Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

German Edition: DOI:

Selective Formation of a Trisubstituted Alkene Motif by *trans*-Hydrostannation/Stille Coupling: Application to the Total Synthesis and Late-Stage Modification of 5,6-Dihydrocineromycin B**

*Stephan M. Rummelt, Johannes Preindl, Heiko Sommer, and Alois Fürstner**

anie_201501608_sm_miscellaneous_information.pdf

Crystallographic Information

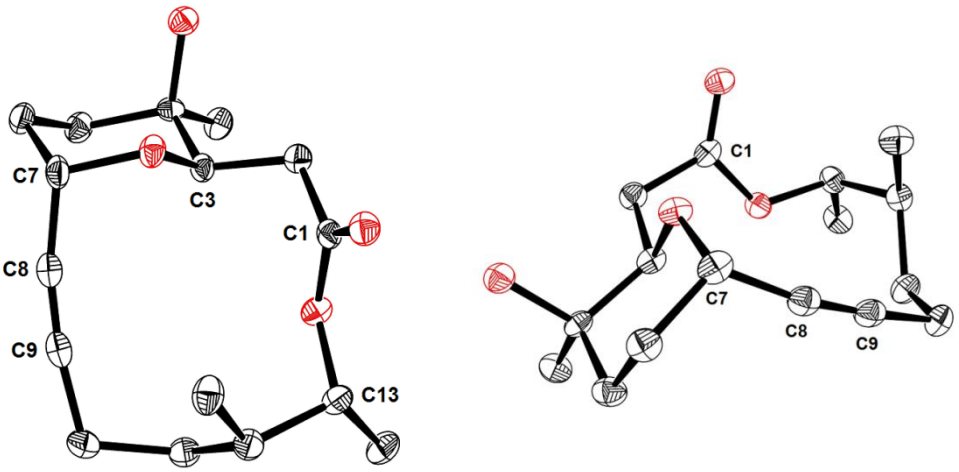


Figure S-1. Structure of compound **20** in the solid state in two different orientations (cineromycin numbering scheme); all hydrogen atoms are omitted for clarity

CCDC 1048778 contains the supporting crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

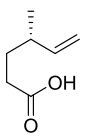
X-ray Crystal Structure Analysis of Compound 20. X-ray Crystal Structure Analysis of 8977: $C_{16}H_{24}O_4$, M_r = 280.35 g · mol^{-1}, colorless plate, crystal size 0.30 x 0.12 x 0.03 mm, orthorhombic, space group $P2_12_12_1$, a = 7.2789(9) Å, b = 10.7001(13) Å, c = 19.387(2) Å, V = 1510.0(3) Å^3, T = 100 K, Z = 4, D_{calc} = 1.233 g·cm^3, λ = 1.54178 Å, μ(Cu-K_α) = 0.707 mm^{-1}, Empirical absorption correction (T_{min} = 0.37, T_{max} = 0.69), Bruker-AXS Proteum X8 diffractometer, 4.561 < θ < 55.082°, 17540 measured reflections, 1896 independent reflections, 1741 reflections with $I > 2\sigma(I)$, Structure solved by direct methods and refined by full-matrix least-squares against F^2 to R_1 = 0.034 [$I > 2\sigma(I)$], wR_2 = 0.084, 186 parameters, absolute structure parameter = –0.01(13), H atoms riding, extinction coefficient = 0.0054(8), S = 1.042, residual electron density 0.2 / –0.2 e Å^{-3}.

Preparative Results

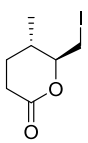
General. All reactions were carried out under Ar in flame-dried glassware. The solvents were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Mg/anthracene), CH_2Cl_2, MeCN (CaH_2), toluene, benzene (Na/K), MeOH (Mg). DMF and NEt_3 were dried by an absorption solvent purification system based on molecular sieves. DBU, TMEDA and pyridine were purified by distillation over CaH_2 and transferred under Ar. Flash chromatography: Merck silica gel 60 (40–63 µm). NMR: Spectra were recorded on a Bruker AV 400 spectrometer 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

($CDCl_3$: $\delta_C \equiv 77.16$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.26$ ppm) For clarity, Sn–H couplings of the vinylic protons were omitted in the multiplet analysis but are given in brackets. ^{119}Sn NMR spectra were recorded on a Bruker AV VIII 300 spectrometer using Me_4Sn as external standard. IR: Spectrum One (Perkin-Elmer) spectrometer, wavenumbers ($\widetilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ 3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan). Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Strem) were used as received; CuTC was purchased from Aldrich. $Zn(OTf)_2$ was dried at 120 °C at $1x10^{-2}$ mbar for 12 h. $[Cp^*RuCl_2]_n$ [1] and $[(Ph_3SiO)_4Mo{\equiv}CPh]K$ (**21**)[2] were prepared according to literature procedures and were stored under Argon. Commercial Bu_3SnH is stabilized with 0.05% of 3,5-di-*tert*-butyl-4-hydroxytoluene, which was not removed in the reactions described herein.

***(S)*-4-Methylhex-5-enoic acid (5).** Ozone was bubbled through a solution of *(S)*-citronellene (**4**) (14.6 g, 105 mmol) in CH_2Cl_2 (600 mL) at –78 °C for 3.5 h. The progress of the reaction was carefully monitored by TLC. Once the substrate was consumed, the mixture was treated with Me_2S (40 mL, 540 mmol) and allowed to warm to room temperature. The solution was washed with water and brine and dried over $MgSO_4$, the drying agent was filtered off and the solvent evaporated. The crude aldehyde was dissolved in *t*BuOH/water (2:1, 525 mL) and NaH_2PO_4 (38.0 g, 316 mmol) and H_2O_2 (30% *w/w* in water, 62 mL, 546 mmol) were successively introduced. The mixture was cooled to 0 °C before $NaClO_2$ (57.4 g, 634 mmol) was added in portions. The ice bath was removed and stirring continued for 21 h. For work up, the mixture was extracted with Et_2O and the combined organic phases were repeatedly extracted with sat. aq. $NaHCO_3$. The combined aqueous layers were carefully acidified with aq. HCl (2 M) and then extracted with Et_2O (3 x). The combined organic layers were washed with brine and dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/*tert*-butyl methyl ether, 2:1) afforded the title compound as a colorless oil (10.9 g, 80%). $[a]_D^{20}$: +10.2 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.55 – 9.00 (bs, 1H), 5.63 (ddd, *J* = 17.5, 10, 7.5 Hz, 1H), 5.05 – 4.92 (m, 2H), 2.40 – 2.30 (m, 2H), 2.16 (hex., *J* = 7.0 Hz, 1H), 1.76 – 1.53 (m, 2H), 1.02 ppm (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.0, 142.4, 113.0, 36.6, 31.0, 30.2, 19.3 ppm. IR (film): $\tilde{\nu}$ = 3079, 2962, 2929, 2871, 2672, 1715, 1455, 1416, 1376, 1276, 914 cm^{-1}; HR (EI): *m/z* calcd. for $[C_7H_{11}O_2^-]$: 127.0765; found 127.0764.



(5*S*,6*S*)-6-(Iodomethyl)-5-methyltetrahydro-2*H*-pyran-2-one (S-1). Iodine (19.3 g, 76.1 mmol) was added in one portion to a solution of acid **5** (3.25 g, 25.4 mmol) in CH_3CN (81 mL). The dark red mixture was stirred at room temperature for 3 h before it was diluted with *tert*-butyl methyl ether. The reaction was quenched with sat. aq. $Na_2S_2O_3$, the layers were separated and the aqueous layer was extracted with *tert*-butyl methyl ether. The combined extracts

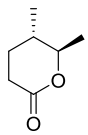


[1] T. D. Tilley, R. H. Grubbs, J. E. Bercaw, *Organometallics* **1984**, *3*, 274-278.

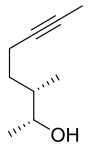
[2] J. Heppekausen, R. Stade, A. Kondoh, G. Seidel, R. Goddard, A. Fürstner *Chem. Eur. J.* **2012**, *18*, 10281-10299.

were dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue (d.r.: 7.5:1, NMR) by flash chromatography (silica, hexanes/Et_2O, 1:1) afforded the title compound as a diastereomerically pure white solid (4.73 g, 73%). Mp = 70-72 °C. $[a]_D^{20}$: –10.5 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (dt, *J* = 9.3, 3.4 Hz, 1H), 3.53 (dd, *J* = 11.4, 3.0 Hz, 1H), 3.38 (dd, *J* = 11.4, 3.8 Hz, 1H), 2.65 (ddd, *J* = 18.1, 6.4, 3.3 Hz, 1H), 2.53 (ddd, *J* = 17.9, 6.8, 11.1 Hz, 1H), 1.99 – 1.87 (m, 2H), 1.74 – 1.61 (m, 1H), 1.01 ppm (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.5, 82.8, 33.6, 29.9, 27.2, 17.0, 9.0 ppm. IR (film): $\tilde{\nu}$ = 2963, 2937, 2876, 1735, 1461, 1416, 1342, 1291, 1249, 1227, 1177, 1101, 1038, 1006 cm^{-1} HR-ESI**:** *m/z* calcd. for $[C_7H_{11}IO_2Na]^+$: 276.9696; found 276.9696.

(5*S*,6*R*)-5,6-Dimethyltetrahydro-2*H*-pyran-2-one (6). Tributylstannane (5.90 mL, 21.9 mmol) was added to a solution of compound **S-1** (3.70 g, 14.6 mmol) in benzene (35 mL) and the resulting mixture was stirred at reflux temperature for 2 h. The mixture was allowed to cool before the reaction was quenched with sat. aq. KF. The resulting mixture was stirred for 30 min and then diluted with water. After extraction of the aqueous layer with *tert*-butyl methyl ether, the combined extracts were washed with brine and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/Et_2O, 4:1 to 1:1) afforded the title compound as a colorless oil (1.64 g, 88%). $[a]_D^{20}$: +26.0 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.01 (dq, *J* = 9.6, 6.3 Hz, 1H), 2.58 (ddd, *J* = 17.9, 4.2 Hz, 1H), 2.43 (ddd, *J* = 17.6, 7.4, 10.2 Hz, 1H), 1.94 – 1.83 (m, 1H), 1.69 – 1.48 (m, 2H), 1.31 (d, *J* = 6.3 Hz, 3H), 0.96 ppm (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 82.5, 34.6, 29.7, 27.8, 20.0, 17.3 ppm. IR (film): $\tilde{\nu}$ = 2977, 2937, 2880, 2251, 1726, 1461, 1338, 1351, 1225, 1094, 1045, 912, 727 cm^{-1}. HR-ESI**:** *m/z* calcd. for $[C_7H_{12}O_2Na]^+$: 151.0730; found 151.0729.



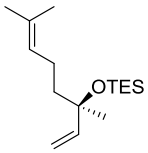
(2*R*,3*S*)-3-Methyloct-6-yn-2-ol (8). CCl_4 (47.8 mL, 495 mmol) was added dropwise over 4 h to a refluxing solution of lactone **6** (1.40 g, 10.9 mmol) and PPh_3 (13.19 g, 50.3 mmol) in THF (220 mL). Once the addition was complete, the reaction was quenched with water and the mixture extracted with *tert*-butyl methyl ether. The combined extracts were washed with brine and dried over $MgSO_4$, the drying agent was filtered off and the solution was concentrated to a volume of ca. 10 mL. Pentane was added and the precipitated solid was filtered off. After repeating this operation 3 times, the solvent was evaporated and the residue was purified by flash chromatography (silica, pentane). Because of its limited stability, the resulting product **7** was immediately used in the next step without characterization.



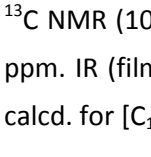
MeLi (1.6 M in Et_2O, 20.4 mL, 32.6 mmol) was added dropwise to a solution of the dichloroolefin **7** (2.12 mg, 10.9 mmol) and $Cu(acac)_2$ (285 mg, 1.09 mmol, 10 mol%) in Et_2O (76 mL) at 0 °C. The mixture was stirred for 14 h at room temperature before the reaction was quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with *tert*-butyl methyl ether, the combined extracts were washed with brine and dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, pentane/Et_2O, 4:1 to 1:1) afforded the title compound as a colorless oil (1.13 g, 74%). $[a]_D^{20}$: –4.6 (c = 1, $CHCl_3$). ^{1}H NMR (400

MHz, $CDCl_3$): δ = 3.73 – 3.62 (m, 1H), 2.31 – 2.17 (m, 1H), 2.17 – 2.03 (m, 1H), 1.76 (t, *J* = 2.6 Hz, 3H), 1.72 – 1.55 (m, 2H), 1.47 – 1.40 (bs, 1H), 1.36 – 1.22 (m, 1H), 1.13 (t, *J* = 6.3 Hz, 3 H), 0.87 ppm (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 79.2, 75.8, 71.6, 39.2, 31.9, 19.6, 16.6, 14.4, 3.6 ppm. IR (film): $\tilde{\nu}$ = 3378, 2968, 2920, 2876, 2454, 1378, 1320, 1092, 1058, 1005, 922 cm^{-1}; HR (EI): *m/z* calcd. for [$C_9H_{16}O$]: 140.11200; found 140.12012.

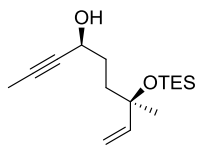
(*R*)-((3,7-Dimethylocta-1,6-dien-3-yl)oxy)triethylsilane (S-2). Et_3SiCl (5.6 mL, 33.5 mmol) was added dropwise to a solution of (*R*)-linalool (4.0 mL, 22.3 mmol), imidazole (3.0 g, 44.6 mmol) and DMAP (1.1 mmol, 0.14 g) in CH_2Cl_2 (40 mL). The mixture was stirred for 15 h before the reaction was quenched with sat. aq. $NaHCO_3$. The organic phase was extracted with CH_2Cl_2, the combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes) afforded the title compound as a colorless oil (5.9 g, 99%). $[\alpha]_D^{20}$: –5.2 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85 (dd, *J* = 17.3, 10.6 Hz, 1H), 5.14 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.09 (ddt, *J* = 8.7, 5.9, 1.5 Hz, 1H), 4.99 (dd, *J* = 10.7, 1.7 Hz, 1H), 2.09 – 1.89 (m, 2H), 1.67 (d, *J* = 1.4 Hz, 3H), 1.59 (s, 3H), 1.54 – 1.41 (m, 2H), 1.29 (s, 3H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.58 ppm (q, *J* = 7.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.6, 131.3, 124.9, 111.8, 75.5, 43.9, 27.5, 25.9, 23.0, 17.7, 7.3, 6.9 ppm. IR (film): $\tilde{\nu}$ = 2955, 2913, 2876, 1457, 1413, 1370, 1238, 1175, 1118, 1047, 1003 cm^{-1}. HR-ESI: calcd. for [$C_{16}H_{32}OSiNa$]$^+$: 291.21146; found 291.21139.



(*R*)-4-Methyl-4-((triethylsilyl)oxy)hex-5-enal (10). Ozone was bubbled through a solution of the silyl ether **S-2** (5.8 g, 21.6 mmol) and pyridine (2.1 mL, 25.9 mmol) in CH_2Cl_2 (100 mL) at –78 °C for 2 h. The progress of the reaction was carefully monitored by TLC. Upon completion, the reaction mixture was filtered through a pad of Celite® into ice water (170 mL) containing Me_2S (3.5 mL, 47.88 mmol). The resulting mixture was warmed to room temperature and stirred for additional 2 h. The layers were separated and the aq. phase was extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 30:1) afforded the title compound as a colorless oil (4.0 g, 77%). $[\alpha]_D^{20}$: +2.5 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.75 (t, *J* = 1.8 Hz, 1H), 5.79 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.16 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.04 (dd, *J* = 10.6, 1.5 Hz, 1H), 2.57 – 2.36 (m, 2H), 1.90 - 1.73 (m, 2H), 1.34 (s, 3H), 0.94 (t, *J* = 7.9 Hz, 9H), 0.58 ppm (q, *J* = 7.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.2, 144.6, 112.9, 74.8, 39.3, 36.0, 27.7, 7.2, 6.8 ppm. IR (film): $\tilde{\nu}$ = 2955, 2912, 2876, 2716, 1726, 1458, 1413, 1372, 1237, 1178, 1125, 1042, 1005 cm^{-1} HR-ESI: *m/z* calcd. for [$C_{13}H_{26}O_2SiNa$]$^+$: 265.15943; found 265.15935.

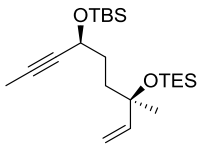


(4*S*,7*R*)-7-Methyl-7-((triethylsilyl)oxy)non-8-en-2-yn-4-ol (S-3). Triethylamine (4.7 mL, 33.6 mmol,) was added dropwise to a suspension of $Zn(OTf)_2$ (11.64 g, 32.0 mmol) and (–)-*N*-methylephedrine (6.03 g, 33.6 mmol) in toluene (110 mL) at room temperature. After stirring for 2 h, liquid propyne (ca. 10 mL) was added via cannula from a Schlenk tube at –78 °C and the resulting mixture was stirred for 45

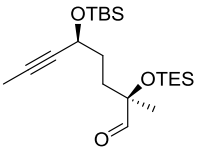


min at room temperature. Next, a solution of aldehyde **10** (3.88 g, 16.0 mmol) in toluene (16 mL) was added dropwise over 5 h. Once the addition was complete, the mixture was stirred for 12 h before the reaction was quenched with sat. aq. NH_4Cl. The aqueous phase was extracted with Et_2O, the combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 10:1) afforded the title compound as a colorless oil (4.26 g, 94%). $[\alpha]_D^{20}$: –3.2 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.15 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.01 (dd, *J* = 10.6, 1.5 Hz, 1H), 4.38 – 4.29 (m, 1H), 2.17 (d, *J* = 5.1 Hz, 1H), 1.83 (d, *J* = 2.1 Hz, 3H), 1.80 – 1.68 (m, 2H), 1.68 – 1.61 (m, 2H), 1.33 (s, 3H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.60 ppm (q, *J* = 7.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.2, 112.3, 80.9, 80.6, 75.4, 63.0, 39.2, 32.9, 27.5, 7.2, 6.8, 3.7 ppm; IR (film): $\tilde{\nu}$ = 3382, 2954, 2914, 2876, 1458, 1413, 1370, 1304, 1237, 1179, 1115, 1048, 1004; HR-ESI: *m/z* calcd. for $[C_{16}H_{30}O_2SiNa]^+$: 305.19073; found 305.19055.

(5*S*,8*R*)-10,10-Diethyl-2,2,3,3,8-pentamethyl-5-(prop-1-yn-1-yl)-8-vinyl-4,9-dioxa-3,10-disila-dodecane (11). *tert*-Butyldimethylchlorosilane (2.50 g, 16.6 mmol) was added in one portion to a solution of alcohol **S-3** (4.26 g, 15.1 mmol) and imidazole (1.23 g, 18.1 mmol) in CH_2Cl_2 (30 mL). The mixture was stirred for 20 h before the reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, the combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 50:1) afforded the title compound as a colorless oil (5.98 g, quant.). $[\alpha]_D^{20}$: –28.1 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (dd, *J* = 17.2, 10.6 Hz, 1H), 5.14 (dd, *J* = 17.3, 1.7 Hz, 1H), 4.98 (dd, *J* = 10.6, 1.7 Hz, 1H), 4.34 – 4.26 (m, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.74 –1.52 (m, 4H), 1.30 (s, 3H), 0.94 (t, *J* = 7.9 Hz, 9H), 0.89 (s, 9H), 0.58 (q, *J* = 7.9 Hz, 6H), 0.11 (s, 3H), 0.08 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.5, 111.9, 81.1, 80.0, 75.3, 63.6, 39.1, 33.8, 27.9, 26.0, 18.4, 7.3, 6.9, 3.7, −4.4, −4.9 ppm. IR (film): $\tilde{\nu}$ = 2955, 2930, 2877, 2857, 1461, 1413, 1362, 1250, 1180, 1083, 1058, 1004 cm^{-1}. HR-ESI: *m/z* calcd. for $[C_{22}H_{44}O_2Si_2Na]^+$: 419.27721; found 419.27696.

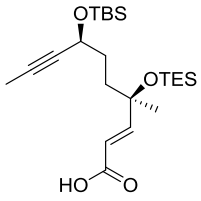


(2*R*,5*S*)-5-((*tert*-Butyldimethylsilyl)oxy)-2-methyl-2-((triethylsilyl)oxy)oct-6-ynal (S-4). Ozone was bubbled through a solution of compound **11** (5.63 g, 14.2 mmol) in CH_2Cl_2 (140 mL) at –78 °C. The progress of the reaction was carefully monitored by TLC. Once the conversion was complete (ca. 1 h), Me_2S (5 mL, 67.6 mmol) was added and the resulting mixture stirred for 1 h at –78 °C and for 2 h at room temperature. Water was introduced and the mixture extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 50:1) afforded the title compound as a colorless oil (3.80 g, 67%). $[\alpha]_D^{20}$: –9.1 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.55 (s, 1H), 4.36 – 4.25 (m, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.77 – 1.63 (m, 3H), 1.63 – 1.52 (m, 1H), 1.27 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.89 (s, 9H), 0.61 (q, *J* = 7.9 Hz, 6H), 0.10 (s, 3H), 0.08 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 205.0, 80.6, 80.4, 80.1, 63.1, 34.6, 32.7, 26.0, 23.0, 18.4, 7.1, 6.7, 3.7, −4.4, −4.9 ppm. IR (film), $\tilde{\nu}$ =



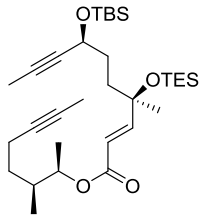
2955, 2931, 2878, 2858, 1738, 1461, 1414, 1362, 1250, 1193, 1084, 1058, 1006 cm^{-1}; HR-ESI: calcd. for $[C_{21}H_{42}O_3Si_2Na]^+$: 421.25647; found 421.25651.

(4*R*,7*S*,*E*)-7-((*tert*-Butyldimethylsilyl)oxy)-4-methyl-4-((triethylsilyl)oxy)dec-2-en-8-ynoic acid (12).



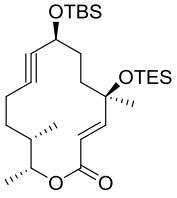
Diethylphosphonoacetic acid (1.48 mL, 9.2 mmol), TMEDA (1.50 mL, 10.0 mmol) and DBU (5.00 mL, 33.4 mmol) were added to a suspension of $Zn(OTf)_2$ (6.68 g, 18.4 mmol) in THF (25 mL) at 0 °C. Aldehyde **S-4** (3.31 g, 8.35 mmol) was introduced, the ice-bath was removed and the mixture stirred for 16 h at room temperature. The reaction was quenched with saturated aq. NH_4Cl and the aqueous layer extracted with CH_2Cl_2 (4 x) The combined extracts were washed with brine, which was re-extracted with CH_2Cl_2 (4 x). The combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solution was concentrated. Purification of the crude product by flash chromatography (silica, hexane/EtOAc, 5:1 to 2:1 to 1:1) afforded the title compound as a colorless oil (2.95 g, 80%). $[\alpha]_D^{20}$: −19.4 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.88 – 10.48 (bs, 1H), 6.97 (d, *J* = 15.4 Hz, 1H), 5.98 (d, *J* = 15.4 Hz, 1H), 4.37 – 4.24 (m, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.79 – 1.60 (m, 3H), 1.58 – 1.48 (m, 1H), 1.38 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.89 (s, 9H), 0.62 (q, *J* = 7.8 Hz, 6H), 0.10 (s, 3H), 0.08 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.6, 157.7, 118.1, 80.8, 80.3, 75.1, 63.1, 38.4, 33.4, 28.2, 25.9, 18.4, 7.2, 6.8, 3.6, –4.5, –4.9 ppm. IR (film) $\tilde{\nu}$ = 2955, 2930, 2877, 2857, 2688, 1697, 1654, 1461, 1415, 1303, 1249, 1162, 1083, 1056, 1004 cm^{-1}. HR-ESI: *m/z* calcd. for $[C_{23}H_{43}O_4Si_2]^-$: 439.27054; found 439.27079.

(*2R,3S*)-3-Methyloct-6-yn-2-yl (4*R*,7*S*,*E*)-7-((*tert*-butyldimethylsilyl)oxy)-4-methyl-4-((triethylsilyl)-oxy)dec-2-en-8-ynoate (13).



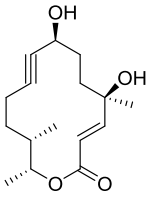
DCC (1.16 g, 5.60 mmol) was added in one portion to a solution of alcohol **8** (635 mg, 4.53 mmol), acid **12** (1.90 g, 4.31 mmol) and DMAP (53 mg, 0.43 mmol) in CH_2Cl_2 (30 mL) at 0 °C. After stirring for 30 min, the mixture was filtered through a plug of Celite® and the filtrate was concentrated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 40:1 to 30:1) afforded the title compound as a colorless oil (2.04 g, 84%). $[\alpha]_D^{20}$: –13.4 (c = 1, CH_3OH). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.83 (d, *J* = 15.5 Hz, 1H), 5.91 (d, *J* = 15.5 Hz, 1H), 4.88 (p, *J* = 6.3 Hz, 1H), 4.30 (ddt, *J* = 5.6, 3.7, 2.1 Hz, 1H), 2.29 – 2.15 (m, 1H), 2.10 (dtq, *J* = 13.6, 8.0, 2.5 Hz, 1H), 1.86 – 1.79 (m, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.77 (t, *J* = 2.5 Hz, 3H), 1.75 –1.61 (m, 4H), 1.59 – 1.49 (m, 1H), 1.36 (s, 3H), 1.29 (dtd, *J* = 9.3, 8.1, 4.6 Hz, 1H), 1.19 (d, *J* = 6.4 Hz, 3H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.65 –0.56 (m, 6H), 0.09 (s, 3H), 0.08 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.6, 154.6, 119.4, 80.8, 79.2, 78.9, 75.7, 75.0, 74.1, 63.2, 38.6, 36.7, 33.5, 31.8, 28.2, 26.0, 18.4, 16.7, 16.3, 14.5, 7.2, 6.8, 3.64, 3.60, −4.4, −4.9 ppm. IR (film): $\tilde{\nu}$ = 2955, 2932, 2120, 1717, 1655, 1459, 1362, 1254, 1159, 1082, 1004, 836, 776, 724 cm^{-1}. HR-ESI**:** *m/z* calcd. for $[C_{32}H_{58}O_4Si_2Na]^+$: 585.37601, found 585.37659.

(*5R,8S,13S,14R,E*)-8-((*tert*-Butyldimethylsilyl)oxy)-5,13,14-trimethyl-5-((triethylsilyl)-oxy)oxacyclo-tetradec-3-en-9-yn-2-one (14). Diyne **13** (800 mg, 1.42 mmol) was added to a suspension of molecular sieves 5 Å (flame dried, 6 g) in toluene (750 mL) at room temperature and the resulting



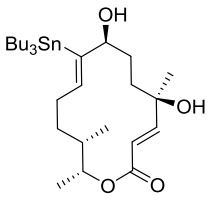
mixture was stirred for 1 hour. [$(Ph_3SiO)_4Mo{\equiv}CPh$]K (**21**) (188 mg, 0.142 mmol, 10 mol%) was then added in one portion and stirring continued for 2 h. The suspension was filtered through a plug of Celite®, which was carefully rinsed with EtOAc. The combined filtrates were concentrated and the residue was purified by flash chromatography (silica, hexanes/EtOAc, 30:1 to 20:1) to furnish the title compound as a colorless oil (672 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.05 (d, *J* = 15.3 Hz, 1H), 5.97 (d, *J* = 15.3 Hz, 1H), 4.68 (dq, *J* = 9.1, 6.3 Hz, 1H), 4.34 (dq, *J* = 8.4, 2.1 Hz, 1H), 2.27 (dddd, *J* = 17.0, 7.0, 5.2, 1.9 Hz, 1H), 2.15 (dddd, *J* = 17.0, 8.6, 5.2, 2.0 Hz, 1H), 1.95 – 1.76 (m, 2H), 1.66 (dtd, *J* = 9.1, 6.8, 3.8 Hz, 1H), 1.62 – 1.54 (m, 2H), 1.54 – 1.35 (m, 2H), 1.32 (s, 3H), 1.27 (d, *J* = 6.3 Hz, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.65 –0.57 (m, 6H), 0.08 (s, 3H), 0.07 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.6, 155.1, 119.0, 85.4, 81.5, 75.5, 74.9, 63.4, 39.2, 37.6, 33.3, 32.9, 27.5, 25.9, 19.2, 18.3, 17.0, 16.9, 7.2, 6.9, –4.3, –4.8 ppm. IR (film): $\tilde{\nu}$ = 2955, 2932, 2877, 1715, 1459, 1342, 1251, 1162, 1106, 1081, 1048, 1005, 976, 836, 777, 724 cm^{-1}. HR-ESI**:** *m/z* calcd. for $[C_{28}H_{52}O_4Si_2Na]^+$: 531.32927, found 531.32964.

(*5R,8S,13S,14R,E*)-5,8-Dihydroxy-5,13,14-trimethyloxacyclotetradec-3-en-9-yn-2-one (15).



HF/pyridine (70% in pyridine, 372 µL, 2.89 mmol) was added dropwise to a solution of compound **14** (545 mg, 0.96 mmol) and pyridine (702 µL, 8.7 mmol) in THF (7 mL). The mixture was stirred for 5 h before additional HF/pyridine (124 µL, 0.96 mmol) was introduced. Stirring was continued for another 12 h before the reaction was quenched with sat. aq. $NaHCO_3$. After extraction of the aqueous layer with EtOAc, the combined extracts were washed with brine and dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 1:1) afforded the title compound as a white crystalline solid (365 mg, 84%). Mp = 150 – 152 °C. $[a]_D^{20}$: –50.2 (c = 1, CH_3OH). ^{1}H NMR (400 MHz, $CDCl_3$) δ **=** 7.17 (d, *J* = 15.6 Hz, 1H), 6.02 (d, *J* = 15.6 Hz, 1H), 4.69 (dq, *J* = 12.5, 6.5 Hz, 1H), 4.50 – 4.37 (m, 1H), 2.39 – 2.25 (m, 1H), 2.25 – 2.13 (m, 1H), 1.87 (m, 3H), 1.80 – 1.66 (m, 4H), 1.48 (p, *J* = 6.3, 5.6 Hz, 2H), 1.34 (s, 3H), 1.29 (d, *J* = 6.3 Hz, 3H), 0.92 ppm (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.2, 154.2, 119.1, 87.2, 80.6, 75.2, 73.3, 62.7, 39.1, 36.9, 32.9, 31.8, 27.3, 19.1, 17.04, 16.96 ppm. IR (film) $\tilde{\nu}$ = 3402, 2972, 2934, 1698, 1455, 1379, 1339, 1268, 1102, 1036, 977 cm^{-1}. HR-ESI**:** *m/z* calcd. for $[C_{16}H_{24}O_4Na]^+$: 303.15665, found 303.15668.

(3*E*,5*R*,8*S*,9*Z*,13*S*,14*R*)-5,8-Dihydroxy-5,13,14-trimethyl-9-(tributylstannyl) oxacyclotetradeca-3,9-dien-2-one (16).



Tributyltin hydride (0.37 mL, 1.38 mmol) was added dropwise over 5 min to a stirred solution of alkyne **15** (336 mg, 1.2 mmol) and [{Cp*$RuCl_2$}$_n$] (18 mg, 5 mol%) in CH_2Cl_2 (15 mL, 0.08 M). The resulting mixture was stirred for 15 min before all volatile materials were evaporated. Purification of the residue by flash chromatography (hexanes/EtOAc, 3:1) afforded the title compound as a pale yellow oil that solidified upon standing (587 mg, 83%). $[a]_D^{20}$: –41.2 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, *J* = 15.6 Hz, 1H), 6.36 (dd, *J* = 9.2, 5.2, J_{Sn-H} = 121.7 Hz, 1H), 5.99 (d, *J* = 15.6 Hz, 1H), 4.58 (dq, *J* = 10.2, 6.3 Hz, 1H), 4.28 –4.04 (m, 1H), 2.09 – 1.93 (m, 2H), 1.89 – 1.80 (m, 1H),

1.80 – 1.66 (m, 3H), 1.56 –1.39 (m, 8H), 1.36 (s, 3H), 1.36 – 1.16 (m, 12H), 1.02 – 0.82 ppm (m, 18H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.0, 153.5, 146.4, 143.0, 119.7, 83.2, 76.3, 73.9, 39.8, 38.3, 34.4, 32.6, 31.5, 29.4, 28.1, 27.5, 19.0, 17.7, 13.8, 11.2 ppm. ^{119}Sn NMR (186 MHz, $CDCl_3$) δ = –54.9 ppm. IR (film): $\tilde{\nu}$ = 3450, 2954, 2924, 2871, 2853, 1698, 1640, 1455, 1377, 1281, 1267, 1153, 1133, 1104, 1044 cm^{-1}. HR-ESI: calcd. for $[C_{28}H_{52}O_4SnNa]^+$: 595.27791, found 595.27750.

(–)-5,6-Dihydrocineromycin B (**3**)**.** $[Pd(PPh_3)_4]$ (29 mg, 0.025 mmol, 5 mol%) was added to a solution of compound **16** (285.7 mg, 0.50 mmol) and flame-dried $[Ph_2PO_2][NBu_4]$ (253 mg, 0.55 mmol) in DMF (2.5 mL). The resulting mixture was stirred for 5 min before CuTC (100 mg, 0.53 mmol) was introduced, followed by MeI (0.75 mmol, 47 µL) *30 seconds later*.[3] The resulting mixture was stirred for 30 min before it was diluted with Et_2O and the reaction was quenched with water. The aqueous layer was extracted with Et_2O, the combined extracts were dried over $MgSO_4$, the drying agent was filtered off and the solution was concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 1:1) afforded the title compound as a white solid (137 mg, 92%). $[\alpha]_D^{20}$: –86.9 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): see Table S-1; ^{13}C NMR (101 MHz, $CDCl_3$): see Table S-2. IR (film): $\tilde{\nu}$ = 3401, 2971, 2935, 2876, 1696, 1639, 1450, 1377, 1268, 1154, 1104, 1041, 985, 755 cm^{-1}. HR-ESI: calcd. for $[C_{17}H_{28}O_4Na]^+$ 319.18798; found 319.18795.

Table S-1. Comparison of the ^{1}H NMR data ($CDCl_3$, δ_H in ppm) of 5,6-dihydrocineromycin B (**3**) prepared herein with the data reported in the literature; numbering scheme as shown in the Insert

Position	Isolation[4]	Zhai et al[5]	Current study
2	5.98 (d, *J* = 15.5 Hz, 1H)	5.95 (d, *J* = 15.9 Hz, 1H)	5.95 (d, *J* = 15.6 Hz, 1H)
3	6.82 (d, *J* = 15.5 Hz, 1H)	6.84 (d, *J* = 15.6 Hz, 1H)	6.84 (d, *J* = 15.6 Hz, 1H)
4			
5	1.95 (m, 2H)	1.89 – 1.75 (m, 1H)	1.89 – 1.76 (m, 1H)
		1.61 – 1.57 (m, 1H)	1.63 – 1.55 (m, 1H)
6	1.81 (m, 1H)	1.73 – 1.67 (m, 2H)	1.73 – 1.67 (m, 2H)
	1.57 (m, 1H)		
7	3.97 (dd, *J* = 15.5, 1.5 Hz, 1H)	3.98 (t, *J* = 6.0 Hz, 1H)	3.98 (t, *J* = 6.1 Hz, 1H)
9	5.49 (m, 1H)	5.51 (dd, *J* = 9.9, 2.7 Hz, 1H)	5.50 (ddd, *J* = 10.4, 3.7, 1.7 Hz, 1H)
10	2.09 (m, 1H)	2.16 – 2.02 (m, 1H)	2.11 (ddt, *J* = 15.0, 10.0, 5.0 Hz, 1H)
	1.80 (m, 1H)	1.89 – 1.75 (m, 1H)	1.89 – 1.76 (m, 1H)
11	1.30 – 1.25 (m, 2H)	1.45 – 1.37 (m, 1H)	1.47 – 1.38 (m, 1H)
		1.32 – 1.25 (m, 1H)	1.34 – 1.25 (m, 1H)
12	1.39 (m, 1H)	1.89 – 1.75 (m, 1H)	1.89 – 1.76 (m, 1H)
13	4.55 (m, 1H)	4.60 – 4.51 (m, 1H)	4.56 (dq, *J* = 10.1, 6.2 Hz, 1H)
4-CH_3	1.34 (s, 3H)	1.35 (s, 3H)	1.35 (s, 3H)
8-CH_3	1.51 (d, *J* = 0.5 Hz, 3H)	1.54 (s, 3H)	1.53 (t, *J* = 1.3 Hz, 3H)
12-CH_3	0.92 (d, *J* = 7.0 Hz, 3H)	0.94 (d, *J* = 6.9 Hz, 3H)	0.94 (d, *J* = 6.9 Hz, 3H)
13-CH_3	1.30 (m, 3H)	1.30 (d, *J* = 6.3 Hz, 3H)	1.29 (d, *J* = 6.2 Hz, 3H)

[3] The order of addition and the timing are important.

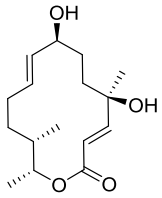
[4] H. J. Schiewe, A. Zeeck *J. Antibiot.* **1999**, *52*, 635-642.

[5] G. Li, X. Yang, H. Zhai *J. Org. Chem.* **2009**, *74*, 1356-1359.

Table S-2. Comparison of the ^{13}C NMR data ($CDCl_3$, δ_C in ppm) of **3** prepared herein with the data reported in the literature; numbering scheme as shown in the Insert

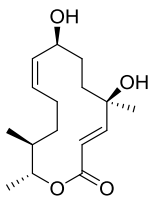
Position	Isolation[4]	Zhai et al.[5]	Current study
1	166.1	166.1	166.2
2	118.9	118.9	119.1
3	153.8	153.8	153.9
4	73.1	73.1	73.3
5	39.0	39.0	39.2
6	29.7	29.3	29.5
7	79.6	79.6	79.9
8	135.2	135.2	135.3
9	128.8	128.8	129.1
10	23.8	23.8	24.0
11	33.2	33.2	33.4
12	38.1	38.1	38.3
13	75.5	75.5	75.7
4-CH_3	28.2	28.2	28.4
8-CH_3	11.1	11.1	11.2
12-CH_3	17.2	17.2	17.4
13-CH_3	19.0	19.0	19.2

(3*E*,5*R*,8*S*,9*E*,13*S*,14*R*)-5,8-Dihydroxy-5,13,14-trimethyloxacyclotetradeca-3,9-dien-2-one (17).



Compound **16** (15 mg, 0.026 mmol) and CuTC (6 mg, 0.032 mmol) were added to a solution of $[Ph_2PO_2][NBu_4]$ (13.3 mg, 0.029 mmol) in DMF (0.15 mL). The mixture was stirred for 1 h before it was diluted with Et_2O and the reaction was quenched with water. The aqueous layer was extracted with Et_2O, the combined extracts were dried over $MgSO_4$, the drying agent was filtered off, and the solution was concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 1:1) afforded the title compound as a colorless oil (6 mg, 78%). $[a]_D^{20}$: –93.5 (c = 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.79 (d, *J* = 15.7 Hz, 1H), 5.95 (d, *J* = 15.7 Hz, 1H), 5.68 (dddd, *J* = 15.4, 9.1, 4.4, 0.8 Hz, 1H), 5.29 (dddd, *J* = 15.4, 8.1, 1.7, 1.0 Hz, 1H), 4.60 (dq, *J* = 10.1, 6.2 Hz, 1H), 4.01 (td, *J* = 8.4, 3.4 Hz, 1H), 2.11 – 1.98 (m, 1H), 1.95 –1.83 (m, 2H), 1.81 – 1.63 (m, 3H), 1.60 – 1.56 (bs, 1H), 1.52 – 1.41 (m, 3H), 1.34 (s, 3H), 1.30 (d, *J* = 6.1 Hz, 3H), 1.27 – 1.23 (bs, 1H), 0.93 ppm (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.1, 154.1, 133.12, 133.05, 119.2, 74.9, 73.6, 73.3, 38.5, 36.7, 32.5, 30.7, 28.3, 27.9, 19.3, 16.8 ppm. IR (film) $\tilde{\nu}$ = 3398, 2962, 2931, 2874, 1697, 1642, 1453, 1377, 1261, 1161, 1101, 1043, 967 cm^{-1}. HR-ESI: calcd. for $[C_{16}H_{26}O_4Na]^+$ 305.17233; found 305.17241.

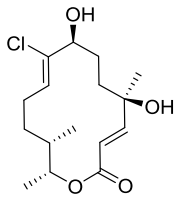
(*3E,5R,8S,9Z,13S,14R*)-5,8-Dihydroxy-5,13,14-trimethyloxacyclotetradeca-3,9-dien-2-one (18).



Hydrogen gas was bubbled through a suspension of $Pd/BaSO_4$ (5% on $BaSO_4$, 0.76 mg) in pyridine (1 mL) until the suspension turned black. A solution of alkyne **15** (20 mg, 71 µmol) in THF (1 mL) was introduced and the mixture was stirred for 3 h under hydrogen atmosphere. The suspension was filtered through a plug of Celite®, the

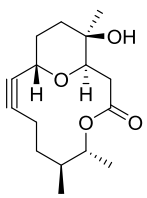
filtrate was concentrated and the residue purified by flash chromatography (silica, hexanes/EtOAc, 1:1) to furnish the title compound as a colorless foam (15 mg, 74%); the product contained ca. 5% of overreduced product formed by saturation of the former triple bond. $[\alpha]_D^{20}$: –31.1 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (d, *J* = 15.7 Hz, 1H), 6.03 (dd, *J* = 15.7, 1.4 Hz, 1H), 5.48 (tdd, *J* = 10.0, 5.6, 0.9 Hz, 1H), 5.37 (ddt, *J* = 10.8, 9.0, 1.1 Hz, 1H), 4.65 (dq, *J* = 9.9, 6.3 Hz, 1H), 4.31 (tt, *J* = 9.3, 1.6 Hz, 1H), 2.20 – 2.08 (m, 1H), 2.04 –1.90 (m, 2H), 1.84 – 1.75 (m, 1H), 1.60 – 1.44 (m, 2H), 1.40 (s, 3H), 1.38 – 1.31 (m, 1H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.27 – 1.21 (m, 2H), 1.21 – 1.04 (m, 2H), 0.93 ppm (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.0, 153.0, 133.1, 131.2, 120.8, 76.2, 74.0, 69.7, 41.1, 39.1, 35.0, 31.6, 29.0, 27.8, 19.3, 17.2 ppm. IR (film): $\tilde{\nu}$ = 3402, 2925, 1694, 1454, 1378, 1260, 1043, 730 cm^{-1}. HR-ESI: calcd. for $[C_{16}H_{26}O_4Na]^+$ 305.17233; found 305.17227.

(3*E*,5*R*,8*S*,9*Z*,13*S*,14*R*)-9-Chloro-5,8-dihydroxy-5,13,14-trimethyloxacyclotetradeca-3,9-dien-2-one



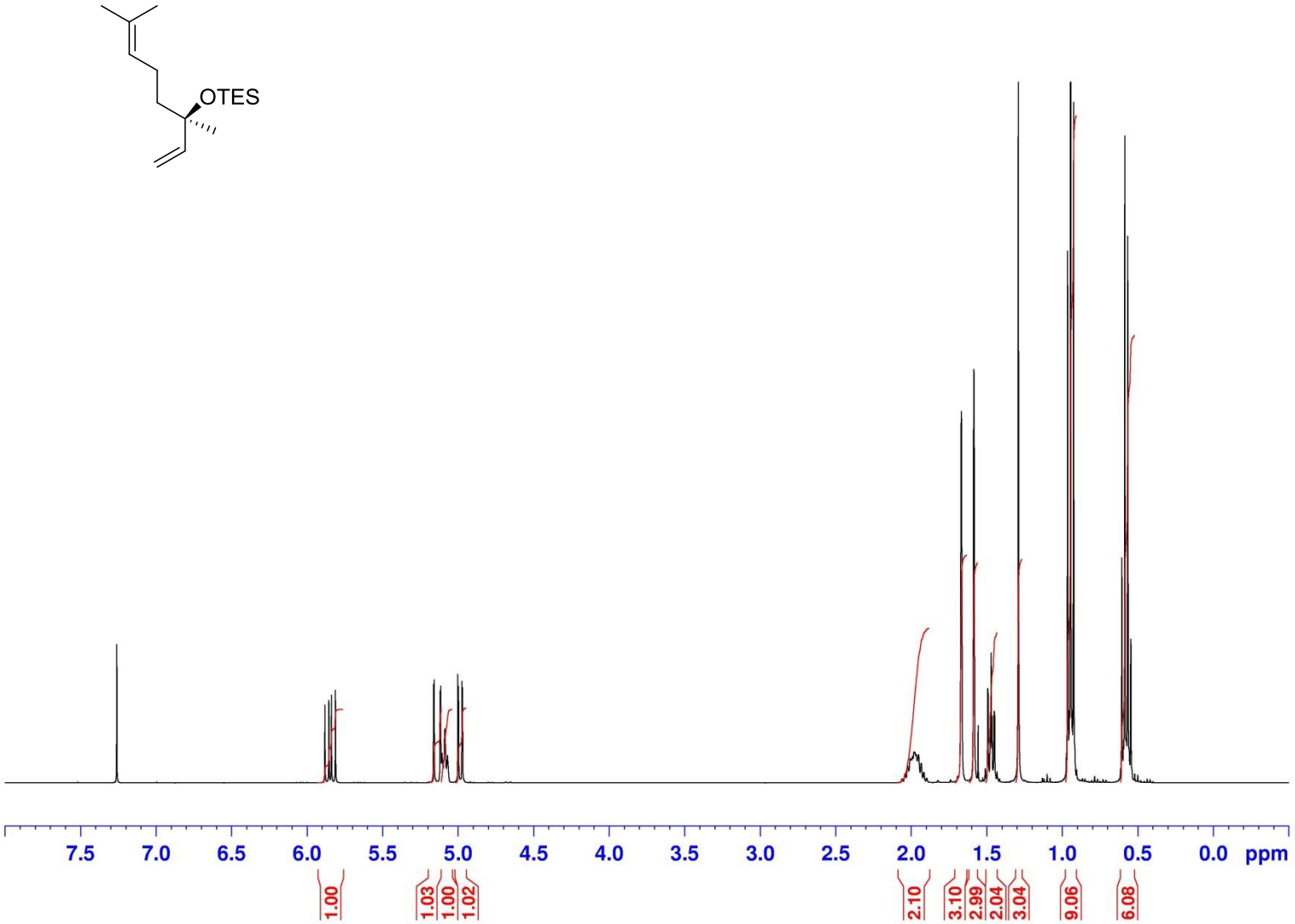
(19). Copper(II)chloride (25 mg, 0.19 mmol) was added in one portion to a solution of stannane **16** (42 mg, 0.07 mmol) in THF (0.35 mL) and the resulting mixture was stirred for 23 h. The reaction was quenched with water and the aqueous layer extracted with CH_2Cl_2. The combined extracts were washed with brine and dried over $MgSO_4$, the drying agent was filtered off, and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 2:1) afforded the title compound as a colorless oil (18 mg, 77%). $[\alpha]_D^{20}$: –24.3 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (d, *J* = 15.7 Hz, 1H), 5.98 (d, *J* = 15.4 Hz, 1H), 5.84 (dd, *J* = 9.3, 4.0 Hz, 1H), 4.56 (dq, *J* = 10.1, 6.2 Hz, 1H), 4.15 – 4.08 (m, 1H), 2.39 –2.28 (m, 1H), 2.05 – 1.87 (m, 4H), 1.82 – 1.69 (m, 3H), 1.59 – 1.49 (m, 2H), 1.48 –1.40 (m, 1H), 1.36 (s, 3H), 1.31 (d, *J* = 6.6 Hz, 3H), 0.95 ppm (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.9, 153.1, 135.0, 129.3, 119.7, 76.7, 75.5, 73.0, 38.5, 38.4, 32.2, 29.5, 28.7, 24.6, 19.2, 17.3 ppm. IR (film) $\tilde{\nu}$ = 3401, 2964, 2932, 2875, 1696, 1451, 1378, 1263, 1160, 1101, 1044 cm^{-1}. HR-ESI: calcd. for $[C_{16}H_{25}O_4ClNa]^+$ 339.13344; found 339.13336.

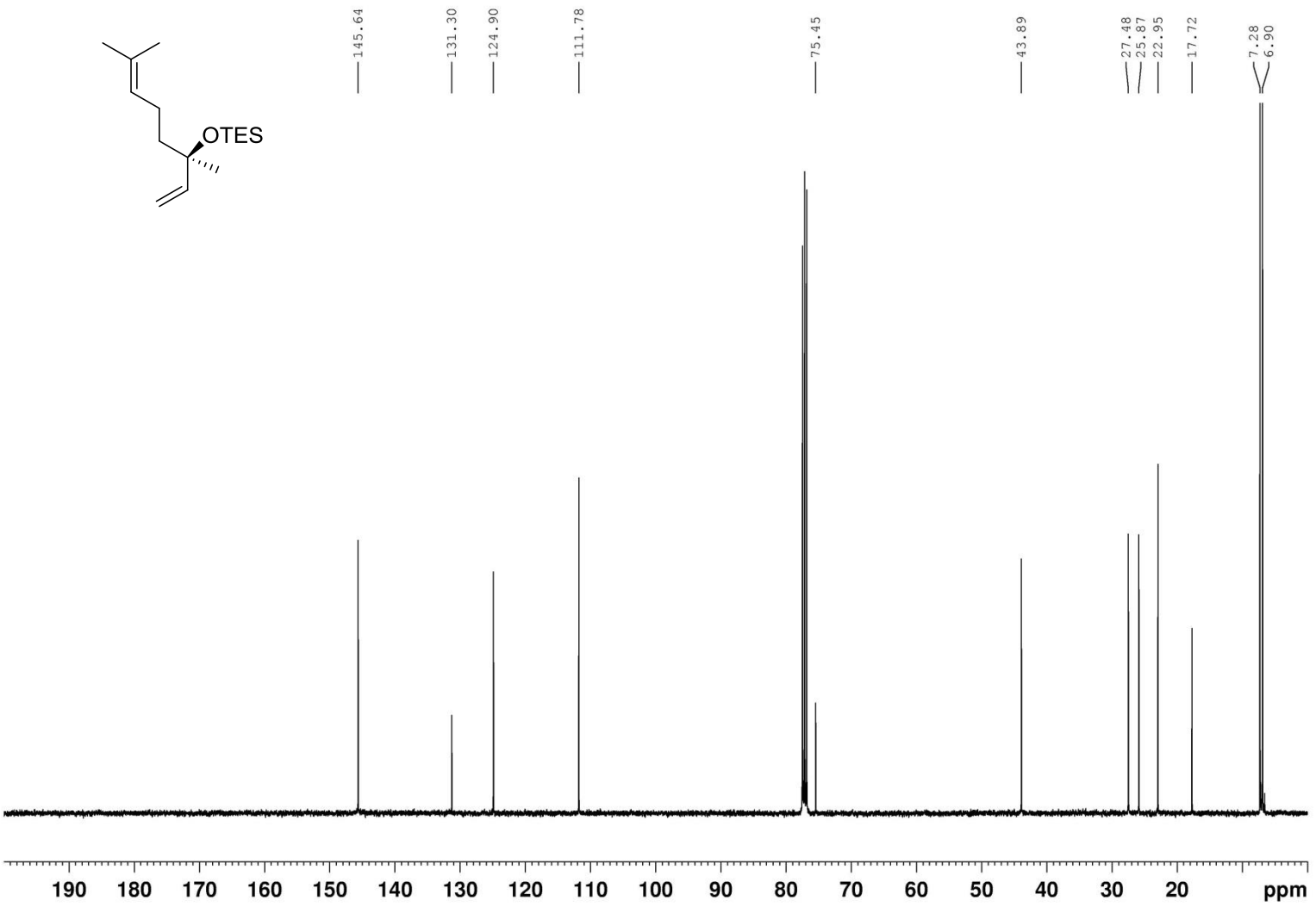
(*1S,5R,6S,11S,14R*)-11-Hydroxy-5,6,14-trimethyl-4,15-dioxabicyclo[12.1.0]pentadec-9-yn-3-one

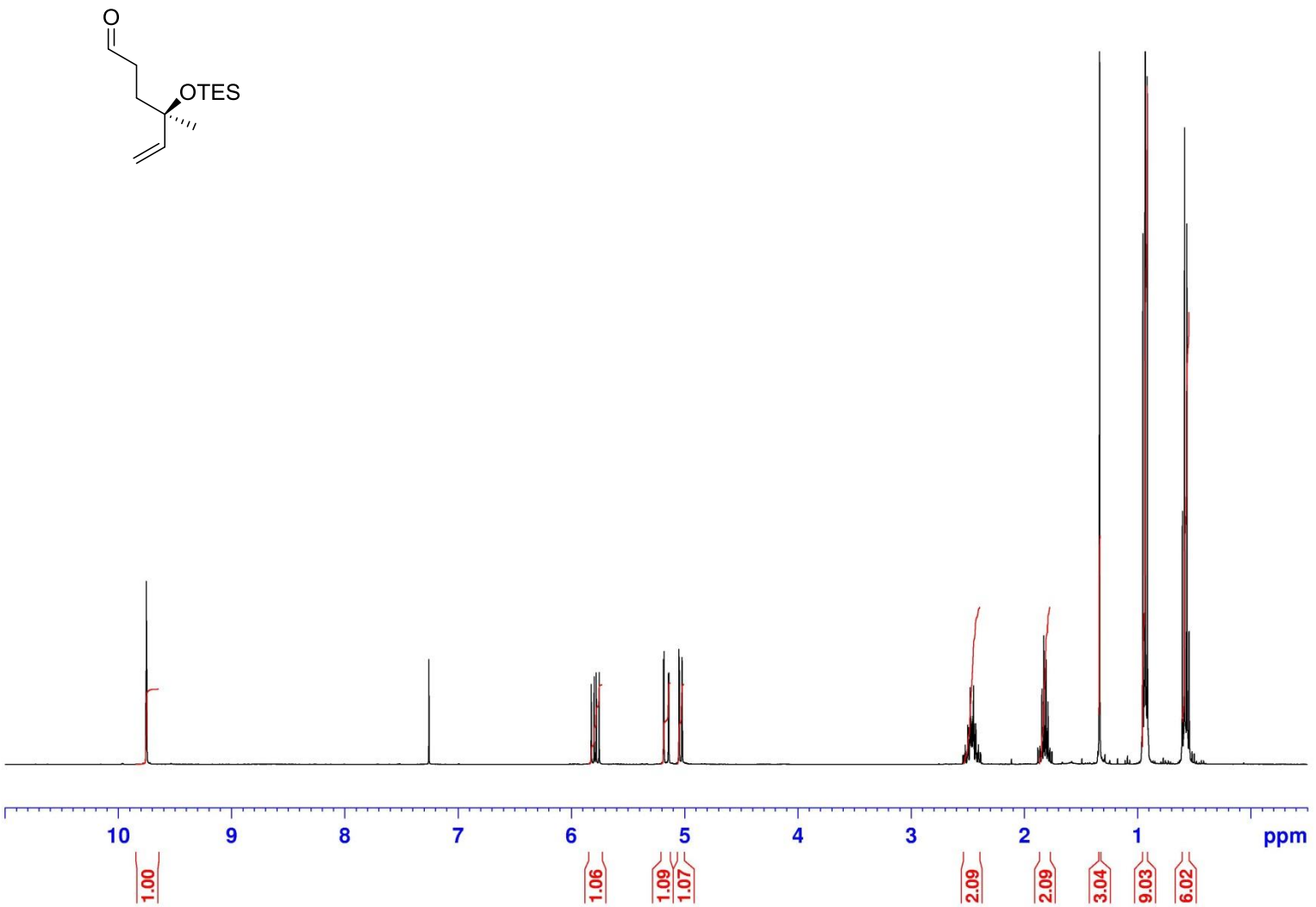


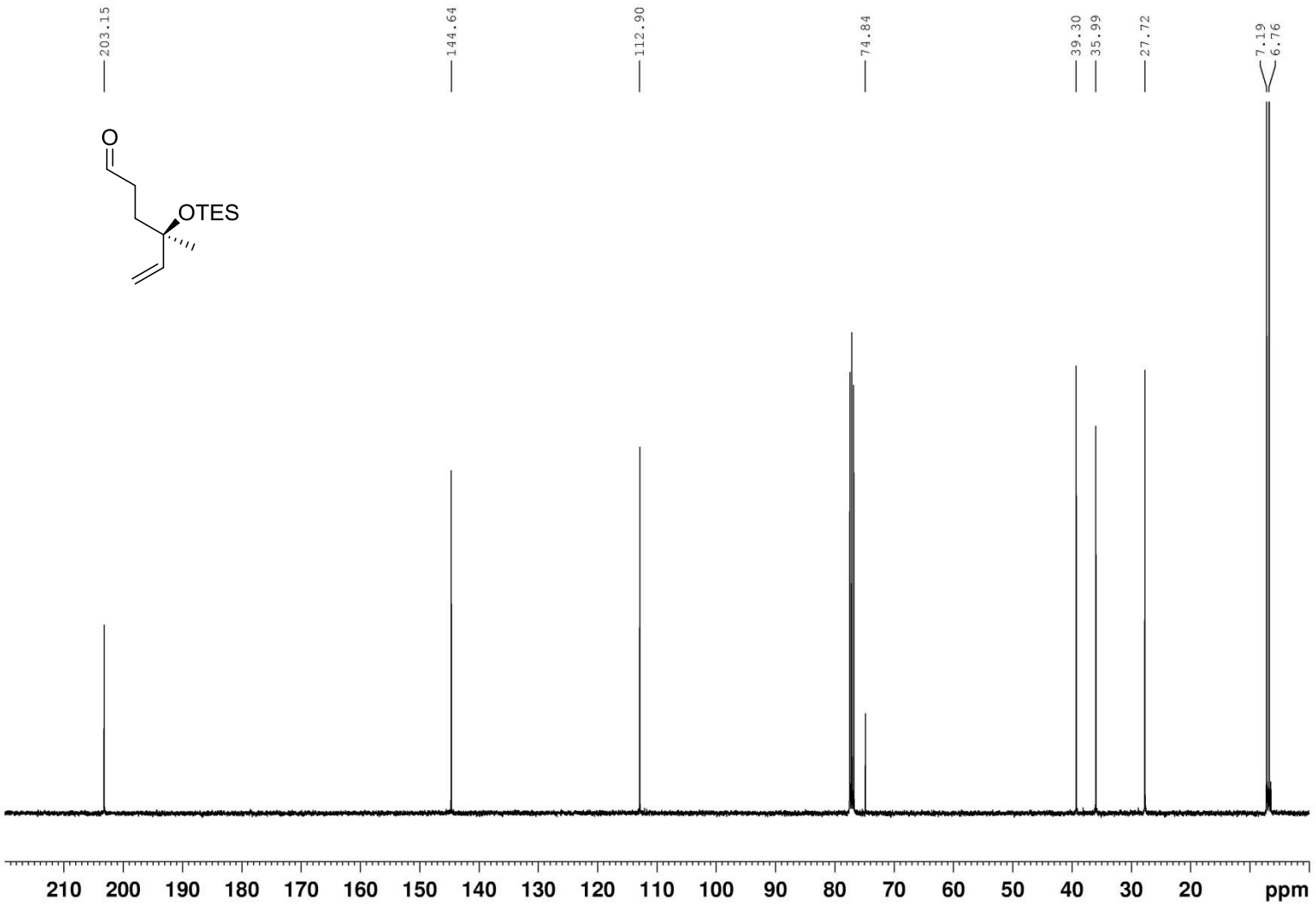
(20). TBAF (1 M in THF, 750 µL, 0.75 mmol) was added dropwise to a solution of compound **14** (127 mg, 0.25 mmol) in THF (10 mL) and the resulting mixture was stirred for 4 h at room temperature. Additional TBAF (1 M in THF, 750 µL, 0.75 mmol) was introduced and stirring continued for another 12 h. The reaction was quenched with water and the aqueous layer extracted with *tert*-butyl methyl ether. The combined extracts were washed with brine and dried over $MgSO_4$, the drying agent was filtered off and the solvent was evaporated. Purification of the residue by flash chromatography (silica, hexanes/EtOAc, 6:1 to 1:1) afforded the title compound as a white crystalline solid (68 mg, 97%). Mp = 101-102 °C. $[\alpha]_D^{20}$: +57.3 (c = 1, CH_3OH). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.79 – 4.69 (m, 2H), 4.59 (dd, *J* = 11.3, 2.0 Hz, 1H), 2.58 (dd, *J* = 14.1, 2.0 Hz, 1H), 2.54 (s, 1H), 2.34 (dd, *J* = 14.1, 11.3 Hz, 1H), 2.23 (ddt, *J* = 7.8, 5.3, 2.6 Hz, 2H), 2.12 – 1.89 (m, 3H), 1.86 – 1.73 (m, 2H), 1.69 –1.58 (m, 1H), 1.53 (dddd, *J* = 14.0, 4.9, 2.4, 1.2 Hz, 1H), 1.28 (d, J = 6.3 Hz, 3H), 1.17 (s, 3H), 1.05 ppm (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.2, 90.4, 79.7, 75.3, 75.2, 68.5, 66.2, 37.5, 36.1, 34.3, 29.7, 25.7, 24.3,

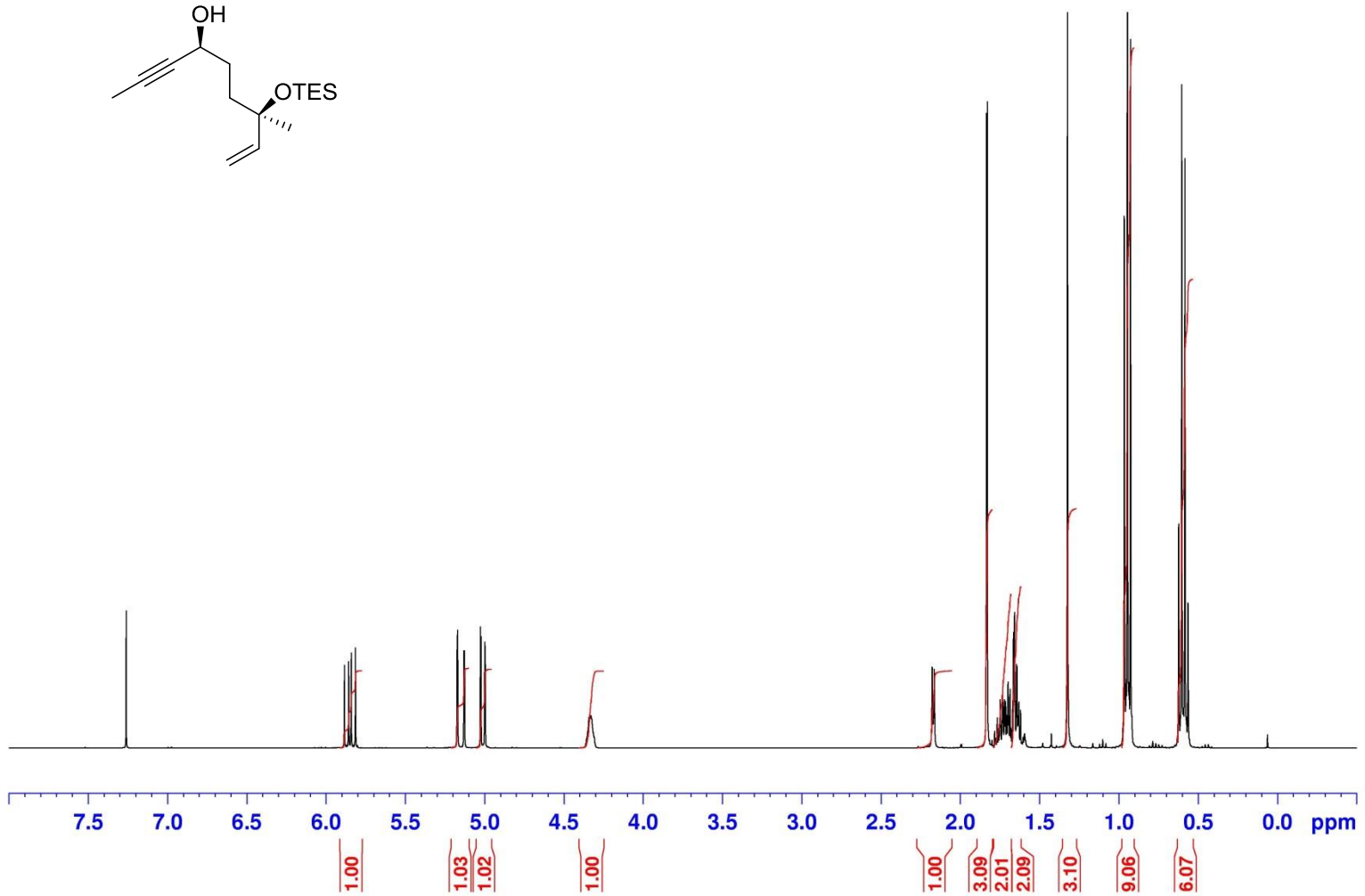
19.1, 16.3, 15.0 ppm. IR (film) $\tilde{\nu}$ = 3468, 2933, 1731, 1449, 1380, 1286, 1247, 1155, 1101, 1061, 1001, 958 cm^{-1}. HR-ESI**:** *m/z* calcd. for $[C_{16}H_{24}O_4Na]^+$: 303.15668; found 303.15668.

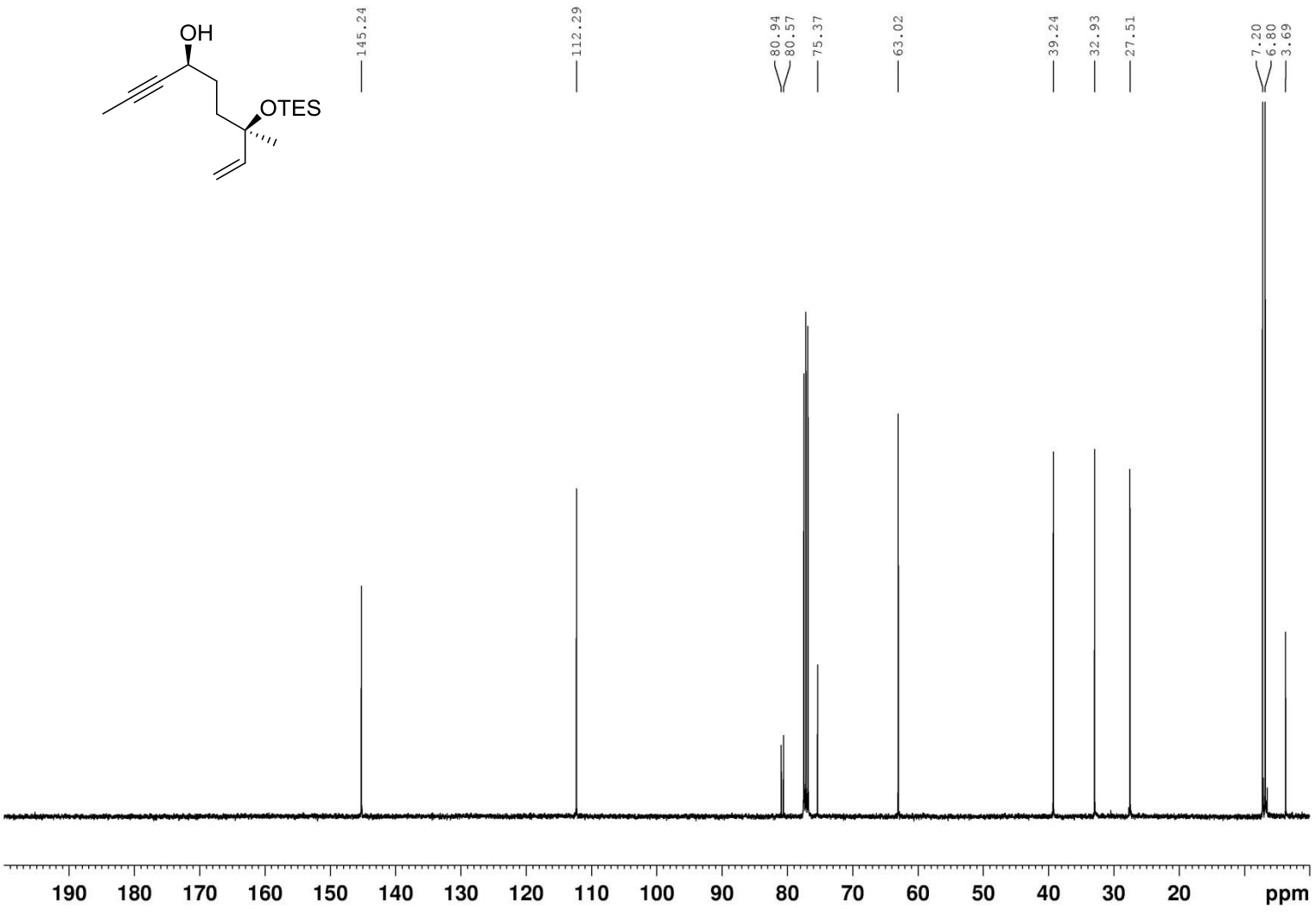

OTES
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.03
1.00
1.02
2.10
3.10
2.99
2.04
3.04
9.06
6.08

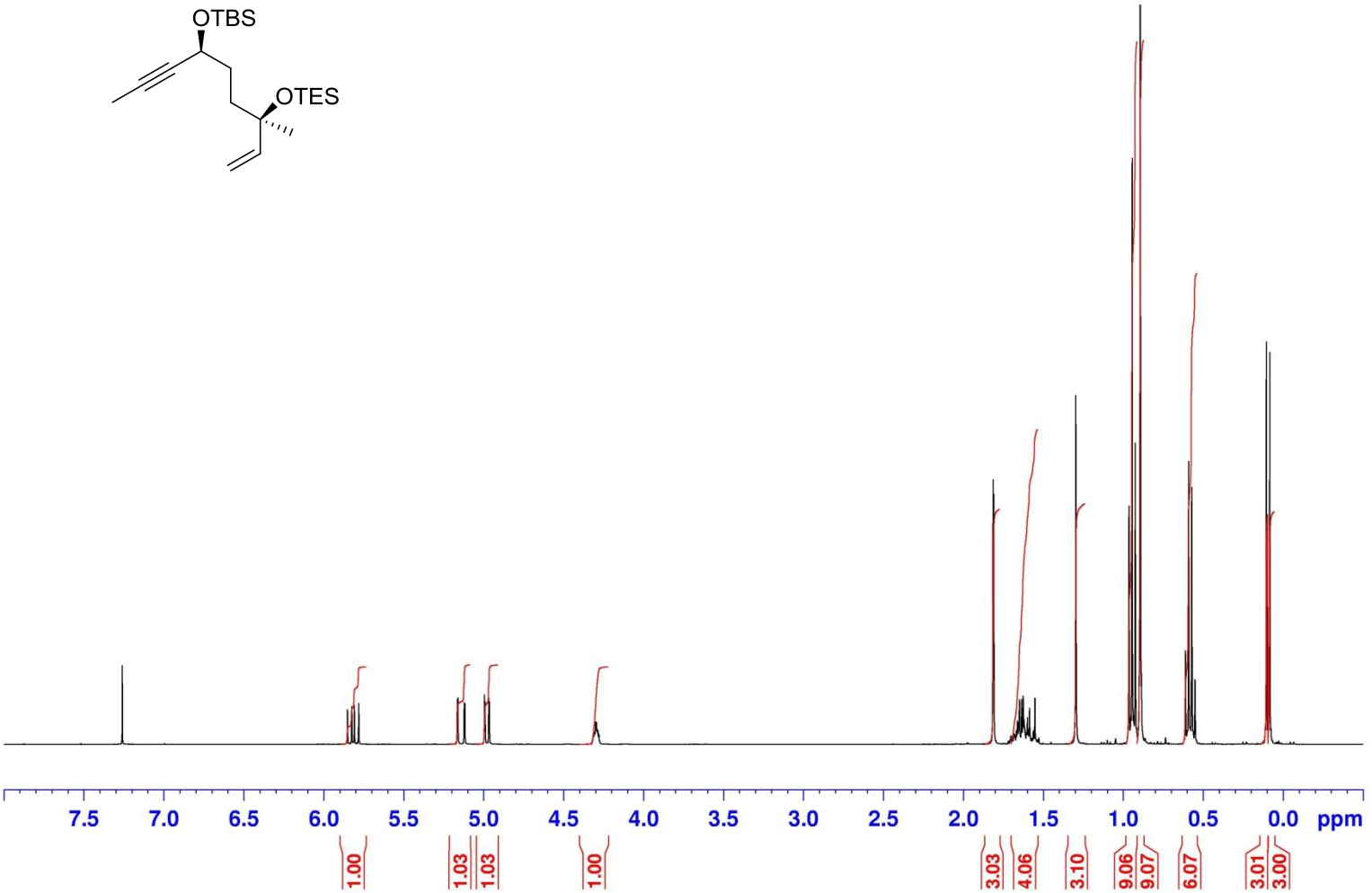

OTES
145.64
131.30
124.90
111.78
75.45
43.89
27.48
25.87
22.95
17.72
7.28
6.90
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

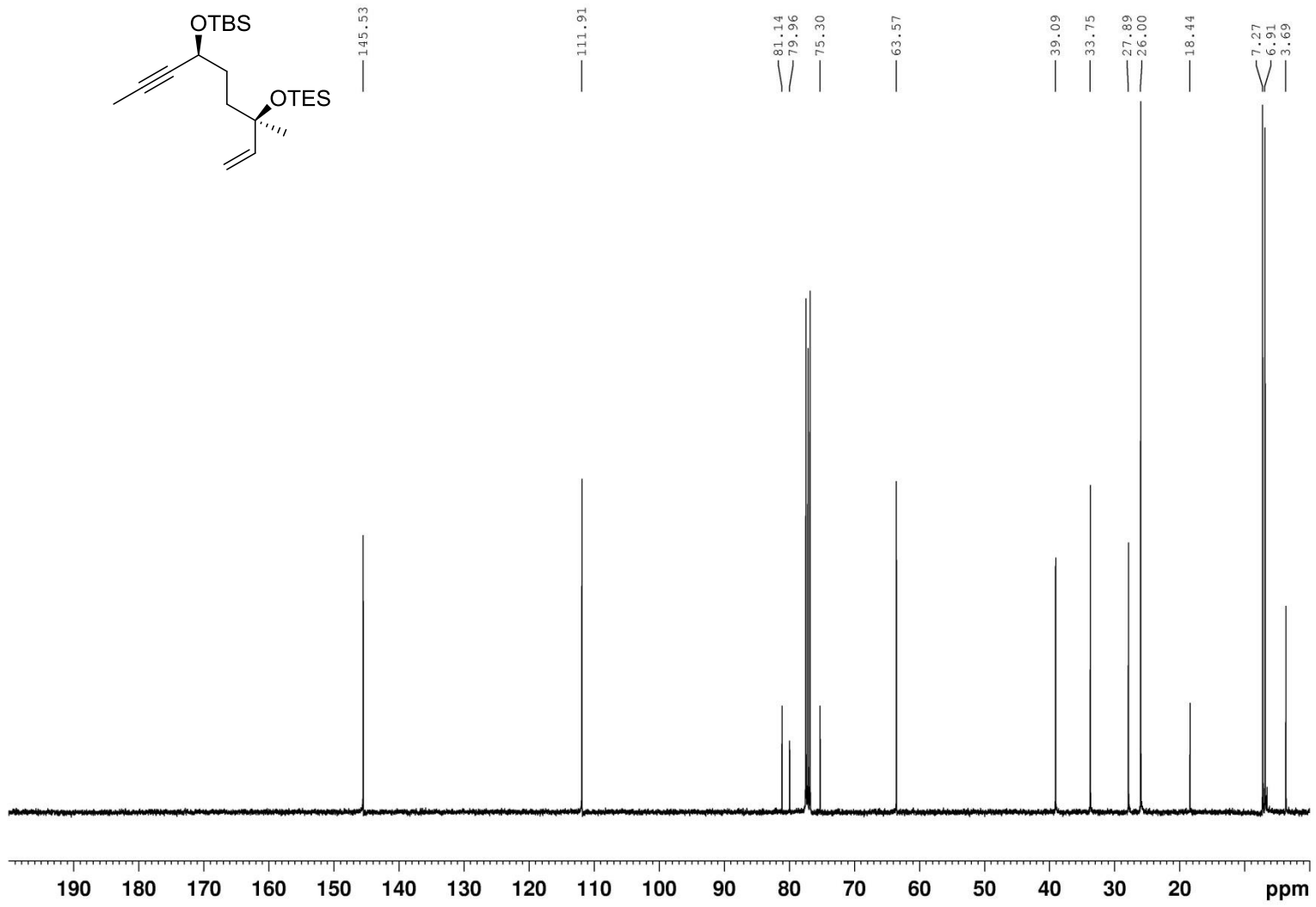

O
OTES
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.06
1.09
1.07
2.09
2.09
3.04
9.03
6.02

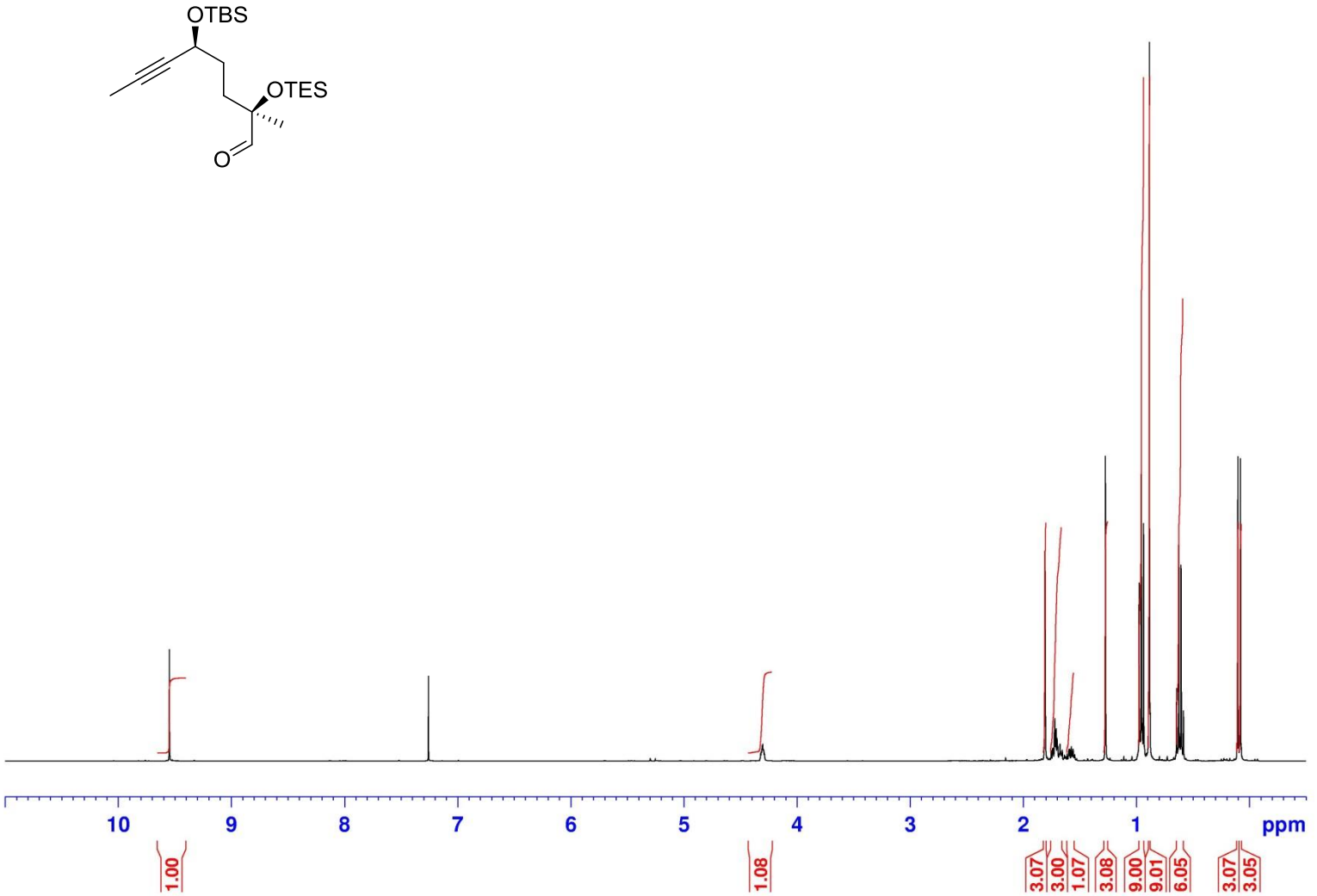

203.15
144.64
112.90
74.84
39.30
35.99
27.72
7.19
6.76
O
OTES
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

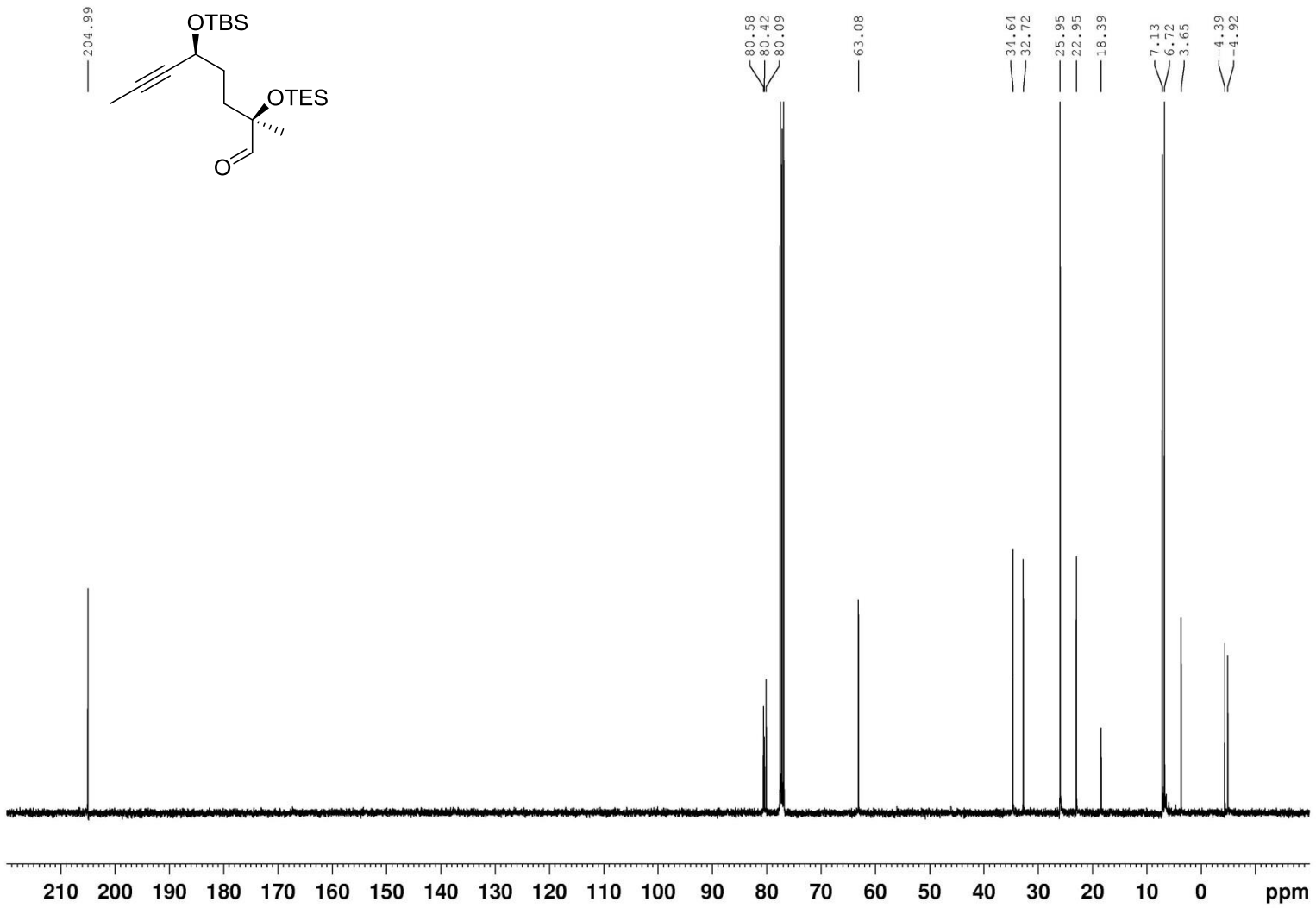

OH
OTES
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.03
1.02
1.00
1.00
3.09
2.01
2.09
3.10
9.06
6.07

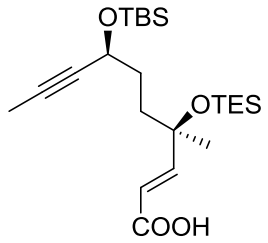

OH
OTES
145.24
112.29
80.94
80.57
75.37
63.02
39.24
32.93
27.51
7.20
6.80
3.69
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


OTBS
OTES
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.03
1.03
1.00
3.03
4.06
3.10
9.06
9.07
6.07
3.01
3.00

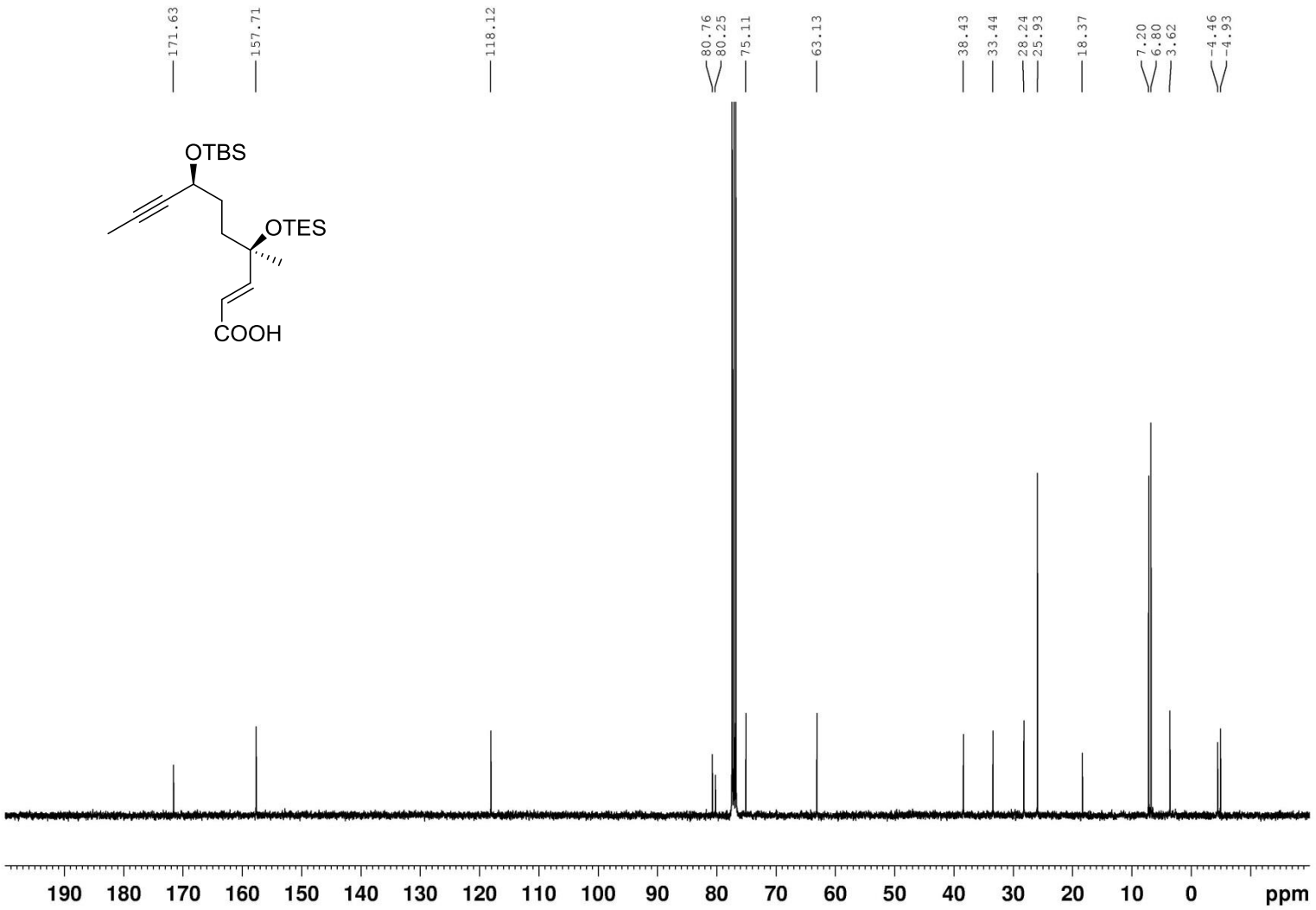

OTBS
OTES
145.53
111.91
81.14
79.96
75.30
63.57
39.09
33.75
27.89
26.00
18.44
7.27
6.91
3.69
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

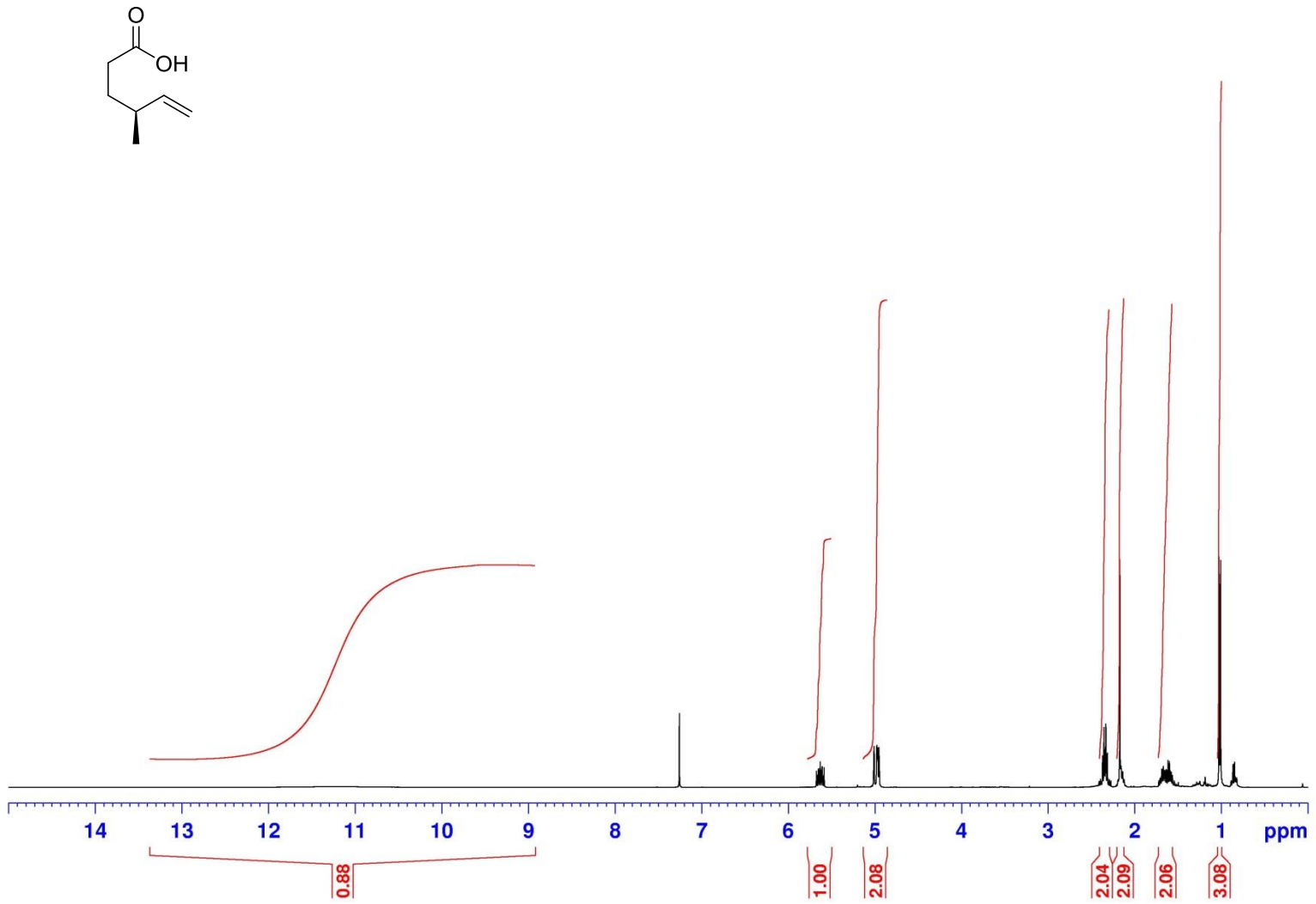

OTBS
OTES
O
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.08
3.07
3.00
1.07
3.08
9.00
9.01
6.05
3.07
3.05

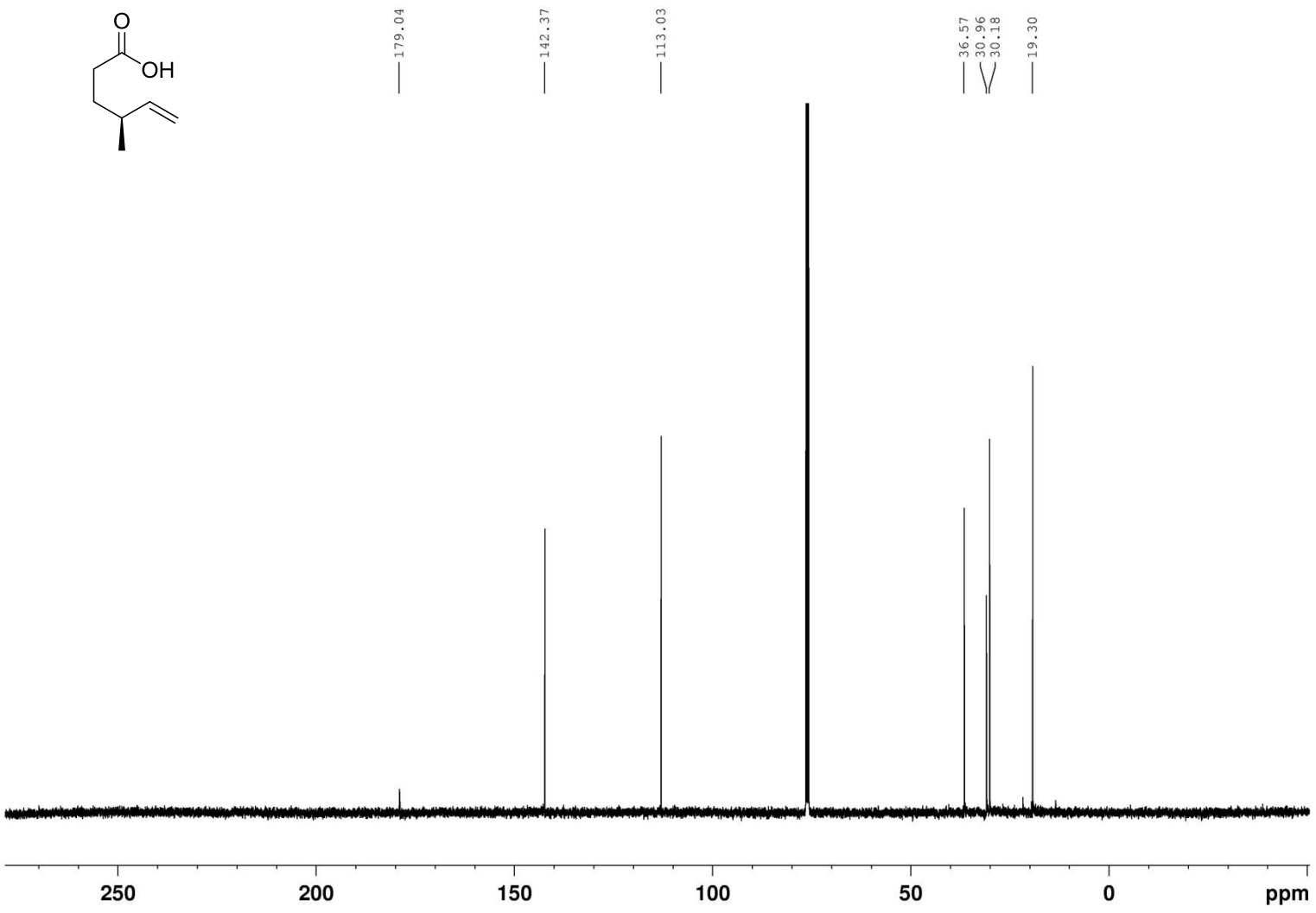

OTBS
OTES
O
204.99
80.58
80.42
80.09
63.08
34.64
32.72
25.95
22.95
18.39
7.13
6.72
3.65
-4.39
-4.92
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

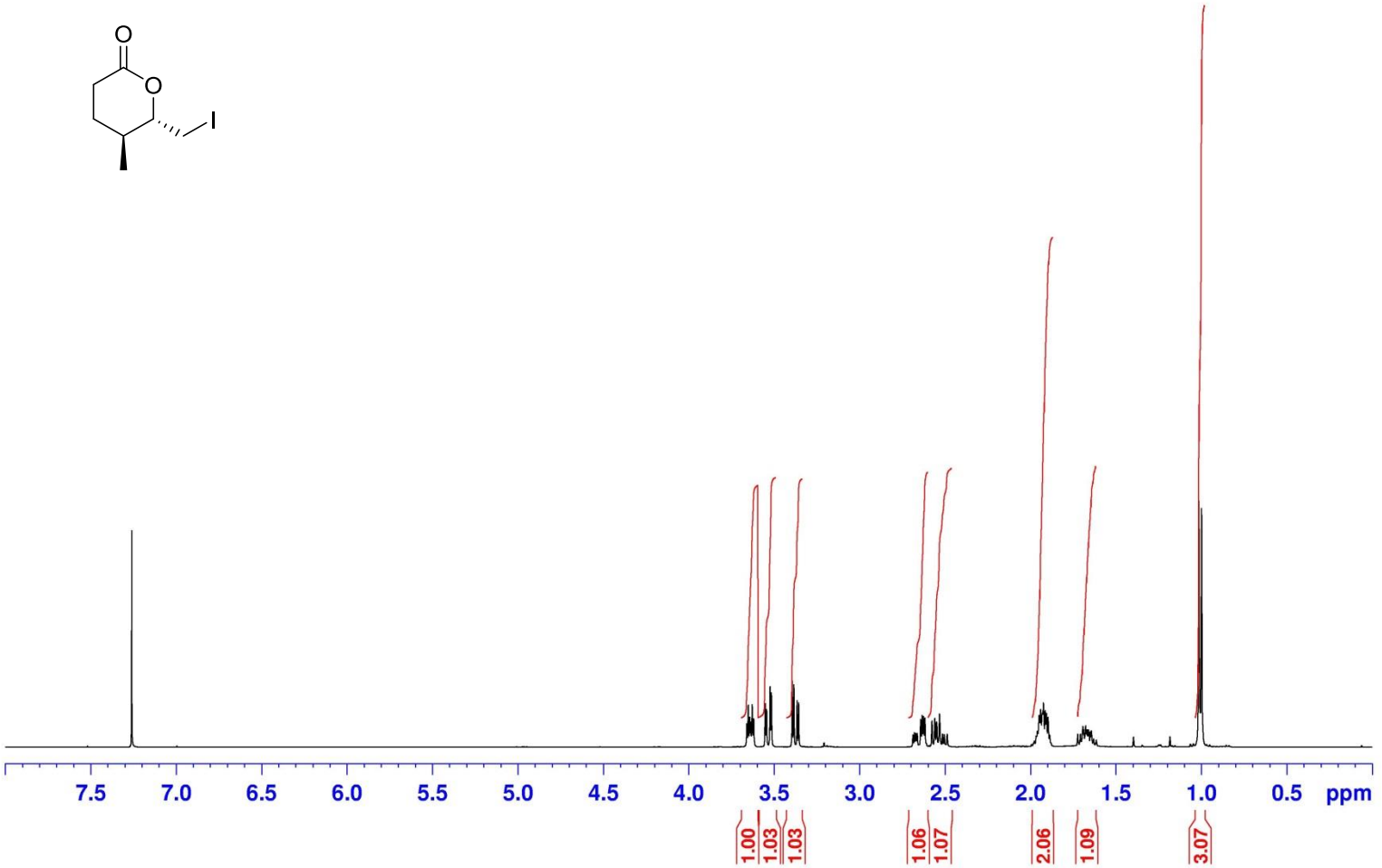

OTBS
OTES
COOH

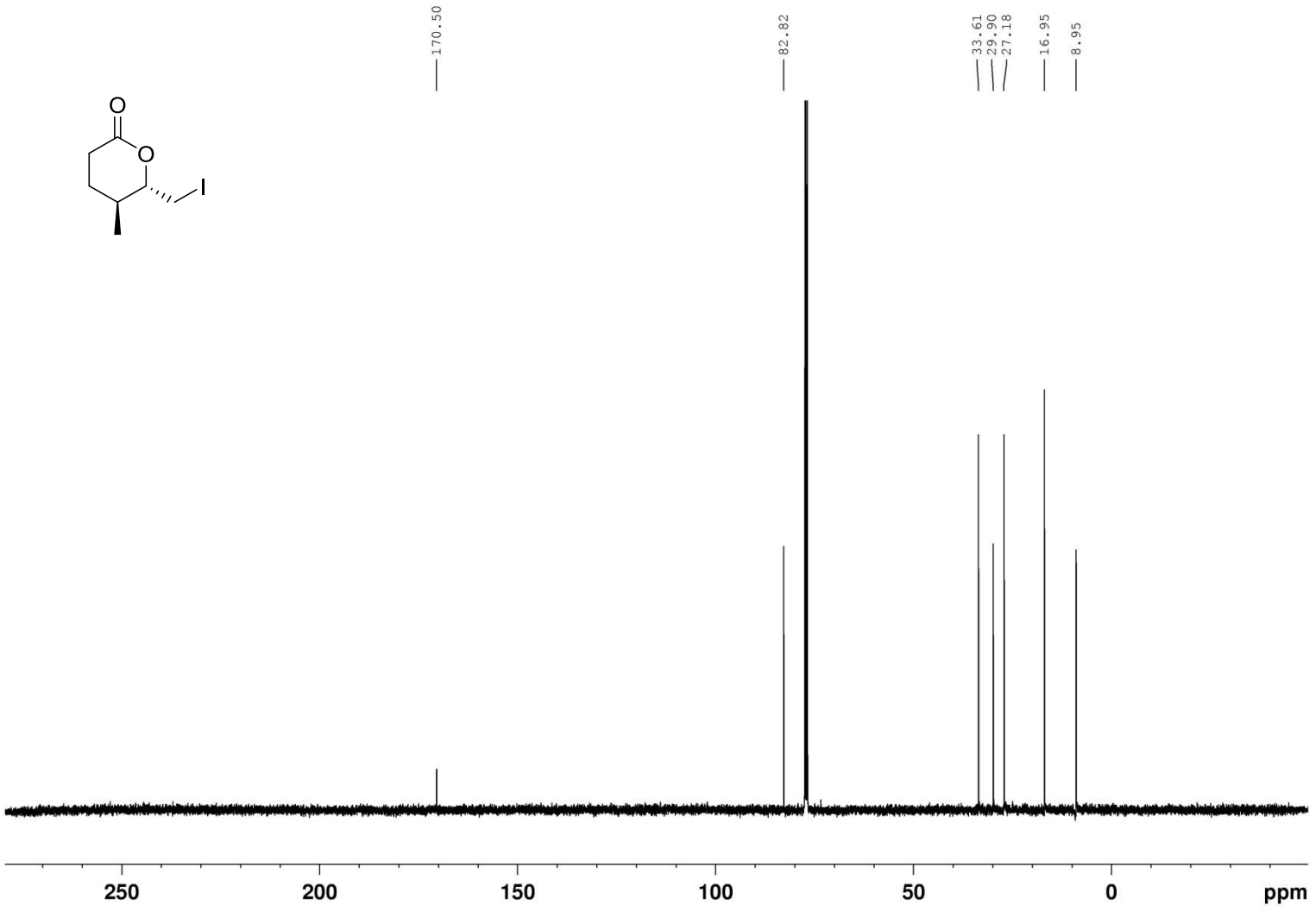
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.74
1.02
1.00
1.02
3.08
3.03
1.09
3.02
9.04
9.07
6.04
3.04
3.07

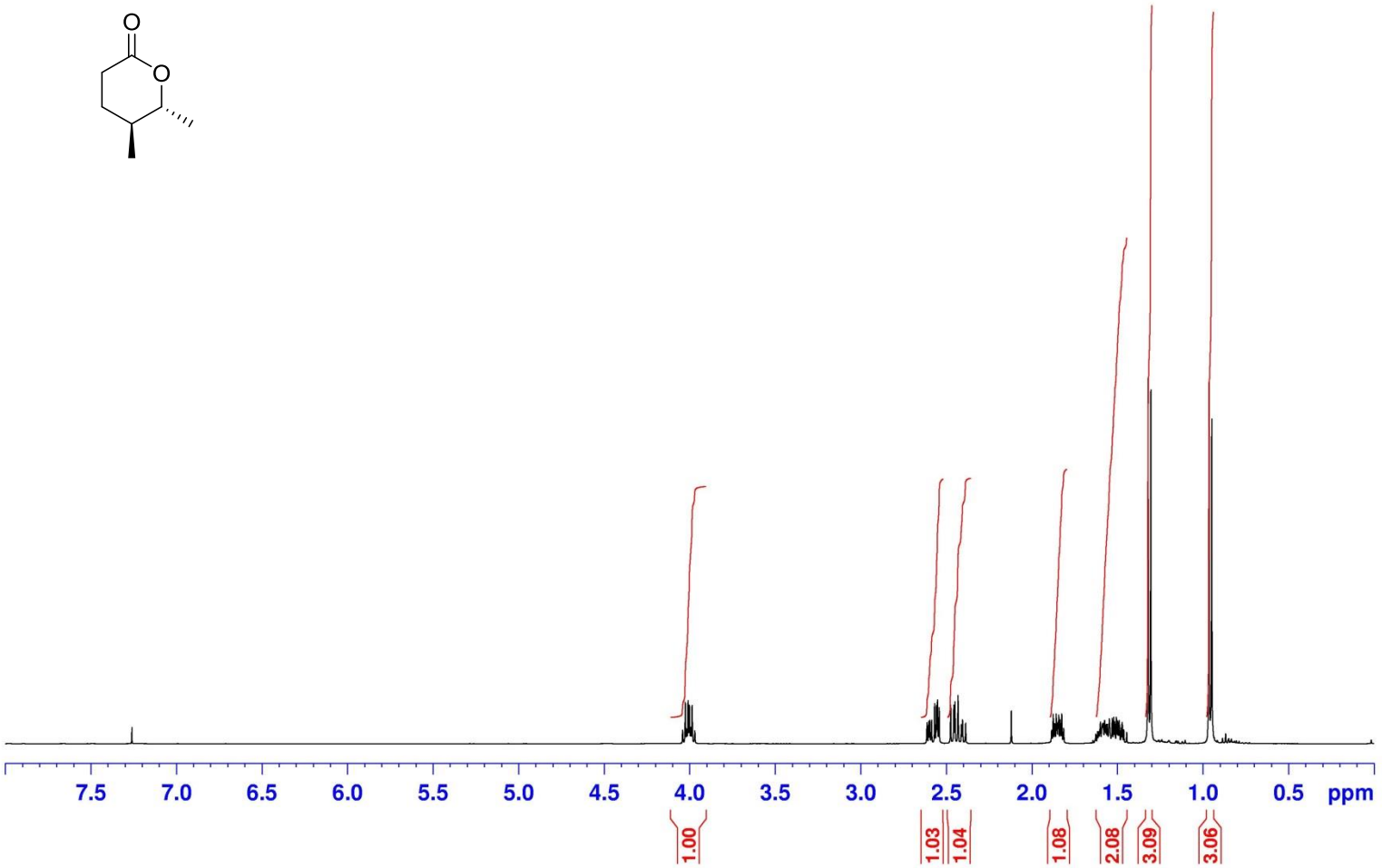

171.63
157.71
118.12
80.76
80.25
75.11
63.13
38.43
33.44
28.24
25.93
18.37
7.20
6.80
3.62
-4.46
-4.93
OTBS
OTES
COOH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

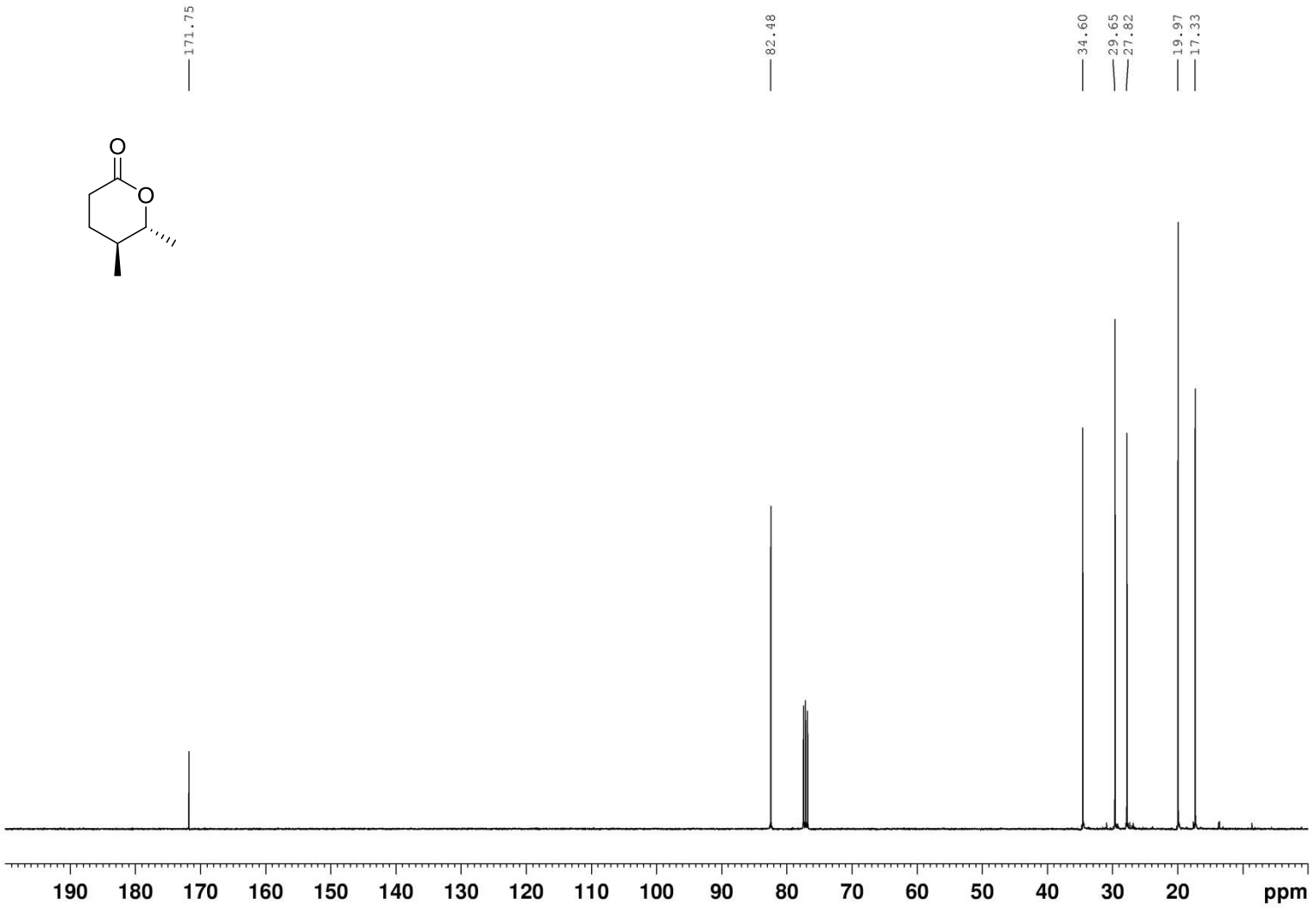

O
OH
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.88
1.00
2.08
2.04
2.09
2.06
3.08

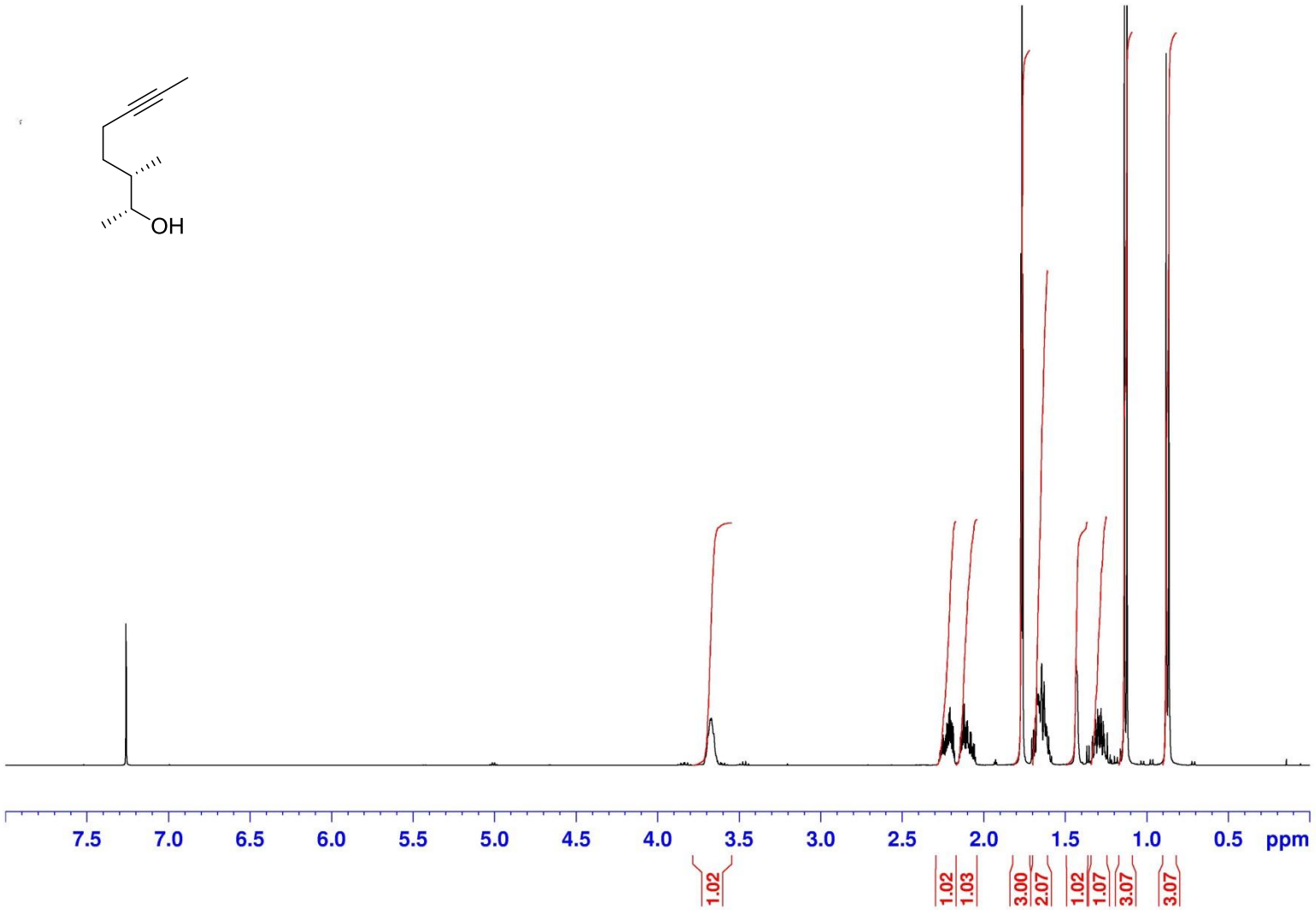

O
OH
179.04
142.37
113.03
36.57
30.96
30.18
19.30
250
200
150
100
50
0
ppm

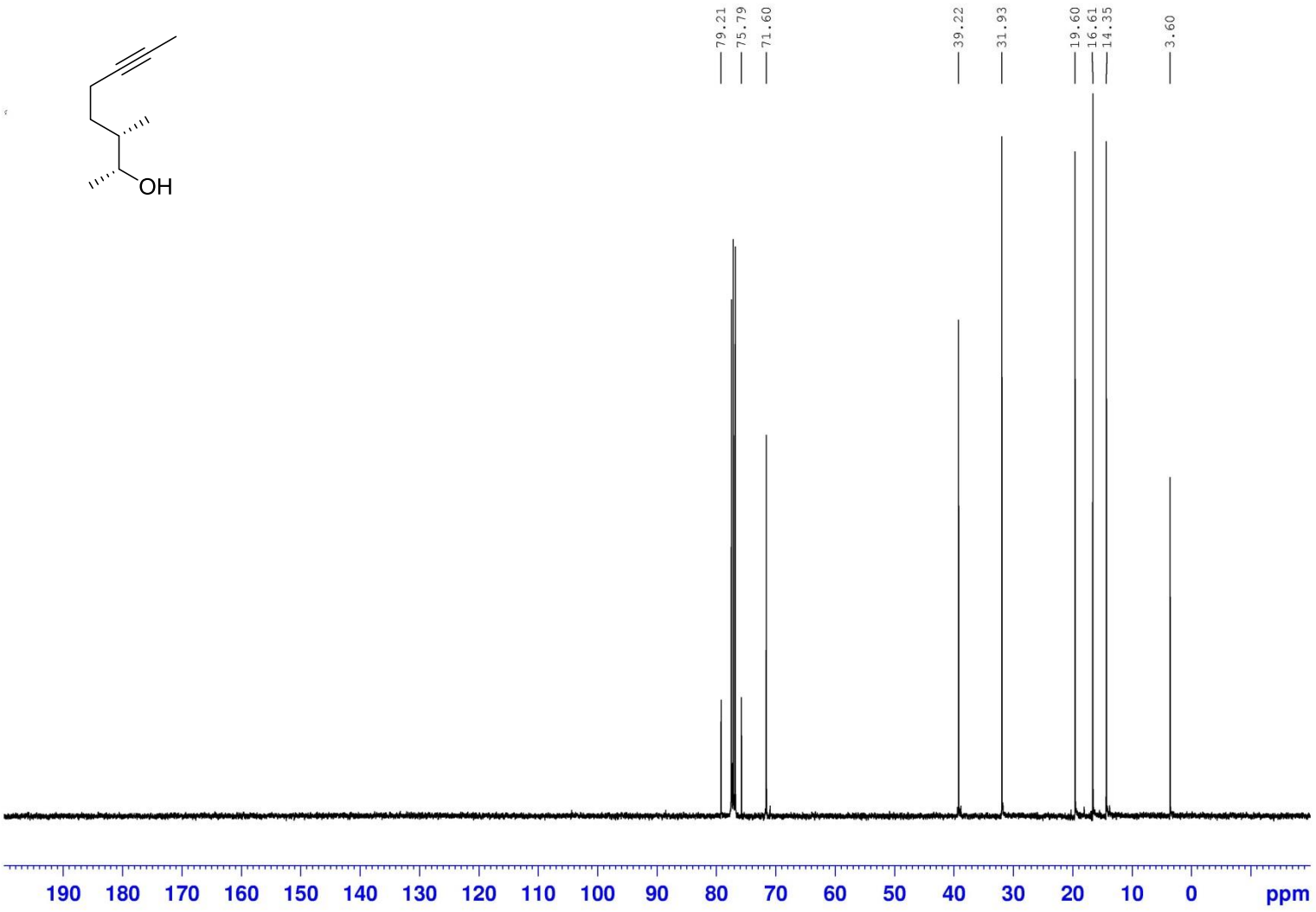

O
O
I
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.03
1.03
1.06
1.07
2.06
1.09
3.07

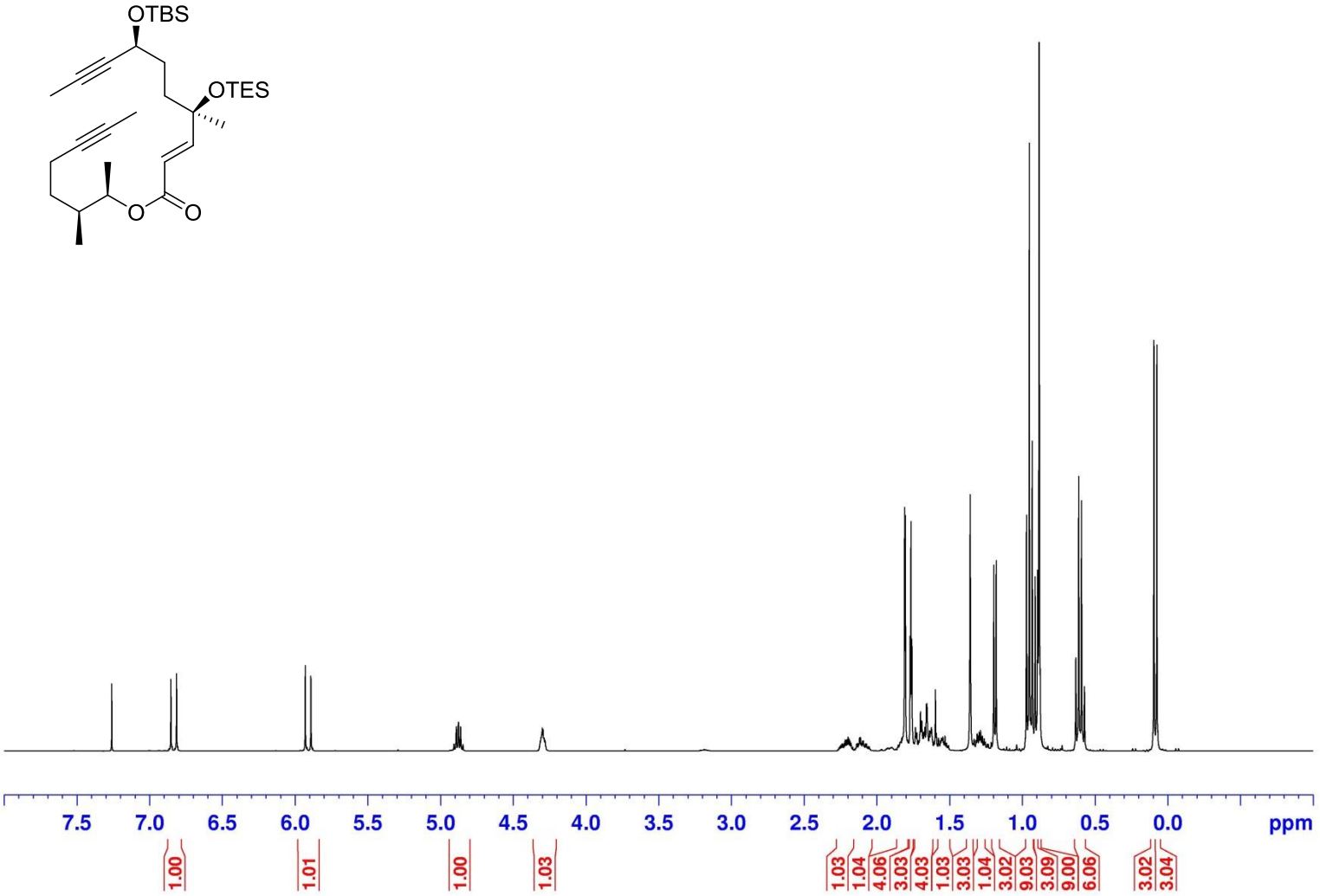

170.50
82.82
33.61
29.90
27.18
16.95
8.95
O
O
I
250
200
150
100
50
0
ppm

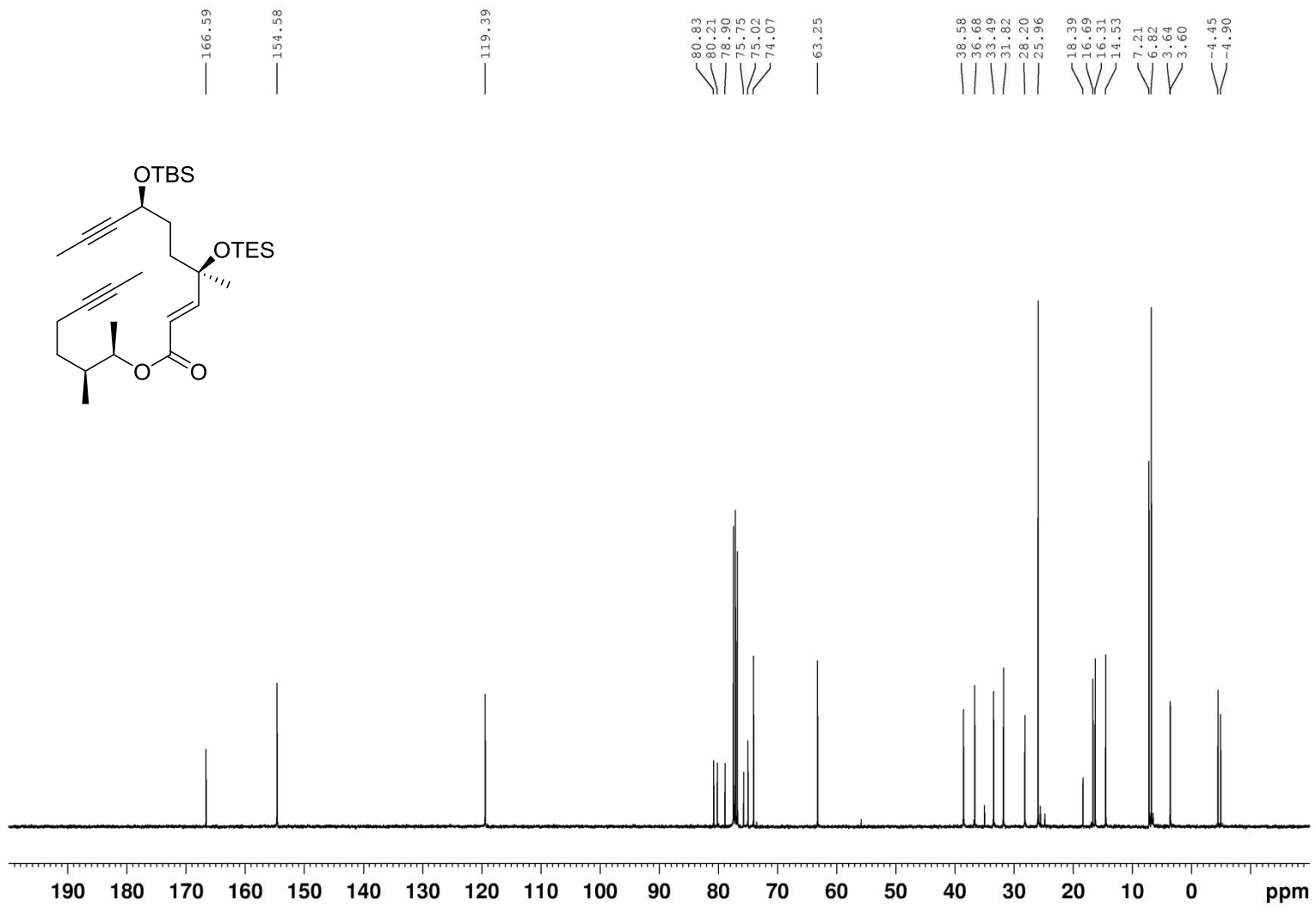

O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.03
1.04
1.08
2.08
3.09
3.06

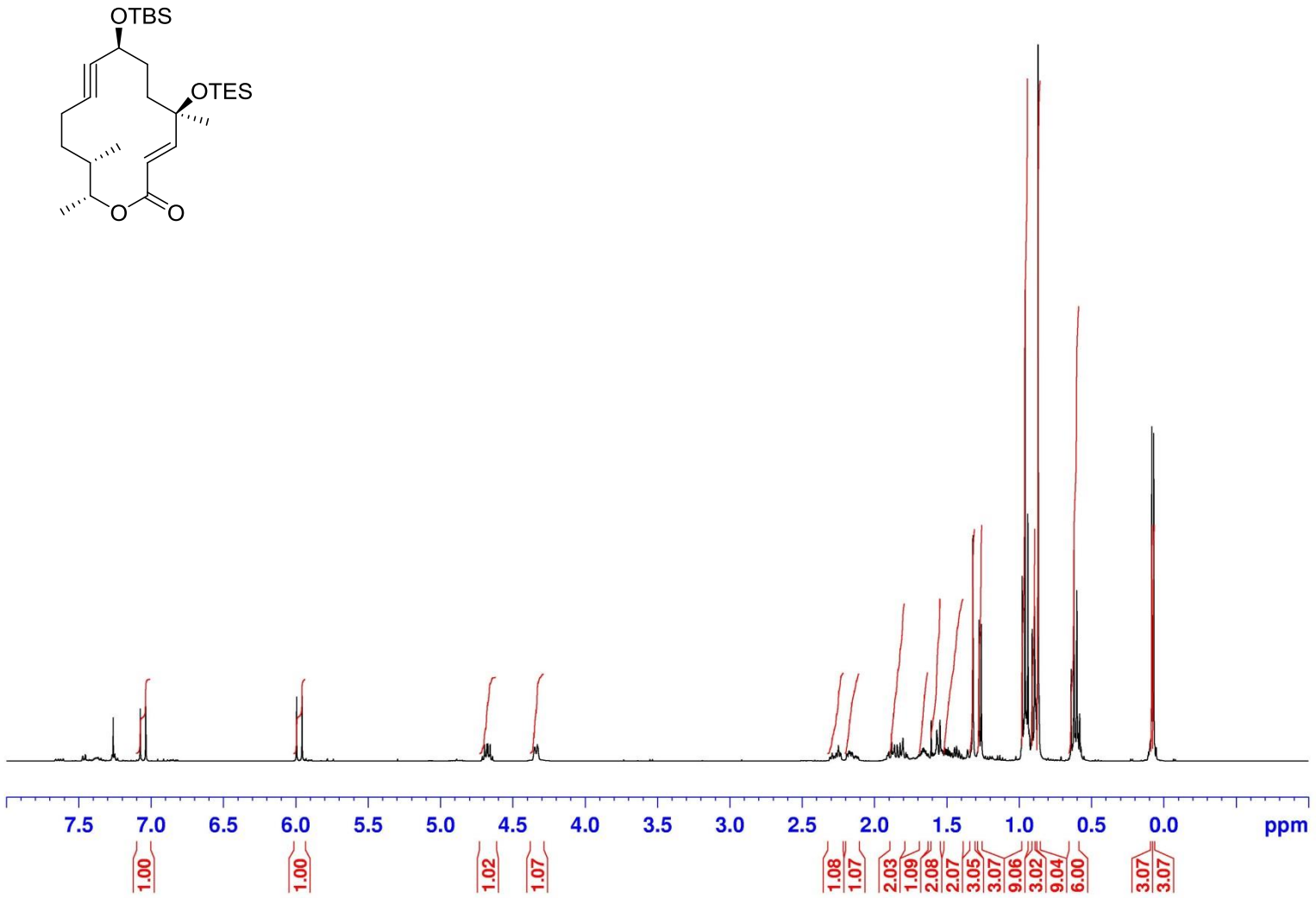

171.75
82.48
34.60
29.65
27.82
19.97
17.33
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

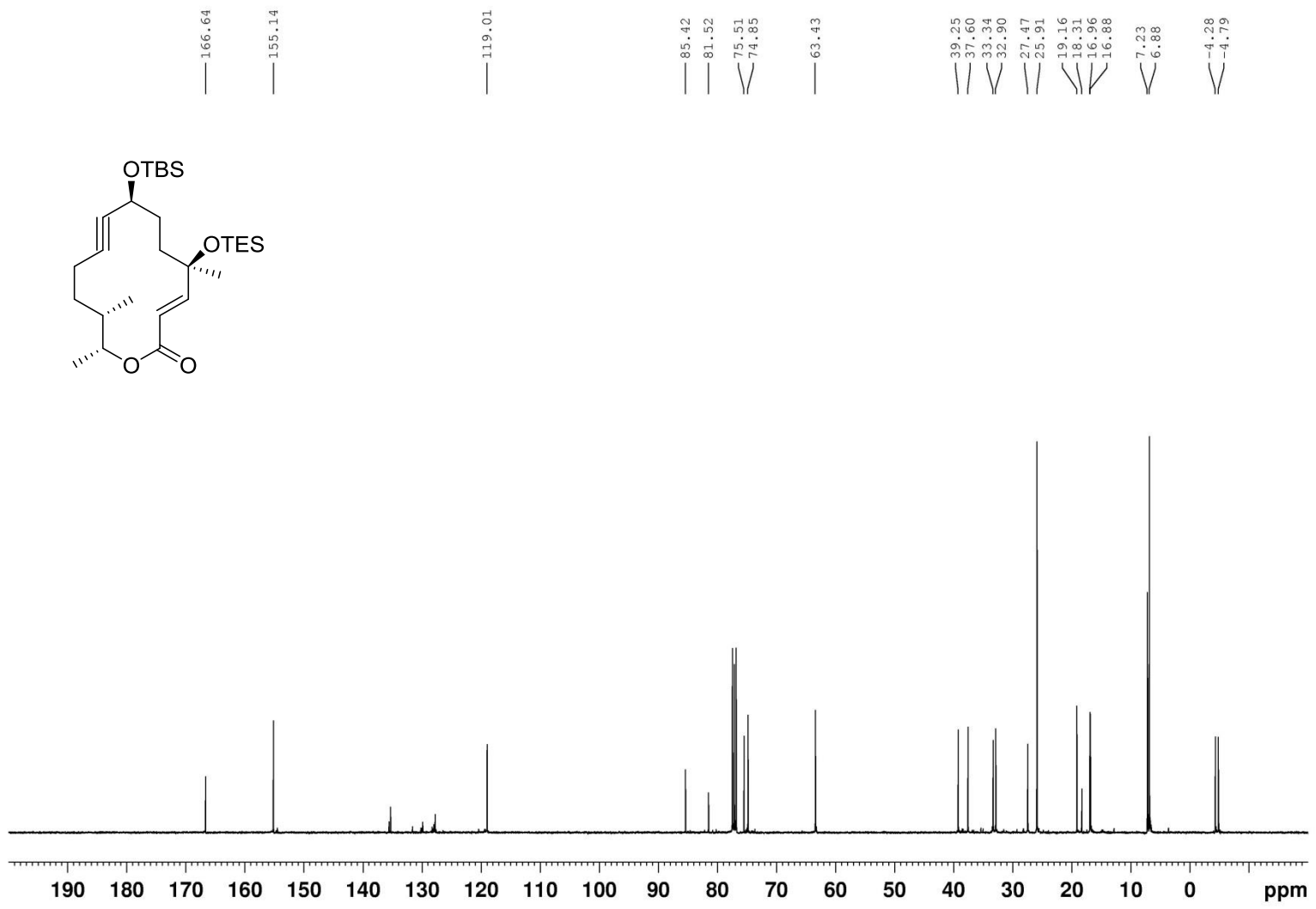

OH
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.02
1.02
1.03
3.00
2.07
1.02
1.07
3.07
3.07

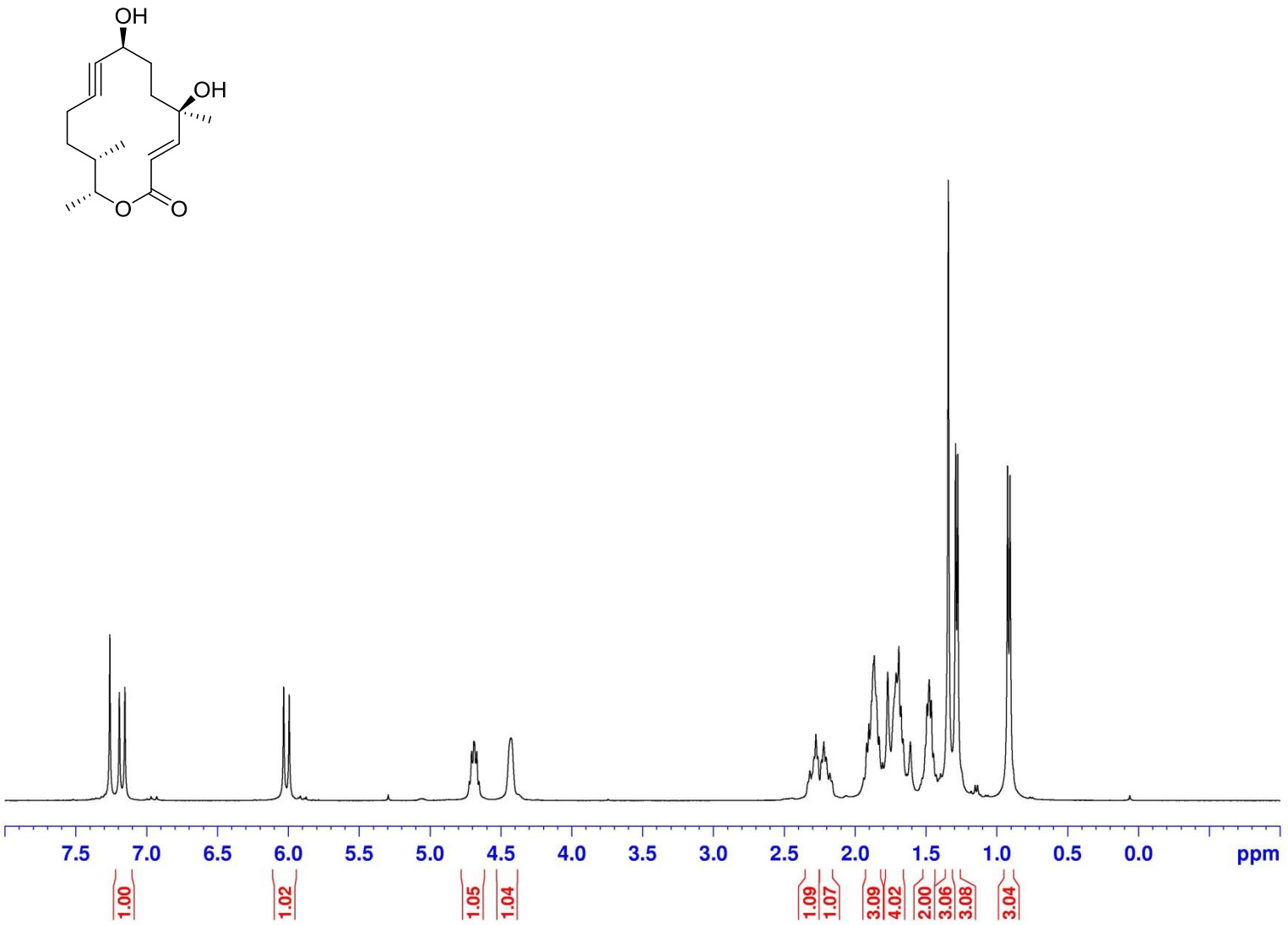

OH
79.21
75.79
71.60
39.22
31.93
19.60
16.61
14.35
3.60
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

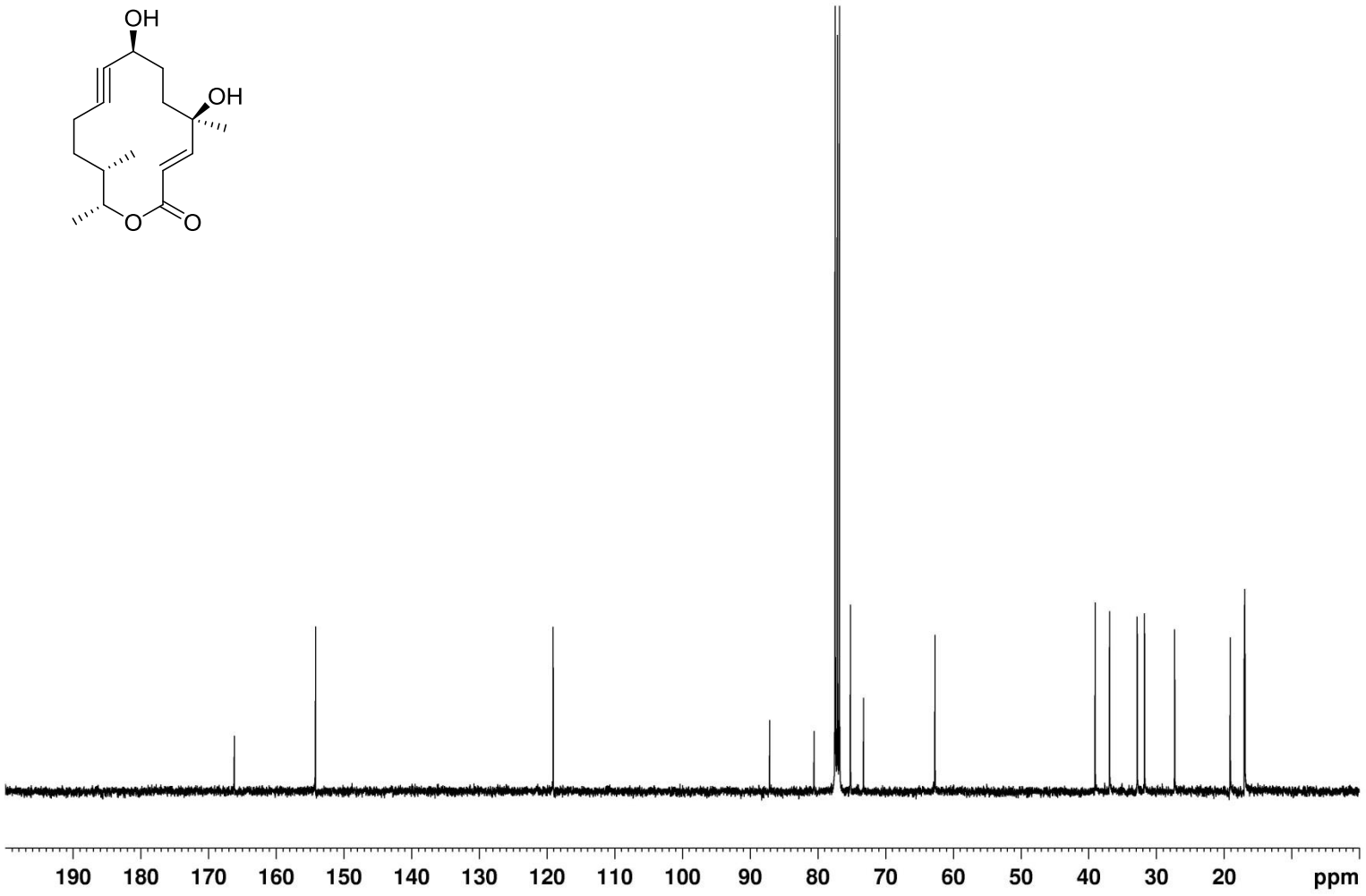

OTBS
OTES
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.01
1.00
1.03
1.03
1.04
4.06
3.03
4.03
1.03
3.03
1.04
3.02
9.03
3.09
9.00
6.06
3.02
3.04

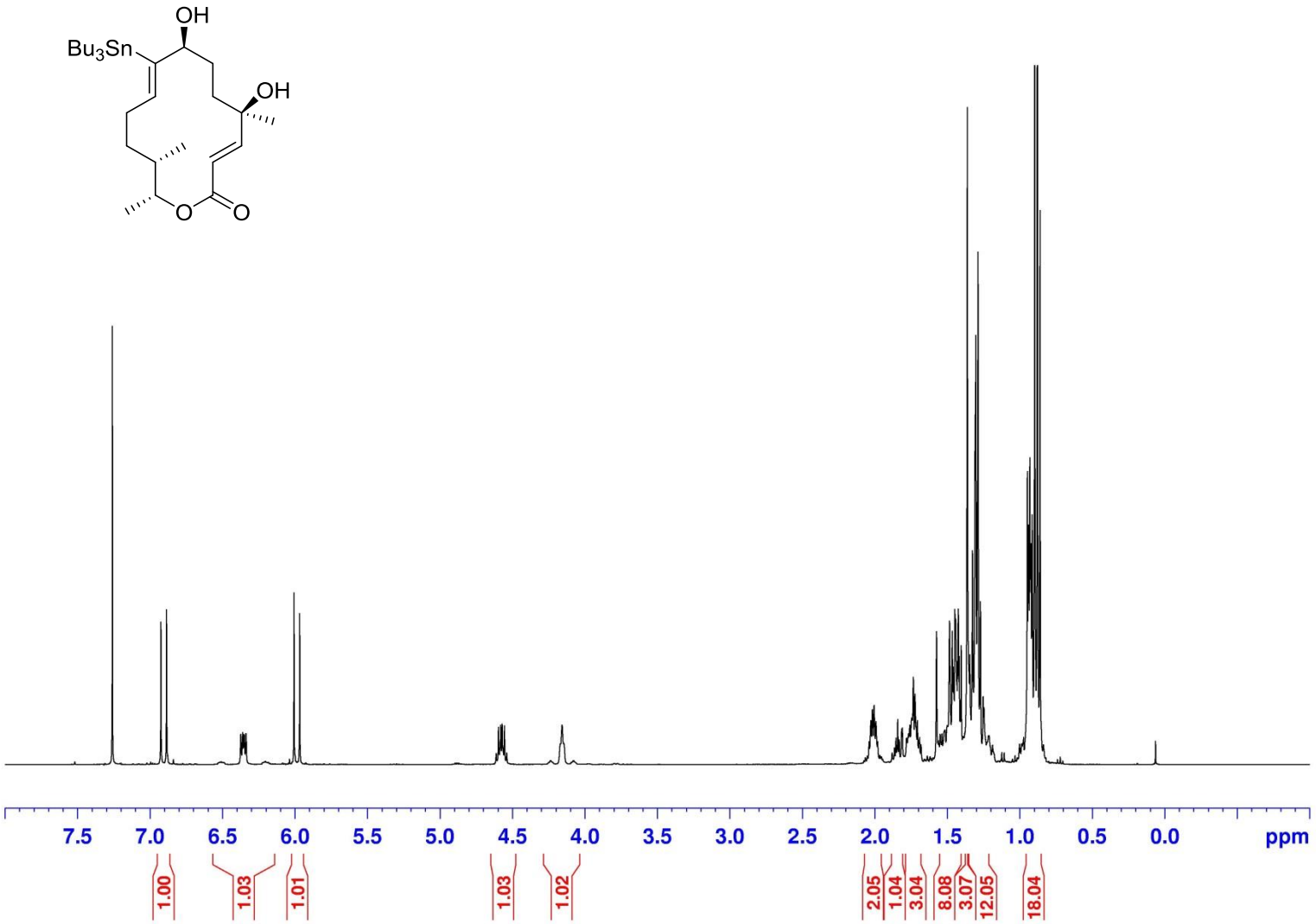

166.59
154.58
119.39
80.83
80.21
78.90
75.75
75.02
74.07
63.25
38.58
36.68
33.49
31.82
28.20
25.96
18.39
16.69
16.31
14.53
7.21
6.82
3.64
3.60
-4.45
-4.90
OTBS
OTES
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

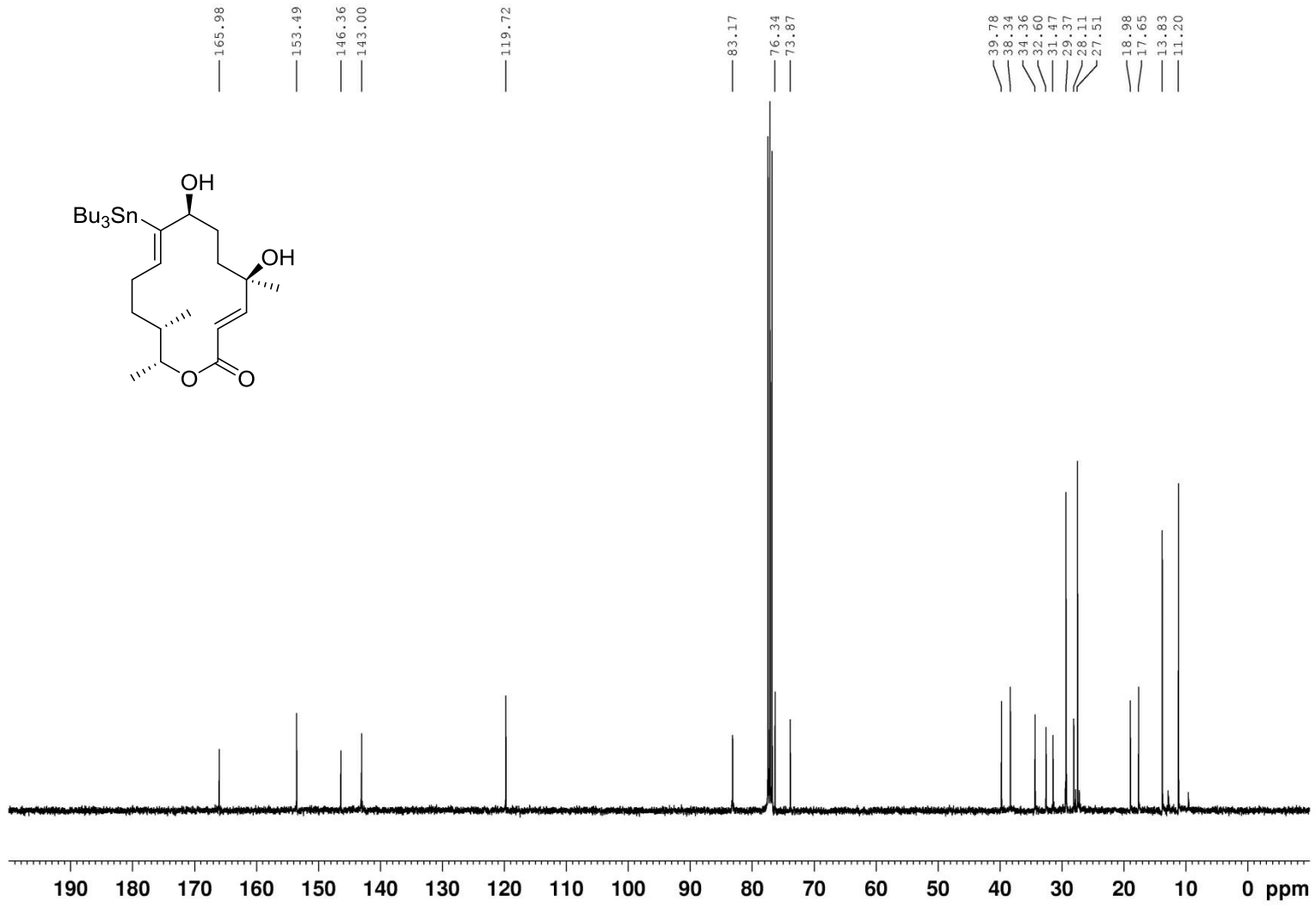

OTBS
OTES
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.00
1.02
1.07
1.08
1.07
2.03
1.09
2.08
2.07
3.05
3.07
9.06
3.02
9.04
6.00
3.07
3.07

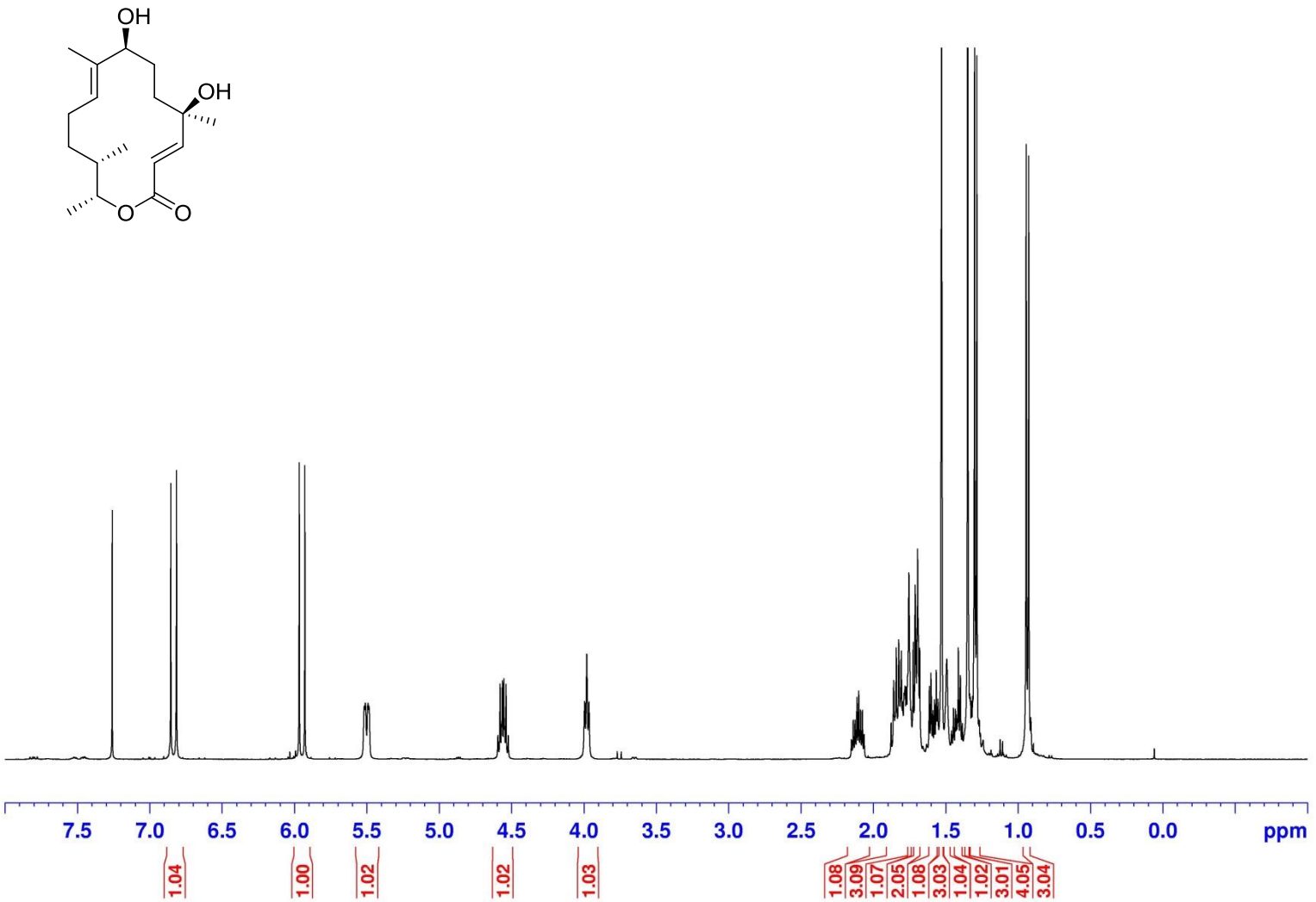

166.64
155.14
119.01
85.42
81.52
75.51
74.85
63.43
39.25
37.60
33.34
32.90
27.47
25.91
19.16
18.31
16.96
16.88
7.23
6.88
-4.28
-4.79
OTBS
OTES
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

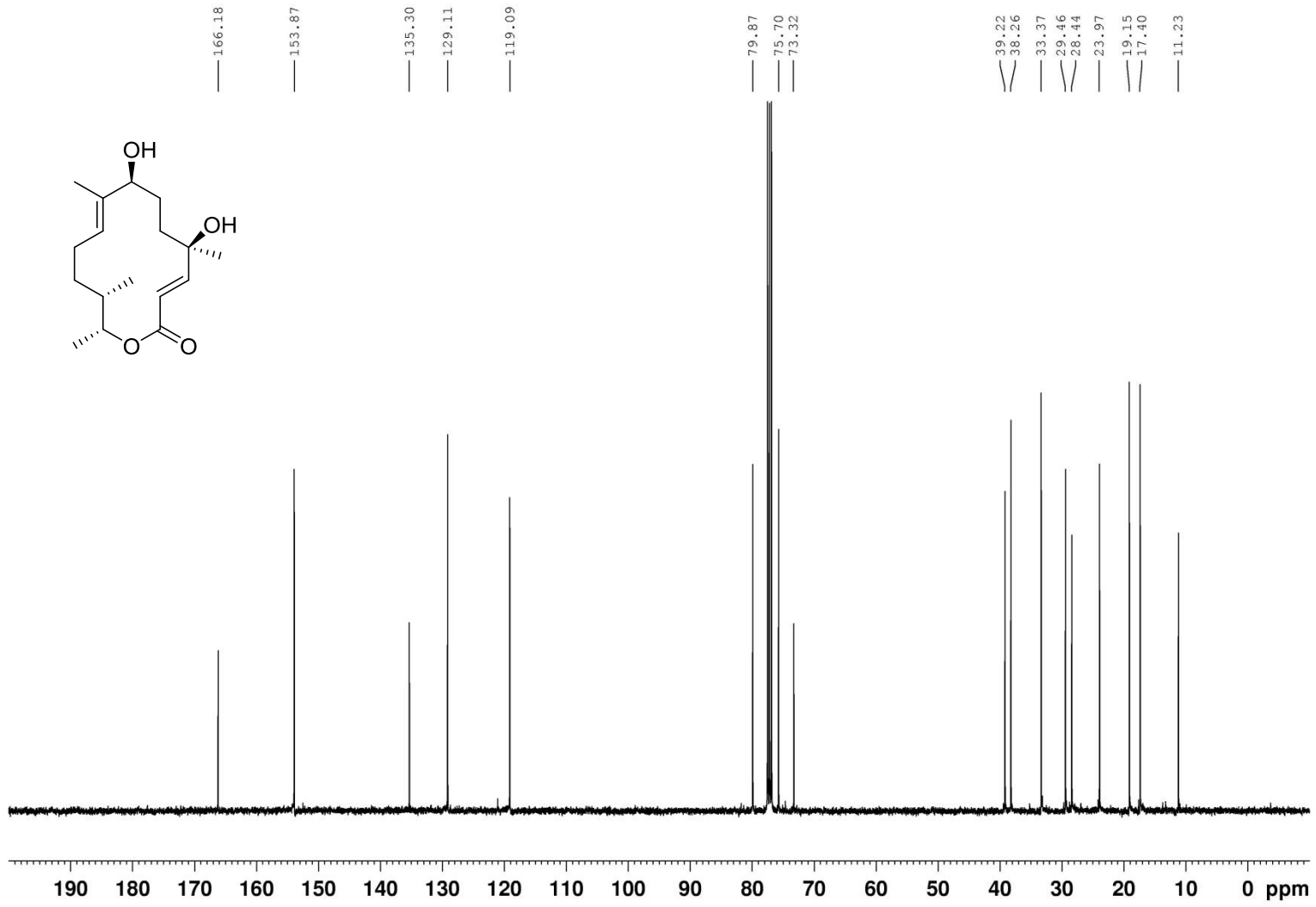

OH
OH
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.02
1.05
1.04
1.09
1.07
3.09
4.02
2.00
3.06
3.08
3.04

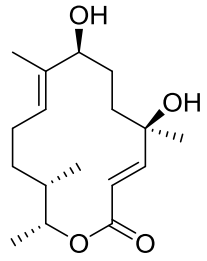

OH
OH
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


OH
Bu3Sn
OH
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.03
1.01
1.03
1.02
2.05
1.04
3.04
8.08
3.07
12.05
18.04


165.98
153.49
146.36
143.00
119.72
83.17
76.34
73.87
39.78
38.34
34.36
32.60
31.47
29.37
28.11
27.51
18.98
17.65
13.83
11.20
OH
Bu3Sn
OH
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

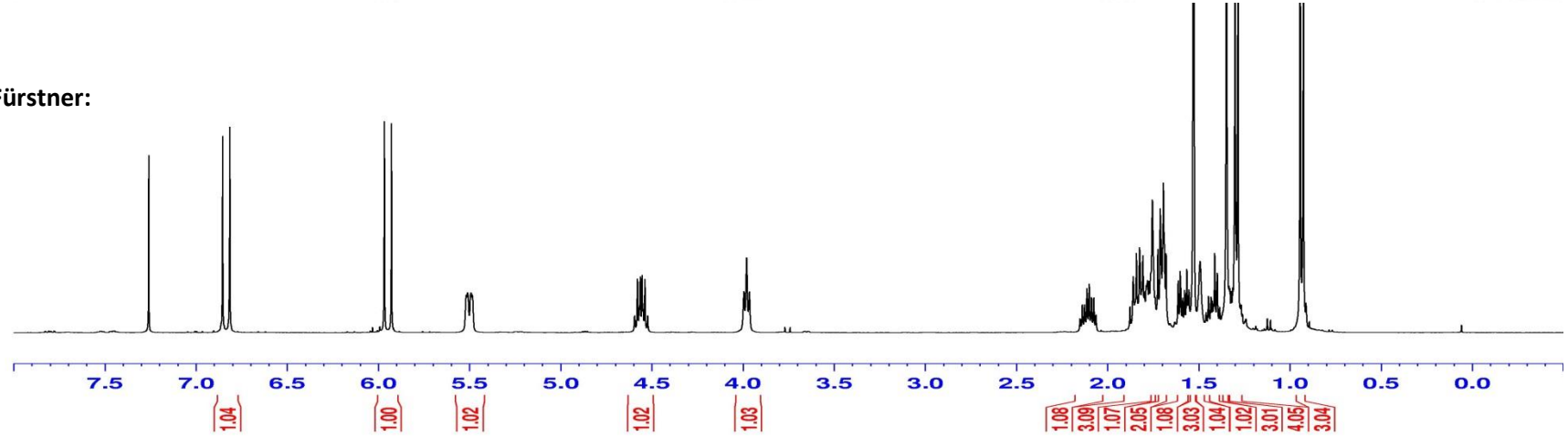

OH
OH
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.04
1.00
1.02
1.02
1.03
1.08
3.09
1.07
2.05
1.08
3.03
1.04
1.02
3.01
4.05
3.04

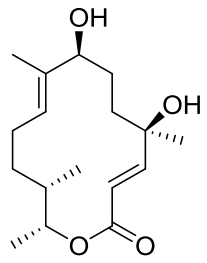

166.18
153.87
135.30
129.11
119.09
79.87
75.70
73.32
39.22
38.26
33.37
29.46
28.44
23.97
19.15
17.40
11.23
OH
OH
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



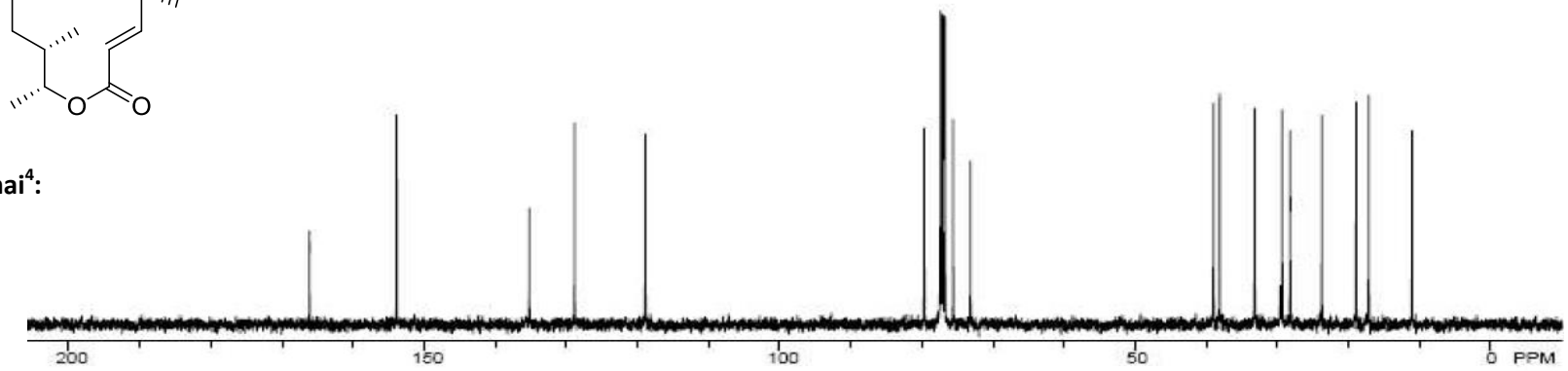
Zhai[4]:

Fürstner:

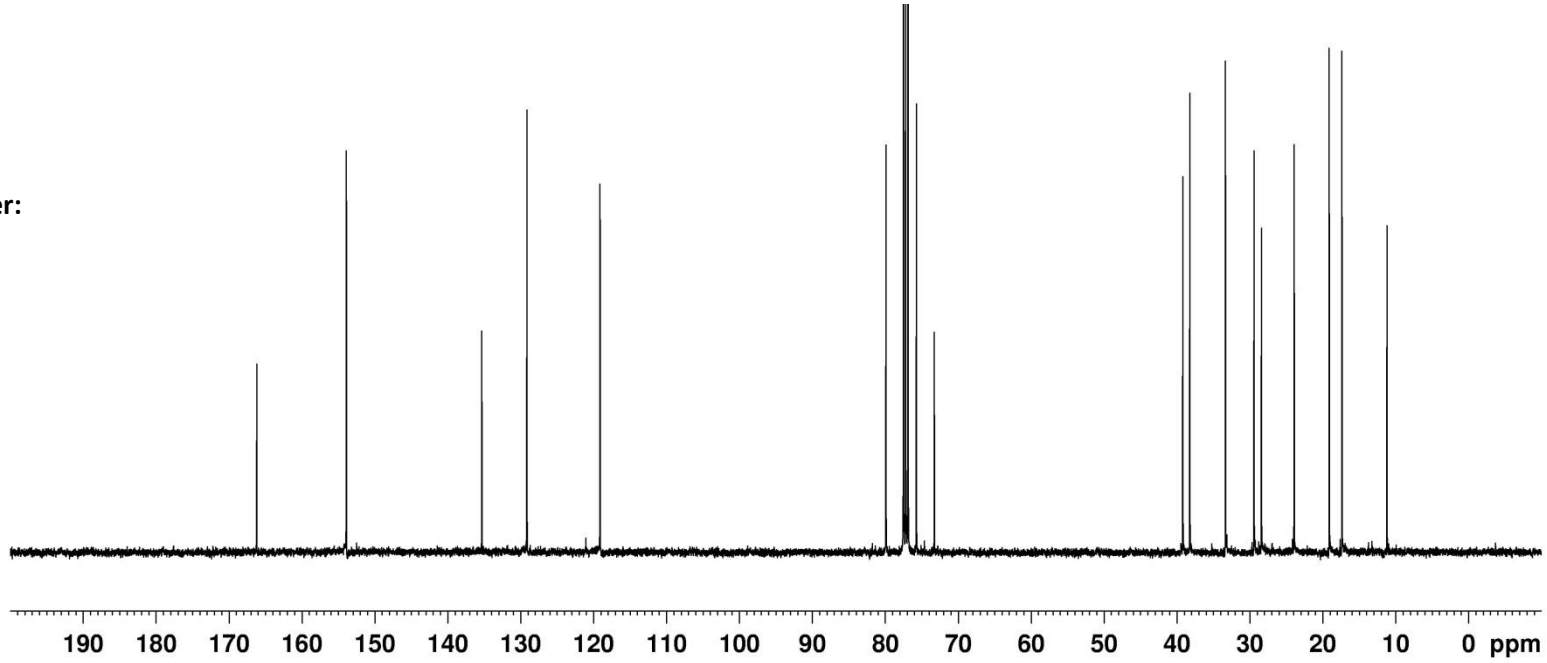


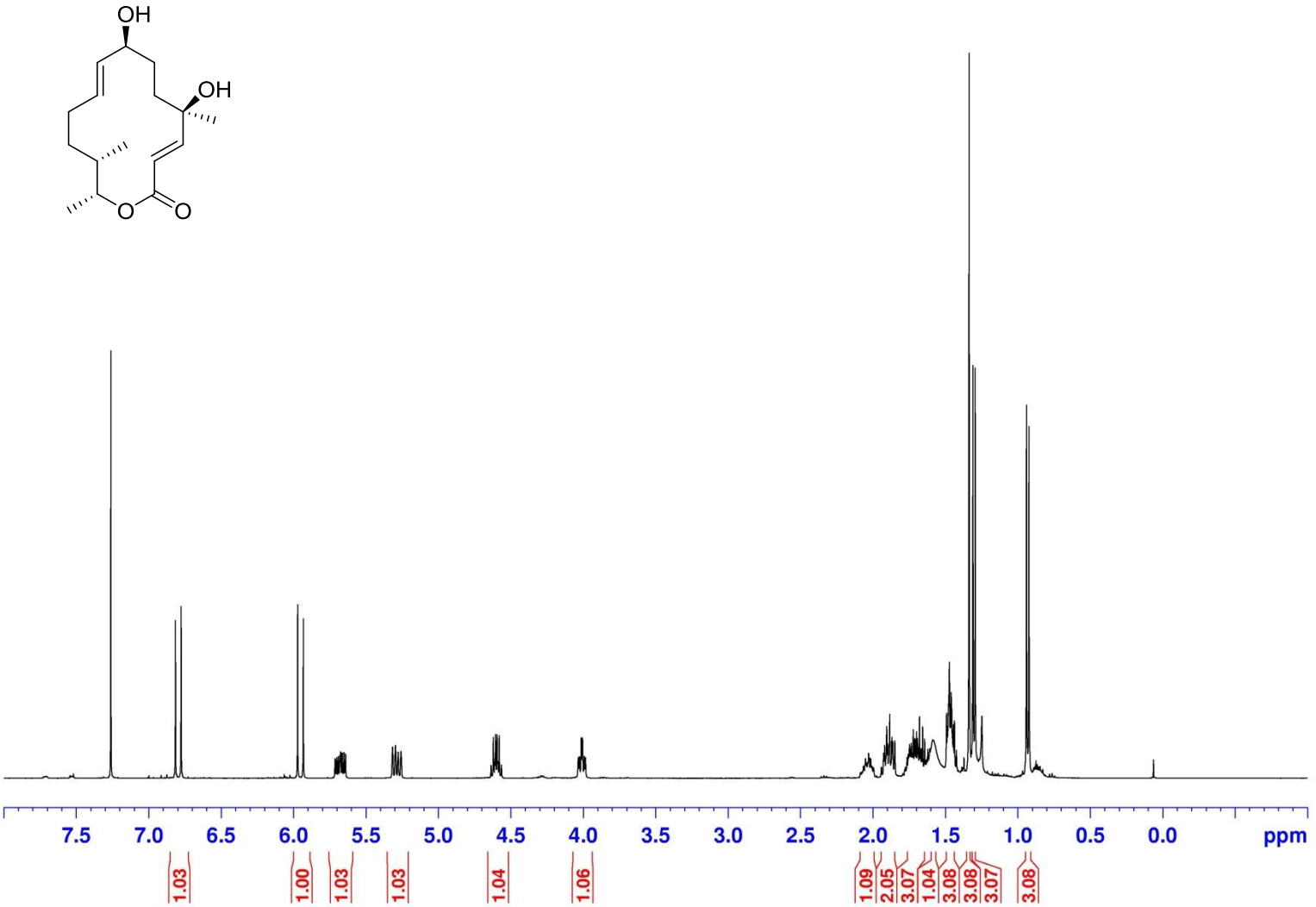


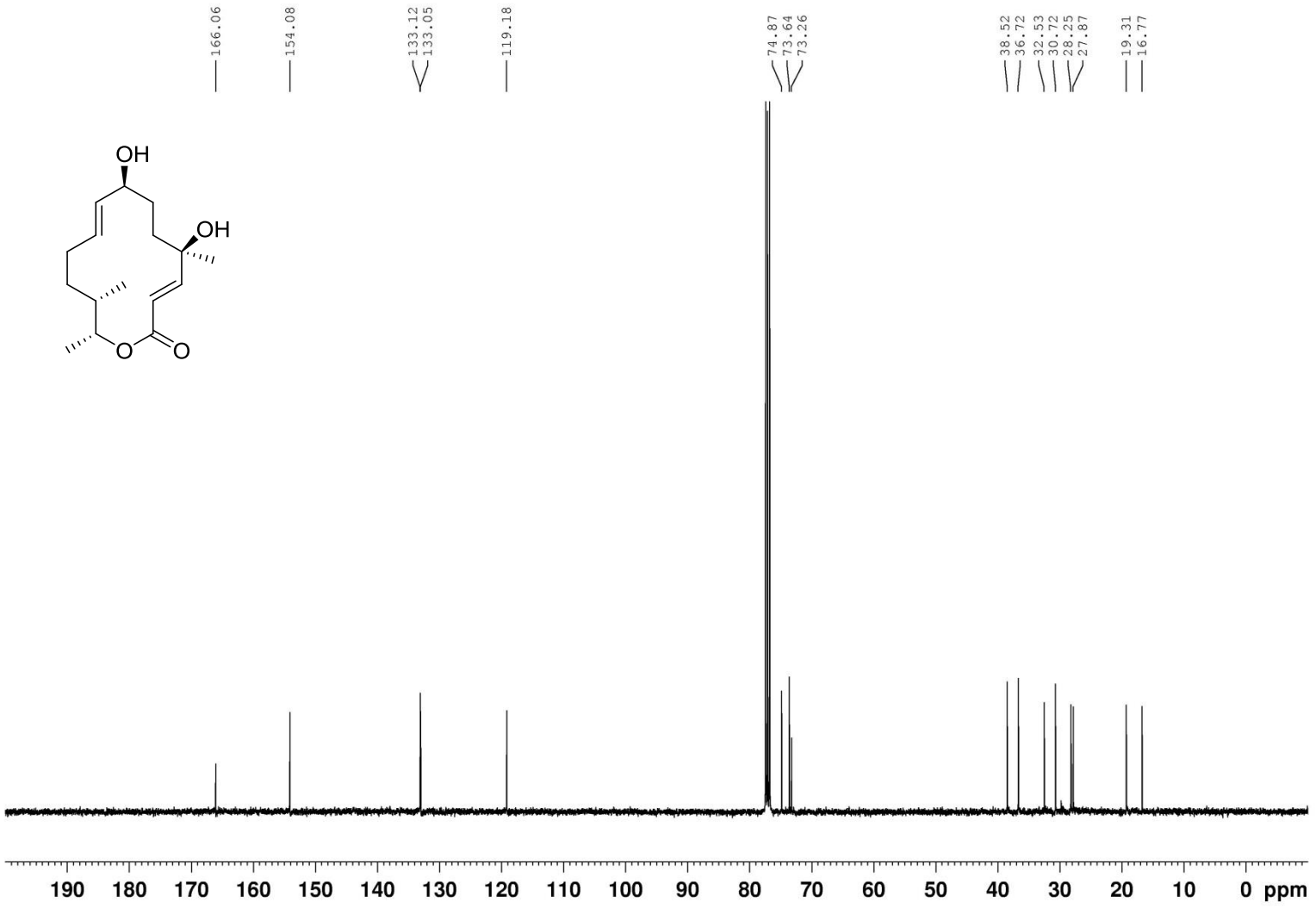
Zhai[4]:

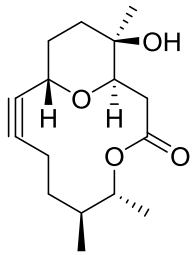


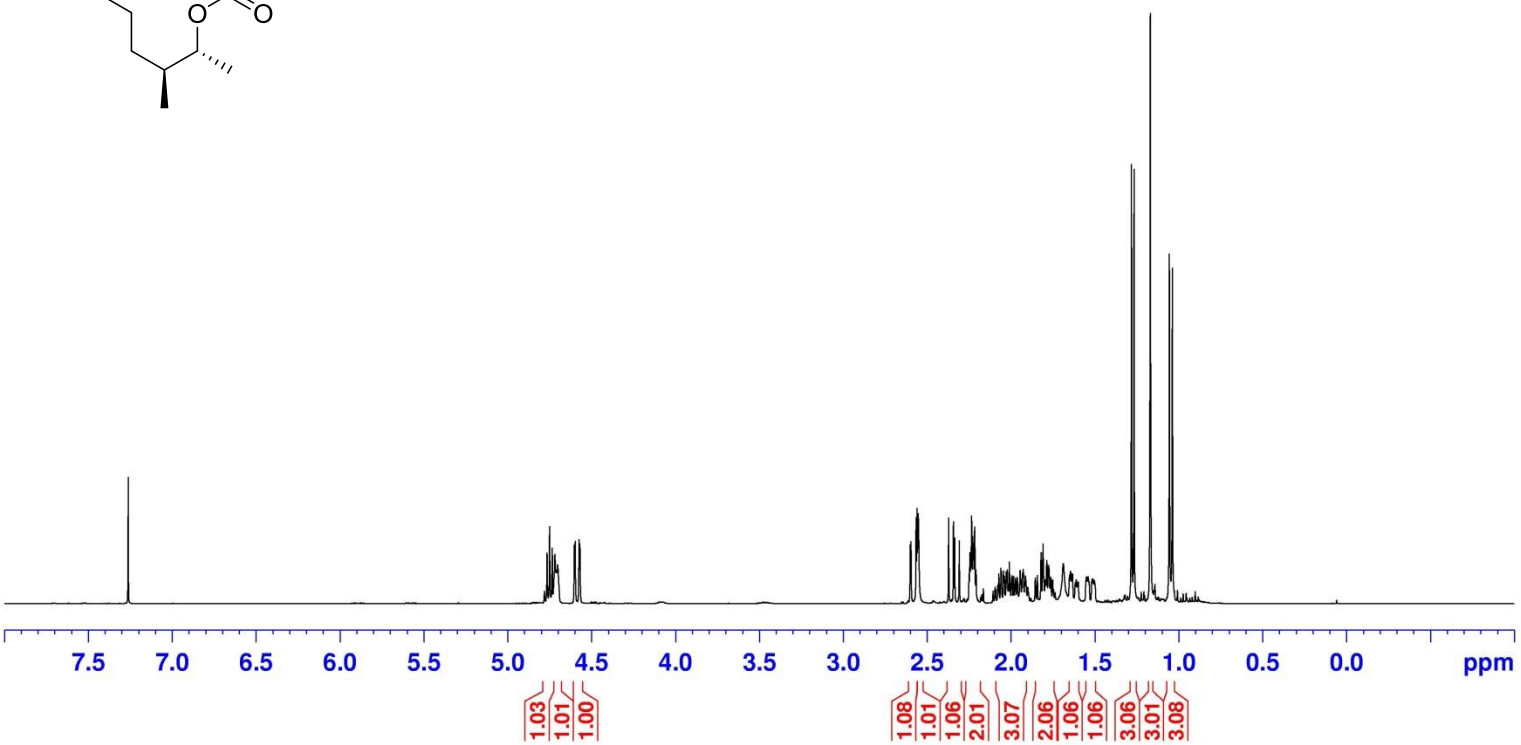
Fürstner:

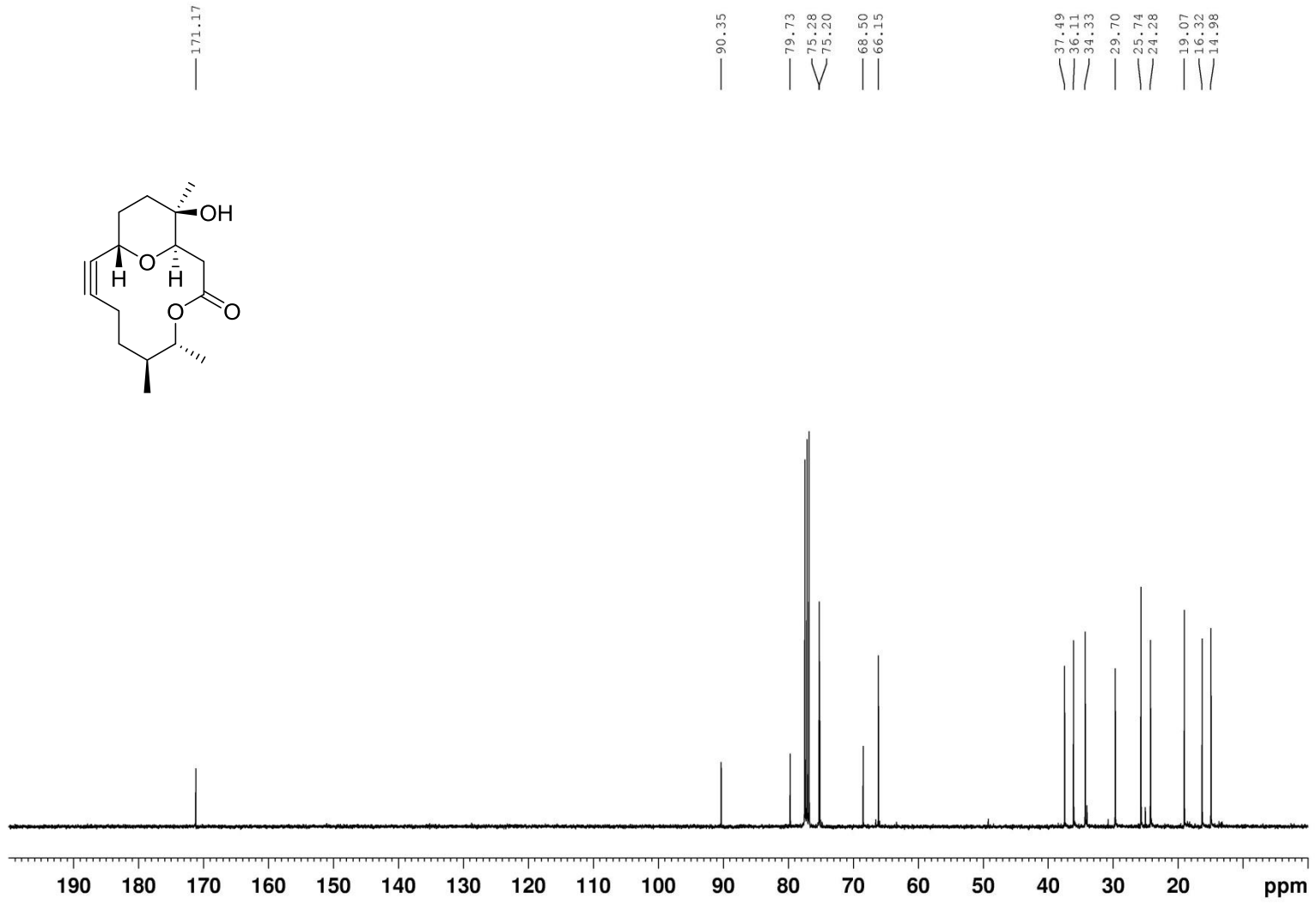


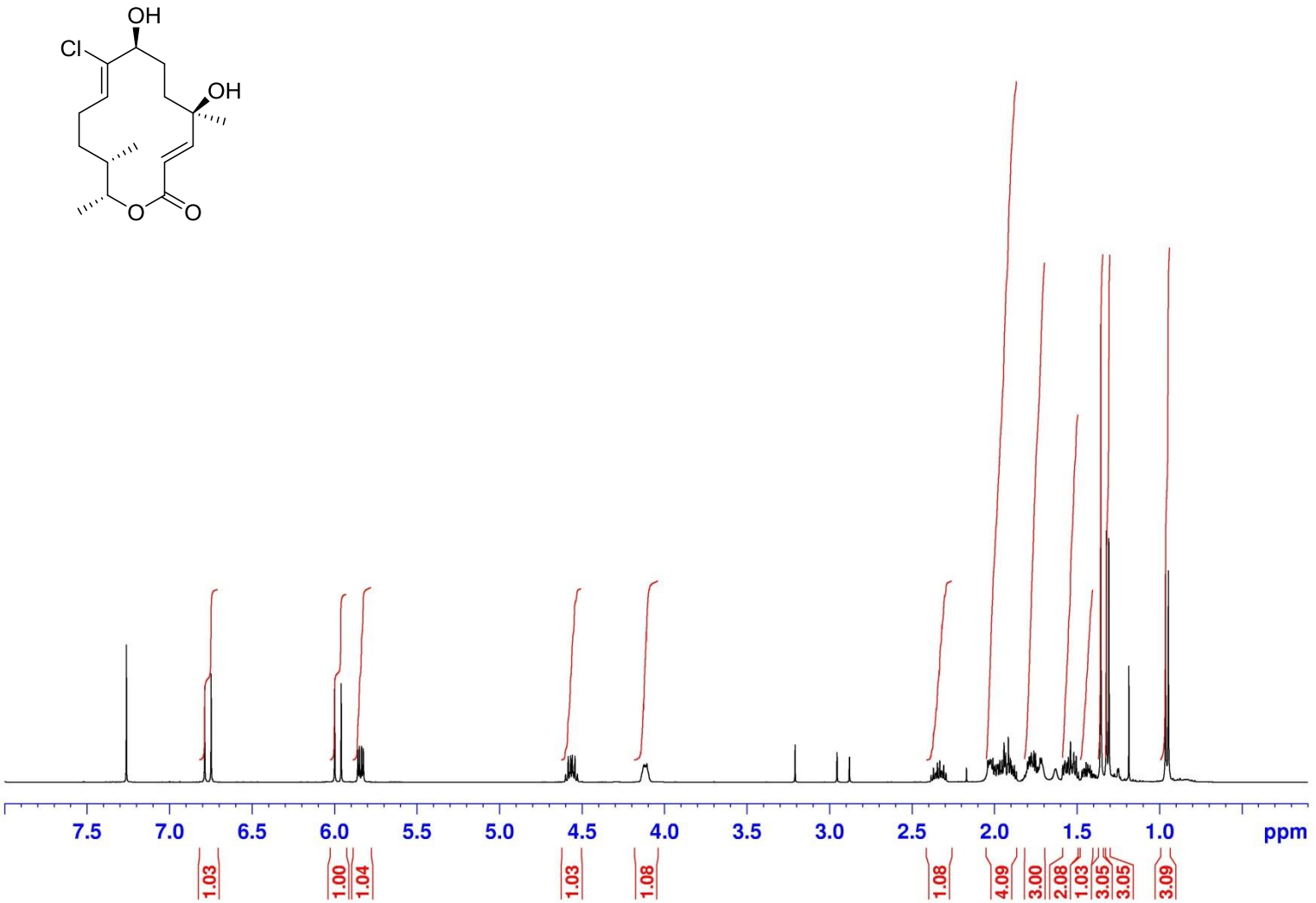

OH
OH
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.03
1.00
1.03
1.03
1.04
1.06
1.09
2.05
3.07
1.04
3.08
3.08
3.07
3.08

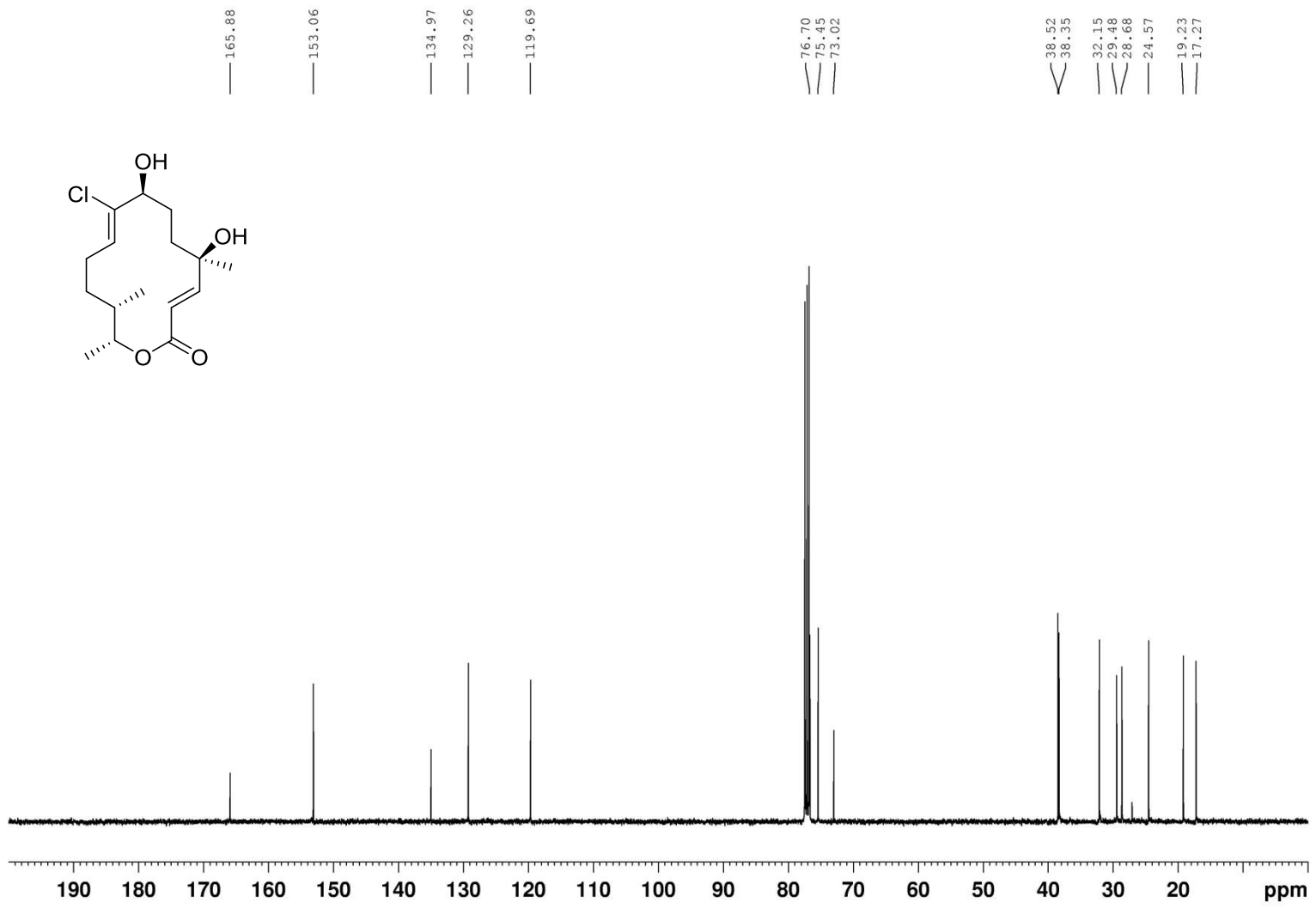

166.06
154.08
133.12
133.05
119.18
74.87
73.64
73.26
38.52
36.72
32.53
30.72
28.25
27.87
19.31
16.77
OH
OH
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

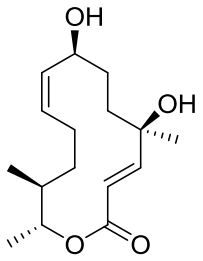

OH
O
H
H
O
O

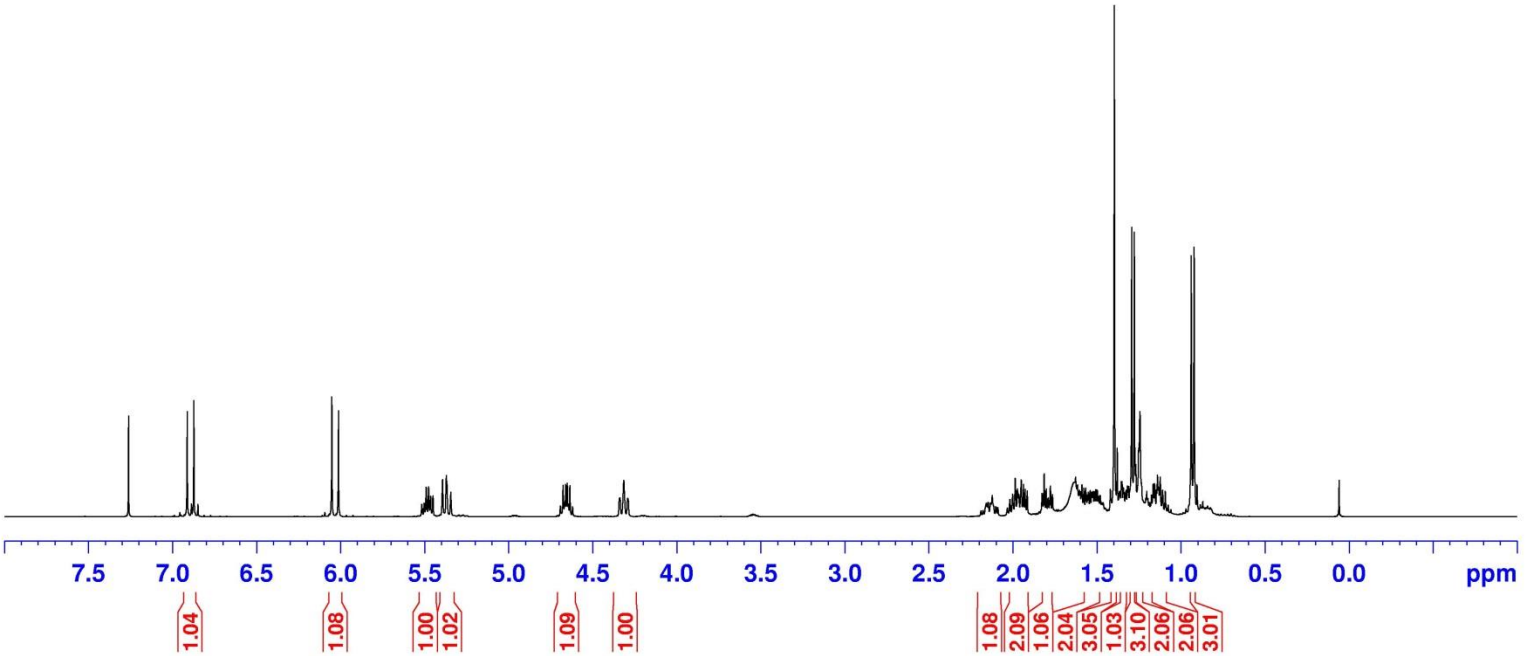

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.03
1.01
1.00
1.08
1.01
1.06
2.01
3.07
2.06
1.06
1.06
3.06
3.01
3.08

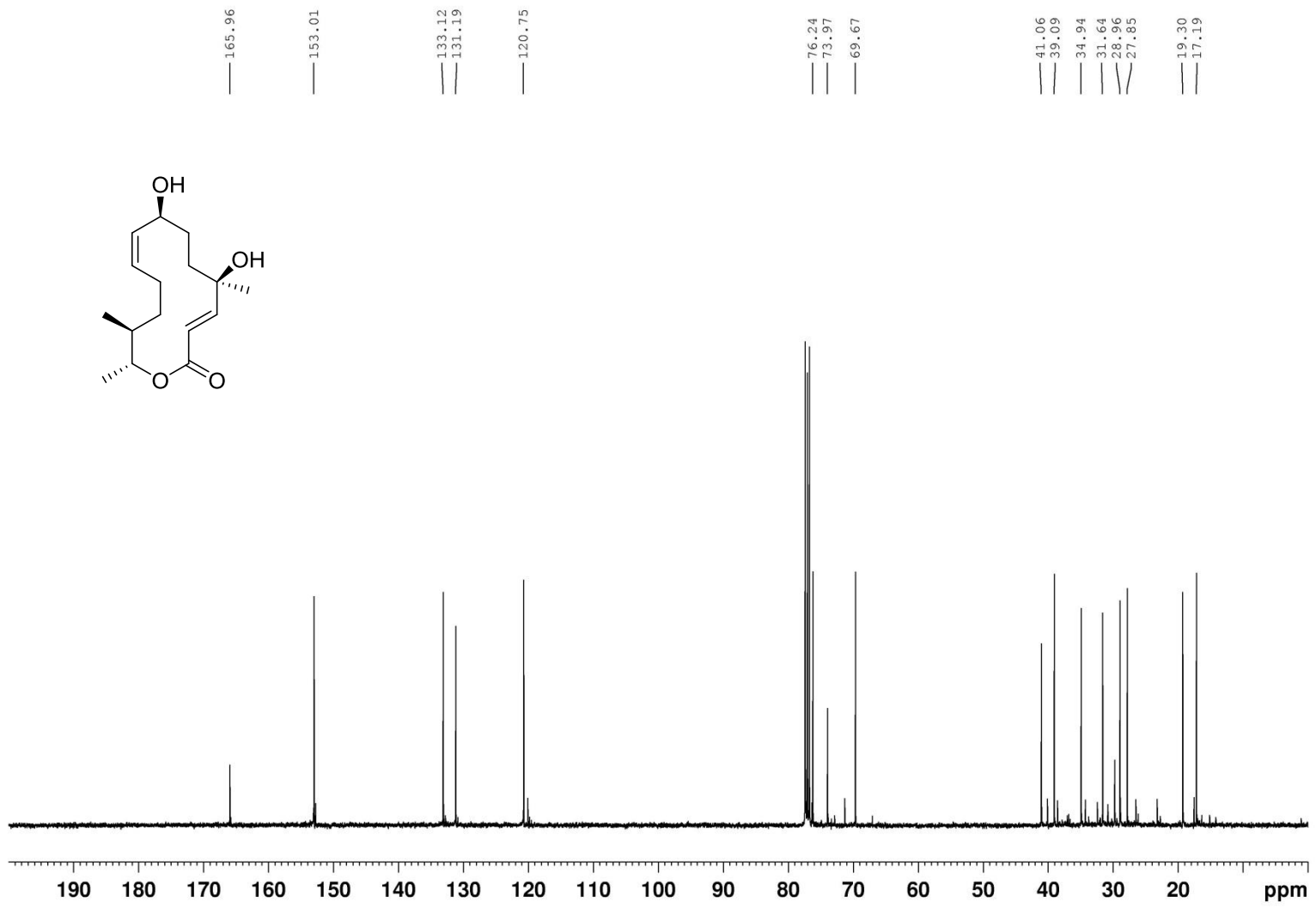

171.17
90.35
79.73
75.28
75.20
68.50
66.15
37.49
36.11
34.33
29.70
25.74
24.28
19.07
16.32
14.98
OH
O
H
H
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


OH
Cl
OH
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.03
1.00
1.04
1.03
1.08
1.08
4.09
3.00
2.08
1.03
3.05
3.05
3.09


165.88
153.06
134.97
129.26
119.69
76.70
75.45
73.02
38.52
38.35
32.15
29.48
28.68
24.57
19.23
17.27
OH
Cl
OH
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


OH
OH
O
O


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.04
1.08
1.00
1.02
1.09
1.00
1.08
2.09
1.06
2.04
3.05
1.03
3.10
2.06
2.06
3.01


165.96
153.01
133.12
131.19
120.75
76.24
73.97
69.67
41.06
39.09
34.94
31.64
28.96
27.85
19.30
17.19
OH
OH
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm