixture was partitioned between sat. aq. NH_4Cl (20 mL) and *tert*-butyl methyl ether (100 mL), the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 150 mL), the combined organic phases were washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 10:1 to 4:1) to give the desired alcohol as a colorless oil.



Imidazole (3.01 g, 44.2 mmol) and *tert*-butyldimethylsilyl chloride (5.0 g, 33.2 mmol) were added to a solution of this material in DMF (1.0 mL). After stirring for 10 min, sat. aq. $NaHCO_3$ (10 mL) was added and the resulting mixture was extracted with *tert*-butyl methyl ether (3 x 30 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/ *tert*-butyl methyl ether, 15:1) to afford the title compound as a colorless oil (6.85 g, 67%). $[\alpha]_{D}^{20}$ = 8.7 (c = 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 5.81 (s, 1H), 4.83–4.74 (m, 1H), 4.05 (td, *J* = 6.4, 6.4, 1.6 Hz, 1H), 3.67 (s, 3H), 2.64 (dd, *J* = 13.0, 6.1 Hz, 1H), 2.47 (dd, *J* = 13.3, 6.3 Hz, 1H), 2.24 (d, *J* = 1.2 Hz, 3H), 1.78 (d, *J* = 2.2 Hz, 3H), 1.60–1.37 (m, 5H), 1.27 (d, *J* = 13.4 Hz, 1H), 1.20 (s, 3H), 1.09 (s, 9H), 0.90 (s, 9H), 0.14 (s, 3H), 0.07 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1, 158.7, 117.7, 84.5, 82.5, 78.9, 63.7, 60.4, 60.0, 50.6, 40.6, 34.3, 34.2, 34.1, 26.0, 20.6, 20.4, 20.4, 19.5, 18.3, 17.2, 3.4, −3.9, −4.8 ppm; IR (film) ν = 2929, 2857, 1720, 1648, 1435, 1223, 1148, 1076, 832, 776 cm^{-1}; MS (ESI): *m*/*z*: 466 [*M*+H^+], 488 [*M*+Na^+]; HRMS (ESI)*: m/z* calcd. for $C_{26}H_{48}NO_4Si$ [*M*+H^+]: 466.33471, found: 466.33486.

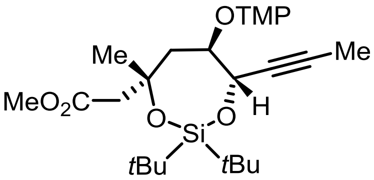


Methyl (*3S,5R,6S*)-6-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-3-methyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)non-7-ynoate (7). A mixture of copper (I) chloride (36.0 mg, 0.364 mmol), sodium *tert*-butoxide (89.8 mg, 0.934 mmol,), and (*S,S*)-Me-Duphos (112 mg, 0.366 mmol) in THF (3 mL) was stirred for 30 min at 0 °C. Bis(pinacolato)diboron (1.87 g, 7.36 mmol) was added to the mixture and stirring was continued for 10 min before a solution of compound **6** (2.86 g, 6.14 mmol) in THF (2 mL) was introduced, followed by MeOH (1 mmol, 0.40 mL). After stirring for 2 d, the mixture was adsorbed on silica and purified by flash chromatography to provide the crude borylated ester.

Sodium perborate tetrahydrate (22.7 g, 73.8 mmol) was added to a solution of this crude material in THF/H_2O (10 mL, 1:1) at ambient temperature. The mixture was warmed to 90 °C and stirred at this temperature for 2 d. For work-up, the mixture was diluted with water (20 mL) and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 10:1 to 4:1) to afford the title compound as a colorless oil (2.21 g, 74%). $[\alpha]_{D}^{20}$ = 1.5 (c = 1.2, $CHCl_3$); ^1H NMR

(400 MHz, $CDCl_3$): δ = 6.86 (s, 1H), 4.43 (dq, *J* = 4.2, 2.1, 2.1, 2.1 Hz, 1H), 4.33 (ddd, *J* = 7.4, 4.1, 1.2 Hz, 1H), 3.65 (s, 3H), 2.54 (d, *J* = 3.3 Hz, 2H), 2.31 (dd, *J* = 16.1, 7.3 Hz, 1H), 2.20–2.04 (m, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.61–1.53 (m, 3H), 1.51–1.39 (m, 3H), 1.34 (s, 3H), 1.29 (s, 3H), 1.26 (s, 3H), 1.22 (s, 3H), 1.11 (s, 3H), 0.90 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 82.6, 81.3, 79.2, 68.9, 65.3, 62.2, 60.3, 51.3, 49.6, 40.8, 39.8, 39.7, 33.6, 33.2, 27.6, 27.0, 25.8, 21.3, 21.1, 18.2, 17.0, 3.4, −4.4, −5.0 ppm; IR (film) ν = 2929, 2856, 1738, 1472, 1436, 1364, 1251, 1131, 1095, 1064, 835, 777 cm^{-1}; MS (ESI): *m*/*z*: 484 [*M*+H^+], 506 [*M*+Na^+]; HRMS (ESI)*: m/z:* calcd. for $C_{26}H_{50}NO_5Si$ [*M*+H^+]: 484.34528, found: 484.34527.

Methyl 2-((4*S*,6*R*,7*R*)-2-(*tert*-butyl)-4-methyl-7-(prop-1-yn-1-yl)-6-((2,2,6,6 tetramethyl-piperidin-1-yl)oxy)-1,3,2-dioxasilepan-4-yl)acetate (S2). A solution of tetrabutylammonium fluoride (1 M in THF, 0.13 mL, 0.130 mmol) was added to a solution of compound **7** (61.3 mg, 0.127 mmol) in THF (1.0 mL) at 0 °C. The resulting solution was stirred at this temperature for 30 min before the reaction was quenched with sat. aq. NH_4Cl (4 mL). The aqueous layer was extracted with EtOAc (3 x10 mL), the combined extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/EtOAc, 4:1 to 1:1) to give a colorless oil.



2,6-Lutidine (0.15 mL, 1.29 mmol) and di-*tert*-butylsilyl ditriflate (60 μL, 0.184 mmol) were successively added to a solution of this crude material in CH_2Cl_2 (1.6 mL) at 0 °C. The resulting mixture was stirred at ambient temperature for 5 h. sat.aq. $NaHCO_3$ (2 mL) was added, the aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 10:1) to afford the title compound as a colorless oil (10.7 mg, 17%). $[\alpha]_D^{20}$ = −16.7 (c = 1.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.33 (dq, *J* = 9.1, 2.1, 2.1, 2.1 Hz, 1H), 4.17 (t, *J* = 9.1, 9.1 Hz, 1H), 3.68 (s, 3H), 2.79 (d, *J* = 15.0 Hz, 1H), 2.75 (d, *J* = 14.7 Hz, 1H), 2.59 (d, *J* = 14.7 Hz, 1H), 1.86 (d, *J* = 2.2 Hz, 3H), 1.76 (dd, *J* = 15.1, 9.3 Hz, 1H), 1.62–1.54 (m, 2H), 1.52 (s, 3H), 1.48–1.38 (m, 4H), 1.28 (s, 3H), 1.23 (s, 3H), 1.07 (s, 3H), 1.05 (s, 3H), 1.03 (s, 9H), 0.99 (s, 9H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 171.3, 80.9, 80.4, 80.2, 73.6, 68.3, 61.2, 59.4, 51.2, 45.9, 43.2, 40.7, 40.3, 34.5, 34.4, 30.2, 28.1, 27.8, 27.4, 20.8, 20.7, 20.7, 20.6, 17.2, 3.5 ppm; IR (film) ν = 2969, 2934, 2858, 1744, 1474, 1436, 1361, 1200, 1129, 1106, 1031, 826, 645 cm^{-1}; MS (ESI): *m/z*: 509 [*M*+H^+], 532 [*M*+Na^+]; HRMS (ESI)*: m/z:* calcd. for $C_{28}H_{52}NO_5Si$ [*M*+H^+]: 510.36093, found: 510.36114.

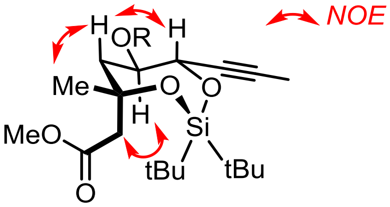
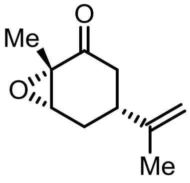
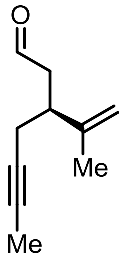


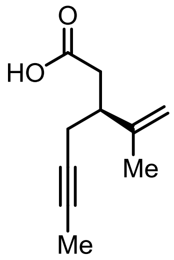
Figure S1. Determination of the relative stereochemistry;
R = 2,2,6,6 tetramethyl-piperidin-1-yl (TMP)

(*1S,4R,6S*)-1-Methyl-4-(prop-1-en-2-yl)-7-oxabicyclo[4.1.0]heptan-2-one (S3). A solution of (*R*)-(–)-carvone (10 g, 66.6 mmol) in MeOH (150 mL) was cooled to –20 °C. aq. NaOH (32 wt%, 2.5 mL, 20 mmol) and aq. H_2O_2 (35 wt%, 8.5 mL, 175 mmol) were added dropwise to this solution at –20 °C. The resulting mixture was stirred at 0 °C for 4 h before the reaction was quenched by careful addition of sat. aq. $Na_2S_2O_3$ (100 mL). Diethyl ether and water were added and the phases were separated. The aqueous layer was extracted with diethyl ether (3 x 200 mL), and the combined organic layers were washed with brine and dried with $MgSO_4$. After filtration, the solvent was removed under vacuum to afford the title compound as a colorless oil, which was directly used in the next step (11.2 g, quant.). $[\alpha]_D^{20}$ = 85.6 (c = 1.7, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 4.78 (t, *J* = 1.5, 1.5 Hz, 1H), 4.71 (s, 1H), 3.45–3.42 (m, 1H), 2.72 (tt, *J* = 11.1, 11.1, 4.5, 4.5 Hz, 1H), 2.58 (ddd, *J* = 17.7, 4.7, 1.4 Hz, 1H), 2.41–2.33 (m, 1H), 2.02 (dd, *J* = 17.6, 11.6 Hz, 1H), 1.89 (ddd, *J* = 14.8, 11.1, 1.3 Hz, 1H), 1.71 (s, 3H), 1.41 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 205.5, 146.3, 110.5, 61.3, 58.8, 41.8, 35.0, 28.7, 20.6, 15.3 ppm; IR (film) ν = 2935, 1646, 1439, 1377, 1118, 890, 814 cm^{-1}; MS (EI): *m/z* (%): 105 (100), 123 (46); HRMS (ESI): *m/z:* calcd. for $C_{10}H_{14}NNa$ [*M*+Na^+]: 189.08860, found: 189.08868.



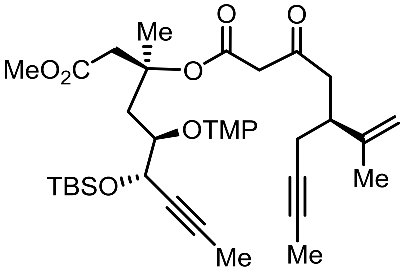


(*S*)-3-(Prop-1-en-2-yl)hept-5-ynal (10). Tosylhydrazide (2.46 g, 13.2 mmol) was added in portions to a stirred solution of compound **S3** (1.83 g, 12.0 mmol) in HOAc/CH_2Cl_2 (1:1, 34 mL) at 0 °C. The mixture was allowed to slowly warm to 10 °C. After stirring for 2 h, crushed ice (20 g) was added and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (5 × 200 mL), and the combined organic phases were neutralized with ice-cold sat. aq. $NaHCO_3$ and dried over Na_2SO_4. The solvent was removed under vacuum and the residue purified by flash chromatography on silica (pentane/*tert*-butyl methyl ether, 10:1) to afford the title compound as a colorless oil (932 mg, 52%). $[\alpha]_D^{20} = -18.1$ (c = 0.52, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 9.72 (dd, *J* = 2.6, 1.8 Hz, 1H), 4.83 (p, *J* = 1.5, 1.5, 1.5, 1.5 Hz, 1H), 4.79 (dt, *J* = 1.6, 0.9, 0.9 Hz, 1H), 2.85–2.75 (m, 1H), 2.69 (ddd, *J* = 16.6, 6.1, 1.8 Hz, 1H), 2.52 (ddd, *J* = 16.5, 8.3, 2.5 Hz, 1H), 2.38–2.29 (m, 1H), 2.21 (ddq, *J* = 16.6, 7.8, 2.5, 2.5, 2.5 Hz, 1H), 1.77 (t, *J* = 2.6, 2.6 Hz, 3H), 1.72 (dd, *J* = 1.5, 0.8 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.9, 145.6, 112.0, 78.0, 76.5, 46.3, 40.6, 23.7, 20.2, 3.4 ppm; IR (film) ν = 2920, 1722, 1646, 1436, 1260, 1016, 895 cm^{-1}; MS (EI): *m*/*z* (%): 41 (100), 91 (94), 107 (47); HRMS (ESI): *m/z:* calcd. for $C_{10}H_{15}O$ [M+H^+]: 151.11174, found: 151.11185.



(*S*)-3-(Prop-1-en-2-yl)hept-5-ynoic acid (11). Sodium chlorite (8.30 g, 91.8 mmol) was added in portions to a stirred solution of compound **10** (6.92 g, 46.1 mmol), 2-methyl-2-butene (25 ml, 235 mmol) and sodium dihydrogen phosphate (24.7 g, 225 mmol) in *t*BuOH/H_2O (180 mL, 2:1) at 0 °C. The mixture was stirred at this temperature for 10 min before the reaction was quenched with sat. aq. $Na_2S_2O_3$ (24 mL). After extraction with EtOAc (3 × 200 mL), the combined organic phases were washed with brine, dried over Na_2SO_4 and filtered. The solvent was evaporated under vacuum and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 15:1 to 2:1) to afford the title compound as a colorless oil (7.19 g, 94%). $[\alpha]_D^{20} = -19.2$ (c = 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 4.82–4.81 (m, 1H), 4.79 (s, 1H), 2.73–2.68 (m, 1H), 2.68–2.64 (m, 1H), 2.50–2.42 (m, 1H), 2.32 (ddq, *J* = 16.7, 5.2, 2.5, 2.5, 2.5 Hz, 1H), 2.21 (ddq, *J* = 16.8, 7.5, 2.5, 2.5, 2.5 Hz, 1H), 1.75 (dd, *J* = 2.5, 2.5 Hz, 3H), 1.72 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.2, 145.6, 111.7, 77.6, 76.4, 42.0, 37.5, 23.5, 20.2, 3.4 ppm; IR (film) ν = 2920, 1648, 1432, 1289, 1163, 894 cm^{-1}; MS (EI): *m*/*z* (%): 41 (87), 91 (100), 121 (41); HRMS (ESI): *m/z:* calcd. for $C_{10}H_{13}O_2$ [M–H^+]: 165.09211, found: 165.09213.

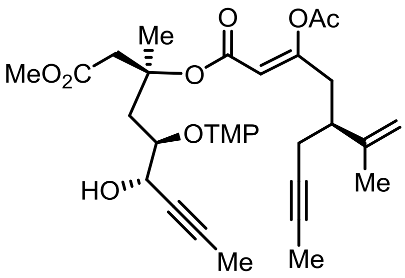
Methyl (*3S,5R,6S*)-6-((*tert*-butyldimethylsilyl)oxy)-3-methyl-3-(((S)-3-oxo-5-(prop-1-en-2-yl) non-7-ynoyl)oxy)-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy) non-7-ynoate (15). Compound **12** (1.29 g, 6.26 mmol)[2] was added to a solution of 4-dimethylaminopyridine (127 mg, 1.04 mmol), triethylamine (1.75 mL, 12.6 mmol) and dicyclohexylcarbodiimide (2.15 g, 10.4 mmol) in CH_2Cl_2 (10 mL) at ambient temperature. After 5 min, a solution of acid **11** (1.04 g, 6.26 mmol) in THF (10 mL) was added and stirring continued for 20 h. The mixture was concentrated and the residue triturated with diethyl ether (20 mL) and H_2O (20 mL). The biphasic suspension was filtered and the filter cake was carefully washed with diethyl ether (3 x 30 mL) and H_2O (3 x 30 mL) until the remaining urea became colorless. The filtrate was extracted with H_2O (5 x 50 mL), the combined aqueous phases were cooled to 0 °C, acidified to pH 2-3 with solid citric acid and extracted with $CHCl_3$ (5 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated ($T \leq 30$°C).



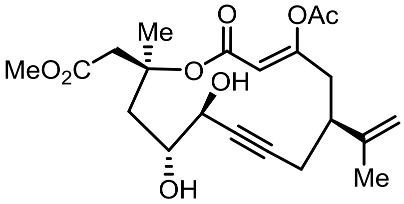
The crude compound **13** (1.01 g, 2.09 mmol) thus formed was added to a solution of **7** (1.01 g, 2.09 mmol) in toluene (6 mL) and the resulting mixture was stirred at 60 °C for 1.5 h. sat. aq. $NaHCO_3$ (20 mL) was added, the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 10:1) to afford the title compound as a yellow oil (1.39 g, quant.). $[\alpha]_D^{20}$ = +18.9 (c = 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.1 (s, 0.3H, minor), 5.21 (dt, *J* = 3.0, 2.0, 2.0 Hz, 1H), 4.93 (s, 0.3H, minor), 4.81 (tt, *J* = 3.0, 3.0, 1.5, 1.5 Hz, 0.3H), 4.80 (tt, *J* = 1.7, 1.7, 0.9, 0.9 Hz, 0.7H), 4.77–4.76 (m, 1H), 4.15–4.11 (m, 1H), 3.66 (s, 2H), 3.65 (s, 1H), 3.41 (d, *J* = 15.3 Hz, 0.7H), 3.34 (d, *J* = 15.3 Hz, 0.7H), 3.22 (dd, *J* = 25.7, 15.0 Hz, 1H), 3.00 (dd, *J* = 19.6, 14.9 Hz, 1H), 2.83 (dd, *J* = 14.8, 5.0 Hz, 0.6H), 2.79– 2.70 (m, 1.4H), 2.44–2.20 (m, 5H), 1.80 (dd, *J* = 3.8, 2.3 Hz, 2H), 1.79 (q, *J* = 2.6, 2.6, 2.6 Hz, 1H), 1.77–1.75 (m, 3H), 1.72–1.70 (m, 6H), 1.50–1.38 (m, 5H), 1.30–1.25 (m, 1H), 1.15 (t, *J* = 6.1, 6.1 Hz, 9H), 1.05 (s, 3H), 0.88 (s, 9H), 0.16 (s, 3H), 0.08–0.07 (m, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.7, 176.3, 172.1, 170.7, 170.5, 166.2, 146.2, 145.6, 112.0, 111.4, 91.8, 83.1, 83.0, 82.7, 82.2, 81.7, 79.6, 77.5, 76.7, 62.7, 62.6, 60.3, 59.8, 51.4, 51.4, 50.8, 45.7, 43.7, 43.1, 42.8, 40.8, 40.5, 38.3, 38.3, 38.2, 34.8, 34.3, 26.1, 25.6, 25.2, 23.5, 23.2, 20.8, 20.6, 19.9, 18.4, 17.2, 17.2, 3.5, 3.5, 3.5, –3.5, –4.3

ppm; IR (film) ν = 2929, 2856, 1741, 1646, 1249, 1204, 1164,1134, 1084, 1063, 894 cm^{-1}; MS (ESI): *m*/*z*: : 674 [*M*+H$^+$], 696 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{38}H_{64}NO_7$ [*M*+H$^+$]: 674.44466, found: 674.44461.

Methyl (*3S,5R,6S*)-6-hydroxy-3-methyl-3-(((*S*)-3-oxo-5-(prop-1-en-2-yl)non-7-ynoyl)oxy)-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)non-7-ynoate (16). Triethylamine (0.47 mL, 3.37 mmol), acetic anhydride (0.32 mL, 3.39 mmol) and 4-dimethylaminopyridine (27.6 mg, 0.226 mmol) were added to a stirred solution of compound **15** (760 mg, 1.13 mmol) in CH_2Cl_2 (5.6 mL) at –40 °C. After stirring at this temperature for 2 h, the reaction was quenched with sat. aq. $NaHCO_3$ (5 mL) and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 filtered and evaporated. The residue was passed through a pad of silica, eluting with hexanes/*tert*-butyl methyl ether (10:1) to provide the corresponding enol acetate as a colorless oil, which was used in the next step without further characterization.

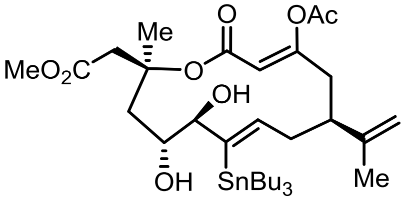


aq. HF (1.5 mL) was added to a solution of this compound in THF (15 mL) at 0 °C. After 10 min, stirring was continued at ambient temperature for 2 h. The mixture was then poured into sat. aq. $NaHCO_3$ (100 mL) at 0 °C and the aqueous phase was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 10:1 to 4:1) to afford the title compound as a colorless oil (498 mg, 73%). $[\alpha]_{D}^{20}$ = 17.8 (c = 2.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.72 (s, 1H), 5.65 (s, 1H), 4.80–4.77 (m, 1H), 4.75–4.71 (m, 1H), 4.67 (s, 1H), 4.49 (dt, *J* = 7.0, 3.3, 3.3 Hz, 1H), 3.65 (s, 3H), 3.20 (d, *J* = 15.1 Hz, 1H), 3.10 (dd, *J* = 14.4, 8.9 Hz, 1H), 2.98–2.87 (m, 2H), 2.51–2.43 (m, 1H), 2.39 (dd, *J* = 15.4, 7.3 Hz, 1H), 2.26–2.19 (m, 2H), 2.14 (s, 3H), 2.06 (dd, *J* = 15.4, 3.5 Hz, 1H), 1.81 (d, *J* = 2.3 Hz, 3H), 1.74 (t, *J* = 2.5, 2.5 Hz, 3H), 1.68 (s, 3H), 1.66 (s, 3H), 1.52–1.41 (m, 5H), 1.37 (s, 3H), 1.29 (s, 3H), 1.17 (s, 3H), 1.08 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.4, 167.8, 165.0, 164.6, 145.6, 112.2, 111.9, 82.7, 81.0, 78.4, 78.0, 77.1, 77.0, 67.3, 61.3, 60.7, 51.4, 44.4, 42.7, 40.9, 40.4, 39.6, 34.7, 33.9, 33.4, 25.3, 23.4, 21.1, 21.0, 20.7, 19.1, 17.0, 3.6, 3.4 cm^{-1}; IR (film) ν = 2923, 2873, 1764, 1717, 1655, 1473, 1437, 1365, 1198, 1169, 1094, 1021, 896, 753 cm^{-1}; MS (ESI): *m*/*z*: 602 [*M*+H$^+$], 624 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{34}H_{52}O_8N$ [*M*+H$^+$]: 602.36874, found: 602.36895.



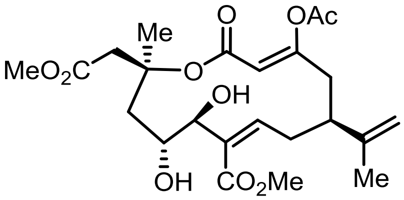
Methyl 2-((*2S,4R,5S,9S,Z*)-11-acetoxy-4,5-dihydroxy-2-methyl-13-oxo-9-(prop-1-en-2-yl) oxacyclotridec-11-en-6-yn-2-yl)acetate (17). A solution of silanol **24** (51.0 mg, 0.0648 mmol) in toluene (1 mL) was added to complex **23** (37.7 mg, 0.0648 mmol) at ambinent temperature.[3] After stirring for 10 min, the resulting catalyst solution was added to a solution of diyne **16** (130 mg, 0.216 mmol) in refluxing toluene (97 mL). After 15 min, the mixture was allowed to cool to ambient temperature, filtered through a pad of Celite and the filtrate was concentrated. The crude material was passed through a pad of silica, eluting with hexanes/EtOAc (4:1).

Zinc dust (565 mg, 8.64 mmol) was added to a solution of this compound in HOAc/THF/H_2O (0.75 mL, 3:1:1). The suspension was vigorously stirred for 2 h at room temperature before all insoluble materials were filtered off through a pad of Celite. The filtrate was diluted with sat. aq. $NaHCO_3$ (10 mL), the aqueous phase was extracted with EtOAc (3 x 20 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/EtOAc, 4:1 to 1:1) to afford the title compound as a colorless oil (67.4 mg, 76%). $[\alpha]_D^{20}$ = 8.5 (c = 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.54 (d, *J* = 0.6 Hz, 1H), 4.75 (t, *J* = 1.5, 1.5 Hz, 1H), 4.69 (s, 1H), 4.51 (s, 1H), 4.07 (ddd, *J* = 8.6, 5.9, 2.6 Hz, 1H), 3.74 (d, *J* = 5.6 Hz, 1H), 3.68–3.64 (m, 1H), 3.64 (s, 3H), 3.34 (dd, *J* = 14.5, 4.9 Hz, 1H), 2.99 (d, *J* = 14.6 Hz, 1H), 2.64 (dd, *J* = 14.4, 11.0 Hz, 1H), 2.57 (d, *J* = 16.4 Hz, 1H), 2.48 (d, *J* = 3.4 Hz, 1H), 2.42 (ddt, *J* = 11.0, 9.1, 4.5, 4.5 Hz, 1H), 2.30 (ddd, *J* = 16.9, 4.1, 1.7 Hz, 1H), 2.21 (ddd, *J* = 16.8, 8.8, 3.0 Hz, 1H), 2.04 (s, 3H), 1.99 (dd, *J* = 16.2, 8.5 Hz, 1H), 1.65 (s, 3H), 1.63 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 167.9, 164.9, 163.0, 144.7, 114.0, 112.7, 85.4, 83.1, 81.3, 71.5, 67.1, 52.1, 44.5, 42.3, 39.8, 33.4, 25.6, 23.9, 21.0, 19.9 ppm; IR (film) ν = 3447, 3080, 2923, 2853, 1739, 1698, 1437, 1200, 1078, 1016, 889 cm^{-1}; MS (ESI): *m*/*z*: 431 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{21}H_{28}O_8Na$ [*M*+Na$^+$]: 431.16764, found: 431.16747.



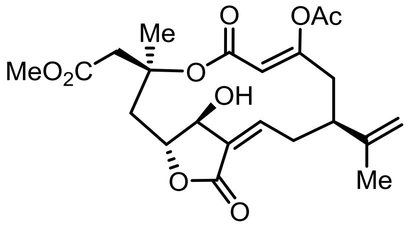
Methyl 2-((*2S,4R,5R,6Z,9S,11Z*)-11-acetoxy-4,5-dihydroxy-2-methyl-13-oxo-9-(prop-1-en-2-yl)-6-(tributylstannyl)oxacyclotrideca-6,11-dien-2-yl)acetate (18). A solution of tributyltin hydride (53 μL, 0.197 mmol) in CH_2Cl_2 (0.7 mL) was added dropwise over 20 min to a stirred orange solution of $[Cp^*RuCl]_4$ (2.0 mg, 1.8 µmol) and compound **17** (67.4 mg, 0.165 mmol) in CH_2Cl_2 (0.14 mL) under Ar at 23°C. Once the addition was complete, all volatile materials were evaporated under argon. The crude material was purified by flash chromatography on silica (hexanes/*tert*-butyl methyl ether, 4:1 to 2:1) to afford the title compound as a yellow oil (76.2 mg, 66%). $[\alpha]_D^{20}$ = 24.2 (c = 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.22 (ddd, *J* = 10.0, 5.1, 1.8 Hz, 1H), 5.54 (d, *J* = 0.6 Hz, 1H), 4.82 (t, *J* = 1.5, 1.5 Hz, 1H), 4.66 (s, 1H), 4.50 (s, 1H), 3.91 (ddd, *J* = 8.0, 4.7, 3.1 Hz, 1H), 3.71 (s, 3H), 3.66 (s, 1H), 3.64 (s, 1H), 3.04 (d, *J* = 6.2 Hz, 1H), 3.00 (d, *J* = 5.5 Hz, 1H), 2.76 (dd, *J* = 14.6, 10.9 Hz, 1H), 2.36 (d, *J* = 2.4 Hz, 1H), 2.24 (ddd, *J* = 20.4, 8.9, 4.4 Hz, 4H), 2.10 (s, 3H), 1.92–1.80 (m, 1H), 1.73 (s, 3H), 1.66 (s, 3H), 1.32 (dq, *J* = 13.7, 7.2, 7.2, 6.6 Hz, 12H), 1.00–0.95 (m, 6H), 0.88 (t, *J* = 7.3, 7.3 Hz, 9H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 167.8, 165.0, 163.6, 148.8, 145.7, 137.9, 113.8, 111.9, 83.3, 80.6, 73.9, 52.1, 46.3, 41.2, 39.7, 35.3, 32.8, 29.2, 29.2, 27.8, 27.5, 26.8, 25.7, 21.0, 20.7, 17.5, 13.7, 13.6, 12.2 ppm; ^{119}Sn NMR (186 MHz, $CDCl_3$): δ = −58.3 ppm; IR (film) ν = 3503, 2955, 2923, 2853, 1742, 1700, 1374, 1190, 1069, 1015, 892 cm^{-1}; MS (ESI): *m*/*z*: 723 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{33}H_{56}O_8SnNa$ [*M*+Na$^+$]: 723.28887, found: 723.28927.

Methyl (*2S,4R,5S,6Z,9S,11Z*)-11-acetoxy-4,5-dihydroxy-2-(2-methoxy-2-oxoethyl)-2-methyl-13-oxo-9-(prop-1-en-2-yl)oxacyclotrideca-6,11-diene-6-carboxylate (19). *p*-Benzoquinone (10.5 mg, 0.0971 mmol), Ph_3As (7.9 mg, 0.0258 mmol) and $Pd(OAc)_2$ (2.9 mg, 0.0129 mmol) were added to a solution of compound **18** (45.3 mg, 0.0648 mmol) and trifluoroacetic acid (2 μL, 0.0259 mmol) in MeOH (1.6 mL). The Schlenk flask was flushed for 5 min with CO before the mixture was stirred under CO atmosphere (balloon) at room temperature for 2 h. The mixture was diluted with EtOAc and filtered through a pad of Celite. sat.aq. $NaHCO_3$ (5 mL) was added to the filtrate and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash

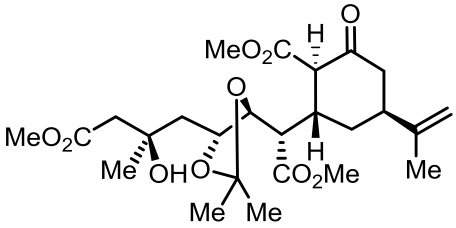


chromatography (hexanes/ EtOAc, 2:1 to 1:2) to afford the title compound as a white solid (17.3 mg, 57%). $[\alpha]_D^{20}$ = 4.0 (c = 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.34 (t, *J* = 8.1, 8.1 Hz, 1H), 5.52 (s, 1H), 4.88–4.77 (m, 1H), 4.74 (d, *J* = 4.2 Hz, 1H), 4.71 (s, 1H), 3.96 (t, *J* = 6.6, 6.6 Hz, 1H), 3.79 (s, 3H), 3.70 (dd, *J* = 16.0, 1.4 Hz, 1H), 3.69 (s, 3H), 3.00–2.91 (m, 3H), 2.84 (d, *J* = 4.7 Hz, 1H), 2.53 (dd, *J* = 14.5, 11.0 Hz, 1H), 2.41–2.28 (m, 3H), 2.08 (s, 3H), 1.91 (dd, *J* = 16.4, 7.9 Hz, 1H), 1.75 (s, 3H), 1.71 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.2, 167.9, 167.3, 164.8, 163.0, 146.0, 140.4, 132.8, 114.0, 111.9, 83.2, 75.7, 72.1, 51.9, 51.8, 45.0, 40.7, 39.6, 32.6, 32.3, 25.5, 21.0, 20.0 ppm; IR (film) ν = 3481, 2952, 1697, 1648, 1436, 1355, 1128, 1062, 889,804 cm^{-1}; MS (ESI): *m/z*: 469 [*M*+H$^+$], 491 [*M*+Na$^+$]; HRMS (ESI)*: m/z:* calcd. for $C_{23}H_{32}O_{10}Na$ [*M*+Na$^+$]: 491.18877, found: 491.18832.

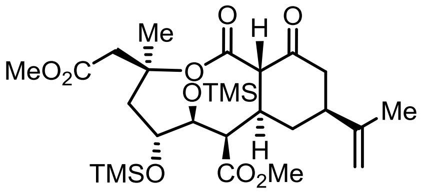
Methyl 2-((1*R*,3*S*,6*Z*,9*S*,11*Z*,15*S*)-7-acetoxy-15-hydroxy-3-methyl-5,13-dioxo-9-(prop-1-en-2-yl)-4,14-dioxabicyclo[10.2.1]pentadeca-6,11-dien-3-yl)acetate (20). A solution of CF_3COOH (0.4 μL, 5.1 μmol) in CH_2Cl_2 (0.1 mL) was added to a solution of **19** (2.0 mg, 4.3 μmol) in CH_2Cl_2 (0.1 mL) at ambient temperature. The mixture was stirred at this temperature for 2 h, the solvent was removed under argon and the residue was purified by flash chromatography (hexanes/EtOAc, 4:1 to 2:1) to afford the title compound as a colorless oil (1.7 mg, 91%). $[\alpha]_D^{20}$ = 5.0 (c = 0.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.31 (t, *J* = 8.3, 8.3 Hz, 1H), 5.62 (s, 1H), 5.07 (s, 1H), 4.85–4.79 (m, 1H), 4.70 (s, 1H), 4.45 (d, *J* = 10.2 Hz, 1H), 3.83 (s, 3H), 3.27 (d, *J* = 17.5 Hz, 1H), 3.15 (d, *J* = 17.4 Hz, 1H), 2.92–2.80 (m, 2H), 2.61–2.47 (m, 2H), 2.43–2.32 (m, 2H), 2.10 (s, 3H), 1.81 (dd, *J* = 15.4, 10.3 Hz, 1H), 1.76 (s, 3H), 1.70 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.2, 167.7, 166.7, 164.6, 162.9, 145.8, 140.3, 133.1, 113.4, 112.2, 80.9, 79.2, 70.6, 52.2, 45.8, 43.4, 37.7, 33.5, 33.2, 27.0, 21.0, 19.7 ppm; IR (film) ν = 2924, 1707, 1437, 1195, 1105, 1026, 459 cm^{-1}; MS (ESI)*: m/z*: 459 [*M*+Na$^+$]; HRMS (ESI): *m/z:* calcd. for $C_{22}H_{28}O_9Na$ [*M*+Na$^+$]: 459.16290, found: 459.16255.



Methyl (1*R*,2*R*,4*S*)-2-((*S*)-1-((4*S*,5*S*)-5-((*R*)-2-hydroxy-4-methoxy-2-methyl-4-oxobutyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-methoxy-2-oxoethyl)-6-oxo-4-(prop-1-en-2-yl)cyclohexane-1-carboxylate (30): 2,2-Dimethoxypropan (40 μL, 0.325 mmol) and PPTS (3.1 mg, 12.3 μmol) were added to a stirred solution of **19** (2.0 mg, 4.3 μmol) in DMF (40 μL) at ambient temperature and the resulting mixture was stirred for 12 h. The reaction was quenched with sat. aq.$NaHCO_3$ (1.0 mL), the aqueous layer was extracted with ether (3 x 5 mL), dried over Na_2SO_4 and evaporated. The crude material was purified by flash chromatography (hexanes/ EtOAc, 6:1 to 2:1) to give product **29** which was immediately used in the next step. This compound was dissolved in MeOH (0.8 mL). Cs_2CO_3 (5.5 mg, 16.9 μmol) was added at 0 °C and the resulting mixture was stirred for 20 min before the reaction was quenched with aq. NH_4Cl (0.5 mL). The aqueous phase was extracted with EtOAc (3 x 5 mL), the combined extracts were dried over $MgSO_4$, the solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 4:1 to 1:1) to afford the title compound **30** as a colorless oil (0.9 mg, ≈ 42%; *the samples invariably contained ca. 5-10% of an unidentified impurity, which could not be removed by flash chromatography*) $[\alpha]_D^{20}$ = 20 (c = 0.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.85–4.81 (m, 1H), 4.76 (s, 1H), 4.53 (ddd, *J* = 10.3, 5.6, 3.1 Hz, 1H), 4.25 (dd, *J* = 9.9, 5.6 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.67 (s, 3H), 3.45 (d, *J* = 11.4 Hz, 1H), 2.77 (dd, *J* = 9.9, 2.1 Hz, 1H), 2.67 (d, *J* = 15.2 Hz, 1H), 2.56–2.42 (m, 3H), 2.38 (dt, *J* = 11.9, 2.9, 2.9 Hz, 1H), 2.25 (td, *J* = 13.3, 13.3, 0.9 Hz, 1H), 2.08 (d, *J* = 13.9 Hz, 1H), 1.88–1.79 (m, 2H), 1.76 (s, 3H), 1.68–1.57 (m, 1H), 1.42 (s, 3H), 1.38 (s, 3H), 1.28 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 204.9, 172.4, 171.6, 170.7, 146.2, 110.6, 108.5, 76.1, 74.2, 70.8, 59.4, 52.4, 51.8, 51.6, 50.5, 46.0, 45.8, 43.1, 39.5, 38.1, 35.9, 27.9, 27.5, 25.7, 20.4. ppm; IR (film) ν = 2924, 1735, 1437, 1217, 756 cm^{-1}; MS (ESI)*:* *m/z*: 521 [*M*+Na$^+$]; HRMS (ESI): *m/z:* calcd. for $C_{25}H_{38}O_{10}Na$ [*M*+Na$^+$]: 521.23563, found: 521.23572.



Methyl (*3S,5S,6S,7S,7aS,9S,11aS*)-3-(2-methoxy-2-oxoethyl)-3-methyl-1,11-dioxo-9-(prop-1-en-2-yl)-5,6-bis((trimethylsilyl)oxy)dodecahydrobenzo[c]oxonine-7-carboxylate (32a).



Imidazole (72.0 mg, 1.06 mmol) and trimethylsilyl chloride (0.13 mL, 1.02 mmol) were added to a solution of compound **19** (8.0 mg, 0.0171 mmol) in DMF (0.2 mL) at ambient temperature. After stirring for 4 h, the reaction was quenched with sat.aq. $NaHCO_3$ (2 mL) and the aqueous layer was extracted with EtOAc (3 x 3 mL). the combined organic phases were washed with birne, dried over Na_2SO_4, filtered and evaporated.

The residue was dried in vacuum for 30 min before it was passed through a pad of silica, eluting with hexanes/EtOAc (8:1) to provide the hydrolysis-prone compound **31a** as a colorless oil. Characteristic data: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.20 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.82 (s, 1H), 4.79–4.76 (m, 1H), 4.68 (s, 1H), 3.96 (d, *J* = 7.5 Hz, 1H), 3.81 (s, 3H), 3.64 (s, 3H), 1.77 (s, 3H), 1.61 (s, 3H) ppm.

A solution of Barton's base **33** (8.8 mg, 0.0514 mmol) in CH_3CN (0.2 mL) was added to a solution of **31a** in CH_3CN (0.1 mL) at 0 °C. After stirring for 1 min, the mixture was adsorbed on silica and the product purified by flash chromatography (hexanes/EtOAc, 8:1) to afford the title compound as a colorless oil (5.5 mg, 56%). $[\alpha]_D^{20}$ = –38.3 (c = 0.12, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.79 (t, *J* = 1.5 Hz, 1H), 4.71 (q, *J* = 1.1 Hz, 1H), 4.28 (dd, *J* = 10.5, 1.4 Hz, 1H), 4.12 (dt, *J* = 8.0, 1.3 Hz, 1H), 3.74 (d, *J* = 12.2 Hz, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.39 (d, *J* = 15.0 Hz, 1H), 3.23 (d, *J* = 15.0 Hz, 1H), 3.03 (tt, *J* = 12.6, 3.9 Hz, 1H), 2.94 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.50 (ddd, *J* = 14.1, 3.5, 2.2 Hz, 1H), 2.44 (d, *J* = 15.1 Hz, 1H), 2.37 (tt, *J* = 12.6, 3.0 Hz, 1H), 2.23 (dd, *J* = 15.2, 7.9 Hz, 1H), 2.15 (dd, *J* = 13.4 Hz, 1H), 1.90 (dt, *J* = 13.4, 3.0 Hz, 1H), 1.73–1.72 (m, 3H), 1.57 (s, 3H), 1.17 (q, *J* = 12.8 Hz, 1H), 0.16 (s, 9H), 0.04 (s, 9H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 205.0, 173.6, 171.1, 170.8, 146.6, 110.2, 80.7, 78.3, 76.0, 60.5, 55.9, 51.6, 51.1, 46.4, 45.8, 43.1, 42.3, 39.2, 35.2, 27.6, 20.4, 0.22, –0.10 ppm; IR (film) ν = 2954, 2855, 1740, 1252, 1160, 1057, 842 cm^{-1}; MS (ESI) *: m/z*: 588 [*M*+NH_4^+], 593 [*M*+Na^+]; HRMS (ESI)*: m/z* calcd. for $C_{27}H_{46}O_9Si_2Na$ [*M*+Na^+]: 593.25726, found: 593.25710.

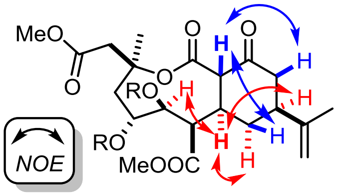
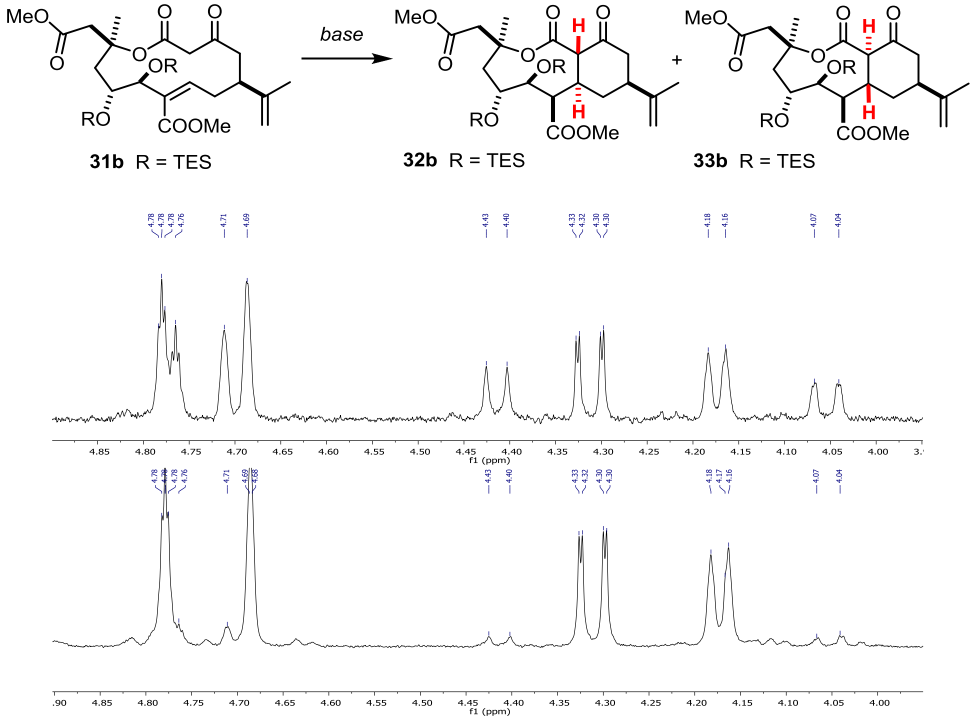
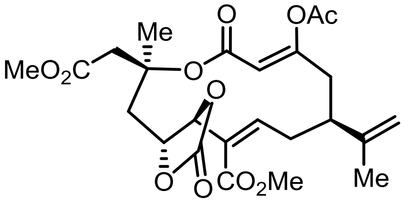


Figure S2. Relevant NOE contacts at the ring junction; R = TMS

Scheme S1. Influence of the Base on the Stereochemical Outcome of the Transannular Michael Addition[a]

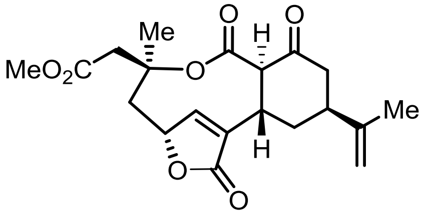


[a] Characteristic region of the ^{1}H NMR spectrum ($CDCl_3$) of the crude reaction mixture; top: Cs_2CO_3, CH_2Cl_2, MeOH/H_2O; bottom: 2-*tert*-butyl-1,1,3,3,-tetramethylguanidine (Barton's base, **33**), MeCN



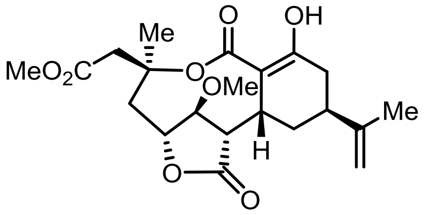
Methyl (*3aS,5S,8Z,11S,13Z,14aS*)-9-acetoxy-5-(2-methoxy-2-oxoethyl)-5-methyl-2,7-dioxo-11-(prop-1-en-2-yl)-3a,4,5,7,10,11,12,14a-octahydro-[1,3]dioxolo[4,5-d][1]oxacyclotridecine-14-carboxylate (25). Triphosgene (54.5 mg, 0.184 mmol) was added in small portions to a solution of compound **19** (17.2 mg, 0.036 mmol) in CH_2Cl_2/pyridine (7:1, 1.14 mL) at 0 °C and the resulting mixture was stirred at this temperature for 3 h. The reaction was quenched at 0 °C with sat. aq. $NaHCO_3$ (4 mL) and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash chromatography on silica (hexane/EtOAc, 3:2) to afford the title compound as a colorless oil (17.6 mg, 97%). $[\alpha]_D^{20}$ = 9.0 (c = 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.51 (t, *J* = 6.4, 6.4 Hz, 1H), 5.64 (s, 1H), 5.37 (d, *J* = 8.2 Hz, 1H), 5.25 (td, *J* = 8.7, 8.5, 3.2 Hz, 1H), 4.92 (s, 1H), 4.79 (q, *J* = 1.1, 1.1, 1.1 Hz, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.39–3.35 (s, 1H), 3.06 (d, *J* = 15.1 Hz, 1H), 2.99 (d, *J* = 15.1 Hz, 1H), 2.95–2.88 (m, 2H), 2.58 (dd, *J* = 16.5, 9.1 Hz, 2H), 2.53 (dt, *J* = 9.0, 4.7, 4.7 Hz, 1H), 2.37 (dd, *J* = 16.5, 2.5 Hz, 1H), 2.14 (s, 3H), 1.80 (s, 3H), 1.59 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 169.7, 167.9, 165.4, 165.1, 163.9, 154.0, 124.8, 113.2, 111.3, 80.4, 77.4, 53.4, 52.0, 51.9, 41.8, 32.0, 29.7, 27.8, 26.8, 22.1, 21.1, 17.5, 13.6, 1.0 ppm; IR (film) ν = 2948, 1800, 1677, 1594, 1366, 1257, 1165, 1019, 835, 754 cm^{-1}; MS (ESI): *m*/*z*: 512 [*M*+NH_4^+], 517 [*M*+Na^+]; HRMS (ESI)*: m/z:* calcd. for $C_{24}H_{30}O_{11}Na$ [*M*+Na^+]: 517.16803, found: 517.16811.

Methyl 2-((*3S*,*5R*,*8aS*,*10S*,*12aR*,*Z*)-3-methyl-1,7,12-trioxo-10-(prop-1-en-2-yl)-4,5,8a,9,10,11,12,12a-octahydro-1*H*,3*H*,7*H*-5,8-(metheno)benzo[g][1,5]dioxecin-3-yl)acetate

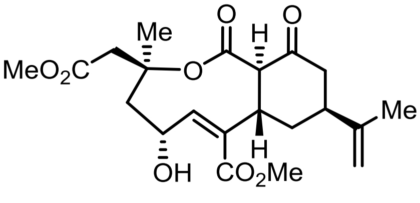


(27). Caesium carbonate (19.3 mg, 0.0592 mmol) was added to a solution of compound **25** (5.6 mg, 0.0113 mmol) in $CH_2Cl_2/CCl_3CH_2OH/H_2O$ (0.65 mL, 3:1:1) at 0 °C. The mixture was stirred for 10 min at this temperature and for 3 h at ambient temperature before the reaction was quenched with sat. aq. NH_4Cl (5 mL). The aqueous phase was extracted with EtOAc (3 x 4 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica (hexanes/EtOAc, 1:1) to afford the title compound as a colorless oil (3.7 mg, 87%). $[\alpha]_D^{20}$ = –4.5 (c = 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (d, *J* = 1.5 Hz, 1H), 5.27 (d, *J* = 8.5 Hz, 1H), 4.99 (s, 1H), 4.79 (s, 1H), 3.65 (s, 3H), 3.43 (d, *J* = 12.1 Hz, 1H), 3.36 (d, *J* = 15.1 Hz, 1H), 3.22 (td, *J* = 12.2, 12.1, 3.4 Hz, 1H), 3.07 (d, *J* = 15.1 Hz, 1H), 2.88 (s, 1H), 2.81 (ddd, *J* = 13.9, 12.5, 5.6 Hz, 1H), 2.70 (ddd, *J* = 15.4, 3.3, 1.7 Hz, 1H), 2.57–2.53 (m, 1H), 2.53–2.49 (m, 1H), 2.39 (d, *J* = 15.2 Hz, 1H), 2.17 (dtd, *J* = 14.0, 3.5, 3.3, 1.8 Hz, 1H), 1.77 (s, 3H), 1.56 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.0, 172.6, 169.9, 168.3, 152.9, 145.5, 130.9, 113.8, 82.9, 78.2, 60.4, 51.8, 46.0, 44.0, 40.4, 38.5, 36.8, 28.3, 27.4, 22.2 ppm; IR (film) ν = 2918, 2850, 1736, 1440, 1360, 1139, 1083, 797 cm^{-1}; MS (ESI): *m*/*z*: 394 [M+NH_4^+], 399 [M+Na^+]; HRMS (ESI) *m/z:* calcd. for $C_{20}H_{24}O_7Na$ [M+Na^+]: 399.14142, found: 399.14155.

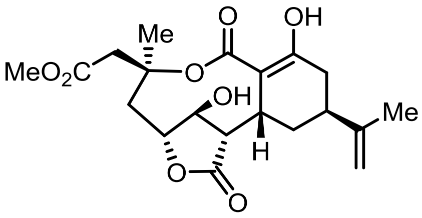
Methyl 2-((*3S,5R,8S,8aR,10S,13S*)-12-hydroxy-13-methoxy-3-methyl-1,7-dioxo-10-(prop-1-en-2-yl)-4,5,7,8,8a,9,10,11-octahydro-1*H*,3*H*-5,8-methanobenzo[g][1,5]dioxecin-3-yl)acetate (28). Caesium carbonate (131.1 mg, 0.402 mmol) was added to a solution of compound **25** (17.6 mg, 0.0356 mmol) in $CH_2Cl_2/MeOH/H_2O$ (3 mL, 3:2:1) at 0 °C. The resulting mixture was stirred for 10 min at 0°C and for another 60 min at ambient temperature. sat.aq. NH_4Cl (5 mL) was added and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography on silica (hexanes/EtOAc, 1:1) to afford the title compound as a colorless oil (12.5 mg, 86%). A second fraction consisted of compound **26** (1.6 mg, 11%). $[\alpha]_D^{20}$ = –79.0 (c = 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 12.01 (s, 1H), 4.85 (s, 1H), 4.70 (s, 1H), 4.61 (d, *J* = 6.5 Hz, 1H), 4.07 (t, *J* = 1.8, 1.8 Hz, 1H), 3.68 (s, 3H), 3.34 (s, 3H), 3.08 (d, *J* = 15.2 Hz, 1H), 2.85 (d, *J* = 15.2 Hz, 1H), 2.80 (t, *J* = 6.0, 6.0 Hz, 1H), 2.66 (d, *J* = 6.1 Hz, 1H), 2.62–2.55 (m, 1H), 2.54–2.51 (m, 2H), 2.33 (dd, *J* = 14.9, 6.3 Hz, 1H), 2.31–2.24 (m, 1H), 2.08–2.00 (m, 1H), 1.87 (ddd, *J* = 13.7, 8.4, 5.8 Hz, 1H), 1.78 (s, 6H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 176.2, 174.4, 170.0, 169.8, 146.3, 110.3, 98.3, 93.2, 82.8, 80.9, 56.3, 55.3, 51.7, 45.4, 42.4, 36.5, 36.3, 36.2, 34.0, 26.1, 21.4 ppm; IR (film) ν = 2920, 2851, 1770, 1661, 1219, 1096, 803, 728 cm^{-1}; MS (ESI): *m/z*: 409 $[M+H^+]$, 431 $[M+Na^+]$; HRMS (ESI) *m/z:* calcd. for $C_{21}H_{28}O_8Na$ $[M+Na^+]$: 431.16764, found: 431.16799.



Methyl (*3S,5R,7aS,9S,11aR,Z*)-5-hydroxy-3-(2-methoxy-2-oxoethyl)-3-methyl-1,11-dioxo-9-(prop-1-en-2-yl)-1,3,4,5,7a,8,9,10,11,11a-decahydrobenzo[c]oxonine-7-carboxylate (26). $[\alpha]_D^{20}$ = –30.0 (c = 0.16, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ = 6.07 (d, *J* = 10.1 Hz, 1H), 5.69 (td, *J* = 10.9, 10.8, 3.1 Hz, 1H), 4.94 (s, 1H), 4.66 (s, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.53 (d, *J* = 6.7 Hz, 1H), 3.37–3.29 (m, 1H), 2.94 (dd, *J* = 15.0, 6.3 Hz, 1H), 2.90 (s, 1H), 2.76 (d, *J* = 15.0 Hz, 1H), 2.65 (d, *J* = 14.2 Hz, 1H), 2.56 (dd, *J* = 14.5, 10.8 Hz, 1H), 2.50 (d, *J* = 14.2 Hz, 1H), 2.38 (td, *J* = 13.6, 13.6, 4.2 Hz, 1H), 2.08 (dd, *J* = 14.8, 3.1 Hz, 1H), 1.87 (d, *J* = 14.8 Hz, 1H), 1.74 (s, 3H), 1.68 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 205.7, 169.6, 168.4, 166.7, 145.9, 145.0, 131.5, 113.4, 83.0, 67.1, 59.2, 52.1, 51.9, 44.4, 44.0, 39.4, 36.3, 25.8, 24.6, 22.3 ppm; IR (film) ν = 3468, 2953, 1709, 1437, 1216, 1163,

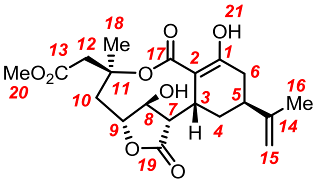


1028, 908 cm^{-1}; MS (ESI): *m/z*: 409 [M+H$^+$], 426 [M+NH$_4^+$], 431 [M+Na$^+$]; HRMS (ESI) *m/z:* calcd. for $C_{21}H_{28}O_8Na$ [M+Na$^+$]: 431.16764, found: 431.16756.



Sinulariadiolide ((–)-1). A solution of boron tribromide (1 M in CH_2Cl_2, 0.26 mL, 0.26 mmol) was slowly added to a solution of compound **28** (6.3 mg, 0.0154 mmol) and 2-methyl-2-butene (20 µL, 0.1882 mmol) in CH_2Cl_2 (0.23 mL) at –78°C. After 10 min, the reaction was warmed to –15 °C and stirring was continued at this temperature for 9 h. The reaction was quenched with anhydrous Et_2O (0.3 mL) at –78°C. The resulting solution was stirred for 2 min before sat. aq. $NaHCO_3$ (0.3 mL) was added dropwise to the vigorously stirred mixture. After 15 min, the mixture was allowed to reach ambient temperature. The aqueous phase was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine, dried over Na_2SO_4 and filterred. The filtrate was evaporated and the residue purified by flash chromatography on silica (hexanes/EtOAc, 2:3) to afford the title compound as a white solid (4.4 mg, 72%). $[\alpha]_D^{20}$ = –179 (c = 0.3, $CHCl_3$) [ref. 4: $[\alpha]_D^{20}$ = +91.1 (c = 0.3, $CHCl_3$)]; for the ^{1}H NMR and ^{13}C NMR data, see Tables S1 and S2; IR (film) ν = 3461, 2951, 1738, 1660, 1372, 1217, 1164, 1027, 756 cm^{-1}; MS (ESI): *m/z*: 417 [M+Na$^+$]; HRMS (ESI) *m/z:* calcd. for $C_{20}H_{26}O_8Na$ [M+Na$^+$]: 417.15199, found: 417.15218.

Table S1. Comparison of the ^{1}H NMR Data of Sinulariadiolide in $CDCl_3$; Arbitrary Numbering Scheme as Shown in the Insert



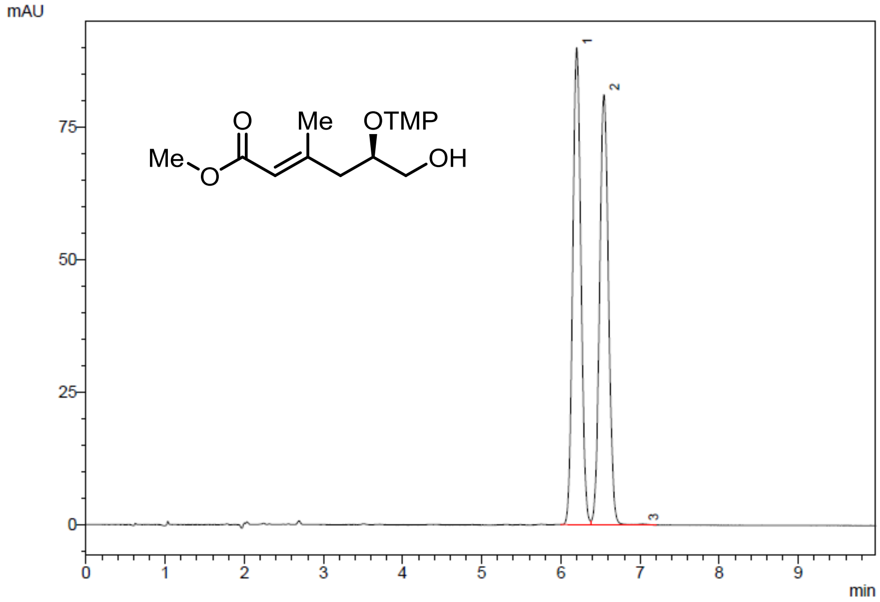
Position	Literature[4]		Synthetic sample		Δδ (ppm)
	δ (ppm)	*J* (Hz)	δ (ppm)	*J* (Hz)	
3	2.87	(t, *J* = 5.5)	2.87	(t, *J* = 6.0)	0
4a	1.85	(ddd, *J* = 5.5, 8.4,13.2)	1.85	(ddd, *J* = 5.7, 8.4,13.6)	0
4b	2.04	(ddd, *J* = 2.9, 6.7, 13.2)	2.04	(ddd, *J* = 2.8, 6.8, 13.0)	0
5	2.65	m	2.66–2.63	m	
6a	2.26	(dd, *J* = 6.7, 18.3)	2.29–2.26	m	
6b	2.55	(dd, *J* = 5.7, 18.3)	2.55	(dd, *J* = 6.0, 18.6)	0
7	2.56	(d, *J* = 1.8)	2.56	(d, *J* = 1.7)	0
8	4.59	brs	4.60	brs	–0.01
9	4.56	(d, *J* = 6.3)	4.56	(d, *J* = 6.3)	0
10a	2.28	(dd, *J* = 6.3, 14.8)	2.28	(dd, *J* = 6.0, 15.0)	0
10b	2.62	(d, *J* = 14.8)	2.63	(d, *J* = 14.8)	–0.01
12a	2.80	(d, *J* = 15.3)	2.80	(d, *J* = 15.4)	0
12b	3.09	(d, *J* = 15.3)	3.11	(d, *J* = 15.4)	–0.02
15a	4.68	s	4.68	s	
15b	4.83	s	4.84	s	–0.01
16	1.79	s	1.78	s	0.01
18	1.77	s	1.77	s	0
20	3.67	s	3.68	s	–0.01
21	12.0	s	12.0	s	0

Table S2. Comparison of the ^{13}C NMR Data of Sinulariadiolide in CDCl$_3$; Numbering Scheme as Shown in the Insert to Table S1

Position	Literature[4] δ (ppm)	Synthetic sample δ (ppm)	**Δδ** (ppm)
19	176.5	176.3	0.2
1	174.5	174.5	0
17	170.1	170.1	0
13	169.8	169.8	0
14	146.5	146.4	0.1
15	110.2	110.2	0
2	98.3	98.2	0.1
9	86.0	85.9	0.1
8	83.8	83.8	0
11	80.8	80.8	0
7	58.5	58.4	0.1
20	51.7	51.7	0
12	45.3	45.1	0.2
10	41.8	41.7	0.1
4	37.0	36.9	0.1
3	36.3	36.2	0.1
5	36.2	125.1	0
6	34.0	33.9	0.1
18	26.1	26.2	–0.1
16	21.4	21.5	–0.1

0.2 µL MFA-MA-627-01 Racemat (in 200 µL ACN)
150 mm Chiralcel OZ-3R, 4.6 mm i.D.
Acetonitril/Wasser = 60:40
1.0 mL/min, 19.0 MPa, 298 K
220 nm

<<Oven>>
Valve R : 6



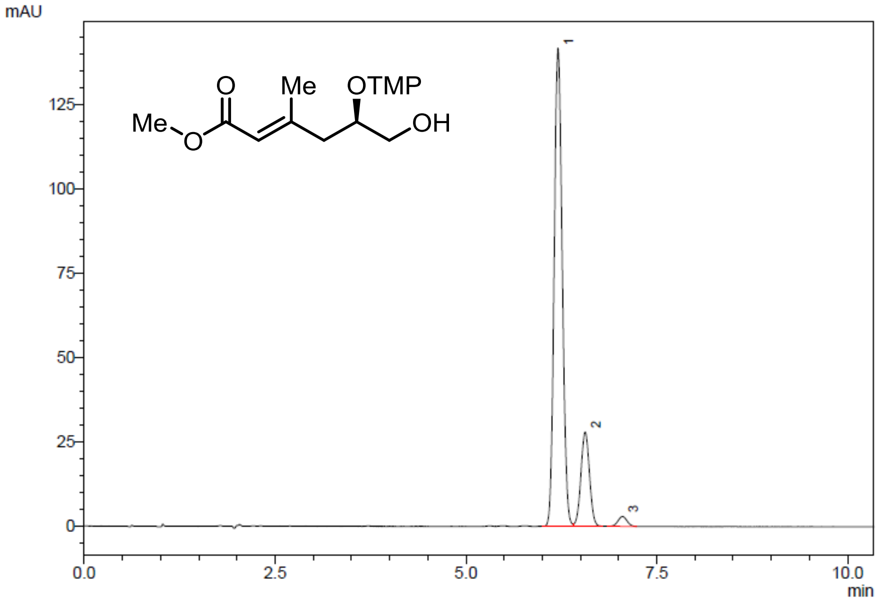
1 220nm,4nm

PDA Ch1 220nm

Peak #	Ret. Time	Area %	Name
1	6.20	50.52	1. enantiomer
2	6.54	49.36	2. enantiomer
3	7.03	0.12	
Total		100.00	

0.3 µL MFA-MA-626-01 Racemat (in 200 µL ACN)
150 mm Chiralcel OZ-3R, 4.6 mm i.D.
Acetonitril/Wasser = 60:40
1.0 mL/min, 19.4 MPa, 298 K
220 nm

<<Oven>>
Valve R : 6



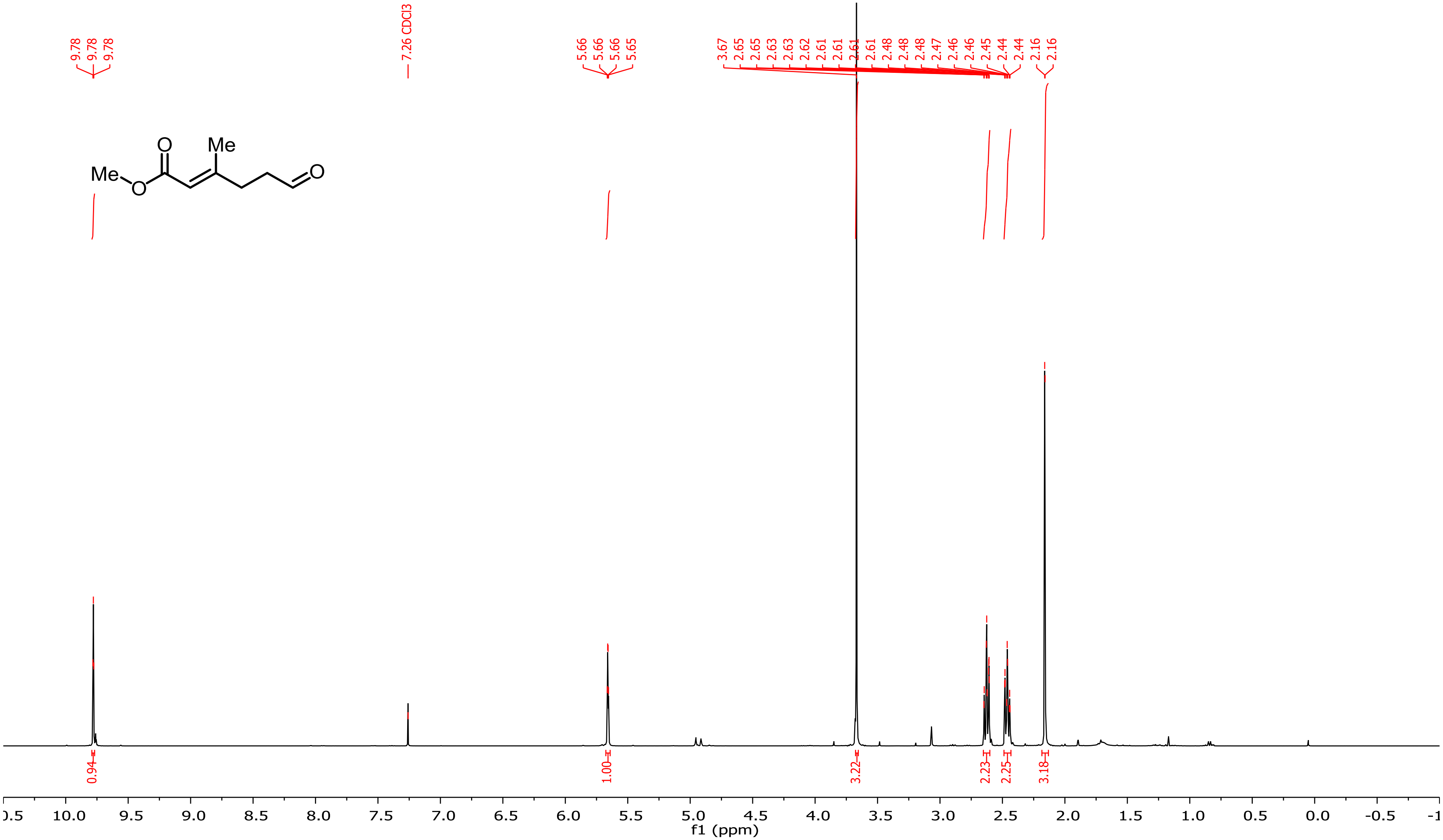
1 220nm,4nm

PDA Ch1 220nm

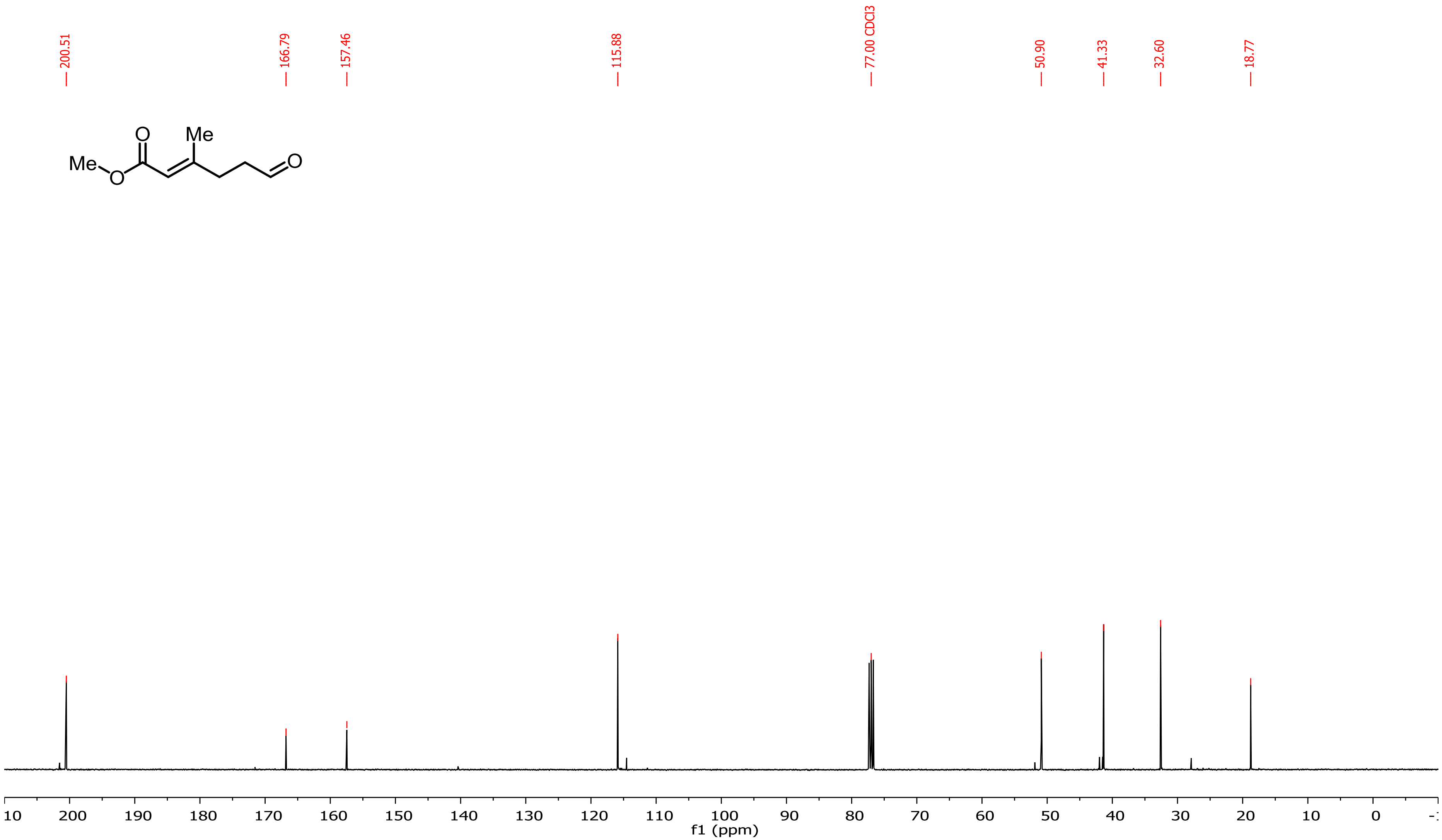
Peak #	Ret. Time	Area %	Name
1	6.21	81.09	1. enantiomer
2	6.56	17.05	2. enantiomer
3	7.05	1.86	
Total		100.00	

ee = 65.3 %

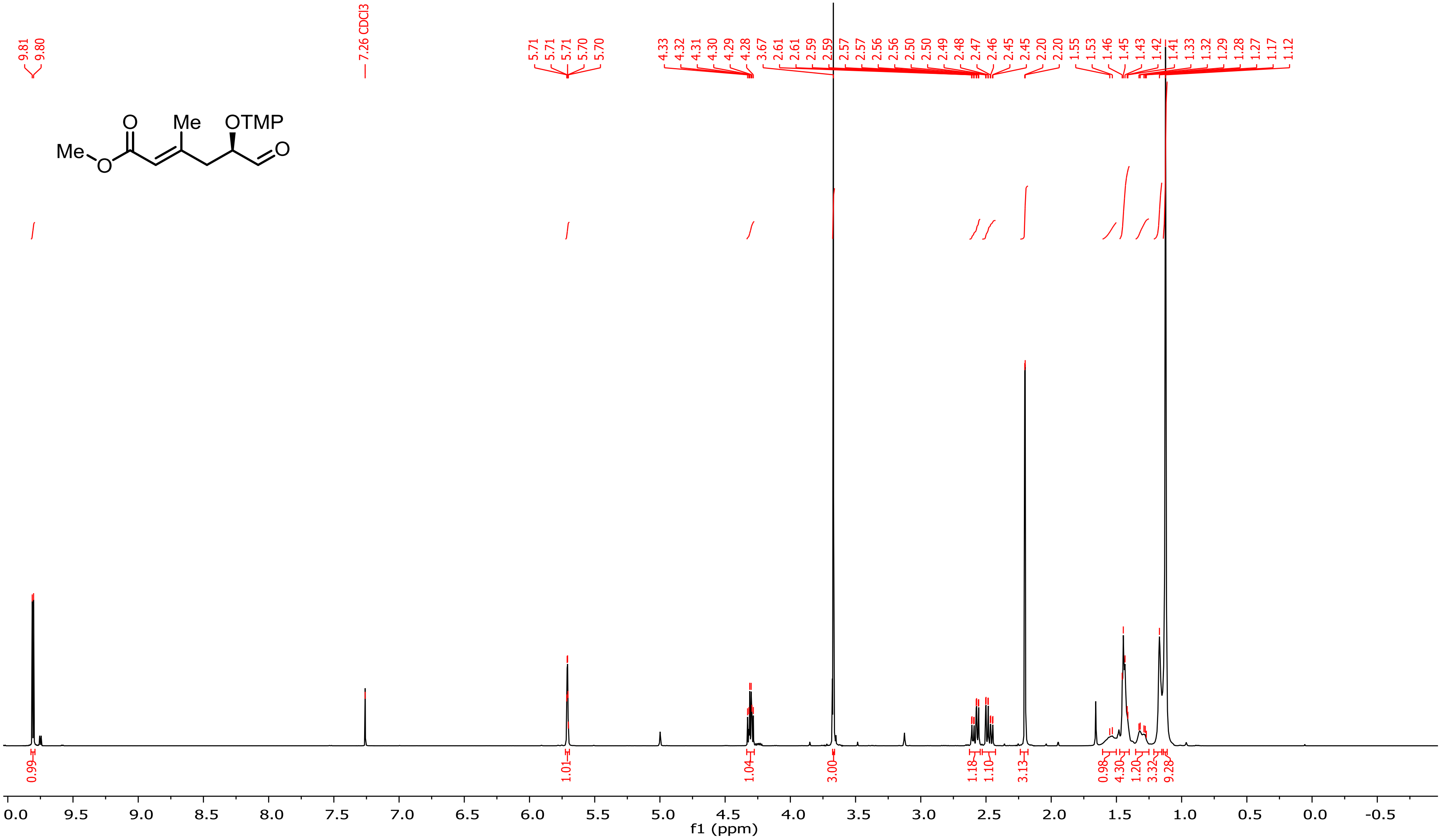
^{1}H NMR Spectrum of 4 (400 MHz, $CDCl_3$)



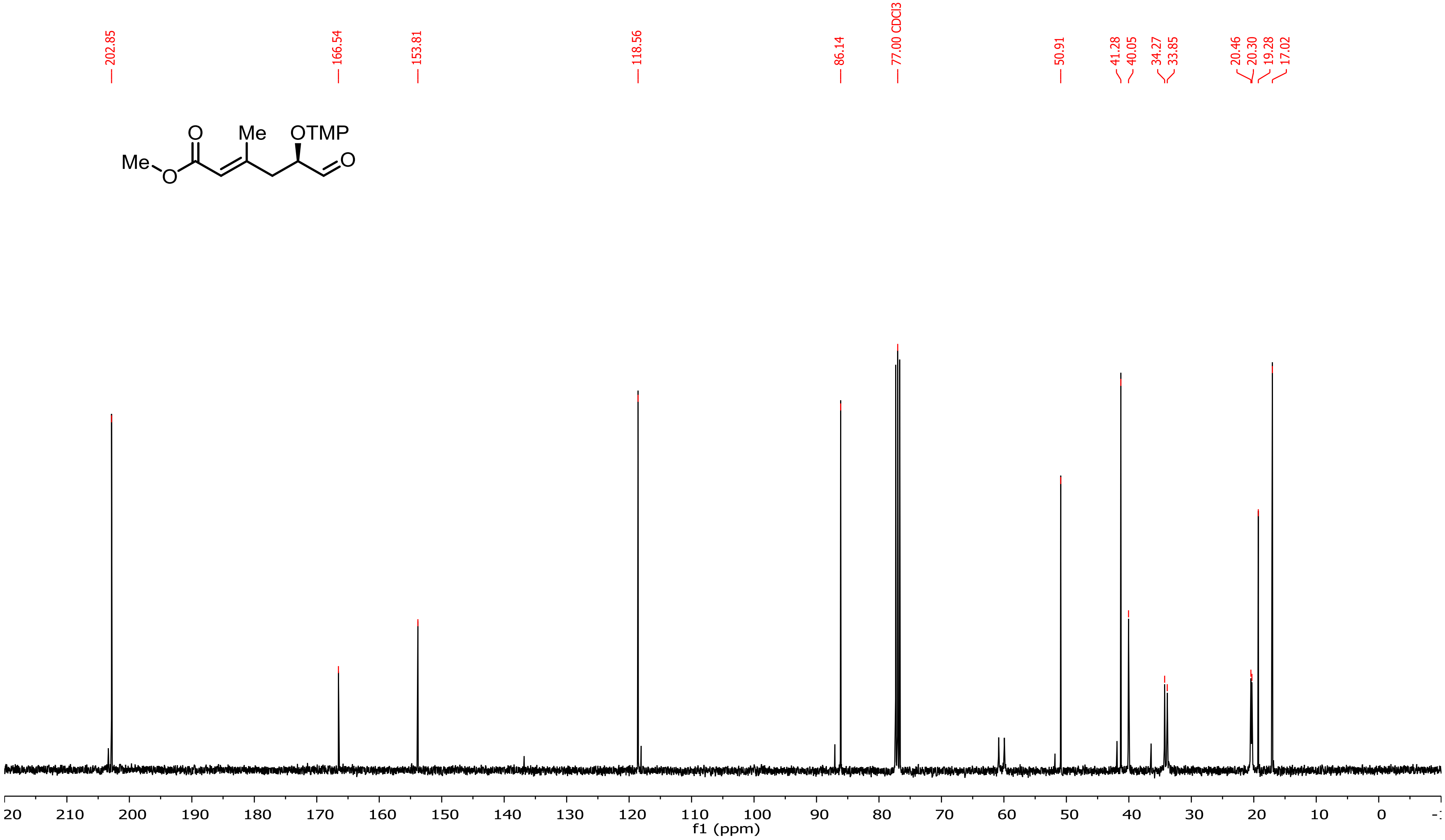
^{13}C NMR Spectrum of 4 (101 MHz, CDCl$_3$)



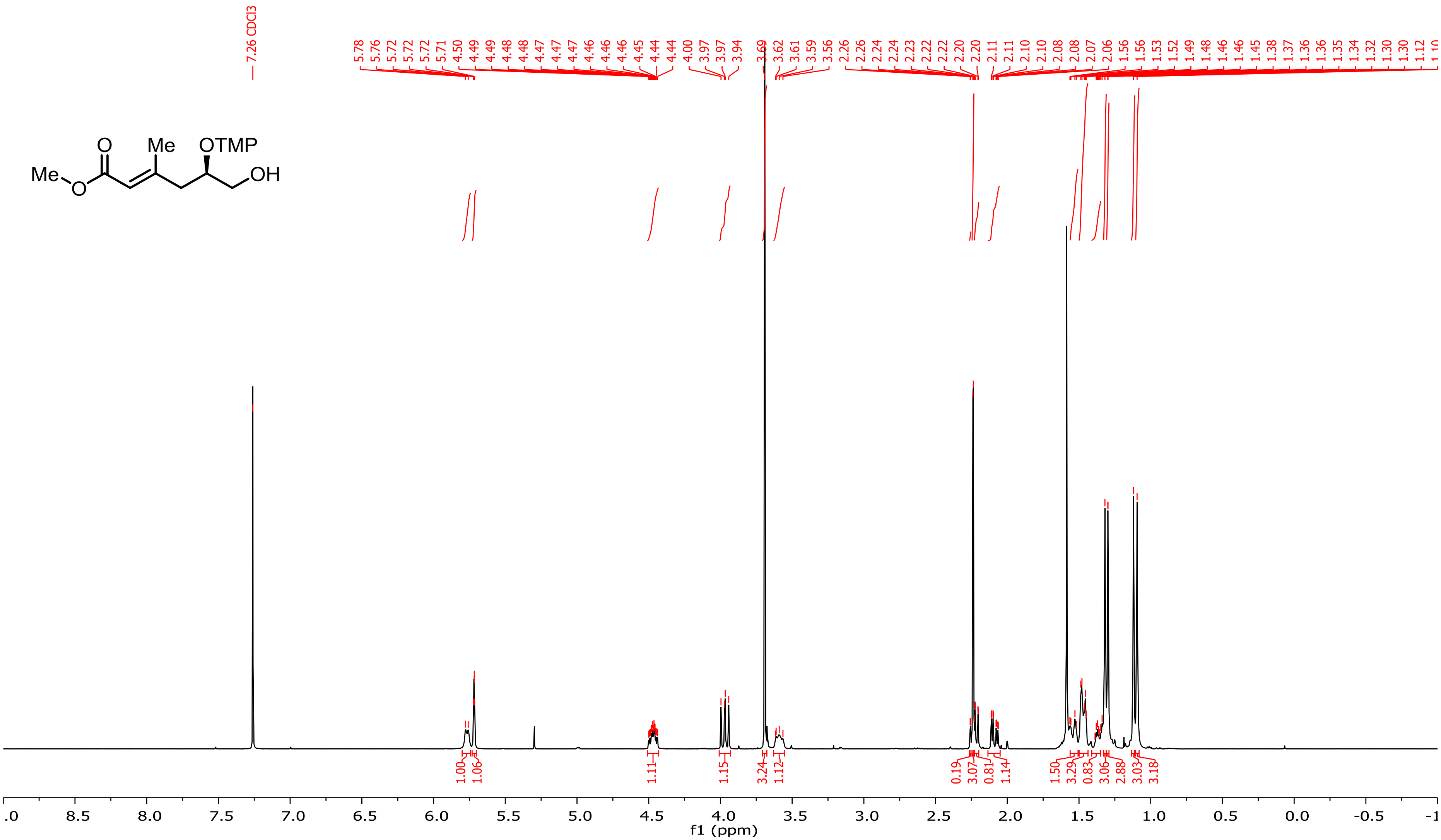
^{1}H NMR Spectrum of 5 (400 MHz, CDCl$_3$)



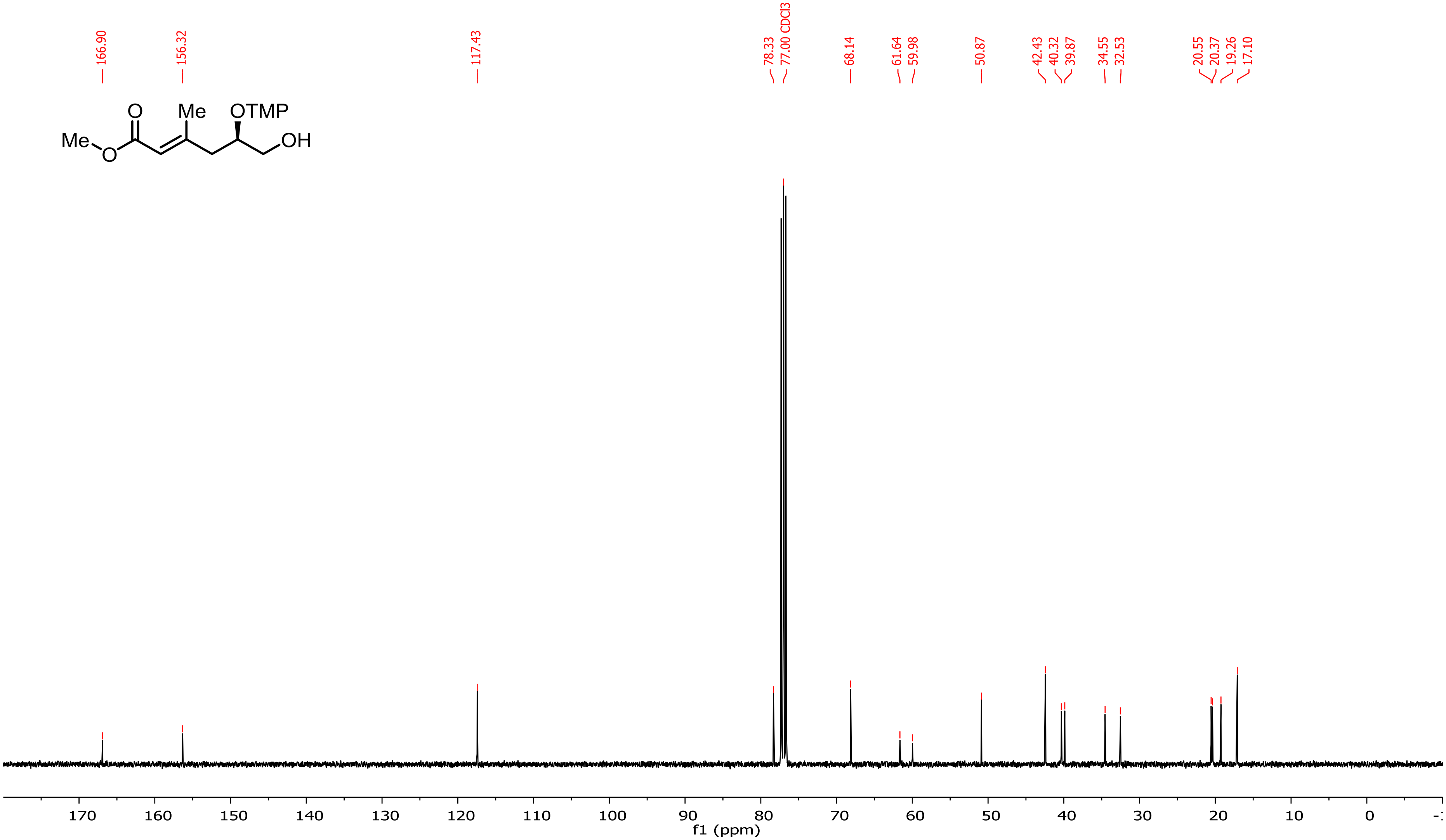
^{13}C NMR Spectrum of 5 (101 MHz, $CDCl_3$)



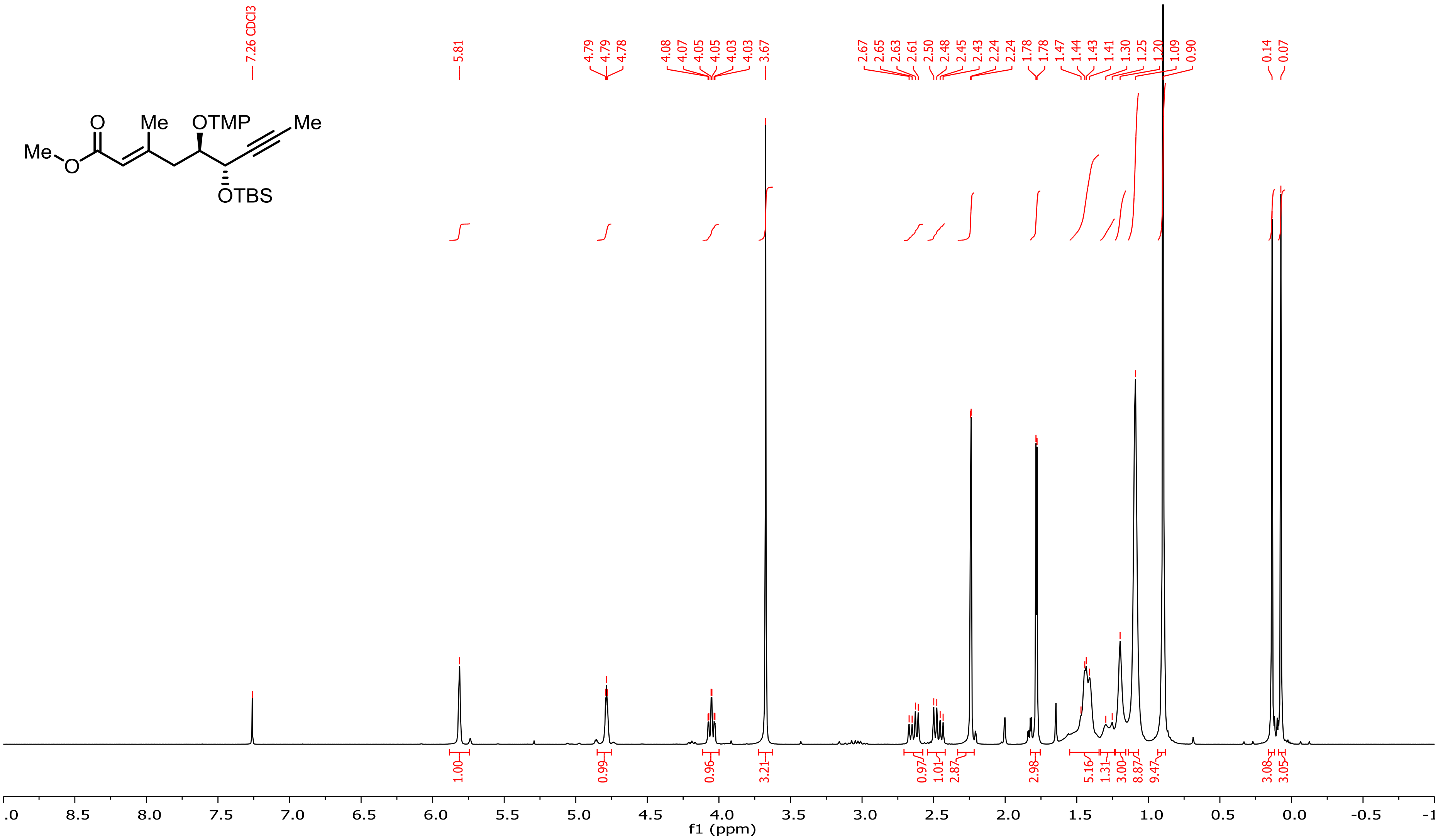
^{1}H NMR Spectrum of S1 (400 MHz, CDCl$_3$)



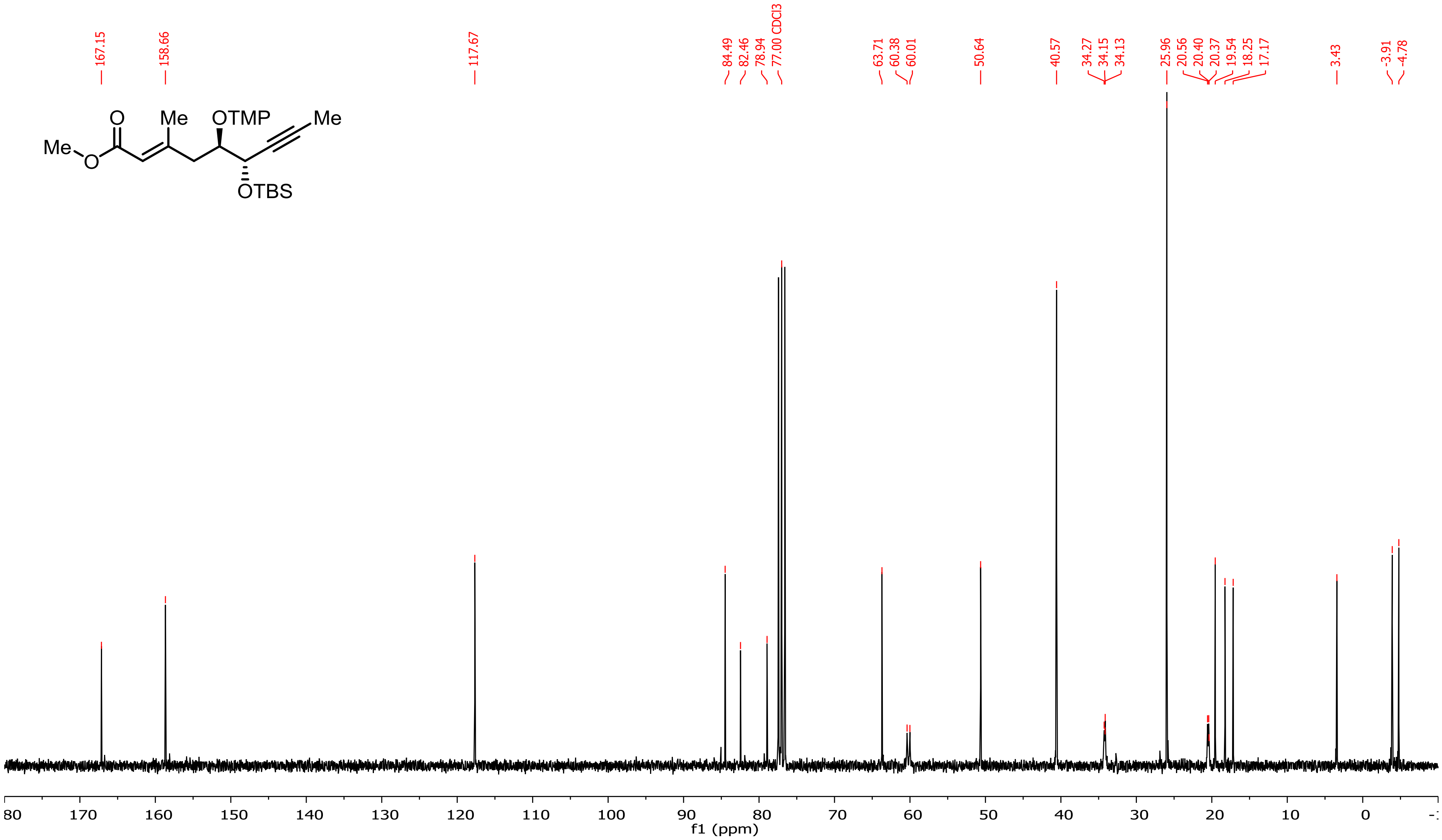
^{13}C NMR Spectrum of S1 (101 MHz, $CDCl_3$)



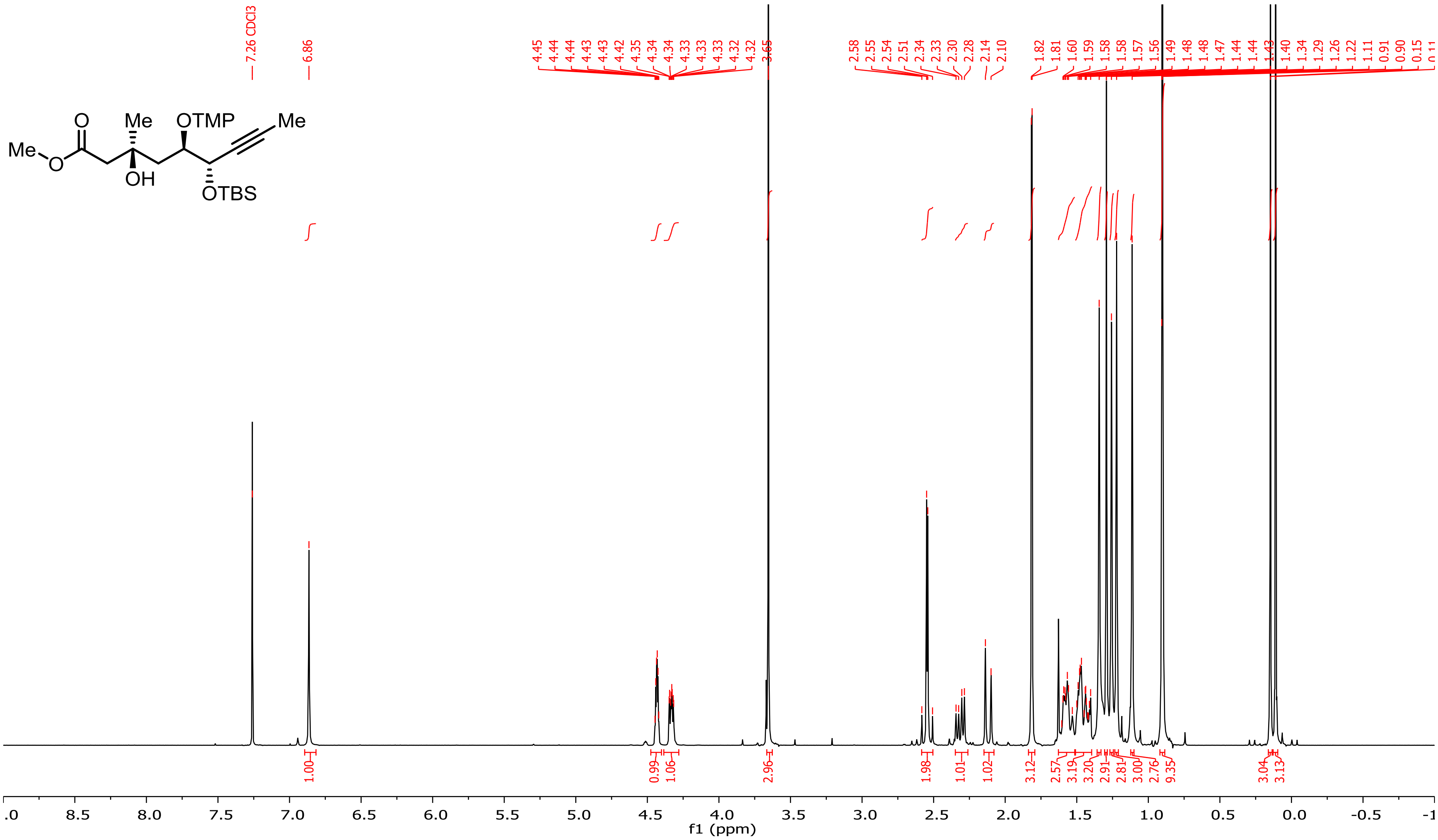
^{1}H NMR Spectrum of 6 (400 MHz, CDCl$_3$)



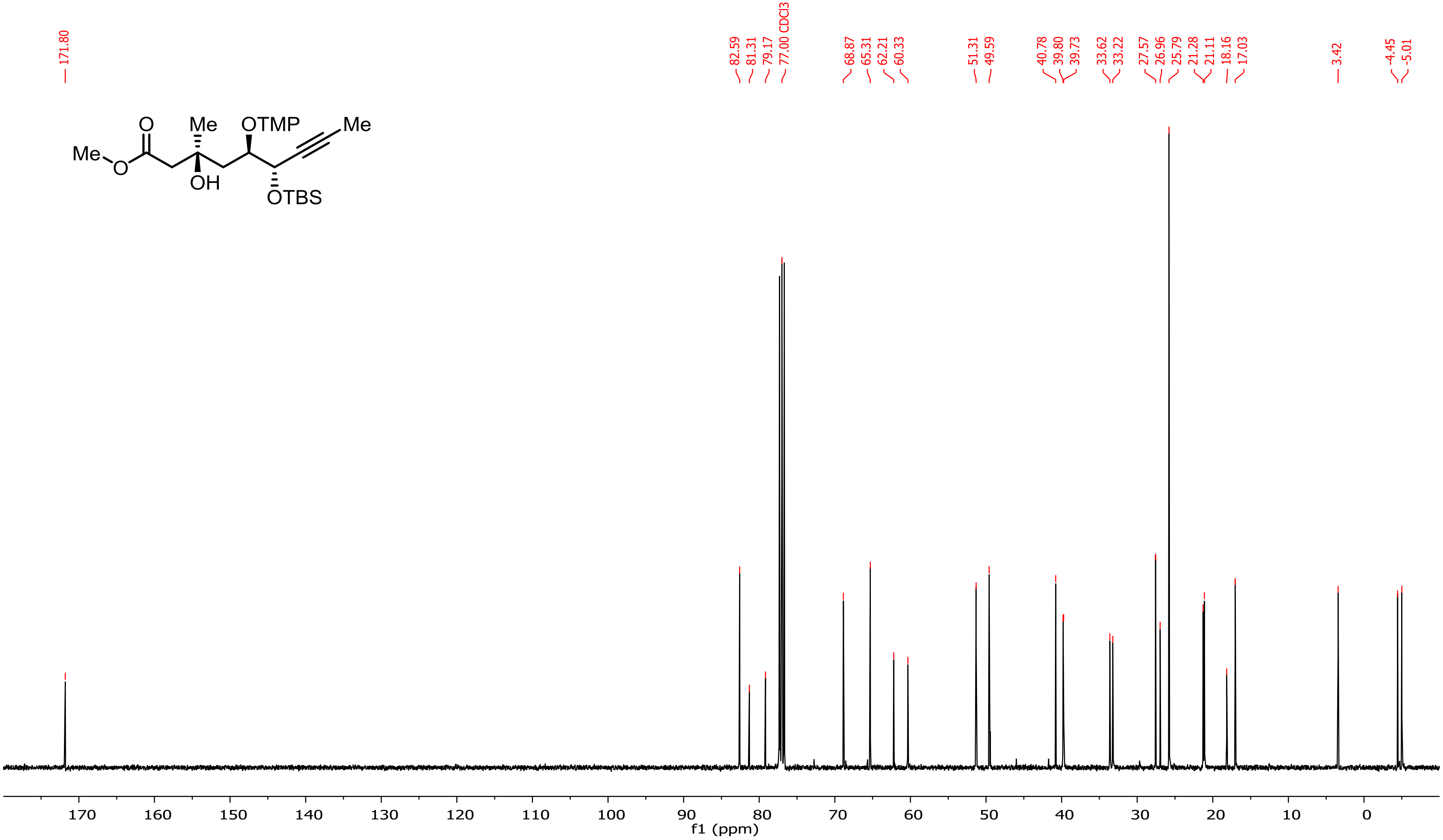
^{13}C NMR Spectrum of 6 (75 MHz, CDCl$_3$)



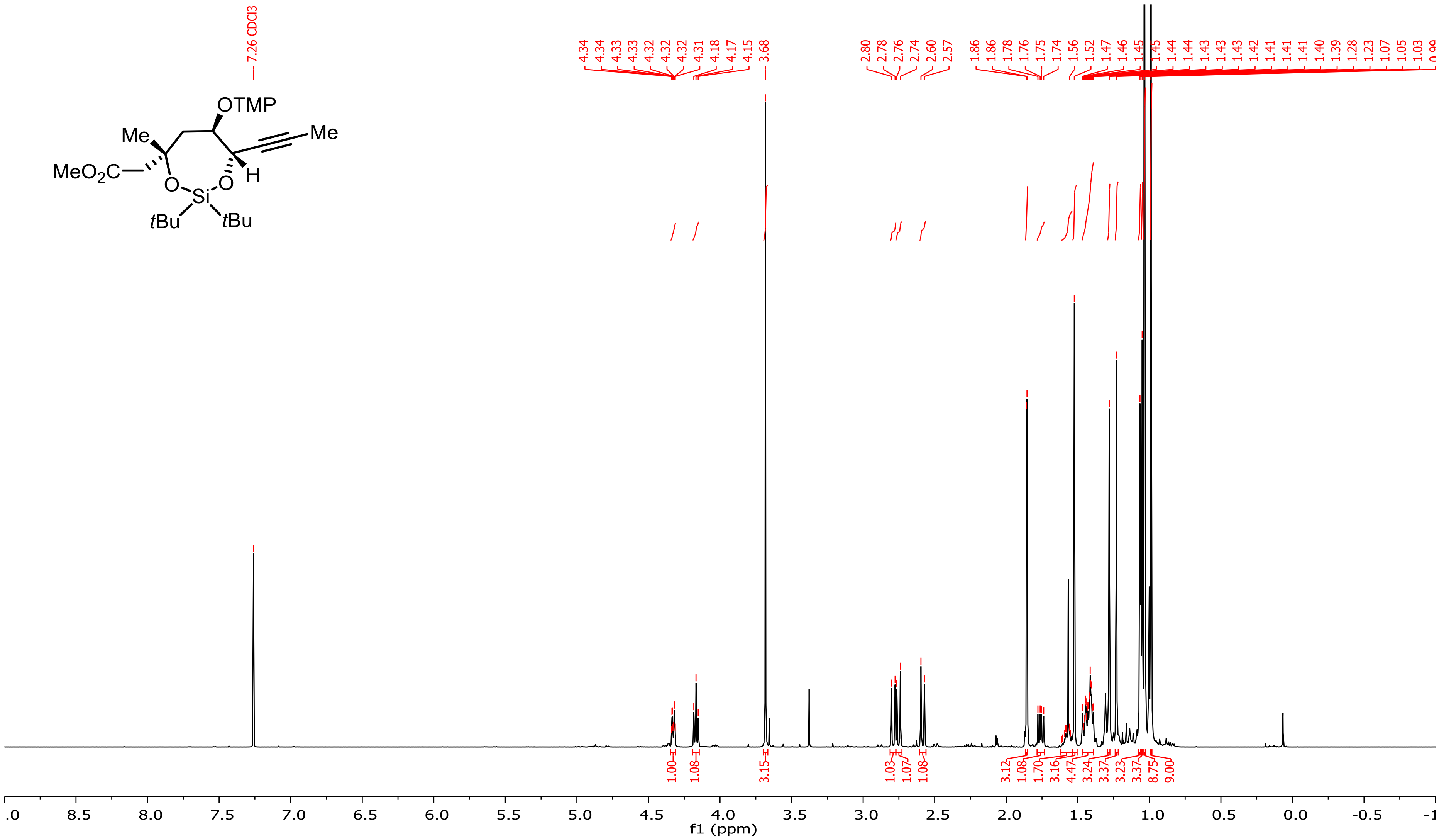
^{1}H NMR Spectrum of 7 (400 MHz, $CDCl_3$)



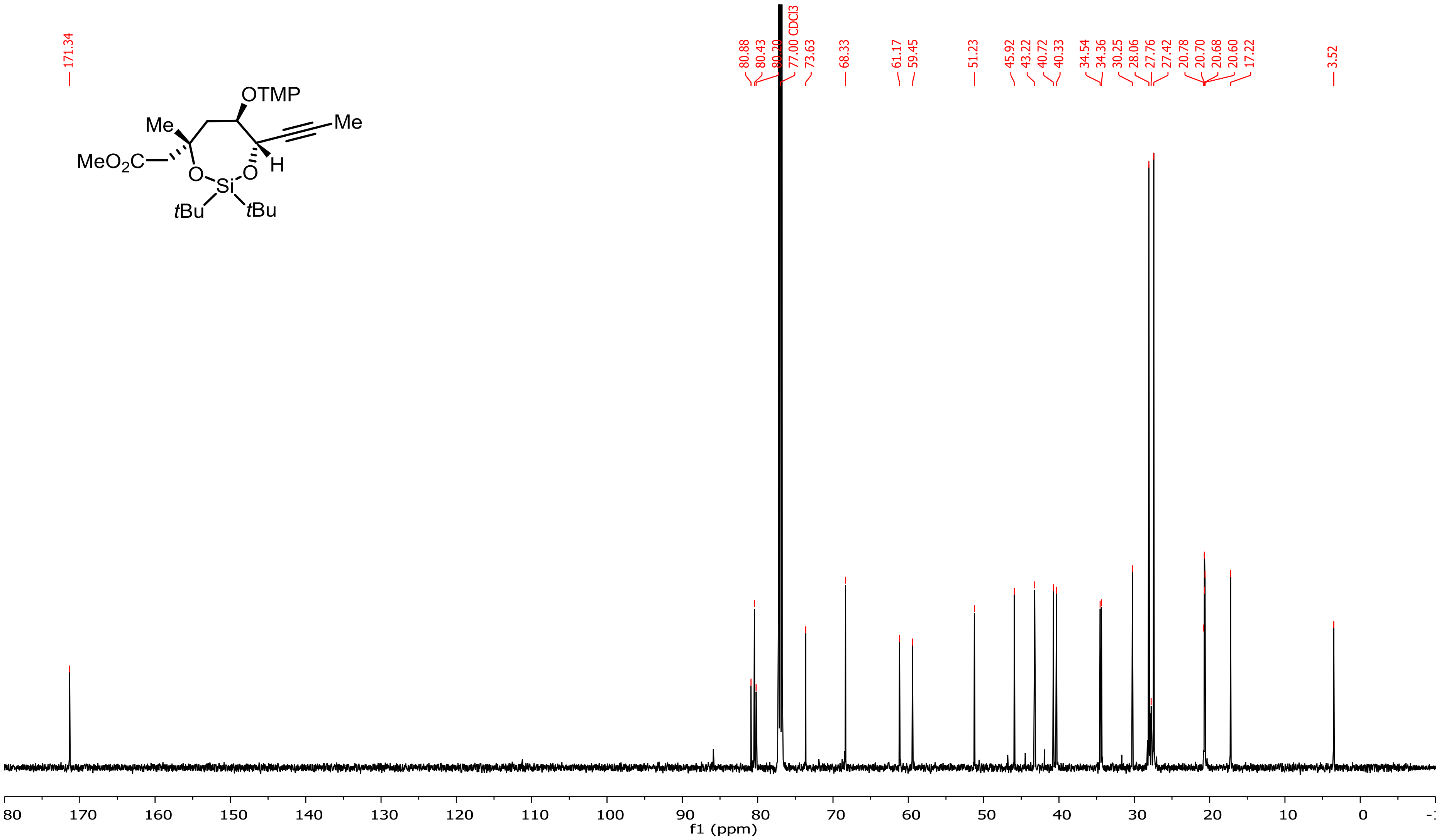
^{13}C NMR Spectrum of 7 (101 MHz, CDCl$_3$)



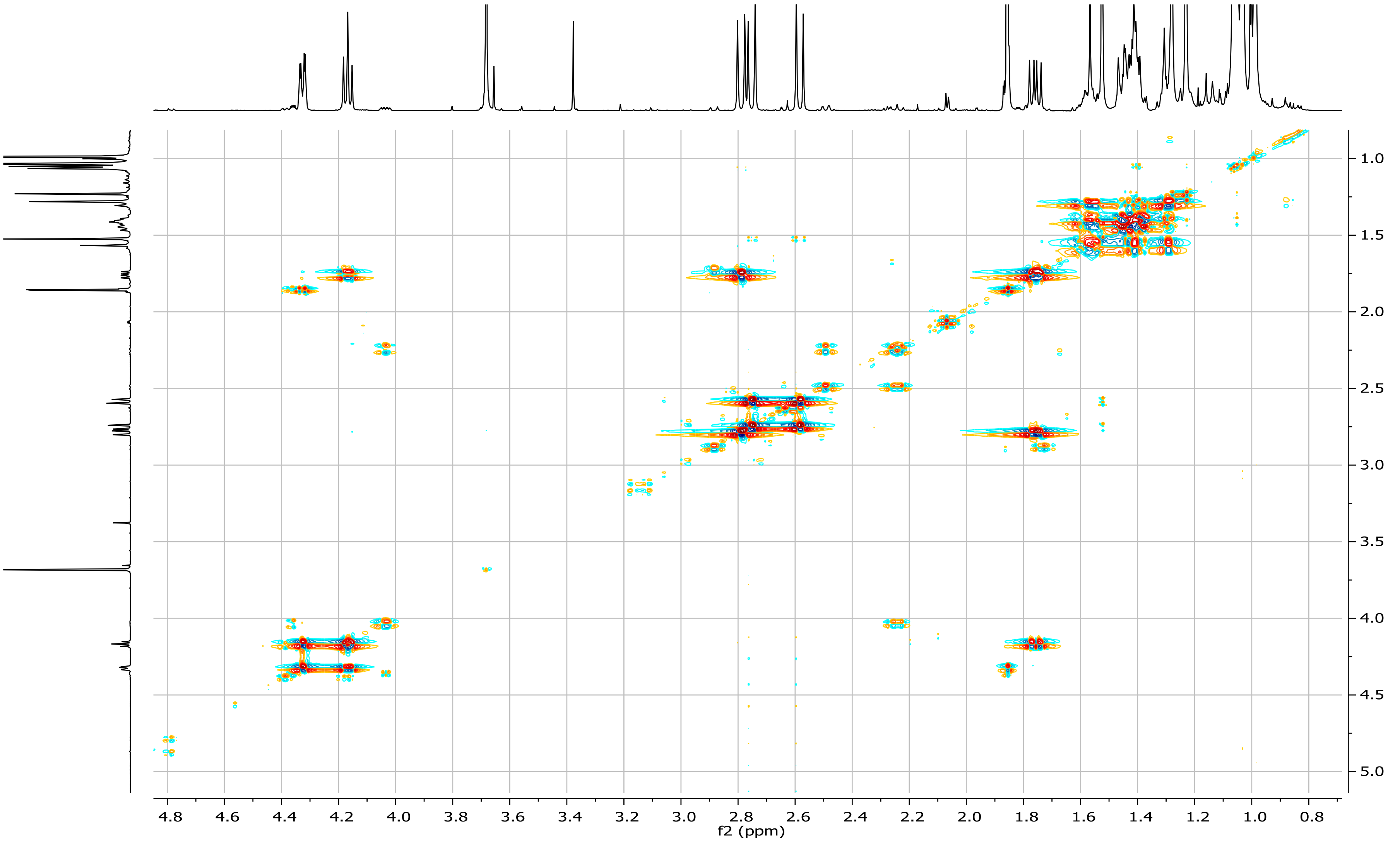
^{1}H NMR Spectrum of S2 (600 MHz, $CDCl_3$)



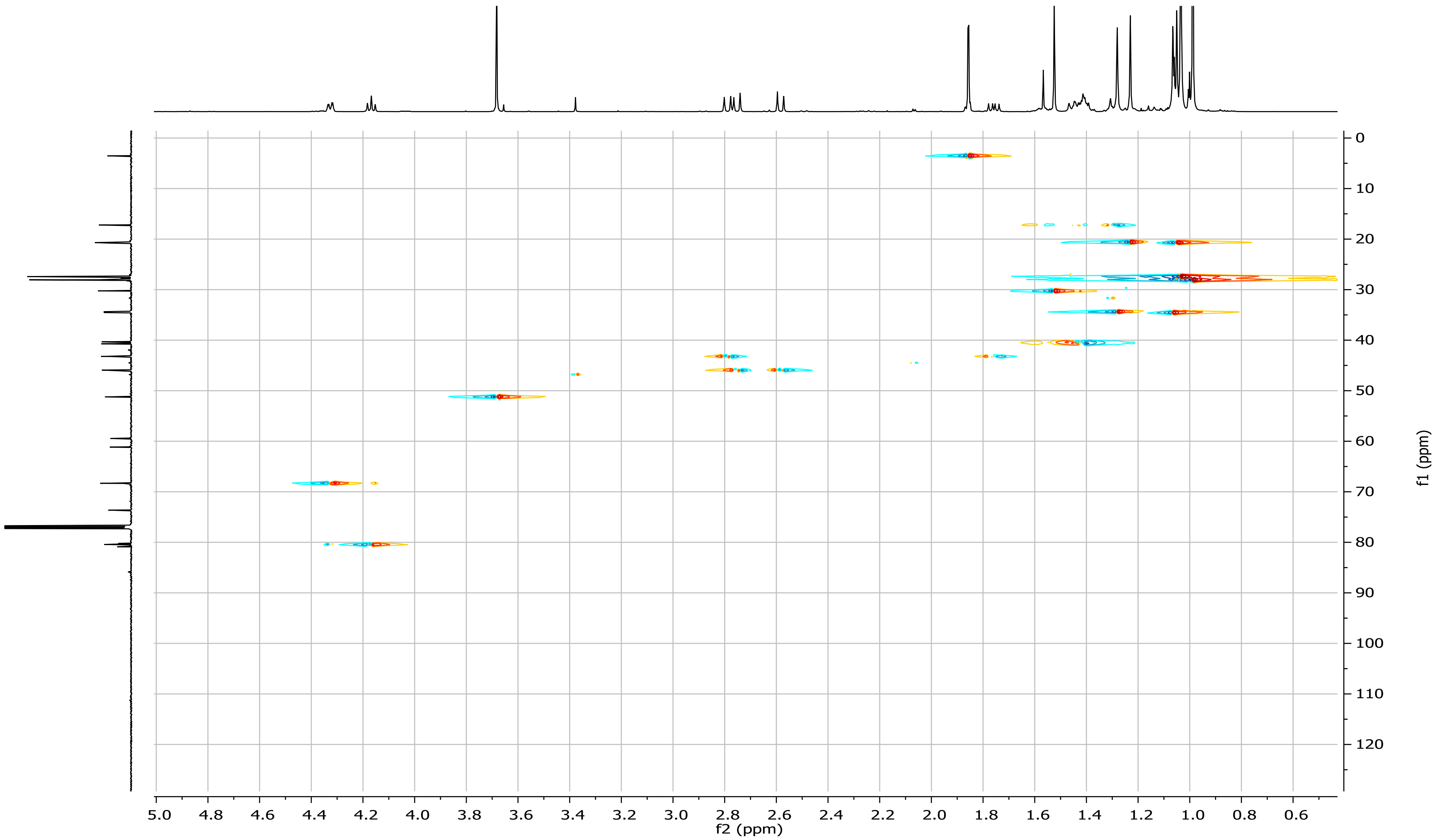
^{13}C NMR Spectrum of S2 (151 MHz, CDCl$_3$)



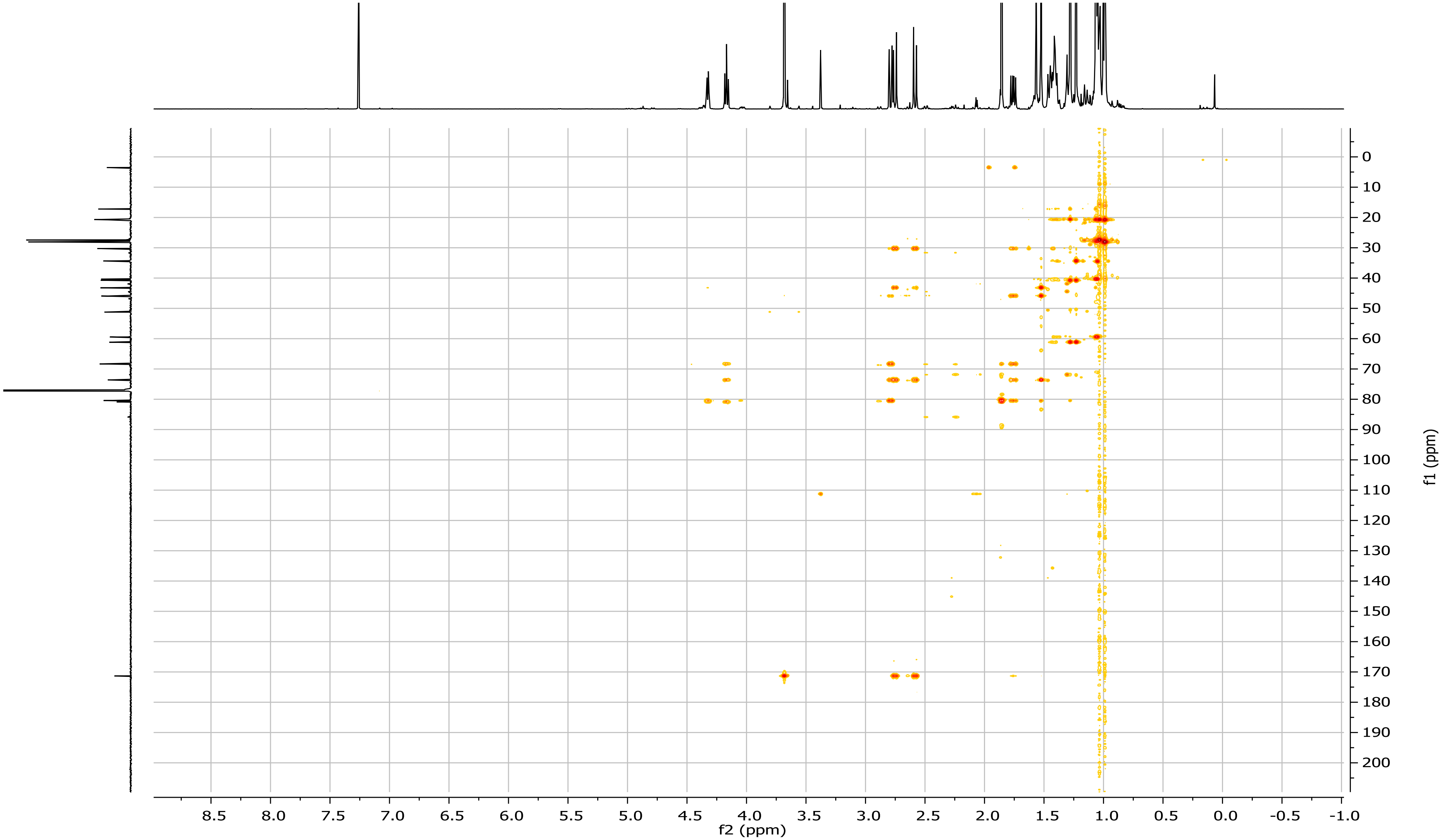
COSY Spectrum of S2



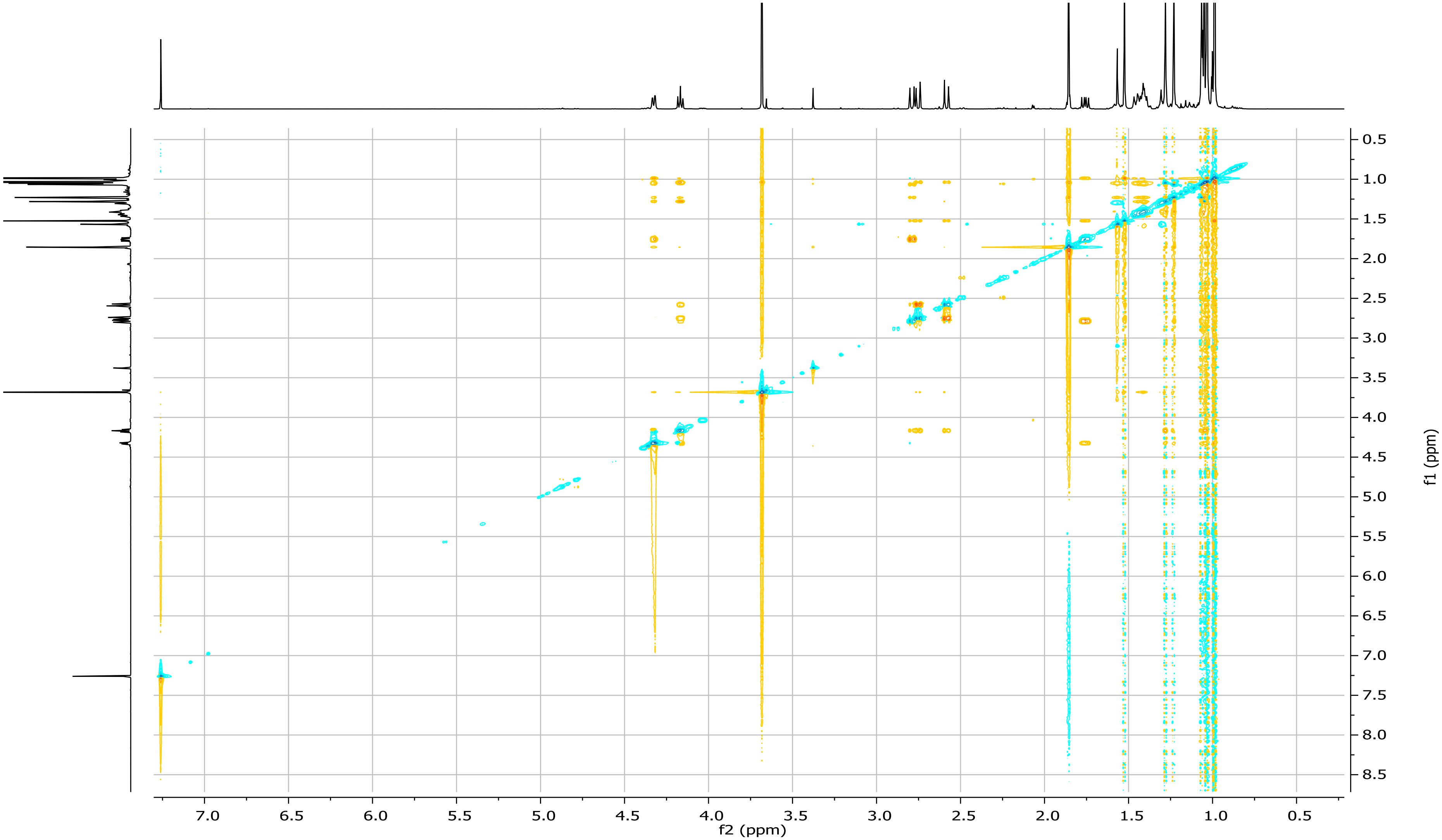
HSQC Spectrum of S2



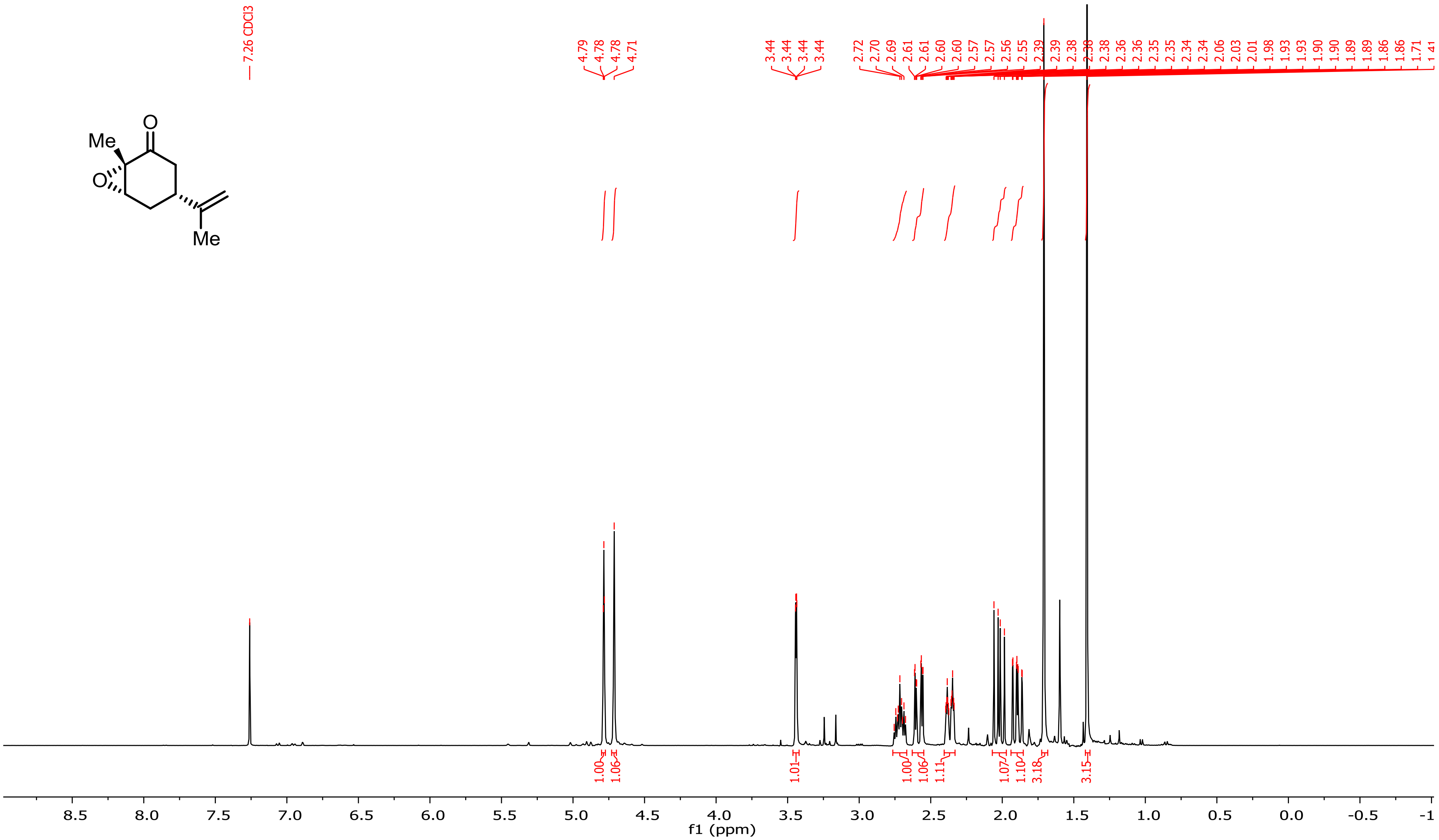
HMBC Spectrum of S2



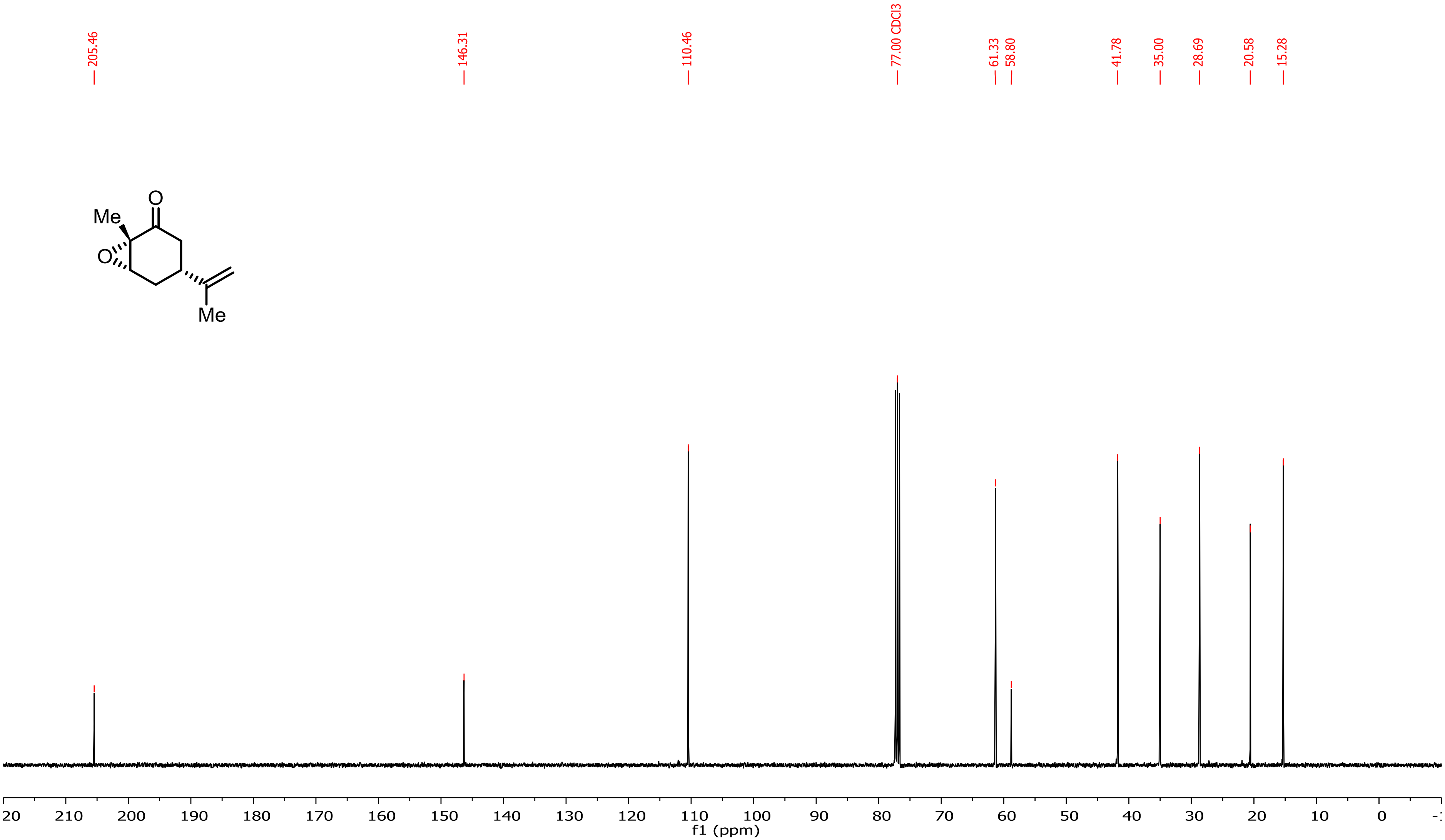
NOESY Spectrum of S2



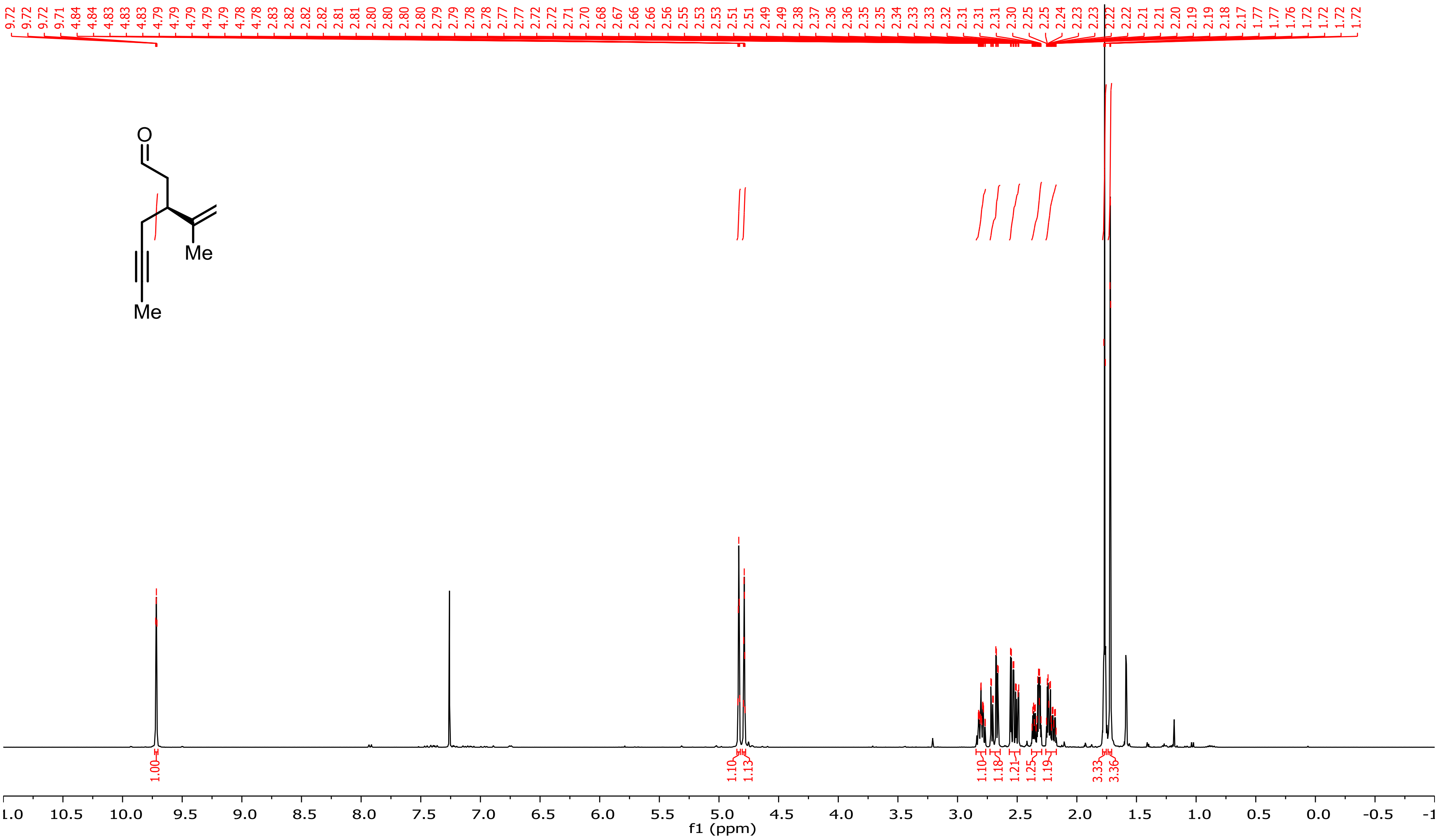
^1H NMR Spectrum of S3 (400 MHz, $CDCl_3$)



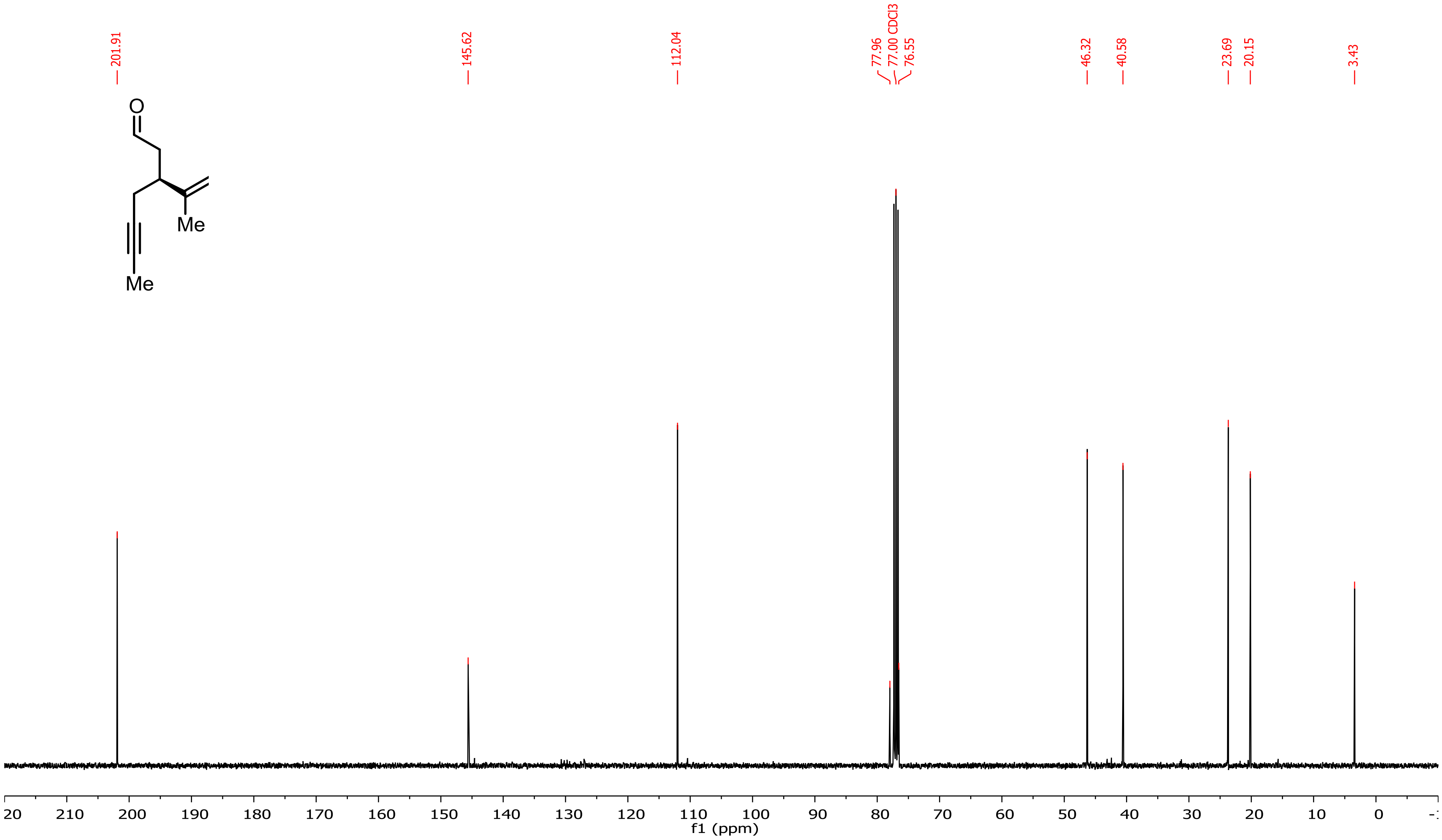
^{13}C NMR Spectrum of S3 (101 MHz, $CDCl_3$)



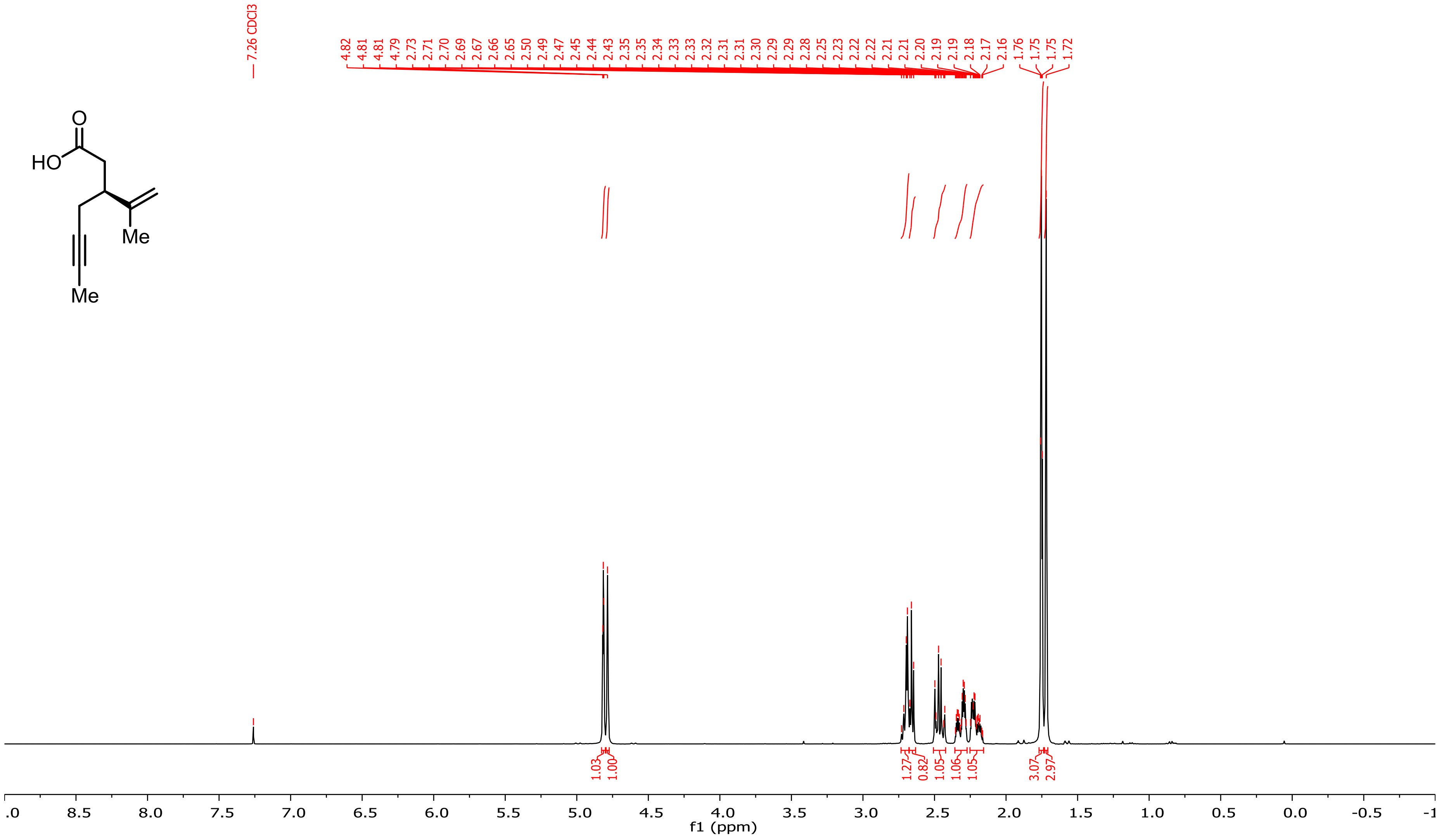
^{1}H NMR Spectrum of 10 (400 MHz, CDCl$_3$)



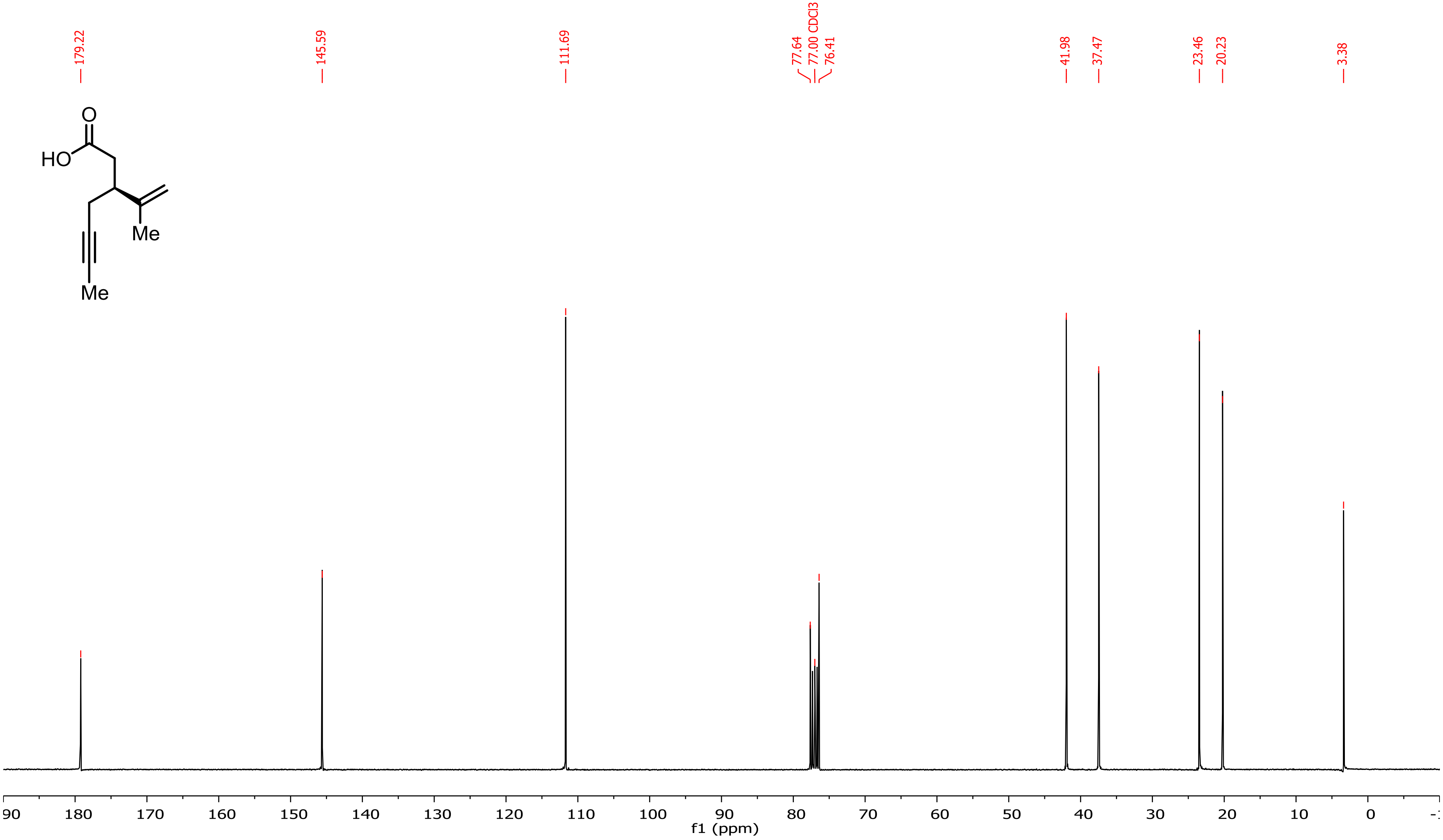
^{13}C NMR Spectrum of 10 (101 MHz, $CDCl_3$)



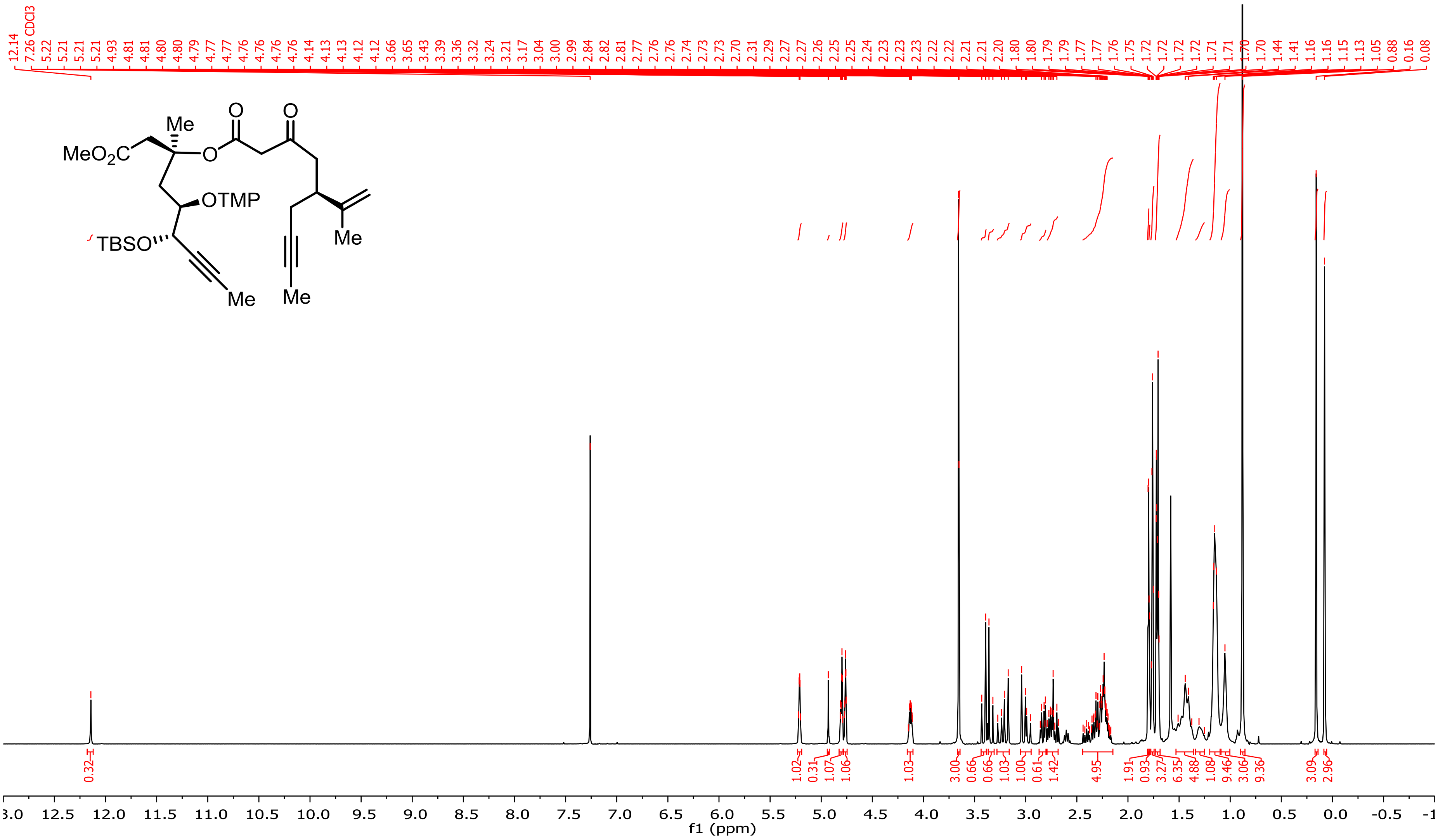
^{1}H NMR Spectrum of 11 (400 MHz, CDCl$_3$)



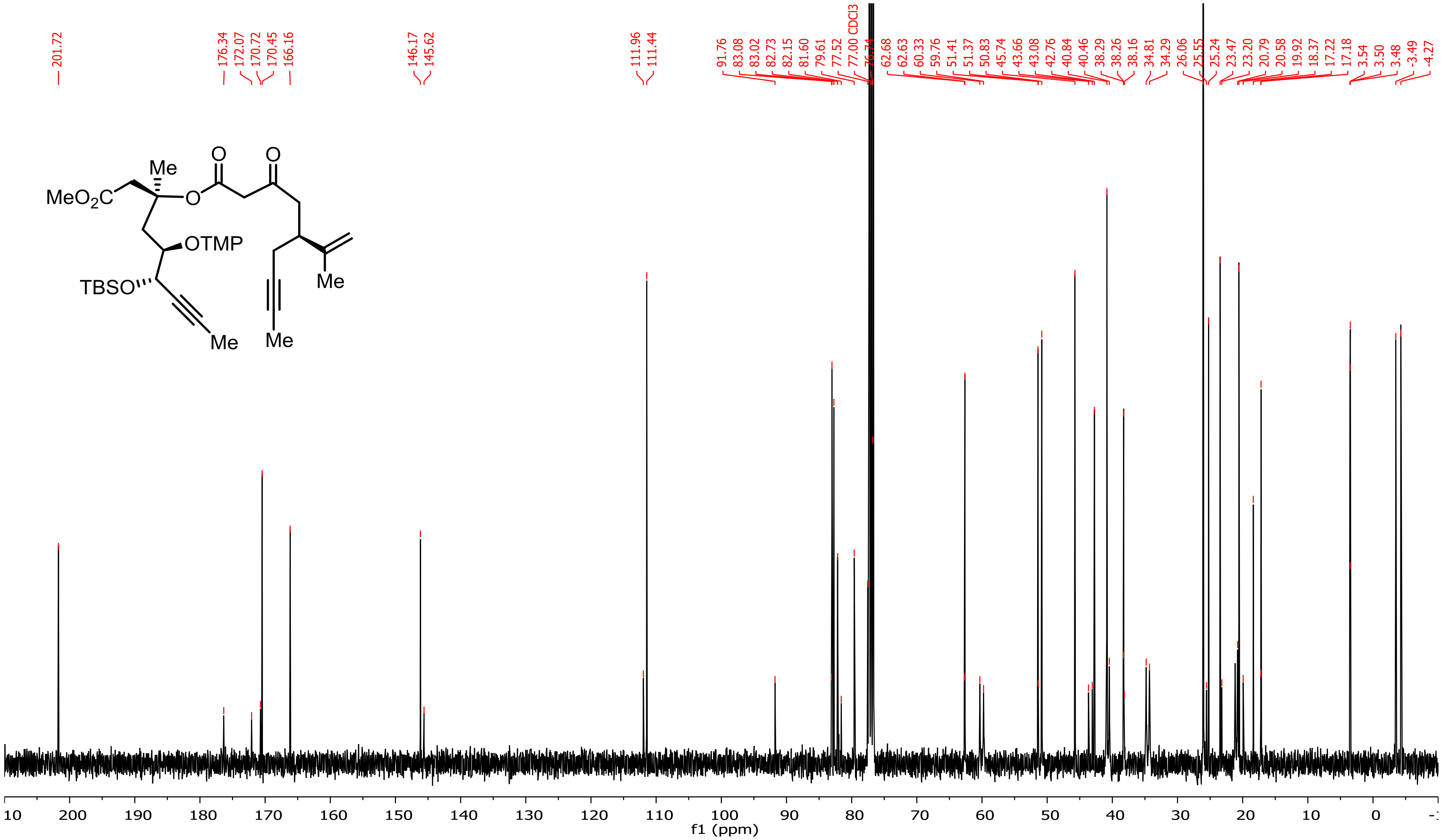
^{13}C NMR Spectrum of 11 (101 MHz, $CDCl_3$)



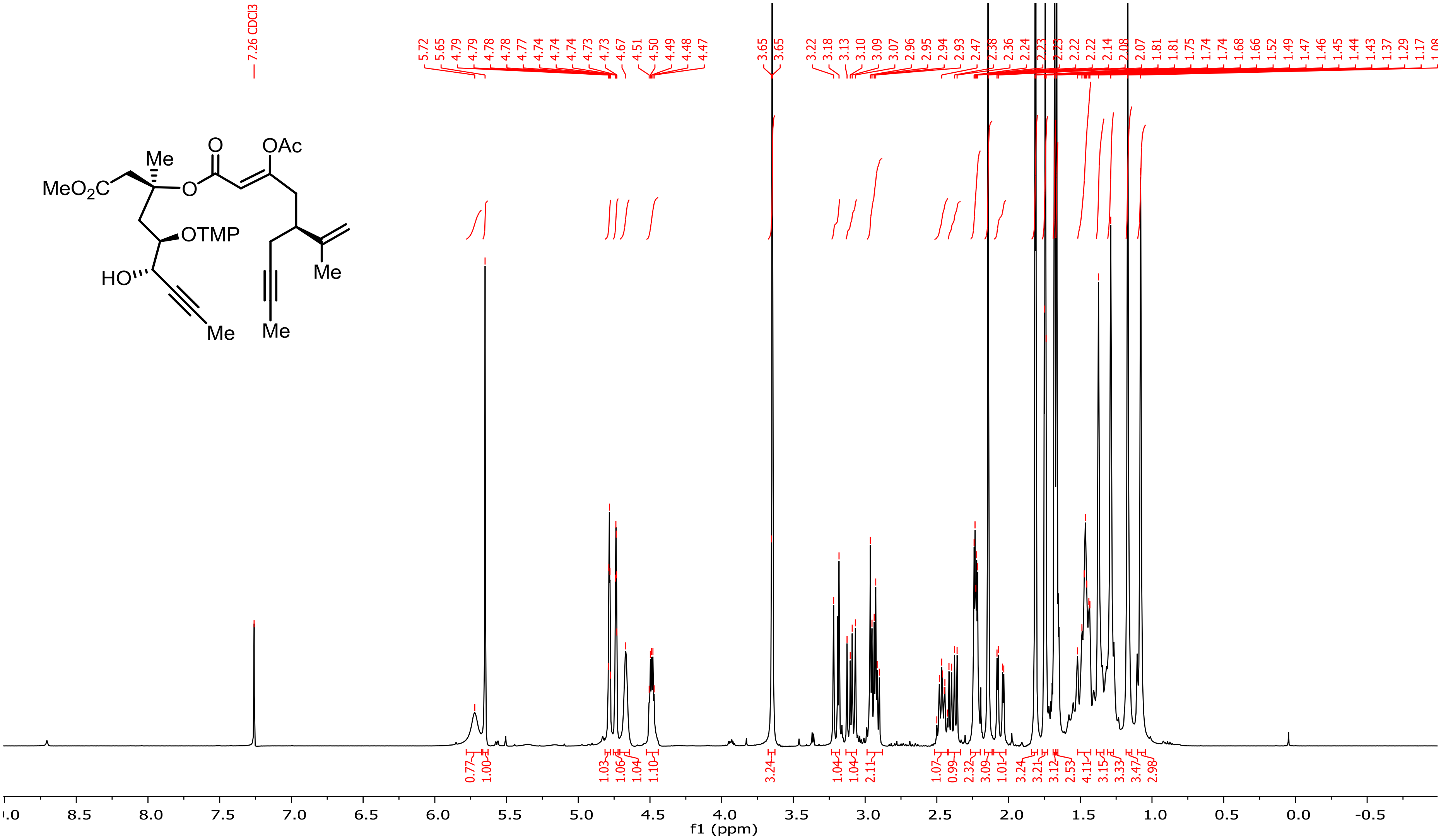
^{1}H NMR Spectrum of 15 (400 MHz, CDCl$_3$)



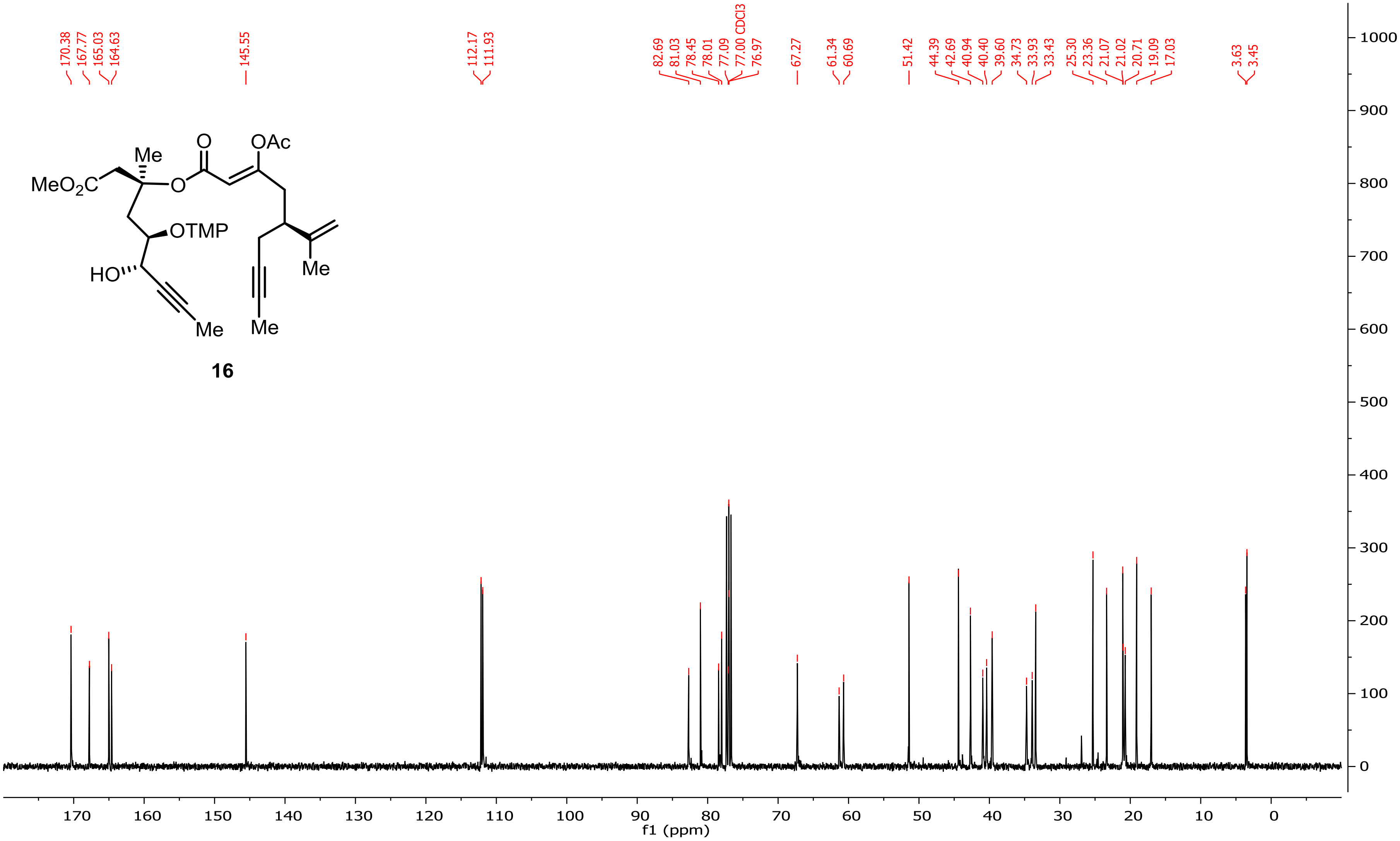
^{13}C NMR Spectrum of 15 (101 MHz, CDCl$_3$)



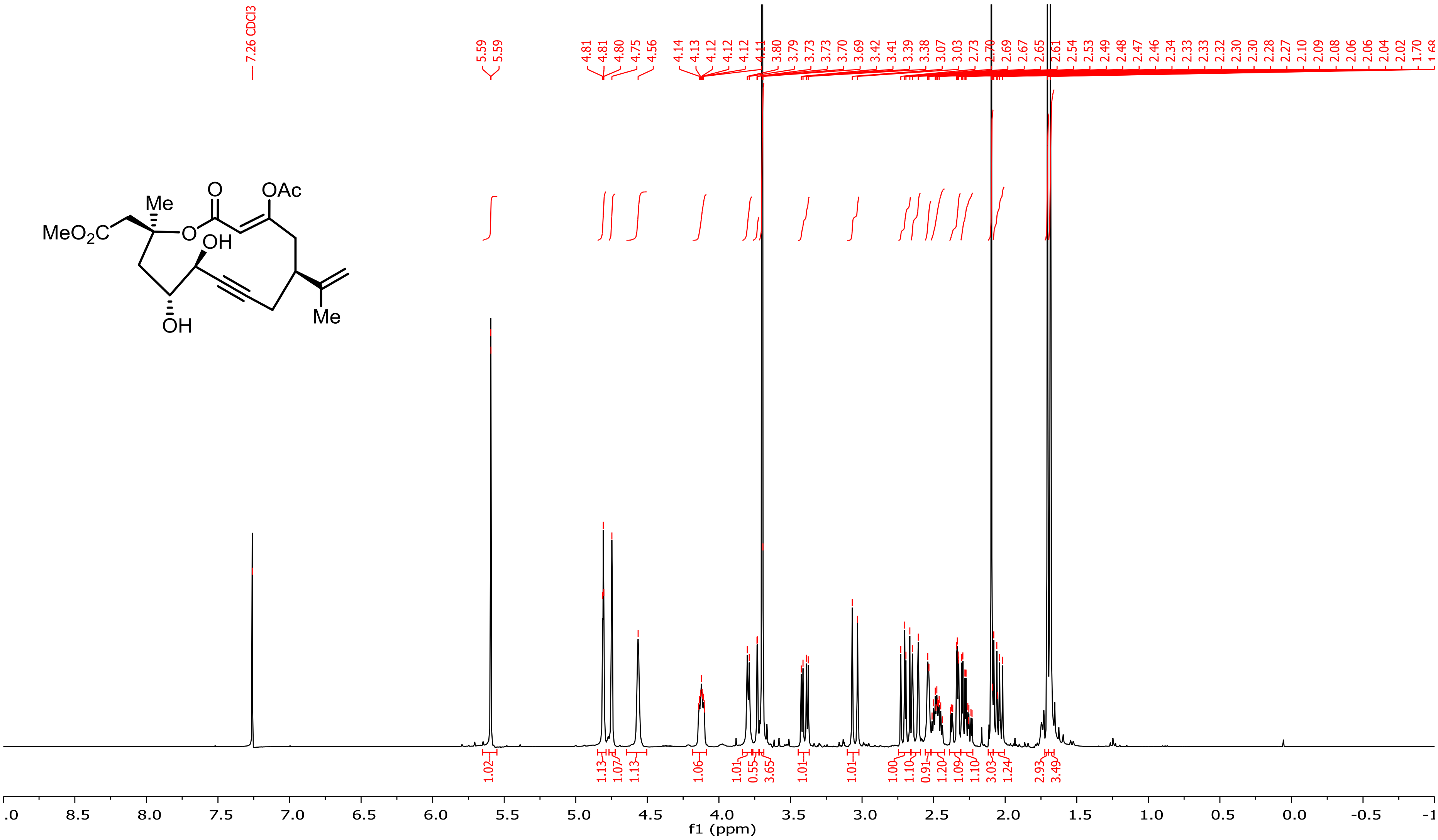
^{1}H NMR Spectrum of 16 (400 MHz, $CDCl_3$



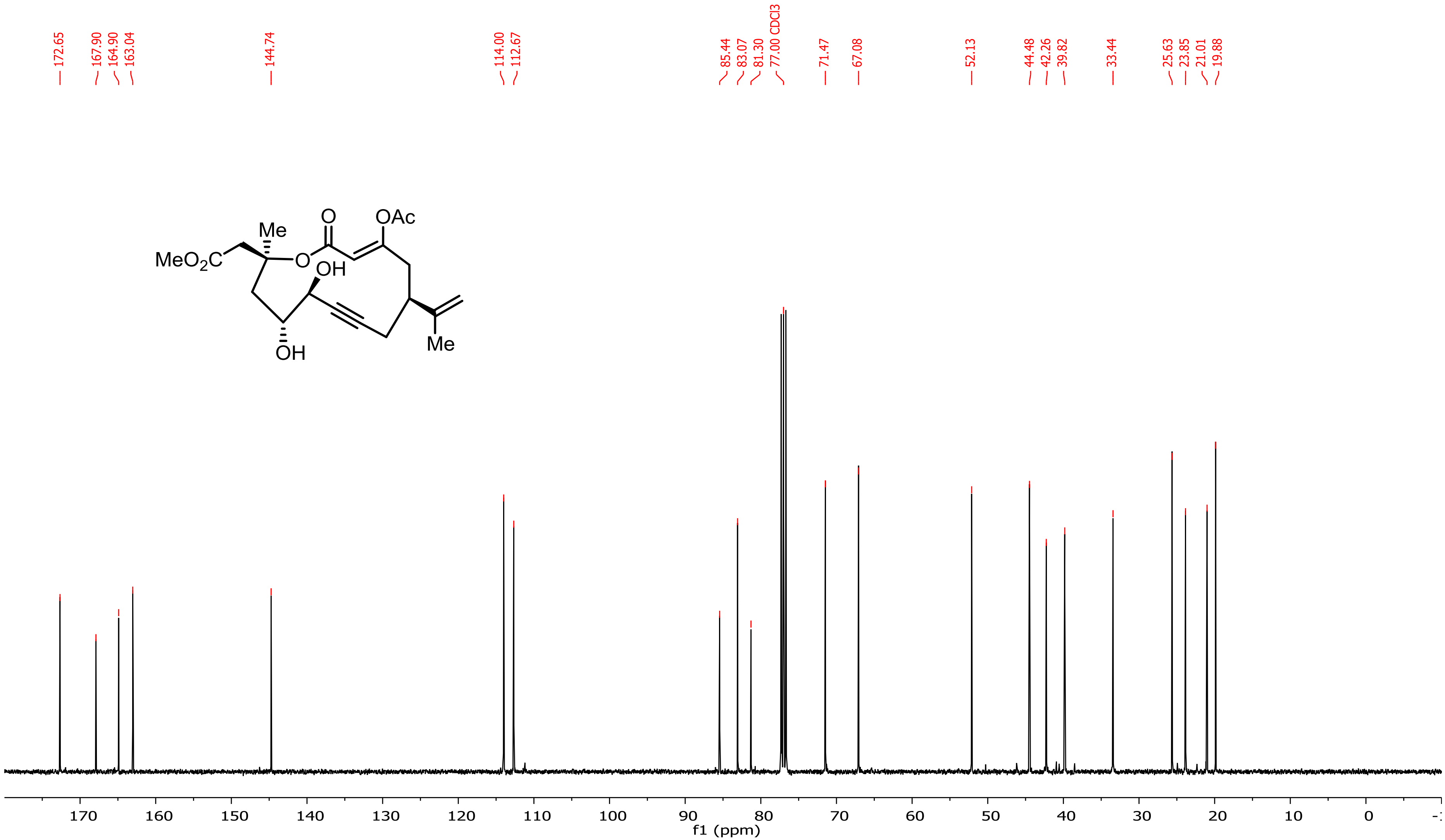
^{13}C NMR Spectrum of 16 (101 MHz, CDCl$_3$)



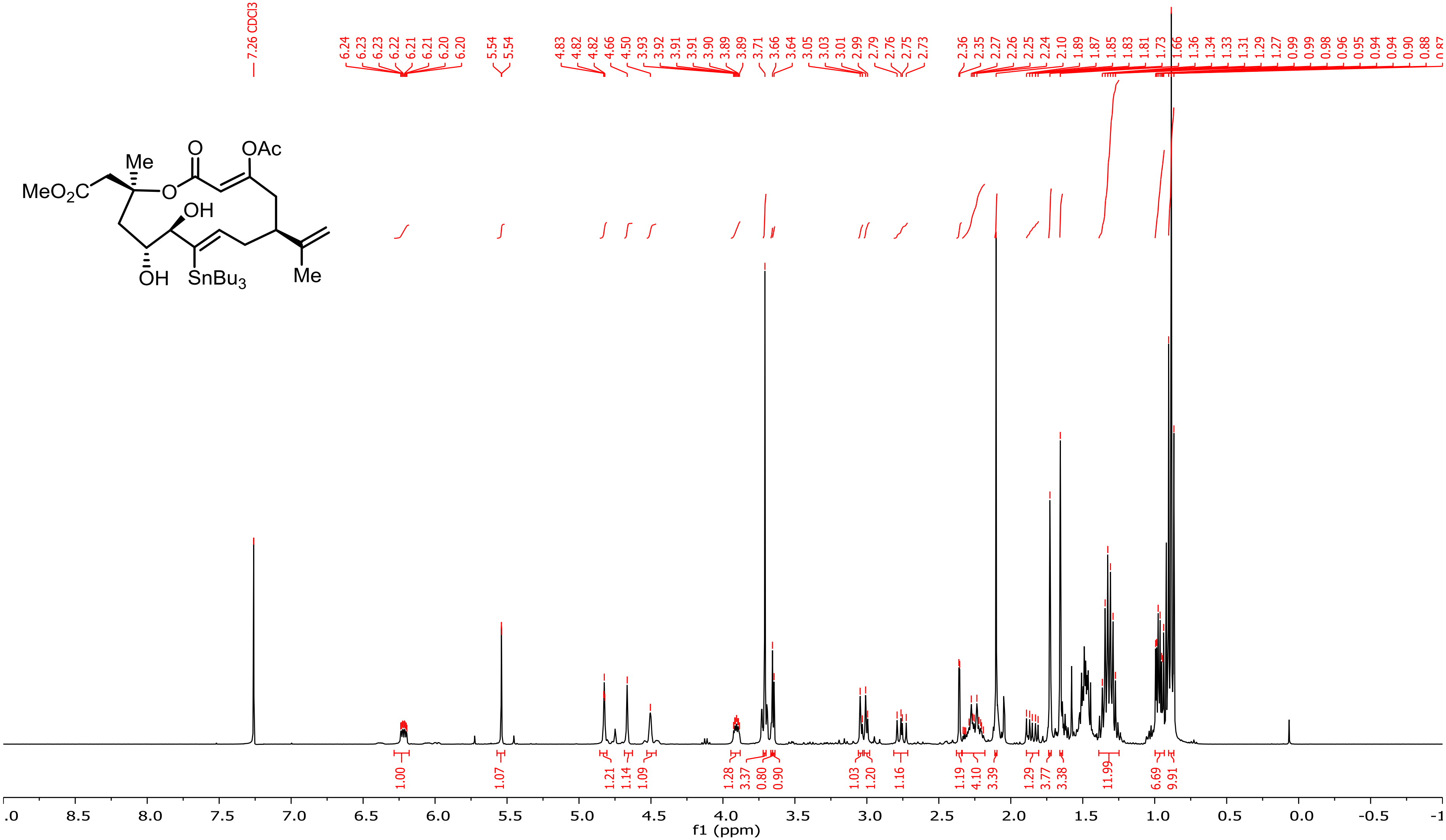
^{1}H NMR Spectrum of 17 (400 MHz, $CDCl_3$)



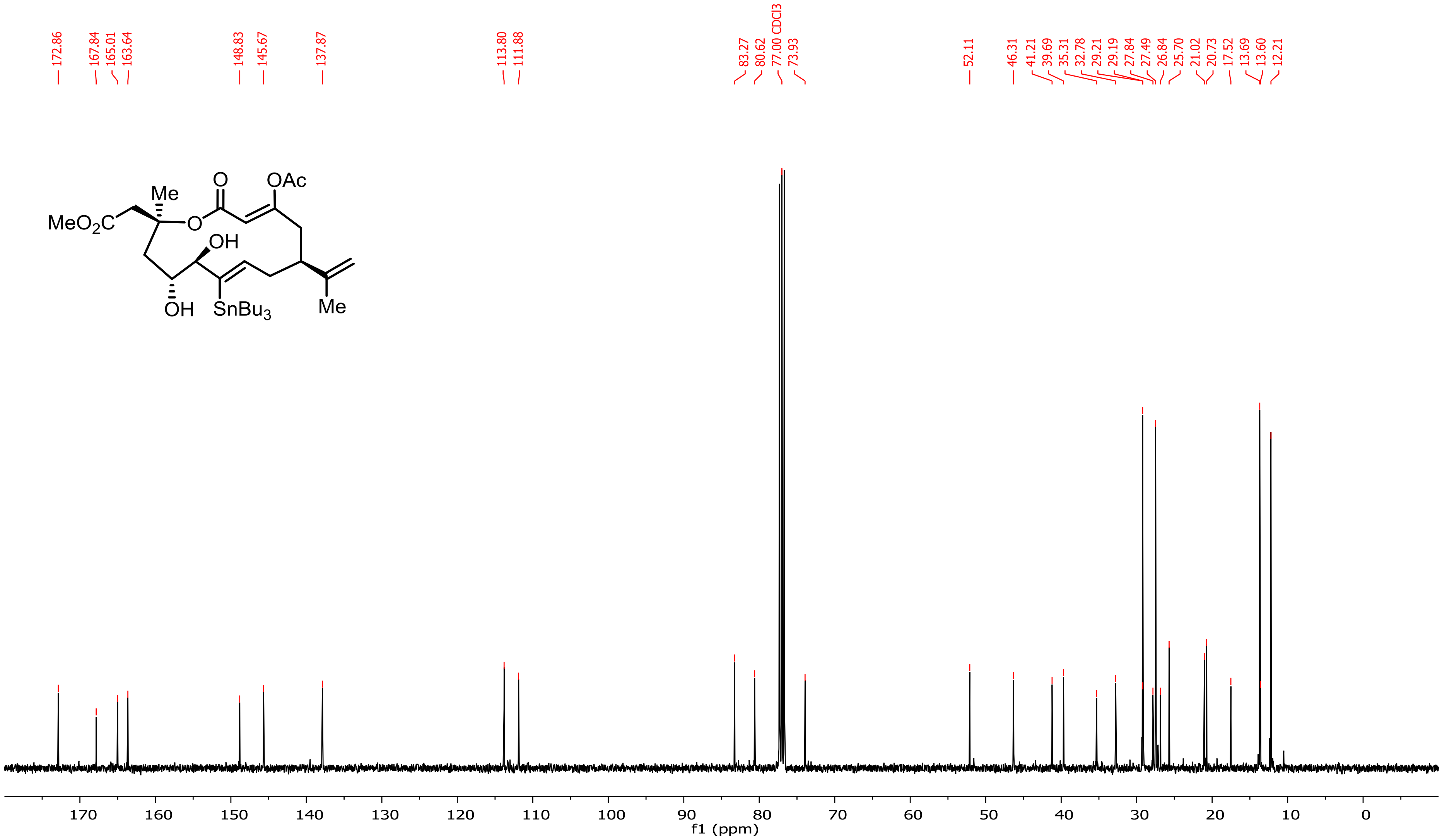
^{13}C NMR Spectrum of 17 (101 MHz, $CDCl_3$)



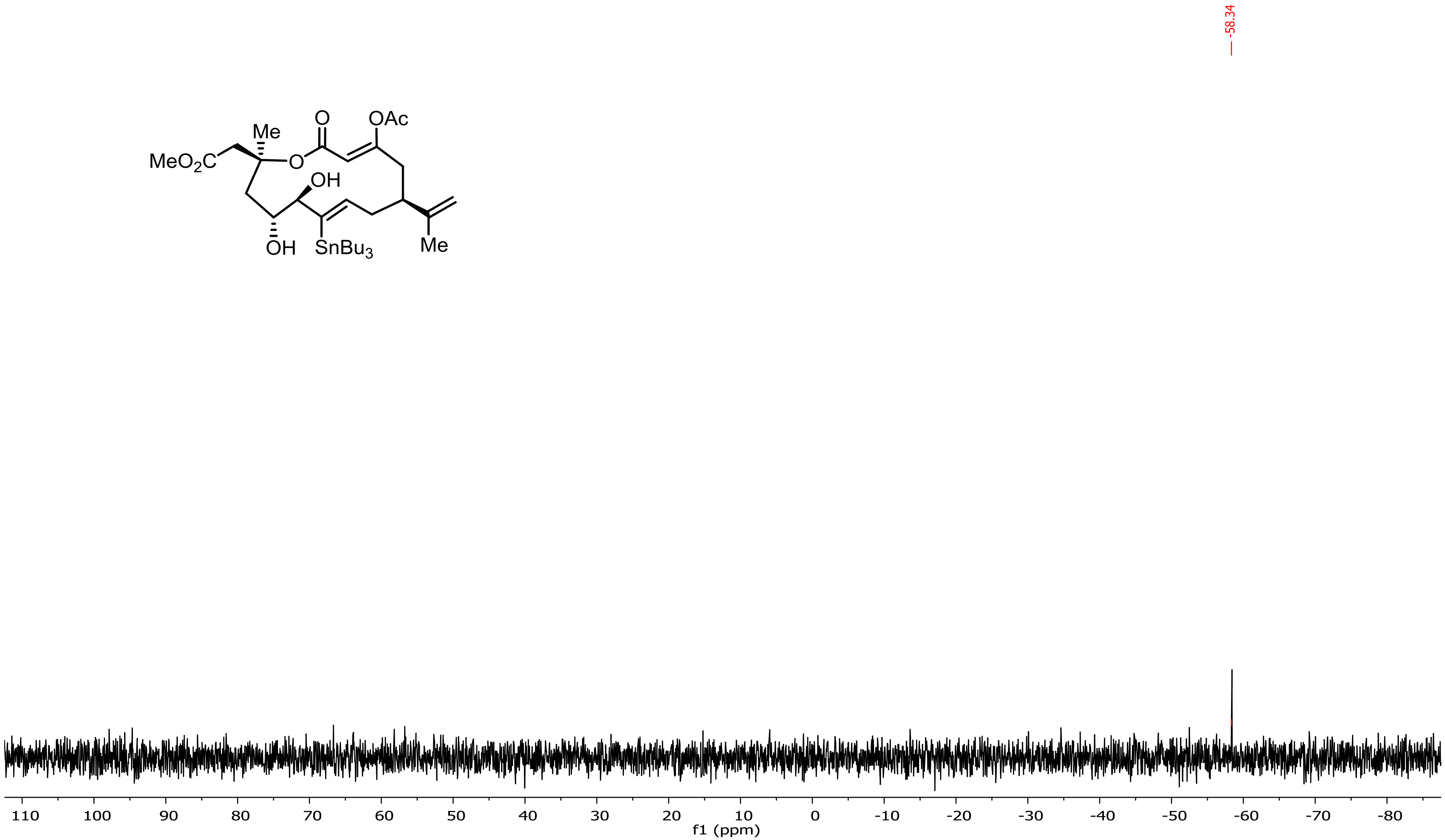
^{1}H NMR Spectrum of 18 (400 MHz, CDCl$_3$)



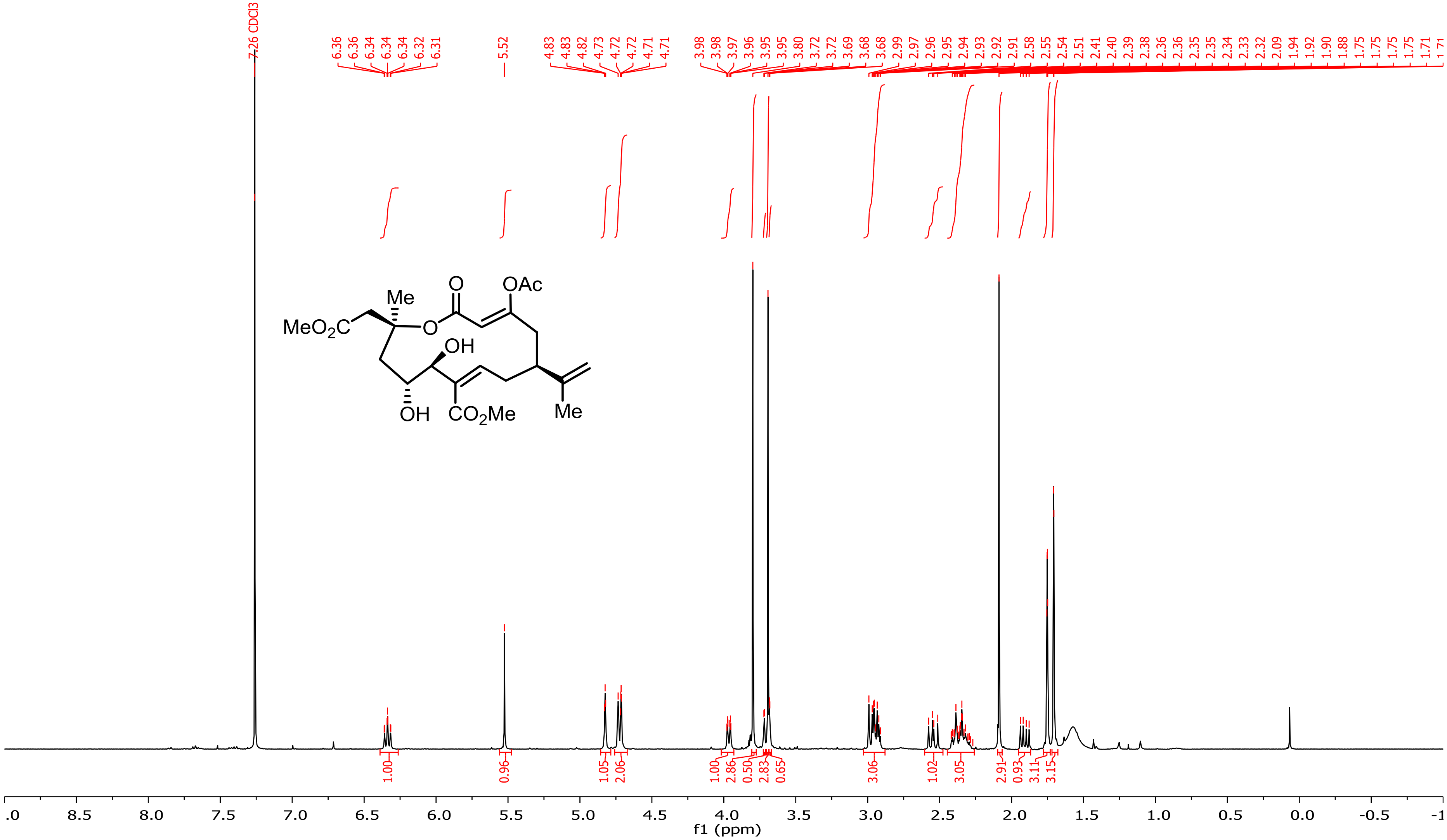
^{13}C NMR Spectrum of 18 (101 MHz, CDCl$_3$)



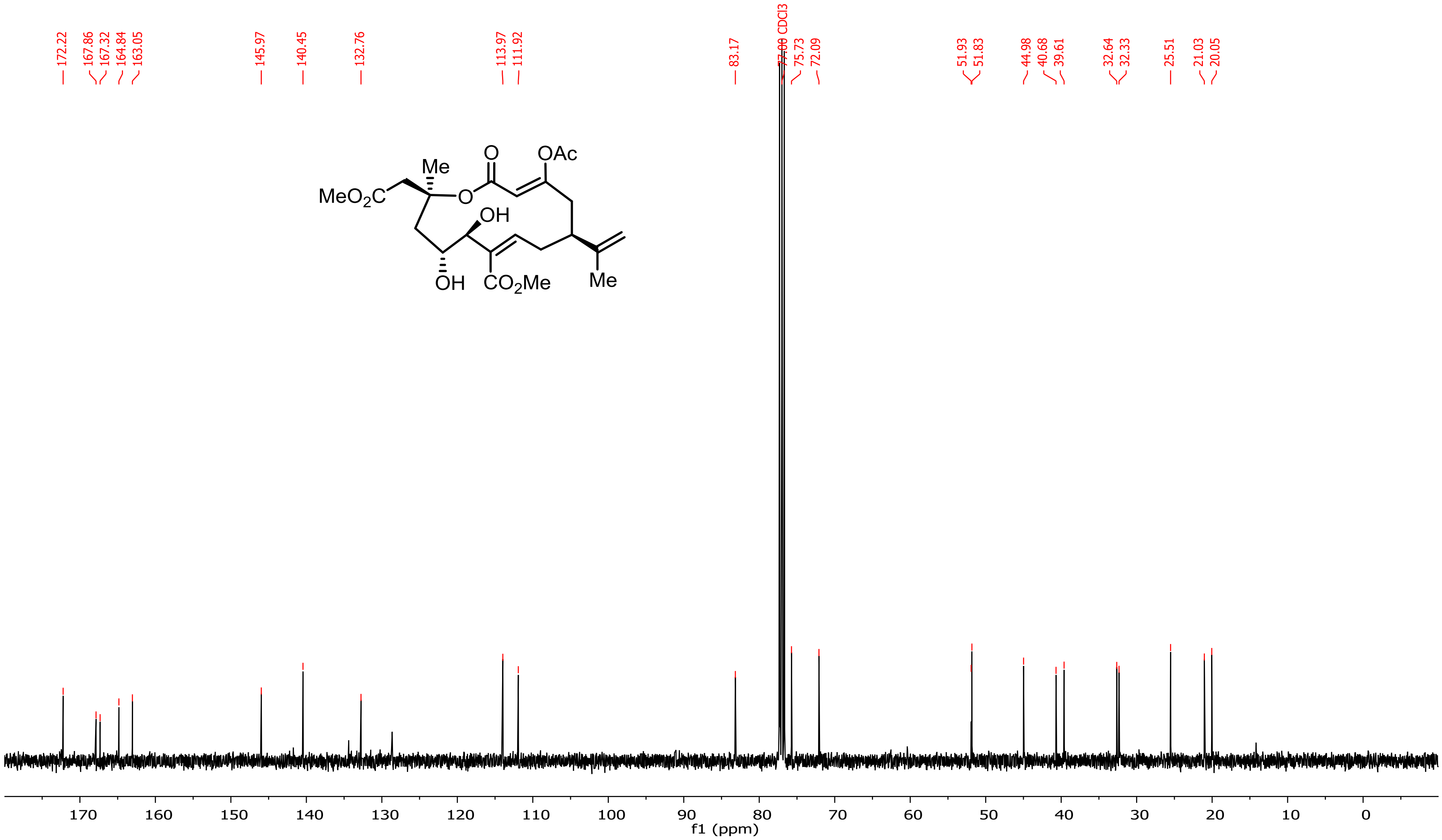
^{119}Sn NMR Spectrum of 18 (186 MHz, $CDCl_3$)



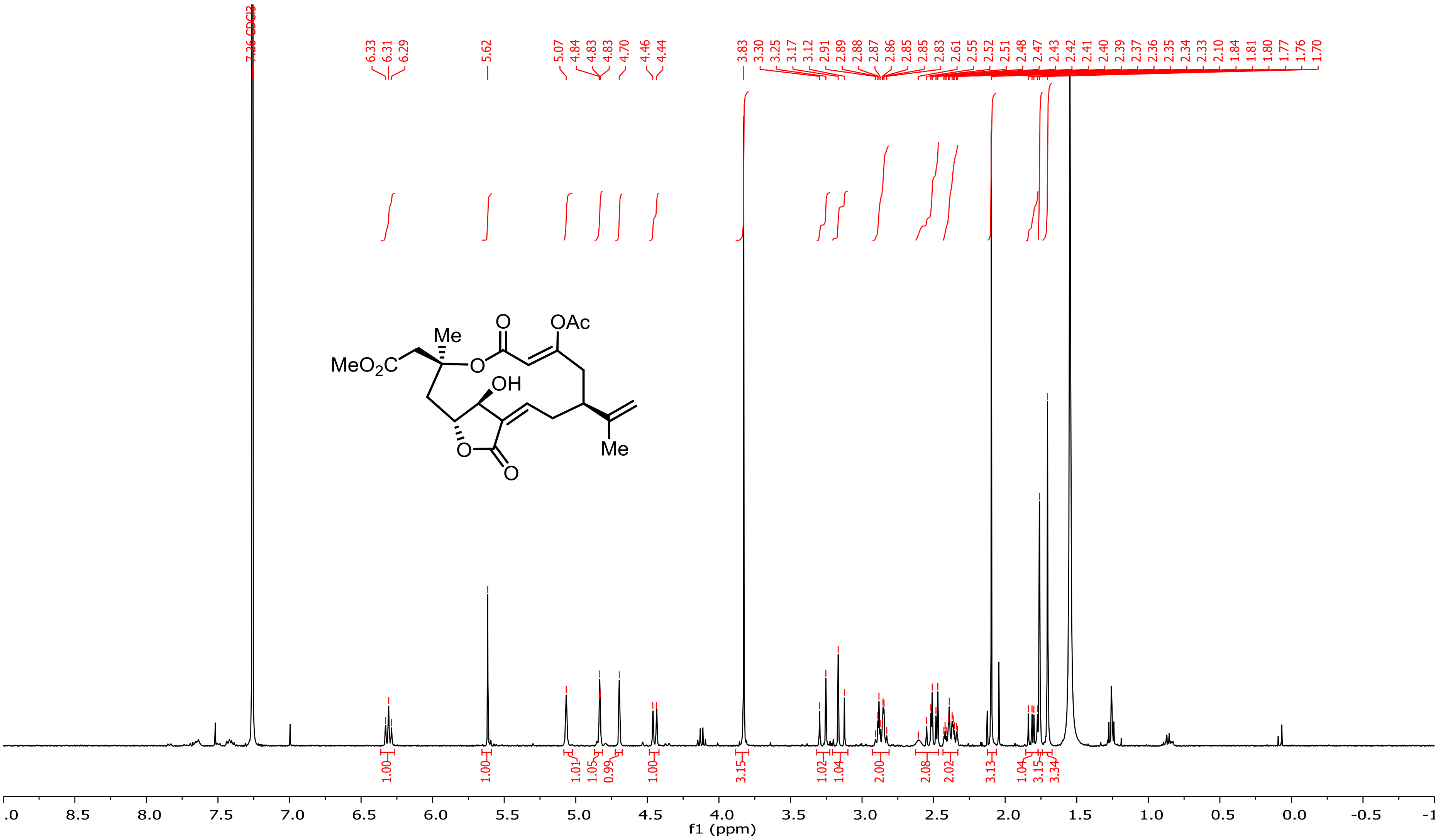
^{1}H NMR Spectrum of 19 (400 MHz, $CDCl_3$)



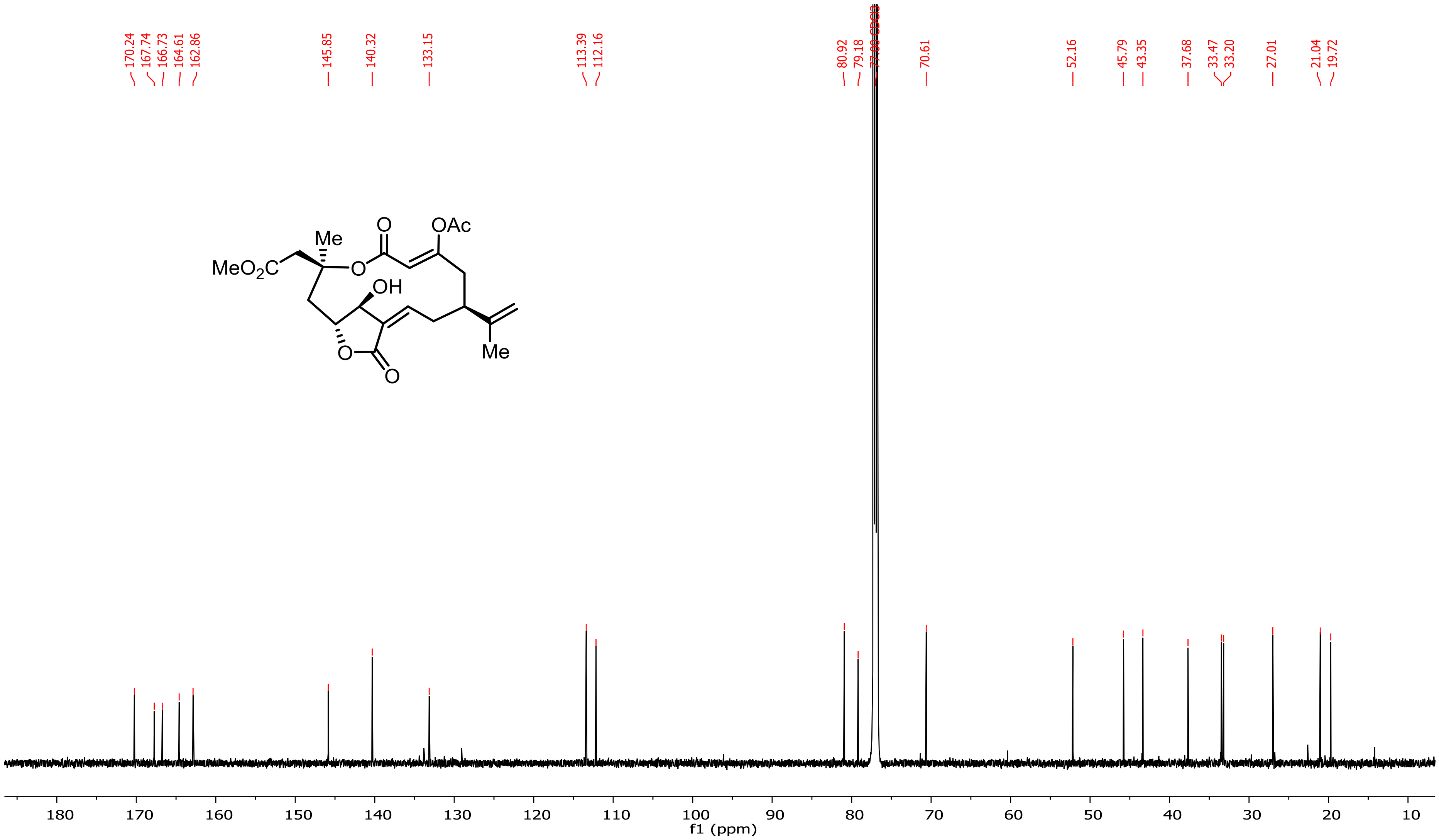
^{13}C NMR Spectrum of 19 (101 MHz, CDCl$_3$)



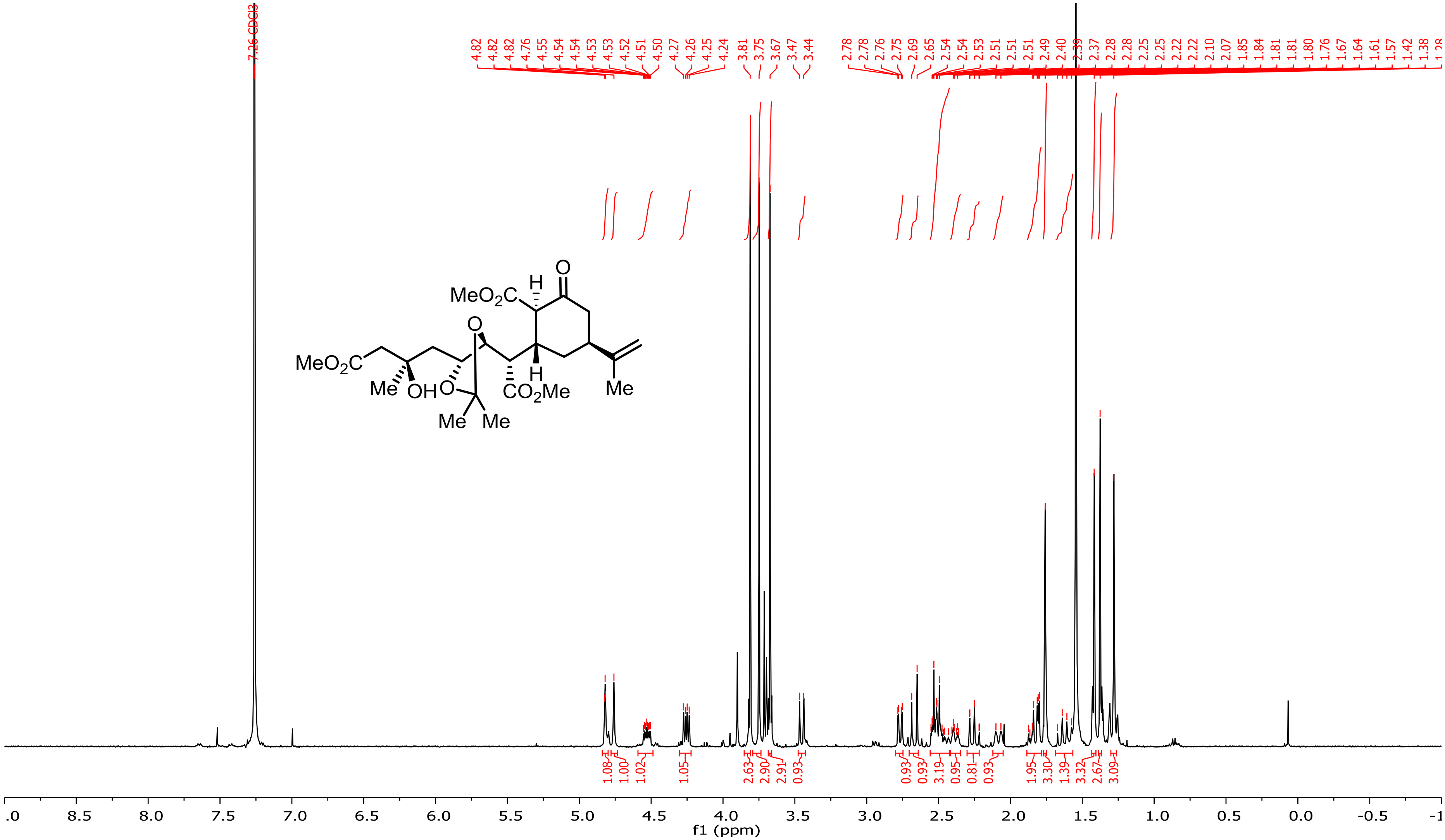
^{1}H NMR Spectrum of 20 (400 MHz, $CDCl_3$)



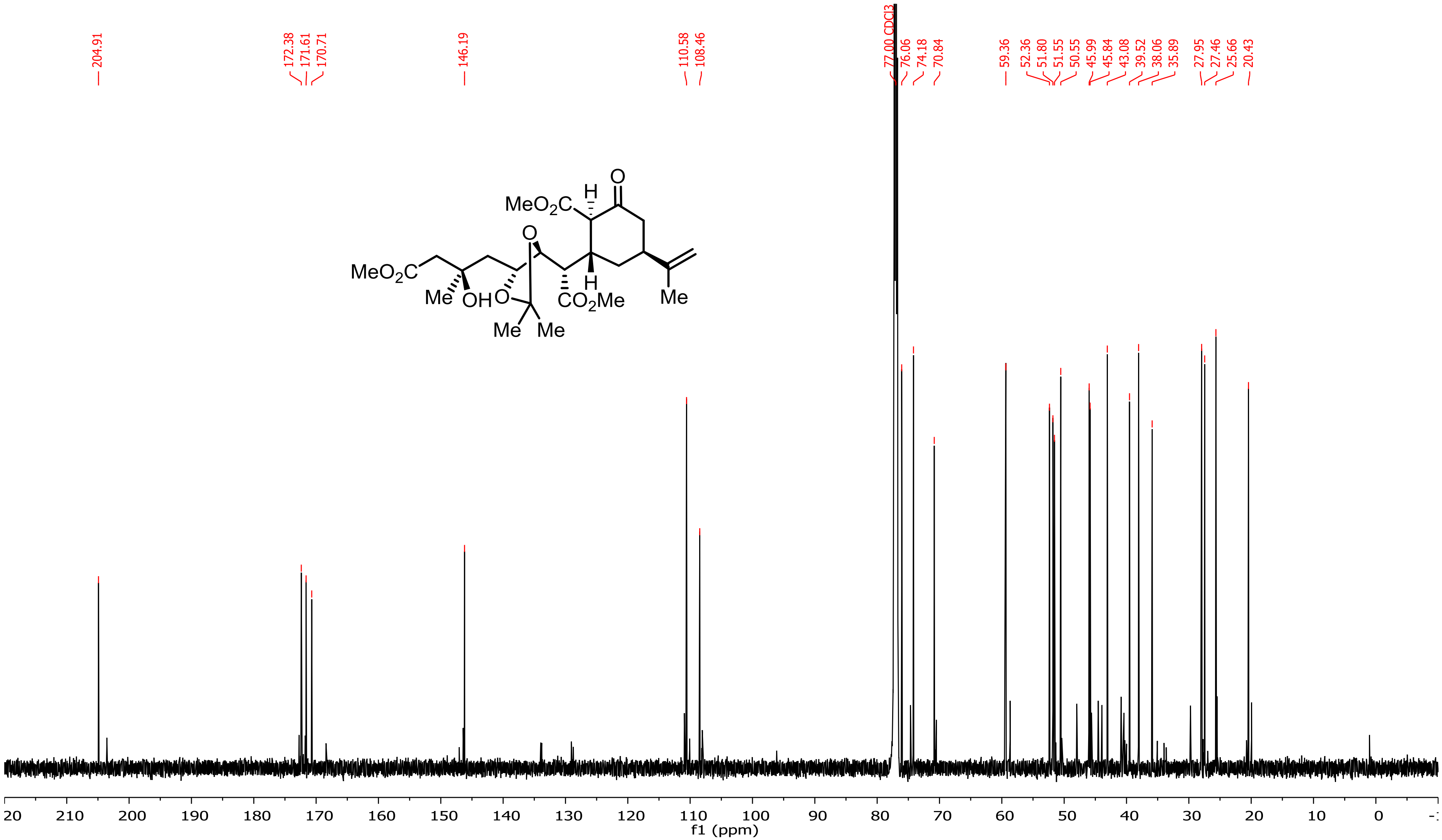
^{13}C NMR Spectrum of 20 (151 MHz, CDCl$_3$)



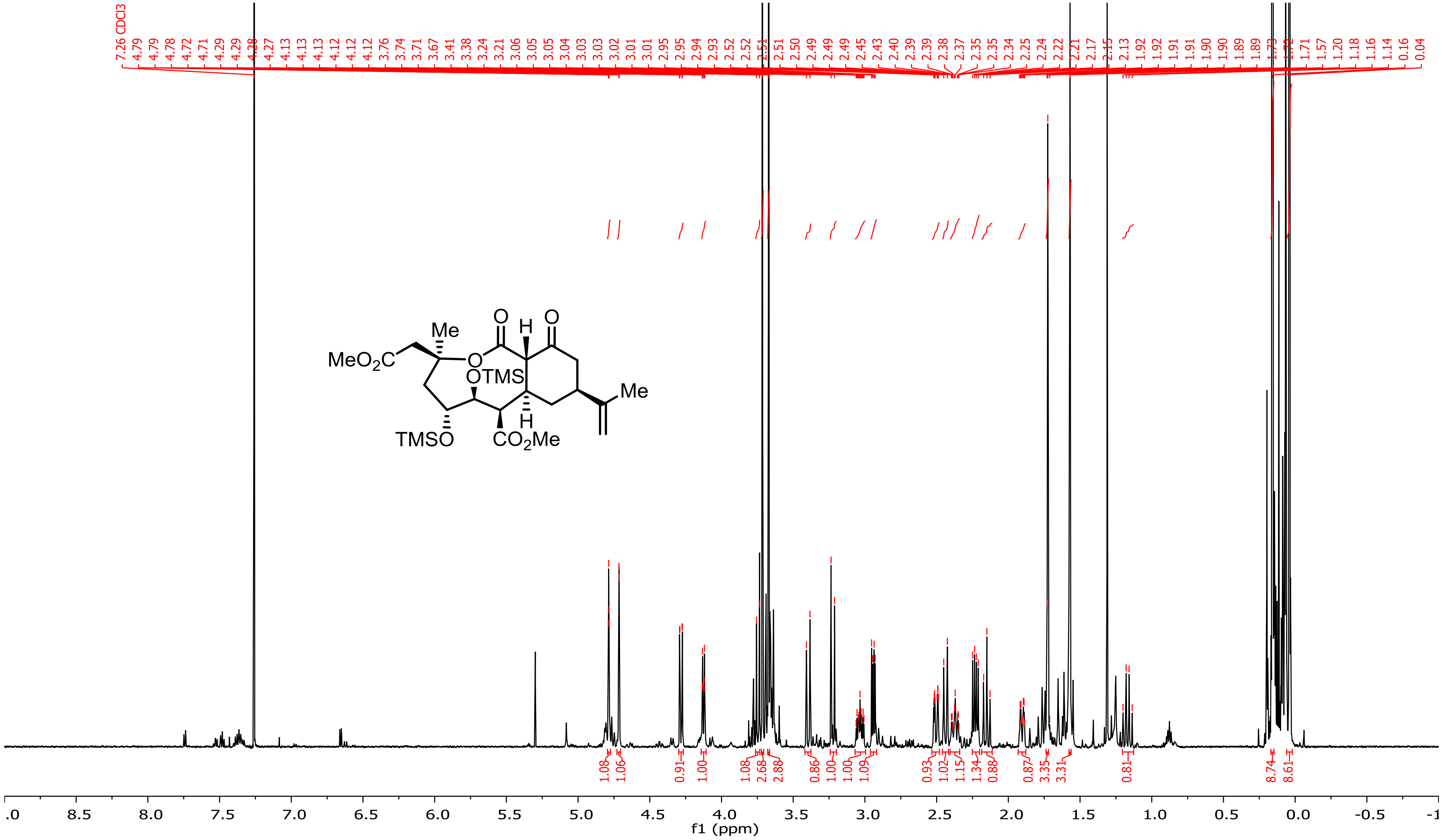
^{1}H NMR Spectrum of 30 (400 MHz, CDCl$_3$) (+ *ca. 5-10% of an unidentified impurity, which could not be removed by flash chromatography)*



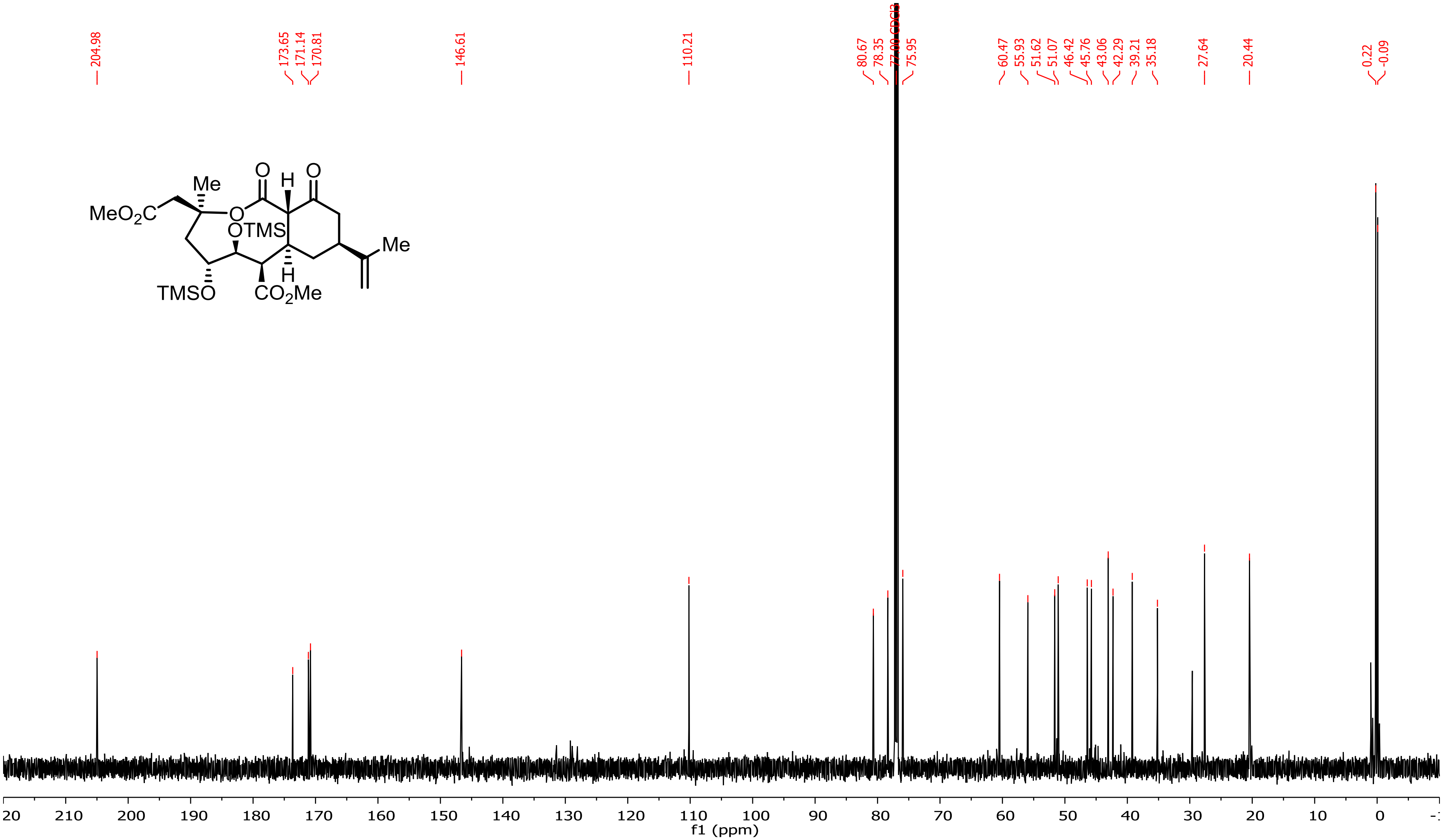
^{13}C NMR Spectrum of 30 (151 MHz, CDCl$_3$) (+ *ca. 5-10% of an unidentified impurity, which could not be removed by flash chromatography)*



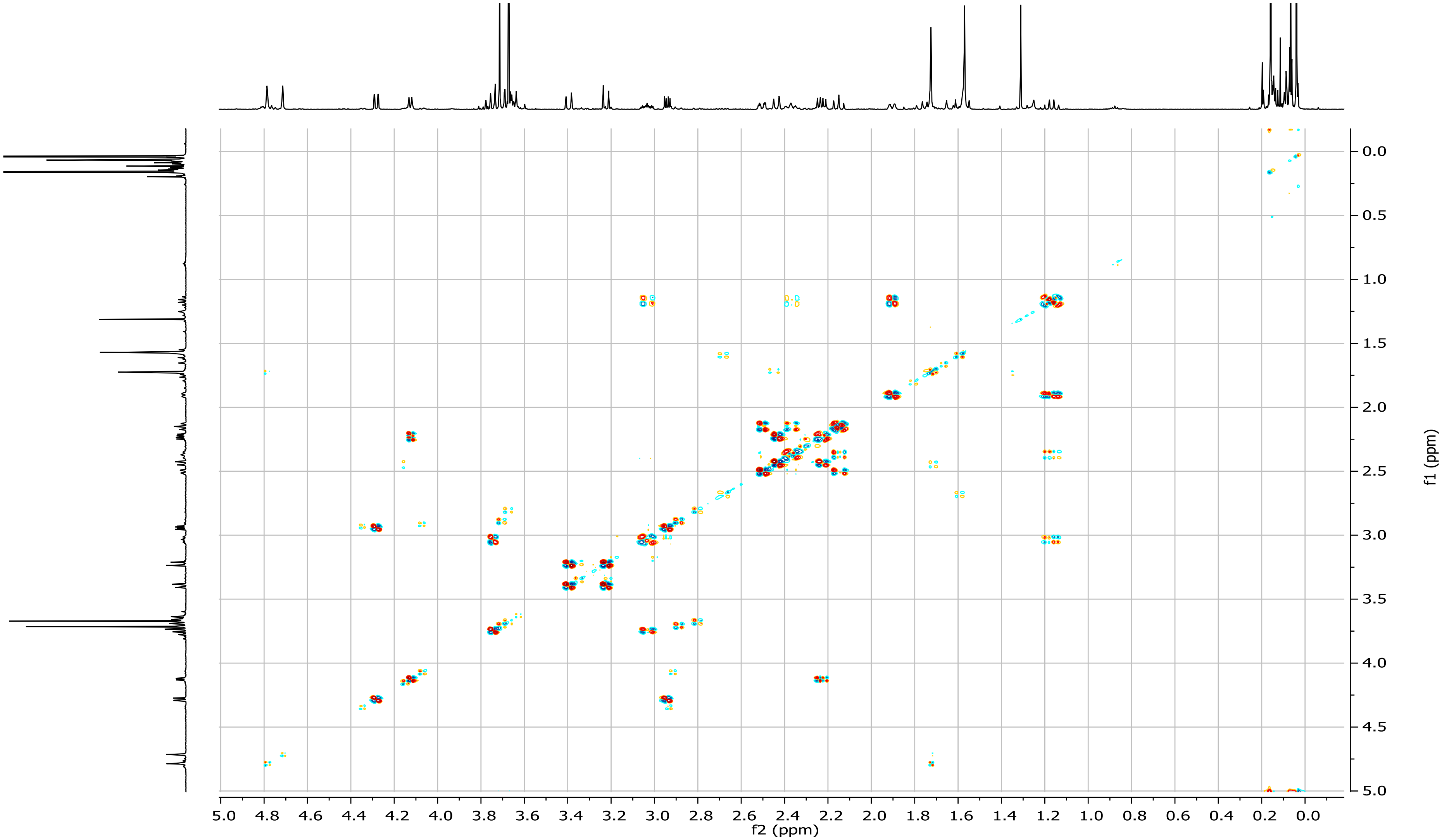
^{1}H NMR Spectrum of 32 (600 MHz, $CDCl_3$)



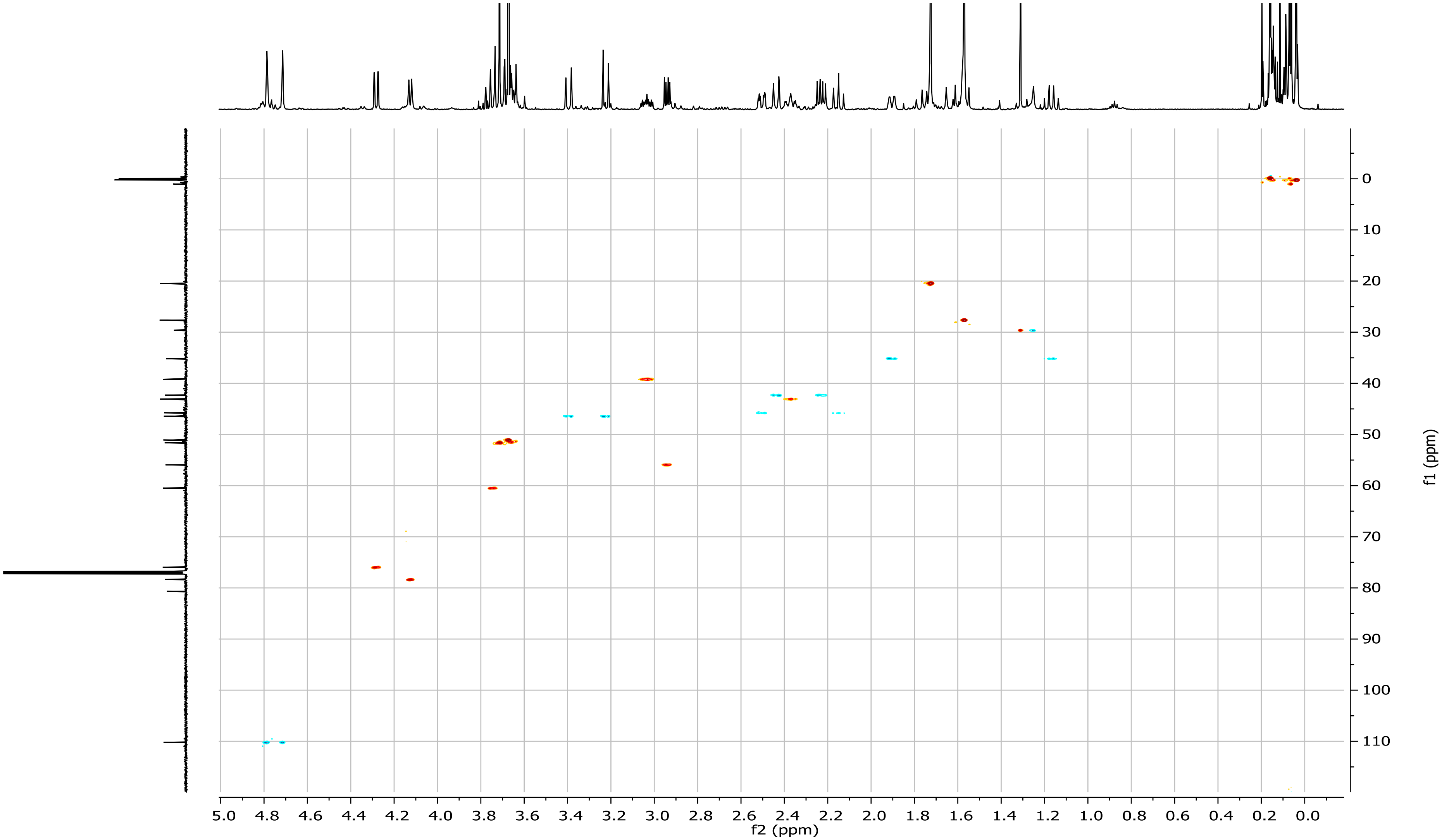
^{13}C NMR Spectrum of 32 (151 MHz, CDCl$_3$)



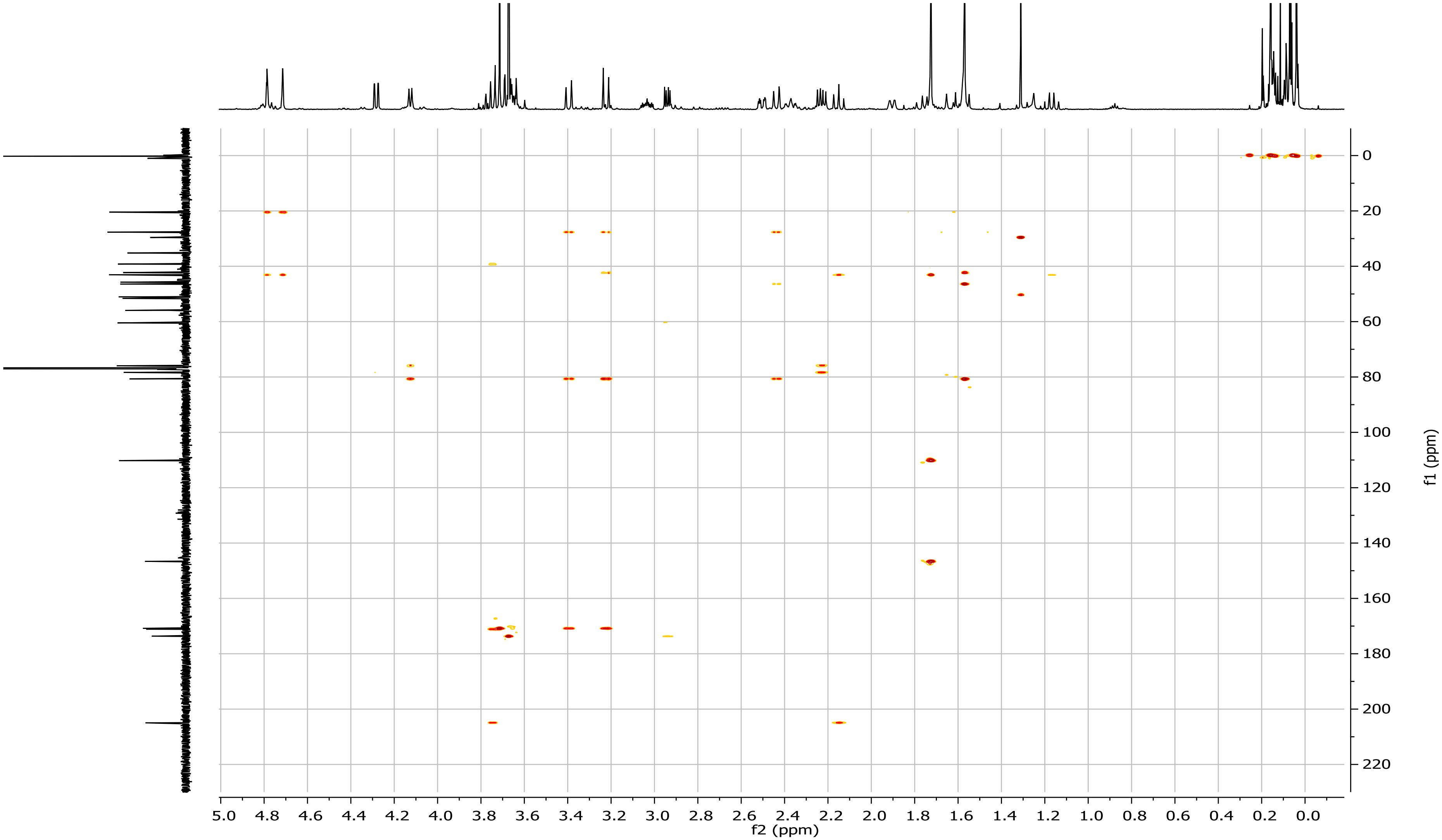
COSY Spectrum of 32



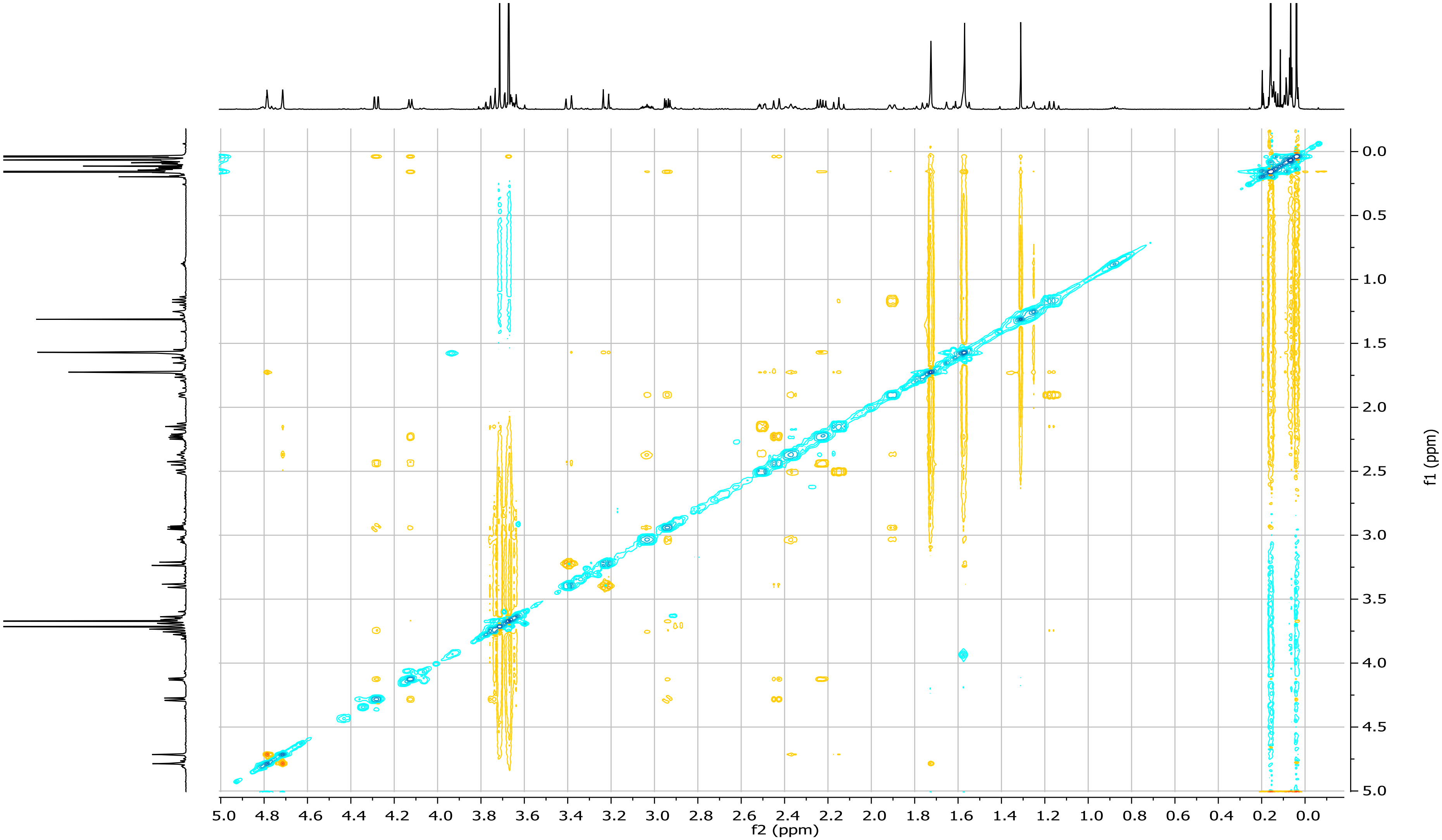
HSQC Spectrum of 32



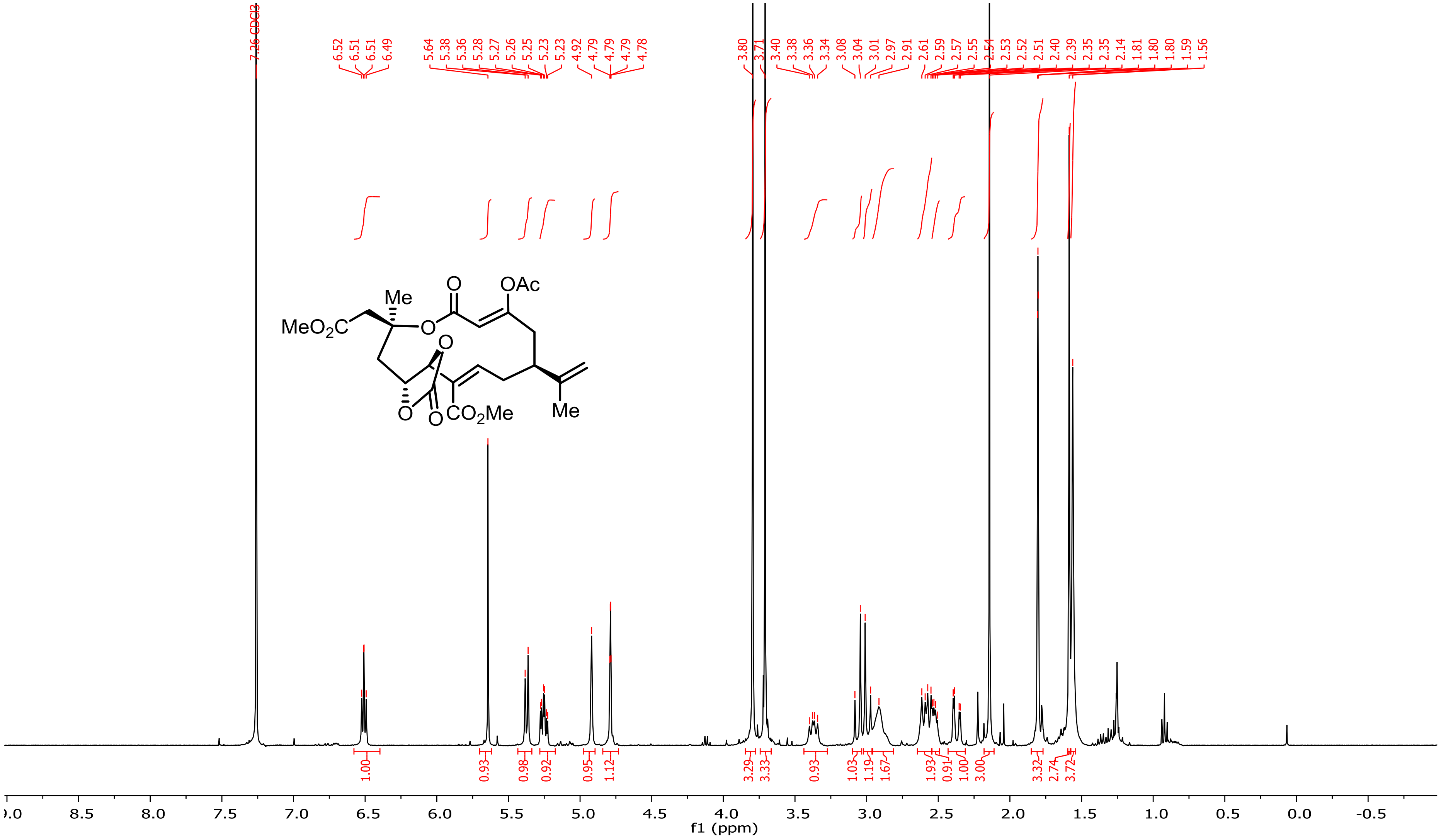
HMBC Spectrum of 32



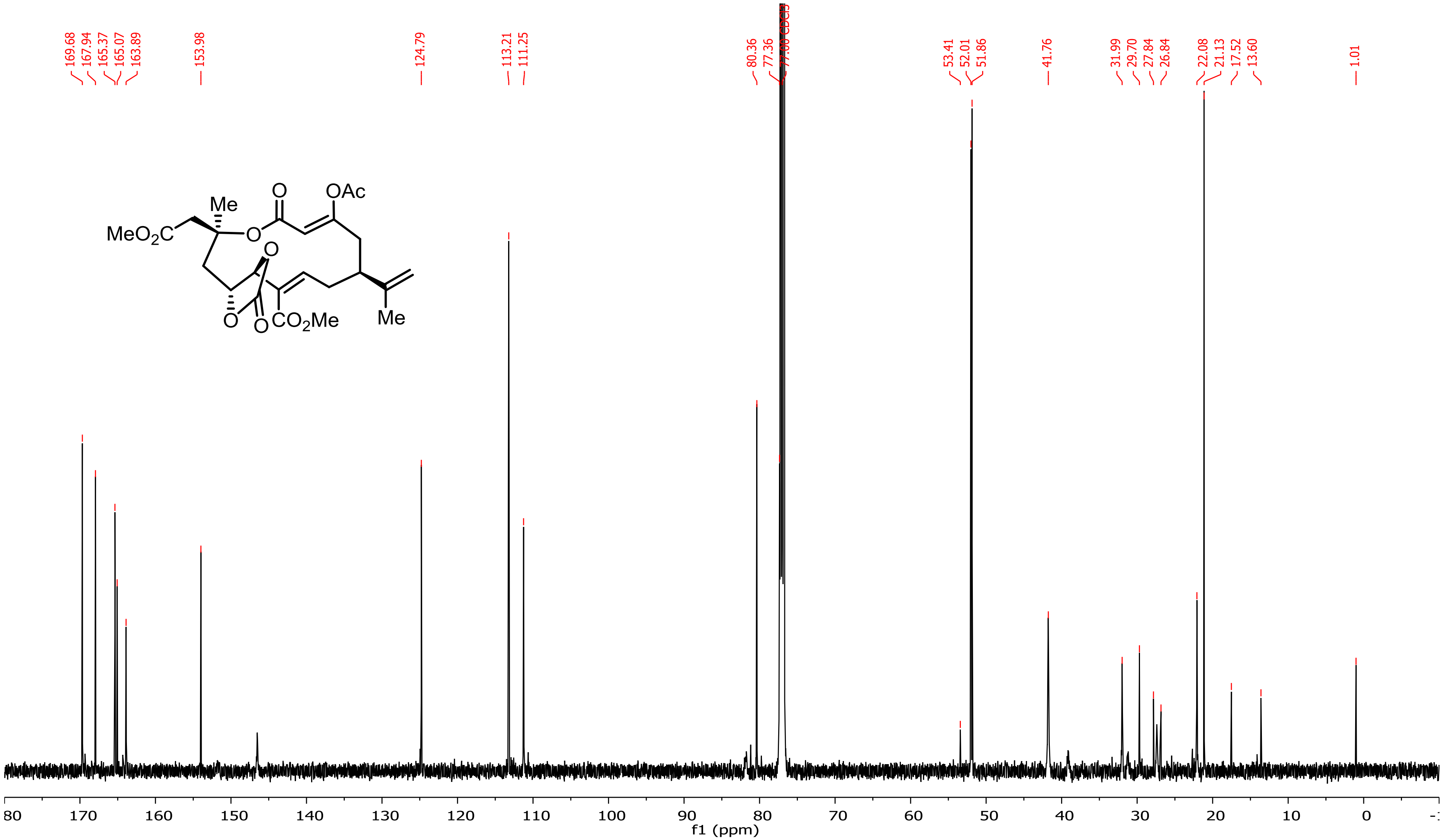
NOESY Spectrum of 32



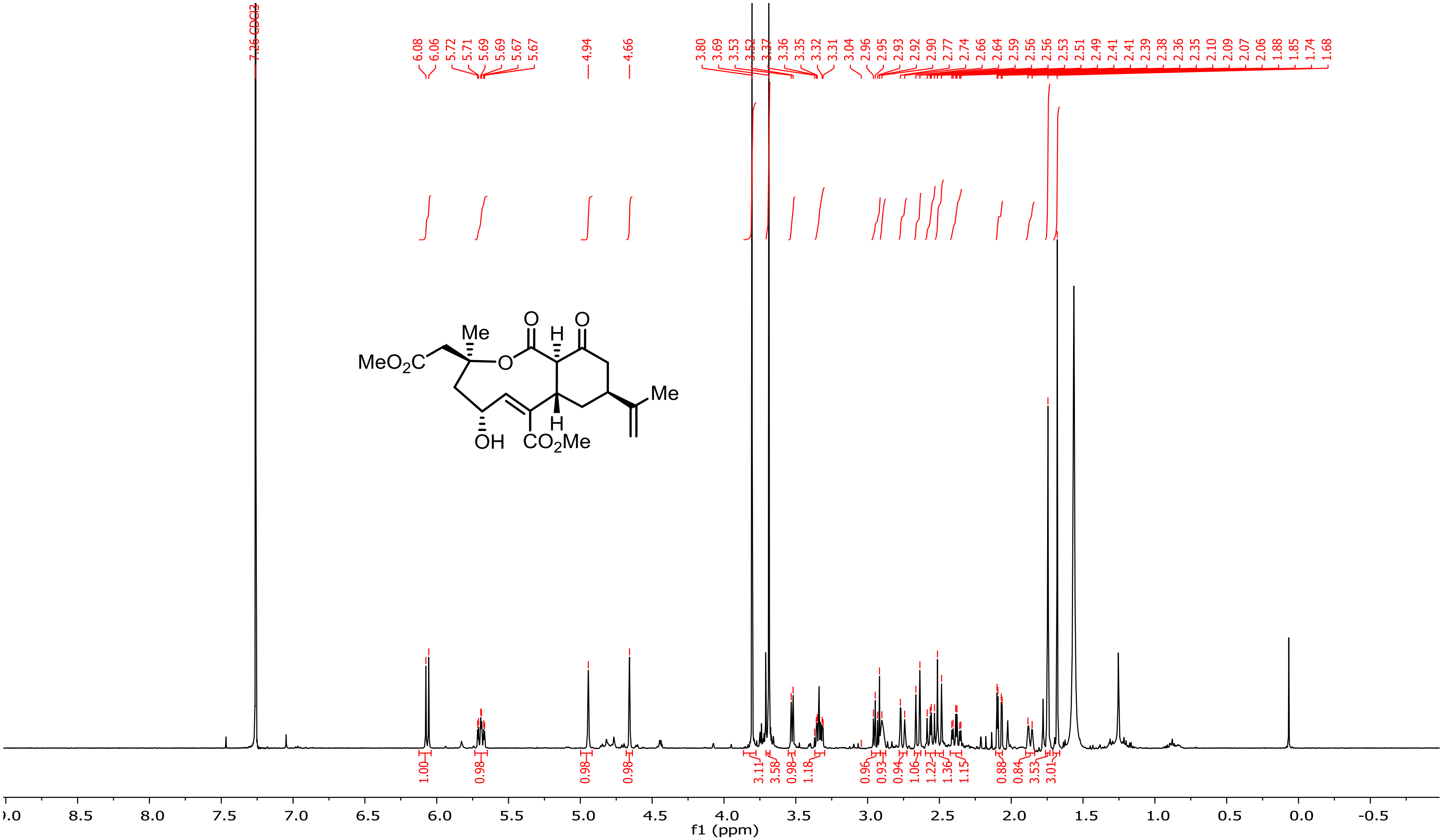
^{1}H NMR Spectrum of 25 (400 MHz, CDCl$_3$)



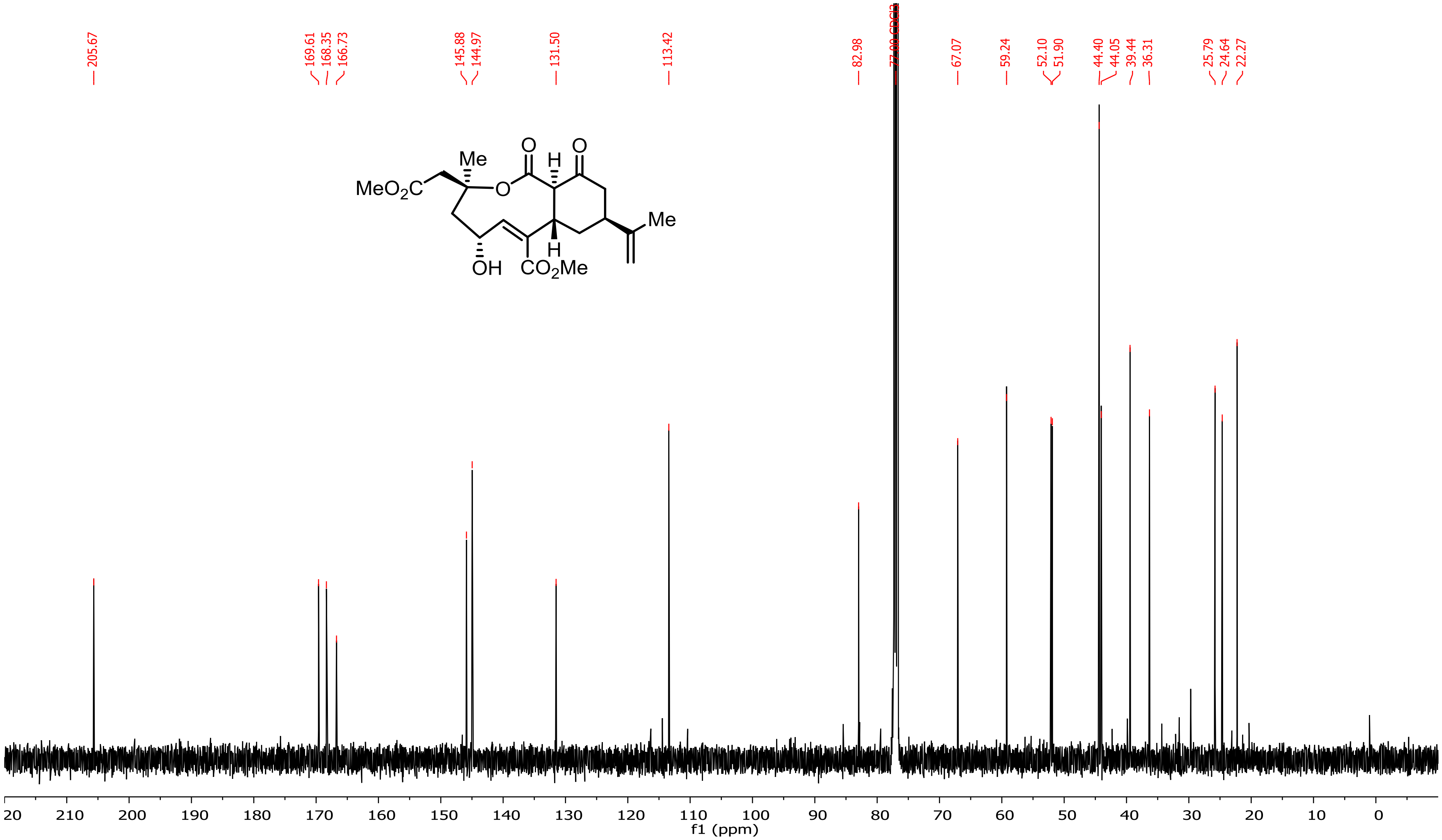
^{13}C NMR Spectrum of 25 (151 MHz, CDCl$_3$)



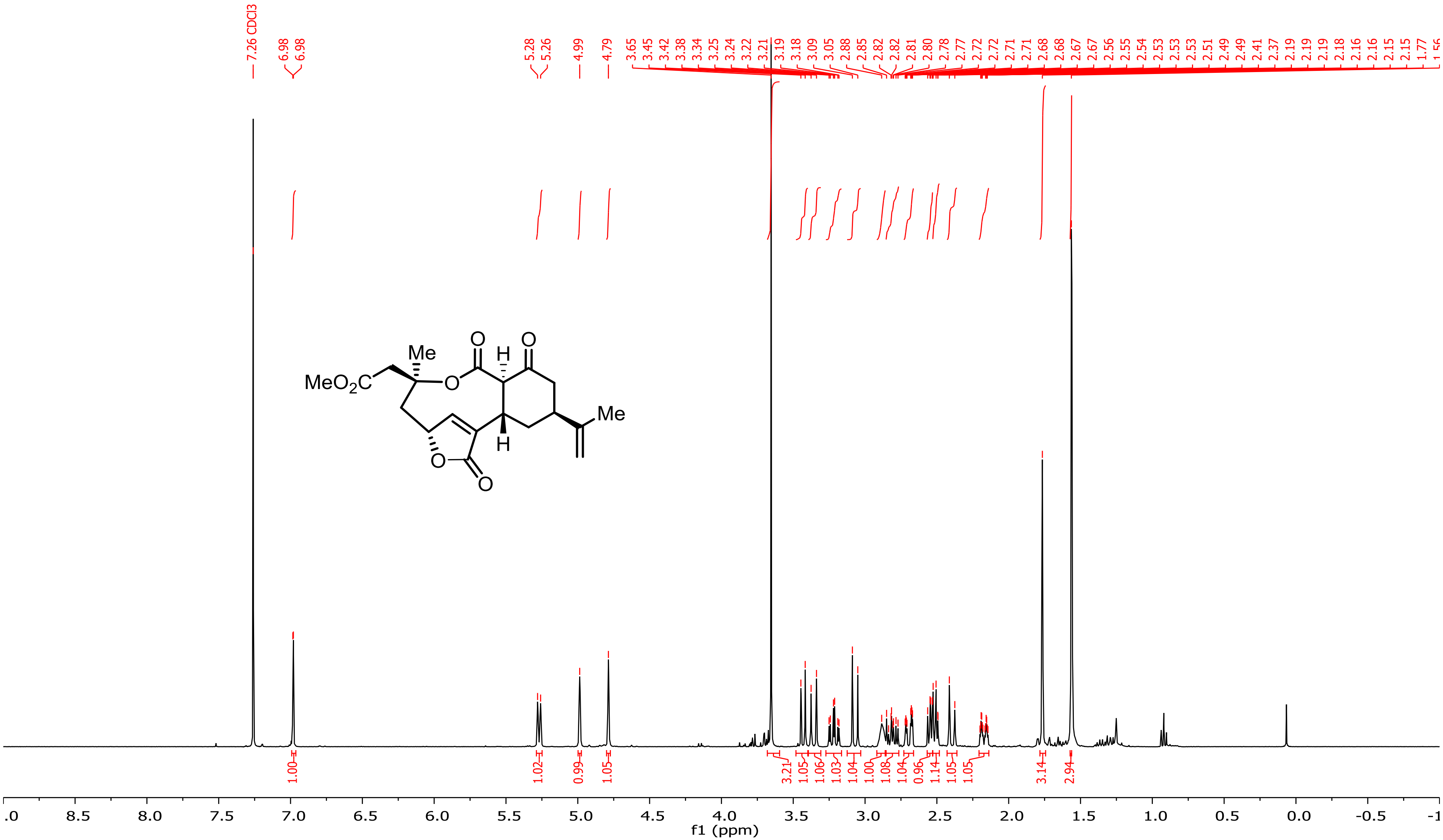
^{1}H NMR Spectrum of 26 (500 MHz, CDCl$_3$)



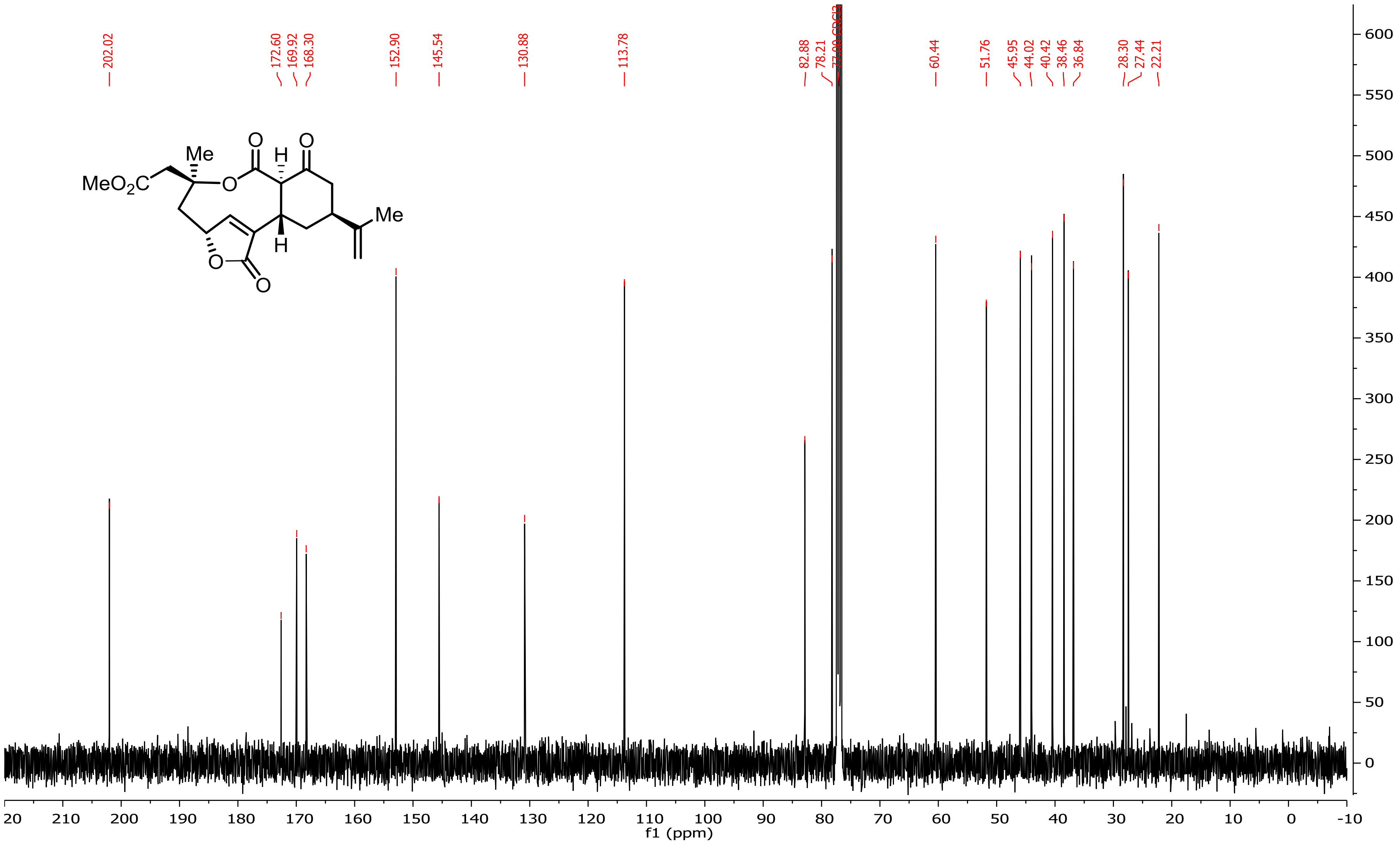
^{13}C NMR Spectrum of 26 (126 MHz, $CDCl_3$)



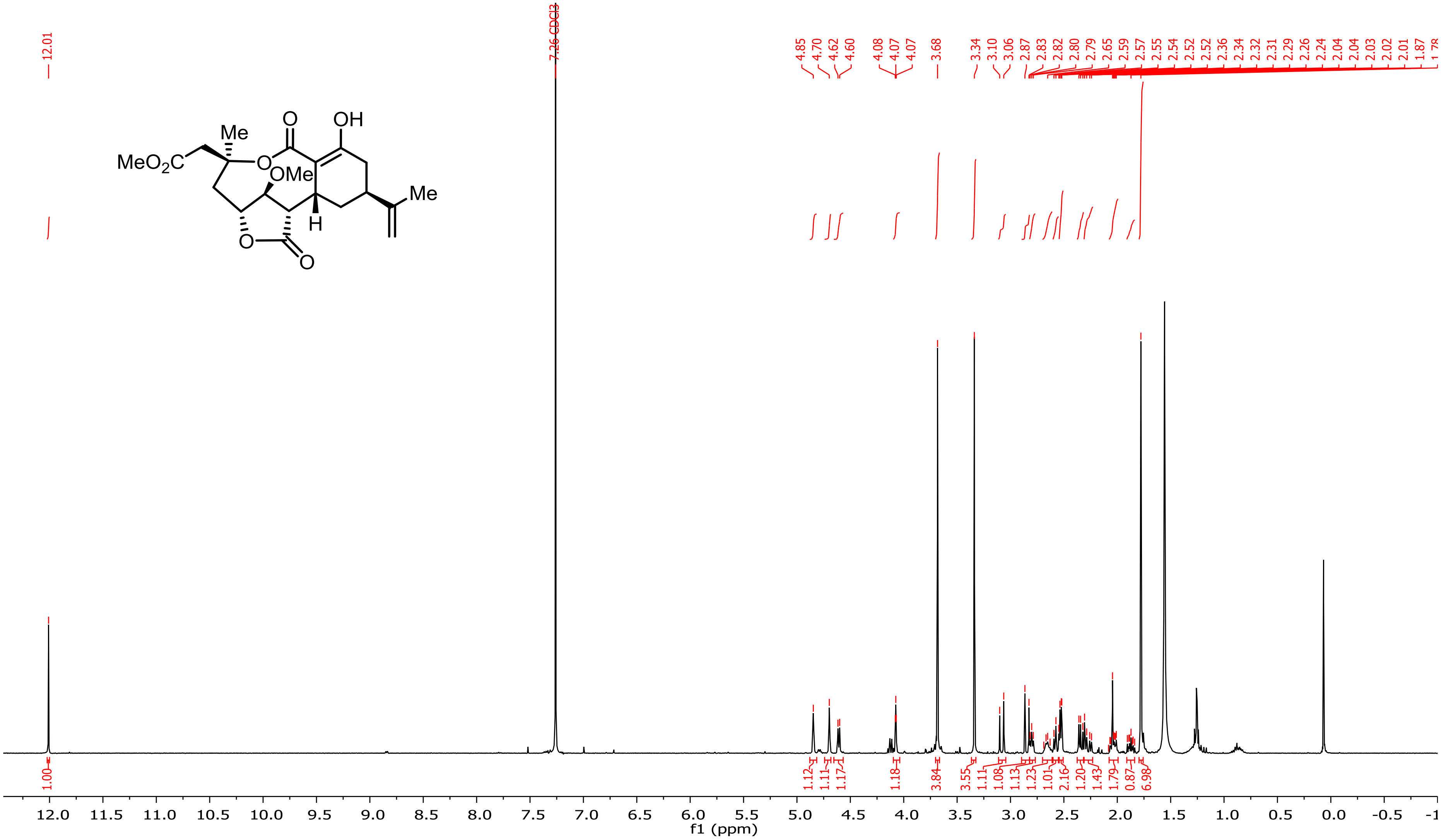
^{1}H NMR Spectrum of 27 (400 MHz, $CDCl_3$)



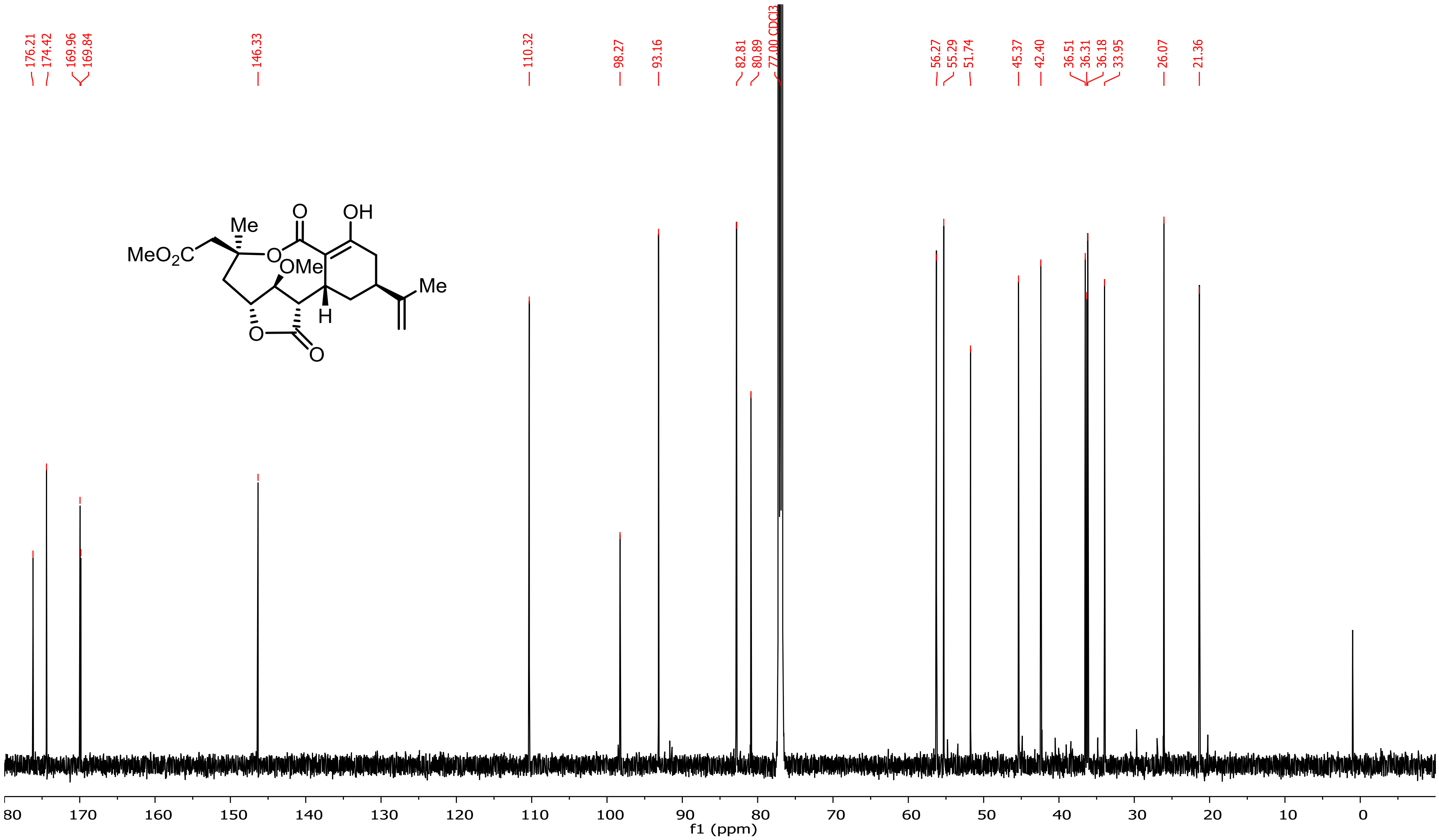
^{13}C NMR Spectrum of 27 (101 MHz, CDCl$_3$)



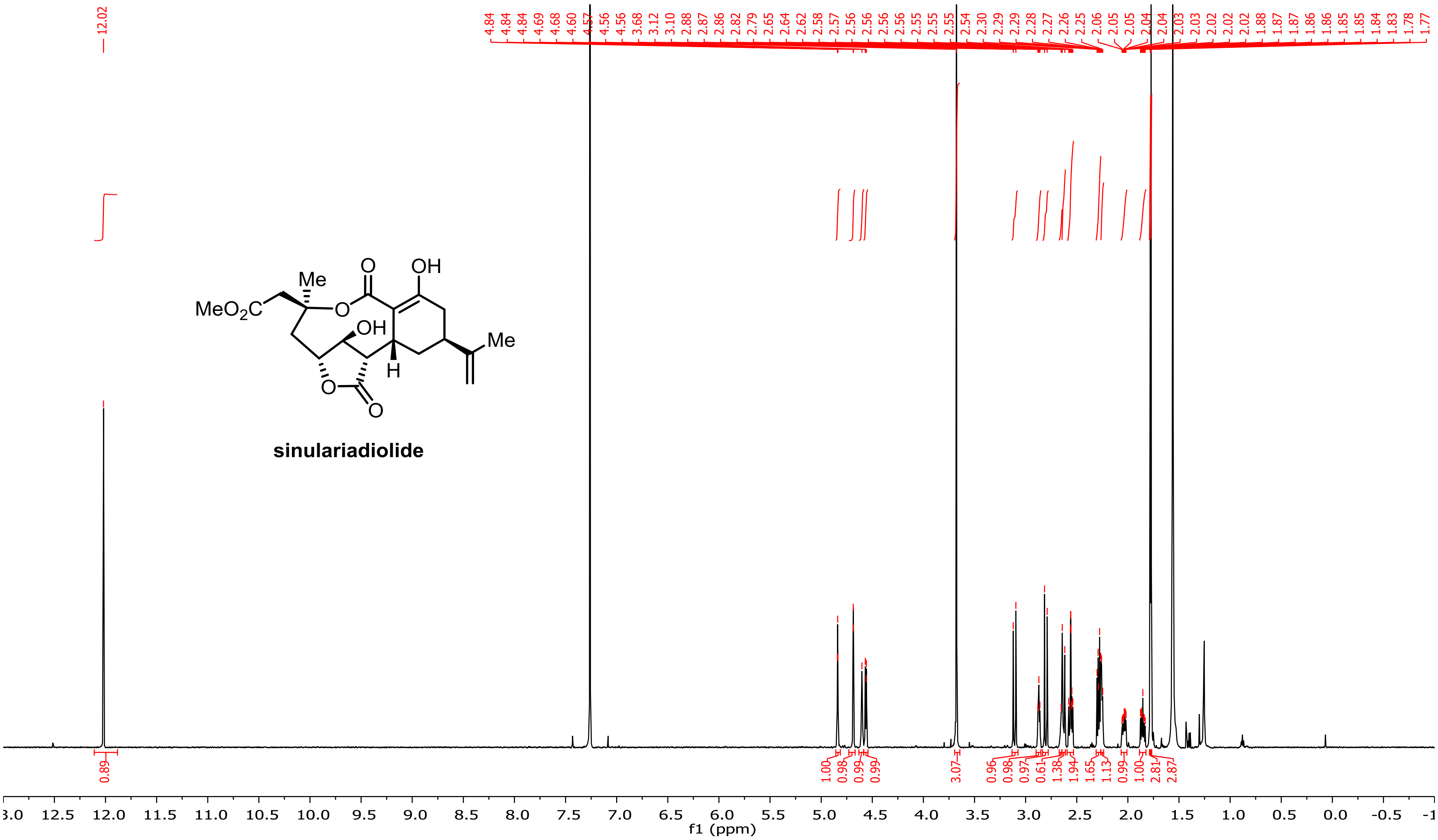
^{1}H NMR Spectrum of 28 (400 MHz, $CDCl_3$)



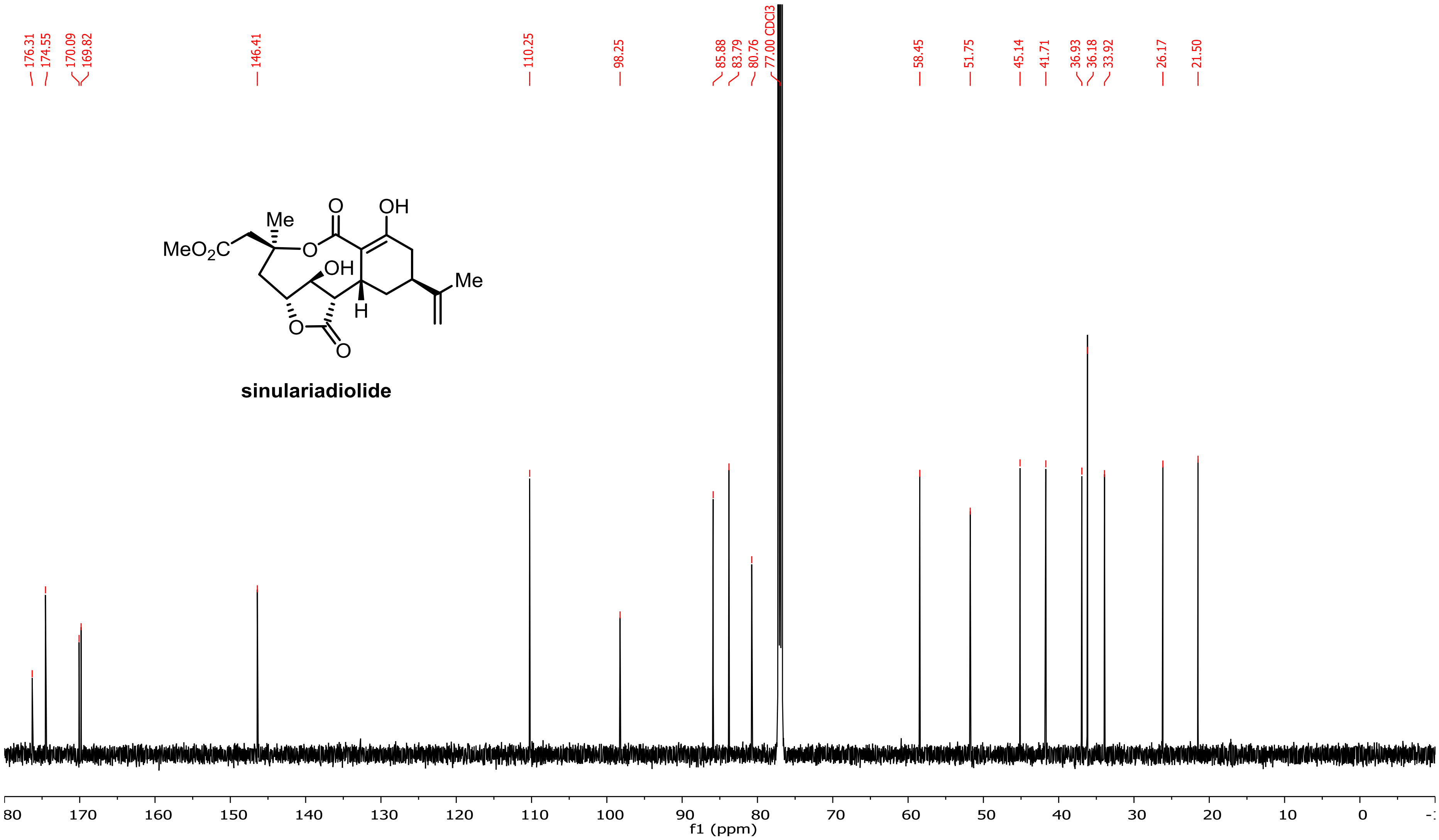
^{13}C NMR Spectrum of 28 (151 MHz, CDCl$_3$)

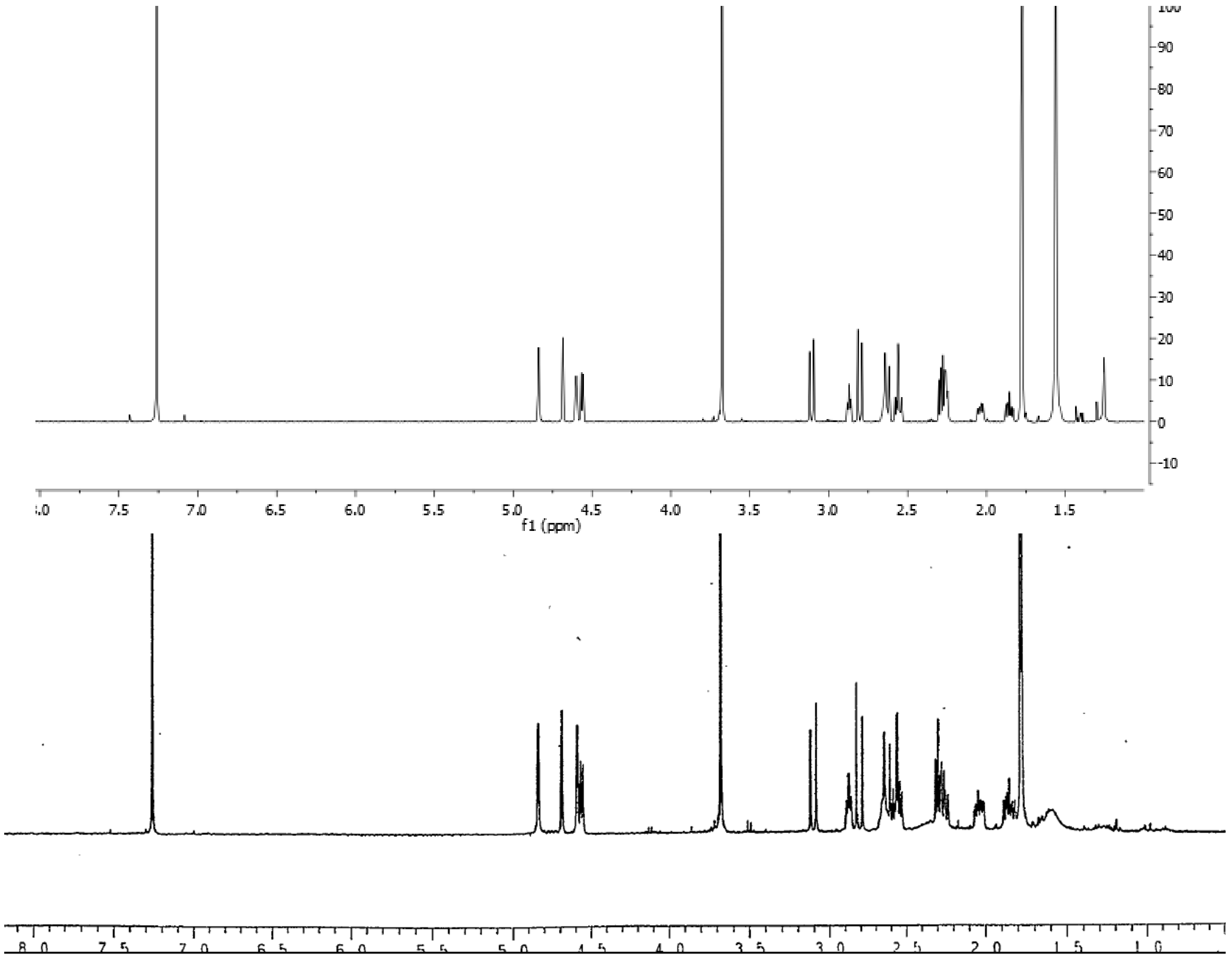


^{1}H NMR Spectrum of Sinulariadiolide (1) (600 MHz, $CDCl_3$)

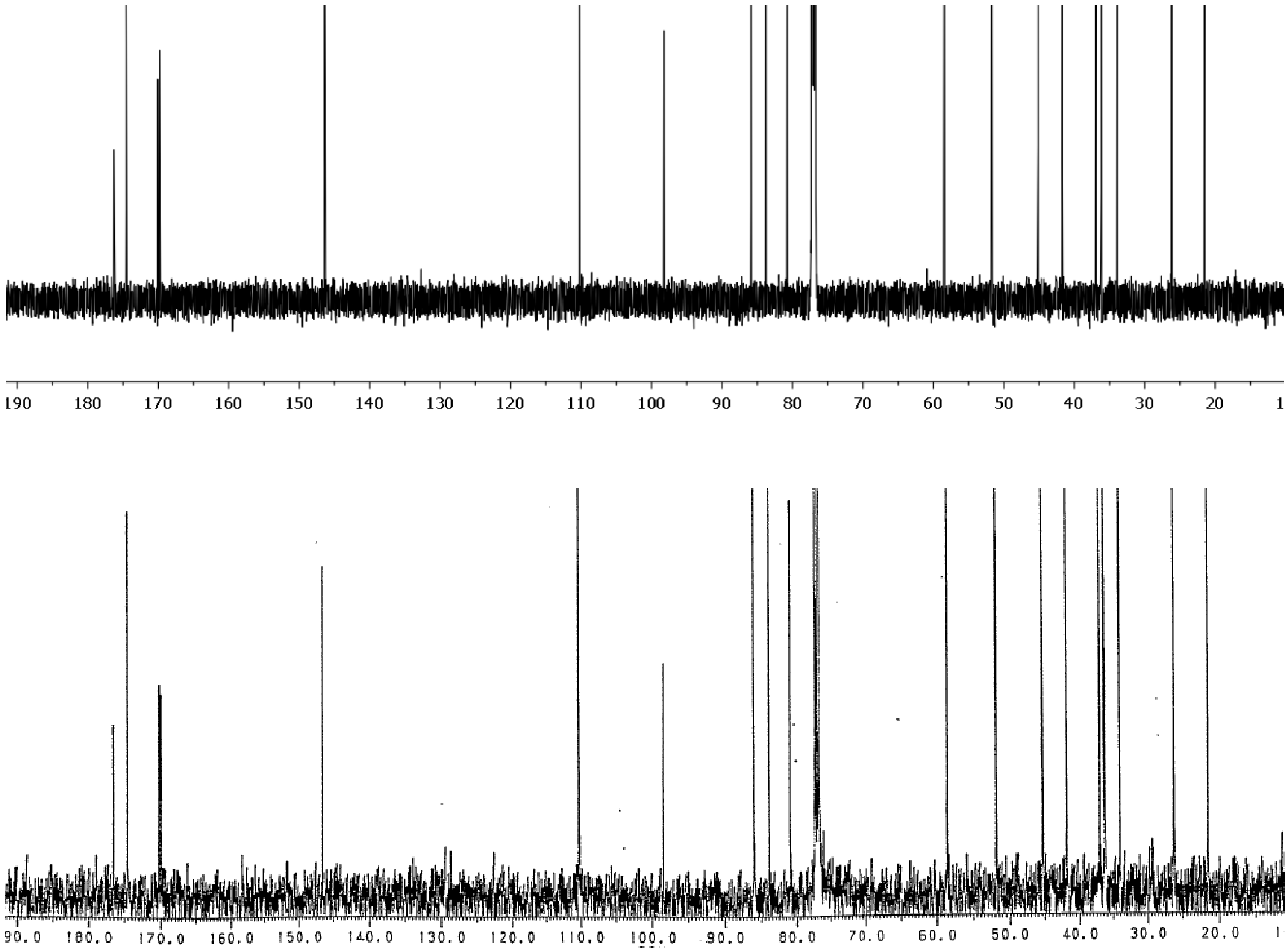


^{13}C NMR Spectrum of Sinulariadiolide (1) (151 MHz, CDCl$_3$)





Comparison of the ^{1}H NMR spectrum of synthetic sinulariadiolide (–)-**1** (top) and the spectrum of the natural product (bottom)



Comparison of the ^{13}C NMR spectrum of synthetic sinulariadiolide (–)-**1** (top) and the spectrum of the natural product (bottom)

References

[1] M. C. Holland, J. B. Metternich, C. Daniliuc, W. B. Schweizer, R. Gilmour, *Chem. Eur. J.* **2015**, *21*, 10031.

[2] A. N. Kost, L. N. Khaimov, Y. Dzhurakulov, K. K. Khaidarov, L. D. Lebedeva, A. L. Kotov, *Chem. Heterocycl. Compd.* **1975**, *11*,1263.

[3] S. Schaubach, K. Gebauer, F. Ungeheuer, L. Hoffmeister, M. K. Ilg, C. Wirtz, A. Fürstner, *Chem. Eur. J.* **2016**, *22*, 8494.

[4] K. Iguchi, K. Kajiyama, H. Miyaoka, Y. Yamada, *J. Org. Chem.* **1996**, *61*, 5998.