Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Divergent Total Synthesis of the Antimitotic Agent Leiodermatolide**

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SUPPORTING INFORMATION

Divergent Total Synthesis of the Antimitotic Agent Leiodermatolide

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List of Contents

Crystallographic Information

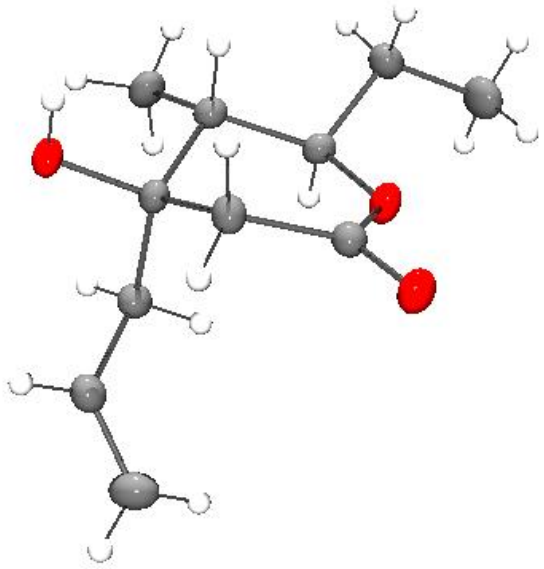


Figure S1. Structure of the allylation compound *ent*-**25** in the solid state.

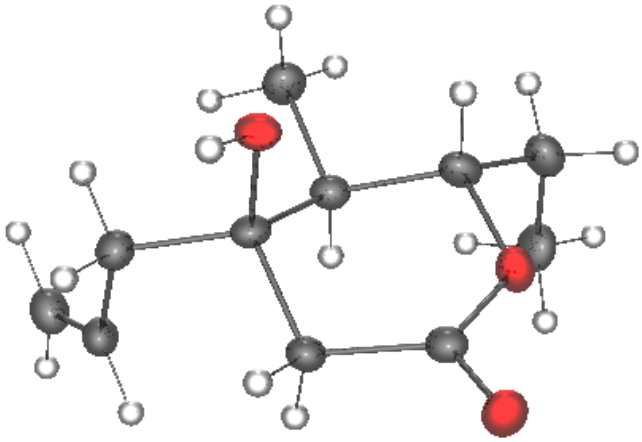


Figure S2. Structure of the allylation compound **23** in the solid state.

X-ray diffraction data for both compounds were collected using a Bruker AXS X8 Proteum diffractometer housed in front of a FR591 rotating anode equipped with graded multilayer focusing optics (Cu Kα, λ = 1.54184 Å) employing ϕ and ω scans to cover reciprocal space up to 67° 2θ with 99% completeness. The structures were solved by direct methods using SHELXS-97, atomic positions and displacement parameters were refined using fullmatrix least-squares based on Fsqd using SHELXL-97.[1]

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre and can be obtained free of charge by applying to: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, United Kingdom, quoting reference numbers CCDC 896726 (**23**) and 896727 (*ent*-**25**).

Crystal data for compound 23: $C_{11}H_{18}O_3$, M = 198.25g mol^{-1}, colorless, crystal dimensions 0.30 x 0.11 x 0.07 mm, monoclinic $P2_1$(no. 4), at 100 K, a = 9.1535(5), b = 5.5655(3), c = 11.1241(6) Å, β = 103.613(2), V = 550.78(5) Å^3, Z = 2, ρ = 1.195 Mgm^{-3}, μ = 0.695 mm^{-1}. Integration of raw data yielded a total of 12661 reflections, merged into 1825 unique reflections with R_{int} = 0.042 after applying Lorentz, polarisation and absorption correction. Refinement of 138 parameters using all reflections converged at R = 0.027, *wR2* = 0.066, highest residual electron density peak 0.1 Å^3.

Crystal data for compound *ent*-25: $C_{11}H_{18}O_3$, M = 198.25g mol^{-1}, colorless, crystal dimensions 0.64 x 0.05 x 0.04 mm, monoclinic $P2_1$ (no. 4), at 100 K a = 7.1017(4), b = 10.4344(5), c = 8.2612(4) Å, β = 113.6280(10), V = 560.85(5) Å^3, Z = 2, ρ = 1.174 Mgm^{-3}, μ = 0.682 mm^{-1}. Integration of raw data yielded a total of 12794 reflections, merged into1858 unique reflections with R_{int} =0.046 after applying Lorentz, polarisation and absorption correction. Refinement of 131 parameters using all reflections converged at R = 0.031, *wR2* =0.084, highest residual electron density peak 0.2 Å^3.

[1] G. M. Sheldrick, *Acta Cryst. Sect. A: Found. Crystallogr.* **2008**, *A64*, 112-122.

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), hexane, toluene (Na/K), MeOH (Mg), DMF (MS 4Å), DMSO (distilled over CaH_2, stored over MS 4Å). Flash chromatography: Merck silica gel 60 (40–63 μm) or Florisil (60-100 mesh). NMR: Spectra were recorded on Bruker DPX 300, AV 400, AV 500 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 $CDCl_3$: $\delta_H \equiv 7.24$ ppm; CD_2Cl_2: $\delta_C \equiv 53.8$ ppm; residual ^1H: $\delta_H \equiv 5.32$ ppm; C_6D_6: $\delta_C \equiv 128.0$ ppm; residual C_6D_5H: $\delta_H \equiv 7.15$ ppm, [D_6]-DMSO: $\delta_C \equiv 39.52$ ppm, residual $CD_2HS(O)CD_3$: $\delta_H \equiv 2.50$ 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.

Diethyl 2-(diiodomethyl)-2-methylmalonate (4). A solution of diethyl methylmalonate (**3**) (9.81 mL, 57.0 mmol) in Et_2O (20 mL) was added over 30 min to a suspension of NaH (1.65 g, 69.0 mmol) in Et_2O (100 mL), causing the mixture to reach reflux temperature while vigorous evolution of H_2 was noticed. Once the addition was complete, the mixture was stirred at reflux for 1.5 h before solid CHI_3 (22.6 g, 57.0 mmol) was added. Stirring was continued at reflux temperature for 12 h before the mixture was cooled to 0 °C and excess NaH was carefully quenched with aq. HCl (1 M, 100 mL). After stirring for 20 min, the layers were separated and the aqueous phase was extracted with Et_2O (3 x 65 mL). The combined organic layers were washed with brine (80 mL), dried over Na_2SO_4 and concentrated to give the title compound as a pale brown oil, which was used in the next without further purification (24.9 g, 99%). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.73 (br s, 1H), 4.18 (dq, 4H, J = 7.1 Hz, 1.4 Hz), 1.75 (s, 3H), 1.25 ppm (t, 6H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 62.6, 62.1, 20.3, 13.9, -26.0 ppm; IR (film): $\tilde{\nu}$ = 1731, 1447, 1380,

1366, 1261, 1207, 1162, 1093, 1074, 1015, 859 cm^{-1}; MS (EI) *m*/*z* (%): 440 (12), 313 (9), 241 (22), 213 (27), 195 (17), 167 (12), 113 (7), 85 (12), 41 (16), 39 (23), 29 (100), 27 (15); HRMS (ESI): *m*/*z*: calcd. for $C_9H_{14}O_2I_2Na$ [M^++Na]: 462.88737, found 462.88705. The analytical and spectroscopic data are in agreement with those reported in the literature.[2]

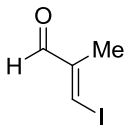
(*E*)-3-Iodo-2-methylacrylic acid (5). KOH (15.9 g, 283 mmol) and water (60 mL) were added to a solution of crude malonate **4** (24.8 g, 56.3 mmol) in EtOH (180 mL), and the resulting red solution was stirred at reflux temperature for 4 h. After cooling and evaporation of all volatile materials, the residue was dissolved in aq. K_2CO_3 (10%, 150 mL), which was then carefully acidified with conc. HCl at 0°C. Extraction with CH_2Cl_2 (8 x 50 mL) was followed by drying of the combined organic layers over Na_2SO_4 and evaporation of the solvent. The residue was purified by flash chromatography (hexanes/EtOAc, 9:1 + 0.5% HOAc) to yield the title compound as a pale yellow solid (8.58 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.28 (br s, 1H), 8.00 (q, 1H, *J* = 1.2 Hz), 2.03 ppm (d, 3H, *J* = 1.2 Hz); ^{13}C NMR (100 MHz, CDCl3): δ = 169.3, 139.0, 102.1, 19.8 ppm; IR (film): $\tilde{\nu}$ = 3079, 2966, 2596, 1682, 1593, 1409, 1379, 1296, 1235, 1108, 991, 915, 838, 727, 685 cm^{-1}; MS (EI) *m*/*z* (%): 212 (56), 167 (6), 127 (6), 85 (75), 57 (12), 45 (14), 43 (11), 41 (28), 40 (16), 39 (100), 38 (18), 37 (9), 29 (18); HRMS (EI): *m*/*z*: calcd. for $C_4H_5O_2I$ [*M*]: 211.93343, found 211.93359. The analytical and spectroscopic data are in agreement with those reported in the literature.[3]

(*E*)-3-Iodo-2-methylprop-2-en-1-ol. A solution of acid **5** (8.4 g, 39.6 mmol) in Et_2O (25 mL) was added over 20 min to a suspension of $LiAlH_4$ (1.65 g, 43.6 mmol) in E_2O (60 mL) at 0°C. After additional 30 min at this temperature, the ice bath was removed and the mixture stirred at ambient temperature for 2.5 h. The excess $LiAlH_4$ was carefully quenched with sat. aq. Na_2SO_4 (130 mL) and the mixture diluted with H_2SO_4 (2 M, 60 mL) and Et_2O. The aqueous layer was extracted with Et_2O (3 x 40 mL), the combined organic phases were washed with aq. K_2CO_3 (10%, 50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the remaining oil by flash chromatography (pentane/Et_2O, 4:1) gave the title compound as a

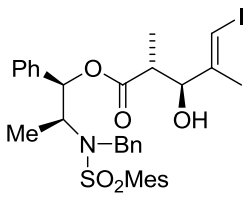
[2] R. Baker, J. L. Castro, *J. Chem. Soc. Perkin Trans. 1*, **1990**, 47-65.
[3] D. Menche, J. Hassfeld, J. Li, K. Mayer, S. Rudolph, *J. Org. Chem.* **2009**, *74*, 7220-7229.

colorless oil (3.6 g, 49%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.25 (m, 1H), 4.09 (d, 2H, *J* = 5.4 Hz), 1.85 – 1.81 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.2, 77.3, 67.1, 21.3 ppm; IR (film): $\tilde{\nu}$ = 3295, 2912, 2851, 1620, 1433, 1376, 1274, 1252, 1145, 1066, 1008, 942, 829, 771, 665 cm^{-1}; MS (EI) *m*/*z* (%): 198 (75), 183 (5), 127 (9), 71 (100), 53 (28), 43 (59), 31 (57), 39 (61), 38 (12), 31(34), 29(14), 27(26); HRMS (EI): *m*/*z*: calcd. for C_4H_7IO [*M*]: 197.95416, found 197.95410. The analytical and spectroscopic data are in agreement with those reported in the literature.[2]

(*E*)-3-Iodo-2-methylacrylaldehyde (6). MnO_2 (11.1 g, 127 mmol) was added in three portions to a vigorously stirred solution of (*E*)-3-iodo-2-methylprop-2-en-1-ol (2.52 g, 12.7 mmol) in CH_2Cl_2 (35 mL), causing a slight exothermic reaction. After 3.5 h, the mixture was filtered through a pad of flame-dried Celite, which was rinsed with CH_2Cl_2 (2 x 10 mL). The combined filtrates were evaporated and the residue briefly dried in high vacuum to give the title compound as a pink oil (2.46 g, 98%). Due to the unstable nature of this compound, it was dissolved in CH_2Cl_2 (10 mL) containing 4Å MS and immediately used in the next step. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.52 (s, 1H), 7.8 (q, 1H, *J* = 1.2 Hz), 1.92 (d, 3H, *J* = 1.2 Hz) ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.4, 150.8, 109.4, 16.4 ppm; IR (film): $\tilde{\nu}$ = 2921, 2842, 1691, 1591, 1294, 1099, 1027, 1015, 798, 679 cm^{-1}; MS (EI) *m*/*z* (%): 196 (99), 167 (14), 127 (8), 69 (86), 41 (59), 30 (11), 39 (100), 38 (13), 29 (8); HRMS (EI): *m*/*z*: calcd. for C_4H_5IO [*M*]: 195.93852, found 195.93837.



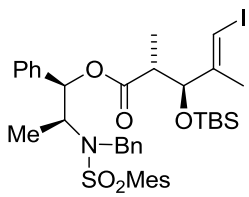
(2*R*,3*S*,*E*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 3-hydroxy-5-iodo-2,4-dimethylpent-4-enoate (8). NEt_3 (0.904 mL, 6.52 mmol) and (1*R*,2*S*)-2-(*N*-benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl propionate (**7**)[4] (2.61 g, 5.43 mmol) were dissolved in CH_2Cl_2 (45 mL) and the solution cooled to -78°C. A solution of dicyclohexyboryl triflate (2.13 g, 6.52 mmol) in pentane (12 mL) was then added over 12 min to give a yellow suspension, which was kept at this temperature for 5 h. A solution of freshly prepared aldehyde **6** (2.45 g, 12.5 mmol) in CH_2Cl_2 (10 mL) was then added and stirring continued for 1.5 h before the cooling bath was removed and the mixture allowed to reach room temperature. After 3 h, the reaction



[4] T. Inoue, J.-F. Liu, D. C. Buske, A. Abiko, *J. Org. Chem*. **2002**, *67*, 5250-5256.

was quenched with pH 7 buffer (30 mL) and treated with MeOH (100 mL) and aq. H_2O_2 (35% *w/w*, 15 mL) overnight. The solvent was removed in vacuo, the residue dissolved in CH_2Cl_2 (150 mL) and the organic phase washed with H_2O (60 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried over Na_2SO_4 and evaporated. ^{1}H NMR analysis of the crude product showed a diastereomeric ratio of 13:1. Purification of the residue by flash chromatography yielded the title compound as a white solid (2.79 g, 76%, single isomer). $[\alpha]_{20}^{D}$ = +45.0 (c = 0.95, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 – 7.13 (m, 8H), 6.87 (s, 2H), 6.86- 6.82 (m, 2H), 6.28 (s, 1H), 5.83 (d, 1H, *J* = 4.0 Hz), 4.73 (d, 1H, *J* = 16.7 Hz), 4.54 (d, 1H, *J* = 16.7 Hz), 4.23 (dd, 1H, *J* = 8.9, 3.8 Hz), 4.09 (dq, 1H, *J* = 4.0, 7.0 Hz), 2.73 (d, 1H, *J* = 4.1 Hz, OH), 2.64 – 2.52 (m, 1H), 2.48 (s, 6H), 2.26 (s, 3H), 1.80 (d, 3H, *J* = 1.1 Hz), 1.15 (d, 3H, *J* = 7.0 Hz), 0.94 ppm (d, 3H, *J* = 7.23 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0, 146.9, 142.6, 140.3, 138.5, 138.1, 133.4, 132.1, 128.5, 128.3, 128.0, 127.6, 127.2, 125.9, 81.2, 78.6, 78.5, 56.8, 48.2, 43.3, 22.9, 20.9, 18.8, 14.1, 13.3 ppm; IR (film): $\tilde{\nu}$ = 3496, 1741, 1604, 1496, 1455, 1379, 1317, 1151, 1117, 1031, 1011, 929, 858, 752, 730, 698, 659 cm^{-1}; MS (EI) *m*/*z* (%): 406 (1), 317 (20), 316 (100), 183 (5), 119 (17), 91 (60), 57 (3), 41 (3); HRMS (ESI): *m*/*z*: calcd. for $C_{32}H_{38}NO_5ISNa$ [M^++Na]: 698.14076, found 698.14108. The analytical and spectroscopic data are in agreement with those reported in the literature.[2]

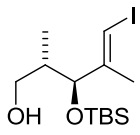
(2*R*,3*S*,*E*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 3-(*tert*-butyldimethylsilyloxy)-5-iodo-2,4-dimethylpent-4-enoate.



2,6-Lutidine (0.863 mL, 7.43 mmol) was added via syringe to a stirred solution of alcohol **8** (2.51 g, 3.71 mmol). The mixture was cooled to 0°C before TBSOTf (1.28 mL, 5.57 mmol) was slowly added. After stirring for 2 h at 0°C, the reaction was quenched with sat. aq. NH_4Cl, the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL), the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated to give a white solid, which was used in the next step without further purification (2.89 g, 95%). An analytically pure sample was obtained by flash chromatography (hexanes/EtOAc, 9:1). $[\alpha]_{20}^{D}$ = +36.3 (c = 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, 2H, *J* = 7.3 Hz), 7.30 – 7.22 (m, 3H), 7.19 – 7.13 (m, 1H), 7.07 (t, 2H, *J* = 7.5 Hz), 6.85 (s, 2H), 6.7 (d, 2H, *J* = 7.3 Hz),

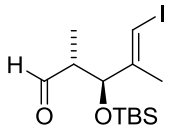
6.18 (s, 1H), 5.67 (d, 1H, *J* = 6.0 Hz), 4.85 (d, 1H, *J* = 16.1 Hz), 4.37 (d, 1H, *J* = 16.1 Hz), 4,29 (d, 1H, *J* = 9.3 Hz), 4.04 (dq, 1H, *J* = 6.6, 6.6 Hz), 2.61 (dq, 1H, *J* = 9.1, 7.3 Hz), 2.39 (s, 6H), 2.29 (s, 3H), 1.73 (d, 3H, *J* = 0.8 Hz), 1.16 (d, 3H, *J* = 6.9 Hz), 0.80 (s, 9H), 0.74 (d, 3H, *J* = 7.2 Hz), -0.03 (s, 3H), -0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9, 147.5, 142.4, 140.4, 138.5, 138.0, 132.9, 132.1, 128.4, 128.4, 128.2, 127.9, 127.4, 126.4, 80.6, 79.2, 77.7, 56.6, 48.1, 44.7, 25.7, 22.8, 20.9, 18.6, 18.1, 14.9, 13.8, -5.1, -5.1 ppm; IR (film): $\tilde{\nu}$ = 2956, 2935, 2857, 1743, 1605, 1455, 1379, 1325, 1254, 1154, 1072, 1030, 1011, 929, 857, 836, 777, 729, 698, 659. cm^{-1}; MS (EI) *m*/*z* (%): 406 (23), 317 (21), 316 (100), 183 (6), 132 (7), 119 (20), 91 (62), 73 (11); HRMS (ESI): *m*/*z*: calcd. for $C_{38}H_{52}NO_5ISSiNa$ [M^++Na]: 812.22724, found 812.22802.

(2*S*,3*S*,*E*)-3-(*tert*-Butyldimethylsilyloxy)-5-iodo-2,4-dimethylpent-4-en-1-ol. DIBAl-H



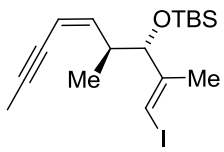
(1 M in toluene, 9.38 mL, 9.38 mmol) was added over a period of 12 min to a solution of the above silyl ether (2.89 g, 95% pure, 3.48 mmol) in toluene (25 mL) at -78°C. After stirring 2 h at this temperature, the excess DIBAl-H was carefully quenched with MeOH (2 mL). The mixture was diluted with *tert*-butyl methyl ether (20 mL) and aq. sat. Rochelle's salt solution (30 mL). The resulting mixture was stirred overnight at ambient temperature before the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 30 mL). The combined extracts were washed with brine (25 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 9:1) to give the title compound as a colorless oil (1.07 g, 83% over two steps). $[\alpha]_{20}^{D}$ = -32.3 (c = 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.18 (s, 1H), 4.00 (d, 1H, *J* = 8.0 Hz), 3.61 (dd, 1H, *J* = 4.5, 0.7 Hz), 3.60 (d, 1H, *J* = 4.8 Hz), 2.44 (t, 1H, *J* = 5.68 Hz), 1.88 – 1.78 (m, 1H), 1.76 (d, 3H, *J* = 1.0 Hz), 0.88 (s, 9H), 0.78 (d, 3H, *J* = 7.0 Hz), 0.06 (s, 3H), -0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.8, 82.8, 79.3, 66.2, 38.7, 25.8, 19.5, 18.1, 14.0, -4.8, -5.3 ppm; IR (film): $\tilde{\nu}$ = 339, 2956, 2928, 2884, 2857, 1615, 1471, 1462, 1376, 1361, 1252, 1140, 1064, 1037, 1004, 982, 938, 834, 774, 672 cm^{-1}; MS (EI) *m*/*z* (%): 313 (46), 311 (23), 271 (18), 185 (52), 171 (16), 115 (6), 111 (9), 75 (100), 73 (44), 53 (6), 45 (5), 43 (5), 41 (6); HRMS (ESI): *m*/*z*: calcd. for $C_{13}H_{27}O_2ISiNa$ [M^++Na]: 393.07172, found 393.07146.

(2*R*,3*S*,*E*)-3-(*tert*-Butyldimethylsilyloxy)-5-iodo-2,4-dimethylpent-4-enal (9). A



solution of (2*S*,3*S*,*E*)-3-(*tert*-butyldimethylsilyloxy)-5-iodo-2,4-dimethylpent-4-en-1-ol (600 mg, 1.62 mmol) in CH_2Cl_2 (6 mL) was added to a suspension of Dess-Martin periodinane (756 mg, 1.78 mmol) in CH_2Cl_2 (10 mL) at 0°C. After stirring for 15 min, the mixture was allowed to warm to room temperature and stirring continued for 2 h. The reaction was quenched with sat. $Na_2S_2O_3/Na_2CO_3$ (1:1, 10 mL), the aqueous phase extracted with CH_2Cl_2 (3 x 10 mL), and the combined extracts were dried over Na_2SO_4 and evaporated. The residue was suspended in hexane/EtOAc (9:1) and the resulting suspension filtered through a short pad of SiO_2. Concentration of the filtrate under reduced pressure gave the rather unstable aldehyde, which was immediately used in the next step (586 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.73 (d, 1H, *J* = 2.7 Hz), 6.28 (s, 1H), 4.27 (d, 1H, *J* = 8.4 Hz), 2.59 (dqd, 1H, *J* = 8.4, 7.1, 2.5 Hz), 1.79 (d, 3H, *J* = 1.0 Hz), 0.88 (d, 3H, *J* = 7.1 Hz), 0.85 (s, 9H), 0.03 (s, 3H), -0.03 ppm (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.8, 147.6, 80.1, 79.0, 50.1, 25.6, 19.0, 18.0, 10.8, -4.8, -5.4 ppm.

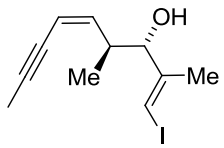
***tert*-Butyl-((1*E*,3*S*,4*S*,5*Z*)-1-iodo-2,4-dimethylnona-1,5-dien-7-yn-3-yloxy)dimethylsi-**



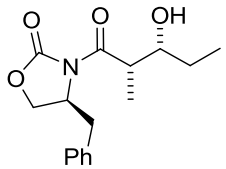
lane. A precooled (-78°C) solution of KHMDS (0.729 g, 3.66 mmol) in THF (6 mL) was added to a solution of sulfone **10** (1.00 g, 3.98 mmol) in THF (6 mL) at –55°C, causing a color change to dark-red. After stirring for 30 min at this temperature, a precooled (-78°C) solution of aldehyde **9** (586 mg, 1.59 mmol) in THF (3 mL) was added dropwise and the resulting mixture stirred for 13 h at -55°C before it was poured into brine (15 mL) and warmed to ambient temperature. *tert*-Butyl methyl ether (20 mL) and H_2O (5 mL) were added, the aqueous phase was extracted with *tert*-butyl methyl ether (2 x 20 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography yielded the title compound as a colorless oil (364 mg, 56%). $[\alpha]_{20}^{D}$ = +100.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.09 (m, 1H), 5.61 (dd, 1H, *J* = 10.3, 10.0 Hz), 5.39 (dq, 1H, *J* = 10.8, 2.3 Hz), 3.98 (d, 1H, *J* = 5.4 Hz), 2.92 (ddq, 1H, *J* = 9.3, 6.5, 6.4 Hz), 1.94 (d, 3H, *J* = 2.4 Hz), 1.76 (d, 3H, *J* = 0.9 Hz), 0.91 (d, 3H, *J* = 6.9 Hz), 0.86 (s, 9H), 0.01 (s, 3H), -0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.2, 143.7, 109.8, 89.4, 80.8, 78.0, 76.6, 39.5, 25.7, 20.6, 18.2, 17.1, 4.4, -4.9, -5.2

ppm; IR (film): $\tilde{\nu}$ = 2956, 2928, 2885, 2856, 2332, 2330, 2324, 1615, 1471, 1462, 1361, 1252, 1081, 1019, 1005, 938, 862, 833, 773, 749, 673 cm^{-1}; MS (EI) *m*/*z* (%): 347 (6), 312 (16), 311 (100), 146 (7), 127 (8), 115 (12), 91 (6), 75 (13), 73 (70), 59 (9), 53 (7); HRMS (ESI): *m*/*z*: calcd. for $C_{17}H_{29}OISiNa$ [M^++Na]: 427.09246, found 427.09258.

(1*E*,3*S*,4*S*,5*Z*)-1-Iodo-2,4-dimethylnona-1,5-dien-7-yn-3-ol (11). TBAF (1 M in THF, 1.42 mL, 1.42 mmol) was added to a solution of the above silyl ether (230 mg, 0.568 mmol) in THF (5 mL) at 0°C and the mixture stirred at this temperature for 3.5 h before it was quenched with water (5 mL), sat. aq. sat. NH_4Cl (2 mL) and *tert*-butyl methyl ether (10 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 10 mL), and the combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (hexanes/EtOAc, 9:1) to yield alcohol **11** as a colorless oil (163 mg, 99%). $[\alpha]_{20}^{D}$ = +24.0 (c = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.24 (s, 1H), 5.64 (dd, 1H, *J* = 10.3 Hz, 10.1 Hz), 5.55 (dq, 1H, *J* = 10.7 Hz, 2.1 Hz), 3.91 (dd, 1H, *J* = 8.0 Hz, 3.1 Hz), 2.97 (dqd, 1H, *J* = 9.2, 7.2, 7.1 Hz), 1.97 (d, 3H, *J* = 2.2 Hz), 1.88 (d, 1H, *J* = 3.3 Hz), 1.83 (d, 3H, *J* = 0.8 Hz), 0.90 ppm (3H, d, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.2, 142.9, 111.8, 90.8, 80.7, 79.6, 76.0, 38.8, 19.4, 16.8, 4.4 ppm; IR (film): $\tilde{\nu}$ = 3535, 3419, 2962, 2916, 2873, 2853, 1615, 1454, 1399, 1377, 1271, 1143, 1117, 1072, 1005, 933, 753, 671 cm^{-1}; MS (EI) *m*/*z* (%): 290 (1), 197 (59), 163 (10), 95 (9), 94, (100), 93 (16), 91(26)79 (89), 77 (40), 60 (5), 65 (9), 53 (10), 51 (7), 43 (12), 4 1 (6), 39 (25), 29 (5); HRMS (EI): *m*/*z*: calcd. for $C_{11}H_{15}OI$ [*M*]: 290.01676, found 290.01657.

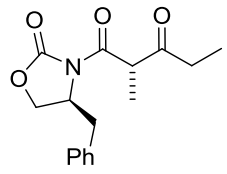


(*S*)-4-Benzyl-3-((2*S*,3*R*)-3-hydroxy-2-methylpentanoyl)oxazolidin-2-one. Bu_2BOTf (1 M in CH_2Cl_2, 49 mL, 49 mmol) was slowly added to a solution of ketone **12** (9.7 g, 41.6 mmol) in CH_2Cl_2 (92 mL) at 0 °C. Et_3N (7.6 mL, 55 mmol) was then added at such a rate as to keep the internal temperature below 2°C. Once the addition was complete, the mixture was cooled to -78 °C before freshly distilled propionaldehyde (4.4 mL, 46.4 mmol) was introduced. The mixture was stirred for 30 min at –78°C before the CO_2/acetone bath was replaced by an ice bath. Stirring was continued for 1 h and the reaction quenched with aq. phosphate buffer (46 mL, pH 7) and MeOH (138 mL)



(T < -6 °C). Next, a 1:2 mixture of MeOH and 30% aqueous H_2O_2 (138 mL) was carefully added such that the internal temperature never rose above 10 °C. The mixture was stirred for 1 h once the addition was complete. After concentration on a rotary evaporator (bath-temperature ca. 30 °C), Et_2O (50 mL) was added to the slurry and the aqueous phase extracted with Et_2O (3 x 50 mL). The combined extracts were washed with aq. sat. $NaHCO_3$ (12 mL) and brine (12 mL) before being dried over $MgSO_4$. Evaporation of the solvent and flash chromatography (hexanes/EtOAc, 3:1) of the residue, followed by recrystallization of the product from Et_2O/hexanes afforded the title compound as a white solid (11.71 g, 97%). $[\alpha]_{20}^{D}$ = + 20.8 (*c* = 1.38, $CHCl_3$), ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 – 7.25 (m, 3H), 7.22 – 7.16 (m, 2H), 4.68 (ddq, 1H, *J* = 13.7, 6.9, 3.4 Hz), 4.27 – 4.12 (m, 2H), 3.89 – 3.80 (m, 1H), 3.80 – 3.70 (m, 1H), 3.24 (dd, 1H, *J* = 13.4, 3.3 Hz), 2.76 (dd, 1H, *J* = 13.4, 9.5 Hz), 1.88 (br s, 1H), 1.66 – 1.32 (m, 2H), 1.23 (d, 3H, *J* = 7.0 Hz), 0.96 ppm (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6, 153.0, 135.0, 129.4, 129.0, 127.4, 73.0, 66.2, 55.1, 41.7, 37.8, 26.7, 10.4, 10.2 ppm; IR (film): $\tilde{\nu}$ = 3466, 2969, 1778, 1696, 1455, 1385, 1210, 1113, 1030, 969, 762, 749, 702 cm^{-1}; MS (EI) *m*/*z* (%): 292 (7), 291 (30), 273 (9), 244 (46), 233 (30), 178 (42), 158 (100), 142 (12), 134 (63), 133 (20), 117 (38), 116 (23), 115 (49), 97 (26), 91 (56), 86 (80), 77 (7), 69 (34), 57 (45), 42 (15); HRMS (ESI): *m*/*z*: calcd. for $C_{16}H_{21}NO_4Na$ [M^++Na]: 314.13628, found 314.13637. The analytical and spectroscopic data are in agreement with those reported in the literature.[5]

(*S*)-1-((*S*)-4-Benzyl-2-oxo-oxazolidin-3-yl)-2-methylpentane-1,3-dione (13). The aldol



product obtained in the previous step (5.70 g, 19.6 mmol) was dissolved in CH_2Cl_2 (92 mL) and DMSO (92 mL) and the solution cooled to -15 °C. Et_3N (8.20 ml, 58.8 mmol) was introduced followed by a very slow addition of a solution of SO_3·pyridine (9.40 g, 58.8 mmol) in DMSO (92 mL). The resulting mixture was stirred for 3 h. For workup, Et_2O (400 mL) was added and the organic phase washed with aq. $KHSO_4$ (1 M, 400 mL), sat. aq. $NaHCO_3$ (400 mL) and brine (400 mL). After drying of the organic layer over $MgSO_4$ and concentration *in vacuo*, the residue was purified by flash chromatography

[5] J. R. Gage, D. A. Evans, *Org. Synth.* **1989**, *68*, 83-91.

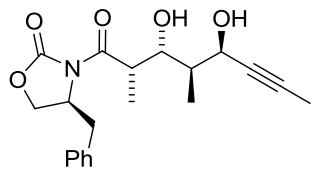
(hexanes/EtOAc, 6:1 → 3:1) to give product **13** as a white solid (4.96 g, 88%). Mp = 71-72 °C (hexanes); $[\alpha]_{20}^{D}$ = +137.4 (*c* = 0.91, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39 – 7.29 (m, 3H), 7.27 – 7.18 (m, 2H), 4.82 – 4.70 (m, 1H), 4.62 (q, 1H, *J* = 7.3 Hz), 4.31 – 4.09 (m, 2H), 3.33 (dd, 1H, *J* = 13.3, 3.3 Hz), 2.85 – 2.57 (m, 3H), 1.46 (d, 3H, *J* = 7.3 Hz), 1.09 ppm (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.2, 170.3, 153.8, 135.1, 129.4, 129.0, 127.3, 66.5, 55.3, 52.7, 38.0, 34.0, 12.9, 7.5 ppm; IR (film): $\tilde{\nu}$ = 2985, 1760, 1718, 1702, 1455, 1390, 1360, 1250, 1213, 1125, 1082, 1082, 1051, 1010, 974, 763, 748, 703 cm^{-1}; MS (EI) *m*/*z* (%): 289 (15) [M^+], 260 (15), 233 (15), 178 (10), 142 (25), 117 (40), 91 (25), 65 (5), 57 (100), 42 (5); HRMS (ESI): *m*/*z*: calcd. for $C_{16}H_{19}NO_4Na$ [M^+ + Na]: 312.12062, found 312.12043. The analytical and spectroscopic data are in agreement with those reported in the literature.[6]

But-2-ynal (14). But-2-ynol (5.0 mL, 66 mmol) was added to a vigorously stirred suspension of MnO_2 (activated, 65 g, 748 mmol) in Et_2O (7 mL). Additional Et_2O (17 mL) was then added and the mixture stirred at ambient temperature overnight. After filtration through a pad of Celite and careful evaporation of the filtrate at ≤ 40°C bath temperature, the residue was distilled (b.p. 75-80 °C) under Ar to give but-2-ynal as a pale yellow liquid, which must be stored at low temperature (1.99 g, 44%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.13 (dd, *J* = 1.8, 0.9 Hz, 1H), 2.05 ppm (d, *J* = 1.0 Hz, 3H). The analytical and spectroscopic data are in agreement with those reported in the literature.[7]

(2*S*,4*R*,5*R*)-1-((*S*)-4-Benzyl-2-oxo-oxazolidin-3-yl)-5-hydroxy-2,4-dimethyloct-6-yne-1,3-dione (15). Et_3N (0.78 mL, 5.66 mmol) was added dropwise to a solution of $Sn(OTf)_2$ (2.36 g, 5.66 mmol) in CH_2Cl_2 (27 mL). After cooling to -30 °C, a solution of ketone **13** (1.56 g, 13.07 mmol) in CH_2Cl_2 (9 mL) was slowly introduced and the mixture stirred for 1 h at this temperature before it was cooled to -78 °C and but-2-ynal (1.8 ml, 29 mmol) was added dropwise. After an additional 45 min, the mixture was diluted with CH_2Cl_2 (30 mL) and added to a vigorously stirred aq.

[6] D. A. Evans, H. P. Ng, J. S. Clark, D. L. Rieger, *Tetrahedron*, **1992**, *48*, 2127-2142.
[7] H. J. Bestmann, K. H. Koschatzky, W. Schaetzke, J. Suess, O. Vostrowsky, *Liebigs Ann. Chem.* **1981**, *9*, 1705-1720.

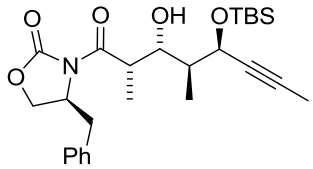
solution of $NaHSO_4$ (1 M, 80 mL) at 0 °C. This slurry was stirred for 10 min before the aqueous phase was extracted with CH_2Cl_2 (4 x 80 mL). The combined extracts were washed with aq. sat. $NaHCO_3$ (120 mL), dried over Na_2SO_4 and concentrated. Flash chromatography of the residue afforded the title compound as a white solid (1.05 g, 55%, 88% brsm). $[\alpha]_{20}^{D}$ = + 101.1 (*c* = 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 – 7.25 (m, 3H), 7.23 – 7.14 (m, 2H), 4.90 (q, 1H, *J* = 7.3 Hz), 4.78 – 4.68 (m, 1H), 4.60 (s, 1H), 4.31 – 4.21 (m, 1H), 4.17 (dd, 1H, *J* = 9.1, 2.8 Hz), 3.28 (dd, 1H, *J* = 13.4, 3.2 Hz), 3.02 – 2.88 (m, 1H), 2.76 (dd, 1H, *J* = 13.3, 9.6 Hz), 2.40 (s, 1H), 1.82 (d, 3H, *J* = 1.8 Hz), 1.47 (d, 3H, *J* = 7.2 Hz), 1.36 ppm (d, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.3, 170.5, 153.7, 135.0, 129.3, 129.0, 127.4, 82.5, 78.0, 66.4, 63.3, 55.2, 51.8, 50.3, 37.9, 12.7, 12.0, 3.4 ppm; IR (film): $\tilde{\nu}$ = 3511, 2940, 1775, 1716, 1690, 1454, 1357, 1212, 1117, 998, 913, 762, 735, 703 cm^{-1}; MS (EI) *m*/*z* (%): 357 (2), 339 (2), 311 (2), 289 (40), 260 (17), 233 (30), 204 (1), 178 (29), 159 (3), 156 (5), 142 (19), 134 (38), 125 (33), 117 (78), 112 (100), 107 (26), 101 (16), 97 (3), 91 (74), 86 (73), 83 (25), 79 (24), 77 (13), 69 (32), 65 (19), 57 (89), 42 (30), 39 (28), 29 (26); HRMS (ESI): *m*/*z*: calcd. for $C_{20}H_{23}NO_5Na$ [M^+ + Na]: 380.14685, found 380.14704.

(*S*)-4-Benzyl-3-((2*S*,3*R*,4*S*,5*R*)-3,5-dihydroxy-2,4-dimethyloct-6-ynoyl)oxazolidin-2-one. 

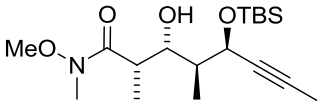
$Me_4NBH(OAc)_3$ (3.72 g, 14.2 mmol) was dissolved in MeCN (260 mL) and HOAc (160 mL) and the resulting mixture cooled to -50 °C. A solution of compound **15** (1.01 g, 2.83 mmol) in MeCN (34 mL) was added and the mixture warmed to +10 °C overnight. The mixture was then poured into a pre-cooled (0 °C) mixture of sat. aq. solution of Rochelle salt (140 mL) and *tert*-butyl methyl ether (140 mL). Under vigorous stirring, saturated $NaHCO_3$-solution and solid $NaHCO_3$ were added in small portions until no further gas evolution could be observed. The phases were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (4 x 100 mL). The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to obtain the desired diol (1.00 g, 98%) as a mixture of diastereomers (2:92:4:1:0.5 as determined by HPLC: 50 mm Ultra HAT Pro 18, 120 A, 2 μm, ∅ 3.0 mm, MeOH/H_2O = 60:40, 0.5 mL/min, 308 K, 27.4 MPa). $[\alpha]_{20}^{D}$ = + 36.0 (*c* =1.1, $CHCl_3$); ^{1}H NMR (400

MHz, $CDCl_3$): δ = 7.35 – 7.25 (m, 3H), 7.21 – 7.15 (m, 2H), 4.75 – 4.66 (m, 1H), 4.45 (s, 1H), 4.27 – 4.15 (m, 3H), 4.14 – 4.01 (m, 1H), 3.89 – 3.76 (m, 2H), 3.22 (dd, 1H, *J* = 13.4, 3.4 Hz), 2.82 – 2.73 (m, 1H), 2.06 – 1.93 (m, 1H), 1.84 (t, 3H, *J* = 3.6 Hz), 1.24 (dd, 3H, *J* = 13.8, 7.0 Hz), 0.91 – 0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1, 152.7, 134.9, 129.4, 129.0, 127.5, 81.9, 78.3, 73.7, 67.3, 66.2, 54.9, 39.7, 39.1, 37.8, 12.9, 9.7, 3.6; IR (film): $\tilde{\nu}$ = 3417, 2974, 2921, 1778, 1698, 1455, 1388, 1287, 978, 762, 702 cm^{-1}; MS (EI) *m*/*z* (%): 359 (1), 341 (3), 308 (1), 273 (68), 262 (7), 244 (3), 233 (38), 183 (3), 178 (50), 165 (14), 159 (4), 149 (4), 142 (12), 136 (11), 134 (29), 126 (13), 117 (57), 109 (34), 103 (8), 96 (100), 91 (71), 86 (74), 80 (44), 77 (11), 69 (35), 67 (11), 65 (17), 57 (51), 41 (32), 39 (18), 29 (23), 27 (9); HRMS (ESI): *m*/*z*: calcd. for $C_{20}H_{25}NO_5Na$ [M^+ + Na]: 382.16250, found 382.16199.

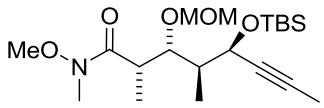
(*S*)-4-Benzyl-3-((2*S*,3*R*,4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxy-2,4-dimethyloct-6-ynoyl)oxazolidin-2-one. Et_3N (0.97 mL, 4.2 mmol) and TBSOTf (0.78 mL, 5.6 mmol) were successively added to a solution of the above diol (1.00 g, 2.78 mmol) in CH_2Cl_2 (15 mL) at -78 °C. After stirring for 3 h, the reaction was quenched with sat. aq. $NaHCO_3$ and the resulting mixture warmed to ambient temperature. The aqueous phase was extracted with CH_2Cl_2 (3 x 15 mL), and the combined extracts were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 9:1 → 7:1) to obtained the title compound as a colorless oil (1.17 g, 89%). $[\alpha]_{20}^{D}$ = + 36.8 (*c* =1.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 – 7.24 (m, 3H), 7.23 – 7.17 (m, 2H), 4.73 – 4.62 (m, 2H), 4.26 – 4.05 (m, 3H), 3.91 (d, 1H, *J* = 2.0 Hz), 3.85 (qd, 1H, *J* = 6.9, 2.4 Hz), 3.31 (dd, 1H, *J* = 13.3, 3.2 Hz), 2.74 (dt, 1H, *J* = 16.7, 8.4 Hz), 1.86 – 1.73 (m, 4H), 1.26 – 1.18 (m, 3H), 0.95 (d, 3H, *J* = 7.0 Hz), 0.87 (s, 9H), 0.12 (s, 3H), 0.11 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.5, 153.0, 135.4, 129.4, 128.9, 127.3, 82.1, 78.5, 72.6, 66.4, 66.1, 55.6, 41.8, 40.3, 37.8, 25.8, 18.1, 11.7, 9.1, 3.5, -4.5, -5.4 ppm; IR (film): $\tilde{\nu}$ = 3509, 2928, 1782, 1702, 1680, 1455, 1387, 1360, 1285, 1242, 1209, 1104, 1050, 1019, 984, 938, 836, 777, 702, 678 cm^{-1}; MS (EI) *m*/*z* (%): 473 (M+, 6), 416 (21), 398 (3), 348 (4), 341 (3), 337 (7), 336 (32), 324 (329, 318 (10), 306 (14), 290 (5), 273 (8), 262 (4), 252 (44), 239 (14), 233 (14), 183 (100), 178 (41), 165 (5), 159 (42), 147 (85), 143 (53),



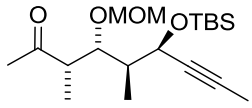
136 (5), 133 (6), 127 (9), 119 (14), 117 (32), 115 (25), 109 (20), 97 (14), 91 (27), 81 (8), 77 (6), 75 (72), 73 (49), 57 (11), 29 (5); HRMS (ESI): *m*/*z*: calcd. for $C_{26}H_{39}NO_3SiNa$ [M^+ + Na]: 496.24897, found 496.24907.

(2*S*,3*R*,4*S*,5*R*)-5-(*tert*-Butyldimethylsilyloxy)-3-hydroxy-*N*-methoxy-*N*,2,4-trimethyloct-6-ynamide (16). 

$AlMe_3$ (2 M in heptane, 4.2 mL, 8.31 mmol) was carefully added (exothermic reaction) to a solution of *N*,*O*-dimethylhydroxylamine hydrochloride (0.811 g, 8.31 mmol) in THF (7 mL) at 0 °C and the resulting suspension was stirred for 15 min at this temperature and for 75 min at room temperature. The mixture was then cooled to -70 °C before a solution of (*S*)-4-benzyl-3-((2*S*,3*R*,4*S*,5*R*)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxy-2,4-dimethyloct-6-ynoyl)oxazolidin-2-one (see above, 1.05 g, 2.22 mmol) in THF (10 mL) was slowly added. The mixture was warmed to -10°C over 8 h before it was poured into a chilled (0°C) sat. aq. Rochelle salt solution (300 mL). The resulting suspension was stirred for 45 min and then repeatedly extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 6:1) to afford the title compound as a colorless oil that solidified in the fridge (715 mg, 90%). $[\alpha]_{20}^{D}$ = +46.5 (*c* = 0.79, $CHCl_3$); mp ≈ 13 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.86 – 4.82 (m, 1H), 4.05 (s, 1H), 3.75 (dd, 1H, *J* = 9.2, 2.4 Hz), 3.69 (s, 3H), 3.18 (s, 3H), 3.06 – 2.92 (m, 1H), 1.80 (d, 3H, *J* = 2.2 Hz,), 1.73 – 1.63 (m, 1H), 1.11 (d, 3H, *J* = 7.1 Hz,), 0.95 (d, 3H, *J* = 6.9 Hz,), 0.86 (s, 9H), 0.11 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.3, 80.5, 80.3, 71.7, 63.1, 61.4, 42.2, 36.0, 32.0, 25.8, 18.1, 10.4, 9.5, 3.4, -4.6, -5.3 ppm; IR (film): $\tilde{\nu}$ = 3458, 2956, 2932, 2857, 1639, 1462, 1416, 1388, 1361, 1292, 1251, 1178, 1146, 1113, 1056, 1016, 998, 863, 833, 776, 684 cm^{-1}; MS (EI) *m*/*z* (%): 357 (1), 326 (2), 302 (3), 300 (47), 297 (13), 241 (9), 232 (3), 225 (6), 220 (34), 217 (24), 208 (27), 183 (100), 174 (7), 164 (16), 159 (8), 153 (16), 143 (24), 138 (7), 127 (7), 117 (30), 115 (42), 109 (17), 97 (19), 87 (9), 85 (11), 81 (12), 75 (90), 73 (64), 62 (8), 61 (12), 59 (12), 45 (7), 41 (8), 29 (14); HRMS (ESI): *m*/*z*: calcd. for $C_{18}H_{35}NO_4SiNa$ [M^+ + Na]: 380.22276, found 380.22281.

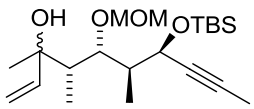
(2*S*,3*R*,4*S*,5*R*)-5-(*tert*-Butyldimethylsilyloxy)-*N*-methoxy-3-(methoxymethoxy)-*N*,2,4-trimethyloct-6-ynamide (17). 

iPr_2NEt (3.01 mL, 18.2 mmol) and MOMCl (0.691 mL, 9.10 mmol) were added to a solution of **16** (650 mg, 1.82 mmol) in DMF (5 mL) and the resulting slightly fuming mixture stirred at 50 °C for 18 h. After cooling, *tert*-butyl methyl ether (20 mL) and brine (30 mL) were introduced and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 15 mL). The combined extracts were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexanes/EtOAc, 29:1 → 8:1) to furnish product **17** as a colorless oil (651 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.64 – 4.43 (m, 3H), 3.97 (dd, 1H, *J* = 8.8, 2.7 Hz), 3.65 (s, 3H), 3.31 (s, 3H), 3.15 (s, 3H), 2.96 (qd, 1H, *J* = 6.9, 2.7 Hz), 1.80 (d, 3H, *J* = 2.2 Hz), 1.78 – 1.68 (m, 1H), 1.09 (d, 3H, *J* = 7.0 Hz), 0.98 (d, 3H, *J* = 6.9 Hz), 0.86 (s, 9H), 0.12 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 98.1, 96.0, 80.9, 79.6, 62.7, 61.0, 56.3, 44.2, 38.1, 25.8, 18.2, 14.2, 10.9, 9.7, 3.5, -3.9, -5.0 ppm; IR (film): $\tilde{\nu}$ = 2931, 2890, 2857, 1672, 1463, 1408, 1377, 1250, 1168, 1143, 1031, 1002, 940, 920, 834, 776, 673 cm^{-1}; MS (EI) *m*/*z* (%): 370 (5), 357 (3), 356 (12), 344 (51), 341 (10), 312 (6), 300 (5), 282(11), 274 (16), 271 (34), 260 (8), 253 (7), 239 (10), 234 (14), 227 (15), 223 (18), 208 (32), 183 (62), 179 (25), 157 (19), 149 (12), 127 (12), 119 (15), 115 (28), 105 (16), 97 (28), 89 (73), 73 (84), 59 (179, 45 (100), 29 (6) ; HRMS (ESI): *m*/*z*: calcd. for $C_{20}H_{39}NO_5SiNa$ [M^+ + Na]: 424.24897, found 424.24886.

(3*S*,4*R*,5*S*,6*R*)-6-(*tert*-Butyldimethylsilyloxy)-4-(methoxymethoxy)-3,5-dimethylnon-7-yn-2-one. 

MeMgCl (2.76 M in THF, 1.76 mL, 4.86 mmol) was added dropwise to a solution of compound **17** (650 mg, 1.62 mmol) in Et_2O (15.0 mL) at 0 °C and the resulting mixture was stirred for 2 h. The reaction was quenched with brine (15 mL), the aqueous phase was extracted with Et_2O (3 x 10 mL), and the combined extracts were dried over Na_2SO_4 and concentrated to give the desired ketone as a colorless oil which was used as such in the next step (562 mg, 97%, > 98% pure). An analytically pure sample was obtained by flash chromatography (hexanes/EtOAc, 29:1 → 8:1). $[\alpha]_{20}^{D}$ = +64.1 (*c* = 0.88, hexanes); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.65 – 4.43 (m, 3H), 4.03 (dd, 1H, *J* = 9.2, 1.9 Hz), 3.21 (s, 3H), 2.58 (qd, 1H, *J* = 6.9, 1.8 Hz), 2.19 (s, 3H), 1.81 (d, 3H, *J* = 2.2 Hz), 1.79 – 1.70 (m,

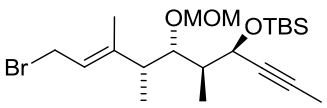
1H), 1.05 (d, 3H, J = 6.9 Hz,), 0.98 (d, 3H, J = 6.9 Hz), 0.88 (s, 9H), 0.14 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.0, 97.9, 81.4, 80.5, 79.9, 62.7, 55.9, 49.5, 44.1, 28.1, 25.9, 18.2, 11.0, 8.2, 3.5, -3.8, -4.5 ppm; IR (film): $\tilde{\nu}$ = 2931, 2857, 1716, 1462, 1360, 1251, 1188, 1142, 1090, 1058, 1032, 918, 834, 777, 677 cm^{-1}; MS (EI) *m*/*z* (%): 311 (1), 299 (1), 293 (3), 255 (4), 239 (12), 237 (99, 229 (59, 227 (9), 225 (4), 197 (27), 183 (86), 163 (46), 159 (27), 157 (15), 153 (15), 119 (19), 115 (18), 97 (21), 89 (57), 75 (55), 74 (6), 59 (17), 45 (100), 43 (46), 41 (8); HRMS (ESI): *m*/*z*: calcd. for $C_{19}H_{36}O_5SiNa$ [M^+ + Na]: 379.22751, found 379.22734.

(4*S*,5*R*,6*S*,7*R*)-7-(*tert*-Butyldimethylsilyloxy)-5-(methoxymethoxy)-3,4,6-trimethyldec-1-en-8-yn-3-ol (18). 

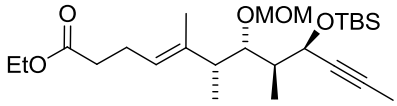
Vinylmagnesium bromide (1.0 M in THF, 3.15 mL, 3.15 mmol) was slowly added at –78°C to a solution of the ketone obtained in the previous step (562 mg, 1.58 mmol) in THF (15 mL). The mixture was slowly warmed to ambient temperature (2 h) and stirred for an additional 2 h. Sat. aq. NH_4Cl (25 mL) was then introduced and the aqueous phase extracted with Et_2O (3 x 12 mL). The combined extracts were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1 → 8:1) to provide alcohol **18** as a mixture of isomers (2:1, ^{1}H NMR) (530 mg, 87%). $[\alpha]_{20}^{D}$ = + 47.4 (c = 0.69, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, data given for the major isomer): δ = 5.92 – 5.68 (m, 1H), 5.39 – 5.16 (m, 1H), 5.12 – 4.95 (m, 1H), 4.79 – 4.59 (m, 2H), 4.56 – 4.44 (m, 1H), 4.05 – 3.78 (m, 2H), 3.37 (s, 3H), 1.89 – 1.76 (m, 3H), 1.76 – 1.52 (m, 3H), 1.31 (s, 1H), 1.18 (d, 2H, J = 0.7 Hz), 1.03 - 1.01 (m, 2H), 0.95 – 0.90 (m, 3H), 0.89 – 0.83 (m, 9H), 0.16 – 0.05 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, data given for the major isomer): δ = 146.7, 111.5, 99.5, 82.7, 81.4, 80.4, 75.9, 63.1, 55.8, 44.5, 41.9, 27.3, 25.9, 18.1, 11.2, 7.1, 3.5, -3.6, -5.0; IR (film): $\tilde{\nu}$ = 3483, 2931, 2857, 1462, 1380, 1361, 1250, 1209, 1143, 1032, 920, 833, 814, 776, 678 cm^{-1}; MS (EI) *m*/*z* (%): 384, 339, 253 (1), 215 (4), 185 (11), 183 (100), 157 (9), 143 (10), 127 (7), 119 (7), 115 (9), 97 (11), 89 (22), 75 (24), 73 (37), 59 (6), 45 (34) ; HRMS (ESI): *m*/*z*: calcd. for $C_{21}H_{40}O_4SiNa$ [M^+ + Na]: 407.25881, found 407.25918.

(5*S*,6*S*,7*R*)-5-((*R*,*E*)-5-Bromo-3-methylpent-3-en-2-yl)-6,9,9,10,10-pentamethyl-7-(prop-1-ynyl)-2,4,8-trioxa-9-silaundecane (19). Pyridine (0.32 mL, 3.92 mmol) was added at 0°C to a solution of alcohol **18** (502 mg, 1.31 mmol) in Et_2O (6.1 mL), followed

by very slow addition of PBr_3 (1.0 M in toluene, 3.13 mL, 3.13 mmol). The resulting mixture was stirred for 3 h at 0 °C before it was diluted with Et_2O (20 mL). The reaction was carefully quenched with sat. aq. $NaHCO_3$ (100 mL) and the aqueous phase extracted with Et_2O (3 x 20 mL), the combined extracts were dried over Na_2SO_4, filtered through a short pad of SiO_2 and evaporated. The residue was very sensitive and therefore immediately used in the next reaction (556 mg, 95%). ^{1}H NMR (400 MHz, C_6D_6): δ = 5.49 – 5.42 (m, 1H), 4.95 (ddd, 1H, *J* = 4.8, 2.3, 2.3 Hz), 4.60 (d, 1H, *J* = 6.6 Hz), 4.47 (d, 1H, *J* = 6.6 Hz), 3.75 (dd, 1H, *J* = 8.4, 2.7 Hz), 3.66 (dd, 2H, *J* = 8.4, 2.1 Hz), 3.17 (s, 3H), 2.16 (dq, 1H, *J* = 6.8, 1.1 Hz), 2.04 – 1.96 (m, 1H), 1.55 (d, 3H, *J* = 1.0 Hz), 1.50 (d, 3H, *J* = 2.2 Hz), 1.13 (d, 3H, *J* = 6.8 Hz), 1.06 (s, 9H), 0.97 (d, 3H, *J* = 6.9 Hz), 0.36 (s, 3H), 0.28 ppm (s, 3H); HRMS (ESI): *m*/*z*: calcd. for $C_{21}H_{39}BrO_3SiNa$ [M^++Na]: 469.17442, found 469.17489.



(6*R*,7*S*,8*S*,9*R*,*E*)-Ethyl 9-(*tert*-butyldimethylsilyloxy)-7-(methoxymethoxy)-5,6,8-trimethyldodec-4-en-10-ynoate. *n*BuLi (1.6 M in hexanes, 14.6 mL, 23.4 mmol) was added to a solution of diisopropylamine (3.47 mL, 24.7 mmol) in THF (20 mL) at 0 °C and the resulting mixture stirred for 1 h.

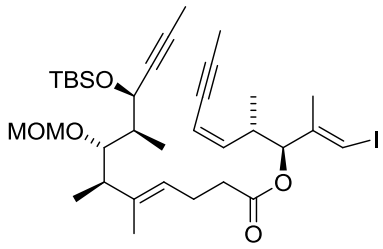


In parallel, CuI (8.9 g, 46.8 mmol) was suspended in THF (40 mL) and the suspension cooled to -110 °C (cooling bath: $Et_2O/CO_2/N_2$). EtOAc (2.43 mL, 24.7 mmol) was added via syringe followed by the very slow addition of the freshly prepared LDA-solution via canula. The mixture was warmed over 3 h to -30 °C, causing the color of the slurry from grey to yellow-brown. A solution of allyl bromide **19** (580 mg, 1.30 mmol) in THF (5 mL) was then slowly introduced and the mixture stirred for 2.5 h. Prior to work up, the suspension was cooled to -60 °C before the reaction was quenched with aq. NH_4Cl/NH_4OH (9:1; 63 g NH_4Cl, 17.5 mL 30% aqueous NH_4OH, filled up to 350 mL with H_2O). The aqueous phase was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography of the residue (hexanes/EtOAc, 100:0 → 19:1) afforded the title compound as a pale yellow oil (369 mg, 62%). $[\alpha]_{20}^{D}$ = + 16.0 (*c* = 0.24, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.17 (t, 1H, *J* = 6.3 Hz), 4.56 (ddd, 1H,

J = 5.6, 2.1, 2.0 Hz), 4.52 (dd, 1H, *J* = 6.3 Hz), 4.43 (d, 1H, *J* = 6.3 Hz), 4.11 (q, 2H, *J* = 7.1 Hz), 3.61 (dd, 1H, *J* = 7.8, 3.6 Hz), 3.32 (s, 3H), 2.31 (m, 4H), 2.26 – 2.17 (m, 1H), 1.80 (d, 3H, *J* = 2.1 Hz), 1.78 – 1.71 (m, 1H), 1.64 (s, 3H), 1.24 (t, 3H, *J* = 7.1 Hz), 0.96 (dd, 6H, *J* = 6.9, 4.7 Hz), 0.88 (s, 9H), 0.13 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.3, 138.98, 123.1, 98.0, 81.2, 80.6, 80.6, 63.2, 60.2, 55.9, 44.3, 42.8, 34.2, 25.8, 23.6, 18.2, 15.8, 14.2, 12.5, 11.1, 3.4, -4.1, -5.1 ppm; IR (film): $\tilde{\nu}$ = 2956, 2929, 2857, 1727, 1462, 1374, 1249, 1143, 1116, 1093, 1033, 919, 835, 814, 777, 676 cm^{-1}; MS (EI) *m*/*z* (%): 439, 397 (1), 365 (1), 329 (4), 283 (13), 253 (3), 211 (6), 183 (100), 169 (11), 157 (17), 115 (9), 95 (17), 89 (17), 73 (29), 45 (31); HRMS (ESI): *m*/*z*: calcd. for $C_{25}H_{46}O_5SiNa$ [M^+ + Na]: 477.30067, found 477.30085.

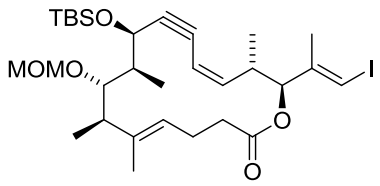
(6*R*,7*S*,8*S*,9*R*,*E*)-9-(*tert*-Butyldimethylsilyloxy)-7-(methoxymethoxy)-5,6,8-trimethyl-dodec-4-en-10-ynoic acid (20). TMSOK (521 mg, 4.06 mmol) was added to a solution of the ethyl ester described above (369 mg, 0.812 mmol) in Et_2O (48 mL). The suspension was stirred for 48 h before being carefully neutralized with solid CO_2 and sat. aq. NH_4Cl. The aqueous phase was extracted with EtOAc (5 x 25 mL) and the combined extracts were washed with brine (40 mL), dried over Na_2SO_4 and concentrated. The crude acid **20**, obtained as a pale yellow oil was judged pure and therefore used without further purification in the next step (347 mg, quant.). $[\alpha]_{20}^{D}$ = +44.7 (*c* = 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.5 – 9.5 (br s, 1H), 5.16 (t, 1H, *J* = 6.1 Hz), 4.56 – 4.53 (m, 1H), 4.52 (d, 1H, *J* = 6.3 Hz), 4.43 (d, 1H, *J* = 6.3 Hz), 3.60 (dd, 1H, *J* = 7.8, 3.5 Hz), 3.32 (s, 3H), 2.42 – 2.29 (m, 4H), 2.28 – 2.20 (m, 1H), 1.80 (d, 3H, *J* = 2.7 Hz), 1.78 – 1.71 (m, 1H), 1.64 (s, 3H), 0.97 (t, 6H, *J* = 7.2 Hz), 0.89 (s, 9H), 0.12 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.7 139.3, 122.8, 98.0, 81.2, 80.7, 80.6, 63.2, 55.9, 44.3, 42.8, 33.8, 25.9, 23.4, 18.2, 15.8, 12.5, 11.1, 3.5, -4.1, -5.0 ppm; IR (film): $\tilde{\nu}$ = 3095, 2929, 2857, 2333, 2171, 1712, 1463, 1377, 1250, 1143, 1033, 923, 834, 777, 676 cm^{-1}; MS (EI) *m*/*z* (%): 411, 337 (1), 307 (3), 283 (12), 227 (6), 183 (100), 173 (8), 157 (16), 154 (14), 115 (9), 97 (8), 89 (14), 75 (16), 73 (30), 45 (48); HRMS (ESI): *m*/*z*: calcd. for $C_{23}H_{42}O_5SiNa$ [M^+ + Na]: 449.26937, found 449.26952.

(6*R*,7*S*,8*S*,9*R*,*E*)-((1*E*,3*S*,4*S*,5*Z*)-1-Iodo-2,4-dimethylnona-1,5-dien-7-yn-3-yl) 9-(*tert*-butyldimethylsilyloxy)-7-(methoxymethoxy)-5,6,8-trimethyldodec-4-en-10-ynoate



(29). EDCI·HCl (83.1 mg, 0.433 mmol) was added to a solution of alcohol **11** (114 mg, 0.393 mmol) in CH_2Cl_2 (2.8 mL) and the resulting mixture cooled to 0°C. Next, DMAP (52.9 mg, 0.433 mmol) was introduced in three portions and the mixture stirred for 10 min before a solution of acid **20** (185 mg, 0.433 mmol) in CH_2Cl_2 (2.5 mL) was slowly added. Stirring was continued for 30 min at 0°C before the ice bath was removed. After 5 h at ambient temperature, the mixture was poured into brine (10 mL) and diluted with CH_2Cl_2 (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 8 mL), the combined organic phases were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 29:1 $\rightarrow$ 19:1) to give the title compound as a colorless oil (244 mg, 89%). $[\alpha]_{20}^{D}$ = +80.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.26 (s, 1H), 5.56 (dd, 1H, *J* = 10.1, 10.0 Hz), 5.43 (dq, 1H, *J* = 10.7, 2.2 Hz), 5.19 (1H, d, *J* = 7.4 Hz), 5.16 – 5.10 (br t, 1H), 4.56 – 4.52 (m, 1H), 4.51 (d, 1H, *J* = 6.3 Hz), 4.43 (d, 1H, *J* = 6.2 Hz), 3.60 (dd, 1H, *J* = 7.7, 3.6 Hz), 3.32 (s, 3H), 3.12 (ddq, 1H, *J* = 9.3, 7.1, 7.1 Hz), 2.37 – 2.27 (m, 4H), 2.27 – 2.19 (m, 1H), 1.96 (d, 3H, *J* = 2.2 Hz), 1.83 (d, 3H, *J* = 0.8 Hz), 1.80 (d, 3H, *J* = 2.1 Hz), 1.79 – 1.73 (m, 1H), 1.63 (s, 3H), 0.97 (d, 3H, *J* = 6.8 Hz), 0.96 (d, 3H, *J* = 6.9 Hz), 0.92 (d, 3H, *J* = 6.9 Hz), 0.87 (s, 9H), 0.12 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2, 144.6, 142.1, 139.0, 123.0, 111.0, 98.0, 90.3, 81.2, 80.8, 80.7, 80.4, 80.1, 76.1, 63.3, 56.0, 44.4, 42.8, 37.1, 34.3, 25.9, 23.7, 20.5, 18.2, 16.8, 15.8, 12.5, 11.1, 4.4, 3.5, -4.0, -5.0 ppm; IR (film): $\tilde{\nu}$ = 2955, 2928, 2856, 1738, 1618, 1461, 1376, 1248, 1142, 1117, 1091, 1075, 1061, 1031, 938, 920, 833, 775, 675 cm^{-1}; MS (EI) *m*/*z* (%): 458 (5), 283 (28), 185 (16), 184 (16), 183 (100), 174 (5), 169 (26), 163 (5), 159 (6), 157 (15), 153 (12), 146 (40), 145 (17), 137 (11), 131(29), 115 (7), 97 (6), 93 (8), 91 (8), 89 (16), 82 (8), 73 (29), 45 (39); HRMS (EI): *m*/*z*: calcd. for $C_{34}H_{55}IO_5SiNa$ [M^++Na]: 721.27557, found 721.27549.

Compound 30. *All glassware used for the ring closing alkyne metathesis reaction was flame-dried under vacuum and backfilled with Argon after cooling to room-temperature (3 cycles). All solvents used were freshly distilled (toluene from Na/K, CH_2Cl_2 from CaH_2), stored over 4Å MS and degassed by 4 freeze-pump-thaw cycles prior to use.* A stock solution of activated catalyst was prepared as follows: CH_2Cl_2 (205 µL, 3.26 mmol) was added to a solution of complex **34** (80.0 mg, 0.128 mmol)[8,9] in toluene (6.4 mL). The resulting brown solution was stirred for 30 min to give a 0.194 M stock solution of the active catalyst.



Diyne **29** (150 mg, 0.215 mmol) was azeotropically dried with toluene (3 x 2 mL). It was then transferred as a toluene solution to a two-necked round-bottom flask equipped with a reflux condenser and septum. Additional toluene was added to reach a total volume of 150 mL. The solution was heated to 100°C and an aliquot of the activated catalyst solution (0.33 mL, 0.065 mmol, 0.30 eq.) was introduced via syringe. The reaction was stirred at 100°C for 7 h before a second aliquot of the catalyst solution (0.11 mL, 0.022 mmol, 0.10 eq.) was added. Stirring was continued at 100°C for further 12 h. After reaching ambient temperature, the mixture was diluted with Et_2O (200 mL) to slowly form a brown precipitate which was filtered off through a short pad of SiO_2, eluting with Et_2O (250 mL). The pale brown filtrate was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 39:1 → 19:1) to provide a mixture of *N-tert*-butyl-3,5-dimethylaniline and the desired product. The amine was removed at 60°C under high vacuum overnight to leave the desired compound as a pale yellow oil (99.2 mg, 72%). $[\alpha]_{20}^{D}$ = +83.0 (c = 0.57, *n*-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.34 (d, 1H, *J* = 1.0 Hz), 5.63 (dd, 1H, *J* = 10.6, 9.6 Hz), 5.54 (dd, 1H, *J* = 10.6, 1.6 Hz), 5.36 – 5.30 (m, 1H), 5.24 (d, 1H, *J* = 9.6 Hz); 4.73 (d, 1H, *J* = 6.8 Hz), 4.62 (d, 1H, *J* = 6.8 Hz), 4.37 (dd, 1H, *J* = 9.1, 1.1 Hz), 3.43 (d, 1H, *J* = 9.2 Hz), 3.39 (s, 3H), 3.17 (dddd, 1H, *J* = 16.5, 9.7, 6.9, 6.8 Hz), 2.98 – 2.88 (m, 1H), 2.45 – 2.36 (m, 1H), 2.35 – 2.19 (m, 3H), 2.07 (dddd, 1H, *J* = 15.5, 7.2, 7.2, 0.6 Hz), 1.83 (d, 3H, *J* = 1.0 Hz), 1.48 (s, 3H), 1.07 (d, 3H, *J* = 7.1 Hz), 1.00 (d, 3H, *J* = 7.0 Hz), 0.89 (s, 9H), 0.82 (d, 3H, *J* = 6.9 Hz), 0.11 (s, 3H),

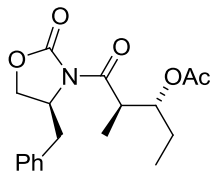
[8] C. C. Cummins, *Chem. Commun*. **1998**, 1777-1786.
[9] A. Fürstner, C. Mathes, C. W. Lehmann, *Chem. Eur. J*. **2001**, *7*, 5299-5317.

0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 144.6, 144.3, 137.4, 126.4, 110.3, 98.9, 96.9, 87.0, 82.5, 82.0, 80.6, 63.9, 56.0, 46.0, 42.0, 37.7, 34.6, 25.8, 22.5, 19.5, 18.2, 17.4, 16.6, 16.3, 12.1, -4.5, -5.1 ppm; IR (film): $\tilde{\nu}$ = 2957, 2929, 2856, 1732, 1617, 1462, 1377, 1361, 1257, 1143, 1058, 1031, 990, 932, 858, 835, 801, 775, 753, 672 cm^{-1}; MS (pos. ESI) *m*/*z* (%): 683 (M+K, 30), 667 (M+Na, 100); HRMS (EI): *m*/*z*: calcd. for $C_{30}H_{49}IO_5SiNa$ [M^++Na]: 667.22862, found 667.22903.

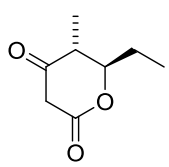
(*S*)-4-Benzyl-3-((2*R*,3*R*)-3-hydroxy-2-methylpentanoyl)oxazolidin-2-one.[10] *i*Pr_2NEt (3.35 mL, 19.7 mmol) was added to a cooled (0°C) solution of *ent*-**12** (4.00 g, 17.1 mmol) and freshly destilled (*n*Bu)$_2$BOTf (7.38 mL, 34.2 mmol) in Et_2O (40 mL). After stirring for 45 min at 0°C, the yellow suspension was cooled to -78°C before a precooled (-78°C) solution of freshly destilled propionaldehyde (1.62 mL, 22.2 mL) in Et_2O (10 mL) was slowly introduced. After an additional 30 min, the reaction was quenched by addition of solid tartaric acid (13 g) and the mixture stirred at ambient temperature for 2 h. The reaction was partitioned between ether and H_2O, and the combined organic layers were washed with sat. aq. $NaHCO_3$ (2 x 40 mL). A mixture of MeOH/30% H_2O_2 (3:1, 50 mL) was added under vigorous stirring at 0°C and the resulting mixture stirred for 1 h at room temperature before it was extracted with Et_2O (2 x 30 mL). The combined extracts were washed with $NaHCO_3$ and brine (30 mL each), dried over Na_2SO_4 and concentrated. The crude material was purified by flash chromatography (hexanes/EtOAc, 3:1) to give the title compound as an off-white solid (3.69 g, 74%, 11:1 dr.), along with additional 350 mg of mixed fractions. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 – 7.29 (m, 2H), 7.28 – 7.25 (m, 1H), 7.23 – 7.19 (m, 2H), 4.67 (ddd, 1H, *J* = 13.0, 6.8, 3.2 Hz), 4.21 – 4.12 (m, 2H), 3.90 (dq, 1H, *J* = 6.9, 6.9 Hz), 3.65 (dddd, 1H, *J* = 8.3, 8.3, 7.4, 3.5 Hz), 3.31 (dd, 1H, *J* = 13.5, 3.4 Hz), 2.76 (dd, 1H, *J* = 13.4, 9.6 Hz), 2.56 – 2.52 (m, 1H), 1.73 – 1.63 (m, 1H), 1.54 – 1.41 (m, 1H), 1.20 (d, 3H, *J* = 6.9 Hz), 1.00 ppm (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.9, 153.6, 135.2, 129.4, 129.0, 127.3, 76.0, 66.0, 55.6, 42.9, 37.9, 27.8, 14.6, 9.8 ppm; IR (film): $\tilde{\nu}$ = 3516, 2967, 2936, 2879, 1775, 1695, 1455, 1385, 1351, 1291, 1209, 1111, 1051, 1015, 969, 762, 749, 702 cm^{-1}; MS (EI) *m*/*z* (%): 291 (10), 244 (28), 233 (18), 178 (32), 158 (15), 142 (13), 134 (24), 133 (16), 118 (14),

[10] Prepared according to: B. R. Raimundo, C. H. Heathcock, *Synlett* **1995**, 1213-1214.

117 (51), 116 (25), 115 (42), 97 (27), 96 (11), 92 (39), 91 (100), 86 (87), 85 (25), 77 (11), 70 (13), 69 (37), 65 (29), 59 (57), 58 (19), 57 (89), 56 (24), 45 (27), 43 (22), 42 (33), 41 (38), 39 (18), 31 (42), 30 (15), 29 (73), 28 (22), 27 (33); HRMS (EI): *m*/*z*: calcd. for $C_{16}H_{21}NO_4Na$ [M^++Na]: 314.13628, found 314.13570.

(2*R*,3*R*)-1-((*S*)-4-Benzyl-2-oxooxazolidin-3-yl)-2-methyl-1-oxopentan-3-yl acetate (21). 

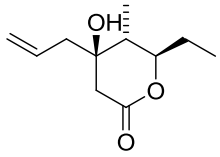
Et_3N (2.20 mL, 15.8 mmol) and freshly distilled acetic anhydride (1.40 mL, 14.6 mmol) were successively added to a solution of the above alcohol (3.55 g, 12.1 mmol) in CH_2Cl_2 (36 mL). The mixture was cooled to 0°C and DMAP (296 mg, 2.40 mmol) was introduced. After 30 min, the ice bath was removed and stirring continued for 90 min before the reaction was quenched with sat. NH_4Cl (20 mL). The aqueous phase was extracted with CH_2Cl_2 (2 x 25 mL), the combined organic layers were washed with brine (30 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 4:1 $\rightarrow$ 3:1) to give the title compound as a single diastereomer in the form of a white solid (3.26 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 – 7.29 (m, 2H), 7.28 – 7.25 (m, 1H), 7.22 – 7.18 (m, 2H), 5.23 (ddd, 1H, *J* = 8.1, 8.0, 3.6 Hz), 4.70 – 4.63 (m, 1H), 4.20 – 4.10 (m, 3H), 3.25 (dd, 1H, *J* = 13.1, 3.3 Hz), 2.68 (dd, 1H, *J* = 13.3, 9.7 Hz), 2.00 (s, 3H), 1.88 – 1.78 (m, 1H), 1.63 – 1.52 (m, 1H), 1.17 (d, 3H, *J* = 7.1 Hz), 0.92 ppm (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6, 170.1, 153.0, 135.1, 129.4, 129.0, 127.4, 75.7, 65.8, 55.3, 40.8, 37.8, 24.1, 21.0, 14.0, 8.8 ppm; IR (film): $\tilde{\nu}$ = 3029, 2978, 2944, 2883, 1782, 1737, 1699, 1491, 1455, 1378, 1349, 1291, 1208, 1111, 1098, 1049, 1016, 962, 884, 840, 762, 741, 726, 698 cm^{-1}; MS (EI) *m*/*z* (%): 273 (14), 244 (27), 178 (11), 157 (14), 117 (19), 97 (86), 96 (18), 91 (32), 69 (23), 57 (10), 43 (100), 41 (16), 29 (13); HRMS (EI): *m*/*z*: calcd. for $C_{18}H_{23}NO_5Na$ [M^++Na]: 356.14684, found 356.14686.

(5*R*,6*R*)-6-Ethyl-5-methyldihydro-2H-pyran-2,4(3H)-dione (22). 

A pre-cooled solution (-78°C) of LiHMDS (4.5 g, 27.0 mmol) in THF (50 mL) was added via canula to a solution of acetate **21** (3.00 g, 9.01 mmol) in THF (50 mL) at -78°C. After 1 h, the mixture was poured into sat. NH_4Cl/H_2O/MeOH (1:1:1, 250 mL) and diluted with EtOAc (150 mL). The organic phase containing the chiral auxiliary was separated, which could be

recovered by flash chromatography (hexanes/EtOAc, 1:1). The aqueous phase was acidified with HCl (1 M) to pH 2 and then extracted with CH_2Cl_2 (3 x 60 mL). The combined organic layers were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexanes/EtOAc, 3:1 $\rightarrow$ 1:1) to yield the desired ß-ketoester as a white solid (1.17 g, 83%). $[\alpha]_{20}^{D}$ = -14.4 (c = 0.55, Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.25 (ddd, 1H, *J* = 10.5, 7.6, 3.0 Hz), 3.53 (d, 1H, *J* = 19.1 Hz), 3.41 (d, 1H, *J* = 19.2 Hz), 2.40 (dq, 1H, *J* = 10.4, 7.1 Hz), 1.93 (tdd, 1H, *J* = 14.8, 7.3, 3.0 Hz), 1.69 (qdd, 1H, *J* = 14.7, 7.4, 7.3 Hz), 1.15 (d, 3H, *J* = 7.1 Hz), 1.08 ppm (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.7, 167.2, 81.2, 46.3, 45.8, 25.4, 10.7, 8.5 ppm; IR (neat): $\tilde{\nu}$ = 3205, 2969, 2928, 2763, 2346, 1652, 1587, 1450, 1395, 1376, 1323, 1275, 1260, 1220, 1152, 1127, 1084, 1055, 1039, 991, 964, 903, 872, 850, 823, 750, 697 cm^{-1}; MS (EI) *m*/*z* (%): 156 (12), 127 (20), 98 (70), 97 (14), 85 (58), 70 (29), 69 (16), 57 (35), 56 (100), 55 (34), 43 (12), 42 (41), 31 (18), 39 (13), 29 (35), 28 (25), 27 (20); HRMS (EI): *m*/*z*: calcd. for $C_8H_{12}O_3$ [*M*]: 156.07865, found 156.07866.

(4*R*,5*R*,6*R*)-4-Allyl-6-ethyl-4-hydroxy-5-methyltetrahydro-2*H*-pyran-2-one (*ent*-25).



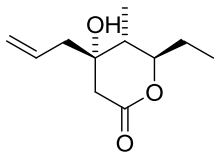
To a cold (0°C) solution of ß-ketoester **22** (84.6 mg, 0.542 mmol) in THF (3.5 mL) was slowly added a precooled (0°C) solution of the freshly prepared Soderquist reagent (1*R*)-**24** (150 mg, 0.596 mmol)[11] in THF (2 mL). After stirring at 0°C for 4 h, the mixture was diluted with hexanes (15 mL) and *N*,*N*-dimethylethanolamine[12] (53.0 mg, 0.596 mmol) was introduced. The resulting cloudy solution was stirred overnight under reflux. For work up, sat. aq. NH_4Cl (35 mL) was added at ambient temperature and the resulting mixture was extracted with EtOAc (4 x 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (silica gel 60 (15 x 40 µm), hexanes/EtOAc, 2.5:1 $\rightarrow$ 2:1) to yield the desired isomer (77.3 mg, 72%) as white needles. A crystal suitable for X-ray analysis was obtained by slowly cooling a concentrated solution of the compound in hexanes/CH_2Cl_2 (92:8) to –40°C. $[\alpha]_{20}^{D}$ = +1.8 (c = 0.56, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.70 (dddd, 1H, *J* = 17.1, 10.1, 7.5,

[11] E. Canales, K. G. Prasad, J. A. Soderquist, *J. Am. Chem. Soc.* **2005**, *127*, 11572-11573.

[12] Efforts to recover the borane by treatment with *N*-methylpseudoephedrine (as reported in ref. [11]) failed, since the obtained precipitate always contained significant quantities of the product and impurities.

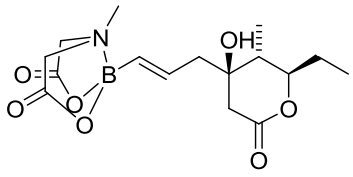
7.1 Hz), 5.02 (dddd, 1H, *J* = 10.1, 1.9, 0.9, 0.8 Hz), 4.95 (ddd, 1H, *J* = 17.1, 3.3, 1.4 Hz), 3.44 (ddd, 1H, *J* = 10.2, 7.4, 2.9 Hz), 2.57 (d, 1H, *J* = 16.4 Hz), 2.18 (dd, 1H, *J* = 16.5, 1.1 Hz), 1.98 (ddq, 1H, *J* = 13.9, 6.8, 1.1 Hz), 1.90 (br s, 1H), 1.78 – 1.71 (m, 1H), 1.55 (dq, 1H, *J* = 10.1, 6.9 Hz), 1.51 – 1.41 (m, 1H), 1.32 – 1.21 (m, 1H), 0.90 (t, 3H, *J* = 7.3 Hz), 0.57 ppm (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, C_6D_6): δ = 168.4, 132.2, 120.2, 82.5, 71.0, 43.1, 42.9, 38.9, 27.0, 10.7, 9.1 ppm; IR (neat): $\tilde{\nu}$ = 3434, 3078, 2974, 2939, 1721, 1640, 1463, 1377, 1247, 1163, 1085, 1042, 1006, 919, 838, 796 cm^{-1}; MS (EI) *m*/*z* (%): 157 (25), 127 (9), 111 (9), 99 (45), 98 (11), 95 (37), 71 (100), 67 (14), 57 (37), 55 (35), 53 (29), 43 (60), 42 (43), 41 (96), 40 (13), 39 (44), 29 (73), 27 (42); HRMS (EI): *m*/*z*: calcd. for $C_{11}H_{18}O_3Na$ [M^++Na]: 221.11481, found 221.11457.

(4*S*,5*R*,6*R*)-4-Allyl-6-ethyl-4-hydroxy-5-methyltetrahydro-2*H*-pyran-2-one (*ent*-23).



Prepared analogously from β-ketoester **22** (40.8 mg, 0.262 mmol) and (1*S*)-**24** as a white solid (45.6.3 mg, 88%). ^{1}H NMR analysis of the crude product before flash chromatography indicated a diastereomeric ratio of 7.5:1 in favor of **23**. A crystal suitable for X-ray analysis was obtained by slowly cooling a concentrated solution of the compound in hexanes/CH_2Cl_2 (92:8) to –40°C. ^{1}H NMR (500 MHz, C_6D_6): δ = 5.45 (dddd, 1H, *J* = 17.1, 9.9, 7.3, 7.3 Hz), 4.94 (dddd, 1H, *J* = 10.1, 1.7, 0.7, 0.7 Hz), 4.88 (ddd, 1H, *J* = 17.0, 3.2, 1.3 Hz), 4.21 (ddd, 1H, *J* = 10.5, 7.7, 2.8 Hz), 2.48 (d, 1H, *J* = 17.3 Hz), 2.38 (br s, 1H), 2.21 (d, 1H, *J* = 17.3 Hz), 2.00 (dd, 1H, *J* = 13.7, 7.3 Hz), 1.90 (dd, 1H, *J* = 13.7, 7.6 Hz), 1.59 – 1.50 (m, 1H), 1.19 – 1.29 (m, 2H), 0.91 (t, 3H, *J* = 7.3 Hz), 0.63 ppm (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 131.6, 120.6, 82.3, 71.1, 44.4, 42.3, 38.9, 25.8, 9.6, 8.6 ppm; IR (film): $\tilde{\nu}$ = 3429, 2978, 2935, 1710, 1460, 1442, 1385, 1326, 1261, 1107, 1008, 987, 919, 702 cm^{-1}; MS (EI) *m*/*z* (%): 157 (26), 127 (9), 111 (9), 99 (45), 98 (12), 95 (37), 71 (100), 67 (16), 57 (37), 55 (30), 53 (29), 43 (60), 42 (43), 41 (96), 40 (13), 39 (44), 29 (73), 27 (43); HRMS (EI): *m*/*z*: calcd. for $C_{11}H_{18}O_3Na$ [M^++Na]: 221.11481, found 221.11461.

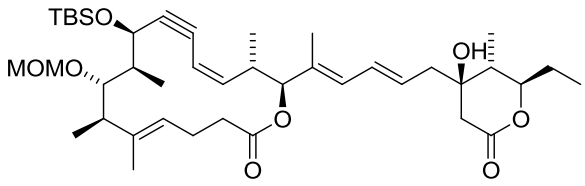
MIDA ester *ent*-28. A flame-dried Schlenk flask was charged with the ruthenium



carbene complex **27** (25.8 mg, 30.4 µmol) and the vinylboronic acid derivative **26** (116.6 mg, 0.637 mmol), evacuated and backfilled with Ar (3 cycles). A solution of the homoallylic alcohol *ent*-**25** (120.4 mg, 0.607 mmol) in

CH_2Cl_2 (6 mL) was then introduced and the flask fitted with a reflux condenser and an Argon bubbler, allowing the generated ethane to evaporate. The reaction mixture was heated to 40°C for 16 h. After cooling to room-temperature, DMSO (300 µL) was added and the mixture stirred for 8 h. It was then concentrated under reduced pressure and the resulting residue purified by flash chromatography (*tert*-butyl methyl ether/MeCN, 3:1) to yield the title compound as a white solid (174 mg, 81%). $[\alpha]_D^{20}$ = +4.4 (c = 0.88, MeCN); ^{1}H NMR (400 MHz, [D_6]-DMSO): δ = 6.05 (ddd, 1H, *J* = 17.7, 8.1, 5.6 Hz), 5.44 (d, 1H, *J* = 17.7 Hz), 4.91 (s, 1H), 4.22 (d, 1H, *J* = 7.3 Hz), 4.17 (d, 1H, *J* = 7.4 Hz), 3.99 – 3.90 (m, 3H), 2.75 (s, 3H), 2.61 (d, 1H, *J* = 16.3 Hz), 2.33 (dd, 1H, *J* = 14.0, 5.4 Hz), 2.25 (d, 1H, *J* =16.4 Hz), 2.08 (dd, 1H, *J* = 13.9, 8.4 Hz), 1.81 – 1.69 (m, 2H), 1.57 – 1.47 (m, 1H), 0.93 (d, 3H, *J* = 6.8 Hz), 0.92 ppm (t, 3H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, [D_6]-DMSO): δ = 170.3, 169.2, 169.1, 139.3, 130.4 (br), 82.8, 70.7, 61.3, 61.2, 46.7, 43.0, 42.4, 41.0, 26.2, 11.0, 9.0 ppm; IR (film): $\tilde{\nu}$ = 3504, 2953, 1745, 1716, 1639, 1464, 1375, 1286, 1247, 1223, 1118, 1029, 1001, 987, 958, 893, 859, 841, 779, 723 cm^{-1}; MS (ESI) *m/z 376.2* [M^++Na]; HRMS (ESI): *m/z*: calcd. for $C_{16}H_{24}BNO_7Na$ [M^++Na]: 376.15518, found 376.15433.

Compound 31a. A solution of compound **30** (54 mg, 0.0838 mmol) in THF/H_2O (3:1, 0.84 mL, degassed by three freeze-pump-thaw cycles) was added to a degassed solution of MIDA ester (+)-*ent*-**28** (35.5 mg, 0.0807 mmol) and $Pd(PPh_3)_4$ (19.4 mg, 0.0168 mmol). Thallium ethoxide (35.6 µL, 0.503 mmol) was added via syringe to the resulting yellow mixture, which was stirred for 2.5 h at room temperature before being diluted with *tert*-butyl methyl ether (5 mL) and transferred to a round-bottom flask fitted with a stirbar. Aqueous HCl (0.5 M, 6 mL) was introduced (pH ~ 2) and the mixture stirred for 2.5 h. H_2O (10 mL) was added and the aqueous phase was extracted with *tert*-butyl methyl ether (4 x 10 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 2.5:1 → 2:1) to give the title compound as a white solid (30.3 mg, 56%). $[\alpha]_{20}^{D}$ = +206.5 (c = 0.94, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): see Table S-1; ^{13}C NMR (125 MHz, $CDCl_3$): see Table S-1; IR (film): $\tilde{\nu}$ = 3465,



2960, 2930, 2857, 1727, 1463, 1389, 1332, 1250, 1144, 1060, 1035, 1005, 985, 918, 859, 837, 776, 755, 733, 669 cm^{-1}; MS (pos. ESI) *m*/*z* (%): 737.5 (M+Na, 100); HRMS (EI): *m*/*z*: calcd. for $C_{41}H_{66}O_8SiNa$ [M^++Na]: 737.441191, found 737.44227.

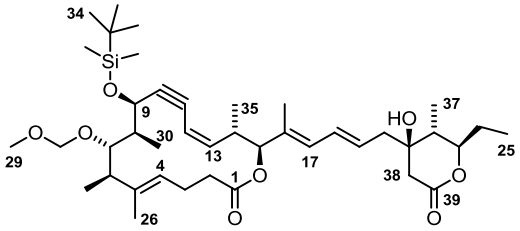


Table S-1: ^1H and ^{13}C data of product **31a**; numbering scheme as shown in the Insert.

	^1H (500 MHz, $CDCl_3$)					^{13}C (125 MHz, $CDCl_3$)	
Nr	**δ (ppm)**	**Integral**	**Splitting**	**COSY**	***J* (Hz)**	**δ (ppm)**	**HMBC**
1	-	-	-	-	-	172,2	2a, 2b, 15
2a	2,41	1H	dd	2b, 3a, 3b	13.9, 6.9	34,7	3, 4
2b	2.33 - 2.25	1H	m	2a, 3a, 3b	-		
3a	2.23 - 2.31	1H	m	2a, 2b, 3b	-	22,5	2, 4
3b	2.19 - 2.23	1H	m	2a, 2b, 3a	-		
4	5,37	1H	dd	3a, 3b	6.6, 3.9	126,7	3a, 3b, 26
5	-	-	-	-	-	137,2	3b, 26, 27
6	2,96	1H	br s	27	-	46,1	7, 26
7	3,42	1H	br d	-	7,8	87,2	27, 28a, 28b, 30
8	2.05 - 2.13	1H	m	9, 30	-	41,9	9, 30
9	4,36	1H	dd	8,12	9.3, 1.1	63,9	8, 30
10	-	-	-	-	-	96,6	8, 9, 12
11	-	-	-	-	-	82,2	9, 12, 13
12	5,53	1H	dd	9, 13	10.6, 1.5	109,9	4, 9, 13, 14
13	5,66	1H	dd	12, 14	10.5, 10.4	145,1	9, 12, 14, 15, 35
14	3,20	1H	ddq	13, 15, 35	10.1, 10.1, 6.8	37,6	12, 13, 15
15	5,09	1H	d	14	9,7	82,6	14, 17, 35, 36
16	-		-	-	-	134,3	14, 15, 17, 18, 19, 36
17	6,04	1H	dd	18, 36	10.8, 0.8	128,8	15, 18, 19, 36
18	6,35	1H	dd	17, 19	15.1, 10.8	131,7	17, 20a, 20b, 36
19	5,70	1H	ddd	18, 20a, 20b	15.3, 7.7, 7.7	127,1	17, 20a, 20b, 36
20a	2.33 - 2.38	1H	m	2a, 2b, 3b	-	37,8	18, 19, 20a,b, 22
20b	2.16 - 2.22	1H	m	2a, 2b, 3a	-		
21	-	-	-	-	-	71,5	19, 20, 38, 22
22	1,92	1H	dq	24, 38	10.3, 6.9	42,5	23, 37, 38a
23	3,93	1H	ddd	24, 22	10.2, 7.3, 3.0	83,5	22, 24b, 25, 37
24a	1,83	1H	ddq	23, 25	14.7, 7.3, 3.0	26,8	23, 24, 25
24b	1,61	1H	ddq	23, 25	14.6, 7.3, 7.3		
25	1,01	3H	t	24	7,1	8,9	23, 24
26	1,46	3H	s	4	-	12,0	4
27	0.98-1.05	3H	m	6	-	17,4	-
28a	4,73	1H	d	28b	6,9	99,0	29
28b	4,62	1H	d	28a	6,9		
29	3,39	3H	s	-	-	56,0	28a, 28b

30	1,08	3H	d	8	7,1	16,8	8
31	0,11	3H	s	-	-	-4,5	32
32	0,07	3H	s	-	-	-5,1	31
33	-	-	-	-	-	18,2	31, 32
34	0,89	9H	s	-	-	25,8	-
35	0,82	3H	d	14	6,8	16,6	13, 14, 15
36	1,76	3H	d	17	0,8	12,1	15,17
37	1,02	3H	d	22	6,9	11,1	22, 23, 38a
38a	2,78	1H	d	38b	16,8	42,8	22, 38
38b	2,37	1H	d	38a	16,8		
39	-	-	-	-	-	170,1	38a, 38b
OH	1,95	1H	br s	-	-	-	-

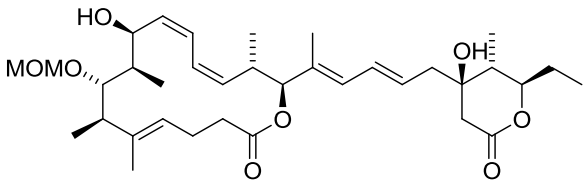
Compound 31. This diastereomer was obtained analogously in 55% isolated yield using MIDA ester (–)-**28** $[\alpha]_D^{20}$ = +117.3 (c = 0.88, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.31 (dd, 1H, *J* = 15.0, 10.9 Hz), 6.01 (d, 1H, *J* = 11.0 Hz), 5.70 (ddd, 1H, *J* = 15.0, 7.5, 7.5 Hz), 5.65 (dd, 1H, *J* = 10.3, 10.2 Hz), 5.52 (dd, 1H, *J* = 10.8, 0.9 Hz), 5.37 – 5.32 (m, 1H), 5.07 (d, 1H, *J* = 9.8 Hz), 4.71 (d, 1H, *J* = 6.8 Hz), 4.61 (d, 1H, *J* = 6.8 Hz), 4.35 (d, 1H, *J* = 8.8 Hz), 3.92 (ddd, 1H, *J* = 10.0, 7.3, 2.9 Hz), 3.41 (br d, 1H, *J* = 7.6 Hz), 3.38 (s, 3H), 3.24 – 3.13 (m, 1H), 3.00 – 2.80 (br s, 1H), 2.77 (d, 1H, *J* = 16.7 Hz), 2.45 – 2.37 (m, 2H), 2.35 (d, 1H, *J* = 16.7 Hz), 2.33 – 2.24 (m, 2H), 2.23 – 2.12 (m, 2H), 2.08 (ddd, 1H, *J* = 15.4, 7.6, 7.5 Hz), 1.90 (ddd, 1H, *J* = 16.8, 6.9, 6.9 Hz), 1.83 (ddq, 1H, *J* = 14.7, 7.3, 2.8 Hz), 1.73 (s, 3H), 1.60 (ddq, 1H, *J* = 14.7 Hz, 7.3, 7.3 Hz), 1.45 (s, 3H), 1.06 (d, 3H, *J* = 7.1 Hz), 1.02 – 0.97 (m, 9H), 0.87 (s, 9H), 0.80 (d, 3H, *J* = 6.9 Hz), 0.09 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.2, 170.2, 145.1, 137.0, 134.0, 131.4, 128.9, 127.4, 126.7, 109.8, 98.9, 96.5, 87.2, 83.6, 82.5, 82.2, 71.5, 63.9, 56.0, 46.1, 42.7, 42.6, 41.8, 37.8, 37.6, 34.6, 26.8, 25.7, 22.4, 18.1, 17.4, 16.8, 16.5, 12.1, 11.9, 11.2, 8.9, -4.5, -5.2; IR (film): $\tilde{\nu}$ = 3448, 2961, 2930, 2857, 1724, 1462, 1377, 1248, 1144, 1058, 1032, 1004, 983, 919, 858, 835, 750, 667 cm^{-1}; MS (EI) *m*/*z* (%): 714 (5), 696 (4), 657 (4), 425 (5), 381 (13), 357 (8), 325 (7), 299 (9), 267 (12), 249 (27), 222 (72), 173 (11), 171 (14), 169 (68), 159 (11), 157 (16), 145 (13), 143 (11), 137 (18), 133 (18), 119 (17), 107 (16), 95 (25), 89 (36), 81 (20), 75 (41), 73 (100), 72 (24); HRMS (EI): *m*/*z*: calcd. for $C_{41}H_{66}O_8SiNa$ [M^++Na]: 737.441192, found 737.44302.

Propargylic alcohol S36a. TBAF (1 M in THF, 92.6 µL, 0.093 mmol) was slowly added to a suspension of silyl ether **31a** (26.5 mg, 0.037 mmol) and activated 4Å molecular sieves in THF (0.5 mL) at 0°C. After 40 min, the reaction was quenched with H_2O/brine (2:1, 4 mL) and diluted with EtOAc (3 mL). The aqueous layer was extracted with EtOAc (3 x 4 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was quickly purified by flash chromatography (Florisil, hexanes/EtOAc, 2:1 → 1:2), keeping the contact time with the Florisil as short as possible. The white solid (17.2 mg, 76%) thus obtained was immediately used in the next step as it decomposes upon storage in a freezer. ^{1}H NMR (400 MHz, C_6D_6): δ = 6.31 (dd, 1H, *J* = 15.0, 10.9 Hz), 6.13 (d, 1H, *J* = 10.9 Hz), 5.58 (dt, 1H, *J* = 15.0, 7.5 Hz), 5.53 – 5.46 (m, 3H), 5.41 – 5.36 (m, 1H), 5.10 (br t, 1H, *J* = 2.5 Hz), 4.39 (s, 2H), 3.44 (ddd, 1H, *J* = 10.2, 7.5, 2.9 Hz), 3.41 (dd, 1H, *J* = 8.7, 2.7 Hz), 3.37 – 3.27 (m, 1H), 3.10 (s, 3H), 2.95 (d, 1H, *J* = 2.9°Hz), 2.61 – 2.52 (m, 1H), 2.56 (d, 1H, *J* = 16.3 Hz), 2.29 – 2.15 (m, 3H), 2.15 – 2.09 (m, 1H), 2.05 (d, 1H, *J* = 16.2 Hz), 2.09 – 2.00 (m, 2H), 1.84 (dd, 1H, *J* = 14.1, 7.6 Hz), 1.71 (s, 3H), 1.51 – 1.41 (m, 2H), 1.40 (s, 3H), 1.33 (d, 3H, *J* = 7.1 Hz), 1.24 (ddq, 1H, *J* = 14.5, 7.3, 7.2 Hz), 1.00 (d, 3H, *J* = 7.1 Hz), 0.93 (d, 3H, *J* = 6.8 Hz), 0.89 (t, 3H, *J* = 7.3 Hz), 0.58 ppm (d, 3H, *J* = 6.8 Hz); IR (film): $\tilde{\nu}$ = 3457, 2970, 2934, 1728, 1455, 1377, 1246, 1189, 1149, 1091, 1022, 987, 843, 755 cm^{-1}; HRMS (ESIpos): *m*/*z*: calcd. for $C_{35}H_{52}O_8Na$ [M^++Na]: 623.35544, found 623.35527.

Isomer S36. This diastereomer was obtained analogously in 85% yield. ^{1}H NMR (400 MHz, C_6D_6): δ = 6.36 (dd, 1H, *J* = 14.9, 10.8 Hz), 6.15 (d, 1H, *J* = 10.8 Hz), 5.73 (dt, 1H, *J* = 15.0, 7.5 Hz), 5.53 – 5.46 (m, 3H), 5.41 – 5.35 (m, 1H), 5.08 (br t, 1H, *J* = 2.7 Hz), 4.41 (s, 2H), 3.52 (ddd, 1H, *J* = 10.0, 7.4, 2.8 Hz), 3.42 (dd, 1H, *J* = 8.6, 2.5 Hz), 3.36 – 3.26 (m, 1H), 3.12 (s, 3H), 3.12 – 3.10 (m, 1H), 2.65 (d, 1H, *J* = 16.4 Hz), 2.56 (dq, 1H, *J* = 7.4, 7.3 Hz), 2.30 – 2.15 (m, 6H), 2.14 – 2.02 (m, 2H), 1.93 (dd, 1H, *J* = 14.3, 7.7 Hz), 1.74 (s, 3H), 1.61 (dd, 1H, *J* = 15.9, 9.1, 6.9, 2.2 Hz), 1.50 (ddq, 1H, *J* = 14.6, 7.2, 3.1 Hz), 1.41 (s, 3H), 1.33 – 1.23 (m, 1H), 1.32 (d, 3H, *J* = 7.1 Hz), 1.01 (d,

3H, *J* = 7.0 Hz), 0.93 (d, 3H, *J* = 6.9 Hz), 0.91 (t, 3H, *J* = 7.3 Hz), 0.67 ppm (d, 3H, *J* = 6.8 Hz); IR (film): $\tilde{\nu}$ = 3454, 2972, 2932, 1727, 1462, 1379, 1246, 1193, 1151, 1090, 1029, 1022, 986, 844, 759 cm^{-1}; HRMS (ESIpos): *m*/*z*: calcd. for $C_{35}H_{52}O_8Na$ [M^++Na]: 623.35544, found 623.35513.

Bis-diene 32a. A solution of propargyl alcohol **S36a** (14.0 mg, 0.0241 mmol) in THF



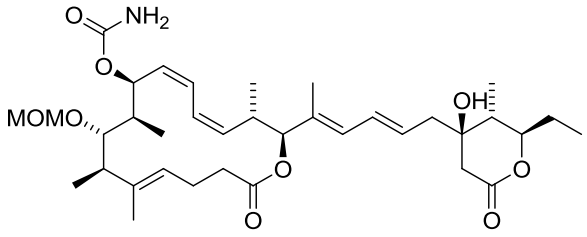
(0.3 mL) was added to a suspension of freshly prepared Zn(Cu/Ag)[13] (1.3 g) in degassed MeOH/H_2O (1:1, 1.1 mL) and the resulting mixture was stirred at 50°C for 18 h. After cooling to room-temperature, the mixture was diluted with EtOAc (5 mL) and filtered through a short pad of Celite, which was carefully rinsed with EtOAc (140 mL) and EtOH (15 mL). The combined filtrates were concentrated under reduced pressure to ca. 1/10 of the original volume and then washed with brine/H_2O (1:1, 15 mL). The aqueous phase was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (Florisil, hexanes/EtOAc, 2:1 $\rightarrow$ 1:1) to give the title compound as a white solid (11.7 mg, 81%). $[\alpha]_{20}^{D}$ = -40.1 (c = 0.76, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.45 (dd, 1H, *J* = 11.3, 11.2 Hz), 6.40 (dd, 1H, *J* = 15.0, 10.9 Hz), 6.29 (dd, 1H, *J* = 11.3, 11.3 Hz), 6.10 (d, 1H, *J* = 11.0 Hz), 5.76 (ddd, 1H, *J* = 15.1, 7.6, 7.6 Hz), 5.57 (dd, 1H, *J* = 10.6, 10.3 Hz), 5.29 (d, 1H, *J* = 10.7, 10.5 Hz), 5.15 – 5.10 (m, 1H), 5.09 (d, 1H, *J* = 10.4 Hz), 5.04 (d, 1H, *J* = 10.1 Hz), 4.73 (d, 1H, *J* = 6.3 Hz), 4.64 (d, 1H, *J* = 6.3 Hz), 3.91 (ddd, 1H, *J* = 10.0, 7.3, 2.9 Hz), 3.41 (s, 3H), 3.35 (d, 1H, *J* = 10.4 Hz), 3.04 – 2.94 (m, 1H), 2.90 – 2.80 (br s, 1H), 2.73 (d, 1H, *J* = 16.6 Hz), 2.62 – 2.54 (m, 1H), 2.40 (d, 1H, *J* = 14.2, 7.9 Hz), 2.36 (d, 1H, *J* = 16.6 Hz), 2.35 – 2.30 (m, 3H), 2.27 – 2.18 (m, 3H), 2.06-2.02 (m, 1H), 1.92 (s, 1H), 1.93 – 1.87 (m, 1H), 1.84 (ddq, 1H, *J* = 7.4, 7.4, 2.8 Hz), 1.80 (s, 3H), 1.64 (ddq, 1H, *J* = 14.4, 7.2, 7.1 Hz), 1.44 (s, 3H), 1.09 (d, 3H, *J* = 7.1 Hz), 1.07 (d, 1H, *J* = 7.3 Hz), 1.02 (d, 3H, *J* = 6.9 Hz), 1.01 (t, 3H, *J* = 7.4 Hz), 0.88 (d, 3H, *J* = 0.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 170.2, 137.1,

[13] Zn(Cu/Ag) was prepared according to: W. Boland, N. Schroer, C. Sieler, M. Feigel, *Helv. Chim. Acta* **1987**, *70*, 1025-1040. Reproducible results were obtained when all solvents used for preparation or washing were carefully degassed by bubbling Argon trough the solvents for 30 min.

136.4, 134.1, 132.4, 131.6, 129.7, 128.3, 126.4, 124.5, 124.3, 100.0, 89.4, 83.9, 82.9, 72.1, 65.0, 56.6, 48.1, 43.3, 43.0, 39.1, 38.7, 35.3, 33.8, 27.2, 26.4, 22.4, 16.7, 16.5, 12.1, 11.6, 11.4, 9.2; IR (film): $\tilde{\nu}$ = 3457, 2966, 2934, 1729, 1455, 1367, 1244, 1147, 1089, 1019, 985, 949, 918, 863, 736 cm^{-1}; HRMS (ESIpos): *m*/*z*: calcd. for $C_{35}H_{54}O_8Na$ [M^++Na]: 625.37109, found 625.37162.

Compound 32. This diastereomer was obtained analogously in 89% yield. $[\alpha]_{20}^{D}$ = -72.0 (c = 0.66, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): see Table S-2; ^{13}C NMR (150 MHz, CD_2Cl_2): see Table S-2; IR (film): $\tilde{\nu}$ = 3447, 2966, 2932, 1729, 1456, 1415, 1368, 1243, 1206, 1147, 1089, 1020, 985, 918, 863, 783, 748, 736, 700 cm^{-1}; HRMS (ESIpos): *m*/*z*: calcd. for $C_{35}H_{54}O_8Na$ [M^++Na]: 625.37109, found 625.37092.

Allylic carbamate 33a. A solution of trichloroacetyl isocyanate (1.0 M in CH_2Cl_2, 16.4 µL, 0.0164 mmol) was added to a precooled solution (-78°C) of the allylic alcohol **32a** (9.0 mg, 0.015 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred at -78°C for 2 h, before being quenched with MeOH (0.1 mL) at this temperature. After warming and concentration under reduced pressure, the residue was dissolved in CH_2Cl_2 (1 mL) and the solution soaked on basic Al_2O_3. After 1.5 h, the alumina was loaded onto a short pad of Celite, which was eluted with EtOAc/EtOH (9:1, 12 mL). The solvent was evaporated and the residue purified by flash chromatography (Florisil, hexanes/EtOAc, 1:1 → 1:2) to furnish the title compound as a white foam (6.1 mg, 63%). $[\alpha]_{20}^{D}$= -43.7 (c = 0.31, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 6.69 (dd, 1H, *J* = 10.8, 10.6 Hz), 6.40 (dd, 1H, *J* = 15.0, 10.9 Hz), 6.32 (dd, 1H, *J* = 10.8, 10.6 Hz), 6.10 (d, 1H, *J* = 10.8 Hz), 5.92 (d, 1H, *J* = 9.2 Hz), 5.76 (ddd, 1H, *J* = 15.1, 7.6, 7.6 Hz), 5.50 (dd, 1H, *J* = 5.50 Hz), 5.36 -5.33 (m, 1H), 5.11 – 5.08 (m, 1H), 5.08 (d, 1H, *J* = 10.3 Hz), 4.70 (d, 1H, *J* = 6.70 Hz), 4.58 (d, 1H, *J* = 6.72 Hz), 4.56 – 4.44 (br s, 2H), 3.90 (ddd, 1H, *J* = 10.1, 7.4, 2.9 Hz), 3.38 (s, 3H), 3.30 (d, 1H, *J* = 9.8 Hz), 3.03 – 2.95 (m, 1H), 2.73 (d, 1H, *J* = 16.5 Hz), 2.54 – 2.46 (br s, 1H), 2.40 (dd, 1H, *J* = 14.0, 7.8 Hz), 2.36 (d, 1H, *J* = 16.5 Hz), 2.33 – 2.27 (m, 1H), 2.26 – 2.15 (m, 3H), 2.05 -1.94 (m, 2H), 1.93 – 1.91 (m, 1H), 1.89 (dq, 1H, *J* = 10.5,



7.1 Hz), 1.84 (ddq, 1H, *J* = 7.4, 7.3, 3.1 Hz), 1.79 (s, 3H), 1.62 (ddq, 1H, *J* = 14.7, 7.4, 7.3 Hz), 1.26 (s, 3H), 1.13 (d, 3H, *J* = 7.1 Hz), 1.09 (d, 3H, *J* = 6.6 Hz), 1.01 (d, 3H, *J* = 6.8 Hz), 1.01 (t, 3H, *J* = 7.3 Hz), 0.87 ppm (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 172.3, 170.2, 156.2, 137.3, 136.8, 134.1, 131.7, 129.7, 129.2, 128.1, 126.1, 125.1, 124.9, 98.8, 85.9, 83.7, 82.7, 72.1, 67.3, 56.2, 48.2, 43.1, 42.9, 38.6, 38.6, 34.9, 33.8, 27.1, 22.3, 16.7, 16.7, 13.7, 12.0, 11.6, 11.3, 9.2 ppm; IR (film): $\tilde{\nu}$ = 3441, 3368, 2969, 2931,1729, 1603, 1376, 1208, 1147, 1059, 1035, 917, 747 cm^{-1}; MS (ESI) *m*/*z* (%): 684.4 (100); HRMS (ESIpos): *m*/*z*: calcd. for $C_{36}H_{55}NO_9K$ [M^++K]: 684.35084, found 625.35135.

Compound 33. This diastereomer was obtained analogously in 84% yield. $[\alpha]_{20}^{D}$ = -66.4 (c = 0.94, CD_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): see Table S-3; ^{13}C NMR (150 MHz, CD_2Cl_2): see Table S-3; IR (film): $\tilde{\nu}$ = 3452, 3365, 2965, 2931, 1723, 1602, 1455, 1376, 1312, 1259, 1209, 1146, 1092, 1058, 1033, 954, 916, 863, 801, 748, 710, 679 cm^{-1}; HRMS (ESIpos): *m*/*z*: calcd. for $C_{36}H_{55}NO_9Na$ [M^++Na]: 668.37800, found 668.37740.

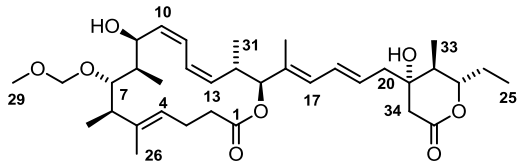


Table S-2: ^{1}H and ^{13}C data of the semi-reduced product **32**; numbering scheme as shown in the Insert.

	^{1}H NMR (CD_2Cl_2, 600 MHz)					^{13}C NMR (CD_2Cl_2, 150 MHz)	
Nr	**δ (ppm)**	**Integral**	**Splitting**	**COSY**	***J* (Hz)**	**δ (ppm)**	**HMBC**
1	-	-	-	-	-	172.4	2, 15
2a	2.31 - 2.36	1H	m	2b, 3a	-	33.7	1, 3, 5, 26
2b	1.91 - 1.96	1H	m	2a, 3b	-		
3	2.15 - 2.23	2H	m	2a, 2b, 4	-	22.2	1, 2, 4, 26
4	5.09 - 5.14	1H	m	3a, 3b, 26	-	126.3	2, 3, 6, 26
5	-	-	-	-	-	137.01	3, 6, 7, 26, 27
6	2.54 - 2.63	1H	m	7, 27	-	47.9	4, 5, 7, 26, 27
7	3.35	1H	d	6	10.6	89.3	6, 9, 27, 28, 30
8	1.62 - 1.69	1H	m	30	-	38.9	7, 9, 10, 30
9	5.04	1H	d	10	9.8	65.0	7, 8, 11, OH1, 30
10	5.57	1H	dd	9, 11	9.9, 10.8	132.2	8, 9, 12, OH1
11	6.29	1H	dd	10, 12	10.9, 11.4	124.3	9, 12, 13, 14
12	6.45	1H	dd	11, 13	10.7, 11.4	124.4	10, 13, 14, 31
13	5.28	1H	dd	12, 14	10.4, 10.7	136.3	11, 14, 15, 31
14	2.98 - 3.03	1H	m	13, 15, 31	-	35.1	12, 13, 15, 31
15	5.09	1H	d	14	10.4	82.9	13, 14, 16, 17, 31, 32
16	-	-	-	-	-	133.8	14, 15, 17, 18
17	6.09	1H	d	18	10.9	129.7	15, 16, 18, 19, 32
18	6.38	1H	dd	17, 19	11.0, 15.0	131.4	17, 20, 32
19	5.77	1H	ddd	20a, 20b	7.5, 7.5, 15.0	128.5	17, 18, 20, 21
20a	2.41	1H	dd	19, 20b	14.0, 7.2	38.5	18, 19, 21, 22, 34
20b	2.16 - 2.22	1H	m	19, 20a	-		
21	-	-	-	-	-	72.0	19, 20a, 20b, 22, 34
22	1.88	1H	dq	23, 33	10.0, 6.9	43.2	20, 33, 34,
23	3.91	1H	ddd	22, 24a, 24b	10.0, 7.4, 2.8	83.8	22, 24, 25
24a	1.83	1H	ddq	23, 24b, 25	7.3, 7.4, 3.0	27.1	23, 25
24b	1.60	1H	ddq	23, 24b, 25	7.3, 7.3, 7.4		
25	1.00	3H	t	24a, 24b	7.3	9.2	24
26	1.43	3H	s	4	-	11.3	4, 5, 6
27	1.09	3H	d	6	6.8	16.4	5, 7, 30
28a	4.72	1H	d	28b	6.5	99.8	7, 29
28b	4.63	1H	d	28a	6.5		
29	3.40	3H	s	-	-	56.6	28
30	1.06	3H	d	8	7.3	12.0	5, 9
31	0.86	3H	d	14	6.7	16.6	13, 14, 15
32	1.79	3H	s	17	-	12.0	15, 17
33	1.01	3H	d	22	6.9	11.5	21, 22
34a	2.72	1H	d	34b	16.5	42.8	21, 35
34b	2.34	1H	d	34a	16.6		
35	-	-	-	-	-	170.3	34a, 34b
OH1	2.91	1H	br s				
OH2	2.17 - 2.26	1H	br s				

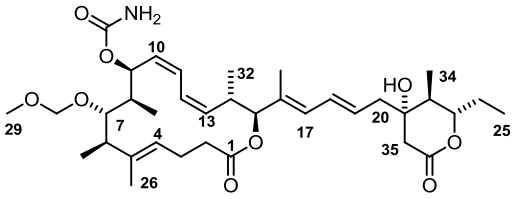


Table S-3: ^{1}H and ^{13}C data of the allylic carbamate **33**; numbering scheme as shown in the Insert.

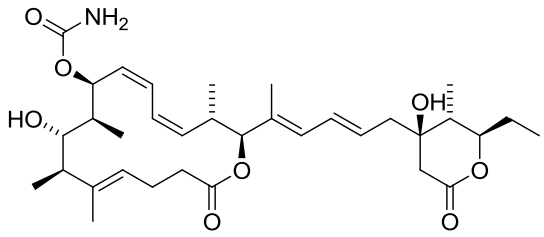
	^{1}H (CD_2Cl_2, 600 MHz)					^{13}C (CD_2Cl_2, 150 MHz)	
Nr	**δ (ppm)**	**Integral**	**Splitting**	**COSY**	***J* (Hz)**	**δ (ppm)**	**HMBC**
1	-	-	-	-	-	172.3	2, 15
2a	2.27 - 2.33	1H	m	2b, 3a	-	33.8	1, 4, 5, 26
2b	1.93 - 2.02	1H	m	2a, 3b	-		
3	2.18 - 2.23	2H	m	2a, 2b, 4	-	22.3	1
4	5.05 - 5.11	1H	m	3a, 3b, 26	-	126.1	6
5	-	-	-	-	-	137.3	3, 26, 27
6	2.45 - 2.55	1H	m	7, 27	-	48.2	6, 26, 27
7	3.30	1H	d	6	9.9	85.9	9, 27, 29
8	1.72 - 1.79	1H	br m	30	-	38.6	30
9	5.92	1H	br d	10	9.3	67.3	7, 11, 12, 30
10	5.50	1H	br dd	9, 11	9.3, 10.0	129.2	12
11	6.32	1H	br dd	10, 12	10.1, 11.1	125.1	9, 13, 15
12	6.68	1H	br dd	11, 13	10.7, 11.0	124.9	10, 14
13	5.29 - 5.36	1H	m	12, 14	-	136.8	11, 14, 15, 32
14	2.95 - 3.03	1H	m	13, 15, 32	-	34.9	12, 13, 15, 32
15	5.08	1H	d	14	10.3	82.7	13, 14, 16, 17, 32, 33
16	-	-	-	-	-	133.9	14, 15, 17, 18, 19, 33
17	6.10	1H	d	18	10.9	129.8	15, 16, 17, 18, 19, 33
18	6.39	1H	dd	17, 19	10.9, 15.1	131.5	17, 20, 33
19	5.77	1H	ddd	18, 20a, 20b	7.6, 7.6, 15.1	128.3	17, 20, 21, 33
20a	2.41	1H	dd	19, 20b	14.0, 7.3	38.6	18, 19, 21, 22, 35
20b	2.19 - 2.22	1H	m	19, 20a	-		
21	-	-	-	-	-	72.1	19, 20, 22, 34, 35
22	1.89	1H	dq	23, 34	9.9, 6.8	43.1	20, 34, 35
23	3.91	1H	ddd	22, 24a, 24b	10.1, 7.4, 2.9	83.8	22, 24, 25, 34
24a	1.84	1H	ddq	23, 24b, 25	7.4, 7.3, 2.8	27.1	23, 25
24b	1.62	1H	ddq	23, 24b, 25	7.3, 7.3, 7.4		
25	1.00	3H	t	24a, 24b	7.4	9.2	24
26	1.43	3H	br s	-	-	11.3	2, 6, 7
27	1.08	3H	d	6	6.6	16.7	5, 6, 7
28a	4.70	1H	d	28b	6.7	98.8	29
28b	4.58	1H	d	28a	6.7	-	-
29	3.38	3H	s	-	-	56.2	28
30	1.13	3H	d	8	7.1	13.7	8, 27
31	-	-	-	-	-	156.3	-
32	0.86	3H	d	14	6.6	16.6	13, 14, 15
33	1.79	3H	d	17	0.7	12.0	15, 16, 17, 19
34	1.01	3H	d	22	7.1	11.6	21, 22
35a	2.73	1H	d	34b	16.5	42.8	21, 36
35b	2.35	1H	dd	34a	16.6, 0.3		
36	-	-	-	-	-	170.3	34a, 34b
NH2	4.51 - 4.66	2H	br s	-	-	-	-
OH1	1.66 - 1.69	1H	br s	-	-	-	-

Leiodermatolide (1). A solution of compound **33** (9.0 mg, 13.9 µmol) in CH_2Cl_2 (1.6 mL) was cooled to -90°C ($Et_2O/CO_2/N_2$ cooling bath) before a solution of freshly prepared Me_2BBr (0.5 M in CH_2Cl_2, 30.6 µL, 15.3 µmol)[14] was carefully added via the cold wall of the flask. The mixture was allowed to reach -78°C and was stirred at this temperature for 1.5 h, when a second aliquot of Me_2BBr (0.5 M, 30.6 µL, 15.3 µmol) was introduced. After additional 1.5 h, the mixture was transferred via canula into a vigorously stirred mixture of sat. $NaHCO_3/H_2O$/THF (1:1:1, 10 mL) and the flask was rinsed with THF (2 x 0.7 mL). After stirring for 10 min, the mixture was diluted with EtOAc (10 mL), the aqueous layer was extracted with EtOAc (3 x 10 mL), the combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by preparative thin layer chromatography (TLC Silica gel 60 F254 (20 x 20 cm), hexanes/EtOAc, 1:2.5) to give the title compound as a white solid (5.1 mg, 61%). $[\alpha]_{24}^{D}$ = –74.3 (c = 0.41, MeOH); ^{1}H NMR (600 MHz, CD_2Cl_2, 4.8 mg in 0.3 mL CD_2Cl_2): δ = 6.53 (dd, 1H, *J* = 11.7, 11.3 Hz), 6.39 (dd, 1H, *J* = 15.3, 10.7 Hz), 6.37 (dd, 1H, *J* = 11.3, 11.2), 6.10 (d, 1H, *J* = 10.9 Hz), 5.89 (d, 1H, *J* = 10.1 Hz), 5.77 (ddd, 1H, *J* = 15.1, 7.6, 7.6 Hz), 5.53 (dd, 1H, *J* = 10.4, 10.4 Hz), 5.35 (dd, 1H, *J* = 10.5, 10.4°Hz), 5.09 (m, 1H), 5.07 (d, 1H, *J* = 10.3 Hz), 4.84 – 4.63 (br s, 2H), 3.91 (ddd, 1H, *J* = 10.1, 7.4, 2.9 Hz), 3.26 (br t, 1H), 2.97 (ddq, 1H, *J* = 10.1, 10.1, 6.7 Hz), 2.73 (d, 1H, *J* = 16.5 Hz), 2.46 (dq, 1H, *J* = 11.2, 5.8 Hz), 2.42 (dd, 1H, *J* = 14.0, 7.3 Hz), 2.35 (dd, 1H, *J* = 16.6, 0.9 Hz), 2.31 (ddd, 1H, *J* = 16.7, 5.8, 3.0 Hz), 2.21 (dd, 1H, *J* = 13.9, 8.0 Hz), 2.27 – 2.17 (m, 3H), 2.13 – 2.06 (br s, 1H), 1.99 (ddd, 1H, *J* = 16.7, 10.6, 3.6 Hz), 1.89 (dq, 1H, *J* = 10.3, 7.0 Hz), 1.83 (ddq, 1H, *J* = 7.4, 7.3, 3.1 Hz), 1.79 (d, 3H, *J* = 0.9 Hz), 1.74 (q, 1H, *J* = 7.2 Hz), 1.62 (ddq, 1H, *J* = 14.7, 7.4, 7.3 Hz), 1.42 (s, 3H), 1.12 (d, 3H, *J* = 6.7 Hz), 1.08 (d, 3H, *J* = 7.3 Hz), 1.02 (d, 3H, *J* = .6.8 Hz), 1.01 (t, 3H, *J* = 7.3 Hz), 0.86 ppm (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (150 MHz, CD_2Cl_2, 4.8 mg in 0.3 mL): δ = 172.2, 170.3, 157.4, 137.6, 137.2, 133.8, 131.5, 129.8, 128.5, 128.4, 126.2, 125.6, 124.1, 83.8, 82.5, 78.2, 72.1, 67.6, 48.5, 43.1, 42.8, 39.3, 38.6, 35.0, 33.7, 27.1, 22.2, 16.6, 16.5, 12.5, 12.0, 11.6, 11.3, 9.2 ppm; IR (film): $\tilde{\nu}$ = 3360, 2963, 2924,

[14] H. Nöth, H. Vahrenkamp, *J. Organomet. Chem*. **1968**, *11*, 399-405.

1708, 1605, 1455, 1375, 1312, 1246, 1207, 1148, 1082, 1056, 1040, 986, 949, 915, 778, 745 cm^{-1}; MS (ESI) *m*/*z* (%): 624.4 (100); HRMS (ESIpos): *m*/*z*: calcd. for $C_{34}H_{51}NO_8Na$ [M^++Na]: 624.35069, found 624.35132.

Leiodermatolide-Isomer 2. Prepared analogously from compound **33a** (3.6 mg, 5.6 µmol) as a white solid (0.6 mg). $[\alpha]_{24}^{D}$ = –58 (c = 0.09, MeOH); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = see Table S5; ^{13}C NMR (150 MHz, CD_2Cl_2): δ = see Table S5; MS (ESI) *m*/*z* (%): 624.4 (100); HRMS (ESIpos): *m*/*z*: calcd. for $C_{34}H_{51}NO_8Na$ [M^++Na]: 624.35069, found 624.35155.



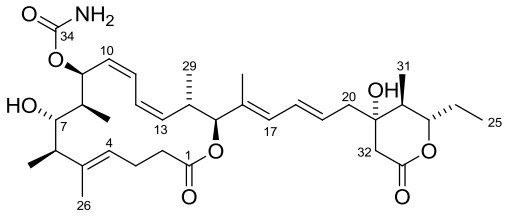


Table S-4: ^{1}H and ^{13}C data of Leiodermatolide (**1**); numbering scheme as shown in the Insert, data was obtained with 0.8 mg in 0.3 mL CD_2Cl_2.

	^{1}H (CD_2Cl_2, 600 MHz)					^{13}C NMR (CD_2Cl_2, 150 MHz)	
Nr	**δ (ppm)**	**Integral**	**Splitting**	**COSY**	***J* (Hz)**	**δ (ppm)**	**HMBC**
1	--	--	--	--	--	172.2	2, 3, 15
2a	2.31	1H	ddd	2b, 3	16.7, n.d.	33.7	3, 4, 26
2b	1.99	1H	ddd	2a, 3	16.7, n.d.		
3	2.20	2H	m	2, 4, 26	--	22.2	2, 4, 5, 26
4	5.09	1H	ddq	3, 26	9.9, 5.5, 1.6	125.6	2, 3, 5, 6, 26
5	--	--	--	--	--	137.2	3, 4, 6, 26, 27
6	2.46	1H	dq	7, 27	10.5, 6.7	48.5	4, 7, 25, 26, 27
7	3.26	1H	br t	OH, 6, 8	9.9	78.2	6, 8, 9, 28
8	1.74	1H	qt	7, 27, 28	7.4, n.d.	39.3	7, 10, 28
9	5.89	1H	d	10	10.0	67.6	7, 28, 11
10	5.53	1H	ddt	9, 11	10.7, 10.0, 1.4	128.5	9, 11, 12, 13
11	6.38	1H	ddt	10, 12	12.0, 10.9	126.2	9, 10, 12, 13
12	6.53	1H	ddt	11, 13	11.8, 11.0, 1.0	124.4	10, 11, 13, 14
13	5.35	1H	ddt	12, 14	10.8, 10.2, 1.4	137.6	11, 12, 14, 15, 29
14	2.98	1H	tq	13, 15, 29	10.2, 6.7	35.0	12, 13, 15, 29, 30
15	5.07	1H	d	14	10.3	82.5	12, 13, 14, 17, 29, 30
16	--	--	--	--	--	134.0	14, 15, 17, 18, 30
17	6.10	1H	dq	18, 30	10.9, 1.4	129.7	15, 16, 18, 19, 30
18	6.40	1H	ddt	17,19, 20	15.1, 10.9, 1.3	131.7	16, 17, 20, 30
19	5.76	1H	dt	18, 20	15.0, 7.6	128.2	17, 20, 30
20a	2.41	1H	dd	19, 20b	14.0, 7.5	38.6	18, 19, 32
20b	2.22	1H	dd	19, 20a	13.8, 7.9		
21						72.1	18, 19, 20, 22, 31, 32
22	1.89	1H	dq	23, 31	10.5, 6.7	43.1	20, 21, 23, 24, 31, 32
23	3.91	1H	ddd	22, 24	10.0, 7.6, 3.1	83.8	22, 24, 25, 31
24a	1.85	1H	ddq	23, 24b, 25	14.5, 7.4, 3.1	27.1	22, 23, 25
24b	1.62	1H	dq	23, 24a, 25	14.6, 7.4		
25	1.01	3H	t	24	7.3	9.2	23, 24
26	1.42.	3H	s	3, 4	-	11.3	3, 4, 5, 6
27	1.12	3H	d	6	6.7	16.5	5, 6
28	1.08	3H	d	8	7.3	12.5	7, 8, 9
29	0.87	3H	d	14	6.7	16.6	13, 14, 15
30	1.79	3H	d	17	1.0	12.0	14, 15, 16, 17, 18, 19
31	1.02	3H	d	22	6.8	11.6	21, 22, 23, 32
32a	2.72	1H	d	32b	16.4	42.8	21, 22, 31, 33
32b	2.35	1H	dd	32a	16.5, 1.0		
33	--	--	--	--	--	170.2	32
34	--	--	--	--	--	157.3	9
NH2	4.66	2H	br s	--	--	--	--
C7-OH	2.16	1H	d	7	7.9	--	--
C21-OH	1.91	1H	s	--	--	--	--

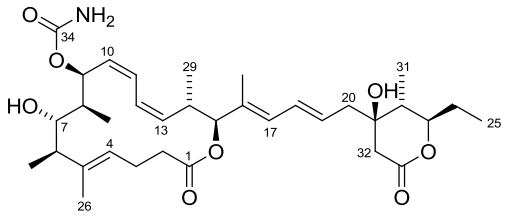


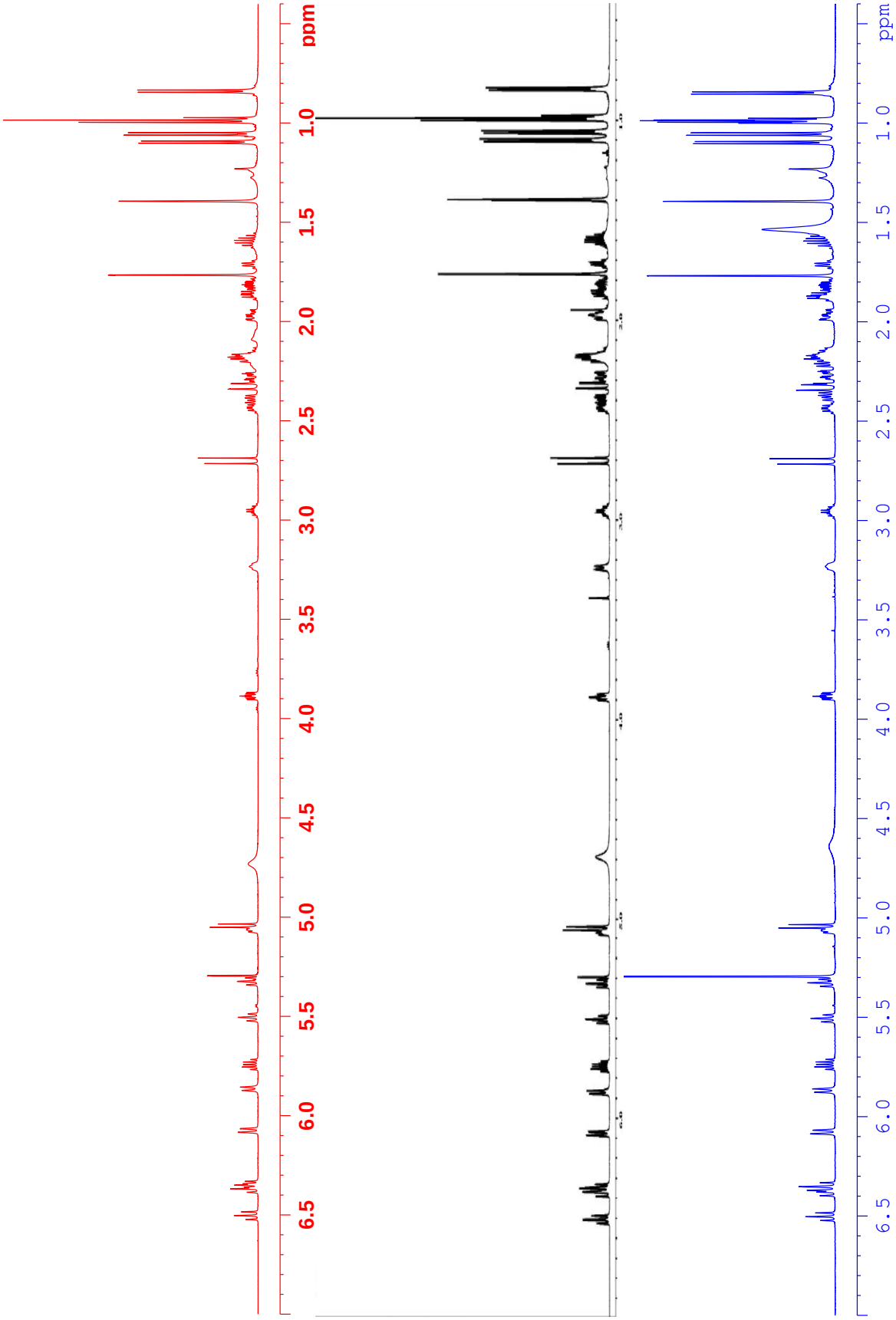
Table S-5: ^{1}H and ^{13}C data of Leiodermatolide-isomer **2**; numbering scheme as shown in the Insert, data was obtained with 0.6 mg in 0.3 mL CD_2Cl_2.

	^{1}H NMR (CD_2Cl_2, 600 MHz)					^{13}C NMR (CD_2Cl_2, 150 MHz)	
Nr	**δ (ppm)**	**Integral**	**Splitting**	**COSY**	***J* (Hz)**	**δ (ppm)**	**HMBC**
1	--	--	--	--	--	172.2	2, 3, 15
2a	2.29	1H	ddd	2b, 3	16.6, n.d.	33.7	3, 4, 26
2b	1.99	1H	ddd	2a, 3	16.7, n.d.		
3	2.20	2H	m	2, 4, 26	--	22.2	2, 4, 5, 26
4	5.09	1H	ddq	3, 26	8.4, 5.2, 1.4	125.6	2, 3, 5, 6, 26
5	--	--	--	--	--	137.3	3, 4, 6, 26, 27
6	2.47	1H	dq	7, 27	10.5, 6.7	48.5	4, 7, 25, 26, 27
7	3.26	1H	br m	OH, 6, 8	--	78.1	6, 8, 9, 28
8	1.74	1H	qt	7, 27, 28	7.3, n.d.	39.3	7, 10, 28
9	5.89	1H	d	10	10.0	67.6	7, 28, 11
10	5.53	1H	ddt	9, 11	10.7, 10.0, 1.3	128.5	9, 11, 12, 13
11	6.38	1H	t	10, 12	11.3	126.2	9, 10, 12, 13
12	6.53	1H	t	11, 13	11.5	124.4	10, 11, 13, 14
13	5.35	1H	ddt	12, 14	10.8, 10.2, 1.4	137.6	11, 12, 14, 15, 29
14	2.98	1H	tq	13, 15, 29	10.2, 6.7	35.0	12, 13, 15, 29, 30
15	5.07	1H	d	14	10.3	82.5	12, 13, 14, 17, 29, 30
16	--	--	--	--	--	134.0	14, 15, 17, 18, 30
17	6.10	1H	dq	18, 30	10.9, 1.4	129.7	15, 16, 18, 19, 30
18	6.40	1H	ddt	17,19, 20	15.0, 10.9, 1.3	131.7	16, 17, 20, 30
19	5.76	1H	dt	18, 20	15.1, 7.6	128.2	17, 20, 30
20a	2.40	1H	dd	19, 20b	14.1, 7.8	38.6	18, 19, 32
20b	2.23	1H	dd	19, 20a	14.2, 7.5		
21						72.1	18, 19, 20, 22, 31, 32
22	1.89	1H	dq	23, 31	10.0, 6.8	43.1	20, 21, 23, 24, 31, 32
23	3.91	1H	ddd	22, 24	10.0, 7.6, 3.1	83.8	22, 24, 25, 31
24a	1.85	1H	ddq	23, 24b, 25	14.5, 7.4, 3.1	27.1	22, 23, 25
24b	1.62	1H	dq	23, 24a, 25	14.6, 7.4		
25	1.01	3H	t	24	7.4	9.2	23, 24
26	1.42.	3H	s	3, 4	-	11.3	3, 4, 5, 6
27	1.12	3H	d	6	6.7	16.5	5, 6
28	1.08	3H	d	8	7.3	12.5	7, 8, 9
29	0.87	3H	d	14	6.7	16.6	13, 14, 15
30	1.79	3H	d	17	0.7	12.0	14, 15, 16, 17, 18, 19
31	1.02	3H	d	22	6.9	11.6	21, 22, 23, 32
32a	2.73	1H	d	32b	16.5	42.9	21, 22, 31, 33
32b	2.36	1H	d	32a	16.6		
33	--	--	--	--	--	170.2	32
34	--	--	--	--	--	157.3	9
NH2	4.67	2H	br s	--	--	--	--
C7-OH	2.17	1H	br s	7	--	--	--
C21-OH	1.91	1H	s	--	--	--	--

Table S-6 Comparison of the ^{13}C NMR shifts (150 MHz, CD_2Cl_2) of leiotermatolide and the synthetic samples **1** and **2**. For this particular comparison, the spectra were calibrated on the well resolved signal C13 (≡ 137.869 ppm); if the spectra of the synthetic samples are calibrated on CD_2Cl_2 $\delta_C \equiv 53.8$ ppm, as otherwise practiced in this paper (see General), all shifts systematically deviate by +0.25 ppm.

Atom No	Literature	Synthetic 1 @ 4 mg in 0.3 mL	Synthetic 1 @ 0.8 mg in 0.3 mL	Synthetic 2
1	172,4	172,4	172,4	172,4
2	34,0	34,0	34,0	34,0
3	22,5	22,5	22,5	22,4
4	125,9	125,9	125,9	125,8
5	137,5	137,5	137,5	137,5
6	48,7	48,8	48,8	48,7
7	78,4	78,4	78,4	78,4
8	39,6	39,5	39,5	39,5
9	68,0	67,9	67,9	67,9
10	128,8	128,7	128,7	128,7
11	126,4	126,4	126,4	126,4
12	124,7	124,6	124,6	124,6
13	137,9	137,9	137,9	137,9
14	35,3	35,2	35,2	35,2
15	82,8	82,8	82,7	82,7
16	134,2	134,1	134,2	134,2
17	130,0	130	129,9	129,9
18	131,8	131,8	131,9	131,9
19	128,5	128,6	128,4	128,7
20	38,9	38,8	38,8	38,8
21	72,3	72,3	72,3	72,3
22	43,4	43,4	43,4	43,3
23	84,1	84,1	84	84
24	27,4	27,4	27,4	27,3
25	9,4	9,4	9,4	9,4
26	11,5	11,5	11,5	11,5
27	16,8	16,8	16,8	16,7
28	12,7	12,7	12,7	12,7
29	16,8	16,8	16,8	16,8
30	12,2	12,2	12,2	12,2
31	11,8	11,8	11,8	11,8
32	43,1	43,0	43,0	43,1
33	170,4	170,5	170,4	170,4
34	157,6	157,6	157,5	157,5

The following color-coded spectra show a direct comparison between the ^{1}H and ^{13}C NMR spectra (CD_2Cl_2, 600 MHz and 150 MHz, respectively) of **natural leiodermatolide (black)** depicted in the Supporting Information of the isolation paper (I. Paterson, S. M. Dalby, J. C. Roberts, G. J. Naylor, E. A. Guzman, R. Isbrucker, T. P. Pitts, P. Linley, D. Divlianska, J. K. Reed, A. E. Wright, *Angew. Chem. Int. Ed*. **2011**, *50*, 3219-3223) with the recorded spectra of **synthetic 1 (red)** and **synthetic 2 (blue)**.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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
6.5
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5.0
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3.0
2.5
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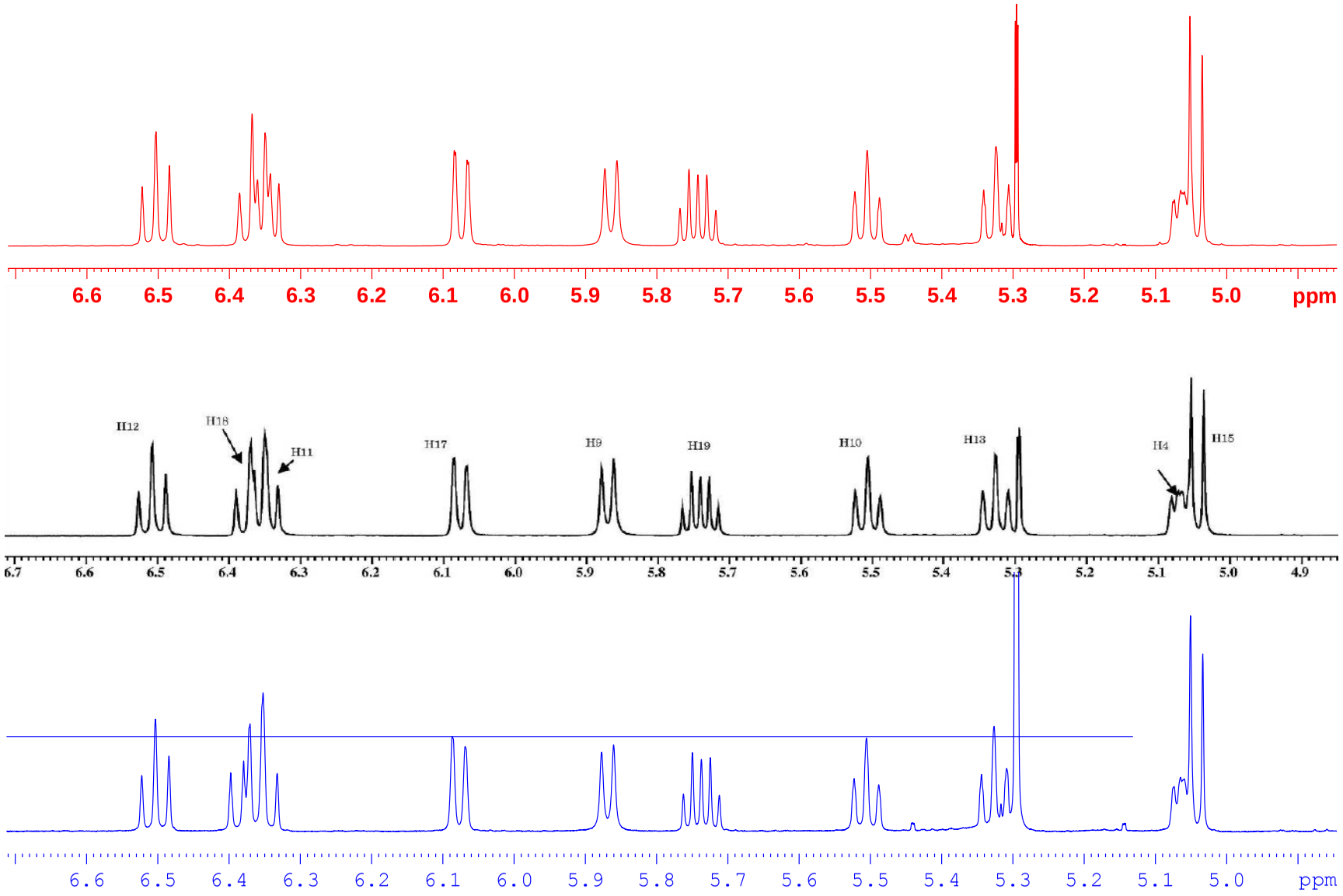
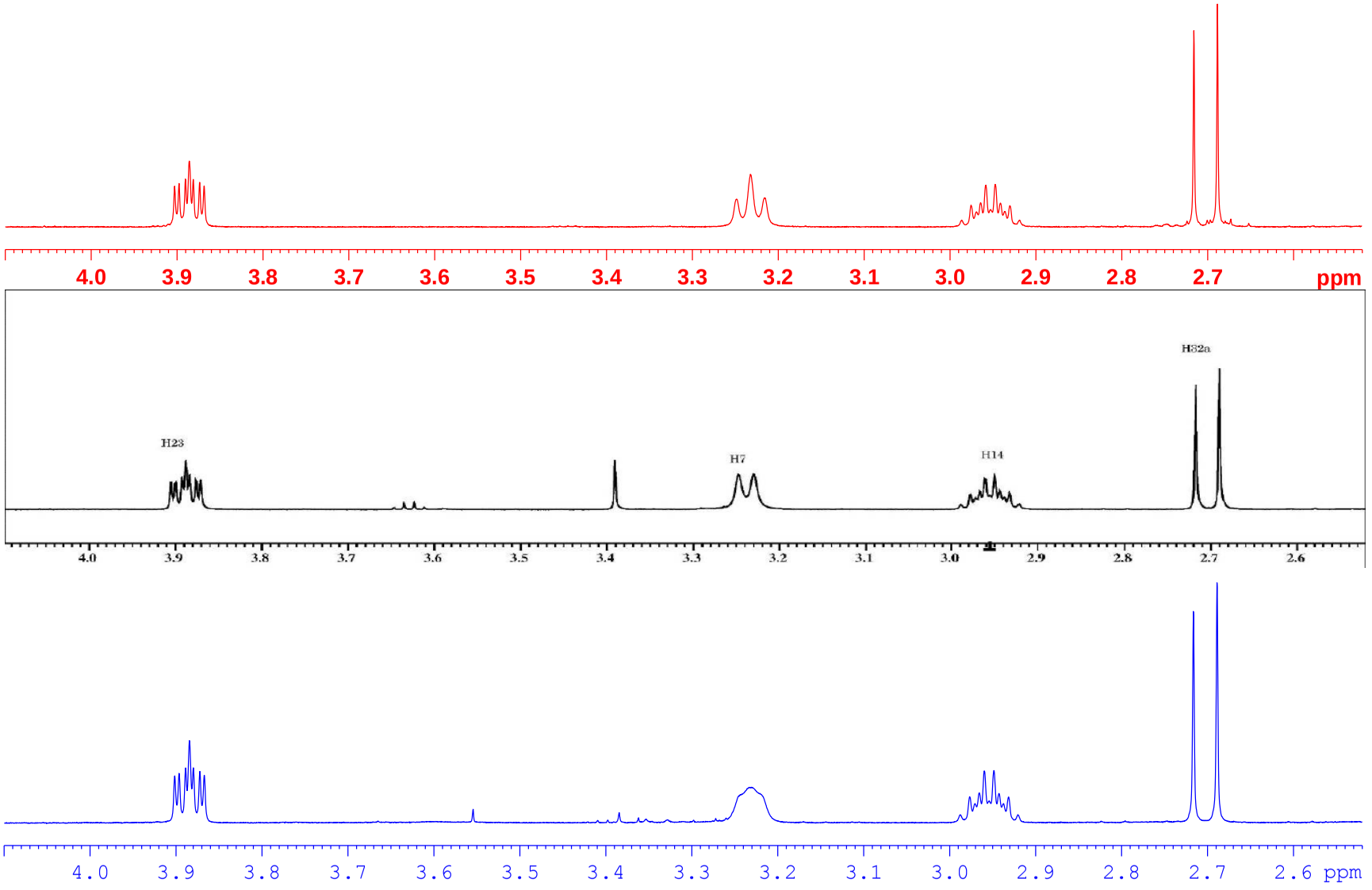
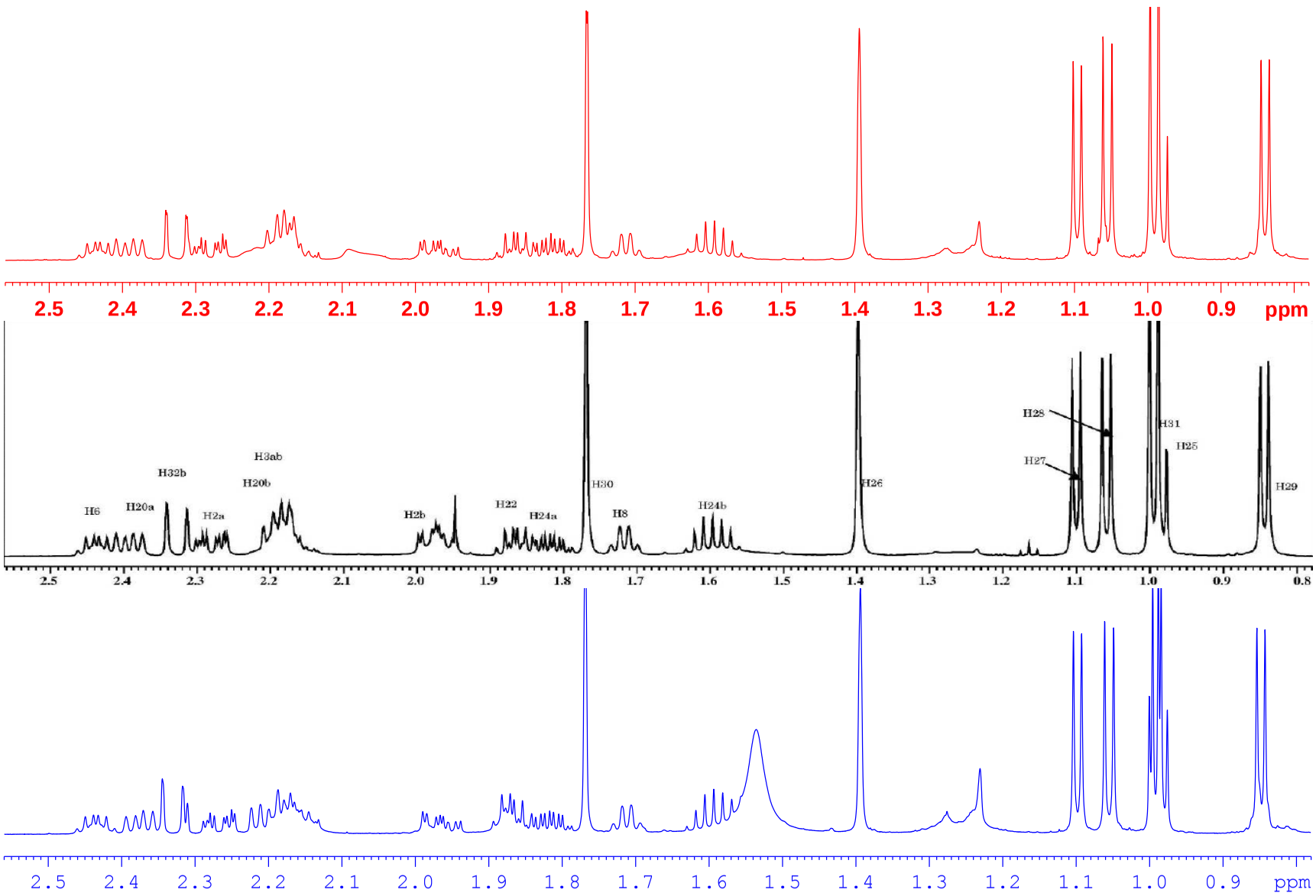
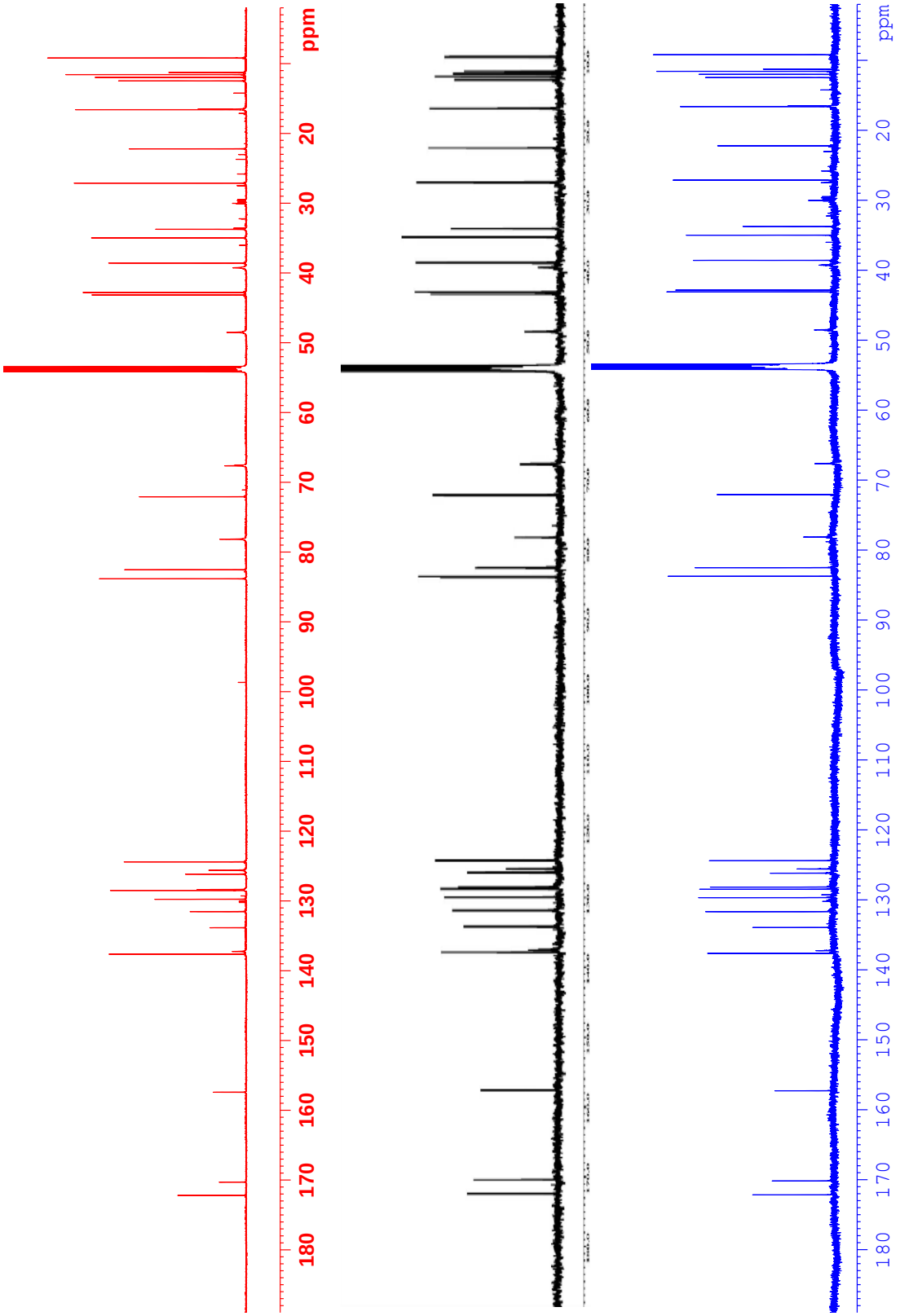
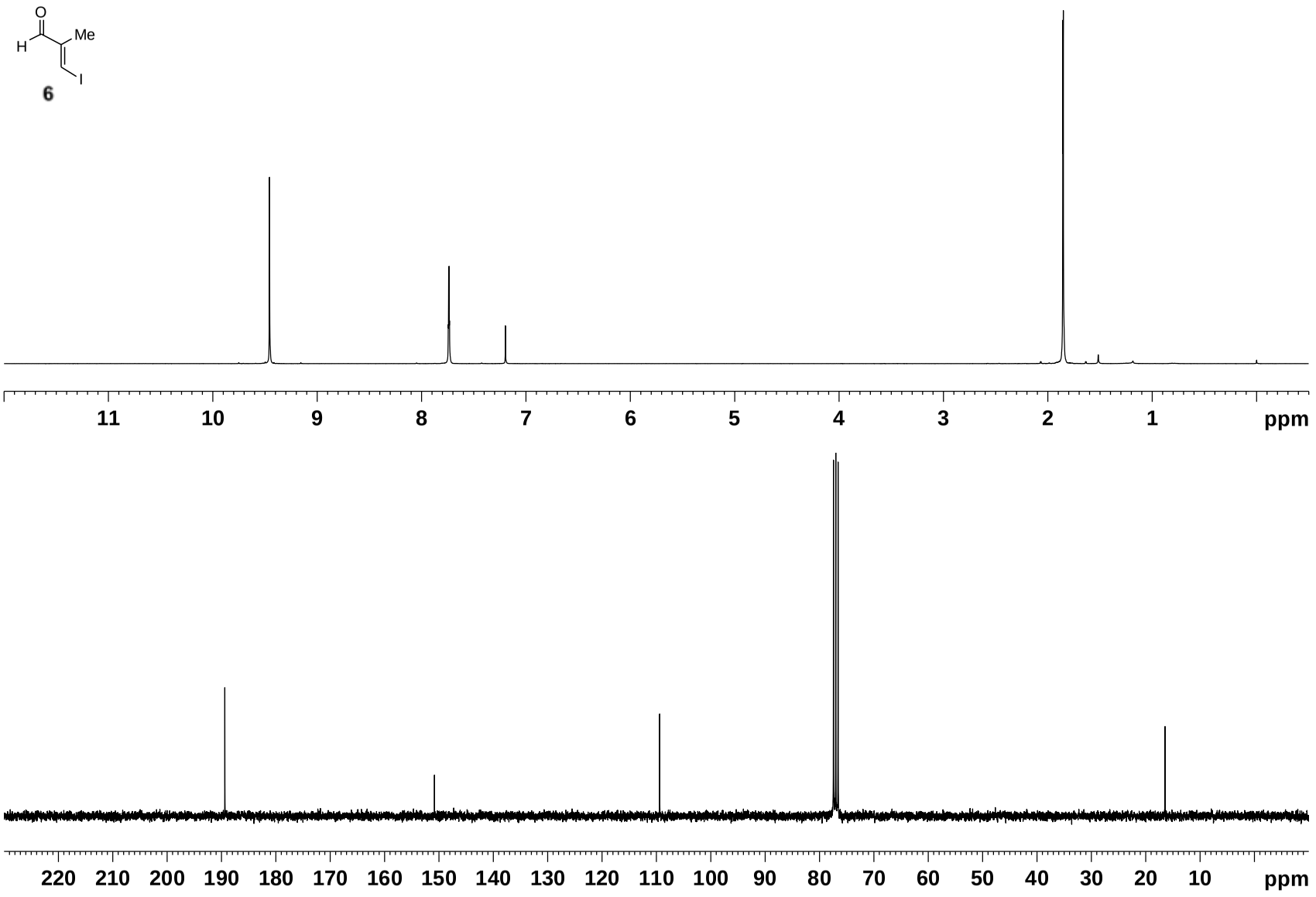
1.5
1.0

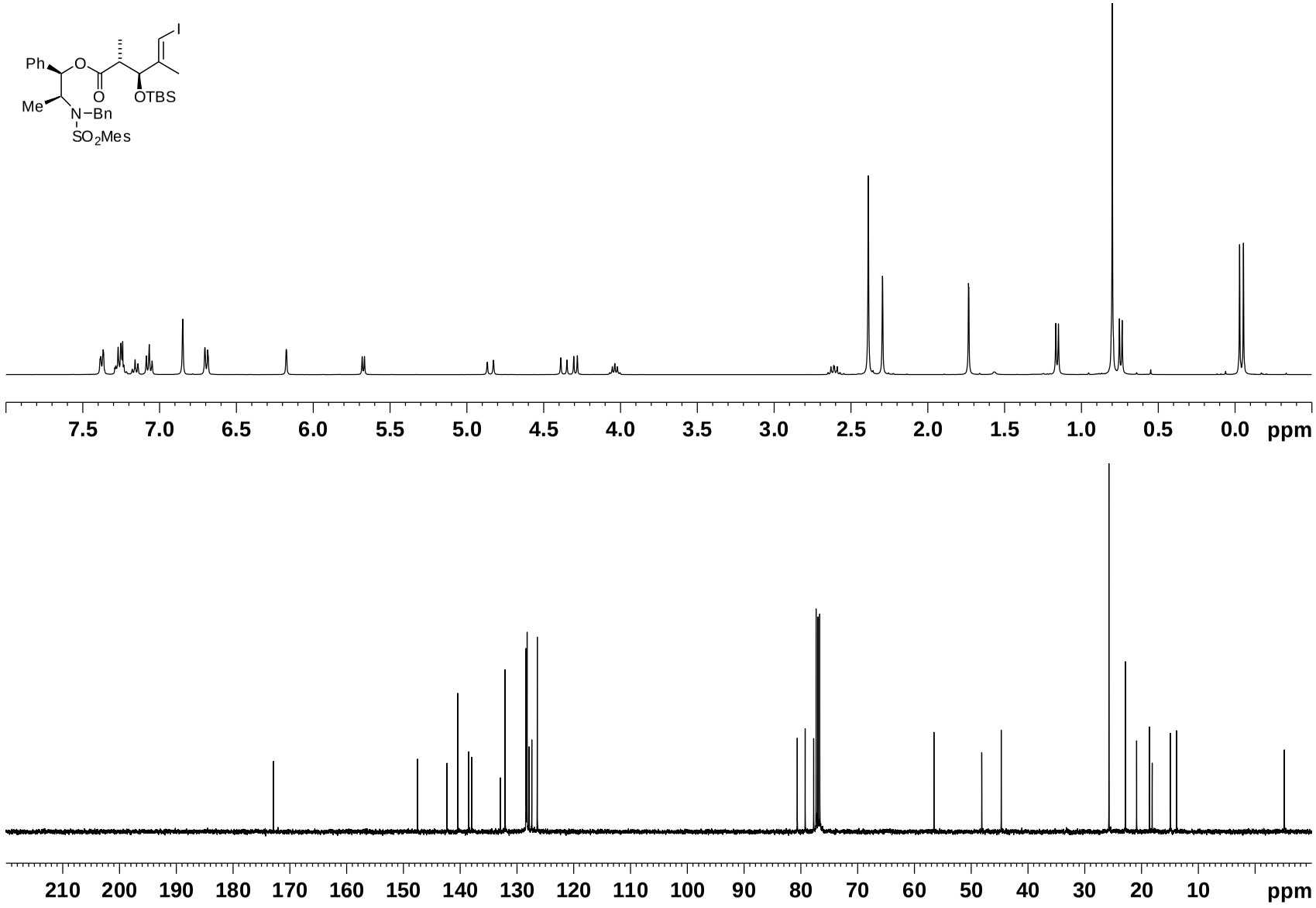

6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 ppm
H12
H18
H11
H17
H9
H19
H10
H13
H4
H15
6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9
6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 ppm

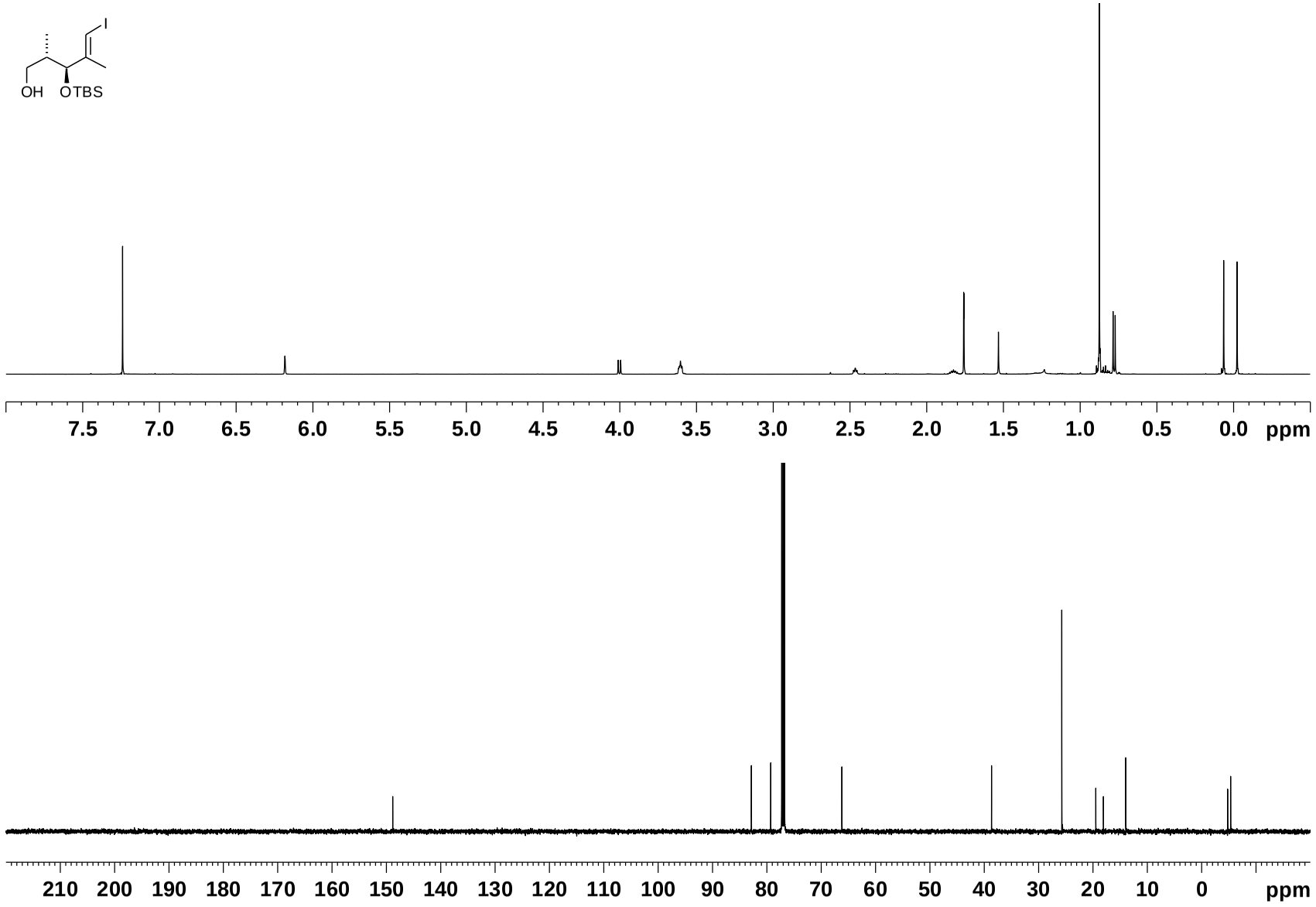

4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 ppm
H23
H7
H14
H32a
4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 ppm

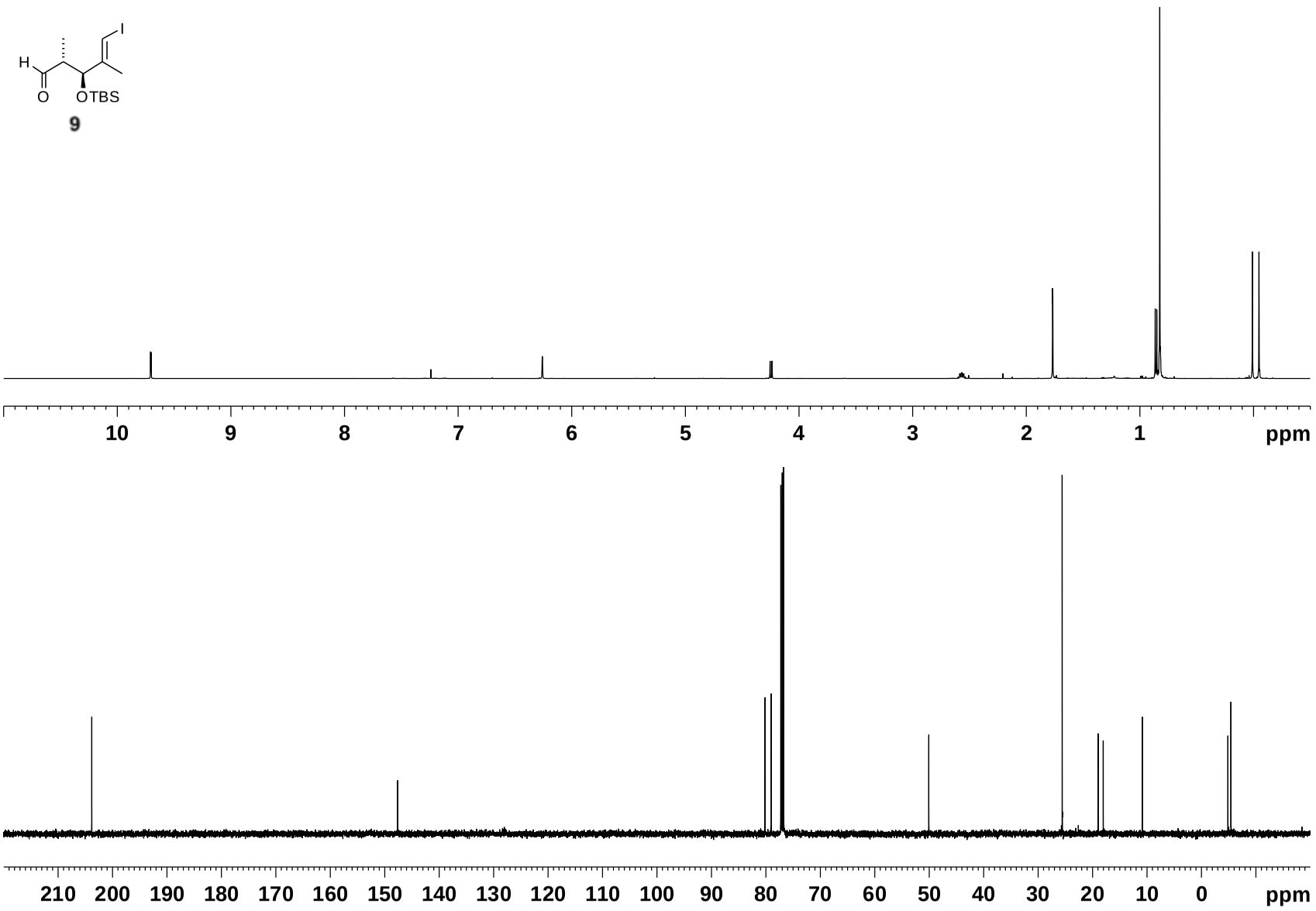

2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 ppm
H6
H20a
H32b
H2a
H3ab
H20b
H2b
H22
H24a
H30
H8
H24b
H26
H28
H27
H31
H25
H29
2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8
2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 ppm

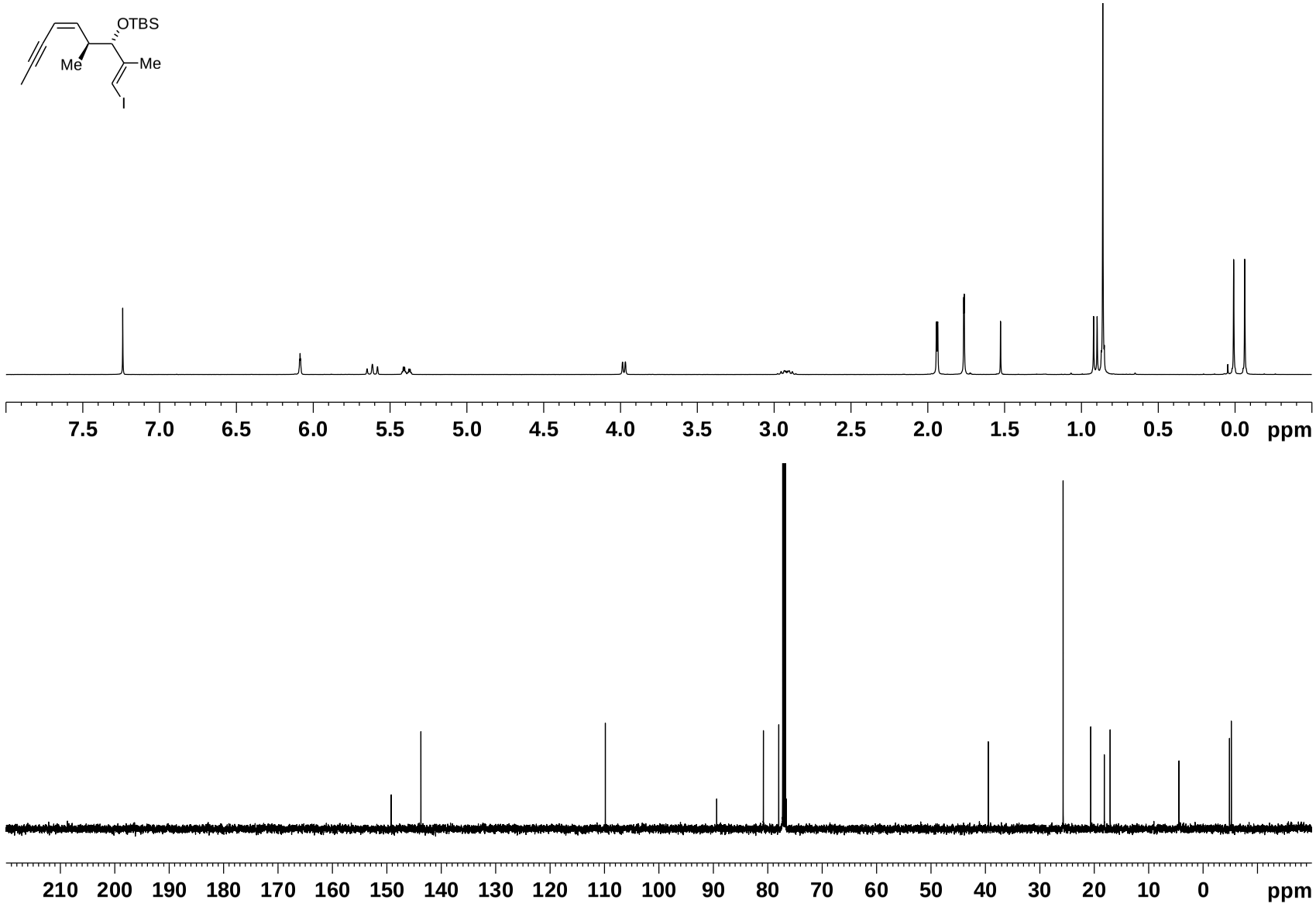

ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

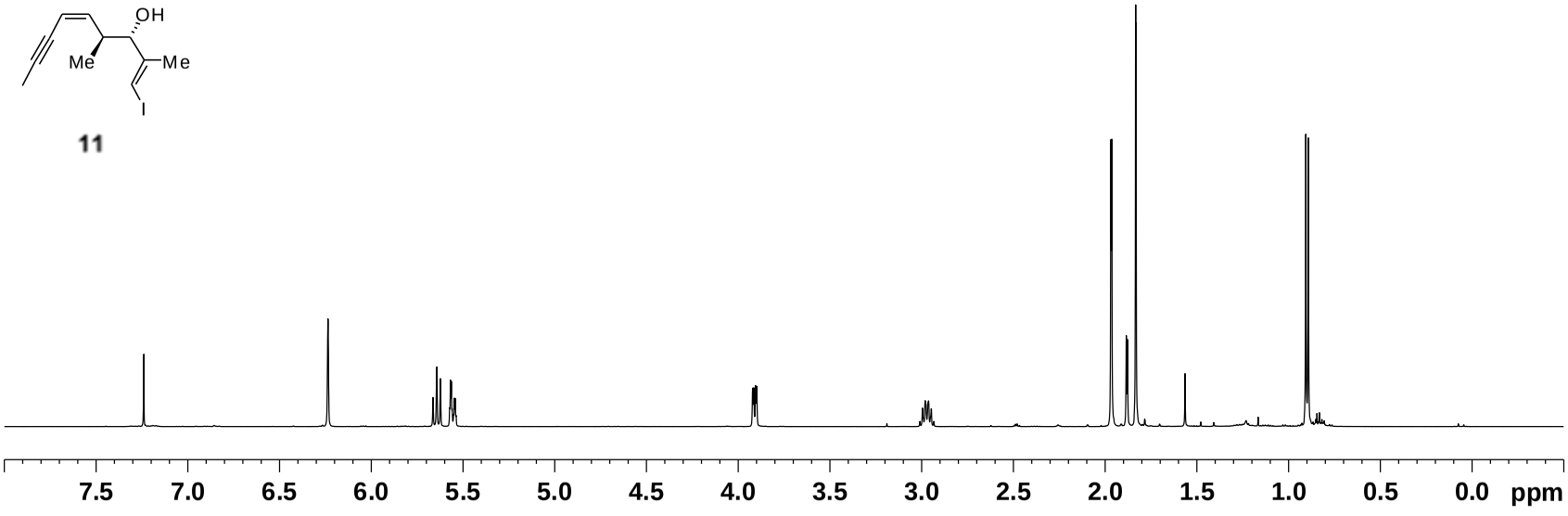

O
H
Me
I
6
11
10
9
8
7
6
5
4
3
2
1
ppm
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Ph
O
O
I
OTBS
Me
N–Bn
SO2Mes
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
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


I
OH
OTBS
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
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

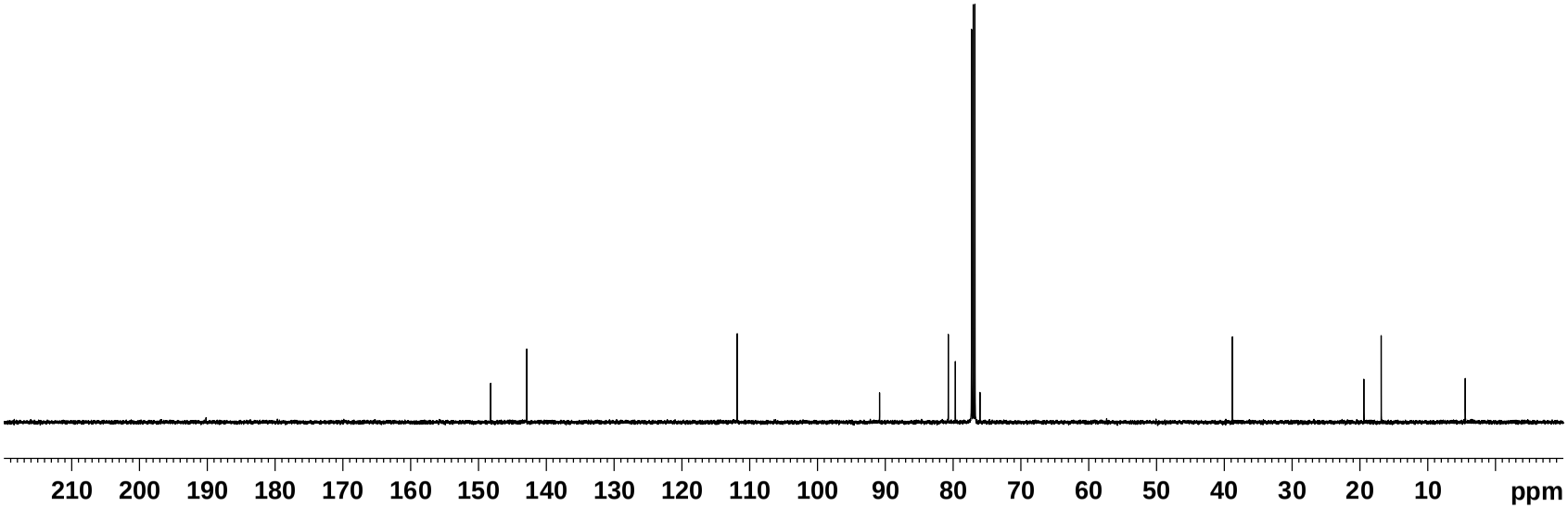

H
O
OTBS
I
9
10
9
8
7
6
5
4
3
2
1
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

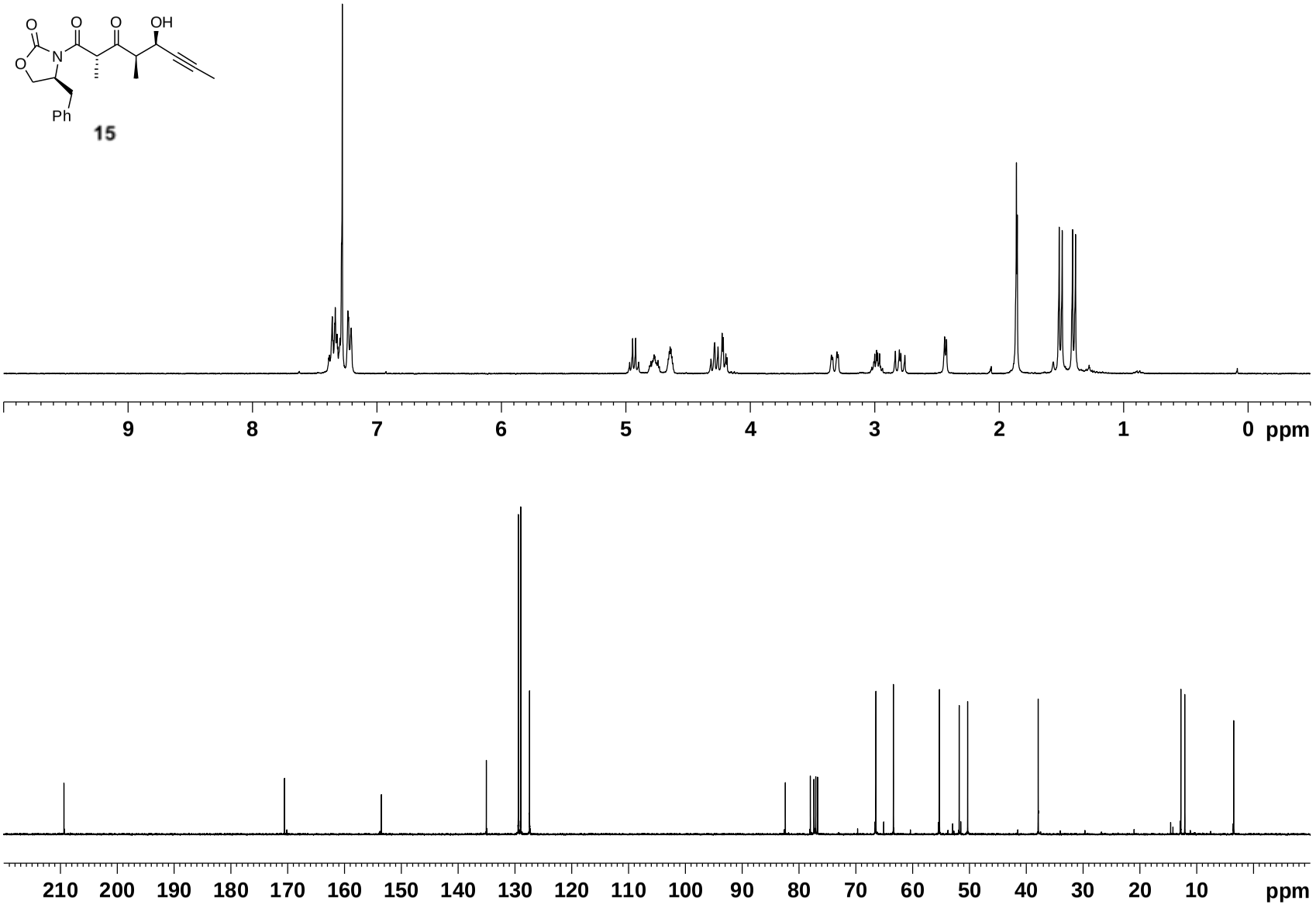

OTBS
Me
Me
I
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

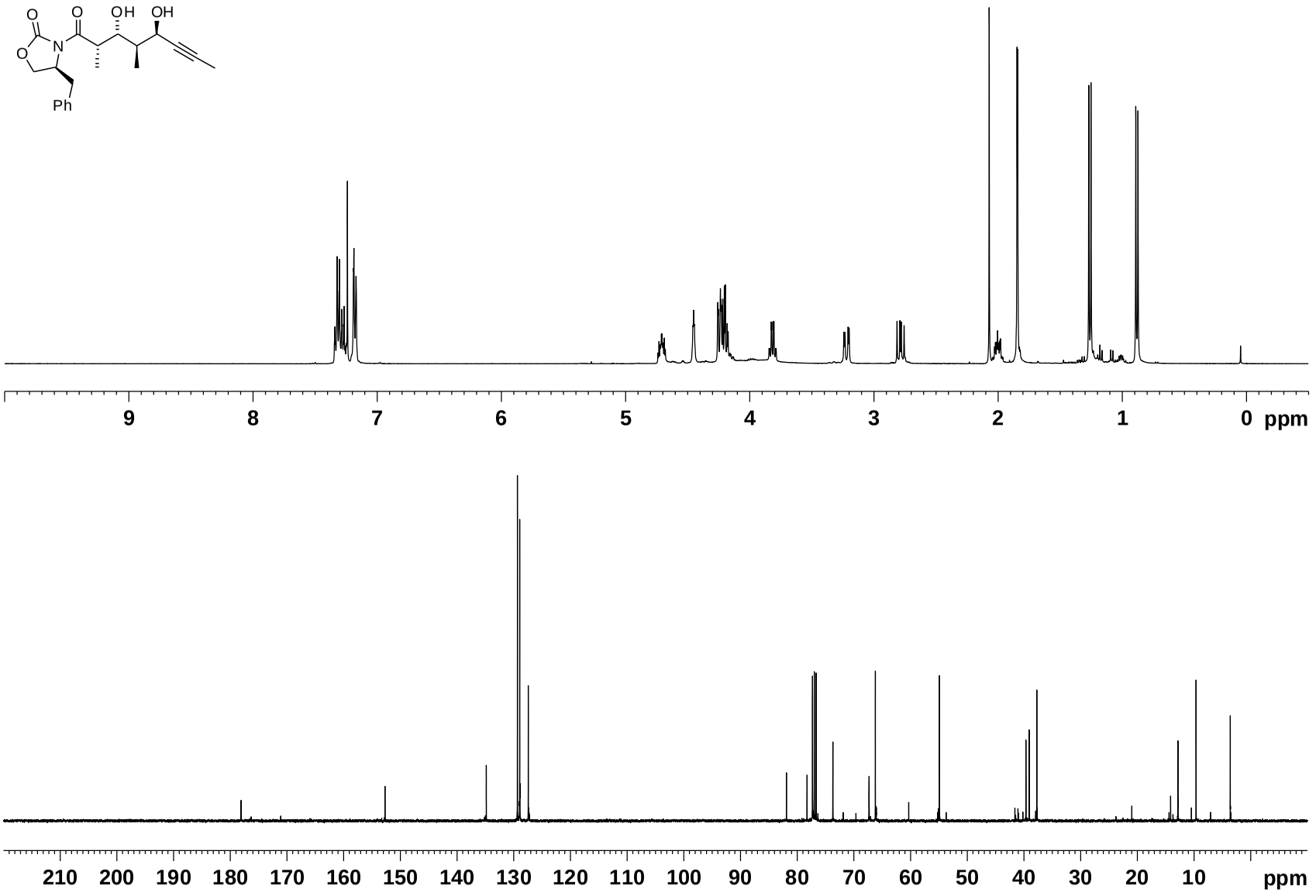

OH
Me
Me
I

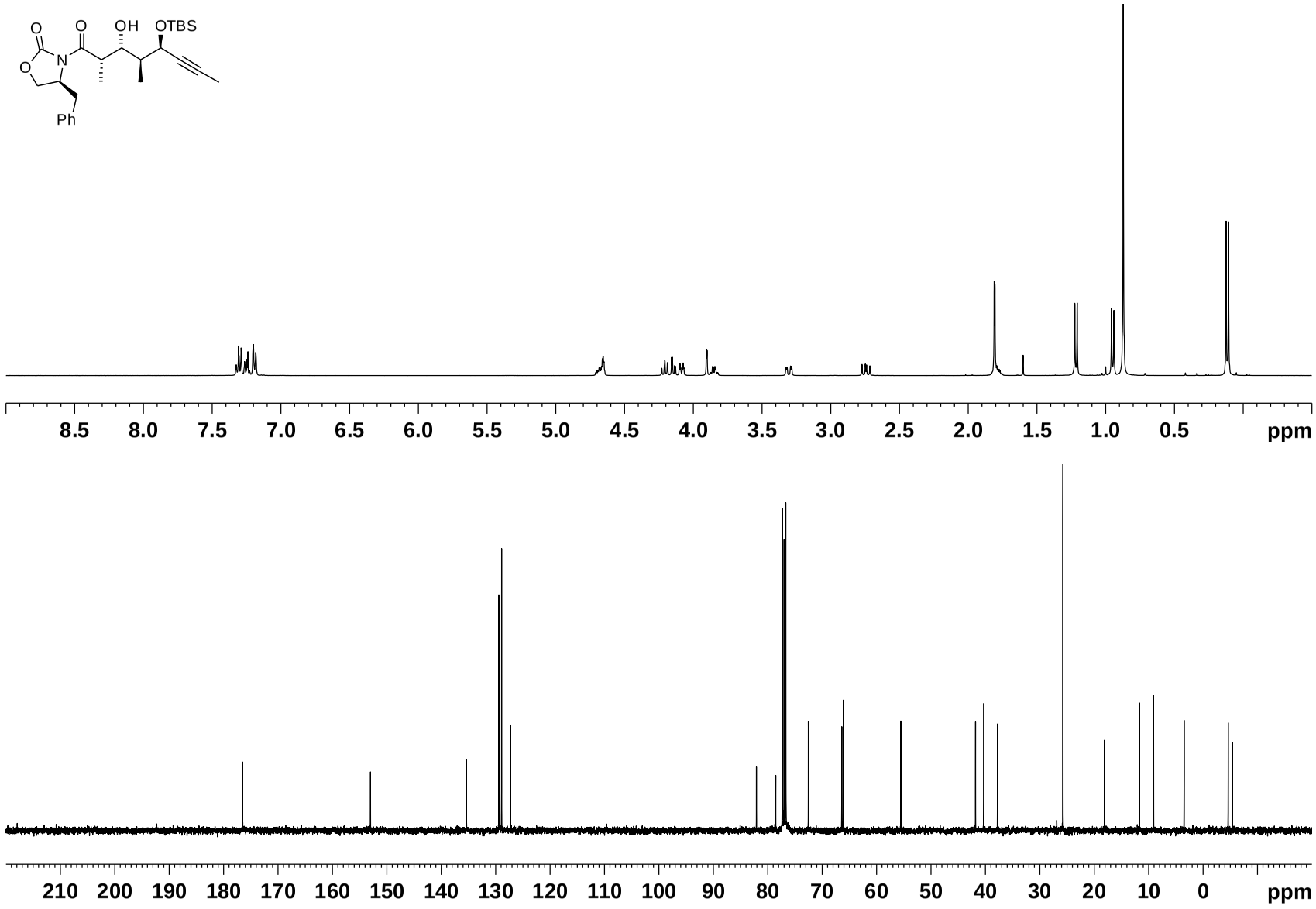
11

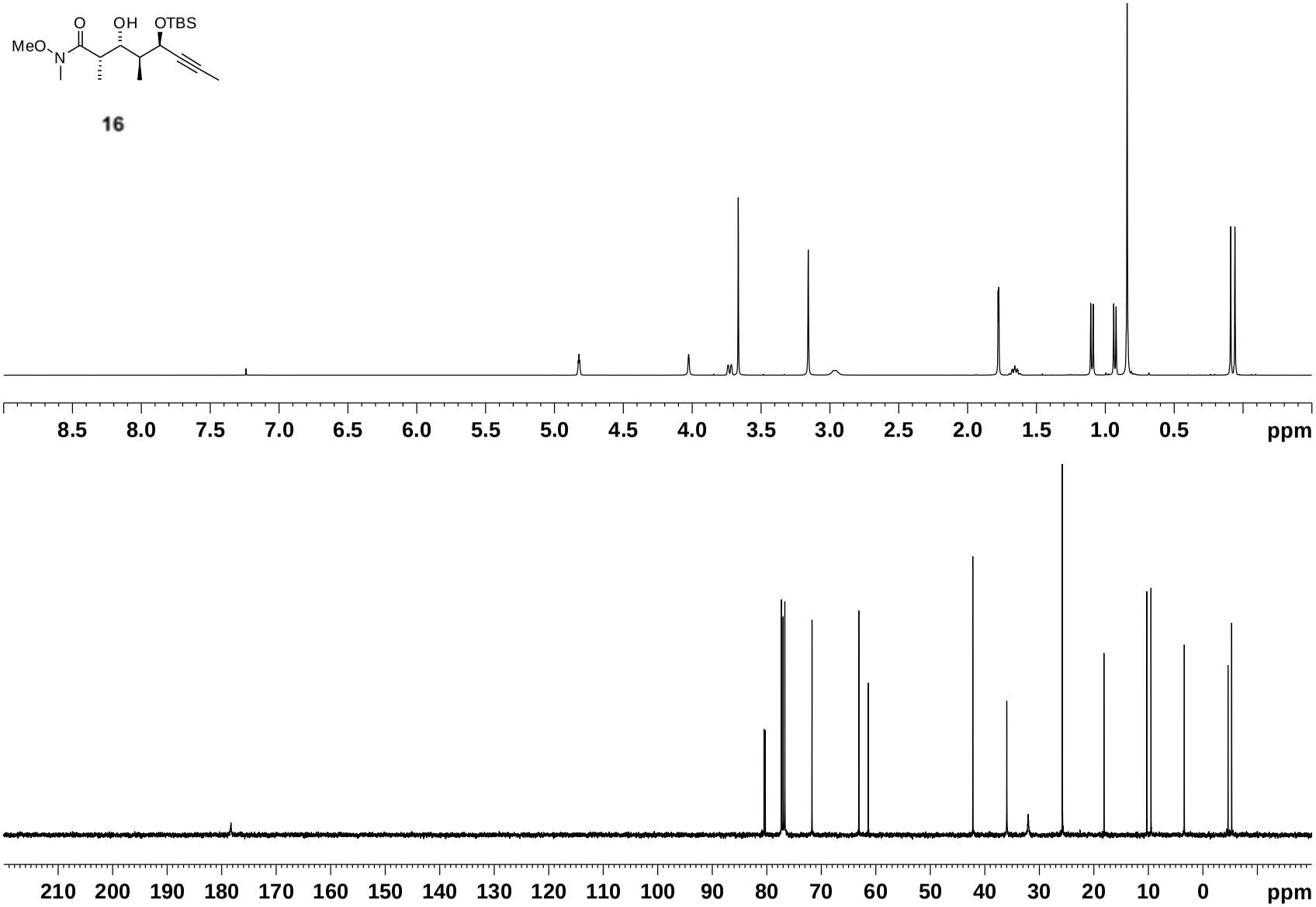
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

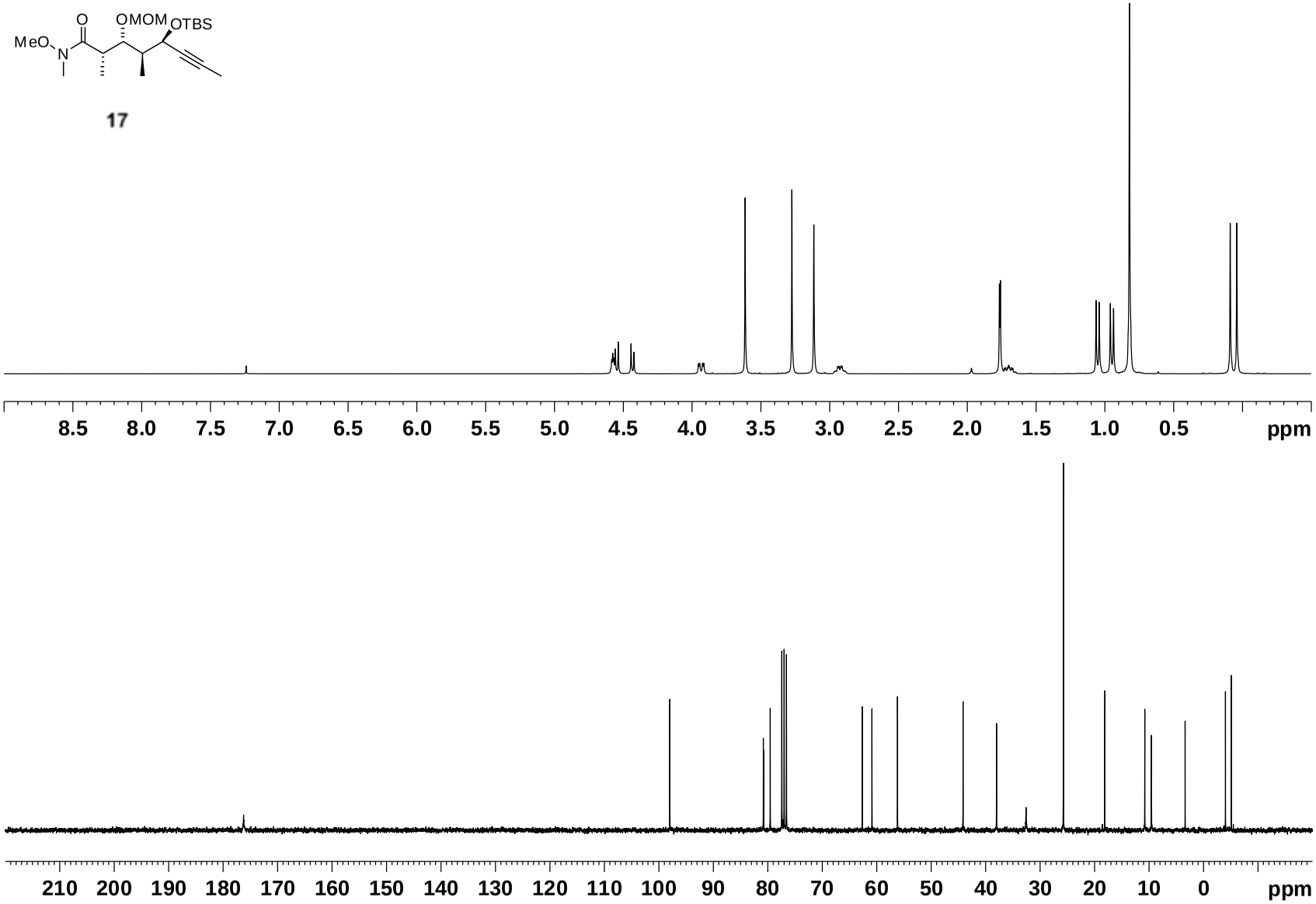

O
O
O
OH
O
N
Ph
15
9
8
7
6
5
4
3
2
1
0 ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

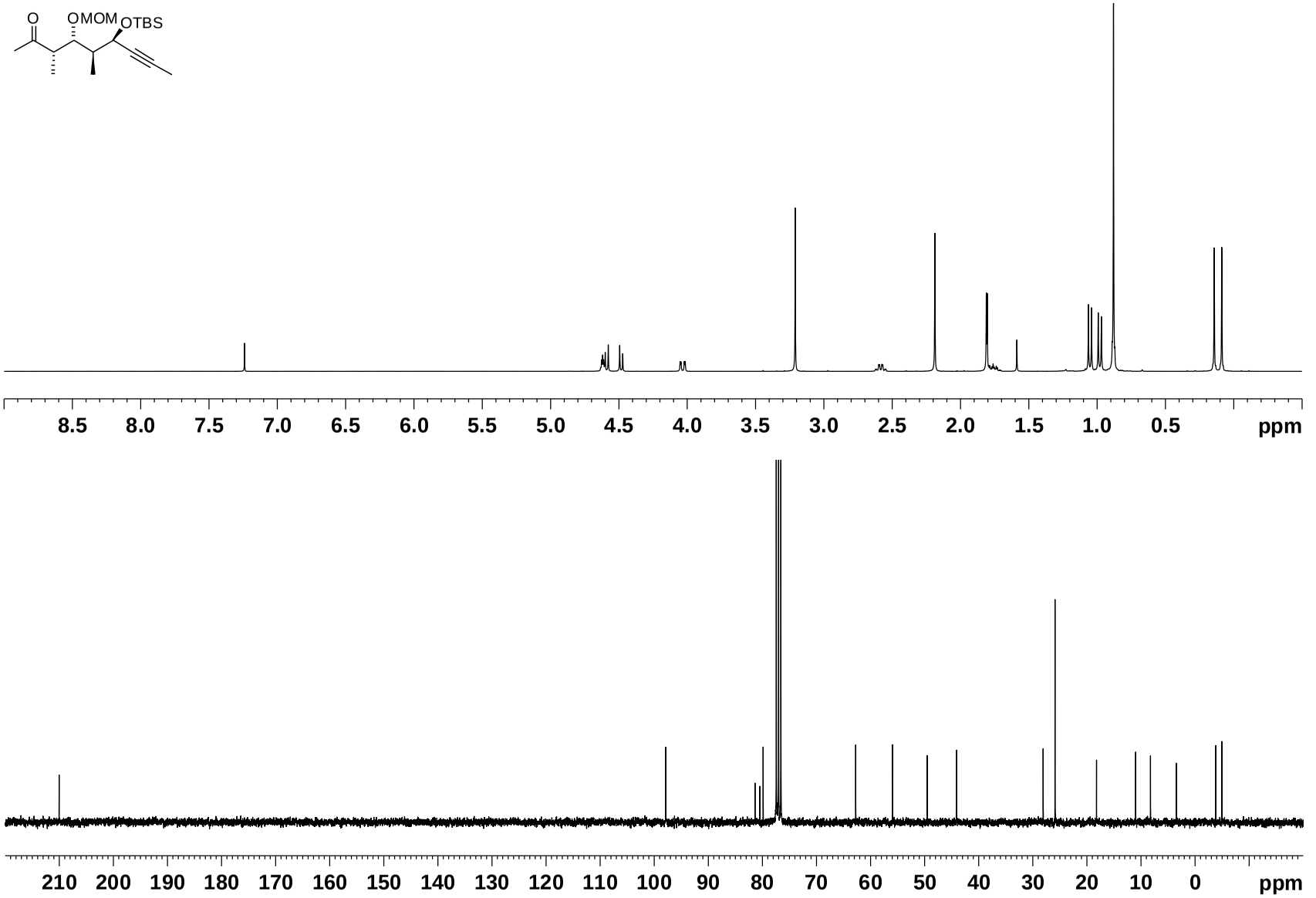

O
O
OH
OH
N
O
Ph
9
8
7
6
5
4
3
2
1
0 ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

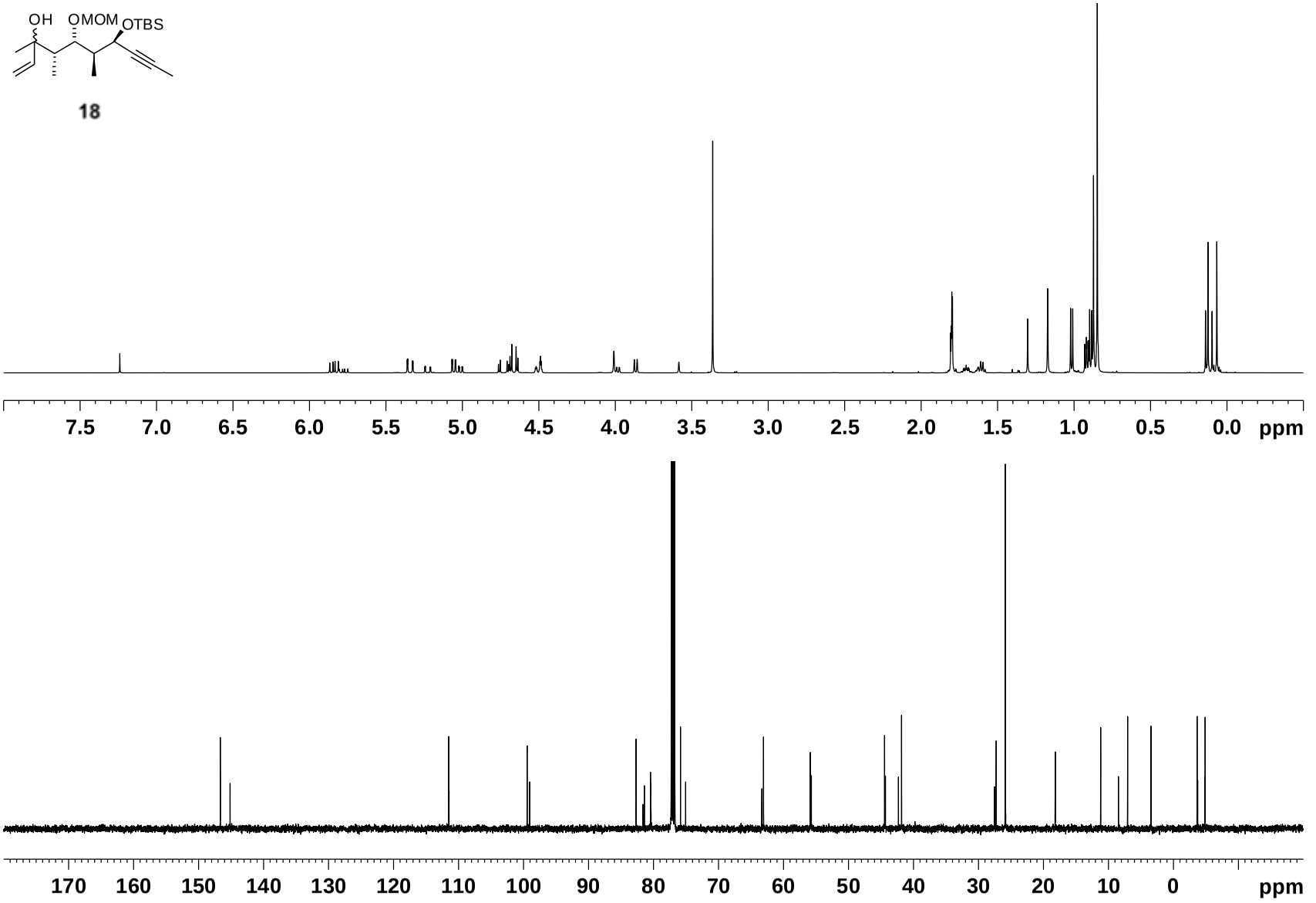

O
O
OH
OTBS
N
O
Ph
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

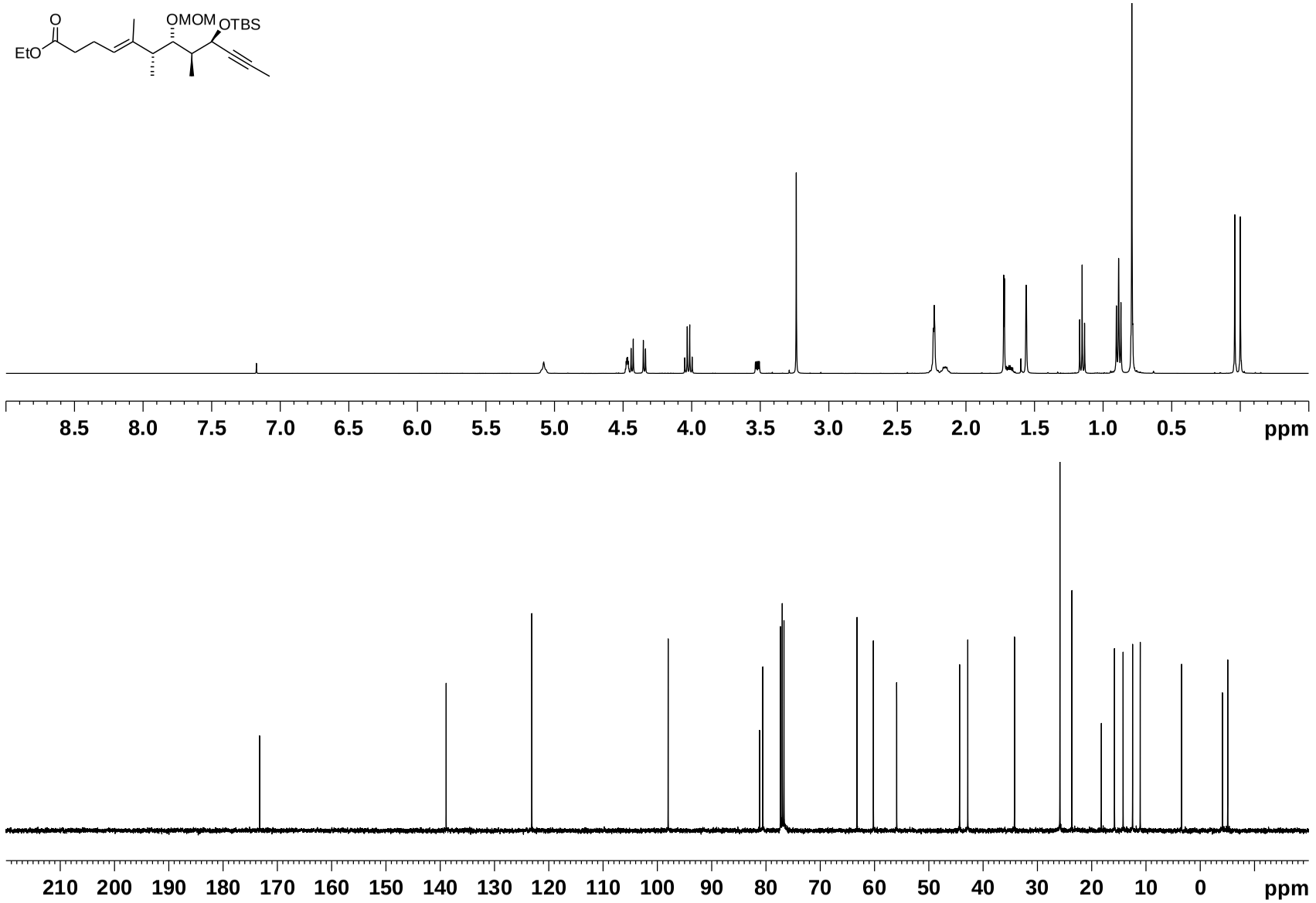

O
OH
OTBS
MeO
N
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

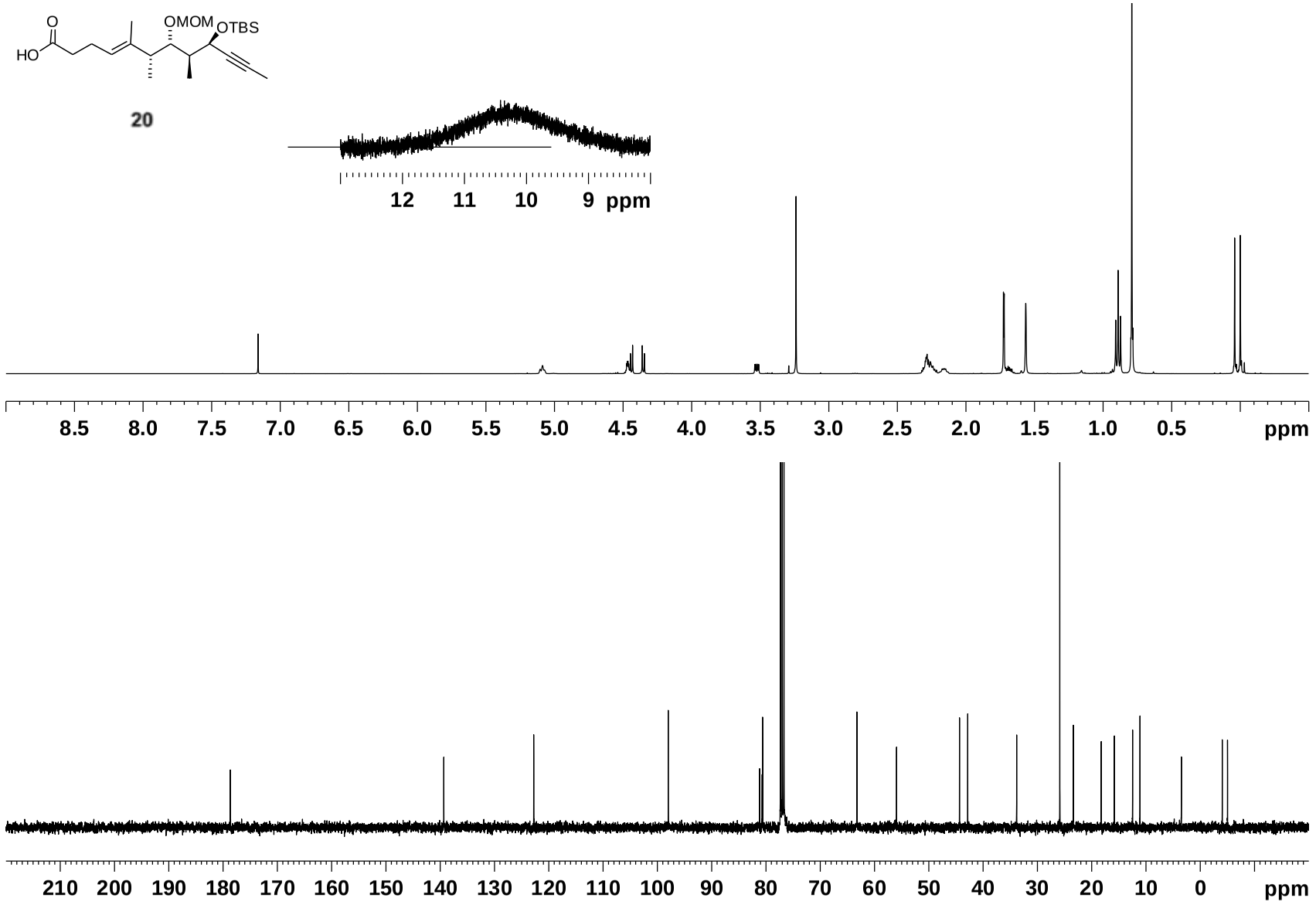
16

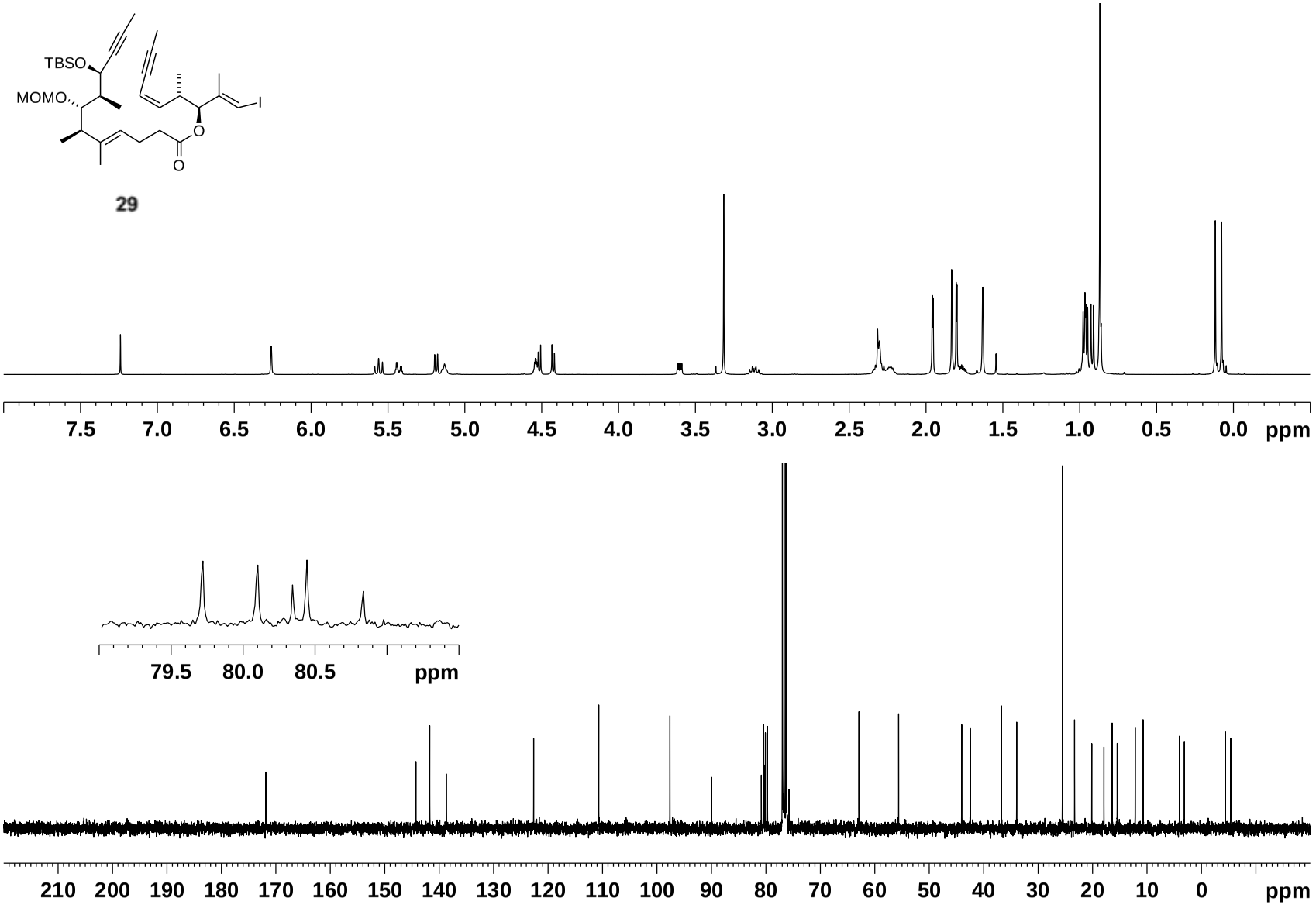

MeO
N
O
OMOM
OTBS
17
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

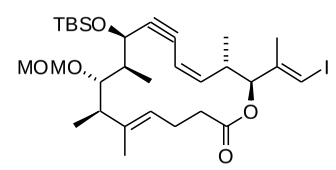

O
OMOM
OTBS
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


OH
OMOM
OTBS
18
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
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
EtO
OMOM
OTBS
8.5 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
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

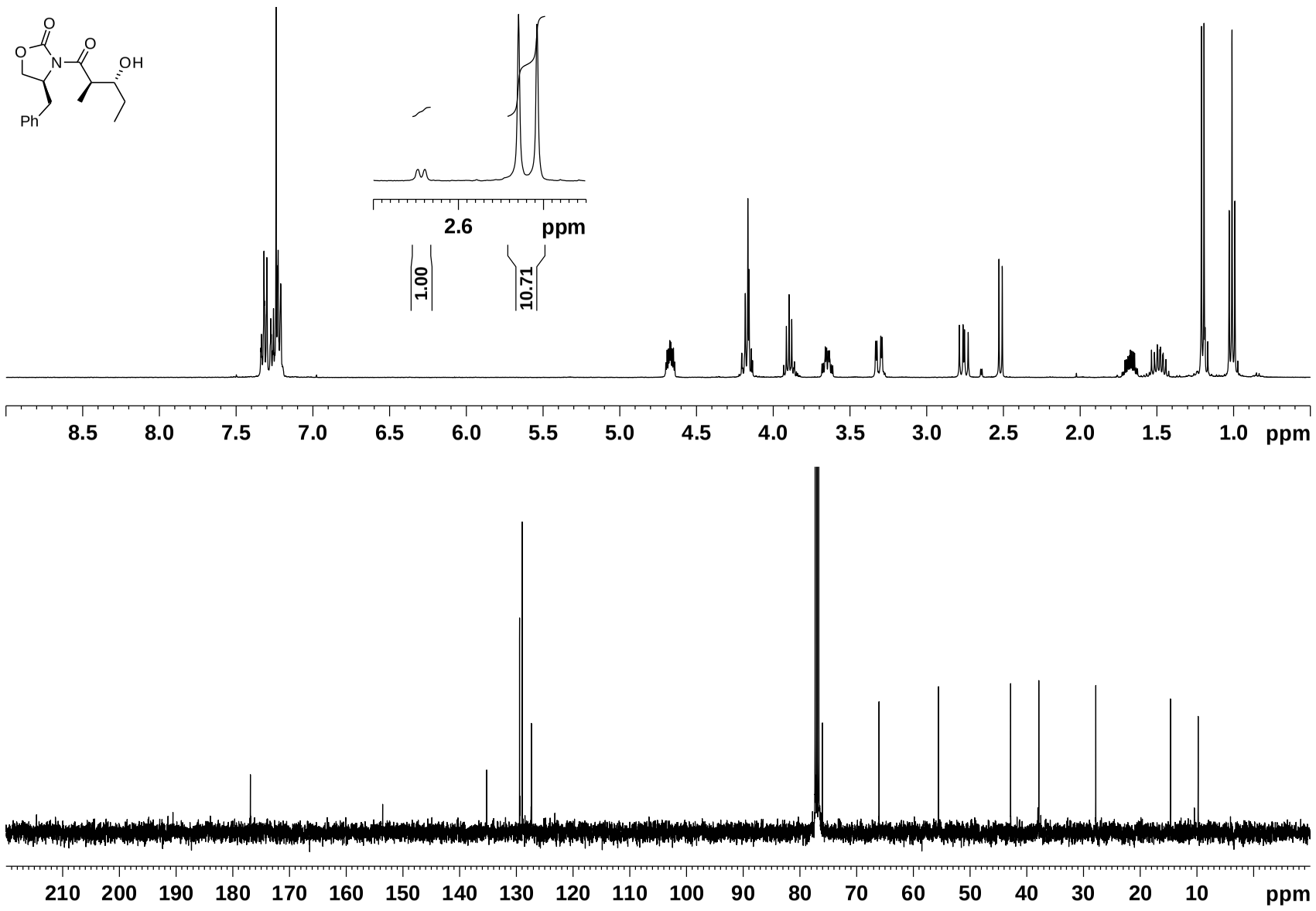

O
HO
OMOM
OTBS
20
12
11
10
9 ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

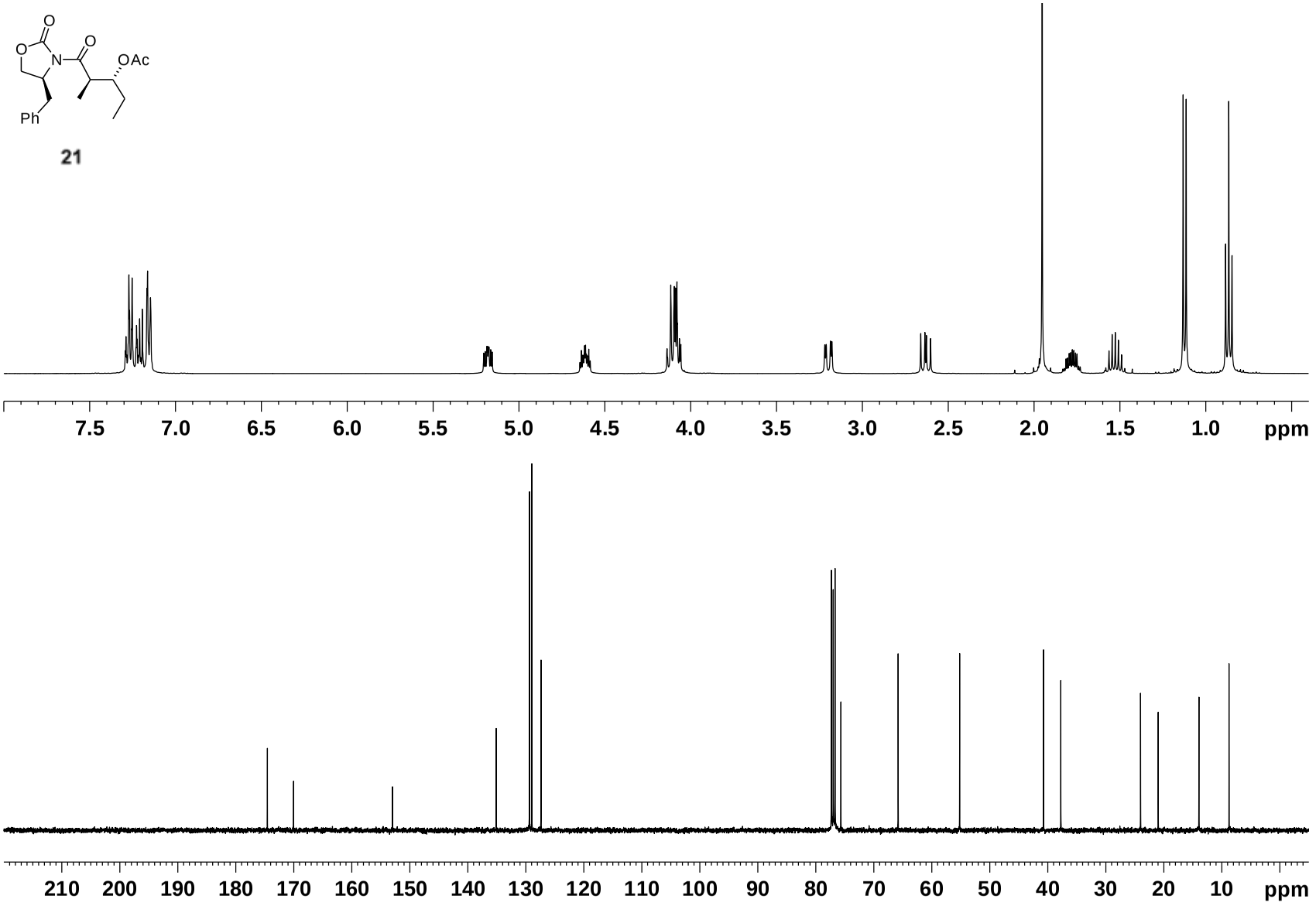

TBSO
MOMO
I
O
O
29
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
79.5 80.0 80.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

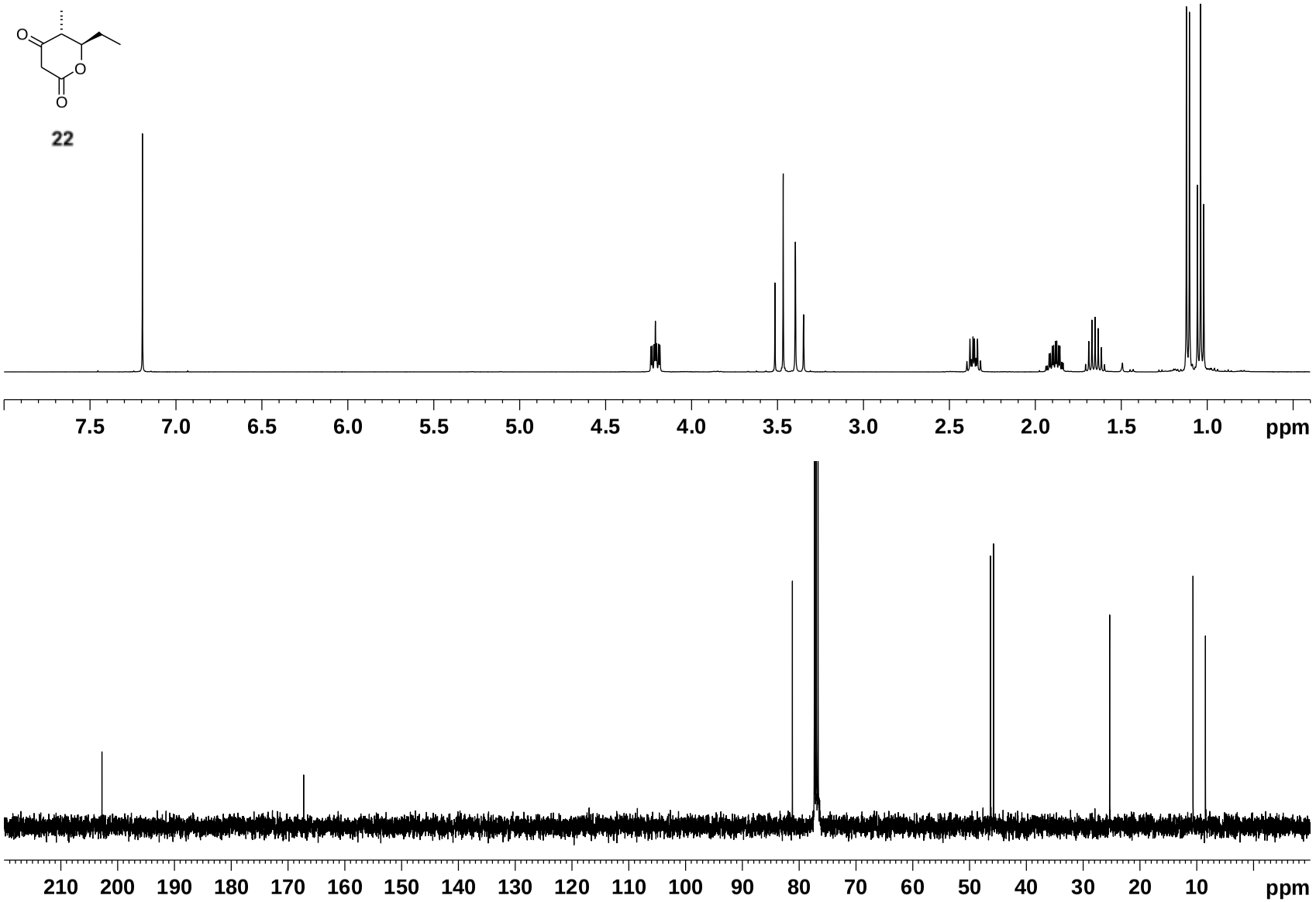

TBSO
MOMO
I
O
O

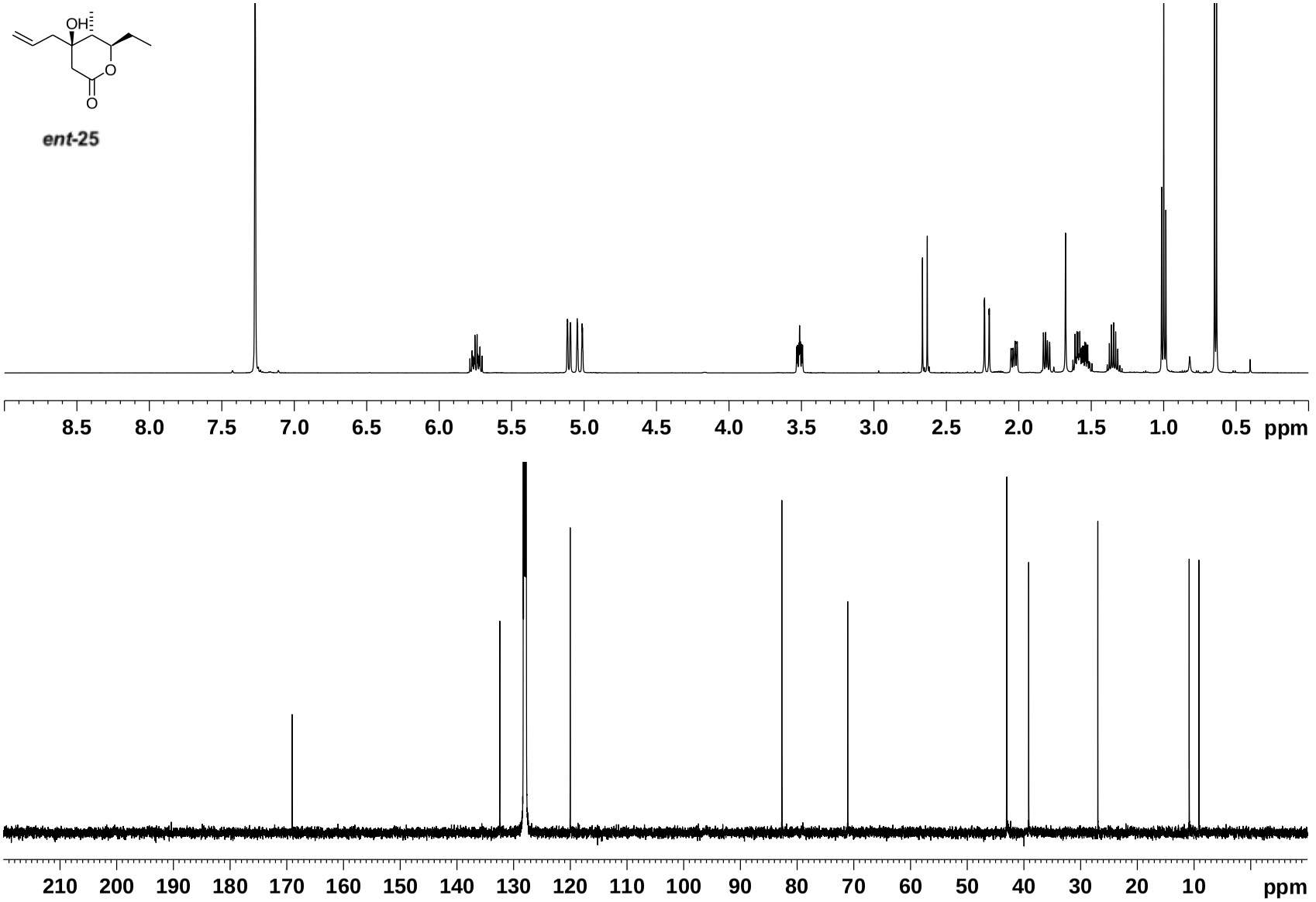
30

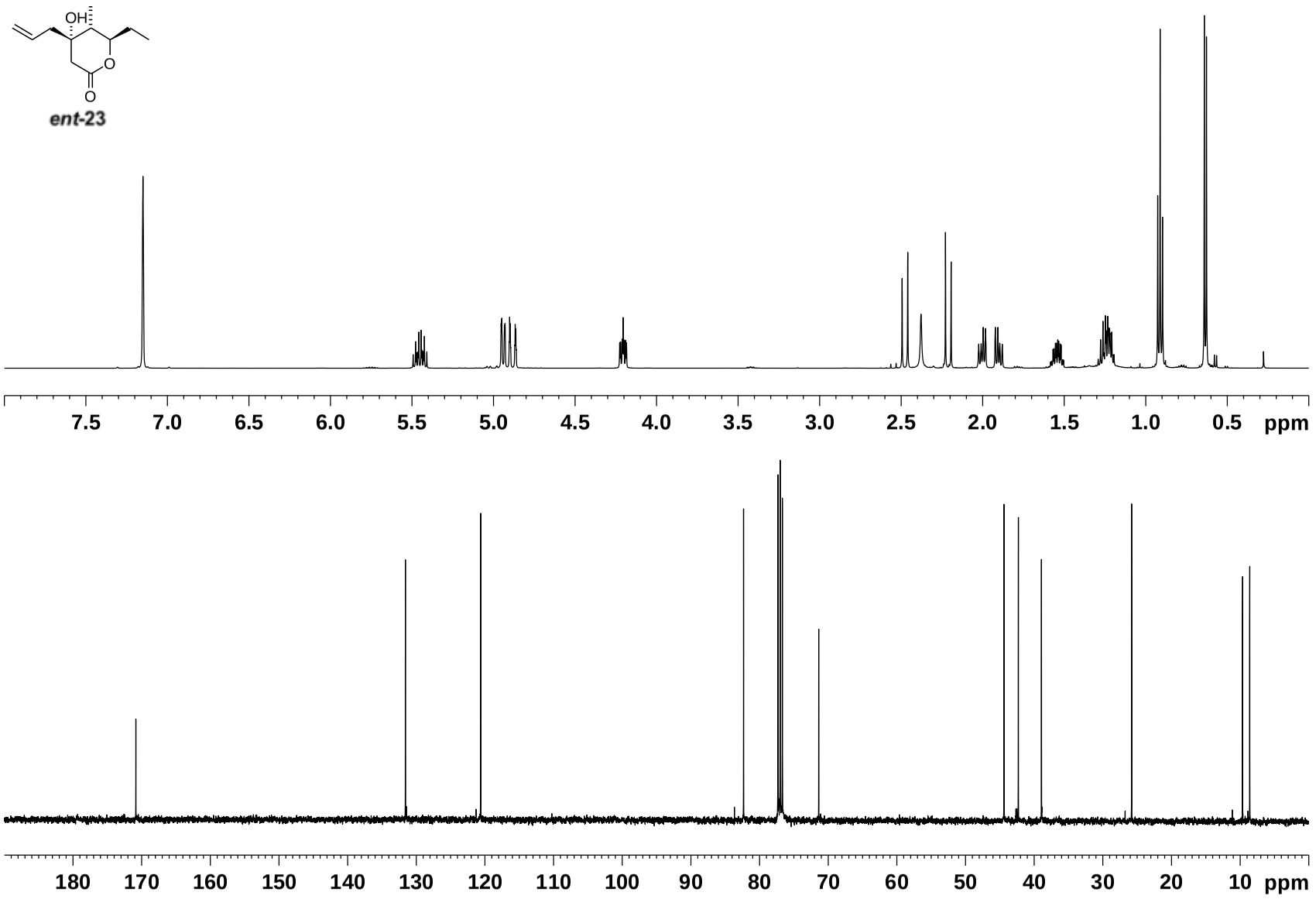
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

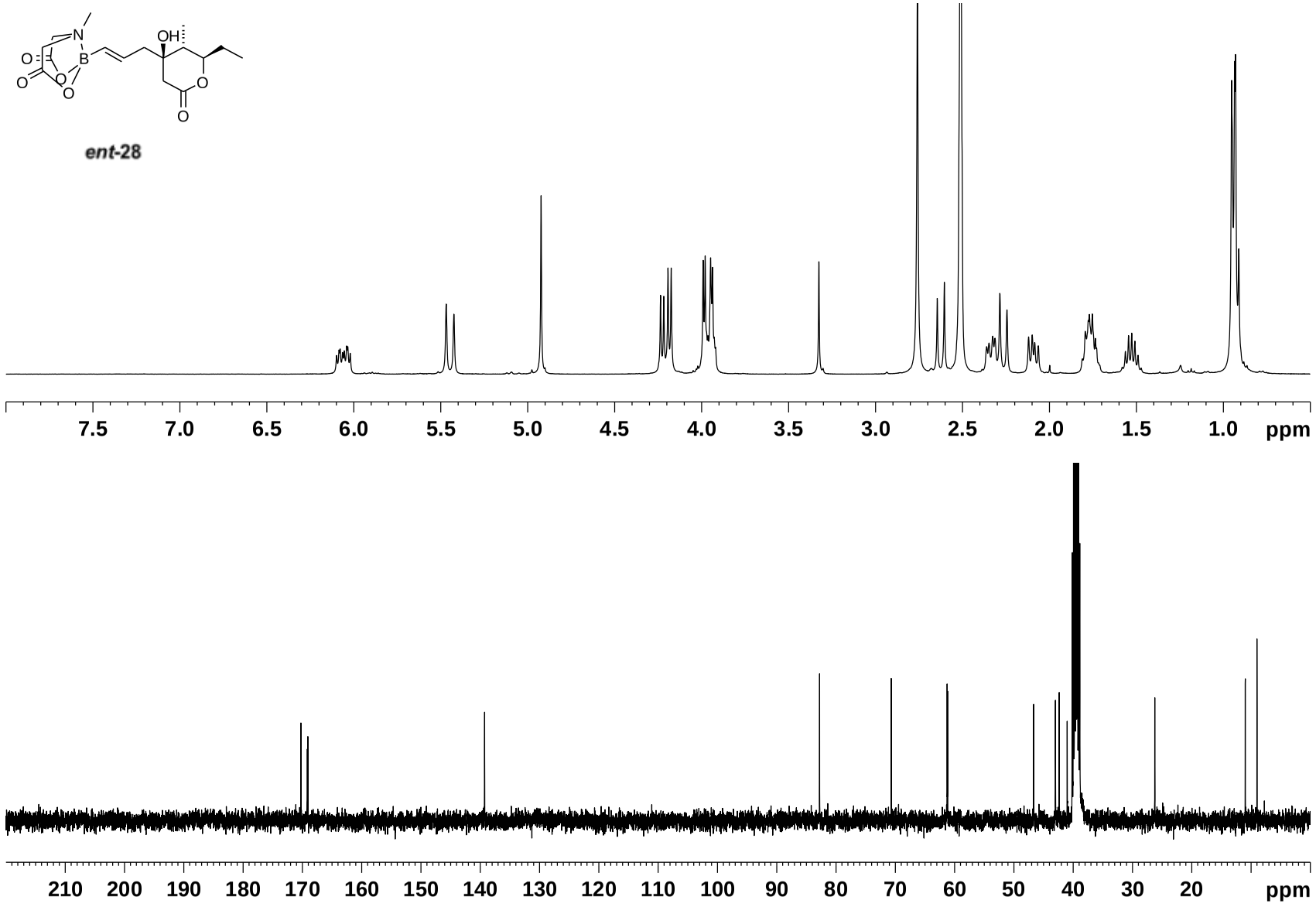

O
O
N
O
OH
Ph
2.6
ppm
1.00
10.71
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

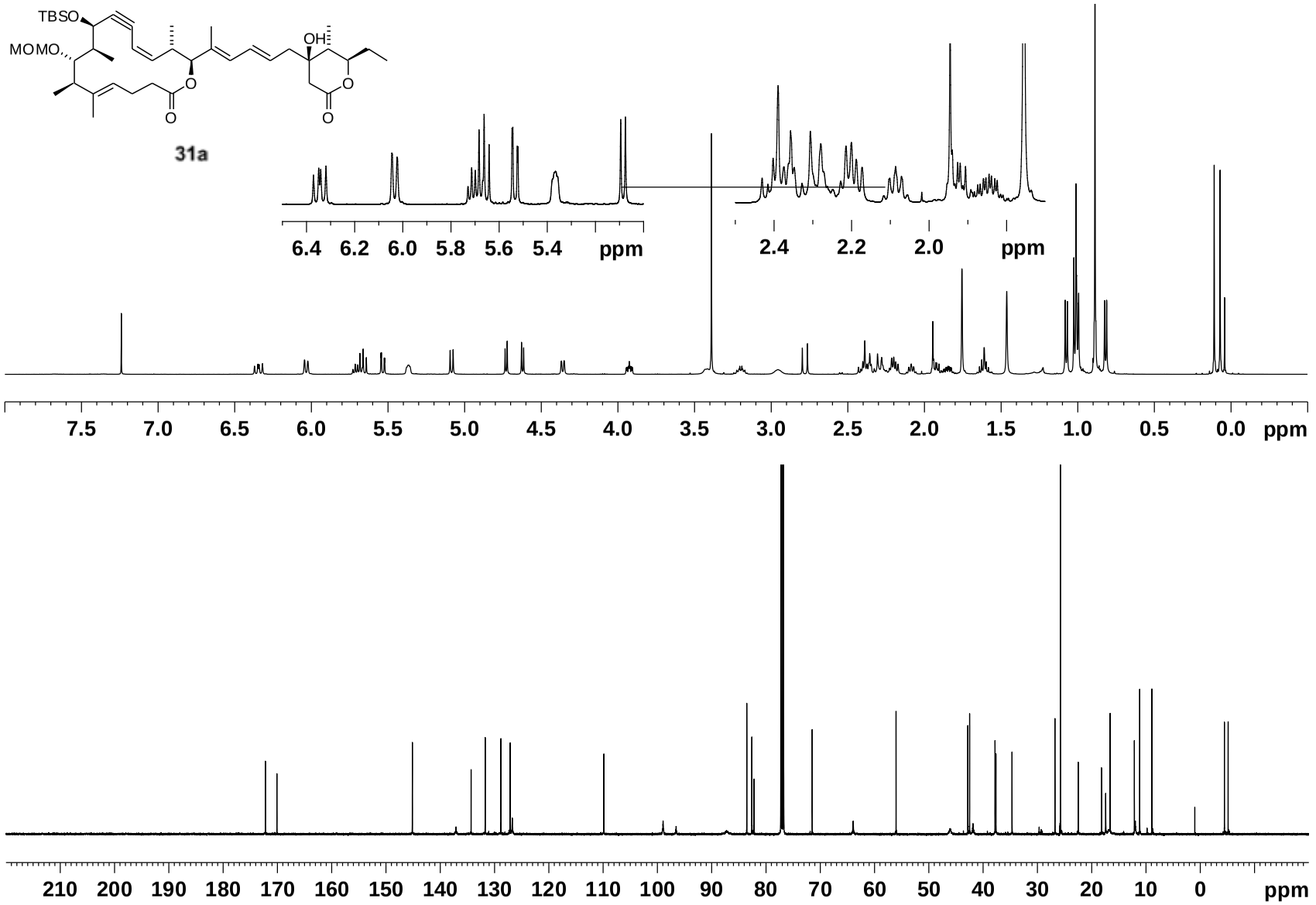

O
O
N
O
OAc
Ph
21
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

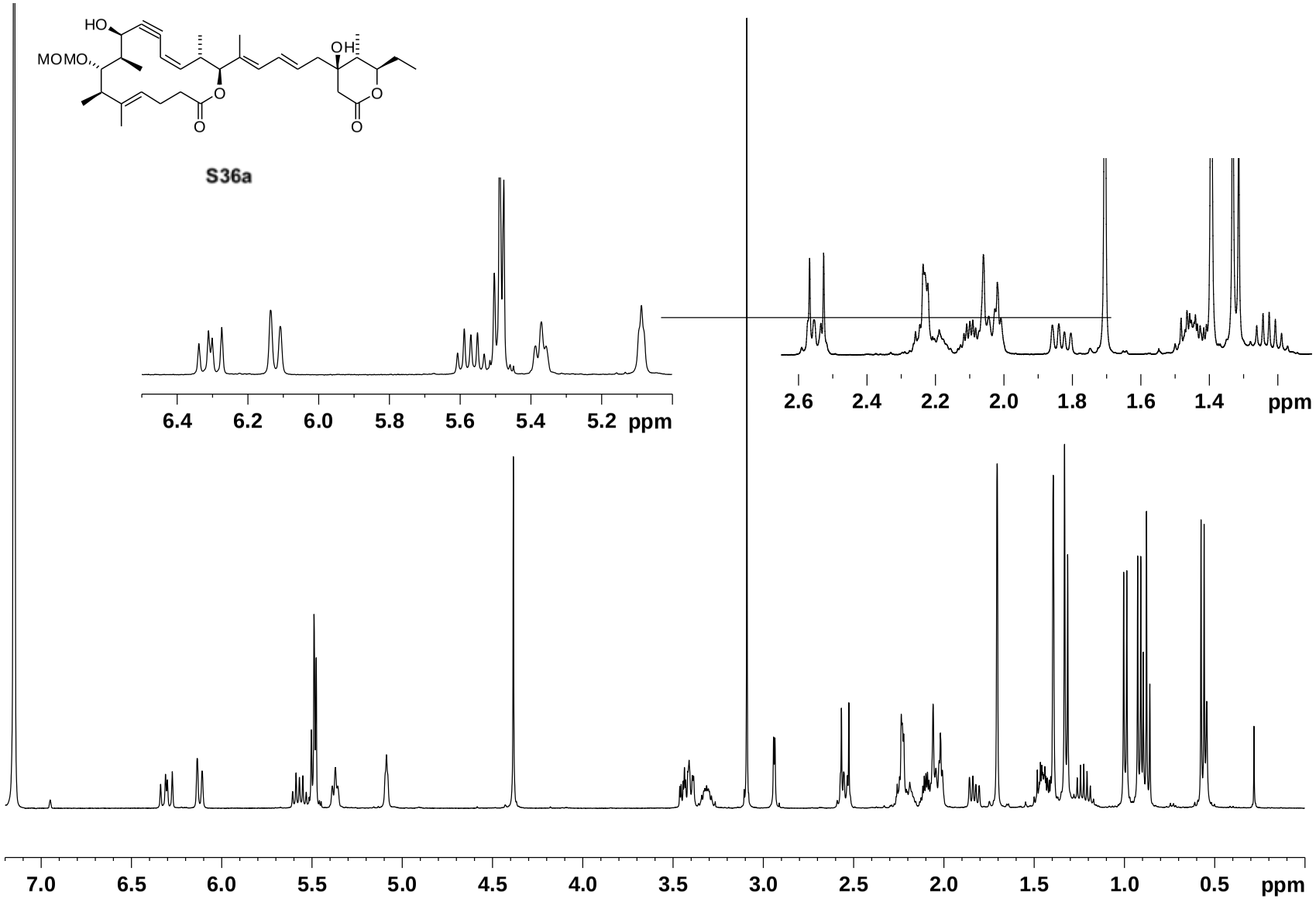

22
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

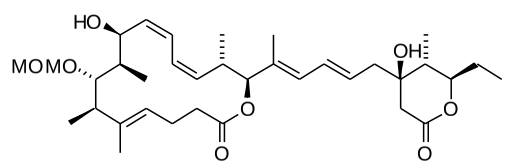

OH
O
O
ent-25
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OH
O
O
ent-23
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
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


OH
N
B
O
O
O
O
O
O
ent-28
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
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

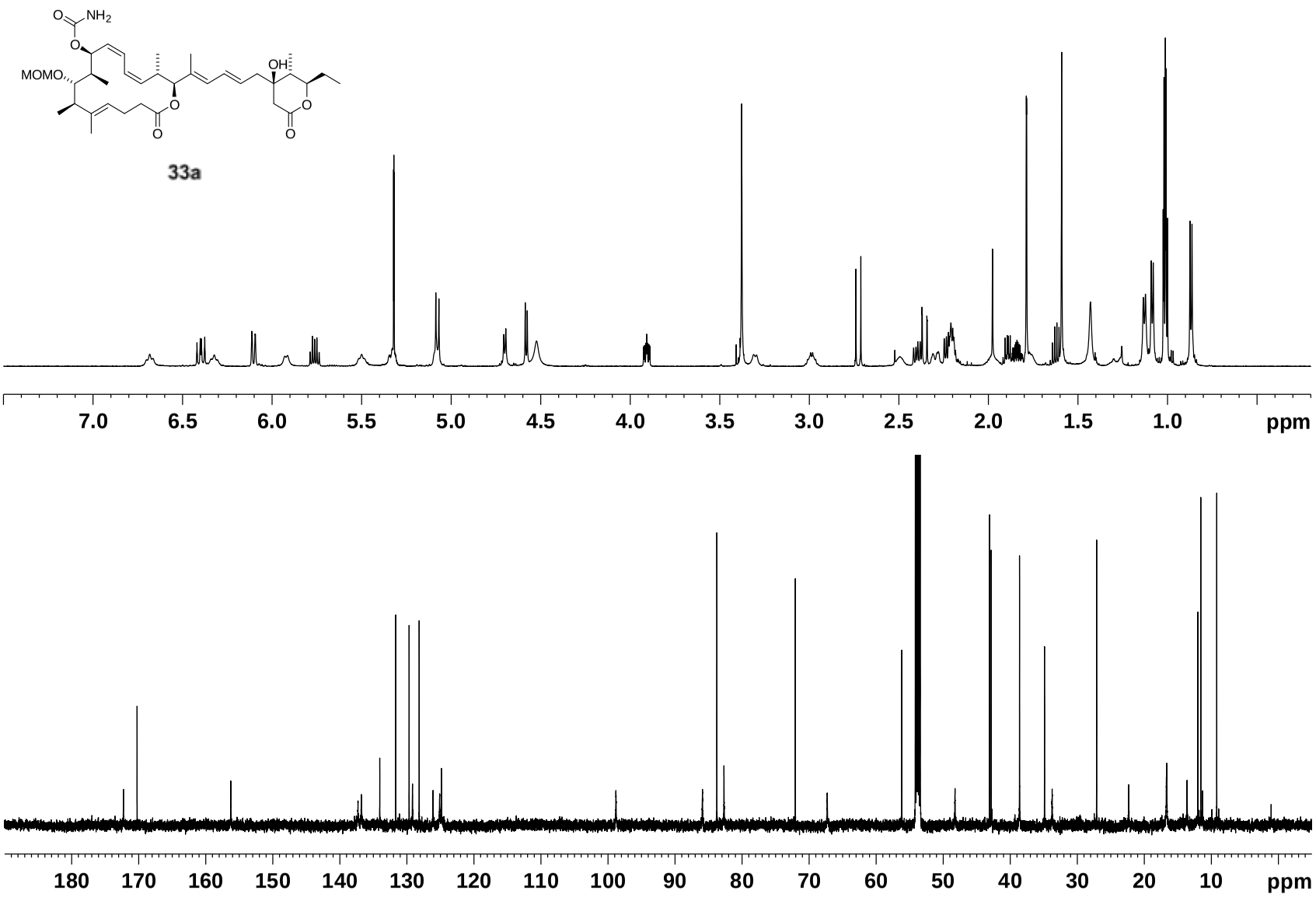

TBSO
MOMO
OH
O
O
O
O
31a
6.4 6.2 6.0 5.8 5.6 5.4 ppm
2.4 2.2 2.0 ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

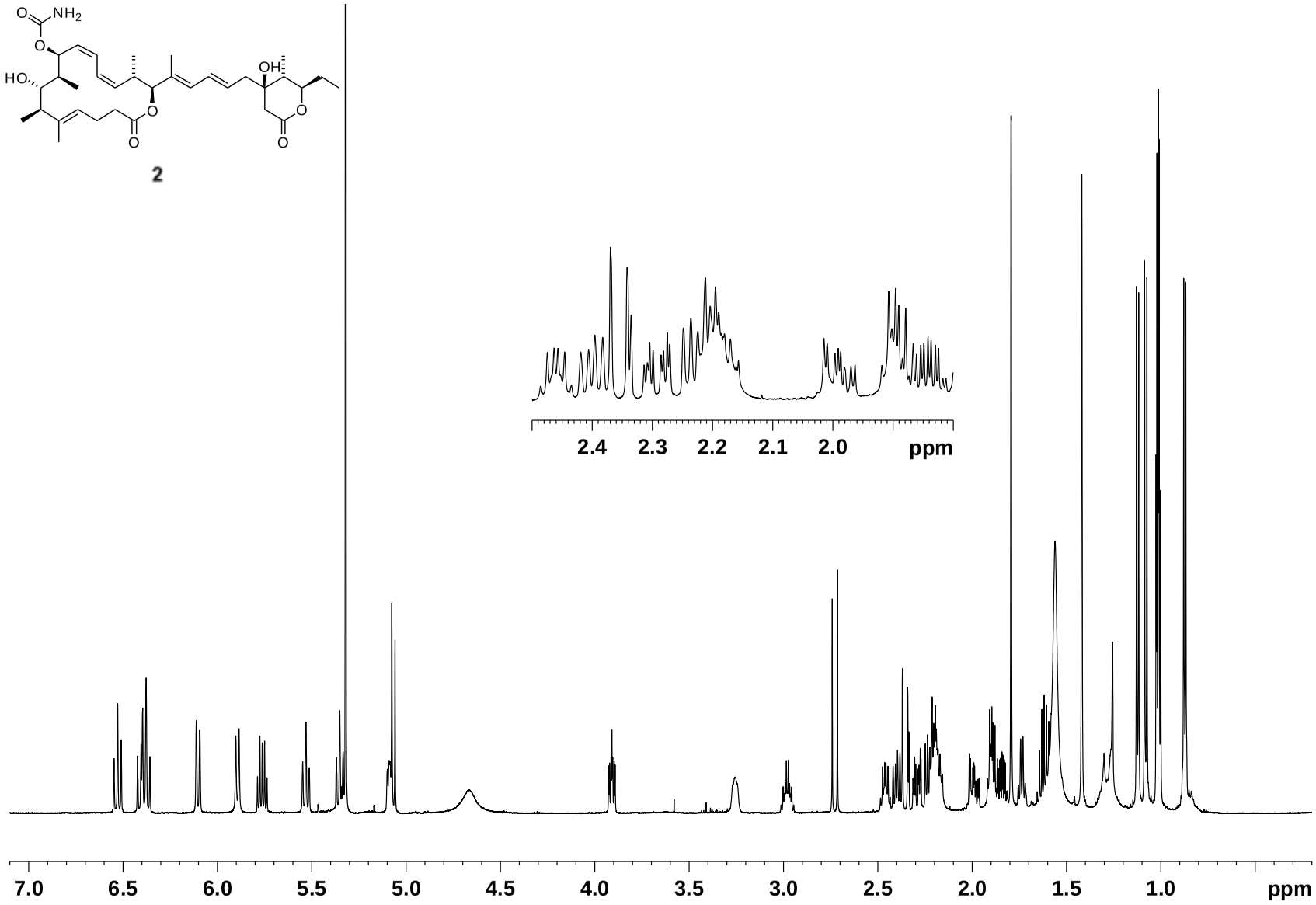

HO
MOMO
OH
O
O
O
O
S36a
6.4
6.2
6.0
5.8
5.6
5.4
5.2
ppm
2.6
2.4
2.2
2.0
1.8
1.6
1.4
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

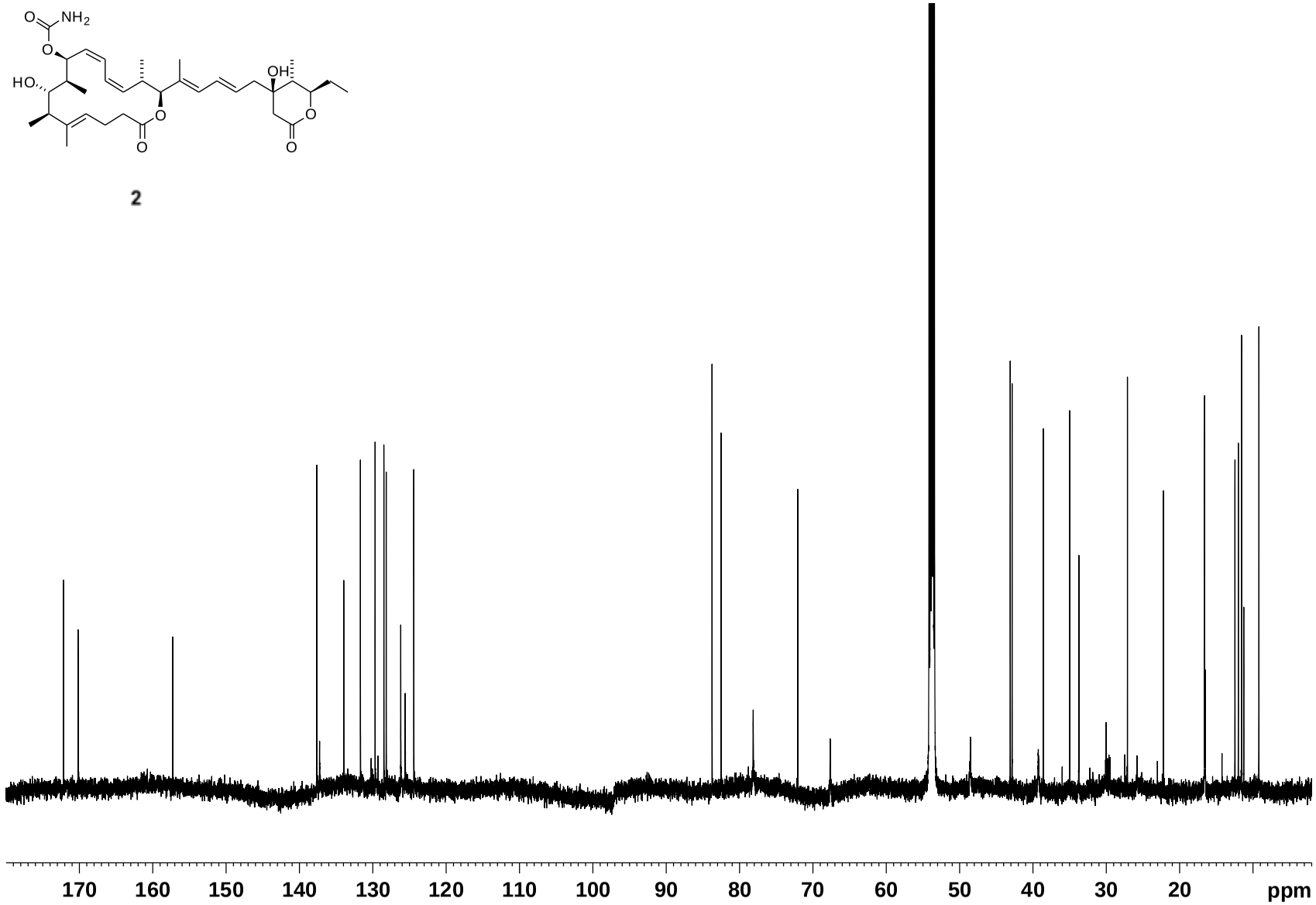

HO
MOMO
OH
O
O
O
O

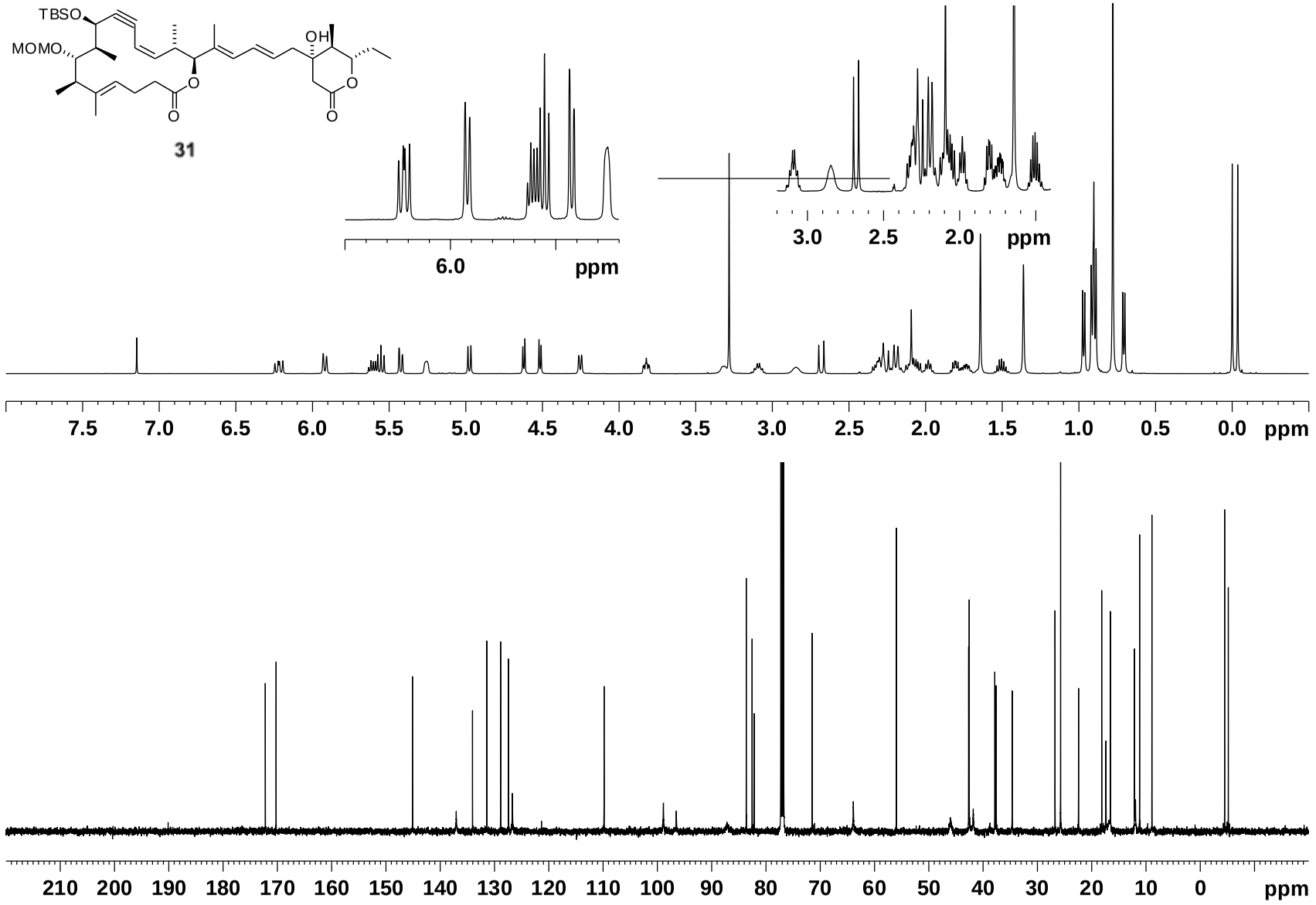
32a

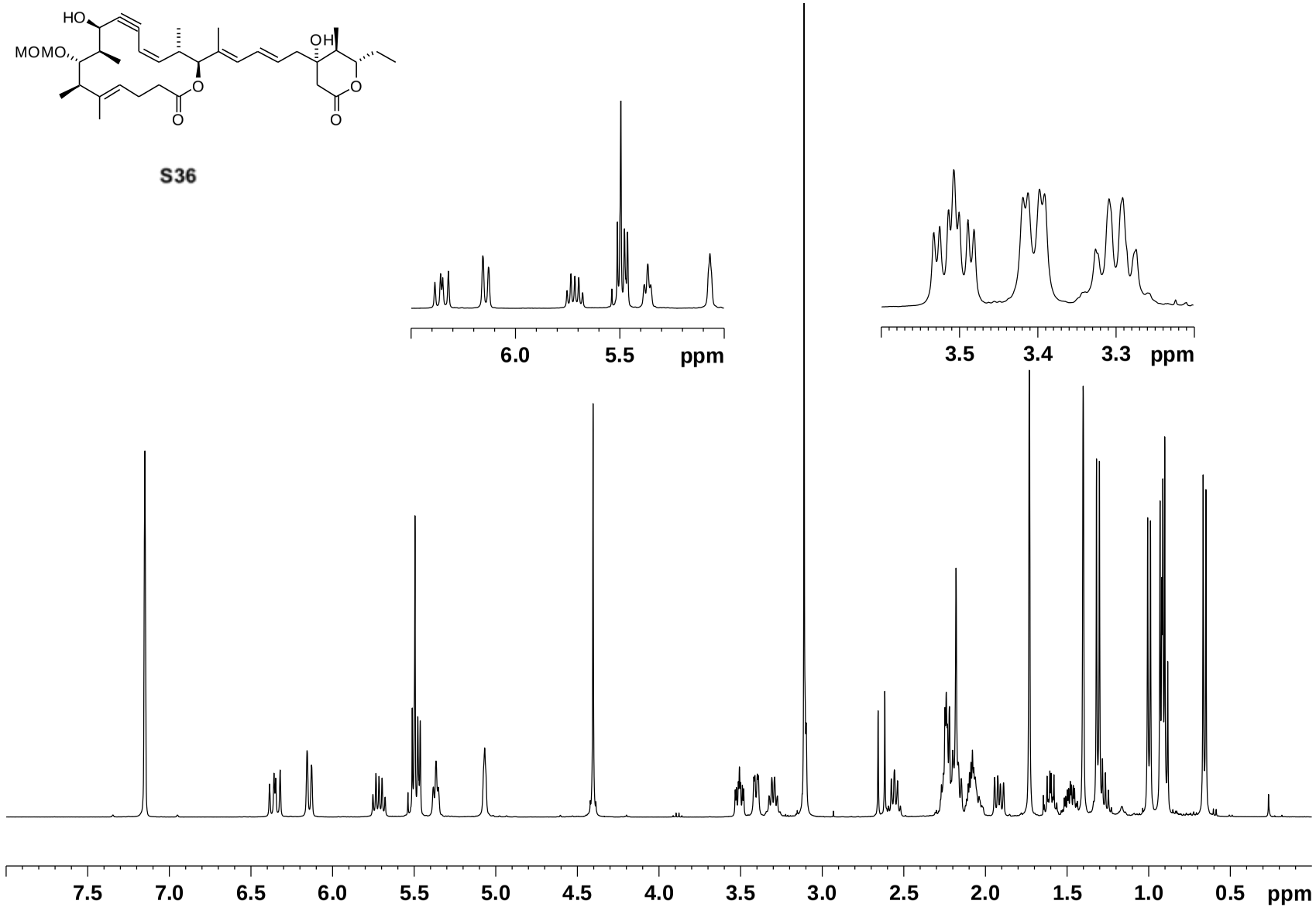
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

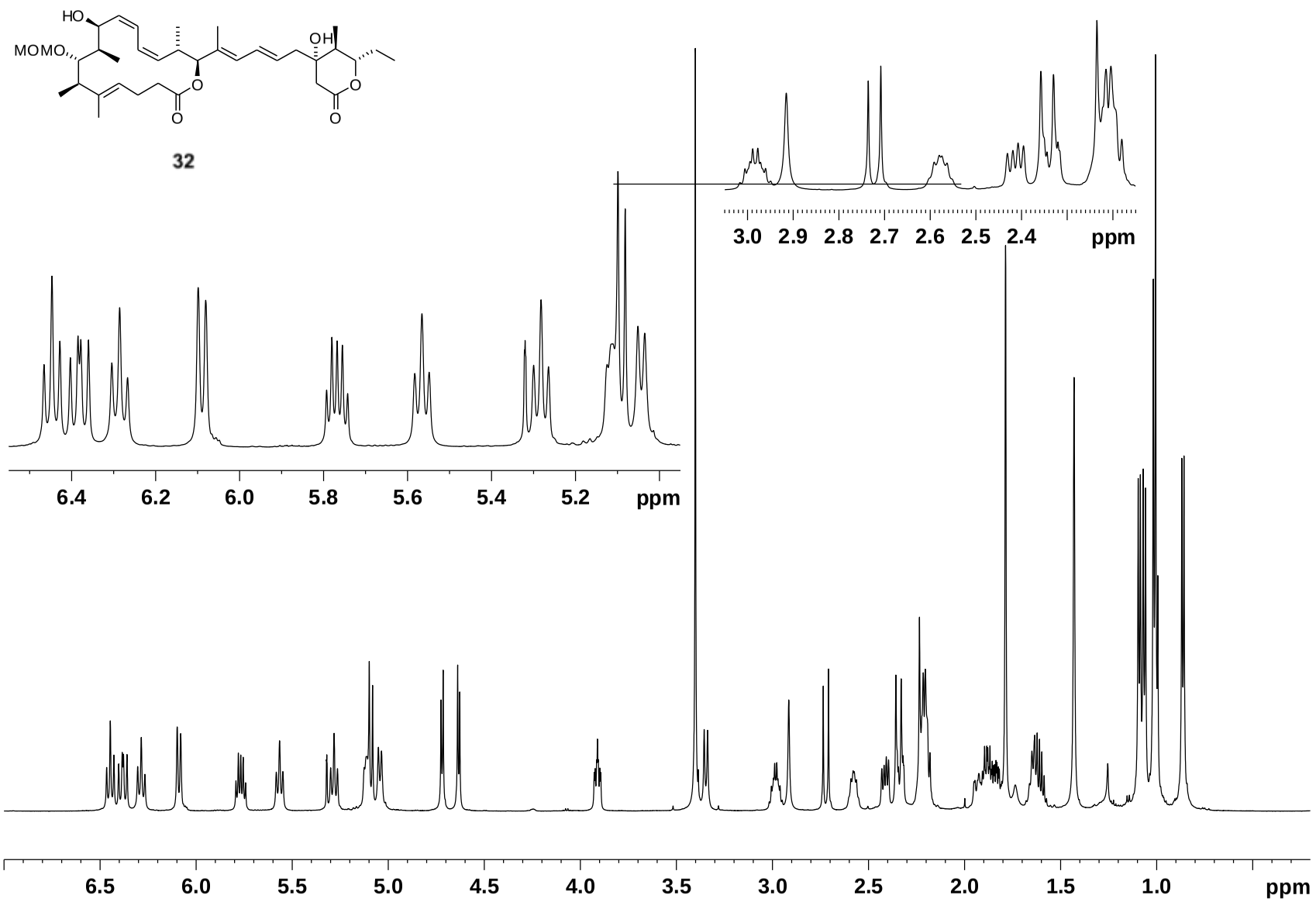

O
NH2
O
MOMO
OH
O
O
O
O
33a
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

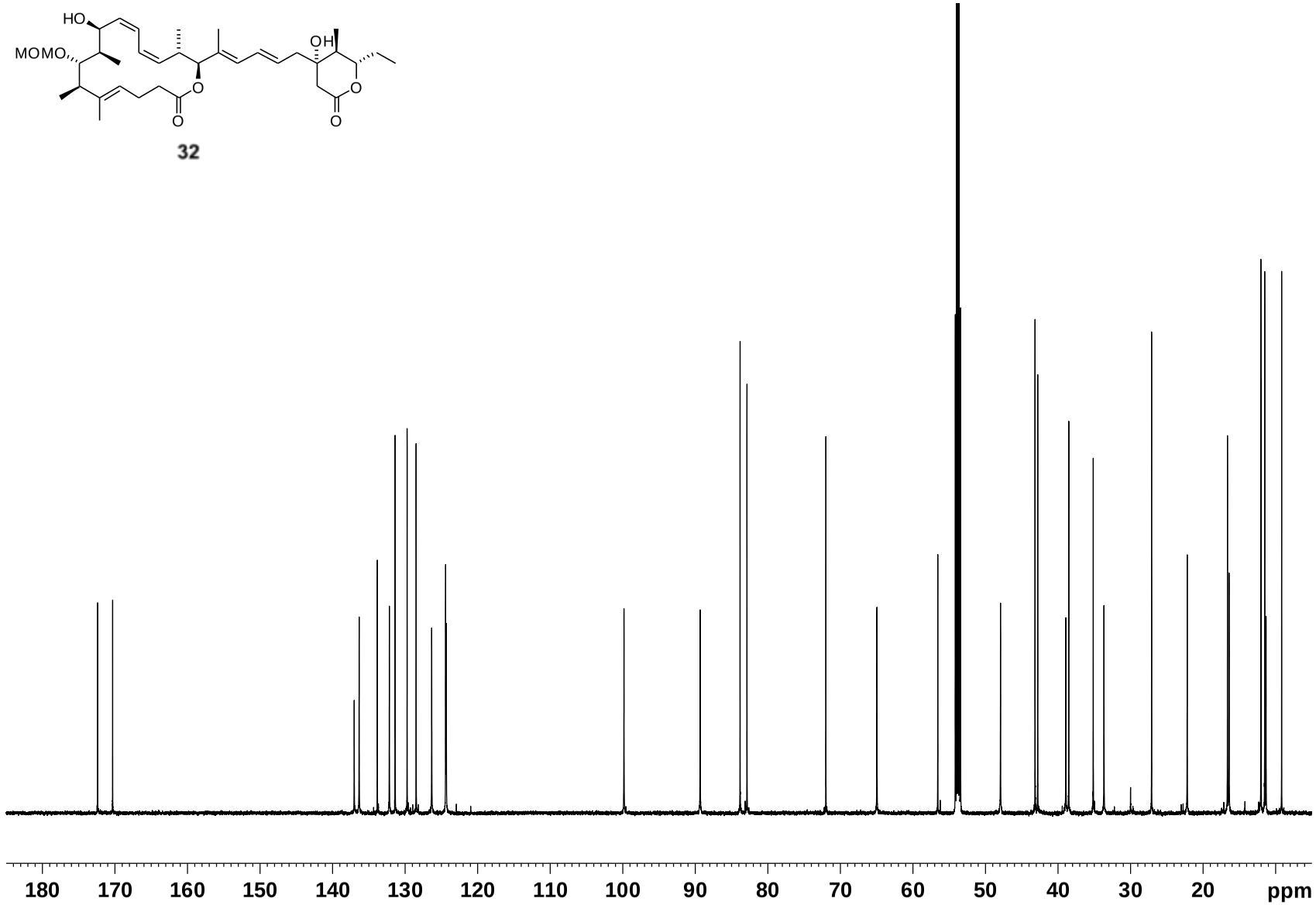

O
NH2
O
HO
OH
O
O
O
O
2
2.4
2.3
2.2
2.1
2.0
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

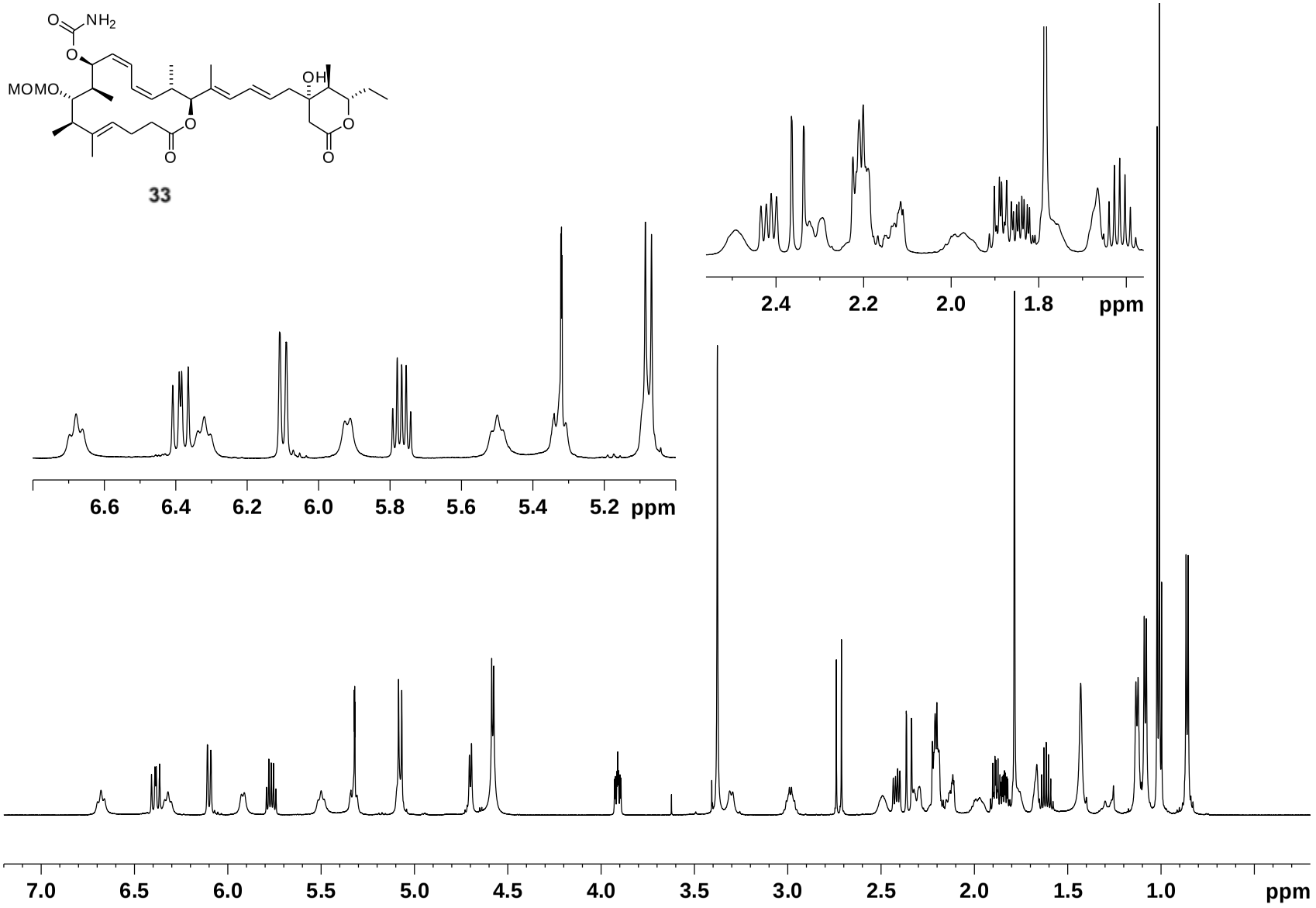

O
NH2
O
HO
OH
O
O
O
O
2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

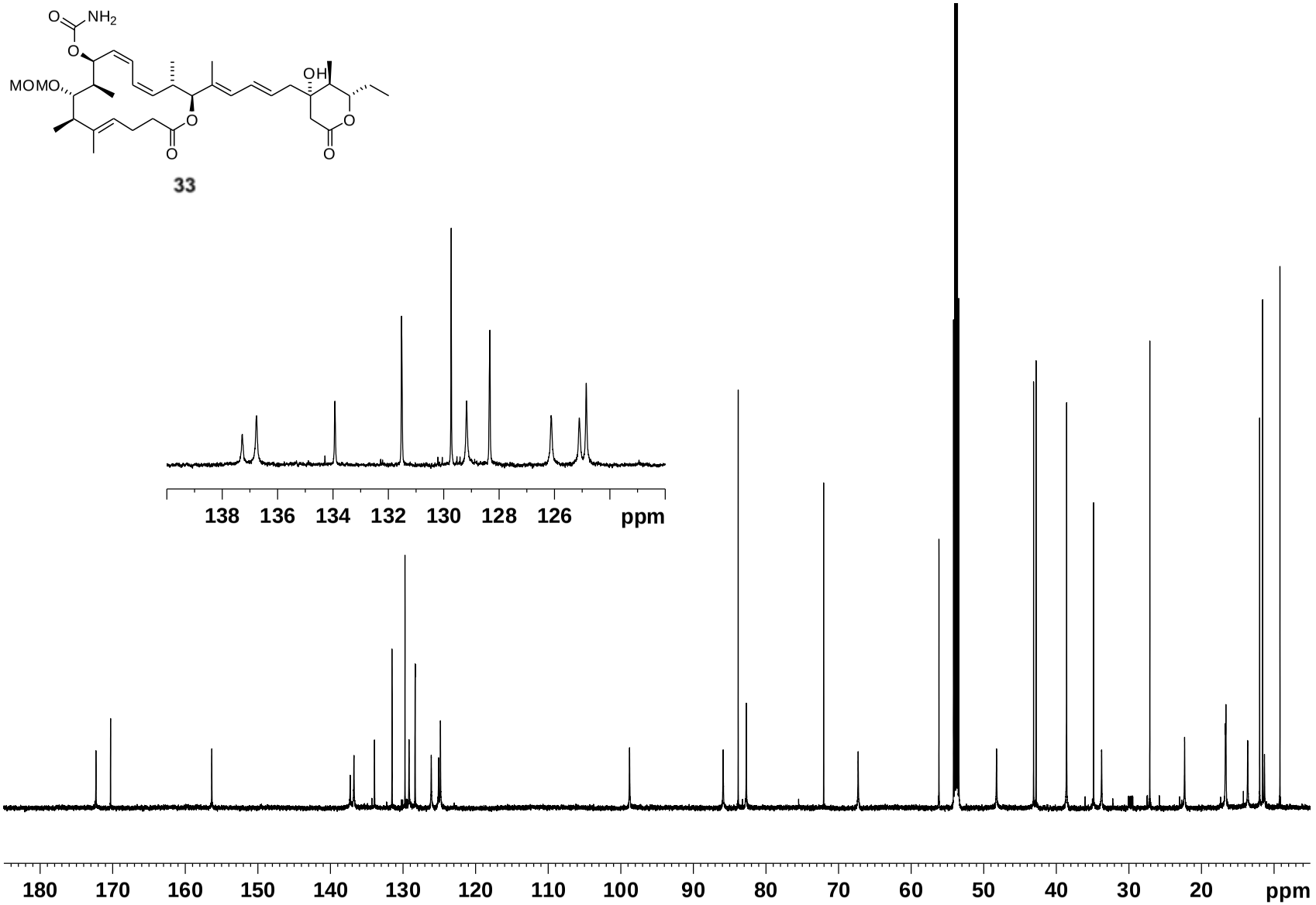

TBSO
MOMO
OH
O
O
O
O
31
6.0
ppm
3.0
2.5
2.0
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

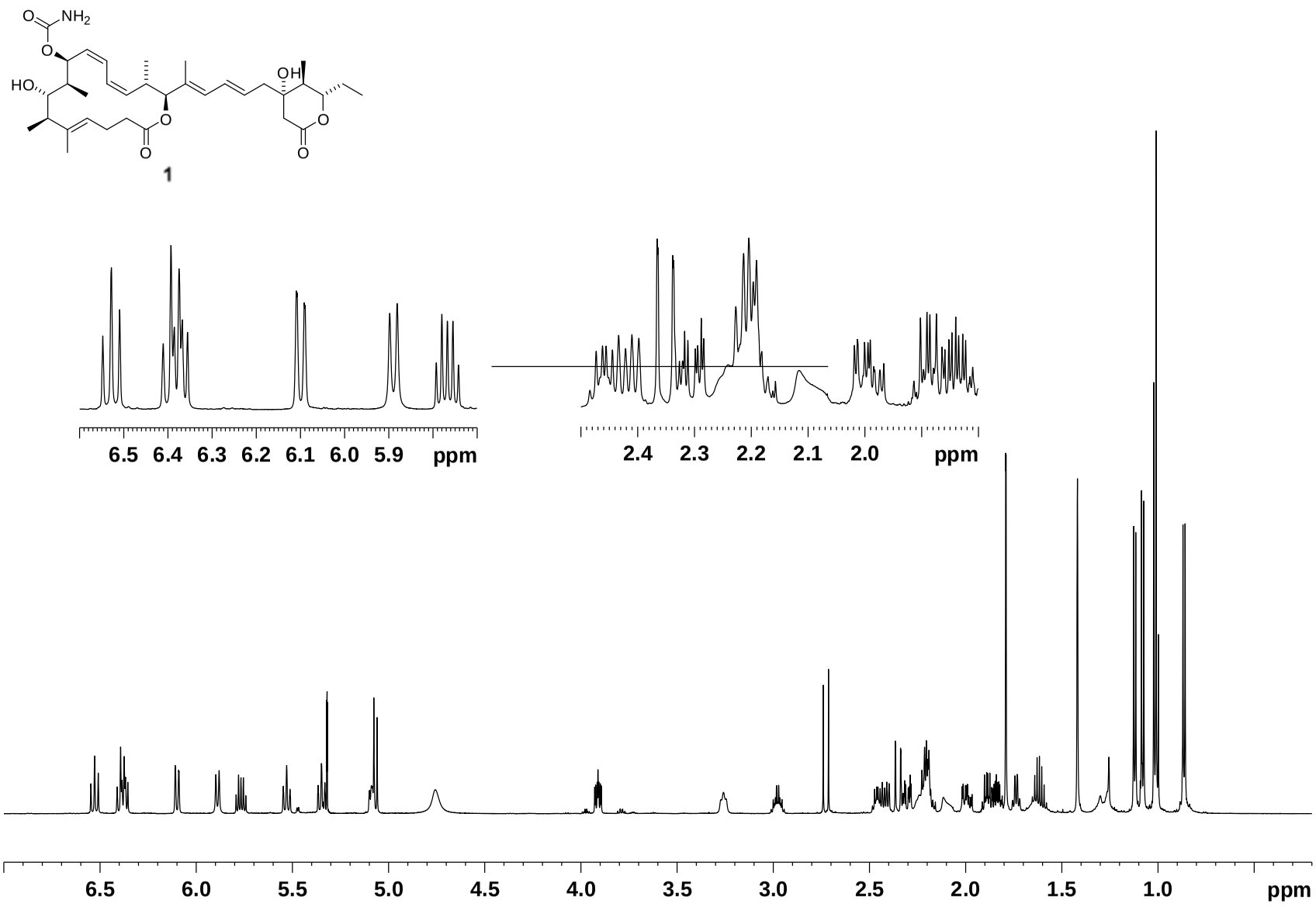

HO
MOMO
OH
O
O
O
O
S36
6.0
5.5
ppm
3.5
3.4
3.3
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

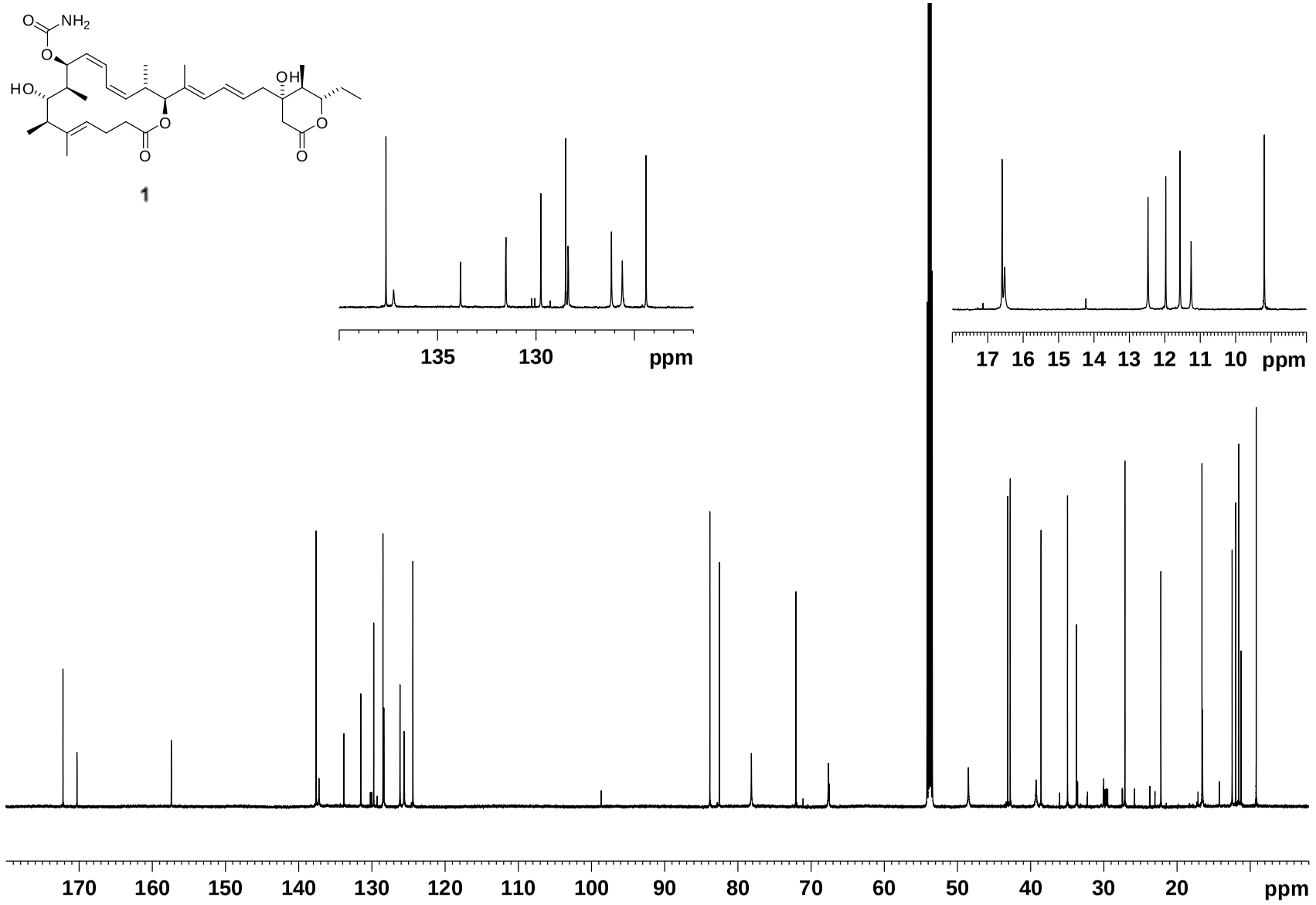

HO
MOMO
OH
O
O
O
O
32
3.0 2.9 2.8 2.7 2.6 2.5 2.4 ppm
6.4 6.2 6.0 5.8 5.6 5.4 5.2 ppm
6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm


HO
MOMO
OH
O
O
O
O
32
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
NH2
O
MOMO
OH
O
O
O
O
33
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
ppm
2.4
2.2
2.0
1.8
ppm
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


O
NH2
O
MOMO
OH
O
O
O
O
33
138
136
134
132
130
128
126
ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
NH2
O
HO
OH
O
O
O
O
1
6.5 6.4 6.3 6.2 6.1 6.0 5.9 ppm
2.4 2.3 2.2 2.1 2.0 ppm
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


O
NH2
O
HO
OH
O
O
O
O
1
135
130
ppm
17 16 15 14 13 12 11 10 ppm
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm