SUPPORTING INFORMATION

Concise Total Synthesis of the Potent Translation and Cell Migration Inhibitor Lactimidomycin

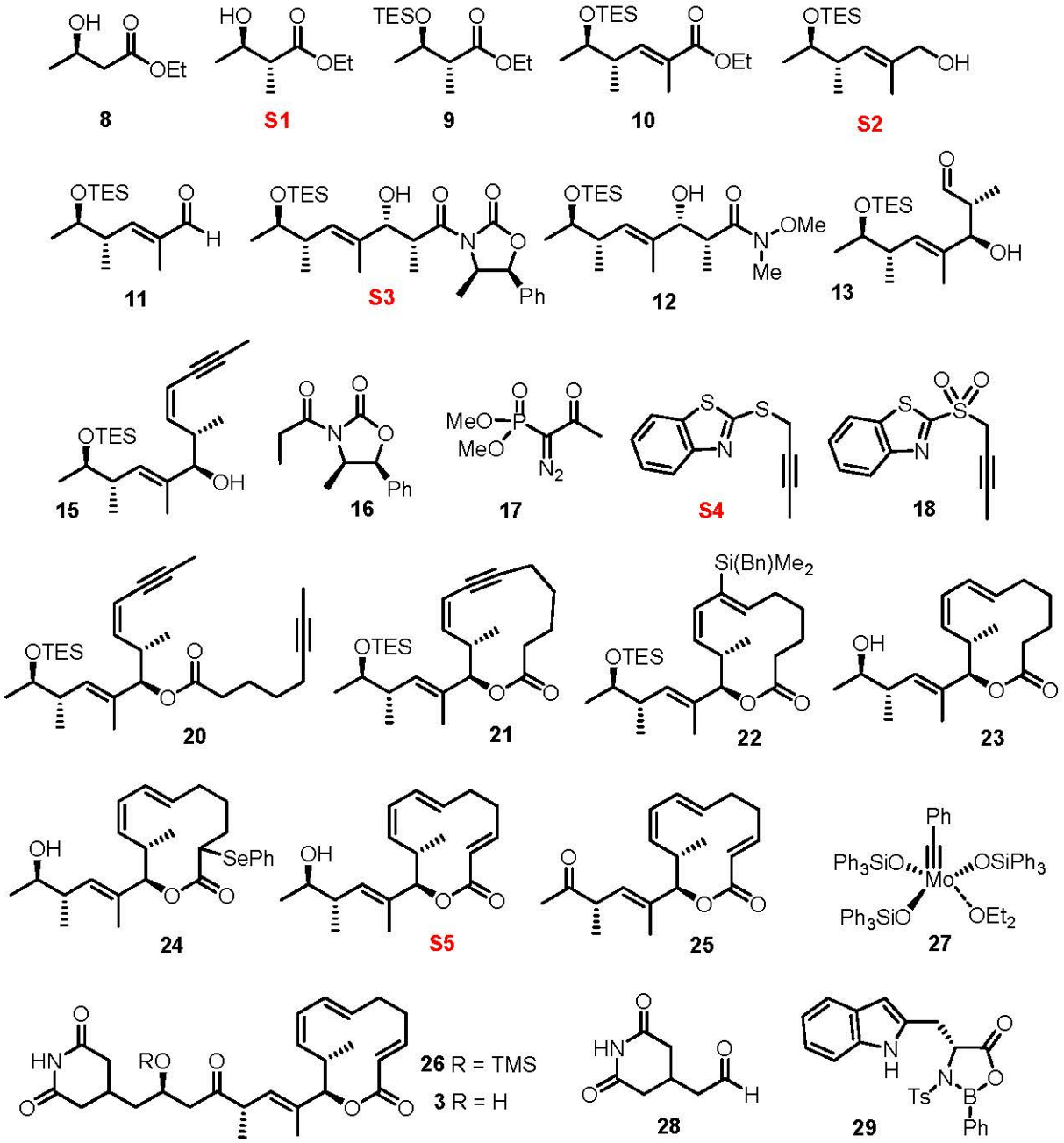
Kevin Micoine and Alois Fürstner*

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

email: fuerstner@kofo.mpg.de

Contents

Full Numbering Scheme



General. All reactions were carried out under Ar in flame-dried glassware. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O, CH_2Cl_2, HMPA (CaH_2), hexane, toluene (Na/K), MeOH (Mg). Flash chromatography (FC): Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on Bruker DPX 300, AMX 300, AV 400, or AVIII 600 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 ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.26$ 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 FT-MS (7 T magnet) or Mat 95 (Finnigan). Unless stated otherwise, all commercially available compounds (Fluka, Lancaster, Aldrich) were used as received.

Procedures & Analytical and Spectral Data

Compound S1: *n*BuLi (1.6 M in hexane, 31.3 mL, 50 mmol) was added dropwise to a solution of diisopropylamine (6.7 mL, 47.7 mmol) in THF (50 mL) at –78 °C. The resulting yellow solution was stirred at this temperature for 1 h before a solution of ethyl (*R*)-3-hydroxybutyrate **8** (3.0 g, 22.7 mmol) in THF (16 mL) and HMPA (6.8 mL) was slowly added via canula. The mixture was allowed to warm to –40 °C for 20 min before it was cooled back to –78 °C and iodomethane (1.77 mL, 28.4 mmol) was introduced. The mixture was stirred at 0 °C for 2 h before the reaction was quenched with sat. aq. NH_4Cl. HCl (1 M) was then added until pH ≈ 7 was reached and the product was extracted with Et_2O (3 x 50 mL). The combined organic layers were dried over $MgSO_4$ and evaporated, and the resiude was purified by flash chromatography (hexanes/EtOAc, 4/1 → 1:1) to give compound **S1** as a pale yellow liquid (3.1 g, 94 %). $[\alpha]_D^{20} = -29.5$ (c = 1.3, $CHCl_3$) [lit.[1] $[\alpha]_D^{20} = -30.3$ (c = 1, $CHCl_3$)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13 (q, *J* = 7.2 Hz, 2 H), 3.84 (qd, *J* = 6.5, 6.5 Hz, 1 H), 2.81 (br s, 1 H), 2.40 (qd, *J* = 7.1, 7.1 Hz, 1 H), 1.23 (t, *J* = 7.2 Hz, 3 H), 1.17 (d, *J* = 6.4 Hz, 3 H), 1.13 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8 (C), 69.2 (CH), 60.4 (CH_2), 46.8 (CH), 20.5 (CH_3), 14.0 (CH_3), 13.8 (CH_3); IR (film): 3446, 2978, 2938, 1715, 1458, 1375, 1259, 1182, 1109, 1074, 1045, 1028, 1001, 966, 924, 894, 862, 756 cm^{-1}; MS (EI): *m/z* (%): 131 (10), 116 (2), 102 (100), 101 (41), 85 (22), 74 (91), 56 (28), 45 (24), 43 (15), 29 (18); HRMS (CI): *m/z* calcd for $C_7H_{15}O_3$ $[M + H]^+$: 147.1021; found 147.1020.

Compound 9: Et_3SiCl (8.9 mL, 53 mmol) was slowly added to a solution of alcohol **S1** (3.1 g, 21.2 mmol) and pyridine (8.6 mL, 106 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The resulting mixture was stirred at ambient temperature for 1 h before the reaction was quenched at 0 °C with sat. aq. $NaHCO_3$ (40 mL). After the evolution of gas had ceased, the aqueous layer was extracted with Et_2O, the combined organic phases were successively washed with sat. aq. $NaHCO_3$ and $CuSO_4$ solution (0.5 M, 4 x 20 mL), dried over $MgSO_4$ and evaporated. The crude product was purified by flash chromatography (hexanes/EtOAc, 1/0 → 7/3), affording compound **9** as a colorless liquid (5.0 g, 91 %). $[\alpha]_D^{20} = -35.2$ (c = 1.1, $CHCl_3$) [lit.[2] $[\alpha]_D^{20} = -38.1$ (c = 1.05, $CHCl_3$)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.11 (q, *J* = 7.1 Hz, 2 H), 4.04 (dq, *J* = 7.4, 6.2 Hz, 1 H), 2.48 (qd, *J* = 7.1, 7.1 Hz, 1 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.13 (d, *J* = 6.1 Hz, 3 H), 1.07 (d, *J* = 7.0 Hz, 3 H), 0.94 (t, *J* = 8.0 Hz, 9 H), 0.58 (q, *J* = 7.7 Hz, 6 H); ^{13}C NMR (100 MHz,

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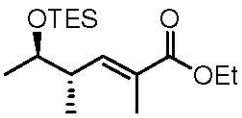
[1] Mori, K.; Ebata, T. *Tetrahedron* **1986,** *42,* 4413-4420.

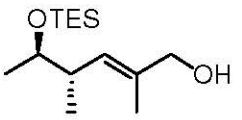
[2] Scheidt, K.; Bannister, T. D.; Tasaka, A.; Wendt, M. D.; Savall, B. M.; Fegley, G. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 6981-6990.

$CDCl_3$): δ = 175.1 (C), 69.9 (CH), 60.1 (CH_2), 46.2 (CH), 20.5 (CH_3), 14.2 (CH_3), 12.5 (CH_3), 6.8 (3 x CH_3), 4.9 (3 x CH_2); IR (film): 2955, 2912, 2877, 1736, 1459, 1415, 1375, 1348, 1318, 1240, 1182, 1163, 1110, 1066, 1035, 1005, 982, 950, 914, 862, 840, 775, 724, 672 cm^{-1}; MS (EI): *m/z* (%): 231 (79), 217 (7), 203 (21), 189 (3), 175 (12), 159 (21), 147 (55), 131 (67), 115 (43), 103 (100), 87 (22), 75 (36), 59 (13), 47 (8), 29 (7); HRMS (ESI): *m/z* calcd for $C_{13}H_{28}O_3SiNa$ $[M + Na]^+$: 283.1700; found 283.1697.

Compound 10: Dibal-H (1 M in CH_2Cl_2, 20 mL, 20 mmol) was added via syringe pump over 30 min to a solution of ester **9** (3.80 g, 14.7 mmol) in CH_2Cl_2 (30 mL) at –78 °C. The resulting mixture was stirred for 1 h at this temperature before it was quenched with ethyl acetate (2 mL) and poured into a sat. aq. solution of Rochelle's salt. The biphasic mixture was vigorously stirred for 2 h until a clean separation of the layers was reached. The aqueous phase was extracted with Et_2O and the combined organic layers were dried over $MgSO_4$ and evaporated. The resulting crude aldehyde was dissolved in THF (100 mL) and (carbethoxyethylidene)triphenylphosphorane (16.5 g, 46 mmol) was added. The mixture was stirred at reflux temperature for 20 h before the solvent was evaporated. Purification of the residue by flash chromatography (hexanes/EtOAc 1/0 → 9/1) gave compound **10** as a colorless liquid (4.05 g, 92 %). $[\alpha]_D^{20} = -15.5$ (c = 1, $CHCl_3$).[3] ^1H NMR (400 MHz, $CDCl_3$): δ = 6.66 (dq, *J* = 13.7, 1.0 Hz, 1 H), 4.17 (qd, *J* = 9.4, 5.5 Hz, 1 H, overlap), 4.14 (qd, *J* = 9.4, 5.6 Hz, 1 H, overlap), 3.70 (dq, *J* = 8.1, 7.9 Hz, 1 H), 2.47 (dqd, *J* = 13.5, 9.1, 6.9 Hz, 1 H), 1.80 (d, *J* = 1.9 Hz, 3 H), 1.24 (t, *J* = 9.6 Hz, 3 H), 1.06 (d, *J* = 8.3 Hz, 3 H), 0.96-0.86 (m, 12 H), 0.53 (q, *J* = 10.5 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3 (C), 144.8 (CH), 127.5 (C), 71.4 (CH), 60.3 (CH_2), 41.0 (CH), 21.2 (CH_3), 15.7 (CH_3), 14.2 (CH_3), 12.6 (CH_3), 6.8 (3 x CH_3), 5.0 (3 x CH_2); IR (film): 2957, 2912, 2877, 1710, 1650, 1458, 1414, 1367, 1295, 1236, 1171, 1141, 1120, 1088, 1063, 1034, 1004, 956, 838, 775, 740, 700, 672 cm^{-1}; MS (EI): *m/z* (%): 271 (31), 256 (29), 242 (2), 225 (8), 199 (7), 175 (67), 159 (100), 147 (7), 131 (75), 115 (68), 103 (18), 87 (31), 75 (16), 59 (12), 47 (5), 29 (6); HRMS (ESI): *m/z* calcd for $C_{16}H_{32}O_3SiNa$ $[M + Na]^+$: 323.2013; found 323.2010.



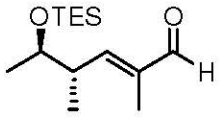
Compound S2: Dibal-H (1 M in CH_2Cl_2, 5.8 mL, 5.8 mmol) was added to a solution of ester **10** (754 mg, 2.5 mmol) in CH_2Cl_2 (6 mL) at –78 °C. The resulting mixture was stirred for 30 min at this temperature and for another 30 min at 0 °C before the reaction was carefully quenched with sat. aq. Rochelle's salt (15 mL). The biphasic mixture was vigorously stirred for 2.5 h before CH_2Cl_2 and water were added. The aqueous phase was extracted with CH_2Cl_2 and Et_2O, the combined organic layers were dried over $MgSO_4$ and evaporated to give compound **S2** as a colorless liquid (631 mg, 98 %). $[\alpha]_D^{20} = -6.6$ (c = 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.30 (d, *J* = 9.6 Hz, 1 H), 4.01 (d, *J* = 0.9 Hz, 2 H), 3.70 (qd, *J* = 6.0, 4.6 Hz, 1 H), 2.42 (dqd, *J* = 9.4, 6.9, 4.3 Hz, 1 H), 1.67 (d, *J* = 1.4 Hz, 3 H), 1.06 (d, *J* = 6.1



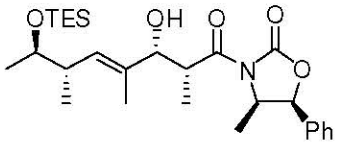
[3] For comparison, the corresponding –OTBS analogue has the following optical rotation: $[\alpha]_D^{20} = -16.2$ (c = 2 in $CHCl_3$), cf. Kinoshita, K.; Williard, P. G.; Koshla, C.; Cane, D. E. *J. Am. Chem. Soc.* **2001,** *123,* 2495-2502.

Hz, 3 H), 0.95 (t, J = 8.1 Hz, 9 H, overlap), 0.94 (m, 3 H, overlap), 0.58 (q, J = 7.7 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.6 (C), 129.0 (CH), 71.6 (CH), 69.1 (CH_2), 39.5 (CH), 20.6 (CH_3), 16.1 (CH_3), 13.9 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2); IR (film): 3336, 2959, 2913, 2876, 1456, 1415, 1376, 1237, 1094, 1067, 1007, 958, 872, 743, 673 cm^{-1}; MS (EI): *m/z* (%): 159 (100), 147 (29), 131 (42), 115 (76), 103 (33), 87 (29), 82 (16), 75 (20), 59 (10), 43 (8), 29 (3); HRMS (ESI): *m/z* calcd for $C_{14}H_{30}O_2SiNa$ [M + Na]$^+$: 281.1907; found 281.1907.

Compound 11: Pyridinium chlorochromate (3.42 g, 15.8 mmol) was added to a solution of alcohol **S2** (3.42 g, 13.2 mmol) in CH_2Cl_2 (80 mL) containing molecular sieves (4 Å, ca. 3 g). The resulting mixture was stirred at room temperature overnight before it was filtered through a pad of silica. The filtrate was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 1/0 → 85/15), affording aldehyde **11** as a yellow liquid (2.66 g, 79 %). $[\alpha]_D^{20}$ = +9.5 (c = 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.41 (s, 1 H), 6.46 (d, J = 9.9 Hz, 1 H), 3.81 (qd, J = 5.9, 5.4 Hz, 1 H), 2.42 (dqd, J = 10.0, 6.8, 4.3 Hz, 1 H), 1.74 (d, J = 1.0 Hz, 3 H), 1.10 (d, J = 6.3 Hz, 3 H), 1.05 (d, J = 6.8 Hz, 3 H), 0.94 (t, J = 8.0 Hz, 9 H), 0.58 (q, J = 8.2 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6 (CH), 157.1 (CH), 139.1 (C), 71.3 (CH), 41.2 (CH), 21.8 (CH_3), 16.2 (CH_3), 9.4 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2); IR (film): 2957, 2911, 2877, 1689, 1641, 1457, 1414, 1375, 1330, 1294, 1238, 1215, 1164, 1130, 1105, 1062, 1005, 957, 925, 881, 830, 723, 672 cm^{-1}; MS (EI): *m/z* (%): 256 (0.14) [M]$^+$, 227 (27), 212 (21), 183 (51), 171 (14), 159 (82), 155 (30), 131 (41), 115 (100), 103 (19), 87 (51), 75 (26), 59 (19), 47 (9), 29 (3); HRMS (ESI): *m/z* calcd for $C_{14}H_{28}O_2SiNa$ [M + Na]$^+$: 279.1751; found 279.1752.



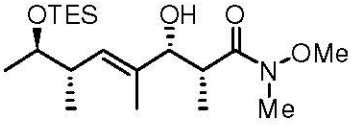
Compound S3: Bu_2OTf (3.6 mL, 14.6 mmol) was added over 30 min to a solution of oxazolidinone **16** (3.11 g, 13.3 mmol)[4] in CH_2Cl_2 at –15 °C. Et_3N (2.2 mL, 16 mmol) was added over 15 min before the mixture was cooled to –78 °C and a solution of aldehyde **11** (3.57 g, 13.9 mmol) in CH_2Cl_2 (10 mL + 5 mL rinse) was slowly introduced via canula over the course of 1 h. The mixture was stirred at –78 °C for 1 h and then warmed to ambient temperature. After stirring for additional 2 h, the reaction was quenched with a mixture of MeOH (6 mL) and pH 7 phosphate buffer (6 mL). Aq. sat. NH_4Cl was introduced and the layers were separated. The aqueous phase was extracted twice with CH_2Cl_2, the combined organic layers were dried over $MgSO_4$ and evaporated, and the crude product was purified by flash chromatography (hexane/EtOAc, 9/1 → 8/2) to give product **S3** as a colorless oil (5.85 g, 90 %). $[\alpha]_D^{20}$ = +22.2 (c = 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46-7.34 (m, 3 H), 7.30 (d, J = 7.2 Hz, 2 H), 5.67 (d, J = 7.0 Hz, 1 H), 5.46 (d, J = 10.0 Hz, 1 H), 4.77 (qd, J = 6.8, 6.8 Hz, 1 H), 4.38 (d, J = 3.6 Hz, 1 H), 4.00 (qd, J = 7.0, 3.8 Hz, 1 H), 3.73 (qd, J = 5.9, 5.3 Hz, 1 H), 2.62 (br s, 1 H), 2.48 (dqd, J = 9.6, 6.8, 4.3 Hz, 1 H), 1.65 (d, J = 1.1 Hz, 3 H), 1.15 (d, J = 6.9 Hz, 3 H), 1.08 (d, J = 6.5 Hz, 3 H), 0.96 (t, J = 8.1 Hz, 9 H, overlap), 0.96 (d, J = 6.9 Hz, 3 H, overlap), 0.90 (d, J = 6.7 Hz, 3 H), 0.59 (q, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6 (C), 152.6 (C),



[4] Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

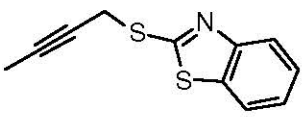
133.3 (C), 133.2 (C), 129.2 (CH), 128.8 (CH), 128.7 (CH), 125.6 (CH), 78.9 (CH), 75.3 (CH), 71.3 (CH), 55.0 (CH), 40.6 (CH), 39.5 (CH), 20.4 (CH_3), 15.8 (CH_3), 14.3 (CH_3), 13.7 (CH_3), 10.2 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2); IR (film): 3528, 2957, 2911, 2876, 1779, 1701, 1455, 1412, 1362, 1341, 1302, 1235, 1193, 1148, 1120, 1090, 1066, 1002, 956, 891, 867, 817, 766, 740, 699 cm^{-1}; MS (EI): *m/z* (%): 489 (< 0.1) $[M]^+$, 347 (41), 318 (14), 313 (42), 274 (4), 227 (10), 212 (5), 183 (11), 159 (100), 136 (28), 131 (54), 115 (74), 87 (29), 75 (12), 57 (13); HRMS (ESI): *m/z* calcd for $C_{27}H_{43}NO_5SiNa$ $[M + Na]^+$: 512.2803; found 512.2801.

Compound 12: Me_3Al (2 M in heptane, 7.5 mL, 15 mmol) was slowly added to a solution of



MeNHOMe·HCl (1.46 g, 15 mmol) in THF at 0 °C and stirring was continued for 20 min at 0°C and for 45 min at ambient temperature. The resulting mixture was cooled to –10 °C before a solution of **S3** (1.96 g, 4 mmol) in THF (10 mL + 3 mL rinse) was slowly added via canula. After 1 h at that temperature, the mixture was poured into an ice-cold mixture of sat. aq. Rochelle's salt and CH_2Cl_2. The biphasic mixture was vigorously stirred for 1 h, the aqueous phase was carefully extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 7/3 → 5/5), affording product **12** as a colorless oil (1.21 g, 81 %). $[\alpha]_D^{20} = -7.4$ (c = 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.44 (d, *J* = 9.8 Hz, 1 H), 4.25 (d, *J* = 2.9 Hz, 1 H), 3.70 (s, 3 H, overlap), 3.74-3.66 (m, 1 H, overlap), 3.18 (s, 3 H), 3.06 (br s, 1 H), 2.47 (dqd, *J* = 9.5, 6.8, 4.2 Hz, 1 H), 1.60 (d, *J* = 1.1 Hz, 3 H), 1.09 (d, *J* = 7.1 Hz, 3 H), 1.05 (d, *J* = 6.3 Hz, 3 H), 0.98-0.90 (m, 12 H), 0.57 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.9 (C), 132.9 (C), 129.2 (CH), 75.4 (CH), 71.2 (CH), 61.4 (CH_3), 39.5 (CH), 37.2 (CH), 31.9 (CH_3), 19.9 (CH_3), 15.3 (CH_3), 13.7 (CH_3), 10.5 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2); IR (film): 3444, 2958, 2912, 2876, 1639, 1458, 1415, 1378, 1294, 1238, 1172, 1093, 1063, 998, 959, 894, 868, 816, 766, 740, 673 cm^{-1}; MS (EI): *m/z* (%): 373 (< 0.1) $[M]^+$, 344 (3), 300 (14), 231 (5), 197 (62), 183 (6), 159 (100), 131 (47), 115 (74), 87 (27), 75 (17), 59 (10), 43 (6); HRMS (ESI): *m/z* calcd for $C_{19}H_{39}NO_4SiNa$ $[M + Na]^+$: 396.2541; found 396.2543.

Compound S4: Triphenylphosphine (13.4 g, 51 mmol), imidazole (8.75 g, 129 mmol) and



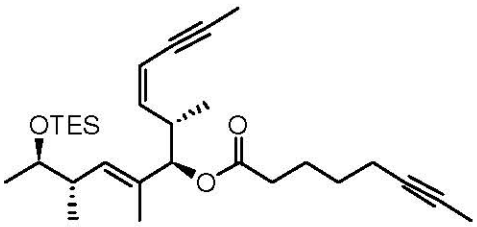
iodine (13.1 g, 51 mmol) were successively added to a virgorously stirred solution of 2-butyn-1-ol (3.0 g, 42.9 mmol) in CH_2Cl_2 (100 mL). The mixture was refluxed for 45 min before it was cooled to ambient temperature and 2-mercaptobenzothiazole (8.6 g, 51 mmol) was introduced. Stirring was continued for 2 h before the reaction was quenched with sat. aq. NH_4Cl. The organic layer was dried over $MgSO_4$ and evaporated, and the residue purified by flash chromatography (hexanes/EtOAc, 90/10) to give compound **S4** as a yellow solid (5.0 g, 53 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.4 Hz, 1 H), 7.77 (d, *J* = 7.9 Hz, 1 H), 7.43 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1 H), 7.31 (ddd, *J* = 7.9, 7.3, 1.3 Hz, 1 H), 4.10 (q, *J* = 2.5 Hz, 2 H), 1.84 (t, *J* = 2.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.5 (C), 153.0 (C), 135.4 (C), 126.1 (CH), 124.4 (CH), 121.7 (CH), 121.0 (CH), 80.6 (C), 73.0 (C), 22.5 (CH_2), 3.7 (CH_3).

Compound 18: *m*-Chloroperbenzoic acid (70% w/w, 22.2 g, 90 mmol) was added to a solution of thioether **S4** (5.0 g, 22.8 mmol) in CH_2Cl_2 (100 mL) and the resulting mixture stirred for 5 h. The reaction was carefully quenched with sat. aq. $NaHCO_3$ until a pH $\geq$ 8 was reached, the organic layer was successively washed with aq. sat. $NaHSO_3$, aq. sat. $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 7/3 $\rightarrow$ 0/1) to give compound **18** as a yellow solid (4.85 g, 85 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 8.1 Hz, 1 H), 8.03 (d, *J* = 7.9 Hz, 1 H), 7.68-7.59 (m, 2 H), 4.35 (q, *J* = 2.6 Hz, 2 H), 1.78 (t, *J* = 2.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3 (C), 152.6 (C), 137.2 (C), 128.1 (CH), 127.7 (CH), 125.6 (CH), 122.3 (CH), 85.9 (C), 65.0 (C), 47.6 (CH_2), 3.8 (CH_3); IR (film): 2958, 2915, 1769, 1697, 1597, 1575, 1552, 1462, 1418, 1325, 1317, 1307, 1263, 1145, 1130, 1086, 1028, 897, 853, 760, 748, 721, 692 cm^{-1}.

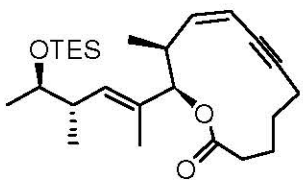
Compound 15: A solution of amide **12** (2.19 g, 5.9 mmol) in THF (20 mL + 15 mL rinse) was slowly added to a suspension of $LiAlH_4$ (0.36 g, 9.4 mmol) in THF (20 mL) at –78 °C and the resulting mixture was stirred at that temperature for 2 h and at 0 °C for 30 min. The reaction was quenched with acetone (5 mL) and poured into an ice-cold mixture of sat. aq. Rochelle's salt and Et_2O. The aqueous layer was extracted with Et_2O, the combined organic phases were washed with brine, dried over $MgSO_4$ and evaporated, affording aldehyde **13**, which was used in the next step without further purification.

A solution of KHMDS (2.0 g, 10 mmol) in THF (10 mL) was added to a solution of sulfone **18** (2.5 g, 10 mmol) in THF (30 mL) at –55 °C. The resulting dark red solution was stirred at this temperature for 30 min before a solution of the crude aldehyde **13** in THF (15 mL + 5 mL rinse) was slowly added. Stirring was continued at –55 °C for 22 h before the reaction was quenched with *tert*-butyl methyl ether and brine. The aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1/0 $\rightarrow$ 9/1) to give product **15** as a yellow liquid (1.22 g, 59 %). $[\alpha]_D^{20}$ = +117.5 (c = 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.56 (dd, *J* = 10.3, 10.3 Hz, 1 H), 5.33 (dq, *J* = 10.6, 2.4 Hz, 1 H), 5.22 (d, *J* = 9.6 Hz, 1 H), 3.83 (d, *J* = 7.9 Hz, 1 H), 3.72 (qd, *J* = 6.2, 3.7 Hz, 1 H), 2.99 (dqd, *J* = 9.8, 7.0, 6.9 Hz, 1 H), 2.41 (dqd, *J* = 9.8, 6.7, 3.6 Hz, 1 H), 1.95 (d, *J* = 2.2 Hz, 3 H), 1.63 (d, *J* = 1.3 Hz, 3 H), 1.57 (br s, 1 H), 1.06 (d, *J* = 6.8 Hz, 3 H), 0.99 (d, *J* = 6.3 Hz, 3 H), 0.98-0.91 (m, 12 H), 0.57 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.8 (CH), 136.3 (C), 129.9 (CH), 108.7 (CH), 89.6 (C), 81.8 (CH), 76.4 (C), 71.3 (CH), 39.2 (CH), 38.5 (CH), 20.4 (CH_3), 16.2 (CH_3), 15.8 (CH_3), 11.8 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2), 4.3 (CH_3); IR (film): 3425, 2957, 2915, 2876, 1456, 1414, 1375, 1296, 1238, 1165, 1130, 1092, 1064, 1003, 958, 909, 870, 838, 817, 774, 740, 723, 673 cm^{-1}; MS (EI): *m/z* (%): 350 (0.3) $[M]^+$, 159 (100), 147 (8), 131 (23), 115 (39), 103 (8), 87 (18), 75 (9), 59 (7), 43 (3); HRMS (ESI): *m/z* calcd for $C_{21}H_{38}O_2SiNa$ $[M + Na]^+$: 373.2533; found 373.2532.

Compound 20: Oct-6-ynoic acid (0.61 g, 4.4 mmol),[5] DMAP (0.54 g, 4.4 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI, 0.84 g, 4.4 mmol) were successively added to a solution of alcohol **15** (1.22 g, 3.5 mmol) in CH_2Cl_2 (20 mL) at 0 °C and the resulting mixture was stirred at this temperature for 30 min and at ambient temperature for 4 h. *tert*-Butyl methyl ether and brine were then added, the aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1/0 → 9/1) to give ester **20** as a yellow liquid (1.59 g, 96 %). $[\alpha]_D^{20}$ = +94.5 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.51 (dd, *J* = 10.5, 10.5 Hz, 1 H), 5.35 (dq, *J* = 10.8, 2.3 Hz, 1 H), 5.25 (d, *J* = 9.6 Hz, 1 H), 5.00 (d, *J* = 8.5 Hz, 1 H), 3.69 (qd, *J* = 6.2, 3.6 Hz, 1 H), 3.12 (dq, *J* = 14.0, 7.6 Hz, 1 H), 2.38 (dqd, *J* = 10.0, 6.6, 3.3 Hz, 1 H), 2.32 (t, *J* = 7.5 Hz, 2 H), 2.13 (tq, *J* = 6.9, 2.2 Hz, 2 H), 1.95 (d, *J* = 2.2 Hz, 3 H), 1.75 (t, *J* = 2.4 Hz, 3 H, overlap), 1.76-1.67 (m, 2 H, overlap), 1.61 (d, *J* = 1.0 Hz, 3 H), 1.54–1.42 (m, 2 H), 1.00-0.89 (m, 18 H), 0.56 (q, *J* = 7.8 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6 (C), 143.3 (CH), 132.1 (C), 131.7 (CH), 109.6 (CH), 90.0 (C), 82.1 (CH), 78.6 (C), 76.2 (C), 75.7 (C), 71.1 (CH), 39.2 (CH), 37.0 (CH), 34.1 (CH_2), 28.4 (CH_2), 24.2 (CH_2), 20.2 (CH_3), 18.4 (CH_2), 16.3 (CH_3), 15.5 (CH_3), 12.4 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2), 4.3 (CH_3), 3.4 (CH_3); IR (film): 2957, 2917, 2875, 1735, 1456, 1415, 1374, 1236, 1166, 1150, 1134, 1092, 1064, 1030, 1005, 959, 869, 836, 740, 724, 675 cm^{-1}; MS (EI): *m/z* (%): 472 (<0.1) $[M]^+$, 335 (7), 225 (8), 174 (11), 159 (100), 145 (3), 131 (17), 115 (31), 87 (15); HRMS (ESI): *m/z* calcd for $C_{29}H_{48}O_3SiNa$ $[M + Na]^+$: 495.3265; found 495.3264.



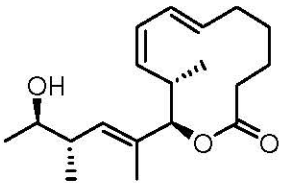
Compound 21: Activated molecular sieves (5 Å, ca. 2 g) were added to a solution of diyne **20** (284 mg, 0.6 mmol) in toluene (200 mL) and the resulting suspension heated to 80 °C before a solution of complex **27** (33 mg, 0.03 mmol) in toluene (3 mL) was introduced. The mixture was stirred at 80 °C for 3 h before it was allowed to reach ambient temperature. Insoluble materials were filtered off through a pad of silica which was carefully rinsed with ethyl acetate. The combined filtrates were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 1/0 → 95/5) to give cycloalkyne **21** as a yellow oil (240 mg, 95 %). When performed analogously with 1.59 g of diyne **20**, 1.18 g (84%) of the desired product **21** were obtained. $[\alpha]_D^{20}$ = +65.2 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 (dd, *J* = 10.5, 9.6 Hz, 1 H), 5.46 (d, *J* = 10.7 Hz, 1 H), 5.31 (d, *J* = 9.8 Hz, 1 H), 5.17 (d, *J* = 4.2 Hz, 1 H), 3.74 (qd, *J* = 5.9, 4.0 Hz, 1 H), 3.30 (dqd, *J* = 9.2, 6.6, 4.3 Hz, 1 H), 2.69 (ddd, *J* = 17.3, 12.0, 2.5 Hz, 1 H), 2.49-2.40 (m, 1 H, overlap), 2.42-2.33 (m, 2 H, overlap), 2.22 (dd, *J* = 17.3, 10.2 Hz, 1H), 2.13-2.00 (m, 1 H), 1.93-1.79 (m, 1 H), 1.62 (d, *J* = 1.3 Hz, 3 H, overlap), 1.69–1.58 (m, 2 H, overlap), 1.05 (d, *J* = 6.1 Hz, 3 H), 1.00-0.91 (m, 15 H), 0.57 (q, *J* = 7.9 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7 (C), 143.9 (CH), 133.6 (CH), 129.9 (C), 110.8 (CH), 94.9 (C), 82.1 (CH), 79.3 (C), 71.4



[5] Song, D.; Blond, G.; Fürstner, A. *Tetrahedron* **2003**, *59*, 6899-6904.

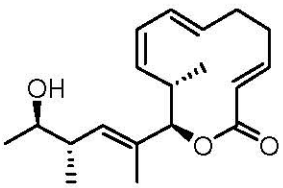
(CH), 39.5 (CH), 37.1 (CH), 32.3 (CH_2), 26.5 (CH_2), 23.9 (CH_2), 20.9 (CH_3), 18.7 (CH_2), 17.2 (CH_3), 16.1 (CH_3), 14.5 (CH_3), 6.9 (3 x CH_3), 5.0 (3 x CH_2); IR (film): 2958, 2932, 2875, 1730, 1455, 1416, 1376, 1344, 1260, 1241, 1194, 1152, 1130, 1100, 1088, 1028, 1006, 973, 909, 803, 767, 726, 699 cm^{-1}; MS (EI): *m/z* (%): 418 (15) [*M*+], 176 (14), 162 (85), 159 (100), 131 (27), 115 (58), 89 (37), 87 (38), 93 (65), 75 (23), 59 (17), 41 (12); HRMS (ESI): *m/z* calcd for $C_{25}H_{42}O_3SiNa$ [M + Na]$^+$: 441.2795; found 441.2789.

Compound 23: [Cp*Ru(MeCN)$_3$]PF$_6$ (30 mg, 0.059 mmol) and benzyldimethylsilane (0.28 mL, 1.77 mmol) were successively added to a solution of cycloalkyne **21** (247 mg, 0.59 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C. The mixture was stirred at this temperature for 20 min until the catalyst had fully dissolved, and for 1 h at ambient temperature. Next, the solvent was slowly evaporated by a stream of Ar, until TLC indicated complete conversion (ca. 30 min). The residue was purified by flash chromatography (hexanes/EtOAc, 95/5 → 90/10) to give product **22**, which was directly used in the next step.



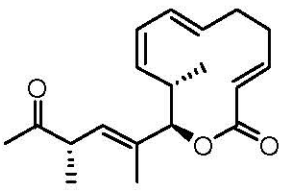
A solution of anhydrous TBAF (1 M in THF, 2.3 mL, 2.3 mmol) was added at 0°C to a solution of alkenylsilane **22** in THF (0.5 mL) and the resulting orange mixture stirred at ambient temperature for 2 h before it was filtered through a pad of silica which was carefully rinsed with ethyl acetate. The combined filtrates were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 90/10 → 85/15) to remove traces of the undesired (*Z*,*Z*)-diene isomer. Product **23** was thus obtained as a colorless oil (115 mg, 64 %). $[\alpha]_D^{20} = -85.8$ (c = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.21 (dd, *J* = 15.3, 10.8 Hz, 1 H), 6.11 (dd, *J* = 10.3, 10.3 Hz, 1 H), 5.74 (dt, *J* = 15.5, 5.2 Hz, 1 H), 5.23 (d, *J* = 9.8 Hz, 1 H), 5.13 (d, *J* = 5.0 Hz, 1 H), 5.05 (dd, *J* = 9.9, 9.9 Hz, 1 H), 3.58 (qd, *J* = 6.2, 6.2 Hz, 1 H), 3.42-3.29 (m, 1 H), 2.40 (ddq, *J* = 9.9, 6.8, 6.6 Hz, 1 H), 2.34-2.26 (m, 3 H), 2.05-1.93 (m, 2 H), 1.64 (d, *J* = 1.4 Hz, 3 H), 1.60-1.46 (m, 3 H), 1.16 (d, *J* = 6.2 Hz, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1 (C), 133.1 (CH), 132.8 (C), 131.3 (CH), 131.1 (CH), 130.1 (CH), 126.5 (CH), 83.1 (CH), 71.5 (CH), 39.9 (CH), 33.3 (CH), 33.2 (CH_2), 30.3 (CH_2), 23.9 (CH_2), 23.0 (CH_2), 20.2 (CH_3), 17.8 (CH_3), 16.3 (CH_3), 14.6 (CH_3); IR (film): 3421, 2967, 2931, 2874, 1722, 1452, 1376, 1245, 1158, 1090, 996, 972, 876, 770, 735, 701 cm^{-1}; MS (EI): *m/z* (%): 306 (1) [*M*+], 164 (100), 149 (7), 136 (23), 135 (20), 120 (59), 107 (24), 94 (24), 79 (32), 68 (25), 55 (13), 41 (18); HRMS (ESI): *m/z* calcd for $C_{19}H_{30}O_3Na$ [M + Na]$^+$: 329.2087; found 329.2091.

Compound S5: *n*BuLi (1.6 M in hexane, 0.48 mL, 0.70 mmol) was added dropwise to a solution of diisopropylamine (0.1 mL, 0.70 mmol) in THF at –78 °C. The resulting yellow solution was stirred at that temperature for 15 min before a solution of compound **23** (54 mg, 0.18 mmol) in THF (1 mL + 1 mL rinse) was added via canula. The resulting mixture was stirred at –20 °C for 20 min before it was warmed to 0 °C, causing a color change to orange. After 10 min, the mixture was cooled to –78 °C and PhSeBr (85 mg, 0.36 mmol) was introduced. The solution was slowly warmed to 0 °C and stirred for 2 h before the reaction was quenched with sat. aq. NH_4Cl. The aqueous phase was extracted with



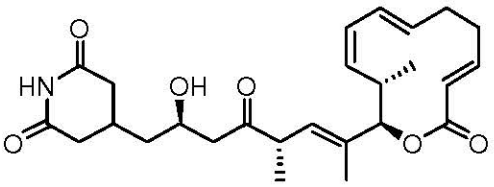
tert-butyl methyl ether, and the combined organic layers were dried over $MgSO_4$ and evaporated to give selenide **24** as a yellow oil, which was directly used in the next step.
A solution of *m*-chloroperbenzoic acid (70 % *w/w*, 88 mg, 0.36 mmol) in CH_2Cl_2 (1 mL) was added to a solution of crude **24** in CH_2Cl_2 (5 mL) at –78°C. After stirring for 1 h at this temperature, diisopropylethylamine (0.12 mL, 0.72 mmol) was introduced and the mixture warmed to ambient temperature. After stirring for 1 h, hexane was added, the solvents were evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 90/10 → 80/20) to give product **S5** as a yellow oil (35 mg, 64 %). $[\alpha]_D^{20} = -232.7$ (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.47 (ddd, *J* = 16.0, 10.4, 5.4 Hz, 1 H), 6.04 (dd, *J* = 10.8, 10.8 Hz, 1 H), 5.74 (dd, *J* = 15.6, 10.6 Hz, 1 H), 5.55 (d, *J* = 16.1 Hz, 1 H), 5.40 (ddd, *J* = 15.3, 8.8, 6.6 Hz, 1 H), 5.35 (d, *J* = 4.5 Hz, 1 H, overlap), 5.33 (d, *J* = 9.5 Hz, 1 H, overlap), 5.10 (dd, *J* = 10.9, 10.9 Hz, 1 H), 3.60 (qd, *J* = 6.2, 6.2 Hz, 1 H), 3.09 (ddq, *J* = 11.7, 6.2, 5.8 Hz, 1 H), 2.59-2.49 (m, 2 H), 2.44 (dqd, *J* = 9.4, 6.5, 3.7 Hz, 1 H), 2.01-1.84 (m, 2 H), 1.72 (d, *J* = 1.2 Hz, 3 H), 1.55 (br s, 1 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 0.99 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7 (C), 146.4 (CH), 134.5 (CH), 133.1 (CH), 131.9 (C), 131.7 (CH), 128.9 (CH), 128.3 (CH), 127.7 (CH), 83.3 (CH), 71.5 (CH), 40.0 (CH), 35.7 (CH), 32.2 (CH_2), 31.1 (CH_2), 20.3 (CH_3), 17.5 (CH_3), 16.4 (CH_3), 14.9 (CH_3); IR (film): 3453, 2964, 2928, 2872, 1709, 1641, 1451, 1376, 1336, 1313, 1259, 1190, 1141, 1085, 1005, 957, 923, 848, 800, 736, 691 cm^{-1}; MS (EI): *m/z* (%): 304 (2) [*M*+], 162 (7), 94 (100), 79 (41), 68 (12), 55 (4), 41 (9); HRMS (ESI): *m/z* calcd for $C_{19}H_{28}O_3Na$ [M + Na]$^+$: 327.1931; found 327.1931.

Compound 25: Dess-Martin periodinane (52 mg, 0.12 mmol)[6] was added to a solution of alcohol **S5** (25 mg, 0.08 mmol) in CH_2Cl_2 (4 mL) at 0 °C. The mixture was stirred at ambient temperature for 1 h 15 min before the solvent was evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 90/10 → 80/20), affording product **25** as a yellow oil (21 mg, 87 %). $[\alpha]_D^{20} = -3.9$ (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.48 (ddd, *J* = 16.0, 10.4, 5.4 Hz, 1 H), 6.05 (dd, *J* = 10.8, 10.8 Hz, 1 H), 5.73 (dd, *J* = 15.6, 10.7 Hz, 1 H), 5.55 (d, *J* = 16.1 Hz, 1 H), 5.41 (ddd, *J* = 15.6, 8.9, 6.5 Hz, 1 H, overlap), 5.39-5.31 (m, 2 H, overlap), 5.08 (dd, *J* = 10.9, 10.9 Hz, 1 H), 3.43 (dq, *J* = 9.4, 6.9 Hz, 1 H), 3.10 (dqd, *J* = 11.7, 6.4, 3.2 Hz, 1 H), 2.60-2.46 (m, 2 H), 2.14 (s, 3 H), 2.02-1.85 (m, 2 H), 1.78 (d, *J* = 1.3 Hz, 3 H), 1.17 (d, *J* = 6.8 Hz, 3 H), 0.92 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.0 (C), 166.5 (C), 146.6 (CH), 134.5 (CH), 133.3 (C), 131.4 (CH), 129.8 (CH), 129.1 (CH), 128.2 (CH), 127.8 (CH), 82.6 (CH), 46.8 (CH), 36.0 (CH), 32.2 (CH_2), 31.2 (CH_2), 27.9 (CH_3), 17.3 (CH_3), 16.1 (CH_3), 14.9 (CH_3); IR (film): 2965, 2931, 2872, 1713, 1642, 1453, 1373, 1353, 1313, 1244, 1188, 1140, 1088, 1001, 957, 872, 848, 829, 799, 768, 733, 701 cm^{-1}; MS (EI): *m/z* (%): 302 (1) [*M*+], 162 (8), 94 (100), 79 (42), 68 (12), 53 (2), 43 (11); HRMS (ESI): *m/z* calcd for $C_{19}H_{26}O_3Na$ [M + Na]$^+$: 325.1774; found 327.1775.



[6] (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155-4156. (b) Meyer, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549-7552.

Lactimidomycin (3): Me_3SiCl (36 µL, 0.28 mmol) and triethylamine (39 µL, 0.28 mmol) were added to a solution of ketone **25** (8.5 mg, 0.028 mmol) in THF (1 mL) at –78 °C. Next, LiHMDS (1 M in THF, 56 µL, 0.056 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate buffer and the product extracted with CH_2Cl_2 (3 x 1 mL). The combined organic phases were dried over $MgSO_4$ and evapoprated to give the corresponding silyl enol ether, which was used in the next step without further purification.



Molecular sieves (4 Å, ca. 100 mg) and aldehyde **28** (4.4 mg, 0.028 mmol)[7] were added to a solution of the crude silyl enol ether in propionitrile (0.5 mL). The mixture was cooled to –78 °C before a solution of compound **29** [prepared upon stirring of a solution of $PhBCl_2$ (3.7 µL, 0.028 mmol) and N-tosyl-*D*-tryptophane (10 mg, 0.028 mmol) in CH_2Cl_2 (0.25 mL) for 1 h, followed by removal of the solvent][8] in propionitrile (0.15 mL) was added dropwise. After stirring for 19 h at –78°C, the reaction was quenched with sat. aq. $NaHCO_3$ (1 mL), the aqueous phase extracted with CH_2Cl_2 (3 x 3 mL), and the combined organic layers were dried over $MgSO_4$ and evaporated. The resulting crude product **26** was dissolved in THF (5 mL) at 0 °C and treated with 0.5 mL of a stock solution of buffered HF·pyridine [prepared from THF (7.25 mL), pyridine (2.69 mL) and HF·pyridine complex (0.54 mL, 70% w/w)]. The mixture was stirred at 0 °C for 2 h and warmed to ambient temperature for 30 min to complete the desilylation. Dilution with CH_2Cl_2 (20 mL), washing of the organic layer with sat. aq. $NaHCO_3$ (10 mL) and $CuSO_4$ solution (1 M, 3 x 10 mL), drying over $MgSO_4$ and evaporation of the solvents left a residue, which was purified by preparative TLC (EtOAc/hexanes, 80/20) to give product **3** as a white solid (7.5 mg, 60 %). $[\alpha]_D^{20} = +6.9$ (c = 0.5, DMSO);[9] $[\alpha]_D^{20} = -7.0$ (c = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.99 (br s, 1 H), 6.47 (ddd, *J* = 16.1, 10.2, 5.2 Hz, 1 H), 6.05 (dd, *J* = 10.8, 10.8 Hz, 1 H), 5.71 (dd, *J* = 15.6, 10.7 Hz, 1 H), 5.54 (d, *J* = 16.1 Hz, 1 H), 5.41 (ddd, *J* = 15.6, 9.1, 6.2 Hz, 1 H), 5.36-5.32 (m, 2 H, overlap), 5.05 (dd, *J* = 10.9, 10.9 Hz, 1 H), 4.13-4.08 (m, 1 H), 3.42 (dq, *J* = 9.7, 6.8 Hz, 1 H), 3.15-3.05 (m, 1 H), 2.82-2.70 (m, 2 H), 2.59-2.56 (m, 2 H), 2.56-2.44 (m, 3 H), 2.37-2.27 (m, 2 H), 2.02-1.85 (m, 2 H), 1.77 (d, *J* = 1.3 Hz, 3 H), 1.60 (ddd, *J* = 14.1, 10.5, 4.9 Hz, 1 H), 1.32 (ddd, *J* = 14.0, 8.9, 2.8 Hz, 1 H), 1.18 (d, *J* = 6.8 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.5 (C), 172.2 (C), 172.1 (C), 166.7 (C), 147.0 (CH), 134.5 (CH), 134.0 (C), 131.2 (CH), 129.5 (CH), 129.0 (CH), 128.3 (CH), 128.2 (CH), 82.4 (CH), 64.8 (CH), 47.5 (CH_2), 46.7 (CH), 40.8 (CH_2), 38.5 (CH_2), 37.2 (CH_2), 36.0 (CH), 32.4 (CH_2), 31.3 (CH_2), 27.1 (CH), 17.6 (CH_3), 16.2 (CH_3), 15.4 (CH_3); IR (film): 3481, 3239, 2925, 2852, 1695,

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[7] Egawa, Y.; Suzuki, M.; Okuda, T. *Chem. Pharm. Bull.* **1963**, *11*, 589.

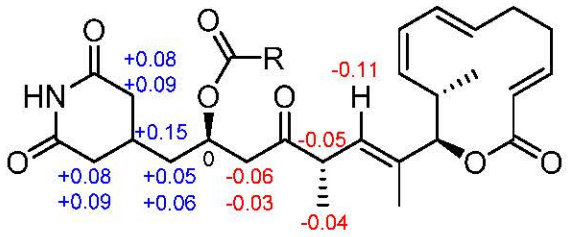
[8] Ishihara, K.; Kondo, S.; Yamamoto, H. *J. Org. Chem.* **2000**, *65*, 9125.

[9] The original isolation paper reports: $[\alpha]_D^{20} = -20$ (c = 0.5, DMSO), cf. Sugawara, K.; Nishiyama, Y.; Toda, S.; Komiyama, N.; Hatori, M.; Moriyama, T.; Sawada, Y.; Kamei, H.; Konishi, M.; Oki, T. *J. Antibiot.* **1992**, *45*, 1433. It seems, however, that this value is incorrect. Prof. B. Shen, University of Wisconsin, kindly informed us that the optical rotation of authentic lactimidomycin produced by the original strain deposited at ATCC is in fact positive in DMSO.

1453, 1376, 1259, 1190, 1145, 1084, 1003, 829, 796, 767, 733, 701 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{26}H_{35}NO_6Na$ $[M + Na]^+$: 480.2357; found 480.2363.

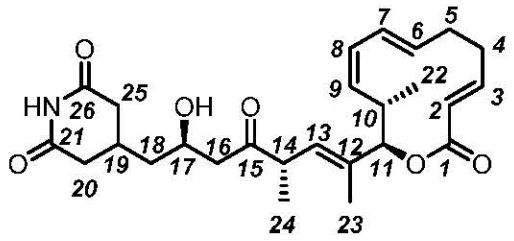
(*R*)-Mosher-ester: ^1H NMR (600 MHz, $CDCl_3$): δ = 7.73 (br s, 1 H), 7.48 (m, 2 H), 7.39 (m, 3 H), 6.47 (ddd, *J* = 15.9, 10.3, 5.4 Hz, 1 H), 6.03 (dd, *J* = 10.8, 10.8 Hz, 1 H), 5.70 (dd, *J* = 15.9, 10.9 Hz, 1 H), 5.52 (d, *J* = 16.1 Hz, 1 H), 5.47 (m, 1 H), 5.41 (m, 1 H), 5.30 (d, *J* = 4.4 Hz, 1 H), 5.28 (d, *J* = 10.3 Hz, 1 H), 5.01 (dd, *J* = 11.0, 11.0 Hz, 1 H), 3.50 (s, 3 H), 3.39 (m, 1 H), 3.07 (m, 1 H), 2.98 (dd, *J* = 17.7, 6.0 Hz, 1 H), 2.70 (m, 1 H), 2.63 (dd, *J* = 17.6, 6.6 Hz, 1 H), 2.56 (m, 1 H), 2.52 (m, 1 H), 2.51 (m, 1 H), 1.83 (m, 1 H), 1.75 (d, *J* = 1.5 Hz, 3 H), 1.71 (m, 1 H), 1.59 (m, 1 H), 1.14 (d, *J* = 6.8 Hz, 3 H), 0.84 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 207.0 (C), 171.2 (C), 171.0 (C), 166.7 (C), 166.2 (C), 147.0 (CH), 134.5 (CH), 134.2 (C), 132.0 (C), 131.2 (CH), 130.0 (CH), 129.5 (CH), 129.0 (CH), 128.8 (CH), 128.2 (CH), 128.2 (CH), 127.1 (CH), 82.4 (CH), 69.5 (CH), 55.7 (CH_3), 46.4 (CH), 44.5 (CH_2), 39.1 (CH_2), 38.1 (CH_2), 36.9 (CH_2), 36.0 (CH), 32.4 (CH_2), 31.3 (CH_2), 26.7 (CH), 17.5 (CH_3), 16.0 (CH_3), 15.4 (CH_3).

(*S*)-Mosher-ester: ^1H NMR (600 MHz, $CDCl_3$): δ = 7.74 (br s, 1 H), 7.47 (m, 2 H), 7.41 (m, 3 H), 6.47 (ddd, *J* = 15.9, 10.4, 5.3 Hz, 1 H), 6.04 (dd, *J* = 10.6, 10.6 Hz, 1 H), 5.71 (dd, *J* = 15.6, 10.6 Hz, 1 H), 5.53 (d, *J* = 16.1 Hz, 1 H), 5.47 (m, 1 H), 5.42 (m, 1 H), 5.29 (d, *J* = 5.0 Hz, 1 H), 5.17 (d, *J* = 9.5 Hz, 1 H), 5.04 (dd, *J* = 11.0, 11.0 Hz, 1 H), 3.45 (s, 3 H), 3.34 (m, 1 H), 3.09 (m, 1 H), 2.95 (dd, *J* = 17.6, 6.1 Hz, 1 H), 2.78 (m, 1 H), 2.60 (m, 1 H), 2.57 (m, 1 H), 2.56 (m, 1 H), 2.52 (m, 1 H), 1.98 (m, 1 H), 1.76 (m, 1 H), 1.74 (d, *J* = 1.3 Hz, 3 H), 1.65 (m, 1 H), 1.10 (d, *J* = 7.0 Hz, 3 H), 0.87 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.9 (C), 171.1 (C), 171.0 (C), 166.7 (C), 166.1 (C), 146.9 (CH), 134.6 (CH), 134.1 (C), 131.7 (C), 131.3 (CH), 130.0 (CH), 129.5 (CH), 129.0 (CH), 128.8 (CH), 128.3 (CH), 128.1 (CH), 127.4 (CH), 82.5 (CH), 69.9 (CH), 55.4 (CH_3), 46.5 (CH), 44.2 (CH_2), 39.1 (CH_2), 38.2 (CH_2), 37.1 (CH_2), 36.0 (CH), 32.4 (CH_2), 31.3 (CH_2), 27.1 (CH), 17.5 (CH_3), 15.9 (CH_3), 15.2 (CH_3).



Scheme S-1. Mosher ester analysis: Shift differences $\delta_S - \delta_R$ in ppm.

Table S-1. Comparison of the recorded ^{1}H NMR data ($CDCl_3$) of lactimidomycin with those reported in the literature;[10] numbering scheme as shown in the Insert.

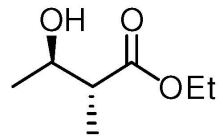


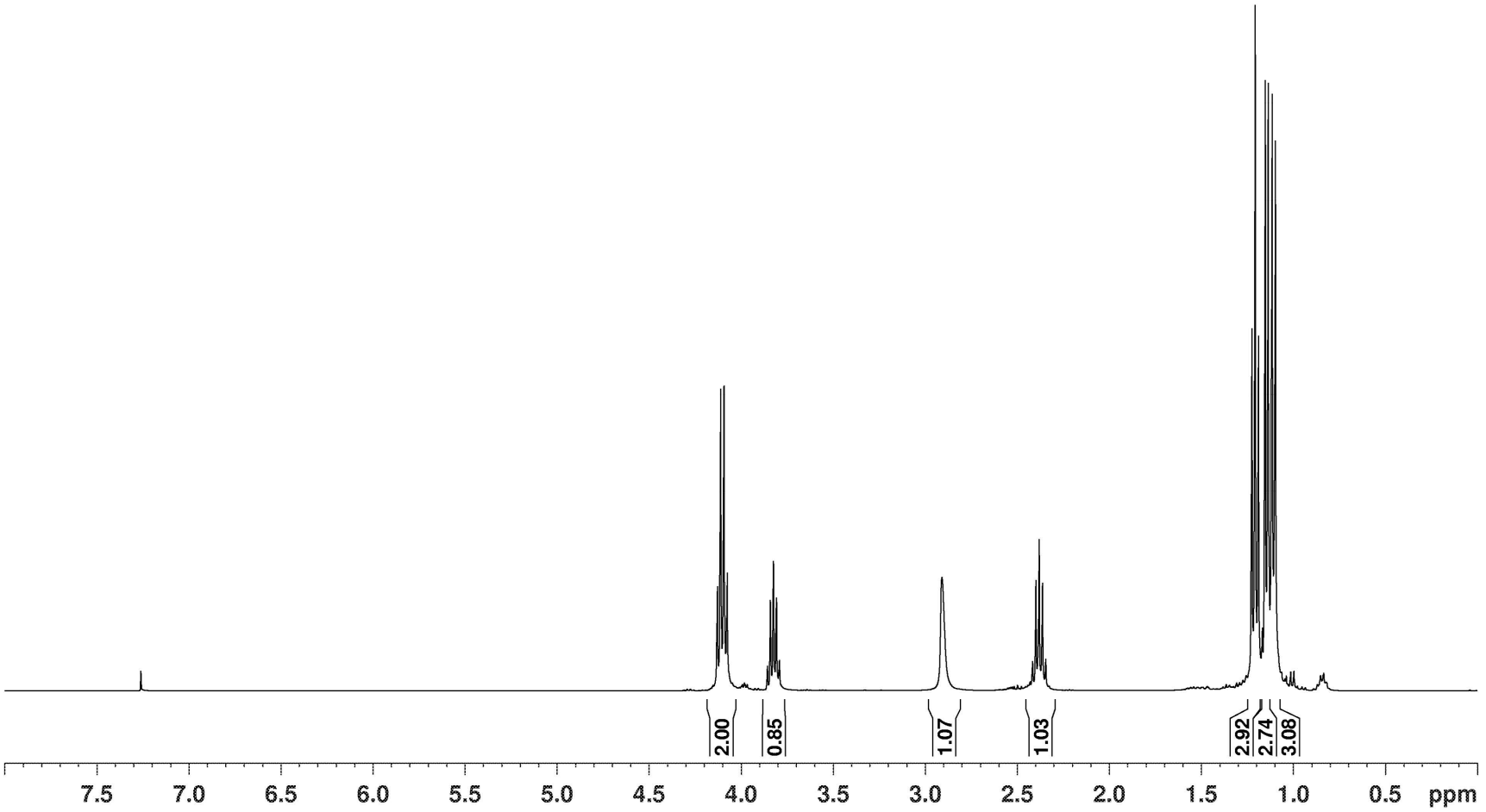
Position	Literature (500 MHz) δ (in ppm) mult. (*J* in Hz)	Experimental (600 MHz) δ (in ppm) mult. (*J* in Hz)	Δδ
2	5.53 d (16.0)	5.54 d (16.1)	+0.01
3	6.49 ddd (16.0, 10.0, 5.0)	6.47 ddd (16.1, 10.2, 5.2)	-0.02
4	1.96 m/2.56 m	1.95 m/2.56 m	-0.01/0
5	1.96 m/2.54 m	1.92 m/2.52 m	-0.04/-0.02
6	5.42 m	5.41 ddd (15.6, 9.1, 6.2)	-0.01
7	5.72 dd (15.5, 10.5)	5.71 dd (15.6, 10.7)	-0.01
8	6.06 t (11.0)	6.05 t (10.8)	-0.01
9	5.06 t (11.0)	5.05 t (10.9)	-0.01
10	3.11 m	3.10 m	-0.01
11	5.34 m	5.34 m	0
13	5.34 m	5.34 m	0
14	3.44 m	3.42 dq (9.7, 6.8)	-0.02
16	2.59 m	2.58 m	-0.01
17	4.12 m	4.11 m	-0.01
18	1.33 ddd (14.0, 9.0, 3.0)	1.32 ddd (14.0, 8.9, 2.8)	-0.01
	1.60 ddd (14.0, 10.5, 4.5)	1.60 ddd (14.1, 10.5, 4.9)	0
19	2.48 m	2.49 m	+0.01
20	2.34 m/2.76 m	2.34 m/2.76 m	0/0
22	0.92 d (6.5)	0.91 d (6.8)	-0.01
23	1.78 d (1.5)	1.77 d (1.3)	-0.01
24	1.19 d (7.0)	1.18 d (6.8)	-0.01
25	2.32 m/2.80 m	2.32 m/2.78 m	0/-0.02
NH	7.98 br s	7.99 br s	+0.01

[10] Ju, J.; Seo, J.-W.; Her, Y.; Lim, S.-K.; Shen, B. *Org. Lett.* **2007**, *9*, 5183-5186.

Table S-2. Comparison of the recorded ^{13}C NMR data (δ in ppm, $CDCl_3$) of lactimidomycin with those reported in the literature.[10]

Position	Literature (125 MHz)	Experimental (150 MHz)	Δδ
1	166.7	166.7	0
2	128.4	128.3	-0.1
3	147.0	147.0	0
4	32.4	32.4	0
5	31.4	31.3	-0.1
6	128.2	128.2	0
7	134.6	134.5	-0.1
8	129.6	129.5	-0.1
9	131.1	131.2	+0.1
10	36.1	36.0	-0.1
11	82.5	82.4	-0.1
12	134.1	134.0	-0.1
13	129.1	129.0	-0.1
14	46.8	46.7	-0.1
15	212.5	212.5	0
16	47.6	47.5	-0.1
17	64.9	64.8	-0.1
18	40.9	40.8	-0.1
19	27.3	27.1	-0.2
20	38.6	38.5	-0.1
21	172.2	172.2	0
22	17.7	17.6	-0.1
23	15.4	15.4	0
24	16.3	16.2	-0.1
25	37.3	37.2	-0.1
26	172.1	172.1	0


OH
O
OEt


2.00
0.85
1.07
1.03
2.92
2.74
3.08
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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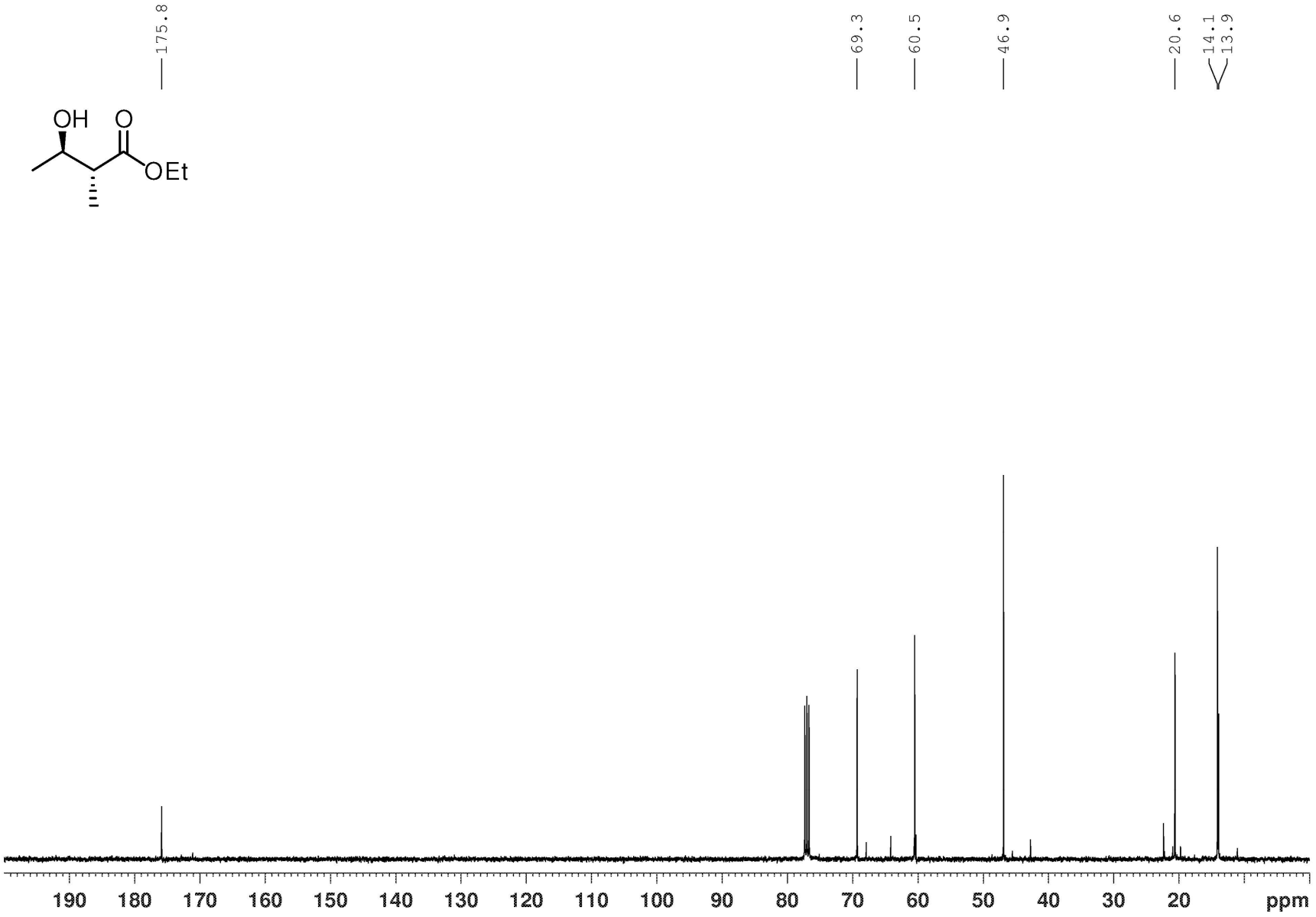
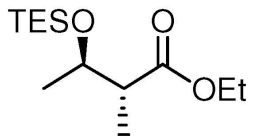
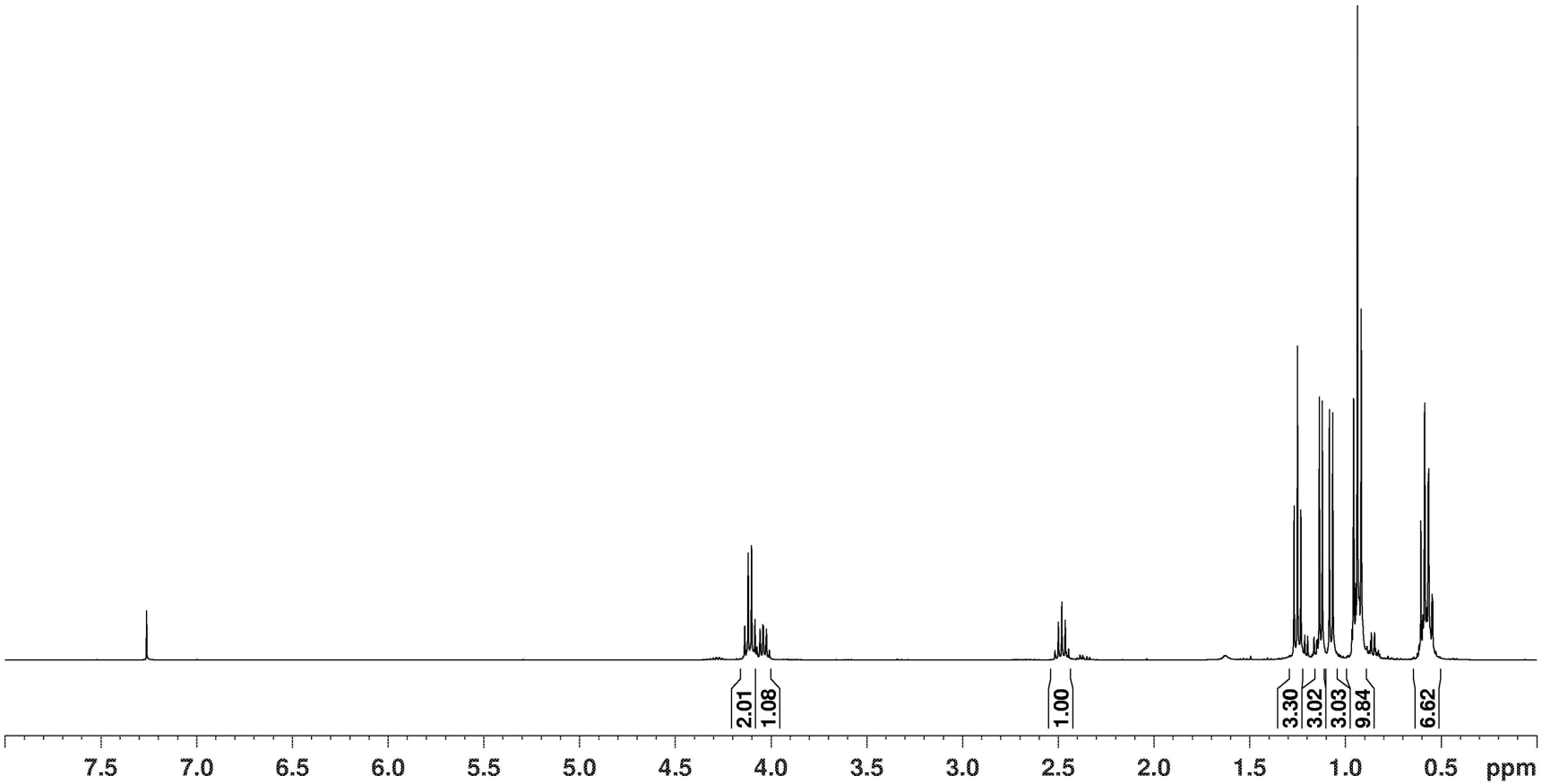
2.0
1.5
1.0
0.5
ppm


175.8
69.3
60.5
46.9
20.6
14.1
13.9
OH
O
OEt
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


TESO
O
OEt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3.02
3.03
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6.5
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4.0
3.5
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2.0
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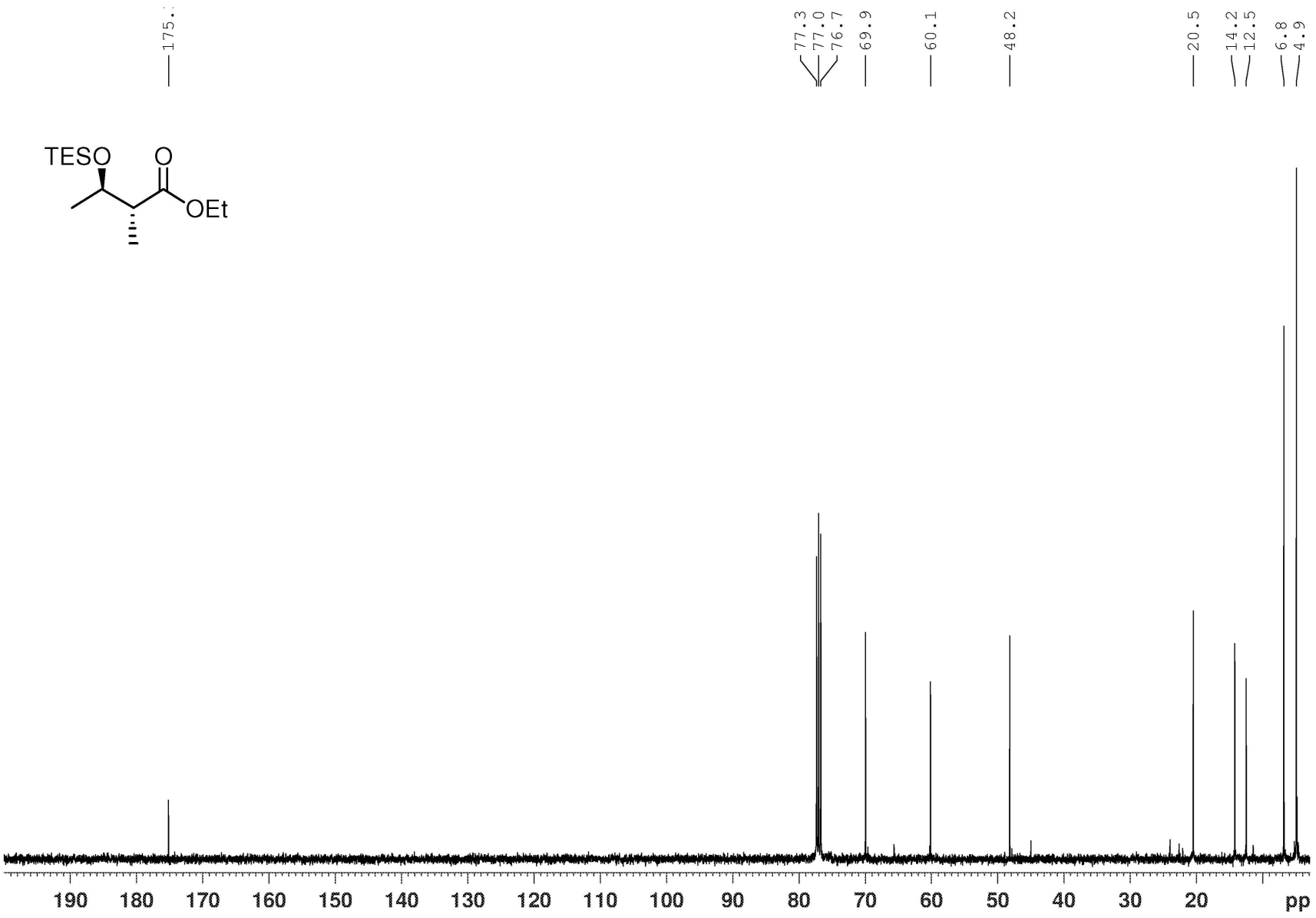
1.0
0.5
ppm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77.0
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69.9
60.1
48.2
20.5
14.2
12.5
6.8
4.9
TESO
O
OEt
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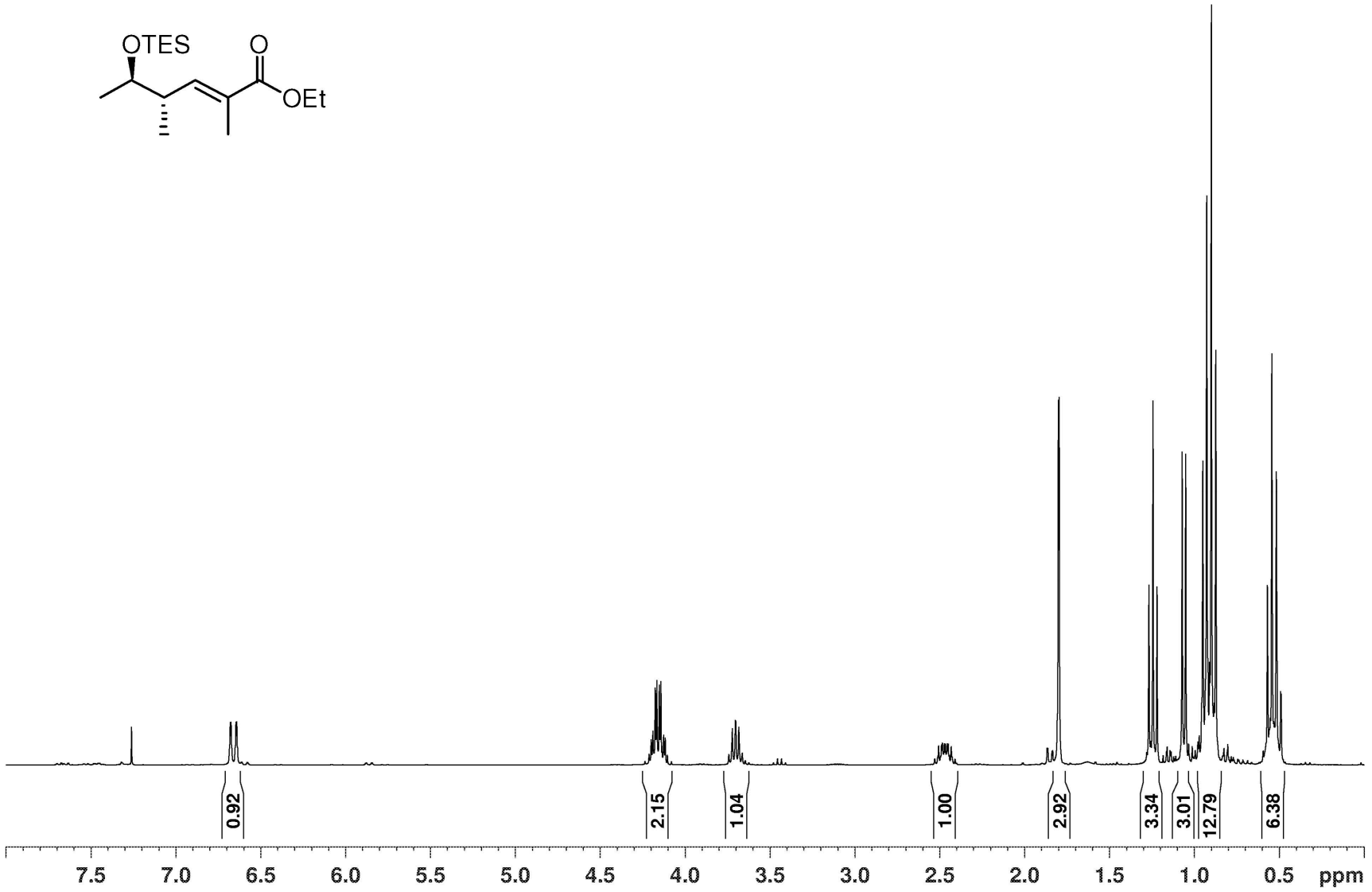
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
pp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O
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1.00
2.92
3.34
3.01
12.79
6.38
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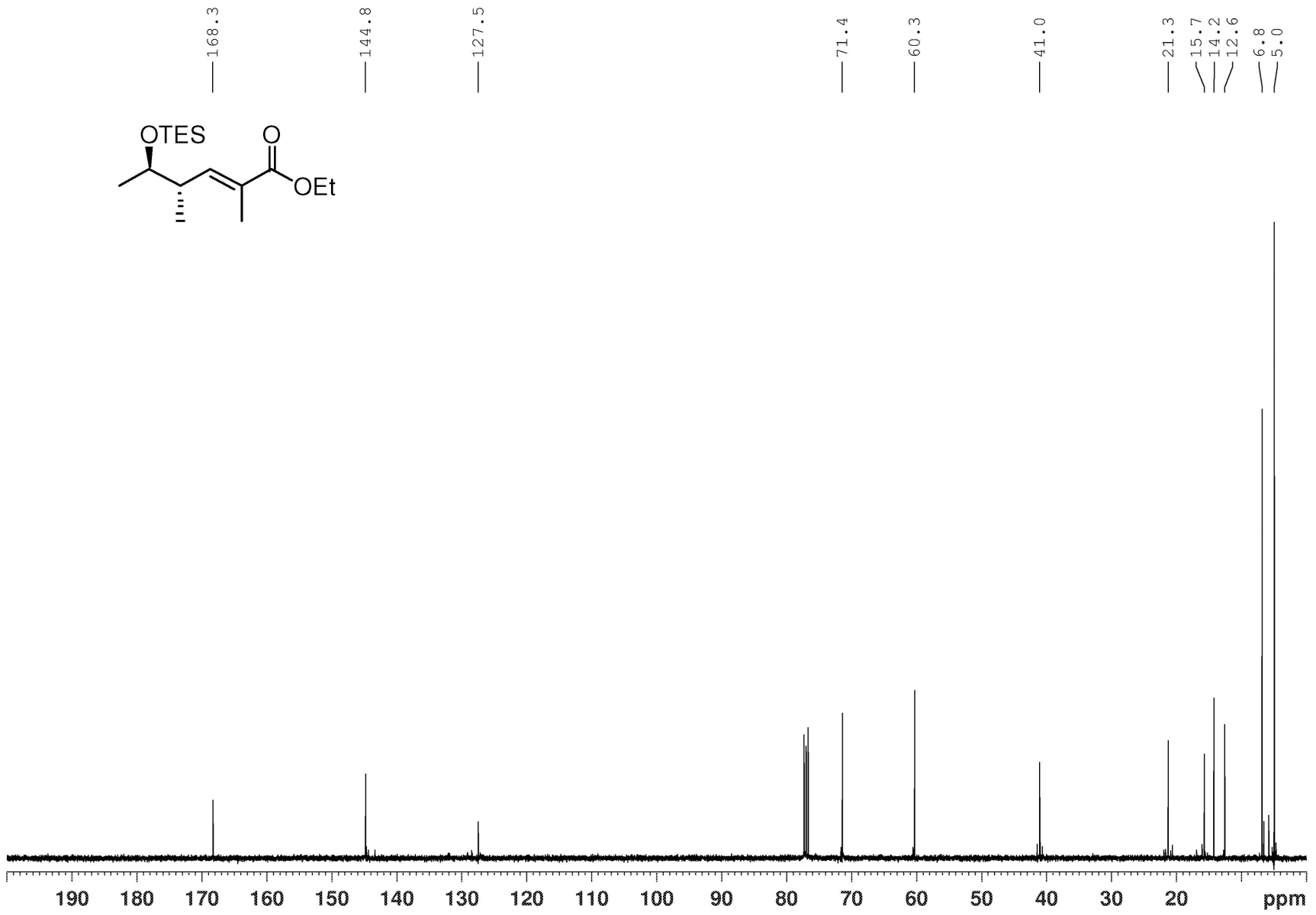
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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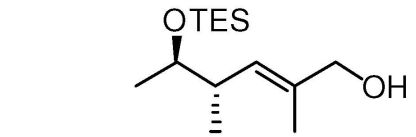
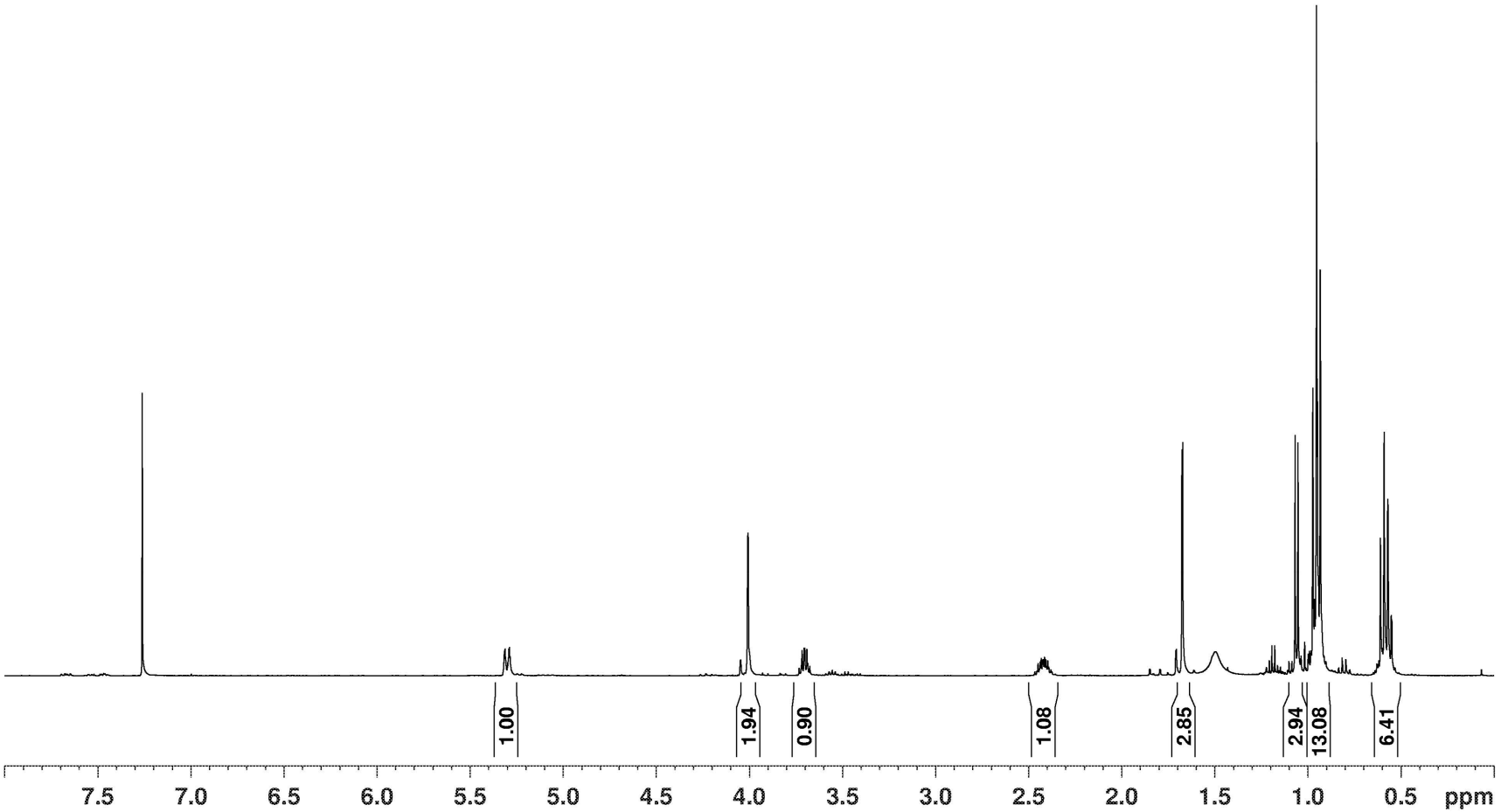
144.8
127.5
71.4
60.3
41.0
21.3
15.7
14.2
12.6
6.8
5.0
OTES
O
OEt
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


OTES
OH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6.5
6.0
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4.0
3.5
3.0
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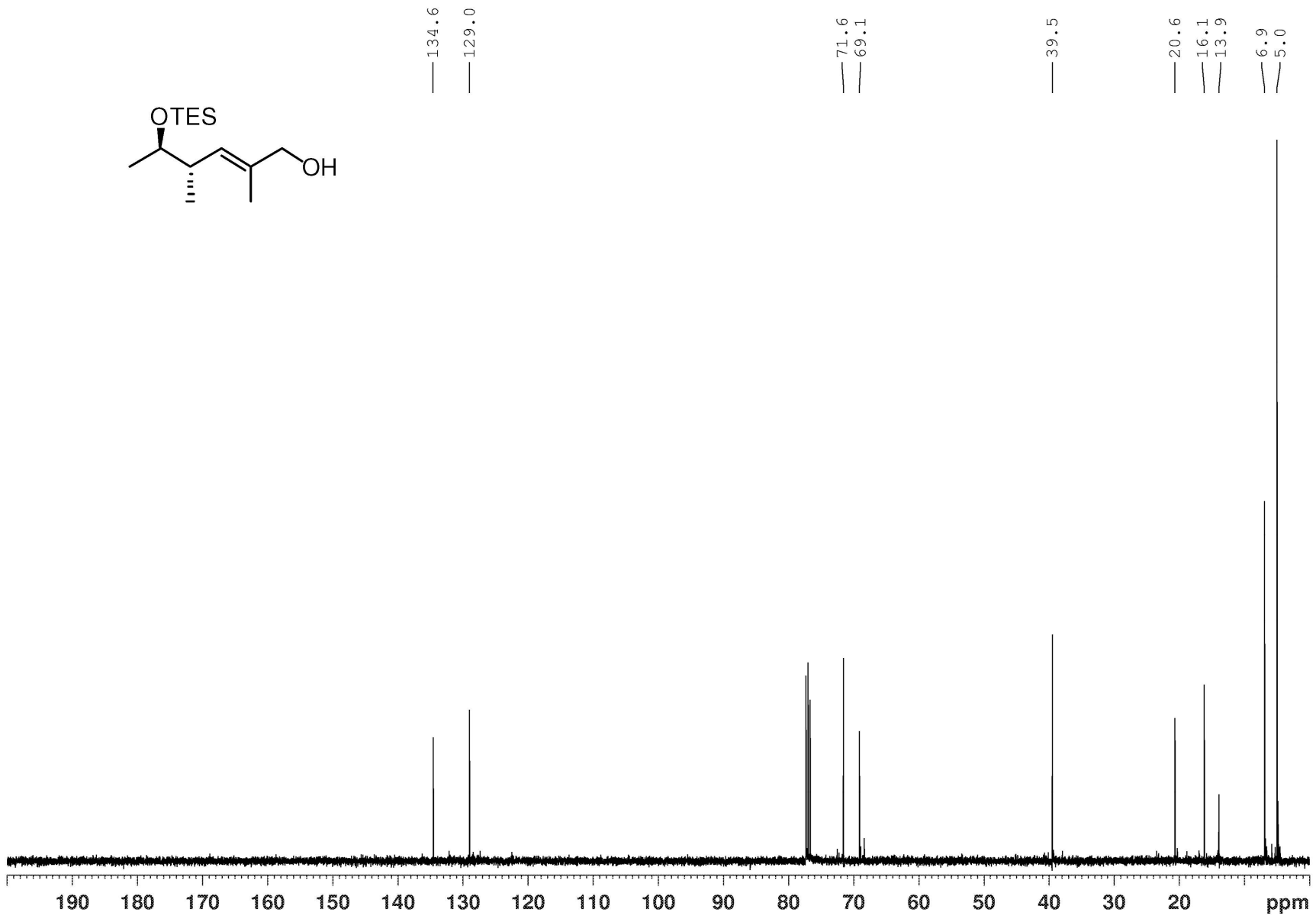
2.0
1.5
1.0
0.5
ppm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39.5
20.6
16.1
13.9
6.9
5.0
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OH
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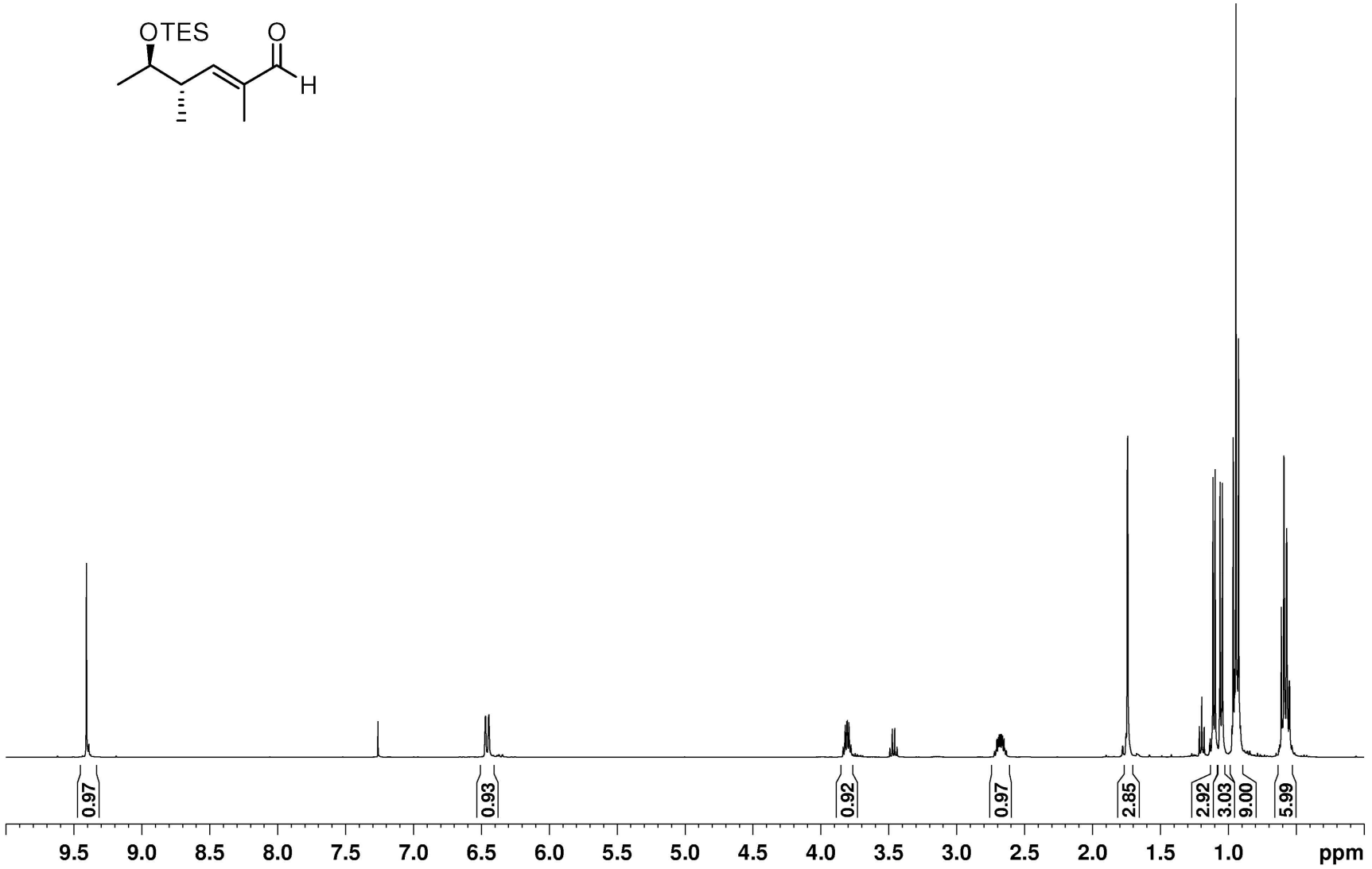
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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H
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0.97
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2.92
3.03
9.00
5.99
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7.0
6.5
6.0
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4.5
4.0
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2.5
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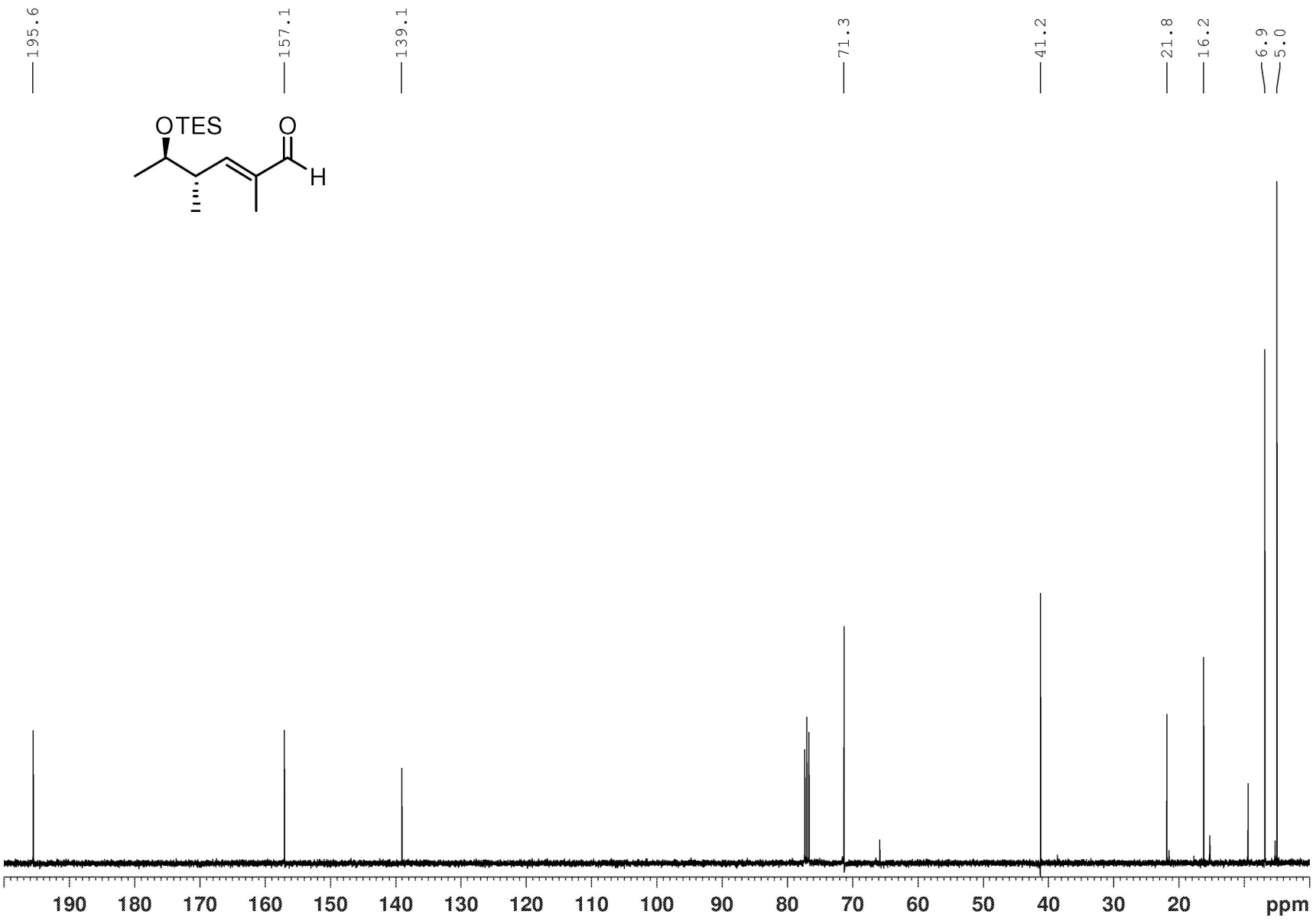
1.5
1.0
ppm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6.9
5.0
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H
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180
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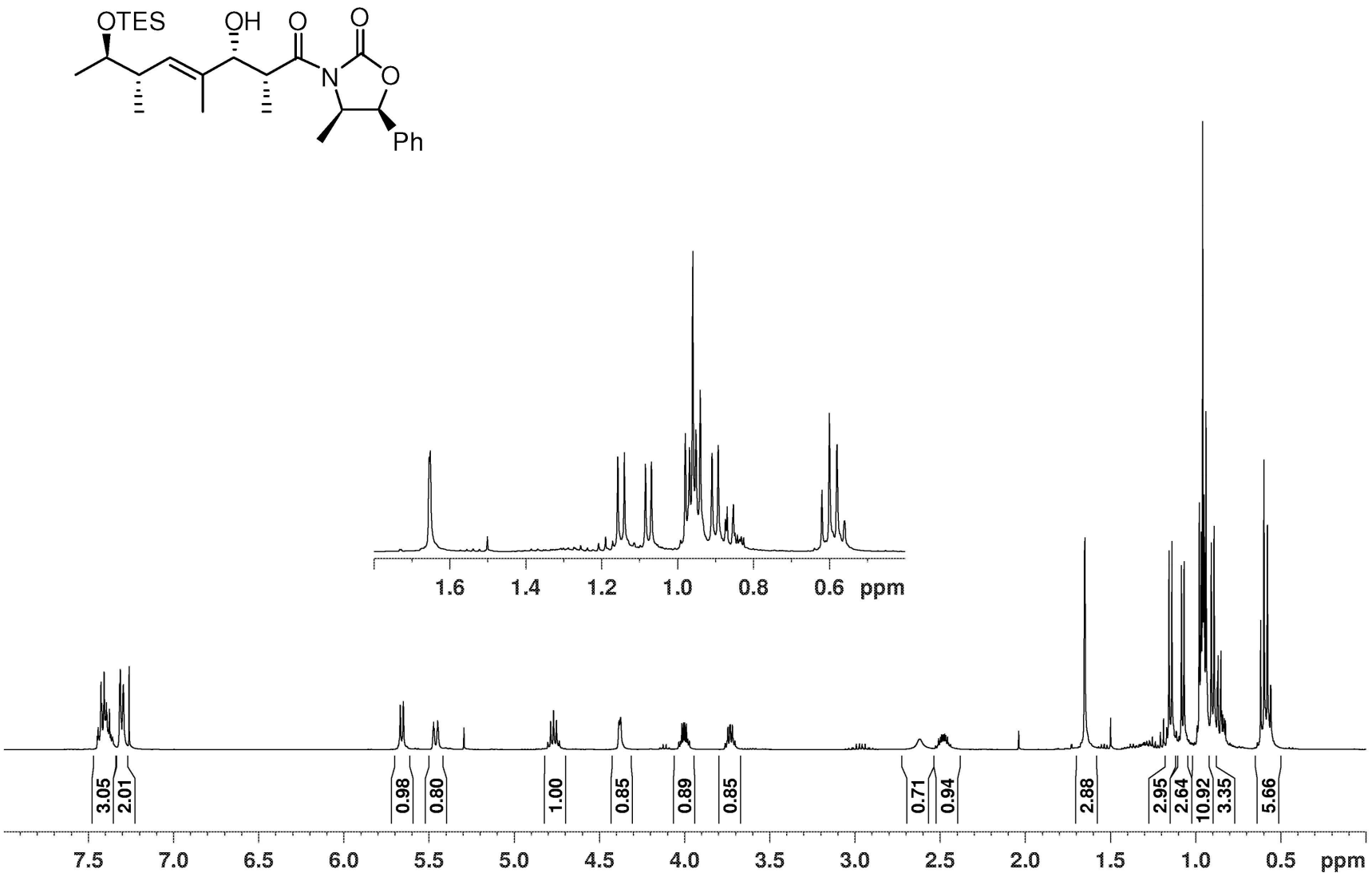
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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O
N
O
Ph
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0.6
ppm
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2.01
0.98
0.80
1.00
0.85
0.89
0.85
0.71
0.94
2.88
2.95
2.64
10.92
3.35
5.66
7.5
7.0
6.5
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2.0
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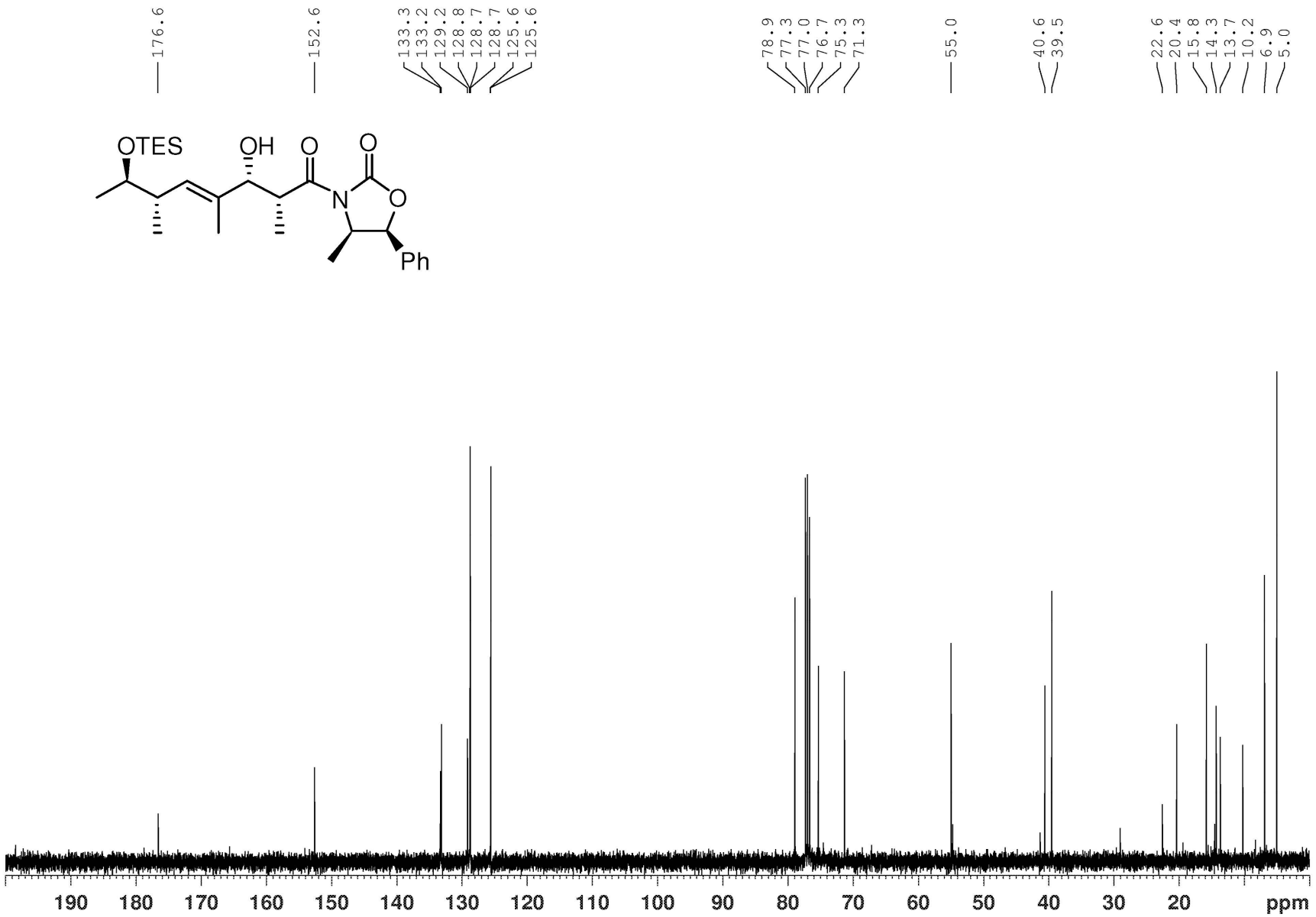
ppm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75.3
71.3
55.0
40.6
39.5
22.6
20.4
15.8
14.3
13.7
10.2
6.9
5.0
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OH
O
O
N
O
Ph
190
180
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120
110
100
90
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70
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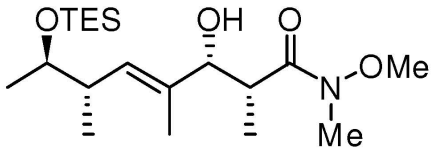
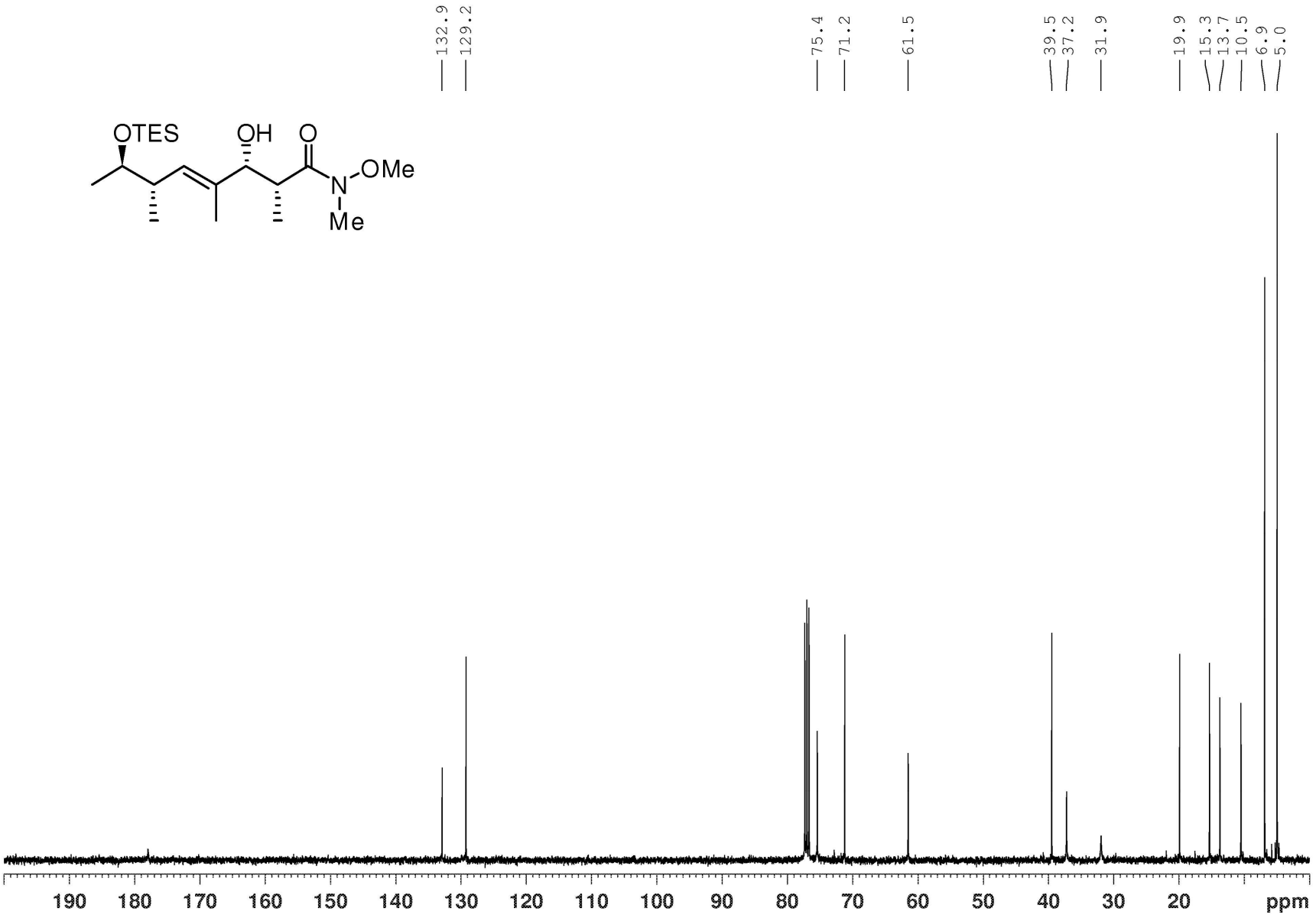
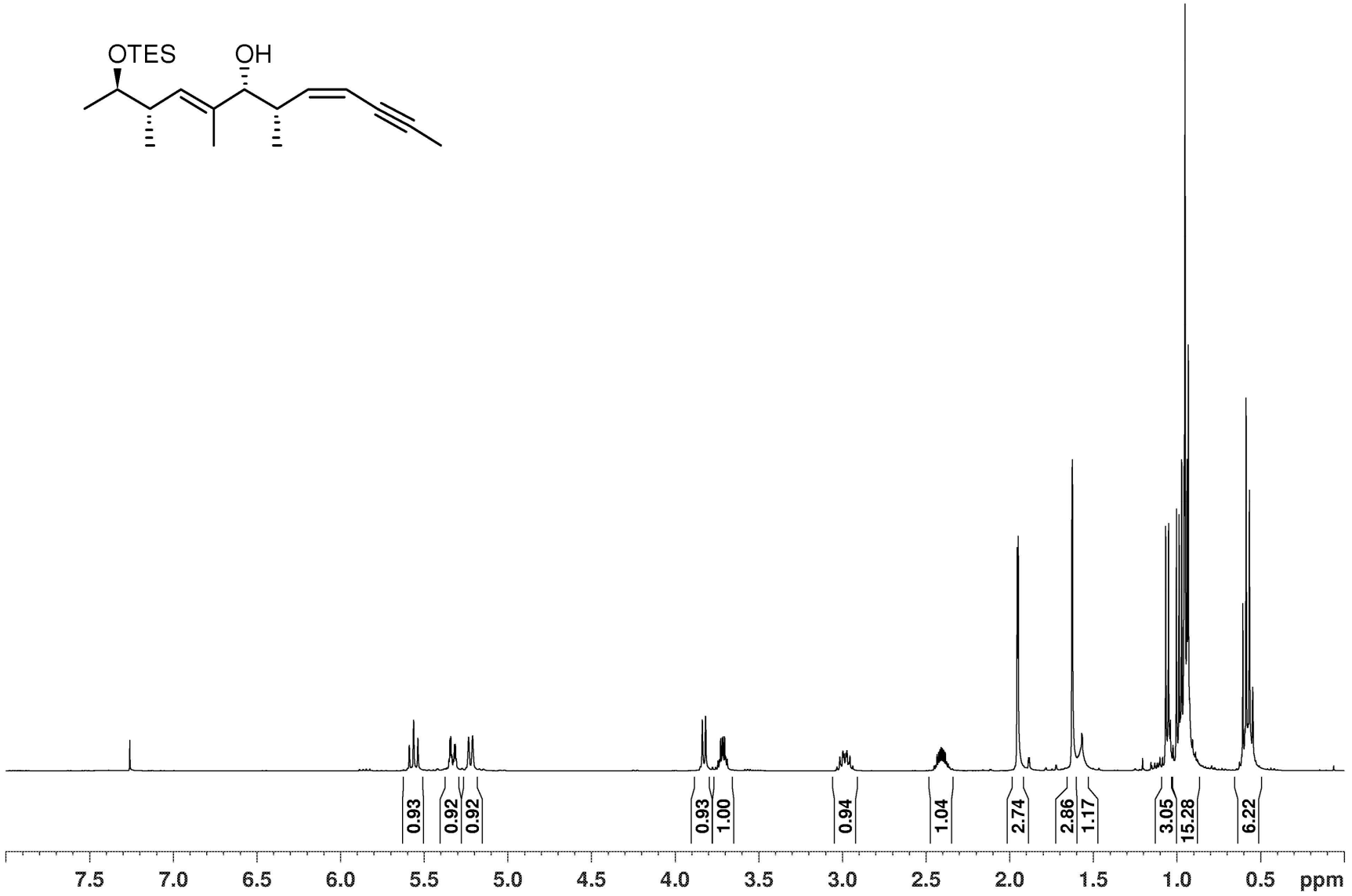
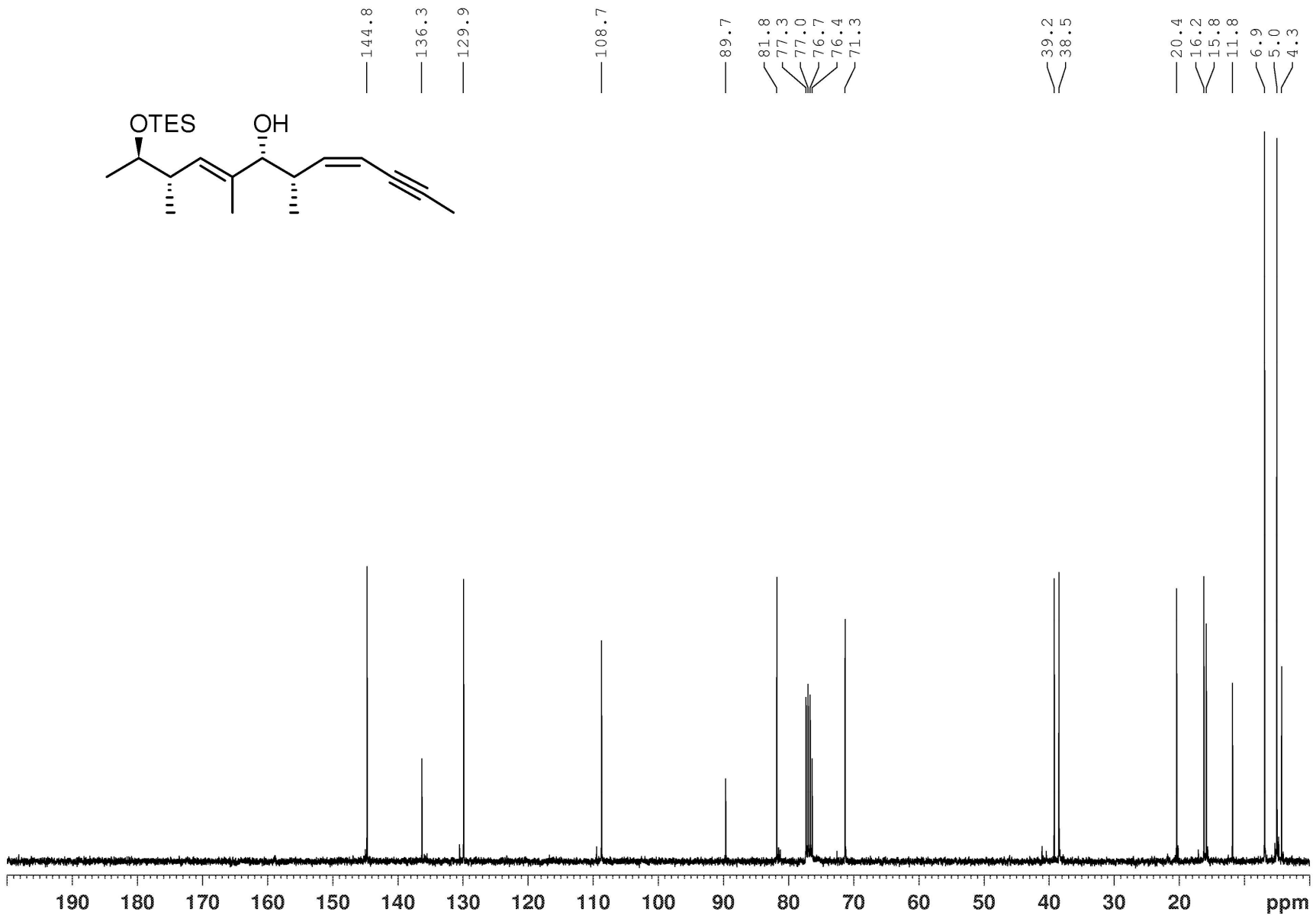
30
20
ppm

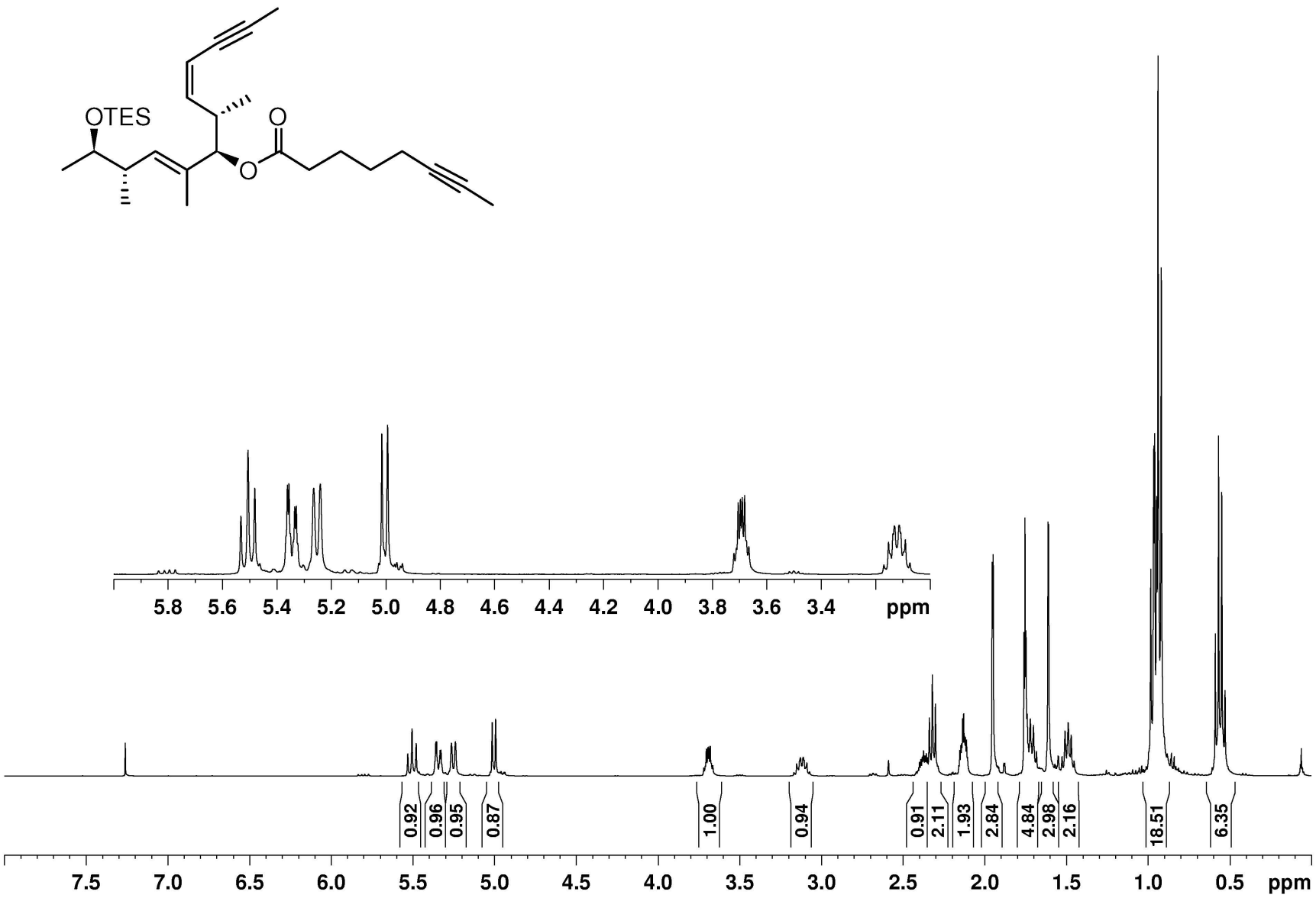

OTES
OH
O
N
OMe
Me

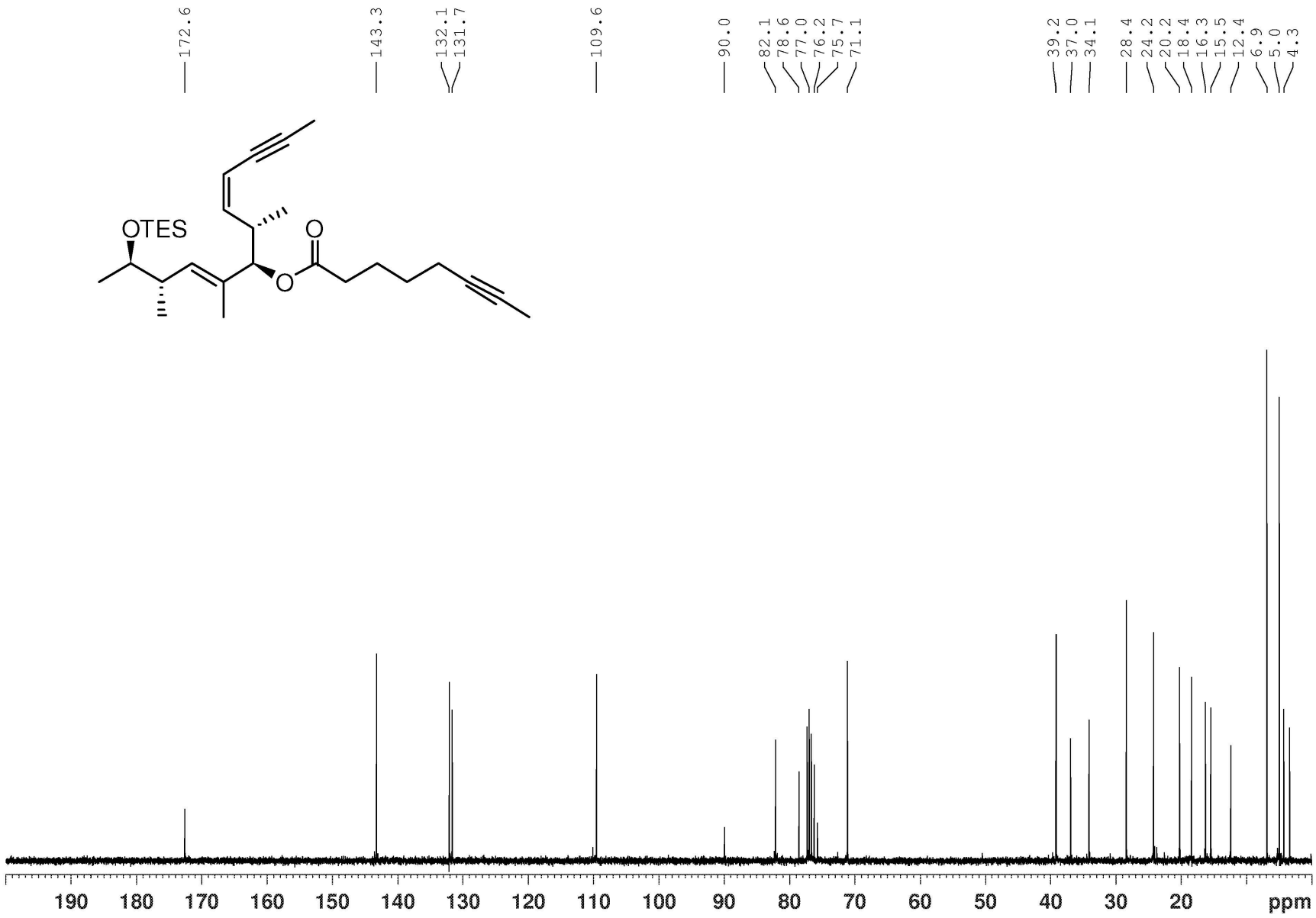
0.96
1.00
4.40
2.98
1.06
1.01
3.05
2.89
2.90
11.86
6.11
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

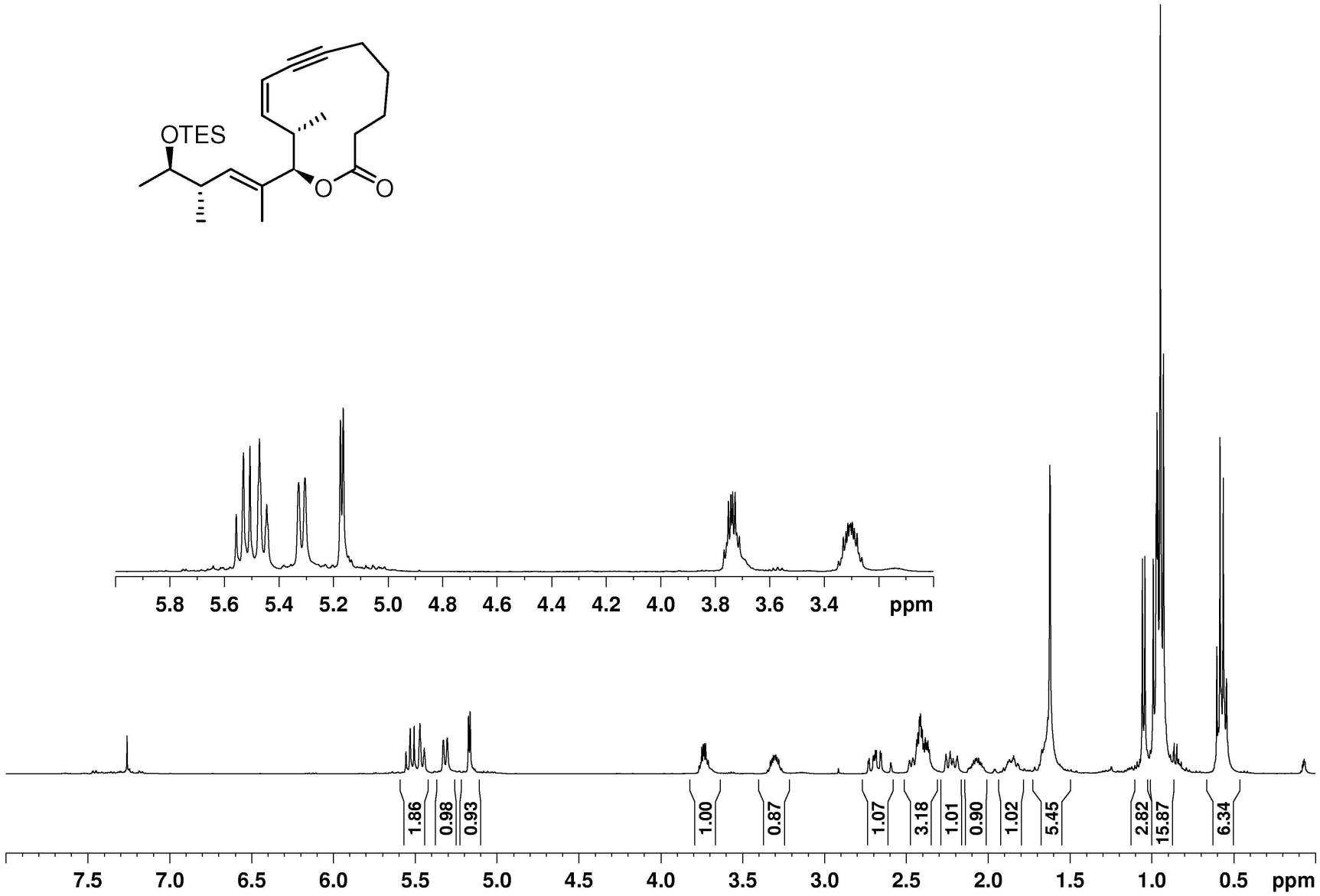

132.9
129.2
75.4
71.2
61.5
39.5
37.2
31.9
19.9
15.3
13.7
10.5
6.9
5.0
OTES
OH
O
N
OMe
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

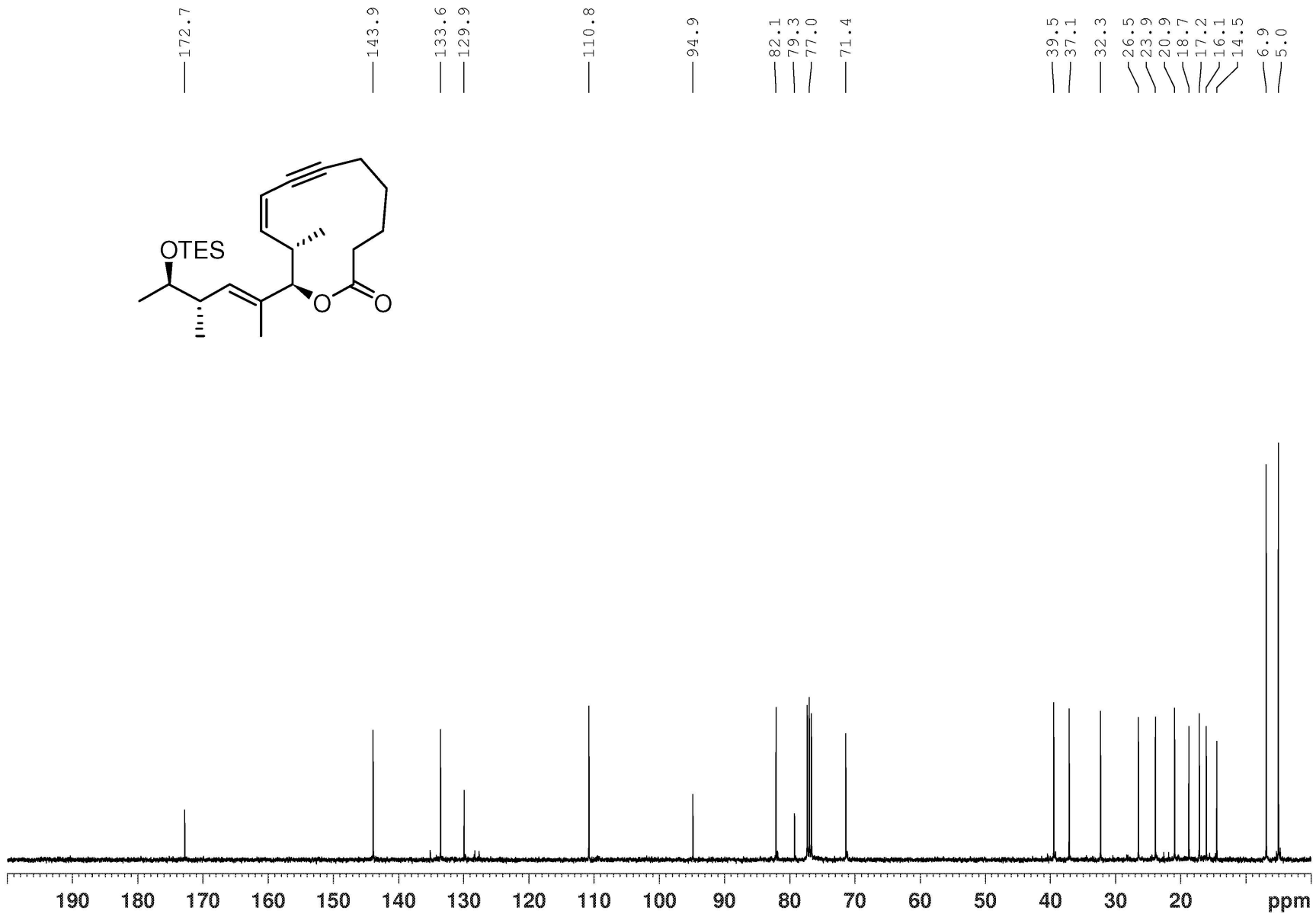

OTES
OH
0.93
0.92
0.92
0.93
1.00
0.94
1.04
2.74
2.86
1.17
3.05
15.28
6.22
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

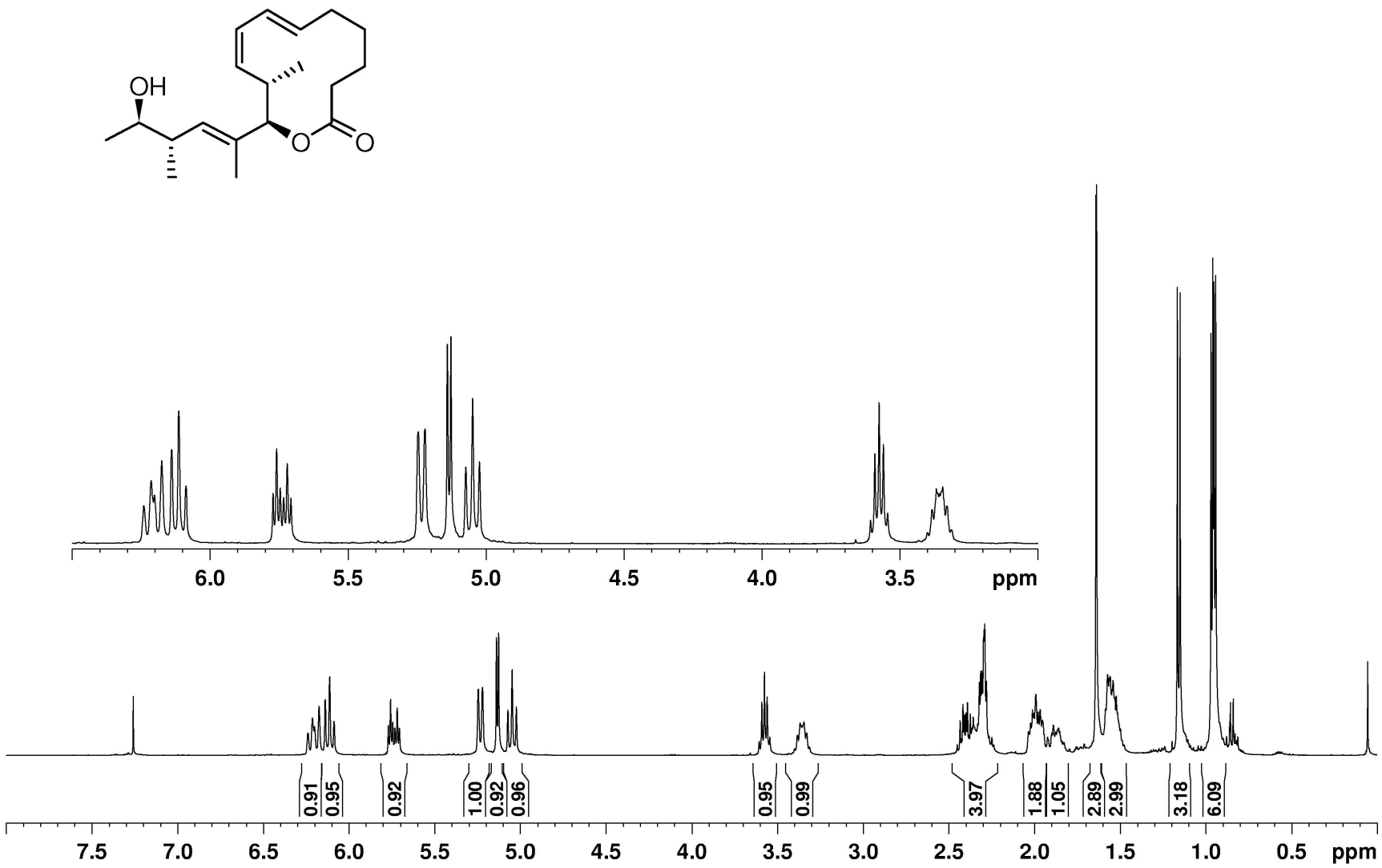

144.8
136.3
129.9
108.7
89.7
81.8
77.3
77.0
76.7
76.4
71.3
39.2
38.5
20.4
16.2
15.8
11.8
6.9
5.0
4.3
OTES
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

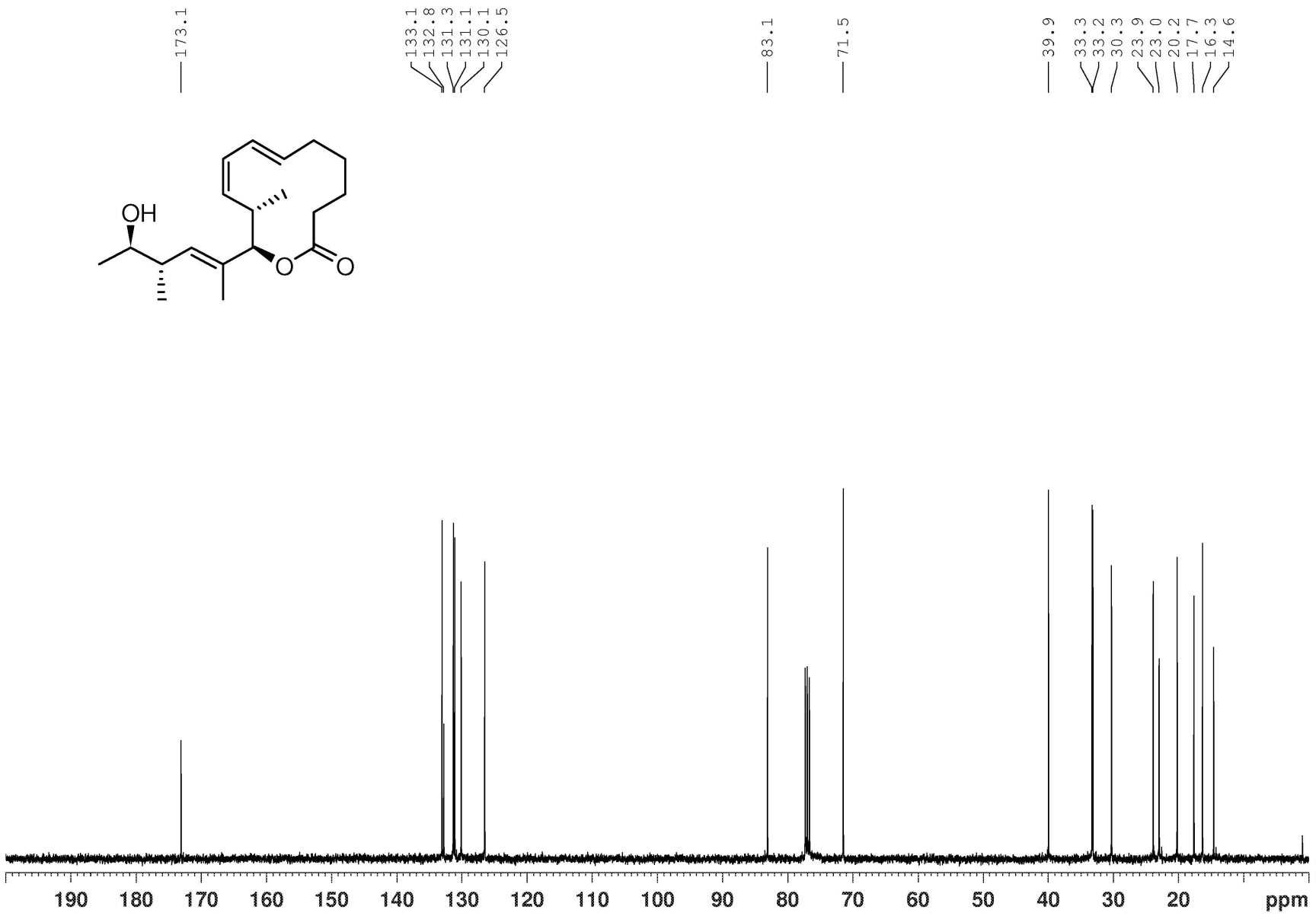

OTES
O
O
5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 ppm
0.92 0.96 0.95 0.87 1.00 0.94 0.91 2.11 1.93 2.84 4.84 2.98 2.16 18.51 6.35
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

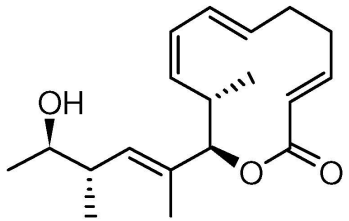

172.6
143.3
132.1
131.7
109.6
90.0
82.1
78.6
77.0
76.2
75.7
71.1
39.2
37.0
34.1
28.4
24.2
20.2
18.4
16.3
15.5
12.4
6.9
5.0
4.3
OTES
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

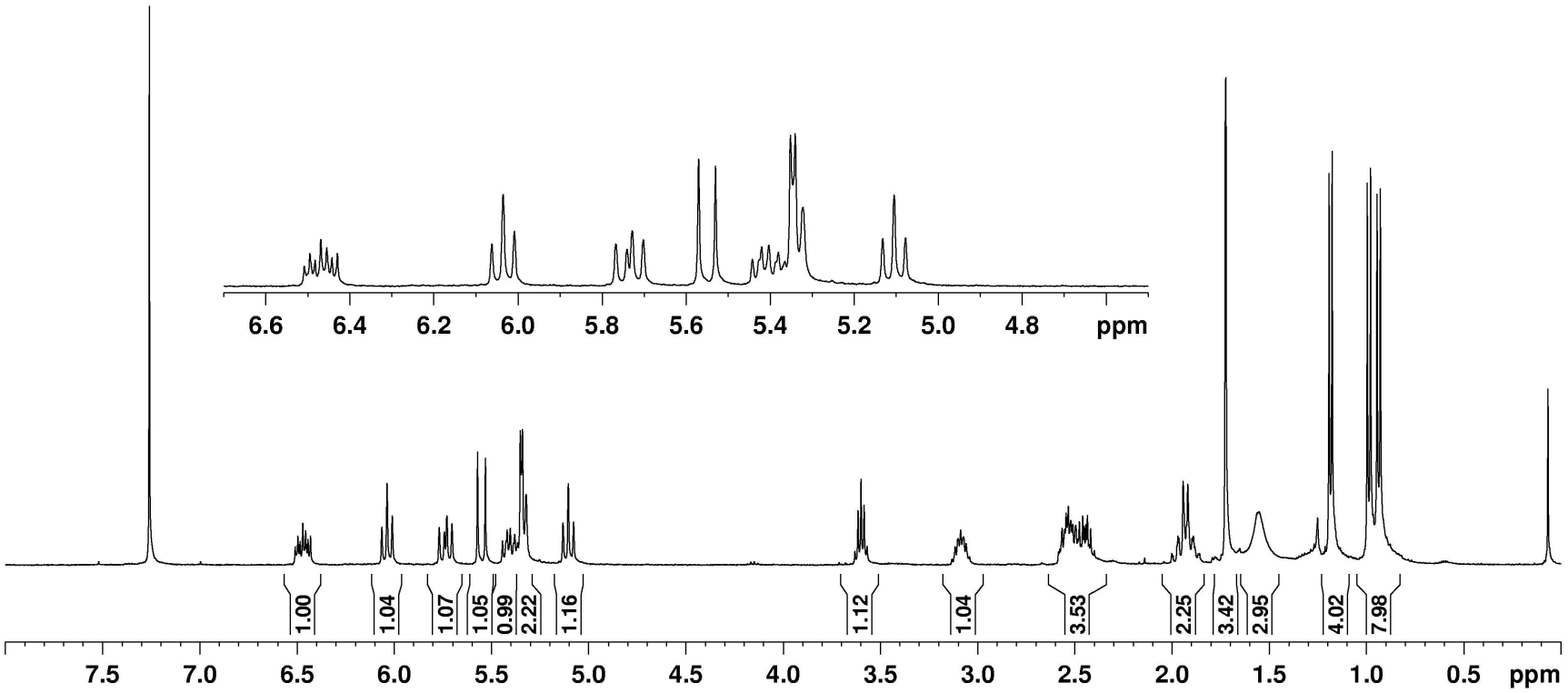

OTES
O
O
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
ppm
1.86
0.98
0.93
1.00
0.87
1.07
3.18
1.01
0.90
1.02
5.45
2.82
15.87
6.34
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

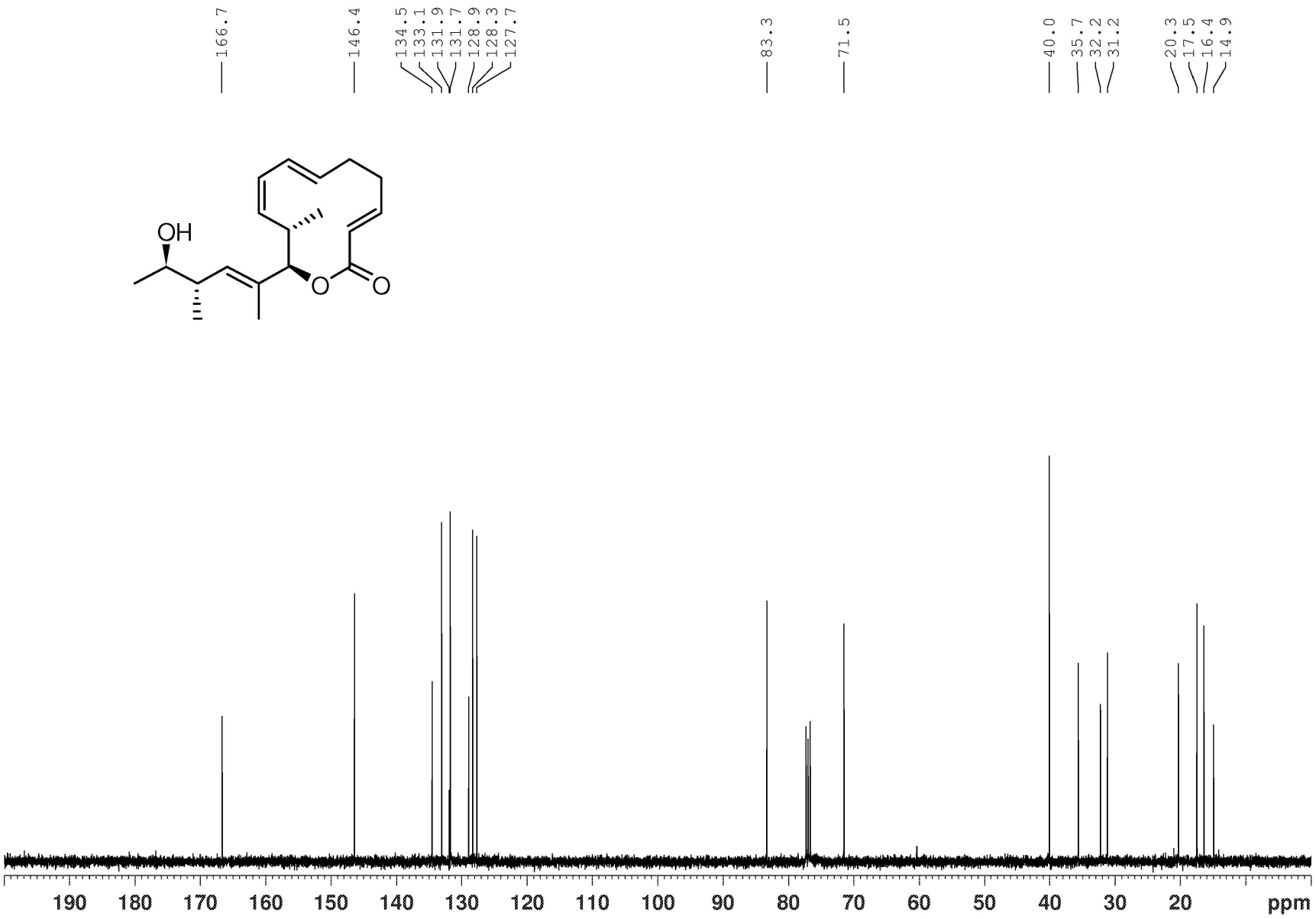

172.7
143.9
133.6
129.9
110.8
94.9
82.1
79.3
77.0
71.4
39.5
37.1
32.3
26.5
23.9
20.9
18.7
17.2
16.1
14.5
6.9
5.0
OTES
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

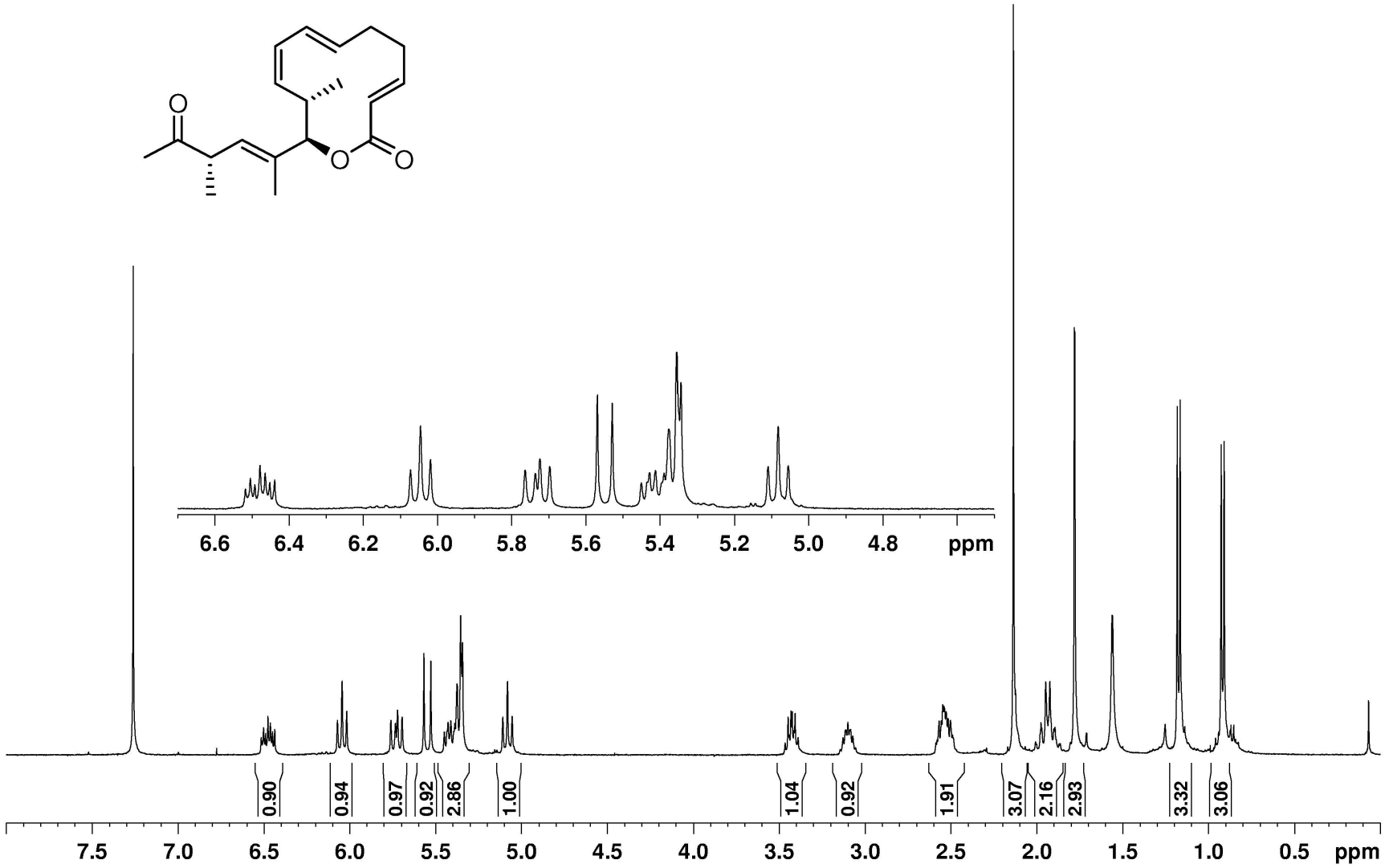

OH
O
O
6.0
5.5
5.0
4.5
4.0
3.5
ppm
0.91
0.95
0.92
1.00
0.92
0.96
0.95
0.99
3.97
1.88
1.05
2.89
2.99
3.18
6.09
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

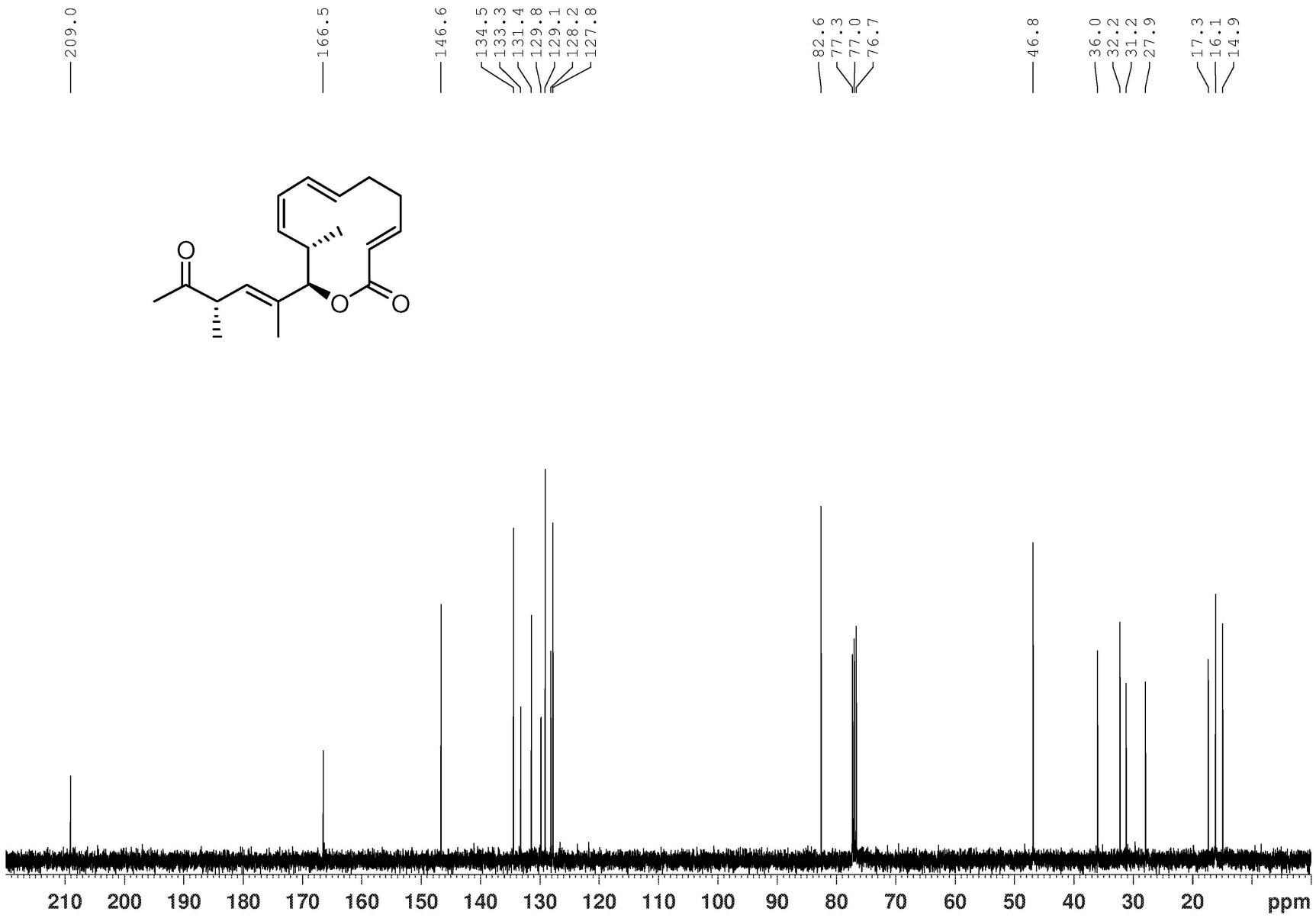

173.1
133.1
132.8
131.3
131.1
130.1
126.5
83.1
71.5
39.9
33.3
33.2
30.3
23.9
23.0
20.2
17.7
16.3
14.6
OH
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

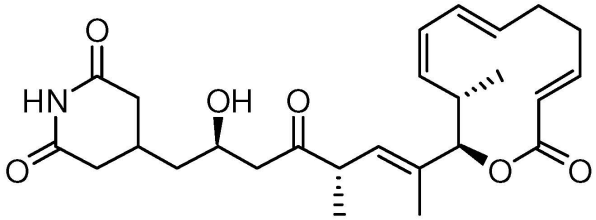

OH
O
O

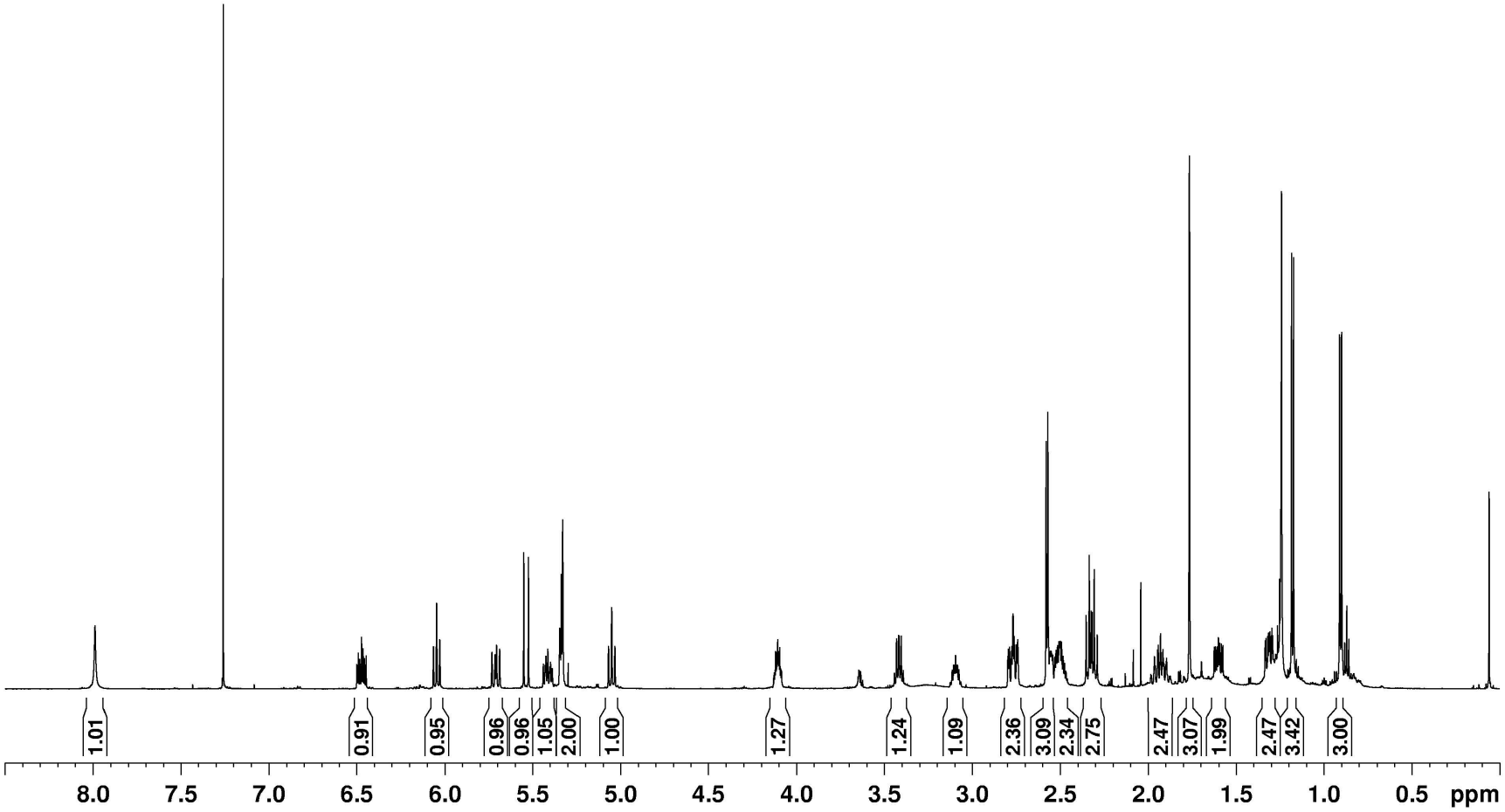

6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
ppm
1.00
1.04
1.07
1.05
0.99
2.22
1.16
1.12
1.04
3.53
2.25
3.42
2.95
4.02
7.98
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

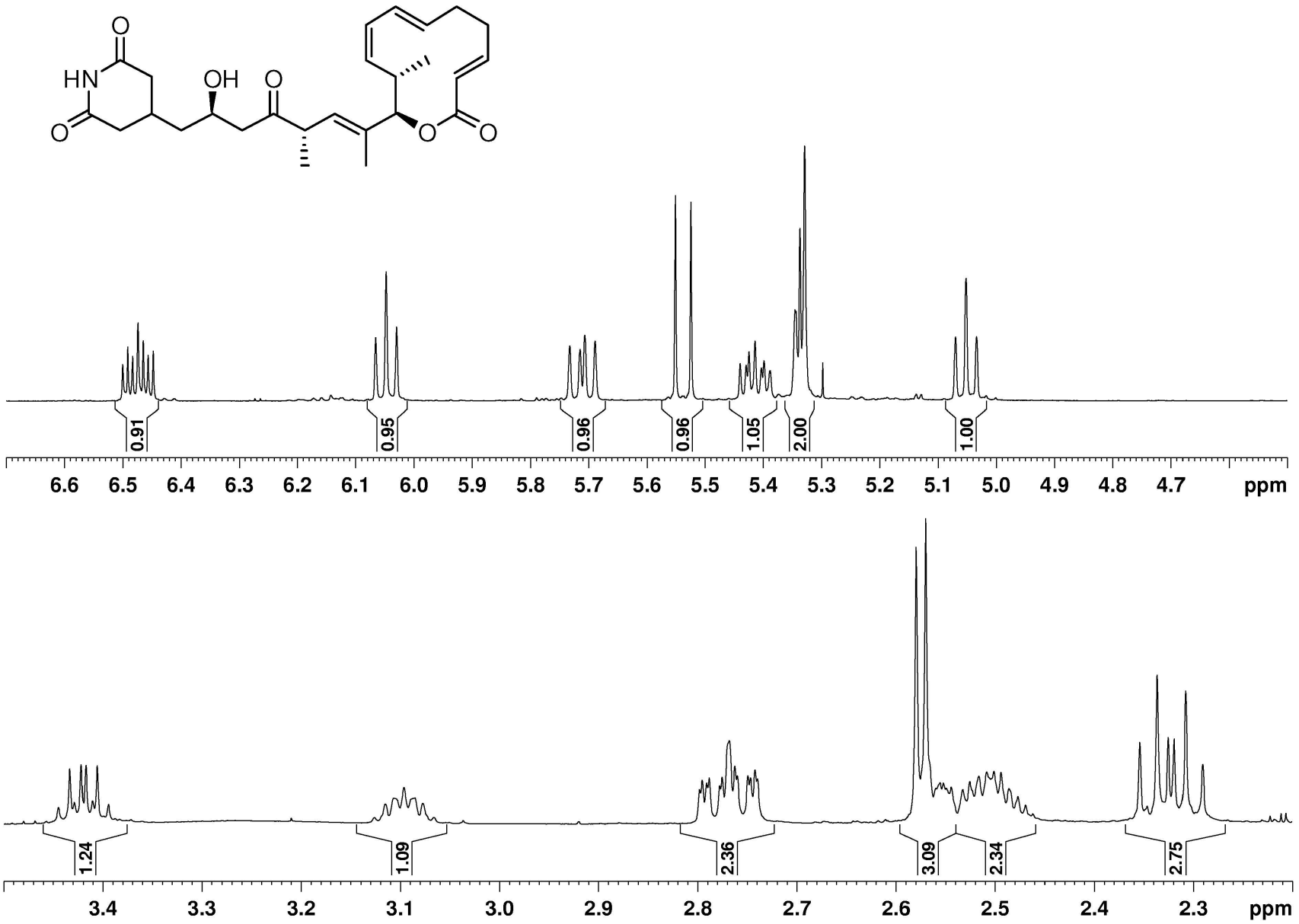

166.7
146.4
134.5
133.1
131.9
131.7
128.9
128.3
127.7
83.3
71.5
40.0
35.7
32.2
31.2
20.3
17.5
16.4
14.9
OH
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

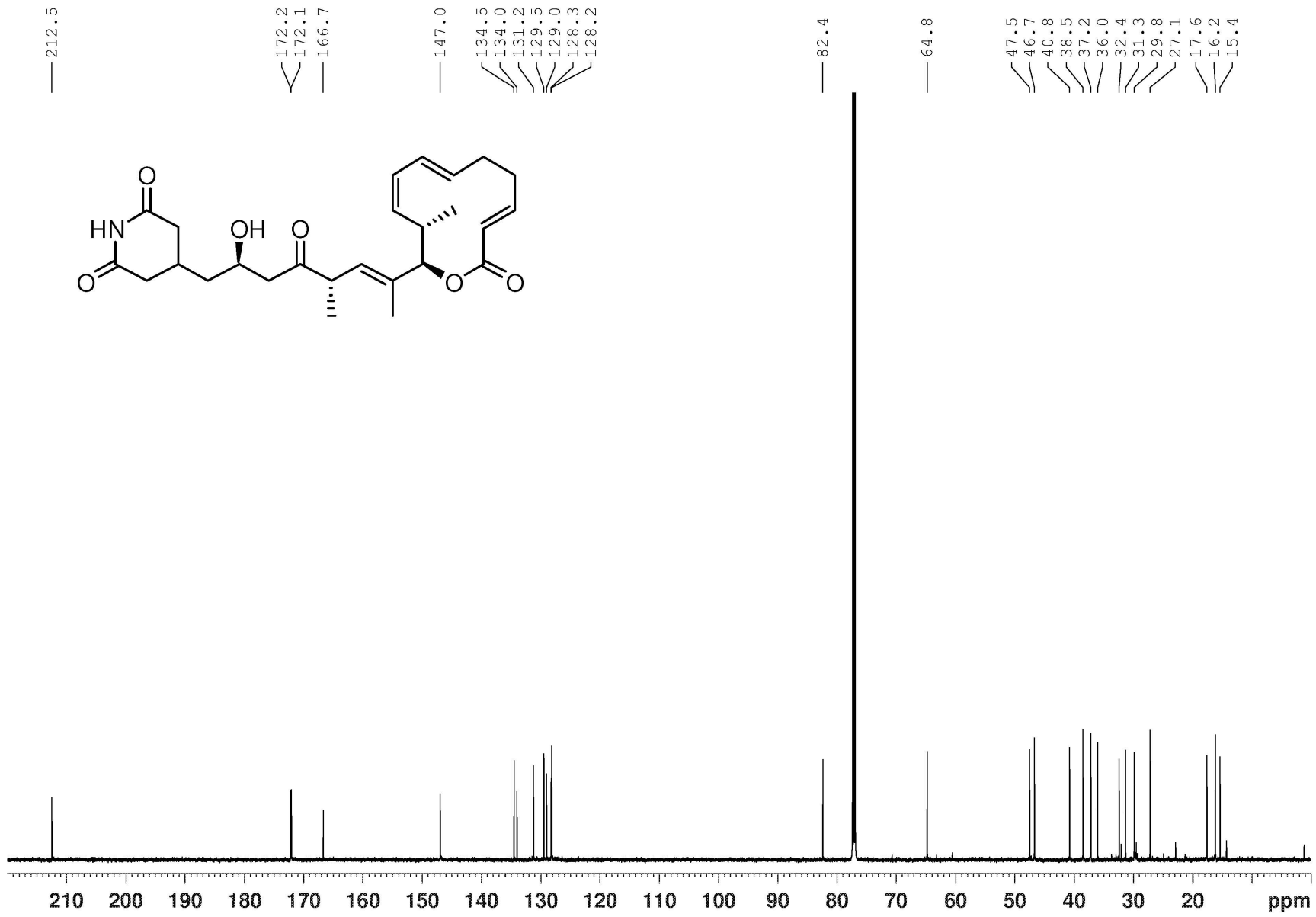

O
O
O
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
ppm
0.90
0.94
0.97
0.92
2.86
1.00
1.04
0.92
1.91
3.07
2.16
2.93
3.32
3.06
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


209.0
166.5
146.6
134.5
133.3
131.4
129.8
129.1
128.2
127.8
82.6
77.3
77.0
76.7
46.8
36.0
32.2
31.2
27.9
17.3
16.1
14.9
O
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
HN
O
OH
O
O
O


1.01
0.91
0.95
0.96
0.96
1.05
2.00
1.00
1.27
1.24
1.09
2.36
3.09
2.34
2.75
2.47
3.07
1.99
2.47
3.42
3.00
8.0
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


HN
O
O
OH
O
O
O
0.91
0.95
0.96
0.96
1.05
2.00
1.00
6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 ppm
1.24
1.09
2.36
3.09
2.34
2.75
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 ppm


212.5
172.2
172.1
166.7
147.0
134.5
134.0
131.2
129.5
129.0
128.3
128.2
82.4
64.8
47.5
46.7
40.8
38.5
37.2
36.0
32.4
31.3
29.8
27.1
17.6
16.2
15.4
HN
O
OH
O
O
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm